frontiers | Research Topics

Quality of stroke care: What could be improved, and how?

Edited by
Aleksandras Vilionskis, Michael V. Mazya, Adam Kobayashi, Aleš Tomek and Janika Kõrv

Published in
Frontiers in Neurology

ISSN 1664-8714
ISBN 978-2-8325-3089-4
DOI 10.3389/978-2-8325-3089-4

About Frontiers

Frontiers is more than just an open access publisher of scholarly articles: it is a pioneering approach to the world of academia, radically improving the way scholarly research is managed. The grand vision of Frontiers is a world where all people have an equal opportunity to seek, share and generate knowledge. Frontiers provides immediate and permanent online open access to all its publications, but this alone is not enough to realize our grand goals.

Frontiers journal series

The Frontiers journal series is a multi-tier and interdisciplinary set of open-access, online journals, promising a paradigm shift from the current review, selection and dissemination processes in academic publishing. All Frontiers journals are driven by researchers for researchers; therefore, they constitute a service to the scholarly community. At the same time, the *Frontiers journal series* operates on a revolutionary invention, the tiered publishing system, initially addressing specific communities of scholars, and gradually climbing up to broader public understanding, thus serving the interests of the lay society, too.

Dedication to quality

Each Frontiers article is a landmark of the highest quality, thanks to genuinely collaborative interactions between authors and review editors, who include some of the world's best academicians. Research must be certified by peers before entering a stream of knowledge that may eventually reach the public - and shape society; therefore, Frontiers only applies the most rigorous and unbiased reviews. Frontiers revolutionizes research publishing by freely delivering the most outstanding research, evaluated with no bias from both the academic and social point of view. By applying the most advanced information technologies, Frontiers is catapulting scholarly publishing into a new generation.

What are Frontiers Research Topics?

Frontiers Research Topics are very popular trademarks of the *Frontiers journals series*: they are collections of at least ten articles, all centered on a particular subject. With their unique mix of varied contributions from Original Research to Review Articles, Frontiers Research Topics unify the most influential researchers, the latest key findings and historical advances in a hot research area.

Find out more on how to host your own Frontiers Research Topic or contribute to one as an author by contacting the Frontiers editorial office: frontiersin.org/about/contact

Quality of stroke care: What could be improved, and how?

Topic editors

Aleksandras Vilionskis — Vilnius University, Lithuania
Michael V. Mazya — Karolinska University Hospital, Sweden
Adam Kobayashi — Cardinal Stefan Wyszyński University, Poland
Aleš Tomek — Charles University, Czechia
Janika Kõrv — University of Tartu, Estonia

Citation

Vilionskis, A., Mazya, M. V., Kobayashi, A., Tomek, A., Kõrv, J., eds. (2023). *Quality of stroke care: What could be improved, and how?* Lausanne: Frontiers Media SA. doi: 10.3389/978-2-8325-3089-4

Table of contents

frontiers | Frontiers in Neurology

TYPE Editorial
PUBLISHED 11 July 2023
DOI 10.3389/fneur.2023.1250872

OPEN ACCESS

EDITED AND REVIEWED BY
Jean-Claude Baron,
University of Cambridge, United Kingdom

*CORRESPONDENCE
Aleksandras Vilionskis
aleksandras.vilionskis@gmail.com

RECEIVED 30 June 2023
ACCEPTED 03 July 2023
PUBLISHED 11 July 2023

CITATION
Vilionskis A and Korv J (2023) Editorial: Quality of stroke care: what could be improved, and how? *Front. Neurol.* 14:1250872. doi: 10.3389/fneur.2023.1250872

Editorial: Quality of stroke care: what could be improved, and how?

Aleksandras Vilionskis[1]* and Janika Korv[2]

[1]Clinic of Neurology and Neurosurgery, Vilnius University, Vilnius, Lithuania, [2]Department of Neurology and Neurosurgery, University of Tartu, Tartu, Estonia

KEYWORDS

quality, stroke care, stroke therapy, stroke unit, stroke rehabilitation

Editorial on the Research Topic
Quality of stroke care: what could be improved, and how?

Stroke is one of the leading contributors to long-term disability and mortality worldwide (1). Its direct and undirect burden is substantial and perhaps will rise in future due to the aging of the population (2). Reperfusion treatment allows to decrease the disability among the survivors, but only a small amount of acute stroke patients receive that modern therapy (3, 4). There are several international initiatives aiming at improvement of care of acute stroke patients and reducing their mortality as disability as well. The stroke care pathway includes all stages from prehospital until rehabilitation and post-stroke care. There are many challenges in each step, and it is crucial to identify the gaps on each stage and to find the ways to improve stroke care.

The aim of our special Research Topic "*Quality of stroke care: what could be improved and how?*" was designed to present the real-world situation regarding stroke services at all stages across different countries and provide some practical recommendations to improve acute stroke care in daily practice. The Research Topic includes 15 manuscripts: 1 review, 11 original research, 1 perspective, 1 study protocol, and 1 brief research report. The research has been conducted in different world regions, including Asia, Europe, USA, and the Middle East.

Chen M. et al. performed an original review of bibliometric analysis of stroke and quality of life and showed, that during the last more than two decades the number of publications increased significantly in all parts of the world. Hot topics in stroke research, main research institutions and contributors in this field were identified.

Al Hashmi et al. evaluated the availability of resources for the management of acute stroke in the Middle East, North Africa, and neighboring areas (MENA+). The study revealed significant differences in stroke care between low-income and high-income countries and stressed the importance of development of stroke target programs. Hwong et al. studied the gaps of implementation of intravenous thrombolysis in Malaysia. The analysis showed that delayed presentation at the scene (67.6%) was identified as the primary factor contributing to the low utilization rate of intravenous thrombolysis. The authors note that the facilitative work process and cohesiveness of team members are the important factors for implementation of modern stroke treatments into daily clinical practice. Ganti et al. studied the impact of arrival time to the emergency department on door-to-needle time of thrombolytic treatment.

A single hospital data showed that nighttime, lack of dedicated stroke team, longer time-to-CT read and arrival as walk-in are associated with the longer door-to-needle time. These data confirm the results from previous studies (5, 6).

Modern guidelines recommend using a stent-retriever for mechanical thrombectomy for the treatment of acute ischemic stroke due to large vessel occlusion (7). However, many centers use other techniques, including aspiration. Narloch et al. show that the success of aspiration-based first-pass recanalization did not decrease significantly with increasing age and might not be avoided in the elderly patients.

Pneumonia is a common post-stroke complication with the prevalence up to 38% (8). Clinical studies confirm that pneumonia is a preventable condition (9). Studies have shown that dysphagia is an independent risk factor of pneumonia, so early diagnosis and treatment of dysphagia result in the decreasing rate of post-stroke pneumonia and improve the outcome (10). Zhang et al. evaluated the effectiveness of smart health-based rehabilitation on patients with dysphagia in a case-control study of 60 poststroke dysphagia patients. Their findings confirm the significant positive effect of smart rehabilitation compared to routine rehabilitation. In another quasi-intervention pilot study of 120 patients Zheng et al. showed that nurse-led hierarchical management based on acute ischemic stroke – associated pneumonia score is useful tool to reduce the incidence of pneumonia.

Up to 50–60% of acute stroke patients have disability and require rehabilitation and post-stroke long-term care. Sarzyńska-Długosz analysis offers a comprehensive understanding of the ideal long-term care model while shedding light on the real-world obstacles faced in putting that model into practice. Chen M. et al. found in their retrospective study that more than half of acute ischemic stroke patients have risk of malnutrition, and severe neurological deficit on admission and older age are its independent risk factors. These results allow us to identify the target group of patients to whom more attention should be paid. Susts et al. evaluated and confirmed that physical inactivity before stroke is the independent predictor of dependency in basic activities of daily living after stroke. Other predictors are older age, female sex, pre-stroke living conditions, previous stroke, and severity of stroke on admission. Pan et al. found that around 50% of young and middle-aged stroke survivors do not return to work after stroke. Among others, they identified the risk factors such as older age, female sex, low education, and no medical insurance. Another conclusion is that there is a direct relationship between the ability to return to work and health-related quality of life. The authors conclude that specific interventions are needed to facilitate returning to work and improving the quality of life after a stroke. Xie et al. investigated the relation between hemiplegic shoulder pain and subluxation and found that there is a high frequency of shoulder pain and local injury after stroke. The authors provide specific recommendations for rehabilitation for this patients group, which can be quickly implemented into the daily practice. Bae et al. analyzed the utilization of post-stroke rehabilitation prior to the introduction of the post-acute rehabilitation system in South Korea in 2017. The authors conclude that before the nationwide rehabilitation system, the rehabilitation treatment was over- and under-supplied. The study confirms the need for development of post-acute rehabilitation system that specifies the subject, duration, and intensity of rehabilitation treatment.

In contrast to acute ischemic stroke there are only a few recommendations for the treatment of intracerebral hemorrhage (11). The benefit of surgical evacuation of intracerebral hematoma is still an unanswered question. Ratcliff et al. present the protocol for a new multi-centered randomized trial. This trial is addressed to patients with supratentorial spontaneous intracerebral hemorrhage using minimally invasive trans-sulcal parafascicular surgery approach. The results of the trial were presented during the 9th European Stroke Organization Conference in May 2023.

An abdominal aortic aneurysm is a dangerous, potentially fatal, but often underdiagnosed condition (12). There is evidence that the prevalence of abdominal aortic aneurysm is higher among TIA patients (13). Loban et al. presents the results of local screening programs in elderly men over past decade, who have had ischemic stroke or TIA. They suggest that there is a strong basis for recommendation to screen acute stroke patients over 60 years for this condition.

In conclusion, the "*Quality of stroke care: what could be improved and how?*" Research Topic provides the latest data in this field. The 15 studies cover all areas of acute stroke from prehospital stage until rehabilitation and provide new insights into improvement of quality of stroke care. Conduction of studies in different regions results in broad implementation of new knowledge into daily clinical practice. We believe that this Research Topic will be a useful reading for improvement of acute stroke care and mapping future directions for research.

Author contributions

AV and JK wrote the final version. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett D, et al. Global and regional burden of stroke during 1990–2010: findings from the global burden of disease study 2010. *Lancet.* (2014) 383:245–55. doi: 10.1016/S0140-6736(13)61953-4

2. Feigin VL, Norrving B, Mensah GA. Global burden of stroke. *Circ Res.* (2017) 120:439–48. doi: 10.1161/CIRCRESAHA.116.308413

3. Lees KR, Bluhmki E, von Kummer R, Brott TG, Toni D, Grotta JC, et al. Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. *Lancet.* (2010) 375: 1695–1703. doi: 10.1016/S0140-6736(10)60491-6

4. Aguiar de. Sousa D, von Martial R, Abilleira S. Access to and delivery of acute ischaemic stroke treatments: a survey of national scientific societies and stroke experts in 44 European countries. *Eur Stroke J.* (2019) 41:3–28. doi: 10.1177/2396987318786023

5. Mikulík R, Kadlecová P, Czlonkowska A, Kobayashi A, Brozman M, Svigelj V, et al. Factors influencing in-hospital delay in treatment with intravenous thrombolysis. *Stroke.* (2012) 43:1578–83. doi: 10.1161/STROKEAHA.111.644120

6. Kõrv J, Vilbo R, Kadlecova P, Kobayashi A, Czlonkowska A, Brozman M, et al. Benefit of thrombolysis for stroke is maintained around the clock: results from the SITS-EAST Registry. *Eur J Neurol.* (2014) 21:112–7. doi: 10.1111/ene.12257

7. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* (2018) 49:e46–e110. doi: 10.1161/STR.0000000000000158

8. Hilker R, Poetter C, Findeisen N, Sobesky J, Jacobs A, Neveling M, et al. Nosocomial pneumonia after acute stroke: implications for neurological intensive care medicine. *Stroke.* (2003) 34:975–81. doi: 10.1161/01.STR.0000063373.70993.CD

9. Kumar S, Selim MH, Caplan LR. Medical complications after stroke. *Lancet Neurol.* (2010) 9:105–18. doi: 10.1016/S1474-4422(09)70266-2

10. Martino R, Foley N, Bhogal S, Diamant N, Speechley M, Teasell R. Dysphagia after stroke: incidence, diagnosis, and pulmonary complications. *Stroke.* (2005) 36:2756–63. doi: 10.1161/01.STR.0000190056.76543.eb

11. Hemphill JC, Greenberg SM, Anderson CS, Becker K, Bendok BR, Cushman M, et al. Guidelines for the Management of Spontaneous Intracerebral Hemorrhage: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke.* (2015) 46:2032–60. doi: 10.1161/STR.0000000000000069

12. Reimerink JJ, Van Der Laan MJ, Koelemay MJ, Balm R, Legemate DA. Systematic review and meta-analysis of population-based mortality from ruptured abdominal aortic aneurysm. *Br J Surg.* (2013) 100:1405–13. doi: 10.1002/bjs.9235

13. van Lindert NHA, Bienfait HP, Gratama JWC, Vriesema H, Hove WT, Vermeulen EGJ, et al. Screening for aneurysm of the abdominal aorta: Prevalence in patients with stroke or TIA. *Eur J Neurol.* (2009) 16:602–7. doi: 10.1111/j.1468-1331.2009.02550.x

frontiers | Frontiers in Neurology

TYPE Original Research
PUBLISHED 28 October 2022
DOI 10.3389/fneur.2022.1016376

OPEN ACCESS

EDITED BY
Aleš Tomek,
Charles University, Czechia

REVIEWED BY
Hrvoje Budincevic,
University Hospital Sveti Duh, Croatia
Albert Akpalu,
University of Ghana, Ghana

*CORRESPONDENCE
Amal. M. Al Hashmi
amal.m.alhashmi@gmail.com

SPECIALTY SECTION
This article was submitted to Stroke, a section of the journal Frontiers in Neurology

RECEIVED 10 August 2022
ACCEPTED 06 October 2022
PUBLISHED 28 October 2022

CITATION
Al Hashmi AM, Shuaib A, Imam Y, Amr D, Humaidan H, Al Nidawi F, Sarhan A, Mustafa W, Khalefa W, Ramadan I, Usman FS, Hokmabadi ES, Ghorbani M, Nassir T, Aladham F, Salmeen A, Kikano R, Muda S, Jose S, Bulushi MA, Sajwani B, Wasay M, Bashir Q, Al Hazzani A, Khoja W, Alkadere R, Osman H, Hussein A, Churojana A, Hammami N, Ozdemir AO, Giray S, Gurkas E, Hussain SI, Sallam AR and Mansour OY (2022) Stroke services in the Middle East and adjacent region: A survey of 34 hospital-based stroke services. *Front. Neurol.* 13:1016376. doi: 10.3389/fneur.2022.1016376

Stroke services in the Middle East and adjacent region: A survey of 34 hospital-based stroke services

Amal. M. Al Hashmi[1]*, Ashfaq Shuaib[2], Yahia Imam[3], Dareen Amr[4], Hani Humaidan[5], Firas Al Nidawi[6], Ahmed Sarhan[7], Wessam Mustafa[8], Wael Khalefa[9], Ismail Ramadan[10], Fritz Sumantri Usman[11], Elyar Sadeghi Hokmabadi[12], Mohammed Ghorbani[13], Temeem Nassir[14], Farid Aladham[15], Athari Salmeen[16], Raghid Kikano[17], Sobri Muda[18], Sachin Jose[19], Manal Al Bulushi[20], Badrai Sajwani[21], Mohammad Wasay[22], Qasim Bashir[23], Adel Al Hazzani[24], Waleed Khoja[25], Radwan Alkadere[26], Haytham Osman[27], Abbashar Hussein[28], Anchalee Churojana[29], Nadia Hammami[30], Atilla Ozcan Ozdemir[31], Semih Giray[32], Erdem Gurkas[33], Seyd Irteza Hussain[34], Abdul Rahman Sallam[35] and Ossama Yassin Mansour[36] on behalf of MENA-SINO Organization

[1]Central Stroke Unit, Neuroscience Directorate, Khoula Hospital, MOH, Muscat, Oman, [2]Division of Neurology, Department of Medicine, University of Alberta, Edmonton, AB, Canada, [3]Neuroscience Institute, Hamad General Hospital, Doha, Qatar, [4]Stroke and Neurointervention Unit, Alexandria University School of Medicine, Alexandria, Egypt, [5]Stroke Unit, Salmaniya Medical Complex, Al Manamah, Bahrain, [6]King Hamad Hospital, Al Muharaq, Bahrain, [7]Al-Hussein University Hospital, Cairo, Egypt, [8]Department of Neurology, Mansoura University Hospital, Mansoura, Egypt, [9]Department of Neurology, Maady Military Hospital, Cairo, Egypt, [10]Department of Neurology, Semoha Emergency Hospital, Alexandria University, Alexandria, Egypt, [11]Stroke Unit, Pelni General Hospital, Jakarta, Indonesia, [12]Neuroscience Research Center, Tabriz University of Medical Science, Tabriz, Iran, [13]Division of Vascular and Endovascular Neurosurgery Firoozgar Hospital, Tehran, Iran, [14]Department of Internal Medicine, Maysan Cardiac Center, MOH, Musan, Iraq, [15]Specialty Hospital, Amman, Jordan, [16]Department of Neurology, Jaber Al Ahmad Hospital, Kuwait City, Kuwait, [17]Lebanese American University, Head of Interventional Radiology, Beirut, Lebanon, [18]Department of Radiology, Pengajar Hospital UPM, FPSK, Universiti Putra Malaysia, Serdang, Malaysia, [19]Statistical Specialist, Oman Medical Specialty Board (OMSB), Muscat, Oman, [20]Stroke Unit, Sultan Qaboos Hospital, MOH of Oman, Salalah, Oman, [21]Stroke Unit, Sohar Hospital, MOH of Oman, Sohar, Oman, [22]Department of Neurology, Aga Khan University, Karachi, Pakistan, [23]Department of Neurology, Services Institute of Medical Sciences, Lahore, Pakistan, [24]Neuroscience Center, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia, [25]Department of Neurology, Prince Sultan Military Medical City, Riyadh, Saudi Arabia, [26]Family Care Hospital, Riyadh, Saudi Arabia, [27]Department of Neurology, National Ribat University, Khartoum, Sudan, [28]Department of Neurology, El Shaab Teaching Hospital, Khartoum, Sudan, [29]Department of Radiology, Siriraj Hospital, Mahidol University, Bangkok, Thailand, [30]National Institute Mongi Ben Hamida of Neurology, Tunis, Tunisia, [31]Interventional Neurology and Neurocritical Care Program, Eskisehir Osmangazi University, Eskişehir, Turkey, [32]Gaziantep University Medical Faculty, Gaziantep, Turkey, [33]Stroke Center, Dr. Lutfi Kirdar City Hospital, Istanbul, Turkey, [34]Neurological Institute, Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates, [35]Department of Neurology, University Hospital of Sana'a, Sanan, Yemen, [36]Department of Neurology, Faculty of Medicine, Alexandria University, Alexandria, Egypt

Background: Acute stroke care is complex and requires multidisciplinary networking. There are insufficient data on stroke care in the Middle East and adjacent regions in Asia and Africa.

Objective: Evaluate the state of readiness of stroke programs in the Middle East North Africa and surrounding regions (MENA+) to treat acute stroke.

Method: Online questionnaire survey on the evaluation of stroke care across hospitals of MENA+ region between April 2021 and January 2022.

Results: The survey was completed by 34/50 (68%) hospitals. The median population serviced by participating hospitals was 2 million. The median admission of patients with stroke/year was 600 (250–1,100). The median length of stay at the stroke units was 5 days. 34/34 (100%) of these hospitals have 24/7 CT head available. 17/34 (50%) have emergency guidelines for prehospital acute stroke care. Mechanical thrombectomy with/without IVT was available in 24/34 (70.6%). 51% was the median (IQR; 15–75%) of patients treated with IVT within 60 min from arrival. Thirty-five minutes were the median time to reverse warfarin-associated ICH.

Conclusion: This is the first large study on the availability of resources for the management of acute stroke in the MENA+ region. We noted the disparity in stroke care between high-income and low-income countries. Concerted efforts are required to improve stroke care in low-income countries. Accreditation of stroke programs in the region will be helpful.

KEYWORDS

stroke care, MENA+ region, MENA-SINO, stroke units, stroke centers

Background

Stroke remains a leading cause of death and disability worldwide (1). Successful prevention and treatment strategies over the last five decades in high-income countries (HICs) have led to a progressive overall decline in mortality resulting in stroke becoming the fifth leading cause of death (2). Unfortunately, similar successes have not been evident in low to upper-middle-income countries (LMICs) where stroke still remains the second most common cause of death (3). Some data suggest that the burden of stroke is increasing in the Middle East and North Africa (MENA) region (3, 4). The MENA region has an estimated population of 411 million (5). A study published in 2010 reported variable stroke incidence rates in the MENA (6). The stroke incidence was 29.8 per 100,000 in Saudi Arabia and 57 per 100,000 people in Bahrain. Furthermore, the 28-day case mortality rates also varied among the MENA countries, ranging from 10% in Kuwait to 31.5% in Iran. Although the rates of strokes are comparable with those reported in high-income countries (HICs), the population of the region is much younger and therefore represents a higher burden. Another study published in 2017 (7) reported incidence rates between 16/100,000 in a prospective population based in Iran and 162/100,000 in Libya. Age-adjusted prevalence was available only from Tunisia at 184/100,000. Mortality for all strokes from the eight countries reported 30-day case fatality ranged from 9.3% in Qatar to 30% in Pakistan.

The MENA-SINO comprises stroke experts from 19 MENA and adjacent (+) regional countries (Bahrain, Egypt, Iran, Indonesia, Iraq, Jordan, Kuwait, Lebanon, Malaysia, Oman, Pakistan, Saudi Arabia, Sudan, Turkey, Thailand, United Arab Emirates (UAE), Yemen, and Qatar).

The main objective of the MENA-SINO+ is to improve education, research, and healthcare in the regional countries. The MENA-SINO organization has regular regional conferences, educational seminars, and exchanges of local and international stroke expert faculty to regional hospitals. In addition, it conducted locally relevant research and guidelines (8–11).

Acute stroke care is complex and requires multidisciplinary networking. Undoubtfully, dedicated efforts made by the regional stroke experts in the last few years have led to improvement in stroke care in the MENA region. Further improvement in stroke care will require the creation of an integrated regional stroke system at the local hospital level and across the MENA region. The lack of data on the readiness of acute stroke care from the MENA and the surrounding region (MENA+) was the driving force for this study.

Objectives

This study aimed to assess the readiness of stroke programs in the Middle East, North Africa, and neighboring areas (MENA+) to manage acute stroke.

Method

The survey

An online survey composed of open and multiple-choice questions aimed at evaluating the hospital demographics, interest in stroke program certification, design of stroke program infrastructure, availability of complementary services, diagnostic capabilities, patient monitoring capabilities, availability of standard operating procedures (SOPs), and existence of effective legislation. The inter-hospital integrated protocol and the availability of various modalities for the treatment of acute stroke were also evaluated.

The survey questionnaire was available as online Supplementary material. The online survey tool (survey monkey, Palo Alto, California, USA; www.surveymonkey.com) was utilized. No compensation was offered to participants, and respondents were limited to a single response per center. The survey included general questions to identify the engagement of participants in acute stroke management and more specific questions related to the availability of facilities for thrombolysis and thrombectomy. If the participant was not actively involved in acute stroke treatment, the survey was terminated automatically.

This survey commenced in April 2021 and ended in January 2022. After 5 months the site was closed, and the data were extracted. Finally, all the survey data were fed into an excel sheet by an assigned key person to secure homogeneity, then it was double check and reviewed by the principal investigator to ensure the validity of the data.

Participants

The survey was distributed through secure internal membership emails of the society, or postings on MENA-SINO web page and distributed to stroke and neuro interventionalists' centers' leaders (stroke program directors, stroke neurologists, neuro interventionalists, neurosurgeons, and neuro-radiologists) affiliated with the Middle East North Africa Stroke and Interventional Neurotherapies Organization (MENA-SINO). The MENA-SINO steering committee approved the study project and the questionnaire. The aim was to have at least one respondent from each of the countries comprising MENA+. Initially, 50 stroke expert affiliated hospitals showed interest to be part of the survey. However, out of the 50 initial responses, only 34 (68%) completed the survey (Appendices 1, 2).

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 28.0. (Armonk, NY: IBM Corp). Numerical data were summarized using the median and interquartile range, whereas categorical data were summarized using the frequency and percentage. Data were subsequently summarized in tables (12).

Result

Demographic data

Bahrain, Egypt, Iran, Indonesia, Iraq, Jordan, Kuwait, Lebanon, Malaysia, Oman, Pakistan, Sudan, Saudi Arabia, Qatar, Thailand, Turkey, Tunisia, United Arab Emirates (UAE), and Yemen took part in the survey. A total of 34 hospitals participated in the survey. 32/34 (94.1%) hospitals were interested in getting their stroke unit certified. The majority of hospitals that responded to the survey were university-based hospitals (19/34 [55.9%]). The remainder of the hospitals were associated with the ministry of health (7/34 [20.6%]), private (5/34 [14.7%]), or military (3/34 [8.8%]). The location of the stroke units/wards in the majority of hospitals was within the neurology department (18/34 [52.9%]) or within the internal medicine departments (9/34 [26.5%]). In the remainder of hospitals, the units were located within the intensive care unit, neurosurgery department, or emergency department, or other areas in the hospitals (7/34 [20.6%]).

Structures

The median catchment population for participating hospitals was 2 million (IQR) (1.0 million−3.05 million). The number of stroke admissions to these hospitals ranged from 36 cases at Family Care Hospital in Riyadh to as high as 10,000 cases at Al-Hussein University Hospital located in Cairo. The median number of patients with stroke admitted per year at these hospitals was 600/year ([IQR] [range: 250–1,100]). The median number of admission to the stroke units/ year was 300/year ([IQR] [range: 77.5–600]).

The median length of stay at these hospitals was 8 days (IQR [range: 7–10]), whereas the median length of stay at the stroke unit was 5 days (IQR [range 5–7]). The median number of the monitored stroke unit beds at the participating hospitals was 8 (IQR [range: 4–11]) vs. 4 (IQR [range: 0–12]) for non-monitored beds (Table 1).

TABLE 1 General structures of the surveyed hospitals.

Variable	Median (IQR)	Minimum–Maximum
Catchment area population	2 million (1 million−3.05 million)	100,000–25 million
# of stroke admission in hospital per year	600 (250–1,100)	36–10,000
# of stroke admission to stroke unit per year	300 (77.5–600)	12–1,600
Total Hospital beds	450 (217.5–1,160)	42–2,500
# of monitored stroke unit beds	8 (4–11)	0–24
# of non-monitored stroke unit beds	4 (0–12)	0–90
Total length stroke patients stay at hospital (in days)	8 (7–10)	2–21
% of patients spending 24-72 hours in stroke unit	50.5% (30–80.75%)	5–100
% of patients spending >72 hours in stroke unit	50% (20–70%)	3–100

TABLE 2 Neuroimaging and monitoring services at surveyed hospitals.

Service availabilities	*n* (%)
CT head 24/7	34 (100)
CT cerebral angiogram 24/7	26 (76.5)
MRI brain 24/7	17 (50.0)
MRA 24/7	15 (44.1)
Neurovascular ultrasound	22 (64.7)
Intra-arterial catheter angiography	21 (61.8)
Routine ECG 24/7	32 (94.1)
Long-term-ECG with arrhythmia/AF detection	31 (91.2)
Echocardiogram	34 (100)
Clinical/biochemical emergency available 24/7	34 (100)
Continuous BP measurement	34 (100)
Pulse oximetry	33 (97.1)
Respiratory monitoring	34 (100)
Temperature recording	34 (100)

Service availabilities

Imaging and monitoring

Head CT scanning is present at all 34 participating hospitals 24 h per day and 7 days per week. Cerebral CT angiogram facilities are delivered 24 h per day and 7 days per week at (26/34 [76.5%]) of the participating hospitals. However, brain MRI service is available only at (17/34 [50%]) of the hospitals. Clinical/biochemical emergency laboratory tests are done 24-hours per day and 7 days per week at all sites (34/34 [100%]) (Table 2).

Other disciplines

Neurosurgical services are found at (33/34 [97%]) of the hospitals. Although the echocardiogram facility is present at all the participating hospitals (34/34 [100%]), cardiology experts are available within the hospital only at (30/34 [88.2%]) sites. Accessibility to internal medicine services is present at (32/34 [94.1%]) of the surveyed hospitals. Radiological department with neuroradiological expertise is found at (30/34 [88.2%]) hospitals, and finally, vascular surgery expertise was only available at (27/34 [79%]) hospitals.

Protocols and guidelines

Stroke informational manuals are available in (27/34 [79.4 %]) hospitals. Nursing manuals were available in (24/34 [82.4%]) of the sites. Only half of these hospitals (17/34 [50%]) have emergency guidelines for prehospital acute stroke care. National Institute of health stroke scale (NIHSS) was the most common scale used to access acute stroke symptoms at these hospitals (26/34 [82.4%]). The remaining 6/34 (17.6%)] hospitals used Glasgow Coma Scale (GCS).

Other facilities

Clinical stroke trials were conducted in (15/34 [44.1%]) of the hospitals. Post-stroke rehabilitation services were present in (30/34 [88.2%]). Tele medical/ tele radiological link with other stroke care facilities was only available in (6/34 [17.6%]) hospitals.

Treatment options delivered for patients with stroke

Intravenous thrombolysis/mechanical thrombectomy

Intravenous thrombolysis (IVT) alone was offered in (7/34 [20.6%]) hospitals. Mechanical thrombectomy with/without IVT was available in (24/34 [70.6%]) hospitals. There were only 3/34 (8.8%) where the two treatments were not available.

The median (IQR) percentage of patients treated with IVT for acute ischemic stroke (AIS) whose treatment is started within or <60 min following arrival to hospital was (51% [15–75%]). The median (IQR) percentage of patients with AIS eligible for IVT who received it within the appropriate time window was (56% [15–82.3%]). The median (IQR) percentage of patients treated with IVT who have a symptomatic hemorrhagic transformation (HT) within 36 h of treatment was (6% [4–10%]). The median percentage (IQR) of patients with AIS treated with endovascular interventions who developed **HT** was (5.5% [2–10%]). The median (IQR) number of decompressive craniotomies in malignant brain infarction was 10/year (3.75–20.25). The median (IQR) number of carotid interventions (surgery/stenting) was 20 /year (5–45) across all hospitals (Table 3).

Other types of treatments

The survey also evaluated if the hospitals had facilities to manage subarachnoid aneurysmal hemorrhages (SAHs). The number of hospitals with adequate facilities to treat SAH was 84% (48.5–84%). Nimodipine (60 mg every 4 h or 30 mg every 2 h) was started within 24 h of diagnosis and continued until 21 days after the hemorrhage or until discharge from the hospital was also an option.

Most hospitals had facilities for the reversal of anticoagulation-related ICH. Median time from arrival to start of treatment to reverse the INR with a procoagulant preparation (e.g., fresh frozen plasma, recombinant factor VIIa, prothrombin complex concentrates) for patients with warfarin-associated intracerebral hemorrhage (ICH) and an elevated INR was 35 min (35–78).

The percentage of patients with stroke or death within 24 h of diagnostic neuro-angiography after the diagnosis of SAH was 4% [4–10% as reported in 32/34 hospitals (two hospitals did not provide the data on this) was] (Table 4).

Discussion

This is the largest study on the availability of stroke services in a large geographical area comprising 19 countries. Our study shows the availabilities of imaging resources and stroke units at the surveyed hospitals. It also highlights a wide range of variability in treatment options for acute stroke in the courtiers included in the survey. Excellent stroke care services are observed in high-income countries with immediate access to thrombolysis and thrombectomy services. Where there has been a serious lack of availability of basic care in the management of acute stroke in low-income countries.

This survey revealed a dichotomy of stroke center representation regionally. On the one hand, tertiary fully

TABLE 3 Treatment options delivered for AIS.

Variable	*n* (%)	Minimum–Maximum
Stroke-relevant scales		
GCS	6 (17.6)	–
NIHSS	28 (82.4)	–
Treatment options available for AIS across Hospitals		
IVT alone	7 (20.6)	–
MT with/without IVT	24 (70.6)	–
Neither	3 (8.8)	–
# of carotid interventions (surgery/stenting) Per Year, median (IQR)	20 (5–45)	(0–200)
# of decompressive craniectomies performed for malignant MCA infarction, median (IQR)	10 (3.75–20.25)	(0–50)
% of patients treated with IVT & developed an sHT within 36 hours of treatment, median (IQR)	6% (4–10%)	(0–39%)
% of AIS patients treated with MT & developed HT, median (IQR)	5.5% (2–10%)	(0–29%)
% of AIS patients eligible for IVT treatment & receive it within the appropriate time window, median (IQR)	56% (15–82.25%)	(0–100%)
% of patients treated for AIS with IVT ≤60 min after arrival, median (IQR)	51% (15–75%)	(0–100%)
% of patients with AIS or TIA for whom an NIHSS score was documented.	78% (32.5–96%)	0–100%
Time from arrival to start of multimodal brain vascular imaging (MRI/MRA or CT/CTA) for IS patients arriving within 6 hours from last seen well, if one of these studies done	35 min (15.5–61 min)	0–100 min

TABLE 4 Treatment options delivered for ICH/SAH.

Variable	Median (IQR)	Minimum–Maximum
% of patients with confirmed aneurysmal SAH & received nimodipine treatment	84% (48.5–100%)	0–100%
(Time from arrival to start treatment to reverse the INR with a procoagulant preparation) for patients with warfarin-associated ICH & an elevated INR (INR ≥1.4).	35 min (10–78 min)	0–100
% of patients with stroke or death within 24 h of diagnostic neuroangiography.	4% (0.25–10%)	0–23%

accredited centers with a standardized level of stroke care are delivered that rival major stroke centers in the West. However, on the other hand, others centers lack the basic measures of stroke care. Therefore, these results may not accurately represent the preparedness of hospitals to serve as accredited stroke centers. However, given the scarcity of data from the region we hope, the information obtained from the current study may allow for more rigorous prospective databases and registries to capture the true burden of stroke in the region.

When compared to prior studies from Asia (13), our research reveals a welcome increase in the number of stroke experts and stroke units and facilities in the region. Unfortunately, we also noted a marked disparity in stroke treatment and stroke research productivity between high- and low-income countries (14). This was particularly evident in Africa where there is a lack of awareness of stroke risk factors and recognition of symptoms of stroke and a general lack of facilities, including stroke units and rehabilitation services.

A key observation in our survey was that most hospitals were interested in stroke certification. Such certification will allow for the improvement of care in hospitals with sub-optimal stroke care. Unfortunately, such certifications have not been developed by most governments and local professionals in the MENA+ region. Our survey offers an opportunity for MENA-SINO to initiate the process in collaboration with local organizations and local governments. Collaboration between local representatives and established international organizations will be useful. The establishment of data sharing with SITS registry has improved data collection related to stroke in the MENA region and has resulted in publications that have had regional relevance (15–20).

Limitations

There are limitations to the study. The survey was sent to a large number of hospitals representing stroke care in high and low-income countries. The majority of the participating hospitals that completed the survey were, however, tertiary hospitals in high-income countries. This may underrepresent reporting from hospitals where stroke care is sub-optimal. Given the nature of self-reporting used in the survey, and in the absence of validation or auditing, response bias may exist. The lower rates of engagement of many hospitals, especially from low-income countries in the survey, may reflect a regional lack of research culture, a lack of protected research time, and a lack of financial incentives to support such activities. The survey respondents were physicians. The underrepresentation of multidiscipline health personnel in the survey is also another limitation. Such involvement may have provided useful information on the delivery of care from the perspective of the allied health personal.

Conclusion

This is the first large study on the availability of resources for the management of acute stroke in the MENA+ region. Our research shows a considerable variance in stroke management in the regions surveyed. Regional and international cooperation is required to advance stroke care and begin accreditation of the region's current stroke programs. Prospective registries and databases with the engagement of stakeholders to ensure engagements of more centers in future studies might help to better understand and classify the current situation of acute stroke services available in the region.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

AAlH: principle investigator, data organization, analysis, and manuscript writing. ASh and YI: contribution to manuscript writing and critical review. DA: data organization. SJ: data analysis. Rest of coauthors were responsible for filling out the survey of their corresponding country and institute.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2022.1016376/full#supplementary-material

References

1. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett D, et al. Global and regional burden of stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. *Lancet.* (2014) 383:245–55. doi: 10.1016/S0140-6736(13)61953-4

2. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M et al. American Heart Association Statistics Committee, Stroke Statistics Subcommittee. Heart disease and stroke statistics-2016 update: a report from the American Heart Association. *Circulation*. (2016) 133:e38–60. doi: 10.1161/CIR.0000000000000350

3. Top 10 causes of death, WHO, 2019. *2021 Heart Disease & Stroke Statistical Update Fact Sheet—Global Burden of Disease.*

4. Feigin VL, Norrving B, Mensah GA. Global burden of stroke. *Circ Res.* (2017) 120:439–48. doi: 10.1161/CIRCRESAHA.116.308413

5. Khan M, Al-Rukn S, Alhazzani AA, Aref H, Moreira T, Wahlgren N. Changing the face of stroke care in the Middle East North Africa region *J Neurol Sci.* (2020) 412:116727. doi: 10.1016/j.jns.2020.116727

6. Jackie T, Masoud M, Laurie A, Stephen RL. The epidemiology of stroke in the Middle East and North Africa. *J Neurol Sci.* (2010) 295:38–40. doi: 10.1016/j.jns.2010.05.016

7. Streletz LJ, Mushtak A, Gad H, Abbasi S,Dimassi DM, Akhtar N et al. Epidemiology of stroke in the MENA region: a systematic review. *Int J Neu Dis.* (2017) 1: 10-21.

8. Al Hashmi AM, Ozdemir AO, Shuaib A, Al-Jehani H, Mansour OY, Alhazzani A, et al. Current recommendations for the management of stroke patients in the middle east in the era of COVID-19 pandemic) statement from the MENA SINO. *J Stroke Cerebrovasc Dis.* (2020) 29:105181. doi: 10.1016/j.jstrokecerebrovasdis.2020.105181

9. Al-Jehani H, John S, Hussain SI, Al Hashmi A, Alhamid MA, Amr D, et al. Consensus statement of the MENA-SINO on implementing care pathway for acute neurovascular emergencies during the COVID-19 pandemic. *Front Neurol.* (2020) 11:928. doi: 10.3389/fneur.2020.00928

10. Al Hashmi A, von Bandemer S, Shuaib A, Mansour OY, Wassy M, Ozdemir AO, et al. Lessons learned in stroke care during COVID-19 pandemic and preparing for future pandemics in the MENA+ region: A consensus statement from the MENA+-SINO. *J Neurol Scie.* (2022) 432:120060. doi: 10.1016/j.jns.2021.120060

11. Al Hashmi AM, Akhtar N, Al Rukin S, Gaba W, Mehrpour M, Shuaib A, et al. Maintaining stroke care in the era of Covid-19: A review of practices implemented in the Gulf and Iran). *Neurology.* (2020) 25:545–53

12. Simpson SH. Creating a data analysis plan: what to consider when choosing statistics for a study. *Can J Hosp Pharm.* (2015) 68:311–7. doi: 10.4212/cjhp.v68i4.1471

13. Suwanwela NC, Poungvarin N. Stroke burden and stroke care system in Asia. *Asian Stroke Advisory Panel.* (2016) 64:46–51 doi: 10.4103/0028-3886.178042

14. Apor ADAO, Pagaling GT. Espiritu AI, Jamora RDG. Stroke research disparity in southeast asia: socioeconomic factors, healthcare delivery, and stroke disease burden. *J Stroke Cerebrovasc Dis.* (2021) 30:105481.

15. Al-Rukn S, Mazya M, Akhtar N, Hashim H, Mansouri B, Faouzi B et al. Stroke in the Middle-East and North Africa: A 2-year prospective observational study of intravenous thrombolysis treatment in the region. Results from the SITS-MENA Registry. *Int J Stroke.* (2020) 15:980–7. doi: 10.1177/1747493019874729

16. Jasne AS, Sucharew H, Alwell K, Moomaw CJ, Flaherty ML, Adeoye O, et al. Stroke center certification is associated with improved guideline concordance. *Am J Med Qual.* (2019) 34:585–9. doi: 10.1177/1062860619835317

17. Abd-Allah F, Wasay M. Roadmap for improved stroke care: implications for global stroke guidelines and action plan *Int J Stroke.* (2015) 10:E52. doi: 10.1111/ijs.12528

18. Ringelstein EB, Meckes-Ferber S, Hacke W, Kaste M, Brainin M, Leys D, et al. European stroke facilities survey: the German and Austrian perspective. *Cerebrovasc Dis.* (2009) 27:138–45. doi: 10.1159/000177922

19. Owolabi MO, Thrift AG, Martins M, Johnson W, Pandian J, Abd-Allah F, et al. The state of stroke services across the globe: Report of World Stroke Organization-World Health Organization surveys. *Int J Stroke.* (2021) 16:889–901. doi: 10.1177/17474930211019568

20. McAlister FA, Majumdar SR, Padwal RS, Fradette M, Thompson A, Buck B. Case management for blood pressure and lipid level control after minor stroke: PREVENTION randomized controlled trial. *CMAJ.* (2014) 186:577–84) doi: 10.1503/cmaj.140053

frontiers | Frontiers in Neurology

TYPE Original Research
PUBLISHED 14 November 2022
DOI 10.3389/fneur.2022.1032676

OPEN ACCESS

EDITED BY
Janika Kõrv,
University of Tartu, Estonia

REVIEWED BY
Hrvoje Budincevic,
University Hospital Sveti Duh, Croatia
Joshua C. Cheng,
Harvard Medical School, United States

*CORRESPONDENCE
Li-Ning Zhang
Zhangln301@163.com

†These authors have contributed equally to this work

SPECIALTY SECTION
This article was submitted to Stroke, a section of the journal Frontiers in Neurology

RECEIVED 31 August 2022
ACCEPTED 28 October 2022
PUBLISHED 14 November 2022

CITATION
Xie H-M, Zhang X-T, Xu L, Wang N, Wang R, Jia Z-S and Zhang L-N (2022) Magnetic resonance imaging findings in painful hemiplegic shoulder patients with or without subluxation: A retrospective cohort study. *Front. Neurol.* 13:1032676. doi: 10.3389/fneur.2022.1032676

Magnetic resonance imaging findings in painful hemiplegic shoulder patients with or without subluxation: A retrospective cohort study

Hui-Min Xie[1†], Xiao-Tan Zhang[1†], Lin Xu[2†], Ning Wang[1], Rui Wang[1], Zi-Shan Jia[1] and Li-Ning Zhang[1*]

[1]Department of Rehabilitation Medicine, The First Medical Centre, Chinese PLA General Hospital, Beijng, China, [2]Department of Radiology, The First Medical Centre, Chinese PLA General Hospital, Beijng, China

The relationship between hemiplegic shoulder pain (HSP) and subluxation is unclear. This study aimed to determine the differences of magnetic resonance imaging (MRI) findings in HSP patients with or without subluxation after stroke, and to analyze the etiology of shoulder pain. This retrospective study included 53 patients with HSP after stroke from September 2013 to February 2020. Patients underwent MRI of the shoulder because of shoulder pain. Clinical characteristics, including age, sex, stroke duration, body mass index, stroke type, visual analog scale score, Brunnstrom stage, and MRI arthrography findings of the affected shoulder, were recorded. Patients were classified into the glenohumeral subluxation (GHS) group ($n = 27$) or non-glenohumeral subluxation (nGHS) group ($n = 26$). We found that patients with HSP may be prone to bursa effusion, rotator cuff injury, ligament injury, and cartilage injury, even though there was no significant difference between the GHS and nGHS groups. MRI revealed 14 cases of long bicipital tendon-glenoid labrum injury (51.8%) in the GHS group and 6 cases (23.1%) in the nGHS group ($p = 0.030$). We also found 10 cases (37%) of glenoid labrum injury in the GHS group and 2 cases (7.7%) in the nGHS group ($p = 0.026$). Eight cases (29.6%) and 1 case (3.8%) of bone marrow edema were found in the GHS and nGHS groups, respectively ($p = 0.033$). Compared with painful hemiplegic shoulder patients without subluxation, patients with subluxation may be more susceptible to some injuries, such as long bicipital tendon-glenoid labrum injury, glenoid labrum injury, and bone marrow edema. During rehabilitation, physicians need to pay attention to these injuries.

KEYWORDS

magnetic resonance imaging, shoulder pain, hemiplegic shoulder, glenohumeral subluxation, hemiplegic shoulder pain

Introduction

Stroke often causes disability among elderly people. Hemiplegic shoulder pain (HSP) is one of the most common complications in patients after a stroke. The incidence of HSP is approximately 17–72% (1). HSP, which is related to depression and a poor quality of life, negatively affects functional recovery of the upper extremity and activities of daily living (ADLs) (2). The pathogenesis of HSP includes shoulder subluxation, adhesive capsulitis, bursitis, shoulder-hand syndrome, among others (3). However, the exact etiology of HSP remains unknown and many complicated factors are involved. Glenohumeral subluxation (GHS) may be considered a potential cause of shoulder pain development (4).

The prevalence of GHS was reported to be 15–81% (2). There is speculation that the peri-articular tissue of the shoulder may be overstretched because of malalignment of the joint. The capsule and ligaments contain high concentrations of pain receptors, which cause shoulder pain (5).

Factors contributing to joint malalignment include rotator cuff weakness, loose ligaments and capsule, and impingement between the humeral head and shoulder suture. GHS commonly occurs in the flaccid stage, which is characterized by areflexia and atonia (6). However, the relationship between HSP and subluxation is unclear. Magnetic resonance imaging (MRI), which is widely used in diagnosing and determining the pathologies of HSP, has been proven to be more advantageous than other imaging techniques because it can clearly show the details of the soft tissue (7).

Thus, the present investigation aimed to determine the differences between MRI findings in HSP patients with subluxation and non-subluxation after stroke, and to analyze the etiology of shoulder pain.

Materials and methods

Patient selection

This was a retrospective cohort study conducted at the rehabilitation center of the First Medical Centre, Chinese PLA General Hospital in Beijing. The data of 53 post-stroke patients with HSP were collected for this study from September 2013 to February 2020 (Figure 1). Inclusion criteria were first-time stroke resulting in HSP and no history of shoulder disorder before stroke onset. Exclusion criteria were history of shoulder trauma and surgery, and severe cognitive impairment. Patients with GHS were categorized into the GHS group, and those without GHS were allocated into the non-glenohumeral subluxation (nGHS) group.

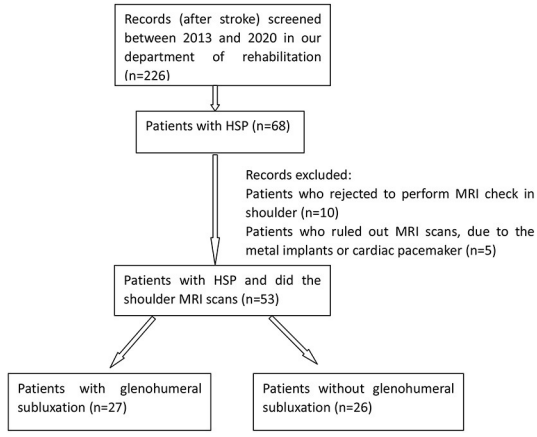


FIGURE 1
Flow chart and retention of patients.

Ethical approval

This study was approved by the Ethics Committee of the Chinese PLA General Hospital (No. S2019-230-01). As an anonymous retrospective study, the need for obtaining informed consent from patients was waived.

Definitions and data collection

The diagnosis of stoke was confirmed based on the patients' history, clinical symptoms, physical examinations, and computed tomography/MRI findings. HSP was diagnosed on the basis of two criteria: visual analog scale (VAS) score ($\geq$4) and limited passive range of motion of the affected shoulder (reduced shoulder abduction and external rotation $\geq$25%) (8).

GHS was diagnosed based on the clinical palpation method, which has been shown to be a reliable screening measure with good inter- and intra-rater reliabilities (9, 10). The patient was seated with their arm relaxed beside their body. The distance between the acromion and humeral head was measured. If the distance was longer than a fingerbreadth, it indicated the presence of subluxation (6). The diagnosis of GHS was made by two examiners, a rehabilitation physician and a physiotherapist, both of whom had > 5 years of experience with stroke patients in the rehabilitation department.

Shoulder MRI was performed once shoulder pain occurred; 3.0 Tesla Skyra MRI (Siemens) was used. Patients were positioned supine with their upper limb in a neutral

Abbreviations: HSP, hemiplegic shoulder pain; GHS, glenohumeral subluxation; MRI, magnetic resonance imaging; VAS, visual analog scale; BMI, body mass index; ADL, activity of daily living; TR, repetition time; TE, echo time; BME, bone marrow edema.

position. An identical MRI protocol of the hemiplegic shoulder was used for all patients, as follows: T1WI-SAG and T1WI-COR: TE/TR 22/600ms, PDWI-SAG: TE/TR 37/3800ms, PDWI-COR: TE/TR 42/3100ms, PDWI-TRA: TE/TR 73/3780ms. The field of view was set to 18 cm, and the image sequences were obtained with a matrix acquisition range of 320 × 256. The slice thickness was 4 mm. The images were read individually by two experienced radiologists.

Age, sex, body weight, height, body mass index (BMI), hemiplegic side, stroke type (ischemic or hemorrhagic), and stroke duration were recorded. The level of motor function was assessed by the Brunnstrom recovery stages of the upper extremity (9), which were defined as follows: I, flaccid stage without any voluntarily muscle movement; II, muscle contraction with weak flexor and/or extensor synergies; III, voluntary movement of the upper limbs without selective activation; IV, selective activation coming; V, more predominant selective activation; VI, proper coordination of isolated movements ignoring speed. The pain of the affected shoulder was evaluated by the VAS. Patients scored the intensity of their shoulder pain in person on a scale from 0 to 10 (10). A VAS score of 0 was defined as no pain, and 10 as the worst pain. The Barthel Index was used to assess patients' ADLs. The Barthel Index is considered to be the best ADL measurement scale. Barthel Index scores are based on the completion status of some tasks, such as bathing, feeding, toileting, stair climbing, dressing, personal hygiene, bowel control, bladder control, ambulation, and chair/bed transfers (11). BMI was determined as weight (kg) divided by height $(m)^2$.

Data analysis

Statistical analysis was performed using SPSS statistical software (version 23; IBM Corp.). The independent samples t-test was used to compare the differences in age, stroke duration, BMI, VAS, and Barthel scores between the groups, while the Pearson's chi-squared test test was used to compare the differences in sex, stroke type, hemiplegic side, and paresthesia between the groups. Normality of the data distribution was checked using the Kolmogorov–Smirnov test. Additionally, the Wilcoxon rank-sum test was used to compare differences in the Brunnstrom recovery stage between the groups. Further, the Pearson's chi-squared test, and Fisher's exact test were utilized to compare differences in MRI findings between the groups. In cases of cells <5 and >0, the chi-square test was used. In case of cells equal to 0 or total numbers <40, Fisher's exact test was used. Statistical significance was defined as $p < 0.05$.

TABLE 1 Clinical features of the patients.

	GHS group ($n = 27$)	nGHS group ($n = 26$)	*P*-value
Age, y, mean (SD)	59.7 (11.4)	56.27 (13.1)	0.082
Gender, female/male, *n*	19/8	20/6	0.589
Stroke duration, *d*, mean (SD)	89.5 (62.8)	102.15 (154)	0.296
BMI, cm/kg^2, mean (SD)	23.7 (3.4)	24.8 (4.1)	0.218
Stroke type (*n*)			0.407
Ischemic	18	20	
Hemorrhage	9	6	
Hemiplegic side (*n*)			0.449
Left	16	18	
Right	11	8	
Paresthesia, *n* (%)	16 (0.59)	10 (0.37)	0.13
Barthel Index, mean (SD)	42.4 (23)	59.6 (22.2)	0.616
VAS, mean (SD)	6.3 (1.7)	5.2 (3.2)	0.375
Brunnstrom stage, *n* (%)			0.002*
I	2	0	
II	14	6	
III	10	10	
IV	0	3	
V	1	7	
VI	0	0	

BMI, body mass index; VAS, visual analog scale; y, year; d, day. *Denotes statistical significance.

Results

Clinical characteristics of the sample

Fifty-three patients (39 men and 14 women; age range, 22–80 years) were included in our study. The GHS group comprised 27 patients, and the nGHS group comprised 26 patients. Mean stroke durations were 89.5 days in the GHS group and 102.15 days in the nGHS group. The numbers of patients with paresthesia in the GHS and nGHS groups were 16 and 10, respectively. There was no significant difference between the groups in age, sex, BMI, stroke duration, hemiplegic side, stroke type, and paresthesia ($p > 0.05$). In the GHS group, the mean Barthel score was 42.4, but in the nGHS group, the mean score was 59.6 ($p = 0.616$). Mean VAS scores were 6.3 and 5.2 in the GHS and nGHS groups, respectively ($p = 0.375$). No significant differences were found in the Barthel and VAS scores between the groups. The ratios of the Brunnstrom stages I/II/III/IV/V/VI in the groups were 2/14/10/0/1/0 and 0/6/10/3/7/0, respectively. There was a significant difference in the Brunnstrom stage between the groups ($p = 0.002$). Demographic characteristics of the two groups are shown in Table 1.

TABLE 2 Comparison of MRI findings between GHS group and nGHS group.

	GHS group ($n = 27$)	nGHS group ($n = 26$)	*P*-value
Bursa effusion	26 (96.3)	26 (100)	NA
Subacromial-subdeltoid bursa	19 (70.4)	19 (73.1)	0.827
Subcoracoid bursa	25 (92.6)	21 (80.8)	0.387
Subscapular bursa-cavity	22 (81.5)	24 (92.3)	0.448
Rotator cuff injury	26 (96.3)	24 (92.3)	0.973
Supraspinatus	25 (92.6)	20 (76.9)	0.227
Infraspinatus	6 (22.2)	2 (7.7)	0.274
Subscapularis	14 (51.9)	14 (53.8)	0.884
Teres Minor	3 (11.1)	0	0.236
Ligament injury	5 (18.5)	4 (15.4)	0.906
Effusion or tendinosis of long head of biceps tendon	20 (74.1)	21 (80.8)	0.56
Synovitis	7 (25.9)	5 (19.2)	0.56
Cartilage injury	3 (11.1)	0	0.236
Bone morrow edema	8 (29.6)	1 (3.8)	0.033*
Long bicipital tendon-glenoid labrum injury	14 (51.8)	6 (23.1)	0.030*
Glenoid labrum injury	10 (37.0)	2 (7.7)	0.026*
Ext	4 (14.8)	0	
Ant, Sup	3 (11.1)	1 (3.8)	
Post, Sup	1 (3.7)	0	
Ant, Inf	1 (3.7)	0	
Ant	1 (3.7)	1 (3.8)	
Post	1 (3.7)	0	

GHS, Glenohumeral subluxation; Nghs, non-glenohumeral subluxation; Ant, anterior; Post, posterior; Sup, superior; Inf, inferior; Ext, Extensive. *Denotes statistical significance.

MRI findings

MRI findings included ligament injury, rotator cuff injury, long head of the biceps tendon injury, bursa effusion, cartilage injury, synovitis, bone morrow edema (BME), long bicipital tendon-glenoid labrum injury, and glenoid labrum injury. No significant differences were found in rotator cuff injury, bursa effusion, cartilage injury, ligament injury, and synovitis between the groups.

In the GHS group, 8/27 patients (29.6%) had a positive MRI finding of BME, but in the nGHS group, only 1/26 patients (3.8%) had such finding ($p = 0.033$). We also found that 14/27 patients (51.8%) had a long bicipital tendon-glenoid labrum injury in the GHS group, whereas 6/26 patients (23.1%) had such injury in the nGHS group ($p = 0.030$). Additionally, 10/27 patients (37.0%) in the GHS group and only 2/26 patients (7.7%) in the nGHS group had a glenoid labrum injury ($p = 0.026$). In the GHS group, 4 patients had extensive injury of the glenoid labrum, and 6 had partial injury (anterior and superior portion 1; posterior and superior portion 1; anterior and inferior portion 1; anterior portion 1; posterior portion 1). In the nGHS group, only 2 patients had partial injury of the glenoid labrum (anterior and superior portion 1; anterior portion 1). See Table 2 for details and Figures 2–4 for examples.

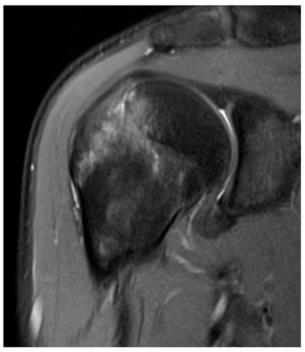


FIGURE 2
Fat suppressed T2 images. The bone marrow edema is shown.

Discussion

In this study, MRI of the affected shoulder was performed in patients with or without subluxation. Shoulder subluxation occurs mostly during the first 3 weeks in patients with HSP after a stroke (12). The incidence rate was reported to range from 32 to 81% (13), and the rate found in our study (51%) falls within this range.

The MRI scans demonstrated rotator cuff injury in 94% of the shoulders of patients in our study. However, in a study conducted by Dogun et al., 63.2% of patients ($n = 68$) with HSP were found to have a rotator cuff injury (7). The difference between their study and ours may be attributed to the different stroke onset durations: Their mean duration was 49 days, whereas ours was 85. Moreover, we found that the rotator cuff injury rate was high regardless of subluxation. In detail, supraspinatus injury rates were 92.6% in the GHS group and 76.9% in the nGHS group. Moreover, about half of patients had subscapularis injury. Contrastingly, the incidence of infraspinatus and teres minor injury was low. The main function of the supraspinatus is to abduct the shoulder, and it is an important posterior stabilizing structure of the shoulder. According to several studies (14, 15) supraspinatus injury is mainly caused by subacromial impingement. When the shoulder is frequently abducted and lifted upward, the supraspinatus tendon becomes easily impacted by the coracoacromial arch, resulting in edema, hyperemia, degeneration, and even tearing. Zhu et al. showed

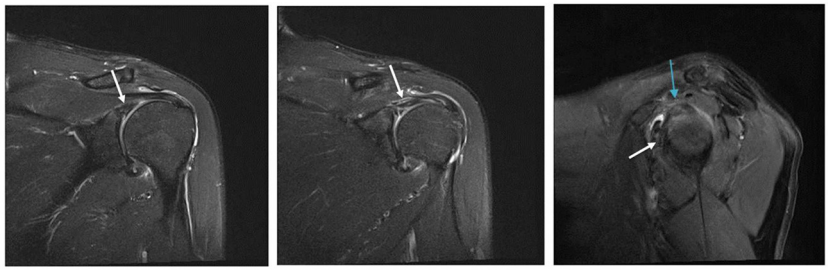


FIGURE 3
Fat suppressed T2 images. The long bicipital tendon-glenoid labrum injury is shown by the white arrow. The sup-glenoid labrum injury is shown by the blue arrow.

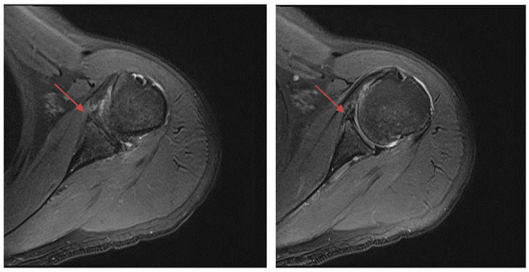


FIGURE 4
Fat suppressed T2 images. The anterior labrum injury is shown by the red arrow.

that when the shoulder was abducted 60°, it bore the greatest stress; additionally, it was beginning to rub between the supraspinatus tendon and the acromion and was thus most prone to injury and pain (16).

The functions of the subscapularis are to internally rotate the shoulder and dynamically stabilize the humeral head. Moreover, the subscapularis is an antagonist to the superior pull of the deltoid and it assists in abduction and adduction of the shoulder (17). External rotation and abduction can cause excessive strain injury of the subscapularis, which results in pain in the front of the shoulder (18). In addition, a frequent overhead throwing motion can cause coracoid impingement, which is closely associated with subscapularis injury. Therefore, rotator cuff injury, especially supraspinatus and subscapularis injury, is one of the causes of HSP. It is important for rehabilitation teams to not schedule exercises that involve moving the upper limbs above 60° with abduction action in patients with HSP. Furthermore, if the patient has a possible subscapular injury, external rotation of the shoulder should be avoided as much as possible.

Supraspinatus injury was recently hypothesized to result in compensation *via* greater force generation through the subscapularis, which could potentially hasten degeneration of the subscapularis (19). Accordingly, we could infer that there may be a correlation between supraspinatus and subscapularis injuries in patients with HSP, but this needs to be confirmed by a study with a large sample size.

Our MRI scans also demonstrated subacromial-subdeltoid bursa effusion in 71.74% of shoulders in patients with HSP, which is consistent with previous reports (53–80.9%) (7, 20, 21). Besides, we found a high subcoracoid bursa effusion and subscapular bursa-cavity effusion rate, even though this was not statistically significant between the groups. It has been suggested that subcoracoid bursa effusion and subscapular bursa-cavity effusion, except subacromial-subdeltoid bursa effusion, may cause HSP.

In a study of 42 fresh cadaveric shoulders, it was found that the function of the subscapularis and subcoracoid bursae is to manage friction of the superficial fibers against the scapular neck, humeral head, and coracoid process (22). Thus, it remains to be explored whether friction of these bone structures is increased after biomechanical changes in hemiplegic patients, resulting in fluid accumulation in the bursa.

Thanks to MRI, BME has been detected in the humeral head of numerous patients with HSP: BME was mostly reported in the femoral head and knee (23, 24). In recent studies, instances of BME were observed in the foot, ankle, wrist, or other bones (25, 26). There are two perspectives about the mechanism of BME: (1) secondary BME, secondary to infection, trauma, or arthritis, is caused by an external force acting on the cancellous bone, resulting in a microfracture of the trabecula bone that increases permeability and rupture of the local capillary, adding to the exosmosis of cell fluid and vascular perfusion; and (2) physiological BME is caused by a long-term external force or change of the normal load of the bone, resulting in bone marrow hyperemia and excessive perfusion of the capillaries. In our study, BME occurred more in patients with subluxation which may be due to (1) rotator cuff weakness and change in gravity

that caused secondary BME and (2) excessive passive movement or incorrect posture that caused physiological BME in flaccid paralysis period. Because of its self-limiting course (24), BME could improve after the paralysis period. Thus, the potential evolution and mechanism of BME in the shoulder requires further study.

Long bicipital tendon-glenoid labrum injury occurred more commonly in the GHS group. It is caused by repeated contraction of the long head of the bicipital tendon or trauma to the humeral head with repeated external rotation and abduction movements (27). Thus, when rehabilitating patients with HSP, especially those with subluxation, physicians should avoid such movements.

We usually divide the labrum into eight directions: anterior, posterior, superior, inferior, anterior superior, anterior inferior, posterior superior, and posterior inferior. We also briefly differentiated the exact location of the simple labrum injury observed herein. MRI findings showed that simple labrum injury was more common in the GHS group than in the nGHS group, and it included extensive anterior superior, posterior superior, anterior inferior, anterior, and posterior injury. Our finding that extensive injury in the anterior superior was the most common injury type differs from findings of shoulder imaging in cases of sports injury (27). This discrepancy implies that the biological stress produced by passive motion is different from that of active motion.

The limitations of this study include the small sample size, absence of MRI images of contralateral healthy shoulders, and retrospective design. A larger scale, controlled clinical trial with a longer-term, longitudinal follow-up is warranted.

Conclusion

On the basis of our MRI findings, we found a high frequency of bursa effusion, rotator cuff injury, and long head of the biceps tendon injury in patients with HSP. Compared to patients with HSP in the non-subluxation group, we found that patients with HSP in the subluxation group were more prone to BME, long bicipital tendon-glenoid labrum injury, and glenoid labrum injury. Thus, in patients with HSP, we recommend that physicians avoid moving the upper limbs above 60° with abduction action. If patients have subluxation, physicians and therapists should plan to reduce the external rotation and abduction movements to prevent rotator cuff injury and long bicipital tendon-glenoid labrum injury during rehabilitation. Patients with subluxation should be moved gently if they require passive actions. Moreover, they should be educated about protecting their shoulders during ADLs. Further studies with a larger sample size are needed to confirm our findings.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving human participants were reviewed and approved by No. S2019 230 01. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

Z-SJ, X-TZ, and L-NZ designed the experiment. H-MX and LX read and checked the MRI images. NW and RW assessed the clinical information of the patients. H-MX wrote the draft of the manuscript. All authors discussed the results, commented on the manuscript, and approved the submitted version.

Acknowledgments

We greatly appreciate the staff at the department of radiology in the Chinese PLA General Hospital for their assistance in this study and the editors of Editage for English language editing. The study was not supported by any external funding.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Yang L, Yang J, He C. The effect of kinesiology taping on the hemiplegic shoulder pain: a randomized controlled trial. *J Healthc Eng.* (2018) 10:8346432. doi: 10.1155/2018/8346432

2. Karaahmet OZ, Gurcay E, Unal ZK, Cankurtaran D, Cakci A. Effects of functional electrical stimulation-cycling on shoulder pain and subluxation in patients with acute–subacute stroke: a pilot study. *Int J Rehabil Res.* (2019) 42:36–40. doi: 10.1097/MRR.0000000000000319

3. Chuang LL, Chen YL, Chen CC, Li YC, Wong AMK, Hsu AL, et al. Effect of EMG-triggered neuromuscular electrical stimulation with bilateral arm training on hemiplegic shoulder pain and arm function after stroke: a randomized controlled trial. *J Neuroeng Rehabil.* (2017) 28:122. doi: 10.1186/s12984-017-0332-0

4. Paci M, Nannetti L, Taiti P, Baccini M, Pasquini J, Rinaldi L. Shoulder subluxation after stroke: relationships with pain and motor recovery. *Physiother Res Int.* (2007) 12:95–104. pri.349. doi: 10.1002/pri.349

5. Anke VB, Gert L, Kristine MO, Vanderstraeten G, Cambier D. A randomized controlled trial on the immediate and long-term effects of arm slings on shoulder subluxation in stroke patients. *Eur J Phys Rehabil Med.* (2017) 53:400–9. doi: 10.23736/S1973-9087.17.04368-4

6. Idowu BM, Ayoola OO, Adetiloye VA, Komolafe MA, Afolabi BI. Sonographic detection of inferior subluxation in post-stroke hemiplegic shoulders. *J Ultrason.* (2017) 17:106–12. doi: 10.15557/JoU.2017.0015

7. Dogun A, Karabay I, Hatipoglu C, Ozgirgin N. Ultrasound and magnetic resonance findings and correlation in hemiplegic patients with shoulder pain. *Top Stroke Rehabil.* (2014) 21:S1–7. doi: 10.1310/tsr21S1-S1

8. Pompa A, Clemenzi A, Troisi E, Mario M, Tonini A, Pace L, et al. Enhanced-MRI and ultrasound evaluation of painful shoulder in patients after stroke: a pilot study. *Eur Neurol.* (2011) 66:175–81. doi: 10.1159/000330657

9. Pong YP, Wang LY, Wang L, Leong CP, Huang YC, Chen YK. Sonography of the shoulder in hemiplegic patients undergoing rehabilitation after a recent stroke. *J Clin Ultrasound.* (2009) 37:199–205. doi: 10.1002/jcu.20573

10. Turner-Stokes L, Jackson D. Assessment of shoulder pain in hemiplegia: sensitivity of the ShoulderQ. *Disabil Rehabil.* (2006) 28:389–95. doi: 10.1080/09638280500287692

11. Shah S, Vanclay F, Cooper B. Improving the sensitivity of the Barthel index for stroke rehabilitation. *J Clin Epidemiol.* (1989) 42:703–9. doi: 10.1016/0895-4356(89)90065-6

12. Stolzenberg D, Siu G, Cruz E. Current and future interventions for glenohumeral subluxation in hemiplegia secondary to stroke. *Top Stroke Rehabil.* (2012) 19:444–56. doi: 10.1310/tsr1905-444

13. Kim YH, Jung SJ, Yang EJ, Paik NJ. Clinical and sonographic risk factors for hemiplegic shoulder pain: a longitudinal observational study. *J Rehabil Med.* (2014) 46:81–7. doi: 10.2340/16501977-1238

14. Kocyigit F, Kuyucu E, Kocyigit A, Herek DT, Savkin R, Aslan UB. Investigation of biomechanical characteristics of intact supraspinatus tendons in subacromial impingement syndrome. *Am J Phys Med Rehabil.* (2016) 95:588–96. doi: 10.1097/PHM.0000000000000450

15. Tuoheti Y, Itoi E, Pradhan RL, Wakabayashi I, Takahashi S, Minagawa H, et al. Apoptosis in the supraspinatus tendon with stage II subacromial impingement. *J Should Elbow Surg.* (2005) 14:535–41. doi: 10.1016/j.jse.2005.01.001

16. Zhu MD, Tang JB, Gao YZ. The study of movement locus of the supraspinatus tendon as the humerus was abducted and its clinical implication. *Chin J Clin Anat.* (2003) 21:375–8.

17. Arpád I, Rita MK. Electromyographic analysis in patients with multidirectional shoulder instability during pull, forward punch, elevation and overhead throw. *Knee Surg Sports Traumatol Arthrosc.* (2007) 15:624–31. doi: 10.1007/s00167-006-0163-1

18. Maura L, Andrew G, Monika K, Evans K, Chen YT. Sonographic findings in subcoracoid impingement syndrome: a case report and literature review. *PM&R.* (2017) 9:204–9. doi: 10.1016/j.pmrj.2016.06.013

19. Gausden EB, Mccarthy MM, Kontaxis A, Kontaxis A, Corpus KT, Gulotta LV, Kelly AM. Subscapularis tendon loading during activities of daily living. *J Should Elbow Surg.* (2016) 26:331–6. doi: 10.1016/j.jse.2016.07.013

20. Wu T, Song HX, Dong Y, Li GH. Ultrasound-guided versus blind subacromial-subdeltoid bursa injection in adults with shoulder pain: a systematic review and meta-analysis. *Semin Arthritis Rheum.* (2015) 45:374–8. doi: 10.1016/j.semarthrit.2015.05.011

21. Távora DG, Gama RL, Bomfim RC, Nakayama M, Silva CE. MRI findings in the painful hemiplegic shoulder. *Clin Radiol.* (2010) 65:789–94. doi: 10.1016/j.crad.2010.06.001

22. Colas F, Nevoux J, Gagey O. The subscapular and subcoracoid bursae: descriptive and functional anatomy. *J Should Elbow Surg.* (2004) 13:454–8. doi: 10.1016/j.jse.2004.02.001

23. Jianchuan W, Lei Y, Benjie W, Dewei Z. Study on correlation between bone marrow edema, stage of necrosis and area ratio of necrosis with the hip pain grading in nontraumatic osteonecrosis of the femoral head. *Open Med.* (2015) 10:440–4. doi: 10.1515/med-2015-0076

24. Manara M, Varenna MA. clinical overview of bone marrow edema. *Reumatismo.* (2014) 66:184–96. doi: 10.4081/reumatismo.2014.790

25. Aizenberg E, Roex EAH, Nieuwenhuis WP, Mangnus L, van der Helm-van Mil AH, Reijnierse M, et al. Automatic quantification of bone marrow edema on MRI of the wrist in patients with early arthritis: a feasibility study. *Magn Reson Med.* (2017) 79:1127–34. doi: 10.1002/mrm.26712

26. Seyed AM, Elly T, Mohammad SS, Narges R, Shervin R. Bone marrow edema syndrome in the foot and ankle. *Foot Ankle Int.* (2016) 37:1364–73. 1071100716664783. doi: 10.1177/1071100716664783

27. Clavert P. Glenoid labrum pathology. *Orthop Traumatol Surg Res.* (2014) 101:S19–24. doi: 10.1016/j.otsr.2014.06.028

frontiers | Frontiers in Neurology

TYPE Original Research
PUBLISHED 24 November 2022
DOI 10.3389/fneur.2022.1048807

OPEN ACCESS

EDITED BY
Michael V. Mazya,
Karolinska University Hospital, Sweden

REVIEWED BY
Matt Silsby,
Westmead Hospital, Australia
Padma Vasantha,
All India Institute of Medical Sciences, India

*CORRESPONDENCE
Wen Yea Hwong
amyhwong@crc.gov.my;
w.y.hwong@umcutrecht.nl

SPECIALTY SECTION
This article was submitted to Stroke, a section of the journal Frontiers in Neurology

RECEIVED 20 September 2022
ACCEPTED 07 November 2022
PUBLISHED 24 November 2022

CITATION
Hwong WY, Ng SW, Tong SF, Ab Rahman N, Law WC, Kaman Z, Wong SK, Puvanarajah SD and Sivasampu S (2022) Stroke thrombolysis in a middle-income country: A case study exploring the determinants of its implementation. *Front. Neurol.* 13:1048807. doi: 10.3389/fneur.2022.1048807

Stroke thrombolysis in a middle-income country: A case study exploring the determinants of its implementation

Wen Yea Hwong[1,2]*, Sock Wen Ng[1], Seng Fah Tong[3], Norazida Ab Rahman[1], Wan Chung Law[4], Zurainah Kaman[4], Sing Keat Wong[5], Santhi Datuk Puvanarajah[5] and Sheamini Sivasampu[1]

[1]Institute for Clinical Research, National Institutes of Health, Ministry of Health Malaysia, Selangor, Malaysia, [2]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands, [3]Department of Family Medicine, Universiti Kebangsaan Malaysia, Selangor, Malaysia, [4]Neurology Unit, Department of Medicine, Sarawak General Hospital, Ministry of Health Malaysia, Kuching, Malaysia, [5]Department of Neurology, Hospital Kuala Lumpur, Ministry of Health Malaysia, Kuala Lumpur, Malaysia

Introduction: Translation of evidence into clinical practice for use of intravenous thrombolysis in acute stroke care has been slow, especially across low- and middle-income countries. In Malaysia where the average national uptake was poor among the public hospitals in 2018, one hospital intriguingly showed comparable thrombolysis rates to high-income countries. This study aimed to explore and provide in-depth understanding of factors and explanations for the high rates of intravenous stroke thrombolysis in this hospital.

Methods: This single case study sourced data using a multimethod approach: (1) semi-structured in-depth interviews and focus group discussions, (2) surveys, and (3) review of medical records. The Tailored Implementation of Chronic Diseases (TICD) framework was used as a guide to understand the determinants of implementation. Twenty-nine participants comprising the Hospital Director, neurologists, emergency physicians, radiologists, pharmacists, nurses and medical assistants (MAs) were included. Thematic analyses were conducted inductively before triangulated with quantitative analyses and document reviews.

Results: Favorable factors contributing to the uptake included: (1) cohesiveness of team members which comprised of positive interprofessional team dynamics, shared personal beliefs and values, and passionate leadership, and (2) facilitative work process through simplification of workflow and understanding the rationale of the sense of urgency. Patient factors was a limiting factor. Almost two third of ischemic stroke patients arrived at the hospital outside the therapeutic window time, attributing patients' delayed presentation as a main barrier to the uptake of intravenous stroke thrombolysis. One other barrier was the availability of resources, although this was innovatively optimized to

minimize its impact on the uptake of the therapy. As such, potential in-hospital delays accounted for only 3.8% of patients who missed the opportunity to receive thrombolysis.

Conclusions: Despite the ongoing challenges, the success in implementing intravenous stroke thrombolysis as standard of care was attributed to the cohesiveness of team members and having facilitative work processes. For countries of similar settings, plans to improve the uptake of intravenous stroke thrombolysis should consider the inclusion of interventions targeting on these modifiable factors.

KEYWORDS

acute stroke care, intravenous thrombolysis, developing countries, translational research, facilitator, barrier

Introduction

Effective management in the early stages of an acute ischemic stroke is crucial to reduce mortality and morbidity. Recent advancement in stroke treatment recommends the use of intravenous thrombolysis within 4.5 h of an acute ischemic stroke (1).

Nevertheless, translation of this evidence into clinical practice remains challenging. In developed countries, the rate of intravenous thrombolysis among patients who presented with acute ischemic stroke ranged from 13.7% in the United States in 2018 (2), 11.7% in the United Kingdom to 20.6% in the Netherlands, both in 2017 (3). The discrepancy between clinical guidelines and actual clinical practice was more apparent among low- and middle-income countries with an average of 3% uptake of the therapy (4).

The extent of success in its adoption were contributed by multiple factors. From the perspective of healthcare providers, lack of training and self-confidence to administer therapy, poor communication, limited resources and incentives were reported as key barriers (5, 6). Guideline awareness, work pride and motivation and regular feedback were identified to facilitate the implementation of stroke thrombolysis (6, 7). A majority of these existing studies however, were performed in high-income countries. Challenges in providing intravenous stroke thrombolysis in resource-poor countries can be significantly different and should be acknowledged, particularly when the burden of stroke is higher in these countries. In Ghana, distinctive factors from the high-income countries were found which included the role of sociocultural beliefs and the lack of coverage for acute care in their national health insurance (8). Furthermore, the importance of understanding barriers and facilitators in the implementation of intravenous stroke thrombolysis in a low- and middle-income country was highlighted in studies assessing the effectiveness of different interventions developed to improve the therapy. These interventions were found to produce similar effects, despite their targets on different aspects of stroke thrombolysis. Given the degree of variability between studies, it has been recommended for selection of intervention to address specific challenges in the given context until better evidence emerges (9).

Malaysia is one of the low- and middle-income countries where local regulatory authorities have approved the use of recombinant tissue plasminogen activator (r-TPA) for acute ischemic stroke (10). Nevertheless, the reported national uptake of intravenous stroke thrombolysis among public hospitals in the country has been poor at 1.6% in 2018 (unpublished data: Hiew FL. Stroke Thrombolysis Survey in Ministry of Health Malaysia. 2019). Intriguingly, one public hospital reported comparable rates of the therapy to high-income countries (11). This study therefore, was set to explore and provide an in-depth understanding of factors and explanations for the high rates of intravenous stroke thrombolysis in this hospital, which could explain its differences in comparison to other hospitals in similar socioeconomic settings.

Abbreviations: TICD, tailored implementation of chronic diseases; MA, medical assistant/assistant medical officer; r-TPA, recombinant tissue plasminogen activator; IDI, In-depth interview; FGD, focus group discussion; ED, emergency department; CT, computed tomography; MRI, magnetic resonance imaging; ESO, European stroke organization; VSM, value stream mapping; TIA, transient ischemic attack.

Methods

Study design

This study adopted a case study methodology. Qualitative case study allows an in-depth understanding and exploration of the phenomenon of interest within the real-world context (12). In this study, this refers to the exploration of reasons for the high rate of thrombolysis. This case study involved a Ministry

of Health hospital which is referred as "Hospital Z." It is a 1,057-bedded tertiary referral center. Neurology unit is placed under the Medical Department where out of 200 beds, an area of 6-beds was established as an acute stroke unit. A weighing bed is reserved for patients indicated for thrombolysis.

Research team

The research team comprised of 4 women and 2 men. SFT is a family medicine specialist with experience in qualitative research. WYH, SWN and NAR are trained in qualitative research, with medical and pharmacy backgrounds, and have been conducting clinically-related stroke research. WYH and NAR hold higher qualifications in epidemiology. SS is a public health specialist who heads health systems research. WCL is a neurologist with specific interest in stroke care.

Researchers have no prior relationships with the participants, except for WCL who has worked directly or indirectly with participants for patient management. WCL was not involved in data collection. His roles were to provide expert opinions to make sense of the data. It was made clear to the participants that the interviews were conducted to understand their experiences in implementing thrombolysis.

Tailored Implementation in Chronic Disease framework

The TICD is an implementation framework which guides understandings on the determinants of implementation change in clinical practice and of recent, in stroke care. There were 57 determinants of practice in seven domains which include factors related to individual health professionals, professional interactions, guidelines, incentives and resources, patients, capacity for organizational change, and social, political and legal (13). As this framework provides an overview of the common barriers and facilitators for programme implementation in clinical practice, it was used as a guide to develop interview guides for data collection. Instinctively, determinants from the framework were also applied when we conducted the initial line by line coding during data analysis.

Data collection

In-depth interviews and focus group discussions

Semi-structured interviews were conducted to provide data on participants' thoughts and work processes that lead to the decision for thrombolysis. Interview guides for each profession were developed based on literature (8, 13, 14), expert opinions, and guided by the TICD framework. The interview guides were pilot-tested among medical professionals outside our study sites and adapted following their feedback (Supplementary material 1).

