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Hybrid (combined endovascular and microsurgical) treatments for cerebrovascular diseases

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Hybrid (combined endovascular and microsurgical) treatments for cerebrovascular diseases

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Editorial: Hybrid (combined endovascular and microsurgical) treatments for cerebrovascular diseases

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Editorial on the Research Topic
Hybrid (combined endovascular and microsurgical) treatments for cerebrovascular diseases

Most cerebrovascular diseases can effectively be treated with microsurgical operations, endovascular procedures or radiation therapy. In some cases, a combination of these techniques may be necessary, either in a staged workflow or simultaneously in a hybrid operation. Technical progress during the last several decades has led to the construction of hybrid operation rooms – combining microsurgical and endovascular facilities in many neurovascular units all over the globe. A classic neurovascular hybrid operation is the surgical exposure of an otherwise inaccessible blood vessel for direct cannulation and endovascular treatment (1, 2). A different form of a hybrid operation is a direct intraoperative control-angiography after microsurgical clipping, which aids in detecting remnants (3) or periprocedural vasospasm (4). However, in such a hybrid approach, the purpose of the endovascular part remains purely diagnostic.

In select cases, a multimodality approach may be needed utilizing both endovascular and microsurgical techniques. For instance, an endovascular aneurysm treatment combined with minimally invasive endoscopic hematoma evacuation (5) or combined clipping/coiling procedures can be used to streamline treatment of a ruptured aneurysm with significant mass effect from the hematoma (6, 7). In addition, microsurgical creation of an extra-intracranial bypass in combination with endovascular aneurysm obliteration may be an alternative for more complex morphologies (8–11). In line with these studies Rennert et al. reports his series of 10 patients with complex, mostly ruptured aneurysms that underwent combined open revascularization (intra-intra or extra-intracranial bypass) and endovascular aneurysm embolization. These cases were not amenable to stand-alone open or endovascular procedures. The combined hybrid approach allowed the authors to recognize and preserve perforator arteries. Many of these modalities focus on unique aspects of either endovascular or microsurgical techniques. There are some hybrid options that utilize some of the endovascular armamentarium in unique ways. A different from of a true hybrid approach for treatment of aneurysms is to achieve

proximal control by means of an endovascular ballon occlusion and treat the aneurysm with microsurgical clipping. This has also been highlighted by the Dallas technique in which balloon occlusion proximally can allow for modulation of aneurysmal dome to allow for easier microsurgical access (12). Similar techniques have also previously been described for some posterior circulation aneurysms (13). The work of Zhang et al. focused on giant paraclinoid aneurysms. They refined the technique and suggested to inject methylene blue into the balloon, in order to improve its visibility, optimize its positioning, and avoid excess radiation exposure.

Although complex aneurysm management is one of the key uses of hybrid cerebrovascular surgery, there are also potential benefits when treating other pathologies including steno-occlusive disease and vascular malformations. The feasibility and potential beneficial effects of presurgical embolization of high-grade arterio-venous malformations (AVMs) in a hybrid operation has been shown several times (14–16). Highly select complex dural fistulas may be treated with a true hybrid approach, if a single modal therapy failed or does not seem to be sufficiently promising (17). Xiao et al. present their series foramen magnum fistulas, underscoring that even in this pathology, there are a small subset that require a hybrid approach.

The optimal treatment strategy for carotid artery stenosis remains controversial (18, 19). Cai et al. share their experience with a hybrid approach (carotid endarterectomy combined with carotid stenting) for complex chronic internal carotid artery occlusion. In their experience, they found revascularization of occluded carotid arteries was safe and feasible and correlated with whether the occluded segment extended past the ophthalmic artery. Similar work in steno-occlusive disease done by Kuo et al. demonstrate a compelling case of a life-threatening innominate artery dissection treated with simultaneous placement of two kissing stents. While one stent was delivered via a percutaneous retrograde endovascular route through the right brachial artery, the second one required a combined hybrid approach, involving open surgical distal clamping of the common carotid artery, and a retrograde endovascular transcarotid approach.

Further articles in this Research Topic cover very rare, interesting cerebrovascular pathological conditions but are not directly related to a therapeutic hybrid approach. As such, Zeng et al. report a *de-novo* formation of an extracranial aneurysm after endovascular embolization of a vertebral epidural arterio-venous fistula in a patient with underlying neurofibromatosis I. The case report of Xu and Li is on the formation of a pseudoaneurysm of the middle meningeal artery after craniotomy with consecutive successful endovascular treatment. Yu et al. reports a study on patients with hypertensive brainstem hemorrhage and found that hematoma volume correlated with the 30-days mortality in these patients. Lastly, with the aim of an optimal patient's monitoring during the operation, Tang et al. present their experience with intraoperative neurophysiological monitoring (MEP/SSEP) during microsurgical clipping of posterior communicating aneurysms, particularly for monitoring the patency and vasospasm of the adjacent anterior choroidal artery.

In summary, the combination of endovascular and microsurgical strategies in a single hybrid operation is both feasible and safe. This approach can address various cerebrovascular disease and its necessity arises in selective complex cases, demanding a sophisticated infrastructure and a high level of specialization and expertise for which we have to train the next generation.

Author contributions

BG: Conceptualization, Project administration, Validation, Writing – original draft, Writing – review & editing. DC: Project administration, Writing – review & editing. KV: Project administration, Writing – review & editing. PG: Project administration, Writing – review & editing. PT: Project administration, Supervision, Writing – review & editing.

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Predictive value of neurophysiological monitoring during posterior communicating artery aneurysm clipping for postoperative neurological deficits

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Objective: This study aimed to evaluate the diagnostic effect of intraoperative neurophysiological monitoring in identifying intraoperative ischemic events and predicting postoperative neurological dysfunction during PCoA aneurysm clipping, as well as to explore the safe duration of intraoperative temporary clipping of the parent artery.
Methods: All 71 patients with PCoA aneurysm underwent craniotomy and aneurysm clipping. MEP and SSEP were used for monitoring during operation to evaluate the influence of MEP/SSEP changes on postoperative neurological function. Receiver operating characteristic (ROC) curve analysis was used to calculate optimal duration of intraoperative temporary clipping.
Results: Patients with intraoperative MEP/SSEP changes were more likely to develop short-term and long-term neurological deficits than those without MEP/SSEP changes ($P < 0.05$). From the ROC curve analysis, the safe time from the initiation of temporary clipping during the operation to the early warning of neurophysiological monitoring was 4.5 min (AUC = 0.735, 95%CI 0.5558-0.912). Taking 4.5 min as the dividing line, the incidence of short-term and long-term neurological dysfunction in patients with temporary clipping >4.5 min was significantly higher than that in patients with temporary clipping ≤4.5 min ($P = 0.015$, $P = 0.018$).
Conclusion: Intraoperative MEP/SSEP changes are significantly associated with postoperative neurological dysfunction in patients with PCoA aneurysms. The optimal duration of temporary clipping of the parent artery during posterior communicating aneurysm clipping was 4.5 min under neurophysiological monitoring.

KEYWORDS

intraoperative neurophysiological monitoring, motor evoked potential, somatosensory evoked potential, posterior communicating artery, aneurysm clipping, temporary clipping

Abbreviations
IONM, intraoperative neurophysiological monitoring; PCoA, Posterior communicating artery; MEP, motor evoked potential; SSEP, somatosensory evoked potential.

Introduction

Posterior communicating artery (PCoA) aneurysms are the second most common aneurysm, accounting for 25 percent of all intracranial aneurysms and 50 percent of all internal carotid artery aneurysms (1, 2). PCoA aneurysms are more prone to rupture than intracranial aneurysms located elsewhere (1). The development of PCoA varies greatly in different individuals, and this difference makes PCoA aneurysms either the most manageable intracranial aneurysm or the most difficult to intervene. At the same time, PCoA sends out multiple important branch vessels to supply blood to important structures such as the surrounding thalamus, caudate nucleus, internal capsule, etc. During craniotomy aneurysm clipping, improper operation affects the normal blood supply of PCoA and its branches, resulting in Complications such as postoperative ischemic brain injury in patients (3). Since the 1970s, intraoperative neurophysiological monitoring (IONM) technology has been used in aneurysm surgery to avoid neurological deficits caused by transient postoperative ischemia (4). At present, IONM is widely used in intracranial aneurysm clipping, among which motor evoked potential (MEP) and somatosensory evoked potential (SSEP) are safe and effective methods for real-time monitoring of acute cerebral ischemic injury (5). In addition, MEP and SSEP monitoring plays an important role in preventing ischemic brain injury caused by occlusion of parent artery for too long during surgery. In recent decades, many teams have studied the optimal safe time for temporary clipping of the parent artery during surgery, but so far, there is still no unified definition standard (6–8). In clinical practice, we have found that many studies are imprecise in defining the safe duration of temporary clipping, because aneurysms in different locations tolerate cerebral ischemia differently. Therefore, the ideal standard for predicting intraoperative cerebral ischemia should be determined according to the location of the aneurysm and the actual situation during the operation. In this study, we chose PCoA aneurysm as the entry point to study the application of IONM to analyze the specific correlation between the safe duration of temporary clipping and the location of the aneurysm, in order to provide more information for the clinical application of IONM. For reference, the specific content is reported as follows.

Materials and methods

Patient population

A total of 71 patients with PCoA aneurysms in neurosurgery of Qingdao University Affiliated Hospital from April 2019 to May 2022 were retrospectively included, and were diagnosed by preoperative CT, CTA and/or DSA. All patients underwent craniotomy to clip the aneurysm. There were 14 males and 57 females, ranging in age from 37 to 81 years old, with an average of (61.62 ± 9.35) years old. Aneurysm rupture occurred in 29 cases, and 42 cases did not rupture. Aneurysm size: <5 mm in 29 cases, 5–10 mm in 31 cases, and 10–25 mm in 11 cases. There were 31 patients with temporary clipping of parent artery during operation, and 40 patients without temporary clipping. This study was approved by the ethics committee of our hospital. All patients gave informed consent to participate in the study.

Surgical procedure

The microsurgical approach is the pterional approach. After the aneurysm is exposed through fine dissection, the neck of the aneurysm is carefully separated and identified, and the parent artery is temporarily clipped according to the specific situation during the operation. Neurophysiological monitoring technology is applied throughout the operation. A decrease in MEP and SSEP amplitude of more than 50% is considered a significant change requiring early warning and intervention after excluding anesthetic and physiological effects. When the amplitude of MEP and SSEP monitoring decreases to the alarm threshold, the surgeon will be informed immediately, and the cause of ischemia will be determined according to the actual operation during the operation, and the operation will be stopped and adjusted accordingly, including releasing temporary clips, releasing brain retractors, adjusting aneurysm clips, applying papaverine wet compresses and other surgical operations, and continuing the operation after the abnormal MEP and (or) SSEP return to the baseline level.

Intraoperative MEP and SSEP monitoring

All patients were treated with intravenous inhalation anesthesia. Typically, intraoperative muscle relaxants are not administered after induction of anesthesia. The Cadwell Cascade 32-lead intraoperative evoked potential monitoring system was used, and the corresponding IONM scheme was designed according to the location of the aneurysm. According to the international EEG 10/20 standard, electrodes are placed and parameters are set: (1) SSEP monitoring, the recording electrodes are spiral electrodes, the upper limbs are placed at C3′ and C4′, the lower limbs are placed at Cz, and the reference electrodes are placed at FPz. The stimulation electrodes were needle electrodes, the upper limb was the median nerve of the wrist, and the lower limb was the posterior tibial nerve of the ankle. Constant current

monophasic pulse stimulation was used, the stimulation frequency was 2.79 Hz, the stimulation interval was 200 μs, the current stimulation intensity was 15–35 mA, the sensitivity was 1–10 μV, the band-pass was 30–500 Hz, the duration was 50–100 ms, and the average superposition was 100–200 times. (2) MEP monitoring, the stimulation electrodes are placed on C3, C4 or C1, C2, the two act as reference electrodes for each other, the recording electrodes are placed on the upper limb abductor pollicis brevis and the lower limb adductor muscle, and short series of electrical stimulation is used, generally given 5–8 single series of stimulation, each single stimulation duration 50 ms, stimulation interval 1–2 ms, stimulation voltage 100–400 V, sensitivity 50–200 μV, bandpass 100–3000 Hz, analysis time 100 ms. MEP and SSEP were recorded once after anesthesia and before opening of the dura to obtain baseline values. After the dura mater was opened, MEP and SSEP were recorded routinely every 5 min, and MEP and SSEP should be recorded frequently when the operation proceeded to critical steps, such as temporary clipping of the parent artery and adjustment of aneurysm clips. In the event of a warning, the surgeon should take appropriate measures, such as lifting the temporary occlusion or adjusting the clip placement, to restore the MEP and SSEP amplitudes and prevent ischemic injury.

Outcome criteria and evaluation

The curative effect evaluation of 71 patients was based on 1 day and 3 months after surgery, and the score (Glasgow Outcome Scare, GOS) was used to evaluate the prognosis. The higher the score, the better the prognosis and vice versa. Neurological deficits at 1 day after surgery were defined as short-term neurological deficits, while neurological deficits at 3 months postoperatively were defined as long-term neurological deficits. Postoperative evaluation of all patients after surgery was performed by a neurosurgeon and a neurophysiological monitoring physician.

Statistical analysis

Statistical analysis was performed using SPSS 26.0 software. Measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$), and comparisons between groups were expressed by t test or nonparametric test; enumeration data were expressed by number of cases or percentages, and comparisons between groups were expressed by χ^2 test or Fisher's exact test. $P < 0.05$ was considered to be statistically significant. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal duration of intraoperative temporary clipping and ischemia tolerance time for changes in MEP/SSEP.

Results

The relationship between intraoperative MEP/SSEP changes and clinical characteristics of patients with PCoA aneurysm

Of all 71 patients with PCoA aneurysm, 21 (29.6%) showed IONM changes, 17(23.9%) showed MEP changes, 11(15.5%) showed SSEP changes, and 7 (9.9%) showed combined MEP and SSEP changes. The characteristics of patients classified according to the occurrence of MEP/SSEP changes are summarized in Table 1. There were no differences in gender, age, aneurysm size, and rupture of patients with or without MEP/SSEP changes, but the incidence of temporary clipping in patients with MEP/SSEP changes was significantly higher than that in patients without changes ($P < 0.05$).

Intraoperative MEP/SSEP monitoring results and postoperative neurological dysfunction

Of the 17 patients with PCoA aneurysms with significant intraoperative MEP changes, 8 (47.1%) had short-term neurological deficits and 4 (23.5%) had long-term neurological deficits. Of the 54 patients with no intraoperative MEP change, 3 (5.6%) had short-term neurological deficits and 1 (1.9%) had long-term neurological deficits. Patients with intraoperative MEP changes were more likely to develop short-term and long-term neurological deficits than those without MEP changes ($P < 0.001$, $P < 0.05$, Fisher's exact probability, Table 2). Among 11 aneurysm patients with significant intraoperative SSEP changes, 5 (45.5%) had short-term neurological deficits and 3 (27.3%) long-term neurological deficits. Of the 60 patients with no intraoperative SSEP changes, 6 (10.0%) had short-term neurological deficits and 2 (3.3%) had long-term neurological deficits. Overall, the conclusions are consistent with those obtained from the MEP monitoring described above ($P < 0.05$, chi-square test, $P < 0.05$, Fisher's exact probability, Table 3).

There were 31 patients with temporary clipping during operation. From the ROC curve analysis, it can be seen that the safe duration from the initiation of temporary clipping to the occurrence of MEP/SSEP warning was 4.5 min respectively (area under the curve (AUC) = 0.735, 95% confidence interval [CI] 0.558–0.912, Figure 1). The duration of temporary clipping was longer than 4.5 min in 15 patients, of which 7 (46.7%) patients developed short-term neurological deficits after surgery, and 5 (33.3%) patients developed long-term functional deficits. Temporary clipping time of 16 patients was within 4.5 min, of which only 1 patient (6.25%) developed short-term neurological dysfunction, and none (0%) developed long-term neurological dysfunction. The odds

TABLE 1 Clinical characteristics of 71 patients with posterior communicating artery aneurysm.

Parameter	Total ($n = 71$)	MEP			SSEP		
		MEP changes ($n = 17$)	No MEP changes ($n = 54$)	P	SSEP changes ($n = 11$)	No SSEP changes ($n = 60$)	P
Age				0.258			0.129
Mean ± SD	61.62 ± 9.35	63.06 ± 10.31	61.17 ± 9.09		61.73 ± 6.44	61.60 ± 9.84	
Gender				0.806			0.889
Male	14	3	11		2	12	
Female	57	14	43		9	48	
SAH				0.245			0.735
Yes	29	9	20		5	24	
No	42	8	34		6	36	
Size (mm)				0.095			0.468
<5	29	5	25		4	25	
5–10	31	7	23		4	27	
10–25	11	5	6		3	8	
Temporary clipping				0.000			0.006
Yes	31	14	17		9	22	
No	40	3	37		2	38	

of postoperative short-term and long-term neurological dysfunction were significantly higher in patients with temporary clipping >4.5 min than in patients with temporary clipping ≤4.5 min ($P = 0.015$, $P = 0.018$, Fisher's exact probability, Table 4).

Intraoperative MEP/SSEP changes and GOS score

The GOS scores at 1 day (short-term) and 3 months (long-term) after surgery were compared in patients with or without intraoperative MEP/SSEP changes. On 1 day after surgery, patients with no intraoperative MEP change had significantly higher GOS scores than those with MEP change (4.89 ± 0.46 vs. 4.24 ± 0.97, $P < 0.001$, Mann–Whitney U test, Table 2). At 3-momth follow-up, the results were the same (4.98 ± 0.14 vs. 4.65 ± 0.70, $P < 0.05$, Mann–Whitney U test, Table 2). For intraoperative SSEP monitoring follow-up results, 1 day after surgery, SSEP did not change vs. SSEP changed (4.87 ± 0.50 vs. 4.00 ± 1.00, $P < 0.001$, Mann–Whitney U test, Table 3). At 3-month follow-up, there was no change in SSEP vs. change in SSEP (4.95 ± 0.29 vs. 4.64 ± 0.67, $P < 0.05$, Mann–Whitney U test, Table 3).

TABLE 2 Relationship between intraoperative MEP and postoperative neurological dysfunction and GOS score.

	MEP changes (n, %)	No MEP changes (n, %)	Total ($n = 71$)	P
Short-term neurological dysfunction (n,%)				<0.001
Yes	8 (47.1%)	3 (5.6%)	11	
No	9 (52.9%)	51 (94.4%)	60	
Long-term neurological dysfunction (n,%)				<0.05
Yes	4 (23.5%)	1 (1.9%)	5	
No	13 (76.5%)	53 (98.1%)	66	
GOS				
1-day follow-up	4.24 ± 0.97	4.89 ± 0.46		<0.001
3-month follow-up	4.65 ± 0.70	4.98 ± 0.14		<0.05

TABLE 3 Relationship between intraoperative SSEP and postoperative neurological dysfunction and GOS score.

	SSEP changes (n, %)	No SSEP changes (n, %)	Total (n, %)	P
Short-term neurological dysfunction (n,%)				<0.05
Yes	5 (45.5%)	6 (10.0%)	11	
No	6 (54.5%)	54 (90.0%)	60	
Long-term neurological dysfunction (n,%)				<0.05
Yes	3 (27.3%)	2 (3.3%)	5	
No	8 (72.7%)	58 (96.7%)	66	
GOS				
1-day follow-up	4.00 ± 1.00	4.87 ± 0.50		<0.001
3-month follow-up	4.64 ± 0.67	4.95 ± 0.29		<0.05

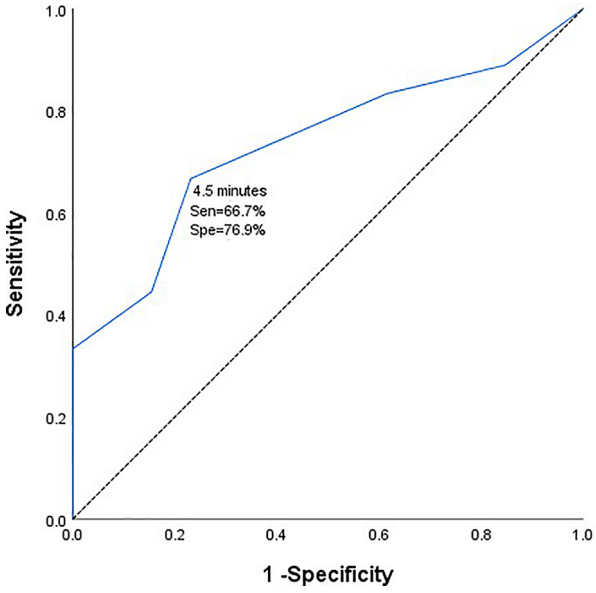

FIGURE 1
Receiver operating characteristic curve of duration of intraoperative temporary clipping and electrophysiological monitoring and warning.

Discussion

At present, MEP and SSEP monitoring are commonly used electrophysiological monitoring techniques in craniotomy aneurysm clipping, and are also important means to predict whether patients will develop new neurological dysfunction after surgery. Intraoperative cerebral ischemia is an important cause of postoperative neurological dysfunction and even death. Intraoperative continuous SSEP and MEP monitoring can evaluate the integrity of the nervous system in real time, detect intraoperative cerebral ischemia and brain tissue damage in time, and then take corresponding intervention measures, which greatly reduces postoperative complications.

TABLE 4 Relationship between temporary clipping time and postoperative neurological dysfunction.

	Temporary clipping duration		Total ($n = 31$)	P
	≤4.5 min	>4.5 min		
Short-term neurological dysfunction (n,%)				0.015
Yes	1 (6.25%)	7 (46.7%)	8	
No	15 (93.75%)	8 (53.3%)	23	
Long-term neurological dysfunction (n,%)				0.018
Yes	0 (0%)	5 (33.3%)	5	
No	16 (100%)	10 (66.7%)	26	

In our study, the incidence of postoperative new neurological dysfunction was 47.1% (8/17) and 5.6% (3/54) in patients with and without intraoperative MEP changes, respectively, and the GOS score was 4.24 ± 0.97 and 4.89 ± 0.46. For SSEP, the incidence was 45.5% (5/11) and 10.0% (6/60), and the GOS scores were 4.00 ± 1.00 and 4.87 ± 0.50, respectively. Our analysis showed that intraoperative MEP and SSEP changes were significantly associated with new postoperative neurological deficits and lower quality of life. Our review of the literature found that other research groups have come to the same conclusion. Nakagawa I et al. believed that intraoperative MEP changes could reliably predict postoperative neurological dysfunction, in which the permanent loss of intraoperative MEP would lead to severe postoperative neurological dysfunction (9). Guo D et al. reported that postoperative neurological function and quality of life in patients with significant changes in MEP were significantly lower than those in patients with no changes in MEP (10). A meta-analysis by Thirumala PD et al. showed that patients with intraoperative changes in SSEP were 7 times more likely to develop postoperative neurological dysfunction than those without changes (11). From this we can see that patients with significant intraoperative changes in MEP and SSEP have a significantly increased risk of developing new neurological deficits after surgery and have a worse prognosis.

During clipping of a PCoA aneurysm, temporary clipping of the parent artery is often required to completely stop blood flow to the aneurysm. The risk of postoperative ischemia-induced neurological deficits greatly increases with prolonged temporary clipping. IONM can monitor patients for intraoperative cerebral cortical ischemia and subcortical ischemia during the temporary clipping of the blood supply of the parent artery (12). Temporary clipping has been used in intracranial aneurysm clipping since 1928, and despite evolving medical techniques and surgical strategies, controversy over the maximum allowable duration and safety of temporary clipping remains unanswered (13). In a noncontemporaneous prospective analysis of 132 patients with aneurysms at Massachusetts General Hospital from 1991 to 1993, the safe duration of intraoperative temporary clipping should not exceed 20 min (14). In 2014, Griessenauer CJ et al. came to a similar conclusion. They concluded that the longest duration of intraoperative temporary clipping in SAH and unruptured aneurysms was 19.4 min and 16.1 min, respectively, and within these timeframes, patients did not experience neurological deficits postoperatively (15, 16). With the advancement of medical technology and the application of intraoperative neurophysiological techniques, we can detect ischemic changes faster before clinical manifestations in patients, thereby improving the safety of temporary clipping. A 2020 study by Kameda et al. reported a safe time of 5 min for the longest interim clip under intraoperative neurophysiological monitoring (17). Our team published a

report in 2021 that temporary clipping of the parent artery should not exceed 6 min. In this study, we analyzed the safe duration from the initiation of temporary clipping to the change in intraoperative MEP/SSEP monitoring of 4.5 min for the specificity of PCoA aneurysm location (AUC = 0.735, 95% CI 0.558-0.912). Moreover, the incidence of short-term and long-term neurological dysfunction was significantly higher in patients with temporary clipping >4.5 min than in patients with temporary clipping ≤4.5 min ($P = 0.015$, $P = 0.018$, Fisher's exact probability). From this we can see that the safe time of temporary clipping is different for different locations and characteristics of aneurysms, and we believe that 4.5 min is the best cut-off value for temporary clipping in PCoA aneurysm clipping. This finding extends our past findings and represents a new step toward an individualized prediction system for postoperative neurological dysfunction in patients with aneurysms.

In this study, MEP/SSEP changes occurred in 21 cases, including 18 cases due to prolonged temporary clipping of the internal carotid artery during surgery, 3 cases due to mis-clamping of important perforating vessels of PCoA, and 11 cases with new neurological dysfunction after operation. It can be seen that IONM plays an important role in predicting intraoperative cerebral ischemia and preventing new postoperative neurological dysfunction. It is worth mentioning that we found that only significant changes in MEP occurred in 3 patients who had mis-clamped important perforators due to PCoA, but no changes in SSEP. This also confirms to some extent that MEP monitoring is superior to SSEP in predicting motor impairment caused by subcortical perforator ischemia (18). However, MEP is less sensitive than SSEP in predicting cerebral cortical ischemia, and MEP is greatly affected by anesthesia factors, and its waveform is less stable than SSEP. In the current monitoring of intracranial aneurysm clipping surgery, MEP as a supplement to SEP, combined monitoring of the two can reduce the probability of cerebral cortical and subcortical ischemia during operation, and provide a reliable theoretical basis for the time limit of parent artery occlusion during operation.

