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Prognostic value of temporalis muscle thickness as a marker of sarcopenia in intracerebral hemorrhage

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Introduction: Estimating the prognosis of spontaneous intracerebral hemorrhage (ICH) is of great importance. It has not been conclusively clarified whether sarcopenia is predictive for the functional outcome in ICH. Determining the temporalis muscle thickness (TMT) may be helpful for estimating sarcopenia. An association of TMT with outcome (mRS) has been shown in cerebellar ischemia and traumatic brain injury.

Methods: The present retrospective study of 488 consecutive patients with ICH aimed to investigate the association of sarcopenia as assessed by TMT with mRS. In addition to biometric data, ICH subtype and severity [modified ICH score (mICH)], occurrence of complications and mRS at discharge and after 90 days were recorded. The influence of sarcopenia assessed by TMT as the surrogate marker using head imaging (cCT, cMRT) on mRS was analyzed by ordinal regression analysis. Dichotomization into sarcopenic and non-sarcopenic patients was carried out using standard threshold values.

Results: Finally, 322 patients were analyzed [median (IQR) age: 77 (66–83) years; 57.5% male]. Sarcopenic patients were older ($P < 0.001$), had lower BMI ($P = 0.025$) and higher mICH scores ($P < 0.001$) compared to non-sarcopenic patients. There was no significant difference in the overall distribution of mRS scores between sarcopenic and non-sarcopenic patients at discharge (unadjusted common OR: 1.28; 95% CI: 0.85–1.92; $P = 0.236$), but at 90 days favoring the non-sarcopenic over the sarcopenic group (unadjusted common OR: 1.41; 95% CI: 1.07–2.12; $P = 0.049$). The results did not subsist statistical adjustment to candidate covariates by multivariate ordinal regression.

Discussion: In conclusion, sarcopenia as assessed by TMT seems to have limited prognostic value in ICH.

KEYWORDS

intracerebral hemorrhage, prognosis, sarcopenia, temporal muscle thickness, modified ranking scale

Introduction

Spontaneous intracerebral hemorrhage (ICH) accounts for 10–15% of all stroke with mortality up to 61% at 1 month after bleeding (1, 2). Given severe neurological dysfunction and impaired consciousness, ICH survivors often require admission to the intensive care unit (ICU) or neurological ICU (NICU) (3). Along with this,

incidence of ICH increases with higher age (4). Despite improvements in care and treatment, functional outcome in those elder patients with ICH is not always as favorable as expected. Therefore, additional efforts to identify novel prognostic markers and improve patient outcomes are required. Sarcopenia, defined as the loss of skeletal muscle mass, is recognized to increase after stroke, although it can also be a pre-existing condition especially in the elder age. Both cases have been associated with a worse functional outcome (5, 6), highlighting the importance of measuring skeletal muscle mass as a measure of sarcopenia in a stroke population. However, the role of sarcopenia in ICH remains largely unclear.

The diagnostic tools to assess sarcopenia are based on methods that estimate muscle quantity comprise, among others, magnetic resonance imaging (MRI) and computed tomography (CT) scans of the lumbar muscles obtained on abdominal CT scans (7–9). Estimation by measuring temporalis muscle thickness (TMT) has become a favorable approach for sarcopenia measurement which could be easily, fast and reliable be performed in routine imaging scans. This has been shown in cerebellar ischemia and traumatic brain injury as well (10, 11). The aim of the current study was to investigate the association of sarcopenia and TMT with functional outcome in ICH at hospital discharge and 90 days follow-up.

Methods

Study design

In this retrospective cross-sectional cohort study, we screened the hospital charts of 488 consecutive sICH patients admitted to the Department of Neurology of the University Medicine Rostock between January 2017 and December 2021. After exclusion of patients with insufficient clinical data due to hospital stay length <24 h and patients with loss of follow-up at 90 days, a total of 322 patients were included in the final analysis (see Figure 1 for study flow chart). The study was approved by the Institutional Review Board of the Medical Faculty, University of Rostock (A-2017-0207).

Patients

All patients received standard-of-care treatment according to the European Stroke Organization Guidelines for ICH (12). Basic characteristics like age, sex, body-mass-index (BMI), comorbidities (atrial hypertension, diabetes mellitus, atrial fibrillation, hyperlipoproteinemia, pneumonia) were obtained. Clinical severity of ICH was assessed using the modified ICH score (mICH) (13) and the National Institutes of Health Stroke Scale (NIHSS).