TABLE 1 Distribution of participants by profession and types of interview conducted.

Participants	Number of participants	Types of interview
Neurologists	2	In-depth interview
ED physician and medical officer	2	In-depth interview
Radiologist	1	In-depth interview
Medical Department HOD and medical officers	3	In-depth interview
Hospital director	1	In-depth interview
Radiographers	4	Focus group discussion
ED nurses	4	Focus group discussion
Neurology unit nurses	6	Focus group discussion
ED medical assistants (MAs)	4	Focus group discussion
Pharmacists	2	Focus group discussion
Total	29	

ED, emergency department; HOD, Head of department.

A purposive sampling was conducted among healthcare providers who were directly involved in providing the therapy and senior administrators who were authorized to make decisions. We included healthcare providers with at least 6-months experience in the study site to augment the validity of their shared experience as a reflection of the actual situation. Healthcare providers were chosen from a variety of profession and therefore, with rather different but at times, overlapping roles in the provision of intravenous stroke thrombolysis. As sample size for qualitative research is dependent on the saturation of information necessary to answer the study objectives, we conducted at least one interview for each group of healthcare providers. A reported average number of interviews needed to reach saturation is between 9 and 17 (15).

To facilitate recruitment, phone calls were made to the Heads of Department of each specialty involved. Potential participants were recommended and engagements were made *via* text messages and telephone calls. Thirty-two participants were invited to participate and none declined. However, 3 participants could not attend the interview because of hospital admission ($n = 1$) and emergency calls ($n = 2$). Table 1 shows the distribution of participants, by their professions and the types of interview conducted.

Four researchers (WYH, SWN, SFT, NAR) took turns to conduct the interviews. There were nine IDIs and five FGDs. None of the interviews were repeated. The main language used was English except for the FGDs with the nurses, medical

assistants (MAs) and radiographers, which interviews were conducted in both English and Malay languages. In many healthcare systems, the roles of ground staff including nurses, MAs and radiographers are often considered less important in comparison to clinicians (16). Typically, this steep hierarchical gradient results in the fear to voice out their opinions especially on negatively-related issues. The conduct of FGDs is aimed to encourage staff participation and provision of feedback comfortably in the presence of their peers. Additionally in FGDs, the role of moderators would likely to be perceived as less domineering than interviewers in an IDI. Due to restrictions following COVID-19 pandemic, these interviews were conducted virtually using a video conferencing platform. Each interview lasted about 50 min. Interviews were recorded visually for the purpose of transcribing and to observe non-verbal cues. All records were subsequently transcribed with clear verbatim. Transcripts were not returned to participants but were rechecked randomly to ensure that the contents matched the audio recording.

Surveys and medical record reviews

Quantitative surveys and medical chart reviews were conducted to supplement findings from the qualitative data by evaluating available resources and quantifying reasons for not receiving thrombolysis. For surveys, information on hospital facilities, number of staff, rates of thrombolysis among ischemic stroke patients, and services available were collected in a predetermined data collection sheet. The review of medical records involved obtaining a list of ischemic stroke patients admitted between June and December 2019 from the hospital's stroke registry and having their medical records reviewed to investigate reasons for not receiving thrombolysis. A systematic sampling was conducted by including every 5th patient with a minimum of 15 patients every month. In total, 105 patient records were included.

Data analysis

Data from different sources were analyzed separately before being compiled for cross examination and triangulation.

First, the transcripts were de-identified and compiled using Nvivo 12 software for data management (17). Second, line-by-line coding was performed by WYH and SWN independently using TICD framework as an initial guide to provide a bearing on possible determinants to focus on. During the coding exercise, the codes were not restricted to the categories available within TICD. Instead, codes were also generated inductively based on understanding and in-depth analysis from the transcripts. To ensure congruence, the codes were subsequently compared and discrepancies were resolved in a discussion. Each code was also distinguished by the participants' profession to understand its context and to seek for patterns across the codes. The codes were then categorized into bigger constructs and sorted into domains.

The third step involved analysis of findings from the surveys and medical record reviews descriptively. Next, triangulation of data was performed. This entailed several discussions among the research team on presentation of the main findings based on coded data, transcripts and how the quantitative results supplemented those findings. During these discussions, we also discussed the choice of codes and its transcripts to be presented by looking through different transcripts to ensure that the message quoted is clear, direct and independent. Finally, feedback from content experts and peers who were not directly involved in the data analysis were obtained to aid making sense of the data.

Results

Stroke care services in Hospital Z

Management of stroke cases is handled by the stroke team led by two neurologists. This responsibility is shared across the Emergency, Radiology and Medical Departments. Intravenous stroke thrombolysis has been available since 2013 during office hours but from 2015, the therapy has been expanded to 24 h daily. The number of ischemic stroke admissions increased from 116 patients in 2013 to 610 in 2019. Likewise, the rate of intravenous thrombolysis was about 5% in 2013 and 2014 before it rose to a range between 11.1 and 20.8% in the later years (Table 2).

Admission of acute stroke patients goes through ED. Patients who present with acute neurological deficit during triage assessment would undergo a fast-tracked standardized workflow which includes ED medical officer assessment and a Computed tomography (CT) request before a stroke activation call is prompted. Computed tomography or CT angiography imaging facilities are not available in ED and patients are sent to the Radiology Department located in a different building. Computed tomography imaging facilities are available for 24 h. Although magnetic resonance imaging (MRI) or MR angiography are only available during office hours, its use for acute stroke cases can be requested as necessary.

A dedicated stroke team comprising a neurologist, a medical officer, and a nurse would attend to the patients during office hours. After office hours, the stroke nurse or a medical staff nurse is on standby while the neurologists are available for remote consultations. Once patients are identified to be eligible for thrombolysis, they will be consented and sent to the acute stroke unit. No allocated elevators are available for patient transport.

TABLE 2 Rate of intravenous stroke thrombolysis in Hospital Z from 2013 to 2019[a].

Year	Total admission for ischemic stroke patients	Number of stroke activation calls	Number of patients thrombolyzed	Rate of thrombolysis (%)	Rate of true positive activation calls[b] (%)
2013	116	na	6	5.2	na
2014	249	na	12	4.8	na
2015	368	59	41	11.1	69.5
2016	440	115	62	14.1	53.9
2017	553	124	87	15.7	70.2
2018	568	148	118	20.8	79.7
2019	610	na	92	15.1	na

[a]Sourced from data collection for stroke registry in Neurology Unit in Hospital Z; [b]true positive activation calls refer to stroke activation calls which ended up with thrombolysis being conducted; na: not available.

Factors influencing the uptake of intravenous stroke thrombolysis

The rates of thrombolysis in Hospital Z could be attributed and explained from four main factors discussed below (Figure 1; Supplementary material 2). Figure 2 shows the relationship of the contributing factors to the uptake of thrombolysis. Cohesiveness of team members and facilitative work process were found to ease the service provision. Patient factors and availability of resources impeded the uptake of this therapy although the latter was innovatively optimized.

Cohesiveness of team members

Positive interprofessional team dynamics

Effective engagement among team members

Having effective communication and willingness to engage with team members were key facilitators to achieve effective dynamics within an interdisciplinary team. The neurology team played a significant and engaging role in building rapport and initiating interdisciplinary meetings to facilitate better communication between departments. *"I spent a lot of time going down to the radiology department, talking to the radiologist and making myself known to them* (ID 07)." Similar reflections were provided by participants from other departments: *"She (neurologist) came to ED to discuss with our Head of Department regarding stroke protocol (ID 04)"* and *"Our hospital became more active (in the service provision) since Dr X came. He approached us when he wanted to do this (thrombolysis) and asked us to help facilitate (ID 11)".*

Besides, team members from different professions were interdependent and supportive of each other. One MA reflected (ID 06-01): *"Upon stroke activation, sometimes the stroke team or the ED houseman will push the patients for CT scan. They do not rely on MAs, nurses or porters."* Team members were also approachable. Said one doctor (ID 07): *"Generally, everyone has been somewhat approachable. I think that certainly help in getting and pulling everyone to work together as a team."*

Such culture has benefitted the sustenance of the therapy beyond Hospital Z's boundaries. For example, thrombolysis has been expanded to district hospitals without neurosurgeons in the state with commitments from the neurosurgical department in Hospital Z to back these hospitals up should complications occur.

Joint ownership of responsibility

The joint ownership was demonstrated through trust and confidence in sharing responsibilities. Neurologists trusted the clinical assessments of their medical officers in identifying eligible patients for thrombolysis. Likewise, there was mutual trust between the radiologists and neurologists because the ultimate responsibility to patient care was shared. The neurologists were willing to interpret CT images for stroke patients: *"We tell them (radiologists) that we (are) going to see the scan. They don't have to come and report* (ID 01)." Importantly, the radiologists were comfortable for the task to be handled by the neurologists: *"We are okay with them (neurologists) interpreting the scan. For them (the neurologists) (they need) to have immediate (report), because (they) need to act on the scan finding* (ID 11)."

Besides trust, a positive attitude toward joint sharing of workload from thrombolysis resonated among the participants. Neither did they feel that having thrombolysis has added to their workload nor did they require financial incentives. As noted by one radiographer (ID 08-04): *"I am not burdened because it is indeed our job*" and one nurse said (ID 02-02): *"We only claim off hours. We do not claim (money)."*

Initiatives to cope with constraints of human resources with the aim to improve the quality of stroke care were also seen as a form of joint ownership of responsibility. One doctor explained how they empowered and privileged medical physicians and medical officers to handle the therapy (ID

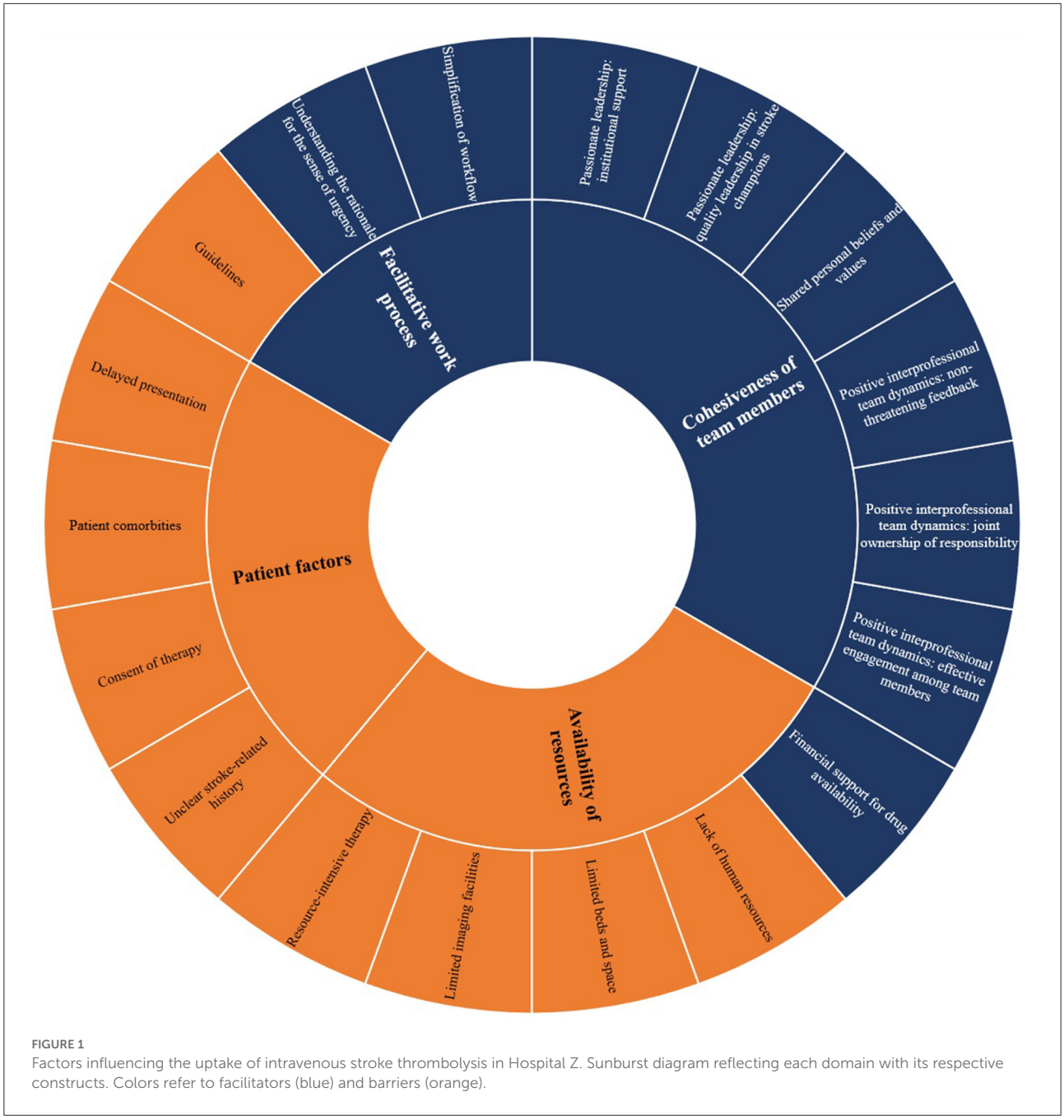


FIGURE 1
Factors influencing the uptake of intravenous stroke thrombolysis in Hospital Z. Sunburst diagram reflecting each domain with its respective constructs. Colors refer to facilitators (blue) and barriers (orange).

07): *"At the moment, we don't have trainees. So, a lot of our bouts (are) being covered by (medical) physicians (and) medical officers. When they receive stroke activations, they are the first to attend to patient and when we said "yes" for thrombolysis, they'll be the one(s) helping to push up patient to the ward, administering thrombolysis and monitoring."* The nurses also had a systematic rotation to support the stroke team: *"So far, there are seven of us. Every month, our nursing sister will arrange the schedule for two nurses (to be on call for stroke activation calls)* (ID 02-06)".

Nevertheless, presence of mixed opinions on sharing the responsibility to decide for thrombolysis could potentially threaten this dynamic. Emphasizing the hesitancy of the emergency physicians, one doctor (ID 04) said: *"Most of us are not there yet. To say that we would take over the decision to thrombolyze, not all of us are used to it."* Furthermore, increase in the number of medical subspecialties has led to issues of patient segregation: *"The moment they go into specialized area (to manage patients from) the general medicine side (would be) like: this is not mine. This is somebody else's* (ID 13)".

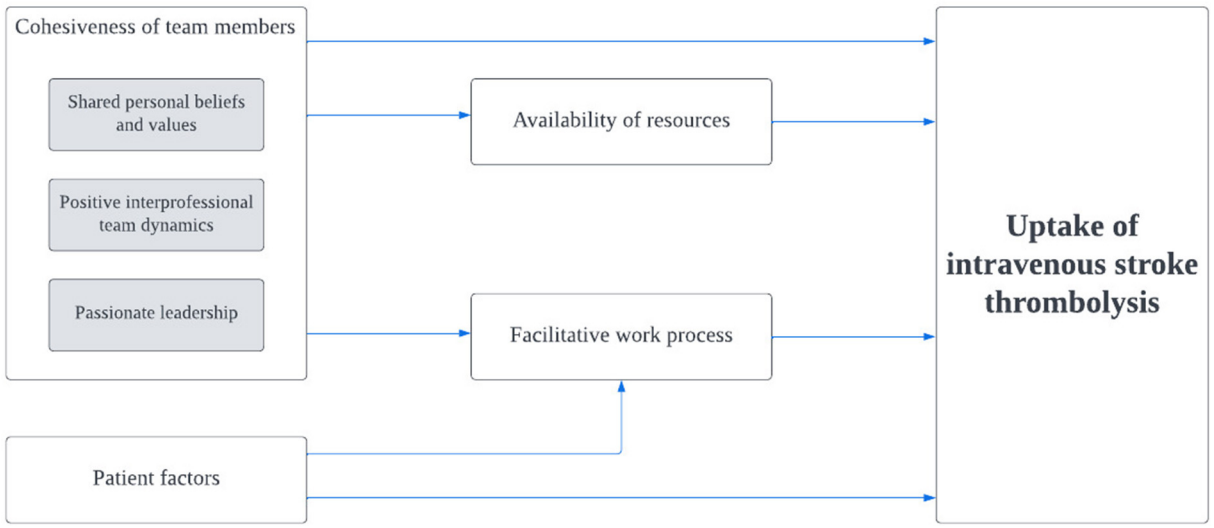


FIGURE 2
Relationship between contributing factors and the uptake of intravenous stroke thrombolysis. Gray boxes refer to constructs within the specified domain.

Non-threatening feedback

A majority of the participants agreed on the importance of having an avenue to provide feedback within and across departments: *"Normally if there is feedback, we will share it in our WhatsApp group. But if there is something confidential that requires face-to-face discussion, we will talk to the staff involved* (ID 06-03)".

Furthermore, feedback was transferred to ground staff although the initial communications only involved higher authorities. Interestingly, having received negative feedback was accepted as a measure of encouragement: *"They (the neurologists) get upset when it's (stroke is) missed sometimes but not overly upset. Appropriately upset. So, we try not to miss. So, the culture is such that we want to do it well* (ID 09)." More importantly, the participants confided on how their team members were often non-judgemental in handling mistakes occurring at work. Said one MA (ID 06-04): *"If he or she (other MA) happens to make a mistake, we will try to resolve it together."* One doctor also recalled (ID 09): *"When we call them (the neurologists), they will come and assess. So, it gives us confidence that we wouldn't be blamed".*

Shared personal beliefs and values

Having the intentions and motivations to optimize the therapy were key values portrayed. One doctor shared (ID 01): *"We can achieve what I believe as universal access of acute thrombolysis across the country. I always believe I wanted to do for others what I want them to do for me. Thus, I will try my level best to treat them. I think that's the main drive."* Echoed by another (ID 07): *"With the introduction of treatments, you can actually help patient(s) to live independent life. That's actually a good motivation for me personally, because you know that your work makes a difference".*

One nurse reflected how her experiences in the use of thrombolysis influenced her beliefs on the treatment outcomes (ID 02-03): *"There are some patients with power 0 who can (improve) to 3. That makes us satisfied. The thrombolysis seems successful."* A doctor also shared his confidence on the low bleeding risk from thrombolysis (ID 01): *"From my own experience, hemorrhagic transformation (that) requires neurosurgical intervention (is) not very common. We (are) talking about <3%. The benefit outweighs the risk. We're talking about 30% of our stroke patients can become normal or near-normal again. That's the minimum".*

Passionate leadership

Quality leadership in stroke champions

The importance of having passionate stroke champions to drive the therapy was reiterated. One doctor said (ID 11): *"I think the person doing it is very important, like—Dr X. I can see his dedication. I think we can all share the enthusiasm."* Ground staff of Hospital Z also shared their views where they appreciated the working personality of the stroke champions: *"Our bosses are quite hands-on. They don't just give order; they will attend even though they are consultants. That gives us confidence* (ID 09)." Besides that, the nature of them sharing the achievements earned from thrombolysis have provided motivations to the staff: *"Dr X does share with us some awards that they achieved. (This brings) some positive reinforcements for the radiographers. They are the ones who do 24 h shift to scan the patients* (ID 11)".

Institutional support

One doctor reflected on the attitude of the higher authorities and other departments in the hospital toward thrombolysis (ID 01): *"Our radiologists, our hospital director and our head (of) department are very supportive".*

Facilitative work process

Simplification of workflow

Difficulties in identifying stroke cases during triaging were attributed to patients with atypical symptoms. *"Patients present with very vague symptoms. The worst would be if the patient keeps on having dizziness but you cannot pinpoint whether there is any obvious neurology deficit or not* (ID 10)".

To address this, a simplified criteria to assess thrombolysis eligibility was established. As explained by one doctor (ID 01): *"We change the (triaging) protocol to acute neurology deficit. We're very lenient for them to activate and call us."* Table 2 showed an initial dip in the percentage of patients who received thrombolysis after a stroke activation call between 2015 and 2016 but subsequently, a sharp increase from 53.9% in 2016 to 79.7% in 2018.

Besides, patients with acute neurology deficits would be fast tracked for stroke activation and CT imaging. Said one doctor (ID 01): *"We default registration for admission, we'll get consent on the way to CT."* Workflow for referrals from district hospitals was also simplified where ambulances from district hospitals without CT imaging were encouraged to bypass their own hospital and send suspected stroke patients to Hospital Z directly. As a result of this streamlining process, healthcare providers found it easy to be familiar with their roles. As explained by one doctor (ID 04): *"Overtime, we get comfortable with it that it becomes a reflex. You say that this is stroke, people would know what to do".*

Parallelly from the medical records review, potential in-hospital delays related to workflows accounted only for 3.8% of patients who missed the opportunity to receive thrombolysis due to a delay in referral for CT imaging ($n = 2$) and a delay in assessment by stroke team ($n = 2$), one of which suffered stroke whilst being an inpatient (Figure 3).

Understanding the rationale for the sense of urgency

It was coherently agreed that stroke cases should be given a priority. One doctor explained (ID 04): *"Once we suspect that it is stroke, we quickly determine that it is acute and within time. We will quickly activate the stroke thrombolysis."* The same sense of urgency for stroke patients was shared in radiology department: *"Whenever you say thrombolysis, the radiographers know that we have to stop our elective case(s) and scan the case first* (ID 11)".

This sense of urgency has been instilled with informal training in the form of briefings, orientations and tagging to senior staff. One doctor highlighted the importance of educating the staff on why stroke cases should be made a priority (ID 11): *"They have to understand why their workflow must be disrupted. I think the point is to make them understand the time constraint. Once they understand that, I think they are more acceptable. Rather than you say, "Thrombolysis, you must scan now." They don't know why".*

Patient factors

Delayed presentation

One suggested reason for delayed presentation was the low public awareness on stroke symptom recognition. One doctor noted (ID 12): *"Once they (patients) have weakness on one side of the body, they will go for massage. When they come, it's already 2 or 3 days (after)."* The public were also unaware of the availability of a time-dependent therapy for stroke: *"(People are) not exposed (to it). Only if they go to the hospital, then would they know about this service* (ID 02-01)." Furthermore, logistic issues, in particular among patients who required hospital transfers due to the lack of CT machines in district hospitals were brought up. Findings from the medical records review supported the importance of this barrier. A total of 67.6% of ischemic stroke patients arrived at the hospital outside the therapeutic window time (Figure 3).

Patient comorbidities

Having comorbidities or a severe stroke may contraindicate patients from the therapy. Figure 3 showed that uncontrolled blood pressure levels and seizure upon onset of stroke constituted 2.9% of the reasons for non- thrombolysis whereas 4.8% had either established infarcts or NIHSS score which was $\geq$25. Patients with poor condition upon arrival could also have their CT imaging delayed, potentially excluding them from the opportunity to be thrombolyzed.

Consent of therapy

The issue of consent largely existed due to influence from family members. One doctor argued that it depended on how the risk benefit explanation was provided (ID 14): *"I have seen thrombolysis refusals, maybe one in fifty? Not very common. Because it depends on how you explain to them. If you tell the family member, we give that (thrombolysis) there's a chance you will improve and if we don't, most likely you'll remain like this. Most of the time, they are quite receptive even though you tell them there is a risk of bleeding".*

Unclear stroke-related history

Unclear patient history and language barrier complicated the triaging assessment and subsequently delayed referrals. Explained by a doctor (ID 07): *"Sometimes the problem (is that) patients and family themselves are not forthcoming with regards to their time of onset of stroke. So, we can't really decide on exactly when was (the actual) onset because the history was so unreliable."* Likewise, this was evident from Figure 3 where

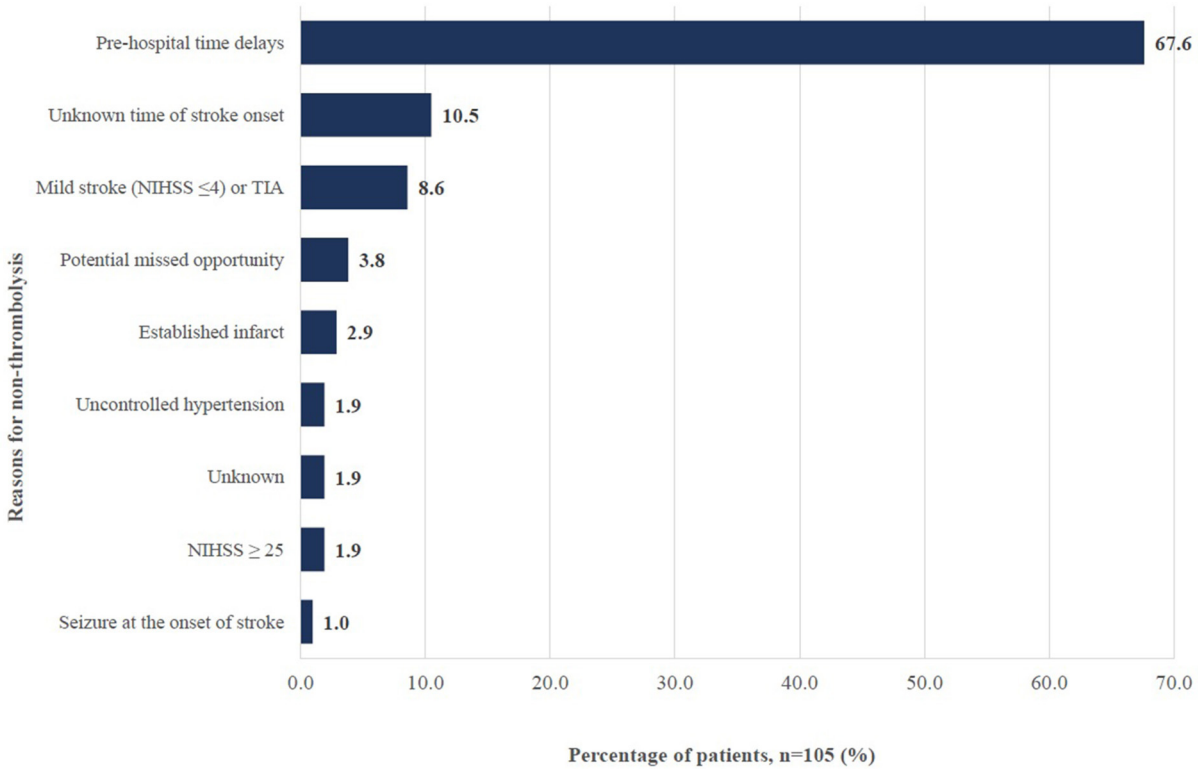


FIGURE 3
Reasons for non-thrombolysis among ischemic stroke patients in Hospital Z between June to December 2019. TIA: Transient ischemic attack; NIHSS: National Institutes of Health Stroke Scale; potential missed opportunity includes those with delayed referral to CT imaging and delayed assessment by stroke team.

10.5% of ischemic stroke patients did not receive thrombolysis because the onset of their stroke was unknown.

Availability of resources

Intravenous stroke thrombolysis is known to be a resource-intensive therapy (ID 01): *"Thrombolysis is labor intensive and we have to respond very quickly. It's every 15 min monitoring. It's costly. We need CT scan. We used to have to call radiologist(s) to get the permission, then we get patient consent for CT and then push their way to CT scan room which is always not next to ED. And then have to interpret CT. There's always a reservation among neurologists in Malaysia because it is labor intensive."* Working around challenges related to resources thus, had not been easy.

Limited imaging facilities

Due to the lack of a CT machine in ED, more time were required to transfer patients to undergo CT imaging. Nevertheless, with the availability of two CT machines since year 2020, many agreed that the process of getting a CT imaging has been sped up. The limited availability of MRI slots however, has made it difficult to extend the window therapy for thrombolysis. As described by one doctor (ID 01): *"we only thrombolyze those with(in) four and half hours. The guidelines now allow thrombolysis up to 9 h and if those patients with wake-up stroke, even up to 12 h which we do not have access to because that requires advanced imaging."* Another doctor explained (ID 07): *"there is only one MRI machine and the queue is extremely long for MRI (even) for normal standard appointments".*

Limited beds and space

The lack of beds and space has made it difficult to conduct thrombolysis and to accommodate another imaging machine in ED. As mentioned by one doctor (ID 11): *"Our emergency department layout and the space are very limited. There's no more space to expand".*

Lack of human resources

There was a unanimous agreement that lack of manpower remained as an existing issue. One doctor said (ID 09): *"Not enough manpower, very busy. You need to run a ward, you need to do rounds, you need to do discharges, you need to attend clinics and then suddenly (when) thrombolysis calls, you have to go and attend."* Echoed by another who shared how remote consultations due to shortage of neurologists occasionally led to

delays (ID 07): *"When you were given images through WhatsApp, depending on your line, the quality of the video that is being sent, sometimes we do miss things. Sometimes it's very difficult to make the judgement call".*

Heavy workload has prevented the conduct of thrombolysis in ED: *"We cannot spend the time to help you to monitor the patient. You can have either three CPR patient coming in 5 min apart or you can have polytrauma coming in* (ID 10)." Similarly, thrombolysis could not be initiated in CT suite for the same reason: *"our CT (functions) 24/7, so they (radiographers) cannot afford to let us dilute the medicine and jab there (CT suite)* (ID 01)".

Furthermore, high turnover among nurses and medical officers was another issue brought up by one doctor (ID 12): *"The problem is training our nurses. Nurses that are specific for acute stroke care. Those are kind of hard to develop (but) once they are promoted, they might be transferred to another place. And then we have to train new nurses again".*

Financial support for drug availability

Despite limited budget allocation, support from the higher authorities and other departments have been crucial in maintaining the availability of r-TPA. Said one doctor (ID 01): *"every time we said we needed it, they've (higher authorities) never said "No." Our usage exceeded many times off budget."* Proper budget planning has also been quoted as one substantial factor to receive enough funding to maintain the therapy: *"our pharmacist is doing a very good job in estimating all these (budget for r-TPA)* (ID 12)".

Discussion

The European Stroke Organization (ESO) aims to have at least 20% of all ischemic stroke patients being treated with thrombolysis by 2020 (18). Malaysia fared worse at nationwide than many other countries, at 1.6% among the public hospitals providing the therapy in 2018 (unpublished data: Hiew FL. Stroke Thrombolysis Survey in Ministry of Health Malaysia. 2019) although the rate in Hospital Z was higher at 20.8% in the same year, achieving the benchmarking rate set by ESO. A survey across 44 European countries reported an average of 7.3% of thrombolysis between 2016 and 2017 whereas country-specific rates in Europe were higher in Czech Republic (23.5% in 2018) and the Netherlands (21.7% in 2016) (Table 3) (3). The reported rates however, were noticeably lower in low and middle-income countries such as Thailand (7.8% in 2019) (19), Vietnam (5.6–8.5% in 2020) (20) and China (5.6% between 2019 and 2020) (21). Direct country comparison of the rates however, was not feasible owing to differences in study methods and reporting years.

In year 2019, Hospital Z has the highest uptake of intravenous stroke thrombolysis amongst other Ministry of Health hospitals in Malaysia. This is intriguing, considering that allocation of resources and hospital policies should be similar across all Ministry of Health hospitals. Geographically, the setting where this hospital is located remains mainly rural with poor access to healthcare services due to logistic difficulties (11). Findings from our case study has clearly observed two main factors facilitating the uptake in this therapy: (1) cohesiveness of team members, especially having positive interprofessional team dynamics and (2) facilitative work process. Patient factors were found to impede the uptake of thrombolysis, where almost two third of ischemic stroke patients arrived at the hospital outside the therapeutic window time, attributing patients' delayed presentation as a main barrier to the uptake of thrombolysis. Similarly, availability of resources was a barrier, although this was innovatively optimized to minimize its impact on the rate of the therapy. Only 3.8% of patients missed the opportunity to receive thrombolysis due to potential in-hospital delays.

One major contributing aspect to cohesiveness among team members was having positive interprofessional team dynamics. The concept of effective communication and understanding of one's role towards teamwork are crucial components to establish an engaging interprofessional team (22). Physician-driven stroke care without adequate involvement of other ground staff has been reported to lead to concerns of marginalization and disconnectedness (8). Having joint ownership of responsibility was another key facilitator. There have been global discussions surrounding the role of other doctors to provide thrombolysis, in particular the emergency and internal medicine physicians. Studies comparing neurologists and non-neurologist doctors on patients' functional outcomes and safety following the provision of intravenous stroke thrombolysis reported no differences between the groups (23, 24). In response to that, institutions in many different countries are adopting this approach to cope with shortages of neurologists; Hospital Z being one of the few in Malaysia.

TABLE 3 Comparison for rate of intravenous stroke thrombolysis by countries[a].

Country	Year	Rate of intravenous stroke thrombolysis (%)
Malaysia	2013	5.2
	2019	15.1
Europe (3)	2016–2017	7.3
United States (2)	2018	13.7
Thailand (19)	2019	7.8
Vietnam (20)	2020	5.6–8.5
China (21)	2019–2020	5.6

[a] Country-specific rates except for Malaysia (rates retrieved from a single hospital Z) and Europe (average estimate among 44 European countries).

Besides healthcare providers' belief and values attributing positively toward the therapy, leadership from the aspect of having quality stroke champions and support from higher authorities has also enabled optimization of available manpower and resources. These facilitators were consistent with findings from other studies; thus, exerting their importance in the uptake of thrombolysis (7, 25).

We also found that facilitative work processes have positively influenced the uptake of thrombolysis. Wang et al. reported how streamlining of workflow reduced in-hospital time delays for endovascular mechanical thrombectomy (26). A simplified pathway to increase the access to CT imaging for acute stroke interventions was also highlighted in the United Kingdom (27). Workflow simplification was quoted to bring about familiarity with one's roles. Understanding respective roles in the work process and that of other team members subsequently would give rise to a routine and coordinated stroke management (25). Furthermore, although the sense of urgency for rapid triage and assessment has often been associated with regular use of a written protocol for thrombolysis (8, 25), this factor was attributed to repetitive hands-on exposures to handle patients for the therapy in Hospital Z. Stecksen et al. echoed this, where lack of knowledge and experience was cited as a barrier to the implementation of stroke thrombolysis guidelines (7).

Consistently, patients' delayed presentation was a main barrier to hyperacute stroke care in Ghana (8). Likewise, 60.5% of Thai patients with ischemic stroke arrived late in the hospital (28) whereas in Lebanon, at 55.2% (29). This delay has been attributed to multiple reasons including but not limited to poor recognition of stroke symptoms, lack of awareness of the availability of a time-dependent therapy as well as poor accessibility (30).

Resource constraint is an issue of priority because a limited budget is almost always present. Results from studies conducted in high-income countries were parallel to our findings where restriction of resources could range from access to imaging facilities, beds, and space for an acute stroke unit, staff capacity, and finances (5, 7). The only difference could be the weightage that these factors carry to influence the uptake of thrombolysis. In a low- and middle-income country like ours, limited imaging facilities and staff especially neurologists are major impediments (8). Adding this limitation with heavy workload and high staff turnover, driving thrombolysis forward is often a major task.

Strengths and weaknesses

The strength of our study lies in the efforts of applying the TICD framework at the initial stage to understand the components for implementation change in clinical practice but subsequently conducting an inductive analysis to derive explanations for the success of the therapy in Hospital Z and how the factors relate to each other, as shown in Figure 2. Furthermore, having quantitative data to triangulate with the qualitative findings not only adds depth to our current analysis but also functions as a strategy to strengthen the validity by connecting information from multiple data sources (31). Independent and cross coding theme derivation and quality checks were also conducted to minimize interpretation bias among researchers. This study described data from a single center. Comparable factors to that in the literature suggests potential generalizability of these findings. We acknowledge the possibility of selection bias as a result of the recruitment strategy but given that the interviews did not result in entirely positive points about the hospital, this bias should be minimal. Hierarchically, recruitment could not have been done without the permission from the Heads of Department.

Implications on research and clinical practice

While acknowledging the ongoing constraints of resources as well as a lack of patients' awareness, what stood out as a lesson learnt was that the success in the uptake of thrombolysis in this hospital was attributed to cohesiveness of team members and having a facilitative work process. Understanding these facilitators which are modifiable within the service provision carry important implications for recommendations of targeted interventions to improve the uptake of the therapy in institutions of similar settings.

First, the theory of opportunistic dialogue where dialogues between team members are problem oriented, largely unplanned and facilitated by co-locations of team members and their commitment to work together can be applied to achieve a cohesive interprofessional team engagement (32). Moving away from the traditional multidisciplinary approach to adopt the concept of interdisciplinary team is pivotal to cultivate ownerships for responsibilities. Multidisciplinary refers to having knowledge from multiple disciplines brought together but each discipline acts from their own perspective within the boundaries of respective discipline. Interdisciplinary on the other hand, is defined as linking and integrating knowledge from different disciplines into one, using a coherent and coordinated approach. In other words, responsibilities are divided between disciplines in a multidisciplinary team. Contrastingly, responsibilities are shared among the different disciplines with interdisciplinary approaches, which provide an excellent learning and working environment where providers from other disciplines are able to learn and conduct tasks that are traditionally the roles of certain disciplines (33). In essence, interdependence is well-understood and

acknowledged among team members in order to improve patient care. Interventions related to behavioral change have been advocated to promote such changes in team dynamics. These interventions were reported to have an increase of two times the odds of thrombolysis rate as compared to usual practice (9).

Second, lean techniques are increasingly used to streamline healthcare work processes. Value Stream Mapping (VSM) for example, has been applied to identify inefficiencies and to create a streamlined workflow to expedite time-dependent stroke care (34). Third, innovative education such as simulation workshops or mock stroke codes to provide hands-on experiences and opportunities to practice are foreseen to enhance familiarity of roles and instill the sense of urgency among healthcare providers. These strategies have been observed to improve the rate of thrombolysis (35, 36).

Fourth, research is an integral part of these recommendations. In the plans to implement any targeted interventions, it is vital to concurrently plan for an evaluation study to look at effectiveness and feasibility and importantly, the sustainability of such interventions. Several trials have been conducted for this purpose, with differing results (35–38).

Conclusions

In conclusion, factors influencing the uptake of intravenous stroke thrombolysis have been identified from multiple aspects. Insight onto these factors is crucial to allow the development of targeted interventions to improve the provision of the therapy in countries of similar settings.

Data availability statement

The datasets presented in this article are not readily available because of ethical and legal restrictions but is available from the corresponding author on reasonable request. Requests to access the datasets should be directed to WYH amyhwong@crc.gov.my.

Ethics statement

The studies involving human participants were reviewed and approved by Medical Research and Ethics Committee, Ministry of Health Malaysia (NMRR ID: 19-3145-51552). The participants provided both their written and verbal informed consent to be interviewed in this study.

Author contributions

WYH: conceptualization, methodology, investigation, formal analysis, and writing-original draft. SWN: investigation, formal analysis, and writing-original draft. SFT: methodology, investigation, formal analysis, and writing-review and editing. NAR: methodology, investigation, and writing-review and editing. WCL: data acquisition, formal analysis, and writing-review and editing. ZK, SKW, and SDP: data acquisition and writing-review and editing. SS: methodology and writing-review and editing. All authors contributed to the article and approved the submitted version.

Funding

This study is funded by the Ministry of Health Malaysia research grant under the project Access to Hyperacute Stroke Care in Malaysia (NMRR 19-3145-51552). Ministry of Health Malaysia had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Acknowledgments

The authors would like to thank the Director General of Health Malaysia for his permission to publish this article.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2022.1048807/full#supplementary-material

References

1. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American heart association/American stroke association. *Stroke.* (2019) 50:e344–418. doi: 10.1161/STR.0000000000000211

2. Asaithambi G, Tong X, Lakshminarayan K, Coleman King SM, George MG. Current trends in the acute treatment of ischemic stroke: analysis from the paul coverdell national acute stroke program. *J Neurointerv Surg.* (2020) 12:574–8. doi: 10.1136/neurintsurg-2019-015133

3. Aguiar de. Sousa D, von Martial R, Abilleira S. Access to and delivery of acute ischaemic stroke treatments: a survey of national scientific societies and stroke experts in 44 European countries. *Eur Stroke J.* (2019) 4:13–28. doi: 10.1177/2396987318786023

4. Khatib R, Arevalo YA, Berendsen MA, Prabhakaran S, Huffman MD. Presentation, evaluation, management, and outcomes of acute stroke in low- and middle-income countries: a systematic review and meta-analysis. *Neuroepidemiology.* (2018) 51:104–12. doi: 10.1159/000491442

5. Baatiema L, Otim ME, Mnatzaganian G. de-Graft Aikins A, Coombes J, Somerset S. Health professionals' views on the barriers and enablers to evidence-based practice for acute stroke care: a systematic review. *Implement Sci.* (2017) 12:74. doi: 10.1186/s13012-017-0599-3

6. Craig LE, McInnes E, Taylor N, Grimley R, Cadilhac DA, Considine J, et al. Identifying the barriers and enablers for a triage, treatment, and transfer clinical intervention to manage acute stroke patients in the emergency department: a systematic review using the theoretical domains framework (TDF). *Implement Sci.* (2016) 11:157. doi: 10.1186/s13012-016-0524-1

7. Stecksén A, Lundman B, Eriksson M, Glader EL, Asplund K. Implementing thrombolytic guidelines in stroke care: perceived facilitators and barriers. *Qual Health Res.* (2014) 24:412–9. doi: 10.1177/1049732313514137

8. Baatiema L. de-Graft Aikins A, Sav A, Mnatzaganian G, Chan CKY, Somerset S. Barriers to evidence-based acute stroke care in Ghana: a qualitative study on the perspectives of stroke care professionals. *BMJ Open.* (2017) 7:e015385. doi: 10.1136/bmjopen-2016-015385

9. Hasnain MG, Attia JR, Akter S, Rahman T, Hall A, Hubbard IJ, et al. Effectiveness of interventions to improve rates of intravenous thrombolysis using behaviour change wheel functions: a systematic review and meta-analysis. *Implement Sci.* (2020) 15:98. doi: 10.1186/s13012-020-01054-3

10. de Souza AC, Sebastian IA, Zaidi WAW, Nasreldein A. Regional and national differences in stroke thrombolysis use and disparities in pricing, treatment availability, and coverage. *Int J Stroke.* (2022) 2022:17474930221082446. doi: 10.1177/17474930221082446

11. King TL, Tiong LL, Kaman Z, Zaw WM, Abdul Aziz Z, Chung LW, et al. hospital-based study on ischaemic stroke characteristics, management, and outcomes in Sarawak: where do we stand? *J Stroke Cerebrovasc Dis.* (2020) 29:105012. doi: 10.1016/j.jstrokecerebrovasdis.2020.105012

12. Yin RK. *Case Study Research: Design and Methods, 5th edn.* Los Angeles, CA: SAGE (2014).

13. Skolarus LE, Sales AE, Zimmerman MA, Corches CL, Landis-Lewis Z, Robles MC, et al. Stroke ready: a multi-level program that combines implementation science and community-based participatory research approaches to increase acute stroke treatment: protocol for a stepped wedge trial. *Implement Sci.* (2019) 14:24. doi: 10.1186/s13012-019-0869-3

14. Sales AE, Ersek M, Intrator OK, Levy C, Carpenter JG, Hogikyan R, et al. Implementing goals of care conversations with veterans in VA long-term care setting: a mixed methods protocol. *Implement Sci.* (2016) 11:132. doi: 10.1186/s13012-016-0497-0

15. Hennink M, Kaiser BN. Sample sizes for saturation in qualitative research: a systematic review of empirical tests. *Soc Sci Med.* (2022) 292:114523. doi: 10.1016/j.socscimed.2021.114523

16. Green B, Oeppen RS, Smith DW, Brennan PA. Challenging hierarchy in healthcare teams - ways to flatten gradients to improve teamwork and patient care. *Br J Oral Maxillofac Surg.* (2017) 55:449–53. doi: 10.1016/j.bjoms.2017.02.010

17. QSR International Pty Ltd. *NVivo (released in March 2020).* (2020). Available online at: https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home

18. European Stroke Organization: Res-Q registry. *Campaign Stroke 2020.* Available online at: https://qualityregistry.eu/cs/members-cs/34-stroke-2020 (accessed May 30, 2022).

19. Tiamkao S, Ienghong K, Cheung LE, Celebi I, Suzuki T, Apiratwarakul K. Stroke incidence, rate of thrombolytic therapy, mortality in Thailand from 2009 to 2021. *Open Access Maced J Med Sci.* (2022) 9:110–5. doi: 10.3889/oamjms.2022.8051

20. Duy Ton Mai X, Luong NK, Nguyen TK, Nguyen HT, Thanh N. Nguyen current state of stroke care in vietnam stroke. *Vasc Interv Neurol.* (2022) 2:e000331. doi: 10.1161/SVIN.121.000331

21. Ye Q, Zhai F, Chao B, Cao L, Xu Y, Zhang P, et al. Rates of intravenous thrombolysis and endovascular therapy for acute ischaemic stroke in China between 2019 and 2020. *Lancet Reg Health West Pac.* (2022) 21:100406. doi: 10.1016/j.lanwpc.2022.100406

22. Cramm JM, Nieboer AP. Professionals' views on interprofessional stroke team functioning. *Int J Integr Care.* (2011) 11:e081. doi: 10.5334/ijic.657

23. Akins PT, Delemos C, Wentworth D, Byer J, Schorer SJ, Atkinson RP. Can emergency department physicians safely and effectively initiate thrombolysis for acute ischemic stroke? *Neurology.* (2000) 55:1801–5. doi: 10.1212/WNL.55.12.1801

24. Chew SH, Looi I, Neoh KK, Ooi J, Cheah WK, Zariah AA. Clinical outcomes of acute stroke thrombolysis in neurologist and non-neurologist centres - a comparative study in Malaysia. *Med J Malaysia.* (2021) 76:12–6.

25. Olson DM, Constable M, Britz GW, Lin CB, Zimmer LO, Schwamm LH, et al. A qualitative assessment of practices associated with shorter door-to-needle time for thrombolytic therapy in acute ischemic stroke. *J Neurosci Nurs.* (2011) 43:329–36. doi: 10.1097/JNN.0b013e318234e7fb

26. Wang H, Thevathasan A, Dowling R, Bush S, Mitchell P, Yan B. Streamlining workflow for endovascular mechanical thrombectomy: lessons learned from a comprehensive stroke center. *J Stroke Cerebrovasc Dis.* (2017) 26:1655–62. doi: 10.1016/j.jstrokecerebrovasdis.2017.04.021

27. Sentinel Stroke National Audit Programme (SSNAP). *Rising to the Challenge. The Fourth SSNAP Annual Report.* London: Royal College of Physicians. 2016 - 2017. p. 13–5.

28. Rakchue P, Poonphol S. Factor influencing pre-hospital delay among acute ischemic stroke patients in rajavithi hospital. *J Thai Stroke Soc.* (2019) 18.

29. El Sayed MJ, El Zahran T. Acute stroke care and thrombolytic therapy use in a tertiary care center in Lebanon. *Emerg Med Int.* (2014) 2014:438737. doi: 10.1155/2014/438737

30. Al Khathaami AM, Mohammad YO, Alibrahim FS, Jradi HA. Factors associated with late arrival of acute stroke patients to emergency department in Saudi Arabia. *SAGE Open Med.* (2018) 6:2050312118776719. doi: 10.1177/2050312118776719

31. Carter N, Bryant-Lukosius D, DiCenso A, Blythe J, Neville AJ. The use of triangulation in qualitative research. *Oncol Nurs Forum.* (2014) 41:545–7. doi: 10.1188/14.ONF.545-547

32. Clarke DJ. Achieving teamwork in stroke units: the contribution of opportunistic dialogue. *J Interprof Care.* (2010) 24:285–97. doi: 10.3109/13561820903163645

33. Jessup RL. Interdisciplinary versus multidisciplinary care teams: do we understand the difference? *Aust Health Rev.* (2007) 31:330–1. doi: 10.1071/AH070330

34. Ford AL, Williams JA, Spencer M, McCammon C, Khoury N, Sampson TR, et al. Reducing door-to-needle times using Toyota's lean manufacturing principles and value stream analysis. *Stroke.* (2012) 43:3395–8. doi: 10.1161/STROKEAHA.112.670687

35. Haesebaert J, Nighoghossian N, Mercier C, Termoz A, Porthault S, Derex L, et al. Improving access to thrombolysis and inhospital management times in ischemic stroke: a stepped-wedge randomized trial. *Stroke.* (2018) 49:405–11. doi: 10.1161/STROKEAHA.117.018335

36. Scott PA, Meurer WJ, Frederiksen SM, Kalbfleisch JD, Xu Z, Haan MN, et al. A multilevel intervention to increase community hospital use of alteplase for acute stroke (INSTINCT): a cluster-randomised controlled trial. *Lancet Neurol.* (2013) 12:139–48. doi: 10.1016/S1474-4422(12)70311-3

37. Dirks M, Niessen LW, Huijsman R, van Wijngaarden J, Minkman MM, Franke CL, et al. Promoting acute thrombolysis for ischaemic stroke (PRACTISE). *Int J Stroke.* (2007) 2:151–9. doi: 10.1111/j.1747-4949.2007.00119.x

38. Levi CR, Attia JA, D'Este C, Ryan AE, Henskens F, Kerr E, et al. Cluster-randomized trial of thrombolysis implementation support in metropolitan and regional australian stroke centers: lessons for individual and systems behavior change. *J Am Heart Assoc.* (2020) 9:e012732. doi: 10.1161/JAHA.119.012732

frontiers | Frontiers in Neurology

TYPE Brief Research Report
PUBLISHED 09 January 2023
DOI 10.3389/fneur.2022.1110067

OPEN ACCESS

EDITED BY
Aleksandras Vilionskis,
Vilnius University, Lithuania

REVIEWED BY
Saulius Taroza,
Saulius Taroza, Lithuania
Hrvoje Budincevic,
University Hospital Sveti Duh, Croatia

*CORRESPONDENCE
Qing-Ping Huang
✉ hqphuli@sina.com

†These authors have contributed equally to this work and share first authorship

SPECIALTY SECTION
This article was submitted to Stroke, a section of the journal Frontiers in Neurology

RECEIVED 28 November 2022
ACCEPTED 16 December 2022
PUBLISHED 09 January 2023

CITATION
Zhang J-R, Wu Y-E, Huang Y-F, Zhang S-Q, Pan W-L, Huang J-X and Huang Q-P (2023) Effectiveness of smart health-based rehabilitation on patients with poststroke dysphagia: A brief research report.
Front. Neurol. 13:1110067.
doi: 10.3389/fneur.2022.1110067

Effectiveness of smart health-based rehabilitation on patients with poststroke dysphagia: A brief research report

Jian-Rong Zhang†, Yu-E Wu†, Yan-Fang Huang, Shu-Qing Zhang, Wen-Li Pan, Jin-Xia Huang and Qing-Ping Huang*

Department of Nursing, Dongguan Houjie Hospital Affiliated to Guangdong Medical University, Dongguan, Guangdong, China

Objective: This study aimed to evaluate the effectiveness of smart health-based rehabilitation on patients with poststroke dysphagia (PSD).

Methods: We recruited 60 PSD patients and randomly allocated them to the intervention ($n = 30$) and control ($n = 30$) groups. The former received the smart health-based rehabilitation for 12 weeks, whereas the latter received routine rehabilitation. Water swallow test (WST), standardized swallowing assessment (SSA), swallow quality-of-life questionnaire (SWAL-QOL), stroke self-efficacy questionnaire (SSEQ), perceived social support scale (PSSS) and nutritional measurements including body weight, triceps skinfold thickness (TSF), total protein (TP), serum albumin (ALB) and serum prealbumin (PA) in both groups were measured.

Results: When the baseline WST, SSA, SWAL-QOL, SSEQ, PSSS and nutritional measurements were examined, there was no significant difference between the intervention group and the control group ($P > 0.05$). After rehabilitation interventions, the WST and SSA scores in the intervention group were significantly lower than those in the control group ($P < 0.01$). The SWAL-QOL, SSEQ and PSSS scores in the intervention group were significantly higher than in the control group ($P < 0.01$). Compared with the control group, the intervention group showed an increase in the serum levels of PA ($P < 0.01$). However, no statistically significant difference existed between the intervention group and the control group in terms of body weight, TSF, TP or ALB ($P > 0.05$).

Conclusions: Overall, our data revealed that smart health-based rehabilitation is significantly beneficial to the swallowing function, quality of life, self-efficacy, and social support for PSD patients when compared with routine rehabilitation. However, nutritional measurements were not significantly improved in such patients under the smart health-based rehabilitation when compared the routine rehabilitation. In the future, it is necessary to extend the intervention

time to further evaluate the long-term efficacy of smart health-based rehabilitation on nutritional measurements of PSD patients.

KEYWORDS

poststroke dysphagia, smart health, rehabilitation, nursing, rehabilitation nurse

1. Introduction

Poststroke dysphagia (PSD), or post stroke swallowing difficulty, is one of the most common complications of ischemic stroke patients (1). Impairment in the central nervous system, cortical, or subcortical parts of the brain after stroke can impair swallowing physiology and further leads to true bulbar paralysis (2). According to epidemiological statistics, the incidence rate of PSD in China is 51–73% (3). If PSD is not intervened in time, it further leads to difficulties in eating and drinking, resulting in malnutrition, aspiration pneumonia, dehydration, and asphyxia, which seriously affects the prognosis of PSD patients (4, 5). PSD not only increases the economic burden of patients and prolongs their hospitalization time, but also brings a greater care burden to their family members (6, 7). Furthermore, PSD patients are prone to mental and psychological problems. For example, major and minor depression occur in 20–65% of PSD patients (8–11). Moreover, studies show that the presence of PSD is associated with anxiety, bringing individual psychosocial consequences such as fear, and frustration (12, 13). At the same time, PSD is one of the key factors causing disability and death of patients (14).

Currently, the conventional swallowing interventions include transcutaneous neuromuscular electrical stimulation (NMES), biofeedback and lingual strength training (15, 16). However, in China, the limited coverage of medical insurance for PSD patients' rehabilitation programs has brought a greater economic burden to PSD patients and their families (17). Since the implementation of the Diagnosis Related Groups (DRG) payment system in China, most PSD patients must transition from inpatient rehabilitation to home-based rehabilitation due to the limitation of the average hospital stay (18). However, China's community rehabilitation medical resources are in relative shortage, especially professional physiotherapists in the community. This leads to the lack of professional home-based rehabilitation guidance for discharged PSD patients, making the rehabilitation effect of most discharged PSD patients unsatisfactory (19).

To date, smart health devices including smartphones, patient-monitoring devices and wireless devices have enabled patients and health care providers to use health information anytime, anywhere by adding modern technology to health care management systems (20). Smart health employs a variety of different features, including smartphone-based applications. China has now exceeded 500 million smartphone users (21). The WeChat smartphone application has been gradually applied to the field of medical rehabilitation in China because it is convenient and fast, with the advantages of quickly sending messages, video, voice, and pictures through the network, supporting multi-group chat and realizing information sharing (22). The use of smart health makes it possible to combine information technology with individualized continuous rehabilitation.

For PSD patients in the rehabilitation period after discharge, home rehabilitation is a long-term process. WeChat's characteristics of interactivity, immediacy and wide area also allow for expanding the continuity of PSD home-based rehabilitation (23). Specifically, home-based rehabilitation exercise videos on a WeChat public account can be watched repeatedly, which is convenient for PSD patients and their caregivers for learning. In WeChat synchronized videos, PSD caregivers can complete the basic rehabilitation training of swallowing function and diet modification for PSD patients under the supervision of physiotherapists, nutritionists and rehabilitation nurses. WeChat groups can also help realize information sharing between health providers and PSD patients, among health provider team members, and even between peer educators and PSD patients (24).

To date, WeChat-based rehabilitation programs have been widely used in several chronic diseases, including for diabetes patients (25), postoperative women with breast cancer (26), and patients with chronic obstructive pulmonary disease (27). However, very few WeChat-based rehabilitation programs have been developed to support PSD patients. Li et al. (28) explored the effects of smart health-based rehabilitation programs on middle-aged stroke patients. However, that study did not focus on PSD patients, and self-efficacy, social support and nutritional status were not included in this research. The aim of this study was to explore the effect of smart health-based rehabilitation

Abbreviations: ALB, serum albumin; DRG, Diagnosis Related Groups; MDT, multidisciplinary team; NMES, neuromuscular electrical stimulation; ASS, power analysis sample size; PSD, poststroke dysphagia; PSSS, perceived social support scale; PA, serum prealbumin; SPSS, statistical product service solutions; SSA, standardized swallowing assessment; SWAL-QOL, swallow quality-of-life questionnaire; SSEQ, stroke self-efficacy questionnaire; TSF, triceps skinfold thickness; TP, total protein; VFSS, videofluoroscopic swallowing study; WST, water swallow test.

programs on patients with PSD in terms of swallowing function, quality of life, self-efficacy, social support and nutritional status.

2. Materials and methods

This was a prospective, parallel-group, randomized, assessor-blinded clinical pilot trial. This clinical trial was approved by the hospital ethics committee, in line with the *Declaration of Helsinki*, and all patients signed informed consent. This study has been registered in the open science framework (OSF) clinical trial registry (Registration number: DOI https://doi.org/10.17605/OSF.IO/T4UDE).

2.1. Participants, selection criteria and randomization

Participants were selected using the following inclusion criteria: (1) age between 40 and 80 years old; (2) first-time stroke was screened through neurological examination by the attending neurologist and confirmed by computed tomography or magnetic resonance imaging findings according to the WHO definition (29); (3) dysphagia following stroke was confirmed by a videofluoroscopic swallowing study (VFSS). Additionally, to control for spontaneous recovery, enrolment into the study had to occur at least 4 weeks after PSD onset. The exclusion criteria were cognitive impairment or severe communication disorders, serious psychologic disorders including major depressive disorder, bipolar disorder, schizophrenia, *etc.*, known history of dysphagia prior to the stroke [(a) other neurological conditions that may explain dysphagia: amyotrophic lateral sclerosis, multiple sclerosis, or Parkinson's disease; (b) swallowing disorders caused by surgery or radiotherapy applied to the head and neck region; (c) dysphagia due to drug toxicity], unstable cardiopulmonary status, head and neck cancer, implanted cardiac pacemaker, nasogastric tube, and history of seizures or epilepsy. Random numbers were generated by the center computer. The random numbers were placed in opaque and sealed envelopes, and PSD patients were randomly assigned to the control group or intervention group in a ratio of 1:1 according to the random allocation order.

2.2. Treatment methods

2.2.1. Control group

According to the guidelines of the European Stroke Organization and European Society for Swallowing Disorders in 2021 (30), the 12-week routine rehabilitation was patient-oriented and adjusted based on PSD patient swallowing function *via* VFSS (31). (1) Oral–facial and laryngeal motor exercises according to the stroke rehabilitation and recovery guideline. (2) Sensorial stimulation of the oral cavity. These sensory stimulation methods were patient-oriented and customized to the patients' swallowing abilities. (3) Diet modification: diet modification and nutritional support were individualized to match the PSD patients' nutritional and functional statuses under the guidance of registered nutritionists and a nutritional support team. Four weeks after PSD onset, according to the stroke rehabilitation and recovery guideline, dysphagia rehabilitation services were delivered by a multidisciplinary team (MDT) of healthcare providers. According to the American Stroke Association guideline, our MDT team includes neurologists who have specialized training or board certification in rehabilitation medicine, rehabilitation nurses, nutritionists, physiotherapists, and speech and language therapists (32). The MDT held case meetings every week. During the meeting, MDT members shared and discussed the patient's rehabilitation care pathway in combination with data from the clinical swallowing evaluations, the results of rehabilitation strategies, the patient's medical condition and clinical judgment.

2.2.2. Intervention group

PSD patients in the intervention group received smart health-based rehabilitation in addition to the routine rehabilitation. The WeChat cloud platform provided continuous rehabilitation training programs for PSD patients, which were set up for five modules: patient symptom assessment and clinical database establishment, health education, smart health-based oral–facial and laryngeal motor exercises and sensorial stimulation exercises, diet modification and WeChat group. (1) Patient symptom assessment and clinical database establishment: rehabilitation nurses first used the Eating Assessment Tool-10 (EAT-10) tool to identify patients with dysphagia. Patients with an EAT-10 score >3 points underwent the water swallow test (WST) test. The EAT-10, WST results and other clinical data were uploaded to the WeChat cloud platform to realize the tracking of the patients' condition and the sharing of information among MDT members. During the follow-up after discharge, the corresponding data on the WeChat cloud platform was updated in real time and become the reference for the MDT to adjust the rehabilitation plan. (2) Health education: hospital information engineers set up the WeChat public account, and the rehabilitation nurses guided patients to follow the WeChat public account when they were discharged to ensure that every patient could obtain health education information through the online platform. The rehabilitation nurses distributed the information of the PSD follow-up health education manual to patients every 2 days through text, pictures, videos and other forms after the PSD patients were discharged from hospital to strengthen their health education. The rehabilitation nurses set up the WeChat theme interactive sign-in form in the WeChat cloud platform to monitor the reading of PSD patients in real time and reply and answer

their questions in time in the cloud platform. (3) Smart health-based oral–facial and laryngeal motor exercises and sensorial stimulation exercises: After discharge from the hospital, the physiotherapists uploaded the sample video of basic swallowing function rehabilitation training to the WeChat cloud platform. The video was prepared by the physiotherapists using electronic products, combined through editing and subtitles. Caregivers of PSD patients could repeatedly watch and learn basic swallowing function rehabilitation skills on the cloud platform at any time to strengthen their proficiency in skill application. In addition, on the terminal of the cloud platform, the physiotherapists supervised and guided the caregivers of PSD patients on tongue muscle training and cheek muscle training (pouting, empty swallowing, etc.) every day in the first week through the video connection of the WeChat cloud platform. In the remaining 11 weeks, the physiotherapists monitored the completion of oral–facial and laryngeal motor exercises and sensory stimulation exercises of PSD patients in real time through the WeChat clock in applet of daily monitoring report of rehabilitation exercises. (4) Diet modification: diet modification was performed on the WeChat MDT platform. First, the nutritionists calculated the calories required by the PSD patients and the proportion of the nutrients according to their medical history, weight and activity ability (data were mainly retrieved from the WeChat cloud platform). On the WeChat MDT platform, the nutritionist informed the nutrition assessment results to the neurologists, and the neurologists issued the food for PSD patients after consultation with the physiotherapists. After discharge from the hospital, the rehabilitation nurses conducted one-to-one online video guidance for three consecutive days based on the WeChat cloud platform. The rehabilitation nurses then conducted examinations with the caregivers of PSD patients once a week through the WeChat cloud platform, and the neurology nurses were responsible for recording them. The records included evaluating the general state and feeding state of the patient before eating, checking the eating environment, state, posture, tableware, food, and eating and feeding methods. The rehabilitation nurses ensured the accuracy of the implementation of the program by the patients' caregivers and answered the different problems encountered by them. The nutritionists conducted weekly video communication through the WeChat cloud platform, re-formulated the food for the next week with the family members, and adjusted the consistency of the food according to the feedback of neurology specialists and physiotherapists on the WeChat MDT platform. (5) WeChat group: the WeChat group included three WeChat subgroups. The first was the WeChat Med subgroup. In this subgroup, in addition to the weekly case meetings of the MDT as in the control group, the MDT members in the WeChat Med subgroup could share real-time information and promote mutual communication and cooperation. The second was the healthcare providers–PSD patients–caregivers of PSD patients WeChat subgroups. In this subgroup, PSD patients could get regular follow-up visits and real-time health guidance online. In the third peer education subgroup, the MDT members invited patients with better disease control and their caregivers to participate and provide social and peer support to PSD patients. All participants received weekly follow-up. After the 12-week smart health-based rehabilitation intervention, the MDT members conducted the final evaluation and follow-up of patients. The follow-up was conducted in the form of a family visit. It included the evaluation of disease status and swallowing function, quality of life, self-efficacy, social support and nutritional status.

2.3. Outcome measures

2.3.1. Primary outcomes

(1) *Swallowing function assessments:* ① *WST.* The rehabilitation nurses gave 2–3 teaspoons of water to the patients with PSD and instructed them to drink it once. The WST evaluation criteria were scored by a 5-point Likert scale (33). ② *Standardized swallowing assessment (SSA).* The swallowing function of patients in the two groups before and after the intervention was evaluated and divided into three parts, with a total possible score of 46 (34). The lower the score, the better the swallowing function.

(2) *Quality of life, self-efficacy and social support assessment:* ① *Swallow quality-of-life questionnaire (SWAL-QOL)* (35). The questionnaire consists of 11 dimensions and 44 items. A 5-point Likert scale was adopted, with a total possible score of 220. A higher score means a better quality of life. ② *Stroke self-efficacy questionnaire (SSEQ)* (36). It includes two dimensions of activity of daily living and self-management efficacy, with a total of 13 items. A 10-point Likert scale was adopted, and the possible score ranged from 0 to 100. Higher scores mean a higher self-efficacy level. ③ *Perceived Social Support Scale (PSSS).* This scale contains 12 items, and each item uses a 1–7 scoring system. The total score of the scale is the sum of item scores, ranging from 12 to 84. The higher the score, the higher the individual's perceived level of social support.

2.3.2. Secondary outcomes

Nutritional measurements: Body weight (kg), triceps skinfold thickness (TSF), biomarker [total protein (TP; g/L), serum albumin (ALB; g/L), serum prealbumin (PA; mg/L)].

2.4. Statistical analysis

Statistical product service solutions (SPSS) 19.0 statistical software (SPSS Inc., Chicago, IL, USA) was used for data

analysis. Data were presented by means (standard deviation, SD) for continuous variables and frequencies and percentage (%) for categorical variables. The independent *t*-test and Chi-square test were used to compare differences between the two groups at the baseline and 12th week. A value of $p < 0.05$ (two-tailed) indicated statistical significance.

3. Results

According to the sample size calculation with the power analysis sample size (PASS) tool ($\alpha = 0.05$, $1\text{-}\beta = 0.8$ and effect size of standardized swallowing assessment score=0.87), a total of 62 patients with PSD were included in this study. From February 2020 to December 2021, 200 participants were screened in this study, and 140 participants were excluded. In the follow-up phase, a participant in the control group was dropped out because he refused to continue to participate; a participant in the intervention group was dropped out because he moved to the other places. Finally, 60 participants (Control group: $n = 30$; Intervention group: $n = 30$) were included for data analysis (Figure 1).

3.1. Comparison of baseline data

There were no significant differences in general data such as age, gender, marital status, education level, stroke events, time post-stroke, types of strokes and healthcare insurance between the intervention group and the control group ($p > 0.05$) (Table 1).

3.2. Comparison of swallowing function between the two groups

In this research, the swallowing function was measured by WST and SAA score. In terms of the WST, in the intervention group, the proportion of participants in Grade I, Grade II, Grade III, Grade IV, and Grade V was 53.33, 30, 6.67, 6.67, and 3.33%, respectively; In the control group, the proportion of participants in Grade I, Grade II, Grade III, Grade IV, and Grade V was 33.33, 13.33, 10, 26.67, and 16.67%, respectively. There was a significant difference in WST between the two groups (χ^2 value = 9.77, *P* value = 0.040) (Figure 2). The SAA score was not statistically significantly different between the intervention group and the

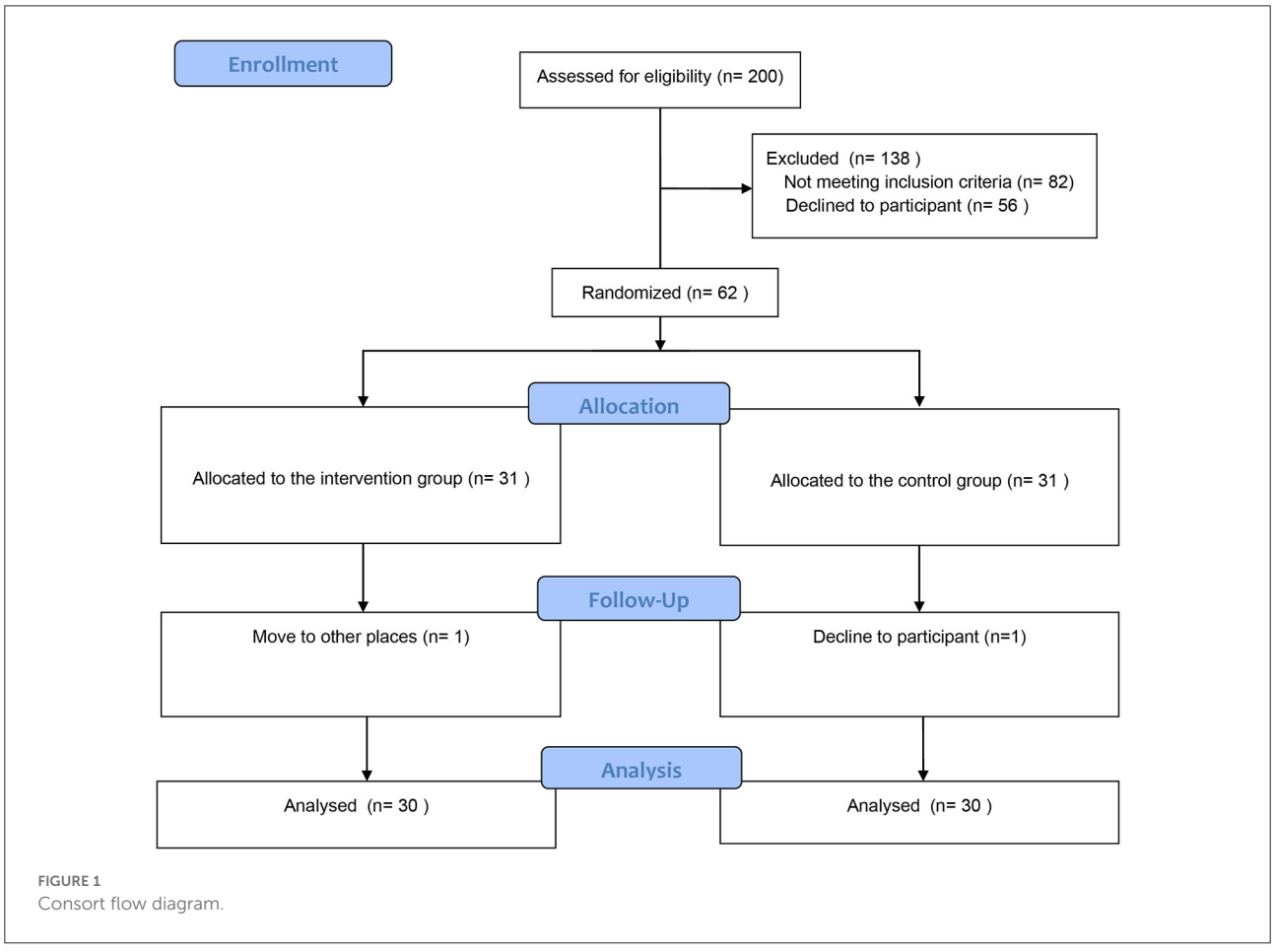


FIGURE 1
Consort flow diagram.

10.3389/fneur.2022.1110067

TABLE 1 Baseline of study characteristics.

Variables	Intervention group ($N = 30$) Mean (SD)	Control group ($N = 30$) Mean (SD)	t	P
Age (years)	68.10 ± 2.34	69.22 ± 3.26	1.53	0.13
Time post-stroke (weeks)	17.37 ± 2.64	18.09 ± 2.53	1.08	0.29
Variables	***N* (%)**	***N* (%)**	χ^2	***P***
Gender			0.32	0.57
Male	20 (66.67)	22 (73.33)		
Female	10 (33.33)	8 (26.67)		
Marital status			0.58	0.45
Married	27 (90.00)	25 (83.33)		
Single	3 (10.00)	5 (16.67)		
Education level			0.53	0.77
Undergraduate	3 (10.00)	6 (20.00)		
High school	6 (20.00)	1 (3.33)		
Middle school	21(70.00)	23 (76.67)		
Type of stroke			1.18	0.28
Ischemic stroke Haemorrhagic	24 (80.00)	27 (90.00)		
Stroke	6 (20.00)	3 (10.00)		
Healthcare insurance			0.60	0.44
Yes	14 (46.67)	17 (56.67)		
No	16 (53.33)	13 (43.33)		

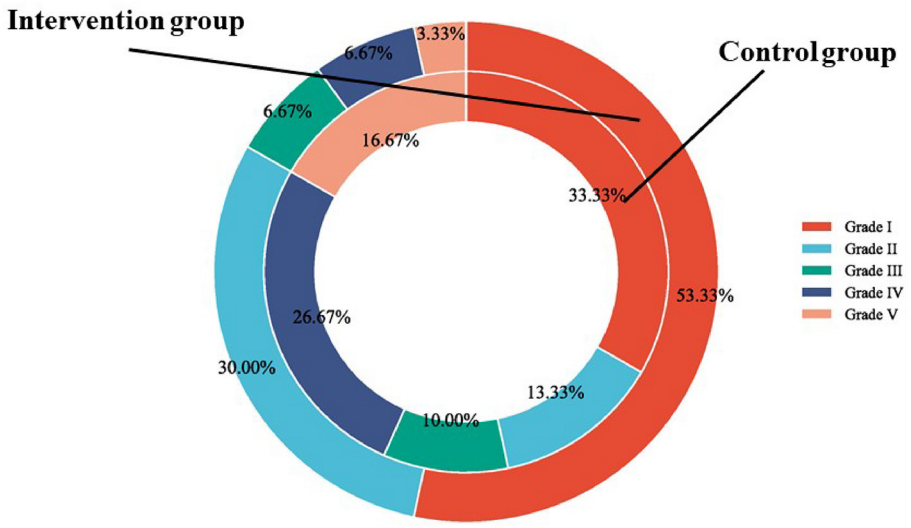


FIGURE 2
Comparison of WST between the two groups.

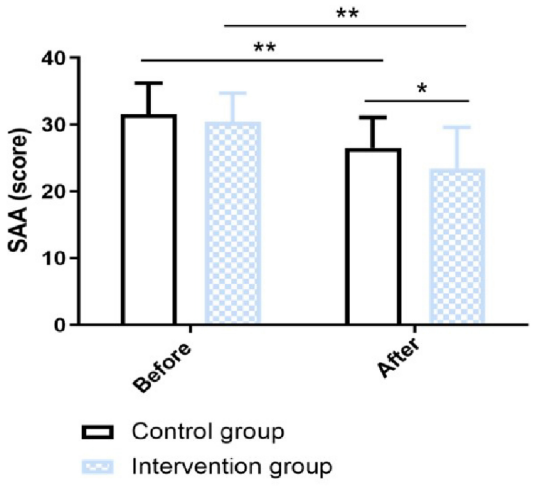


FIGURE 3
Changes in SAA scores between groups. *$P < 0.05$, **$p < 0.01$.

control group before the intervention ($p > 0.05$). After 12-week intervention, the SAA score of the intervention group was significantly improved than that of the control group (χ^2 value $= 2.20$, P value $= 0.032$) (Figure 3).

3.3. Comparison of quality of life, self-efficacy and social support between the two groups

SWAL-QOL were used to assess the health-related quality of life, SSEQ was used to assess the self-efficacy, and PSSS was used to assess the social support between the two groups before and after the intervention. Before intervention, there was no significant difference in the quality of life (Supplementary Figure S1A), self-efficacy (Supplementary Figure S1B) and social support (Supplementary Figure S1C) between the two groups ($P > 0.05$). After intervention, the improvement of quality of life (Supplementary Figure S1A), self-efficacy (Supplementary Figure S1B) and social support (Supplementary Figure S1C) was greater in the intervention group than in the control group ($P < 0.05$) (Supplementary Figure S1).

3.4. Comparison of nutritional measurements between the two groups

As shown in Supplementary Figure S2, before the intervention, there was no significant differences in body weight (Supplementary Figure S2A), triceps skinfold thickness (TSF) (Supplementary Figure S2B), and biomarkers [Total protein (TP) (Supplementary Figure S2C), Serum albumin (ALB) (g/L) (Supplementary Figure S2D), serum prealbumin (PA) (mg/L) (Supplementary Figure S2E)] between the intervention group and control group ($P > 0.05$). After the intervention, compared with the control group, the intervention group showed an increase in the serum levels of PA ($P < 0.01$) (Supplementary Figure S2E). However, there was no statistically significant difference between the intervention group and the control group in terms of body weight (Supplementary Figure S2A), TSF (Supplementary Figure S2B), TP (Supplementary Figure S2C) and ALB (Supplementary Figure S2D) ($P > 0.05$).

4. Discussion

The observation of similar improvements in swallow functional outcomes at 12 weeks post rehabilitation in the control group is also consistent with the findings of a systematic review of nine studies which estimated the impact of MDT based rehabilitation program among PSD patients (37). To explore this issue, MDT team could formulate standardized, individualized and comprehensive rehabilitation plans for PSD patients (38). At the same time, this research reflects the nature and extent of rehabilitation prescribed to PSD patients which were similar, with the main difference lying in the mode of rehabilitation delivery (tele-rehabilitation or not) (39). The difference in mode of service delivery highlights the strength of tele-rehabilitation which often facilitates more interactions between the service users (patients) and the service providers (physiotherapies). Although the swallowing function, quality of life, self-efficacy and social support index data of the two groups after the intervention are significantly improved compared with the baseline data, tele-rehabilitations overcome the barriers related to access to services caused by distance or difficulty of patient's mobility, potentially encouraging continuity of care and reducing the costs of the healthcare system (40).

In this research, after the smart health-based rehabilitation intervention, the WST and SAA scores of patients with PSD significantly decreased when compared with the control group ($P < 0.05$). This somewhat agreed with studies by Wu and Wang (41) and Gandolfi et al. (42). To explore this issue, the sample video of basic swallowing function rehabilitation training on the WeChat cloud platform could set an example for caregivers of PSD patients. Especially after discharge, the caregivers of PSD patients could repeatedly click the video to watch, which strengthens their proficiency in the rehabilitation of basic swallowing function. Videos on the WeChat cloud platform were classified according to the purpose of the swallow function exercise, which could help caregivers of PSD patients understand the benefits

of each exercise on rehabilitation. At the same time, the WeChat punch in applet of daily monitoring report of rehabilitation exercises improved the rehabilitation adherence of caregivers of PSD patients in the implementation of basic swallowing function rehabilitation and ensured the rehabilitation training effect of oral–facial and laryngeal motor exercises and sensorial stimulation exercises (43). Moreover, the smart health-based rehabilitation intervention model could realize the interaction between neurology specialists, rehabilitation nurses, physiotherapists, nutritionists, caregivers of PSD patients and PSD patients through the WeChat cloud platform. Through one-to-one, face-to-face communication, the rehabilitation nurses, physiotherapists and nutritionists in the early stage helped the caregivers establish standardized operating procedures (44).

Enhancing patients' self-efficacy can increase their health status by improving health behavior and ultimately improve their quality of life (45). Bonetti et al. (46) conducted a follow-up survey on 203 patients with stroke after discharge and found that the level of self-efficacy was a strong predictor of the rehabilitation process of swallowing function. In this study, compared with the control group, the smart health-based rehabilitation significantly improved the score of SSEQ ($P < 0.05$). To explore this issue, one-on-one teaching of MDT members enables patients and their caregivers to gain direct experience. After PSD patients were discharged, MDT members continuously corrected the behavior of the caregivers to enhance the accuracy of their direct experience. Furthermore, in the peer education WeChat group, peer education was integrated into the rehabilitation training so that patients and caregivers were supplemented by alternative experience, and their self-efficacy was improved.

Quality of life describes an individual's overall wellbeing based on daily experience. The quality of life of patients with PSD usually decreases due to prolonged eating time, fatigue caused by poor nutritional status, decline in social support, psychological anxiety and depression (12). In this study, the smart health-based rehabilitation effectively enhanced the quality-of-life score of SWAL-QOL for PSD patients. On one hand, smart health-based rehabilitation can effectively improve the WST and SAA scores, enhance the swallowing function of patients, reduce the time of eating and finally improve the quality of life of patients. On the other hand, patients' fatigue in the dimension of quality-of-life scale is closely related to their poor nutritional status (47). Smart health-based rehabilitation can effectively improve the expression level of PA, reduce the patients' sense of fatigue, and finally improve the quality of life of PSD patients.