Conclusions

Regarding the application of IONM in PCoA aneurysms, we have the following three experiences: First, one of the goals of this study was to determine the relationship between intraoperative MEP and SSEP changes and postoperative neurological dysfunction in patients. Patients with changes in MEP and SSEP had a significantly higher risk of postoperative neurological dysfunction than those without changes. Second, the critical thresholds for intraoperative changes from temporary clipping to intraoperative neurophysiological monitoring were 4.5 min, respectively, a finding that has important clinical implications. Third, at present, most neurosurgeons do not have a comprehensive understanding of the application value of IONM in craniotomy and artery clipping. Predictive value, while ignoring the actual application of IONM in predicting ischemic events caused by other reasons (such as excessive clipping of the aneurysm neck, associated clipping of collateral vessels, and incorrect clipping of perforating arteries, etc.) clinical significance.

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

Conception and design: FT, YF. Acquisition of data: JW, WT. Analysis and interpretation of data: FT, SL. Drafting the article: FT. Critically revising the article: YF. Reviewed the submitted version of the manuscript: YF, SL, JW. Statistical analysis: FT, SL. Administrative/technical/material support: all authors. All authors contributed to the article and approved the submitted version.

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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.

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Visualization balloon occlusion-assisted technique in the treatment of large or giant paraclinoid aneurysms: A study of 17 cases series

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Objective: Although balloon-assisted techniques are valuable in aneurysm clipping, repeated angiography and fluoroscopy are required to understand the location and shape of the balloon. This study investigated the value of visualization balloon occlusion-assisted techniques in aneurysm hybridization procedures.

Methods: We propose a visualization balloon technique that injects methylene blue into the balloon, allowing it to be well visualized under a microscope without repeated angiography. This study retrospects the medical records of 17 large or giant paraclinoid aneurysms treated by a visualization balloon occlusion-assisted technique in a hybrid operating room. Intraoperative surgical techniques, postoperative complications, and immediate and long-term angiographic findings are highlighted.

Results: All 17 patients had safe and successful aneurysm clipping surgery with complete angiographic occlusion. Under the microscope, the balloon injected with methylene blue is visible through the arterial wall. The position and shape of the balloon can be monitored in real time without repeated angiography and fluoroscopic guidance. Two cases of intraoperative visualization balloon shift and slip into the aneurysm cavity were detected in time, and there were no cases of balloon misclipping or difficult removal. Of 17 patients, four patients (23.5%) experienced short-term complications, including pulmonary infection (11.8%), abducens nerve paralysis (5.9%), and thalamus hemorrhage (5.9%). The rate of vision recovery among patients with previous visual deficits was 70% (7 of 10 patients). The mean follow-up duration was 32.76 months. No aneurysms or neurological deficits recurred among all patients who completed the follow-up.

Conclusion: Our study indicates that microsurgical clipping with the visualization balloon occlusion-assisted technique seems to be a safe and effective method for patients with large or giant paraclinoid aneurysms to reduce the surgical difficulty and simplify the operation process of microsurgical treatment alone.

KEYWORDS

paraclinoid aneurysms, visualization, balloon occlusion-assisted technique, microsurgical clipping, hybrid operation

Introduction

Paraclinoid aneurysms can be defined as intracranial aneurysms that originate between the distal dural ring and the initial segment of the posterior communicating artery (1). Some patients with paraclinoid aneurysms are likely to present visual acuity and field deficits caused by the aneurysms' proximity to the ophthalmic artery and optic, oculomotor, trochlear, and abducens nerves (2–5). Traditionally, paraclinoid aneurysms are treated with surgical clipping. For large (range from 10 to 25 mm in diameter) and giant (≥25 mm in diameter) paraclinoid aneurysms with a broad neck, calcification, and intraluminal thrombus, direct surgical clipping is complex. It is associated with high mortality and disability rates. Modern advancements in endovascular treatment for these aneurysms have replaced a large portion of surgical clipping. As a novel endovascular treatment, the pipeline embolization device (PED) has been demonstrated to be effective for wide neck and giant aneurysms (6–8). Although the emerging array of advanced endovascular treatment materials has shown exceptional surgical outcomes, the mass effect cannot be reduced, especially in large and giant aneurysms (4, 9–11). Moreover, endovascular therapy is usually not indicated for some patients who cannot tolerate regular anticoagulation therapy, such as in combination with gastrointestinal dysfunction.

A hybrid operating room, known as the "one-stop" operating room, is fully equipped with medical imaging devices, such as high-quality angiographic equipment (12). It created a new procedure named hybrid surgery, which combines endovascular interventions and open surgery, which inherits the advantages of two treatments. Some studies reported that the surgical procedure in treating internal cerebral large or giant aneurysms had an excellent clinical outcome and a low number of complications. In previous studies, a balloon occlusion-assisted technique was used to block the proximal end of the aneurysm or straddle the aneurysm neck better to control the blood flow of the parent artery. As the tension of a giant paraclinoid aneurysm decreases, aneurysmal clips can be precisely placed with promising results (13–16). However, repeated angiography and fluoroscopy are required to understand the location and shape of the balloon during this type of hybrid operation. Meanwhile, there are also some clinical and technical difficulties, such as balloon rupture and displacement, slippage of the distal end of the balloon into the aneurysm cavity, and being mistaken.

We propose a visualization balloon technique in which the balloon is injected with methylene blue, allowing it to visualize well under the microscope without repeated angiography (Figure 1). Moreover, since July 2018, we have been applying this technique in the hybridization operating room to treat paraclinoid aneurysm clipping. This study retrospects the medical records of 17 cases of visualization balloon-assisted technique for the treatment of large or giant paraclinoid aneurysms, reporting on the surgical technique and the results of the postoperative application of this technique.

Material and methods

A retrospective analysis of 17 patients with a paraclinoid aneurysm treated with the visualization balloon occlusion-assisted technique in a hybrid operation room was performed between July 2018 and July 2020. The Wuhan University Zhongnan Hospital Research Ethics Committee approval was not required for this retrospective analysis of deidentified medical data. Written informed consent was waived by this Committee, as it was a retrospective analysis of our usual everyday work. The data of the patients were anonymized for this analysis. The confidential information of the patients was protected according to the national normative.

Patient selection and data collection

Inclusion criteria were as follows: (1) Patients with large (10–25 mm in diameter) or giant (≥25 mm in diameter) aneurysms with a neck width of >5 mm and intraluminal thrombus, aneurysmal wall calcifications or atherosclerosis were included in the study. (2) The aneurysms were confirmed to be paraclinoid aneurysms by CT angiography (CTA) or digital subtraction angiography (DSA) before the operation. (3) No contraindications (heart failure, liver dysfunction, and renal dysfunction) for surgical intervention and craniotomy were present. (4) A one-stop operation involving balloon placement and aneurysm clipping was performed in the same hybrid operation room; no operations were performed in stages or multiple rooms. (5) Only patients in whom the balloon was placed at the neck of the aneurysm instead of the petrous internal carotid artery (ICA) or other positions were included in the study.

Seventeen patients were included in the final analyses. Patients' data were collected and statistically analyzed: basic information; aneurysm characteristics based on preoperative CTA or DSA; CT findings; intraoperative video data; intraoperative and postoperative DSA data; postoperative complications; follow-up data.

Surgical procedures

The ICA balloon occlusion test (BOT), the cross circulation test, and Allcock's test was performed to understand cerebral blood flow compensation. Surgical procedures were performed using a biplane flat panel angiographic suite (UNIQ FD2020 Hybrid-OR, Philips, Eindhoven, The Netherlands) with 3D reconstruction under general anesthesia (Figures 2A, B). The surgical procedure was divided into the following steps:

(1) Balloon placement: After successfully placing the electrophysiological monitoring electrode and the catheter, the Seldinger technique was used to perform angiography of the lesion side carotid artery. Anteroposterior, lateral, and three-dimensional rotational views were obtained to clearly show the aneurysm's morphology, size, direction, and neck width. Next, a 4 × 20 mm Scepter C Occlusion Balloon (MicroVention, USA) was selected for placement at the aneurysm neck, ensuring that the balloon completely covered the aneurysm neck (Figure 2C). After placing the balloon, the contrast agent diluted with methylene blue (1 ml methylene blue was added to 10–20 ml of contrast agent) was used to expand the balloon tentatively, and the pressure required to block the blood supply of the aneurysm entirely was recorded. When satisfactory results were obtained, the balloon was deflated, and the guiding and balloon catheter was fixed correctly to prevent the balloon from shifting during the clipping process. To prevent intravascular thrombosis,

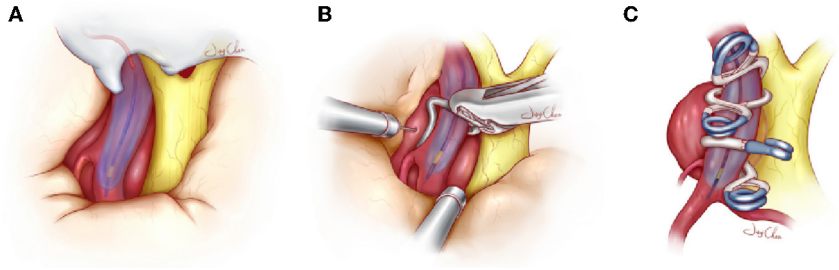

FIGURE 1
Schematic diagram about the visualization balloon occlusion-assisted technique used to treat large and giant paraclinoid aneurysms. **(A)** The balloon is successfully navigated across the neck of the aneurysm and inflated by a contrast agent diluted with methylene blue, which is identified under the microscope. **(B)** Once the balloon is inflated with the aid of microscopic visualization and the blood supply of the aneurysm has been completely blocked, the dome of the aneurysm is punctured or cut to release the remaining hematoma or thrombus. When the aneurysm collapses, the clots and plaques in the cavity are further removed, which facilitates accurate clip placement. **(C)** Accurate tandem clipping is performed with fenestrated clips or straight clips with the aid of the inflated balloon, which provides tactile and visual feedback to the surgeon. During clip closure, the surgeon can distinguish the vessel lumen and contiguous perforating branches from the longitudinal visualization balloon, and this helps to preserve the true lumen of the parent vessel and collateral blood vessels. Once the complete exclusion is confirmed, the deflated balloon and guide catheter are removed.

the catheter was successively washed with heparinized saline during the clip occlusion procedure (500 ml normal saline:500 UI heparin).

(2) Microsurgical clipping of aneurysms with visualization balloon occlusion-assisted technique: After the balloon placement, standard craniotomy was performed with a pterion approach, and the sphenoid ridge and anterior clinoid process were resected in extradural. Generally, it was difficult to completely expose the body and neck of aneurysms with large volumes and high tension. The distal and proximal dural ring of the carotid artery and the outer membrane of the optic canal was sharply separated further to expand the space for exposure of the ICA. Exposure to essential ICA branches, such as the ophthalmic artery and posterior communicating artery, increased surgical safety. After the exposure, the interventional physician dilated the balloon with a contrast agent diluted with methylene blue at a suitable pressure (the experimentally recorded value at the time of balloon insertion before craniotomy). This allowed for clear visualization of the ICA under the microscope (Figure 2D). The blood flow to the aneurysm was blocked entirely (the blocking time was recorded). Usually no more than 5 min per attempt, and the obstruction time should be adjusted in real-time according to the changes observed by monitoring), and the tension of the aneurysm was decreased. If necessary, a puncture or minor incision was made for further decompression by suction. An appropriate aneurysmal clip was applied to reconstruct the ICA and clip the aneurysm while the important branches were well protected (Figure 2E).

(3) After successful clipping, the balloon was deflated and the blood flow to the parent artery was restored (Figure 2F). Angiography of the parent artery was performed after observation of aneurysm obliteration without bleeding. The angiography examination showed that the artery was well perfused with no residual aneurysm neck, no parent artery stenosis, and no inadvertently clipped branch vessel (Figure 2G). If any residual aneurysm, misclipping, or stenosis of the parent artery was present, adjustments were immediately made under the microscope until the angiography showed no problems. The balloon and guiding catheter were withdrawn after successful clip occlusion. After the operation, CT (Xper; Philips, Amsterdam, Netherlands) was immediately performed through the angiography equipment (Philips) to determine whether a hematoma or infarction was present (Figure 2H). This patient gained full consciousness without a neurological deficit (Figure 2I).

Postoperative management and follow-up

After the operation, all patients returned to the neurosurgical intensive care unit (ICU) with endotracheal intubation and were placed on a ventilator to assist their breathing. With the blood pressure controlled, the perfusion maintained, the internal environment stabilized, moderate sedation and analgesia were performed, and the tracheal tube was removed.

Complete aneurysm occlusion was determined based on postoperative angiography. CT examination was performed the next day to determine whether hemorrhage or infarction was present. The sutures were removed on postoperative day 7, and the patients were discharged when they no longer had discomfort and had undergone all relevant examinations, including CTA. Regular follow-up was conducted after discharge, and DSA reexamination was generally performed 3–6 months after the surgery.

Results

Patient and aneurysm characteristics

Between July 2018 and July 2020, 17 patients with 17 large and giant paraclinoid aneurysms were treated using microsurgical clipping assisted by a visualization balloon occlusion-assisted technique (Table 1). A total of 6 men (35.3%) and 11 women (64.7%) with an average age of 59.65 years were enrolled in this study. A history of preoperative visual deficit, hypertension, diabetes, and coronary artery disease was present in 10 (58.8%), seven (41.2%), one (5.9%), and one (5.9%), respectively. Overall, there were four cases (23.5%) with subarachnoid hemorrhage (SAH).

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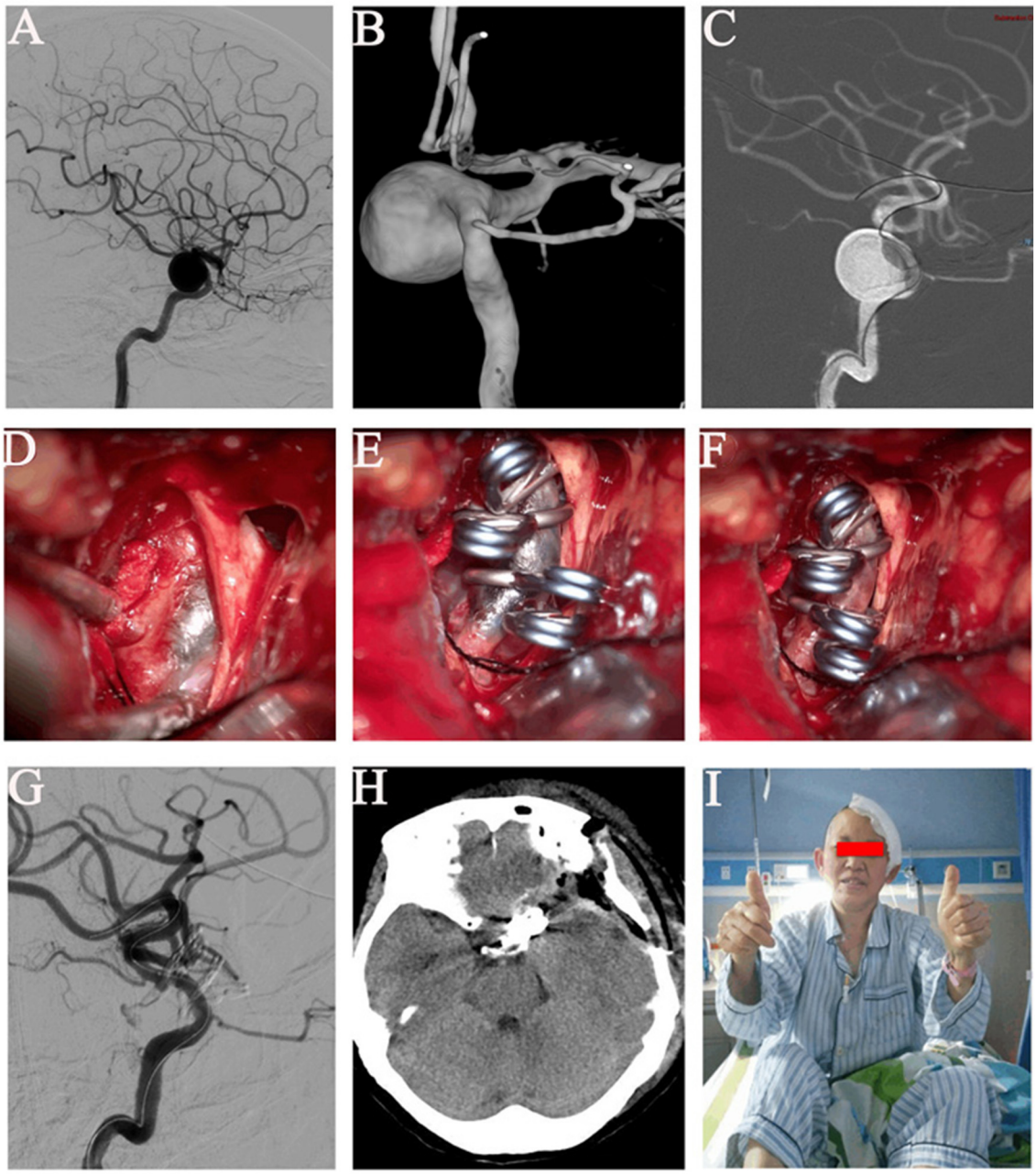

FIGURE 2
Images of a left giant paraclinoid aneurysm. **(A)** Angiography of a left wide-necked giant paraclinoid aneurysm of the internal carotid artery. **(B)** Three-dimensional digital subtraction angiography of the left wide-necked giant paraclinoid aneurysm. **(C)** The balloon was successfully inserted into the position of the neck of the aneurysm. **(D)** The balloon was dilated with methylene blue and could be clearly seen under the microscope, and the balloon adhered well to the wall. The blood supply of the aneurysm was completely blocked. **(E)** When the neck was blocked, the aneurysm was successfully clipped and the parent artery was reconstructed. **(F)** The balloon was withdrawn after the aneurysm had been satisfactorily clipped. **(G)** Digital subtraction angiography of the left internal carotid artery after successful clip occlusion showed no parent artery stenosis, no residual aneurysm, and a well-perfused distal vessel. **(H)** Head computed tomography on postoperative day 2. **(I)** This patient gained full consciousness without a neurological deficit.

There were 17 large or giant paraclinoid aneurysms treated with microsurgical clipping assisted by a visualization balloon occlusion-assisted technique. Eleven (64.7%) aneurysms were located on the left, and six (35.3%) were on the right. The aneurysm size ranged from 13.3 to 27.4 mm (mean, 20.08 mm). Fourteen (82.4%) aneurysms measured 10–25 mm, and three (17.6%) were $\geq$25 mm. The neck size of all aneurysms was >5 mm (mean, 9.49 $\pm$ 1.73 mm).

Postoperative and follow-up

According to the postoperative angiography studies, all 17 lesions were excluded entirely from the parent vessel. All aneurysms were clipped (complete exclusion in 100% on follow-up angiography). There was no parent artery stenosis or distal embolization of an intraluminal thrombus.

The overall short-term disability rate was 23.5%. Two patients developed a pulmonary infection, and one exhibited abducens nerve paralysis. These complications were mild and were resolved entirely by pharmaceutical therapy after the operation. One patient presented with a small amount of thalamus hemorrhage, mixed aphasia, and contralateral limb hemiparesis after the operation. No severe complications occurred, such as postoperative carotid thrombosis or parent artery stenosis. Among the 17 patients, 10 (58.8%) had preoperative vision deficits. Seven patients recovered their vision after surgical decompression of the optic apparatus, and three patients had no improvement. The rate of vision recovery among patients with previous visual deficits was 70% (7 of 10 patients). Other than these instances, no new occurrence of visual impairment was observed in the other patients.

The follow-up duration ranged from 24 to 48 months (mean, 32.76 ± 7.57 months). Sixteen (94.1%) patients had good clinical outcomes [modified Rankin Scale (mRS) score of 0–1]. DSA examination showed no aneurysmal recurrence or new neurological deficits during the follow-up period.

Discussion

For many years, treating aneurysms in the paraclinoid region has been a significant challenge for neurosurgeons because of the complex anatomical structure, narrow operative space, and high mortality and disability rates. In particular, large and giant aneurysms are often wide-necked and calcified and may contain an intraluminal thrombus. Direct clipping is not easy to be performed, and the incomplete aneurysm obliteration rate and parent artery stenosis rate are high, potentially reaching 15% (17). It is vital to control the proximal blood flow of the parent artery during the operation. Several studies have shown that the proximal blood flow of the parent artery can be controlled through cervical vascular exposure and blockage, which plays an essential promoting role in the surgical clipping of such aneurysms (14, 18, 19). However, because of the retrograde blood flow of the posterior communicating artery, ophthalmic artery, cavernous sinus segment of the ICA, and perforating branches, high tension of the aneurysm still exists. In this regard, some researchers have further introduced the balloon-assisted retrograde suction decompression method to reduce the aneurysm tension further (13, 15, 16, 20). This method makes surgical treatment of aneurysms in this segment possible. However, other reports have questioned its safety, proposing that this technology further increases the rate of embolic events, cerebral vasospasm, and other postoperative complications (21).

Since the beginning of the twenty-first century, with the development of hybrid operations and successful applications in neurosurgery, the advantages of neurological interventions and microsurgery have been effectively complementary. Neurosurgeons can not only perform microsurgeries but also directly conduct angiography, interventional embolization treatment, and immediate postoperative observation, which can significantly improve the success rate of surgery and reduce complications. For complex paraclinoid aneurysms, the balloon occlusion-assisted technique has been successfully performed by some neurosurgeons and neurointerventionists in hybrid operating rooms. In 2004, Thorell et al. (16) reported the successful clipping of giant paraclinoid aneurysms by the balloon occlusion-assisted technique at the level of the aneurysm neck, and no surgery-related complications were observed. In addition, the postoperative visual defects were improved. Other successful cases have since been reported in major clinical centers (15, 22). Chao et al. from West China Hospital of Sichuan University performed a clinical study in which 24 patients underwent microsurgical clipping with the balloon occlusion-assisted technique in the neck of the aneurysm, which achieved good clinical results (20). Nevertheless, repeated angiography and fluoroscopy are always needed during this hybrid operation. Meanwhile, these events, such as balloon rupture and displacement, slippage of the distal end of the balloon into the aneurysm cavity, and being mistaken, are inevitable.

In this study, we place the balloon on the level of the aneurysm neck in a way that covers the entire orifice of the aneurysm and thus wholly blocks the blood supply of the aneurysm, and then microclipping the aneurysm. This technique has two significant advantages. First, the balloon is placed by endovascular intervention, allowing it to quickly reach an area difficult to reach by craniotomy and effectively avoiding the trauma and pain caused by cervical vascular exposure. More importantly, the proximal and distal ends of the parent artery can be controlled more effectively simultaneously, blocking the parent artery's blood flow and nearby perforators. This can markedly reduce the tension of the aneurysm and provide more space for successful exposure of the aneurysm and adjacent perforator vessels. Even coils placed in the aneurysm, intraluminal thrombi, and sclerotic plaques can be removed to treat more complex aneurysms. This reduces bleeding and thrombotic events and thus decreases the incidence of complications. All aneurysms were safely clipped in our series. There were no cases of severe bleeding or distal embolization of an intraluminal thrombus.

Seventeen patients were treated with a Scepter balloon for the blocking in this study because it provided improved guidance in microsurgery after blocking, with better plasticity, more substantial flexibility, and more excellent controllability. After the inflation of the balloon, the aneurysm needed exposure under micromanipulation and the parent artery needed reshaping, which necessitated greater flexibility and plasticity of the balloon; these requirements were met by the Scepter balloon (MicroVention, USA). At the same time, methylene blue was added to the contrast agent filling balloon to allow the balloon in the internal carotid artery to be identified under the microscope. At least three aspects highlight the innovation of this technology. First, the position and adherence of the balloon can be observed in real time during the operation without intraoperative radiologic or fluoroscopic guidance. Second, through direct observation of the visualization balloon, the operator can avoid serious complications caused by accidental puncture and injury of the balloon in the process of puncture and aspiration of the tumor cavity or incision of the aneurysm for decompression. Third, the displacement and detaching of the balloon can be observed in real-time during the process of clip reconstruction, which can effectively avoid clipping mistakes in the balloon. In addition, the parent artery can be better reconstructed with the support of the filling balloon, and stenosis of the parent artery after surgery can be avoided effectively.

All 17 patients underwent methylene blue balloon dilatation and blocking during microsurgery in this series. No radiographic examination and repeated device switching were needed throughout the process, significantly simplifying the operative procedure. During the operation, two cases with balloon displacement and slippage into the aneurysm cavity were found in time and

TABLE 1 Summary of patient and aneurysm characteristics.

No. of case	Age/Sex	Comorbidities	Vision deficits	Aneurysm					Occlusion time (s)	Complications	Follow-up (m)	mRS	
				Treatment history	SAH	Side	Diameter (mm)	Neck (mm)				Pre-operative	Post-operative
1	65/F	No	Yes	No	Yes	R	21.6	10.7	424	Pulmonary infection	48	3	1
2	79/F	Hypertension, diabetes	No	No	No	R	17.5	8.5	415	No	44	1	0
3	58/F	No	Yes	No	No	L	23.6	11.4	367	No	41	0	0
4	47/M	No	No	Coiling	No	L	18.3	9.2	749	Pulmonary infection	40	1	1
5	58/M	Hypertension	No	No	No	L	14.5	7.1	302	No	39	0	0
6	55/M	Hypertension	Yes	No	No	R	26.7	11.7	558	Thalamus hemorrhage	38	1	2
7	53/F	No	No	No	No	R	19.7	9.4	289	No	35	1	0
8	63/M	Hypertension	Yes	No	No	L	13.3	6.9	267	No	32	0	0
9	50/F	Coronary heart disease	No	No	Yes	R	25.2	12.8	622	No	30	2	0
10	75/F	Hypertension	No	No	No	R	16.4	7.6	356	No	29	0	0
11	51/M	No	Yes	Coiling	Yes	L	22.8	10.4	737	Visual loss	28	4	1
12	75/F	No	No	Clipping	Yes	L	16.7	8.3	426	No	27	2	0
13	55/F	No	Yes	Coiling	No	L	23.3	10.6	683	No	26	1	0
14	48/M	No	Yes	No	No	L	27.4	11.4	655	No	26	1	0
15	73/F	Hypertension	Yes	No	Yes	L	14.8	7.4	297	VI paralysis	25	2	1
16	55/F	Hypertension	Yes	No	No	L	17.4	8.3	306	No	25	1	0
17	54/F	No	Yes	Coiling	No	L	22.1	9.6	591	No	24	1	0

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without balloon misclipping. All 17 aneurysms were successfully clipped, and angiography was performed immediately after the surgery. There was no residual aneurysm, parent artery stenosis, or perforator misclipping. The rate of good mRS score after the operation was 100%; at the same time, it also significantly improved the patients with preoperative visual impairment, with an improvement rate of 70%. Therefore, the visualization balloon occlusion-assisted technique is safe and effective for microsurgical clipping recurrent paraclinoid aneurysms after stent-assisted coil embolization.