The topology of ICH was assessed by an experienced board-certified neuroradiologist (D.C.) blinded to the hypothesis investigated here by using cerebral CT or MRI. Since insular localization of ICH has been shown to influence functional outcome it was included in further analyses of candidate factors (14). Hemorrhage was considered to involve the insular region when at least a portion of the insula was compromised, regardless of affecting other brain regions. We determined whether there was insular involvement based on the identification of the appropriate ASPECTS region (15). The occurrence of intraventricular hemorrhage (IVH) was determined. ICH volume was estimated in cubic centimeters by the formula $ABC/2$ according to Kothari et al. (16) [see Wittstock and co-workers for details (14)]. The most likely cause of bleeding was determined considering the clinical and radiological characteristics and classified as follows: arterial hypertension, cerebral amyloid angiopathy according to the modified Boston criteria (17), hemorrhagic diathesis due to therapeutic anticoagulation.

Functional outcome [modified Rankin scale (mRS)] was assessed at hospital discharge as well as at 90 days follow-up, death rate was additionally determined at day 7.

TMT measurement

TMT was assessed in CT or MRI scans at admission according to the method presented previously by Ravera et al. and Steindl et al. (18, 19). In detail, TMT was manually measured on the patient's baseline brain CT scan using the method introduced by Katsuki et al. (20). Slice thickness was set at 5 mm and the CT axial image was manually fixed to obtain a symmetric cut. TMT was measured bilaterally, perpendicular to the long axis of the temporal muscle. Three determinations were taken for each side: one at the level of the orbital roof, identified by comparing a sagittal cut, another at 5 mm above the orbital roof and the last at 5 mm below the orbital roof. The mean of the three measurements was calculated on both the left and the right side. Once the right and left means were obtained, the final TMT, expressed in millimeters, was measured by calculating the mean between the two values.

Based on the results, patients were further divided into two groups (sarcopenic vs. non-sarcopenic) as recommended by the European Working Group on Sarcopenia in Older People (EWGOP) and based on previously reported cut-off values (mean TMT 6.3 mm for male and 5.2 mm for female patients) (19, 21).

Statistical analysis

Statistical comparisons between groups, Mann–Whitney U-test or Kruskal–Wallis test were used for comparison of parametric data, and Pearson Chi^2-test or Fisher exact test for the comparison of non-parametric data as appropriate. For ordinal data, we used the Jonckheere–Terpstra test. *Post-hoc* analyses results were presented with Bonferroni adjustment. To test whether there was an association between categorical clinical variables and the outcome of interest, univariate and multivariate binary logistic (for in-hospital death as dependent outcome variable) or ordinal regression analyses (for mRS as dependent outcome measure) were performed. To select relevant covariates, we performed Mann–Whitney U-test and Chi^2/Fisher Exact test in combination with univariate regression models to determine the predictive values and Odds ratios (OR) with 95% confidence intervals (95%CIs) of the candidate covariates age, sex,

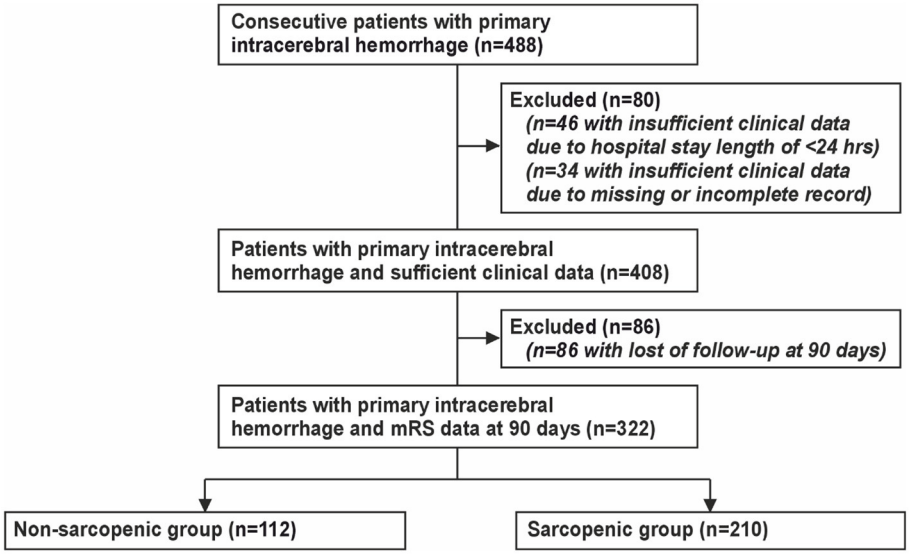

FIGURE 1
Study flowchart.