Malnutrition is very common in patients with PSD. At present, the malnutrition evaluation indexes of PSD include body weight, TSF, TP, ALB and PA. These measurements are recommended in the European Stroke Organization and European Society for Swallowing Disorders guidelines to monitor the nutritional status of PSD (30). Peng et al. (48) found that enteral nutritional suspension (TPF-FOS) JEVITY could effectively improve the expression of PA in stroke patients, but no statistical significance existed in weight, TSF, TP, ALB or other indicators compared with the control group ($P > 0.05$). In line with the results of Peng et al. (48), smart health-based rehabilitation can only improve the expression of PA in patients with PSD, and no significant difference existed in other nutritional indexes compared with the control group ($P > 0.05$). Body weight, TSF, TP and other indicators are not easy to change in a short time and are affected by oedema. Although ALB has always been the main index of nutritional risk assessment and prognosis in patients with PSD, its level cannot reflect the nutritional status of patients early and dynamically. However, the half-life of PA is only 2 days, and it can have significant changes in short-term protein supplementation (49). The continuous monitoring of PA levels can be used as a dynamic monitoring index of malnutrition.

This study has some limitations. The development time of smart health-based rehabilitation programs in China is relatively short. Moreover, smart health-based rehabilitation programs cannot be blind to implementers and patients, which may lead to performance bias. Furthermore, the intervention time is relatively short at only 12 weeks. Additionally, to control for initial spontaneous recovery, we included PSD patients with a minimum limit of 4 weeks by referring to the published literature (16, 50, 51). However, we still cannot completely rule out some positive effects of patients' spontaneous recovery on outcome measurements. Considering the medical ethical requirement, we could not include PSD patients with a minimum limit of 6–7 months. Moreover, we also could not set up a non-rehabilitation group to explore the outcome impact of PSD patients' spontaneous recovery rehabilitation. Furthermore, the National Institutes of Health Stroke Scale (NIHSS) is accepted as the definitive clinical examination to assess the neurological impairment severity of stroke patients (52). Conventional neuroradiological tools, such as CT and MRI, are useful to reveal radiological markers of neuropathology in PSD patients (53). However, due to the limitation of research funds, we did not collect data in this brief research study on the neurological impairment severity and neuroradiological markers independently associated with PSD outcomes. We would build the collection of these data into a further full-scale study.

5. Conclusion

Overall, our data revealed that smart health-based rehabilitation is significantly beneficial to the swallowing function, quality of life, self-efficacy, and social support for Chinese PSD patients when compared with routine

rehabilitation. However, nutritional measurements were not significantly improved in such patients under the smart health-based rehabilitation when compared the routine rehabilitation. In the future, it is necessary to extend the intervention time to further evaluate the long-term efficacy of smart health-based rehabilitation on nutritional measurements of PSD patients in China.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by Dongguan Houjie Hospital Affiliated to Guangdong Medical University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the individual(s), and minor(s)' legal guardian/next of kin, for the publication of any potentially identifiable images or data included in this article.

Author contributions

J-RZ and Y-EW: conceptualization, data curation, and writing. Y-FH: software. S-QZ and W-LP: analysis. J-XH: validation. Q-PH: supervision and funding acquisition. All authors read and approved the final manuscript.

Funding

This research was supported by Dongguan Science and Technology of Social Development Program (20211800904942).

Acknowledgments

We thank Cambridge Proofreading company for editing our language.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2022.1110067/full#supplementary-material

References

1. Ortega O, Martín A, Clavé P. Diagnosis and management of oropharyngeal dysphagia among older persons, state of the art. *J Am Med Dir Assoc.* (2017) 18:576–82. doi: 10.1016/j.jamda.2017.02.015

2. Jones CA, Colletti CM, Ding MC. Post-stroke dysphagia: recent insights and unanswered questions. *Curr Neurol Neurosci Rep.* (2020) 20:61. doi: 10.1007/s11910-020-01081-z

3. Wu S, Wu B, Liu M, Chen Z, Wang W, Anderson CS, et al. Stroke in China: advances and challenges in epidemiology, prevention, and management. *Lancet Neurol.* (2019) 18:394–405. doi: 10.1016/S1474-4422(18)30500-3

4. Martino R, Foley N, Bhogal S, Diamant N, Speechley M, Teasell R. Dysphagia after stroke: incidence, diagnosis, and pulmonary complications. *Stroke.* (2005) 36:2756–63. doi: 10.1161/01.STR.0000190056.76543.eb

5. Sharma JC, Fletcher S, Vassallo M, Ross I. What influences outcome of stroke–pyrexia or dysphagia? *Int J Clin Pract.* (2001) 55:17–20.

6. Allen J, Greene M, Sabido I, Stretton M, Miles A. Economic costs of dysphagia among hospitalized patients. *Laryngoscope.* (2020) 130:974–9. doi: 10.1002/lary.28194

7. Davis C, Namasivayam-MacDonald AM, Shune SE. Contributors to poststroke dysphagia-related caregiver burden. *Am J Speech Lang Pathol.* (2021) 30:1061–73. doi: 10.1044/2021_AJSLP-20-00250

8. Pohjasvaara T, Leppävuori A, Siira I, Vataja R, Kaste M, Erkinjuntti T. Frequency and clinical determinants of poststroke depression. *Stroke.* (1998) 29:2311–7. doi: 10.1161/01.STR.29.11.2311

9. Eastwood MR, Rifat SL, Nobbs H, Ruderman J. Mood disorder following cerebrovascular accident. *Br J Psychiatry.* (1989) 154:195–200. doi: 10.1192/bjp.154.2.195

10. Aström M, Adolfsson R, Asplund K. Major depression in stroke patients. A 3-year longitudinal study. *Stroke.* (1993) 24:976–82. doi: 10.1161/01.STR.24.7.976

11. Gainotti G, Azzoni A, Marra C. Frequency, phenomenology and anatomical-clinical correlates of major post-stroke depression. *Br J Psychiatry.* (1999) 175:163–7. doi: 10.1192/bjp.175.2.163

12. Ekberg O, Hamdy S, Woisard V, Wuttge-Hannig A, Ortega P. Social and psychological burden of dysphagia: its impact on diagnosis and treatment. *Dysphagia.* (2002) 17:139–46. doi: 10.1007/s00455-001-0113-5

13. Eslick GD, Talley NJ. Dysphagia: epidemiology, risk factors and impact on quality of life–a population-based study. *Aliment Pharmacol Ther.* (2008) 27:971–9. doi: 10.1111/j.1365-2036.2008.03664.x

14. Arnold M, Liesirova K, Broeg-Morvay A, Meisterernst J, Schlager M, Mono ML, et al. Dysphagia in acute stroke: incidence, burden and impact on clinical outcome. *PLoS ONE.* (2016) 11:e0148424. doi: 10.1371/journal.pone.0148424

15. Rogus-Pulia N, Robbins J. Approaches to the rehabilitation of dysphagia in acute poststroke patients. *Semin Speech Lang.* (2013) 34:154–69. doi: 10.1055/s-0033-1358368

16. Simonelli M, Ruoppolo G, Iosa M, Morone G, Fusco A, Grasso MG, et al. Stimulus for eating. The use of neuromuscular transcutaneous electrical stimulation in patients affected by severe dysphagia after subacute stroke: a pilot randomized controlled trial. *NeuroRehabilitation.* (2019) 44:103–10. doi: 10.3233/NRE-182526

17. Tang Q, Liang B, Liang R, Zhang S, Zhu L. Study on optimization and evaluation system of traditional Chinese medicine rehabilitation program for swallowing disorder after stroke. *Medicine (Baltimore).* (2021) 100:e25731. doi: 10.1097/MD.0000000000025731

18. Zeng JQ. The pilot results of 47 148 cases of BJ-DRGs-based payment in China. *Int J Health Plann Manage.* (2019) 34:1386–98. doi: 10.1002/hpm.2818

19. Fang WJ, Zheng F, Zhang LZ, Wang WH, Yu CC, Shao J, et al. Research progress of clinical intervention and nursing for patients with post-stroke dysphagia. *Neurol Sci.* (2022) 43:5875–84. doi: 10.1007/s10072-022-06191-9

20. Wang J, Wang Y, Wei C, Yao NA, Yuan A, Shan Y, et al. Smartphone interventions for long-term health management of chronic diseases: an integrative review. *Telemed J E Health.* (2014) 20:570–83. doi: 10.1089/tmj.2013.0243

21. Zapata BC, Fernández-Alemán JL, Idri A, Toval A. Empirical studies on usability of mHealth apps: a systematic literature review. *J Med Syst.* (2015) 39:1. doi: 10.1007/s10916-014-0182-2

22. Chen X, Zhou X, Li H, Li J, Jiang H. The value of WeChat application in chronic diseases management in China. *Comput Methods Programs Biomed.* (2020) 196:105710. doi: 10.1016/j.cmpb.2020.105710

23. Zhang X, Zhao J, Zheng L, Li X, Hao Y. Implementation strategies to improve evidence-based practice for post-stroke dysphagia identification and management: a before-and-after study. *Int J Nurs Sci.* (2022) 9:295–302. doi: 10.1016/j.ijnss.2022.06.010

24. Donnan GA. Multidisciplinary stroke management [Editorial]. *Int J Stroke.* (2012) 7:275. doi: 10.1111/j.1747-4949.2012.00821.x

25. Xia SF, Maitiniyazi G, Chen Y, Wu XY, Zhang Y, Zhang XY, et al. Web-Based TangPlan and WeChat combination to support self-management for patients with type 2 diabetes: randomized controlled trial. *JMIR Mhealth Uhealth.* (2022) 10:e30571. doi: 10.2196/30571

26. Zhou K, Wang W, Zhao W, Li L, Zhang M, Guo P, et al. Benefits of a WeChat-based multimodal nursing program on early rehabilitation in postoperative women with breast cancer: A clinical randomized controlled trial [Randomized Controlled Trial]. *Int J Nurs Stud.* (2020) 106:103565. doi: 10.1016/j.ijnurstu.2020.103565

27. Jiang Y, Liu F, Guo J, Sun P, Chen Z, Li J, et al. Evaluating an intervention program using wechat for patients with chronic obstructive pulmonary disease: randomized controlled trial. *J Med Internet Res.* (2020) 22:e17089. doi: 10.2196/17089

28. Li Y, Zhang S, Song J, Tuo M, Sun C, Yang F. Effects of self-management intervention programs based on the health belief model and planned behavior theory on self-management behavior and quality of life in middle-aged stroke patients. *Evid Based Complement Alternat Med.* (2021) 2021:8911143. doi: 10.1155/2021/8911143

29. World Health Organization. *International Classification of Diseases and Related Health Problems, 10th revision*. Geneva: Elsevier (1992).

30. Dziewas R, Michou E, Trapl-Grundschober M, Lal A, Arsava EM, Bath PM, et al. European stroke organisation and european society for swallowing disorders guideline for the diagnosis and treatment of post-stroke dysphagia. *Eur Stroke J.* (2021) 6:89–106. doi: 10.1177/23969873211039721

31. Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, et al. Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* (2016) 47:e98–e169. doi: 10.1161/STR.0000000000000098

32. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke.* (2019) 50:e344–418. doi: 10.1161/STR.0000000000000211

33. Chen PC, Chuang CH, Leong CP, Guo SE, Hsin YJ. Systematic review and meta-analysis of the diagnostic accuracy of the water swallow test for screening aspiration in stroke patients. *J Adv Nurs.* (2016) 72:2575–86. doi: 10.1111/jan.13013

34. Jiang JL, Yu JL, Wang JH, Wang YY, Wang WH. Evaluation of the Chinese version of the swallowing screen in stroke patients with dysphagia. *Ci Ji Yi Xue Za Zhi.* (2019) 31:270–5. doi: 10.4103/tcmj.tcmj_158_18

35. McHorney CA, Robbins J, Lomax K, Rosenbek JC, Chignell K, Kramer AE, et al. The SWAL-QOL and SWAL-CARE outcomes tool for oropharyngeal dysphagia in adults: III. Documentation of reliability and validity. *Dysphagia.* (2002) 17:97–114. doi: 10.1007/s00455-001-0109-1

36. Jones F, Partridge C, Reid F. The stroke self-efficacy questionnaire: measuring individual confidence in functional performance after stroke. *J Clin Nurs.* (2008) 17:244–52. doi: 10.1111/j.1365-2702.2008.02333.x

37. Broderick P, Horgan F, Blake C, Ehrensberger M, Simpson D, Monaghan K. Mirror therapy for improving lower limb motor function and mobility after stroke: a systematic review and meta-analysis. *Gait Posture.* (2018) 63:208–220. doi: 10.1016/j.gaitpost.2018.05.017

38. Grigonyte M, Kraujelyte A, Januskeviciute E, Semys G, Kriukelyte O, Kontrimaviciute E, et al. The impact of the pandemic on acute ischaemic stroke endovascular treatment from a multidisciplinary perspective: a nonsystematic review. *Int J Environ Res Public Health.* (2021) 18:9464. doi: 10.3390/ijerph18189464

39. Chen J, Jin W, Zhang XX, Xu W, Liu XN, Ren CC. Telerehabilitation approaches for stroke patients: systematic review and meta-analysis of randomized controlled trials. *J Stroke Cerebrovasc Dis.* (2015) 24:2660–8. doi: 10.1016/j.jstrokecerebrovasdis.2015.09.014

40. Dee M, Lennon O, O'Sullivan C. A systematic review of physical rehabilitation interventions for stroke in low and lower-middle income countries [Systematic Review]. *Disabil Rehabil.* (2020) 42:473–501. doi: 10.1080/09638288.2018.1501617

41. Wu JX, Wang YJ. Effect of continuous family nursing intervention on the family rehabilitation of the stroke patients with swallowing disorder. *J Nurs Train.* (2017) 32:1698–700. doi: 10.16821/j.cnki.hsjx.2017.18.023

42. Gandolfi M, Smania N, Bisoffi G, Squaquara T, Zuccher P, Mazzucco S. Improving post-stroke dysphagia outcomes through a standardized and multidisciplinary protocol: an exploratory cohort study. *Dysphagia.* (2014) 29:704–12. doi: 10.1007/s00455-014-9565-2

43. Gao SS, Wang YJ, Zhang GX, Zhang WT. Rehabilitation guidance for hip fracture patients during the COVID-19 pandemic using chat software: a new model. *J Back Musculoskelet Rehabil.* (2021) 34:337–42. doi: 10.3233/BMR-200324

44. Dorje T, Zhao G, Scheer A, Tsokey L, Wang J, Chen Y, et al. SMARTphone and social media-based Cardiac Rehabilitation and Secondary Prevention (SMART-CR/SP) for patients with coronary heart disease in China: a randomised controlled trial protocol. *BMJ Open.* (2018) 8:e021908. doi: 10.1136/bmjopen-2018-021908

45. Lev EL, Owen SV. A measure of self-care self-efficacy. *Res Nurs Health.* (1996) 19:421–9. doi: 10.1002/(SICI)1098-240X(199610)19:5<421::AID-NUR6>3.0.CO;2-S

46. Bonetti D, Johnston M. Perceived control predicting the recovery of individual-specific walking behaviours following stroke: testing psychological models and constructs. *Br J Health Psychol.* (2008) 13(Pt 3):463–78. doi: 10.1348/135910707X216648

47. Zhang Q, Schwade M, Smith Y, Wood R, Young L. Exercise-based interventions for post-stroke social participation: a systematic review and network meta-analysis. *Int J Nurs Stud.* (2020) 111:103738. doi: 10.1016/j.ijnurstu.2020.103738

48. Peng B, Su YY, Cui LY, Wang SS, Guan YT, Zhou D, et al. Safety and efficacy of enteral nutritional suspension (TPF-FOS) JEVITY in acute stroke [Multicenter Study]. *Zhonghua Yi Xue Za Zhi.* (2011) 91:2634–7. doi: 10.3760/cma.j.issn.0376-2491.2011.37.014

49. Cohen DL, Roffe C, Beavan J, Blackett B, Fairfield CA, Hamdy S, et al. Post-stroke dysphagia: a review and design considerations for future trials. *Int J Stroke.* (2016) 11:399–411. doi: 10.1177/1747493016639057

50. Sproson L, Pownall S, Enderby P, Freeman J. Combined electrical stimulation and exercise for swallow rehabilitation post-stroke: a pilot randomized control trial. *Int J Lang Commun Disord.* (2018) 53:405–17. doi: 10.1111/1460-6984.12359

51. Hägglund P, Hägg M, Levring Jäghagen E, Larsson B, Wester P. Oral neuromuscular training in patients with dysphagia after stroke: a prospective, randomized, open-label study with blinded evaluators. *BMC Neurol.* (2020) 20:405. doi: 10.1186/s12883-020-01980-1

52. Puetz V, Dzialowski I, Hill MD, Demchuk AM. The alberta stroke program early CT score in clinical practice: what have we learned? *Int J Stroke.* (2009) 4:354–64. doi: 10.1111/j.1747-4949.2009.00337.x

53. Benjamini D, Iacono D, Komlosh ME, Perl DP, Brody DL, Basser PJ. Diffuse axonal injury has a characteristic multidimensional MRI signature in the human brain. *Brain.* (2021) 144:800–16. doi: 10.1093/brain/awaa447

frontiers | Frontiers in Neurology

TYPE Original Research
PUBLISHED 07 February 2023
DOI 10.3389/fneur.2023.1094232

OPEN ACCESS

EDITED BY
Aleksandras Vilionskis,
Vilnius University, Lithuania

REVIEWED BY
Michal Karlinski,
Institute of Psychiatry and Neurology (IPiN), Poland
Taiki Yoshida,
Fujita Health University, Japan

*CORRESPONDENCE
Tamar Abzhandadze
✉ tamar.abzhandadze@gu.se

SPECIALTY SECTION
This article was submitted to Stroke, a section of the journal Frontiers in Neurology

RECEIVED 09 November 2022
ACCEPTED 09 January 2023
PUBLISHED 07 February 2023

CITATION
Susts J, Reinholdsson M, Sunnerhagen KS and Abzhandadze T (2023) Physical inactivity before stroke is associated with dependency in basic activities of daily living 3 months after stroke. *Front. Neurol.* 14:1094232. doi: 10.3389/fneur.2023.1094232

Physical inactivity before stroke is associated with dependency in basic activities of daily living 3 months after stroke

Jevgenijs Susts[1,2], Malin Reinholdsson[3,4], Katharina Stibrant Sunnerhagen[3,5] and Tamar Abzhandadze[3,4]*

[1]Department of Education and Science, National Rehabilitation Center "Vaivari", Jurmala, Latvia, [2]Faculty of Residency, Riga Stradins University, Riga, Latvia, [3]Department of Clinical Neuroscience, Institute of Neuroscience and Physiology, University of Gothenburg, The Sahlgrenska Academy, Gothenburg, Sweden, [4]Department of Occupational Therapy and Physiotherapy, Sahlgrenska University Hospital, Gothenburg, Sweden, [5]Rehabilitation Medicine, Neurocare, Sahlgrenska University Hospital, Gothenburg, Sweden

Background: Physical inactivity is a leading risk factor for non-communicable diseases, including stroke. Moreover, physical inactivity before stroke is associated with stroke severity, which, in turn, can cause disability. However, it remains unclear whether physical inactivity before stroke is associated with dependency in basic activities of daily living (ADL).

Aim: The aim of this study was to evaluate whether physical inactivity before stroke influences ADL dependency 3 months after stroke.

Methods: This longitudinal study was based on data from three Swedish registries. Patients with acute stroke who were admitted to the Sahlgrenska University Hospital between 9 November 2014 and 30 June 2019 were included in the study. Baseline data were collected from the three stroke units, and self-reported questionnaires were used to collect 3-month follow-up data. Physical inactivity before stroke was the primary independent variable that was self-reported using the Saltin–Grimby physical activity level scale. ADL dependency was a composite measure of three tasks: mobility, dressing, and toilet use. A binary logistic regression analysis was used to explain the association between physical inactivity before stroke and basic ADL 3 months after stroke.

Results: In total, 3,472 patients were included in the study. The median age was 75 years, 49% of the patients were physically inactive before stroke, and 75% had a mild stroke. ADL dependency at follow-up was reported to be 32%. Physically inactive patients, compared with physically active patients, had 2.35 times higher odds for ADL dependency 3 months after stroke (odds ratio 2.30 [95% CI 1.89 – 2.80]). The model correctly classified 84% of the patients (the area under the receiver operating characteristic curve was 0.84 [95% CI, 0.83 – 0.86]).

Conclusion: The findings of this study suggest that physical inactivity before stroke is associated with dependency in basic ADL 3 months after stroke. In addition, older age, female sex, pre-stroke living conditions, need for help, previous stroke, and admission stroke severity are significant contributors to dependency.

KEYWORDS

pre-stroke, physical activity, independence, assistance, functional outcome, exercise, sedentary behavior

1. Introduction

Stroke is associated with a high burden on the healthcare system due to the loss of disability-adjusted life years (1, 2). Some level of assistance is required in 26–44% of stroke survivors (3, 4). By 2047, the number of stroke survivors in Europe is estimated to increase by 27% (5). After stroke, patients and their relatives turn to healthcare professionals for evaluating their recovery prognosis and assessing their need for assistance in activities of daily living (ADL) (2, 6, 7).

There are several modifiable and non-modifiable risk factors for stroke (8). Hypertension, hyperlipidemia, diabetes, smoking, physical inactivity, unhealthy diet, and obesity can increase stroke incidence (8). However, a few studies have explored whether these factors can influence functional outcomes. The risk factor of physical inactivity is estimated to be present among 31% of the global population, with continuously growing numbers (9). Physical inactivity is defined as not meeting the international recommendations of at least 150 min of moderate-intensity physical activity per week (10). Furthermore, there are conflicting results regarding how physical activity before stroke influences ADL after stroke (11, 12).

Studies have shown that additional factors, including older age, stroke severity, and ADL dependency before stroke, influence stroke-related functional outcomes (7, 13, 14). Moreover, men tend to have better functional outcomes, which may be related to a younger average age when experiencing their first stroke (15). Reperfusion therapy is associated with better outcomes in patients with moderate-to-severe ischemic stroke (16). Meanwhile, living alone is not associated with worse functional outcomes, although it is associated with higher mortality rates (17, 18).

Previous studies on physical inactivity before stroke have mostly looked at small samples and rarely evaluated how it influences dependency after stroke (12). While physical inactivity is acknowledged as a risk factor for stroke, it is also important to know whether it can influence functional outcomes after stroke. This study aimed to evaluate whether physical inactivity before stroke influences ADL dependence 3 months after stroke.

2. Materials and methods

2.1. Ethics statement

This study was approved by the Swedish Ethics Review Authority (#2021-03324, 13 July 2021). According to the Swedish Data Protection Authority, the handling of data generated within the framework of quality registries is exempt from the requirement for informed consent from participants. Furthermore, the Personal Data Act (Swedish Law #1998:204, issued 29 April 1998) allows data from medical charts to be collected for clinical purposes and quality control without written-informed consent. Data collection and handling in this study followed the General Data Protection Regulation of Sweden (2018).

2.2. Study design and population

This longitudinal and registry-based study was a part of the research project Consequences After Stroke in Gothenburg (COASTGOT). Data were retrieved from three Swedish registries, including Väststroke, Riksstroke, and Statistics Sweden (SCB). Väststroke is a local quality registry for stroke with three stroke units at the Sahlgrenska University Hospital (SU) registering data. The catchment area for hospitals' basic care is 700,000 people, and specialized care is for 1.7 million people. Riksstroke is a national quality registry for stroke, covering over 90% of patients admitted to Swedish hospitals (19). SCB is Sweden's governmental, national statistics center.

This study included patients who were admitted to the SU between 1 November 2014 and 30 June 2019, were ≥18 years at the onset, had a stroke diagnosis (I61, non-traumatic intracerebral hemorrhage; I63, cerebral infarction; and I64, stroke not specified as hemorrhage or infarction), and had registered data on physical activity level before stroke and ADL 3 months after the stroke. Patients who died ≤93 days before follow-up were excluded from the analysis.

2.3. Procedure

Data from Väststroke, Riksstroke, and SCB were merged by statisticians at Riksstroke and SCB using the patients' personal identification numbers. Thereafter, personal identification numbers were replaced with serial numbers. SCB held the code key, and the researchers received a pseudonymized data file. The major reason for merging the data was the variety of variables available using several registries.

Data in Väststroke were registered by healthcare professionals working in the stroke units. Physiotherapists assessed and registered the level of physical activity during their first encounter with the patient. In addition, information was obtained from the next of kin when the patient could not respond, and medical doctors assessed stroke severity on hospital admission.

The baseline data on Riksstroke were registered by Riksstroke nurses working in the stroke units. Medical charts of patients were used as data sources. Three-month follow-up data, including information on basic ADL, were collected using self-reported postal questionnaires. In case of no response, a reminder letter was sent.

Data from the SCB were registered by governmental institutions. The authors retrieved information on the sociodemographic characteristics of patients and data on death after stroke. This study is reported in accordance with the STROBE guidelines for cohort studies (20).

2.4. Variables

The physical activity before stroke was assessed with Saltin–Grimby physical activity level scale (SGPALS) (21, 22). The SGPALS has four levels: (1) physically inactive, (2) light physical activity for at least 4 h/week, (3) moderate physical activity and training for at least 2–3 h/week, and (4) high-intensity physical training for competitive sports several times/week. The physical activity level refers to the year before the stroke. For statistical analysis, SGPALS was dichotomized into the physically inactive group including level 1 versus the physically active group with levels 2–4 (23). The SGPALS has good predictive validity (11, 22, 23).

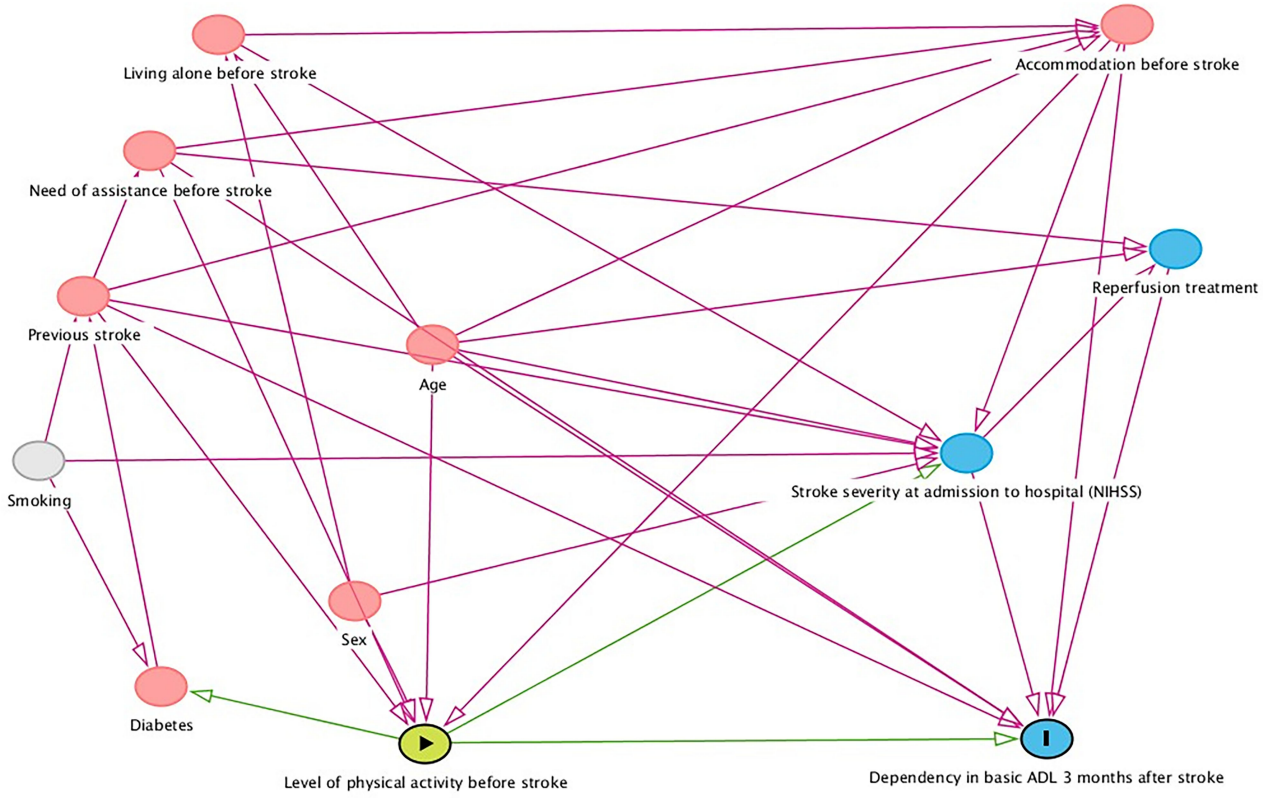


FIGURE 1
Directed acyclic graph showing factors that might confound the relationship between level of physical activity before stroke and dependency in basic activities of daily living (ADL) 3 months after stroke. NIHSS, National Institutes of Health Stroke Scale.

The outcome variable was a composite measure with three basic ADLs: mobility, dressing, and toilet use. Mobility had three response categories that are as follows: (1) able to move around without help both indoors and outdoors (use of walking aid permitted), (2) able to move around without help indoors but not outdoors (use of walking aid permitted), and (3) need help from another person when moving around or bedridden. Levels 2 and 3 were considered dependent in mobility. Dressing and toilet use were binary variables describing "I need help" or "I can manage myself." Dependency in basic ADL 3 months after stroke was defined as the need for help in at least one of the three basic ADLs (24).

The stroke severity was assessed during hospital admission using the National Institutes of Health Stroke Scale (NIHSS) (25). The score range of NIHSS is from 0 to 42 points, with a higher score indicating a more severe stroke. Stroke severity was stratified based on the NIHSS scores as follows: no neurological symptoms according to NIHSS (NIHSS 0 p), mild stroke (NIHSS 1–5 p), moderate stroke (NIHSS 6–14 p), and severe stroke (NIHSS $\geq$ 15 p).

Other variables included in the analysis were demographic characteristics (sex and age), ADLs (a composite measure of three basic ADLs before stroke), accommodation before the onset of stroke, comorbidities (previous stroke and diabetes), and reperfusion treatments. Notably, all variables were binary yes/no, except age, which was analyzed as a continuous variable. Accommodation before stroke was stratified into people who lived in their own homes without help, in their own homes with help, or in nursing homes (or equivalent) (19).

2.5. Data analysis

The difference between included and excluded patients was analyzed using the Mann–Whitney U-test for continuous variables and the chi-square test for categorical variables. The characteristics of the study sample are described as mean and standard deviation (SD), median and interquartile range (IQR), minimum–maximum, or numbers and frequencies (n [%]). The levels of physical activity before stroke were stratified into three groups for describing the characteristics of the study sample, and physical activity levels 3 and 4 were merged, as level 4 comprised only 11 observations. The statistical difference between the physical activity groups was studied with the Kruskal–Wallis test for independent continuous variables and the chi-square test for independent categorical variables.

2.5.1. Choosing the regression model

A binary logistic regression analysis was performed to explain the dependency in basic ADL 3 months after stroke, as the outcome was a binary variable (ADL dependency defined as an event, "1").

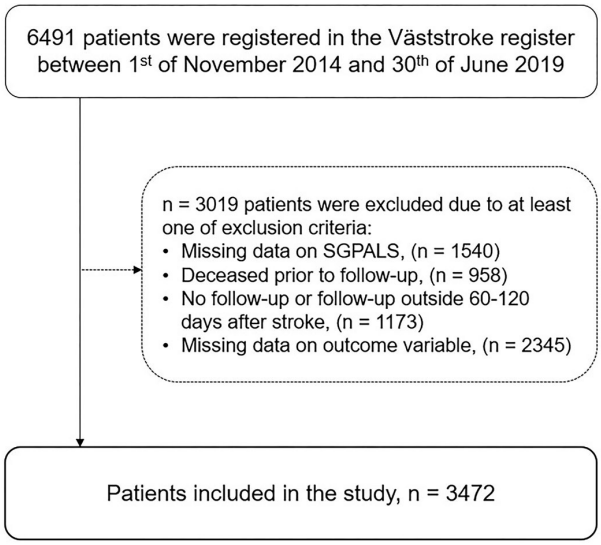


FIGURE 2
Flowchart of the study participants (SGPALS, Saltin–Grimby physical activity level scale).

2.5.2. Selection of explanatory variables

The primary explanatory variable was physical inactivity before stroke, with 10 potential independent variables. A directed acyclic graph (DAG) was created to make the regression model parsimonious and clinically relevant (Figure 1). The DAG model selected the five variables: age at stroke onset, accommodation before stroke, need for assistance before stroke, previous stroke, and stroke severity at admission to hospital for minimal adjustment variables to estimate the direct effect of physical inactivity before stroke on dependency in basic ADL 3 months after stroke. Although the DAG model did not select sex, it was still entered into the model as a variable regarded as clinically important (26).

2.5.3. Fitting and evaluation of the regression models

All categorical explanatory variables were checked for ≥10 observations per outcome category. Multicollinearity between explanatory variables was studied by exploring the correlation coefficients and variance inflation factor (VIF). In the correlation analysis, the phi value was used to compare nominal variables, and Spearman's rho was used for continuous variables. A correlation of $r < \pm 0.7$ was considered as not having multicollinearity (27). A VIF coefficient of less than two was regarded as acceptable.

The regression model was evaluated using the following tests: omnibus test ($p < 0.05$, good fit), Hosmer–Lemeshow test ($p > 0.05$, good fit), and Nagelkerke R^2 test (a value closer to 1 was anticipated). The area under the receiver operating characteristic curve (AUC, a value closer to 1 was anticipated) was used to evaluate the model's ability to discriminate patients who were ADL-dependent from patients who were not. The binary logistic regression results at the variable level were evaluated with β coefficient, odds ratio (OR) with 95% confidence interval (CI), and a *p*-value. A sensitivity analysis was performed on the subgroup of patients who were fully independent before stroke.

Analyses were performed on a group of people who were physically inactive and physically active before stroke. The test variables were ADL dependence before stroke (no/yes) and 3 months after stroke (no/yes). Transition probabilities for each event were calculated. All analyses were performed using the SPSS software (IBM Corp. IBM SPSS Statistics for Windows, version 28.0. Armonk, NY). All statistical tests were two-sided at an alpha of 5%.

3. Results

In total, 3,472 patients were included in the study from the dataset that comprised 6,491 patients (Figure 2). Significant differences were found between included patients ($n = 3,472$) and excluded patients ($n = 3,019$) with more severe strokes on admission (median NIHSS score six points, $p < 0.001$), older age (median 77 years, $p < 0.001$), and more women (49%, $p < 0.01$) among the excluded patients.

Of 3,472 patients, 49% ($n = 1,712$) were physically inactive before stroke, 44 % (n = 1,521) reported light physical activity, and 7% (n = 239) reported moderate-/high-intensity physical activity and training (Table 1). Moreover, the median age of patients was 75 years, and 54% were men (Supplementary Table 1). ADL dependency before stroke was reported by 19% ($n = 311$) of the physically inactive group and 2% ($n = 30$) of the physically active group ($p < 0.001$). Patients who were dependent at the 3-month follow-up were older, with a higher proportion of physical inactivity, and had a more severe stroke than independent patients (Supplementary Table 1).

At the 3-month follow-up, dependency in basic ADL was reported by 32% ($n = 1,119$) of the patients, three times higher compared to that before stroke ($n = 342$, 10%). Patients who were dependent in basic ADL at follow-up were more often physically inactive before stroke (73%) than independent patients (38%).

The multivariable binary logistic regression analysis showed that physically inactive patients had 2.30 times higher odds for ADL dependency 3 months after stroke (OR 2.30 [95% CI 1.89–2.80]) than physically active patients. The variance of the model was 41% (Nagelkerke R square, 0.41). The regression model correctly classified 84% of the patients (AUC 0.84 [95% CI, 0.83–0.86]) as described in Table 2.

The multivariable binary logistic regression analysis on the subgroup of the patients, who were independent before stroke, showed that physically inactive patients had 2.18 times higher odds for ADL dependency 3 months after stroke (OR 2.18 [95% CI 1.79–2.66]) than physically active patients. However, the variance and classification accuracy of the model were lower compared to the full model, 30 % (Nagelkerke R square, 0.30) and 80 % (AUC 0.80 [95% CI, 0.78–0.82]), respectively (Supplementary Table 2).

3.1. Subgroup analysis

The transition probability from ADL independence before stroke to ADL dependency 3 months after stroke was 0.36 and 0.16 in patients who were physically inactive and active before stroke, respectively (Figure 3).

10.3389/fneur.2023.1094232

TABLE 1 Characteristics of the study sample stratified based on the levels of physical activity before stroke.

Characteristics	Levels of physical activity before stroke, SGPALS			
	Physically inactive	Light physical activity	Moderate/high intensity physical activity and training	*P*-value
	n = 1,712	*n* = 1,521	*n* = 239	
Age, years				<0.001#
Mean (SD)	76.1 (12.3)	71.6 (12.6)	61.5 (16.1)	
Median (IQR [min-max])	78 (16 [19–100])	73 (16 [20–99])	65 (20 [20–95])	
Sex, n (%)				<0.001
Male	810 (47)	891 (59)	177 (74)	
Female	902 (53)	630 (41)	62 (26)	
Help in ADL or instrumental activities before stroke, n (%)				<0.001
No	1,126 (71)	1,384 (95)	231 (100)	
Yes	471 (29)	75 (5)	1 (<1)	
Accommodation before stroke, n (%)				<0.001
Own accommodation without help	1,226 (72)	1,438 (95)	238 (100)	
Own accommodation with help	344 (20)	72 (5)	0 (0)	
Nursing home	*136 (8)*	10 (<1)	0 (0)	
Other	5 (<1)	0 (<1)	1 (< 1)	
Pre-morbid conditions				
Independent in basic ADL before stroke, n (%)	1,352 (81)	1,480 (98)	239 (100)	<0.001
Living alone before stroke, no, n (%)	934 (55)	563 (37)	68 (29)	<0.001
Diabetes, yes, n (%)	383 (22)	233 (15)	8 (3)	<0.001
Previous stroke, yes, n (%)	320 (19)	184 (12)	14 (6)	<0.001
Stroke type, n (%)				0.44
Hemorrhagic stroke	150 (9)	140 (9)	16 (7)	
Ischemic stroke	1,562 (91)	1,381 (91)	223 (93)	
Stroke severity at admission (NIHSS)				<0.001#
Mean (SD)	4.7 (5.6)	3.5 (5.1)	3.0 (4.7)	
Median (IQR [min-max])	3 (6 [0–29])	1 (4 [0–28])	1 (4 [0–23])	
Reperfusion treatment, n (%)				<0.001
Yes	258 (16)	290 (21)	54 (24)	
No	1,343 (84)	1,117 (79)	173 (76)	

Statistics: #Kruskal–Wallis test and chi-square test.
IQR, interquartile range; SD, standard deviation; NIHSS, National Institutes of Health Stroke Scale; SGPALS, Saltin–Grimby physical activity level scale; ADL, activities of daily living.
Variables with missing data n (%): previous stoke 9 (<1); stroke severity 176 (5); reperfusion treatment 237 (7); accommodation before stroke 2 (<1); living alone before stroke 29 (<1); need of assistance before stroke 184 (5); diabetes 4 (<1).

Furthermore, a sensitivity analysis was performed on a group of patients with no prior ADL dependency. As shown in the Sankey diagram (Figure 4), despite stroke severity, physically inactive patients showed a trend toward dependency in basic ADLs 3 months after stroke.

4. Discussion

This study showed that patients who were physically inactive before stroke had higher odds of ADL dependency 3 months after stroke. In addition, we revealed that sociodemographic factors, pre-stroke living conditions, previous stroke, and admission stroke severity were significant factors. Physically active patients have a less severe stroke (28), which may be induced by a higher cardiovascular and neuromuscular reserve (29).

Moreover, physically inactive patients were often ADL-dependent 3 months after stroke, regardless of ADL ability before stroke. Although this study emphasizes on physical inactivity, the results support seven previous studies reviewed by Victorisson et al. where an association was found between a higher level of physical activity before stroke and less post-stroke disability (12). These

TABLE 2 Results of the multivariable binary logistic regression analysis for explaining dependency in basic activities of daily living 3 months after stroke.

Explanatory variables	β (SE)	Adjusted *P*-value	Adjusted OR (95% CI)
Physically inactive before stroke (SGPALS, level 1)	0.83 (0.10)	<0.001	2.30 (1.89–2.80)
Age (range 19–100 y)	0.06 (0.01)	<0.001	1.06 (1.05–1.07)
Female sex	0.28 (0.10)	0.008	1.33 (1.09–1.61)
Ref. Own accommodation without help			
Own accommodation with help	0.62 (0.17)	<0.001	1.87 (1.34–2.62)
Nursing home	1.28 (0.32)	<0.001	3.58 (1.92–6.68)
Living alone before stroke	0.26 (0.11)	0.81	1.03 (0.84–1.26)
Need help before stroke	0.91 (0.16)	<0.001	2.49 (1.83–3.39)
Stroke severity at admission to the hospital (NIHSS, range 0–29 p)	0.31 (0.01)	<0.001	1.14 (1.12–1.16)
Previous stroke	0.45 (0.14)	0.001	1.57 (1.19–2.05)

Statistics: binary logistic regression analysis. Predicted outcome: dependency in basic activities of daily living 3 months after stroke. Missing data, n = 351.
Model evaluation metrics: Hosmer–Lemeshow test, p = 0.10; Omnibus test for the model, p <0.001; Nagelkerke R square, 0.41. The area under the receiver operating characteristic curve, 0.84 (95% CI, 0.83–0.86). SGPALS, Saltin–Grimby physical activity level scale; NIHSS, National Institutes of Health Stroke Scale; β, unstandardized regression coefficients; SE, standard error; OR, odds ratio; CI, confidence intervals.

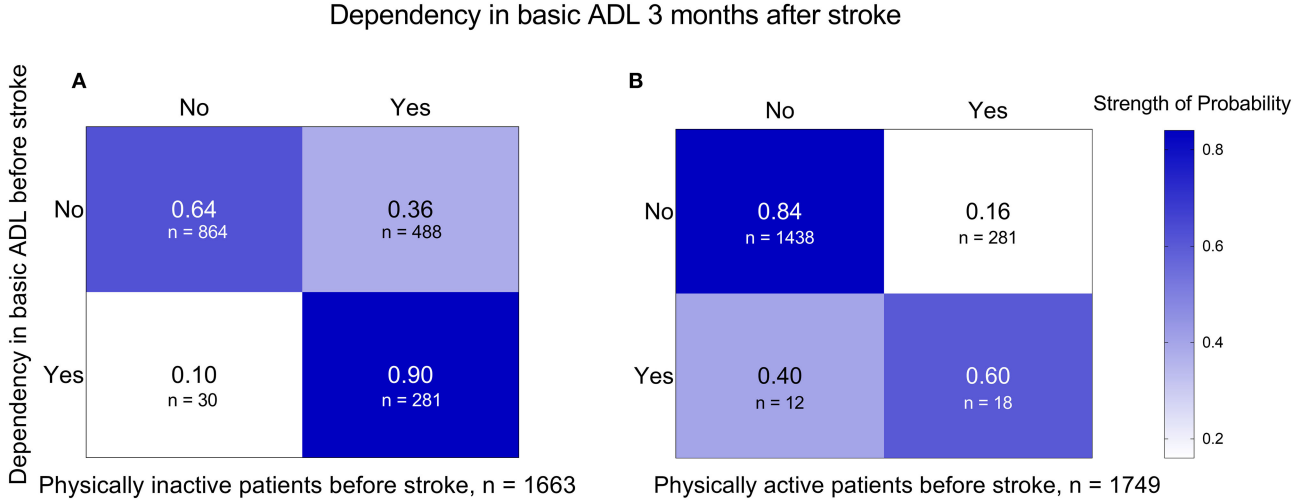


FIGURE 3
Transition probabilities from basic ADLs before stroke to basic ADLs 3 months after stroke in subgroups of patients who were physically inactive **(A)** and physically active **(B)** before stroke. ADL, activities of daily living.

findings support the hypothesis that physical inactivity before stroke is associated with ADL dependency after stroke. Nevertheless, four studies in this review reported no association (12). These conflicting results may be explained by different factors. First, the assessment scales for physical activity and ADL differed. Second, the timing of assessments varied. Third, the stroke cohorts differed in terms of their stroke characteristics.

In this study, other contributors to ADL dependency in addition to physical inactivity before stroke were sociodemographic factors, pre-stroke living conditions, previous stroke, and admission stroke severity. These results could be explained by the complexity of ADL ability considering that body functions and structures, as well as daily life engagement, can be impaired after stroke (7, 13, 30). Old age and high-stroke severity are well-known predictors of ADL dependency after stroke, confirming the results of our study (13). Moreover, female sex and previous stroke were associated with ADL dependency 3 and 12 months after stroke (24). Age and previous stroke were related to other factors in the regression model. Elderly patients and patients with comorbidities are more likely to live alone, in nursing homes, or need assistance in everyday life (31, 32). Unexpectedly, living alone before stroke was not associated with dependency 3 months after stroke. This result conflicts with a previous study that showed a positive association between living alone and ADL dependency 1 year after stroke (33).

This study has several strengths and limitations. The study was based on consecutively collected data from three stroke units. A large sample of patients had both ischemic and hemorrhagic stroke; the majority had mild strokes, and the median age was 75 years. Therefore, our sample can be assumed to be representative of the Swedish stroke population (26). However, a large number of participants were excluded from the analysis, mainly due to missing data on the primary explanatory variable and the outcome variable. This could lead to bias regarding the study sample. Therefore, the results should be interpreted with caution.

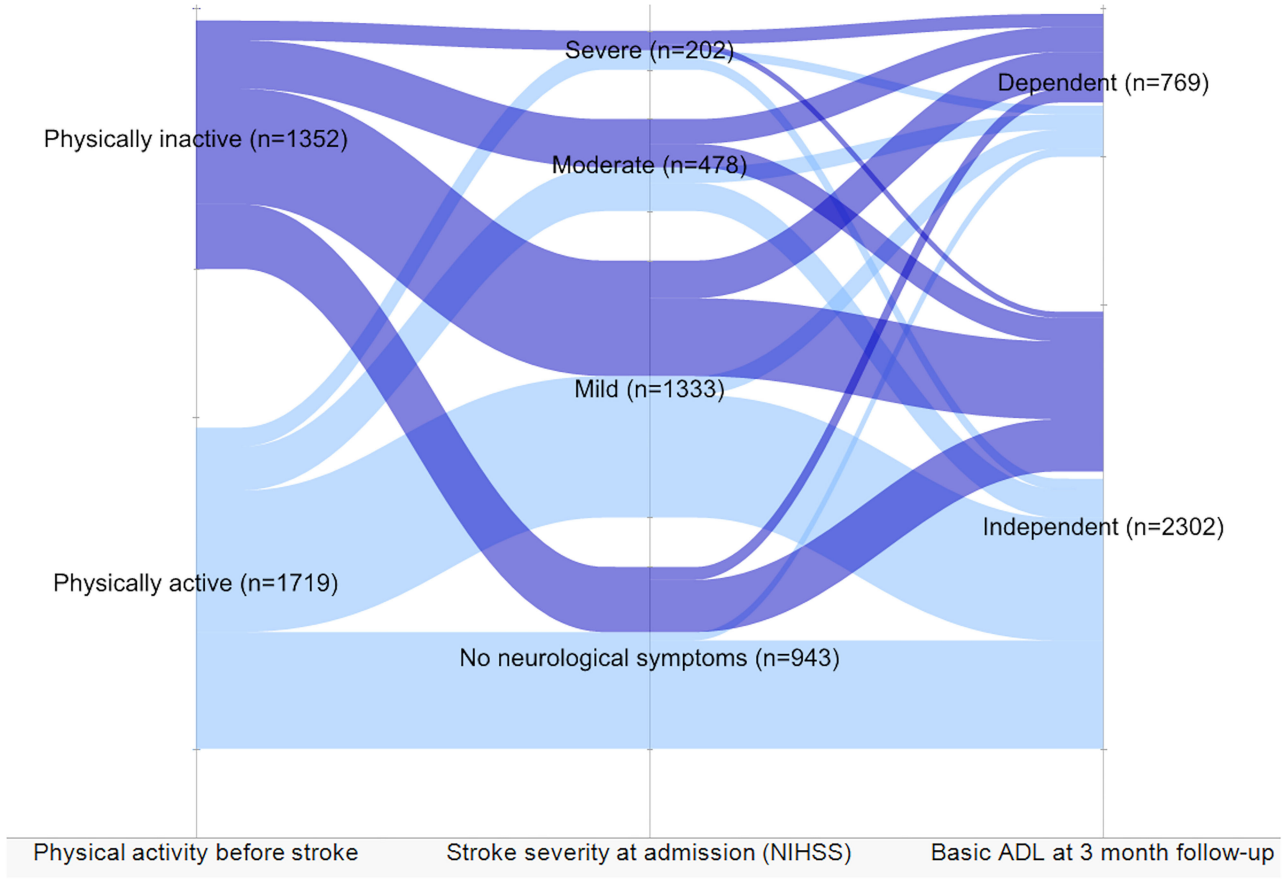


FIGURE 4
Level of dependency in activities of daily living (ADL) and stroke severity in patients independent before stroke based on the level of physical activity before stroke. The patients divided by physical activity level before stroke showed stroke severity and dependency 3 months after stroke.

The study sample comprised patients with a wide range of pre- and post-stroke conditions and abilities. However, patients without a 3-month follow-up were older and had a more severe stroke, which could have influenced their ability to answer the questionnaires. Moreover, this group included a higher proportion of patients living in nursing homes and deceased patients.

The data were collected in clinical settings and represented a combination of patient-reported information and assessments performed by trained healthcare staff at stroke units. However, retrospectively collected data are associated with recall bias, particularly in populations with an increased risk of cognitive deficit. The next of kin was contacted by healthcare staff to reduce the risk of bias.

Physical activity before stroke was evaluated using the SGPALS. Although objective measurements are considered more accurate, they are not feasible for registry-based studies. The self-reported instruments are considered reliable and feasible for large samples (11, 29). The use of self-reported data to compare the results of different studies is problematic. In addition, the study outcome was a composite measured by three basic ADL questions, which were validated and are commonly used in Riksstroke-based studies (34). There are many assessment instruments that can be used for measuring the level of dependency after stroke; however, elaborating on these instruments can be difficult in a nationwide stroke registry that collects self-reported data.

5. Conclusion

The findings of this study suggest that physical inactivity before stroke is one factor associated with dependency in basic ADL 3 months after stroke. In addition, older age, female sex, pre-stroke living conditions, need for help, previous stroke, and admission stroke severity are also significant contributors to dependency. This study supports previous findings on the importance of physical activity in preventing the negative consequences of stroke. Therefore, promoting a physically active lifestyle could be a way to reduce the burden of stroke on society. However, these findings require additional knowledge. Future studies should investigate the levels of physical activity that are beneficial in decreasing stroke-related dependency. In addition to physical activity, it is important to investigate the influence of pre-stroke sedentary behavior on stroke outcomes.

Data availability statement

The datasets presented in this article are not readily available because of ethical and privacy restrictions. Requests to access the datasets should be directed to KS, ks.sunnerhagen@neuro.gu.se.

Ethics statement

This study was approved by the Swedish Ethics Review Authority (#2021-03324, July 13, 2021). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

JS: conceptualization of the study, manuscript drafting, data analysis, and interpretation of the results. MR: data acquisition, manuscript drafting, and interpretation of the results. KS: data acquisition, conceptualization of the study, and interpretation of results. TA: conceptualization of the study, data analysis, and interpretation of the results. All authors critically revised the manuscript for intellectual content and approved the final version.

Funding

This study was funded by the Swedish Heart and Lung Foundation, Swedish state under an agreement between the Swedish government and county councils, the ALF agreement (ALFGBG-71980), the Swedish Brain Foundation, Greta and Einar Asker's Foundation, Rune and Greta Almöv's Foundation for Neurological Research, Hjalmar Svensson's Research Foundation, Doktor Felix Neubergh's Foundation, and Renée Eander's Foundation.

Acknowledgments

The authors thank the study participants, caregivers, and staff who collected and registered the data.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2023.1094232/full#supplementary-material

References

1. Barbosa PM, Ferreira LN, Cruz VT, Silva A, Szrek H. Healthcare, clinical factors and rehabilitation predicting quality of life in first-time stroke patients: a 12-month longitudinal study. *J Stroke Cerebrovasc Dis.* (2022) 31:106300. doi: 10.1016/j.jstrokecerebrovasdis.2021.106300

2. Stinear C. Prediction of recovery of motor function after stroke. *Lancet Neurol.* (2010) 9:1228–32. doi: 10.1016/S1474-4422(10)70247-7

3. Katan M, Luft A. Global burden of stroke. *Semin Neurol.* (2018) 38:208–11. doi: 10.1055/s-0038-1649503

4. Sennfält S, Ullberg T. Informal caregivers in stroke: Life impact, support, and psychological wellbeing—A Swedish Stroke Register (Riksstroke) study. *Int J Stroke.* (2020) 15:197–205. doi: 10.1177/1747493019858776

5. Wafa HA, Wolfe CD, Emmett E, Roth GA, Johnson CO, Wang Y. Burden of stroke in Europe: thirty-year projections of incidence, prevalence, deaths, and disability-adjusted life years. *Stroke.* (2020) 51:2418–27. doi: 10.1161/STROKEAHA.120.029606

6. Tan E, Gao L, Collier JM, Ellery F, Dewey HM, Bernhardt J, et al. The economic and health burden of stroke among younger adults in Australia from a societal perspective. *BMC Public Health.* (2022) 22:1–11. doi: 10.1186/s12889-021-12400-5

7. Veerbeek JM, Kwakkel G, van Wegen EE, Ket JC, Heymans MW. Early prediction of outcome of activities of daily living after stroke: a systematic review. *Stroke.* (2011) 42:1482–8. doi: 10.1161/STROKEAHA.110.604090

8. Feigin VL, Stark BA, Johnson CO, Roth GA, Bisignano C, Abady GG, et al. Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Neurol.* (2021) 20:795–820. doi: 10.1016/S1474-4422(21)00252-0

9. Kohl HW. 3rd, Craig CL, Lambert EV, Inoue S, Alkandari JR, Leetongin G, et al. The pandemic of physical inactivity: global action for public health. *Lancet.* (2012) 380:294–305. doi: 10.1016/S0140-6736(12)60898-8

10. Bull FC, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *Br J Sports Med.* (2020) 54:1451–62. doi: 10.1136/bjsports-2020-102955

11. Kramer SF, Hung SH, Brodtmann A. The impact of physical activity before and after stroke on stroke risk and recovery: a narrative review. *Curr Neurol Neurosci Rep.* (2019) 19:1–9. doi: 10.1007/s11910-019-0949-4

12. Viktorisson A, Reinholdsson M, Danielsson A, Palstam A, Sunnerhagen KS. Pre-stroke physical activity in relation to post-stroke outcomes–linked to the International Classification of Functioning, Disability and Health (ICF): a scoping review. *J Rehabil Med.* (2022) 54:jrm00244. doi: 10.2340/jrm.v53.51

13. Kwakkel G, Kollen B. Predicting activities after stroke: what is clinically relevant? *Int J Stroke.* (2013) 8:25–32. doi: 10.1111/j.1747-4949.2012.00967.x

14. Sennfalt S, Pihlsgard M, Norrving B, Ullberg T, Petersson J. Ischemic stroke patients with prestroke dependency: Characteristics and long-term prognosis. *Acta Neurol Scand.* (2021) 143:78–88. doi: 10.1111/ane.13328

15. Harvey RL. Predictors of functional outcome following stroke. *Phys Med Rehabil Clin N Am.* (2015) 26:583–98. doi: 10.1016/j.pmr.2015.07.002

16. Prabhakaran S, Ruff I, Bernstein RA. Acute stroke intervention a systematic review. *Jama-J Am Med Assoc.* (2015) 313:1451–62. doi: 10.1001/jama.2015.3058

17. Reid JM, Gubitz GJ Dai D, Kydd D, Eskes G, Reidy Y, et al. Predicting functional outcome after stroke by modelling baseline clinical and CT variables. *Age Ageing.* (2010) 39:360–6. doi: 10.1093/ageing/afq027

18. Redfors P, Isaksen D, Lappas G, Blomstrand C, Rosengren A, Jood K, et al. Living alone predicts mortality in patients with ischemic stroke before 70 years of age: a long-term prospective follow-up study. *BMC Neurol.* (2016) 16:80. doi: 10.1186/s12883-016-0599-y

19. Asplund K, Asberg KH, Appelros P, Bjarne D, Eriksson M, Johansson A, et al. The Riks-Stroke story: building a sustainable national register for quality assessment of stroke care. *Int J Stroke.* (2011) 6:99–108. doi: 10.1111/j.1747-4949.2010.00557.x

20. Vandenbroucke JP, Elm Ev, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Ann Intern Med.* (2007) 147:W-163-W-94. doi: 10.7326/0003-4819-147-8-200710160-00010-w1

21. Saltin B, Grimby G. Physiological analysis of middle-aged and old former athletes: comparison with still active athletes of the same ages. *Circulation.* (1968) 38:1104–15. doi: 10.1161/01.CIR.38.6.1104

22. Grimby G, Börjesson M, Jonsdottir I, Schnohr P, Thelle D, Saltin B. The "Saltin–Grimby physical activity level scale" and its application to health research. *Scand J Med Sci Sports.* (2015) 25:119–25. doi: 10.1111/sms.12611

23. Rodjer L, Jonsdottir IH, Rosengren A, Bjorck L, Grimby G, Thelle DS, et al. Self-reported leisure time physical activity: a useful assessment tool in everyday health care. *BMC Public Health.* (2012) 12:693. doi: 10.1186/1471-2458-12-693

24. Ullberg T, Zia E, Petersson J, Norrving B. Changes in functional outcome over the first year after stroke an observational study from the Swedish Stroke Register. *Stroke.* (2015) 46:389–94. doi: 10.1161/STROKEAHA.114.006538

25. Kasner SE. Clinical interpretation and use of stroke scales. *Lancet Neurol.* (2006) 5:603–12. doi: 10.1016/S1474-4422(06)70495-1

26. Eriksson M, Åsberg S, Sunnerhagen KS, von Euler M, Collaboration R. Sex differences in stroke care and outcome 2005–2018: Observations from the Swedish Stroke Register. *Stroke.* (2021) 52:3233–42. doi: 10.1161/STROKEAHA.120.033893

27. Daniel WW, Cross CL. *Biostatistics: Basic Concepts and Methodology for the Health Sciences.* Hoboken, NJ: Wiley. (2017).

28. Reinholdsson M, Palstam A, Sunnerhagen KS. Prestroke physical activity could influence acute stroke severity (part of PAPSIGOT). *Neurology.* (2018) 91:e1461–e7. doi: 10.1212/WNL.0000000000006354

29. Stroud N, Mazwi TML, Case LD, Brown RD, Brott TG, Worrall BB, et al. Prestroke physical activity and early functional status after stroke. *J Neurol Neurosur Ps.* (2009) 80:1019–22. doi: 10.1136/jnnp.2008.170027

30. Wurzinger H, Abzhandadze T, Rafsten L, Sunnerhagen KS. Dependency in activities of daily living during the first year after stroke. *Front Neurol.* (2021) 12:736684. doi: 10.3389/fneur.2021.736684

31. Kjörk EK, Gustavsson M, El-Manzalawy N, Sunnerhagen KS. Stroke-related health problems and associated actions identified with the post-stroke checklist among nursing home residents. *BMC Cardiovasc Disord.* (2022) 22:1–9. doi: 10.1186/s12872-022-02466-3

32. Sennfalt S, Pihlsgard M, Petersson J, Norrving B, Ullberg T. Long-term outcome after ischemic stroke in relation to comorbidity - an observational study from the Swedish Stroke Register (Riksstroke). *Eur Stroke J.* (2020) 5:36–46. doi: 10.1177/2396987319883154

33. Ursin MH, Ihle-Hansen H, Fure B, Tveit A, Bergland A. Effects of premorbid physical activity on stroke severity and post-stroke functioning. *J Rehabil Med.* (2015) 47:612–7. doi: 10.2340/16501977-1972

34. Palmcrantz S, Sommerfeld DK. Development and validation of the Swedish national stroke register Riksstroke's questionnaires in patients at 3 and 12 months after stroke: a qualitative study. *BMJ Open.* (2018) 8:e018702. doi: 10.1136/bmjopen-2017-018702

frontiers | Frontiers in Neurology

TYPE Original Research
PUBLISHED 23 February 2023
DOI 10.3389/fneur.2023.1078251

OPEN ACCESS

EDITED BY
Michael V. Mazya,
Karolinska University Hospital, Sweden

REVIEWED BY
Birgitta Langhammer,
Oslo Metropolitan University, Norway
Steven Kittner,
University of Maryland, United States

*CORRESPONDENCE
Lan Xu
✉ xulan1108@sina.com

†These authors have contributed equally to this work and share first authorship

SPECIALTY SECTION
This article was submitted to Stroke, a section of the journal Frontiers in Neurology

RECEIVED 24 October 2022
ACCEPTED 31 January 2023
PUBLISHED 23 February 2023

CITATION
Pan X, Wang Z, Yao L and Xu L (2023) The reasons for not returning to work and health-related quality of life among young and middle-aged patients with stroke: A cross-sectional study.
Front. Neurol. 14:1078251.
doi: 10.3389/fneur.2023.1078251

The reasons for not returning to work and health-related quality of life among young and middle-aged patients with stroke: A cross-sectional study

Xi Pan[1†], Zhi Wang[1†], Lin Yao[2] and Lan Xu[2*]

[1]Department of Neurology, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu, China, [2]Nursing Department, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu, China

Objectives: This study aimed to explore the reasons and influencing factors for non-return to work (non-RTW) within 1 year among young and middle-aged patients with stroke and to assess their health-related quality of life (HRQoL) at 1 year across different reasons.

Methods: The study was conducted as a telephone-based cross-sectional survey. Seven hundred eighty-nine young and middle-aged patients with stroke aged between 18 and 54 years for men and 18 and 49 years for women in the electronic medical system were included. Data collection included demographic characteristics, socioeconomic status, behavioral habits, history of chronic diseases, work status, reasons for non-RTW, and HRQoL.

Results: Of 789 patients, 435 (55.1%) (mean [SD] age, 47.7 [7.8] years) did not return to work within 1 year after stroke. Among the patients who did not RTW, 58.9% were unable to work, 9.7% retired early, 11.03% became full-time homemakers or were unemployed, and 20.5% were reluctant to work. The disordered multiclass logistic regression model showed that the factors influencing the reasons for non-RTW included age, gender, education, income, health insurance, diabetes comorbidity, ability to perform activities of daily living, and mobility of the right upper extremity. Furthermore, patients who were unable to work had significantly lower HRQoL compared to those who had RTW, followed by those who retired early.

Conclusions: More than half did not RTW within 1 year in our study. The results will help inform future research to identify interventions to promote RTW and improve HRQoL for young and middle-aged patients with stroke.

KEYWORDS

young and middle-aged stroke, non-return to work, factor, quality of life, category, patient-reported outcomes

1. Introduction

Recent data show that the incidence of stroke is increasing among young and middle-aged people and is highest in Asians compared to that in other ethnic groups (1, 2). According to reports, nearly 40% of patients with stroke are of working age, an age group whose specific social characteristics dictate a higher willingness to return to work (RTW) after a stroke (3). RTW is the primary goal of the rehabilitation process for most working-age patients (4), and it is closely related to the patient's quality of life, physical and mental health, subjective wellbeing, and life satisfaction (5).

Unfortunately, it can be challenging for stroke sufferers to return to work (6). Several studies have demonstrated that with proper rehabilitation, most young and middle-aged post-stroke survivors can achieve functional independence and high activity levels (1, 7). Nevertheless, the proportion of patients with stroke who do not return to work ranges from 25 to 50% (8–10). Exploring the reasons for non-RTW among young and middle-aged patients with stroke and the associated factors require clinical practice by identifying the types of non-RTW that may occur in different patients and that can be improved through rehabilitation (4, 11, 12). Although previous research has explored the factors impacting non-RTW after stroke, such as gender and advanced age (8–10), most studies have evaluated non-RTW as a whole and cannot differentiate between various non-RTW types and their associated factors. However, some qualitative studies have been conducted to explore the related causes and influencing factors (4, 11), but the researchers' opinions and thoughts may introduce bias in interpreting the results, resulting in a lack of objectivity and the inability to identify relevant influencing factors.

To the best of our knowledge, no specific study has been conducted that quantitatively describes the reason for non-RTW following stroke, and its associated factors are mainly unclear. In addition, it is uncertain whether the reported reasons for non-RTW are related to health-related quality of life (HRQoL). Therefore, the aims of this study were to (1) quantify reasons for non-RTW among young and middle-aged patients with stroke; (2) identify factors predicting different reasons for non-RTW, focusing mainly on sociodemographic and clinical characteristics factors; and (3) investigate the impact of different reasons for non-RTW on HRQoL.

2. Methods

The study was conducted as a telephone-based cross-sectional survey. The central review committee of the First Affiliated Hospital of Soochow University approved the study protocol (No. 2022025).

2.1. Participants

All patients were admitted to our neurology department between 1 July 2020 and 1 July 2021, with a diagnosis of a first-time stroke. From July 2021 to July 2022, young and middle-aged patients with stroke who had been discharged from the electronic medical system for 1 year were eligible to be surveyed by telephone. Of the 1,136 patients recorded in the electronic medical record system, 789 patients were included in this study based on the following criteria: (i) first stroke, (ii) the diagnosis of stroke (hemorrhage stroke, ischemic stroke, or hemorrhagic stroke combined with ischemic stroke), (iii) working age (18–59 years for men and 18–54 years for women) at the stroke onset, and (iv) active employment status (full-time or part-time competitive employment, or self-employment) at the stroke onset. We excluded patients who had stopped working before the onset and those with other critical illnesses, such as heart failure, respiratory failure, malignant tumors, severe trauma, and other acute diseases.

2.2. Data collection

A trained research assistant administered the telephone survey to participants over the phone. After obtaining verbal consent, a 20-min telephone survey was conducted.

Patient characteristics included baseline demographic characteristics (age, gender, and marital status), socioeconomic status (per capita monthly household income and education level), behavioral habits (smoking and alcohol consumption), history of comorbid chronic diseases (hypertension, diabetes, dyslipidemia, coronary heart disease, and atrial fibrillation), the stroke type, the degree of functional dependence at discharge, limb muscle strength, stroke complications (dysarthria, visual deficiency, swallowing disturbances, reduced bladder control, and sensory disturbances), and the occupational type before the onset. Among them, demographic characteristics, the history of comorbid chronic diseases, the stroke type, the degree of functional dependence at discharge, limb muscle strength, and stroke complications were obtained from the electronic medical record. Moreover, socioeconomic status, behavioral habits, and occupational type before the onset was obtained during the 20-min interview.

Age was categorized into 25–34, 35–44, and 45–55. The education level was categorized into primary school (Elementary school and below), junior high school, secondary school, or college and above. Family per capita monthly income (income level), which is equal to family income divided by the number of family members, was categorized as "<1000," "1001–3000," "3001–5000," and ">5000." The degree of functional dependence is scored according to the activities of daily living (ADL) scale: 100 points mean no dependence, 60–99 points mean mild dependence, 40–60 points mean moderate dependence, and <40 points mean severe dependence. The muscle strength of the left upper limb, the right upper limb, the left lower limb, and the right lower limb was evaluated with a clinical examination (levels 0–5). If the muscle strength of the limb is below grade 4, the limb is considered dysfunctional.

2.3. Outcome

The outcome of this study was RTW after stroke, defined as active employment at the former or new occupation (full-time or part-time competitive job, or self-employment) based on these follow-up questions: (i) "Have you been able to return to work?"; (ii) "Have you changed work?"; (iii) "What is the reason for changing work?"; and (iv) "What is your reason for not returning to work?" Patients who did not return to work within 12 months were classified as non-RTW for the following reasons: (1) unable to work (if the patient reports being unable to work due to physical dysfunction), (2) early retirement (if a patient reported retiring after stroke but had not yet reached retirement age), (3) full-time homemaker or unemployed (if a patient reported becoming a full-time homemaker or being laid off after stroke), and (4) reluctance to work (if a patient reported being unable to return to work due to other reasons such as work stress, the new crown epidemic, their children's demands, or for unspecified reasons).

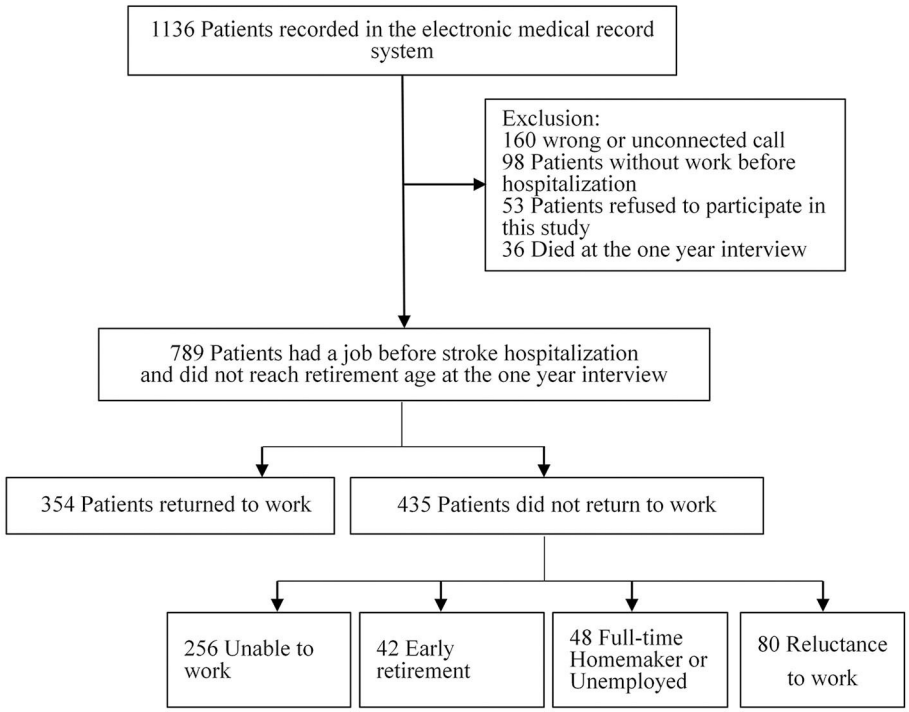


FIGURE 1
Flowchart of patient enrollment.

An additional outcome variable was health-related quality of life (HRQoL), which was measured using the health utility value of EQ-5D-5L (13), which is comprised of a five-level descriptive health classifier questionnaire and a visual analog scale (EQ-VAS). The descriptive questionnaire evaluates five dimensions (5D): mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. There are five response levels (5L) for each size, ranging from no problems to extreme problems. Using the latest EQ-5D-5L health utility value conversion table based on the Chinese population, the EQ-5D-5L health status was converted into health utility values to describe the respondents' HRQoL. The health utility values range from −0.391 to 1, with zero denoting death, one representing perfect health, and negative values indicating that the current health state is worse than death. The health dimensions of the EQ-5D-5L were dichotomized into "no limitations" ("no problems") and "limitations" (from "slight problems" to "unable"). The Cronbach's coefficient was 0.761 in the study.

2.4. Statistical analysis

This study used descriptive statistics such as mean, standard deviation, and frequency to describe the demographic characteristics and reasons for RTW and HRQoL variables. The chi-square test was used to compare patient characteristics between the RTW and four non-RTW groups. We fitted a disordered multiclass logistic regression model to evaluate the association between patient characteristics and the four reasons for non-RTW, with RTW as the reference. Furthermore, descriptive statistics for the EQ-5D dimensions, EQ-5D index, and EQ-VAS were calculated. Differences in the distribution of continuous variables over different categorical groups were evaluated using the Kruskal–Wallis test, and where differences were detected, Dunn's test was used for pairwise comparisons. For nominal variables, a chi-square test was used as applicable. All statistical tests were performed using a two-sided α value of 0.05. Analyses were conducted using SPSS, version 22.0.

3. Results

3.1. Baseline patient characteristics

The final study sample included 1,136 patients in the electronic medical record system (Figure 1). Among the 789 patients, 576 (73.0%) were men, and 740 (93.8%) were patients with ischemic stroke, 153 (19.4%) had a college degree or higher, 169 (21.4%) were physical workers. The mean (SD) age of these patients was 47.68 (7.8) years; 647 (82.0%) were aged 40 years or older. The six common chronic diseases in the population were hypertension (456 [57.8%]), diabetes (160 [20.3%]), dyslipidemia (18 [2.3%]), atrial fibrillation (19 [2.4%]), coronary heart disease (17 [2.2%]), and kidney disease (13 [1.7%]). The five common dysfunctions owing to stroke were dysarthria (155 [19.7%]), visual deficiency (19 [2.4%]), dysphagia (45 [5.7%]), reduced bladder control (24 [3.0%]), and sensory disturbance (108 [13.7%]) (Table 1).

10.3389/fneur.2023.1078251

TABLE 1 Distribution and comparison of reasons for non-RTW among young and middle-aged patients with stroke.

Variable	Return to work ($n = 354$)	Unable to work ($n = 256$)	Early retirement ($n = 42$)	Full-time homemaker or unemployed ($n = 48$)	Reluctance to work ($n = 89$)	*P*
Age at onset						0.000*
18–30	12 (70.6)	1 (5.9)	0 (0.0)	2 (11.8)	2 (11.8)	
30–40	68 (62.4)	23 (21.1)	1 (0.9)	5 (4.6)	12 (11.0)	
40–50	150 (56.6)	77 (29.1)	3 (1.1)	16 (6.0)	19 (7.2)	
50	124 (31.2)	165 (41.5)	37 (9.3)	25 (6.3)	47 (11.8)	
Gender						0.000*
Male	286 (49.7)	191 (33.2)	27 (4.7)	23 (4.0)	49 (8.5)	
Female	68 (31.9)	76 (35.2)	14 (6.6)	24 (11.7)	31 (14.6)	
Education						0.000*
Elementary school and below	36 (28.1)	54 (42.2)	4 (3.1)	16 (12.5)	18 (14.1)	
Junior high school	122 (38.5)	131 (41.0)	19 (6.0)	19 (6.3)	26 (8.2)	
High school/secondary school	95 (54.3)	49 (28.0)	11 (6.3)	7 (4.0)	13 (7.4)	
College and above	95 (62.1)	27 (17.7)	6 (3.9)	4 (2.6)	21 (13.7)	
Family per capita monthly income						0.000*
<1000	5 (13.9)	22 (61.1)	0 (0.0)	5 (13.9)	4 (11.1)	
1001–3000	47 (30.7)	66 (43.1)	7 (4.6)	16 (10.5)	17 (11.1)	
3001–5000	132 (50.0)	81 (30.3)	15 (5.7)	15 (5.7)	22 (8.3)	
>5000	131 (57.7)	62 (27.3)	6 (2.6)	5 (2.2)	23 (10.1)	
Medical insurance	277 (48.2)	176 (30.6)	30 (5.2)	35 (6.1)	57 (9.9)	0.018*
Prior smoking	73 (52.9)	48 (34.8)	5 (3.6)	6 (4.1)	6 (4.4)	0.050
Prior drinking	45 (45.9)	42 (42.9)	4 (4.1)	1 (1.0)	6 (6.1)	0.048*
Stroke type						0.093
Ischemic	340 (46.0)	240 (32.3)	39 (5.3)	45 (6.2)	76 (10.3)	
Hemorrhagic	14 (30.4)	24 (52.2)	2 (4.4)	2 (4.4)	4 (8.7)	
Mixed	0 (0)	3 (100)	0 (0.0)	0 (0.0)	0 (0.0)	
Chronic diseases						
Hypertension	183 (40.1)	181 (39.7)	26 (5.7)	26 (5.7)	40 (8.8)	0.001*
Diabetes	54 (33.8)	61 (38.1)	15 (9.4)	15 (9.4)	15 (9.4)	0.002*
Dyslipidemia	13 (72.2)	2 (11.1)	0 (0.0)	2 (11.1)	1 (5.6)	0.090
Atrial fibrillation	9 (47.4)	7 (36.8)	1 (5.3)	1 (5.3)	1 (5.3)	0.968
Coronary heart disease	5 (29.4)	7 (41.2)	2 (11.8)	2 (11.8)	1 (5.9)	0.414
Kidney disease	5 (38.5)	6 (46.2)	1 (7.7)	0 (0.0)	1 (7.7)	0.784
Daily life dependence						0.000*
No dependency	246 (58.9)	84 (20.1)	23 (5.5)	23 (5.5)	42 (10.1)	
Mild dependence	71 (35.0)	84 (41.4)	9 (4.4)	16 (7.9)	23 (11.3)	
Moderate dependence	24 (35.8)	28 (40.3)	4 (6.0)	4 (7.5)	7 (10.5)	
Heavy dependence	13 (12.9)	71 (70.3)	5 (5.0)	4 (4.0)	8 (7.9)	
LU extremity dysfunction	15 (18.8)	51 (63.8)	4 (5.0)	5 (6.3)	5 (6.3)	0.000*
LL extremity dysfunction	9 (15.5)	38 (65.5)	3 (5.2)	3 (5.2)	5 (8.6)	0.000*

(Continued)

TABLE 1 (Continued)

Variable	Return to work ($n = 354$)	Unable to work ($n = 256$)	Early retirement ($n = 42$)	Full-time homemaker or unemployed ($n = 48$)	Reluctance to work ($n = 89$)	*P*
RU extremity dysfunction	7 (8.9)	57 (72.2)	6 (7.6)	2 (2.5)	7 (8.9)	0.000*
RL extremity dysfunction	4 (6.7)	48 (80.0)	3 (5.0)	2 (3.3)	3 (5.0)	0.000*
Dysarthria	43 (27.7)	83 (53.6)	4 (2.6)	5 (3.2)	20 (12.9)	0.000*
Visual deficiency	7 (36.8)	6 (31.6)	2 (10.5)	1 (5.3)	3 (15.8)	0.735
Dysphagia	8 (17.8)	33 (73.3)	0 (0.0)	2 (4.4)	2 (4.4)	0.000*
Reduced bladder control	3 (12.5)	20 (83.3)	1 (4.2)	0 (0.0)	0 (0.0)	0.000*
Sensory disturbance	40 (37.0)	44 (40.7)	3 (2.8)	7 (6.5)	14 (13.0)	0.205
Pre-stroke occupation						0.001*
Non-physical	102 (67.6)	30 (19.2)	5 (3.3)	2 (2.0)	12 (8.0)	
Physical	98 (58.0)	48 (28.4)	1 (0.6)	8 (4.7)	14 (8.3)	
Combination	146 (50.5)	96 (33.2)	16 (5.5)	17 (5.9)	14 (4.8)	

*P-value < 0.05.

TABLE 2 Work status within 1 year among young and middle-aged patients with stroke ($n = 789$).

Work status	$n = 789$
RTW	354 (44.9)
Returned to their original work	291 (36.9)
Changed work owing to stroke	37 (4.7)
Changed work owing to other reasons	26 (3.3)
Non-RTW	435 (55.1)
Unable to work	256 (32.5)
Early retirement	42 (5.2)
Full-time homemakers or were unemployed	48 (6.1)
Reluctance to work	89 (11.3)

RTW, return to work.

3.2. Non-return to work

In total, 354 patients (44.9%) returned to work within 1 year after discharge from a stroke. Among them, 291 patients (36.9%) returned to their original work, 37 patients (4.7%) changed work owing to stroke, and 26 patients (3.3%) changed work for other reasons. Among the 435 patients who did not RTW, 256 (32.5%) were unable to work owing to stroke, 42 (5.2%) retired early owing to stroke, 48 (6.1%) became full-time homemakers or were unemployed, and 89 (11.3%) showed reluctance to work (Table 2).