Limitations

First, there are inherent limitations in the present study since it is a retrospective study. Second, the number of cases in this study was small and there was only one observation group and no control group. Therefore, the study results need to be validated by case–control studies with strict inclusion and exclusion criteria.

Conclusion

In consideration of patients with large or giant paraclinoid aneurysms, microsurgical clipping of complicated large and giant paraclinoid aneurysms with the visualization balloon occlusion-assisted technique in a hybrid operating room is a safe and effective combined surgical method. It significantly reduces surgical difficulty and simplifies the operation process. This technique can allow for accurate placement of aneurysmal clips, safely reconstruct the parent artery, relieve clinical symptoms, reduce complications, ease the mass effect, and reduce the high recurrence rate after embolization. Future clinical studies are needed to explore this finding further.

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 the Ethics Committee of Wuhan University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

JC and WZ: conceptualization and validation. JC: methodology, funding acquisition, and supervision. WS and YZ: software. YZ: formal analysis. LY: data curation. TZ and YC: writing the original draft preparation. YC and WW: writing, reviewing, and editing. ZL: visualization. ZX: project administration. All authors have read and agreed to the published version of the manuscript.

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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.

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Clinical features, angio-architectural phenotypes, and treatment strategy of foramen magnum dural arteriovenous fistulas: a retrospective case series study

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Background: The rarity and complex angioarchitecture of foramen magnum dural arteriovenous fistulas (DAVFs) make its treatment difficult and controversial. We aimed to describe their clinical features, angio-architectural phenotypes, and treatments, through a case series study.

Methods: We first retrospectively studied cases of foramen magnum DAVFs treated in our Cerebrovascular Center, and then reviewed the published cases on Pubmed. The clinical characteristics, angioarchitecture, and treatments were analyzed.

Results: A total of 55 patients were confirmed with foramen magnum DAVFs, which included 50 men and 5 women, with a mean age of 52.8 years. Most patients presented with subarachnoid hemorrhage (SAH) (21/55) or myelopathy (30/55), depending on the venous drainage pattern. In this group, 21 DAVFs were supplied by only the vertebral artery (VA), three by only the occipital artery (OA), three by only the ascending pharyngeal artery (APA), and the remaining 28 DAVFs were supplied by two or three of these feeding arteries. Most cases (30/55) were treated with only endovascular embolization, 18 cases (18/55) with only surgical disconnection, five cases (5/55) with combined therapy, and two cases rejected treatment. The angiographic outcome of complete obliteration was achieved in most patients (50/55). In addition, two cases of foramen magnum DAVFs were treated by us in a Hybrid Angio-Surgical Suite (HASS) with good outcomes.

Conclusions: Foramen magnum DAVFs are rare and their angio-architectural features are complicated. The treatment option (microsurgical disconnection or endovascular embolization) should be weighed carefully, and combined therapy in HASS could be a more feasible and less invasive treatment option.

KEYWORDS

foramen magnum DAVF foramen magnum, dural arteriovenous fistula, subarachnoid hemorrhage, myelopathy, Hybrid Angio-Surgical Suite

Introduction

Foramen magnum dural arteriovenous fistula (DAVF) is a subset of craniocervical DAVF with the fistula point around the foramen magnum. Generally, the foramen magnum region lies in the bilateral occipital area that runs laterally up to the jugular foramen and includes both the inner and outer sides of the occipital bone (1). Most foramen magnum DAVFs are presented with myelopathy or subarachnoid hemorrhage, depending on the pattern of venous drainage (1). Foramen magnum DAVFs are rare, representing only 1.5–2.3% of all intracranial DAVFs (1, 2), and their rarity and complicated angioarchitectures make the treatment difficult and controversial.

Generally, microsurgical disconnection of the shunt was the predominant treatment option for the foramen magnum DAVFs before 2010 (3–5). However, in the past decade, with remarkable advances in the endovascular techniques providing highly flexible hydrophilic-coated catheters and new non-adhesive liquid embolic agents, such as Onyx and N-butyl-cyanoacrylate (NBCA) glue, endovascular embolization of the fistula has become an alternative option for treating the foramen magnum DAVFs (6–8). It has been reported that ∼80% of the foramen magnum DAVFs in the literature were treated endovascularly (9). Nevertheless, the incomplete obliteration and reoccurrence of the fistula after endovascular embolization could not be underestimated, and some cases even required staged or salvage combined surgeries (1, 10). Recently, a combined surgical-endovascular technique in a hybrid operating room (Hybrid Angio-Surgical Suite, HASS) has emerged as a solution to the complexity of cerebrovascular surgery, and this technique has been an effective treatment option for DAVFs complicated by inaccessible arterial and transvenous approaches (11, 12). Coincidentally, we applied this concept of a HASS to treat two complicated cases of foramen magnum DAVFs with good outcomes.

In this retrospective observational case series, we first studied the cases of foramen magnum DAVFs treated in our Cerebrovascular Center, and then reviewed the published cases of foramen magnum DAVFs (4, 5, 7–10, 13–29), aiming to obtain a comprehensive understanding of the clinical symptoms, angioarchitectures, pathophysiological mechanisms and treatments for foramen magnum DAVFs.

Methods

Patients

In this retrospective case series, we reviewed clinical charts, radiological images, and operative notes of 13 consecutive patients who were diagnosed with foramen magnum DAVFs from January 2002 until April 2021. All patients were managed at the Neurosurgery Department, Renji Hospital, Shanghai Jiao Tong University School of Medicine. All available imaging studies were reviewed and analyzed. All the patients had digital subtraction angiography (DSA) of the bilateral internal and external carotid arteries and the vertebral arteries that carefully analyzed the arterial feeders, the location of the fistula, and the venous drainage patterns. Patients who presented with myelopathy had a complete spine MRI and spine DSA. All the patients gave consent to be enrolled and have their data published.

In addition, we found 78 published reports when we searched for "dural arteriovenous fistula foramen magnum" on PubMed, 26 of which included sufficient clinical descriptions and adequate angiographic architecture of the foramen magnum DAVFs.

Data collection

The variables collected and analyzed include demographic profiles such as age and gender, clinical presentation and the duration of symptoms, and angio-architectural features of the fistulas including the location, arterial supply, venous drainage pattern, and presence of venous aneurysms. Treatment modalities, outcomes, and follow-up information were also documented and analyzed.

Data analysis

All the data were analyzed and interpreted by the senior investigator with extensive knowledge of vascular neuroanatomy and angio-architectural interpretation. No statistical analysis software was warranted.

Results

There were 55 patients (including 13 of our current cases) who were angiographically confirmed with foramen magnum DAVFs, which included 50 men (90.9%) and 5 women (9.1%). The mean age was 52.8 years, ranging from 20 to 83 years (Supplementary Table 1).

Clinical presentation

Most patients presented with subarachnoid hemorrhage (SAH) or myelopathy (debility of bilateral limbs and/or urinary retention) after symptoms appeared, with 30 cases (54.5%) of myelopathy, 21 cases (38.2%) of SAH, and 4 cases (7.3%) of other etiologies (three intracranial hematomas, and one trigeminal neuralgia).

Angioarchitecture

Generally, foramen magnum DAVFs have three important arterial supplies: the neuromeningeal trunk of the ascending pharyngeal artery (APA), the meningeal branches of the vertebral artery (VA), and the mastoid branches of the occipital artery (OA). As listed in Table 1, of the 55 cases in this case series study, 21 cases were supplied by only the VA; 3 cases were supplied by only the OA; 3 cases were supplied only by the APA, and the remaining 28 cases were supplied by two or three of these feeding arteries. Thus, more than half of these cases were not supplied by only one feeding artery, but by two or even three feeding arteries. In addition, as listed in Table 1, foramen magnum DAVFs usually first drain into

TABLE 1 Clinical and angioarchitectural characteristics and treatments of foramen magnum DAVFs.

	Case	Age	Gender	Clinical presentation	Feeding arteries	Venous drainage	Treatment	Angiographic outcome
Guo et al. (3)	1	47	M	SAH	VA	MV	Surgical disconnection	CO
	2	51	M	SAH	VA	MV	Surgical disconnection	CO
	3	35	M	SAH	OA, APA	MV, COS	Surgical disconnection	CO
	4	40	M	SAH	OA	MV, SS, COS	Treatment rejected	No follow up
Guo et al. (6)	5	45	M	SAH	VA	MV, COS	Embolization	CO
Present cases	6	30	M	SAH	VA	MV, COS	Treatment rejected	No follow up
	7	36	M	SAH	VA	MV	Surgical disconnection	CO
	8	40	M	SAH	VA	MV	Surgical disconnection	CO
	9	53	F	SAH	OA	COS	Embolization	CO
	10	52	M	SAH	VA	COS	Embolization	CO
	11	63	M	SAH	VA	MV	Surgical disconnection	CO
	12	62	M	Myelopathy	VA	MV, ASV	Surgical disconnection in HASS	CO
	13	60	M	SAH	VA	MV	Embolization in HASS	CO
Rivierez et al. (13)	14	50	M	SAH	VA	MV	Surgical disconnection	NR
Slaba et al. (14)	15	36	M	Myelopathy	VA, OA	MV	Embolization	CO
Reinges et al. (4)	16	58	M	Myelopathy	VA	MV	Surgical disconnection	CO
	17	63	F	Myelopathy	VA	MV	Surgical disconnection	CO
	18	48	M	Myelopathy	VA	MV	Surgical disconnection	CO
Kim et al. (15)	19	36	M	Cerebellar and 4th ventricular hematoma	VA, OA	MV	Embolization	CO
Chng et al. (16)	20	67	M	Myelopathy	APA, OA, VA	Straight sinus	Embolization	Incomplete
Takami et al. (5)	21	69	M	Myelopathy	VA, OA	MV	Surgical disconnection	CO
	22	60	M	Myelopathy	VA	MV	Embolization+ Surgical disconnection	CO
Spiotta et al. (8)	23	49	M	Myelopathy	APA	Cervical radicular vein	Embolization	CO
Liang et al. (7)	24	50	M	Myelopathy	VA, OA	MV	Embolization	CO
	25	61	M	Myelopathy	OA	MV	Embolization	CO
	26	36	M	SAH	VA, OA	MV, Coronal venous plexus	Embolization	CO
	27	55	M	Myelopathy	VA, APA	MV	Embolization	CO
	28	49	F	Myelopathy	VA, APA, OA	MV	Embolization	CO
Gilard et al. (17)	29	59	M	SAH	VA	Superior petrous sinus	Surgical disconnection	CO

(Continued)

TABLE 1 (Continued)

	Case	Age	Gender	Clinical presentation	Feeding arteries	Venous drainage	Treatment	Angiographic outcome
Mendes et al. (18)	30	72	M	Occipital hematoma	VA	Marginal sinus, Superior petrosal sinus	Embolization	CO
Pop et al. (19)	31	38	M	Seizure, Myelopathy	APA, OA	ASV, cortical temporal vein	Embolization	CO
Hiramatsu et al. (20)	32	53	M	Myelopathy	APA, OA	PSV	Embolization+ Surgical disconnection	CO
Llacer et al. (21)	33	68	M	Myelopathy	VA, OA	ASV	Embolization	CO
Raheja et al. (22)	34	59	M	Myelopathy	VA	MV	Surgical disconnection	CO
Do et al. (23)	35	57	M	Myelopathy	VA	PSV	Surgical disconnection	CO
Kim et al. (24)	36	48	M	SAH	APA	Suboccipital venous plexus, sigmoid sinus	Embolization	CO
Motebejane et al. (25)	37	45	M	Myelopathy	APA, VA	PSV	Embolization	CO
	38	54	M	Myelopathy	APA, VA	PSV	Embolization	CO
	39	71	M	Myelopathy	APA, VA	ASV, PSV	Embolization	CO
	40	57	M	Myelopathy	APA, VA	ASV	Embolization	CO
	41	47	M	Myelopathy	APA, VA	ASV, PSV	Embolization	CO
	42	67	M	Myelopathy	APA, VA	ASV	Embolization	CO
	43	62	F	Myelopathy	APA, VA	ASV, MV	Embolization	CO
	44	70	M	Myelopathy	APA, VA	ASV	Embolization	CO
	45	49	M	Myelopathy	APA, VA	Pontomesencephalic vein, MV	Embolization	CO
	46	53	M	SAH	APA, VA	Pontomesencephalic vein	Embolization	CO
	47	42	M	SAH	APA, VA	Pontomesencephalic vein	Embolization	CO
	48	51	M	SAH	APA, VA	MV, Jugular bulb	Embolization	CO
Sattur et al. (26)	49	63	F	Myelopathy	VA	ASV	Surgical disconnection	CO
Iampreechakul et al. (10)	50	20	M	Seizure, Medullary hemorrhage	PICA, VA, APA, OA	Petrosal vein, basal vein of Rosenthal, vein of Galen	Embolization additional combined treatment	Incomplete
Chen et al. (9)	51	35	M	Trigeminal neuralgia	APA, OA	Vein of Galen, PSV	Surgical disconnection	CO
Kakizaki, et al. (1)	52	65	M	SAH	APA, VA	MV, anterior pontomesencephalic vein, basal veins of Rosenthal	Embolization + Surgical disconnection	CO
Artemiadis et al. (27)	53	63	M	Myelopathy	APA	MV, ASV	Embolization	No follow up
Gadot, et al. (28)	54	83	M	Myelopathy	VA	MV	Surgical disconnection	CO
Okamoto, et al. (29)	55	50	M	SAH	APA, VA, OA	Straight sinus, superior petrosal sinus	Embolization + surgical disconnection	CO

APA, ascending pharyngeal artery; ASV, anterior spinal vein; CO, complete obliteration; COS, confluence of sinuses; F, female; HASS, Hybrid-Surgical Suite; hOR, hybrid operating room; M, male; MV, medullary vein; OA, Occipital artery; PSV, posterior spinal vein; SAH, subarachnoid hemorrhage; VA, vertebral artery.

the bridging medullary veins, but some DAVFs then drain into the intracranial cerebral veins or the spinal veins.

Treatments

Almost all the patients adopted treatments (two patients rejected treatment). Most cases (30/55) were treated with only endovascular embolization, while 18 cases (18/55) were treated with only surgical disconnection, and 5 cases (5/55) with combined therapy (endovascular embolization and microsurgical disconnection) because of incomplete embolization or DAVF reoccurrence.

Follow-up and outcome

With follow-up duration ranging from 6 months to 2 years, all the treated patients recovered well. All the patients were followed with cerebral DSA. The angiographic outcome of complete obliteration was achieved in all the patients who underwent surgery or combined therapy, and in 30 of 35 patients who received endovascular embolization.

Illustrative cases

Case 12

A 62-year-old male patient presented with a 2-month history of progressive difficulty in walking and bilateral extremity weakness and numbness. He reported no pain but described balance issues and urinary and bowel incontinence episodes. Physical examinations revealed the muscle strength of his distal limbs was grade 4. His Hoffman's and Babinski's signs were both positive. The superficial sensation of his lower body was not intact, with a sensory level at T10.

Cervical spine magnetic resonance imaging (MRI) showed an expanded spinal brain stem and a longitudinal extensive cervical cord enlargement with obvious edema. Vascular flow voids were also demonstrated in front of the cervical cord (Figure 1A). The presence of brainstem and cervical cord edema, as well as the vascular flow voids in front of the cervical cord, were strong indicators of a DAVF. The clinicians strongly advised pursuing further angiographic investigations. A complete spine DSA was negative, while the cerebral DSA demonstrated a DAVF located at the foramen magnum supplied by the meningeal branch of the left VA (Figures 1B–D). The fistula was draining through the bridge-medullary veins into the dilated tortuous anterior spinal vein (SPV) (Figures 1B–D; Supplementary material Video 1). After consultation with the multidisciplinary team of the Cerebrovascular Center, a surgical disconnection of the fistula in HASS was considered to be the treatment option. During the operation, the right femoral artery catheterization was first performed. With the patient in the park bench position on his right side, the foramen magnum was osteoclastically enlarged, followed by a partial hemilaminectomy of C1(Figure 1E; Supplementary material Video 2). After opening the dura, a large tortuous vein was visible at the level of the foramen magnum. It originated near the dural penetration of the left vertebral artery and formed a "C" pattern crawling between the vertebral artery and the medulla (Figure 1F). After an aneurysm min-clip was temporarily applied to the origin of the fistula (Figure 1F), intra-operative DSA was performed and revealed the complete disappearance of the DAVF (Figure 1G; Supplementary material Video 3). Thus, electrical coagulation and disconnection of the fistula at its origin from the dura were performed. After the operation, a repeated cerebral DSA confirmed the complete obliteration of the fistula (Figure 1H; Supplementary material Video 4). The postoperative course was uneventful, and his limb's motor and sensory function gradually recovered. Cerebral angiography 6 months later confirmed the disappearance of the DAVF.

Case 13

A 60-year-old male presented with a sudden onset of severe headache and loss of consciousness for 2 h. Emergent cranial CT revealed diffuse SAH and 4th ventricular hematoma (Figure 2A) (Fisher grade IV). The patient was in a deep coma with tracheal intubation (GCS 7, Hunt Hesse IV). Emergent complete cerebral DSA revealed a DAVF located at the foramen magnum supplied by the meningeal branch of the right VA, draining into the enlarged tortuous medullary vein (Figure 2B). As the patient's neurological state was very poor and the only feeding artery was not small, trans-arterial embolization *via* the meningeal branch of the VA in HASS was considered as the treatment option. In addition, microsurgical disconnection of the fistula was regarded as the alternative option, if the endovascular approach failed.

Under general anesthesia, catheterization was performed *via* the transfemoral approach. The Marathon microcatheter (MTI-EV3, Irvine, CA, USA) was dimethylsulfoxide (DMSO)-compatible, and smoothly entered the feeding artery. The microcatheter tip was placed as close as possible to the DAVF nidus to ensure that the liquid embolic agent could penetrate and occlude the lesion. Once the microcatheter tip was advanced to reach the optimal position (Figure 2C), the injection of Onyx-18 (MTI-EV3) was carried out. Whenever any venous migration appeared, the injection was stopped to allow for solidification and subsequently the injection was continued until the DAVF was completely obliterated (Figure 2D). After the embolization, continuous lumbar drainage of bloody cerebrospinal fluid was applied to the patient for 5 days. The patient woke up from a coma 1 week later and recovered well without any neurological deficit 1 month later. Follow-up angiography at 6 months did not reveal any fistula residual or recurrence (Figures 2E, F).

Discussion

From these 55 cases, foramen magnum DAVFs appeared to be much more common in men (90.9%), with a median age of 52.8 years. Most patients presented with myelopathy or SAH after symptoms appeared, with 30 cases (54.5%) of myelopathy, 21 cases (38.2%) of SAH, and 4 cases (7.3%) of other etiologies (three intracranial hematomas, and one trigeminal neuralgia). The

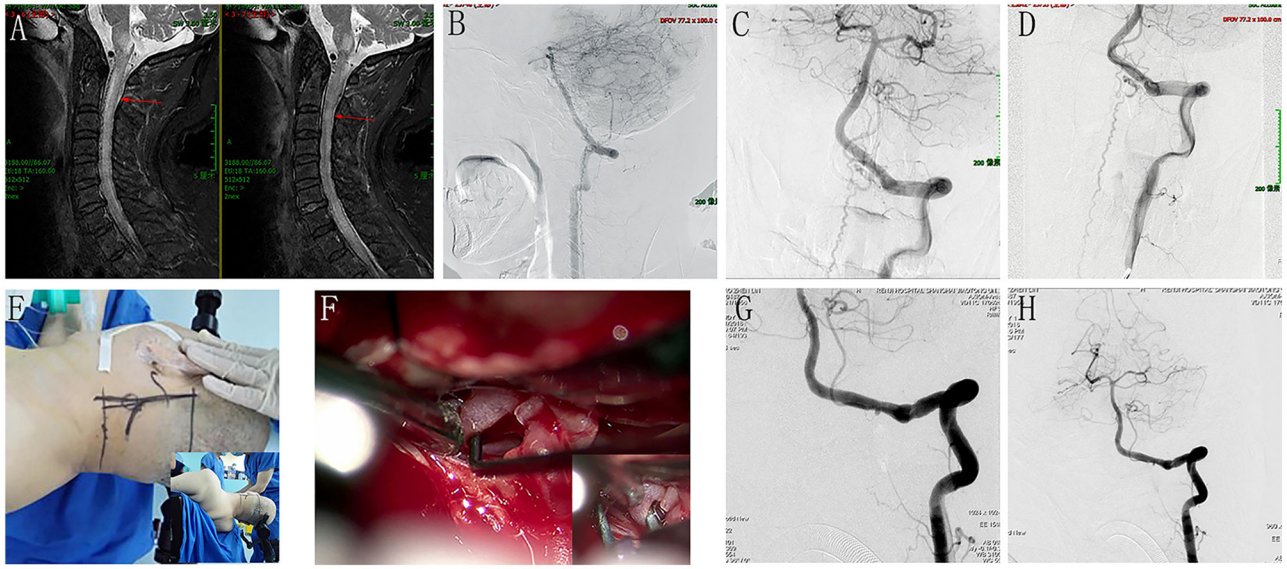

FIGURE 1
Perioperative neuroimages of Case 12. A cervical spine MRI showed an expanded spinal brain stem and a longitudinal extensive cervical cord enlargement with obvious edema, and vascular flow voids was also demonstrated in front of the cervical cord **(A)**. The cerebral DSA demonstrated a DAVF located at the foramen magnum supplied by the meningeal branch of left VA, and the fistula was draining through the bridge-medullary veins into the dilated tortuous anterior spinal vein **(B)**, lateral view; **(C)**, anteroposterior view; **(D)**, oblique view with magnification. **(E)** showed the incision line and the operation position (park bench position). F demonstrated a large tortuous vein was visible at the level of the foramen magnum, and it originated near the dural penetration of the left vertebral artery and formed a "C" pattern crawling between the vertebral artery and the medulla. **(F)** showed an aneurysm min-clip was temporarily applied to the origin of the fistula to occlude the shunt. Intraoperative DSA revealed the complete disappearance of the DAVF **(G)**. After electrical coagulation and disconnection of the fistula at its origin from the dura, repeat cerebral DSA confirmed the complete obliteration of the fistula **(H)**.

pathophysiological mechanism underlying SAH or myelopathy is presumed to involve venous hypertension, although it is not entirely understood (1, 3, 10). The DAVFs around the foramen magnum could drain into the bridging medullary veins and then to the intracranial cerebral veins or the spinal veins (1). Drainage into the cortical or perimedullary spinal veins increases the pial venous pressure, resulting in aggressive neurologic outcomes including SAH, cerebral hemorrhage, or congestive venous myelopathy (3, 10). Almost all the patients in this study experienced symptoms associated with SAH (38.2%) or myelopathy (54.5%), depending on the pattern of venous drainage.

Anatomically, foramen magnum DAVFs have three important arterial supplies: the neuromeningeal trunk of the APA, the meningeal branches of the VA, and the mastoid branches of the OA (1, 3, 5). As listed in Table 1, among the 55 cases, 21 cases were supplied by only the VA; 3 cases were supplied by only the OA; 3 cases were supplied only by the APA, and the remaining 28 cases were supplied by two or three of these feeding arteries. Therefore, to reduce the incidence of missed or misdiagnosed foramen magnum DAVFs, accurate recognition of six arteries (including the bilateral external carotid arteries, the internal carotid arteries, and the vertebral arteries) and their branches is necessary during the angiography (3).

The dangerous clinical presentations of foramen magnum DAVFs require rapid and aggressive treatment. However, their rarity and complicated angioarchitectures make the treatment difficult and controversial. Generally, microsurgical disconnection of the fistula has been the predominant treatment option for foramen magnum DAVFs before 2010 (3–5). In the past decade, with remarkable advances in endovascular techniques providing highly flexible hydrophilic-coated catheters and new non-adhesive liquid embolic agents, such as Onyx and N-butyl-cyanoacrylate (NBCA) glue, endovascular embolization of the fistula has become an alternative option for treating foramen magnum DAVFs (6–8).

There are abundant anastomoses with surrounding blood vessels in the meningeal branches of VA at the craniocervical junction (1, 3, 5, 30), and embolized materials like Onyx or N-butyl-cyanoacrylate glue (NBCA) can easily migrate or reflux to the basilar and vertebral arteries (1). Therefore, the foramen magnum DAVFs supplied exclusively by the VA are preferably treated with direct microsurgery. As in our current cases, microsurgical disconnection (6/9) was dominantly chosen to treat the foramen magnum DAVFs with VA to be the only feeding artery. On the other hand, in most of the cases supplied by the external carotid artery, the microcatheter was guided sufficiently proximal to the fistula site and the fistula was completely obliterated by using Onyx or NBCA from the external carotid artery. Thus, for DAVFs supplied by the external carotid artery and its branches, endovascular embolization could be preferred (7, 25). During the embolization, the catheter tip should be advanced beyond the hypoglossal or jugular foramina to prevent occlusion of the vasa nervosum.