NIHSS at admission, ICH volume, intraventricular hemorrhage, mICH score, length of hospital stay, surgical intervention, pneumonia, and atrial fibrillation (see Supplementary Table S1). Prior to calculate multivariate regressions, assumptions of normality, homoscedasticity, independence of errors and absence of multicollinearity, were checked. For survival analyses, we performed univariate and multivariate Cox proportional hazards models to estimate hazard ratios (HRs) with 95%CIs and *P*-values for pairwise comparisons. The proportional hazards assumption was tested using log-log plots. Kaplan-Meier curve was used to visually compare the time to death after ICH onset in non-sarcopenic and sarcopenic patients.

Analyses were conducted using SPSS, version 25.0 (SPSS, Chicago, IL), and all *P*-values were two-sided and values of <0.05 were deemed statistically significant (due to the limited sample size in our retrospective study, α adjusting of *P*-values was not carried out in order to preserve statistical power).

Results

Demographic and clinical characteristics

A total of 488 consecutive patients treated for ICH were screened, 80 were excluded ($n = 46$ due to hospital stay length of <24 h and $n = 34$ due to insufficient clinical data). Another 86 patients were excluded due to loss of follow-up at 90 days (Figure 1). Out of 322 ICH patients (median age 77 years, IQR 66.0–83.0 years, 57.5% men), 294 patients (91.9%) showed supratentorial ICH, whereas 28 (8.1%) displayed infratentorial bleeding. Forty-three patients (27%) displayed insular involvement. Intraventricular hemorrhage occurred in 210 (65.2%) ICH patients. The median value of NIHSS at admission was 9 (IQR 4–15). Detailed demographic and clinical characteristics are illustrated in Table 1.

Association of TMT with demographic and clinical characteristics

TMT values measured in the study cohort were significant higher in male than in female subjects [median (IQR) value 5.8 (5.3–6.6) vs. 4.8 (4.1–5.4); $P<0.001$]. Significant correlation (Spearman rho, *P*-value) could be found for age (−0.52, 95% CI: −0.43 to −0.59; $P < 0.001$) as well as for BMI (0.29, 95% CI: −0.17 to −0.41; $P < 0.001$). Further analysis did not reveal any correlations with atrial fibrillation, pneumonia, hypertension, diabetes hyperlipoproteinemia, statin use, therapy with TAH as well as oral anticoagulation (data not shown).

Association of sarcopenia with demographic and clinical characteristics

The full cohort was divided into a sarcopenic (65.2% of patients) and a non-sarcopenic group (34.8% of patients) based on the previously reported cut-off values (Table 1) (19). Sarcopenic patients were significantly older than non-sarcopenic patients (Table 1) and the frequency of sarcopenia displayed a clear age-dependency ranging from 25% in patients of age group <50 years over 39% in age group 50–59 years, 48% in age group 60–69 years and 68% in age group 70–79 years up to 84% in age group 80+ years ($P < 0.001$, Chi^2 test). Concerning other demographic and clinical characteristics, sarcopenic patients had significant higher NIHSS at admission, greater ICH volumes and higher mICH scores as compared to non-sarcopenic patients. The frequency of hypertension and atrial fibrillation (AF) as well was higher in sarcopenic vs. non-sarcopenic patients (Table 1). There were neither differences regarding the etiology of sICH nor the rate of pneumonia between sarcopenic vs. non-sarcopenic patients (Table 1).

TABLE 1 Demographics, baseline clinical characteristics and management data of cohort with data at 90 days.