3.3. Factors for non-return to work

Baseline data showed that factors influencing the reason for non-RTW included age at onset, gender, education level, per capita monthly household income, medical insurance, hypertension, diabetes mellitus, daily life dependence, the muscle strength of the four limbs, and pre-stroke occupation (Table 1). Furthermore, with different reasons for non-RTW as dependent variables (with RTW as the control) and variables with statistical significance in the univariate analysis as independent variables, an unordered multiclass logistic regression analysis was performed. The multinomial logistic regression modeling results are presented in Table 3. Younger patients are less likely to be unable to work and retire earlier than older patients. Patients aged 40–50 years were less likely than those aged 50 years or older to be reluctant to work (odds ratio [OR], 0.371; 95% CI, 0.142–0.966). Female patients were more likely than male patients to be at home full time (OR, 2.793; 95% CI, 1.054–7.403) and to be reluctant to work (OR, 2.433; 95% CI, 1.037–5.710). The likelihood of being unable to work decreases as education increases (OR, 0.687; 95% CI, 0.514, 0.919). As monthly per capita household income increases, the possibility of being unable to work (OR, 0.684; 95% CI, 0.505–0.926) and being at home full time (OR, 0.433; 95% CI, 0.244–0.767) decreases. Patients with medical insurance were less likely to be unable to work (OR, 0.511; 95% CI, 0.296–0.882), to retire early (OR, 0.249; 95% CI, 0.079–0.787), and to be reluctant to work (OR, 0.284; 95% CI, 0.125–0.646) than those without medical insurance. Patients with diabetes were more likely to choose early retirement than those without diabetes (OR, 4.585; 95% CI, 1.459–14.404). The likelihood of being unable to work increases as the dependence on daily life increases (OR, 1.630; 95% CI, 1.273–2.087). Patients who cannot lift their right upper limb are more likely to be unable to work (OR, 8.174; 95% CI, 2.409–27.733) and to retire early (OR, 26.894; 95% CI, 2.853–253.551) than those who can lift their right upper limb. Dysphagia, dysarthria, dysuria, and sensory disorder after a stroke had no significant effect on the reasons for non-RTW (Table 3). Figure 2 summarizes Table 3, a visualization of the statistically significantly associated variables with at least one of the four non-RTW reasons.

TABLE 3 Factors of reasons for non-RTW: Multinomial logistic regression (vs. RTW).

	Unable to work		Early retirement		Full-time Homemaker or Unemployed		Reluctance to work	
Variable	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Age at onset								
18-30	€	0.997	-	-	2.18 (0.18, 26.35)	0.540	0.00 (0.00, 0.00)	-
30-40	0.30 (0.14, 0.66)	0.003	0.05 (0.01, 0.43)	0.007	0.67 (0.15, 2.90)	0.587	0.61 (0.21, 1.77)	0.362
40-50	0.43 (0.25, 0.73)	0.002	0.04 (0.01, 0.33)	0.003	0.78 (0.28, 2.17)	0.632	0.37 (0.14, 0.97)	0.042
50	Ref	-	Ref		Ref		Ref	
Female	1.66 (0.93, 2.96)	0.089	3.11 (0.94, 10.49)	0.064	2.79 (1.05, 7.40)	0.039	2.43 (1.04, 5.71)	0.041
Education	0.69 (0.51, 0.92)	0.011	1.25 (0.67, 2.32)	0.484	0.58 (0.33, 1.04)	0.066	1.01 (0.61, 1.66)	0.974
Family per capita monthly income	0.68 (0.51, 0.93)	0.014	1.07 (0.51, 2.21)	0.864	0.43 (0.24, 0.77)	0.004	0.99 (0.59, 1.66)	0.959
Medical insurance	0.51 (0.30, 0.88)	0.016	0.25 (0.08, 0.79)	0.018	0.52 (0.19, 1.42)	0.199	0.28 (0.13, 0.65)	0.003
Prior drinking	0.93 (0.45, 1.93)	0.841	2.58 (0.55, 12.18)	0.231	0.44 (0.05, 3.75)	0.451	0.51 (0.11, 2.45)	0.397
Hypertension	1.29 (0.78, 2.11)	0.323	0.49 (0.17, 1.47)	0.204	0.91 (0.36, 2.32)	0.845	0.64 (0.29, 1.42)	0.272
Diabetes	1.25 (0.68, 2.29)	0.472	4.59 (1.46, 14.40)	0.009	1.78 (0.62, 5.19)	0.285	1.21 (0.41, 3.56)	0.731
Daily life dependence	1.63 (1.27, 2.09)	0.000	0.93 (0.43, 2.03)	0.855	1.27 (0.80, 2.03)	0.316	1.31 (0.84, 2.03)	0.232
LU extremity dysfunction	3.16 (0.94, 10.66)	0.064	0.68 (0.01, 43.00)	0.855	6.58 (0.95, 45.42)	0.056	0.57 (0.02, 13.33)	0.725
LL extremity dysfunction	0.72 (0.15, 3.51)	0.680	18.04 (0.24, 1386.92)	0.192	0.49 (0.04, 6.37)	0.585	1.62 (0.06, 44.40)	0.775
RU extremity dysfunction	8.17 (2.41, 27.73)	0.001	26.89 (2.85, 253.55)	0.004	6.83 (0.77, 60.32)	0.084	3.68 (0.44, 31.02)	0.231
RL extremity dysfunction	1.60 (0.33, 7.76)	0.561	0.00 (0.00, -)	0.997	0.86 (0.04, 18.04)	0.923	0.97 (0.06, 16.93)	0.981
Dysarthria	1.31 (0.67, 2.55)	0.427	0.50 (0.05, 4.64)	0.541	0.73 (0.16, 3.29)	0.677	1.20 (0.36, 4.01)	0.773
Dysphagia	0.78 (0.20, 3.13)	0.728	0.00 (0.00, -)	0.998	1.79 (0.18, 18.00)	0.621	0.00 (0.00, .c)	0.998
Reduced bladder control	1.70 (0.27, 10.87)	0.577	0.00 (0.00, -)	0.999	0.00 (0.00, 0.00)	-	0.00 (0.00, -)	0.998
Pre-stroke occupation								
Non-physical	Ref		Ref		Ref		Ref	
Physical	1.70 (0.87, 3.34)	0.120	1.96 (0.49, 7.80)	0.343	2.19 (0.54, 8.94)	0.274	0.86 (0.30, 2.46)	0.782
Combination	0.85 (0.38, 1.87)	0.683	0.11 (0.01, 1.63)	0.109	0.75 (0.14, 4.04)	0.739	0.97 (0.274, 3.40)	0.957

€: Not analyzed because cell size <5; OR, odds ratio; CI, confidence interval; RTW, return to work.

10.3389/fneur.2023.1078251

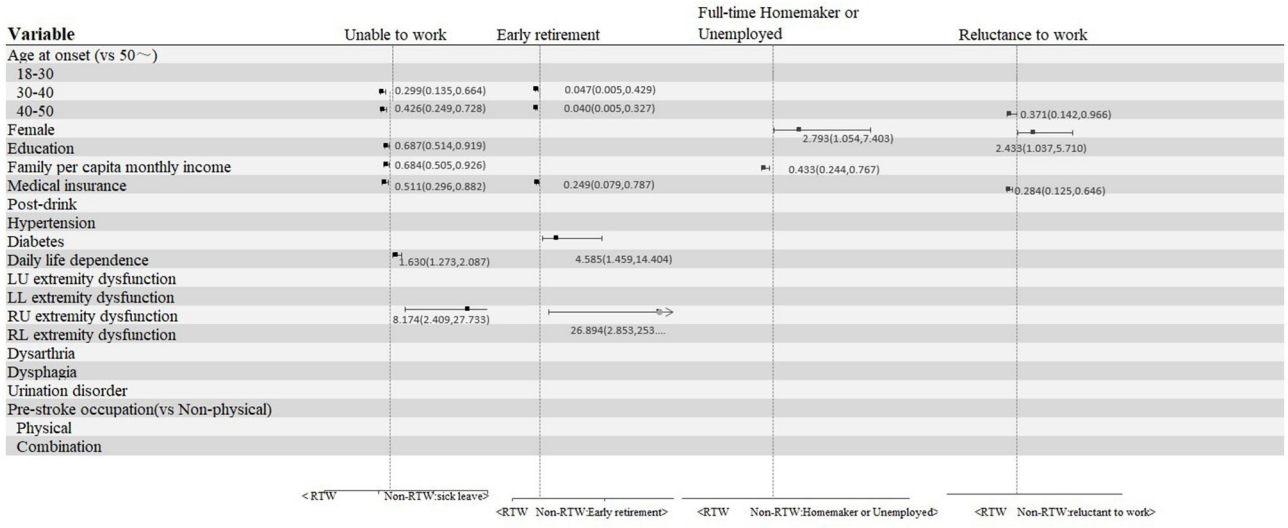


FIGURE 2
Variables statistically significantly associated with at least one of the four non-RTW reasons.

3.4. Health-related quality of life in the non-RTW groups

The most prominent problem in the "unable to work" group was the usual activities (38.94%). The most significant problem in the "early retirement" group was mobility (31.71%). In the other three groups, including those who had returned to work, the most prominent problem was pain/discomfort (13.38, 17.50, and 14.49%), as shown in Figure 3. Compared to patients who had RTW, those who were unable to work reported higher rates of health problems in all dimensions of the EQ-5D-5L; those who retired early reported higher rates of health problems in the mobility, self-care, and usual activities dimensions (30.95, 16.67, and 19.05%); and those who were reluctant to work reported the higher rates of health problems in the self-care dimension (6.74%). When stratified by gender, male patients had similar rates of health problems as the overall population, while female patients who were unable to work had higher rates of health problems in the mobility, self-care, and usual activities dimensions (36.84, 28.95, and 36.84%). Female patients who retired early had higher rates of health problems in their usual activities (14.29%). Female patients who were reluctant to work had an increased proportion of self-care health problems (16.13%) (Table 4). Furthermore, compared to patients who had RTW, patients who were unable to work had significantly lower EQ-5D index and EQ-5D VAS ($P < 0.05$), male patients who retired early had significantly lower EQ-5D index and EQ-5D VAS ($P < 0.05$), and female patients who retired early had significantly lower EQ-5D VAS ($P < 0.05$). There was no significant difference between the female patients who were reluctant to work and those who were unable to work in terms of the EQ-5D score. Male patients who were full-time homemakers or unemployed had the second-lowest EQ-5D VAS, behind those who were unable to work and those who retired early, although the difference was not statistically significant (Table 5; Figures 4, 5).

4. Discussion

We found that more than half of previously employed individuals did not return to work within 1 year of being hospitalized for a stroke. Among those who were non-RTW, 32.45% were unable to work due to health reasons, 5.23% retired early, 6.08% were full-time homemakers or were unemployed, and 11.28% were reluctant to work. Moreover, our study explored various demographic, socioeconomic, and clinical factors associated with reasons for non-RTW, which the association may be informative when planning interventions for recovery after stroke. Furthermore, the HRQoL of patients who were unable to work was significantly lower than those who had RTW, followed by those who retired early. In addition, female patients who were reluctant to work had a lower EQ-5D index second only to those who were unable to work, which may be related to a higher rate of limitations with self-care. Similarly, male patients who were unable to work, retired early, and stayed at home full time had lower EQ-5D VAS.

In the present study, <50% of patients with stroke returned to work within 1 year after discharge from the hospital. This rate is relatively lower compared to other countries, where rates have ranged between 50 and 75% over the past two decades (8–10). Several factors may explain this observation. First, the accessibility of post-stroke rehabilitation services in China is poor, and the vocational rehabilitation system is not well developed (14). Vocational rehabilitation can effectively facilitate the RTW of patients with stroke, improving their mood, physical function, participation, health-related quality of life, work self-efficacy, and confidence (15, 16). Second, the age-based retirement policy implemented in the country could have a role. Currently, men retire at 60 and women at 55. Given that 50.44% of the study participants were 50 and over, pension policies hampered RTW motivation, especially for women whose retirement age was 5 years younger. Previous studies

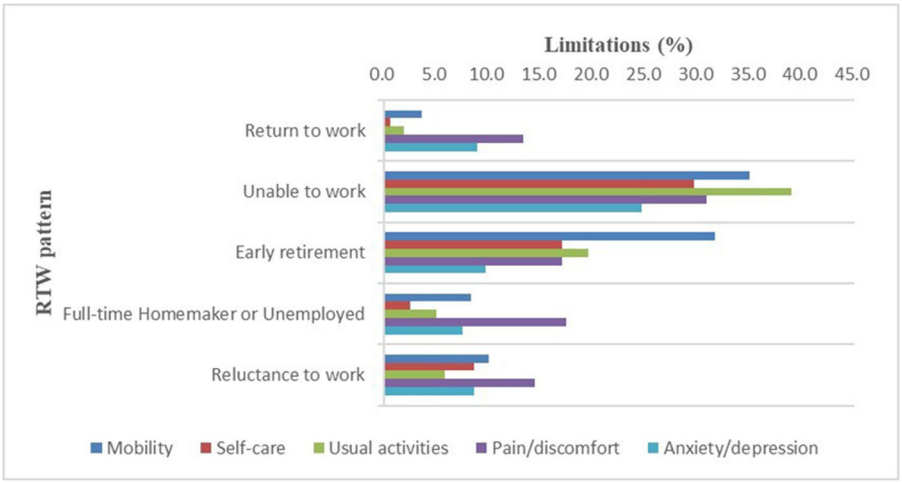


FIGURE 3
Limitations (%) per health domain of the EQ-5D-5L among patients who have returned to work and the four groups of patients who have not returned to work.

TABLE 4 Percentage of health problems in five dimensions of EQ-5D-5L, stratified by gender [*n* (%)].

		MO	SC	UA	PD	AD
Total	Return to work ($n = 354$)	13 (3.7)	2 (0.6)	6 (1.7)	42 (11.9)	28 (7.9)
($n = 789$)	Unable to work ($n = 256$)	93 (36.3)*	67 (26.2)*	88 (34.4)*	70 (27.4)*	56 (21.9)*
	Early retirement ($n = 42$)	13 (31.0)*	7 (16.7)*	8 (19.1)*	7 (16.7)	4 (9.5)
	Full-time Homemaker or Unemployed ($n = 48$)	4 (8.3)	1 (2.1)	2 (4.2)	7 (14.6)	3 (6.3)
	Reluctance to work ($n = 89$)	8 (9.0)	6 (6.7)*	4 (4.5)	10 (11.2)	6 (6.7)
Male	Return to work ($n = 286$)	11 (3.9)	2 (0.7)	6 (2.1)	28 (9.8)	21 (7.3)
($n = 576$)	Unable to work ($n = 191$)	65 (34.0)*	45 (23.6)*	60 (31.4)*	46 (24.2)*	41 (21.5)*
	Early retirement ($n = 27$)	10 (37.0)*	6 (22.2)*	6 (22.2)*	4 (14.8)	2 (7.4)
	Full-time Homemaker or Unemployed ($n = 23$)	1 (4.4)	0 (0.0)	0 (0.0)	3 (13.0)	1 (4.4)
	Reluctance to work ($n = 49$)	4 (8.2)	1 (2.0)	1 (2.0)	4 (8.2)	1 (2.0)
Female	Return to work ($n = 68$)	2 (2.9)	0 (0.0)	0 (0.0)	14 (20.6)	7 (10.3)
($n = 213$)	Unable to work ($n = 76$)	28 (36.8)*	22 (29.0)*	28 (36.8)*	24 (31.6)	15 (19.7)
	Early retirement ($n = 14$)	3 (21.4)	1 (7.1)	2 (14.3)*	3 (21.4)	2 (14.3)
	Full-time Homemaker or Unemployed ($n = 24$)	3 (12.5)	1 (4.2)	2 (8.3)	4 (16.7)	2 (8.3)
	Reluctance to work ($n = 31$)	4 (12.9)	5 (16.1)*	3 (9.7)	6 (19.4)	5 (16.1)

*Comparisons to return to work group, *P*-value < 0.05. MO, mobility; SC, self-care; UA, usual activities; PD, pain/discomfort; AD, anxiety/depression.

have shown that the rate of RTW after stroke varies within and between countries. For example, the rate is 59% to 68% in the United States (10, 17), 65% to 74% in Sweden (8, 18, 19), 70% in Israel (20), 75% in Germany (21), 75% in Finland (22), 72% in the Netherlands (23), 50% in Denmark (9), and 55% in Japan (24). Across countries, there may be differences in sampling practices, current unemployment rates, sickness benefits, insurance assistance, social assistance programs, or employment protection laws.

We identified several sociodemographic and clinical characteristics associated with reasons for non-RTW. Many studies have reported that daily life dependence and right upper limb paralysis after stroke adversely affect RTW (23, 25). In particular, the right upper extremity hand function is essential in early rehab, as it directly affects the ability to work. However, the corresponding confidence intervals are wide, making it impossible to determine the true effect. Similar results suggest that socioeconomic levels, such as age, education level, income,

TABLE 5 Health-related quality of life across different reasons for non-RTW, stratified by gender.

	EQ-5D index			EQ-5D VAS		
	Total	Male	Female	Total	Male	Female
Return to work	0.98 ± 0.5	0.98 ± 0.1	0.97 ± 0.1	85.0 ± 14.0	85.7 ± 13.1	81.8 ± 17.2
Unable to work	0.86 ± 0.2*	0.86 ± 0.2*	0.83 ± 0.2*	74.6 ± 18.4*	74.4 ± 18.8*	75.0 ± 17.3*
Early retirement	0.94 ± 0.1	0.93 ± 0.1*	0.95 ± 0.1	77.7 ± 14.2*	78.3 ± 14.3*	76.4 ± 14.5
Full-time Homemaker or Unemployed	0.98 ± 0.1	0.98 ± 0.1	0.98 ± 0.0	82.8 ± 13.1	80.5 ± 15.5	84.6 ± 11.0
Reluctance to work	0.95 ± 0.2	0.98 ± 0.1	0.89 ± 0.3	83.4 ± 17.6	84.0 ± 15.6	82.5 ± 20.6

*Comparisons to return to the work group, P-value < 0.05.

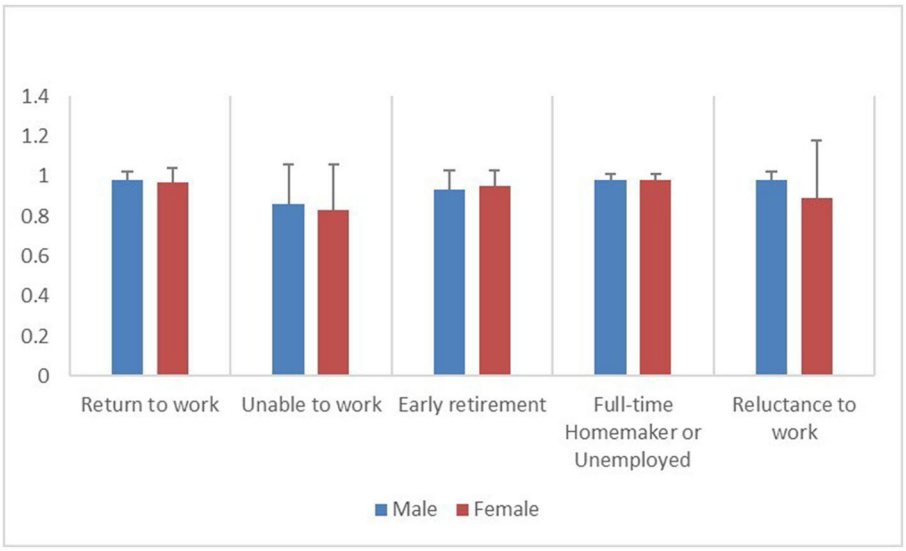


FIGURE 4
Distribution of EQ-5D index among patients who have returned to work and the four groups of patients who have not returned to work, stratified by gender.

and medical insurance, may be an additional important factor in determining RTW. This result is consistent with earlier Swedish and international studies (8). Meanwhile, patients aged 40–50 years were 0.629 times less likely to be reluctant to work than those aged 50 or older. This could be because middle-aged patients in this age group bear the financial burden of supporting their parents and children simultaneously, and traditional Chinese culture dictates that they are less likely to be unwilling to work when they are able to do so. Furthermore, people with diabetes were more likely to choose early retirement. Patients with diabetes have to consistently consider their diet, exercise, medication, and blood glucose monitoring in their job routines, which can have a detrimental effect on their treatment and make managing the disease even more complicated, potentially leading to early retirement.

More importantly, we report the HRQoL associated with non-RTW attributed to different reasons. Patients unable to work had the lowest 1-year health-related quality of life, which was related to the effects of stroke. Moreover, patients who were unable to work had the highest rates of health problems in all five dimensions of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression at 1-year post-stroke, and this category accounted for 32.45% of all the young and middle-aged stroke population in this study. This indicates that stroke has a significant impact on physical functioning and that boosting recovery from the condition is the most effective approach to increasing RTW rates within 1 year. However, it is worth noting that female patients who were reluctant to work had an EQ-5D index second only to those who were unable to work, which may be related to a higher rate (16.13%) of limitations with self-care. Similarly, male patients who were unable to work retired early and stayed at home full time had lower EQ-5D VAS. This may be due to the fact that male patients are typically the primary breadwinners in their families, their eagerness to RTW is greater, and their self-reported quality of life is lower when they are unable to return to work. Life satisfaction studies indicate that RTW improves health and wellbeing after stroke and is more important than non-RTW for overall life satisfaction. This difference was pronounced for male patients (26, 27).

This research is subject to certain limitations. First, the researcher's classification of the reasons for not returning to work may be subjective, and some patients may report multiple reasons

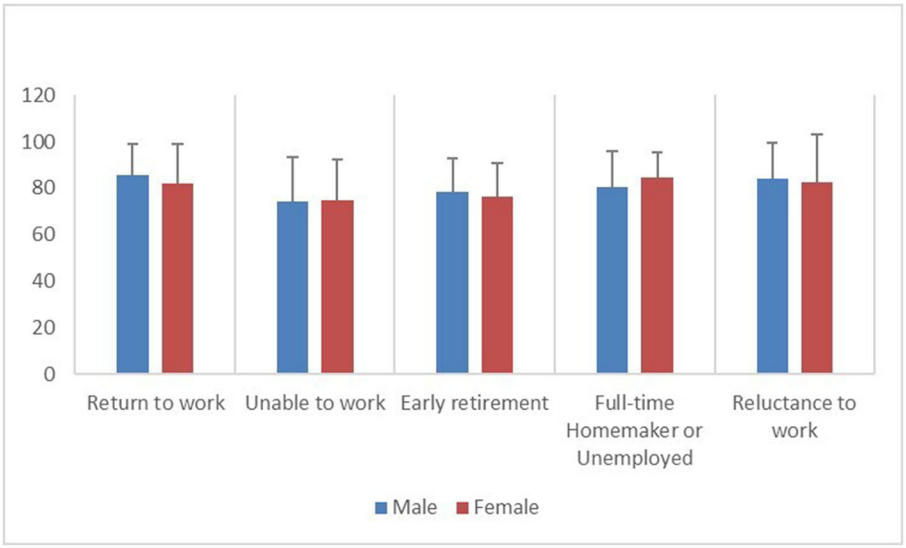


FIGURE 5
Distribution of EQ-5D VAS among patients who have returned to work and the four groups of patients who have not returned to work, stratified by gender.

for non-RTW, and for such patients, we ask for the main reason for non-RTW. Second, although 89 of the 435 patients (20.5%) in our study who failed to RTW declared that they left the workforce for reasons of being reluctant to work or to give a reason, we did not have detailed explanations for these decisions. We did not collect information about patient-reported work conditions or job quality, including job stress, job satisfaction, and job safety. Information about patient-reported work conditions, in addition to health and socioeconomic characteristics, is important. This information may help determine patient-centered interventions supporting RTW. Finally, our study included only patients with stroke from a single center, which may caution us from generalizing to a larger population. Furthermore, the sample size available for the study resulted in wide 95% confidence intervals. Larger sample sizes should be considered in future studies to increase the precision of effect estimates.

5. Conclusion

More than half of young and middle-aged patients with stroke did not RTW within 1 year. Our study highlights the most frequently cited reasons for non-RTW, how they vary across sociodemographic and clinical profile factors, and their impact on HRQoL at 1 year. In vocational rehabilitation, more focus should be directed to female patients who were reluctant to work and male patients who were full-time homemakers or unemployed.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by the Central Review Committee of the First Affiliated Hospital of Soochow University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

XP: paper writing and data analysis. ZW: data collection and data organization. LY: data compilation and data analysis. LX: project preparation and thesis revision. All authors contributed to the article and approved the submitted version.

Funding

This work was supported by the National Science Foundation of China (No. 72104168), Chinese Nursing Association Research Fund (No. ZHKY202218), Suzhou 32nd Batch of Science and Technology Development Plan (Medical and Health Technology Innovation) (2021) (Nos. SKY2021036 and SKJY2021066), and the First Hospital of Soochow University nursing hospital level project (No. HLYJ-2022-05).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Ekker MS, Verhoeven JI, Vaartjes I, van Nieuwenhuizen KM, Klijn CJ, de Leeuw FE. Stroke incidence in young adults according to age, subtype, sex, and time trends. *Neurology.* (2019) 92:e2444–54. doi: 10.1212/WNL.0000000000007533

2. Jacob MA, Ekker MS, Allach Y, Cai M, Aarnio K, Arauz A. Global differences in risk factors, etiology, and outcome of ischemic stroke in young adults-a worldwide meta-analysis: the goal initiative. *Neurology.* (2022) 98:e573–88. doi: 10.1212/WNL.0000000000013195

3. P Duong PK, Egan MY, Meyer MJ, Morrison TL. Intention to return to work after stroke following rehabilitation in ontario. *Can J Occup Ther.* (2020) 87:221–6. doi: 10.1177/0008417420905706

4. Balasooriya-Smeekens C, Bateman A, Mant J, De Simoni A. Barriers and facilitators to staying in work after stroke: insight from an online forum. *BMJ Open.* (2016) 6:e009974. doi: 10.1136/bmjopen-2015-009974

5. Langhammer B, Sunnerhagen KS, Sällström S, Becker F, Stanghelle JK. Return to work after specialized rehabilitation-an explorative longitudinal study in a cohort of severely disabled persons with stroke in seven countries: the sunnaas international network stroke study. *Brain Behav.* (2018) 8:e01055. doi: 10.1002/brb3.1055

6. Norstedt M. The (im)possibilities of returning to work after a stroke. *Work.* (2017) 56:637–47. doi: 10.3233/WOR-172521

7. Maaijwee NA, Rutten-Jacobs LC, Schaapsmeerders P, Van Dijk EJ, de Leeuw FE. Ischaemic stroke in young adults: risk factors and long-term consequences. *Nat Rev Neurol.* (2014) 10:315–25. doi: 10.1038/nrneurol.2014.72

8. Glader EL, Jonsson B, Norrving B, Eriksson M. Socioeconomic factors' effect on return to work after first stroke. *Acta Neurol Scand.* (2017) 135:608–13. doi: 10.1111/ane.12639

9. Larsen LP, Biering K, Johnsen SP, Andersen G, Hjollund NH. Self-rated health and return to work after first-time stroke. *J Rehab Med.* (2016) 48:339–45. doi: 10.2340/16501977-2061

10. Turi ER, Conley Y, Crago E, Sherwood P, Poloyac SM, Ren D. Psychosocial comorbidities related to return to work rates following aneurysmal subarachnoid hemorrhage. *J Occup Rehabil.* (2019) 29:205–11. doi: 10.1007/s10926-018-9780-z

11. Gard G, Pessah-Rasmussen H, Brogårdh C, Nilsson Å, Lindgren I. Need for structured healthcare organization and support for return to work after stroke in Sweden: experiences of stroke survivors. *J Rehab Med.* (2019) 51:741–8. doi: 10.2340/16501977-2591

12. Soeker MS, Olaoye OA. Exploring the experiences of rehabilitated stroke survivors and stakeholders with regard to returning to work in South- West Nigeria. *Work.* (2017) 57:595–609. doi: 10.3233/WOR-172590

13. Golicki D, Niewada M, Karlińska A, Buczek J, Kobayashi A, Janssen MF. Comparing responsiveness of the EQ-5D-5L, EQ-5D-3L and EQ VAS in stroke patients. *Q Life Res.* (2015) 24:1555–63. doi: 10.1007/s11136-014-0873-7

14. Schwarz B, Claros-Salinas D, Streibelt M. Meta-synthesis of qualitative research on facilitators and barriers of return to work after stroke. *J Occup Rehabil.* (2018) 28:28–44. doi: 10.1007/s10926-017-9713-2

15. Bin Zainal MN, Pei Wen PK, Sien NY, Kee KM, Chieh KJ, Asano M. Supporting people with stroke to return to work in singapore: findings from a pilot vocational rehabilitation program. *Am J Occup Ther.* (2020) 74:7406205040p1–9. doi: 10.5014/ajot.2020.041376

16. Frank A. Vocational rehabilitation: supporting ill or disabled individuals in (to) work: a UK perspective. *Healthcare.* (2016) 4:46. doi: 10.3390/healthcare4030046

17. Van Patten R, Merz ZC, Mulhauser K, Fucetola R. Multivariable prediction of return to work at 6-month follow-up in patients with mild to moderate acute stroke. *Arch Phys Med Rehab.* (2016) 97:2061–7. doi: 10.1016/j.apmr.2016.06.006

18. Palstam A, Westerlind E, Persson HC, Sunnerhagen KS. Work-related predictors for return to work after stroke. *Acta Neurol Scand.* (2019) 139:382–8. doi: 10.1111/ane.13067

19. Westerlind E, Abzhandadze T, Rafsten L, Persson HC, Sunnerhagen KS. Very early cognitive screening and return to work after stroke. *Top Stroke Rehabil.* (2019) 26:602–7. doi: 10.1080/10749357.2019.1645440

20. Fride Y, Adamit T, Maeir A, Ben Assayag E, Bornstein NM, Korczyn AD. What are the correlates of cognition and participation to return to work after first ever mild stroke? *Top Stroke Rehabil.* (2015) 22:317–25. doi: 10.1179/1074935714Z.0000000013

21. Hackett ML, Glozier N, Jan S, Lindley R. Returning to paid employment after stroke: the Psychosocial Outcomes In StrokE (POISE) cohort study. *PLoS One.* (2012) 7:e41795. doi: 10.1371/journal.pone.0041795

22. Hiltunen S, Putaala J, Haapaniemi E, Tatlisumak T. Long-term outcome after cerebral venous thrombosis: analysis of functional and vocational outcome, residual symptoms, and adverse events in 161 patients. *J Neurol.* (2016) 263:477–84. doi: 10.1007/s00415-015-7996-9

23. van der Kemp J, Kruithof WJ, Nijboer TC, van Bennekom CA, van Heugten C, Visser-Meily JM. Return to work after mild-to-moderate stroke: work satisfaction and predictive factors. *Neuropsychol Rehabil.* (2019) 29:638–53. doi: 10.1080/09602011.2017.1313746

24. Saeki S, Toyonaga T. Determinants of early return to work after first stroke in Japan. *J Rehab Med.* (2010) 42:254–8. doi: 10.2340/16501977-0503

25. Aarnio K, Rodriguez-Pardo J, Siegerink B, Hardt J, Broman J, Tulkki L. Return to work after ischemic stroke in young adults: A registry-based follow-up study. *Neurology.* (2018) 91:e1909–17. doi: 10.1212/WNL.0000000000006510

26. Eriksson G, Aasnes M, Tistad M, Guidetti S, von Koch L. Occupational gaps in everyday life one year after stroke and the association with life satisfaction and impact of stroke. *Top Stroke Rehabil.* (2012) 19:244–55. doi: 10.1310/tsr1903-244

27. Wang R, Zhang T, Langhammer B. Activities of daily living and life satisfaction of persons with stroke after rehabilitation in China: a longitudinal descriptive study. *Top Stroke Rehabil.* (2019) 26:113–21. doi: 10.1080/10749357.2018.1550615

frontiers | Frontiers in Neurology

TYPE Original Research
PUBLISHED 09 March 2023
DOI 10.3389/fneur.2023.1067706

OPEN ACCESS

EDITED BY
Michael V. Mazya,
Karolinska University Hospital, Sweden

REVIEWED BY
Susan Alderman,
University of Texas Health Science Center at Houston, United States
Mona Laible,
Ulm University, Germany

*CORRESPONDENCE
Meijuan Lan
✉ lanmj@zju.edu.cn

SPECIALTY SECTION
This article was submitted to Stroke, a section of the journal Frontiers in Neurology

RECEIVED 12 October 2022
ACCEPTED 16 February 2023
PUBLISHED 09 March 2023

CITATION
Chen Y, Yang H, Lan M, Wei H and Chen Y (2023) The controlling nutritional status score and risk factors associated with malnutrition in patients with acute ischemic stroke. *Front. Neurol.* 14:1067706. doi: 10.3389/fneur.2023.1067706

The controlling nutritional status score and risk factors associated with malnutrition in patients with acute ischemic stroke

Yuanyuan Chen, Hongyan Yang, Meijuan Lan*, Hui Wei and Yanqin Chen

Nursing Department, The Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China

Objectives: Malnutrition is an independent risk factor for poor outcomes in patients who suffered an acute ischemic stroke (AIS). The controlling nutritional status (CONUT) score can provide information for nutritional management in AIS patients. However, the risk factors associated with the CONUT score have not been established to date. Therefore, in this study, we aimed to investigate the CONUT score of patients with AIS and explore the potential risk factors associated with it.

Methods: We conducted a retrospective review of the data from consecutive AIS patients who were recruited in the CIRCLE study. Within 2 days of admission, we gathered the CONUT score, the Nutritional Risk Screening 2002, the Modified Rankin Scale, the National Institutes of Health Neurological Deficit Score (NIHSS), and demographic data from medical records. We used chi-squared tests to examine admission, and a logistic regression analysis was performed to explore the risk factors associated with CONUT in patients with AIS.

Results: A total of 231 patients with AIS participated in the study, with a mean age of 62.32 ± 13.0 years and a mean NIHSS of 6.77 ± 3.8. Of these patients, 41(17.7%) had hyperlipidemia. In terms of nutritional assessment, 137(59.3%) patients with AIS had high CONUT scores, 86(37.2%) patients with AIS had low or high BMI, and 117(50.6%) patients with AIS had NRS-2002 scores below 3. The chi-squared tests showed that age, NIHSS, body mass index (BMI), and hyperlipidemia were associated with the CONUT score ($P < 0.05$). The logistic regression analysis showed that low NIHSS scores (OR = 0.055 95% CI: 0.003–0.893), younger age (OR = 0.159 95% CI: 0.054–0.469), and hyperlipidemia (OR = 0.303 95% CI: 0.141–0.648) were independently associated with lower CONUT scores ($P < 0.05$), whereas BMI was not found to be independently associated with the CONUT.

Conclusions: More than half of the patients with AIS were at risk of malnutrition, with age and neurological deficits being identified as risk factors for nutritional control. Hyperlipidemia was found to be a protective factor of the CONUT, while NRS-2002 and BMI did not affect the nutritional control in patients with AIS.

KEYWORDS

risk factor, acute stage, ischemic stroke, controlling nutritional status, malnutrition

Introduction

It is well-known that nutrition is an independent predictor of outcomes in patients with acute ischemic stroke (AIS) (1). AIS patients with malnutrition show a higher frequency of pneumonia, other infections, and bedsores (2). Malnutrition also indicates poor prognosis, such as prolonged hospital stays and disability-related hospital costs (3). In addition, a previous study suggested that malnutrition may negatively affect functional recovery (4). Patients with AIS are vulnerable to the risk of malnutrition because of dysphagia, impaired consciousness, and the inability to maintain an adequate and healthy diet (5). Thus, ensuring proper nutrition is available to patients with AIS is essential to their recovery.

The early evaluation of nutritional status is crucial for developing appropriate nutrition support for patients with AIS. At hospital admission, the prevalence of malnutrition ranged from 7 to 34% in patients with AIS (6). The wide prevalence range may be attributed to the heterogeneous nutritional assessment methods. The European Society for Clinical Nutrition and Metabolism (ESPEN) has the diagnostic criteria for malnutrition but does not assess the risk of malnutrition (7). Although there is no gold standard for screening the risk of malnutrition, there are several nutritional assessment tools, including the Nutritional Risk Screening 2002 (NRS-2002) (8), the Malnutrition Universal Screening Tool (MUST) (9), the Geriatric Nutritional Risk Index (GNRI) (10), the Prognostic Nutritional Index (PNI) (4), the Subjective Global Assessment (SGA) (11), and anthropometric measurements (12). These tools have been used to evaluate nutritional status in patients with various disorders, but they are not always appropriate for patients with emerging diseases such as stroke because of the difficulties in gathering nutritional information (13). Thus, developing a simple and valid tool to assess the risk of malnutrition is significant for nutrition intervention in patients with AIS.

The controlling nutritional status (CONUT) score was initially proposed by Ignacio de Ulíbarri et al. (14) and is used for hospitalized patients. Then, the CONUT score was used for patients with AIS. The CONUT score is a comprehensive and appropriate tool for assessing nutritional status and a more vital prognostic marker for functional recovery in patients with AIS compared to others (15, 16). Furthermore, the CONUT score has predictive validity for all-cause mortality after 3 months in patients who have suffered a stroke (17). In other words, the CONUT score, as a convenient and cost-effective index, can reflect the nutritional status and functional outcomes of patients with AIS.

However, research on the CONUT score focused on its validity and prediction ability in patients with AIS (18). Considering the fact that malnutrition is relatively common in stroke survivors and could result in serious outcomes, identifying the risk factors for the CONUT in patients with AIS is essential. Therefore, this study aimed to identify potential risk factors that might influence the CONUT score in patients with AIS.

Methods

Sample and procedures

In this study, we conducted a retrospective review of the data from consecutive patients who were recruited in the CIRCLE study (19) (ClinicalTrials.gov ID: NCT03702452) between 21 November 2018 and 19 November 2019. The CIRCLE study was designed to verify whether nursing-directed rehabilitation in patients who suffered ischemic strokes can compensate for the lack of professional rehabilitation therapists (20). The inclusion criteria were as follows: (1) patients aged between 18 and 90 years; (2) those having a diagnosis of ischemic stroke by CT or MRI and having met the diagnostic criteria prescribed by the WHO; (3) having an initial ischemic stroke within 7 days with limb dysfunction (muscle strength of the limbs is <5); (4) those maintaining consciousness (National Institutes of Health Neurological Deficit Score consciousness level 0 or 1); and (5) those who signed an informed consent form. The exclusion criteria were as follows: (1) patients with blood vessels that were recanalized after thrombolysis or thrombectomy; (2) those with cardiopulmonary dysfunction; a history of craniocerebral trauma, fracture trauma, or rheumatoid arthritis; or a physical disability or other diseases that have an impact on the disabled limb; (3) those with cognitive impairment or other mental illness that prevents cooperation with researchers; and (4) those with diseases that affect lymphocyte count. A total of 231 patients were included in this study.

Ethics approval

Informed consent was obtained from the participants before the study, and the human ethics committee approved the protocols of the Second Affiliated Hospital of Zhejiang University. All clinical investigations were conducted according to the principles expressed in the Helsinki Declaration.

Evaluation

All the participants were administered the CONUT score, the Nutritional Risk Screening 2002 (NRS-2002), the Modified Rankin Scale (MRS), and the National Institutes of Health Neurological Deficit Score (NIHSS). Demographic data [age, gender, educational background, body mass index (BMI), the limbs' muscles, hypertension, hyperlipidemia, and diabetes] were gathered from medical records within 2 days from admission.

The controlling nutritional status score

The CONUT scores calculated from the serum albumin concentration, total peripheral lymphocyte count, and total cholesterol concentration are listed in Table 1. The range of the CONUT scores is from 0 to 12; a score of 0 or 1 indicates a normal nutritional status, and higher scores indicate a worse

TABLE 1 Scoring system for the CONUT score.

Parameter	None	Light	Moderate	Severe
Serum albumin (g/dL)	≥3.5	3.00–3.49	2.50–2.99	<2.50
Score	0	2	4	6
Total lymphocyte count (/mm^3)	≥1,600	1,200–1,599	800–1,199	<800
Score	0	1	2	3
Total cholesterol (mg/dL)	≥180	140–179	100–139	<100
Score	0	1	2	3

nutritional status (14). According to the original stratification of the CONUT score (normal nutritional status: 0–1; mild malnutrition: 2–4; moderate malnutrition: 5–8; severe malnutrition: 9–12) (21), a CONUT score of 0–4 was used to define the lower risk of malnutrition, and a CONUT score of 5–12 was used to define the higher risk of malnutrition (moderate or severe) in this study. The CONUT score is an effective tool for early detection and continuous control of hospital undernutrition in cases of stroke (18). The samples were collected and analyzed within 2 days of admission.

Nutritional Risk Screening 2002

The NRS-2002 score was calculated from BMI, weight loss over the past 3 months, food intake in recent weeks, and the presence of a fatal disease. Patients with a score of ≥3 were considered at risk of malnutrition (8). The sample was obtained within 2 days of admission.

Modified Rankin Scale

The modified Rankin Scale (MRS) was used to assess the function of patients who suffered a stroke. The MRS ranged from 0 to 6. The range of 0 indicated a normal function status, and higher ranges indicated a worse function status (22). We also recorded the function result 2 days after admission.

National Institutes of Health Neurological Deficit Score

The NIHSS assesses the degree of neurological deficits. It consists of 11 parameters, with a maximum score of 42 points. A score of 0 or 1 indicates a normal neurological status, and higher scores suggest a severe neurological deficit (23). In this study, we recorded the neurological deficit result within 2 days of admission for each patient.

Statistical analysis

Data analysis was conducted using SPSS 24.0. All statistical tests were two-tailed, and an alpha of 0.05 was used to indicate significance. The categorical data were statistical frequencies, including age, gender, education background, muscle of limbs, BMI, NIHSS, MRS, NRS 2002, dysphagia, hypertension, diabetes, and hyperlipidemia, and the chi-squared tests were used to examine the data. Then, a logistic regression analysis with backward stepwise selection ($P > 0.10$ for exclusion) was performed to examine the association between the CONUT score, age, BMI, hyperlipidemia, and the NIHSS.

Patient and public involvement

Patients and/or the public were not involved in this research's design, conduct, reporting, or dissemination plans.

Results

Clinical characteristics of patients with AIS

We administered a questionnaire to 231 patients with AIS. The sample comprised 70.1% male participants with a mean age of 62.32 ± 13.0 years. The mean NIHSS score was 6.77 ± 3.8. The mean MRS score was 3.87 ± 0.4. The mean score of the MRC scale was 2.31 ± 1.7 in the upper limbs and 2.87 ± 1.5 in the lower limbs. Comorbidities consisted of hypertension (68.0%), dysphagia (39.4%), hyperlipidemia (17.7%), and diabetes (26.8%). Regarding nutritional assessment, 137 (59.3%) patients with AIS had high CONUT scores, 86 (37.2%) patients with AIS had low or high BMI, and the NRS-2002 scores of 117 (50.6%) patients with AIS were below 3. The demographic characteristics of the 231 patients with AIS are summarized in Table 2.

Risk factors for the CONUT in patients with AIS

Table 2 shows that age, NIHSS, BMI, and hyperlipidemia were associated with the CONUT score ($P < 0.05$), according to the results of the univariate analysis. A logistic regression analysis revealed that those patients with AIS who had low NIHSS scores (0–1) were independently associated with lower CONUT scores compared with those with high NIHSS scores (OR = 0.055 95% CI: 0.003–0.893). Younger age (18–44 years) was independently associated with lower CONUT scores than older age (OR = 0.159 95% CI: 0.054–0.469). AIS patients with hyperlipidemia were independently associated with lower CONUT scores (OR = 0.303 95% CI: 0.141–0.648). BMI was not shown to be independently associated with the CONUT scores (Table 3).

10.3389/fneur.2023.1067706

TABLE 2 Demographic and clinical information for all participants with CONUT.

Characteristic	Total	Low CONUT ($n = 94$)	High CONUT ($n = 137$)	*P*
Age				<0.001**
18–45 y	25/231	17/94	8/137	
46–69 y	140/231	61/94	79/137	
>70 y	66/231	16/94	50/137	
Men	162/231	61/94	101/137	0.150
Education				0.263
Incomplete elementary school	100/231	36/94	64/137	
Elementary school	73/231	36/94	37/137	
Upper secondary school	43/231	15/94	28/137	
University	15/231	7/94	8/137	
NHISS				0.002*
0–1	13/231	11/94	2/137	
2–4	69/231	32/94	37/137	
5–14	144/231	50/94	94/137	
15–20	5/231	1/94	4/137	
MRS				0.396
3	35/231	17/94	18/137	
4	191/231	76/94	115/137	
5	5/231	1/94	4/137	
BMI				0.005*
<18.5	7/231	1/94	6/137	
18.5–24.9	145/231	49/94	96/137	
25–29.9	70/231	38/94	32/137	
30–34.9	9/231	6/94	3/137	
NRS2002				0.133
<3	114/231	52/94	62/137	
≥3	117/231	42/94	75/137	
Dysphagia	91/231	30/94	61/137	0.054
Hypertension	157/231	65/94	92/137	0.749
Diabetes	62/231	24/94	38/137	0.710
Hyperlipidemia	41/231	28/94	13/137	<0.001**
Muscle strength of upper limb				0.079
0	59/231	17/94	42/137	
1	25/231	7/94	18/137	
2	22/231	13/94	9/137	
3	43/231	21/94	22/137	
4	74/231	33/94	41/137	
5	8/231	3/94	5/137	
Muscle strength of lower limb				0.064
0	31/231	7/94	24/137	

(Continued)

TABLE 2 (Continued)

Characteristic	Total	Low CONUT ($n = 94$)	High CONUT ($n = 137$)	*P*
1	18/231	5/94	13/137	
2	21/231	8/94	13/137	
3	61/231	30/94	31/137	
4	80/231	32/94	48/137	
5	20/231	12/94	8/137	

*Statistically significant at $p < 0.05$; **statistically significant at $p < 0.001$.
CONUT, controlling nutritional status; NNIHSS, National Institutes of Health Neurological Deficit Score; MRS, Modified Rankin Scale; NRS-2002, Nutritional Risk Screening 2002.

TABLE 3 Logistic regression analysis of CONUT.

Factor	*B*	SE	Wald	*P*-value	OR	95% CI
NHISS (15–20)						
NHISS (0–1)	−2.906	1.425	4.158	0.041*	0.055	0.003–0.893
NHISS (2–4)	−0.849	1.221	0.483	0.487	0.428	0.039–4.686
NHISS (5–14)	−0.469	1.205	0.152	0.697	0.625	0.059–6.633
Age (above 70 y)						
Age (18–45 y)	−1.839	0.553	11.078	0.001*	0.159	0.054–0.469
Age (46–69 y)	−0.945	0.366	6.662	0.10	0.389	0.190–0.947
Hyperlipidemia	−1.195	0.388	9.469	0.002*	0.303	0.141–0.648
Constant	2.103	1.206	3.043	0.081	8.189	N/A

*Statistically significant at $p < 0.05$.
CONUT, Controlling Nutritional Status; NNIHSS, National Institutes of Health Neurological Deficit Score.

Discussion

In this study, the main findings are as follows: (1) More than half of the patients with AIS are at risk for malnutrition or poor nutritional control; (2) older age is independently associated with poor nutritional control; (3) the degree of neurological deficit affects the nutritional control of patients with AIS (severe neurological deficits indicate bad nutritional status); (4) hyperlipidemia is also an independent factor of nutritional status in patients with AIS; and (5) the nutritional assessment of the NRS-2002 and BMI may not affect the nutritional control in patients with AIS.

The CONUT score as a nutritional risk assessment tool is easy to obtain from biochemical parameters, which reflect the risk of malnutrition because of the comprehensive assessment of nutritional status. This study found that more than half of the patients with AIS are under poor nutritional control. This result is similar to the study by Naito et al. (16). In other words, patients who suffered a stroke are likely to experience nutritional problems in the acute stage. It is essential to evaluate the nutritional status of patients with AIS because malnutrition may worsen clinical outcomes (17). Exploring the risk factors for nutritional status can help prevent malnutrition.

In this study, older age was a poor prognosticator for nutritional control. For older adults, natural age-related changes could increase the risk of malnutrition (24). If they suffered acute stroke events, increased protein requirements, alterations to appetite, and declining sensory function could worsen their condition. A previous study showed that advanced age was the main risk factor for malnutrition in patients who suffered a stroke and that it affects recovery (25). In other words, the risk of malnutrition is higher in older patients with AIS, leading to poor outcomes. This study also showed that the risk of malnutrition increases with age.

The NIHSS is a scale that reflects neurological deficits. This study showed that the NIHSS is the independent factor of the CONUT score. In brief, the degree of neurological deficit affects the nutritional control of patients with AIS. AIS patients with critical neurological deficits often have reduced consciousness levels, dysphagia, facial or arm weakness, reduced mobility, cognitive impairments, and poor oral hygiene (26). In the acute stage of a stroke, dysphagia is a significant factor in developing malnutrition, which occurs in 30–50% of patients (27). The disturbance of consciousness may cause patients to not be fed in time after they suffer a stroke, leading to malnutrition. The presence of depression, cognitive impairments, and language deficits could hinder effective communication about food preferences and satiety, leading to malnutrition, particularly with regard to protein intake (28). Moreover, the paralysis of dextromanuality and weakness affects patients' food intake, leading to a premature suspension of feeding (29). In summary, the neurological deficit is an important factor of CONUT in patients with AIS.

In this study, we found an interesting result: AIS patients with hyperlipidemia were associated with lower CONUT scores. In other words, hyperlipidemia may result in a low risk of malnutrition. Cholesterol, an item of the CONUT score, is a part of blood fat, which might be the main reason why

hyperlipidemia affects malnutrition. Since hyperlipidemia is a risk factor for cardiovascular and cerebrovascular diseases, maintaining an average blood fat level is crucial for health (30).

In contrast, BMI was not found to be independently associated with the CONUT scores. The most likely explanation is that only seven patients with AIS in the study had a low BMI. Moreover, the risk of malnutrition in the acute stage may not immediately lead to a low BMI soon, meaning that BMI does not reflect current changes in nutrition but is an indicator of malnutrition.

Implications for practice

This study highlights the risk factors associated with malnutrition in patients with AIS and emphasizes the need for early nutritional evaluation and intervention. Close attention should be paid to older patients, especially those with severe neurological deficits. Effective nutritional intervention measures should be developed to decrease the occurrence of malnutrition.

Limitations

This study has some limitations. First, the CONUT score for the chronic stage was not collected; therefore, it was impossible to compare the nutritional control status at different stages. Second, the sample size may be more significant to obtain more stable results. Finally, only one hospital's patients with AIS were included, which may create a representational bias, that is, the representation of all hospitalized individuals was missing, and the study findings might not apply to all patients with AIS.

Conclusion

The risk of malnutrition is high among patients with AIS. The CONUT score can reflect malnutrition. The significant risk factors associated with the CONUT score are older age, severe neurological deficits, and hyperlipidemia. The NRS-2002 and BMI may not be effective screening tools for identifying the risk of malnutrition in the acute stage of patients with stroke.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The Human Ethics Committee approved the protocols of The Second Affiliated Hospital of Zhejiang University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

YuC and ML provided critical feedback, edits to drafts of the paper, and managed subsequent revisions. HY contributed to the design of the study and facilitated data acquisition. YaC and HW contributed to the data acquisition and analysis. All authors read and approved the final manuscript.

Funding

This study was funded by the National Natural Science Foundation of China (No: 81871839).

Acknowledgments

The authors would like to thank the patients with AIS for participating in this research. They are also equally grateful for the assistance of the staff in the department of neurology at The Second Affiliated Hospital, Zhejiang University School of Medicine.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Yoo SH, Kim JS, Kwon SU, Yun SC, Koh JY, Kang DW. Undernutrition as a predictor of poor clinical outcomes in acute ischemic stroke patients. *Arch Neurol.* (2008) 65:39–43. doi: 10.1001/archneurol.2007.12

2. FOOD Trial Collaboration. Poor nutritional status on admission predicts poor outcomes after stroke: observational data from the FOOD trial. *Stroke.* (2003) 34:1450–6. doi: 10.1161/01.STR.0000074037.49197.8C

3. Marco E, Sánchez-Rodríguez D, Dávalos-Yerovi VN, Duran X, Pascual EM, et al. Malnutrition according to ESPEN consensus predicts hospitalizations and long-term mortality in rehabilitation patients with stable chronic obstructive pulmonary disease. *Clin Nutr.* (2019) 38:2180–6. doi: 10.1016/j.clnu.2018.09.014

4. Scrutinio D, Lanzillo B, Guida P, Passantino A, Spaccavento S, Battista P. Association between malnutrition and outcomes in patients with severe ischemic stroke undergoing rehabilitation. *Arch Phys Med Rehabil.* (2020) 101:852–60. doi: 10.1016/j.apmr.2019.11.012

5. Lieber AC, Hong E, Putrino D, Nistal DA, Pan JS, Kellner CP. Nutrition, energy expenditure, dysphagia, and self-efficacy in stroke rehabilitation:

a review of the literature. *Brain Sci.* (2018) 8:218. doi: 10.3390/brainsci8120218

6. Aliasghari F, Izadi A, Khalili M, Farhoudi M, Ahmadiyan S, Deljavan R. Impact of premorbid malnutrition and dysphagia on ischemic stroke outcome in elderly patients: a community-based study. *J Am Coll Nutr.* (2019) 38:318–26. doi: 10.1080/07315724.2018.1510348

7. Cederholm T, Bosaeus I, Barazzoni R, Bauer J, Van Gossum A, Klek S, et al. Diagnostic criteria for malnutrition-An ESPEN Consensus Statement. *Clin Nutr.* (2015) 34:335–40. doi: 10.1016/j.clnu.2015.03.001

8. Kondrup J, Allison SP, Elia M, Vellas B, Plauth M, Educational and Clinical Practice Committee, European Society of Parenteral and Enteral Nutrition (ESPEN). ESPEN guidelines for nutrition screening 2002. *Clin Nutr.* (2003) 22:415–21. doi: 10.1016/S0261-5614(03)00098-0

9. van der Schueren MA, Guaitoli PR, Jansma EP, de Vet HC. Nutrition screening tools: does one size fit all? a systematic review of screening tools for the hospital setting. *Clin Nutr.* (2014) 33:39–58. doi: 10.1016/j.clnu.2013.04.008

10. Kang MK, Kim TJ, Kim Y, Nam KW, Jeong HY, Kim SK, et al. Geriatric nutritional risk index predicts poor outcomes in patients with acute ischemic stroke-Automated undernutrition screen tool. *PLoS ONE.* (2020) 15:e0228738. doi: 10.1371/journal.pone.0228738

11. Martineau J, Bauer JD, Isenring E, Cohen S. Malnutrition determined by the patient-generated subjective global assessment is associated with poor outcomes in acute stroke patients. *Clin Nutr.* (2005) 24:1073–7. doi: 10.1016/j.clnu.2005.08.010

12. Kimura Y, Yamada M, Kakehi T, Itagaki A, Tanaka N, Muroh Y. Combination of low body mass index and low serum albumin level leads to poor functional recovery in stroke patients. *J Stroke Cerebrovasc Dis.* (2017) 26:448–53. doi: 10.1016/j.jstrokecerebrovasdis.2016.10.008

13. Akimoto T, Hara M, Morita A, Uehara S, Nakajima H. Relationship between nutritional scales and prognosis in elderly patients after acute ischemic stroke: comparison of controlling nutritional status score and geriatric nutritional risk index. *Ann Nutr Metab.* (2021) 77:116–23. doi: 10.1159/000515212

14. Ignacio de Ulíbarri J, González-Madroño A, de Villar NG, González P, González B, Mancha A, et al. CONUT: a tool for controlling nutritional status first validation in a hospital population. *Nutr Hosp.* (2005) 20:38–45.

15. Kokura Y, Kimoto K, Okada Y, Kawakita S. The Controlling Nutritional Status score as a functional prognostic marker in patients with acute stroke: a multicenter retrospective cohort study. *Nutrition.* (2020)79–80:110889. doi: 10.1016/j.nut.2020.110889

16. Naito H, Hosomi N, Nezu T, Kuzume D, Aoki S, Morimoto Y, et al. Prognostic role of the controlling nutritional status score in acute ischemic stroke among stroke subtypes. *J Neurol Sci.* (2020) 416:116984. doi: 10.1016/j.jns.2020.116984

17. López Espuela F, Roncero-Martín R, Zamorano JDP, Rey-Sanchez P, Aliaga-Vera I, et al. Controlling Nutritional Status (CONUT) Score as a predictor of all-cause mortality at three months in stroke patients. *Biol Res Nurs.* (2019) 21:564–70. doi: 10.1177/1099800419860253

18. Lee EC, Jeong YG, Jung JH, Moon HI. Validity of the controlling nutritional status score as a nutritional assessment tool early after stroke. *Int J Rehabil Res.* (2022) 45:58–64. doi: 10.1097/MRR.0000000000000503

19. Wang JM, Chen YY, Zhang YP, Li M, Jin JF. Rehabilitation nursing for motor functional recovery of acute ischaemic stroke: study protocol for a randomised controlled trial. *BMJ Open.* (2020) 10:e037391. doi: 10.1136/bmjopen-2020-037391

20. Wang JM, Zhang YP, Chen YY, Li M, Yang HY, Chen JH, et al. Effectiveness of rehabilitation nursing versus usual therapist-led treatment in patients with acute ischemic stroke: a randomized non-inferiority trial. *Clin Interv Aging.* (2021) 21:1173–84. doi: 10.2147/CIA.S306255

21. Fukushima K, Ueno Y, Kawagishi N, Kondo Y, Inoue J, Kakazu E, et al. The nutritional index 'CONUT' is useful for predicting long-term prognosis of patients with end-stage liver diseases. *Tohoku J Exp Med.* (2011) 224:215–9. doi: 10.1620/tjem.224.215

22. Saver JL, Chaisinanunkul N, Campbell BCV, Grotta JC, Hill MD, Khatri P, et al. Standardized nomenclature for modified rankin scale global disability outcomes: consensus recommendations from stroke therapy academic industry roundtable XI. *Stroke.* (2021) 52:3054–62. doi: 10.1161/STROKEAHA.121.034480

23. Chalos V, van der Ende NAM, Lingsma HF, Mulder MJHL, Venema E, et al. National institutes of health stroke scale: an alternative primary outcome measure for trials of acute treatment for ischemic stroke. *Stroke.* (2020) 51:282–90. doi: 10.1161/STROKEAHA.119.026791

24. Bardon LA, Corish CA, Lane M, Bizzaro MG, Loayza Villarroel K, Clarke M, et al. Ageing rate of older adults affects the factors associated with, and the determinants of malnutrition in the community: a systematic review and narrative synthesis. *BMC Geriatr.* (2021) 21:676. doi: 10.1186/s12877-021-02583-2

25. Sabbouh T, Torbey MT. Malnutrition in stroke patients: risk factors, assessment, and management. *Neurocrit Care.* (2018) 29:374–84. doi: 10.1007/s12028-017-0436-1

26. Mould J. Nurses must control of the nutritional needs of stroke patients. *Br J Nurs.* (2009)18:1410–4. doi: 10.12968/bjon.2009.18.22.45572

27. Crary MA, Humphrey JL, Carnaby-Mann G, Sambandam R, Miller L, Silliman S. Dysphagia, nutrition, and hydration in ischemic stroke patients at admission and discharge from acute care. *Dysphagia.* (2013) 28:69–76. doi: 10.1007/s00455-012-9414-0

28. Corrigan ML, Escuro AA, Celestin J, Kirby DF. Nutrition in the stroke patient. *Nutr Clin Pract.* (2011) 26:242–52. doi: 10.1177/0884533611405795

29. Westergren A. Nutrition and its relation to mealtime preparation, eating, fatigue and mood among stroke survivors after discharge from hospital - a pilot study. *Open Nurs J.* (2008) 2:15–20. doi: 10.2174/1874434600802010015

30. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, et al. 2021 Guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association. *Stroke.* (2021) 52:e364–467. doi: 10.1161/STR.0000000000000375

frontiers | Frontiers in Neurology

TYPE Study Protocol
PUBLISHED 16 March 2023
DOI 10.3389/fneur.2023.1126958

OPEN ACCESS

EDITED BY
Aleksandras Vilionskis,
Vilnius University, Lithuania

REVIEWED BY
Craig S. Anderson,
University of New South Wales, Australia
Christian Fung,
University of Freiburg Medical Center, Germany

*CORRESPONDENCE
Gustavo Pradilla
✉ gpradil@emory.edu

SPECIALTY SECTION
This article was submitted to Stroke, a section of the journal Frontiers in Neurology

RECEIVED 18 December 2022
ACCEPTED 27 February 2023
PUBLISHED 16 March 2023

CITATION
Ratcliff JJ, Hall AJ, Porto E, Saville BR, Lewis RJ, Allen JW, Frankel M, Wright DW, Barrow DL and Pradilla G (2023) Early Minimally Invasive Removal of Intracerebral Hemorrhage (ENRICH): Study protocol for a multi-centered two-arm randomized adaptive trial. *Front. Neurol.* 14:1126958. doi: 10.3389/fneur.2023.1126958

Early Minimally Invasive Removal of Intracerebral Hemorrhage (ENRICH): Study protocol for a multi-centered two-arm randomized adaptive trial

Jonathan J. Ratcliff[1,2], Alex J. Hall[1], Edoardo Porto[3], Benjamin R. Saville[4,5], Roger J. Lewis[4,6], Jason W. Allen[2,7], Michael Frankel[2], David W. Wright[1], Daniel L. Barrow[3] and Gustavo Pradilla[3]*

[1]Department of Emergency Medicine, Emory University School of Medicine, Atlanta, GA, United States, [2]Department of Neurology, Emory University School of Medicine, Grady Hospital, Atlanta, GA, United States, [3]Department of Neurosurgery, Emory University School of Medicine, Atlanta, GA, United States, [4]Berry Consultants LLC, Austin, TX, United States, [5]Department of Biostatistics, Vanderbilt University Medical Center, Nashville, TN, United States, [6]Department of Emergency Medicine, Harbor-UCLA Medical Center, UCLA, Torrance, CA, United States, [7]Department of Radiology and Imaging Sciences, Emory University School of Medicine, Atlanta, GA, United States

Background: Intracerebral hemorrhage (ICH) is a potentially devastating condition with elevated early mortality rates, poor functional outcomes, and high costs of care. Standard of care involves intensive supportive therapy to prevent secondary injury. To date, there is no randomized control study demonstrating benefit of early evacuation of supratentorial ICH.

Methods: The Early Minimally Invasive Removal of Intracerebral Hemorrhage (ENRICH) Trial was designed to evaluate the minimally invasive trans-sulcal parafascicular surgery (MIPS) approach, a technique for safe access to deep brain structures and ICH removal using the BrainPath® and Myriad® devices (NICO Corporation, Indianapolis, IN). ENRICH is a multi-centered, two-arm, randomized, adaptive comparative-effectiveness study, where patients are block randomized by ICH location and Glasgow Coma Score (GCS) to early ICH evacuation using MIPS plus standard guideline-based management vs. standard management alone to determine if MIPS results in improved outcomes defined by the utility-weighted modified Rankin score (UWmRS) at 180 days as the primary endpoint. Secondary endpoints include clinical and economic outcomes of MIPS using cost per quality-adjusted life years (QALYs). The inclusion and exclusion criteria aim to capture a broad group of patients with high risk of significant morbidity and mortality to determine optimal treatment strategy.

Discussion: ENRICH will result in improved understanding of the benefit of MIPS for both lobar and deep ICH affecting the basal ganglia. The ongoing study will lead to Level-I evidence to guide clinicians treatment options in the management of acute treatment of ICH.

Trial registration: This study is registered with clinicaltrials.gov (Identifier: NCT02880878).

KEYWORDS

intracerebral hemorrhage (ICH), minimally invasive trans-sulcal parafascicular surgery, lobar ICH, deep ICH, minimally invasive surgery (MIS)

Introduction

Intracerebral hemorrhage (ICH) accounts for 10–15% of all strokes and its prevalence continues to increase with an aging population. ICH-related early mortality rates range from 35 to 52% (1). Among survivors, only 10–25% return to functional independence, with an estimated annual cost of care and productivity losses of approximately 12.7 billion US dollars (2–5). Clinical outcomes following an ICH are negatively affected by the mechanical complications of mass effect leading to concomitant tissue infarction and intracranial hypertension. In addition, the hematoma in the brain parenchyma mediates a secondary inflammatory cascade.

An effective therapy for ICH patients has been elusive despite several well-designed clinical trials focused on surgical evacuation (6, 7), hemostasis augmentation (8), and blood-pressure reduction (9–11), among other interventions, all of which have failed to improve functional outcomes.

The role of surgery in the care of supratentorial ICH has been limited to life-saving clot evacuation, decompressive craniectomy, or a combination of these two procedures. Despite preclinical evidence supporting the role of hematoma evacuation on early correction of intracranial hypertension and prevention of secondary injury mechanisms, surgical intervention for supratentorial ICH remains unproven in randomized clinical trials (12).

Technology and technique development in support of minimally invasive surgery (MIS) has been encouraged by the hypothesis that prior randomized surgical trials failed to demonstrate benefit in part due to cortical and white matter tract injury incurred while accessing the clot with traditional techniques and tools. Indeed, surgical clot evacuation remains appealing based on the existing preliminary data, which continue to support the time-dependent pathophysiology of ICH, and that early removal of clot mitigates injury to surrounding tissue (13–15). Recent reports describing the safety of image-guided catheter placement for aspiration followed by infused thrombolytics in the MISTIE II trial have produced promising results supporting the premise of tissue preservation and the benefit of clot reduction (16).

Since the MISTIE approach was first described, multiple technological advances have occurred in diagnostic imaging, intraoperative frameless navigation, and navigable port-based minimally invasive access. The preliminary experiences reported by Labib et al. and Bauer et al. suggest that minimally invasive trans-sulcal parafascicular surgery (MIPS) is safe, prevents rebleeding, and maximizes clot evacuation (17, 18). In these studies, intervention occurred as early as 16 and 6.2 h, respectively, suggesting that MIPS may be safely performed while preserving eloquent white matter tracts and producing excellent clot reduction, without significant risk of hemorrhage recurrence, even when surgery is performed early.

To further evaluate this strategy, a randomized clinical trial was designed to assess the clinical benefit of a standardized MIS approach. The proposed MIPS approach was developed to provide atraumatic access, high-resolution visualization, and intraoperative tools for maximal clot evacuation and definitive hemostasis. In this article, we describe the design and methods for the Early Minimally Invasive Removal of Intracerebral Hemorrhage (ENRICH) trial and provide the rationale for the choice of design parameters.

Methods and analysis

Study objective

The primary objective of the ENRICH trial is to determine if early ICH evacuation using MIPS results in improved outcomes for patients with an ICH. The primary hypothesis is that MIPS will result in an improvement in the 180-day utility-weighted modified Rankin Scale (UWmRS) when compared to patients treated with standard guideline-based management. To address the primary objective, we have designed an adaptive clinical trial with a sample size between 150 and 300 subjects, with frequent interim analyses to determine if early stopping rules are met and if patient population enrichment per hemorrhage location should occur. Randomization between MIPS and standard management groups will be equal and patients will be block randomized by ICH location, anterior basal ganglia (ABG) vs. lobar location as well as Glasgow Coma Score (GCS) with a threshold for stratification <9 vs. ≥ 9. At each interim analysis, the enrollment scheme defined by hemorrhage location can be adapted based on the *a priori* enrichment plan.

Secondary aims of the study will evaluate the economic and clinical benefits, and the safety of MIPS compared to standard management. The clinical benefit of MIPS is thought to be a function of clot removal while minimizing white matter injury. Therefore, we will determine if the percent volume of ICH reduction is associated with improved UWmRS at discharge, 30, and 90 days between the treatment groups. The economic effect of MIPS for ICH will be evaluated by quantifying the cost per quality-adjusted life-year (QALY) gained through MIPS at 30, 90, 120, and 180 days. Safety of MIPS will be assessed: (1) by determining the effect of MIPS on mortality when compared to standard management at 30 days; (2) by assessing post-operative rebleeding associated with clinical deterioration following MIPS. Rebleeding will be defined by a growth in hemorrhage volume between an initial non-contrast head computed tomography scan (NCCT) and a follow-up NCCT obtained within 24 h of the index NCCT. Lastly, we will evaluate the impact of time from onset of symptoms to MIPS on the UWmRS.

Study design and method

ENRICH is an adaptive, two-arm, randomized comparative effectiveness study, where eligible patients are block randomized

Abbreviations: ABG, anterior basal ganglia; CSG, Clinical Standardization Guidelines; DSMB, Data and Safety Monitoring Board; ED, emergency department; EDC, electronic data capture; GCS, Glasgow Coma Score; HUI, Health Utilities Index; ICH, intracerebral hemorrhage; LKN, last known normal; MIPS, minimally invasive trans-sulcal parafascicular surgery; MIS, minimally invasive surgery; MM, medical monitor; NCCT, non-contrast head computed tomography scan; NIHSS, National Institutes of Health Stroke Scale; QALYs, quality-adjusted life years; SLT, Scientific Leadership Team; UWmRS, utility-weighted modified Rankin score.

by ICH location (ABG vs. lobar) and GCS to early ICH evacuation using the MIPS approach plus standard management vs. standard guideline-based management alone. Scheduled interim analyses, beginning after 150 patients have been enrolled, will guide the adaptive sample size and study enrichment (Figure 1). A maximum of 300 subjects will be enrolled.

All randomized subjects are to be treated according to the study protocol, clinical standardization guidelines, and MIPS surgical standardization guidelines. Subjects are followed for 6 months or death (Table 1).

Pre-randomization procedures

On arrival at the study hospital emergency department (ED), rapid evaluation and treatment will occur per routine including a physical assessment (GCS and National Institutes of Health Stroke Scale-NIHSS), NCCT, head CT angiogram, laboratory evaluation, and appropriate resuscitation (Figure 2). Participating neurosurgeons are instructed to contact the local Investigator on Call (IOC) for subject eligibility.

The IOC will review eligibility criteria and the patient's clinical information (Table 2). Once the patient meets eligibility criteria and informed consent has been obtained from the patient or legally authorized representative, the subject may be randomized using the central electronic data capture (EDC) portal.

Study treatment

Subjects randomized to MIPS will have the intervention performed as close to the time of randomization as possible. Study protocol requires subjects to enter the OR within 24 h from last known normal (LKN), with a goal of arrival in the OR within 8 h. MIPS is to be performed in accordance with the study surgical manual (Supplementary Datasheet 1). All surgically randomized cases are video recorded, with the first two surgical cases from each site reviewed by the study's lead neurosurgeon (GP) to objectively assess adherence to the surgical protocol. Following surgery, care will follow the Clinical Standardization Guidelines (CSG) for management (Supplementary Datasheet 2).

In the standard treatment arm, subjects will be treated according to the CSG. The decision for surgical intervention with an external ventricular drain for CSF diversion or ICP control/monitoring, decompressive craniectomy, clot evacuation using traditional techniques, or both is left to the treating neurosurgeon. As traditional surgical techniques, such as decompressive hemicraniectomy, remain available to the treating team in the standard management arm, cross-over from this arm to MIPS is strictly not permitted.

Post-randomization in-hospital assessment

General neurologic evaluation, as assessed by the NIHSS and the GCS, will be monitored daily for the first 7 days following randomization. General laboratory and neuroimaging performed per routine medical care will be collected during this time. A daily checklist will be completed to identify clinical parameters that may be uncorrected and inconsistent with the CSG for care.

Post-discharge follow up

The outcomes battery includes mRS, NIHSS, GCS, and Health Utilities Index (HUI). The full in-person outcomes battery will occur at 180 days (± 14 days) post-randomization. This assessment will be conducted with both the subject and the primary caregiver/family member to corroborate subject responses. The mRS will also be collected on day 30 (± 7 days) and day 90 (± 14 days) via telephone communication. The 30, 90, and 180-day mRS are audio recorded for blinded adjudication. The 30, 90, 120, and 180-day HUI will be collected by telephone unless visit is conducted in person.

Primary efficacy analysis

The primary efficacy endpoint is the UWmRS scale at 180 days post-randomization (Table 3). The primary analysis will be performed on all subjects randomized in the ENRICH study. Subjects will be analyzed according to the group they are randomized to, referred to as the intent to treat population. Let Δ be the mean difference in UWmRS between treatment groups (MIPS—standard management) in the ITT population, in which a positive value indicates MIPS benefit.

The following hypothesis will be tested:

H_0: $\Delta \leq 0$, i.e., the mean difference in UWmRS between treatment groups is ≤ 0

H_1: $\Delta > 0$, i.e., the mean difference in UWmRS between treatment groups is >0.

If the Bayesian model-based posterior probability of MIPS benefit (i.e., $\Delta > 0$) is ≥ 0.975, then the study will demonstrate superiority of MIPS vs. standard management.

Adaptive sample size and enrichment plan

A trial update will be performed when the number of patients enrolled is equal to 150, 175, 200, 225, 250, and 275 patients. The purpose of the trial updates is to determine whether one or two ICH locations meet futility criteria, or whether the current sample size is sufficient to achieve success on the primary outcome. At each trial update, one of the following three decisions will be made:

1) Stop accrual to patients with ICH in either ABG, Lobar, or both locations due to futility.

    a. If accrual stops in only one of the two locations, this creates population enrichment.
    b. If accrual stops in both locations, the trial is stopped for futility.

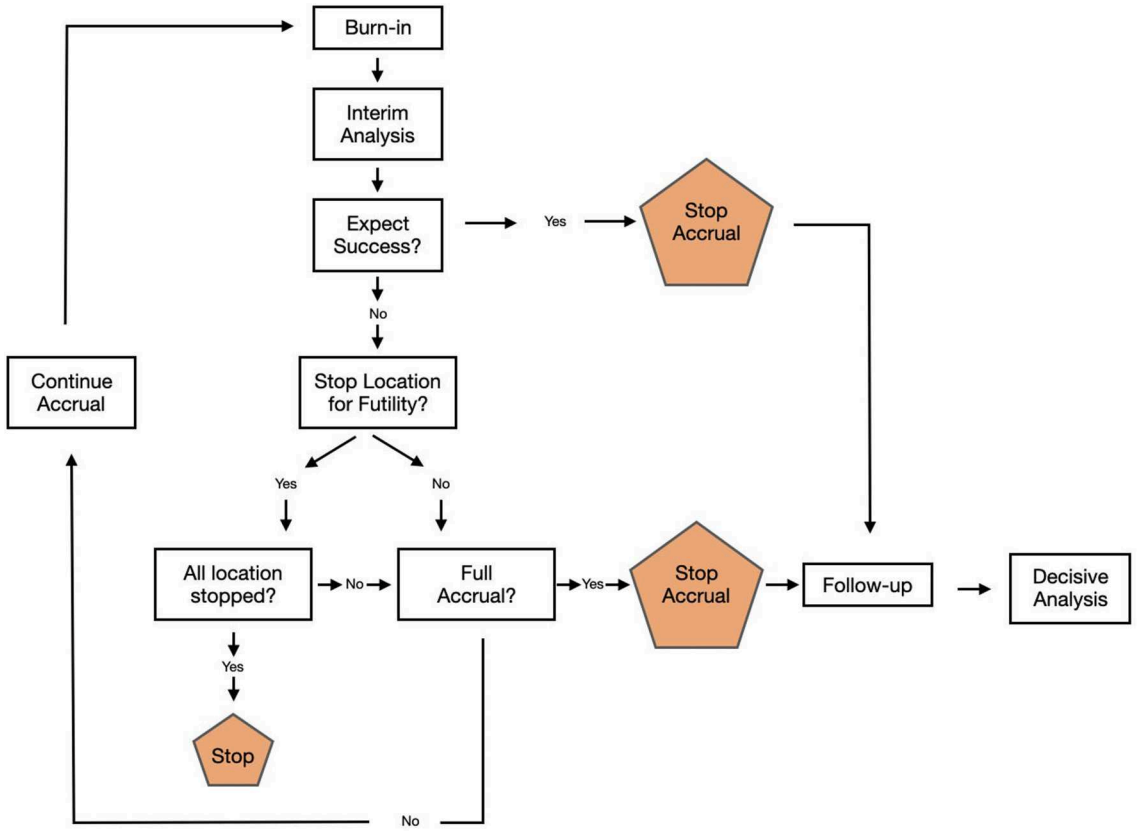


FIGURE 1
Study flow chart.

2) Stop accrual of all patients due to expected success in the pooled ABG/Lobar population. If enrollment is stopped due to expected success, the primary analysis will occur 180 days after the last patient is enrolled.
3) Continue accruing patients without changes.

If the trial does not stop for futility, the primary analysis will occur 180 days after the last patient is enrolled. If enrichment takes place at any point in the trial, and subsequently the primary analysis criteria are met, superiority is only claimed for the location that did not meet the futility criteria, despite the final evaluation including patients from both locations.

In order to stop accrual within a location due to futility, the following two criteria must be met:

1) The Bayesian model-based probability of a clinically meaningful difference (a mean difference of UWmRS of at least 0.075) between surgery and control is <0.20.
2) At least 30 patients have complete 180-day outcomes within the location.

To trigger stopping of accrual for expected success, two criteria must be met:

1) The Bayesian model-based probability of a difference in mean UWmRS utility is ≥ 0.99.
2) At least 60 patients have completed 180-day outcomes.

Statistical modeling

The primary analysis will be based on a pre-specified Bayesian hierarchical model which assumes a constant treatment effect across hemorrhage locations, but in which the mean UWmRS in the control group may differ between locations. Missing data will be addressed via Bayesian multiple imputation, in which 90-day UWmRS values are used to inform the likelihood of 180-day values for patients with missing 180-day UWmRS outcomes. The interim updates will incorporate two models: (1) a model equivalent to the primary analysis model for monitoring expected success in the overall study population; and (2) a Bayesian hierarchical model in which the treatment effect is allowed to vary between hemorrhage locations for the purpose of monitoring futility. Both models used in the interim updates will incorporate longitudinal modeling, in which 90-day UWmRS values are used to inform the likelihood of 180-day values for patients with incomplete information.

Sample size justification

Virtual trial simulations were used to quantify the statistical power and Type I error (Supplementary Datasheet 3). With an adaptive sample size of 150–300 subjects and a base "expected" set of assumptions regarding patient accrual, dropout, distribution of mRS for control and treatment groups, prevalence of ABG/Lobar

TABLE 1 SPIRIT figure.

	Study period								
	Enrolment	Allocation	Post-allocation						Close-out
			Pre-discharge		Post-discharge				
Timepoint	t_1	t_2	t_3 = within 24 h from LKN	t_4 = within 7 days from allocation	t_5 = discharge	t_6 = 30 days	t_7 = 90 days	t_8 = 120 days	t_9 = 180 days
ENROLMENT									
Physical assessment, NCCT, CT angiogram, lab, appropriate resuscitation	x								
Eligibility screen	x								
Informed consent	x								
Allocation		x							
INTERVENTIONS									
MIPS			x						
Standard treatment			According to CSG						
ASSESSMENTS									
Neurologic evaluation, lab, neuroimaging, CSG checklist			←	→					
ICH reduction in association with improved UWmRS					x	x	x		x
Economic effect: QALY						x	x.	x	x
Adverse event monitoring	x		←	→	x	x	x	x	x
Safety: mortality			←					→	
Safety: rebleeding			x						
mRS	x					x	x		x
HUI						x	x	x	x
NIHSS and GCS	x			x	x				x

locations, and treatment benefit in either one or both locations, the Bayesian primary analysis has approximately 90% or greater power for detecting superiority of treatment vs. control for a mean UWmRS difference in both ABG/Lobar locations of 0.15 or larger (i.e., a 15% absolute increase in utility weighted mRS), with an approximate one-sided Type I error <0.025. In addition, the trial design and analysis provide approximately 60–90% power for detecting treatment superiority if there is a mean benefit on UWmRS of 0.15 or larger in one of the two locations.

Primary safety objective

The primary safety objectives will be evaluated by the rate of mortality and/or rebleeding at 30 days, which will be compared between the two groups using a Pearson's chi-square test and the difference in hemorrhage volume between index CT and 24-h follow-up CT, which will be compared between the two groups using a two-sided *t*-test (or Wilcoxon rank sum test if the normality assumption is violated).