As shown in Table 1, most cases (30/55) were treated with only endovascular embolization, 18 cases (18/55) with only surgical disconnection, and 5 cases (5/55) with combined therapy (endovascular embolization and microsurgical disconnection) because of incomplete embolization or DAVF reoccurrence. The

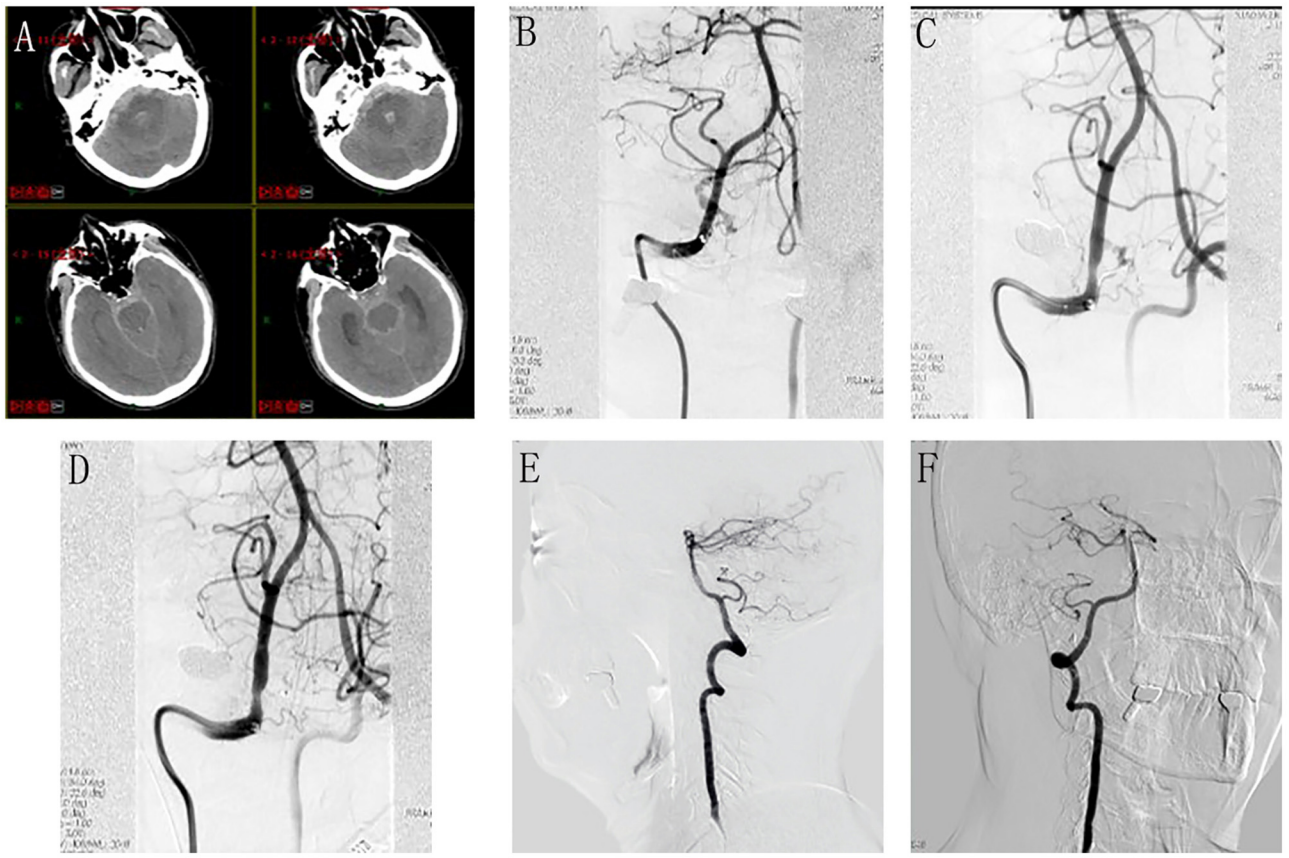

FIGURE 2
Perioperative neuroimages of Case 13. Emergent cranial CT revealed diffuse SAH and 4th ventricular hematoma **(A)**. Emergent cerebral DSA revealed a DAVF located at the foramen magnum supplied by the meningeal branch of the right VA, draining into the enlarged tortuous medullary vein **(B)**. During the procedure, the microcatheter tip was advanced to reach the optimal position **(C)**; the injection of Onyx was continued until the DAVF was completely obliterated **(D)**. Follow-up angiography at 6 months did not reveal any fistula residual or recurrence **(E)**, lateral view; **(F)**, anteroposterior view.

angiographic outcome of complete obliteration was achieved in all the patients who underwent surgery or combined therapy, and in 30 of 35 patients who received endovascular embolization. Nevertheless, the incomplete obliteration and reoccurrence of the fistula after endovascular embolization could not be underestimated, and some cases even required staged or salvage combined surgeries (1, 10). According to Hiramatsu et al., complication rates of the overall embolization procedure is 15.8% in craniocervical junction DAVF (20). Specifically, cranial nerve palsy may occur after Onyx injection, possibly due to the neurotoxicity of Onyx or dimethyl sulfoxide, or occlusion of the vasa nervorum due to dangerous extracranial-intracranial anastomoses (31–33). Drawing from our experience, for the patients with extracranial-intracranial anastomoses, a non-detachable balloon catheter was inflated in the VA across the C1 branch origin to prevent reflux of the embolized materials into the VA during the embolization.

Notwithstanding alternative treatment options in recent years, microsurgical disconnection of the shunt appears to be a more effective and reliable method of treatment. The surgery can be performed *via* the far lateral suboccipital craniotomy with a C1 laminectomy or hemilaminectomy (3). Microsurgery has also been useful in cases with symptoms caused by the mass effect of the dilated venous pouch and the shunt fistula (1). Chen et al. reported that trigeminal neuralgia due to a foramen magnum DAVF compression was completely relieved after surgical disconnection (9). In addition, although seldom reported, surgery-related complications (intracranial hematoma, intracranial infection, etc.,) cannot be completely avoided.

No treatment is perfect. To achieve complete obliteration of the fistula through minimally invasive procedures, combined therapy might be a better option, especially for the complex foramen magnum DAVFs. However, it often needs staging or additional surgery. Early studies with intraoperative portable DSA (early "hybrid surgery") showed that intraoperative angiogram altered surgical management, frequently by avoiding additional surgery. Recently, the concept of a Hybrid Angio-Surgical Suite (HASS) has emerged as a solution to the complexity of cerebrovascular surgery and the need for immediate intraoperative feedback (11, 12). It combines the capacity of both the operating room and interventional suite—a standard operating room equipped with a biplane or single-plane angiogram machine. The HASS is becoming

a standard facility for many hospitals around the world, and many neurosurgeons and neuro-interventionists use it for the treatment of cerebrovascular diseases (11).

Coincidentally, we treated two cases of foramen magnum DAVFs in HASS with good outcomes. The use of HASS for foramen magnum DAVFs could have the following advantages: 1) the HASS can afford immediate intraoperative feedback (for example, the accurate anatomic location of the fistula, the complete obliteration of the fistula after surgical disconnection); 2) the HASS could immediately provide surgical obliteration when the endovascular approach fails; 3) the HASS with open surgery could supply alternative access for endovascular embolization when the regular trans-arterial and trans-venous approaches fail. In short, HASS provides a less invasive and more feasible alternative for the treatment of difficult foramen magnum DAVFs.

Conclusion

Foramen magnum DAVFs are rare, with only 55 cases being reported till now. Their angioarchitecture is complicated, with three possible feeder arteries (APA, VA, and OA), draining into the bridging medullary veins and then to the intracranial cerebral veins or the spinal veins, leading to SAH or myelopathy. Their rarity and angio-architectural complexity make their treatment difficult and controversial. Generally, microsurgical disconnection of the fistula appears to be a more effective and reliable method of treatment, while endovascular embolization is a more recent and popular treatment option for selected cases. However, we suggest that all foramen magnum DAVFs should be managed in HASS if available because HASS could provide a less invasive and more feasible alternative treatment strategy.

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 Ethics Committee of Renji Hospital, School of Medicine, Shanghai Jiaotong University. 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

LG, ZX, and WG designed the study, analyzed data, and wrote the article. HZ and XZ collected the data. JD and JW assisted in analyzing the data and revised the article. All authors contributed to the article 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

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2023.1121075/full#supplementary-material

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Combined open revascularization and endovascular treatment of complex intracranial aneurysms: case series

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Background and purpose: The treatment of complex intracranial aneurysms can be challenging with stand-alone open or endovascular techniques, particularly after rupture. A combined open and endovascular strategy can potentially limit the risk of extensive dissections with open-only techniques, and allow for aggressive definitive endovascular treatments with minimized downstream ischemic risk.

Materials and methods: Retrospective, single-institution review of consecutive patients undergoing combined open revascularization and endovascular embolization/occlusion for complex intracranial aneurysms from 1/2016 to 6/2022.

Results: Ten patients (4 male [40%]; mean age 51.9±8.7years) underwent combined open revascularization and endovascular treatment of intracranial aneurysms. The majority of aneurysms, 9/10 (90%), were ruptured and 8/10 (80%) were fusiform in morphology. Aneurysms of the posterior circulation represented 8/10 (80%) of the cases (vertebral artery [VA] involving the posterior inferior cerebellar artery [PICA] origin, proximal PICA or anterior inferior cerebellar artery/PICA complex, or proximal posterior cerebral artery). Revascularization strategies included intracranial-to-intracranial (IC-IC; 7/10 [70%]) and extracranial-to-intracranial (EC-IC; 3/10 [30%]) constructs, with 100% postoperative patency. Initial endovascular procedures (consisting of aneurysm/vessel sacrifice in 9/10 patients) were performed early after surgery (0.7±1.5days). In one patient, secondary endovascular vessel sacrifice was performed after an initial sub-occlusive embolization. Treatment related strokes were diagnosed in 3/10 patients (30%), largely from involved or nearby perforators. All bypasses with follow-up were patent (median 14.0, range 4–72 months). Good outcomes (defined as a Glasgow Outcomes Scale ≥4 and modified Rankin Scale ≤2) occurred in 6/10 patients (60%).

Conclusion: A variety of complex aneurysms not amenable to stand-alone open or endovascular techniques can be successfully treated with combined open and endovascular approaches. Recognition and preservation of perforators is critical to treatment success.

KEYWORDS

cerebral revascularization, bypass, aneurysm, neuroendovascular approach, embolization

Introduction

Treatment of complex, non-saccular intracranial aneurysms has increasingly involved endovascular therapies, in particular flow diversion, due to an ability to remodel diseased vessels from the inside in a minimally invasive manner (1). Intrasaccular devices similarly have the potential to change treatment paradigms for selected wide-necked saccular aneurysms (2). Limitations to these technologies nonetheless exist, particularly in the setting of ruptured aneurysms where flow diversion (or stent/coil constructs) requires the use of dual anti-platelet agents (increasing the risk of hemorrhage with ventricular catheters), and both flow diversion and intrasaccular devices can often have continued aneurysm filling (maintaining a small but significant risk of re-rupture) (3, 4). Although newer flow diversion technologies are being investigated that require only a single anti-platelet agent, concerns regarding significant morbidity and mortality from ischemic complications or post-treatment aneurysmal re-bleeding (occurring in up to 21% of patients) remain based on data from preliminary studies (5).

Open management of complex aneurysms, in particular cerebral bypass, remains an important tool for vascular neurosurgeons (6). Combined approaches that leverage the respective advantages of open and endovascular treatments, while avoiding their risks, can also be tailored to optimize the treatment of select aneurysms. For example, for fusiform or complex saccular ruptured aneurysms where a definitive treatment is desired, a combined strategy of open revascularization followed by endovascular deconstruction can be used to limit the risk of additional dissection with open-only techniques (i.e., for clip trapping), and allow for endovascular vessel sacrifice (or aggressive aneurysm treatment that may risk parent vessel occlusion) without downstream ischemic risk. We herein report our experience with combined open bypass and endovascular management of complex cerebral aneurysms.

Materials and methods

This study was performed in compliance with Health Insurance Portability and Accountability Act and local institutional review board (IRB) regulations. Patient consent was obtained based on institutional guidelines.

Data from all patients undergoing combined open revascularization and endovascular treatment for the management of intracranial aneurysms from 1/2016 to 6/2022 was retrospectively collected from an IRB-approved, prospectively maintained database. Recorded data included: patient demographics (age, gender), presenting symptoms, clinical status, Glasgow Coma Scale (GCS) score, aneurysm characteristics, surgical and endovascular details, treatment/overall complications, and neurologic outcomes (Glasgow outcomes scale [GOS] and modified Rankin Scale [mRS] scores at discharge and last follow up). Descriptive statistics were used to report continuous data (mean ± standard deviation).

Management and planning of combined open revascularization and endovascular treatment of all patients in this series was based on multidisciplinary (open and endovascular) neurosurgical review of the patient, and neurovascular and pathologic anatomy. Surgical details for open revascularization strategies are described previously (7–11). All patients were maintained on aspirin in the peri-operative and post-operative period to promote bypass patency. Secondary endovascular procedures were performed as early as possible after revascularization to secure the aneurysm (in cases of rupture) and to promote bypass patency. Systemic heparinization was not used during endovascular procedures for ruptured aneurysms or for procedures immediately following open surgery. Neuromonitoring was used for both open and endovascular procedures. Balloon test occlusion (BTO) was performed if feasible based on vascular anatomy to aid in treatment planning prior to endovascular vessel sacrifice.

Results

Ten patients (4 male [40%]; mean age 51.9 ± 8.7 years) underwent combined endovascular and open treatment of intracranial aneurysms (Figure 1; Table 1). Most aneurysms presented ruptured, 9/10 (90%), and 3/10 (30%) patients had undergone prior aneurysm treatments or treatment attempts. Aneurysm locations included: 5 (50%) involving the vertebral artery (VA)/posterior inferior cerebellar artery (PICA) origin, 2 (20%) of the proximal PICA or anterior inferior cerebellar artery (AICA)/PICA complex, 2 (20%) of the anterior communicating artery (Acomm) or A1/2 junction, and 1 (10%) of the proximal posterior cerebral artery (PCA). All (8/8) of the aneurysms involving the posterior circulation were fusiform, while aneurysms involving the anterior circulation were traumatic/pseudoaneurysm (1/2; 50%) or saccular (1/2; 50%) in morphology. Bypass strategies included both extracranial-to-intracranial (EC-IC) and intracranial-to-intracranial (IC-IC) constructs and included PICA-PICA side-to-side (5/10; 50%), V3-PICA with a descending branch of the lateral circumflex artery (DLCFA) interposition graft (2/10; 20%), A3-A3 side-to-side (2/10; 20%), and occipital artery (OA)-P4 with a DLCFA interposition graft (1/10; 10%). Mean temporary clip time was 38.5 ± 8.9 min, and immediate bypass patency was 100%. Initial endovascular procedures were performed early after surgery (mean 0.7 ± 1.5 days) to reduce rupture risk and promote bypass patency, and included vessel sacrifice in 9/10 patients (90%) (Table 2). Two patients underwent multiple endovascular embolizations. In one patient, a non-occlusive post-bypass endovascular strategy was initially employed for a fusiform VA aneurysm involving the proximal left PICA to preserve flow to the dominant anterior spinal artery (ASA) located immediately distal to the aneurysm, although further aneurysmal growth necessitated a delayed vessel sacrifice. The second patient had an initial post-bypass endovascular strategy of aggressive re-coiling of a recurrent/re-ruptured Acomm aneurysm arising from an unpaired A1 (including Acomm sacrifice), followed by delayed flow diversion/coiling for aneurysm re-growth.

Strokes from any etiology occurred in 5/10 patients (50%). Treatment related strokes were diagnosed in 3/10 patients (30%) and included a lateral medullary stroke after PICA-PICA bypass and VA sacrifice, thalamic/occipital strokes after PCA bypass/sacrifice, and an ASA stroke after V3-PICA bypass and delayed VA sacrifice. In 2/10 patients (20%) strokes were from vasospasm. Mean GOS and mRS at discharge were 3.8 ± 0.9 and 2.7 ± 2.0, respectively. Follow up data was available in 6/10 patients (60%). Over a median follow up of 14.0 months (range 4–72), all bypasses were patent and mean GOS and mRS were 4.5 ± 0.5 and 1.2 ± 1.3, respectively. Good outcomes

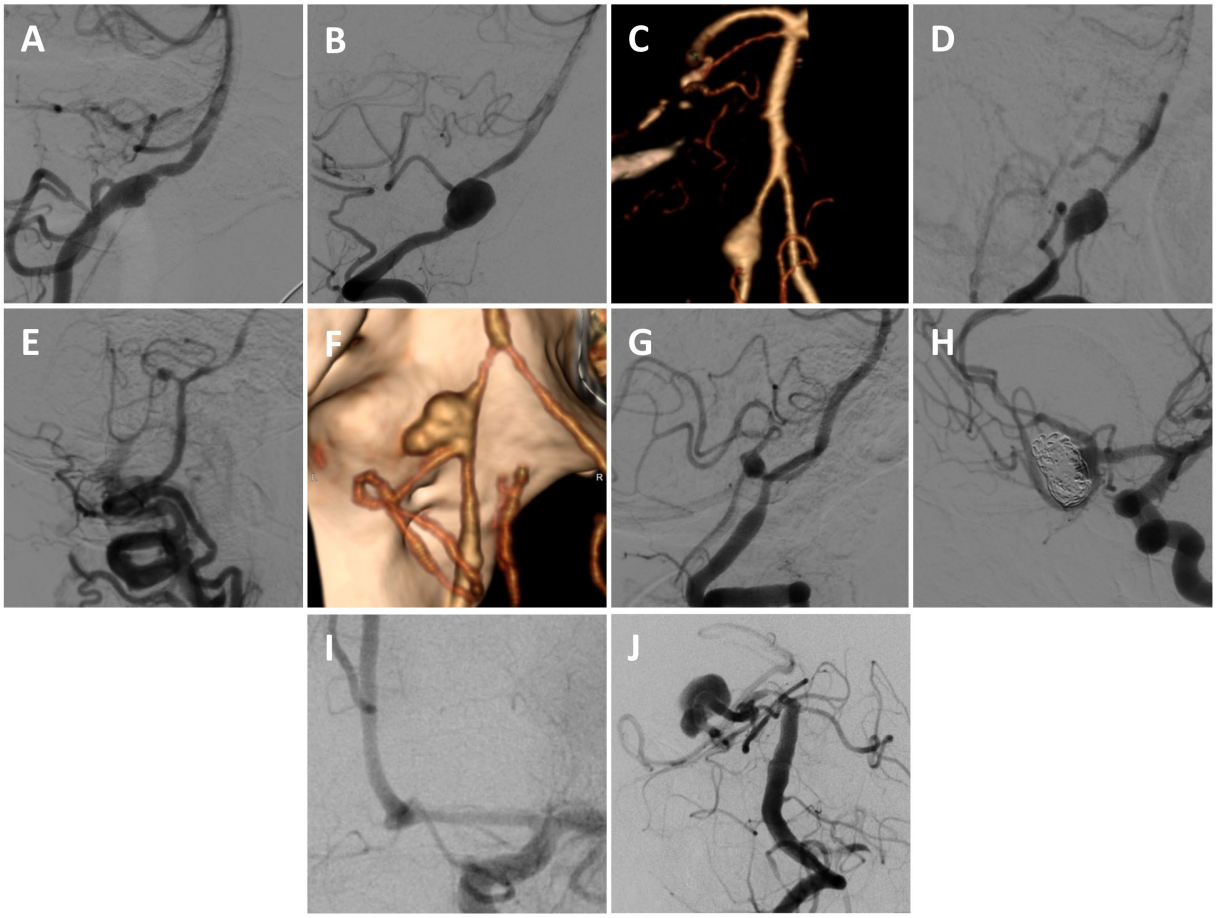

FIGURE 1
Treated aneurysms. **(A)** Left VA fusiform ruptured aneurysm involving the proximal left PICA (lateral angiogram of left VA). **(B)** Right VA fusiform ruptured aneurysm involving the proximal right PICA (lateral angiogram of the right VA). **(C)** Left VA fusiform ruptured aneurysm involving the proximal left PICA (3D-reconstruction). **(D)** Right VA fusiform ruptured aneurysm involving the proximal right PICA (lateral angiogram of the right VA). **(E)** Right proximal AICA/PICA fusiform ruptured aneurysm involving the vessel origin (lateral angiogram of the right VA, also demonstrating an iatrogenic right cervical VA-venous fistula from an unsuccessful prior endovascular treatment attempt). **(F)** Left VA fusiform ruptured aneurysm involving the proximal left PICA (3D-reconstruction). **(G)** Left proximal PICA fusiform ruptured aneurysm (lateral angiogram of left VA). **(H)** Recurrent ruptured and partially coiled Acomm aneurysm arising from an azygous left A1 (oblique angiogram of the left ICA). **(I)** Left A1-2 junction traumatic ruptured pseudoaneurysm (oblique angiogram of the left ICA). **(J)** Large right fusiform P2 aneurysm with a proximal dysplastic P1 (AP angiogram of the left VA).

(defined as a GOS $\geq$ 4 and mRS $\leq$ 2) occurred in 6/10 patients (60%) overall.

Case examples

Patient #7

A 59-year-old female who was recovering at an outside hospital from a perforated diverticulum experienced a severe acute headache followed by a seizure and was found to have diffuse subarachnoid hemorrhage (SAH) and obstructive hydrocephalus from a ruptured left proximal PICA fusiform aneurysm (Hunt and Hess 3, Fisher 4) (Figures 2A,B). She was stabilized with an external ventricular drain and transferred to our facility. She was recommended for a combined open revascularization and endovascular aneurysm/vessel occlusion on multidisciplinary review. As the contralateral PICA was not favorable for IC-IC bypass a V3 to left tonsillar PICA bypass using a DLCFA interposition graft was performed after a suboccipital craniotomy and C1 laminectomy. Immediately afterwards, the left PICA aneurysmal segment was internally embolized with coils (Figures 2C,D). She had an uneventful hospital course without complications (Figure 2E). On four-month follow up she was performing all activities of daily living independently.

Patient #8

A 61-year-old male with a history of coil embolization of a ruptured (Hunt and Hess 1, Fisher 2), large, multilobed Acomm aneurysm arising from an unpaired left A1 presented 3 months later with SAH (Hunt and Hess 2, Fisher 3) and intraparenchymal hemorrhage, with aneurysm re-growth (Figures 3A–C). A repeat coil embolization was performed, leaving a neck residual to preserve the Acomm (Figure 3D). He was recommended for a right anterior cerebral artery (ACA) revascularization to allow aggressive Acomm aneurysm coiling and possible Acomm sacrifice given the rapid re-growth of the lesion. He underwent an A3-A3 bypass followed by aneurysm embolization with Acomm sacrifice 5 days

TABLE 1 Patient summary.

Patient #	Age/ Sex	Presenting symptoms	Ruptured (Y/N)	Initial SAH grade	Initial GCS	Stroke at presentation	Previous aneurysm treatment	Aneurysm	Revascularization procedure	Temporary clip time (minutes)	Anastomosis patency	Endovascular procedure	Treatment-related stroke	Other notable events	GOS at D/c	mRS at D/c	F/u (months)	Anastamosis patency on F/u	GOS at F/u	mRS at F/u
1	41/F	Severe HA -> LOC	Y	HH4F4	9	Chronic right superior frontal gyrus stroke	N	Left VA fusiform aneurysm involving the proximal left PICA	PICA-PICA bypass	38	Y	Coil embolization/vessel sacrifice of left VA aneurysm	N	N	5	0	60	Y	5	0
2	41/M	HA, blurry vision	Y	HH1F2	15	N	N	Right VA fusiform aneurysm involving the proximal right PICA	PICA-PICA bypass	40	Y	Coil embolization/vessel sacrifice of right VA aneurysm	N	N	5	0	n/a	n/a	n/a	n/a
3	44/M	Severe HA, nausea	Y	HH1F3	15 - re-rupture upon transfer from OSH requiring intubation	N	N	Left VA fusiform aneurysm involving the proximal left PICA	Left V3 to left tonsillar PICA bypass w/ DLCFA interposition graft	30	Y	Coil embolization of left VA aneurysm; secondary coil/ liquid embolic embolization/ sacrifice of left VA aneurysm after expansion	ASA stroke following VA artery sacrifice	N	3	5	n/a	n/a	n/a	n/a
4	48/F	HA -> seizure	Y	HH3F3	13	N	N	Right VA fusiform aneurysm involving the proximal right PICA	PICA-PICA bypass	50	Y	Coil/liquid embolic embolization/vessel sacrifice of right VA aneurysm	N	Severe vasospasm - delayed right lateral medullary stroke	3	3	72	Y	4	3
5	66/F	HA, nausea -> AMS	Y	HH4F4	10	Right cerebellar strokes	Previous unsuccessful coil attempt; iatrogenic right cervical VA-venous fistula s/p stenting	Right proximal AICA/ PICA fusiform aneurysm involving the vessel origin	PICA-PICA bypass	40	Y	Coil embolization/vessel sacrifice of right AICA/ PICA aneurysm; coil/liquid embolic embolization/ sacrifice of right VA at level of C2 fistula	N	N	3	4	19	Y	5	0
6	57/F	LOC	Y	HH4F4	8	N	N	Left VA fusiform aneurysm involving the proximal left PICA	PICA-PICA bypass	28	Y	Coil/liquid embolic embolization/vessel sacrifice of left VA aneurysm	Left lateral medullary stroke following VA artery sacrifice	N	3	5	n/a	n/a	n/a	n/a
7	59/F	HA -> seizure	Y	HH3F4	8	N	N	Left proximal PICA fusiform aneurysm	Right V3 to left tonsillar PICA bypass w/ DLCFA interposition graft	51	Y	Coil embolization/vessel sacrifice of left PICA aneurysm	N	N	4	2	4	Y	4	2
8	61/M	HA -> AMS	Y	HH2F3	13	N	Coiling after initial rupture, re-coiling after growth and re-rupture with significant residual aneurysm	Large, multilobed saccular Acomm aneurysm arising from an unpaired left A1	A3-A3 bypass	48	Y	Coil embolization of residual Acomm aneurysm with Acomm sacrifice; delayed flow diversion and coiling of recurrent aneurysm	N	N	5	1	8	Y	5	0
9	49/F	Iatrogenic injury during transsphenoidal resection of recurrent pituitary tumor	Y	HH4F4	6T	Left fronto-basal	N	Left A1-2 junction pseudoaneurysm	A3-A3 bypass	32	Y	Coil embolization/vessel sacrifice of pseudoaneurysm and left A1-2 junction	N	Severe vasospasm - delayed bilateral ACA strokes; required decompressive hemicraniectomy	3	5	n/a	n/a	n/a	n/a
10	53/M	Indidental	N	n/a	15	N	Aborted flow diversion endovascular treatment	Large right fusiform P2 aneurysm with proximal dysplastic vessel	Right OA to P4 bypass w/ DLCFA interposition graft	28	Y	Coil embolization/vessel sacrifice of right P2 aneurysm	Small right thalamic and occipital strokes following PCA sacrifice	N	4	2	9	Y	4	2

A1, first segment of the anterior cerebral artery; A2, second segment of the anterior cerebral artery; A3, third segment of the anterior cerebral artery; ACA, anterior cerebral artery; Acomm, anterior communication artery; AICA, anterior inferior cerebellar artery; AMS, altered mental status; ASA, anterior spinal artery; DLCFA, descending branch of the lateral circumflex artery; F, female; GCS, Glasgow coma score; HA, headache; HH/F, Hunt & Hess and Fisher score; LOC, loss of consciousness; M, male; N, no; n/a, not applicable; OA, occipital artery; P2, second segment of the posterior cerebral artery; P4, fourth segment of the posterior cerebral artery; PCA, posterior cerebral artery; PICA, posterior inferior cerebellar artery; V3, third segment of the vertebral artery; VA, vertebral artery; Y, yes.