	Total cohort ($n = 322$)	Non-sarcopenic group ($n = 112$)	Sarcopenic group ($n = 210$)	*P*-value
Males/females, *n* (%)	185 (57.5%)/137 (42.5%)	70 (62.5%)/42 (37.5%)	115 (54.8%)/95 (45.2%)	0.181[$]
Age (years), median (IQR)	77.0 (66.0–83.0)	67.5 (58.0–78.8)	80.0 (74.0–84.0)	**<0.001***
BMI (kg/m^2), median (IQR)	25.9 (23.5–29.1)	26.4 (24.2–30.2)	25.5 (23.2–28.3)	**0.025***
TMT (mm), median (IQR)	5.4 (4.7–6.2)	6.5 (5.5–6.9)	4.9 (4.4–5.6)	**<0.001***
Sarcopenia, *n* (%)	210 (65.2%)	–	–	–
Length of hospital stay (days), median (IQR)	14 (9–20)	16 (10–22)	13 (8–20)	0.053*
NIHSS at admission, median (IQR)	9 (4–15)	8 (3–15)	9 (4–15)	0.708*
Hemorrhage-related parameters				
Modified ICH score, median (IQR)	4 (3–6)	3 (2–5)	4 (3–6)	**<0.001[#]**
ICH volume (ml), median (IQR)	14.6 (5.8–36.7)	15.4 (6.2–35.3)	14.0 (5.5–36.9)	0.751*
Supra-/infratentorial hemorrhage, *n* (%)	294 (91.9%)/28 (8.1%)	104 (92.9%)/8 (7.1%)	190 (90.5%)/20 (9.5%)	0.470[$]
Insular/non-insular hemorrhage, *n* (%)	79 (24.5%)/243 (75.5%)	31 (27.7%)/81 (72.3%)	48 (22.9%)/162 (77.1%)	0.338[$]
Intraventricular hemorrhage (IVH), *n* (%)	145 (45%)	52 (46.4%)	93 (44.3%)	0.713[$]
Accompanied SAH, *n* (%)	73 (22.7%)	23 (20.5%)	50 (23.8%)	0.504[$]
Surgical therapy, *n* (%)	19 (5.9%)	11 (9.8%)	8 (3.4%)	**0.029[$]**
Hemorrhage etiology				
Anticoagulation associated, *n* (%)	78 (24.2%)	22 (19.6%)	56 (26.7%)	0.161[$]
Hypertension associated, *n* (%)	264 (82.0%)	90 (80.4%)	174 (82.9%)	0.578[$]
Amyloid angiopathy associated, *n* (%)	79 (24.5%)	25 (22.3%)	54 (25.7%)	0.500[$]
Comorbidities				
Arterial hypertension, *n* (%)	312 (96.9%)	104 (92.9%)	208 (99.0%)	**0.004[$]**
Pneumonia, *n* (%)	139 (43.2%)	49 (43.8%)	90 (42.9%)	0.878[$]
Diabetes mellitus, *n* (%)	95 (29.5%)	32 (28.6%)	63 (30.0%)	0.789[$]
Hyperlipoproteinemia, *n* (%)	141 (43.8%)	46 (32.6%)	95 (45.2%)	0.473[$]
Treatment with statin, *n* (%)	109 (33.9%)	35 (31.3%)	74 (35.2%)	0.471[$]
Artrial fibrillation, *n* (%)	114 (35.4%)	28 (25.0%)	86 (41.0%)	**0.004[$]**

Values are median and interquartile ranges (IQR, in brackets) or *n* (%). Significant *p*-values are provided as bold values.
ICH, Intracranial hemorrhage; BMI, body mass index; TMT, temporalis muscle thickness; NIHSS, National Institute of Health Stroke Scale; IVH, intraventricular hemorrhage; SAH, subarachnoidal hemorrhage; mRS, modified ranking scale.
*Mann-Whitney *U*-test.
[$]Pearson Chi^2 or Fisher exact test as appropriate.
[#]Jonckheere-Terpstra test.

Association of TMT with functional outcome and mortality in ICH

Univariate regression models showed that TMT was associated with all major outcome parameters (mRS, death) at hospital discharge and at 90 days, with patients with higher TMT values having a more favorable outcome (see Table 2 for respective ORs). In contrast, TMT was not associated with early mortality rate at 7 days after ICH onset (Table 2). However, adjustment of ORs using multivariate regression models with variables influencing the outcome showed no significant associations of TMT and functional outcome/death at 7 days after ICH onset, hospital discharge and 90 days follow-up (Table 2).

Notably, after exclusion of age as a covariate, which was correlated to TMT, common OR for TMT from multivariate logistic ordinal regression at hospital discharge was 0.75 (95% CI: 0.60–0.94; $P = 0.012$). Common OR for TMT from multivariate logistic ordinal regression at 90 days follow-up was 0.85 (95% CI: 0.68–1.06; $P = 0.152$).

Association of sarcopenia with functional outcome and mortality in ICH

As displayed in Figure 2, there was no significant difference in functional outcome between sarcopenic and non-sarcopenic

TABLE 2 Odds ratios for functional outcomes by TMT and by non-sarcopenic vs. sarcopenic patient group.