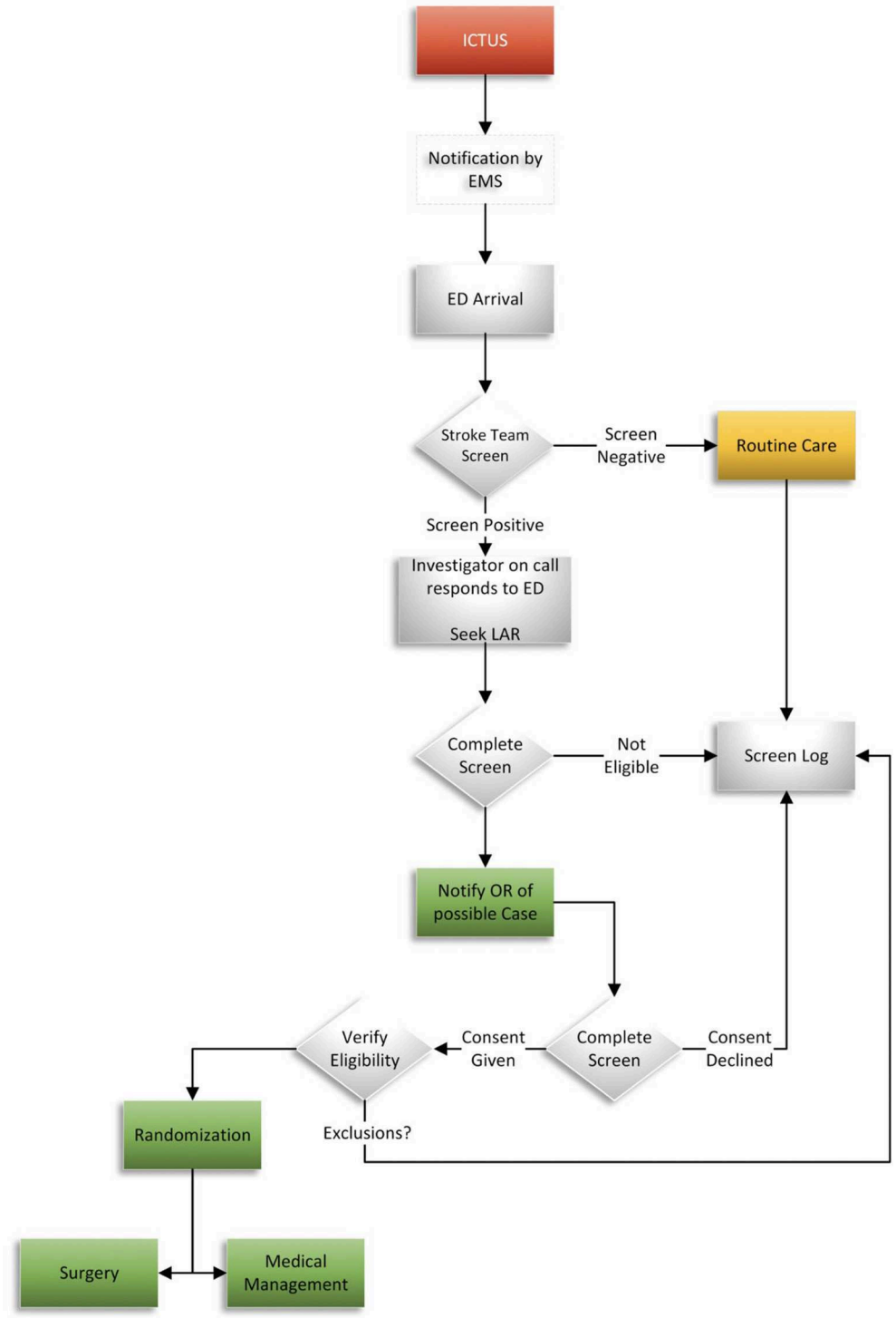


FIGURE 2
Subject flow chart.

Secondary endpoints

The secondary endpoints were selected to provide supportive information on safety and efficacy. These secondary endpoints include:

- Postoperative rebleeding associated with deterioration following MIPS (no hypothesis test).
- ICU and in-hospital length of stay (two-sided *t*-test).
- mRS at discharge, 30 and 90 days (ordinal logistic regression; treatment as explanatory variable).

TABLE 2 Inclusion and exclusion criteria.

Study inclusion criteria	• Age 18–80 years • Pre-randomization head CT demonstrating an acute, spontaneous, primary ICH • ICH volume between 30 and 80 ml as calculated by the ABC/2 method • Study intervention can reasonably be initiated within 24 h after the onset of stroke symptoms. If the actual time of onset is unclear, then the onset will be considered the time that the subject was last known to be well • Glasgow Coma Score GCS 5–14 • Historical Modified Rankin Score 0 or 1
Study exclusion criteria	• Ruptured aneurysm, arteriovenous malformation (AVM), vascular anomaly, Moyamoya disease, venous sinus thrombosis, mass or tumor, hemorrhagic conversion of an ischemic infarct, recurrence of a recent (<1 year) ICH, as diagnosed with radiographic imaging • NIHSS <5 • Bilateral fixed dilated pupils • Extensor motor posturing • Intraventricular extension of the hemorrhage is visually estimated to involve >50% of either of the lateral ventricles • Primary thalamic ICH • Infratentorial intraparenchymal hemorrhage including midbrain, pontine, or cerebellar • Use of anticoagulants that cannot be rapidly reversed • Evidence of active bleeding involving a retroperitoneal, gastrointestinal, genitourinary, or respiratory tract site • Uncorrected coagulopathy or known clotting disorder • Platelet count <75,000, INR >1.4 after correction • Patients requiring long-term anti-coagulation that needs to be initiated <5 days from index ICH • End stage renal disease • Patients with a mechanical heart valve • End-stage liver disease • History of drug or alcohol use or dependence that, in the opinion of the site investigator, would interfere with adherence to study requirements • Positive urine or serum pregnancy test in female subjects without documented history of surgical sterilization or is post-menopausal • Known life-expectancy of <6 months • No reasonable expectation of recovery, DNR, or comfort measures only prior to randomization • Participation in a concurrent interventional medical investigation or clinical trial • Inability or unwillingness of subject or legal guardian/representative to give written informed consent • Homelessness or inability to meet follow up requirements

- Impact of percent ICH reduction with MIPS on mRS at 180 days (ordinal logistic regression; %ICH reduction as explanatory variable).
- Impact of end-of-treatment (EOT) volume with MIPS on mRS at 180 days (ordinal logistic regression; EOT volume as explanatory variable).
- Proportion of patients with mRS at 180 days equal to 0, 1, 2, or 3 (chi-square test).
- Ordinal mRS at 180 days (Wilcoxon rank sum test).
- Overall survival through 180 days (log-rank test and Cox proportional hazards model).

TABLE 3 mRS values to utility weights mapping.

mRS	Utility weights
0	1.0
1	0.91
2	0.76
3	0.65
4	0.33
5	0
6	0

Economic outcome analysis

The ENRICH economic evaluation will assess the primary endpoint: the relative cost-effectiveness of MIPS vs. standard management at 180 days with the effect measured in terms of quality-adjusted life-years (QALYs). QALYs will be calculated from the results of the HUI. Secondary analysis will also: (1) inform how adoption of MIPS will intersect with new and forthcoming Medicare reimbursement policies; and (2) provide evidence on clinical cost-effectiveness.

For the primary endpoint, an incremental analysis will be undertaken to determine the cost per QALY gained through MIPS calculated as: $(C_{MIP} - C_{std})/(QALY_{MIP} - QALY_{std})$ where C_I = cost per treatment arm and QALYI = QALYs per treatment arm.

Safety monitoring

At each Data and Safety Monitoring Board (DSMB) meeting, members will be presented with group comparisons with respect to mortality, occurrence of rebleed and hemorrhage expansion, unexplained and unexpected surgical complications, and other SAEs. The DSMB will also be presented group A–B comparative rates of adverse events to identify any unexpected trends.

An independent medical monitor (MM) will review every SAE for causality and expectedness. For events that are deemed potentially high-risk for future subjects, the DSMB will be provided a report and any necessary additional A–B analysis to make recommendations about study continuation.

The DSMB is a fully independent group of experts selected to advise the ENRICH leadership team, site investigators, and study sponsor and to periodically review and evaluate study data for participant safety, study conduct and progress, and efficacy.

Rationale for early treatment window

The pathophysiology of ICH is time-dependent; therefore, subjects enrolled in ENRICH and randomized to MIPS will have surgery within 24 h of LKN, with a goal of 8 h. Following the initial ICH, a secondary cascade of inflammation-mediated and pro-apoptotic signaling pathways is initiated, contributing

to the poor outcomes (13–15). Previous attempts at ultra-early intervention showed discouraging results using conventional craniotomy (19, 20). Collateral damage of eloquent tissue during surgery remained an important challenge in these studies in addition to poor visualization, and suboptimal hemostasis, all of which we hypothesize have been improved upon with MIPS. Considering the preclinical biological evidence available, a time window of 24 h will allow for early intervention and facilitate institutional and logistic support.

Rationale for specified eligibility criteria

Eligibility criteria were formulated to investigate a population of ICH patients with high risk for poor outcomes that may also benefit from intervention experiencing a significant event unrelated to a vascular anomaly (21, 22). Patients with a hemorrhage volume <30 ml may benefit from MIPS but any observed relative benefit is likely to be small in magnitude as many of these patients may have reasonable outcomes with supportive medical care. Patients with hematoma volume exceeding 80 ml often have dismal outcomes and poor presenting exams limiting the expected benefit of this intervention. Additionally, clot evacuation for hemorrhages exceeding 80 ml is generally believed to be life-saving and functional improvement is rarely observed (12).

Primary thalamic hemorrhages have been excluded, despite the potential benefit from MIPS, for two principal reasons: (1) thalamic hemorrhages frequently lead to significant midbrain injury, and (2) hemorrhages in this location often have delayed recovery extending beyond 180-days (23).

Direct oral anticoagulants (DOAC) that cannot be reversed are necessarily excluded from the ENRICH trial due to potential untoward risk of hemorrhage expansion and rebleeding. FDA has recently approved agents for reversal of anticoagulation effects of some DOACs (24, 25), as a result, ENRICH excludes patients based on the ability to reverse the effect of the direct inhibitors.

Rationale for randomization

Randomization minimizes the influence of bias often seen in observational studies of existing therapies. The MIPS technique uses the FDA-cleared BrainPath® and Myriad® (NICO Corporation Indianapolis, IN) devices. Both tools are widely available and have been used in over 40,000 cases of different neurosurgical pathologies including primary and metastatic brain tumors among several others (internal communication, NICO Corporation). Despite this reality, superiority to well-instituted standard management has not yet been established. Therefore, randomization is an ethical and rigorous tool in understanding the potential benefit that MIPS may offer.

Rationale for the enrichment strategy

Lobar and deep ABG hemorrhages behave differently in prior surgical studies. The STICH trial suggested that more superficial hemorrhages might respond favorably to clot removal in the absence of intraventricular hemorrhage (19). While this hypothesis was not supported in the subsequent STICH II trial, it remains biologically plausible that access to superficial clots may result in less iatrogenic injury (7). As such, we decided to handle these two distinct hemorrhage groups separately so that if we established futility in one group, the investigation into the relative benefits of the other may proceed.

Rationale for preventing cross over to MIPS

Intentional cross-over from standard management to MIPS is not permitted in this trial. Deteriorating subjects, regardless of randomization assignment may be provided the most aggressive life-saving care available. The most recent national guidelines in the care of the ICH patient detail Class IIb evidence for surgical clot evacuation, decompressive craniectomy, or the combination in the life-saving care of the ICH patient. These procedures, done under traditional techniques may be performed at the discretion of the clinical team, regardless of randomization assignment.

Rationale for blinded adjudication of outcome

Because this study includes surgical intervention, outcomes cannot be reasonably performed in a blinded manner due to evidence of surgery. Therefore, a unique blinded adjudication process for the mRS was designed to minimize the effect of bias on the primary outcome. The ENRICH team enlisted an experienced Neuropsychologist, who is blinded to treatment allocation, to review audio recordings of subject mRS interviews. Following review of the audio recording the Neuropsychologist enters their assessment into the EDC. Discordance in the mRS value between the site and the Neuropsychologist are adjudicated by case discussion between the blinded and unblinded assessors. The final determination is made by the blinded Neuropsychologist.

Rationale for cost per quality-adjusted life year gained assessment

ICH is a condition with high morbidity, and often early fatality rate. Should the MIPS approach be superior to standard management it is likely that cost of care of ICH patients may increase in the acute setting, even though the procedure may impact ICU length of stay, ICU-related complications, in-hospital length of stay, or length and complexity of post-acute rehabilitation, all of which may result in overall decreased cost in the long term. By utilizing the QALY metric, the cost can be analyzed in the context of patient outcomes. By convention, an intervention is deemed cost-effective if the treatment is in the range of $100,000–200,000 per QALY gained.

Rationale for the primary outcome and follow up period

Patient-centered outcomes in stroke research are increasingly desirable. The utility is a measure that expresses the desirability of a specific outcome to a patient. The UWmRS converts the arbitrarily distinguished mRS to a patient-centered scale with distances between the items that better reflect societal and patient beliefs of the desirability of a particular outcome (26). The use of UWmRS also improves statistical efficiency when compared to the ordinal mRS. Statistical analysis of the ordinal mRS often leads to dichotomizing the outcome, reducing the power to detect treatment effects through collapsing important categories of health outcomes, or ordinal analysis, which does not account for the varied importance represented in the distance between each of the categories. The UWmRS may be analyzed as a continuous measure allowing the full use of the obtained data.

A 6-month follow-up term for the primary outcome was selected with the understanding that ICH survivors may continue to improve up to a year or more after the event. ICH trials have moved to a 6-month outcome and we have selected a similar outcome to permit comparison between trials.

Rationale for site selection

Participating sites have been carefully selected based on prior experience with the MIPS approach, annual ICH volume, partnership between neurocritical care and neurosurgery, and experience of the research team. Selected sites are visited in person by a member of the Scientific Leadership Team (SLT) as well as for Site Initiation Visits prior to full engagement. A minimum of 10 sites will be involved in this study.

Study organization and funding

Trial design, leadership, and conduct are overseen by the SLT at Emory University and representatives of the sponsor. Berry Consultants supports the SLT with the study's adaptive clinical trial design and one unblinded statistician (BS) performed the interim analyses. The trial sponsor and funder is the NICO Corporation. The sponsor will perform monitoring at all sites to ensure data quality and integrity, and the protection of the rights and safety of subjects through a contract research organization (IQVIA).

Discussion

Generalizability

The ENRICH clinical trial has been designed to enhance the care of ICH patients. The overall stroke community is desperately seeking an effective treatment for ICH that directly results in improved functionality. The broad inclusion criteria were designed to focus on those ICH patients with high risk of significant morbidity and mortality. This selection represents a large number of ICH patients and a cohort in whom scientific progress is imperative. Exclusion criteria were also selected with three guiding principles: (1) In whom might early clot evacuation prove beneficial? (2) In whom might the MIPS approach prove harmful? and (3) The ethical imperative to complete the trial with a fullness of scientific understanding that permits the improvement of care of these patients.

The ENRICH trial and the MIPS approach being studied is not being tested for every patient with an ICH, but rather a cohort of patients in whom the risk-benefit profile might lead to overall improvement.

Expected impact of the proposed trial

There are no Level I evidence-based surgical options in the acute management of ICH. This trial is designed to determine if MIPS for ICH evacuation, performed within 24 h from LKW, results in improved functional outcome and economic benefit. Surgical evacuation following spontaneous ICH is an appealing treatment option; nonetheless, when studied, surgery has not been observed to be efficacious. It is believed that previous negative studies were due in part to trauma that occurs with accessing the ICH, heterogeneity in surgical and medical care, and patient selection. The ENRICH clinical trial improves upon these limitations with technology that permits access to deep structures with minimal trauma. This trial will significantly contribute to scientific literature guiding the optimal management of these medically complex patients.

Dissemination

The trial results will be disseminated through publications in peer-reviewed journals, presentations at scientific conferences, and media channels.

The datasets generated during the study will be available upon reasonable request.

Ethics statement

The studies involving human participants were reviewed and approved by Emory University Institutional Ethical Review Boards. The patients/participants provided their written informed consent to participate in this study.

Author contributions

GP, JR, AH, BS, and RL were responsible for the conceptualization, methodology, and writing the original draft. EP, BS, JA, MF, DW, and DB were responsible for reviewing and editing the protocol. All authors contributed to the article and approved the submitted version.

Funding

This study received funding from NICO Corporation. The SLT at Emory University and representatives of the funder

oversee trial design, leadership, and conduct. The SLT oversees all clinical trial activities including design, protocol development, protocol amendments, database development, and final analyses and interpretation of data. The funder will perform monitoring at all sites to ensure data quality and integrity, and the protection of the rights and safety of subjects through a contract research organization.

Conflict of interest

Authors BS and RL are employed by Berry Consultants LLC. Berry Consultants LLC supports the SLT with the study's adaptive clinical trial design.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Author disclaimer

Research reported in this publication was supported by the NICO Corporation and coordinated through Emory University. The content is solely the responsibility of the authors and does not necessarily represent the official views of NICO Corporation or other supporting entities.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2023.1126958/full#supplementary-material

References

1. Macellari F, Paciaroni M, Agnelli G, Caso V. Neuroimaging in intracerebral hemorrhage. *Stroke.* (2014) 45:903–8. doi: 10.1161/STROKEAHA.113.003701

2. Cheung RT, Zou LY. Use of the original, modified, or new intracerebral hemorrhage score to predict mortality and morbidity after intracerebral hemorrhage. *Stroke.* (2003) 34:1717–22. doi: 10.1161/01.STR.0000078657.22835.B9

3. Clarke JL, Johnston SC, Farrant M, Bernstein R, Tong D, Hemphill JC III. External validation of the ICH score. *Neurocrit Care.* (2004) 1:53–60. doi: 10.1385/NCC:1:1:53

4. Hemphill JC III, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score: a simple, reliable grading scale for intracerebral hemorrhage. *Stroke.* (2001) 32:891–7. doi: 10.1161/01.STR.32.4.891

5. Ruiz-Sandoval JL, Chiquete E, Romero-Vargas S, Padilla-Martínez JJ, González-Cornejo S. Grading scale for prediction of outcome in primary intracerebral hemorrhages. *Stroke.* (2007) 38:1641–4. doi: 10.1161/STROKEAHA.106.478222

6. Mendelow AD, Gregson BA, Fernandes HM, Murray GD, Teasdale GM, Hope DT, et al. Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): a randomised trial. *Lancet.* (2005) 365:387–97. doi: 10.1016/S0140-6736(05)70233-6

7. Mendelow AD, Gregson BA, Rowan EN, Murray GD, Gholkar A, Mitchell PM. Early surgery versus initial conservative treatment in patients with spontaneous supratentorial lobar intracerebral haematomas (STICH II): a randomised trial. *Lancet.* (2013) 382:397–408. doi: 10.1016/S0140-6736(13)60986-1

8. Mayer SA, Brun NC, Begtrup K, Broderick J, Davis S, Diringer MN, et al. Efficacy and safety of recombinant activated factor VII for acute intracerebral hemorrhage. *N Engl J Med.* (2008) 358:2127–37. doi: 10.1056/NEJMoa0707534

9. Qureshi AI, Palesch YY, Barsan WG, Hanley DF, Hsu CY, Martin RL, et al. Intensive blood-pressure lowering in patients with acute cerebral hemorrhage. *N Engl J Med.* (2016) 375:1033–43. doi: 10.1056/NEJMoa1603460

10. Wang X, Arima H, Heeley E, Delcourt C, Huang Y, Wang J, et al. Magnitude of blood pressure reduction and clinical outcomes in acute intracerebral hemorrhage: intensive blood pressure reduction in acute cerebral hemorrhage trial study. *Hypertension.* (2015) 65:1026–32. doi: 10.1161/HYPERTENSIONAHA.114.05044

11. Anderson CS, Heeley E, Huang Y, Wang J, Stapf C, Delcourt C, et al. Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. *N Engl J Med.* (2013) 368:2355–65. doi: 10.1056/NEJMoa1214609

12. Hemphill JC III, Greenberg SM, Anderson CS, Becker K, Bendok BR, Cushman M, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* (2015) 46:2032–60. doi: 10.1161/STR.0000000000000069

13. Venkatasubramanian C, Mlynash M, Finley-Caulfield A, Eyngorn I, Kalimuthu R, Snider RW, et al. Natural history of perihematomal edema after intracerebral hemorrhage measured by serial magnetic resonance imaging. *Stroke.* (2011) 42:73–80. doi: 10.1161/STROKEAHA.110.590646

14. Gebel JM Jr, Jauch EC, Brott TG, Khoury J, Sauerbeck L, Salisbury S, et al. Natural history of perihematomal edema in patients with hyperacute spontaneous intracerebral hemorrhage. *Stroke.* (2002) 33:2631–5. doi: 10.1161/01.STR.0000035284.12699.84

15. Wu TY, Sharma G, Strbian D, Putaala J, Desmond PM, Tatlisumak T, et al. Natural history of perihematomal edema and impact on outcome after intracerebral hemorrhage. *Stroke.* (2017) 48:873–9. doi: 10.1161/STROKEAHA.116.014416

16. Hanley DF, Thompson RE, Muschelli J, Rosenblum M, McBee N, Lane K, et al. Safety and efficacy of minimally invasive surgery plus alteplase in intracerebral haemorrhage evacuation (MISTIE): a randomised, controlled, open-label, phase 2 trial. *Lancet Neurol.* (2016) 15:1228–37. doi: 10.1016/S1474-4422(16)30234-4

17. Labib MA, Shah M, Kassam AB, Young R, Zucker L, Maioriello A, et al. The safety and feasibility of image-guided brainpath-mediated transsulcul hematoma evacuation: a multicenter study. *Neurosurgery.* (2017) 80:515–24. doi: 10.1227/NEU.0000000000001316

18. Bauer AM, Rasmussen PA, Bain MD. Initial single-center technical experience with the brainpath system for acute intracerebral hemorrhage evacuation. *Oper Neurosurg (Hagerstown).* (2017) 13:69–76. doi: 10.1227/NEU.0000000000001258

19. Morgenstern LB, Frankowski RF, Shedden P, Pasteur W, Grotta JC. Surgical treatment for intracerebral hemorrhage (STICH): a single-center, randomized clinical trial. *Neurology.* (1998) 51:1359–63. doi: 10.1212/WNL.51.5.1359

20. Steiner T, Vincent C, Morris S, Davis S, Vallejo-Torres L, Christensen MC. Neurosurgical outcomes after intracerebral hemorrhage: results of the Factor Seven for Acute Hemorrhagic Stroke Trial (FAST). *J Stroke Cerebrovasc Dis.* (2011) 20:287–94. doi: 10.1016/j.jstrokecerebrovasdis.2009.12.008

21. Gregson BA, Broderick JP, Auer LM, Batjer H, Chen XC, Juvela S, et al. Individual patient data subgroup meta-analysis of surgery for spontaneous supratentorial intracerebral hemorrhage. *Stroke.* (2012) 43:1496–504. doi: 10.1161/STROKEAHA.111.640284

22. Zhou X, Chen J, Li Q, Ren G, Yao G, Liu M, et al. Minimally invasive surgery for spontaneous supratentorial intracerebral hemorrhage: a meta-analysis of randomized

controlled trials. *Stroke.* (2012) 43:2923–30. doi: 10.1161/STROKEAHA.112.667535

23. Hill MD, Muir KW. INTERACT-2: should blood pressure be aggressively lowered acutely after intracerebral hemorrhage? *Stroke.* (2013) 44:2951–2. doi: 10.1161/STROKEAHA.113.002790

24. *RP. Idarucizumab Approval Letter. Administration UFD* (2015).

25. *Malarkey M. BW. Andexxa (Coagulation Factor Xa (Recombinant), Inactivated-Zhzo) Approval Letter. Administration UFD* (2018).

26. Chaisinanunkul N, Adeoye O, Lewis RJ, Grotta JC, Broderick J, Jovin TG, et al. Adopting a patient-centered approach to primary outcome analysis of acute stroke trials using a utility-weighted modified Rankin scale. *Stroke.* (2015) 46:2238–43. doi: 10.1161/STROKEAHA.114.008547

frontiers | Frontiers in Neurology

TYPE Perspective
PUBLISHED 23 March 2023
DOI 10.3389/fneur.2023.1129516

OPEN ACCESS

EDITED BY
Aleksandras Vilionskis,
Vilnius University, Lithuania

REVIEWED BY
Hrvoje Budincevic,
University Hospital Sveti Duh, Croatia
Christian Boehme,
Innsbruck Medical University, Austria

*CORRESPONDENCE
Iwona Sarzyńska-Długosz
✉ isarzynska@ipin.edu.pl

SPECIALTY SECTION
This article was submitted to Stroke, a section of the journal Frontiers in Neurology

RECEIVED 22 December 2022
ACCEPTED 01 March 2023
PUBLISHED 23 March 2023

CITATION
Sarzyńska-Długosz I (2023) An optimal model of long-term post-stroke care. *Front. Neurol.* 14:1129516. doi: 10.3389/fneur.2023.1129516

An optimal model of long-term post-stroke care

Iwona Sarzyńska-Długosz*

Second Department of Neurology, Institute of Psychiatry and Neurology, Warsaw, Poland

Stroke is a major healthcare challenge that is increasing worldwide. The burden of stroke is significant for the affected individuals as well as for the general population; high-quality care is needed to reduce its negative impacts. This article synthesized information from systematic reviews, guidelines, and primary literature on stroke care and post-stroke rehabilitation and proposes an optimal strategy for long-term post-stroke care. It also highlights the unmet needs of patients who experienced a stroke in terms of early diagnosis of complications and adequate, comprehensive therapy.

KEYWORDS

stroke, standard of care, rehabilitation, spasticity, complication

Introduction

Stroke is one of the greatest public healthcare challenges for the global population. In 2019, there were 12.2 million incident cases and 101 million prevalent cases of stroke worldwide, representing increases of 70 and 85%, respectively, from 1990 (1). The lifetime risk of having a stroke has increased by 50% over the past 17 years, and 1 in 4 people will have a stroke in their lifetime (2). Stroke was also the second-leading cause of death in 2019, with 6.55 million deaths (11.6% of the total), which increased by 43% from 1990 to 2019 (1). Moreover, mathematical models have predicted a 36% increase in the number of stroke events in the European Union (EU) combined with Iceland, Norway, and Switzerland between 2000 and 2025 (3, 4). The disease burden of stroke is accompanied by a substantial economic burden: the total (direct and indirect) costs of stroke were estimated to be $40.1 billion annually in the United States (US) (5) and €45 billion in the EU (3).

Mortality rates alone do not provide the full picture of stroke burden. Stroke survivors are at a high risk of having a stroke in the future; a meta-analysis of 13 studies based on stroke registries estimated the cumulative risk of stroke recurrence as 3.1% in 30 days, 11.1% in 1 year, 26.4% in 5 years, and 39.2% in 10 years (6). Stroke was the fifth leading cause of disability-adjusted life years (DALYs) in 1990 but was the third leading cause by 2010 (7); from 1990 to 2019, DALYs due to stroke increased by 32.0%, accounting for 143 million DALYs in 2019, with 3% of men and 2% of women in the US experiencing disability due to stroke (8). Stroke not only affects the patients but also has a prolonged physical, emotional, and financial impact on their family and friends; up to 48% of caregivers of patients who experienced stroke report health problems and two-thirds have experienced a decline in their social activities (9, 10). As the number of stroke survivors is predicted to increase from 3,718,785 in 2015 to 4,631,050 in 2035 (3), there is an urgent need for improvements in every aspect of stroke care.

The quality of healthcare is defined as "the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge" (11). Stroke prognosis largely depends on acute-phase care: patients with suspected stroke should be admitted to the hospital as quickly as possible and assessed and treated within a few hours to improve outcomes. The in-hospital acute stroke care pathway is well-established (Figure 1): patients who experienced an acute stroke are transferred directly to stroke units from the emergency department and remain there for the duration of the inpatient stay (12). Stroke units provide multidisciplinary care and rehabilitation by staff specialized in stroke care. The effectiveness of high-quality stroke units is paramount: regardless of age, sex, disability, or stroke type, patients who receive organized in-patient care in a stroke unit have higher survival rates and achieve independence more rapidly, and they will be sooner able to return to their own home (12). At present, stroke unit networks are well-developed in many European countries (13–19) but there is a lack of consistency in the application of treatment guidelines (20).

The provision of multidisciplinary, coordinated, structured rehabilitation, and appropriate specialist post-stroke health services—not only immediately after discharge from the stroke unit but also for months and years afterward—is critical for minimizing the long-term sequelae of stroke (21). This study aimed to deliver current information on high-quality long-term services for reducing stroke burden based on systematic reviews, guidelines, and primary literature on stroke care to optimize long-term post-stroke care.

Rehabilitation settings and patient eligibility

Following a stroke, all survivors need care, support, and education; however, formal rehabilitation is only needed by patients with neurologic deficits affecting their functions. Although 20% of survivors of stroke (or over 30% of those treated with intravenous thrombolysis) fully recover by 2 weeks post-stroke (22), another 20% of them have severe functional deficits and require lifelong assistance with basic activities of daily living (ADL) despite rehabilitation (23, 24), and the remaining survivors have varying degrees of disability and need specific post-stroke rehabilitation (24). An optimal post-acute stroke care pathway to manage these patients is outlined in Figure 2.

In determining the most appropriate form of rehabilitation after discharge from the stroke unit, it is important to take into account the patient's general medical condition, neurologic findings, degree of disability (evaluated using standardized tests), mental and psychological statuses, and ability to participate in a rehabilitation program as well as the availability of caregiver support. Rehabilitation needs should be evaluated by a clinician experienced in neurologic assessment or by a multidisciplinary team as soon as the patient's medical and neurologic condition permits (24–26) to determine the appropriate intensity of rehabilitation and allocation of relevant resources.

Criteria for a comprehensive in-hospital rehabilitation program include a stable general condition, the ability to learn, sufficient physical endurance to sit unsupported for at least 1 h, and the ability to actively participate in rehabilitation (24). Initiation of such a rehabilitation program should be reserved for patients who have more than one type of disability and require the services of 2 or more rehabilitation disciplines (e.g., physiotherapy, occupational therapy, speech therapy, and neuropsychological therapy) (27). Patients with moderate disabilities and sufficient physical endurance to tolerate intensive rehabilitation (often at least 3 h per day of physically demanding activities) are the best candidates for such a program.

The decision of whether to admit patients who experienced a severe stroke to an in-hospital rehabilitation program is not straightforward. Severe stroke is defined as unconsciousness at the onset with severe unilateral or bilateral paresis (28, 29) or an early Functional Independence Measure (FIM) score of <40 (30). Stroke severity may also be influenced by medical comorbidities that impact overall disability and make rehabilitation more challenging. Patients who experienced a severe stroke are less likely to achieve functional independence even over the long term (31); in these patients, younger age and the presence of a caregiver (32, 33) determine the extent of functional improvement with rehabilitation, although the provision of multidisciplinary stroke care in a highly specialized facility over an extended period can achieve significant results, to the extent that some will not require long-term care in a nursing facility and can be discharged with strong support from their family and the community (24). For severe stroke patients who are unable to participate in or are contraindicated for intensive multidisciplinary rehabilitation, appropriate care and rehabilitation should be provided in long-term care facilities (24).

Patients who experienced a mild stroke (early FIM score >80) can undergo rehabilitation at outpatient facilities, which potentially allows them to be more involved in self-care and take greater responsibility for their recovery. Outpatient stroke rehabilitation can be divided into early supported discharge (ESD), hospital-based outpatient rehabilitation, and community-based rehabilitation (34). ESD arose from the recognition that many survivors of stroke prefer being at home following a stroke and was developed to reduce the length of hospital stay and provide multidisciplinary rehabilitation in a patient's own home. Members of the ESD team should have specialized stroke care knowledge and should include a physiotherapist, an occupational therapist, and a nurse. A coordinator facilitates weekly meetings and assigns therapists to each patient (35). This approach to rehabilitation has been shown to reduce the duration of hospitalization in the stroke unit and the number of patients requiring institutional care following discharge and increase patients' independence in ADL at 6 months (36, 37).

The condition of patients who experienced a stroke may deteriorate after they are discharged from the hospital, resulting in a loss of independence in ADL and necessitating long-term institutional care (38). Outpatient therapy should be initiated following discharge from in-hospital stroke units as a continuation of therapy and may include hospital-based "day," hospital programs, or home-based rehabilitation consisting of occupational therapy without or with physiotherapy (39).

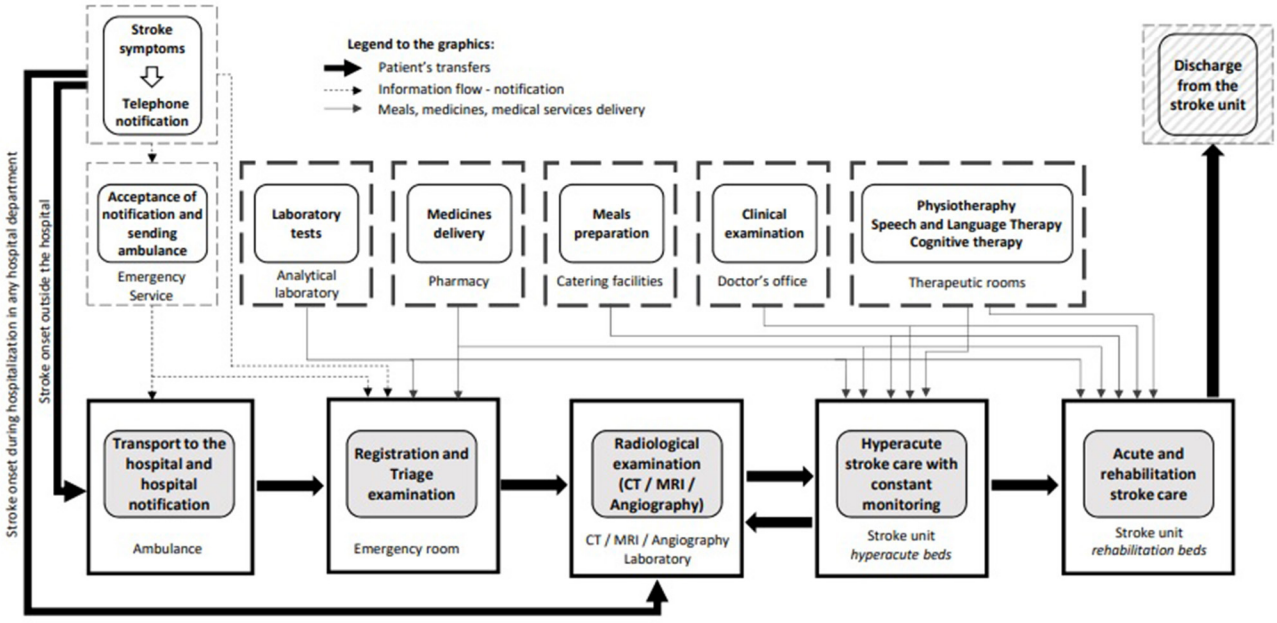


FIGURE 1
In-hospital acute stroke care pathway (unpublished - drawn by Jarosław Gębski, Polish Society of Health Economics, Warsaw, Poland).

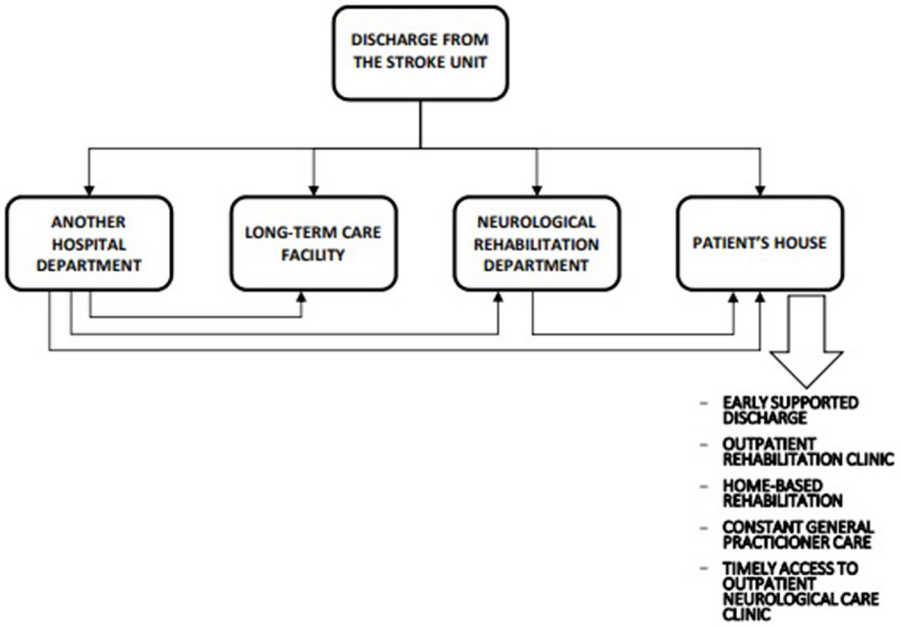


FIGURE 2
Optimal postacute stroke care pathway (unpublished - drawn by Jarosław Gębski, Polish Society of Health Economics, Warsaw, Poland).

Stroke rehabilitation requires long-term commitment (for at least 3–5 years after the stroke) (34); patients in the chronic phase (>6 months after the stroke) should have access to rehabilitation to prevent secondary complications resulting from immobilization and maintain a functional state (40, 41). Rehabilitation has many benefits even if it is not initiated early on, as functional improvements post-stroke can continue for a long period (20) although the patient's rehabilitation needs will evolve. For chronic stroke, the most effective mode of delivery of physiotherapy/occupational therapy is through a community rehabilitation program—which is usually home-based (42) or a self-management program—carried out under the periodic supervision and instruction of a therapist (20). An important factor limiting the provision of proper and continuous post-stroke rehabilitation is the

insufficient number of rehabilitation professionals and nursing staff with specialist knowledge in the field of stroke.

Spasticity management

Spasticity management is important for helping patients adhere to their care plan and setting realistic expectations regarding post-stroke rehabilitation. Spasticity, a complex movement disorder, is a common post-stroke complication caused by excessive muscle tone and stretch reflex resulting in clonus and spasms (43, 44) that contributes to functional impairment and reduces patients' ADL and quality of life (45, 46). The prevalence of post-stroke spasticity ranges from 19 to 92%; the timing of onset varies (44, 47, 48) and typically emerges between 1 and 6 weeks after the stroke (49). The anatomic pattern and severity of spasticity depend on the neurologic deficit, age at stroke onset, and lesion location and size. The heterogeneity of the manifestations of spasticity makes the rehabilitation process highly challenging. A standardized approach is needed to ensure that patients with post-stroke spasticity are diagnosed in a timely manner and receive care soon after its onset (50, 51). Patients with spasticity also need to be informed about their condition and the available treatments. Acute stroke teams often overlook early signs of spasticity, although early recognition of the symptoms could lead to receiving earlier treatment, achieving better outcomes, and avoiding long-term complications (52, 53). The post-stroke checklist was developed as an easy-to-use tool to identify and facilitate the proper treatment of long-term complications of a stroke, including spasticity (54). Patients with weakness or problems with limb dexterity, especially of the upper limb, that interfere with ADL and increase muscle stiffness in at least 1 joint at 4–12 weeks post-stroke are at high risk of developing severe spasticity and should be directly referred to a specialist who can administer botulinum toxin treatment and perform physiotherapy assessment (53).

Secondary stroke prevention and management of early complications

Patients who experienced a chronic stroke have better outcomes when they receive effective treatment within an integrated care system with regular follow-up and self-management support (55, 56). They often receive complex information about risk factors for stroke recurrence, secondary prevention methods, treatment of comorbidities, lifestyle changes, and rehabilitation strategies at the time of discharge from the hospital. Providing this information can allow patients (and their families) to better care for their illnesses. The self-management model of care is essential for improving outcomes; therefore, stroke teams must support stroke survivors in transitioning to this care model (56–58).

General practitioners (GPs) play an integral role in the management of post-stroke patients. From the hospital, a GP should receive all the necessary information about the patient for secondary prevention and proper monitoring of medication use and lifestyle modifications in the primary care settings. In routine practice, the GP can identify deterioration in a patient's functioning post-discharge and arrange a referral for further therapy (59). The GP's involvement in stroke survivors' care alleviates their dependence (as well as that of their caregivers) on specialists and allows patients to better understand and manage their condition.

Another important element of post-stroke care is timely access to outpatient specialist neurologic care clinics linked to hospital services and primary care, with an initial visit at 6 months post-stroke and then one time a year as a long-term follow-up. The purpose of these visits is to monitor the patient's neurologic status and assess the occurrence and treatment of complications such as post-stroke cognitive disorders, depression, or epilepsy (29, 56, 59).

Summary and conclusion

Experts have long suggested organizational solutions and goals of proper care for patients who experienced a stroke (20, 60, 61). Based on these recommendations, many countries are systematically improving the quality of acute stroke care, including the creation of better-functioning stroke unit networks. Current healthcare policy trends in many countries point to broader implementation of intravenous thrombolysis and mechanical thrombectomy, which are consistent with the ischemic stroke treatment guidelines (62). The proportion of patients receiving specific therapy for ischemic stroke is increasing, with successful outcomes in many cases. However, although doctors caring for patients in the acute phase are constantly improving their qualifications and acquiring highly specialized knowledge to implement acute stroke interventions properly and safely, they lack opportunities and time to develop competencies in neurorehabilitation and long-term post-stroke care.

Significant improvements in patient outcomes and healthcare savings may be afforded by improved access to rehabilitation and specialist outpatient neurologic care and their integration with primary care. Effective long-term post-stroke care requires optimal pathways and facilities for patients in different clinical conditions. The efficient organization of all hospital and community practice settings for post-stroke patients requires investment in infrastructure and continuous training of all healthcare professionals to ensure adequate provision of care. Decisions based on the principle of the effectiveness of continuous stroke care will ensure the most beneficial allocation of limited financial resources. As most post-stroke patients spend most of their lives outside of formal healthcare settings, it is essential to expand and coordinate partnerships with government sectors (e.g., the Ministry of Work and Social Policy), the private healthcare sector, non-governmental organizations, and community groups.

The optimal model of post-stroke care is not widely used because of a lack of coordination of such care and the dearth of medical professionals who can provide highly specialized post-stroke rehabilitation and long-term care. This study summarized the frequently overlooked problems in post-stroke patient care and outlined the necessary steps to organize a network of post-stroke care centers (both inpatient and outpatient) in individual countries with the active involvement of primary care physicians. A limitation of the proposed pathway is that it was developed based on the experience of experts and not on data from studies evaluating the effectiveness of such an approach; despite a general acknowledgment of the need for better organization of long-term

stroke care, there is insufficient research and evidence to support experts' recommendations.

Currently, in many countries, patients who have had a stroke are monitored indirectly based on population health statistics. Some countries maintain stroke registries or conduct observational studies to monitor patients in the year after a stroke (21), but most registries focus solely on the quality of early stroke care. The creation of a register—for example, as an extension of the Registry of Stroke Care Quality that is organized based on the Stroke Action Plan for Europe—for long-term assessment of the quality of post-stroke care would allow for an easier analysis of the effectiveness of the proposed care scheme.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

IS-D contributed to the conception and design of the article, collected and organized the data, wrote the first draft of the manuscript, and revised, edited, and approved the final submitted version of the manuscript.

Funding

This research was supported by the National Center for Research and Development (grant no. IS-2/200/NCBR/2015 entitled The Lean Management Project in Healthcare (LeanOZ), project manager: Prof. dr hab. Tomasz Hermanowski).

Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Neurol.* (2021) 20:795–820. doi: 10.1016/S1474-4422(21)00252-0

2. Feigin VL, Brainin M, Norrving B, Martins S, Sacco RL, Hacke W, et al. World Stroke Organization (WSO): global stroke fact sheet 2022. *Int J Stroke.* (2022) 17:18–29. doi: 10.1177/17474930211065917

3. Stevens E, Emmet E, Wang Y, McKevitt C, Wolfe CDA. *The Burden of Stroke in Europe: The Challenge for Policy Makers*. Stroke Alliance for Europe (2017). p. 1–131. Available online at: https://www.stroke.org.uk/sites/default/files/the_burden_of_stroke_in_europe_-_challenges_for_policy_makers.pdf (accessed December 09, 2022).

4. Truelsen T, Piechowski-Józwiak B, Bonita R, Mathers C, Bogousslavsky J, Boysen G. Stroke incidence and prevalence in Europe: a review of available data. *Eur J Neurol.* (2006) 13:581–98. doi: 10.1111/j.1468-1331.2006.01138.x

5. Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, et al. Heart disease and stroke statistics – 2018 update. A report from the American Heart Association. *Circulation.* (2018) 137:e67–492. doi: 10.1161/CIR.0000000000000573

6. Mohan KM, Wolfe CD, Rudd AG, Heuschmann PU, Kolominsky-Rabas PL, Grieve AP. Risk and cumulative risk of stroke recurrence: a systematic review and meta-analysis. *Stroke.* (2011) 42:1489–94. doi: 10.1161/STROKEAHA.110.602615

7. Murray CJL, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet.* (2012) 380:2197–223. doi: 10.1016/S0140-6736(12)61690-0

8. Centers for Disease Control and Prevention. Prevalence and most common causes of disability among adults: United States, 2005. *Morb Mortal Wkly Rep.* (2009) 58:421–6.

9. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensach GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990–2010: findings from the Global Burden of Diseases Study 2010. *Lancet.* (2014) 383:245–55. doi: 10.1016/S0140-6736(13)61953-4

10. Salter K, Hellings C, Foley N, Teasell R. The experience of living with stroke: a qualitative meta-synthesis. *J Rehabil Med.* (2008) 40:595–602. doi: 10.2340/16501977-0238

11. Lohr KN (ed.) *Medicare: A Strategy for Quality Assurance*. Volume I. Washington, DC: The National Academy Press (1990). p. 21.

12. Stroke Unit Trialists' Collaboration. Organised inpatient (stroke unit) care for stroke. *Cochrane Database Syst Rev.* (2013) 9:CD000197. doi: 10.1002/14651858.CD000197.pub3

13. Appelros P, Jonsson F, Asberg S, Asplund K, Glader E-L, Asberg KH, et al. Trends in stroke treatment and outcome between 1995 and 2010: observations from riks-stroke, the Swedish stroke register. *Cerebrovasc Dis.* (2014) 37:22–9. doi: 10.1159/000356346

14. Członkowska A, Skowrońska M, Niewada M. Stroke service in Central and Eastern Europe. *Int J Stroke.* (2007) 2:276–8. doi: 10.1111/j.1747-4949.2007.00152.x

15. Budincevic H, Tiu C, Bereczzki D, Korv J, Tsiskaridze A, Niederkorn K, et al. Management of ischemic stroke in Central and Eastern Europe. *Int J Stroke.* (2015) 10:125–7. doi: 10.1111/ijs.12575

16. Członkowska A, Niewada M, Sarzyńska-Długosz I, Kobayashi A, Skowrońska M. Ten years of stroke programmes in Poland: where did we start? Where did we get to? *Int J Stroke.* (2010) 5:414–6. doi: 10.1111/j.1747-4949.2010.00470.x

17. Sarzyńska-Długosz I, Skowrońska M, Członkowska A. Organization of acute stroke services in Poland – polish stroke unit network development. *Neurol Neurochir Pol.* (2013) 47:3–7. doi: 10.5114/ninp.2013.32934

18. Wiedmann S, Heuschmann PU, Hillmann S, Busse O, Wiethölter H, Walter GM, et al. The quality of acute stroke care – an analysis of evidence-based indicators in 260 000 patients. *Dtsch Arztebl Int.* (2014) 111:759–65. doi: 10.3238/arztebl.2014.0759

19. Royal College of Physicians, Clinical Effectiveness and Evaluation Unit on behalf of the Intercollegiate Stroke Working Party. Stroke Sentinel National Audit Programme. *Changes over Time: 4 Years data April 2013 – March 2017 Public Report.* England: Royal College of Physicians (2017).

20. Norrving B, Barrick J, Davalos A, Dichgans M, Cordonnier Ch, Guekht A, et al. Action plan for stroke in Europe 2018–2030. *Eur Stroke J.* (2018) 3:309–6. doi: 10.1177/2396987318808719

21. Boehme Ch, Toell T, Lang W, Knoflach M, Kiechl S. Longer term patient management following stroke: a systematic review. *Int J Stroke.* (2021) 16:917–26. doi: 10.1177/17474930211016963

22. Kelly-Hayes M, Wolf PA, Kannel WB, Sytkowski B, D'Agostino RB, Gresham GE. Factors influencing survival and need for institutionalization following stroke: the Framingham Study. *Arch Phys Med Rehabil*. (1988) 69:415–8.

23. Pfeffer MM, Reding MJ. Stroke rehabilitation. In: Lazar RB, editor. *Principles of Neurological Rehabilitation*. New York, NY, McGraw Hill (1998). p. 105–19.

24. Teassel R, Hyssein N, Foley N. *Evidence-Based Review of Stroke Rehabilitation. Managing the Stroke Rehabilitation Triage Process.* (2018). Available online at: http://www.ebrsr.com/evidence-review/4-managing-stroke-rehabilitation-triage-process (accessed December 09, 2022).

25. Asberg KH, Nydevik I. Early prognosis of stroke outcome by means of Katz Index of activities of daily living. *Scand J Rehabil Med*. (1991) 23:187–91.

26. Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, et al. Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. (2016) 47:e98–169. doi: 10.1161/STR.0000000000000098

27. Agency for Health Care Policy and Research. *Post-stroke Rehabilitation: Assessment, Referral, and Patient Management*. U.S. Department of Health and Human Services Public Health Service (1995). p. 1-32.

28. Garraway M. Stroke rehabilitation units: concepts, evaluation, and unresolved issues. *Stroke*. (1985) 16:178–181. doi: 10.1161/01.STR.16.2.178

29. Garraway WM, Akhtar AJ, Smith DL, Smith ME. The triage of stroke rehabilitation. *J Epidemiol Community Health*. (1981) 35:39–44. doi: 10.1136/jech.35.1.39

30. Ween JE, Alexander MP, D'Esposito M, Roberts M. Factors predictive of stroke outcome in a rehabilitation setting. *Neurology*. (1996) 47:388–92. doi: 10.1212/WNL.47.2.388

31. Stineman MG, Fiedler RC, Granger CV, Maislin G. Functional task benchmarks for stroke rehabilitation. *Arch Phys Med Rehabil*. (1998) 79:497–504. doi: 10.1016/S0003-9993(98)90062-4

32. Pereira S, Graham JR, Shahabaz A, Salter K, Foley N, Meyer M, et al. Rehabilitation of individuals with severe stroke: synthesis of best evidence and challenges in implementation. *Top Stroke Rehabil*. (2012) 19:122–31. doi: 10.1310/tsr1902-122

33. Pereira S, Foley N, Salter K, McClure JA, Meyer M, Brown J, et al. Discharge destination of individuals with severe stroke undergoing rehabilitation: a predictive model. *Disabil Rehabil*. (2014) 36:727–31. doi: 10.3109/09638288.2014.902510

34. Saikaley M, Iruthayarajah J, Foley N, Richardson M, Allen L, Cotoi A, et al. *Evidence-Based Review of Stroke Rehabilitation. Outpatient Rehabilitation*. (2018). Available online at: http://www.ebrsr.com/evidence-review/7-outpatient-stroke-rehabilitation (accessed December 09, 2022).

35. Fisher RJ, Gaynor C, Kerr, M, Langhorne P, et al. A consensus on stroke: early supported discharge. *Stroke*. (2011) 42:1392–7. doi: 10.1161/STROKEAHA.110.606285

36. Fearon P, Langhorne P, Early Supported Discharge Trialists. Services for reducing duration of hospital care for acute stroke patients. *Cochrane Database Syst Rev*. (2012) 9:CD000443. doi: 10.1002/14651858.CD000443.pub3

37. Langhorne P, Baylan S, Early Supported Discharge Trialists. Early supported discharge services for people with acute stroke. *Cochrane Database Syst Rev*. (2017) 7:CD000443. doi: 10.1002/14651858.CD000443.pub4

38. Legg L, Langhorne P, Outpatient Service Trialists. Rehabilitation therapy services for stroke patients living at home: systematic review of randomised trials. *Lancet*. (2004) 363:352–6. doi: 10.1016/S0140-6736(04)15434-2

39. Outpatient Service Trialists. Therapy-based rehabilitation services for stroke patients at home. *Cochrane Database Syst Rev*. (2003) 1:CD002925. doi: 10.1002/14651858.CD002925

40. Ferrarello F, Baccini M, Rinaldi LA, Cavellini MC, Mossello E, Masotti G, et al. Efficacy of physiotherapy interventions late after stroke: a meta-analysis. *J Neurol Neurosurg. Psychiatry*. (2011) 82:136–43. doi: 10.1136/jnnp.2009.196428

41. Green J, Young J, Forster A, Collen F, Wade D. Combined analysis of two randomized trials of community physiotherapy for patients more than one year post stroke. *Clin Rehabil*. (2004) 18:249–52. doi: 10.1191/0269215504cr747oa

42. Gilbertson L, Langhorne P. Home-based occupational therapy: stroke patients' satisfaction with occupational performance and service provision. *Br J Occup Ther*. (2000) 63:464–68. doi: 10.1177/030802260006301002

43. Lance JW. The control of muscle tone, reflexes and movement: Robert Wartenberg lecture. *Neurology*. (1980) 30:1303–13. doi: 10.1212/WNL.30.12.1303

44. Li S, Francisco GE. New insights into the pathophysiology of post-stroke spasticity. *Front Hum Neurosci*. (2015) 9:192. doi: 10.3389/fnhum.2015.00192

45. Doan QV, Brashear A, Gillard PJ, Varon SF, Vandenburgh AM, Turkel CC, et al. Relationship between disability and health-related quality of life and caregiver burden in patients with upper limb poststroke spasticity. *PM R*. (2012) 4:4–10. doi: 10.1016/j.pmrj.2011.10.001

46. Welmer AK, von Arbin M, Widen Holmqvist L, Sommerfeld DK. Spasticity and its association with functioning and health-related quality of life 18 months after stroke. *Cerebrovasc Dis*. (2006) 21:247–53. doi: 10.1159/000091222

47. Ward AB. A literature review of the pathophysiology and onset of post-stroke spasticity. *Eur J Neurol*. (2012) 19:21–7. doi: 10.1111/j.1468-1331.2011.03448.x

48. Wissel J, Manack A, Brainin M. Toward an epidemiology of post-stroke spasticity. *Neurology*. (2013) 80:S13–9. doi: 10.1212/WNL.0b013e3182762448

49. Balakrishnan S, Ward AB. The diagnosis and management of adults with spasticity. *Handb Clin Neurol*. (2013) 110:145–60. doi: 10.1016/B978-0-444-52901-5.00013-7

50. Picelli A, Baricich A, Cisari C, Paolucci S, Smania N, Sandrini G, on behalf of the Italian Real-Life Survey Group. The Italian real-life post-stroke spasticity survey: unmet needs in the management of spasticity with botulinum toxin type A. *Funct Neurol*. (2017) 32:89–96. doi: 10.11138/FNeur/2017.32.2.089

51. Barnesa M, Kocerb S, Fernandezc MM, Balcaitiened M, Fheodoroffe K. An international survey of patients living with spasticity. *Dis Reh*. (2017) 39:1428–34. doi: 10.1080/09638288.2016.1198432

52. Wissel J, Verrier M, Simpson DM, Charles D, Guinto P, Papapetropoulos S, Snnerhagen KS. Post-stroke spasticity: predictors of early development and considerations for therapeutic intervention. *PM R*. (2015) 7:60–66. doi: 10.1016/j.pmrj.2014.08.946

53. Bavikatte G, Subramanian G, Ashford S, Allison R, Hicklin D. Early identification, intervention and management of post-stroke spasticity: expert consensus recommendations. *J Centr Ner Sys Dis*. (2021) 13:1–8. doi: 10.1177/11795735211036576

54. Philp I, Brainin M, Walker MF, Ward AB, Gillard P, Shields AL, et al. Development of a post-stroke checklist to standardize follow-up care for stroke survivors. *J Stroke Cerebrovasc Dis*. (2013) 22:e173–80. doi: 10.1016/j.jstrokecerebrovasdis.2012.10.016

55. Epping-Jordan JE, Pruitt SD, Bengoa R, Wagner EH. Improving the quality of health care for chronic conditions. *Qual Saf Health Care*. (2004) 13:299–305. doi: 10.1136/qshc.2004.010744

56. Clarke DJ, Forster A. Improving post-stroke recovery: the role of the multidisciplinary health care team. *J Multidiscip Healthc*. (2015) 8:433–42. doi: 10.2147/JMDH.S68764

57. Bodenheimer T, Lorig K, Holman H, Grumbach K. Patient self-management of chronic disease in primary care. *JAMA*. (2002) 288:2469–75. doi: 10.1001/jama.288.19.2469

58. Sadler E, Wolfe CDA, McKevitt C. Lay and health care professional understandings of self-management: A systematic review and narrative synthesis. *SAGE Open Med*. (2014) 2:2050312114544493. doi: 10.1177/2050312114544493

59. Smith LN, James R, Barber M, Ramsay S, Gillespie D, Chung C, et al. Rehabilitation of patients with stroke: summary of SIGN guidance. *BMJ*. (2010) 340:c2845. doi: 10.1136/bmj.c2845

60. Adams HP Jr. The importance of the Helsingborg declaration on stroke management in Europe. *J Intern Med*. (1996) 240:169–71. doi: 10.1046/j.1365-2796.1996.38858000.x

61. Kjellström T, Norrving B, Shatchkute A. Helsingborg Declaration 2006 on European stroke strategies. *Cerebrovasc Dis*. (2007) 23:231–41. doi: 10.1159/000097646

62. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2018 Guidelines for the early management of patients with acute ischemic stroke. A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. (2018) 49:e46–110. doi: 10.1161/STR.0000000000000158

frontiers | Frontiers in Neurology

TYPE Original Research
PUBLISHED 30 March 2023
DOI 10.3389/fneur.2023.1126472

OPEN ACCESS

EDITED BY
Janika Kõrv,
University of Tartu, Estonia

REVIEWED BY
Silke Walter,
Saarland University Hospital, Germany
Hrvoje Budincevic,
University Hospital Sveti Duh, Croatia

*CORRESPONDENCE
Latha Ganti
✉ latha.ganti@ucf.edu

SPECIALTY SECTION
This article was submitted to Stroke, a section of the journal Frontiers in Neurology

RECEIVED 17 December 2022
ACCEPTED 06 March 2023
PUBLISHED 30 March 2023

CITATION
Ganti L, Mirajkar A, Banerjee P, Stead T, Hanna A, Tsau J, Khan M and Garg A (2023) Impact of emergency department arrival time on door-to-needle time in patients with acute stroke. *Front. Neurol.* 14:1126472. doi: 10.3389/fneur.2023.1126472

Impact of emergency department arrival time on door-to-needle time in patients with acute stroke

Latha Ganti[1,2,3,4]*, Amber Mirajkar[4], Paul Banerjee[3,4], Tej Stead[5], Andrew Hanna[6], Joshua Tsau[7], Mohammed Khan[4] and Ankur Garg[1,4]

[1]Department of Neurology, University of Central Florida College of Medicine, Orlando, FL, United States, [2]Department of Emergency Medicine, University of Central Florida College of Medicine, Orlando, FL, United States, [3]Polk County Fire Rescue, Bartow, FL, United States, [4]HCA Florida Osceola Hospital, Kissimmee, FL, United States, [5]Department of Mathematics and Physics, Brown University, Providence, RI, United States, [6]Division of Pediatric Emergency Medicine, University of Florida, Jacksonville, FL, United States, [7]Department of Emergency Medicine, UT San Antonio, San Antonio, TX, United States

Background: This study aimed to identify which emergency department (ED) factors impact door-to-needle (DTN) time in acute stroke patients eligible for intravenous thrombolysis. The purpose of analyzing emergency department factors is to determine whether any modifiable factors could shorten the time to thrombolytics, thereby increasing the odds of improved clinical outcomes.

Methods: This was a prospective observational quality registry study that included all patients that received alteplase for stroke. These data are our hospital data from the national Get With The Guidelines Registry. The Get With The Guidelines® Stroke Registry is a hospital-based program focused on improving care for patients diagnosed with a stroke. The program has over five million patients, and hospitals can access their own program data. The registry promotes the use of and adherence to scientific treatment guidelines to improve patient outcomes. The time of patient arrival to the ED was captured *via* the timestamp in the electronic health record. Arriving between Friday 6 p.m. and Monday 6 a.m. was classified as "weekend," regardless of the time of arrival. Time to CT, time-to-lab, and presence of a dedicated stroke team were also recorded. Emergency medical services (EMS) run sheets were used to verify arrival *via* ambulance.

Results: Forty-nine percent of the cohort presented during the day shift, 24% during the night shift, and 27% on the weekend. A total of 85% were brought by EMS, and 15% of patients were walk-ins. The median DTN time during the day shift was 37 min (IQR 26–51, range 10–117). The median DTN time during the night shift was 59 min (IQR 39–89, range 34–195). When a dedicated stroke team was present, the median DTN time was 36 min, compared to 51 min when they were not present. The median door-to-CT time was 24 min (IQR 18–31 min). On univariate analyses, arriving during the night shift ($P < 0.0001$), arriving as a walk-in ($P = 0.0080$), and longer time-to-CT ($P < 0.0001$) were all associated with longer DTN time. Conversely, the presence of a dedicated stroke team was associated with a significantly shorter DTN time ($P < 0.0001$).

Conclusion: Factors that contribute most to a delay in DTN time include arrival during the night shift, lack of a dedicated stroke team, longer time-to-CT read,

and arrival as a walk-in. All of these are addressable factors from an operational standpoint and should be considered when performing quality improvement of hospital protocols.

KEYWORDS

intravenous thrombolysis, door-to- puncture time, acute ischemic stroke, stroke system of care, emergency medicine

Introduction

It is common knowledge that, in acute ischemic stroke (AIS), expeditious thrombolysis with tissue plasminogen activator (tPA) has markedly positive outcomes. Shorter time to thrombolytics—often referred to as door-to-needle (DTN) time—not only reduces mortality and symptomatic intracranial hemorrhage, but also results in higher rates of independent ambulation at discharge, discharge to home, and better functional outcomes at 3 months (1). While thrombolytics are approved to be given in the 4.5 h following the onset of stroke symptoms (with several exceptions), there is a push to give them as soon as possible, with a common mantra being "time is brain." Giving thrombolytics as soon as 45 min following presentation to the emergency department (ED) results in improved all-cause mortality or all-cause re-admission at 1 year, although it did not impact re-admission for stroke or other cardiovascular diseases (1).

Furthermore, the updated stroke guidelines by the American Heart Association (AHA) and the American Stroke Association (ASA) (2) reflect this drive to administer thrombolytics within an hour of patient arrival, supported by additional medical associations, such as the American College of Cardiology (3). However, studies have shown that only 30%−50% of American patients with stroke have been treated within the 60-min window (4, 5). These findings motivate intensive efforts to accelerate hospital presentation and thrombolytic treatment in patients with AIS.

The 2018 AHA/ASA Guidelines for the Early Management of Patients with Acute Ischemic Stroke also addressed the pre-hospital approach to patients demonstrating stroke-like symptoms. The use of emergency medical services (EMS) has been associated with earlier arrival to the ED (<3 h), quicker evaluation, shorter door-to-imaging time (<25 min), more rapid administration of thrombolytics (<60 min), and more eligible patients administered thrombolytics (6). Given the time-sensitive nature of AIS, the public has been encouraged to call EMS if they experience stroke-like symptoms; however, only 60% of patients with stroke are brought by EMS (7). One of the largest benefits of EMS transporting the patient is the advance notice provided, allowing the ED to assemble the hospital stroke team for rapid evaluation and care. Furthermore, advance notice allows the Radiology department to allocate a CT scanner for the patient with stroke, minimizing time wasted if another patient is being scanned. Streamlined protocols across providers and specialties have shown a reduction in DTN time, regardless of the time of day or academic vs. community center (8, 9).

Many of these studies, however, were performed in Canada or in large established academic U.S. hospitals (6–9). There is a paucity of studies at community hospitals in the American southeast, especially in Florida. A major effort to remedy this, from 2010 to 2015, was the National Institute of Neurologic Disorders and Stroke (NINDS)-funded Florida-Puerto Rico (FL-PR) Collaboration to Reduce Stroke Disparities (CReSD) Study. The main findings were that the achievement of DTN time ≤60 min and DTN time ≤45 min was highest in South Florida (50%, 23%), while lowest in West and Central Florida (28%, 11%) (5). Thus, our study in Central Florida aimed to identify whether the time of day when the patient presented to our ED and whether they arrived *via* ambulance impacted the DTN time.

Methods

This is a prospective observational quality registry study that included all patients at our institution who received alteplase in the ED. Our institution sees over 80,000 patient visits per year, has a comprehensive stroke center, and is home to both neurology and emergency medicine residency programs. Of the 80,000 ED visits, ∼500 are for acute ischemic stroke, and we deliver acute thrombolysis for ∼25%. The current study consisted of consecutive patients over a 12-month period that presented as stroke alerts and received thrombolytic therapy. The University Institutional Review Board gave an exempt determination for this study #SBE-1814176.

Our acute stroke protocol begins with notification from emergency medical services (EMS) personnel for patients transported *via* ambulance. Our prehospital protocol to screen for stroke includes the Los Angeles Motor Score (LAMS), baseline functional status, and current anticoagulant (5). Immediately upon notification, a "stroke alert" is announced on the overhead pager, and stroke team members are individually notified on their hospital cellular phones. The stroke team consists of a neurology resident physician, a neurology advanced registered nurse practitioner, the CT and lab technicians, the ED pharmacist, and the ED physicians. During the period of this study, our institution did not have 24/7 coverage by the stroke team. The team is, thus, able to mobilize before patient arrival when prehospital notification is received. Upon arrival, the patient is transported to a designated "stroke bed," which automatically weighs the patient. The thrombolytic dosing is calculated based on this weight and is readied in case the patient would qualify for thrombolysis. The patient's blood is obtained for laboratory analysis en route to the CT scanner, and thrombolytics are administered in the CT scanner room itself if the patent is a candidate.

The DTN time along with other stroke metrics was captured in the Get with the Guidelines® -Stroke (GWTG) registry, to which our institution belongs. GWTG-Stroke is the American Heart Association's (AHA) collaborative performance improvement program, demonstrated to improve adherence to evidence-based care of patients hospitalized with stroke (6). Hospital data are entered into GWTG by trained and monitored abstractors using explicit protocols, precisely defined variables, and standardized abstraction instruments, as delineated by the AHA. Missing, conflicting, and ambiguous chart elements are coded per AHA GWTG instructions. Abstractors are blinded to any study hypotheses, as they are data entry personnel who work for the stroke service and are not part of the research team.

The time of patient arrival to the ED was captured *via* the timestamp in the electronic health record (EHR) and categorized as either being during the "day shift" (6 a.m.−6 p.m.) or the "night shift" (6 p.m.−6 a.m.). Arriving between Friday 6 p.m. and Monday 6 a.m. was classified as "weekend," regardless of the time of arrival. This classification is based on the shift times of the emergency department physicians as well as the stroke team. The mode of arrival was classified as arrival *via* EMS vs. walk/drove in. Our logic in selecting these two factors is that they are potentially ones that we would be able to influence.

TABLE 1 Cohort demographics.

	Day shift ($n = 82$)	Night shift ($n = 25$)
Age	Median 67 (IQR 57–81 years)	Median 59 (IQR 44–70 years)
Sex	49% female ($n = 41$)	32% female
History of prior stroke	27% ($n = 22$)	32% ($n = 8$)
History of diabetes	41% ($n = 34$)	12% ($n = 3$)
Underwent thrombectomy	29% ($n = 24$)	16% ($n = 4$)
Race	46% white, 35% Hispanic, 13% black, 6% mixed	36% white, 32% Hispanic, 24% black, 8% mixed
Time to CT	Median = 22 (IQR 18–28 min)	Median = 30 (IQR 19–42 min)
Time to Lab	Median = 41 (IQR 32–56 min)	Median = 42 (IQR 34–58 min)
NIHSS in the ED	Median = 10 (IQR 6–17)	Median = 7.5 (IQR 2.5–15 min)
Arrival *via* walk-in	6%	28%

CT, computed tomography; NIHSS, National Institutes of Health Stroke Scale; ED, emergency department; IQR, interquartile range; min, minutes.

Results

The cohort consisted of 107 patients, 44% of whom were women. The racial distribution was 44% white, 35% Hispanic, 16% black, and 5% mixed race. The median age was 67 with an interquartile range of 55–79 years. Twenty-eight percent had a history of a prior stroke, while 36% had a history of diabetes. The median NIHSS at admission was 10 with an interquartile range of 5–17 and a range from 1 to 34. The median NIHSS at discharge was 2 with an interquartile range of 0–6 and a range from 0 to 34. The median door-to-CT time was 24 min (IQR 18–31 min). The median door-to-lab result time was 41.5 min (IQR 32–58). Twenty-four percent underwent thrombectomy in addition to thrombolysis.

Forty-nine percent of the cohort presented during the day shift, 24% during the night shift, and 27% on the weekend. A total of 85% were brought by EMS, and 15% of patients were walk-ins. The median DTN time during the day shift was 37 min (IQR 26–51, range 10–117). The median DTN time during the night shift was 59 min (IQR 39–89, range 34–195). When a dedicated stroke team was on duty, the median DTN time was 36 min compared to 51 min when they were not present. Table 1 presents the cohort demographics categorized by arrival during the day or night shift.

Univariate factors associated with increased DTN time included: arriving during the night shift ($P < 0.0001$) not arriving *via* EMS ($P = 0.0080$), and during the absence of a dedicated stroke team ($P < 0.0001$). Time to CT was also significantly associated with DTN time ($P < 0.0001$). Interestingly, time-to-lab was not statistically significant. During the day shift, the median door-to-CT time was 22 min (IQR 18–29, range 5–129) compared to 31.5 min (IQR 18–42, range 13–82) during the night shift. Arrival *via* EMS occurred in 75% of cases during the night shift, but in 88% of cases during the day shift. The time-to-CT was also significantly different for those who did and did not arrive *via* EMS. The median time-to-CT for patients arriving *via* EMS was 21.5 min (IQR 17–28, range 5–129 min). By contrast, the median DTN time for patients not arriving by EMS was 37 min (IQR 25.5–50, range 19–62 min).

None of the other factors, including age, sex, history of diabetes or prior stroke, or NIHSS in the ED, were significant. In a multivariate model that included all of these factors, the same univariate factors remained statistically significant.

Of these univariate results, the ones that were most interesting to our team were the time of patient arrival (day vs. night shift and weekday vs. weekend shift) and mode of arrival, as these are operational factors that we could potentially address. We performed a two-way analysis of variance (ANOVA), which is a whole-model test that determines whether at least one pair of means is significantly different from each other. After rejecting the null hypothesis ($P < 0.0001$), we followed up with Tukey's multiple-comparison procedure, a conservative test that adjusts for multiple comparisons, and found that night shift patients had a significantly longer DTN time than day shift patients ($P < 0.0001$) and weekend patients ($P = 0.0272$).

To determine the effect sizes, we performed a least-squares linear regression model. This model yields a line that makes the vertical distance from the data points to the regression line as small as possible. It is referred to as a "least squares" because the best line of fit is one that minimizes the variance (the sum of squares of the errors). The predicted DTN time ($R^2 = 0.281$) was determined by the following approximate formula: 48.5 min + 18.1 min (if the patient is a walk-in) + the value for shift time. Values for shift time were as follows: −16.0 min if the day shift, +15.3 min if the night shift, and +0.6 min if the weekend shift. Both the shift type

10.3389/fneur.2023.1126472

TABLE 2 Reasons for delay in door-to-needle (DTN) time.

Reason for delay in DTN time
Patient was brought in by EMS as a drug overdose
Transfer from free-standing ED and delay in getting INR
Patient unstable
Chest pain and concern for aortic dissection, needed to wait for chest CTA
Patient improved then worsened
Atypical stroke symptoms; needed intubation and repeat CT to rule out bleeding due to worsening neuro symptoms
Chest pain and need to rule out aortic dissection
Neurology delay in calling back
Patient with dementia, unable to give a reliable time of onset
Elevated blood pressure requiring control prior to tPA
Patient initially presented as a drug overdose
Patient presented with a complaint of chest pain initially
Unclear about anticoagulant use (patient with a history of atrial fibrillation)
Patient with waxing/waning symptoms

EMS, emergency medical services; ED, emergency department; INR, international normalized ratio; CTA, computed chest tomography; CT, computed tomography; tPA, tissue plasminogen activator.

($P < 0.0001$) and arrival by walk-in ($P = 0.0095$) were statistically significant. As the weekend shift contains both day and night shifts, the effect size is close to zero for weekend patients, as the changes in DTN time by shift type cancel each other out.

As the weekend shift seems to be a flawed grouping of data (because it groups both night and day shifts together and the main difference exists between these two groups), we repeated our linear regression model with the exclusion of the weekend patients ($n = 74$, P-value through ANOVA <0.0001, $R^2 = 0.36$). We found that both arrivals during the night shift ($P < 0.0001$) and arrival by walk-in ($P = 0.0047$) were significantly associated with higher DTN times. The predictive formula for DTN time, in this case, was: 32.2 min, plus 21.5 min if arriving *via* walk-in, plus 30.8 min if arriving *via* night shift.

Our second linear regression model, which excluded patients who arrived on the weekend, was found to have a much better coefficient of determination in predicting DTN times. This is not because weekend patients are unique, but rather a result of the patient grouping in our database. The effect of weekend vs. weekday is dwarfed by the effect of day vs. night shift, which were initially both included as "weekend patients."

Six patients in our cohort suffered a post-tPA hemorrhage. While not statistically significant, the median DTN time for those with a hemorrhage was 44 min (IQR 29–74) vs. 40.5 min (IQR 30–58) in those who did not have a post-tPA hemorrhage.

We reviewed each of the cases in which there was a prolonged DTN time. The majority of these cases had to do with not immediately recognizing that the presentation was an acute stroke. A disproportionate number of these cases occurred during the night shift (Table 2).

Discussion

Our study sought to ascertain the factors influencing DTN time at our mid-sized academic community ED in the Southeastern United States. The data show that a patient's DTN time was longer if they arrived as a walk-in or if they arrived during the night shift.

There are several possible reasons why our data showed a statistically significantly higher DTN time at night, despite the stroke protocol for all times of the day being the same.

First, the night shift is inconsistently staffed, with many nights having no dedicated stroke team covering, so it falls to the ED team to see all patients including patients with stroke. ED resident staffing is also decreased at night, with fewer senior residents, and there is usually a team consisting of one senior resident and two interns. With fewer helping hands, each individual has more tasks, and all of these tasks can slow down the process.

In the National Institute of Neurologic Disorders and Stroke (NINDS)-funded Florida-Puerto Rico (FL-PR) Collaboration to Reduce Stroke Disparities (CReSD) Study, researchers also identified significant differences in DTN time when comparing regular hours (Monday–Friday, 7:01 a.m.−5:59 p.m.) to off hours (Monday–Friday 6 p.m.−7 a.m., all day Saturday, all day Sunday, and government holidays) (5). They observed off-hours DTN time to be greater than work hours DTN time likely secondary to increased difficulty obtaining collateral information as well as fewer stroke specialists and staff at night, during weekends, and on holidays. They also found statistically significant reduced DTN time if the patient was brought in by ambulance (5). Walk-in patients do not have the luxury of giving the ED advance notice.

This mirrors our data, which showed an increased DTN time if the patient walked into the ED as opposed to arriving by ambulance. Advanced notice allows the ED personnel and stroke team to prioritize their tasks in the anticipation of giving their undivided attention to a stroke patient. Another explanation for improved DTN time in patients brought by EMS is their ability to correctly identify patients with possible stroke, thereby expediting their care. Many prehospital stroke scales exist, with a sensitivity as high as 85% and a specificity as high as 97% (10). A county-wide EMS stroke protocol found a Los Angeles Motor Score of >4 has excellent predictive validity for identifying patients with large vessel occlusions, resulting in accurate transport decisions to comprehensive stroke centers where thrombolytics are administered promptly, often while the patient is on the way to the angiography suite (11–13). Partnering with one's EMS agency results in more expeditious care, including shorter door-to-physician and door-to-CT time, and greater odds of receiving thrombolysis (14).

Finally, there may be some lingering bias between walk-in patients and EMS patients, namely that patients brought in by ambulance are sicker. Anchoring bias is also very prevalent. Whichever first working "diagnosis" is made is the one that sticks. Therefore, for example, if EMS deems the patient to be a "stroke alert" then stroke protocol in the ED proceeds regardless of any downstream thoughts of alternative diagnoses. Similarly, if EMS brings in a decreased level of consciousness patient but labels them an overdose rather than a stroke, then the natural tendency is for the ED to proceed down the overdose protocol initially. We

actually did see this exact scenario in our cohort. This results in a delayed door-to-needle time when the stroke is ultimately found to be the cause.

Our study did not survey the perspectives of physicians and other medical staff, but it would be an aspect to explore in future. While we can only speculate the contributing factors to the data seen in this study, other areas in which future research is needed are the assessments of demographics in those who received thrombolytics, as well as the degree of sickness upon presentation. If a patient must be stabilized prior to undergoing a CT scan and/or administering thrombolytics because of blood pressure, airway compromise, or other condition, this will increase DTN time.

Limitations

This is a single-center study performed in the Southeastern USA, and thus limited by the population and protocols of this region. Nevertheless, our findings underscore the importance of 24/7 stroke team presence and the importance of our EMS partners.

Conclusion

Our prospective observational study in a real-world community emergency department showed that arrival during the night shift and as a walk-in rather than *via* ambulance resulted in a significantly longer DTN time. Contributing factors to these findings include fewer staff at night and a delay in identifying patients with acute stroke. Ongoing assessment of local factors that prolong DTN times is an important way to expedite thrombolytics for our patients and address quality metrics.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by University of Central Florida Institutional Review Board. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

LG conceived the study and wrote the manuscript. PB, MK, and AG supervised the conduct of the study. TS provided the statistical analyses. AH and JT collected the data. All authors contributed to the revising the original draft manuscript, read the final version of the paper, and have approved it for submission.

Funding

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Author disclaimer

The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

References

1. Man S, Xian Y, Holmes DN, Matsouaka RA, Saver JL, Smith EE, et al. Association between thrombolytic door-to-needle time and 1-year mortality and readmission in patients with acute ischemic stroke. *JAMA*. (2020) 323:2170–84. doi: 10.1001/jama.2020.5697

2. Powers W, Rabinstein A, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. (2018) 49:e46–99. doi: 10.1016/j.jvs.2018.04.007

3. McDermott M. *2018 AHA/ASA Stroke Early Management Guidelines*. Washington, DC: American College of Cardiology (2018).