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TABLE 2 Summary of treatment details.

Patient #	Aneurysm	Bypass	Endovascular procedure	Days after open bypass	Aneurysm dimensions (mm)	BTO	Balloon-assisted intervention	Guide/ intermediate catheters (in)	Microcatheter/ wire (in)	Implants	Liquid embolic	Intraprocedural heparinization	Antiplatelets
1	VA/proximal PICA	PICA-PICA	Embolization/ sacrifice	0	10×6×5	N	Y - extra-compliant balloon	0.070 ID delivery (VA)	0.017 ID microcatheter; 0.014 microwire	Balloon catheter: 5 coils, 6–3 mm diameter; Microcatheter: 9 coils, 4–2 mm diameter	Y - Non-adhesive liquid embolic	N	Aspirin
2	VA/proximal PICA	PICA-PICA	Embolization/ sacrifice	0	11×10×9	N	N	0.087 ID guide (subclavian); 0.054 ID intermediate (VA)	0.017 ID microcatheter; 0.014 microwire	19 coils, 10–1 mm diameter	N	N	Aspirin
3	VA/proximal PICA	V3-DLCFA-PICA	Embolization	1	7×6×5	N	N	0.087 ID guide (subclavian); 0.055 ID intermediate (VA)	0.017 ID microcatheter; 0.012 microwire	5 coils, 6–2 mm diameter	N	N	Aspirin
3			Embolization/ sacrifice	9	9×7×5 - filling around coil mass	Y - extra-compliant balloon	Y - extra-compliant balloon	0.087 ID guide (subclavian); 0.055 ID intermediate (VA)	0.017 ID microcatheter; 0.012 microwire	8 coils, 4–1.5 mm diameter	Y - Non-adhesive liquid embolic	Partial (2000 U) to balance risk of thrombosis and enlarging aneurysm	Aspirin
4	VA/proximal PICA	PICA-PICA	Embolization/ sacrifice	0	9×5×5	N	N	0.087 ID guide (subclavian); 0.055 ID intermediate (VA)	0.017 ID microcatheter; 0.014 microwire	11 colils, 7–2 mm diameter	Y - Non-adhesive liquid embolic	N	Aspirin
5	Proximal AICA/ PICA	PICA-PICA	Embolization/ sacrifice of aneurysm; Embolization/ sacrifice of proximal VA fistula	0	5×3×3	N	N	0.087 ID guide (subclavian); 0.055 ID intermediate (VA)	0.016 ID microcatheter; 0.014 microwire	AICA/PICA: 7 coils, 3–1 mm diameter; VA fistula: 21 coils, 3.5–2 mm diameter	Y - Non-adhesive liquid embolic	N	Aspirin
6	VA/proximal PICA	PICA-PICA	Embolization/ sacrifice	1	8×4×3	N	Y - extra-compliant balloon	0.087 ID guide (subclavian); 0.070 ID intermediate (VA)	0.017 ID microcatheter; 0.014 microwire	Microcatheter: 3 coils, 6–4 mm diameter; Balloon catheter: 5 coils, 4–2 mm diameter	Y - Non-adhesive liquid embolic	N	Aspirin

(Continued)

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TABLE 2 (Continued)

Patient #	Aneurysm	Bypass	Endovascular procedure	Days after open bypass	Aneurysm dimensions (mm)	BTO	Balloon-assisted intervention	Guide/ intermediate catheters (in)	Microcatheter/ wire (in)	Implants	Liquid embolic	Intraprocedural heparinization	Antiplatelets
7	Proximal PICA	V3-DLCFA-PICA	Embolization/ sacrifice	0	5 × 3 × 3	N	N	0.087 ID guide (subclavian); 0.055 ID intermediate (VA)	0.016 ID microcatheter; 0.014 microwire	12 coils, 4–1.5 mm diameter	N	N	Aspirin
8	Acomm from an unpaired A1	A3-A3	Embolization/ Acomm sacrifice	5	Originally 12 × 11 × 11; 9 × 4 × 3 at time of bypass/ embolization	N	N	0.087 ID guide (proximal ICA); 0.055 ID intermediate (distal ICA)	0.017 ID and 0.016 ID microcatheters; 0.014 microwire	13 coils, 5–1.5 mm diameter	N	N	Aspirin
8			Flow diversion/ embolization	45	7 × 4 × 3 at time of flow diversion/ embolization	Attempted but unable to track compliant balloon to A1/2 junction	N	0.10 ID guide (CCA); 0.044 ID intermediate (distal ICA)	Flow diversion: 0.022 ID microcatheter; 0.014 microwire; Embolization: 0.017 ID microcatheter; 0.014 microwire	Flow diverter, 3.5 × 16 mm; 21 coils, 6–2 mm diameter	N	Y	Aspirin, Prasugrel
9	A1-2 pseudoaneurysm	A3-A3	Embolization/ sacrifice	0	3 × 2 × 2	N	N	0.088 ID delivery (ICA)	0.017 ID microcatheter; 0.014 microwire	5 coils, 3–2.5 mm diameter	N	N	Aspirin
10	P2	OA-DLCFA-P4	Embolization/ sacrifice	0	16 × 12 × 11	Y - mini compliant balloon	N	0.087 ID guide (subclavian); 0.055 ID intermediate (VA)	0.017 ID microcatheter; 0.014 microwire	17 coils, 12–1.5 mm diameter	N	N	Aspirin

A1, first segment of the anterior cerebral artery; A2, second segment of the anterior cerebral artery; A3, third segment of the anterior cerebral artery; Acomm, anterior communication artery; AICA, anterior inferior cerebellar artery; BTO, balloon test occlusion; DLCFA, descending branch of the lateral circumflex artery; ID, inner diameter; N, no; n/a, not applicable; OA, occipital artery; P2, second segment of the posterior cerebral artery; P4, fourth segment of the posterior cerebral artery; PICA, posterior inferior cerebellar artery; V3, third segment of the vertebral artery; VA, vertebral artery; Y, yes.

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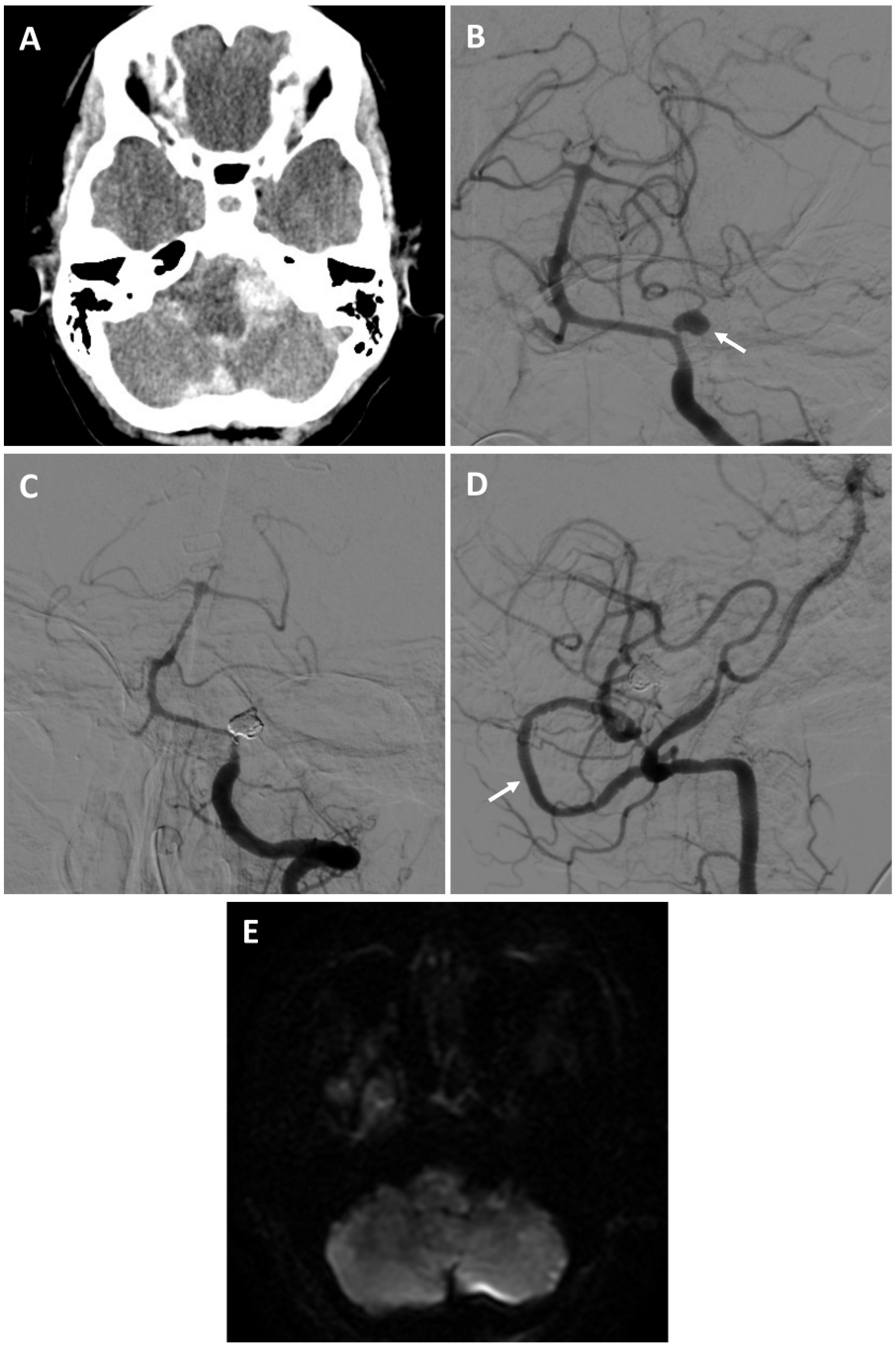

FIGURE 2
Patient #7. A 59-year-old female experienced a Hunt and Hess 3, Fisher 4 SAH from a left proximal PICA fusiform aneurysm [**(A)** axial non-contrast head CT; **(B)** AP angiogram of the left vertebral artery (arrow highlighting aneurysm)]. She underwent a V3 to PICA bypass using a DLCFA interposition graft, followed by internal PICA aneurysm embolization. She had no strokes and an uneventful recovery. On 4-month follow was performing all activities of daily living independently. Angiogram demonstrating PICA occlusion [**(C)** AP left vertebral artery injection, and patent bypass **(D)** lateral right vertebral artery injection (arrow highlights bypass)]. **(E)** Post-procedural MRI (axial DWI) demonstrated no strokes.

later (as the aneurysm dome was already secure), allowing for filling of the right ACA through the bypass (Figures 3E,F). He had an uneventful post-operative course and was discharged home without focal neurologic deficits. On 3-month repeat angiogram the aneurysm had re-grown and the Acomm was patent (Figure 3G). A BTO was attempted to assess the bypass, however, the balloon was unable to be positioned. Flow diversion across the left A1-2 and repeat aneurysm coiling (including re-sacrifice of the Acomm) was performed (Figures 3H,I). After an uneventful recovery, he was discharged home neurologically intact. On 4-month follow-up angiogram there was no residual aneurysm, and the bypass was patent.

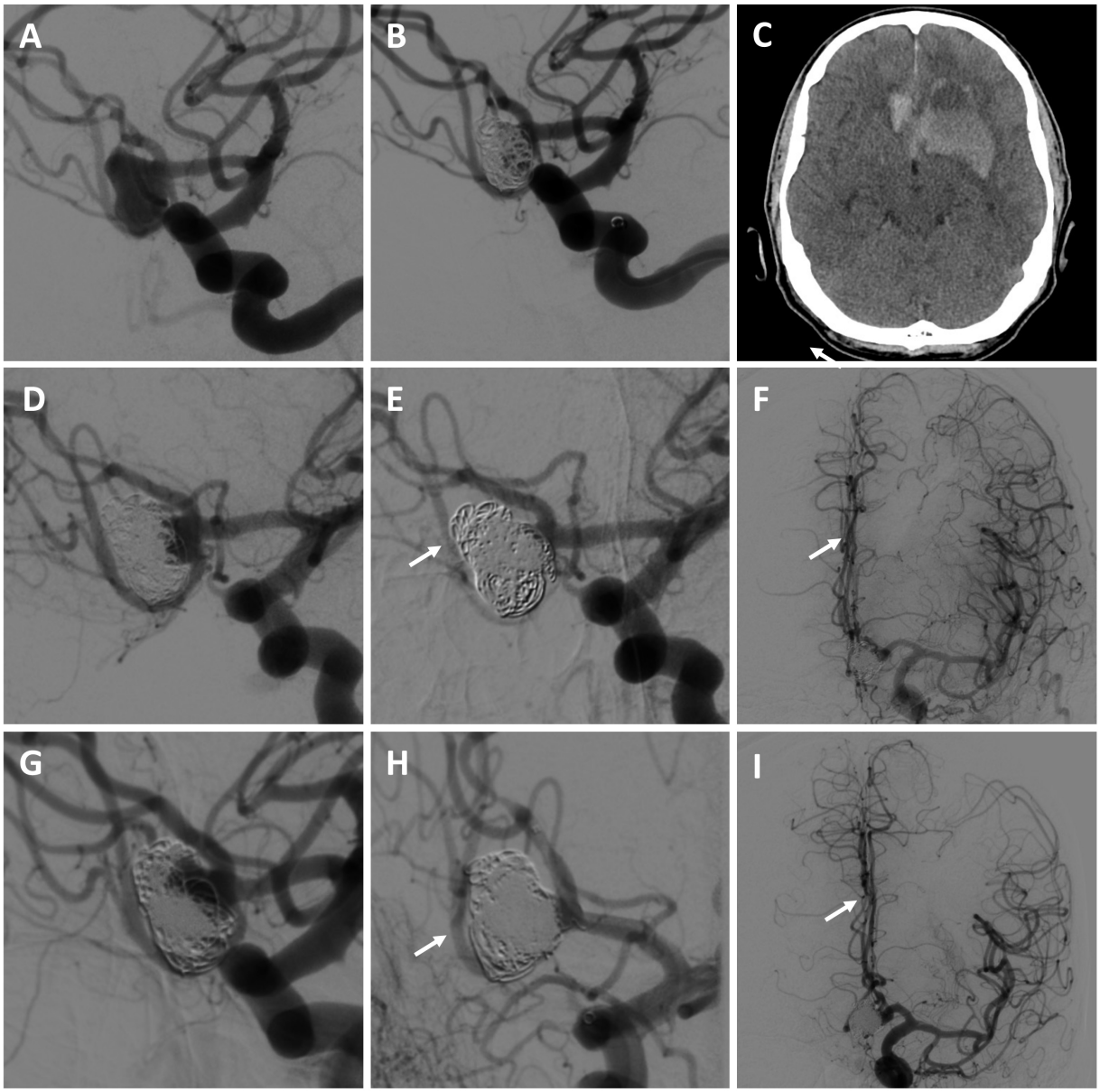

FIGURE 3
Patient #8. A 61-year-old male presented with SAH and intraparenchymal hemorrhage from a previously embolized Acomm aneurysm arising from an unpaired left A1 [**(A)** left ICA angiogram demonstrating initial Acomm aneurysm, and after coil embolization **(B)**; **(C)** head CT demonstrating SAH and IPH]. A repeat coil embolization was performed, leaving a neck residual to preserve the Acomm [**(D)** post re-coiling angiogram demonstrating a neck residual and patent Acomm]. An A3-A3 bypass was performed, followed by repeat aneurysm embolization with Acomm sacrifice [**(E,F)** post-treatment angiogram demonstrating no residual aneurysm and filling of the right ACA through the bypass (highlighted by arrows)]. **(G)** 3-month repeat angiogram demonstrated aneurysm re-growth and an open Acomm, treated with flow diversion across the left A1-2 and repeat aneurysm coiling (including Acomm re-sacrifice) [**(H,I)** post-treatment angiogram demonstrating no residual aneurysm and filling of the right ACA through the bypass (highlighted by arrows)]. On follow up, the bypass was open and there was no aneurysm recurrence. The patient was neurologically intact and living independently.

Patient #10

A 53-year-old male with a history of chronic kidney disease was referred for a large right fusiform P2 aneurysm with a proximal dysplastic P1 vessel (Figures 4A,B) after an unsuccessful attempt at flow diversion at an outside facility. He was neurologically intact. He was recommended for a combined open revascularization and endovascular internal embolization on multidisciplinary review, with a plan to keep the proximal P1 open, despite its dysplastic appearance, to preserve perforator flow. He underwent an uneventful right OA to P4 bypass with a DLCFA interposition graft. The same day he underwent a right P1 BTO that confirmed bypass patency and did not result in neurologic changes. This was followed by a coil embolization/vessel sacrifice of the right P2 aneurysm (Figures 4C–E). Flow into the proximal right P1 was preserved. He experienced a small right thalamic stroke following aneurysm sacrifice (Figure 4F), likely from perforators off the severely diseased and sacrificed P2 segment, as well as a small right occipital stroke.

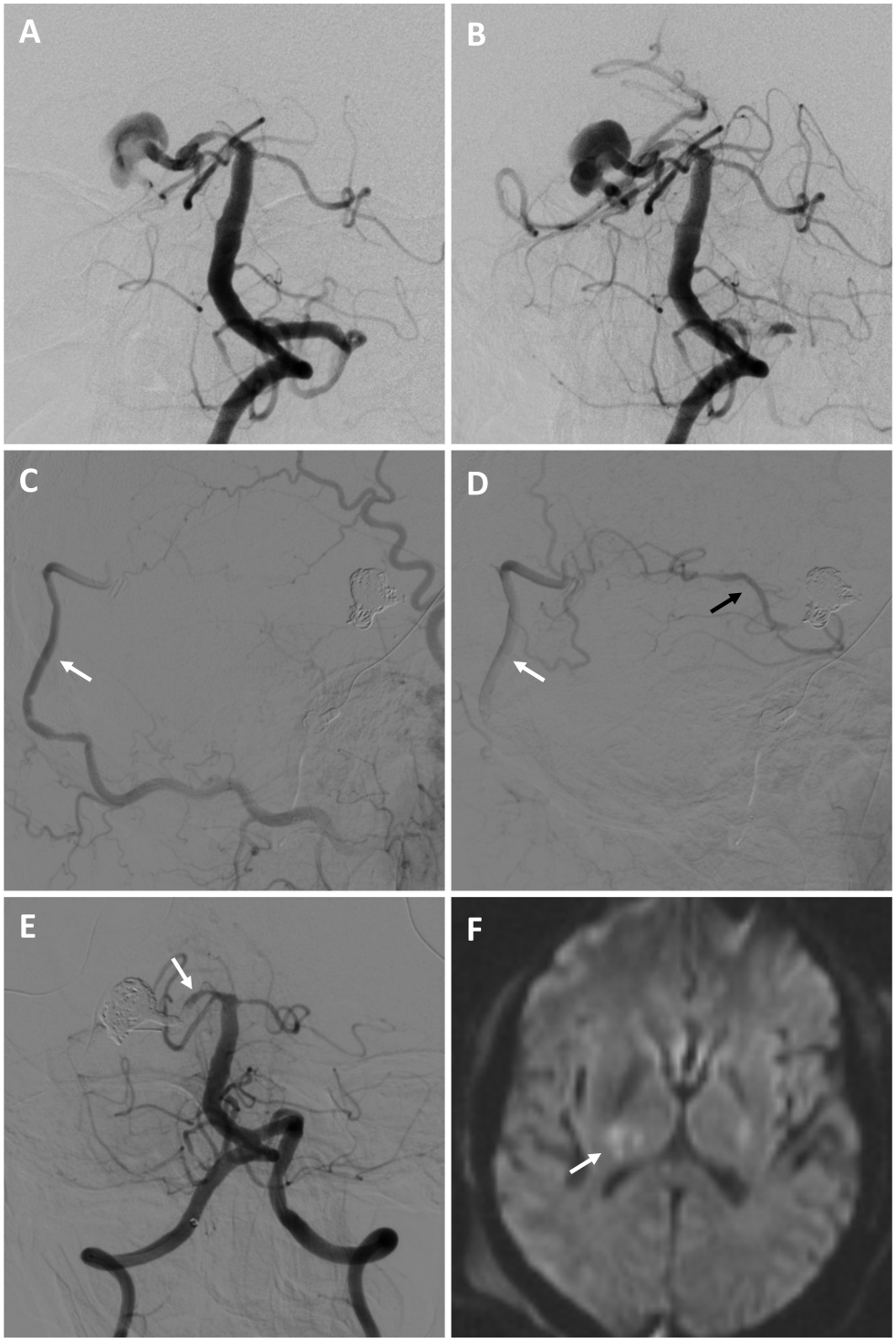

FIGURE 4
Patient #10. A 53-year-old male was referred for a large right fusiform P2 aneurysm with a proximal dysplastic P1 vessel [**(A,B)** AP angiogram of the left vertebral artery]. A prior attempt at flow diversion was aborted due to unfavorable anatomy. He underwent a right OA to P4 bypass with a DLCFA interposition graft, followed by a coil embolization/vessel sacrifice of the right P2 aneurysm (keeping the proximal right P1 patent) after BTO [**(C,D)** serial lateral images from a right external carotid artery injection demonstrating patency of the bypass (white arrows) and backfilling of the PCA territory (black arrow)]. The right P1 was kept open to preserve perforator flow [**(E)** AP angiogram of the right vertebral artery (arrow highlights right P1)]. Post-operatively he experienced a small right thalamic stroke [**(F)** axial diffusion-weighted MRI, arrow highlighting stroke], likely from perforators off the severely diseased and sacrificed P2 segment, as well as a small right occipital stroke of unclear etiology (not shown). He had left mild hemiparesis and a partial left hemianopsia. This significantly improved on 9-month follow, where he was living at home and performing all activities of daily living independently.

This resulted in mild left hemiparesis and a partial left hemianopsia that required a short inpatient rehabilitation stay. On 9-month follow up he was living at home and performing all activities of daily living independently.

Discussion

Combining open and endovascular techniques has established utility for a variety of cerebrovascular pathologies, including complex arteriovenous malformations, arteriovenous fistulas, and aneurysms (12–22). Such approaches are especially useful for aneurysms that can be challenging to treat with purely open or endovascular options, including ruptured giant, blister, fusiform, dissecting, heavily calcified, or pseudoaneurysms in difficult to access locations and with associated perforating vessels or scar tissues from prior treatments (13). Described strategies include both endovascular therapy after surgical treatment (i.e., coil embolization after partial clipping of incompletely exposed or recurrent aneurysms, or endovascular occlusion/vessel sacrifice after bypass, as used herein), and open surgical treatment after endovascular therapy (i.e., definitive clipping after dome-protection of ruptured aneurysms unable to be completely coiled, or surgical debulking to reduce mass effect after endovascular occlusion) (12, 13, 15).

Our data add to prior works supporting the use of cerebral bypass combined with endovascular embolization for complex intracranial aneurysms (13, 14, 16, 17, 19, 21, 23–26). Although previously described for lesions throughout the anterior and posterior circulation, we have found these constructs most useful for the treatment of aneurysms less surgically accessible, particularly in the posterior circulation such as those located on the distal VA, proximal PICA, and proximal PCA (80% of cases in this series). In our experience, complex aneurysms of the anterior circulation (internal carotid artery [ICA], middle cerebral artery [MCA], and even ACA) can often be directly addressed with open surgery algorithms due to their more easily accessible anatomy, which facilitates direct visualization of perforators for precise clip application during vessel ligation, trapping or aneurysm/vessel reconstruction (8, 27–31). This is not always feasible or advisable though, as evidenced by the two ACA cases in this series where a combined open and endovascular approach was used to avoid manipulation of an unstable A1/A2 pseudoaneurysm and a multiply ruptured partially coiled wide-necked Acomm aneurysm.

As demonstrated in this series, the combined approach is easily tailored to a variety of aneurysms and anatomical variations. Emerging data supports the technical and safety profile of IC-IC versus EC-IC constructs (8, 9, 32–35), and we prefer to use PICA-PICA bypass for revascularization during treatment of complex proximal PICA or VA/PICA aneurysms when the contralateral PICA anatomy is favorable. This also avoids the need for dissection of the often torturous OA or harvest of an interposition graft (as needed with other EC-IC options), or performance of a deep anastomosis (as needed with excision and re-anastomosis/re-implantation strategies) (9, 33). In cases where the contralateral PICA is not favorable for side-to-side IC-IC bypass, the DLCFA is well-sized for PICA revascularization and can be used as an interposition graft with a V3, OA, or even the contralateral PICA as a donor vessel (10, 11). Regardless of the bypass strategy used, when combined with endovascular sacrifice of the proximal PICA (and VA as needed), extended skull base approaches to reach the distal VA/PICA origin anterolateral to the brainstem can be avoided. With this approach, after vessel sacrifice the distal PICA fills anterograde from its anastomosis at the tonsillar segment, while the proximal PICA (including brainstem perforators) fills in a retrograde fashion to the point of occlusion. A similar concept can be employed for complex proximal ACA aneurysms by combining an A3-A3 bypass with endovascular vessel sacrifice or aggressive aneurysm treatments that risk vessel occlusion. This strategy avoids the need for long interposition grafts to reach into the interhemispheric fissure from the external carotid artery (ECA) circulation for ACA revascularization, while also avoiding surgical manipulation of the perforator rich A1/A2 region for aneurysms with expected scarring or wall friability. For PCA revascularizations as part of combined treatments of complex proximal PCA aneurysms, IC-IC constructs are less favorable, and we prefer to use a DLCFA interposition graft to connect the OA to a P3 or P4 vessel (again avoiding a time-consuming full OA dissection) (7, 10, 11). This can be followed by proximal PCA endovascular sacrifice, avoiding temporal lobe retraction and potential venous compromise from an additional open subtemporal approach, as well as the manipulation of often sub-optimally visualized sensitive proximal PCA perforators.