	Outcome rate[a]			Univariate logistic/ ordinal regression[c]		Multivariate logistic/ ordinal regression[d]	
	Non-sarcopenic ($n = 112$)	Sarcopenic ($n = 210$)	*P*-value[b]	Unadjusted odds ratio (95% CI)	*P*-value	Adjusted odds ratio (95% CI)	*P*-value
TMT (mm) as marker for sarcopenia							
mRS at discharge				0.83 (0.70–0.99)	**0.033**	0.95 (0.73–1.24)	0.708
mRS 6 (death) at discharge				0.76 (0.60–0.96)	**0.021**	0.95 (0.60–1.53)	0.838
90-days mRS[§]				0.78 (0.65–0.92)	**0.004**	0.99 (0.76–1.29)	0.919
mRS 6 (death) at 7 days				0.83 (0.62–1.11)	0.201	0.93 (0.59–1.45)	0.741
mRS 6 (death) at 90 days				0.75 (0.61–0.94)	**0.012**	0.98 (0.64–1.49)	0.914
Non-sarcopenic vs. sarcopenic group -sarcopenic vs. sarcopenic group							
mRS at discharge, median (IQR)	4.0 (2.0–5,8)	4.0 (3.0–6.0)	0.236	1.29 (0.85–1.92)	0.236	1.15 (0.70–1.90)	0.577
mRS 6, (death) at discharge *n* (%)	28 (25.0%)	67 (31.9%)	0.196	1.41 (0.84–2.36)	0.197	1.28 (0.79–3,45)	0.347
90-days mRS[§], median (IQR)	3.0 (2.0–6.0)	4.0 (2,0–6.0)	0.104	1.41 (1.07–2.12)	0.049	1.01 (0.61–1.67)	0,968
mRS 6 (death) at 7 days, *n* (%)	14 (12.5%)	33 (15.7%)	0.437	1.31 (0.67–2.56)	0.437	1.14 (0.45–2.90)	0.781
mRS 6 (death) at 90 days, *n* (%)	34 (30.4%)	76 (36.2%)	0.293	1.32 (0.81–2.15)	0.270	1.12 (0.76–4.21)	0.632

ICH, Intracranial hemorrhage; BMI, body mass index; TMT, temporalis muscle thickness; NIHSS, National Institute of Health Stroke Scale; IVH, intraventricular hemorrhage; SAH, subarachnoidal hemorrhage; mRS, modified ranking scale. Significant *p*-values are provided as bold values.

[a]Number and (%) for death rate and median (IQR) for mRS.

[b]*P*-values are from Pearson Chi² tests (death rate) or Jonckheere-Terpstra tests (mRS).

[c]Odds ratios and *P*-values from univariate ordinal or binary logistic regression analyses. An odds ratio >1 for the continuous variable (TMT) indicates a higher risk at higher values of TMT, while an odds ratio >1 for dichotomous risk factor (non-sarcopenic vs. sarcoopenic group) indicates a higher risk in the sarcopenic group.

[d]Adjustment of odds ratios for relevant covariates were performed by multivariate ordinal or binary logistic regression with predictive variables from univariate analyses (covariates for data at hospital discharge: sex, age, NIHSS at admission, ICH volume, insular hemorrhage, intraventricular hemorrhage, accompanied subarachnoidal hemorrhage, surgical therapy, pneumonia, atrial fibrillation, anticoagulation, and hypertension; covariates for data at 90 days: sex, age, NIHSS at admission, ICH volume, insular hemorrhage, intraventricular hemorrhage, accompanied subarachnoidal hemorrhage, pneumonia, atrial fibrillation, anticoagulation, and hypertension; covariates for data at 7 days: age, NIHSS at admission, ICH volume, insular hemorrhage, intraventricular hemorrhage and pneumonia).

patients at hospital discharge (unadjusted common OR: 1.28; 95% CI: 0.85–1.92; $P = 0.236$) and no difference in mortality rates at 7 days after ICH onset (unadjusted OR: 1.31; 95% CI: 0.67–2.56; $P = 0.437$) and at hospital discharge (unadjusted common OR: 1.41; 95% CI: 0.84–2.36; $P = 0.197$), but a significant difference at 90 days follow-up was observed favoring the non-sarcopenic group over the sarcopenic group (unadjusted common OR: 1.41; 95% CI: 1.07–2.12; $P = 0.049$). However, after adjustment of ORs using multivariate regression models with variables influencing the outcome revealed no significant associations of sarcopenia and functional outcome/death at 7 days after ICH onset, hospital discharge or 90 days follow-up (Table 2).

Influence of other candidate risk factors on functional outcome and mortality in ICH

Univariate regression analyses revealed that several clinical candidate risk factors of unfavorable outcome such as sex, age, pneumonia as well as major ICH imaging parameters including ICH volume, intraventricular hemorrhage and insular localization were associated with functional outcome at hospital discharge and 90 days follow-up (see Supplementary Tables S1, S2). Multivariate regression analysis confirmed sex, age, NIHSS at admission, ICH volume, insular localization, intraventricular hemorrhage and pneumonia as significant predictors for functional outcome at hospital discharge (Supplementary Table S3). At 90 days follow-up, multivariate regression analysis showed associations of sex, age, NIHSS at admission, ICH volume, intraventricular hemorrhage and pneumonia with functional outcome (Supplementary Table S4). Early death rate at 7 days after ICH onset was mainly associated with age, ICH parameters and pneumonia (Supplementary Table S5).