4. Fonarow GC, Zhao X, Smith EE, Saver JL, Reeves MJ, Bhatt DL, et al. Door-to-needle times for tissue plasminogen activator administration and clinical outcomes in acute ischemic stroke before and after a quality improvement initiative. *JAMA*. (2014) 311:1632–40. doi: 10.1001/jama.2014.3203

5. Oluwole SA, Wang K, Dong C, Ciliberti-Vargas MA, Gutierrez CM Yi L, et al. Disparities and trends in door-to-needle time: the FL-PR CReSD Study (Florida-Puerto Rico Collaboration to Reduce Stroke Disparities). *Stroke*. (2017) 48:2192–7. doi: 10.1161/STROKEAHA.116.016183

6. Ekundayo OJ, Saver JL, Fonarow GC, Schwamm LH, Xian Y, Zhao X, et al. Patterns of emergency medical services use and its association with timely stroke treatment: findings from get with the guidelines–stroke. *Circ Cardiovasc Qual Outcomes*. (2013) 6:262–9. doi: 10.1161/CIRCOUTCOMES.113.000089

7. Mochari-Greenberger H, Xian Y, Hellkamp AS, Schulte PJ, Bhatt DL, Fonarow GC, et al. Racial/ethnic and sex differences in emergency medical services transport

among hospitalized US Stroke patients: analysis of the national get with the guidelines-stroke registry. *J Am Heart Assoc.* (2015) 4:e002099. doi: 10.1161/JAHA.115.002099

8. Kamal N, Shand E, Swanson R, Hill MD, Jeerakathil T, Imoukhuede O, et al. Reducing door-to-needle times for ischaemic stroke to a median of 30 minutes at a community hospital. *Can J Neurol Sci.* (2019) 46:51–6. doi: 10.1017/cjn.2018.368

9. Köhrmann M, Schellinger PD, Breuer L, Dohrn M, Kuramatsu JB, Blinzler C, et al. Avoiding in hospital delays and eliminating the three-hour effect in thrombolysis for stroke. *Int J Stroke.* (2011) 6:493–7. doi: 10.1111/j.1747-4949.2011.00585.x

10. Stead TG, Banerjee P, Ganti L. Real-world field performance of the Los Angeles motor scale as a large vessel occlusion screen: a prospective muticentre study. *Cerebrovasc Dis.* (2021). doi: 10.1159/000516116

11. Abboud ME, Band R, Jia J, Pajerowski W, David G, Guo M, et al. Recognition of stroke by ems is associated with improvement in emergency department quality measures. *Prehosp Emerg Care.* (2016) 20:729–36. doi: 10.1080/10903127.2016.1182602

12. Stead TG, Ganti L, Banerjee P. Large vessel occlusion identification through prehospital administration of stroke scales: a county-wide emergency medical services prospective research protocol. *Cureus.* (2019) 11:e5931. doi: 10.7759/cureus.5931

13. Ganti L, Oostema JA. How accurate are the stroke severity scales for identifying large vessel occlusions? *Ann Emerg Med.* (2020) 75:494–6. doi: 10.1016/j.annemergmed.2019.07.022

14. Ganti L, Banerjee P, Falco W. Partnering with your EMS agency to improve stroke outcomes. ACEP E-QUAL webinar. Available online at: https://vimeo.com/465118080/4349c3db4e (accessed January 20, 2023).

frontiers | Frontiers in Neurology

TYPE Review
PUBLISHED 11 April 2023
DOI 10.3389/fneur.2023.1143713

OPEN ACCESS

EDITED BY
Janika Kõrv,
University of Tartu,
Estonia

REVIEWED BY
Aleksandra Pikula,
University of Toronto,
Canada
Dejian Yu,
Nanjing Audit University,
China

*CORRESPONDENCE
Xiaomei Guo
✉ gxm4725@163.com

†These authors have contributed equally to this work and share first authorship

SPECIALTY SECTION
This article was submitted to Stroke, a section of the journal Frontiers in Neurology

RECEIVED 13 January 2023
ACCEPTED 20 March 2023
PUBLISHED 11 April 2023

CITATION
Chen M, Zhang Y, Dong L and Guo X (2023) Bibliometric analysis of stroke and quality of life.
Front. Neurol. 14:1143713.
doi: 10.3389/fneur.2023.1143713

Bibliometric analysis of stroke and quality of life

Mengtong Chen[1,2†], Yuting Zhang[1,2†], Lijuan Dong[1] and Xiaomei Guo[1*]

[1]Department of Nursing, Zhongshan Hospital of Traditional Chinese Medicine, Zhongshan, Guangdong, China, [2]Clinical Medical College of Acupuncture, Moxibustion, and Rehabilitation, Guangzhou University of Chinese Medicine, Guangzhou, Guangdong, China

Objective: To perform a bibliometric analysis of stroke and quality of life studies between 2000 and 2022 using VOSviewer and CiteSpace.

Methods: The literature data source for this study was the Web of Science Core Collection. CiteSpace and VOSviewer were used to analyze publications in relation to authors, countries, institutions, journals, references, and keywords.

Results: A total of 704 publications were obtained for the bibliometric analysis. The number of publications has gradually increased over 23years, with an annual increase of 728.6%. Kim S is the most prolific author in the field (10 publications), and the United States and Chinese University of Hong Kong have the most publications. Stroke is the most prolific journal with the most citations per paper (91.58) and the highest impact factor (IF 2021, 10.17). The most high-frequency keywords are "stroke," "quality of life," "rehabilitation," and "depression."

Conclusion: A bibliometric analysis of stroke and quality of life over the last 23 years provides future research directions.

KEYWORDS

stroke, quality of life, bibliometric analysis, CiteSpace, VOSviewer

1. Introduction

Stroke is an acute cerebrovascular disease caused by the sudden rupture of a blood vessel in the brain or the blockage of a blood vessel that prevents blood from flowing to the brain. It is a group of diseases that cause brain tissue damage, including ischemic and hemorrhagic strokes. The Global Burden of Disease Study 2017 reported that China had approximately 2 million deaths due to stroke in 2017 (1, 2) and that stroke has become the second leading cause of death worldwide (3). The American Heart Association and the American Stroke Association predict that the total annual cost of stroke expenditure will reach $24,067 million by 2030 (4), imposing a huge global social and economic burden. After a stroke occurs, approximately half of the survivors have physical, psychological, and social impairments. These impairments will lead to increased dependency on activities of daily living, mood changes, and social distancing (5), which have a significant impsignificantly impact patients' quality of survival of life (QOL) refers to a person's sense of well-being, life goals, autonomy, ability to assume valuable roles, and the ability to participate in important relationships (6) and covers physical health, material health, social health, emotional health, development, and activity (7). Standardized scale rating methods are commonly used to evaluate QOL, and commonly used scales include the EuroQol Five Dimensions Questionnaire (EQ-5D) (8), Barthel Index (BI) (9), Health Status Survey

Questionnaire SF36 (10), Stroke Specific Quality of Life Scale (SS-QOL) (11), Hamilton Anxiety Scale (HAMA) (12), Hamilton Depression Scale (HAMD) (12). Functional status, depression, social support, age, gender and race were important predictors of quality of life, among which functional status and depression were the most important determinants (5).

Traditional reviews emphasize the content of the articles and do not reveal the topical issues and collaborations. Bibliometric analysis is a mathematical and statistical method that uses software to extract literature data such as authors, countries, institutions, keywords, cited authors, and cited journals to reveal the macroscopic pattern of a field through quantitative analysis (13), which can effectively explore the development of a subject (14). Bibliometrics has a wide range of applications, including Biomedicine, Humanities and Social Sciences, Engineering and Technology, Economic Management, etc. (15). Current bibliometric analysis software includes CiteSpace (16) (Drexel University, Philadelphia, PA, the United States) and VOSviewer (17) (Leiden University, Leiden, Netherlands), through software-generated collaborative networks and co-occurrence networks, etc., we can identify potential collaborators, and the evolution of thematic research hotspots provides scholars with a dynamic development process in the field. It is useful for scholars to have a comprehensive understanding of the current state of research in the field (18) and to predict the future research hotpots. The literature related to stroke and quality of life has a tendency to increase year by year, but a bibliometric analysis of the topic of stroke and quality of survival has not been conducted; therefore, a bibliometric analysis of the topic is necessary to help researchers understand the hot spots and emerging trends in the field of stroke and quality of life.

2. Materials and methods

2.1. Search strategy

The Web of Science Core Collection (WoSCC) was used as the source of bibliographic data. Web of Science has been widely accepted by researchers as a high-quality digital literature resource database and is generally considered the most suitable database for bibliometric analysis, and the citation index was chosen as Science Citation Index Expanded (SCI-EXPANDED) - 1900-present in order to ensure comprehensive and accurate search data. Search strategy: TI = (stroke* OR "Cerebrovascular Accident*" OR CVA* OR "Cerebrovascular Apoplexy" OR "Brain Vascular Accident*" OR "Cerebrovascular Stroke*" OR Apoplexy OR "Cerebral Stroke*" OR "Acute Stroke*" OR "Acute Cerebrovascular Accident*") and TI = ("quality of life" OR "QOL" OR "Life Quality" OR "Health-Related Quality Of Life" OR "Health Related Quality Of Life" OR "HRQOL"). The search period was limited to January 1, 2000, to November 1, 2022, with Article and Review selected as the document type and English as the language. 704 articles were obtained after de-duplication.

2.2. Analytical tools

Microsoft Excel 2019 was used to produce annual, and annual cumulative publication volume and citation co-citation count graphs for analyzing the global output and trends of papers related to stroke and quality of survival. CiteSpace 6.1.R3 and VOS Viewer 1.6.17 were used to produce network graphs to extract and analyze the number of publications (including output, authors, journals, countries, and institutions), citation frequency (including co-cited authors, co-cited journals, and co-cited literature), and co-occurring keywords to track research trends and hotspots. Both software is information visualization software based on the Java platform. CiteSpace is used to generate collaborative networks (including authors, countries, and institutions), co-citation networks (co-cited authors), and co-occurrence networks (strongest burst references, keywords). In CiteSpace network mapping, the larger the node, the higher the number of articles represented or the higher the frequency of co-occurrence, and the nodes between VOS Viewer is used to generate co-occurrence network (keywords), co-citation network (cited journals, co-cited literature). VOS Viewer generates the clustering view (Figure 1) and density view (Figure 2B) respectively In the cluster view, the color of the node represents the cluster it belongs to, the size of the node represents the frequency of co-occurrence, the line between the nodes represents the co-occurrence (or co-citation) relationship, and the thicker or thinner of them indicates the co-occurrence (or co-citation) intensity. In the density view, each node on the plot is filled with color according to the density of the elements around that node, the higher the density, the closer to red; on the contrary, the lower the density, the closer to blue.

2.3. Research ethics

The study was conducted as a bibliometric analysis. All data sources were available on the Internet, and no animal or human subjects were involved. Therefore, permission was not required from the ethics committee.

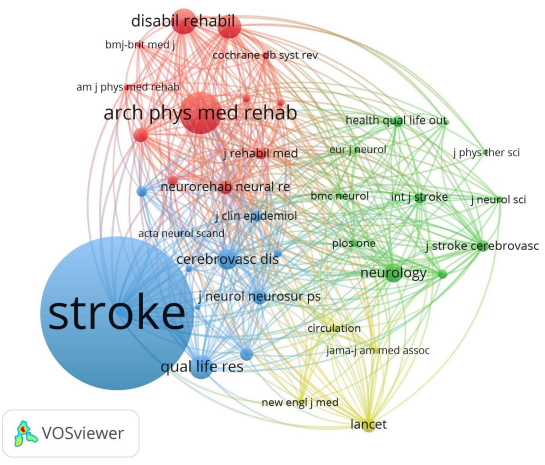


FIGURE 1
Map of co-cited journals with publications.

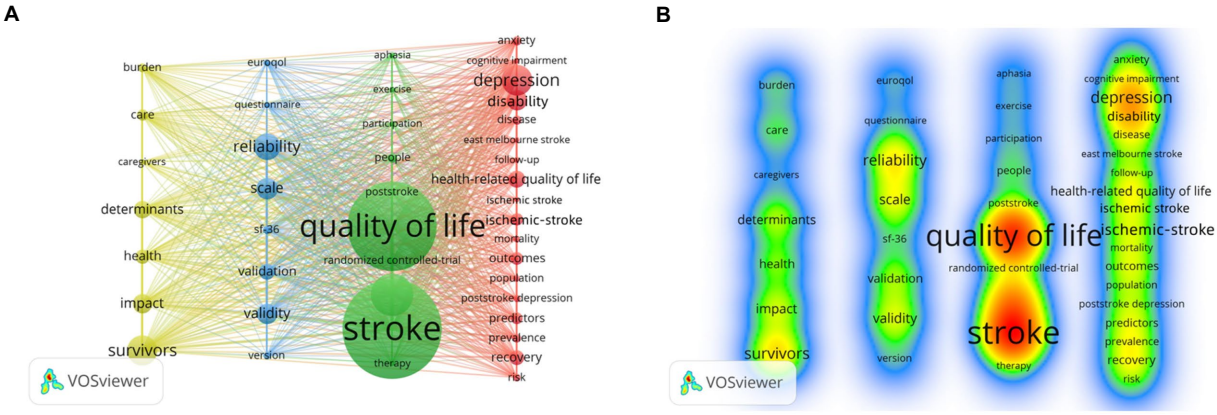


FIGURE 2
(A) Map of co-occurring keywords with occurrences. **(B)** Map of keywords density.

3. Results

3.1. Analysis of publications outputs and citations

Between January 1, 2000, and November 1, 2022, the Web of Science Core Collection included 704 articles that met the inclusion criteria, including 668 articles and 36 reviews, with an average annual yield of 31 articles (Figure 3). We obtained graphs of the number of publications and citations (Figure 4) using Microsoft Excel. Overall, there is a steady growth trend in the number of articles published and frequently cited, with an annual increase of 728.6% (from 7 articles in 2000 to 51 articles in 2022). We fitted a polynomial to the cumulative annual number of publications (Figure 4A) with a growth trend model of $R^2 = 0.9991$, predicting that more articles on quality of life after stroke will be published in the future. Figure 4B shows that 704 papers were cited 18,922 times (H-index 68), with an average citation per paper of 26.88 and an average annual citation frequency of 823, with 2,236 citations in 2021, the highest ever, and 1734 citations in the first 10 months of 2022. 1,677 citations in 2022, which is 29.42 times that of the overview.

3.2. Analysis of authors and co-cited authors

Author collaboration mapping was generated by CiteSpace (Figure 5A), and a total of 3,261 authors were involved in 704 publications. The size of nodes represents their publication volume, and Table 1 lists the top five authors in terms of publication volume, with Kim S ranking first (10 publications), followed by Kim J (9 publications), and Anderson C (8 publications) in third place. The connecting lines between nodes represent the existence of collaborative relationships among authors, and we performed a cluster analysis of the author collaboration network using keywords to extract cluster labels, forming a total of five key clusters (Figure 5B). By calculating the centrality, we found that the highest centrality in author collaboration was 0.03, and centrality greater than 0.1 was considered an important node, which indicates that the connection between authors is not strong and the collaboration between authors should be strengthened in the future.

The network diagram of co-cited authors is shown in Figure 6. Among all co-cited authors, Williams LS from Indiana University School of Medicine ranked first with 158 cited times, followed by Duncan PW, Ware JE, with 144 and 138 cited times, respectively, and the fourth and fifth co-cited authors were Carod-artal FJ (117 cited times) and Sturm JW (114 cited times). Among all co-cited authors, Ali M was the first with a high centrality of 0.21, followed by Anderson C (0.2), Ahlsio B (0.14), Dorman PJ (0.13), and Brott T (0.12), all of whom are influential researchers in the field.

3.3. Analysis of countries and institutions

An analysis of the country collaboration network through CiteSpace (Figure 7A) showed that a total of 66 countries or regions contributed to publications related to stroke and quality of life, and the top five countries in terms of number of publications were the United States, China, Australia, South Korea, and the United Kingdom, with the exception of China, which is a developing country, and the remaining four countries are all developed countries, which shows that developed countries play an important role in this research field. The purple circle represents the centrality, and the center of the study is the most important one. The purple circle represents centrality, and centrality greater than 0.1 is considered an important node. The United States, Australia, the United Kingdom, Nigeria, and Singapore are the top five countries in terms of centrality and have an important impact on global scientific research cooperation. The countries or regions contributing in this area are shown in the world map in Figure 8.

Figure 7B shows a map of institutional collaboration networks in each country and region. Four of the top five institutions in terms of number of publications are from China and one from Australia, with Chinese University of Hong Kong ranking first (20 publications), Chang Gung University ranking second (15 publications), and National Taiwan University ranking third (15 publications). Using CiteSpace to calculate the mediated centrality of research institutions, we found that three of the top five countries for centrality were from

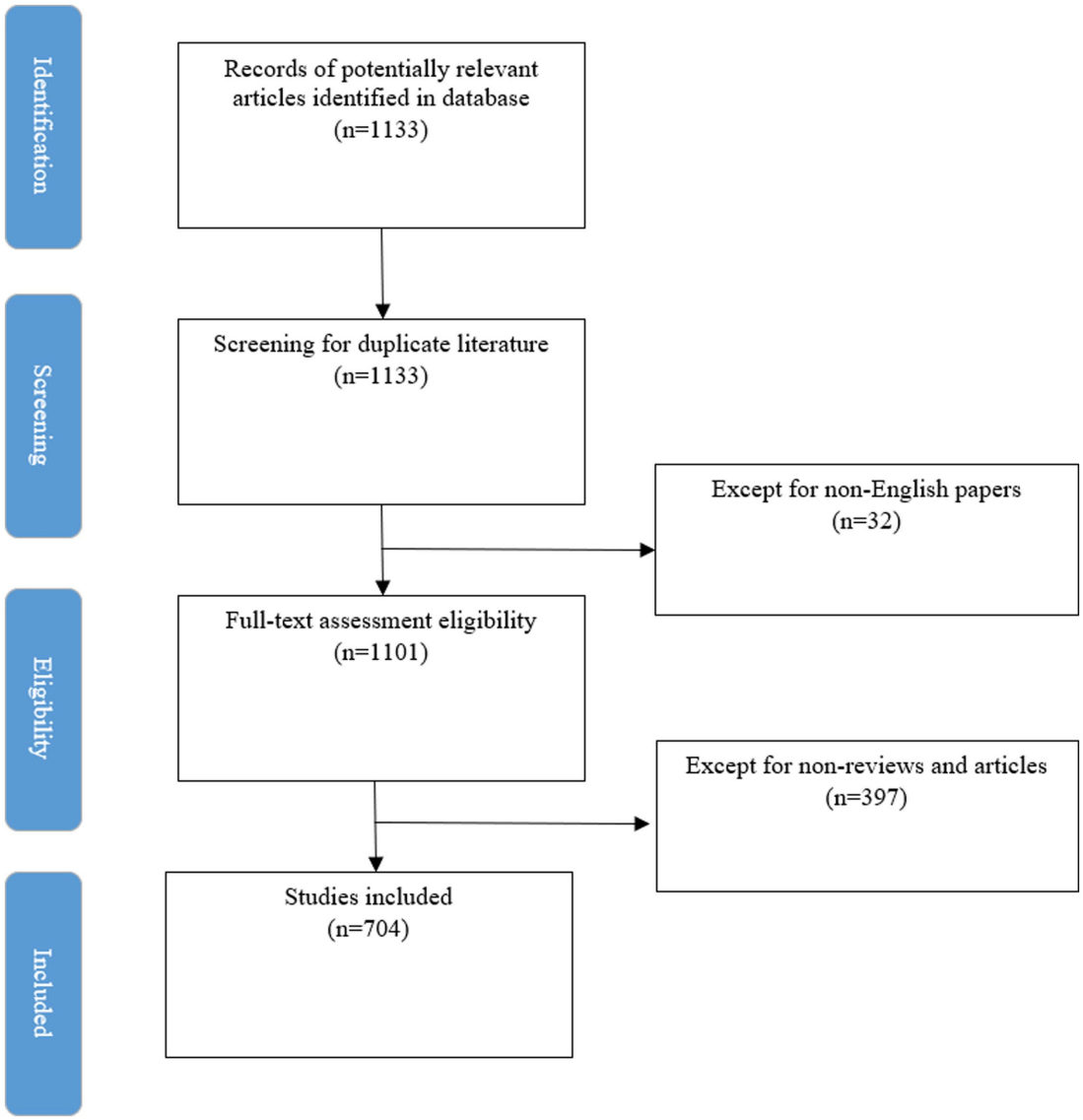


FIGURE 3
The flow chart of screening process.

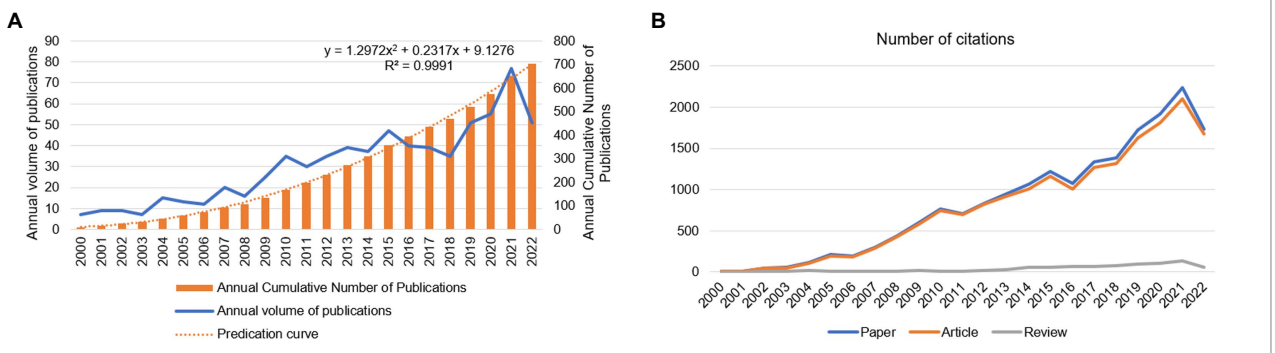


FIGURE 4
The number of publications and citations. **(A)** The number of publication outputs and growth trend from 2000 to 2022. **(B)** The number of annual citations from 2000 to 2022.

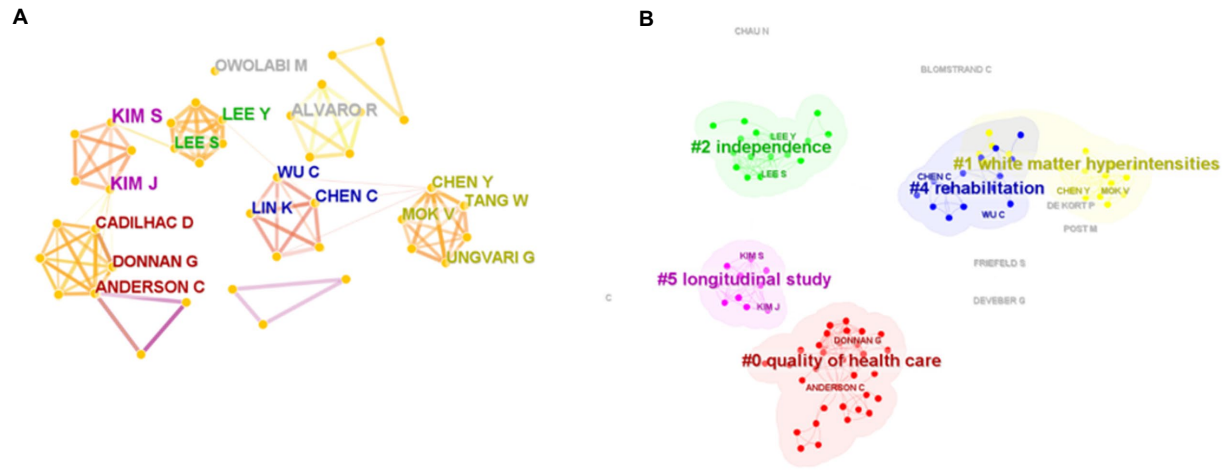


FIGURE 5
(A) Map of authors with publications. **(B)** Map of clustering of authors.

TABLE 1 Top five active authors and co-cited authors.

Rank	Author	Count	Co-cited author	Cited times	Co-cited author	Centrality
1	Kim S	10	Williams LS	158	Ali M	0.21
2	Kim J	9	Duncan PW	144	Anderson C	0.2
3	Anderson C	8	Ware JE	138	Ahlsio B	0.14
4	Chen C	8	Carod-artal FJ	117	Dorman PJ	0.13
5	Alvaro R	8	Sturm JW	114	Brott T	0.12

Australia, with Deakin University ranking first with a mediated centrality of 0.06. As an international comprehensive university, it is one of the youngest but most dynamic universities in Australia, in addition to the Deakin University Language Centre being one of the best language schools in Australia. The third-ranked university, King's College London, is from the UK and the fifth-ranked university, Chonnam National University, is from South Korea. The centrality of the research institutions is all less than 0.1, indicating that inter-institutional links are not strong and inter-institutional cooperation should be strengthened in the future.

3.4. Distribution of journals and co-cited journals

A total of 222 journals have published papers on the quality of life and stroke. Figure 9 shows a dual- map of journals. The left is the citation map, the right is the cited map, and the curves are citation linkages. The linkage trajectories provide an interdisciplinary understanding of the field, and the *z*-Scores function highlights the more fluid trajectories, with higher scores indicated by thicker linkages. In this case, publications in the neurology, sports, ophthalmology (pink trajectory) domain are clearly influenced by publications in the psychology, education, social ($z = 4.46$, $f = 24{,}732$) and health, nursing, medicine ($z = 4.34$, $f = 24{,}120$) domains. In addition, publications in the medicine, medical, clinical (green trajectory) domains were influenced by publications in the health, nursing, medicine ($z = 1.89$, $f = 11{,}736$) domain. Table 2 lists the top 10 academic journals that published papers related to the quality of survival after stroke research. Sorted by publications, Stroke tops the list with 53 articles and plays a significant role in the field. It was followed by Topics in stroke rehabilitation (28 articles) and Disability and rehabilitation (27 articles). The average impact factor of the top 10 journals was 3.709, with the highest impact factor being the most prolific stroke (IF = 10.17). The vast majority of journals are based in the United Kingdom, with all journals based in developed countries.

For further analysis of journal co-citations, we used VOSviewer software to perform a citation co-citation analysis of 38 journals with a threshold of 100 citations, which resulted in Figure 1, with four clusters corresponding to the four colors in the figure. The red clusters are mainly journals in the field of rehabilitation medicine, focusing on the application of rehabilitation techniques and comprehensive care tools in stroke disease; The green and blue clusters are mainly journals in neurology and healthy quality of life assessment, which tend to have more research on the prevention, diagnosis and management of stroke-related diseases and the assessment of medical therapies and quality of life, and are dedicated to reducing the global burden of stroke; The yellow clusters are mainly comprehensive journals of clinical medicine, which contain many relevant clinical and laboratory trials that provide information on how to improve patient prognosis. A review of articles from these journals can provide theoretical and empirical support for this study. Table 3 and Figure 1 show that the most cited is Stroke (4131), followed by Archives of physical medicine and rehabilitation (980), and Disability and rehabilitation (579).

Centrality was calculated by CiteSpace software and the journal with the highest centrality is Physical therapy (0.07) as seen in Table 3.

3.5. Analysis of co-cited references

To analyze the co-citation of the literature, we used VOSviewer to plot the total number of references as 15,318, set the minimum number of co-citations of the literature as 35, and screened 33 papers for co-citation analysis of the cited literature, and constructed a network within the field of stroke and quality of life research (Figure 10).

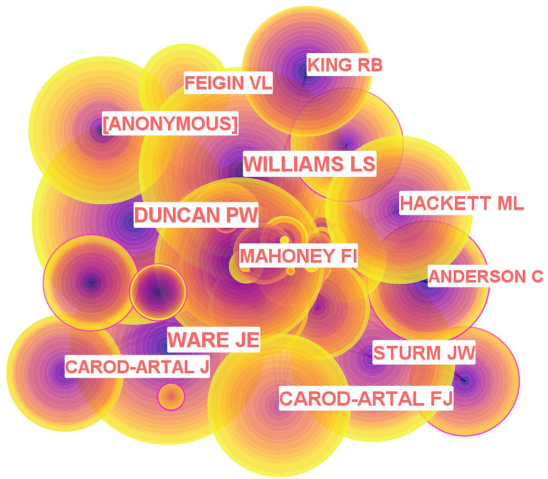


FIGURE 6
Map of co-cited authors with publications.

Table 4 lists the top 10 most frequently cited articles, involving 9 clinical studies, 1 review, and highly cited literature mostly published from 1996 to 2005. The most frequently cited are Williams et al. (11) (120 times), Sturm et al. (19) (100 times). The literature for the green clusters in Figure 10 focuses on the assessment of the characteristics of HRQOL-related scales in stroke patients. The most common generic scale for assessing HRQOL in stroke patients is the SF-36 (20), which has a floor effect in terms of physical functioning, but it is limited in that it does not reflect well the level of social functioning of patients and tends to trigger a ceiling effect (19). Therefore, it should be supplemented with specific stroke HRQOL scales, such as SS-QOL (11) and SIS (21) scales, which have better reliability, validity and responsiveness. In addition, we should use a patient-centered approach to participate in scale production (22) with robust psychometric and quality-of-life measures, and patients should be involved in each stage of scale development. The red and blue clustered literature focuses on how overall and domain-specific HRQOL is assessed in stroke survivors with caregivers at different times and the main predictors of quality of life after stroke. The independent determinant of HRQOL in stroke survivors is functional status, which is low, resulting in social isolation and reduced social activity with little social support, making a depression in stroke survivors frequent (23). The quality of life of stroke survivors is highly correlated with demographic variables, such as gender, age, and racial. Women, especially older women, who have survived after stroke have lower levels of all measures of quality of life and much higher rates of depression than men. This is because in many countries, women take on the responsibility for household management and have greater difficulty maintaining this role after stroke. Multiple studies using data from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study have found that blacks have lower rates of blood pressure control than whites with or without stroke (24). Racial differences in the incidence of cardiovascular events and quality of life of stroke survivors are largely due to differences in healthy lifestyles

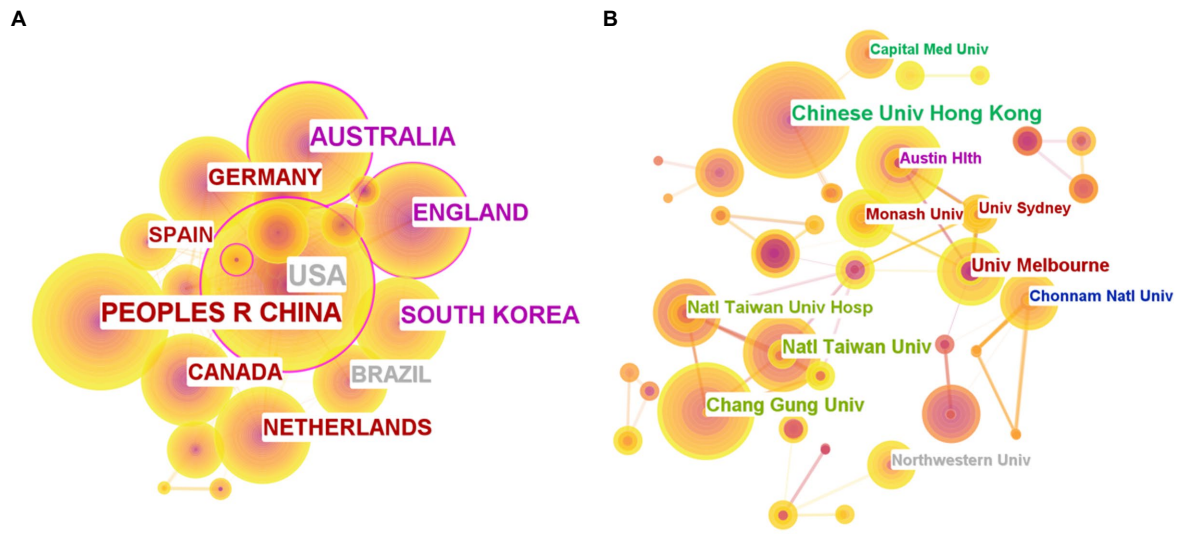


FIGURE 7
(A) Map of countries. **(B)** Map of institutions.

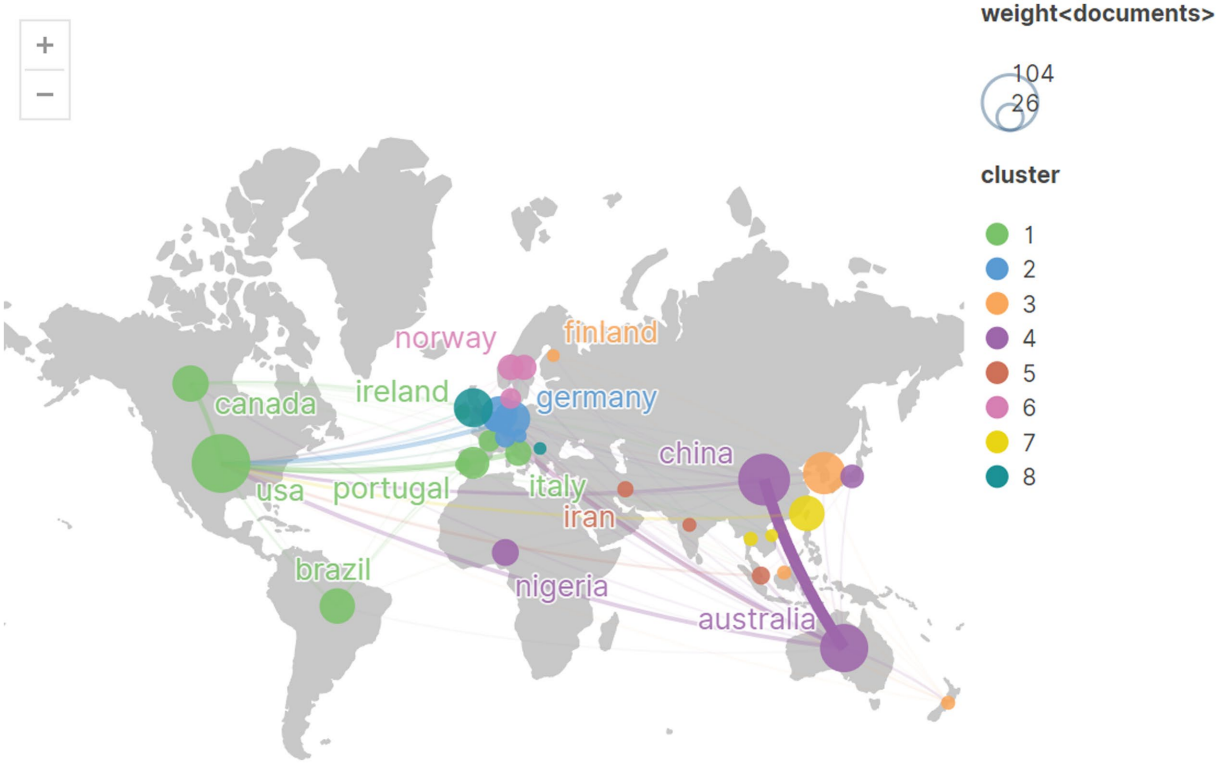


FIGURE 8
The distribution of countries/region.

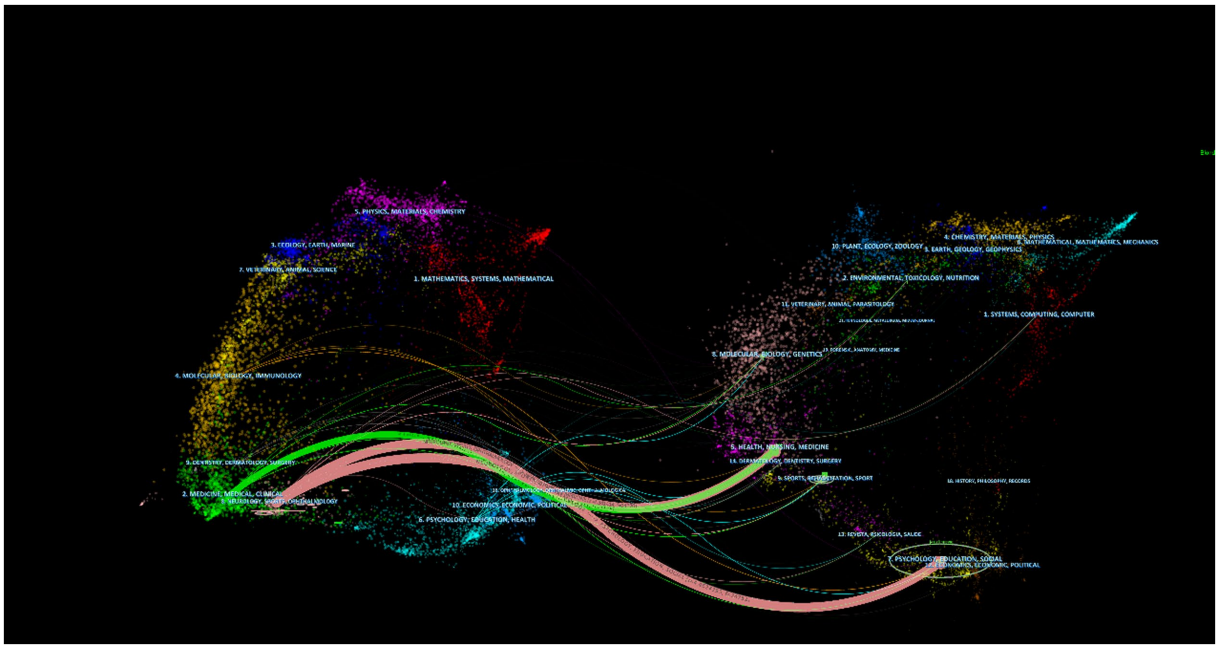


FIGURE 9
The dual-map overlay of journals with publications.

TABLE 2 Top 10 academic journals based on publications.

Rank	Source (Abbreviations)	Publications	Citations	Average Citations/ Publications	Country	IF (2021)
1	Stroke	53	4,854	91.58	United States	10.17
2	Topics in stroke rehabilitation (top stroke rehabil)	28	566	20.21	United Kingdom	2.177
3	Disability and rehabilitation (disabil rehabil)	27	554	20.52	United Kingdom	2.439
4	Journal of stroke and cerebrovascular diseases (j stroke cerebrovasc)	25	301	12.04	United Kingdom	2.677
5	Quality of life research (qual life res)	25	768	30.72	Netherlands	3.44
6	Archives of physical medicine and rehabilitation (arch phys med rehab)	24	1,216	50.67	United Kingdom	4.06
7	Health and quality of life outcomes (health qual life out)	22	486	22.09	United Kingdom	3.077
8	Cerebrovascular diseases (cerebrovasc dis)	18	1,045	58.06	Switzerland	3.104
9	Neurorehabilitation	15	110	7.33	Netherlands	1.986
10	Journal of rehabilitation medicine (j rehabil med)	12	384	32.00	United Kingdom	3.959

TABLE 3 Top five co-cited journals in terms of counts and centrality.

Rank	Co-cited counts	Cited journal (Abbreviations)	Centrality	Cited journal (Abbreviations)
1	4,131	Stroke	0.07	Physical therapy (phys ther)
2	980	Archives of physical medicine and rehabilitation (arch phys med rehab)	0.06	International journal of rehabilitation research (int j rehabil res)
3	579	Disability and rehabilitation (disabil rehabil)	0.06	American journal of physical medicine & rehabilitation (am j phys med rehab)
4	529	Clinical rehabilitation (clin rehabil)	0.06	Acta psychiatrica scandinavica (acta psychiat scand)
5	525	Quality of life research (qual life res)	0.05	Journal of the neurological sciences (j neurol sci)

across groups (25). We considered the top 10 references based on the number of citations as valuable references. These references are landmark references in the field and set the stage for future research.

3.6. Analysis of co-occurring keywords

The keyword co-occurrence map reflects the core themes and research hotspots in the field of quality of life after stroke research. As of November 2022, a total of 2016 keywords have appeared in the field of stroke and quality of life. In the VOSview software, we set the frequency of displayed co-occurrence to at least 25 times. Thus, a total of 43 focused keywords were included (Figure 2A). We used Pajek software to arrange the keywords in columns according to different clusters, with nodes indicating keywords; the larger the node area, the more frequently the keyword appears, and the lines between the nodes indicate the strength of association. Figure 2B shows the density view, the density size depends on the number and importance of keywords, and this figure is used to quickly observe the knowledge and the research density of the domain. We found four different colored clusters, with red clusters representing studies of stroke disease progression and related complications, green clusters representing studies of clinical treatments for stroke and changes in functional outcomes after stroke, blue clusters representing studies of

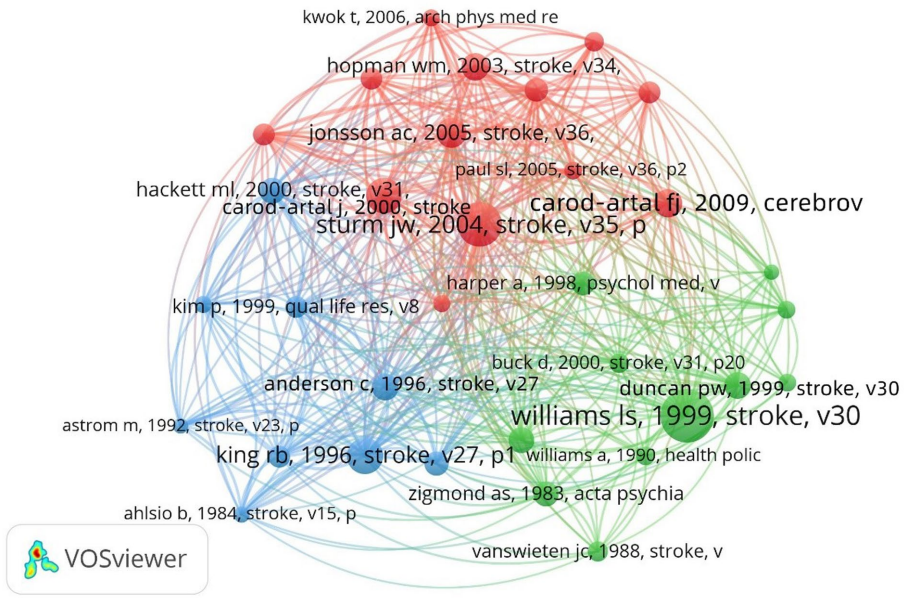


FIGURE 10
Map of co-cited references with citations.

standardized quality-of-life assessment measures and measurement tools after stroke, and yellow representing studies of factors related to the level of health care and the magnitude of caregiver burden for stroke patients (Table 5). To get a clearer picture of the specifics of the keywords, the high-frequency keyword assemblies with a co-occurrence frequency of more than 80 are presented in Table 6, and as seen in Figure 2B and Table 6, "stroke" (451 times), "quality of life" (403 times), "rehabilitation "(194 times), "depression" (140 times), and "survivors" (138 times) constitute the representative terms and hot topics in this field.

Depression refers primarily to post-stroke depression, which is a treatable condition, and early intervention can prevent its progression to chronic depression, thereby slowing the recovery process. In addition to stroke survivors, the psychological status of family caregivers should also be taken into account, and studies have shown that the prevalence of depression in caregivers is twice as high as that in older adults in the community (26). The important predictor of depression is social support (27). The isolation and reduced social activities caused by physical disability in stroke survivors predispose to depression, while the patient's functional status, level of dependency, and family and social support can determine the quality of life of the caregiver (23). Stroke survivors will receive intensive rehabilitation in the hospital and will be less motivated to rehabilitate after discharge from the hospital, when it is more important to enhance home rehabilitation, including promoting low to moderate intensity physical activity, muscle strengthening exercises and reducing sedentary behavior, and changing poor sleep habits (short <6 h or long >8 h of sleep) (28). Caregivers are trained by professionals during patient rehabilitation, and group exercises and group activities are provided in the community to promote socialization and reintegration of stroke patients into community life (29). In addition, it is necessary to strengthen mental health management for stroke survivors and family caregivers by providing interventions such as support groups and counseling.

4. Discussion

The field of health quality of life research for stroke survivors is a multidisciplinary research area that combines clinical medicine and rehabilitation medicine and has received a great deal of attention from the community, which makes it an iterative and updated research topic. This paper analyzes 23 years of relevant research in this field. Using the VOSview and CiteSpace software, trends in the field are reviewed, and a bibliometric-based analysis of core authors in the research field, highly productive and closely collaborating national institutions, core journals in the field, valuable cited references, and topical keywords in the field is conducted.

4.1. General information and global trends for stroke and quality of life

Based on data collected in the Web of Science core collection, between 2000 and 2022, 704 articles on stroke and quality of life were published by 3,261 authors from 1,271 institutions in 66 countries worldwide in 222 journals, citing 15,318 references from 4,211 journals. 18,922 times, with an increasing trend in the number of publications year by year. The rapid growth of published papers indicates that researchers are paying more attention to the quality of life after stroke. To our knowledge, this is the first article based on WoSCC and using bibliometric and visual analysis methods to assess stroke and quality of life, which may inform the direction of future research. Figure 4A shows the temporal distribution of publications

TABLE 4 Top 10 co-cited references in terms of citations.

Rank	Title	citations	year	First author	Journal	Document Type
1	Development of a Stroke-Specific Quality of Life Scale	120	1999	Williams LS	Stroke	Article
2	Quality of Life After Stroke: The North East Melbourne Stroke Incidence Study (NEMESIS)	100	2004	Sturm JW	Stroke	Article
3	Quality of Life After Stroke	82	1996	King RB	Stroke	Article
4	Quality of Life Among Stroke Survivors Evaluated 1 Year After Stroke: Experience of a Stroke Unit	80	2000	Carod-artal J	Stroke	Article
5	Determinants of Quality of Life in Stroke Survivors and Their Informal Caregivers	68	2005	Jonsson AC	Stroke	Article
6	Quality of Life after Stroke: The Importance of a Good Recovery	63	2009	Carod-artal FJ	Cerebrovascular Diseases	review
7	Quality of Life During and After Inpatient Stroke Rehabilitation	62	2003	Hopman WM	Stroke	Article
8	Validation of the Short Form 36 (SF-36) Health Survey Questionnaire Among Stroke Patients	61	1996	Anderson C	Stroke	Article
9	The Stroke Impact Scale Version 2.0. Evaluation of Reliability, Validity, and Sensitivity to Change	61	1999	Duncan PW	Stroke	Article
10	Health-Related Quality of Life Among Long-Term Survivors of Stroke: Results From the Auckland Stroke Study, 1991–1992	59	2000	Hackett ML	Stroke	Article

in the field of quality of life after stroke, and although the number of publications declined considerably during 2015–2018, the annual number of papers increased dramatically from 2018 to 2021, reaching 77 papers and 2,236 citations in 2021 (Figure 4). Despite the overall decreasing trend in stroke mortality and morbidity worldwide, the socioeconomic burden of stroke survivors remains high and several countries are gradually starting to focus on the healthy quality of life of stroke survivors. The growing trend of publications indicates that this research area has received increasing attention from scholars in recent years, and we predict a great potential for growth in this research area.

4.2. Quality of global publications on stroke and quality of life

4.2.1. Authors and co-cited authors

In this study, CiteSpace helped to identify the core authors with the highest number of publications and citations (Figures 5, 6), reflecting the authors' contributions to the field and their collaborations. KIM S, who has the highest number of publications, works at Korea University College of Nursing and leads a team studying the relationship between Type D personality and quality of life in post-stroke patients. Type D personality has a high rate of stroke recurrence and high frequency of antidepressant medication use, and this study helps to reduce stroke recurrence, increase healthy behaviors in post-stroke patients and improve quality of survival (19). Donnan G and Anderson C, who have formed a partnership in the field of quality of health care, work at the National Stroke Institute at the University of Melbourne and Anderson C works at the University of Sydney, and their team has conducted observational studies of post-stroke patients using a follow-up approach to encourage stroke patients to participate in rehabilitation and receive medication and related care programs to improve HRQOL (20, 30); Author Chen C and author Wu C focused their research on rehabilitation therapies to improve patient function through common rehabilitation interventions, such as modern rehabilitation robotic assistive technology and traditional Chinese health care techniques (31–33).

Author Kim S and author Kim J focus on longitudinal studies, as one of the important research methods in psychology, longitudinal study is a continuous observation of a population or individuals in that population to understand the dynamics of disease, nutritional health status or a health event over time. Cross-sectional associations cannot explain the relationship between post-stroke depression and quality of life, therefore Kim J et al. conducted a study on the longitudinal impact of depression on quality of life in stroke patients and found that post-stroke depression was associated with low quality of life in the acute phase of stroke and had a persistent negative impact on patients, emphasizing the need to assess patients for depression after the onset of stroke, in addition to medical interventions (34).

Similarly, we clustered and grouped the author co-citation networks using keywords, and the main research topics were Validity, neglect, Marathi, poststroke fatigue, and response shift, represented by William LS, Duncan PW, Carod-artal FJ, and The first cited article, Development of a Stroke-Specific Quality of Life Scale, was published 462 times in 1999 by Williams LS et al. Williams LS led the team that developed the SS-QoL, a patient-centered outcome measure designed to assess HRQOL specific to stroke patients. The SS-QoL is a patient-centered outcome measure designed to assess patient-specific HRQOL and has the advantage of being valid, reliable, and responsive, and is commonly used to assess the quality of life in stroke patients (11). More attention to the research results of core authors in this field will help to open our minds and promote research innovation.

TABLE 5 Clusters of co-occurring keywords in areas.

Cluster	Color	Keywords
1		Anxiety; cognitive impairment; depression; disability; disease; east Melbourne stroke; follow-up; health-related quality; ischemic stroke; ischemic-stroke; mortality; outcomes; population; poststroke depression; predictors; prevalence; recovery; risk.
2		Aphasia; exercise; participation; people; poststroke; quality of life; randomized controlled-trial; stroke; therapy.
3		Questionnaire; reliability; scale; sf-36; validation; validity; version; euroqol.
4		Burden; care; caregivers; determinants; health; survivors.

4.2.2. Countries and institutions

Combined with Table 7 it can be seen that the United States is the most published country in this field and is the central partner of other countries. The United States ranked first in the number and centrality of publications in quality of life after stroke research, with 104 publications and a centrality of 0.33. Stroke is the second leading cause of death worldwide, and as a developed country, stroke has also posed a major socioeconomic threat to the United States, so the United States has invested significant and research and medical resources to study stroke. Every year, the United States promotes awareness of the prevention and treatment of hypertension through various means. In addition, the United States, Australia, and the United Kingdom are the core research forces in the collaborative network and work closely with other countries.

We used CiteSpace to cluster institutions and extracted cluster labels from the titles to obtain a total of seven clusters, the largest cluster was labeled long-term quality, and the main cited article was Early mobilization and quality of life after stroke findings from avert published in neurology in 2019, the University of Melbourne was the institution with the most citations in this cluster, and the University of Melbourne is both a high volume of publications and a high centrality (Table 8). The second largest cluster was labeled life scale, and the most cited institution was National Taiwan University, which was also the third most prolific institution; the third largest cluster was labeled kosco study, and the Jeonnam National University was the most cited institution in this cluster. In addition, Chinese institutions accounted for 81.6% of the top five publications (Table 8). According to the census, China's population growth rate is much less than the prevalence of cerebrovascular disease, and as the world's most populous and rapidly aging country, we speculate that China faces a great challenge in reducing stroke morbidity and mortality, and therefore institutions in China are investing more research in this research area resources and efforts.

National and institutional collaboration helps researchers in this field to share resources and exchange knowledge and ideas, which is essential for the development of scientific research. Therefore, stronger collaborative networks should be established among more countries and institutions.

4.2.3. Journals and co-cited journals

A total of 704 papers on stroke and quality of life were published in 223 journals. From the dual-map of journals (Figure 9), the cited

TABLE 6 Top 10 keywords.

Rank	Occurrences	Keyword	Rank	Occurrences	Keyword
1	451	Stroke	6	122	Reliability
2	403	Quality of life	7	98	Scale
3	193	Rehabilitation	8	93	Validity
4	140	Depression	9	93	Disability
5	138	Survivors	10	88	Impact

TABLE 7 Top five countries in terms of count and centrality.

Rank	Country	Count	Country	Centrality
1	United States	104	United States	0.33
2	China	81	Australia	0.31
3	Australia	70	United Kingdom	0.17
4	South Korea	54	Nigeria	0.1
5	United Kingdom	46	Singapore	0.1

TABLE 8 Top five institutions in terms of count and centrality.

Rank	Institution	Count	Institution	Centrality
1	Chinese University of Hong Kong	20	Deakin University	0.06
2	Chang Gung University	15	University of Melbourne	0.05
3	National Taiwan University	15	King's College London	0.04
4	University of Melbourne	14	Austin and Repatriation Medical Centre	0.04
5	National Taiwan University Hospital	12	Chonnam National University	0.03

journals were concentrated in neurology, sports, ophthalmology, medicine, medical, clinical, which are called frontiers of research. The cited journals are mainly in the fields of psychology, education, social, health, nursing, medicine, which are called knowledge base.

Table 2 shows that the top 10 journals account for 35% of the total, with the exception of Stroke, which has an IF = 10.17, and the remaining nine journals with low IFs, which we believe lack some groundbreaking discoveries and innovations in the field. Diseases (58.06) and Archives of physical medicine and rehabilitation (50.67), indicating that these three journals contain high quality articles and have received much attention in the field of stroke and quality of life. With 53 papers published over the past 23 years, Stroke is the most preferred journal for those in the field of stroke and quality of life research. As shown in Figure 1 and Table 3, the most frequently cited journal is Stroke, with 4,131 citations, and the first cited paper on quality of life in stroke survivors was also from Stroke, making Stroke arguably the most influential core journal in the field. In terms of centrality, an important journal in the field of stroke and quality of life research is Physical therapy (Table 3), which works closely with other journals. In addition, by combining Tables 2, 3, we found that four journals, Stroke, Disability and Rehabilitation, Quality of life research, and Archives of physical medicine and rehabilitation, are both important citation-giving and cited journals, and the articles in these journals reflect the underlying theories in this field of research. Future scholars should pay more attention to these journals in order to quickly access the latest international information and research advances in stroke and quality of life.

4.3. Research hotpot for stroke and quality of life.

4.3.1. Co-cited references with the strongest citation bursts

A burst reference is a reference that has been cited frequently over a period of time, representing a considerable interest and concern of the researcher in a certain field. Therefore, analyzing the clues of burst references can effectively identify the research hotspots and research frontiers in the field (16). Table 9 lists the top 20 co-cited literature with the strongest citation bursts from 2000 to 2022. The light blue bar indicates that the reference has not yet appeared, the dark blue bar indicates that the reference has started to appear, and the red line represents the burst time.

The first appearance of co-cited literature related to outbreaks was in 2000. The authors of the top three strongest sources of outbreaks were Sturm JW, Carod-artal FJ, and Jonsson AC. with the highest citation intensity ($n = 13.49$ citation bursts) coming from Sturm JW (35) and his team published in Stroke, who had previously studied disability data in community stroke survivors (36), and although disability is the most relevant patient clinical outcome, quality of life may be more relevant from the patient's perspective (22). They assessed 2 years after stroke using Assessment of Quality of Life (AQOL) and most survivors had severely impaired HRQQL, and the determinants of HRQOL were disability, physical impairment, anxiety, and depression. Predictors were age, female, initial NIHSS score, neglect and low socioeconomic status. Carod-artal et al. (29) reviewed HRQOL assessment and determinants in stroke survivors. They described the need for HRQOL measurement tools in clinical practice and commonly used assessment scales. Many factors predict HRQOL in stroke survivors, with functional status and long-term disability being determinants, and psychosocial factors such as depression also affecting HRQOL and functional recovery in stroke survivors. In addition, they found that stroke caregivers who lacked family support and professional support also had generally lower HRQOL. Jonsson et al. (23) also found that caregivers may be under considerable stress and that caregivers have poorer quality of life than patients in terms of emotional and spiritual factors. The determinants of quality of life for caregivers are their own age and the functional status of the patient. Stroke research therefore needs to focus more on the overall functional capacity of survivors, comorbidities and psychosocial factors, and stroke rehabilitation needs to be survivor and caregiver oriented.

There are three articles with reference bursts ending in 2022, and these are commonly cited in recent years, which shows that the content and views in these references are hot spots that tend to be popular. de Wit et al. (37) used the EQ-VAS z-Norm score to compare the long-term HRQOL levels of stroke survivors with population normal levels and found that stroke had a 5-year stroke survivor's HRQOL The effect of stroke on HRQOL was highly variable, with lower HRQOL scores associated with functional status, female, higher age (38), and lower socioeconomic status (39), but the study was limited by not considering psychosocial factors. Ramos-lima et al. (38) found that the most relevant predictor of QOL was functional status during assessment, and that patients with left hemisphere stroke usually have language impairment and worse HRQOL, so lifestyle changes and encouragement of physical activity are necessary. In addition, they found that orthotic use, although

TABLE 9 Top 20 references with the strongest citation bursts.

References	Year	Strength	Begin	End	2000–2022
Williams et al.	1999	6.83	2000	2004	
King et al.	1996	6.46	2000	2001	
Carod-artal et al.	2000	6.5	2002	2005	
Kim et al.	1999	6.19	2002	2004	
Sturm et al.	2004	**13.49**	2005	2009	
Hopman et al.	2003	6.48	2005	2008	
Jonsson et al.	2005	**11.5**	2006	2010	
Nichols-larsen et al.	2005	5.96	2006	2010	
Paul et al.	2005	6.19	2007	2010	
Haacke et al.	2006	7.46	2008	2011	
Kwok et al.	2006	6.96	2008	2011	
Patel et al.	2007	9.92	2009	2012	
Muus et al.	2007	5.64	2009	2012	
Carod-artal et al.	2009	**12.05**	2011	2014	
Dhamoon et al.	2010	5.94	2012	2015	
Abubakar et al.	2012	6.14	2014	2017	
Bushnell et al.	2014	7.6	2015	2019	
De Wit et al.	2016	6.38	2019	**2022**	
Ramos-lima et al.	2018	9.06	2020	**2022**	
Kwon et al.	2018	5.7	2020	**2022**	

The bold values in table refer to the three co-cited references whose citation burst strength is greater than 10.

improving gait performance and controlling abnormal kinematics due to coordination deficits, also had a negative impact on HRQOL. Kwon et al. (40) evaluated the factors influencing HRQOL in stroke survivors and suggested that the development of rehabilitation programs must be tailored to the physical performance level of stroke survivors. Therefore, we need to pay attention to psychosocial factors that affect the health quality of life of survivors, and for post-stroke depression, the community should provide comprehensive medical care including depression screening and treatment. In addition, because it is difficult for stroke survivors to return to work and inadequate financial support limits medical care and participation in activities, which in turn exacerbates the lower quality of life of stroke survivors (41, 42), vocational rehabilitation should also receive attention.

4.3.2. Keywords with the strongest citation bursts

Burst keywords are keywords that are frequently cited over a period of time and can reflect the cutting-edge topics in that research area. Table 10 shows the 20 most frequently cited keywords. The most cited keywords in the early stage include quality of life, stroke outcome, health status, and reliability, which shows that the quality of survival and scale reliability of patients after stroke are popular topics in the early stage of research in this field; The popular keywords in recent years include disease (2018–2022), care (2018–2022), global burden (2018–2022), and anxiety (2019–2022). The four research trends are as follows:

(1) Disease: Hypertension, diabetes mellitus, and obesity are considered risk factors for the occurrence of stroke (43), and the quality of survival of post-stroke patients includes depression in addition to these disease factors. suYeon Kwon et al. (40) suggested that rehabilitation interventions for post-stroke depression should be developed, and vocational rehabilitation and individualized physical activity should be developed to improve post-stroke patients' HROQL (40).

(2) Care: Effective care after stroke has an important impact on improving the quality of patient survival. In the acute phase of stroke, the goal of care is to stabilize the patient's condition through acute treatment. Rehabilitation, an important component of effective care, should be intervened as early as possible after the patient's condition is stabilized. The goal of early rehabilitation is to encourage active participation of the patient, with support and education provided by

TABLE 10 Top 20 keywords with the strongest citation bursts.

Keywords	Year	Strength	Begin	End	2000–2022
Quality of life	2000	9.28	2000	2003	
Stroke outcome	2000	6.43	2000	2010	
Health status	2000	5.36	2000	2007	
Reliability	2000	3.86	2000	2006	
Health-related quality of life	2000	4.52	2003	2006	
East Melbourne stroke	2000	6.62	2007	2013	
Follow up	2000	4.45	2008	2015	
Determinant	2000	4.4	2008	2011	
Induced movement therapy	2000	4.07	2009	2010	
Randomized controlled trial	2000	4.07	2010	2016	
Community	2000	4	2013	2014	
Poststroke	2000	4.32	2016	2022	
Therapy	2000	4.15	2016	2022	
Trial	2000	3.98	2016	2020	
Risk factor	2000	4.55	2017	2019	
Disease	2000	4.7	2018	2022	
Care	2000	4.52	2018	2022	
Global burden	2000	3.97	2018	2022	
EQ-5D	2000	4.2	2019	2020	
Anxiety	2000	4.13	2019	2022	

caregivers and family members; the goal of late rehabilitation is to restore somatic function for social reintegration as much as possible (44).

(3) Global burden: The burden caused by stroke continues to increase globally (45). With approximately 2 million deaths due to stroke in China in 2017, stroke has become the leading cause of death. By documenting lifestyle, environmental and occupational exposures, and metabolic risk factors, it is possible to quantify the magnitude of the stroke burden associated with various risks and to identify prevention strategies at the global, regional, and national levels to reduce the social and economic burden of stroke (46, 47).

(4) Anxiety: There is a correlation between psychological factors and quality of life after stroke (48). The higher the level of depression and anxiety after stroke, the lower the patients' HRQOL scores (37), and the development of rehabilitation programs is important to improve quality of life and reduce mortality, such as the development of qigong exercises as a complementary and alternative form of medicine that can reduce mental distress caused by stroke (32).

4.4. Significance

4.4.1. Significance of published content to the study

Factors influencing QOL in stroke survivors can be categorized into demographic variables, associated vascular risk factors, neurological dysfunction, functional status, cognitive and behavioral factors, psychological factors, and social variables. Among these, the most relevant predictor of QOL is functional status. Therefore, programs tailored to the functional status of stroke survivors can help provide a better quality of life. In addition, the high prevalence of depression after stroke confirms the need for assessment and

intervention for depression. The variables associated with depression are stay-at-home status, feminization, inadequate social support, rehabilitation, depression screening and community interventions for stroke survivors must take into account the support of other family members or caregivers, and the mental status of caregivers cannot be ignored. Therefore, post-stroke rehabilitation should be multifaceted, with mental health education along with improvement of physical function to improve the patient's post-stroke quality of life.

4.4.2. The practical significance of the study

This study uses data visualization to summarize and express complex information in the field of post-stroke quality of life research, which has important implications for hospitals, medical students, and the community engaged in stroke research. First, this study summarizes the current state of research and predictors of quality of life after stroke, emphasizing that psychosocial factors such as depression or anxiety cause the same or greater decline in quality of life than physical disability (49), suggesting that hospitals, universities and community should not only focus on the functional status of stroke patients, but should place a high priority on the psychological status of survivors and caregivers. This study can spread the knowledge of cerebrovascular diseases to the public and raise the awareness of cerebrovascular accident prevention, which is important to reduce the incidence of stroke. Secondly, this study summarized the important cooperative forces, classic literature, key literature and research hotspots in this field, and summarized the research progress and emerging research hotspots in the field of stroke and quality of life, which has great reference value for the scientific research of hospitals and universities engaged in stroke.

4.5. Strengths and limitations

To the best of our knowledge, this is the first article based on WoSCC and using bibliometric and visual analysis methods to assess 23 years of stroke and quality of life. This study includes 704 papers describing the current state of research on stroke and quality of life in terms of authors, countries, institutions, journals, references, and keywords, demonstrating the research base in the field, and also includes emergent references and emergent keywords that help to identify the research hotspots and future trends in the field.

However, this study also has some limitations. First, due to CiteSpace software and technical limitations, we only included relevant literature from the English database WoSCC and did not consider other databases; Second, this study chose English as inclusion criteria and sent out non-English articles, which may lead to research bias in published literature; Third, bibliometrics cannot fully consider the validity and scientific rigor of publications, and citation indicators may be influenced by the time of publication, and recently published studies may be underestimated, but we believe that our findings effectively represent global research in the field of post-stroke quality of life studies.

5. Conclusion

Through a visual analysis of stroke and quality of life research over the past 23 years, this study presents the current research findings and possible future research directions in stroke and quality of life. Kim S, Williams LS, Anderson C, and Ali M are important authors in this field, the United States, Australia and the United Kingdom are core research forces, and the Chinese University of Hong Kong in China has made the largest contribution in this field. The University of Melbourne is an important research institution, and stroke is the most influential core journal in the field. The main research interests are stroke disease progression and related complications, standardized post-stroke quality of life assessment measures and tools, care and rehabilitation of stroke survivors, and the global burden of disease. Topics related to post-stroke depression and anxiety, rehabilitation, care, and scales are emerging research hotspots. This analysis may enable academic collaboration and communication among countries, institutions, and scholars should be enhanced, and provides a useful basis for researchers to further understand the research hotspots, research priorities, and emerging trends in the field of stroke and quality of life.

Author contributions

MC and YZ contributed significantly to analysis and manuscript preparation, performed the data analyses, and wrote the manuscript. LD helped perform the analysis with constructive discussions. XiG contributed to the conception of the study. All authors contributed to the article and approved the submitted version.

Funding

This study was supported by Zhongshan Social Public Welfare and Basic Research Program (2021B1055).

Acknowledgments

The authors would like to express their appreciation to C. M. Chen, who developed the free software CiteSpace, and Van Eck and Waltman, who developed the free software VOSviewer.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Collaborators GBDCOD. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the global burden of disease study 2017. *Lancet*. (2018) 392:1736–88. doi: 10.1016/S0140-6736(18)32203-7

2. Zhou M, Wang H, Zeng X, Yin P, Zhu J, Chen W, et al. Mortality, morbidity, and risk factors in China and its provinces, 1990-2017: a systematic analysis for the global burden of disease study 2017. *Lancet*. (2019) 394:1145–58. doi: 10.1016/S0140-6736(19)30427-1

3. Johnson W, Onuma O, Owolabi M, Sachdev S. Stroke: a global response is needed. *Bull World Health Organ*. (2016) 94:634–634A. doi: 10.2471/BLT.16.181636

4. Ovbiagele B, Goldstein LB, Higashida RT, Howard VJ, Johnston SC, Khavjou OA, et al. Forecasting the future of stroke in the United States: a policy statement from the American Heart Association and American Stroke Association. *Stroke*. (2013) 44:2361–75. doi: 10.1161/STR.0b013e31829734f2

5. Tennant A, Geddes J, Fear J. Outcome following stroke. *Disabil Rehabil*. (1997) 19:278–84. doi: 10.3109/09638289709166539

6. Carod-Artal FJ, Egido JA. Quality of life after stroke: the importance of a good recovery. *Cerebrovasc Dis*. (2009) 27:204–14. doi: 10.1159/000200461

7. Felce D, Perry J. Quality of life: its definition and measurement. *Res Dev Disabil*. (1995) 16:51–74. doi: 10.1016/0891-4222(94)00028-8

8. Pickard AS, Johnson JA, Feeny DH, Shuaib A, Carriere KC, Nasser AM. Agreement between patient and proxy assessments of health-related quality of life after stroke using the EQ-5D and health utilities index. *Stroke*. (2004) 35:607–12. doi: 10.1161/01.STR.0000110984.91157.BD

9. Chaiyawat P, Kulkantrakorn K. Effectiveness of home rehabilitation program for ischemic stroke upon disability and quality of life: a randomized controlled trial. *Clin Neurol Neurosurg*. (2012) 114:866–70. doi: 10.1016/j.clineuro.2012.01.018

10. Cameron LJ, Wales K, Casey A, Pike S, Jolliffe L, Schneider EJ, et al. Self-reported quality of life following stroke: a systematic review of instruments with a focus on their psychometric properties. *Qual Life Res*. (2022) 31:329–42. doi: 10.1007/s11136-021-02944-9

11. Williams LS, Weinberger M, Harris LE, Clark DO, Biller J. Development of a stroke-specific quality of life scale. *Stroke*. (1999) 30:1362–9. doi: 10.1161/01.STR.30.7.1362

12. Zhu W, Jiang Y. Determinants of quality of life in patients with hemorrhagic stroke: a path analysis. *Medicine (Baltimore)*. (2019) 98:e13928. doi: 10.1097/MD.0000000000013928

13. Hicks D, Wouters P, Waltman L, Rijcke SD, Rafols I. Bibliometrics: the Leiden manifesto for research metrics. *Nature*. (2015) 520:429–31. doi: 10.1038/520429a

14. Yu D, Xu Z, Pedrycz W. Bibliometric analysis of rough sets research. *Appl Soft Comput*. (2020) 94:106467. doi: 10.1016/j.asoc.2020.106467

15. Yu D, Xu Z, Fujita H. Bibliometric analysis on the evolution of applied intelligence. *Appl Intell*. (2018) 49:449–62. doi: 10.1007/s10489-018-1278-z

16. Chen C. CiteSpace II: detecting and visualizing emerging trends and transient patterns in scientific literature. *JASIST*. (2006) 57:359–77. doi: 10.1002/asi.20317

17. van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. *Scientometrics*. (2010) 84:523–38. doi: 10.1007/s11192-009-0146-3

18. Yu D, Kou G, Xu Z, Shi S. Analysis of collaboration evolution in AHP research: 1982–2018. *Int J Inform Technol Decis Mak*. (2021) 20:7–36. doi: 10.1142/s0219622020500406

19. Sturm JW, Donnan GA, Dewey HM, Macdonell RA, Gilligan AK, Srikanth V, et al. Quality of life after stroke: the north East Melbourne stroke incidence study (NEMESIS). *Stroke*. (2004) 35:2340–5. doi: 10.1161/01.STR.0000141977.18520.3b

20. Kim SR, Kim S, Cho BH, Yu S, Cho KH. Influence of type D personality on health promoting Behaviours and quality of life in stroke patients: a cross-sectional study in South Korea. *J Stroke Cerebrovasc Dis*. (2021) 30:105721. doi: 10.1016/j.jstrokecerebrovasdis.2021.105721

21. Duncan PW, Wallace D, Lai SM, Johnson D, Embretson S, Laster LJ. The stroke impact scale version 2.0 evaluation of reliability, validity, and sensitivity to change. *Stroke*. (1999) 30:2131–40. doi: 10.1161/01.STR.30.10.2131

22. Buck D, Jacoby A, Massey A, Ford G. Evaluation of measures used to assess quality of life after stroke. *Stroke*. (2000) 31:2004–10.

23. Jonsson AC, Lindgren I, Hallstrom B, Norrving B, Lindgren A. Determinants of quality of life in stroke survivors and their informal caregivers. *Stroke*. (2005) 36:803–8. doi: 10.1161/01.STR.0000160873.32791.20

24. Akinyelure OP, Jaeger BC, Moore TL, Hubbard D, Oparil S, Howard VJ, et al. Racial differences in blood pressure control following stroke: the REGARDS study. *Stroke*. (2021) 52:3944–52. doi: 10.1161/STROKEAHA.120.033108

25. Diaz KM, Booth JN 3rd, Calhoun DA, Irvin MR, Howard G, Safford MM, et al. Healthy lifestyle factors and risk of cardiovascular events and mortality in treatment-resistant hypertension: the reasons for geographic and racial differences in stroke study. *Hypertension*. (2014) 64:465–71. doi: 10.1161/HYPERTENSIONAHA.114.03565

26. Morimoto T, Schreiner AS, Asano H. Caregiver burden and health-related quality of life among Japanese stroke caregivers. *Age Ageing*. (2003) 32:218–23. doi: 10.1093/ageing/32.2.218

27. Carod-Artal J., Egido J.A., Gonza'lez, JL and Seijas, EVd. (2000). Quality of life among stroke survivors evaluated 1 year after stroke experience of a stroke unit. *Stroke* 31, 2995–3000, doi: 10.1161/01.STR.31.12.2995

28. Ezeugwu VE, Manns PJ. Sleep duration, sedentary behavior, physical activity, and quality of life after inpatient stroke rehabilitation. *J Stroke Cerebrovasc Dis*. (2017) 26:2004–12. doi: 10.1016/j.jstrokecerebrovasdis.2017.06.009

29. Hopman WM, Verner J. Quality of life during and after inpatient stroke rehabilitation. *Stroke*. (2003) 34:801–5. doi: 10.1161/01.STR.0000057978.15397.6F

30. Cadilhac DA, Andrew NE, Lannin NA, Middleton S, Levi CR, Dewey HM, et al. Quality of acute care and long-term quality of life and survival: the Australian stroke clinical registry. *Stroke*. (2017) 48:1026–32. doi: 10.1161/STROKEAHA.116.015714

31. Wu C-Y, Yang C-L, Chuang L-L, Lin K-C, Chen H-C, Chen M-D, et al. Effect of therapist-based versus robot-assisted bilateral arm training on motor control, functional performance, and quality of life after chronic stroke: a clinical trial. *Phys Ther*. (2012) 92:1006–16. doi: 10.2522/ptj.20110282

32. Chen CH, Hung KS, Chung YC, Yeh ML. Mind-body interactive qigong improves physical and mental aspects of quality of life in inpatients with stroke: a randomized control study. *Eur J Cardiovasc Nurs*. (2019) 18:658–66. doi: 10.1177/1474515119860232

33. Lin K-C, Chang Y-F, Wu C-Y, Chen Y-A. Effects of constraint-induced therapy versus bilateral arm training on motor performance, daily functions, and quality of life in stroke survivors. *Neurorehabil Neural Repair*. (2009) 23:441–8. doi: 10.1177/1545968308328719

34. Kim ES, Kim JW, Kang HJ, Bae KY, Kim SW, Kim JT, et al. Longitudinal impact of depression on quality of life in stroke patients. *Psychiatry Investig*. (2018) 15:141–6. doi: 10.30773/pi.2017.10.11

35. Sturm JW, Donnan GA, Dewey HM, Macdonell RAL, Gilligan AK, Thrift AG. Determinants of handicap after stroke: the north East Melbourne stroke incidence study (NEMESIS). *Stroke*. (2004) 35:715–20. doi: 10.1161/01.STR.0000117573.19022.66

36. King RB. Quality of life after stroke. *Stroke*. (1996) 27:1467–72.

37. De Wit L, Theuns P, Dejaeger E, Devos S, Gantenbein AR, Kerckhofs E, et al. Long-term impact of stroke on patients' health-related quality of life. *Disabil Rehabil*. (2017) 39:1435–40. doi: 10.1080/09638288.2016.1200676

38. Ramos-Lima MJM, Brasileiro IC, Lima TL, Braga-Neto P. Quality of life after stroke: impact of clinical and sociodemographic factors. *Clinics (São Paulo)*. (2018) 73:e418. doi: 10.6061/clinics/2017/e418

39. Panício MI, Mateus L, Ricarte IF, Figueiredo MMD, Fukuda TG, Seixas JC, et al. The influence of patient's knowledge about stroke in Brazil: a cross sectional study. *Arq Neuropsiquiatr*. (2014) 72:938–41. doi: 10.1590/0004-282X20140167

40. Kwon S, Park JH, Kim WS, Han K, Lee Y, Paik NJ. Health-related quality of life and related factors in stroke survivors: Data from Korea National Health and nutrition examination survey (KNHANES) 2008 to 2014. *PLoS One*. (2018) 13:e0195713. doi: 10.1371/journal.pone.0195713

41. Corr S, Wilmer S. Returning to work after a stroke: an important but neglected area. *Br J Occup Ther*. (2003) 66:186–92. doi: 10.1177/030802260306600502

42. Whyte EM, Mulsant BH. Post stroke depression: epidemiology, pathophysiology, and biological treatment. *Biol Psychiatry*. (2002) 52:253–64. doi: 10.1016/S0006-3223(02)01424-5

43. Boehme AK, Esenwa C, Elkind MS. Stroke risk factors, genetics, and prevention. *Circ Res*. (2017) 120:472–95. doi: 10.1161/CIRCRESAHA.116.308398

44. Wissel J, Olver J, Sunnerhagen KS. Navigating the poststroke continuum of care. *J Stroke Cerebrovasc Dis*. (2013) 22:1–8. doi: 10.1016/j.jstrokecerebrovasdis.2011.05.021

45. Katan M, Luft A. Global burden of stroke. *Semin Neurol*. (2018) 38:208–11. doi: 10.1055/s-0038-1649503

46. Feigin VL, Roth GA, Naghavi M, Parmar P, Krishnamurthi R, Chugh S, et al. Global burden of stroke and risk factors in 188 countries, during 1990-2013: a systematic analysis for the global burden of disease study 2013. *Lancet Neurol*. (2016) 15:913–24. doi: 10.1016/S1474-4422(16)30073-4

47. Ma Q, Li R, Wang L, Yin P, Wang Y, Yan C, et al. Temporal trend and attributable risk factors of stroke burden in China, 1990-2019: an analysis for the global burden of disease study 2019. *Lancet Public Health*. (2021) 6:e897–906. doi: 10.1016/S2468-2667(21)00228-0

48. van Mierlo ML, Schroder C, van Heugten CM, Post MW, de Kort PL, Visser-Meily JM. The influence of psychological factors on health-related quality of life after stroke: a systematic review. *Int J Stroke*. (2014) 9:341–8. doi: 10.1111/ijs.12149

49. Kim P, Warren S, Madill H, Hadley M. Quality of life of stroke survivors. *Qual Life Res*. (1999) 8:293–301. doi: 10.1023/A:1008927431300

frontiers | Frontiers in Neurology

TYPE Original Research
PUBLISHED 11 April 2023
DOI 10.3389/fneur.2023.1131322

OPEN ACCESS

EDITED BY
Adam Kobayashi,
Cardinal Stefan Wyszyński University, Poland

REVIEWED BY
Hrvoje Budincevic,
University Hospital Sveti Duh, Croatia
Iwona Sarzyńska-Długosz,
Institute of Psychiatry and Neurology (IPiN), Poland

*CORRESPONDENCE
Henri Paul Bienfait
✉ p.bienfait@gelre.nl

SPECIALTY SECTION
This article was submitted to Stroke, a section of the journal Frontiers in Neurology

RECEIVED 08 January 2023
ACCEPTED 14 March 2023
PUBLISHED 11 April 2023

CITATION
Loban M, Gratama JWC, Klemm PL, Van Leeuwen RB, Vriesema H and Bienfait HP (2023) High prevalence of abdominal aortic aneurysm in older men with cerebrovascular disease: Evaluation of a local screening program. *Front. Neurol.* 14:1131322. doi: 10.3389/fneur.2023.1131322

High prevalence of abdominal aortic aneurysm in older men with cerebrovascular disease: Evaluation of a local screening program

M. Loban[1], J. W. C. Gratama[2], P. L. Klemm[3], Roeland B. Van Leeuwen[1], H. Vriesema[4] and Henri Paul Bienfait[1]*

[1]Department of Neurology, Gelre Hospital, Apeldoorn, Netherlands, [2]Department of Radiology, Gelre Hospital, Apeldoorn, Netherlands, [3]Department of Vascular Surgery, Gelre Hospital, Apeldoorn, Netherlands, [4]Department of Biometrics, Gelre Hospital, Apeldoorn, Netherlands

Introduction: Patients with cerebrovascular disease may suffer from other vascular morbidities, such as abdominal aortic aneurysm (AAA). Previously, a high prevalence of AAA has been demonstrated in men 60 years of age and older who have experienced TIA or stroke. This report evaluates the results of a decade's operation of a local screening program for AAA in this selected neurologic population.

Methods: Men aged ≥60 years and admitted to the neurology ward of a community-based hospital in the Netherlands from 2006 to 2017 with a diagnosis of TIA or stroke were selected for screening. The diameter of the abdominal aorta was assessed by abdominal ultrasonography. Patients with detected AAA were referred for evaluation by a vascular surgeon.

Results: AAA was detected in 72 of 1,035 screened patients (6.9%). AAAs with a diameter of 3.0–3.9 cm accounted for 61.1% of the total aneurysms found; AAAs with a diameter of 4.0–5.4 cm accounted for 20.8% of the total; and large aneurysms with a diameter of ≥5.5 cm accounted for 18.1% of all aneurysms discovered. A total of 18 patients (1.7%) underwent elective aneurysm repair.

Discussion: The detection rate of AAA in older men with cerebrovascular disease was roughly 5-fold the detection rate in known European screening programs in older men from the general population. The proportion of large AAAs (≥5.5 cm) was also substantially higher. These findings reveal a previously unknown co-morbidity in patients with cerebrovascular disease and may be helpful for cardiovascular management of this large group of neurologic patients. Current and future AAA screening programs may also benefit from this knowledge.

KEYWORDS

stroke, ischemic attack, transient, aortic aneurysm, abdominal, mass screening, prevalence

Introduction

Cerebrovascular disease is one of the sequelae of systemic atherosclerotic vascular disease. Patients who experience transient ischemic attack (TIA) and stroke may suffer from other vascular morbidities, such as abdominal aortic aneurysm (AAA). AAA is a potentially fatal condition with a high rate of mortality when the aneurysm ruptures (1). Elective aneurysm repair reduces mortality, and its perioperative risks are decreasing (2). However, AAA is a silent disease, and most aneurysms are detected by chance on imaging studies conducted for other purposes. When AAA is detected, patients are often put under the surveillance of a vascular surgeon. Elective AAA repair is recommended for large AAAs (≥5.5 cm) when the rupture risk outweighs the surgery risks (3).

In 2009, our research group demonstrated high prevalence of AAA in TIA or stroke patients (4). The subpopulation with the highest risk of AAA was men aged ≥60 years, regardless of stroke type, TOAST classification, and presence of known cardiovascular risk factors. The results of the study were in line with large studies on the prevalence of AAA, indicating the highest prevalence in older men. However, the detection rate observed in our study, of 11% in older men who have experienced TIA or stroke, roughly twofold the prevalence observed in older men from the general population in known trials (4–7). In light of these results, a local screening program for AAA has been implemented focusing on older men who have experienced TIA or stroke.