Although the overall stroke rate was 50% in this series (5 patients), treatment-related strokes occurred in three patients (30%), with the remaining two patients (20%) having delayed strokes from vasospasm. With the use of multiple treatments in a combined approach, the additional risk of each procedure should be offset by its advantages. The 100% bypass patency and low open surgery complication rate herein is similar to the 97% patency reported in a recent large series of 430 cerebral bypasses (36). These data support the relative efficacy of bypass in experienced hands, and justify the addition of an open procedure to minimize the ischemic risk associated with stand-alone end-vessel sacrifice (37, 38). Vessel sacrifice by any means (open or endovascular) is nonetheless associated with the risk of both downstream and perforator strokes, with bypass mitigating the downstream risk but not the risk of perforator stroke if they arise directly from the diseased vessel and a trapping/occlusive (rather than proximal Hunterian ligation) strategy is used. In all the patients in this series, endovascular embolization was selected to avoid unfavorable open dissections, with any significant angiographically visualized perforators preserved and a minimum length of vessel sacrificed to secure the aneurysm.

Understanding perforator anatomy is crucial to designing a treatment strategy that minimizes stroke risk. Along the V4 VA, critical perforators (including the ASA) are variable but thought to be more common distal to the PICA origin (39–41). Accordingly, although brainstem strokes from perforator infarcts can occur from sacrifice anywhere along the V4 vessel, sacrifice of the segment distal to the PICA is thought to be higher risk than more proximally (39, 42). This is true even with selective sacrifice only at the level of disease, where although it is presumed that perforators within the pathologic segment have likely already been occluded, a stump effect from inadequate outflow can extend the length of vessel occlusion based on local arterial anatomy independent of sacrifice technique (42). Even with visualization and early angiographic preservation of perforators, their patency is thus not guaranteed with deconstructive options. This is demonstrated in the patient that experienced an ASA stroke in this series, which occurred after endovascular vessel sacrifice despite

angiographic visualization of the ASA just distal to the aneurysm and allowing it to backfill from the contralateral VA. Learning from this case, we have since allowed ASA anatomy to dictate the treatment strategy of VA/PICA aneurysms, with Hunterian ligation or bypass/clip trapping used for ASAs arising from the aneurysm itself or just distal, respectively (allowing for direct, real-time assessments of ASA viability with clip placement and the potential for strategy modifications if changes are seen with vessel flow or neuromonitoring), and combined open bypass and endovascular occlusion used for cases where the ASA is removed from the aneurysm and the potential for a stump effect is low (43). Similarly, with PICA-PICA bypass, avoidance of tension on the PICAs is critical to maintain lateral medullary perforator patency, a potential contributing factor in the patient in this series with a lateral medullary stroke after PICA-PICA bypass and occlusion of a VA/PICA aneurysm. In this patient, mobilization of the ipsilateral PICA was needed to reach the contralateral vessel for bypass, potentially placing the proximal PICA perforators at risk and decreasing retrograde demand within this vessel. Learning from this, EC-IC PICA bypass has since been used if there is any concern for PICA tension with a PICA-PICA construct.

Perforators play a similarly important role in the treatment of proximal PCA aneurysms. Although these vessels can be difficult to visualize, the proximal PCA is perforator-rich and sacrifice should be avoided whenever possible (44). In the patient that experienced a small thalamic stroke from PCA perforators, this occurred despite keeping a portion of the diseased segment of the PCA proximal to the aneurysm open to allow for perforator filling (with the stroke likely from occlusion of a small vessel arising more distally along the sacrificed and grossly dysplastic P2). This situation is difficult to predict, and although it would likely have also occurred with clip trapping, may have been avoided with a bypass/proximal ligation strategy. Emerging technologies such as high-resolution cone beam computed tomography scans, which can visualize small vessels with high resolution, may help identify critical perforators pre-operatively and inform treatment planning focused on their preservation (45). BTOs may be helpful to assess bypass adequacy and predict tolerance of vessel occlusion prior to sacrifice (especially for vessels other than the VA with no expected redundancy, and/or to assess for potential stump affect with nearby critical perforators). It can nonetheless be challenging to position the balloon properly when sacrifice of smaller or more torturous vessels is planned (i.e., an ACA as in patient 8). BTOs are also not entirely predictive, as the BTO and final occlusion sites often differ slightly. Highlighting this point, patient 3 and patient 10 experienced an ASA and PCA perforator stroke, respectively, after unremarkable BTOs of the VA and P1 prior to aneurysm embolization/sacrifice.

With use of combined open and endovascular approaches in general, if there is concern for significant perforator occlusion with aneurysm embolization, proximal vessel occlusion or open clipping at a perforator-free area can be considered, allowing retrograde filling of the aneurysm and perforators through the bypass (i.e., Hunterian ligation). This must nonetheless be balanced by the reduced but ongoing rupture risk with continued aneurysm filling with this approach (46). Open clip trapping can also be used if a significant perforator is near but not emerging from the aneurysm and the proximal and distal vessel are surgically accessible.

An analysis of outcomes for the other main treatment options for complex intracranial aneurysms highlights the significant challenges of managing this patient population. Flow diversion is the main endovascular option for the treatment of nonsaccular ruptured aneurysms, but is associated with a 21 to 26% rate of ischemic/hemorrhagic complications with use of either standard devices and dual anti-platelet regimens, or newer devices and single agent anti-platelets across all anatomic sites (4, 5). While good neurologic outcomes have been reported with flow diversion for the treatment of fusiform VA aneurysms involving the PICA origin (representing 50% of the cases in the series), complete aneurysm occlusion occurs in <60% of cases, while PICA/VA occlusion can occur in up to 10% of cases (47). A variety of other endovascular options exist for complex non-saccular dissecting lesions, such as placement of multiple stents, stent-assisted coiling, and internal trapping with stenting (described as an alternative to flow diversion if a daughter vessel is involved), but are associated with 12.5 to 25% rates of infarction or aneurysm recurrence (48). Similarly, although selected complex saccular aneurysms not amenable to primary coiling and treatable with stenting or intrasaccular devices can have low rates of procedure-related hemorrhagic/thrombotic or external ventricular drainage–related events (<10% overall), persistent aneurysm filling with unclear long-term implications can occur in a significant proportion (17–46%) of cases. (2, 49). Nonetheless, the algorithm for aneurysms at our institution is endovascular management first, with more complex open or combined approaches reserved for lesions deemed to be poor candidates for stand-alone endovascular therapies (including flow diversion) on multidisciplinary review. While a direct comparison of open-only treatment strategies for the heterogenous complex aneurysm mix in this series is challenging, data from a recent series of 42 patients with largely ruptured dissecting aneurysms of the vertebrobasilar system (the majority of patients in our series) reflects the often poor baseline neurologic conditions of these patients, with good outcomes reported in less than 50% of patients with a variety of open treatments (50). The 60% overall rate of good outcomes in our series (despite 90% of patients having ruptured aneurysms), is consistent with prior data demonstrating the utility of a combined endovascular and open approach for otherwise difficult-to-treat aneurysms (16, 17).

Limitations of this study include its single-institution, retrospective design, and small patient size reflective of the relative rarity of complex aneurysms requiring combined treatments. Four patients (40%) were also lost to follow up, a reflection of the quaternary referral nature of our institution where transfer back to the referring center is often required after completion of the acute treatment stage. Finally, as expertise in both complex open revascularization and endovascular techniques is critical for the successful implementation of this strategy, the generalizability of this data is most pertinent to other high-volume bypass centers.

Conclusion

Combined open revascularization and endovascular embolization can be used for select complex aneurysms not amenable to stand-alone open or endovascular techniques.

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 University of Southern California 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

RR and JR contributed to the design and conception of the study. RR, VN, JR, JC, MT, AAm, and WM developed plans for and participated in the clinical care of included patients. AAb and NA organized and maintained the database. RR, VN, AAb, and NA collected data. RR drafted the manuscript. All authors contributed to the article 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.

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Case report: A hybrid open and endovascular approach for repairing a life-threatening innominate artery dissection using the simultaneous kissing stent technique

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Managing acute innominate artery (IA) dissection associated with severe stenosis is challenging due to its rarity, possible complex dissection patterns, and compromised blood flow to the brain and upper extremities. This report describes our treatment strategy for this challenging disease using the kissing stent technique. A 61-year-old man had worsening of an acute IA dissection secondary to an extension of a treated aortic dissection. Four possible treatment strategies for kissing stent placement were proposed based on different approaches (open surgical or endovascular) and accesses (trans-femoral, trans-brachial, or trans-carotid access). We chose to place two stents simultaneously via a percutaneous retrograde endovascular approach through the right brachial artery and a combined open surgical distal clamping of the common carotid artery with a retrograde endovascular approach through the carotid artery. This hybrid approach strategy highlights the three key points for maintaining safety and efficacy: (1) good guiding catheter support is obtainable through retrograde, rather than antegrade, access to the lesion, (2) concomitant cerebral and upper extremity reperfusion is guaranteed by placing kissing stents into the IA, and (3) peri-procedural cerebral emboli are prevented by surgical exposure of the common carotid artery with distal clamping.

KEYWORDS

arterial dissection, hybrid approach, innominate artery, kissing stent, stenosis

1. Introduction

Acute symptomatic innominate artery (IA) dissection is challenging to manage when it presents with concomitant worsening of cerebral and upper extremity ischemia. Different revascularization methods, such as endovascular, open surgery, or combined approaches, have been proposed for IA dissection, but each has its pros and cons (1). Theoretically, the optimal treatment strategy in this emergency situation accomplishes three major goals: (1)

timely recanalization of the IA, (2) reperfusion of the cerebral and upper extremities, and (3) cerebral embolization prevention during the revascularization procedure (1).

This case report discusses our treatment strategy for a patient with acute IA dissection associated with tight stenosis, complex dissection configuration, and emergency flow compromise.

2. Case description

A 61-year-old male was admitted to our emergency department after the onset of sudden chest pain. The patient's neurological findings were normal, but their blood pressure was 92/72 mmHg without right and left differences. Furthermore, their pulse rate was 55 beats/min, and their respiratory rate was 22 breaths/min. Whole body contrast-enhanced computed tomography (CECT) revealed an aortic dissection extending from the ascending to the descending aorta, which also involved the IA and extended into the right common carotid artery (CCA) (Figures 1A, B). The patient, therefore, underwent emergency aortic graft placement for the ascending aorta.

The patient recovered well immediately after the operation. On postoperative day 2, the patient became lethargic, and his blood pressure in the right arm dropped to ∼50/40 mmHg. CECT of the neck revealed a progression of the IA dissection, tight narrowing of the residual IA true lumen, and involvement of the right CCA and subclavian artery (SA) orifices (Figures 1C, D). Perfusion magnetic resonance imaging of the brain showed marked right-sided hemispheric hypoperfusion (Figures 1E, F).

To obtain cerebral and upper extremity reperfusion, we planned to reconstruct the IA bifurcation using a simultaneous kissing stent technique. After comparing the pros and cons of four kissing stent reconstruction strategies (Figure 2) designed based on different approaches (endovascular or a combined endovascular and open approach) and different accesses (trans-femoral, trans-brachial, or trans-carotid access), we chose a combined open and endovascular approach (Strategy D in Figure 2) for the lesion because it could provide better guiding catheter support for the endovascular procedures and prevent peri-procedural cerebral emboli. As for the stent selection, we chose two self-expanding closed-cell stents of the same size, in order to provide an appropriate contact with the vessel wall, better coverage of the atheromatous lesions, and to minimize stent compromise by another stent during deployment. Based on the pre-treatment CECT, the diameters of IA, proximal CCA, and proximal SA were 15.1 mm (residual true lumen: 1.5 mm), 7.9 mm (residual true lumen: 1.9 mm), and 6.8 mm, respectively; in order to reduce the squeezing pressure on the dissected vessel, we chose stent size slightly smaller than the maximal CCA diameter, i.e., two 7 × 50-mm Wallstents (Boston Scientific), for IA reconstruction. This

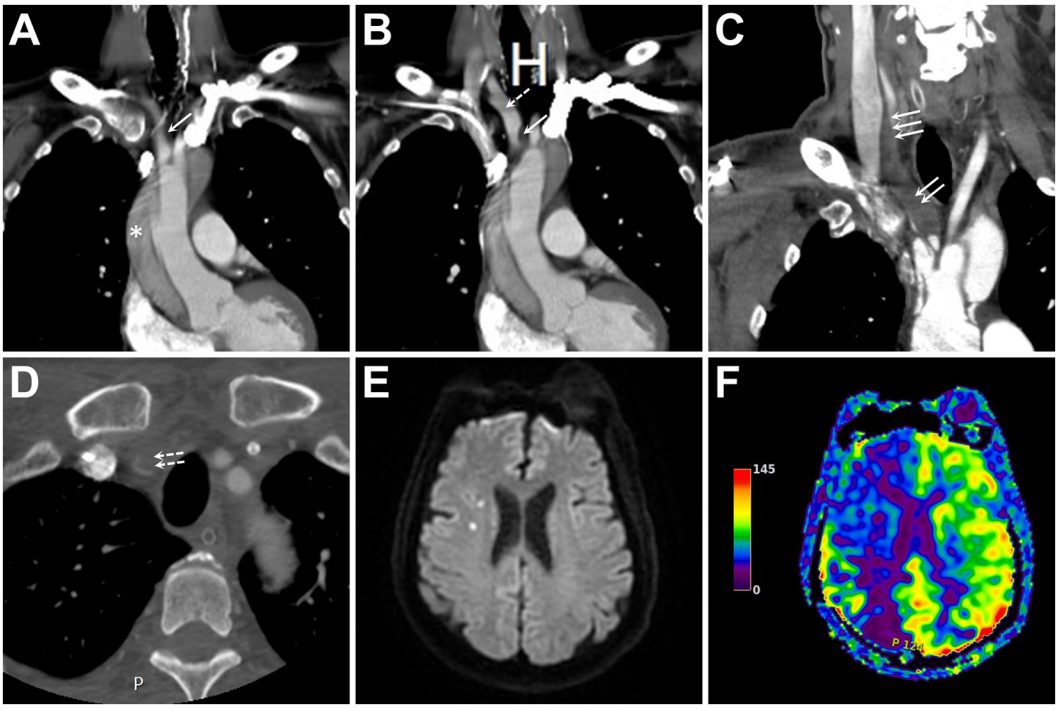

FIGURE 1
(A, B) Initial contrast-enhanced computed tomography (CECT) of the neck and chest in two consecutive coronal sections show an aortic dissection (asterisk) with innominate artery (IA) extension (single solid arrow). At this point, the main IA trunk remained patent without flow-limiting stenosis (single dashed arrow). **(C, D)** Coronal **(C)** and axial **(D)** images of CECT two days following ascending aortic grafting show expansion of the dissection's false lumen (double solid arrows), the distal extension of the dissection involving common carotid artery (triple solid arrows) and subclavian artery (double dashed arrows), and nearly complete occlusion of the main IA trunk and its bifurcation. **(E, F)** Diffusion-weighted imaging and arterial spin labeling perfusion magnetic resonance imaging of the brain reveal few embolic spots **(E)** associated with a large hypoperfusion in the right hemisphere **(F)**.

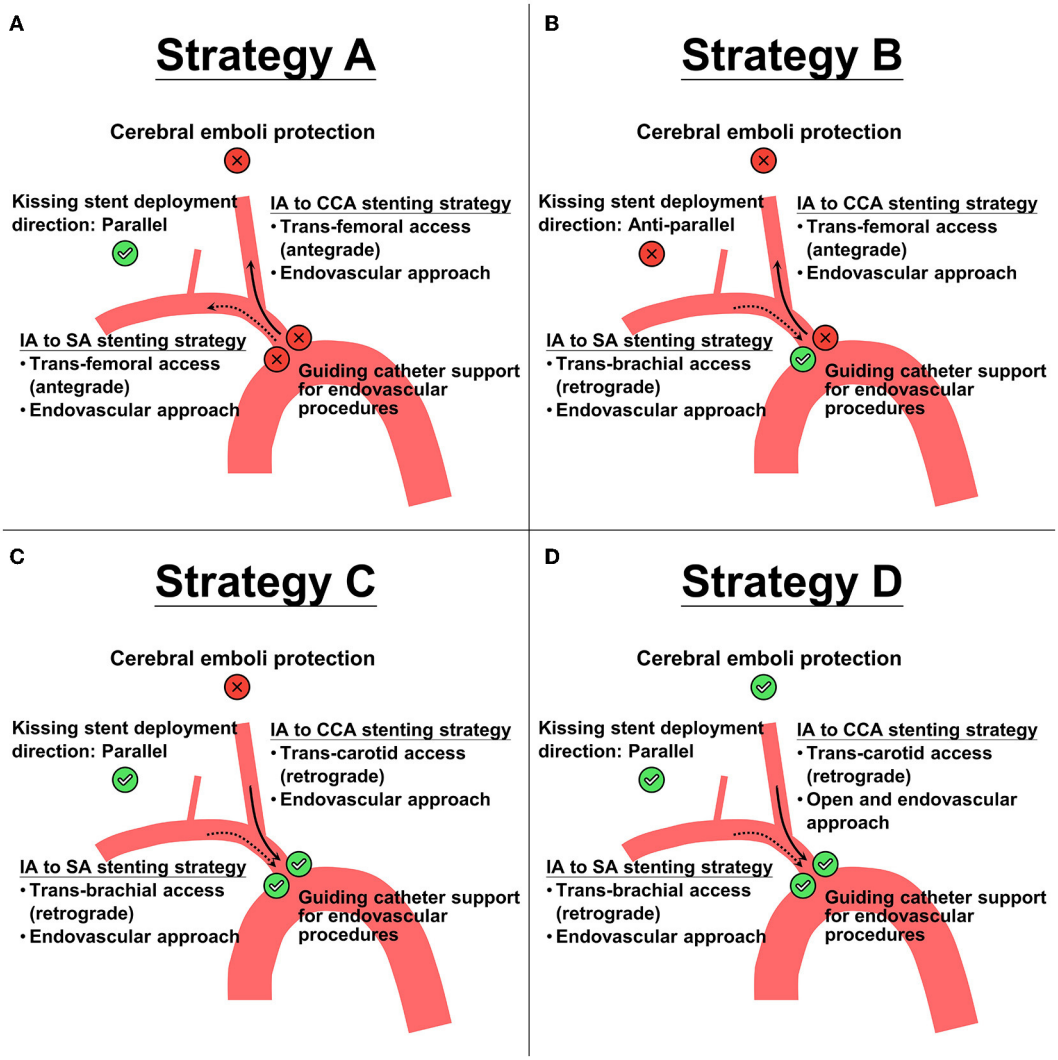

FIGURE 2
Four proposed treatment strategies **(A–D)** for kissing stent placements based on different accesses (trans-femoral, trans-brachial, or trans-carotid access) and different approaches (endovascular or a combined endovascular and open approach). Check-sign (with green circle background) and cross-sign (with red circle background) indicate the pros and cons, respectively, of the corresponding choice. Notice that strategy A and B have 1 pro and 3 cons, strategy C has 3 pros and 1 con, and strategy D has 4 pros and 0 cons. Solid arrow represents the direction of endovascular procedure in innominate artery (IA) to common carotid artery (CCA) stenting strategy. Dashed arrow represents the direction of endovascular procedure in IA to subclavian (SA) stenting strategy.

stent size suited the diameter of proximal SA (6.8 mm), and the overall diameter of the resulting kissing stents (i.e., 14 mm) was also appropriate for the dissected IA segment.

The whole procedure was performed in the hybrid operating room equipped with a biplane angiography system (Artis Q biplane Siemens, Erlangen, Germany). The patient was loaded with 300 mg of aspirin and 300 mg of clopidogrel before the procedure. A standard surgical approach to the right carotid bifurcation was performed by making an incision and dissecting along the medial aspect of the right sternocleidomastoid muscle. A roadmap of the target lesion, together with the CCA and SA, was obtained using a 5F H1 diagnostic angiocatheter placed via trans-femoral access, with its tip in the IA orifice (Figure 3A). An 18-gauge needle was used to retrogradely puncture the exposed CCA, followed by the insertion of a 10 cm 8 French sheath. Meanwhile, a 6F Neuron 088 sheath was also retrogradely placed within the right subclavian artery via the trans-brachial access. Through each guiding sheath, a 300-cm 0.014" guidewire was navigated through the tight stenosis within IA to reach the descending aorta. With the distal CCA clamped, balloon dilatation at the IA was performed using an over-the-wire 12-mm Mustang dilating balloon (Boston Scientific, Marlborough, MA, USA), which was retrogradely advanced through the wire at the CCA. Through both microwires, two 7 × 50-mm Wallstents (Boston Scientific) were then simultaneously deployed in parallel from the IA to CCA and from the IA to SA (Figure 3B). Two 7-mm Sterling balloons (Boston Scientific) were then simultaneously used to post-dilate the deployed stents. After confirming the proper stent opening, the CCA sheath was removed, and all potential debris within the CCA was expelled by flushing the CCA through the puncture

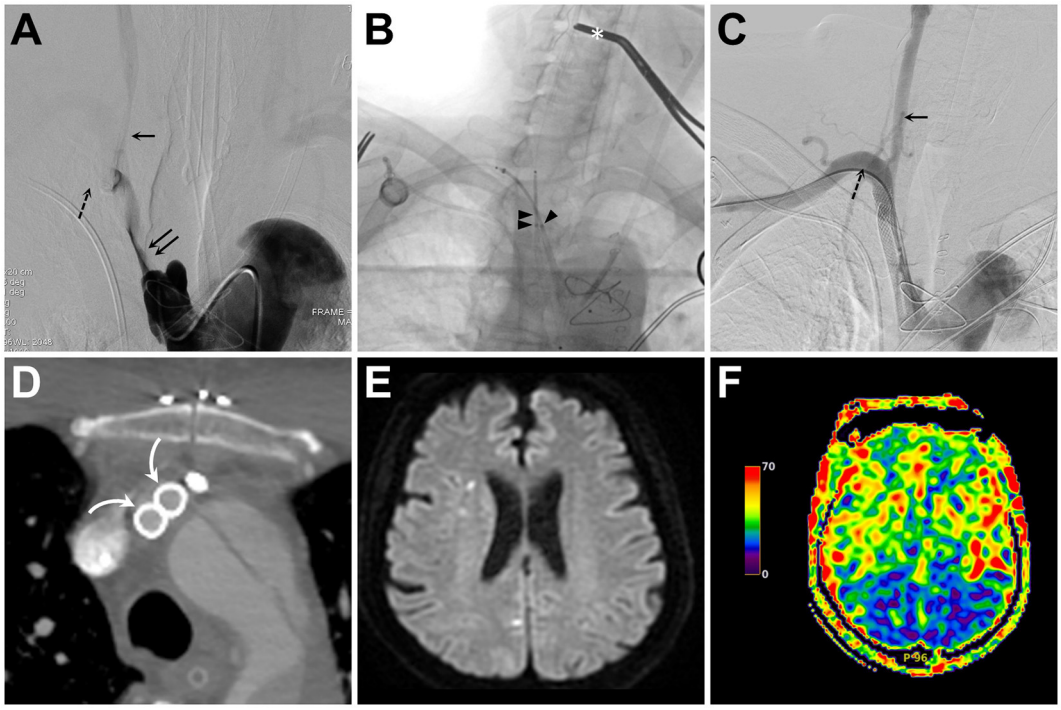

FIGURE 3
(A) Intra-innominate artery (IA) angiogram obtained from a transfemoral-placed angiocatheter reveals tight stenosis of the IA true lumen (double solid arrows) and compromised flow to the common carotid artery (CCA, single solid arrow) and subclavian artery (SA, single dashed arrow). **(B)** Fluoroscopic snapshot of the middle part of the kissing stenting procedure reveals simultaneous retrograde deployment of two Wallstents via a trans-brachial (single arrowhead) and a trans-carotid (double arrowheads) access. Also, notice the distal CCA clamp (asterisk) used for cerebral embolic protection during balloon angioplasty and stent deployment. **(C, D)** Following IA recanalization, both catheter angiography **(C)** and axial contrast-enhanced computed tomography **(D)** confirm good opening and apposition of both stents [curved arrow in **(D)**] and successful CCA (solid arrow) and SA (dashed arrow) recanalization **(C)**. **(E, F)** Diffusion-weighted imaging and arterial spin labeling perfusion magnetic resonance imaging of the brain show no increase in embolic spots **(E)** and symmetric hemispheric perfusion **(F)**.

arteriotomy with heparinized saline. The arteriotomy was closed with a 6–0 Prolene suture, and the distal CCA clamp was removed. A final angiography and CECT showed the patent stents and successful CCA and SA reperfusion (Figures 3C, D).

The postoperative systolic blood pressure of the right upper extremity returned to normal. The patient also regained consciousness, and postoperative perfusion brain magnetic resonance imaging showed symmetric cerebral perfusion without new ischemic stroke (Figures 3E, F). The patient was treated with daily aspirin 100 mg and clopidogrel 75 mg for 3 months, followed by daily aspirin 100 mg. The patient remained neurologically intact, with a modified Rankin scale of 0, at 12 month follow-up.

3. Discussion

Ischemic stroke is one of the main issues after acute type A aortic dissection repair, with an incidence rate around 13% (2). Many factors are thought to be associated with this high ischemic stroke rate. One is the cerebral hypoperfusion secondary to the severe narrowing of the true lumen of the ascending aorta (3). The next common factor will be the progression of the dissection to the supra-aortic vessels including IA and CCA; in this situation, the mechanism of ischemic stroke can be explained by either emboli from thrombus within the false lumen or by a watershed damage secondary to the severe narrowing of the ICA or CCA (3). Therefore, in patients who received type A aortic dissection repair, CTA of both supra-aortic, extracranial, and intracranial arteries should be investigated thoroughly when ischemic stroke occurs, in order to delineate the possible ischemic etiology. As demonstrated in our patient, the mechanism of acute cerebral ischemia was hypoperfusion secondary to the severe narrowing of the IA dissection, and further surgical or endovascular treatment is mandatory because IA dissection progresses and even compromises the cerebral and upper extremity flow.