Influence of TMT and sarcopenia on survival after ICH

Univariate Cox regression analysis showed that TMT but not sarcopenia was significantly associated with survival after ICH, with patients with higher TMT values having a greater chance of survival [HR for TMT: 0.78 (95% CI: 0.65–0.94; $P = 0.006$); HR for sarcopenia: 1.38 (95%CI: 0.92–2.07; $P = 0.124$); Kaplan-Meier survival curve showing the association between sarcopenia and survival after ICH is displayed in Supplementary Figure S1]. However, adjustment of HRs using multivariate Cox regression models with variables influencing survival showed no significant associations of TMT and sarcopenia with survival (Supplementary Table S6).

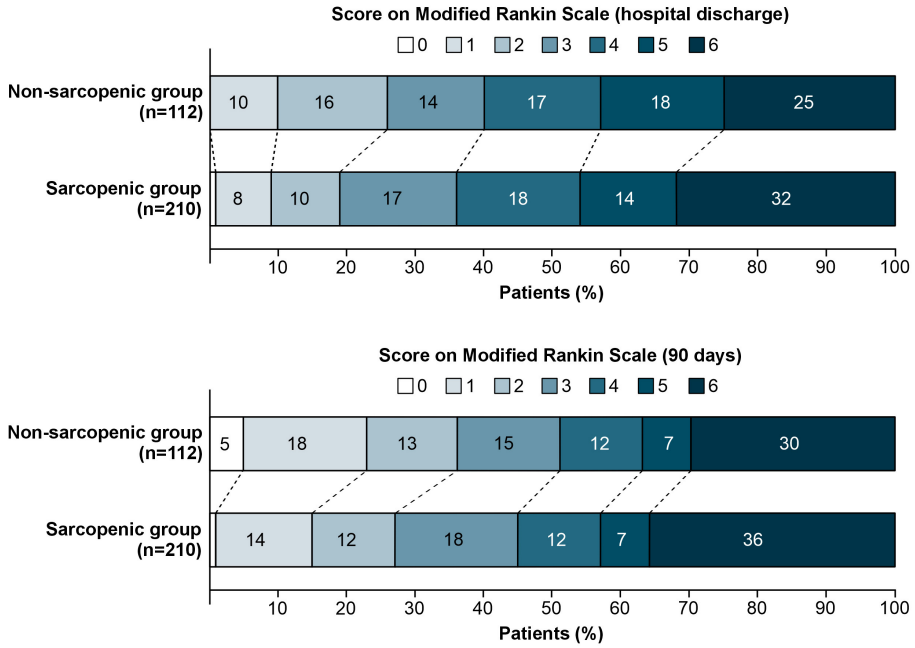

FIGURE 2
Modified rankin scale scores at discharge from hospital and at 90 days. Shown are the results of the ordinal analysis of the modified Rankin scale scores at discharge from hospital (upper panel) and at 90 days (lower panel). Scores range from 0 to 6, with 0 indicating no neurologic deficit, 1 no clinically significant disability, 2 slight disability (able to handle own affairs without assistance but unable to carry out all previous activities), 3 moderate disability requiring some help (e.g., with shopping, cleaning, and finances but able to walk unassisted), 4 moderately severe disability (unable to attend to bodily needs without assistance and unable to walk unassisted), 5 severe disability (requiring constant nursing care and attention), and 6 death. There was no significant difference between the non-sarcopenic and sarcopenic patient group at discharge (unadjusted common odds ratio: 1.28; 95% CI: 0.85–1.92; $P = 0.236$), but a significant difference at 90 days favoring the non-sarcopenic group over the sarcopenic group in the overall distribution of scores (unadjusted common odds ratio: 1.41; 95% CI: 1.07–2.12; $P = 0.049$).

Importantly, after exclusion of age as a covariate, which was correlated to TMT and sarcopenia, Cox regression analyses showed direct association of survival after ICH and TMT with a HR of 0.76 (95% CI: 0.61–0.94; $P = 0.013$) and increased survival for non-sarcopenic as compared to sarcopenic patients with a HR of 1.67 (95% CI: 1.08–2.58; $P = 0.021$).

Discussion

The aim of the presented investigation was to elucidate the relationship between sarcopenia assessed by TMT measurement and ICH outcome. Since we did not detect relevant age-independent associations between TMT itself or sarcopenia with functional outcome, TMT seems to have limited prognostic value in ICH. Adjustment of ORs using multivariate regression models with variables influencing the outcome showed no significant associations of TMT and functional outcome/death at 7 days after ICH onset, hospital discharge and 90 days follow-up. Adjustment of HRs using multivariate Cox regression models with variables influencing survival showed no significant associations of TMT and sarcopenia with survival. However, other candidate factors affecting the prognosis of ICH such as sex, age, disease severity at admission, ICH volume, intraventricular hemorrhage, insular localization and pneumonia were confirmed to be associated with functional outcome or death after ICH.