Since the late 2000s, nationwide screening programs for AAA have gradually been implemented in England and Sweden, and partially implemented in the United States, to reduce AAA-related mortality in men above 65 years of age (8–11). In multiple countries, the effectiveness of screening for AAA has been or is still being investigated, but this has not resulted in the implementation of screening programs with broad coverage (11). In a recent report, the Dutch Health Council did not advise routine population screening for AAA in the Netherlands after an extensive evaluation of existing trials and screening programs implemented worldwide (12). Although reports evaluating the existing large screening programs in England and Sweden do show clear benefits in terms of AAA-related mortality and low costs per quality-adjusted life-year (QALY) gained, the true prevalence of AAA in the screened groups turned out to be lower than expected (13–16). Multiple recent reports show a decreasing prevalence of AAA (17–19). This may imply a reduction in effectiveness of the existing screening programs and raises the need for adjustment of current screening strategies. Selecting a subpopulation with a higher detection rate of AAA may increase screening efficiency.

In the current report, we present the results over the past decade of our local screening program for AAA in older men who have experienced TIAs and stroke, and outline its clinical consequences for this group of patients. In addition, screening program outcomes are discussed in light of the results of other known screening programs worldwide.

Methods

This study was performed at a community-based teaching hospital in the Netherlands. Screening for AAA was implemented as part of the stroke workup for men aged ≥60 years admitted to the Department of Neurology with a diagnosis of TIA or stroke, in accordance with the findings of our previous study at the same hospital (4). Prospectively collected data on all patients admitted to the neurology department were used to identify patients who underwent this screening. Patient files were used to retrieving clinical data including sex, age, date of occurrence of the cerebrovascular event, type of cerebrovascular event, date of abdominal aorta measurement and maximal diameter of the abdominal aorta, and (if applicable) the results of surveillance by the vascular surgeon and the date and type of eventual surgery.

All men aged ≥60 years admitted to the Department of Neurology between January 2006 and December 2017 with a diagnosis of TIA or stroke were eligible for screening. The diagnosis was made by an attending neurologist. Exclusion criteria were subarachnoid hemorrhage; short life expectancy; expected poor functional outcome with expected discharge to a nursing home; clinical condition not allowing transportation within the hospital or making this undesirable; known AAA; previous abdominal aneurysm repair; and earlier radiological evaluation for AAA.

Screening was performed *via* ultrasonography of the abdominal aorta by an attending radiologist. AAA was defined as a maximal anterior–posterior diameter of the abdominal aorta of ≥3.0 cm. The ultrasonography was carried out in parallel to the usual stroke workup administered during the same admission. The in-room duration of the ultrasonography exam was under 5 min. Patients with a newly discovered AAA were referred to a vascular surgeon for surveillance and eventual elective repair of the AAA.

The Institutional Review Board of our institution approved the screening program.

Results

From January 2006 to December 2017, 1,037 male patients aged ≥60 years and admitted to the Department of Neurology with a diagnosis of stroke or TIA were selected for AAA screening. The median age at the time of admission and screening was 73 (IQR: 67; 79). A total of 642 patients (61.9%) had a diagnosis of acute ischemic stroke, 40 (3.9%) had an intracerebral hematoma (ICH), and 355 (34.2%) were diagnosed with a transient ischemic attack (TIA). A reliable measurement of the diameter of the abdominal aorta was successfully obtained in 1,034 patients (99.7%).

Abdominal aortic aneurysm (anterior–posterior diameter ≥3.0 cm) was found in 72 patients (6.9%). In 44 patients (4.2%), the size of the AAA was between 3.0 and 3.9 cm; in 15 cases (1.4%), the diameter was between 4.0 and 5.4 cm; and in the remaining 13 patients (1.3%), the size of the aneurysm was equal to or exceeded 5.5 cm. Thus, AAAs with a diameter of 3.0–3.9 cm accounted for 61.1% of the total aneurysms discovered; those with a diameter of 4.0–5.4 cm accounted for 20.8% of the total; and large aneurysms with a diameter of ≥5.5 cm accounted for 18.1% of all those discovered. The median age of men with a newly discovered AAA was 77 (IQR: 69; 83) years.

A total of 26 patients did not undergo follow-up with a vascular surgeon: in 13 cases this was for unknown reasons/the patients were lost to follow-up; seven patients were not followed up due to deterioration of their clinical condition; one patient died before

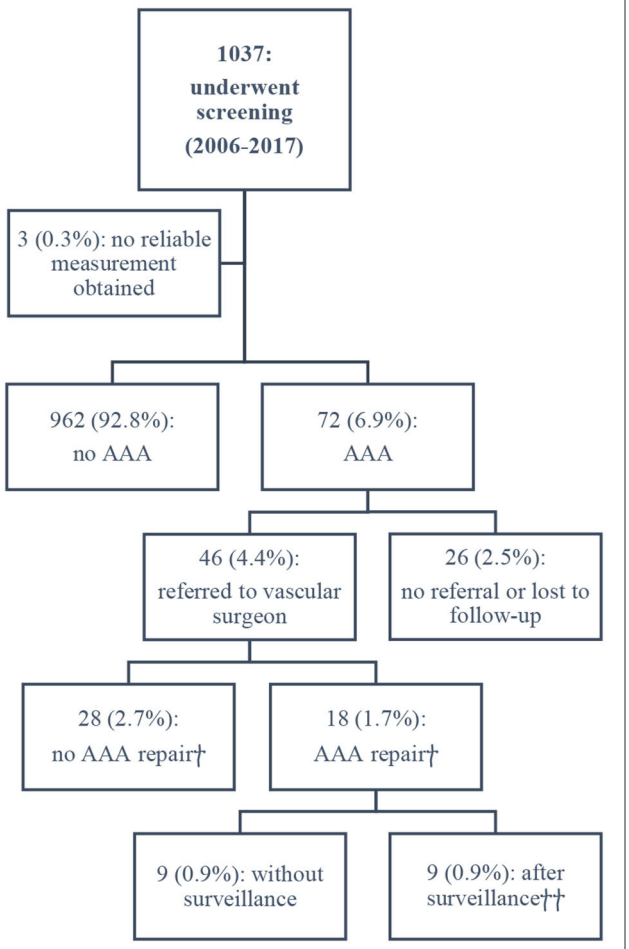


FIGURE 1
Outcomes of the screening program. †Based on available data as of August 2018. ††Median surveillance period: 40 months.

the follow-up appointment could take place; three declined follow-up; and two moved to another region. A total of 48 patients were evaluated by a vascular surgeon. As of August 2018, 28 of these were either known to be still under the surveillance of a vascular surgeon or surveillance had ended due to stability of the size of the AAA. One patient was indicated for aneurysm repair after 48 months of follow-up but declined surgery. A total of 18 patients (1.7%) underwent surgery: nine within a short period (1–15 weeks) after AAA was discovered and nine after a follow-up period with a median duration of 40 months (range: 7–128 months). Four patients underwent an open procedure, and 14 patients underwent endovascular aneurysm repair (EVAR). Two patients underwent re-operation due to major peri-operative complications, both after EVAR; two patients needed a second surgery due to technical failure of endovascular abdominal aortic aneurysm repair; one patient had a ruptured aortic aneurysm 4 years after initial surgery (EVAR) due to progression of the disease. No aneurysm-related or peri-operative deaths are known to have occurred in our patient population.

The results of the screening program are summarized in Figure 1.

The actual screening rate among all men admitted with TIA or stroke and aged ≥60 years was ∼45%. Due to the retrospective nature of the analysis, the data from the years 2006–2009 regarding the screening rate among eligible patients are incomplete; i.e., it is unknown how many patients did not undergo echographic aorta measurement between 2006 and 2009 due to exclusion criteria or logistical failures. During the years 2010–2017, 1,295 potentially eligible patients were evaluated at our stroke department. A total of 574 patients (44.3%) underwent screening and 721 (55.7%) did not. In 192 patients (14.8%), screening was not performed due to poor clinical condition or expected poor functional recovery; 72 patients (5.6%) had a known AAA; 132 (10.2%) had already participated in our screening program during a prior admission; 90 (7.0%) had undergone recent abdominal imaging without any signs of AAA; 13 (1.0%) did not give consent or were urgently transferred to another hospital; and in 222 cases (17.1%), no clear reason why screening was not performed could be identified. As mentioned above, the exact screening rate for the years 2006–2009 is unknown. However, there is no objective reason to assume that there was a substantial difference in the screening rate compared to the years 2010–2017.

Discussion

This report evaluates the results of a local screening program for AAA over a period of 11 years. The screening program was implemented following a preliminary study detecting a group of patients at risk of AAA (men aged ≥60 years with a diagnosis of TIA or stroke). The program was designed, on the one hand, to improve the cardiovascular risk management of patients with known cerebrovascular morbidity; and, on the other hand, to maximize the detection of asymptomatic but potentially fatal conditions in the region (with a population of >200,000).

The screening rate in older men admitted with TIA or stroke was ∼45%; 17% of potentially eligible patients were not screened due to logistic failures, and the remaining proportion of patients did not meet the inclusion criteria due to poor clinical condition or having previously undergone aorta imaging. It should be noted that 5.6% of patients were excluded from screening due to already-known AAA. The prevalence of asymptomatic AAA discovered among the screened patients was 6.9%, among which 18.1% of patients had large aneurysms with a diameter of ≥5.5 cm. The prevalence of AAA discovered was lower than the previously demonstrated prevalence of 11% in a comparable cohort at our institution. This decrease is in line with the results from other screening programs worldwide, showing a lower true prevalence of AAA than that identified in large RCTs.

Nevertheless, the detection rate of AAA in this screening setting, with a focus on a select group of patients with cerebrovascular disease, was substantially higher than the detection rate in other European screening programs with unselected men from the general population (Table 1). A recent report on the Veteran Affairs AAA screening program (USA) shows an AAA detection rate comparable to that of our cohort (20). It must be noted that a substantial proportion of the US cohort did not meet the initial age and gender inclusion criteria for screening; thus, the comparison with our Dutch cohort must be made with caution. Nevertheless, we do not have a clear explanation for the high

TABLE 1 Comparison of outcomes between known screening programs.

Screening program	Screened group	Period of screening	Number of subjects	AAA detected	Large AAA (≥5.5 cm) at first scan	AAA repair surgery (including surgery after period of surveillance)
ACVA (Netherlands; current report)	Men ≥ 60 y/o admitted with stroke or TIA	2006–2017	1,037	72 (6.9%)	13 (1.3%)	18 (1.7%)
NAAASP (England) (16)	One-time screening at age 65	2009–2013	700,000	9,388 (1.3%)	755 (0.1%)	870 (0.1%)
SASS (Sweden) (13)	One-time screening at age 65	2006–2014	253,896	3,891 (1.5%)	Appr. 272 (0.1%)†	Appr. 1,100 (0.4%)†
VANCHCS AAA screening (USA) (20)	Veterans 65–75 y/o who have smoked >100 cigarettes in their lifetime††	2007–2016	19,649	1,232 (6.3%)	44 (0.2%)	54 (0.3%)
UCC-SMART (Netherlands) (18)	Patients 40-80 y/o with a history of manifest atherosclerotic disease	1996—2018	5,540 (men)	136; men: 2.5%	6 (0.1%)	49 (0.9%)

†Only percentage available; approximate number calculated using published percentages.
††Heterogeneous group, including 18.7% not meeting the age and/or gender inclusion criteria.

detection rate in our study. Remarkably, older men with stroke or TIA in our cohort had at least a fivefold risk of having a large (≥5.5 cm) AAA at first ultrasonography compared to the risk observed in all other known screening programs. The proportion of patients with screening-detected AAAs who underwent surgical repair was also higher in our screening program, which cannot be attributed to more aggressive surgical management. However, there is heterogeneity in this comparison, and some data are unavailable in other reports. Nevertheless, the high detection rate of AAA demonstrated here, especially the high proportion of large AAAs in our cohort of older men with cerebrovascular disease, is remarkable when compared to programs involving screening of unselected older men from the general population (Table 1).

The high prevalence of AAA in our series of studies reveals previously unknown co-morbidity in patients with cerebrovascular disease. To the best of our knowledge, the prevalence of AAA in patients who have experienced TIA or stroke has not been investigated before by any other research group. However, the same association has been reported previously in reverse. A history of cerebrovascular disease is frequent (13.3–27.4%) in patients with known asymptomatic and acute AAA, as is a history of coronary artery disease (18.2–26.7%) (21–23). A history of vascular disease, including TIA or stroke, acute coronary disease, and peripheral artery disease, has been shown to be present in 57% of patients with acute AAA in a study of a series of such patients (21). Patients with known coronary artery disease are at a higher risk of AAA, and higher severity of coronary artery disease is associated with higher prevalence of AAA (24, 25). The prevalence of AAA was found to be 5.7% in a cohort of 438 men with coronary artery disease (24). Another study revealed a comparable prevalence (4.2%) among male patients undergoing coronary angiography, which increased drastically in patients aged ≥65 years (8.6%) and even further in patients with three-vessel coronary disease (14.4%) (25). Since cerebrovascular disease and coronary artery disease may share a common pathophysiological ground, the high prevalence of AAA in patients with coronary artery disease indirectly supports our findings.

Limitations

A limitation of our study may be selection bias. Approximately 45% of eligible patients underwent screening; 38% of patients did not meet the screening criteria, and 17% did not undergo measurement of the aorta diameter for unidentifiable reasons (Figure 1). We assume that these cases were missed because of logistical failures. Another limitation is the generalizability of our findings to other populations. Screening was performed in a community-based hospital in an area with a predominantly Caucasian population, and there are no data regarding the vascular risk factors in the study population. However, the absence of data on such risk factors has a plausible explanation, since in our preliminary study, only male gender and age ≥60 years were found to correlate with higher prevalence of AAA, while other cardiovascular risk factors did not (4). Wide inclusion criteria facilitate rapid identification of patients eligible for screening, which is important in daily practice, especially in a non-academic setting. In this report, a comparison of AAA prevalence was made with the prevalence observed in other screening programs. This comparison has a drawback in the form of heterogenicity of the cohorts. The higher prevalence of AAA in our screening program as compared to other programs may be partly attributed to a slight difference in the age of patients. The median age at the time of screening in our study was 73 years, while in other European screening programs, subjects have received an invitation for screening at the age of 65. Based on the results of our research, we cannot estimate to what extent the older age of patients contributed to the higher rates of detection of AAA, as there was no control group of patients without a diagnosis of TIA or stroke.

Conclusion

The high prevalence of AAA in general, and the larger proportion of large AAAs in older men with cerebrovascular disease, encourages the continuation of the established screening program, as it is likely that it leads to better detection and management of co-morbidity in this large subpopulation of neurologic patients. A screening program for AAA becomes beneficial in terms of cost-effectiveness and reduction of AAA-related mortality when it achieves a detection rate of at least 0.5% (26). It is reasonable to assume that this target for effectiveness has been reached in the case of the current screening program, with a detection rate of nearly 7%, especially when taking into consideration the high proportion of large AAAs with no need for follow-up. However, the life expectancy, and thus the probability of mortality as a result of a ruptured AAA, among patients who have experienced TIA or stroke may differ from that among men in the general population. This may decrease the benefit of the screening method presented. Predictors of mortality or dependency after TIA or stroke (27), such as stroke severity, recurrent stroke, increasing age, and vascular co-morbidity, should be taken into account when selecting men suitable for screening from a population with known cerebrovascular disease.

In conclusion, abdominal aortic aneurysm may be a frequent vascular co-morbidity of cerebrovascular disease, especially in men. This knowledge may be helpful for the cardiovascular management of stroke patients, as well as for the development of current and future population-wide screening programs for AAA (28–30). A further, more expansive review of the literature on this subject strengthens our recommendations (31–37). Screening of men aged ≥60 years with a diagnosis of TIA or stroke for this condition seems to be highly effective and is easy to carry out. Validation of these results in another cohort should be considered by neurological societies. Confirmation of high prevalence of AAA in a similar cohort could lead to new insight into optimal vascular risk management in a large group of neurologic patients.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent from the patients/participants or patients/participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

Author contributions

ML and HB researched literature and conceived the study. HB was involved in gaining ethical approval. ML wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Reimerink JJ, Van Der Laan MJ, Koelemay MJ, Balm R, Legemate DA. Systematic review and meta-analysis of population-based mortality from ruptured abdominal aortic aneurysm. *Br J Surg.* (2013) 100:1405–13. doi: 10.1002/bjs.9235

2. Kmietowicz Z. Deaths from elective repair of abdominal aortic aneurysm fall to new low. *BMJ.* (2012) 345:e8066. doi: 10.1136/bmj.e8066

3. Chaikof EL, Dalman RL, Eskandari MK, Jackson BM, Lee WA, Mansour MA, et al. The society for vascular surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg.* (2018) 67:2–77.e2. doi: 10.1016/j.jvs.2017.10.044

4. van Lindert NHA, Bienfait HP, Gratama JWC, Vriesema H, Hove WT, Vermeulen EGJ, et al. Screening for aneurysm of the abdominal aorta: Prevalence in patients with stroke or TIA. *Eur J Neurol.* (2009) 16:602–7. doi: 10.1111/j.1468-1331.2009.02550.x

5. Lindholt JS, Juul S, Fasting H, Henneberg EW. Screening for abdominal aortic aneurysms: single centre randomised controlled trial. *Br Med J.* (2005) 330:750–2. doi: 10.1136/bmj.38369.620162.82

6. Boll APM, Verbeek ALM, Van De Lisdonk EH, Van Der Vliet JA. High prevalence of abdominal aortic aneurysm in a primary care screening programme. *Br J Surg.* (1998) 85:1090–4.

7. Ashton HA, Buxton MJ, Day NE, Kim LG, Marteau TM, Scott RAP, et al. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. *Lancet.* (2002) 360:1531–9. doi: 10.1016/S0140-6736(02)11522-4

8. Davis M, Harris M, Earnshaw JJ. Implementation of the national health service abdominal aortic aneurysm screening program in England. *J Vasc Surg.* (2013) 57:1440–5. doi: 10.1016/j.jvs.2012.10.114

9. Wanhainen A, Bjrck M. The Swedish experience of screening for abdominal aortic aneurysm. *J Vasc Surg.* (2011) 53:1164–5. doi: 10.1016/j.jvs.2010.10.099

10. LeFevre ML. Screening for abdominal aortic aneurysm: U.S. preventive services task force recommendation statement. *Ann Intern Med.* (2014) 161:281–90. doi: 10.7326/M14-1204

11. Stather PW, Dattani N, Bown MJ, Earnshaw JJ, Lees TA. International variations in AAA screening. *Eur J Vasc Endovasc Surg.* (2013) 45:231–4. doi: 10.1016/j.ejvs.2012.12.013

12. Gezondheidsraad. *Bevolkingsonderzoek Naar Aneurysma van de Abdominale Aorta (AAA).* Den Haag: Gezondheidsraad (2019). Available online at: https://www.

gezondheidsraad.nl/documenten/adviezen/2019/07/09/bevolkingsonderzoek-naar-aneurysma-van-de-abdominale-aorta-aaa (accessed December 1, 2019).

13. Wanhainen A, Hultgren R, Linné A, Holst J, Gottsäter A, Langenskiöld M, et al. Outcome of the Swedish Nationwide abdominal aortic aneurysm screening program. *Circulation.* (2016) 134:1141–8. doi: 10.1161/CIRCULATIONAHA.116.022305

14. Benson RA, Poole R, Murray S, Moxey P, Loftus IM. Screening results from a large United Kingdom abdominal aortic aneurysm screening center in the context of optimizing United Kingdom National Abdominal Aortic Aneurysm Screening Programme protocols. *J Vasc Surg.* (2016) 63:301–4. doi: 10.1016/j.jvs.2015.08.091

15. Hager J, Henriksson M, Carlsson P, Länne T, Lundgren F. Revisiting the cost-effectiveness of screening 65-year-old men for abdominal aortic aneurysm based on data from an implemented screening program. *Int Angiol.* (2017) 36:517–25. doi: 10.23736/S0392-9590.16.03777-9

16. Jacomelli J, Summers L, Stevenson A, Lees T, Earnshaw JJ. Impact of the first 5 years of a national abdominal aortic aneurysm screening programme. *Br J Surg.* (2016) 103:1125–31. doi: 10.1002/bjs.10173

17. Svensjö S, Björck M, Wanhainen A. Update on screening for abdominal aortic aneurysm: a topical review. *Eur J Vasc Endovasc Surg.* (2014) 48:659–67. doi: 10.1016/j.ejvs.2014.08.029

18. de Boer AR, Vaartjes I, van Dis I, van Herwaarden JA, Nathoe HM, Ruigrok YM, et al. Screening for abdominal aortic aneurysm in patients with clinically manifest vascular disease. *Eur J Prev Cardiol.* (2022) 29:1170–6. doi: 10.1093/eurjpc/zwaa014

19. Darwood RJ, Brooks MJ. The impact of decreasing abdominal aortic aneurysm prevalence on a local aneurysm screening programme. *Eur J Vasc Endovasc Surg.* (2012) 44:45–50. doi: 10.1016/j.ejvs.2012.04.010

20. Chun KC, Dolan KJ, Smothers HC, Irwin ZT, Anderson RC, Gonzalves AL, et al. The 10-year outcomes of a regional abdominal aortic aneurysm screening program. *J Vasc Surg.* (2019) 70:1123–9. doi: 10.1016/j.jvs.2019.01.053

21. Howard DPJ, Banerjee A, Fairhead JF, Handa A, Silver LE, Rothwell PM. Population-based study of incidence of acute abdominal aortic aneurysms with projected impact of screening strategy. *J Am Heart Assoc.* (2015) 4:1–14. doi: 10.1161/JAHA.115.001926

22. Kent KC, Zwolak RM, Egorova NN, Riles TS, Manganaro A, Moskowitz AJ, Gelijns AC, Greco G. Analysis of risk factors for abdominal aortic aneurysm in a cohort of more than 3 million individuals. *J Vasc Surg.* (2010) 52:539–48. doi: 10.1016/j.jvs.2010.05.090

23. Li K, Zhang K, Li T, Zhai S. Primary results of abdominal aortic aneurysm screening in the at-risk residents in middle China. *BMC Cardiovasc Disord.* (2018) 18:1–6. doi: 10.1186/s12872-018-0793-5

24. Vänni V, Hernesniemi J, Turtiainen M, Turtiainen J, Hakala T. Screening men with coronary heart disease for abdominal aortic aneurysm: a prospective cohort study. *World J Surg.* (2015) 39:2354–8. doi: 10.1007/s00268-015-3091-8

25. Durieux R. High prevalence of abdominal aortic aneurysm in patients with three-vessel coronary artery disease. *Eur J Vasc Endovasc Surg.* (2014) 47:273–8. doi: 10.1016/j.ejvs.2013.12.011

26. Svensjö S, Mani K, Björck M, Lundkvist J, Wanhainen A. Screening for abdominal aortic aneurysm in 65-year-old men remains cost-effective with contemporary epidemiology and management. *Eur J Vasc Endovasc Surg.* (2014) 47:357–65. doi: 10.1016/j.ejvs.2013.12.023

27. Hankey GJ. Long-term outcome after ischaemic stroke/transient ischaemic attack. *Cerebrovasc Dis.* (2003) 16:14–9. doi: 10.1159/000069936

28. Bains P, Oliffe JL, Mackay MH, Kelly MT. Screening older adult men for abdominal aortic aneurysm: a scoping review. *Am J Mens Health.* (2021) 15:15579883211001204. doi: 10.1177/15579883211001204

29. Sprynger M, Willems M, Van Damme H, Drieghe B, Wautrecht JC, Moonen M. Screening program of abdominal aortic aneurysm. *Angiology.* (2019) 70:407–13. doi: 10.1177/0003319718824940

30. Paraskevas KI, Brar R, Constantinou J, Tsui J, Baker DM. Screening programs for abdominal aortic aneurysms: luxury or necessity? *Angiology.* (2019) 70:385–7. doi: 10.1177/0003319718766740

31. Jacob AD, Barkley PL, Broadbent KC, Huynh TT. Abdominal aortic aneurysm screening. *Semin Roentgenol.* (2015) 50:118–26. doi: 10.1053/j.ro.2014.10.003

32. Campbell A, Waggett H, Armer M, Jacomelli J, Earnshaw JJ. Quality assurance for the NHS abdominal aortic aneurysm screening programme in England. *BJS Open.* (2022) 6:zrab148. doi: 10.1093/bjsopen/zrab148

33. Ali MU, Fitzpatrick-Lewis D, Miller J, Warren R, Kenny M, Sherifali D, et al. Screening for abdominal aortic aneurysm in asymptomatic adults. *J Vasc Surg.* (2016) 64:1855–68. doi: 10.1016/j.jvs.2016.05.101

34. Mussa FF. Screening for abdominal aortic aneurysm. *J Vasc Surg.* (2015) 62:774–8. doi: 10.1016/j.jvs.2015.05.035

35. Mell M. Screening for abdominal aortic aneurysm-A call to arms? *JAMA Netw Open.* (2019) 2:e1917168. doi: 10.1001/jamanetworkopen.2019.17168

36. Benson RA, Meecham L, Fisher O, Loftus IM. Ultrasound screening for abdominal aortic aneurysm: current practice, challenges and controversies. *Br J Radiol.* (2018) 91:20170306. doi: 10.1259/bjr.20170306

37. Earnshaw JJ, Lees T. Update on screening for abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg.* (2017) 54:1–2. doi: 10.1016/j.ejvs.2017.04.002

frontiers | Frontiers in Neurology

TYPE Original Research
PUBLISHED 12 April 2023
DOI 10.3389/fneur.2023.1121836

OPEN ACCESS

EDITED BY
Aleksandras Vilionskis,
Vilnius University, Lithuania

REVIEWED BY
Klára Fekete,
University of Debrecen, Hungary
Michelle Hyczy Tosin,
Rush University, United States

*CORRESPONDENCE
Chen Li
✉ chencare@126.com
Jinglan Luo
✉ tljl@jnu.edu.cn

†These authors have contributed equally to this work

SPECIALTY SECTION
This article was submitted to Stroke, a section of the journal Frontiers in Neurology

RECEIVED 08 January 2023
ACCEPTED 14 March 2023
PUBLISHED 12 April 2023

CITATION
Zheng D, Li S, Ding Y, Chen H, Wang D, Wang H, Xie Y, Li C and Luo J (2023) Effects of nurse-led hierarchical management care on acute stroke patients: A pilot study to promote stroke-associated pneumonia management. *Front. Neurol.* 14:1121836. doi: 10.3389/fneur.2023.1121836

Effects of nurse-led hierarchical management care on acute stroke patients: A pilot study to promote stroke-associated pneumonia management

Dongxiang Zheng[1†], Shengjuan Li[2†], Yan Ding[3], Huaihua Chen[3], Dong Wang[4], Huan Wang[2], Yuyao Xie[2], Chen Li[1*] and Jinglan Luo[5*]

[1]Department of Neurology and Stroke Center, First Affiliated Hospital of Jinan University, Guangzhou, Guangdong, China, [2]School of Nursing, Jinan University, Guangzhou, Guangdong, China, [3]Department of Neurology, The First Affiliated Hospital, Jinan University, Guangzhou, China, [4]Dapeng New District Nan'ao People's Hospital, Shenzhen, China, [5]Department of Internal Medicine, First Affiliated Hospital of Jinan University, Guangzhou, Guangdong, China

Background: Stroke-related pneumonia (SAP) is a common complication in acute ischemic stroke (AIS) patients, and it has adverse effects on the clinical outcomes and increases the burden on patients' families and society. Early identification and individualized care are necessary to reduce the incidence of SAP.

Objective: The present study aimed to explore the effect of nurse-led hierarchical management care based on the acute ischemic stroke-associated pneumonia score (AIS-APS) scale in AIS patients.

Methods: A quasi-intervention pilot study design was adopted for the present study. A total of 120 AIS patients were enrolled and assigned to the intervention group and the control group, with 60 subjects in each group in a tertiary hospital in Guangzhou, China. The control group received routine care, whereas the intervention group was given nurse-led hierarchical management care based on the AIS-APS scale. The intervention duration was more than 7 days, and the incidence of SAP, neurological function, swallowing function, and activities of daily living (ADLs) at discharge were observed. The outcomes were assessed at baseline and at outpatient time.

Results: A total of 120 participants were enrolled in our study. A significant decrease was found in the incidence of SAP in the intervention group (18.3%) compared with that in the control group (41.7%). Positive outcomes were shown in neurology function, swallowing function, and ADL in the intervention group.

Conclusion: Nurse-led hierarchical management care based on AIS-APS can reduce the incidence of SAP, promote AIS patients' neurological function, and maintain patients' ADL. The results of our study indicated that nurse-led hierarchical management care is feasible for AIS patients and provides individualized interventions for patients with different levels of SAP risk. Nurse-led hierarchical management care could be incorporated into routine nursing practice. Further study is needed and expected to solve more clinical problems.

KEYWORDS

ischemic stroke, hierarchical management care, stroke-associated pneumonia, nursing care, pilot study

Introduction

Stroke is an acute cerebrovascular disease that is caused by an ischemic infarction or an intracranial hemorrhage (1). Acute ischemic stroke (AIS) is the leading common type of stroke and accounts for 69.6–70.8% of all strokes (2). AIS with the characteristics of high morbidity, disability, mortality, and recurrence, is one of the main diseases that threatens human life and health (1, 3). AIS is accompanied by impaired consciousness, dysphagia, hemiparesis, and stroke-associated pneumonia (SAP).

The concept of SAP was introduced by Hilker et al. (4). The 2010 Chinese Expert Consensus on the Management of SAP defines it as an inflammation of the lung parenchyma (including the alveolar wall or the interstitial lung in the broader sense) in stroke patients who have not previously had pneumonia. When SAP occurs within 72 h of admission, it is described as an early stage of SAP. Another classification that is being used classifies SAPs into acute (when pneumonia occurs within 1 month after stroke) phase and chronic phase (when pneumonia occurs 1 month later) (5). Other SAPs include pendant pneumonia caused by poor blood circulation, long-term bedrest, and ventilator-associated pneumonia (VAP) induced by ventilator-assisted respiration (6).

Stroke-related pneumonia is a common poststroke complication, with a prevalence of ∼7–38%, and is the leading cause of death in patients in the acute phase, with a 30-day mortality rate of up to 30% (4, 7, 8). SAP is associated with prolonged hospitalization, delayed recovery, difficulty in performing rehabilitation procedures, poorer functional outcomes, higher mortality, and increased financial and nursing burden on patient families (9, 10). Previous studies have shown that SAP can be prevented (11, 12). Therefore, for AIS patients, it is of important clinical significance to accurately predict the risk of SAP and implement effective prevention and control measures in a timely manner.

Currently, some studies have focused on pneumonia using pharmaceutical interventions (13, 14) or invasive treatments, such as a portable fibrobronchoscopic treatment and tube feeding methods (15, 16), respiratory muscle training (17), or standard care bundle intervention in preventing the occurrence of SAP (18). A common limitation of these studies is that they provide a uniform intervention without assessing patients' SAP risk. Comprehensive measures and individualized interventions are needed to reduce the incidence of SAP.

Hierarchical management care involves targeted nursing interventions according to the severity of the patient's condition to ensure that each nursing measure is more suitable for the patient's condition and improves the quality of nursing (19, 20). Recent researchers have shown that hierarchical management methods have promising results in acute cerebral infarction, acute myocardial infarction, and bronchial asthma (21–23), which have attracted researchers' interest in exploring more potential effects.

The acute ischemic stroke-associated pneumonia score (AIS-APS) (8) was developed on the basis of data from the National Stroke Registry of China. One study (24) showed that the AIS-APS scale has good predictive discrimination and accuracy and is an operational tool that can stratify the SAP risk to quickly screen high-risk patients.

In this study, we aimed to explore the effect of nurse-led hierarchical management care based on the AIS-APS scale on patients with AIS. By refining the level of nursing required for different degrees of AIS, a nursing-level classification scheme was implemented to ensure that each nursing intervention is more suitable for the patient's condition and thus provides a reference for clinical nursing.

The primary hypothesis is stated as follows. After the intervention, a lower incidence of SAP in AIS patients was observed in the intervention group.

The secondary hypothesis is stated as follows. After the intervention, the intervention group would show significant improvements in neurological function, better recovery of the swallowing function, and a prognostic quality of life.

By refining the nursing levels of high-risk patients, the nurse-led hierarchical management care based on the AIS-APS scale was implemented to ensure that each nursing measure is more suitable for the patient's condition and thus provides a reference for clinical nursing specialists to prevent SAP.

Materials and methods

Study design and population

We conducted a single-blind non-randomized controlled trial to test our hypothesis. The study was conducted at the First Affiliated Hospital of Jinan University, China, from January 2021 to December 2021. The participants were divided into the intervention group and the control group according to the admission time. The researchers in charge of the outcome evaluation were blinded to the allocation of participants.

The preexperimental results of this study showed that the incidence of SAP in the control group was ∼50% and the incidence of SAP in the intervention group was ∼20%. According to the sample size calculation formula of the two groups of an equally parallel 1:1 design, by taking $\alpha = 0.05$ and $\beta = 0.1$, the sample size needed for this study was estimated with the following formula (25):

$$n = \frac{p_1 \times (1 - p_1) + p_2 \times (1 - p_2)}{(p1 - p2)^2} \times (\mu_{\alpha/2} + \mu_{\beta})^2$$

p1 = 50%, P2 = 20%, $\alpha = 0.05$, $\beta = 0.1$, and substitution into Eq.

$$\frac{0.5 \times (1 - 0.5) + 0.2 \times (1 - 0.2)}{(0.5 - 0.2)^2} \times (1.96 + 1.28)^2 \approx 48$$

According to the aforementioned calculation, each group needs at least 48 patients, considering the dropout rate of 10%, and each group should have collected at least 53 AIS patients to ensure that the study can be carried out.

The participants were recruited by word of mouth and posters. The inclusion criteria for the present study were as follows: (1) should have met the diagnostic criteria in the Guidelines for Acute Ischemic Stroke Treatment (26); (2) should have been admitted

within 72 h of stroke; (3) should have been admitted without the diagnoses of pulmonary infection; (4) should have an age ranging ≥18 years; and (5) should have the length of the intervention of no <7 days. The participants were excluded from the present study, if they had (1) been discharged or died within 24 h; (2) had complicated infectious diseases and lung tumors before admission or other respiratory diseases; (3) had incomplete clinical data; or (4) had severe heart, lung, liver, kidney disease, or malignant tumors.

Ethical considerations

All the participants provided written informed consent prior to the study.

Intervention methods

Intervention group

The team was a multidisciplinary medical, nursing, and technical cooperation team that was composed of an expert group and a research group. The expert group included two neurology clinicians, eight clinical nurses, and one rehabilitation therapist from the neurology intensive care unit, and the research group included one doctor and four nursing master candidate students. The expert group was mainly responsible for the implementation of the interventions and the guidance and supervision of the nursing program, whereas the research group was responsible for the intervention preparation, data collection, and analysis of the findings.

Determination of the hierarchical management care

The included participants were classified into Groups I–III according to the AIS-APS scale. The AIS-APS scale includes 11 indicators in 7 domains: (1) age: 0 for ≤59 years, 2 for 60–69 years, 5 for 70–79 years, and 7 for ≥80 years; (2) medical history/comorbidity (including five indicators): atrial fibrillation, congestive heart failure, chronic obstructive pulmonary disease, and smoking; (3) prestroke dependence; (4) the National Institutes of Health Stroke Scale (NIHSS) score range at admission was assigned as follows: 0–4 for 0, 5–9 for 2, 10–14 for 5, and ≥15 for 8; (5) the Glasgow Coma Scale (GCS) at admission was assigned as follows: 15–13 for 0, 9–12 for 0, and 3–8 for 3; (6) dysphagia for 3; (7) stroke staging: 0 for lacunar infarction, 0 for partial anterior circulation infarction, 2 for complete anterior circulation, and 2 for posterior circulation infarction; and (7) admission blood glucose level. The total scale score of AIS– APS was 35, and according to the results of the AIS-APS scale, the patients were assigned to Group I: low-risk group (0–13 points), II: medium-risk group (14–20 points), or III: high-risk group (21–35 points).

Intervention measures

The intervention lasted from the day of recruitment until day 7 of hospitalization or the day of discharge (in case the patient was hospitalized for more than 7 days). Based on the results of the AIS-APS scale at admission, the AIS-APS hierarchical care was provided by our expert group accordingly, while nurses in charge and supervising physicians dynamically adjusted the nursing care level according to patients' condition during hospitalization. AIS-APS hierarchical care details are shown in Table 1.

Control group

Routine nursing interventions were administered upon admission. Participants in the control group received the usual care.

Outcome evaluations

The measurement tools included general information questionnaires, the National Institute of Health Stroke Scale (NIHSS), the modified Rankin Scale (mRS), the water swallow test (WST), and the ability to perform the Activities of Daily Living (ADL) Scale, which were used for screening patients and assessing the effectiveness of the intervention.

The outcomes were SAP rate, neurological function, swallowing function, and daily life function at discharge time *via* face-to-face interviews by trained research group members.

Two technicians were responsible for the evaluation of the homogeneous comprehensive training received. The research group was blinded to which group the participants belonged to and completed all the measurements.

Primary outcome measures

Stroke-related pneumonia

Chest x-ray examination showed a new or progressive pulmonary infiltration after stroke, combined with two or more of the following clinical symptoms of infection: (1) a temperature ≥38°C; (2) a new cough, sputum, or aggravation of the existing respiratory symptoms, with or without chest pain; (3) solid signs of disease, or pulmonary wet fissure, with leukocytes ≥10×10^9/L or ≤4×10^9/L, with or without a nuclear shift to the left. Routine blood and chest DR examinations were performed at admission and at discharge (or at the end of tube feeding). If the patient is hospitalized with a temperature ≥38°C, or if he or she has a new cough, sputum, or wet cracks in the lung, he or she should receive routine blood and chest x-ray immediately.

Secondary outcome measures

Neurological function

Neurological function was assessed using the NIHSS (27) and the mRS (28). The degree of neurological deficits after admission was evaluated using the NIHSS (scale range: 0–42). The total scale scores of <4, 4–15, and >15 were graded as mild, moderate, and severe, respectively. The mRS was used to assess the degree of dependence on the patient's ability to perform life activities and to determine the degree of disability after a stroke. An mRs scale of

10.3389/fneur.2023.1121836

TABLE 1 Nurse-led hierarchical management care based on APS-AIS scale.

Evaluation at admission	Extremely low-risk stratum ☐ Smooth stratum☐ Intermediate risk stratum☐ High risk stratum☐ Very high-risk stratum☐	
Care measures		
Environment management	1. Open windows for ventilation twice a day, for 30 min each time	
	2. Room temperature 20°C−22°C, humidity 50–60%	
	3. Limit the number of visitors and the visit duration	
	4. Use chlorine-based disinfectant to clean equipment, bed units, and ward floors	
	5. Patients diagnosed with multidrug-resistant bacteria are provided bedside isolation or single-room isolation	
Posture management	1. Assist bedridden patients in attaining proper posture and regularly turn them over and pat their backs	
	2. Encourage patients to use healthy limbs to assist passive movement of affected limbs, such as fork-grip lift training and lower limb bridge exercises	
	3. When the patient is sitting, put both upper limbs on the platform or bedside mobile table, sit firmly and push the patient back and forth alternately; do not make the patient fall down	
	4. Those who have difficulty standing need to do stand-up training first, and start walking training when the patient is able to stand without fatigue.	
	Dietary management	**Airway management**
Extremely low-risk stratum Smooth stratum 0–13	**Patients with water swallow test Level I , Patients with consciousness** 1. Instruct patients to eat through the mouth and correct irrational eating behaviors 2. Create a relatively quiet eating environment	1. Patients should rinse their mouths carefully and brush their teeth well after eating 2. Select a mouthwash according to the patient's oral condition
Intermediate risk stratum 14–20	**With the abovementioned nursing measures, add: (Patients with water swallow test Level II , Patients with consciousness)** 1. According to the V-VST screening results and the condition, patients were given a feeding plan with different food consistency (low, medium, and high consistency) and bite size of 5–20 mL 2. For patients who choke on water alone, use rennet to thicken liquids (juice, milk, tea, soup, etc.) to reduce the chance of accidental aspiration and choking. 2. Patients were moved into a semirecumbent or sitting position while eating and, after the meal, patients maintained the eating position for 20–30 min before returning to the supine position. 3. Hanging "Prevent Aspiration" warning sign on the bedside	**With the above mentioned nursing measures, add:** **Patients who eat *via* mouth:** 1. Remove oral secretions and food residues before eating 2. Instruct patients to properly cough and excrete sputum before eating, observe whether patients choke and cough up sputum during and after eating, and whether the sputum contains food particles. 3. Cooperate with rehabilitation practitioners to guide patients to perform swallowing function training, such as mouth opening exercise, empty swallowing, and masticatory muscle exercise **Patients receiving nasal feeding:** 1. Oral care 2 times/day 2. During the nasogastric feeding process, observe whether there is choking, dyspnea, nausea and vomiting, etc. If any of the above occurs, stop the nasogastric feeding immediately. 3. Replace nasogastric fluid containers and medication utensils with each meal 4. Wash the skin around the intubation and the skin where the tape is fixed daily, and keep it clean and dry
High-risk stratum Very high-risk stratum 21–35	**Patients with water swallow test Level III or V, Patients with impaired consciousness:** 1. Choose the right-sized nasogastric tube 2. Continuous head elevation >30° and verification of tube position before and after feeding, assessment of gastric residual volume 3. The temperature is 38°-40° for nasal fluids not exceeding 200 mL at a time or by enteral nutrition pump infusion. 4. Flush the nasal cannula with 30–50 mL warm water before and after nasal feeding. 5. Maintain semi-recumbent position for 60 min after nasal feeding to avoid food-aspiration-related surgeries 6. Check daily for proper fixation of the nasal feeding tube and any changes in the length of placement	**With the above mentioned nursing measures, add:** **Nasal feeding patients:** 1. Oral care 3 times/day 2. Keep the respiratory tract unobstructed, suction sputum according to the needs of the patient, and perform strict aseptic operation (if necessary, increase the oxygen flow before and after suction) 3. Perform airway humidification, and observe the patient's ventilation and changes in breath sounds during the process 4. Monitor patients for signs and symptoms of infection, including unexplained fever, changes in sputum color and properties, and decreased oxygen saturation 5. Observe the patient's consciousness, heart rate, respiration, blood pressure, blood glucose, and water electrolytes
Health education	1. Instruct the patient's family to make good food choices: Light, easily digestible food, which is moderately viscous and does not easily remain on the mucous membranes such as egg custard, tofu, etc.	
	2. Encourage the patient to use the healthy hand or the affected hand to wash the face, brush the teeth, eat, change clothes, etc., and insist on practicing button fastening and using the toilet.	
	3. Families are instructed on anti-sucking techniques, recognition of aspiration/choking, proper oral hygiene care methods, simple rehabilitation training methods, and prevention of pulmonary infections.	
	4. Patients are followed up regularly to understand the problems that they encounter and to provide timely guidance and assistance.	

2 is the criterion and cutoff value for classifying whether a stroke patient is disabled after stroke.

Swallowing function

The swallowing function was graded according to the WST (29). The purpose of this experiment was to detect aspiration with high precision. In Japan, two methods of 3 ml or 30 ml of water are usually used. We used the 30-ml method to detect aspiration in otherwise normal AIS patients. The sensitivity and specificity of the test were 70 and 71%, respectively. The patients were asked to drink water from a 30-ml glass in their usual manner. Their drinking patterns and their voice changes after drinking were recorded (wet voice). Drinking patterns were defined as follows: Level 1: drink 30 ml of water without choking; Level 2: swallow 30 ml of water multiple times without asphyxia; Level 3: drink 30 ml of water at a time but with a choking sound; Level 4: repeated ingestion of 30 ml of water with asphyxia; and Level 5: choking sound and difficulty in drinking 30 ml of water.

Activities of daily living

A comprehensive assessment of 10 items, such as diet, grooming, self-control, and bed chair transfer, was performed using the ADL (30), each rated at 10 out of 100. The higher the scale, the less help the patient needs and the lower the dependency.

Statistical methods

SPSS 22.0 software was used for conducting statistical analysis. The distribution of data was tested using the Shapiro–Wilk test. Continuous variables that conformed to the normal distribution were described by means and standard deviations (SD), and those that did not conform to the normal distribution were described by medians and quartiles. Categorical data were described in terms of frequency and percentage. Baseline characteristics of the intervention and control groups were compared by independent *t*-tests, nonparametric tests, or chi-squared (x^2) tests. Data from the control and intervention groups were compared using independent and paired *t*-tests (the differences were normally distributed)/nonparametric tests, respectively. A p-value of two-sided tests of <0.05 was considered to be statistically significant.

Results

Baseline characteristics of participants

The recruitment and dropout details of the participants are shown in Figure 1. As a result, 120 eligible participants were recruited in the study (60 in the nurse-led hierarchical management care group and 60 in the control group).

The age of the participants in the intervention group was 62.70 ± 12.52 years, and 41 patients (68%) were men. The age of the participants in the control group was 66.28 ± 10.02 years, and 43 patients (72%) were men. There were no significant differences in demographic features, namely, gender, age, hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, current smoking, and excess alcohol consumption ($p>0.05$). However, in the control group, there were more patients with a partial anterior circulation infarct in the OCSP subtype ($p>0.05$), which means that the patient's condition was more severe (Table 2).

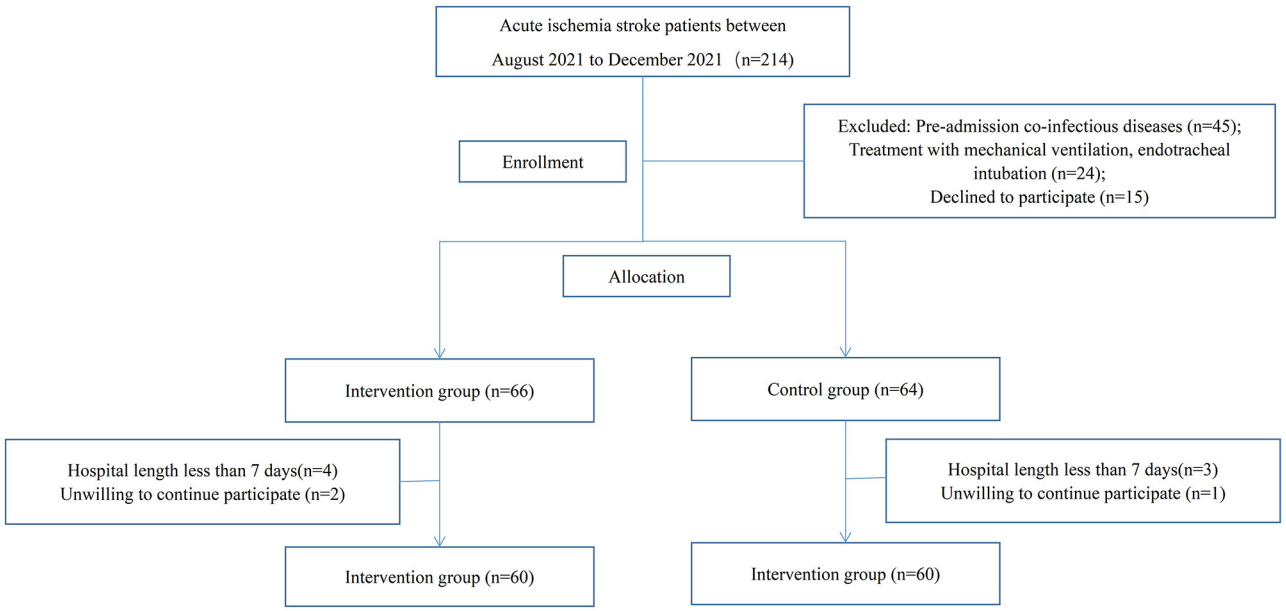


FIGURE 1
Flowchart showing recruitment and dropout of participants.

10.3389/fneur.2023.1121836

TABLE 2 Baseline characteristics of study participants.

Characteristics	Intervention group ($n = 60$)	Control group ($n = 60$)	t or χ^2 value	*P*- value
Sex			0.444	0.659
Male	41	43		
Female	19	17		
Mean age (years)	62.70 ± 12.52	66.28 ± 10.02	0.898	0.492
Hypertension (*n* %)			1.150	0.255
Yes	33 (55.0)	38 (63.3)		
No	27 (45.0)	22 (36.7)		
Diabetes mellitus (n, %)			0.753	0.454
Yes	15 (25.0)	19 (31.7)		
No	45 (75.0)	41 (68.3)		
Dyslipidemia (n, %)			1.843	0.070
Yes	11 (18.3)	4 (6.7)		
No	49 (81.7)	56 (93.3)		
Atrial fibrillation (n, %)			−1.000	0.321
Yes	6 (10.0)	3 (5.0)		
No	54 (90.0)	57 (95.0)		
History of stroke/TIA (n, %)			−2.256	0.028
Yes	14 (23.3)	10 (16.7)		
No	46 (76.7)	50 (83.3)		
Current smoking (n, %)			1.230	0.224
Yes	20 (33.3)	26 (43.3)		
No	40 (66.7)	34 (56.7)		
Excess alcohol consumption (n, %)			0.574	0.568
Yes	7 (11.7)	5 (8.3)		
No	53 (88.3)	55 (91.7)		
OCSP subtype, n, %			2.930	0.005
Lacunar infarction	25 (41.7)	11 (18.3)		
Partial anterior circulation infarct	13 (21.7)	16 (26.7)		
Total anterior circulation infarct	10(16.7)	11 (18.3)		
Posterior circulation infarct	12(20.0)	22 (36.7)		
AIS–APS score			−3.984	0.000
0–6	13	20		
7–13	21	17		
14–20	17	15		
21–27	5	5		
28–35	4	3		
mRS scale			2.390	0.020
0	6	5		
1	31	23		
2	22	30		

(Continued)

TABLE 2 (Continued)

Characteristics	Intervention group ($n = 60$)	Control group ($n = 60$)	t or χ^2 value	*P*- value
3	0	0		
4	1	0		
5	0	1		
NIHSS scale	12.97 ± 7.62	9.83 ± 7.53	1.76	0.083

TIA, transient ischemia attack; OCSP, Oxfordshire community stroke project; AIS–APS, acute ischemic stroke-associated pneumonia score.

Feasibility

The study enrolled participants who were engaged in the intervention during hospitalization. During the intervention period, 10 participants were excluded for intervention duration and personal willingness. All 120 participants completed the intervention program in accordance with a detailed program protocol. In the meantime, expert groups can readily assess the patients' conditions and adjust the nurse-led hierarchical management care level accordingly. Nurses in charge can effectively implement nursing interventions.

SAP

Stroke-related pneumonia occurred in 11 (18.33%) out of 60 patients in the intervention group and 25 (41.67%) out of 60 patients in the control group. The incidence of SAP in the intervention group was lower than that in the control group, and the differences were statistically significant ($p < 0.05$) (Table 3).

Neurological function

The results showed that the NIHSS score was 3.10 ± 4.13 in the intervention group and 4.64 ± 4.93 in the control group ($p < 0.05$), and the mRS score was 1.57 ± 1.21 in the intervention group and 2.84 ± 1.51 in the control group ($p < 0.05$) (Table 3).

Swallowing function

After the intervention, the swallowing function in the intervention group was 1.93 ± 1.08, which was a significant improvement compared to the control group of 1.17 ± 0.42 (Table 3).

ADL

The ADL was higher in the intervention group (76.83 ± 20.65) than in the control group (57.13 ± 29.08), with statistically significant differences ($p<0.05$) (Table 3).

Adverse events

No direct adverse events were observed in the intervention group.

Discussion

Based on our results, it can be concluded that nurse-led hierarchical management care based on AIS-APS exerts a positive effect on the SAP rate and improves stroke prognosis among AIS patients. Furthermore, the results of the present study suggest that hierarchical management care is a suitable intervention that can be led by clinical nurses because it is feasible and efficient.

Neuroinflammation and stroke-induced immunosuppression contribute to stroke-associated infections, such as SAP (31–33). Various risk factors for SAP have been identified, such as male gender, older age, dysphagia, severe stroke, and disturbance of consciousness (34). According to the APS-AIS, we identified patients with low-risk, medium-risk, and high-risk SAP. AIS-APS hierarchical management care was applied to assess acute ischemic stroke patients admitted within 24 h of stroke, and targeted preventive measures and hierarchical management care were given based on the screening results.

Stroke-related pneumonia is associated with increased long-term mortality and poor functional outcome on discharge (10). With the lower incidence of SAP, lower NIHSS and higher mRS scores were observed. Targeted intervention strategies are required to improve the outcomes of SAP patients who survive to hospital discharge.

Dysphagia puts stroke patients at a higher risk of pneumonia, disability, and death, and early dysphagia screening appears to be associated with a reduced risk of stroke-related pneumonia and disability (33, 35). Compared to the study of Liu, in addition to the measures of position management, feeding management, position, airway, and oral hygiene (18), we also included taking environment management, swallowing function rehabilitation, and diet management in our intervention measures. With dysphagia management and rehabilitation intervention, improvement was shown in the swallowing function. In the meantime, target intervention strategies are beneficial in SAP management.

It is feasible for clinical nurses to perform hierarchical management of care because AIS-APS score was obtained on an

TABLE 3 The comparisons in outcomes between two groups after intervention.

Variables	Category	Intervention group	Control group	Statistic	*p*-value
SAP, *n* (%)	Yes	11 (18.33)	25 (41.67)	7.778	0.005*
	No	49 (81.66)	35 (58.33)		
Neurology function	NIHSS score (d, x ± s)	3.10 ± 4.13	4.64 ± 4.93	2.212	0.031*
	mRS score			6.001	0.000*
	0	34	28		
	1	25	26		
	2	1	5		
	3	0	1		
	4	0	0		
	5	0	0		
Swallowing function (d, x ± s)	/	1.93 ±1.08	1.17 ±0.42	5.520	0.003*
ADL (d, x ± s)	/	76.83 ± 20.65	57.13 ± 29.08	4.950	0.000*

SAP, stroke-related pneumonia; ADL, activities of daily living; NIHSS, National Institute of Health stroke scale; mRS, modified Rankin Scale. *$p<0.05$.

operational scale. Before implementation, a clinical care team needs to be established, with members responsible for monitoring and implementing the hierarchical management of care. Training is also needed to teach clinical nurses how to assess the SAP risk using the AIS-APS scale. Hierarchical management care measures require changes according to the evidence-based summary of the reasons for SAP.

Implications for further study

Nurses play an important role in hierarchical management care, but it is necessary to evaluate the process by which the nurses implement these measures. In the meantime, the implementation process should be supervised for maximum effect.

Acute ischemic stroke caused by a large vessel occlusion is often accompanied by greater stroke severity and a much higher prevalence of SAP (36). For further study, we will narrow down our target population and focus on the AIS patients after vascular revascularization therapy.

The role of clinical risk scores in predicting SAP in clinical care or research may lead to bias (37). A further study should focus on developing a risk prediction model based on subjective indicators, such as blood markers.

Limitations

The present study had the following limitations. First, the duration of intervention varies depending on the hospitalization time. Whether a longer intervention time can achieve better outcomes remains unknown. The follow-up time was insufficient to determine long-term patient prognosis. Therefore, further study should extend and standardize the intervention duration. Second, the small convenience sample, while appropriate for a feasibility study, did not provide adequate statistical power and limits generalizability to other populations. Further studies should be well designed, and the sample size should be larger to obtain more positive results.

Conclusion

This pilot study demonstrates that hierarchical management care based on the AIS-APS scale is feasible to be implemented in AIS patients and that it has the potential to decrease the incidence of stroke-related pneumonia and improve patients' prognosis. The present pilot study paves the way for developing hierarchical management nursing programs with generalization and sustainability.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by First Affiliated Hospital of Jinan University (KY-2021-108). The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

DZ, CL, SL, and JL made substantial contributions to conception and design. JL, YD, and HC in charge of the

intervention implementation. DW, HW, and YX in charge of the intervention preparation and data collection. DZ and SL analyzed the data and prepared figures and/or tables. SL and CL wrote the article. All authors contributed to manuscript revision and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Duan R, Xue W, Wang K, Yin N, Hao H, Chu H, et al. Estimation of the LDL subclasses in ischemic stroke as a risk factor in a Chinese population. *BMC Neurol.* (2020) 20:414. doi: 10.1186/s12883-020-01989-6

2. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, et al. Heart disease and stroke statistics-2017 update: a report from the american heart association. *Circulation.* (2017) 135:e146–603. doi: 10.1161/CIR.0000000000000491

3. Yu KJ, Moon H, Park D. Different clinical predictors of aspiration pneumonia in dysphagic stroke patients related to stroke lesion: a STROBE-complaint retrospective study. *Medicine.* (2018) 97:e13968. doi: 10.1097/MD.0000000000013968

4. Hilker R, Poetter C, Findeisen N, Sobesky J, Jacobs A, Neveling M, et al. Nosocomial pneumonia after acute stroke: implications for neurological intensive care medicine. *Stroke.* (2003) 34:975–81. doi: 10.1161/01.STR.0000063373.70993.CD

5. Teramoto S. Novel preventive and therapuetic strategy for post-stroke pneumonia. *Expert Rev Neurother.* (2009) 9:1187–200. doi: 10.1586/ern.09.72

6. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control.* (2008) 36:309–32. doi: 10.1016/j.ajic.2008.03.002

7. Eltringham SA, Kilner K, Gee M, Sage K, Bray BD, Pownall S, et al. Impact of dysphagia assessment and management on risk of stroke-associated pneumonia: a systematic review. *Cerebrovasc Dis.* (2018) 46:99–107. doi: 10.1159/000492730

8. Ji R, Shen H, Pan Y, Wang P, Liu G, Wang Y, et al. Novel risk score to predict pneumonia after acute ischemic stroke. *Stroke.* (2013) 44:1303–9. doi: 10.1161/STROKEAHA.111.000598

9. Katzan IL, Dawson NV, Thomas CL, Votruba ME, Cebul RD. The cost of pneumonia after acute stroke. *Neurology.* (2007) 68:1938–43. doi: 10.1212/01.wnl.0000263187.08969.45

10. Teh WH, Smith CJ, Barlas RS, Wood AD, Bettencourt-Silva JH, Clark AB, et al. Impact of stroke-associated pneumonia on mortality, length of hospitalization, and functional outcome. *Acta Neurol Scand.* (2018) 138:293–300. doi: 10.1111/ane.12956

11. Balami JS, Chen RL, Grunwald IQ, Buchan AM. Neurological complications of acute ischaemic stroke. *Lancet Neurol.* (2011) 10:357–71. doi: 10.1016/S1474-4422(10)70313-6

12. Kumar S, Selim MH, Caplan LR. Medical complications after stroke. *Lancet Neurol.* (2010) 9:105–18. doi: 10.1016/S1474-4422(09)70266-2

13. Harms H, Prass K, Meisel C, Klehmet J, Rogge W, Drenckhahn C, et al. Preventive antibacterial therapy in acute ischemic stroke: a randomized controlled trial. *PLoS ONE.* (2008) 3:e2158. doi: 10.1371/journal.pone.0002158

14. Sluis WM, Westendorp WF, van de Beek D, Nederkoorn PJ, van der Worp HB. Preventive ceftriaxone in patients at high risk of stroke-associated pneumonia. A post-hoc analysis of the PASS trial. *PLoS ONE.* (2022) 17:e0279700. doi: 10.1371/journal.pone.0279700

15. Han Q, Chen C, Fu R, Tan L, Xia L. Portable fibrobronchoscopic treatment for non-severe ischemic stroke-associated pneumonia patients with dysphagia: a pilot study. *Neurol Res.* (2019) 41: 216–22. doi: 10.1080/01616412.2018.1548723

16. Juan W, Zhen H, Yan-Ying F, Hui-Xian Y, Tao Z, Pei-Fen G, et al. A comparative study of two tube feeding methods in patients with dysphagia after stroke: a randomized controlled trial. *J Stroke Cerebrovasc Dis.* (2020) 29:104602. doi: 10.1016/j.jstrokecerebrovasdis.2019.104602

17. Kulnik ST, Birring SS, Moxham J, Rafferty GF, Kalra L. Does respiratory muscle training improve cough flow in acute stroke? Pilot randomized controlled trial. *Stroke.* (2015) 46:447–53. doi: 10.1161/STROKEAHA.114.007110

18. Liu ZY, Wei L, Ye RC, Chen J, Nie D, Zhang G, et al. Reducing the incidence of stroke-associated pneumonia: an evidence-based practice. *BMC Neurol.* (2022) 22:297. doi: 10.1186/s12883-022-02826-8

19. Azami G, Soh KL, Sazlina SG, Salmiah MS, Aazami S, Mozafari M, et al. Effect of a nurse-led diabetes self-management education program on glycosylated hemoglobin among adults with type 2 diabetes. *J Diabetes Res.* (2018) 2018:4930157. doi: 10.1155/2018/4930157

20. Verberne DPJ, van Mastrigt G, Ponds R, van Heugten CM, Kroese M. Economic evaluation of nurse-led stroke aftercare addressing long-term psychosocial outcome: a comparison to care-as-usual. *BMJ Open.* (2021) 11:e039201. doi: 10.1136/bmjopen-2020-039201

21. Chen J, Chen Y. A nurse-led hierarchical management model for the out-of-hospital management of children with bronchial asthma: a prospective randomized controlled study. *Am J Transl Res.* (2021) 13:6488–97.

22. Dai L. Effect of hierarchical nursing management in patients with hypertension complicated with cardiovascular and cerebrovascular risk factors. *Comput Math Methods Med.* (2021) 2021:1246566. doi: 10.1155/2021/1246566

23. Zhang Q, Yu Y. Effects of graded emergency nursing on resuscitation outcomes, prognosis, and nursing satisfaction in patients with acute myocardial infarction. *Am J Transl Res.* (2021) 13:10586–92.

24. Du Q, Li N, Li W, Li J, Yin X, Zhang M, et al. The value of ischemic stroke acute ischemic stroke-associated pneumonia score in predicting stroke-associated pneumonia. *Chin J Emerg Med.* (2016) 25:1268–71. doi: 10.3760/cma.j.issn.1671-0282.2016.10.011

25. Wang R. Methods of sample size estimation in randomized controlled clinical trial design. *Shanghai Med Pharm J.* (2023) 44:48–52. doi: 10.3969/j.issn.1006-1533.2023.01.013

26. Qiu, S., and Xu, Y. (2020). Guidelines for acute ischemic stroke treatment. *Neurosci. Bull.* 36, 1229–1232. doi: 10.1007/s12264-020-00534-2

27. Frankel MR, Morgenstern LB, Kwiatkowski T, Lu M, Tilley BC, Broderick JP, et al. Predicting prognosis after stroke: a placebo group analysis from the national institute of neurological disorders and stroke rt-Pa stroke trial. *Neurology.* (2000) 55:952–9. doi: 10.1212/WNL.55.7.952

28. Banks JL, Marotta CA. Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials: a literature review and synthesis. *Stroke.* (2007) 38:1091–6. doi: 10.1161/01.STR.0000258355.23810.c6

29. Chen PC, Chuang CH, Leong CP, Guo SE, Hsin YJ. Systematic review and meta-analysis of the diagnostic accuracy of the water swallow test for screening aspiration in stroke patients. *J Adv Nurs.* (2016) 72:2575–86. doi: 10.1111/jan.13013

30. Collin C, Wade DT, Davies S, Horne V. The Barthel ADL Index: a reliability study. *Int Disabil Stud.* (1988) 10:61–3. doi: 10.3109/09638288809164103

31. Brott T. Prevention and management of medical complications of the hospitalized elderly stroke patient. *Clin Geriatr Med.* (1991) 7:475–82. doi: 10.1016/S0749-0690(18)30533-0

32. Dylla L, Herson PS, Poisson SN, Rice JD, Ginde AA. Association between chronic inflammatory diseases and stroke-associated pneumonia - an epidemiological study. *J Stroke Cerebrovasc Dis.* (2021) 30:105605. doi: 10.1016/j.jstrokecerebrovasdis.2021.105605

33. Hoffmann S, Harms H, Ulm L, Nabavi DG, Mackert BM, Schmehl I, et al. Stroke-induced immunodepression and dysphagia independently predict stroke-associated pneumonia - The PREDICT study. *J Cereb Blood Flow Metab.* (2017) 37:3671–82. doi: 10.1177/0271678X16671964

34. Li Y, Zhang Y, Ma L, Niu X, Chang J. Risk of stroke-associated pneumonia during hospitalization: predictive ability of combined A(2)DS(2) score and hyperglycemia. *BMC Neurol.* (2019) 19:298. doi: 10.1186/s12883-019-1497-x

35. Al-Khaled M, Matthis C, Binder A, Mudter J, Schattschneider J, Pulkowski U, et al. Dysphagia in patients with acute ischemic stroke: early dysphagia screening may reduce stroke-related pneumonia and improve stroke outcomes. *Cerebrovasc Dis.* (2016) 42:81–9. doi: 10.1159/000445299

36. Zhang B, Zhao W, Wu C, Wu L, Hou C, Klomparens K, et al. SDL index predicts stroke-associated pneumonia in patients after endovascular therapy. *Front Neurol.* (2021) 12:622272. doi: 10.3389/fneur.2021.622272

37. Kishore AK, Vail A, Bray BD, Chamorro A, Napoli MD, Kalra L, et al. Clinical risk scores for predicting stroke-associated pneumonia: a systematic review. *Eur Stroke J.* (2016) 1:76–84. doi: 10.1177/2396987316651759

frontiers | Frontiers in Neurology

TYPE Original Research
PUBLISHED 02 May 2023
DOI 10.3389/fneur.2023.1149531

OPEN ACCESS

EDITED BY
Aleksandras Vilionskis,
Vilnius University, Lithuania

REVIEWED BY
Fabrizio Giammello,
University of Messina, Italy
Saulius Taroza,
Saulius Taroza, Lithuania

*CORRESPONDENCE
Jerzy Narloch
jerzy.narloch@gmail.com

RECEIVED 22 January 2023
ACCEPTED 21 March 2023
PUBLISHED 02 May 2023

CITATION
Narloch J, Piasecki A, Ziecina P, Dębiec A, Wierzbicki M, Staszewski J and Piasecki P (2023) Is aspiration an effective acute stroke treatment in older adults? *Front. Neurol.* 14:1149531. doi: 10.3389/fneur.2023.1149531

Is aspiration an effective acute stroke treatment in older adults?

Jerzy Narloch[1]*, Adam Piasecki[2], Piotr Ziecina[1], Aleksander Dębiec[3], Marek Wierzbicki[1], Jacek Staszewski[3] and Piotr Piasecki[1]

[1]Department of Interventional Radiology, Military Institute of Medicine–National Research Institute, Warsaw, Poland, [2]Faculty of Medicine, Medical University of Warsaw, Warsaw, Poland, [3]Department of Neurology, Military Institute of Medicine–National Research Institute, Warsaw, Poland

Introduction: Clinical outcomes after interventional stroke treatment rely on several factors, with older age being associated with poorer results, which are mainly attributed to patient's comorbidities and medications. The delivery of an aspiration catheter could be hindered by carotid tortuosity, which is more prevalent in elderly patients with increasing age. In this study, we aimed to compare the clinical and angiographic outcomes of a direct aspiration first-pass technique in interventional stroke treatment for elderly patients compared with younger patients.

Materials and methods: A total of 162 patients (92 women and 70 men, aged between 35 and 94 years +/− 12.4 years) were included in this study. Patients who were treated in a comprehensive stroke center due to a large-vessel occlusion stroke using aspiration as the first-choice treatment were included in this study. To evaluate carotid arteries, the tortuosity index (TI) was calculated for each segment of each carotid pathway.

Results: Age correlated significantly with the presence of carotid tortuosity ($R = 0.408$, $p = 0.000$), extracranial length ratio ($R = 0.487$, $p = 0.000$), and overall length ratio ($R = 0.467$, $p = 0.000$). No significant associations were found with coiling, kinking, or intracranial length ratio. Successful aspiration-based recanalization rate decreased with increasing age, and the differences between the age subgroups were not statistically significant. A comparison of the extreme subgroups, i.e., <60 years old vs. ≥80 years old, did not yield a statistically significant change ($p = 0.068$).

Conclusion: Successful aspiration-based recanalization rate decreased with increasing age; however, these differences were not significant. Clinical outcomes did not significantly differ with regard to carotid tortuosity, regardless of the time of assessment. Neither intracranial nor extracranial tortuosity was significantly associated with reperfusion-related complications in either of the age subgroups.

KEYWORDS

stroke, aspiration, elderly, thrombectomy, interventional radiology

Introduction

Clinical outcomes after interventional stroke treatment rely on several factors. Older age is associated with poorer results, which are mainly attributed to patient's comorbidities and medications. Successful recanalization after a single retrieval maneuver is the primary goal of treatment in cases of acute ischemic stroke, and it is an independent factor for good clinical outcomes, regardless of age (1–4).

The results of the ASTER and COMPASS trials have established that, compared with stent-retriever-based techniques, "a direct aspiration first-pass technique" (ADAPT) was a non-inferiority trial in terms of successful recanalization and functional outcomes. Moreover, ADAPT has gained an increasing number of proponents due to its lower cost and faster procedure time (5–7).

Carotid tortuosity, which becomes more prevalent with increasing age, can hinder the delivery of the aspiration catheter (8). Moreover, the navigation of aspiration catheters is further impeded by the branching of the parent artery (in particular, the ophthalmic branch of the internal carotid artery [ICA]). Unfavorable anatomy poses technical challenges that lead to increased procedure time and delays in reperfusion, which affect patient outcomes (5, 8–10).

In this study, we aimed to compare the clinical and angiographic outcomes of elderly patients who received ADAPT as part of interventional stroke treatment with the clinical and angiographic outcomes of younger patients.

Materials and methods

Study design

The primary goal of this study was to assess whether aspiration alone could successfully treat stroke that is caused by a large-vessel occlusion in elderly patients compared with younger patients. Data regarding the modified Rankin score at 1, 3, and 12 months; National Institute of Health Stroke Score (NIHSS) before and after stroke treatment; time from onset-to-groin access; time from onset-to-recanalization; successful reperfusion rate (mTICI 2b-3) (11); first-pass success rate (mTICI 2b-3); periprocedural complication rate; anatomical characteristics; the presence and grade of vessel tortuosity; and aspiration catheter parameters were collected and analyzed retrospectively. The patients were divided into the following groups according to their age: <60 years, ≥60 years, <65 years, ≥65 years, <80 years, and ≥80 years. The groups were created in accordance with the following criteria based on the official definition of old age by the United Nations: 65 years is the most frequently reported age of the patients at the time of hospitalization for interventional stroke treatment, and octogenarians constituted the oldest age group in our study (12). Hemorrhagic transformation of an ischemic infarct was classified according to the European Cooperative Acute Stroke Study (ECASS II) (13).

Study population

Consecutive patients who underwent ADAPT as the first choice of treatment for the treatment of stroke due to a large-vessel occlusion between January 2016 and August 2021 at a comprehensive stroke center were included in the present study. All patients were eligible to receive endovascular treatment according to the American Heart Association/American Stroke Association (AHA/ASA) and European Stroke Organization (ESO)—European Society of Minimally Invasive Neurological Therapy (ESMINT) guidelines. The eligible patients received 0.9 mg/kg of an intravenous recombinant tissue plasminogen activator (rtPA) (14).

Endovascular treatment

All procedures were performed by experienced interventional radiologists (who had performed > 50 endovascular stroke treatment procedures) *via* groin access. Mechanical thrombectomy was performed under local or general anesthesia, depending on the Glasgow Coma Scale (GCS) status of the patient. According to the institutional guidelines, ADAPT was chosen as the first choice of treatment, provided the aspiration catheter was delivered to the occlusion site. After three unsuccessful attempts at aspiration, the stent-retriever was used to continue rescue thrombectomy and such cases were excluded from the analysis.

To confirm the cerebral large-vessel occlusion (LVO), an Impress diagnostic peripheral catheter (Merit Medical, South Jordan, UT, USA) was placed in an 8F Radifocus Super Arrow-Flex Sheath Introducer (Arrow International Inc., PA, USA). The diagnostic catheter was exchanged for a guiding catheter, such as Neuron MAX (Penumbra, Inc., Alameda, CA, USA) or Fubuki (Terumo-MicroVention, Tustin, CA, USA). The following aspiration catheters were used in this study: the React^{TM} 68 and React^{TM} 71 (Medtronic, Minneapolis, MN, USA); SOFIA and SOFIA Plus (Terumo-MicroVention, Tustin, CA, USA); AXS Catalyst 5, 6, and 7 (Stryker, Kalamazoo, MI, USA); or ACE 68, JET7 (Penumbra Inc., Alameda, CA, USA). A Microcatheter Headway 0.021" (Terumo-MicroVention, Tustin, CA, USA) with 0.014" microwire Traxcess (Terumo, Tokyo, Japan) was used to reach the occlusion site. Aspiration passes were performed using ADAPT as described previously (15).

Imaging technique

Computed tomography angiography (CTA) was performed for the region extending from the aortic arch to the vertex of the skull using a 64-row multidetector CT scanner (General Electric LightSpeed VCT, GE Healthcare, Milwaukee, WI, USA) with a helical technique using the following parameters:120 kV, 400 mA, collimation: 40 × 0.625 mm, rotation: 0.5 s, and pitch factor: 0.984.

Automatic bolus triggering at the aortic arch was performed by administering a contrast medium (iomeprol, 350 mg I/mL, Iomeron, Bracco, Milan, Italy) *via* the antecubital vein with an 18-gauge cannula using a coupled power injector (a flow rate of 5 mL/s, 70 mL of contrast medium was injected followed by a 50-mL saline flush).

Image processing and analysis

Dedicated software for visualizing vessel tortuosity was used for the analysis. VesselIQ Xpress (GE Healthcare, Milwaukee, WI, USA) is a post-processing application for the Advantage Workstation (AW) platform that is connected to a local PACS that can be used to analyze two- and three-dimensional CTA images and the data derived from DICOM 3.0 compliant CT scans. It extracts bony structures for the accurate identification of the vessels. The vessels were evaluated in a curved reformat, lumen, or multiple-plane reformat (MPR) view. Tools available for sizing the vessel were utilized once the vessels were visualized.

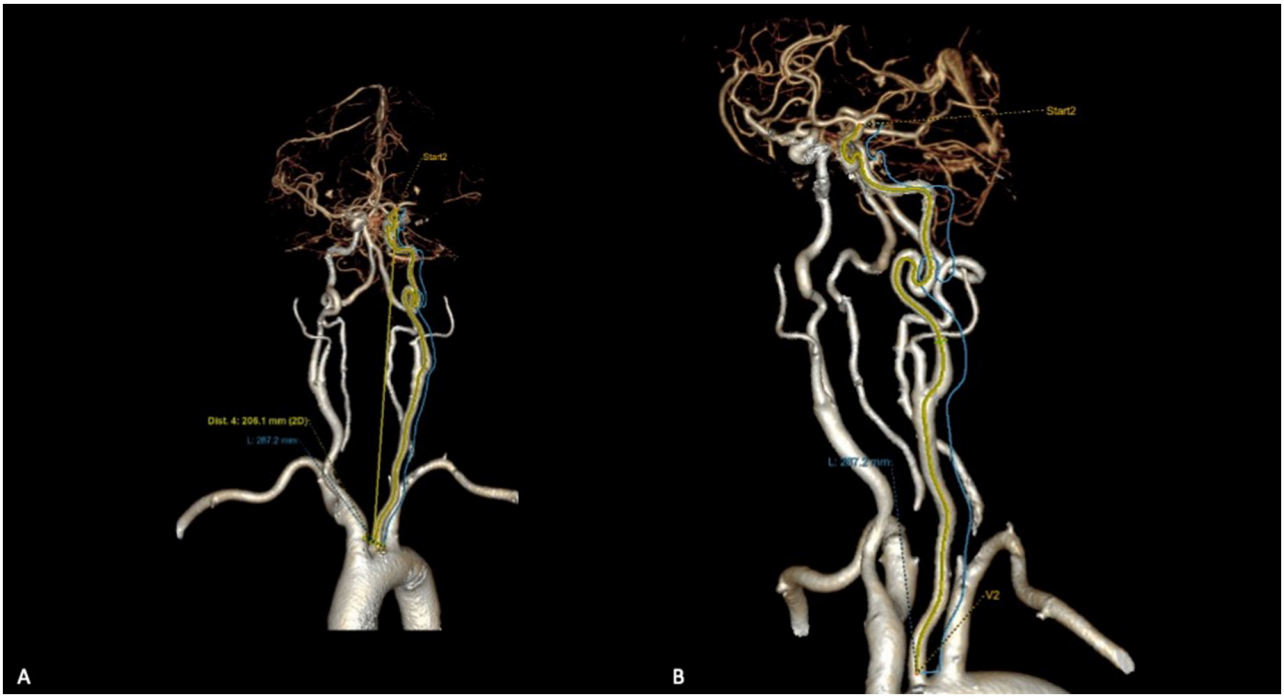


FIGURE 1
Performance of ADAPT in selected age groups. However, none of the differences were statistically significant.

The carotid artery pathway along the centerline was plotted in a three-dimensional space and divided into two main segments: (1) from the aortic arch takeoff (brachiocephalic artery [BCA]/common carotid artery [CCA]) of CCA to the entry of ICA into the skull and (2) intracranial ICA to the bifurcation into the middle cerebral artery (MCA) and anterior cerebral artery (ACA). The tortuosity index (TI) was calculated for each segment of each carotid pathway using the following formula: extracranial TI + intracranial TI = [(centerline distance)/(straight-line distance)−1] × 100. The straight length of the carotid artery pathway was measured individually for the overall length, extracranial, and intracranial segments in the anteroposterior position. Figure 1 presents a sample case of the measurement procedure.

The vertebral artery (VA) from the takeoff to the bifurcation of the basilar artery (BA) was measured in the case of posterior circulation, and two separate segments were created: extracranial and intracranial.

The carotid artery and VA selected for MT access were evaluated. In cases with the occlusion present proximal to the distal measurement landmarks, the contralateral side was evaluated as a surrogate. Using the previously established modified criteria by Wiebel–Fields and Metz (8, 16, 17), dolichoarteriopathy was visually identified and defined as tortuosity, kinking, and coiling.

The images were reviewed and evaluated by two experienced neuroradiologists.

Statistical analysis

The recorded data included categorical variables such as: the modified Rankin score at 1, 3, and 12 months, presence of vessel tortuosity, type of aortic arch, type of periprocedural complications (vasospasm, dissection, embolization in a new territory, subarachnoid hemorrhage, and intracranial hematoma), presence of successful reperfusion (mTICI 2b-3), and presence of first-pass success.

Continuous data included the National Institute of Health Stroke Score (NIHSS) before and after stroke treatment; time from onset-to-groin access; time from onset-to-recanalization; aspiration catheter parameters (internal diameter and external diameter), occluded vessel diameter, and length ratios.

The patients were divided into the following groups according to their ages: <60 years, ≥60 years, <65 years, ≥65 years, <80 years, and ≥80 years. The aforementioned data were compared between these different age groups.

Student's *t*-test and Mann–Whitney U test were used for estimating continuous data. The chi-squared or Fisher's exact test was used for estimating categorical variables. The 95% confidence interval (CI) was calculated. Statistical significance was set at a value of P of < 0.05.

Results

In total, 162 patients met the inclusion criteria in this study. Overall, 92 women and 70 men, aged between 35 and 94 years (+/– 12.4 years), were included in this study. The baseline characteristics, clinical and radiological data of treated patients stratified according to the subgroup are summarized in Table 1.

Spearman's rank correlation analysis

Age was significantly correlated with several clinical characteristics, including the mRS status at 12 months after

TABLE 1 Baseline characteristics, clinical and radiological data of treated patients, divided into age groups: <60 years vs. ≥60 years, <65 years vs. ≥65 years, and <80 years vs. ≥80 years.