Before deciding on a treatment strategy, several challenges or key points regarding the recanalization of severe IA dissection should be considered. First, the IA is typically short in length and large in diameter. Thus, if the artery becomes severely narrowed, the trans-femoral guiding catheter can only be placed in the IA orifice, which is unstable and makes subsequent endovascular procedures difficult. In contrast, retrograde access via the CCA or SA can be confidentially obtained through the true lumen of the dissected IA, and it offers a stable position for the guiding catheter, reducing the risk of catheter dislodgement in the antegrade trans-femoral approach. In other words, endovascular retrograde access to the lesion is more favorable.

Second, the high thrombus burden within the large false lumen will inevitably increase embolic risks during any manipulation maneuver, such as repetitive catheterization, wiring, or balloon angioplasty. Previous literature clearly indicates that, although endovascular treatment of IA stenosis is associated with high technical success, it is also associated with 2–18% of post-interventional ischemic complications (1, 4). In other words, cerebral embolic protection is a key step in the strategic design for IA recanalization. As we chose not to pass the lesion via an antegrade trans-femoral approach, the embolic protection solution will be either endovascularly placing a protection device in the distal CCA via the brachial artery (5), or an open surgical approach for distal CCA clamping (1). We preferred the latter since embolic protection is achieved before any manipulations around the lesion are performed.

Finally, the treatment strategy should also aim to simultaneously preserve the cerebral and upper extremities during IA recanalization. This is crucial because dissection tears can be complicated, and the false lumen of IA dissection, as in our case, may involve the IA bifurcation and the CCA and SA. When balloon angioplasty or stenting is performed at the dissected IA via one of the IA branches, the thrombus may be squeezed, blocking the pathway from the IA to another IA branch (6). Therefore, we opted to adopt a simultaneous kissing stent technique to preserve both IA branches, which is widely used for treating arterial bifurcation lesions, such as aortoiliac occlusive diseases, or left main stem bifurcation coronary artery diseases (7, 8). This technique simultaneously deploys two parallel stents in the same direction to cover the main IA trunk and both IA branches. The important of choosing self-expanding stents and placing both stents in a "simultaneous and parallel" fashion cannot be overemphasized because this minimizes strut compromise by each other during deployment. Post-dilate both stents using two dilatation balloon of the same size in a synchronous inflation and deflation rate further guarantee that both stents will open better without compromise. In our patient, we specifically chose two self-expanding nitinol closed-cell stents of the same diameter for "kissing" because those stents are theoretically advantageous. For example, they provide even radial force for simultaneous expansion, decrease the chance of distal embolization owing to their superior ability to trap thrombotic materials, and reduce radial mismatch areas (7, 9).

All the above considerations formed the basis of our treatment strategy design in Figure 2. To fulfill all the favorable requirements, we chose to recanalize the IA and thus obtain cerebral and upper extremity reperfusion (and provide cerebral embolization protection) by performing retrograde balloon angioplasty and deploying two kissing stents through a percutaneous puncture of the right brachial artery in addition to surgically exposing and puncturing the CCA under distal CCA clamping. Our patient had significant postoperative clinical and radiological improvements and no new embolic strokes following the revascularization procedure, supporting the feasibility of such a treatment strategy.

In conclusion, this case details our treatment strategy for a complex acute IA dissection with severe narrowing in an emergency. Furthermore, we highlight the advantages of a hybrid open and endovascular approach for placing kissing stents for managing challenging IA dissections.

Data availability statement

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

Ethics statement

The studies involving human participants were reviewed and approved by TMU-Joint Institutional Review Board. 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 participant/patient(s) for the publication of this case report.

Author contributions

C-HK wrote the first draft of the manuscript. S-TY, Y-HL, Y-CL, and I-CS performed the procedure and revised the manuscript. All authors read and approved the final 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.

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Case report: An overlooked complication of the dural suture after craniotomy: pseudoaneurysm of the middle meningeal artery with endovascular resolution

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Aneurysms of the middle meningeal artery (MMA) are exceedingly uncommon and mainly result from traumatic brain damage, but this report describes a case of MMA aneurysm induced by cranial surgery. Surgery was performed on a 34-year-old male with cerebrovascular malformation and cerebral hemorrhage. Cerebral angiography revealed no MMA aneurysm before craniocerebral surgery; however, a postoperative angiogram revealed a new MMA aneurysm. Aneurysms of the MMA are uncommon consequences of brain surgery. Based on our findings, the MMA as well as other meningeal arteries should be avoided while suturing the dura mater tent to prevent aneurysms.

KEYWORDS

aneurysm, cerebral angiography, case report, middle meningeal artery (MMA), craniofacial surgery

Introduction

Aneurysms of the middle meningeal artery (MMA) are exceedingly rare. Rupture can result in a variety of intracranial hemorrhages, including epidural haematomas (1), subdural hematomas, and intracerebral hemorrhage (2).

True aneurysms and pseudoaneurysms are the two forms of aneurysms. True aneurysms of the MMA resemble regular cerebral aneurysms, typically originating from their branches, and are usually related to increasing haemodynamic stress or a pathological state in MMAs. Increased blood flow and haemodynamic stress can be caused by many disorders, including arteriovenous malformations (3), Moyamoya disease (4), meningioma (5), and cranial tumor metastases (6). In addition to haemodynamic stress, other pathological states of the MMA, such as Paget's disease, hypertension (7), and type 2 neurofibromatosis (8), can cause aneurysms.

The etiology of pseudoaneurysms of the MMA is either traumatic or medically induced injury. A temporal skull fracture generates a tiny rupture in the vascular wall, which is subsequently occluded by a clot during the acute phase before recanalisation to establish a false lumen. On angiography, pseudoaneurysms frequently lack a neck and are uneven, resulting in delayed and extremely sluggish filling and emptying (9), and possible iatrogenic damage.

In the present case, no obvious MMA aneurysms on angiogram were reported before surgery and prior to discharge. We present the case of a 34-year-old male with an MMA aneurysm which was discovered on an angiogram obtained 12 days after cranial surgery.

Case report

A 34-year-old man presented with loss of consciousness that lasted for 5 h, accompanied with headache and vomiting; hence, he was admitted to the hospital. Computed tomography angiography (CTA) of the brain revealed cerebral hemorrhage in the right temporal lobe and diffuse subarachnoid hemorrhage, raising the possibility of an arteriovenous malformation (AVM) (Figure 1). Subsequently, the patient was transferred to our department for surgery. Intraoperatively, an 8.9 × 7.4 mm vascular malformation in the right temporal lobe, which was fed by the inferior trunk branch of the ipsilateral middle cerebral artery, was discovered on right internal carotid cerebral angiography (Figures 2A–C) (Supplementary Video S1). The Spetzler-Martin AVM grade is 2, and the supplementary grade is 2. No aneurysm was observed in the right MMA during this time (Figure 2D). The patient's

FIGURE 1
Preoperative brain CT images show a right temporal lobe cerebral hemorrhage and a diffuse subarachnoid hemorrhage, suggesting an Arteriovenous Malformation (AVM).

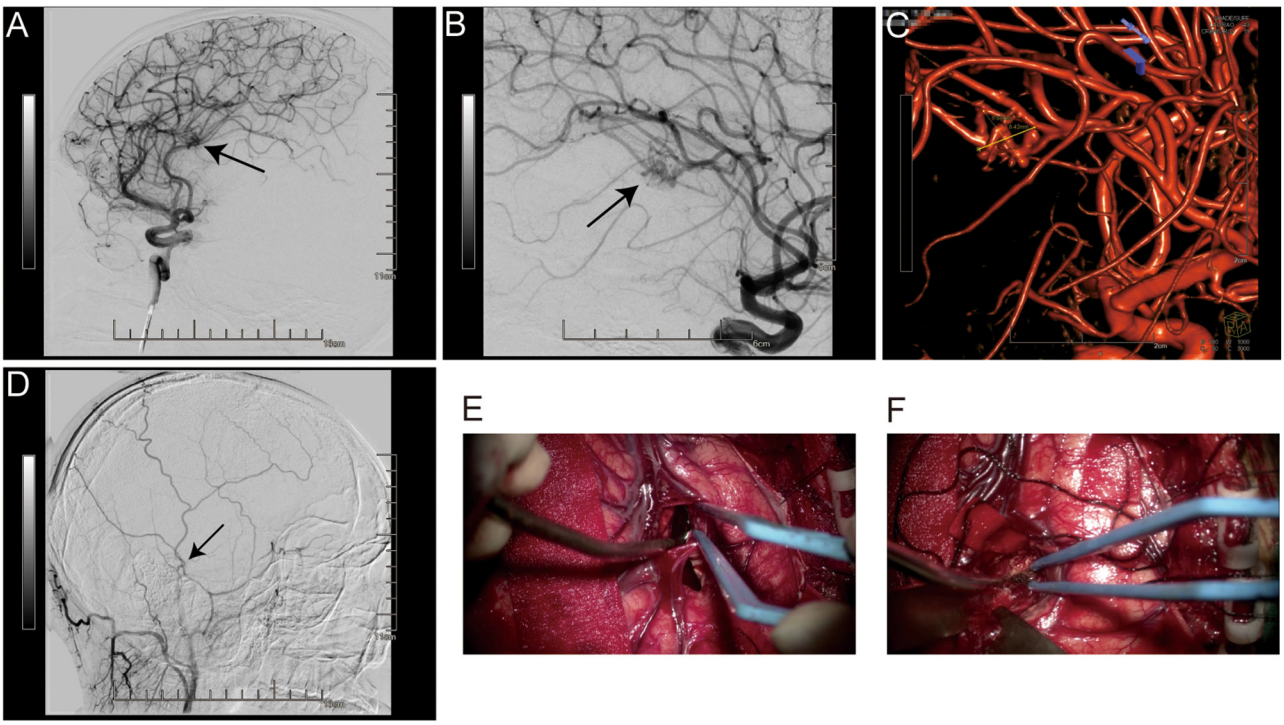

FIGURE 2
Before surgery, a right internal carotid cerebral angiography revealed an 8.9 × 7.4 mm vascular malformation in the right temporal lobe, which is fed by the ipsilateral middle cerebral artery's inferior trunk branch **(A–C)**. The MMA was free of aneurysms **(D)**. The surgical images show a blood clot and a distorted vascular mass in the insular cortex **(E, F)**.

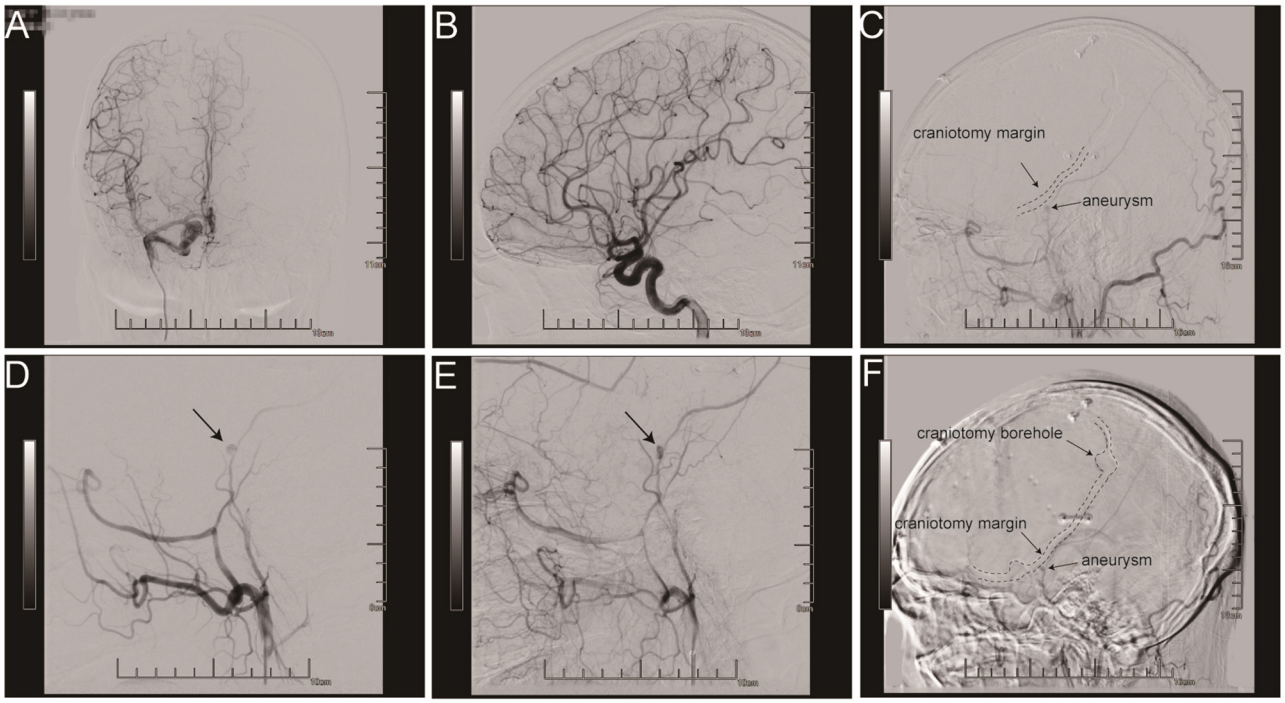

FIGURE 3
A full resection of a cerebral vascular abnormality was identified during the evaluation **(A, B)**. In the cerebral angiography following surgery, a 3.3 × 3.1 mm aneurysm of the right posterior MMA was discovered at the craniotomy cut edge of the skull **(C, F)**. Angiograms demonstrating late filling of a MMA aneurysm and contrast medium stagnation **(D, E)**.

family actively requested surgical treatment. Cerebral vascular malformation excision was performed. Surgical footage showed a blood clot and a distorted vascular mass in the insular cortex (Figures 2E, F). The M3 branch of the middle cerebral artery supplies the blood to the AVM. No drainage veins were seen on DSA, tiny drainage vein was seen during craniotomy. There were no evident dural lacerations or leakage from the MMA during the operation. The patient regained consciousness after surgery with minimal neurological sequelae, and a brain CT scan the next day revealed no cerebral infarction or apparent epidural or subdural hemorrhages.

Cerebral angiography was conducted 12 days after surgery, which revealed that the cerebral vascular abnormality was completely removed (Figures 3A, B); however, a 3.3 × 3.1 mm posterior right MMA aneurysm (Figure 3C) (Supplementary Videos S2, S3) was seen, which was absent on initial cerebral angiography. Because angiography demonstrated late filling of the aneurysmal sac during the arterial phase and contrast medium stagnation, this MMA aneurysm was classified as a pseudoaneurysm (Figures 3D, E). The aneurysm was visible near the cut edge of the skull in the images (Figure 3F). We informed the patient and family that the aneurysm was at risk of rupture. They can choose between endovascular intervention, craniotomy and no further treatment. The patient and family opted for the less invasive endovascular treatment. Endovascular embolisation was performed with an ONYX 18 embolic agent. Right external carotid arteriography revealed the MMA aneurysm found on the last DSA. A 5 ml ONYX 18 embolic agent was progressively injected through a microcatheter into the posterior branch of the MMA (Figure 4). The patient was allowed out of bed and was able to ambulate 2 days after embolisation. The patient provided informed consent to have his case published.

The patient came to our hospital for follow-up after 6 months. DSA revealed no recurrence of AVM and MMA aneurysm (Supplementary Videos S4, S5). Here is the timeline of the patient receiving treatment and follow up (Figure 4C).

Discussion

The pathogenesis of the MMA aneurysm in our case was directly linked to surgery, since it was not initially seen on preoperative angiography but was detected on postoperative angiography. Based on the digital subtraction angiography (DSA) images (Figure 3), we concluded that the MMA aneurysm was induced by dural tenting sutures and craniotomy. We carefully examined the edges of the dura mater during the operation. If the aneurysm was caused by craniotome, then intraoperative hemorrhage and a rupture of the dura mater will be found.

A previous study described an MMA pseudoaneurysm following internal carotid artery trapping and high-flow bypass with a radial artery graft (10). Another study presented an iatrogenic pseudoaneurysm of the MMA after installation of an external ventricular drain (11). However, these studies lacked comprehensive preoperative and postoperative imaging data. Iatrogenic MMA aneurysms were observed at the skull and dural borders in all three

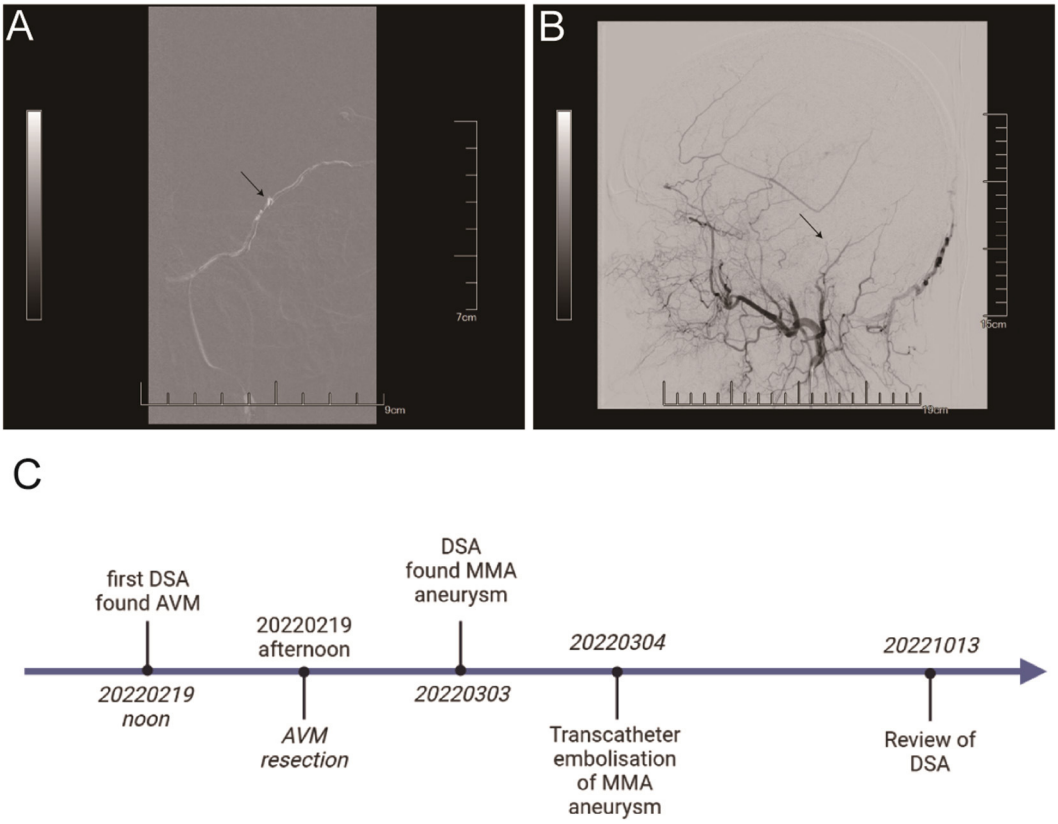

FIGURE 4
The ONYX 18 embolic agent was injected into the right MMA posterior branch **(A)**. There was no evidence of an aneurysm or the posterior branch of the right MMA **(B)**. It's the timeline of the patient receiving treatment and follow up **(C)**.

cases. According to our imaging data, MMA aneurysms were linked to craniocerebral surgery. These examples imply that dural tenting sutures may be associated with MMA aneurysms.

Observations made on a number of patients, including the case presented, reveal the occurrence of epidural and subdural hemorrhage following brain surgery. Since angiography was either not done or initially showed irrelevant findings, these cases have been linked to the placement of dural tenting sutures.

Most pseudoaneurysms and real aneurysms require treatment owing to the risk of rupture. Endovascular embolisation and surgical resection with haematoma evacuation when needed are the treatments of choice for these diseases.

Conclusion

The MMA is a critical landmark when performing brain surgery. The position of the MMA and other meningeal arteries should be meticulously considered when suturing dural tents since it is prone to iatrogenic injury.

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

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

YX wrote the manuscript. XL suggested ideas and provided guidance. Both authors contributed to the article 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

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2023.1173821/full#supplementary-material

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Effect of hematoma volume on the 30-day mortality rate of patients with primary hypertensive brainstem hemorrhage: a retrospective cohort study

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Objective: The purpose of this study is to investigate the effect of hematoma volume on the 30-Day Mortality Rate of patients with Primary Hypertensive Brainstem Hemorrhage (PHBH).

Methods: Retrospective analysis was done on the clinical information of 74 patients who underwent treatment for primary hypertensive brainstem hemorrhage at the Department of Neurosurgery of the 908th Hospital of the Joint Logistic Support Force of the Chinese People's Liberation Army between January 2018 and December 2021. Both univariate and multivariate logistic regression were used to assess clinical signs and risk factors that affect 30-day mortality.

Result(s): In the 74 patients with primary hypertensive brainstem hemorrhage included in this investigation, 46 patients died and 28 patients survived. The mortality rate at 30 days was 62.16%. A statistically significant difference was seen ($P < 0.001$) in the results of the univariate analysis, which suggested that hematoma volume may be a factor affecting the prognosis of patients with hypertensive brainstem hemorrhage. Hematoma volume was further demonstrated to be a risk factor and an independent factor impacting death in patients with brainstem hemorrhage ($P < 0.001$) by multivariate logistic regression analysis (OR: 2.6, 95% CI: 1.7–3.9, $P < 0.001$ Crude Model, OR: 3.6, 95% CI: 1.7–7.7, $P < 0.001$ Multivariate-Adjusted Model). After adjusting for confounding variables such as age, body mass index, sex, history of diabetes mellitus, history of hypertension, admission GCS score, stereotactic aspiration, combined hydrocephalus, admission systolic and diastolic blood pressure, the hematoma volume was revealed to be an independent predictor of 30-day death in patients with brainstem hemorrhage. We discovered by smooth curve fitting that hematoma volume increased in a non-linear manner with 30-day mortality. The 30-day mortality rate did not alter significantly when the hematoma volume was less than 4 ml. When the hematoma volume was greater than 4 ml, the 30-day mortality rate increased rapidly, and when the hematoma volume was 10 ml, the 30-day mortality rate reached the maximum.

Conclusion(s): Hematoma volume is an independent factor affecting 30-day mortality in patients with primary hypertensive brainstem hemorrhage. The severe and extensive neurological damage caused by primary hypertensive brainstem hemorrhage is highly unlikely to be fundamentally altered by a single protocol, and new avenues need to be explored scientifically and continuously.

KEYWORDS

hematoma volume, 30-day mortality, primary hypertensive brainstem hemorrhage, neurological damages, clinical signs and symptoms

Introduction

A spontaneous brainstem hemorrhage known as a primary hypertension brainstem hemorrhage (PHBH), which is unrelated to cavernous hemangioma, arteriovenous malformation, or any other disorders, is connected with hypertension. Primary hypertensive brainstem hemorrhage, which has an abrupt onset, quick progression, and a high fatality rate, is one of the most dangerous varieties of hemorrhagic stroke (1, 2). It primarily affects people between the ages of 40 and 60 and has a 2–4/100,000 yearly incidence rate, with men being more likely than women to be affected (3, 4). When a brainstem hemorrhage occurs, a hematoma typically develops quickly and frequently results in symptoms such as coma, tetraplegia, central fever, respiratory and circulatory failure, among others (5, 6). The hematoma caused by PHBH can quickly expand and result in a rapid deterioration of the patient's condition.

The management of PHBH remains controversial, and there is a need to better understand the factors that influence its prognosis (7). Previous research has shown that the volume of the hematoma is an independent predictor of the outcome in intracerebral hemorrhage (ICH), with a volume of 30 ml being a cutoff for death (8). However, the hematoma volume threshold for mortality outcomes in PHBH has not been adequately clarified. This study aims to investigate the clinical outcomes and risk variables that affect the prognosis of 74 patients with PHBH who received treatment in our department. The study uses a retrospective analysis of the patient's data to examine the relationship between hematoma volume and 30-day mortality in PHBH. Our hypothesis is that the threshold of hematoma volume is an independent predictor of 30-day death in patients with PHBH. By determining the threshold point of hematoma volume, this study aims to provide additional basis for optimizing treatment strategies for brainstem hemorrhage.

Methods

General information

This study comprised 74 PHBH patients who received care at the Department of Neurosurgery of The 908th Hospital of Joint Logistic Support Force of the Chinese People's Liberation Army between January 2018 and December 2021 (**Figure 1**). There were 28 females and 46 males, ranging in age from 30 to 80, with a mean age of 54.4. The Glasgow Coma Scale (GCS) indicated that 29 patients had 6–8 points and 45 cases had 3–5 points. This study was approved by the ethics committee of The 908th Hospital of Joint Logistic Support Force of Chinese People's Liberation Army, and the patients' families signed the informed consent. The data included in this report has never been published, in whole or in part, or offered for publication.

Inclusion and exclusion criteria

The following criteria were used to determine inclusion: 1. Patients with PHBH identified by CT images; Hypertension was defined as SBP 140 mmHg and/or DBP 90 mmHg; 2. GCS score $\leq$8 points, with or without the gradual aggravation of consciousness; 3. Onset time $\leq$24 h; steady circulation and respiration; 4. Full clinical case information.

The following criteria were used to determine exclusion: 1. Secondary brainstem hemorrhage resulting from vascular malformation, metastasis, cavernous hemangioma, or traumatic brain injury; 2. Unstable vital signs and GCS score of 3 points; 3. Complicated by important coagulation disorders or organ failure.

Imaging analysis

All 74 patients with brain computed tomography (CT) examinations had verified brainstem hemorrhage. The Tada formula (9) was used to compute the hematoma volume. All patients underwent a CT scan with a slice thickness of 5 mm, and the size and volume of the hematoma were calculated using the formula $A \times B \times C/2$, where A represents the diameter of the hematoma with the greatest diameter on the axial plane of the CT scan, B represents the diameter of the hematoma perpendicular to A on the same plane, and C represents the total length on the vertical plane (3, 10).

Stereotactic aspiration surgery in PHBH

Equipment and instruments: We used a stereotactic frame to ensure accurate and consistent target localization. The surgical instruments included a high-speed drill with a side-cutting drill bit, a stereotactic biopsy cannula, and an aspiration catheter. A compatible stereotactic planning software was used to determine the coordinates for target localization based on preoperative CT scans.

Patient preparation: Prior to the procedure, the patient was placed under general anesthesia. The stereotactic frame was then fixed to the patient's head, ensuring both comfort and stability. Preopera-tive CT scans were acquired with the stereotactic frame in place, and these images were loaded into the stereotactic planning software to identify the coordinates of the target hematoma site.