Importantly, after exclusion of age as a covariate, which was correlated to TMT and sarcopenia, Cox regression analyses showed direct association of survival after ICH and TMT with a HR of 0.76 (95% CI: 0.61–0.94; $P = 0.013$) and increased survival for non-sarcopenic as compared to sarcopenic patients with a HR of 1.67 (95% CI: 1.08–2.58; $P = 0.021$).

In line with previous published findings, TMT was found to be higher in men than in women (22–24), likely related to the fact that males have more skeletal muscle mass than women both in absolute terms and related to BMI (25). The same studies showed a correlation with age, which was also confirmed in our study with younger patients having a higher TMT (26). Regarding the association of TMT with BMI, data from the literature show inconclusive results: in some studies a positive association between TMT and BMI has been described (6, 24), while in other reports no correlations were found (27). A positive correlation between BMI and TMT was identified in our ICH patient cohort. It is however important to note that BMI is a parameter based on weight and not on body shape, consequently, it does not allow the identification of sarcopenia particularly in obese patients (27). BMI did however not show any significant association with functional outcome.

The prevalence of sarcopenia is variable in the general population, probably due to the absence of uniform criteria (18). In our study, the percentage of patients with sarcopenia was found to be 65%, higher than in other studies mainly referring to populations of community-dwelling subjects (28–31). This could be due to different factors: Firstly, the median age of our study

(77 years) is located in the upper range of related studies (29–32). Since sarcopenia is an age-related disorder, its prevalence is expected to be higher in the elderly population (33, 34). Indeed, we observed a clear age-dependency of sarcopenia frequency also in our cohort. Secondly, the assessment tools for diagnosing sarcopenia largely varied from clinical scoring to quantitative surrogate markers of muscular mass. Indeed, there is no common standard definition of sarcopenia available yet (18). Herein we used TMT as a quantitative surrogate marker of sarcopenia combined with previously generated cut-off values according to the European Working Group on Sarcopenia in Older People (EWGOP) (19, 21). Although the prevalence of sarcopenia in stroke populations may be variable with percentages ranging from 33 to 68% (33–35), our frequency of sarcopenia in an old ICH cohort is well in line with previous reports in similar cohorts.

Outcome prediction models relying on baseline variables can only partly forecast post-ICH outcome, and certain individuals—particularly elderly patients—may still face a lower likelihood of functional recovery (36, 37). In this scenario the investigation of new prognostic markers is of paramount importance, to maximize the benefit to patients while minimizing the harm in this frail population. In previous studies, the association between TMT or sarcopenia and functional outcome was mainly investigated in patients with stroke, subdural hematoma, traumatic brain injury and brain metastases (5, 6, 10, 11, 27, 38). In these studies, a negative correlation between TMT or premorbid sarcopenia and overall survival was demonstrated. In ischemic stroke patients several studies investigated the relationship of TMT/sarcopenia and overall survival with inconsistent results. Li et al. and Ravera et al. showed a negative correlation of TMT and functional outcome as well as overall survival (23, 33). On the other side, Lin et al. reported a positive correlation between TMT and a higher likelihood of functional independence measured by mRS at 90 day in an ischemic stroke cohort, who underwent endovascular therapy for large vessel occlusion without correlation with mortality (39).

In contrast, our data do not demonstrate any relevant age-independent associations between TMT itself or sarcopenia with functional outcome (mRS) or death at hospital discharge and at 90 days in ICH. The relatively high percentage of patients lost to follow-up at 90 days was due to local circumstances. The metropole region of Rostock is located in a wide-ranged rural landscape, has a relatively high mean age of residents and is a highly frequented touristic region.

Thus, sarcopenia as assessed by TMT seems to have only limited prognostic value in ICH. The reasons for this discrepancy might not only be related to different methods for assessing sarcopenia (clinical scoring vs. objective surrogate marker assessment) and study cohort characteristics such as age, but also in differences in temporal dynamics of the various brain disorders including variant recovery trajectories with ICH being associated with high early mortality and early functional disability burden (40–43). It could therefore be that the latency of 90 days until the measurement of functional outcome as used in the present study and as routinely applied in studies in acute brain diseases including ICH (42) is too short to detect the prognostic value of sarcopenia in ICH. Evaluation of cognition or physical fitness in geriatric or ICH patients is mainly based on cooperation, examination or anamnestic data from caregivers. TMT measurement could add an independent measure of sarcopenia in those patients. Existing prognostic scores in ICH such as the modified ICH score (which was used in our study), Functional Outcome in Patients with Primary Intracerebral Hemorrhage score (FUNC) or Modified Emergency Department Intracerebral Hemorrhage score (mEDICH) are not specifically validated in very old patients (44). A recent study (45) showed excellent capability of discriminating the group of elderly patients at risk of short-term death. Additional TMT measurement might add a structural surrogate of sarcopenia in those patients reflecting risk of short-term functional outcome.