Age group	<60	≥60	*p*-value	<65	≥65	*p*-value	<80	≥80	*p*-value
	N/mean	N/mean		N/mean	N/mean		N/mean	N/mean	
Sex	**30 pts**	**132 pts**		**53 pts**	**109 pts**		**128 pts**	**34 pts**	
Women/MEN	12 (40%)/18 (60%)	80 (61%)/52 (39%)	0.032	21 (40%)/32 (60%)	71 (65%)/38 (35%)	0.002	63 (49%)/65 (51%)	29 (85%)/5 (15%)	0.000
Pre-stroke MRS			0.110			0.032			0.058
0	28	88		43	73		98	18	
1	0	18		1	17		10	8	
2	0	3		0	3		2	1	
3	0	1		0	1		1	0	
4	0	0		0	0		0	0	
5	0	3		0	3		2	1	
Side			0.719			0.306			0.567
Left	17	66		27	56		67	16	
Right	11	59		21	49		53	17	
Posterior	2	7		5	4		8	1	
Tandem *yes/no*	8 (27%)/22 (73%)	22 (17%)/109 (83%)	0.160	15 (28%)/38 (72%)	15 (14%)/93 (86%)	0.025	27 (21%)/100 (79%)	3 (9%)/31 (91%)	0.074
Occlusion			0.580			0.525			0.457
ICA-T	12	40		20	32		44	8	
MCA-M1	14	63		22	55		60	17	
MCA-M2	2	21		6	17		16	7	
BA	2	6		4	4		7	1	
PCA-P2	0	2		1	1		1	1	
rTPA *Yes/No*	23 (77%)/7 (23%)	85 (64%) /47 (36%)	0.141	40 (75%)/13 (25%)	68 (62%)/41 (38%)	0.068	87 (68%)/41 (32%)	21 (62%)/13 (38%)	0.313
Complications *Yes/No*	3 (10%)/27 (90%)	17 (13%) /115 (87%)	0.470	5 (9%)/48 (91%)	15 (14%)/94 (86%)	0.304	13 (10%) /115 (90%)	7 (20%)/27 (80%)	0.092
Hemorrhage 24 h *Yes/No*	7 (23%)/20 (67%)	34 (26%)/78 (59%)	0.524	15 (28%)/33 (72%)	27 (25%)/65 (75%)	0.885	31 (24%) /81 (63%)	11 (32%)/17 (50%)	0.336

(Continued)

10.3389/fneur.2023.1149531

TABLE 1 (Continued)

Age group	<60	≥60	*p*-value	<65	≥65	*p*-value	<80	≥80	*p*-value
	N/mean	N/mean		N/mean	N/mean		N/mean	N/mean	
mRS at discharge			0.073			0.156			0.083
0	4	7		5	6		10	1	
1	5	14		6	13		15	4	
2	4	17		9	12		19	2	
3	3	10		6	7		12	1	
4	1	11		2	10		8	4	
5	7	38		14	31		33	12	
6	5	30		9	26		26	9	
Discharged			0.316			0.224			0.044
Home	11	34		15	30		35	10	
Rehab	6	29		14	21		31	4	
Care home	1	14		2	13		8	7	
Other	3	4		4	3		6	1	
Home + rehab	3	10		6	7		12	1	
mRS at 30 days			0.145			0.330			0.046
0	3	8		4	7		9	2	
1	6	9		6	9		14	1	
2	3	16		7	12		17	2	
3	3	18		8	13		19	2	
4	0	12		2	10		8	4	
5	8	33		15	26		31	10	
6	5	24		7	22		21	8	
mRS at 90 days			0.088			0.127			0.011
0	1	5		1	5		4	2	
1	5	9		6	8		14	0	
2	5	17		10	12		19	3	
3	0	11		2	9		9	2	
4	2	12		5	9		13	1	

(Continued)

10.3389/fneur.2023.1149531

TABLE 1 (Continued)

Age group	<60	≥60	*p*-value	<65	≥65	*p*-value	<80	≥80	*p*-value
	N/mean	N/mean		N/mean	N/mean		N/mean	N/mean	
5	3	11		6	8		12	2	
6	1	18		2	17		10	9	
mRS at 12 months			0.013			0.038			0.002
0	1	1		1	1		2	0	
1	6	6		6	6		12	0	
2	0	10		5	5		9	1	
3	2	7		4	5		8	1	
4	0	4		1	3		3	1	
5	0	1		0	1		1	0	
6	1	15		3	13		9	7	
AF *Yes/No*	9 (30%)/21 (70%)	57 (43%)/75 (57%)	0.131	13 (25%)/40 (75%)	53 (49%)/56 (51%)	0.003	43 (34%)/85 (66%)	23 (68%)/11 (32%)	0.000
DB *Yes/No*	3 (10%)/27 (90%)	34 (26%)/98 (74%)	0.047	8 (15%)/45 (85%)	29 (27%)/80 (73%)	0.073	27 (21%)/101 (79%)	10 (29%)/24 (71%)	0.210
LIP *Yes/No*	12 (40%)/18 (60%)	57 (43%)/75 (57%)	0.457	19 (36%)/34 (64%)	50 (46%)/59 (54%)	0.149	55 (43%)/73 (57%)	14 (41%)/20 (59%)	0.505
NT *Yes/No*	12 (40%)/18 (60%)	93 (70%)/39 (30%)	0.002	24 (45%)/29 (55%)	81 (74%)/28 (26%)	0.000	80 (63%)/48 (37%)	25 (74%)/9 (26%)	0.160
COR *Yes/No*	4 (13%)/26 (87%)	33 (25%)/99 (75%)	0.126	10 (19%)/43 (81%)	27 (25%)/82 (75%)	0.264	26 (20%)/102 (80%)	11 (32%)/23 (68%)	0.106
Stroke/TIA *Yes/No*	1 (3%)/29 (97%)	12 (9%)/120 (91%)	0.264	1 (2%)/52 (98%)	12 (11%)/97 (89%)	0.037	9 (7%)/119 (93%)	4 (12%)/30 (88%)	0.278
aTHROMB *Yes/No*	1 (3%)/29 (97%)	23 (17%)/109 (83%)	0.036	3 (6%)/50 (94%)	21 (19%)/88 (81%)	0.016	13 (10%)/115 (90%)	11 (32%)/23 (68%)	0.003
aPLT *Yes/No*	1 (3%)/29 (97%)	24 (18%)/108 (82%)	0.030	4 (8%)/49 (92%)	21 (19%)/88 (81%)	0.040	20 (16%)/108 (84%)	5 (15%)/29 (85%)	0.568
PFO *Yes/No*	6 (20%)/24 (80%)	2 (2%)/130 (98%)	0.001	6 (11%)/47 (89%)	2 (2%)/107 (98%)	0.015	8 (6%)/120 (94%)	0 (0%)/34 (100%)	0.145
Coiling *Yes/No*			0.260			0.357			0.406
	0 (0%)/21 (70%)	6 (5%)/80 (61%)		1 (2%)/34 (64%)	5 (5%)/67 (61%)		4 (3%)/79 (56%)	2 (6%)/22 (65%)	
Kinking *Yes/No*	1 (3%)/20 (67%)	19 (14%)/68 (52%)	0.058	3 (6%)/33 (62%)	17 (16%)/55 (50%)	0.043	16 (13%)/68 (53%)	4 (12%)/20 (59%)	0.527
Tortuosity *Yes/No*	9 (30%)/12 (40%)	67 (51%)/20 (15%)	0.003	15 (28%)/21 (40%)	61 (56%)/11 (21%)	0.000	56 (44%)/28 (22%)	20 (59%)/4 (12%)	0.090

(Continued)

10.3389/fneur.2023.1149531

TABLE 1 (Continued)

Age group	<60	≥60	*p*-value	<65	≥65	*p*-value	<80	≥80	*p*-value
	N/mean	N/mean		N/mean	N/mean		N/mean	N/mean	
Arch type			0.543			0.529			0.687
1	11	63		22	52		56	18	
2	1	8		3	6		6	3	
3	0	1		0	1		1	0	
6	0	1		0	1		1	0	
Vasospasm *Yes/No*	1 (3%)/29 (97%)	3 (2%)/129 (98%)	0.563	1 (2%)/52 (98%)	3 (3%)/106 (97%)	0.604	4 (3%)/124 (97%)	0 (0%)/34 (100%)	0.386
ENT *Yes/No*	0 (0%)/30 (100%)	11 (8%)/121 (92%)	0.097	3 (6%)/50 (94%)	8 (7%)/101 (93%)	0.488	9 (7%)/119 (93%)	2 (6%)/32 (94%)	0.584
Dissection *Yes/No*	0 (0%)/30 (100%)	4 (3%)/128 (97%)	0.437	0 (0%)/53 (100%)	4 (4%)/105 (96%)	0.201	3 (2%)/125 (98%)	1 (3%)/33 (97%)	0.614
SAH *Yes/No*	2 (7%)/28 (93%)	8 (6%)/128 (94%)	0.585	2 (4%)/51 (96%)	8 (7%)/101 (93%)	0.307	4 (3%)/124 (97%)	6 (18%)/28 (82%)	0.006
ICH *Yes/No*	1 (3%)/28 93%)	1 (0.8%)/127 (96%)	0.336	2 (4%)/48 (90%)	0 (0%)/107 (98%)	0.100	2 (2%)/121 (95%)	0 (0%)/34 (100%)	0.613
3DCT			0.177			0.027			0.100
HI1 ECASSII	6	16		12	10		19	3	
HI2 ECASSII	5	26		9	22		25	6	
PH1 ECASSII	0	2		1	1		2	0	
PH2 ECASSII	1	0		1	0		1	0	
Normal	9	48		16	41		45	12	
Final mTICI			0.757			0.994			0.537
0	1	14		5	10		9	6	
1	2	7		3	6		7	2	
2a	3	11		5	9		11	3	
2b	11	37		17	31		41	7	
2c	3	16		6	13		15	4	
3	10	47		17	40		45	12	

(Continued)

10.3389/fneur.2023.1149531

TABLE 1 (Continued)

Age group	<60	≥60	*p*-value	<65	≥65	*p*-value	<80	≥80	*p*-value
	N/mean	N/mean		N/mean	N/mean		N/mean	N/mean	
Final aspiration mTICI			0.502			0.485			0.554
0	3	20		7	16		15	8	
1	3	14		4	13		13	4	
2a	1	16		3	14		14	3	
2b	11	32		18	25		37	6	
2c	2	11		5	8		10	3	
3	10	39		16	33		39	10	
Number of passes			0.124			0.192			0.828
1	16	56		26	46		57	15	
2	10	45		19	36		44	11	
3	4	23		7	20		21	6	
4	0	6		0	6		4	2	
5	0	2		1	1		2	0	
First pass success *Yes/No*	15 (50%)/15 (50%)	46 (35%)/83 (63%)	0.107	23 (43%)/29 (55%)	38 (35%)/69 (63%)	0.187	49 (38%)/76 (59%)	12 (35%)/22 (65%)	0.418
mTICI 2b-3 *Yes/No*	23 (77%)/7 (23%)	82 (62%)/50 (38%)	0.096	38 (72%)/15 (28%)	67 (61%)/42 (39%)	0.134	86 (67%)/42 (33%)	19 (56%)/15 (44%)	0.153
NIHSS initial	15.50	16.00	0.848	15.00	16.00	0.255	16.00	15.50	0.963
NIHSS admission	16.00	16.00	0.881	16.00	16.00	0.993	16.00	16.00	0.786
NIHSS ICU	11.50	14.00	0.294	13.00	14.00	0.234	13.50	16.00	0.249
NIHSS 24 h	6.00	12.00	0.028	8.00	12.00	0.063	10.00	14.00	0.205
NIHSS discharge	5.00	7.00	0.247	6.00	5.00	0.943	5.00	7.00	0.273
Exposure time	23.90	28.82	0.056	26.55	28.57	0.382	27.61	29.03	0.753
Absrobed dose	553.53	611.39	0.494	578.79	611.32	0.648	616.91	539.56	0.174
CM Volume	131.33	131.78	0.869	137.55	128.85	0.209	134.18	122.35	0.201
OTG	265.57	248.47	0.683	269.21	242.93	0.144	259.00	223.79	0.057
OTR	309.90	300.21	0.907	313.43	296.35	0.378	308.67	274.87	0.170

(Continued)

10.3389/fneur.2023.1149531

TABLE 1 (Continued)

Age group	<60 N/mean	≥60 N/mean	*p*-value	<65 N/mean	≥65 N/mean	*p*-value	<80 N/mean	≥80 N/mean	*p*-value
Extracranial length ratio	1.11	1.27	0.000	1.18	1.27	0.000	1.22	1.31	0.004
Intracranial length ratio	1.81	1.73	0.442	1.75	1.74	0.876	1.75	1.72	0.656
Overall length ratio	1.28	1.39	0.001	1.30	1.41	0.000	1.36	1.40	0.010
Occluded vessel diameter	2.93	2.85	0.887	2.92	2.84	0.987	2.95	2.56	0.033
Vessel to ID catheter ratio	1.79	1.75	0.940	1.79	1.74	0.963	1.81	1.55	0.015
Vessel to OD catheter ratio	1.51	1.47	0.882	1.51	1.47	0.984	1.53	1.30	0.013

mRS, modified Rankin Scale; rtPA, recombinant tissue plasminogen activator; AF, atrial fibrillation; BA, basilar artery; DB, diabetes; LIP, hypercholesterolemia; NT, hypertension; COR, coronary heart disease; TIA, transient ischemic stroke; aTHROMB, antithrombotic medication; aPLT, antiplatelet medication; PFO, patent foramen ovale; ENT, embolization in a new territory; SAH, subarachnoid hemorrhage; ICH, intracerebral hemorrhage; mTICI, modified Thrombolysis in Cerebral Infarction scale score; MCA-M1, middle cerebral artery M1 segment; MCA-M2, middle cerebral artery M2 segment; NIHSS, National Institute of Health Stroke Scale; CM, contrast medium (ml); OTG, onset-to-groin time (min); OTR, onset-to-recanalization time (min); ICA-T, internal carotid terminus; ICU, intensive care unit; ID, inner diameter; OD, outer diameter; 3DCT, flat-panel computed tomography; HI1, hemorrhagic infarction type 1; HI2, hemorrhagic infarction type 2; PCA-P2, posterior cerebral artery P2 segment; PH1, parenchymal hematoma type 1; PH2, parenchymal hematoma type 2.

stroke ($R = 0.464$, $p = 0.000$); moderately with the pre-stroke mRS status ($R = 0.320$, $p = 0.000$), death at 12 months after stroke ($R = 0.327$, $p = 0.003$), and atrial fibrillation (AF) ($R = 0.306$, $p = 0.000$); and weakly with hypertension ($R = 0.275$, $p = 0.000$), treatment with antithrombotic agents ($R = 0.285$, $p = 0.000$), and the presence of PFO ($R = -0.253$, $p = 0.0001$). Significant correlations were found in terms of anatomical characteristics, namely, a strong correlation with the presence of carotid tortuosity ($R = 0.408$, $p = 0.000$), extracranial length ratio ($R = 0.487$, $p = 0.000$), and overall length ratio ($R = 0.467$, $p = 0.000$). No significant associations were found with coiling, kinking, or intracranial length ratio.

Modified Thrombolysis in Cerebral Infarction (mTICI2b-3) scale score showed uniform inverse correlations with several clinical, anatomical, and procedure-related parameters, namely, NIHSS in the intensive care unit (ICU), after 24 h, and at discharge ($R = -0.212$, $p = 0.014$, $R = -0.266$, $p = 0.002$, and $R = -0.231$, $p = 0.011$, respectively); mRS at 90 days ($R = -0.361$, $p = 0.000$), 12 months, and death at 12 months ($R = -0.434$, $p = 0.001$; and $R = -0.272$, $p = 0.013$, respectively); the extracranial and overall length ratios ($R = -0.210$, $p = 0.035$, and $R = -0.258$, $p = 0.009$, respectively); exposure time ($R = -0.481$, $p = 0.000$); absorbed dose ($R = -0.434$, $p = 0.000$); contrast medium volume ($R = -0.226$, $p = 0.004$); the presence of any complications ($R = -0.234$, $p = 0.003$); the use of a stent-retriever ($R = -0.647$, $p = 0.000$); and the number of passes ($R = -0.246$, $p = 0.002$).

Successful recanalization was also significantly but weakly correlated with tortuosity ($R = -0.246$, $p = 0.01$). No significant association was observed with first-pass success. Kinking and coiling did not show any significant relationship with the parameters for successful recanalization.

The presence of coiling was weakly but significantly associated with embolization in new territories during ADAPT ($R = 0.264$, $p = 0.006$); however, it showed no significant association with other periprocedural complications, such as vasospasm, dissection, and subarachnoid or intracerebral hemorrhage. None of these adverse events were associated with kinking or tortuosity. First-pass success was not significantly correlated with vessel tortuosity ($p = 0.075$).

Atrial fibrillation was inversely correlated with tandem lesion ($R = -0.237$, $p = 0.003$), first-pass success ($R = -0.156$, $p = 0.01$), and onset-to-groin/reperfusion times ($R = -0.158$, $p = 0.04$; and $R = -0.163$, $p = 0.05$, respectively). Its presence was also associated with a higher mRS status after 90 days ($R = 0.256$, $p = 0.01$).

Successful aspiration

Although successful aspiration-based recanalization rates decreased with increasing age, the differences between the subgroups were not statistically significant. In the subgroup aged <60 years (23 of 30 patients), mTICI2b-3 was achieved in 77% of the cases. In the subgroup aged ≥ 60 years (82 of 132 patients), mTICI2b-3 was achieved in 62% of the cases. When the division was made at 65 years, mTICI2b-3 in those aged <65 years (38 of 53 patients) fell to 72%, while that in those aged ≥ 65 years (67 of 109 patients) fell to 61%. The aspiration recanalization rate in patients aged <80 years (86 of 128 patients) was 67%, while it dropped to 56% in those aged ≥ 80 years (19 of 34 patients).

TABLE 2 Percentage of successful recanalization and first-pass success (FPS) depending on occlusion site and age group.

		Overall	<60	≥60	<65	≥65	<80	≥80
Carotid-T	mTICI2b-3	63.5% *(33/52)*	83.3% *(10/12)*	57.5% *23/40*	75.0% *15/20*	56.3% *18/32*	65.9% *29/44*	44.4% *4/9*
	FPS	30.8% *16/52*	41.7% *5/12*	27.5% *11/40*	35.0% *7/20*	28.1% *9/32*	31.8% *14/44*	22.2% *2/9*
MCA-M1	mTICI2b-3	63.6% *49/77*	71.4% *10/14*	61.9% *39/63*	61.8% *34/55*	68.2% *15/22*	65.0% *39/60*	58.8% *10/17*
	FPS	40.3% *31/77*	64.3% *9/14*	34.9% *22/63*	38.2% *21/55*	45.5% *10/22*	41.7% *25/60*	35.3% *6/17*
MCA-M2	mTICI2b-3	69.6% *16/23*	100.0% *2/2*	66.7% *14/21*	66.7% *4/6*	70.6% *12/17*	75.0% *12/16*	57.1% *4/7*
	FPS	39.1% *9/23*	0.0% *0/2*	42.9% *9/21*	33.3% *2/6*	41.2% *7/17*	43.8% *7/16*	28.6% *2/7*

ex. 33/52 means 32 patients had mTICI2-3 result out of 52 patients with carotid-t occlusion and so on.

A comparison between the extreme subgroups, that is, <60 years vs. ≥ 80 years, did not yield a statistically significant change ($p = 0.068$). The percentages of successful recanalization and first-pass success, depending on the occlusion site, are shown in Table 2. Stacked bar charts comparing the aspiration results in different age subgroups are shown in Figure 2.

Effect of vessel tortuosity

Several correlations associated with vessel tortuosity have been described previously.

Overall, the presence of tortuosity led to a significant increase in the exposure time ($p = 0.011$), followed by the absorbed dose ($p = 0.003$). Notably, the opposite trend was observed for the contrast medium volume ($p = 0.728$). The time from onset-to-groin access and the time from onset-to-recanalization differed significantly between patients with intracranial and extracranial tortuosity ($p = 0.004$ and $p = 0.003$; $p = 0.000$ and $p = 0.004$, respectively).

Neither intracranial nor extracranial tortuosity was significantly associated with reperfusion-related complications in either subgroup (i.e., vasospasm, embolization in a new territory, dissection, and intracerebral hemorrhage), apart from SAH in patients aged ≥80 years ($p = 0.04$) with extracranial vessel elongation. The presence of intracerebral tortuosity was associated with a significant increase in the incidence of SAH with increasing age [≥ 60 years ($p = 0.040$), ≥65 years ($p = 0.033$), and ≥ 80 ($p = 0.021$)].

Extracranial tortuosity was observed significantly more frequently in patients aged ≥80 years with hypercholesterolemia and hypertension ($p < 0.05$). Analogous observations were made in the case of intracerebral tortuosity only for hypercholesterolemia ($p < 0.05$).

History of stroke or transient ischemic stroke and AF; current antithrombotic or antiplatelet therapy; and diagnosis of diabetes did not differ significantly between patients with tortuous intracerebral or extracerebral vessels.

The patient status (i.e., NIHSS, mRS, and death) did not differ significantly with the presence of extracranial tortuosity, regardless of the time of assessment (24 h, 30 days, 3 months, and 12 months after treatment) for any of the subgroups. Overall, NIHSS after 24 h and at discharge were significantly different in patients with intracerebral tortuosity ($p = 0.023$ and $p = 0.050$, respectively).

The ROC analysis did not show any predictive cutoff values for the ratios of inner/outer catheter to the occluded vessel diameters with regard to successful recanalization or first-pass success in any of the groups.

Discussion

Regardless of the mixed results reported by previous studies on aspiration-based thrombectomy, randomized multicenter trials and meta-analyses have demonstrated that ADAPT is successful in achieving recanalization of large occluded intracranial vessels and is non-inferior to stent-retriever-based thrombectomy (5, 18–20). The data showed no significant differences in terms of the success of angiography or clinical outcomes. Successful recanalization determines the prognosis (21). It is believed to be associated with a younger age, a shorter onset-to-clot contact time, an isolated middle cerebral artery M1 segment occlusion, and an rtPA administration (22–26).

Age was previously reported to be associated with clinical outcomes after mechanical thrombectomy, with poorer mRS scores associated with increasing age (27, 28). The older the patient, the higher the incidence of comorbidities, thereby impeding the ability to recover from a stroke. Atrial fibrillation rate increases with age and is associated with a 5-fold increase in the risk of stroke. In a recent meta-analysis, successful reperfusion rates (mTICI-2b/3) were insignificantly different in patients with and without AF (OR, 1.11 [95% CI, 0.78–1.58]; $p = 0.57$). Similarly, symptomatic intracerebral hemorrhage rates were comparable (OR, 1.05 [95% CI, 0.84–1.31]; $p = 0.68$). However, it was not reflected in mortality and functional independence after mechanical thrombectomy. Patients suffering from AF tend to present a lower Alberta Stroke Program Early CT Score (ASPECTS) and a higher NIHSS (29, 30).

In our study population, the mRS at discharge did not differ significantly, regardless of age. Diverging prognosis was observed with increasing observation time, that is, 30 days post-stroke, and the clinical status differed significantly only between

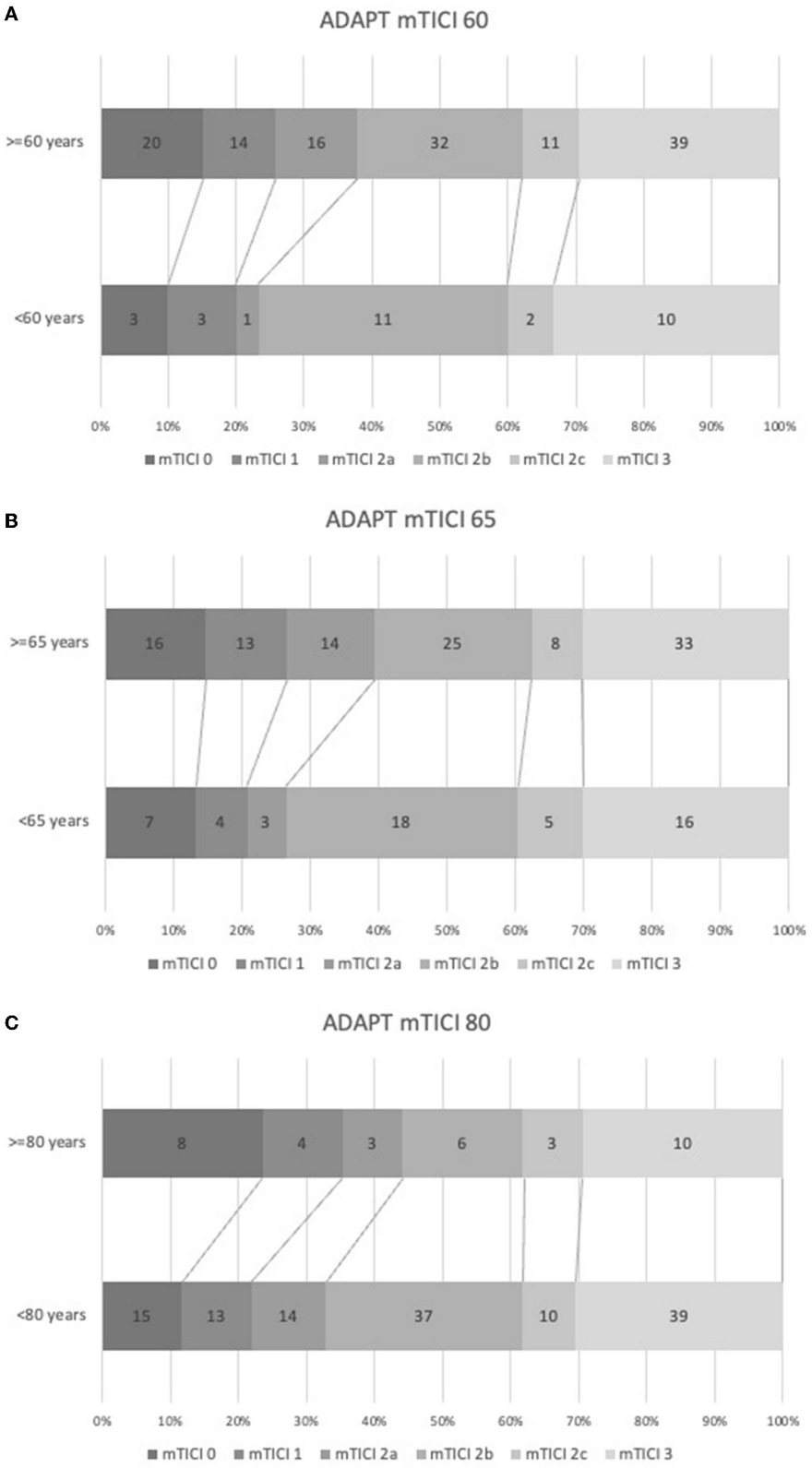


FIGURE 2
Stacked bar charts showing performance of ADAPT in selected age groups, none of the differences were statistically significant.

younger patients and those aged ≥80 years ($p = 0.046$). The difference was more significant in these subgroups after 90 days ($p = 0.011$). All subdivisions differed significantly after 12 months. The effect of comorbidities on clinical outcomes could explain why the neurological status measured by NIHSS did not differ significantly between the subgroups, regardless of the timeframe

(initial, on admission to the hospital, in the ICU, after 24 h, or at discharge).

The presence of AF could exclude the administration of rtPA, in the case of anticoagulant treatment (30). There are mixed reports on the benefits of intravenous thrombolysis (IVT) prior to interventional stroke treatment. The *post hoc* analysis of a recent randomized trial published by Rinkel et al. reported that patients treated with ADAPT had poorer clinical outcomes without IVT; however, it had no impact on successful reperfusion (31). In our series, rtPA showed a weak positive correlation with successful reperfusion (R =0.2, p = 0.014) and was not associated with SAH or intracerebral hemorrhage.

The MR CLEAN Registry showed that the reperfusion rates favored aspiration compared with stent-retrievers in anterior circulation (ICA-T – OR 1.3, MCA-M1 – OR 1.3, and MCA-M2 – OR 1.2) (32). The reported successful reperfusion percentages were 73% for ICA-T, 72% for MCA-M1, and 72% for MCA-M2. Although these results were comparable with our results (64, 64, and 70%, respectively), the first-pass success rates were inferior (43, 58, and 53% vs. 31, 40, and 39%, respectively). This observation could be partially explained by the inclusion of more diverse age groups, which included both younger and older patients (range 35–94 years in our group vs. 62–80 years), where we observed better reperfusion rates in those aged <60 years.

Advanced age is one of the several factors associated with carotid tortuosity, which also includes hypertension, elevated body mass index, and atherosclerosis (8, 33, 34). Their relative capacity to alter the length of the arteries is disputed. Nevertheless, everyday neurovascular interventions, *inter alia*, and stroke treatment are affected by carotid anatomy. Benson et al. found that tortuosity was present in ∼40% of patients undergoing stroke treatment (35). In our study, tortuosity alone was present in up to 77% of patients aged ≥60 years and 83% of those aged > 80 years. Kinking, which becomes less prevalent with age, was present in 23% of patients, whereas coiling affected a maximum of 8% of those patients aged >80 years). No coiling was observed in patients aged <60 years.

Kinks were reported to negatively affect the rates of successful recanalization before; however, no significant complications occurred during mechanical thrombectomy (35). In our study, tortuosity was significantly but weakly correlated with the success of angiography (R = – 0.246, p = 0.01); however, no association was found with any procedure-related adverse events. This could be explained by different anatomy assessment methodologies being used and different age groups being evaluated. We divided the carotid anatomy into two segments: intracranial and extracranial. Only intracranial segment tortuosity was significantly correlated with SAH when performing ADAPT, regardless of age.

Tortuous vessels present a challenge in the delivery of aspiration catheters. Theoretically, the efficacy of ADAPT could be improved by using larger aspiration catheters, a notion that has already been supported by *in vitro* and animal experiments (36). The larger the bore of the catheter, the more difficult the delivery due to hindrance by the meandering anatomy and branching arteries. Successful aspiration relies on adequate catheter diameter. Kyselyova et al. found that the vessel diameter and the catheter-to-vessel ratio affected the effectiveness of clot aspiration (37). In their study, the higher the ratio, the higher the rate of the first aspiration success.

In the COMPASS trial, ADAPT was performed using a 0.068-inch catheter, regardless of the occlusion site. We did not evaluate the performance of specific catheters since their deliverability was not assessed in this study. The catheter characteristics were tapered to the inner and outer diameters, especially in relation to the closed vessel diameter. We performed the ROC analysis to calculate the predictive cutoff value for the ratios of the inner/outer catheter to the occluded vessel diameters with regard to successful recanalization or first-pass success but of no avail. We found that a larger ratio was significantly associated with SAH after ADAPT.

Our study has some limitations. These limitations included its retrospective study design and relatively small sample size. Moreover, the number of passes and the choice of catheters were at the discretion of the operator. Our department's policy permits three unsuccessful attempts before changing the device. We did not consider any attempts where the aspiration catheter could not be delivered to the thrombus in this study. Finally, several calculations, especially with carotid terminus or tandem occlusions, were based on the contralateral artery measurements.

In unselected patients, the successful aspiration-based recanalization rate decreased with increasing age; however, this difference was not significant. Clinical outcomes, such as NIHSS, mRS, and death, did not differ significantly with regard to carotid tortuosity, regardless of the time of assessment (24 h, 30 days, 3 months, and 12 months). Neither intracranial nor extracranial tortuosity was significantly associated with reperfusion-related complications in the subgroups. SAH was significantly more prevalent in the oldest subgroup, although it was clinically inconsequential. In addition, larger catheter-to-occluded vessel ratios were associated with SAH.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Institutional Review Board, Military Institute of Medicine. The patients/participants provided their written informed consent to participate in this study.

Author contributions

The authors confirm contribution to the paper as follows: study conception and design: JN. Data collection: JN, AP, PZ, AD, and MW. Analysis and interpretation of results: JN and AP. Draft manuscript preparation: JN and PP. Manuscript revision: MW, PP, and JS. Supervision: PP and JS. All authors reviewed the results and approved the final version of the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med.* (2015) 372:11–20. doi: 10.1056/NEJMoa1411587

2. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med.* (2015) 372:1009–18. doi: 10.1056/NEJMoa1414792

3. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med.* (2015) 372:1019–30. doi: 10.1056/NEJMoa1414905

4. Zaidat OO, Castonguay AC, Linfante I, Gupta R, Martin CO, Holloway WE, et al. First pass effect: a new measure for stroke thrombectomy devices. *Stroke.* (2018) 49:660–6. doi: 10.1161/STROKEAHA.117.020315

5. Lapergue B, Labreuche J, Blanc R, Barreau X, Berge J, Consoli A, et al. First-line use of contact aspiration for thrombectomy vs. a stent retriever for recanalization in acute cerebral infarction: The randomized ASTER study protocol. *Int J Stroke.* (2018) 13:87–95. doi: 10.1177/1747493017711948

6. Turk AS, Siddiqui A, Fifi JT, De Leacy RA, Fiorella DJ, Gu E, et al. Aspiration thrombectomy vs. stent retriever thrombectomy as first-line approach for large vessel occlusion (COMPASS): a multicentre, randomised, open label, blinded outcome, non-inferiority trial. *Lancet.* (2019) 393:998–1008. doi: 10.1016/S0140-6736(19)30297-1

7. Turk AS, Turner R, Spiotta A, Vargas J, Holmstedt C, Ozark S, et al. Comparison of endovascular treatment approaches for acute ischemic stroke: cost effectiveness, technical success, and clinical outcomes. *J Neurointerv Surg.* (2015) 7:666–70. doi: 10.1136/neurintsurg-2014-011282

8. Togay-Işikay C, Kim J, Betterman K, Andrews C, Meads D, Tesh P, et al. Carotid artery tortuosity, kinking, coiling: stroke risk factor, marker, or curiosity? *Acta Neurol Belg.* (2005) 105:68–72.

9. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet.* (2016) 387:1723–31. doi: 10.1016/S0140-6736(16)00163-X

10. Maus V, Behme D, Kabbasch C, Borggrefe J, Tsogkas I, Nikoubashman O, et al. Maximizing first-pass complete reperfusion with SAVE. *Clin Neuroradiol.* (2018) 28:327–38. doi: 10.1007/s00062-017-0566-z

11. Goyal M, Fargen KM, Turk AS, Mocco J, Liebeskind DS, Frei D, et al. 2C or not 2C: defining an improved revascularization grading scale and the need for standardization of angiography outcomes in stroke trials. *J Neurointerv Surg.* (2014) 6:83–6. doi: 10.1136/neurintsurg-2013-010665

12. Sergei S, Warren S. *New Measures of Population Ageing* (2019).

13. Larrue V, von Kummer R R, Müller A, Bluhmki E. Risk factors for severe hemorrhagic transformation in ischemic stroke patients treated with recombinant tissue plasminogen activator: a secondary analysis of the European–Australasian Acute Stroke Study (ECASS II). *Stroke.* (2001) 32:438–41. doi: 10.1161/01.STR.32.2.438

14. Hacke W, Donnan G, Fieschi C, Kaste M, von Kummer R, Broderick JP, et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. *Lancet.* (2004) 363:768–74. doi: 10.1016/S0140-6736(04)15692-4

15. Kang DH, Hwang YH. Frontline contact aspiration treatment for emergent large vessel occlusion: a review focused on practical techniques. *J Stroke.* (2019) 21:10–22. doi: 10.5853/jos.2018.03076

16. Metz H, Murray-Leslie RM, Bannister RG, Bull JW, Marshall J. Kinking of the internal carotid artery. *Lancet.* (1961) 1:424–6. doi: 10.1016/S0140-6736(61)90004-6

17. Weibel J, Fields WS. Tortuosity coiling, and kinking of the internal carotid artery. I Etiology and Radiographic Anatomy. *Neurology.* (1965) 15:7–18. doi: 10.1212/WNL.15.1.7

18. Kowoll A, Weber A, Mpotsaris A, Behme D, Weber W. Direct aspiration first pass technique for the treatment of acute ischemic stroke: initial experience at a European stroke center. *J Neurointerv Surg.* (2016) 8:230–4. doi: 10.1136/neurintsurg-2014-011520

19. Primiani CT, Vicente AC, Brannick MT, Turk AS, Mocco J, Levy EI, et al. Direct aspiration vs. stent retriever thrombectomy for acute stroke: a systematic review and meta-analysis in 9127 patients. *J Stroke Cerebrovasc Dis.* (2019) 28:1329–37. doi: 10.1016/j.jstrokecerebrovasdis.2019.01.034

20. Qin C, Shang K, Xu SB, Wang W, Zhang Q, Tian DS. Efficacy and safety of direct aspiration vs. stent-retriever for recanalization in acute cerebral infarction: a PRISMA-compliant systematic review and meta-analysis. *Medicine.* (2018) 97:e12770. doi: 10.1097/MD.0000000000012770

21. Imahori T, Tanaka K, Arai A, Shiomi R, Fujiwara D, Mori T, et al. Mechanical thrombectomy for acute ischemic stroke patients aged 80 years or older. *J Stroke Cerebrovasc Dis.* (2017) 26:2793–9. doi: 10.1016/j.jstrokecerebrovasdis.2017.06.060

22. Blanc R, Redjem H, Ciccio G, Smajda S, Desilles JP, Orng E, et al. Predictors of the aspiration component success of a direct aspiration first pass technique (ADAPT) for the endovascular treatment of stroke reperfusion strategy in anterior circulation acute stroke. *Stroke.* (2017) 48:1588–93. doi: 10.1161/STROKEAHA.116.016149

23. Mascitelli JR, Kellner CP, Oravec CS, De Leacy RA, Oermann EK, Yaeger K, et al. Factors associated with successful revascularization using the aspiration component of ADAPT in the treatment of acute ischemic stroke. *J Neurointerv Surg.* (2017) 9:636–40. doi: 10.1136/neurintsurg-2016-012439

24. Anadani M, Ajinkya S, Alawieh A, Vargas J, Chatterjee A, Turk A, et al. Intra-arterial tissue plasminogen activator is a safe rescue therapy with mechanical thrombectomy. *World Neurosurg.* (2019) 123:e604–e8. doi: 10.1016/j.wneu.2018.11.232

25. Consoli A, Rosi A, Coskun O, Nappini S, Di Maria F, Renieri L, et al. Thrombectomy for M1-middle cerebral artery occlusion: angiographic aspect of the arterial occlusion and recanalization: a preliminary observation. *Stroke.* (2018) 49:1286–9. doi: 10.1161/STROKEAHA.117.018987

26. Consoli A, Zhu F, Bourcier R, Dargazanli C, Marnat G, Duhamel A, et al. Effect of the phenotype of the M1-middle cerebral artery occlusion on the recanalization rates in the ASTER trial. *J Neurointerv Surg.* (2020) 12:7–12. doi: 10.1136/neurintsurg-2019-015002

27. Azkune Calle I, Bocos Portillo J, Anton-Ladislao A, Gil Garcia A, Gonzalez Diaz E, Gomez-Beldarrain M, et al. Clinical outcome of mechanical thrombectomy for stroke in the elderly. *J Stroke Cerebrovasc Dis.* (2017) 26:582–8. doi: 10.1016/j.jstrokecerebrovasdis.2016.11.117

28. Kim DH, Kim SU, Sung JH, Lee DH Yi HJ, Lee SW. Significances and outcomes of mechanical thrombectomy for acute infarction in very elderly patients: a single center experience. *J Korean Neurosurg Soc.* (2017) 60:654–60. doi: 10.3340/jkns.2016.1212.004

29. Esmael A, Elsherief M, Eltoukhy K. Predictive value of the alberta stroke program early CT score (ASPECTS) in the outcome of the acute ischemic stroke and its correlation with stroke subtypes, NIHSS, and cognitive impairment. *Stroke Res Treat.* (2021) 2021:5935170. doi: 10.1155/2021/5935170

30. Akbik F, Alawieh A, Cawley CM, Howard BM, Tong FC, Nahab F, et al. Differential effect of mechanical thrombectomy and intravenous thrombolysis in atrial fibrillation associated stroke. *J Neurointerv Surg.* (2021) 13:883–8. doi: 10.1136/neurintsurg-2020-016720

31. Rinkel LA, Treurniet KM, Nieboer D, Kappelhof M, LeCouffe NE, Bruggeman AAE, et al. Effect of intravenous alteplase treatment on first-line stent retriever vs. aspiration alone during endovascular treatment. *Stroke.* (2022) 53:3278–88. doi: 10.1161/STROKEAHA.121.038390

32. Bernsen MLE, Goldhoorn RB, Lingsma HF, van Oostenbrugge RJ, van Zwam WH, Uyttenboogaart M, et al. Importance of occlusion site for thrombectomy technique in stroke: comparison between aspiration and stent retriever. *Stroke.* (2021) 52:80–90. doi: 10.1161/STROKEAHA.120.030031

33. Thomas JB, Antiga L, Che SL, Milner JS, Steinman DA, Spence JD, et al. Variation in the carotid bifurcation geometry of young vs. older adults: implications for geometric risk of atherosclerosis. *Stroke.* (2005) 36:2450–6. doi: 10.1161/01.STR.0000185679.62634.0a

34. Wang HF, Wang DM, Wang JJ, Wang LJ, Lu J, Qi P, et al. Extracranial internal carotid artery tortuosity and body mass index. *Front Neurol.* (2017) 8:508. doi: 10.3389/fneur.2017.00508

35. Benson JC, Brinjikji W, Messina SA, Lanzino G, Kallmes DF. Cervical internal carotid artery tortuosity: a morphologic analysis of patients with acute ischemic stroke. *Interv Neuroradiol.* (2020) 26:216–21. doi: 10.1177/1591019919891295

36. Nikoubashman O, Nikoubashman A, Büsen M, Wiesmann M. Necessary catheter diameters for mechanical thrombectomy with ADAPT. *AJNR Am J Neuroradiol.* (2017) 38:2277–81. doi: 10.3174/ajnr.A5401

37. Kyselyova AA, Fiehler J, Leischner H, Flottmann F, Buhk JH, Frölich AM. Vessel diameter and catheter-to-vessel ratio affect the success rate of clot aspiration. *J Neurointerv Surg.* (2021) 13:605–8. doi: 10.1136/neurintsurg-2020-016459

frontiers | Frontiers in Neurology

TYPE Original Research
PUBLISHED 16 June 2023
DOI 10.3389/fneur.2023.1135568

OPEN ACCESS

EDITED BY
Michael V. Mazya,
Karolinska University Hospital, Sweden

REVIEWED BY
Miljenka-Jelena Jurasic,
Poliklinika Aviva, Croatia
Husna Ahmad Ainuddin,
Universiti Teknologi MARA Puncak Alam, Malaysia

*CORRESPONDENCE
Hyung-Ik Shin
✉ hyungik1@snu.ac.kr

†These authors have contributed equally to this work

RECEIVED 01 January 2023
ACCEPTED 30 May 2023
PUBLISHED 16 June 2023

CITATION
Bae SW, Kwon J and Shin H-I (2023) Over- and under-supply of inpatient rehabilitation after stroke without a post-acute rehabilitation system: a nationwide retrospective cohort study. *Front. Neurol.* 14:1135568. doi: 10.3389/fneur.2023.1135568

Over- and under-supply of inpatient rehabilitation after stroke without a post-acute rehabilitation system: a nationwide retrospective cohort study

Suk Won Bae[1†], Junhyun Kwon[1,2†] and Hyung-Ik Shin[1,3*]

[1]Department of Rehabilitation Medicine, Seoul National University Hospital, Seoul, Republic of Korea, [2]Institute of Health Services Research, Yonsei University College of Medicine, Seoul, Republic of Korea, [3]Department of Rehabilitation Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea

Introduction: This study aimed to investigate the utilization of post-ischemic stroke rehabilitation prior to the introduction of the post-acute rehabilitation system in South Korea in 2017.

Methods: Medical resources utilized for patients with cerebral infarction hospitalized at Regional Cardio-Cerebrovascular Centers (RCCVCs) of 11 tertiary hospitals were tracked until 2019. Stroke severity was classified according to the National Institutes of Health Stroke Scale (NIHSS), and multivariate regression analysis was performed to analyze factors influencing the length of hospital stay (LOS).

Results: This study included 3,520 patients. Among 939 patients with stroke with moderate or greater severity, 209 (22.3%) returned home after RCCVC discharge without inpatient rehabilitation. Furthermore, 1,455 (56.4%) out of 2,581 patients with minor strokes with NIHSS scores ≤4 were readmitted to another hospital for rehabilitation. The median LOS of patients who received inpatient rehabilitation after RCCVC discharge was 47 days. During the inpatient rehabilitation period, the patients were admitted to 2.7 hospitals on average. The LOS was longer in the lowest-income group, high-severity group, and women.

Conclusion: Before the introduction of the post-acute rehabilitation system, treatment after stroke was both over- and under-supplied, thus delaying home discharge. These results support the development of a post-acute rehabilitation system that defines the patients, duration, and intensity of rehabilitation.

KEYWORDS

stroke, rehabilitation, post-acute phase, length of hospital stay, hospitalization

1. Introduction

Stroke is known as one of the leading causes of disability worldwide (1–7). Moreover, it poses a great socioeconomic burden to individuals and society (6, 8). Rehabilitation after acute stroke treatment has been demonstrated to reduce the impairment of body function and limitation of activity, thereby facilitating an early return to home (7, 9, 10).

The guidelines for healthcare professionals from the American Heart Association/American Stroke Association emphasize the need for sustained and coordinated efforts for stroke rehabilitation (11). In many countries, specialized rehabilitation units or hospital systems have been developed to provide stroke survivors with rehabilitation treatment in the post-acute period (12, 13). These rehabilitation hospitals dedicated to the post-acute period are often subject to reimbursement tiers, which are based on a case-mix classification determined by disease group, severity, age, comorbidities, and other variables. For example, the prospective payment system in the United States utilizes prepayment tiers mainly determined by functional independence measures and age (14, 15). Japan's convalescent rehabilitation ward system sets an upper limit on the length of hospitalization that is dependent on disease groups. Additionally, post-acute rehabilitation facilities are evaluated by government or private agencies for indicators such as functional gains and returning home rate (16).

In South Korea, a post-acute rehabilitation hospital system was not introduced until 2019 (17), and reimbursement by the National Health Insurance Service (NHIS) was made in the form of fee-for-service for individual physiotherapy and occupational therapy (18). The payment level made to long-term care hospitals (LTCHs) without deduction did not differ from that of acute care hospitals. However, no criteria were established for the target population for medical rehabilitation or the duration of provision. When patients were hospitalized for rehabilitation treatment, there was also no evaluation system for providers, and payment by the NHIS for rehabilitation treatment was guaranteed for up to 2 years after the stroke (19).

South Korea's post-acute rehabilitation system was launched in 2020 (18). Medical institutions adopting the system allow patients to be admitted within 3 months after stroke and provide inpatient rehabilitation programs for up to 6 months. During this period, providing rehabilitation treatment for up to 4 h daily is possible. The rehabilitation physicians decide the types of treatment to be applied (e.g., gait training and swallowing training). Changes in body function, activity level during hospitalization, and return home rate after discharge are monitored (19).

To evaluate the effects of this system in the future, it is necessary to analyze the use of medical resources related to rehabilitation services to set a baseline before its introduction. No previous studies have described the use of rehabilitation medical resources before the introduction of the post-acute rehabilitation system. Hence, the methodology of this study can serve as a useful reference for countries planning to implement a post-acute rehabilitation system in the future to evaluate the effects after the introduction of this system.

This study aimed to investigate the length of hospital stay (LOS) and related factors for rehabilitation treatment after an ischemic stroke in 2017 before the introduction of the post-acute rehabilitation system.

2. Materials and methods

2.1. Data source

This study tracked the medical resources utilized by patients with ischemic stroke who were hospitalized and discharged from the Regional Cardio-Cerebrovascular Centers (RCCVCs) of 11 tertiary hospitals in 2017 (20). RCCVCs are publicly designated and operated institutions in South Korea for the acute management of thrombolysis in patients with ischemic stroke and ischemic heart disease. Medical information of patients with stroke hospitalized in 11 RCCVCs was registered in the Regional Stroke Center Registry (RSCR) (21). Data were collected from the time of emergency room admission to discharge from the RCCVCs. The RSCR includes information on neurological status at admission and discharge measured by the National Institutes of Health Stroke Scale (NIHSS), medical or surgical interventions, risk factors, and activity levels at admission and discharge measured using the modified Barthel index and modified Rankin scale. For this study, the RSCR data of the patients who were discharged from the RCCVC in 2017 were linked to the data of the relevant patients in the NHIS-National Health Information Database (NHID), and the use of medical resources was tracked until 2019.

The Korean NHIS is a compulsory social health insurance system implemented for all citizens. The NHIS-NHID includes information on demographic and socioeconomic characteristics, births and deaths, healthcare service utilization, and specifics on medical service providers.

2.2. Data linkage

The linkage between the RSCR and NHIS-NHID was implemented by the division of big data management within the NHIS, and the resident registration number of each patient was used as a linkage key. To protect personal information, the NHIS provided connected data to the researchers after deleting the resident registration number. The researchers could access the data only in the secure online environment provided by the NHIS.

This study was approved by the Institutional Review Board of Seoul National University Hospital (IRB No. H-2101-139-1192). The requirement for informed consent was waived because the data in the NHIS were anonymized and de-identified (22).

2.3. Study population

The study population consisted of 6,703 patients with cerebral infarction (ICD-10 codes I63, I67, I68, and I69) admitted to RCCVCs from 1 January 2017 to 31 December 2017. Among these, 6,550 patients were linked to the NHIS-NHID (linkage rate: 97.7%). To track medical resource utilization during the 2 years after discharge, this study analyzed NHIS-NHID data until 2019. In the 255 patients who were hospitalized in RCCVCs in 2017 but discharged in 2018, a tracking period of 2 years could not be achieved. Therefore, these were excluded from the analysis. In this study, severity was classified according to the initial NIHSS score during hospitalization. Since thrombolysis treatment can affect severity (23), 969 patients who received the intervention were excluded from the analysis. Figure 1 presents a schematic of the study population.

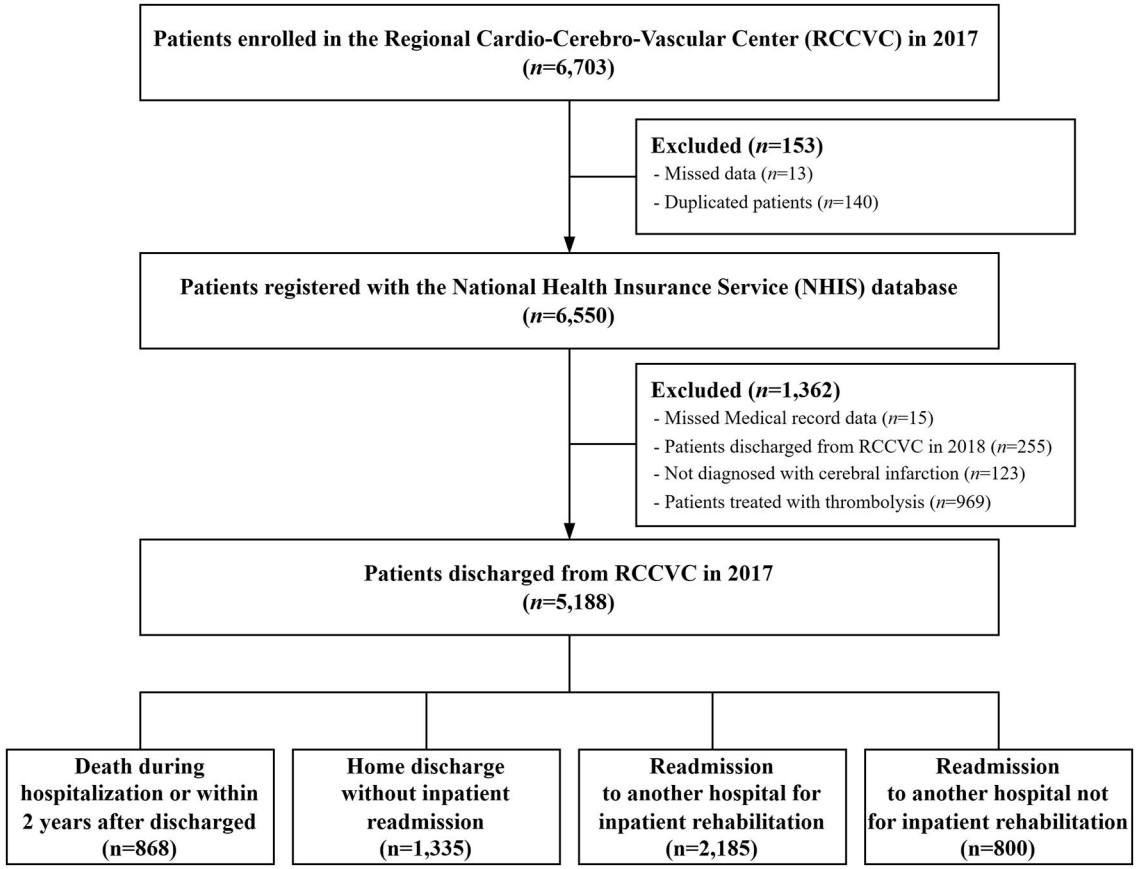


FIGURE 1
Schematic diagram of the study population.

2.4. Outcome variables

The primary outcome variable in this study was the LOS from ER admission to home discharge. Only hospitalization for rehabilitation treatment was investigated and presented. When a patient with a stroke was admitted to several hospitals until home discharge, the LOS at each hospital was summed.

Hospital admission after stroke was also assessed. For example, one hospital was utilized when a patient was discharged home from the RCCVC, and two were used when a patient was discharged from an LTCH, followed by home discharge. The total follow-up period lasted until 31 December 2019. Therefore, all patients were followed up for 2 years after discharge from the RCCVCs.

2.5. Explanatory variable

The NIHSS was used to assess stroke (24). In this study, the initial NIHSS scores were measured and categorized into four severity groups: minor, 0–4; moderate, 5–15; moderate to severe, 6–20; and severe, 21–42 (5).

Additional explanatory variables included age (<65, 65–74, 75–84, and ≥85 years), sex (male or female), and income level. Income level was classified into four different groups according to the level of NHIS co-payment: quartiles 1–4. As the NHIS-NHID has no separate variable for income, NHIS co-payment was considered the patient's income. The lowest group (1st quartile) corresponded to medical aid, and no health insurance co-payment was recorded in this group (22).

Information on the Charlson Comorbidity Index (CCI) was also collected to evaluate patients' comorbidity status before they were admitted to the RCCVCs. Based on the CCI, the severity of comorbidities was categorized as low (0, 1) or high (≥2) (3).

2.6. Statistical analysis

Two groups "not receiving inpatient rehabilitation group (home discharge from RCCVCs)" and "receiving inpatient rehabilitation group (readmission to another hospital for rehabilitation after discharge from RCCVCs)" were compared. We performed a chi-square test and an analysis of variance for the general characteristics of the study population. For the inpatient rehabilitation group, we analyzed the LOS and number of hospital admissions during the 2-year follow-up period after discharge from the RCCVCs. For each variable, the mean and median (interquartile range [IQR]) values were calculated.

TABLE 1 General characteristics of the study population.

Variable	Total		Not receiving inpatient rehabilitation		Receiving inpatient rehabilitation		P-value*
	N	%	*N*	%	*N*	%	
Total	3,520	100.0	1,335	100.0	2,185	100.0	
Median (IQR) length of stay in RCCVC, day	7	6–12	6	5–9	8	6–14	
Age							<0.001
<65 years	1,281	36.4	577	43.2	704	32.2	
65–74 years	957	27.2	368	27.6	589	27.0	
75–84 years	1,070	30.4	342	25.6	728	33.3	
≥85 years	212	6.0	48	3.6	164	7.5	
Sex							<0.001
Male	2,096	59.5	881	66.0	1,215	55.6	
Female	1,424	40.5	454	34.0	970	44.4	
NIHSS							<0.001
0–4	2,581	73.3	1,126	84.3	1,455	66.6	
5–15	855	24.3	206	15.3	649	29.7	
16–20	60	1.7	2	0.1	58	2.7	
21–42	24	0.7	1	0.1	23	1.1	
Income, KRW							0.107
1st quartile	689	19.6	234	17.5	455	20.8	
2nd quartile	570	16.2	222	16.6	348	15.9	
3rd quartile	780	22.2	315	23.6	465	21.3	
4th quartile	1,421	40.4	538	40.3	883	40.4	
Charlson comorbidity index							<0.001
Low (0–1)	1,996	56.7	863	64.6	1,133	51.9	
High (≥2)	1,524	43.3	472	35.4	1,052	48.1	

IQR, interquartile range; RCCVC, Regional Cardio-Cerebrovascular Center; NIHSS, National Institutes of Health Stroke Scale; KRW, Korean Won.
*P-value from χ^2-test (categorical variables), t-test, or ANOVA (continuous variables).

Multivariate regression analysis was used to analyze the factors affecting the LOS. Independent variables included the NIHSS score, age, sex, income level, and CCI. All statistical analyses were performed using the SAS statistical software (version 9.4; Statistical Analysis System Institute, Cary, NC, USA).

3. Results

Among the 5,188 patients linked to the NHIS-NHID, 868 died during hospitalization or within 2 years after discharge from the RCCVCs. Overall, 800 patients were readmitted to a tertiary hospital for purposes other than inpatient rehabilitation, 315 of whom experienced medical complications (Supplementary Table 1). A total of 240 patients had stroke recurrence, and 245 patients had planned readmissions (Supplementary Table 2). Hence, 1,668 patients were excluded from the analysis.

Analyses were performed for the remaining 3,520 patients (Table 1). Among them, 1,335 patients returned home after discharge from the RCCVCs without inpatient rehabilitation, and 2,185 patients were transferred to another hospital for inpatient rehabilitation. Among the 2,581 patients with minor strokes, 1,455 (56.4%) were readmitted to another hospital for inpatient rehabilitation. Meanwhile, of the 939 patients with moderate severity or above, 209 patients (22.3%) returned home after discharge from the RCCVCs without inpatient rehabilitation.

The median LOS in the RCCVCs was 7 (IQR: 6, 12) days for all 3,520 patients, 6 (IQR: 5, 9) days for the "not receiving inpatient rehabilitation" group, and 8 (IQR: 6, 14) days for the "receiving inpatient rehabilitation" group.

The patients in the inpatient rehabilitation group were older and had a higher severity when measured by the NIHSS than those who did not receive inpatient rehabilitation ($P < 0.001$ and $P < 0.001$, respectively). The proportion of women was higher in the inpatient rehabilitation group ($P < 0.001$).

The median LOS from ER admission to home discharge in the inpatient rehabilitation group was 47 (IQR, 17–196) days. During this period, these patients received rehabilitation treatment while being hospitalized at three hospitals sequentially at a median value

TABLE 2 Length of hospital stay and number of hospital admissions in the inpatient rehabilitation group ($N = 2,185$).

Variable	Length of stay (day)*				P-value	Number of hospital admissions*				P-value
	Mean (median)	Q1	–	Q3		Mean (median)	Q1	–	Q3	
Total	191.4 (47)	17	–	196		3.7 (3)	2	–	4	
Age					<0.001					0.001
<65 years	134.8 (30.5)	14	–	113		3.4 (3)	2	–	4	
65–74 years	169.8 (43)	16	–	155		3.8 (3)	2	–	5	
75–84 years	233.0 (62.5)	21	–	302		3.9 (3)	2	–	5	
≥85 years	327.4 (82)	30	–	766.5		4.0 (3)	2	–	4	
Sex					<0.001					0.006
Male	160.1 (36)	15	–	141		3.6 (3)	2	–	4	
Female	230.7 (63)	21	–	279		3.9 (3)	2	–	5	
NIHSS					<0.001					<0.001
0–4	118.0 (29)	14	–	93		3.5 (3)	2	–	4	
5–15	307.9 (128)	39	–	574		4.0 (3)	2	–	5	
16–20	558.8 (719)	117	–	902		4.9 (4)	3	–	6	
21–42	621.0 (845)	224	–	972		4.2 (3)	2	–	5	
Income, KRW					0.050					0.932
1st quartile	226.8 (61)	16	–	276		3.8 (3)	2	–	5	
2nd quartile	191.3 (48)	17	–	223		3.6 (3)	2	–	4	
3rd quartile	176.7 (44)	17	–	171		3.7 (3)	2	–	4	
4th quartile	179.9 (43)	17	–	162		3.7 (3)	2	–	4	
Charlson comorbidity index					0.502					<0.001
Low (0–1)	187.4 (46)	16	–	195		3.5 (3)	2	–	4	
High (≥2)	195.8 (47)	18	–	197.5		3.9 (3)	2	–	5	

Q1, 1st quartile; Q3, 3rd quartile; NIHSS, National Institutes of Health Stroke Scale; KRW, Korean Won.
*Including hospitalizations in Regional Cardio-Cerebrovascular Centers.

(IQR: 2, 4), rather than being admitted to a single hospital (Table 2). Patients with severe stroke had a longer LOS and a higher number of hospital admissions ($P < 0.001$). Female ($P < 0.001$ and $P = 0.006$, respectively) and elderly ($P < 0.001$ and $P = 0.001$, respectively) patients also had a longer LOS and a higher number of hospital admissions. The lowest income level group (Q1) had a longer LOS than that of the other income level groups ($P = 0.050$).

Table 3 describes the multivariate regression model between LOS and the explanatory variables. In this model, LOS was longer with older age and increasing severity. In addition, the LOS was longer for women and Q1, the lowest income group ($P = 0.002$ and $P = 0.020$, respectively).

4. Discussion

Although there are no standard guidelines on the strategies for rehabilitation treatment according to the severity of the stroke, patients with minor stroke (NIHSS 0–4) may generally undergo outpatient-based rather than intensive inpatient rehabilitation. By contrast, patients with moderate or higher stroke severity often require inpatient rehabilitation during the post-acute period (25). This study investigated the rehabilitation healthcare delivery system before the introduction of the post-acute rehabilitation hospital system and identified that rehabilitation after stroke was not properly performed based on severity (9). Before 2000, Japan had no dedicated system in inpatient facilities to provide early and intensive rehabilitation (26). Prior to 2000, Japan faced the same situation as South Korea.

In the US, inpatient rehabilitation facilities are institutions that provide intensive inpatient rehabilitation treatment after an acute period of 13 diseases, including stroke. Patients can undergo intensive multidisciplinary rehabilitation programs. They receive 3 h of treatment for 5 of 7 consecutive days (18, 27). Patients who have completed functional improvement are subject to an active return-to-society program, and those whose condition does not improve discontinue rehabilitation treatment and are transferred to an LTCH (18). The Japanese national insurance system introduced kaifukuki (convalescent) rehabilitation wards (KRW) in 2000 (26). Rehabilitation treatment was limited to 3 h per day, and the maximum length of stay for patients with stroke in the KRW was limited to 150 days. The timing of discharge is set when

TABLE 3 Multivariate regression model for the length of hospital stay in the inpatient rehabilitation group ($N = 2,185$).

Variable	Length of stay (day)*					
	Crude model			Adjusted model†		
	β	SE	P-value	β	SE	P-value
Age						
<65 years	Ref			Ref		
65–74 years	35.0	14.3	0.014	32.0	13.4	0.017
75–84 years	98.2	14.8	<0.001	80.2	14.2	<0.001
≥85 years	192.5	30.9	<0.001	141.1	28.8	<0.001
Sex						
Male	Ref			Ref		
Female	70.6	12.8	<0.001	36.0	11.6	0.002
NIHSS						
0–4	Ref			Ref		
5–15	189.9	14.5	<0.001	179.7	14.3	<0.001
16–20	440.8	51.2	<0.001	420.2	51.7	<0.001
21–42	503.0	81.4	<0.001	470.1	83.7	<0.001
Income, KRW						
1st quartile	46.9	17.9	0.009	38.4	16.5	0.020
2nd quartile	11.3	18.0	0.529	26.5	17.0	0.120
3rd quartile	−3.2	16.1	0.842	9.7	14.6	0.507
4th quartile	Ref			Ref		
Charlson comorbidity index						
Low (0–1)	Ref			Ref		
High (≥2)	8.4	112.5	0.502	1.5	11.7	0.895

SE, standard error; NIHSS, National Institutes of Health Stroke Scale; KRW, Korean Won.
*Including hospitalization in Regional Cardio-Cerebrovascular Centers.
†Statistically estimated from multivariate regression analyses adjusted for all explanatory variables.

patients reach a plateau in activities of daily living according to an interactive evaluation, which has facilitated the home discharge of patients with stroke with severe disability (16).

In our study, among 939 patients with stroke of moderate severity or above, 209 (22.3%) returned home after discharge from the RCCVCs without inpatient rehabilitation (Table 1). In South Korea, rehabilitation services were reimbursed based on the fee-for-service system even before the post-acute rehabilitation hospital system was introduced. Therefore, rehabilitation treatment may not be implemented in the post-acute period in these groups, not for economic reasons, but because the referral system between medical institutions did not work. Since the median LOS in RCCVCs was 6 days or less and outpatient-based rehabilitation treatment is rarely performed in South Korea, rehabilitation services could be undersupplied for these patients (26).

Meanwhile, among 2,581 patients with minor stroke with an NIHSS score of ≤4, 1,455 (56.4%) were readmitted to another hospital for inpatient rehabilitation after discharge from RCCVCs (Table 1). The average (median) LOS was 118.0 (29) days (Table 2). In this group, rehabilitation treatment could be oversupplied. Therefore, this study shows that rehabilitation services could be over- or under-supplied to patients with stroke without systematic provision of medical rehabilitation in the post-acute period (9).

Another characteristic phenomenon demonstrated in this study was that patients with stroke in the inpatient rehabilitation group visited several hospitals after being discharged from the RCCVCs, resulting in prolonged LOS (9, 28). For example, patients with moderate severity (NIHSS 5–15) who were discharged from RCCVCs and transferred to another hospital to receive rehabilitation services were admitted to two additional hospitals before returning home. The median net LOS was 128 days. This phenomenon may be related to the following issues. First, in South Korea, rehabilitation treatment is mainly provided on an inpatient basis, and outpatient-based rehabilitation treatment is rarely performed after discharge to the home. When receiving rehabilitation treatment on an outpatient basis, the out-of-pocket ratio is higher than that of inpatient rehabilitation. In addition, because of hospitalization fees that can be billed to the NHIS, providers prefer inpatient to outpatient rehabilitation. Regardless of severity, patients with stroke who want rehabilitation treatment after discharge from RCCVCs might have no option other than hospitalization. Second, there were no criteria for determining whether inpatient rehabilitation was required in South Korean NHIS in 2017. Instead, if the hospitalization period exceeds 2 weeks, hospitalization reimbursement is deducted, and after 1 month, it is further deducted (26). However, when patients are admitted to another hospital post-discharge, the deduction rate is not applied cumulatively but rather is reset. Therefore, providers might be concerned with the discharge of patients with stroke but are not interested in whether they are discharged home or admitted to another hospital. Third, among the rehabilitation treatment items based on the fee-for-service reimbursement system, patient/family education and counseling for return to home performed by the rehabilitation team were not included. The absence of these services may have delayed the return to home after the stroke.

Several factors influencing LOS may be related to the specific situation in South Korea rather than being universal. First, the long LOS for women may be because women in South Korea have a higher share of household work and fewer people at home to take care of them (29, 30). Considering these environmental factors, women may be more likely to have difficulty returning home than men after a stroke. Second, the longer LOS in the lowest income group (Q1) can be at least partially explained by the fact that 10–30% of co-payments for medical expenses are not applied to the group (31).

This study has some limitations. First, the NHIS-NHID does not contain information on family members or support. Therefore, information on family support could not be obtained, although this is a known factor that affects LOS (32, 33). Second, the RCCVC system in South Korea performs cardio-cerebrovascular thrombolysis, an emergency procedure. Therefore, patients with other types of stroke, such as cerebral hemorrhage, were excluded from this study. Third, only hospitalization for rehabilitation treatment was investigated and presented, and the

rehabilitation treatment itself was not quantitatively analyzed. Because rehabilitation treatment was based on the fee-for-service system as of 2017, it was too complicated to analyze the actual rehabilitation contents and amount of treatment. Fourth, the income level was classified according to the level of NHIS payment. In South Korea, when calculating the NHIS co-payment, the patient's income is determined by salary or tax return, and tax exemption is not included in the calculation. Therefore, patients' incomes in this study may have been underestimated.

In future studies, the use of rehabilitation medical resources and return to home in patients with stroke that occurred after the introduction of the post-acute rehabilitation hospital system in 2020 should be investigated, and the results should be compared with those of this study.

5. Conclusion

In conclusion, before the introduction of the post-acute rehabilitation system in South Korea, rehabilitation treatment after stroke was both over- and under-supplied, and return to home was delayed after discharge from acute care hospitals. Returning home after a stroke was the most delayed in the lowest-income group, high-severity group, and female patients. These results support the need for a post-acute rehabilitation system that specifies the subject, duration, and intensity of rehabilitation treatment. The data reported in this study may serve as basic evidence for planning new systems in countries where a post-acute rehabilitation system has not yet been established.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by the Institutional Review Board of Seoul National University Hospital. Written informed consent from the participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

Author contributions

SB conceived and planned the study, performed the analysis, wrote the original draft with input from all authors, visualized the results, validated the study, and contributed to the interpretation of the results. JK conceived and planned the study, performed the analysis, wrote the original draft with input from all authors, and contributed to the interpretation of the results. H-IS conceived, planned, validated the study, contributed to the interpretation of the results, and supervised the entire process. All the authors have read and approved the final manuscript.

Funding

This study was partially supported by the Cardio-Cerebrovascular Disease Management and Research Service of the Korean Ministry of Health and Welfare and donation of Sir Jung Jin Park.

Acknowledgments

The authors would like to thank Hee-Joon Bae, the chief of the Korea Cardio-cerebrovascular Disease Management and Research Service, for making this study possible, and the chiefs of the Cardio-cerebrovascular Rehabilitation Centers in the RCCVCs for providing data from the RSCR. The chiefs of the Cardio-cerebrovascular Rehabilitation Center who contributed to this study were as follows: Gowun Kim (Kangwon National University Hospital), Yang-Soo Lee (Kyungpook National University Hospital), Eun Shin Lee (Gyeongsang National University Hospital), Jong Hwa Lee (Dong-A University Hospital), Won-Seok Kim (Seoul National University Bundang Hospital), Min Cheol Joo (Wonkwang University Hospital), Chang-Hwan Kim (Inha University Hospital), Min-Keun Song (Chonnam National University Hospital), So Young Lee (Jeju National University Hospital), Sungju Jee (Chungnam National University Hospital), and Heui Je Bang (Chungbuk National University Hospital).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2023.1135568/full#supplementary-material

References

1. GBD Lifetime Risk of Stroke Collaborators. Global, regional, and country-specific lifetime risks of stroke, 1990 and 2016. *N Engl J Med.* (2018) 379:2429–37. doi: 10.1056/NEJMoa1804492

2. Wafa HA, Wolfe CD, Emmett E, Roth GA, Johnson CO, Wang Y. Burden of stroke in Europe: thirty-year projections of incidence, prevalence, deaths, and disability-adjusted life years. *Stroke.* (2020) 51:2418–27. doi: 10.1161/STROKEAHA.120.029606

3. Liu H, Wu X, Cao J, Jiao J, Zhu C, Song B, et al. Effect of comorbidity assessed by the charlson comorbidity index on the length of stay and mortality among immobile hemorrhagic stroke patients younger than 50 years. *Front Neurol.* (2020) 11:487. doi: 10.3389/fneur.2020.00487

4. Wouters A, Nysten C, Thijs V, Lemmens R. Prediction of outcome in patients with acute ischemic stroke based on initial severity and improvement in the first 24 h. *Front Neurol.* (2018) 9:308. doi: 10.3389/fneur.2018.00308

5. Khan MSA, Ahmad S, Ghafoor B, Shah MH, Mumtaz H, Ahmad W, et al. Inpatient assessment of the neurological outcome of acute stroke patients based on the National Institute of Health Stroke Scale (NIHSS). *Ann Med Surg.* (2022) 82:104770. doi: 10.1016/j.amsu.2022.104770

6. Feigin VL, Stark BA, Johnson CO, Roth GA, Bisignano C, Abady GG, et al. Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Neurol.* (2021) 20:795–820. doi: 10.1016/S1474-4422(21)00252-0

7. Stinear CM, Lang CE, Zeiler S, Byblow WD. Advances and challenges in stroke rehabilitation. *Lancet Neurol.* (2020) 19:348–60. doi: 10.1016/S1474-4422(19)30415-6

8. Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW, et al. Heart disease and stroke statistics-—2021 update: a report from the American Heart Association. *Circulation.* (2021) 143:e254–743. doi: 10.1161/CIR.0000000000000950

9. Kim W-S, Bae H-J, Lee H-H, Shin HI. Status of rehabilitation after ischemic stroke: a Korean nationwide study. *Ann Rehabil Med.* (2018) 42:528–35. doi: 10.5535/arm.2018.42.4.528

10. Chen W-C, Hsiao M-Y, Wang T-G. Prognostic factors of functional outcome in post-acute stroke in the rehabilitation unit. *J Formosan Med Assoc.* (2022) 121:670–8. doi: 10.1016/j.jfma.2021.07.009

11. Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, et al. Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* (2016) 47:e98–169. doi: 10.1161/STR.0000000000000098

12. Chu C-L, Chen Y-P, Chen CC, Chen C-K, Chang H-N, Chang C-H, et al. Functional recovery patterns of hemorrhagic and ischemic stroke patients under post-acute care rehabilitation program. *Neuropsychiatr Dis Treat.* (2020) 16:1975–85. doi: 10.2147/NDT.S253700

13. Tung Y-J, Lin W-C, Lee L-F, Lin H-M, Ho C-H, Chou W. Comparison of cost-effectiveness between inpatient and home-based post-acute care models for stroke rehabilitation in Taiwan. *Int J Environ Res Public Health.* (2021) 18:4129. doi: 10.3390/ijerph18084129

14. Yinusa OG, Olowofela OE, Ariyibi ME. Future healthcare payment models in medical entrepreneurship. In: OG Yinusa, editor. *Medical Entrepreneurship: Trends and Prospects in the Digital Age*: Cham: Springer (2023). p. 231-41. doi: 10.1007/978-981-19-6696-5_15

15. Adeoye O, Nyström KV, Yavagal DR, Luciano J, Nogueira RG, Zorowitz RD, et al. Recommendations for the establishment of stroke systems of care: a 2019 update: a policy statement from the American Stroke Association. *Stroke.* (2019) 50:e187–210. doi: 10.1161/STR.0000000000000173

16. Kinoshita S, Abo M, Okamoto T, Miyamura K. Transitional and long-term care system in Japan and current challenges for stroke patient rehabilitation. *Front Neurol.* (2022) 12:711470. doi: 10.3389/fneur.2021.711470

17. Bae SW, Lee M-Y. Association between initiation of rehabilitation and length of hospital stay for workers with moderate to severe work-related traumatic brain injury. *Saf Health Work.* (2023) 16:724–31. doi: 10.1016/j.shaw.2023.04.001

18. Bang MS. Launching of the accreditation system for rehabilitation facility in Korea. *J Kor Med Assoc.* (2020) 63:582–4. doi: 10.5124/jkma.2020.63.10.582

19. Act on Guarantee of Right to Health and Access to Medical Services for Persons with Disabilities. Sejong-si: Korea Ministry of Government Legislation. (2021).

20. Yoon CW, Oh H, Lee J, Rha JH, Woo SI, Lee WK, et al. Comparisons of prehospital delay and related factors between acute ischemic stroke and acute myocardial infarction. *J Am Heart Assoc.* (2022) 11:e023214. doi: 10.1161/JAHA.121.023214

21. Jeong H-Y, Jung K-H, Mo H, Lee C-H, Kim TJ, Park J-M, et al. Characteristics and management of stroke in Korea: 2014–2018 data from Korean Stroke Registry. *Int J Stroke.* (2020) 15:619–26. doi: 10.1177/1747493019884517

22. Lee HR, Yoo JE, Choi H, Han K, Jung JH, Park J, et al. Tuberculosis and risk of ischemic stroke: a nationwide cohort study. *Stroke.* (2022) 53:3401–9. doi: 10.1161/STROKEAHA.122.039484

23. Virta JJ, Strbian D, Putaala J, Kaprio J, Korja M. Characteristics and outcomes of thrombolysis-treated stroke patients with and without saccular intracranial aneurysms. *Stroke.* (2022) 53:3616–21. doi: 10.1161/STROKEAHA.122.040151

24. Mistry EA, Yeatts SD, Khatri P, Mistry AM, Detry M, Viele K, et al. National Institutes of Health Stroke Scale as an outcome in stroke research: value of ANCOVA over analyzing change from baseline. *Stroke.* (2022) 53:e150–5. doi: 10.1161/STROKEAHA.121.034859

25. Olasoji EB, Uhm DK, Awosika OO, Doré S, Geis C, Simpkins AN. Trends in outpatient rehabilitation use for stroke survivors. *J Neurol Sci.* (2022) 442:120383. doi: 10.1016/j.jns.2022.120383

26. Kim E, Lee M, Kim E-H, Kim HJ, Koo M, Cheong IY, et al. Using knowledge translation to establish a model of hospital-based early supported community reintegration for stroke patients in South Korea. *BMC Health Serv Res.* (2021) 21:1–13. doi: 10.1186/s12913-021-07400-5

27. Forrest G, Reppel A, Kodsi M, Smith J. Inpatient rehabilitation facilities: the 3-hour rule. *Medicine.* (2019) 98:e17096. doi: 10.1097/MD.0000000000017096

28. Jung SH. Stroke rehabilitation fact sheet in Korea. *Ann Rehabil Med.* (2022) 46:1–8. doi: 10.5535/arm.22001

29. Han J, Lee HI, Shin Y-I, Son JH, Kim S-Y, Kim DY, et al. Factors influencing return to work after stroke: the Korean Stroke Cohort for Functioning and Rehabilitation (KOSCO) Study. *Br Med J Open.* (2019) 9:e028673. doi: 10.1136/bmjopen-2018-028673

30. Kim SS, Roh YS A. Validation study of the revised caregiving burden instrument in Korean family caregivers of stroke survivors. *Int J Environ Res Public Health.* (2021) 18:2960. doi: 10.3390/ijerph18062960

31. Kong NY, Kim DH. Factors influencing health care use by health insurance subscribers and medical aid beneficiaries: a study based on data from the Korea welfare panel study database. *BMC Public Health.* (2020) 20:1–10. doi: 10.1186/s12889-020-09073-x

32. Camicia M, Lutz BJ, Markoff N, Catlin A. Determining the needs of family caregivers of stroke patients during inpatient rehabilitation using interview, art, and survey. *Rehabil Nurs J.* (2019) 44:328–37. doi: 10.1097/RNJ.0000000000000129

33. Lee HW, Park Y, Jang EJ, Lee YJ. Intensive care unit length of stay is reduced by protocolized family support intervention: a systematic review and meta-analysis. *Intensive Care Med.* (2019) 45:1072–81. doi: 10.1007/s00134-019-05681-3

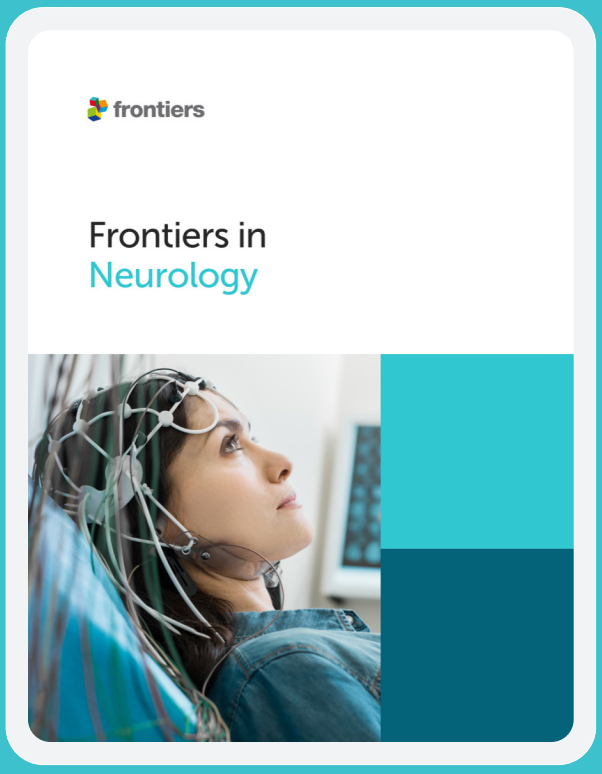
Frontiers in Neurology

Explores neurological illness to improve patient care

The third most-cited clinical neurology journal explores the diagnosis, causes, treatment, and public health aspects of neurological illnesses. Its ultimate aim is to inform improvements in patient care.

Discover the latest Research Topics

See more →



Frontiers

Avenue du Tribunal-Fédéral 34
1005 Lausanne, Switzerland
frontiersin.org

Contact us

+41 (0)21 510 17 00
frontiersin.org/about/contact