Of note, we could confirm a variety of previously known prognostic factors like sex, age, NIHSS at admission, ICH volume, insular localization, intraventricular hemorrhage and pneumonia as substantially associated with functional outcome/death at hospital discharge and 90 days (14, 46).

The present study has several limitations. The main limitations derive from its retrospective nature and the monocentric cohort of patients enrolled. Therefore, e.g., a Charlson Comorbidity index as a compound measure of candidate factors impacting outcome could not be determined (47). However, major comorbidities with potential influence on functional outcome or death within 90 days after ICH onset were documented in patient records (see Table 1 for details). Our results are intended to guide further multicentric prospective validation studies on this topic. The retrospective study design is also conditional for the standard outcome measure latency of up to 90 days, which might be too short to detect relevant prognostic factors for the long-term outcome in ICH. However, already established prognostic factor in ICH were confirmed by the present study such sex, age, symptom severity at admission, several ICH parameters and pneumonia implicating a sufficient validity of our study. Another limit is that no officially accepted TMT cut-off value from literature for the definition of sarcopenia is available: we used the one obtained from the largest population studied and obtained according to current guidelines (19, 21), that also accounted for the difference existing between males and females. On the other hand, a strength of our approach is that our measurement protocol appears to be reliable and easily adoptable in the routine clinical practice, as takes only a few additional minutes and can be potentially automated.

Despite of confirmation of several known prognostic factors like ICH volume, insular localization, intraventricular hemorrhage and others, sarcopenia could not be detected among these. Reasons for this finding remained unclear; larger and prospective studies with longer observation periods are warranted.

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 humans were approved by Institutional Review Board of Medical Faculty, University of Rostock, St.-Georg-Str. 108, 18055 Rostock. The studies were conducted in accordance with the local legislation and institutional

requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

Author contributions

WG: Data curation, Formal analysis, Investigation, Resources, Writing – original draft, Writing – review & editing. JK: Investigation, Resources, Writing – original draft, Writing – review & editing, Data curation. UV: Investigation, Project administration, Resources, Writing – original draft, Writing – review & editing. DC: Investigation, Methodology, Resources, Visualization, Writing – original draft, Writing – review & editing. BZ: Investigation, Resources, Writing – original draft, Writing – review & editing. AR: Investigation, Resources, Writing – original draft, Writing – review & editing. MA: Investigation, Resources, Writing – original draft, Writing – review & editing. DD: Investigation, Methodology, Resources, Visualization, Writing – original draft, Writing – review & editing. S-YW: Investigation, Resources, Writing – original draft, Writing – review & editing. FG: Investigation, Resources, Writing – original draft, Writing – review & editing. TF: Investigation, Resources, Writing – original draft, Writing – review & editing. AS: Data curation, Formal analysis, Investigation, Software, Supervision, Validation, Writing – original draft, Writing – review & editing. MW: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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Conflict of interest

WG reports stock ownerships in AbbVie, AstraZeneca, Bayer AG, Bristol-Myers-Squibb, Eli Lilly & Co., Fresenius SE, Johnson&Johnson, Novartis AG, Pfizer, Viatris. JK reports honoraria for presentations/lectures from Daiichi Sankyo. UV reports stock ownerships in Bayer AG and Roche Holding. AS has received funding from the Deutsche Forschungsgemeinschaft (German Research Association) and the Helmholtz-Association outside the present study. He has received honoraria for presentations/advisory boards/consultations from Global Kinetics Corporation, Esteve, Desitin, Lobsor Pharmaceuticals, STADA, Bial, RG Gesellschaft, Zambon, NovoNordisk and AbbVie outside the present study. He has received royalties from Kohlhammer Verlag and Elsevier Press. He serves as an editorial board member of Stem Cells International. MW reports honoraria for presentations, lectures, consultancies or advisory boards from Bristol-Myers Squibb, Daiichi Sankyo, Bayer Vital, Boehringer Ingelheim, Portola Germany, and AstraZeneca.

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.

Generative AI statement

The author(s) declare that no Gen AI was used in the creation of this manuscript.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2025.1564550/full#supplementary-material

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