Target localization: Using the stereotactic planning software, we calculated the target coordinates (x, y, z) and the entry angle for the surgical trajectory. The target site was chosen to minimize damage to critical structures, such as the brainstem and surrounding vasculature.

Surgical procedure: After sterilizing and draping the surgical site, a small skin incision was made at the entry point. The high-speed drill with a side-cutting drill bit was used to create a small burr hole in the skull. The stereotactic biopsy cannula was then

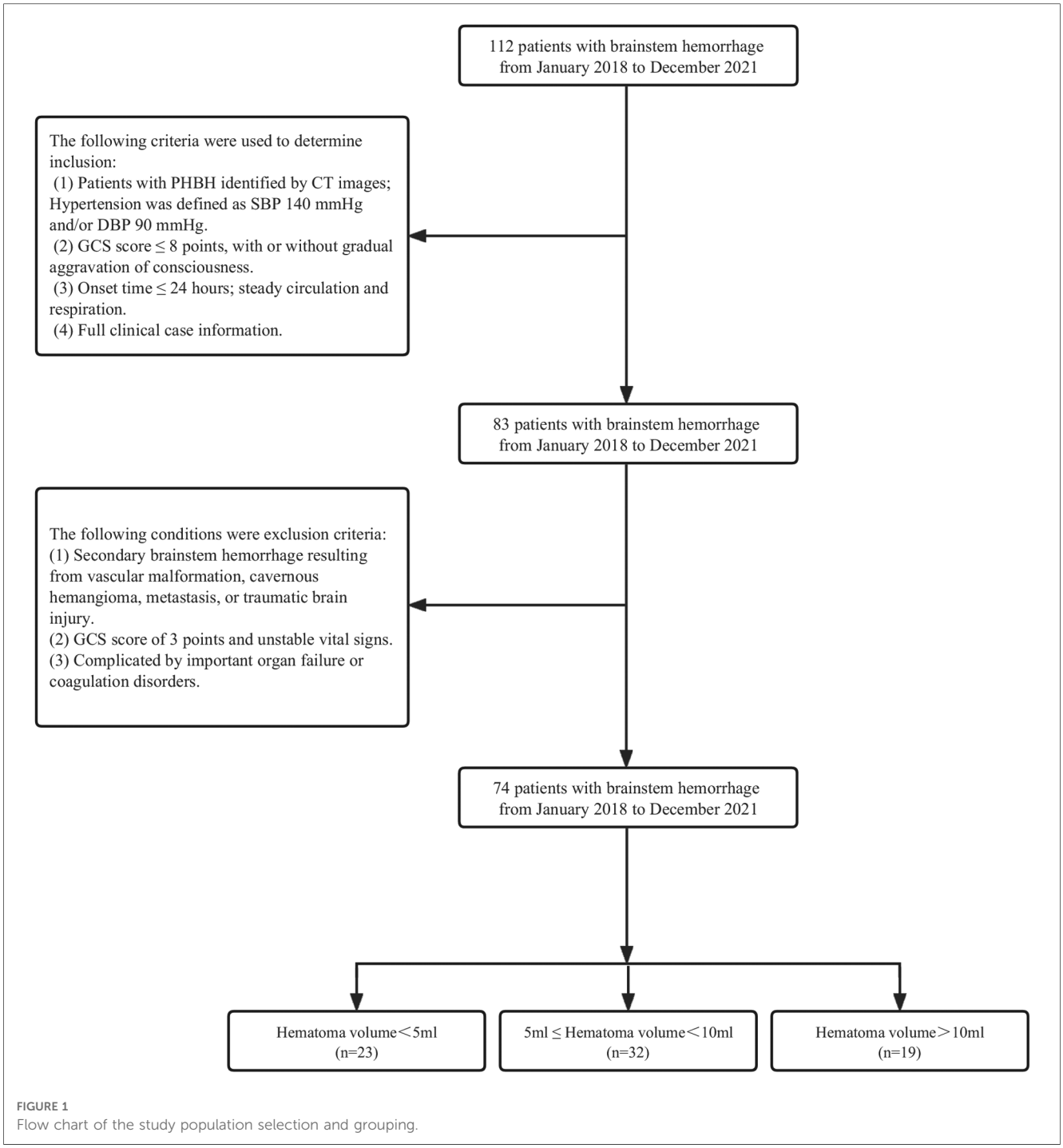

FIGURE 1
Flow chart of the study population selection and grouping.

carefully advanced through the burr hole, guided by the predetermined coordinates and trajectory angle. Once the tip of the cannula reached the hematoma, the aspiration catheter was inserted through the cannula, and the hematoma was gradually aspirated. Throughout the procedure, we carefully monitored the patient's neurological status and vital signs.

Postoperative management: Following the completion of the stereotactic drainage, postoperative CT scans were ob-tained to assess the reduction in hematoma volume and to monitor for any complications, such as rebleeding or infection. The patient was closely monitored in the intensive care unit (ICU) for any changes in neurological status or vital signs, and appropriate medical management was provided as needed.

Efficacy evaluation

The prognosis of survivors was assessed using a modified Rankin scale (mRS) (11), where a score of mRS 3 points indicated a favorable prognosis and a score of mRS 4–6 points indicated bad prognosis (Table 1).

TABLE 1 The modified rankin scale (mRS).

Level	Details of the Modified Rankin Scale
0	No symptoms.
1	No significant disability. Able to carry out all usual activities, despite some symptoms.
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
3	Moderate disability. Requires some help, but able to walk unassisted.
4	Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
6	Dead.

Outcome measures

Our research focused on each subject's vital status, which was categorized as either dead or living as a dichotomous variable. Readily available medical records were used to determine the date of death for the deceased participants. The following demographic, clinical data and 30-day mortality outcome data were analyzed: age, sex, past medical history, GCS score, stereotactic aspiration procedure, combined hydrocephalus, hematoma type, BMI, admission SBP, DBP, and hematoma volume. The hematoma volume was a continuous variable and was grouped into 3 groups according to less than 5 ml, 5–10 ml, and greater than 10 ml (12, 13). The primary outcome was defined as 30-day death. 30-day mortality was defined as a death that occurs within 30 days of the index event, usually admission, surgery, or medication in the hospital.

Statistical analysis

The differences between the groups in terms of demographics, hematoma volume, and 30-day mortality were looked at. The mean and standard deviation were used to express continuous variables (SD). One-way ANOVA was used to compare continuous variables that had a normal distribution, while the Kruskal-Wallis test was used to analyze continuous variables with an atypical distribution. When comparing the distribution of categorical data, Pearson's chi-squared test or Fisher's exact test was used, depending on the situation. Categorical variables were presented as count and proportion. The probable causes of 30-day mortality were examined using univariate logistic regression analysis. To investigate the possible independent association between the hematoma volume and 30-day mortality, multivariate logistic regression analysis was used. As recommended by the STROBE guidelines, this study presents both unadjusted (Crude Model), slightly adjusted (Adjusted Model 1), and fully adjusted (Adjusted Model 2) equations. In the multivariable analysis, the confounding factor is an important issue, we performed some different statistical models to verify the results' stability. In the final model, we adjusted the factors basing the following three rules: 1. We adjusted for variables, if it was added to this model, the matched odds ratio would change by at least 10%. 2. For univariate analysis, we adjusted for variables, of which the p values <0.1. 3. For multivariable analysis, variables were chosen based on previous findings and clinical constraints. The results of these models are shown in (Table 5). The statistical software packages R (The R Foundation; version 4.2.0), and Empower (R) (X&Y solutions, Boston, MA, USA) were used for all statistical analyses. $P < 0.05$ was considered statistically significant.

Results

30-Day mortality in patients with PHBH

Of the 74 patients with primary hypertensive brainstem hemorrhage treated in our department, 46 died and 28 survived. The 30-day mortality rate was 62.16% (Table 2).

Baseline characteristics

A total of 74 patients were divided into three groups based on hematoma volume (HV) as follows: HV < 5 ml ($n = 23$), 5 ≤ HV < 10 ml ($n = 32$), HV ≥ 10 ml ($n = 19$) (Table 3). Table 3 shows the comparison of baseline data, clinical indicators, and 30-day mortality for the 3 groups. No significant differences were observed in age, BMI, admission SBP, DBP, gender, and prior medical history among the different hematoma volume groups (all p values > 0.05). However, 30-day death increased significantly from the lowest HV < 5 ml group to the highest HV ≥ 10 ml group (P < 0.001).

Univariate analysis of 30-Day mortality

Hematoma volume was found to have a significant impact on 30-day mortality by univariate logistic regression analysis (Table 4). Gender, age, hematoma type, prior medical history, BMI, and admission DBP all had a negative impact on 30-day mortality, while GCS score, stereotactic aspiration surgery, combined hydrocephalus, and admission SBP all had a positive impact.

TABLE 2 The 30-day mortality in patients with primary hypertensive brainstem hemorrhage.

	Number of cases (n)	Yes	No	Mortality rate (%)
30-Day mortality rate	$n = 74$	46	28	62.16

TABLE 3 Baseline characteristics of participants ($N = 74$).

Hematoma Volume	T1	T2	T3	*P*-value
	HV < 5 ml	5 ≤ HV < 10 ml	HV ≥ 10 ml	
N	23	32	19	
Age, years	55.26 ± 12.12	56.59 ± 15.77	49.79 ± 14.41	0.256
BMI, kg/m^2	22.39 ± 2.84	22.25 ± 2.90	23.16 ± 3.02	0.543
Admission SBP, mmHg	148.61 ± 12.39	157.91 ± 15.34	165.37 ± 21.06	0.005
Admission DBP, mmHg	87.04 ± 5.94	85.00 ± 7.82	85.21 ± 5.30	0.505
Gender				0.592
Female	10 (43.48%)	10 (31.25%)	8 (42.11%)	
Male	13 (56.52%)	22 (68.75%)	11 (57.89%)	
Prior medical history				0.814
History of hypertension	9 (39.13%)	18 (56.25%)	10 (52.63%)	
History of diabetes	1 (4.35%)	1 (3.12%)	0 (0.00%)	
Hypertension and diabetes	6 (26.09%)	8 (25.00%)	5 (26.32%)	
None	7 (30.43%)	5 (15.62%)	4 (21.05%)	
GCS score				0.011
6–8 points	14 (60.87%)	12 (37.50%)	3 (15.79%)	
3–5 points	9 (39.13%)	20 (62.50%)	16 (84.21%)	
Stereotactic aspiration surgery				0.017
No	7 (30.43%)	2 (6.25%)	1 (5.26%)	
Yes	16 (69.57%)	30 (93.75%)	18 (94.74%)	
Combined hydrocephalus				0.002
No	21 (95.45%)	24 (75.00%)	9 (47.37%)	
Yes	1 (4.55%)	8 (25.00%)	10 (52.63%)	
30-day mortality				<0.001
Survival	20 (86.96%)	8 (25.00%)	0 (0.00%)	
Dead	3 (13.04%)	24 (75.00%)	19 (100.00%)	
Hematoma type				<0.001
Massive type	1 (4.35%)	7 (21.88%)	5 (26.32%)	
Bilateral tegmental type	8 (34.78%)	19 (59.38%)	13 (68.42%)	
Basal tegmental type	9 (39.13%)	6 (18.75%)	1 (5.26%)	
Unilateral tegmental type	5 (21.74%)	0 (0.00%)	0 (0.00%)	

HV, hematoma volume; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; GCS, glasgow coma scale;.

Multivariate logistic regression analysis for 30-day mortality

After adjusting for confounding variables such as age, sex, prior medical history, GCS score, stereotactic aspiration surgery, combined hydrocephalus, BMI, admission SBP, and DBP, hematoma volume was further examined using multivariate logistic regression. According to the findings, hematoma volume was a reliable predictor of 30-day death (Table 5). The odds ratio (OR) of 30-day mortality was 2.25 (95% CI: 1.60, 3.17), 2.26 (95% CI: 1.60, 3.20), and 2.90 (95% CI: 1.58, 5.32) in the crude model, adjusted model 1, and adjusted model 2, respectively, with statistically significant differences ($p < 0.0001$ and 0.0006, respectively). Furthermore, compared with the HV < 5 ml group, the 30-day mortality in the 5 ≤ HV < 10 ml group increased significantly (OR = 20.00 (95% CI: 4.67, 85.57), $P < 0.0001$, OR = 21.25 (95% CI: 4.74, 95.27), $P < 0.0001$ and OR = 32.00 (95% CI: 3.81, 268.58), $P = 0.0014$, respectively). Model failure for the HV ≥ 10 ml group was considered to be due to the small sample size in this group.

Smooth curve fitting analysis for 30-day mortality

To evaluate the non-linear relationship between hematoma volume and the 30-day mortality, a fitting curve was applied (Figure 2). The result of smooth curve fitting revealed a non-linear relationship between hematoma volume and 30-day mortality after adjusting for age, sex, prior medical history, GCS score, stereotactic aspiration surgery, combined hydrocephalus, BMI, admission SBP, and DBP. As the hematoma volume increased, the 30-day mortality showed a trend of slight increase followed by a sharp increase and then saturation.

Preoperative and postoperative imaging

Figure 3—Preoperative Imaging: Figure 3 shows a representative preoperative CT scan of a patient with PHBH. The image demonstrates a hyperdense hematoma in the brainstem region, causing compression of adjacent structures. Figure 4—Postoperative Imaging: Figure 4 presents a postoperative CT

TABLE 4 Univariate logistics regression analysis for 30-day mortality.

Covariate	OR (95%CI)	*P*-value
Age	0.98 (0.95, 1.01)	0.2332
Gender		
Female	Ref	
Male	1.41 (0.54, 3.69)	0.4880
Prior medical history		
History of hypertension	Ref	
History of diabetes	0.48 (0.03, 8.35)	0.6145
Hypertension and diabetes	0.82 (0.26, 2.62)	0.7416
None	0.48 (0.14, 1.59)	0.2297
GCS score		
6–8 points	Ref	
3–5 points	4.38 (1.60, 11.95)	0.0039
Stereotactic aspiration surgery		
No	Ref	
Yes	4.78 (1.12, 20.36)	0.0345
Combined hydrocephalus		
No	Ref	
Yes	7.89 (1.66, 37.54)	0.0094
Hematoma type		
Massive type	Ref	
Bilateral tegmental type	0.00 (0.00, _§)	0.9923
Basal tegmental type	0.00 (0.00, _§)	0.9912
Unilateral tegmental type	0.00 (0.00, _§)	0.9914
BMI	1.05 (0.89, 1.24)	0.5740
Admission SBP	1.05 (1.01, 1.08)	0.0060
Admission DBP	0.99 (0.92, 1.06)	0.6986
Hematoma volume	2.25 (1.60, 3.17)	<0.0001
Hematoma volume		
HV < 5 ml	Ref	
5 ≤ HV < 10 ml	20.00 (4.67, 85.57)	<0.0001
HV ≥ 10 ml	§. (0.00, _§)	0.9931

CI, confidence interval; OR, odds ratio; HV, hematoma volume; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; GCS: glasgow coma scale; § The model failed because of the small sample size.

scan of the same patient, obtained 24 h after the stereotactic aspiration procedure. The image shows a significant reduction in the hema-toma volume, resulting in decreased mass effect and improved anatomical alignment of the brainstem and surrounding structures. **Figure 5**—Postoperative Imaging: **Figure 5** presents a postoperative CT scan of the same patient, obtained 15 days after the stereo-tactic drainage procedure. The image shows the hematoma in brainstem is largely absorbed. These images, along with their accompanying descriptions and analyses, provide visual evidence of the effectiveness of the stereotactic drainage technique in reducing hematoma volume and alleviating mass effect in patients with PHBH.

Discussion

In this retrospective cohort study, hematoma volume was an independent predictor of 30-day mortality in patients with primary hypertensive brainstem hemorrhage. This suggests that hematoma volume may be a very valuable parameter that could provide additional evidentiary support for optimizing treatment strategies. In this study, we also had a surprise finding. There was a nonlinear relationship between hematoma volume and 30-day mortality. When the hematoma volume was less than about 4 ml, the patient's 30-day mortality did not appear to change significantly. And when the hematoma volume was greater than about 4 ml, the patient's 30-day mortality appeared elevated and then rapidly and sharply increased, and when the hematoma volume reached about 10 ml, the 30-day mortality approached saturation. This indicated that the threshold point for hematoma volume and 30-day mortality may be around 4 ml, while the saturation point may be around 10 ml. To our knowledge, this is the first retrospective cohort study to reveal a nonlinear relationship between hematoma volume and 30-day mortality in patients with brainstem hemorrhage.

The two most frequent factors that induce brainstem bleeding are hypertension and atherosclerosis. According to earlier research, brainstem hemorrhage may produce the following pathological injuries. Firstly, the primary harm to the brainstem is generated by the mechanical destruction of hematoma; Secondly, the secondary injury is caused by the compression of hematoma, which results in local tissue ischemia, edoema, or an inflammatory response brought on by hematoma catabolic products (14). It has previously been established that the necrosis

TABLE 5 Multivariate regression for effect of hematoma volume (ml) and 30-day mortality.

Outcome	Crude Model		Multivariate-Adjusted Model 1		Multivariate-Adjusted Model 2	
	β/OR (95%CI)	*P*-value	β/OR (95%CI)	*P*-value	β/OR (95%CI)	*P*-value
Hematoma volume	2.25 (1.60, 3.17)	<0.0001	2.26 (1.60, 3.20)	<0.0001	2.90 (1.58, 5.32)	0.0006
Hematoma volume						
HV < 5 ml	Ref		Ref		Ref	
5 ≤ HV < 10 ml	20.00 (4.67, 85.57)	<0.0001	21.25 (4.74, 95.27)	<0.0001	32.00 (3.81, 268.58)	0.0014
HV ≥ 10 ml	§. (0.00, _§)	0.9931	§. (0.00, _§)	0.9929	§. (0.00, _§)	0.9926

CI, confidence interval.
Crude Model: no adjustment.
Multivariate-Adjusted Model 1 adjusted for age and sex.
Multivariate-Adjusted Model 2 adjusted for age, sex, Prior medical history, GCS score, Stereotactic aspiration surgery, Combined hydrocephalus, BMI, Admission SBP, and DBP.
§ The model failed because of the small sample size.

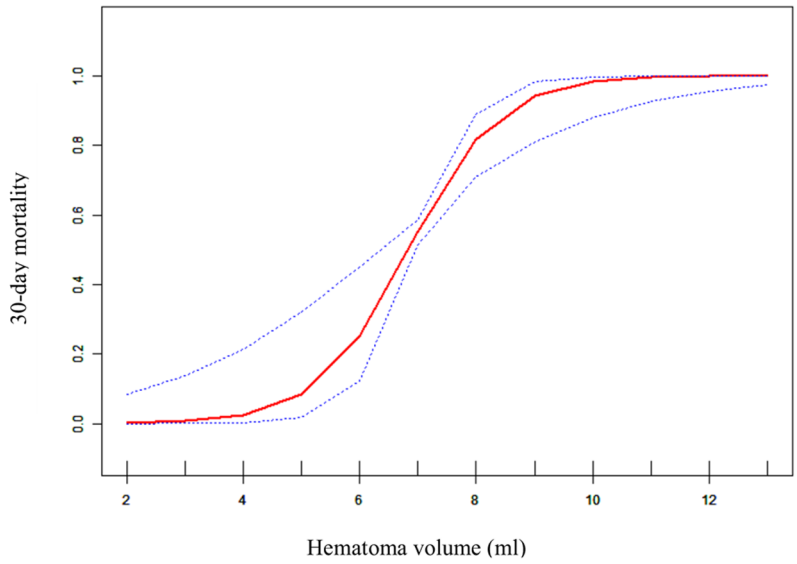

FIGURE 2
Curve fitting diagram of hematoma volume and 30-day mortality. A threshold, nonlinear association between hematoma volume and 30-day mortality was found in a generalized additive model (GAM). Solid rad line represents the smooth curve fit between variables. Blue bands represent the 95% of confidence interval from the fit. All adjusted for age, sex, prior medical history, GCS score, Stereotactic aspiration surgery, combined hydrocephalus, BMI, Admission SBP and DBP.

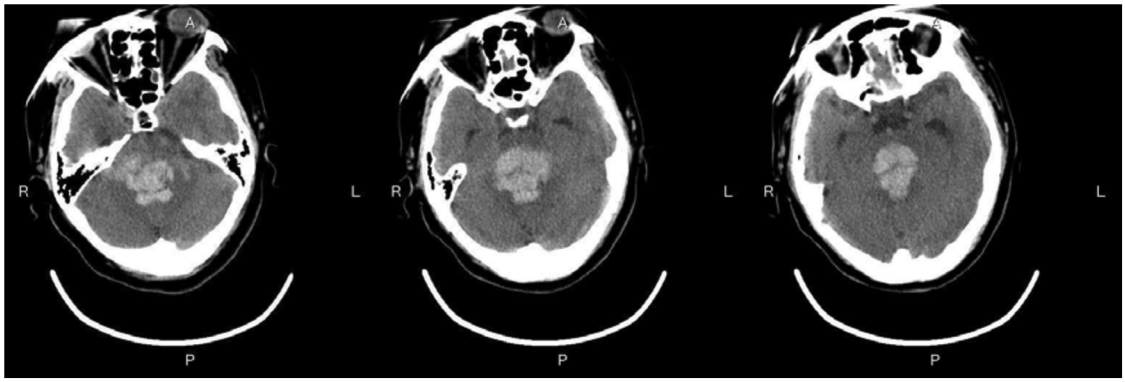

FIGURE 3
Preoperative imaging: Figure 3 shows a representative preoperative CT scan of a patient with PHBH.

of brain tissue surrounding the hematoma starts within six hours of the initiation of intracerebral bleeding, intensifies after twelve hours, and reaches its peak within twenty-four hours (15). As a result, it is crucial to remove the brainstem hematoma as soon as possible following the onset of PHBH in order to minimize primary damage and avoid secondary damage, which is beneficial for maintaining brainstem nerve function (14).

In previous clinical studies of cerebral hemorrhage, brainstem hemorrhage was often excluded, and the guidelines of the American Heart Association (AHA)/American Stroke Association (ASA) did not recommend or even oppose brainstem hematoma evacuation (16). The results of several studies on PHBH in recent years have shown that minimally invasive surgery has a better prognosis than conservative treatment, and active clinical studies have been conducted. The primary surgical approaches for treating PHBH involve hematoma clearing via craniotomy and stereotaxis and/or navigation-guided hematoma puncture and drainage (2, 14). Some patients may benefit from stereotaxis or navigation-guided puncture of brainstem hematoma, according to early research. However, the hematoma cannot be totally cleared with such an approach, and once the bleeding begins, it cannot be halted under direct eyesight, restricting its application (17, 18). A common surgical procedure for the treatment of PHBH is the removal of hematomas by craniotomies, which can be carried out under direct vision while providing simultaneous accurate hemostatic and decompressive effects (2). However, the control of iatrogenic injury is still extremely challenging, and it needs to be carried out by experienced neurosurgeons, and

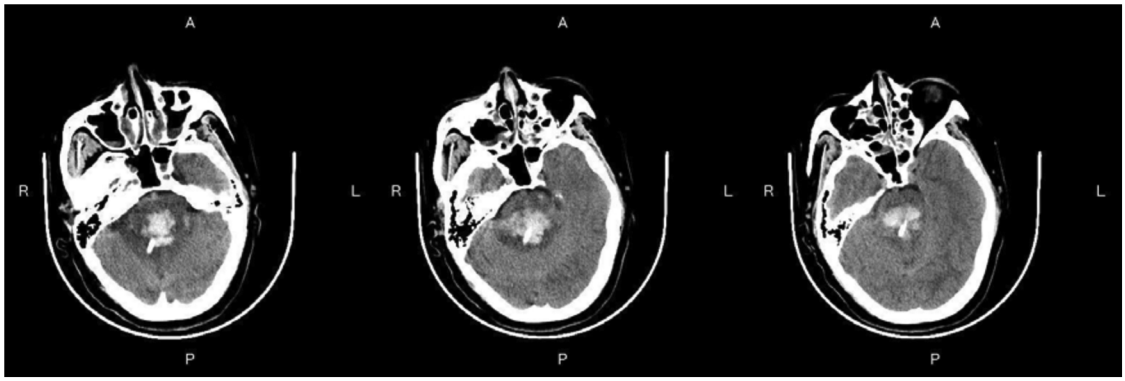

FIGURE 4
Postoperative imaging: Figure 4 presents a postoperative CT scan of the same patient, obtained 24 h after the stereotactic drainage procedure.

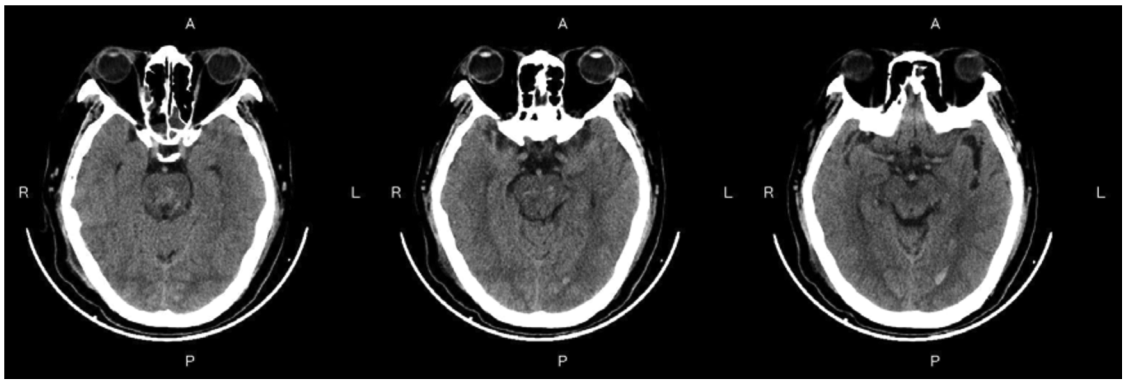

FIGURE 5
Postoperative imaging: Figure 5 presents a postoperative CT scan of the same patient, obtained 15 days after the stereotactic aspiration procedure.

attention should be paid to the operating principles of "no traction of the brainstem, light suction of hematoma, and weak electrocoagulation of the responsible vessel". In this study, we followed Brown's Rule, multiplanar reformatting of brain CT scanning was combined, and individualized surgical approaches were adopted (19).

In this retrospective cohort study, 74 patients with PHBH were included for analysis. 64 patients underwent stereotactic aspiration and 10 patients were treated conservatively with medication. 30-day mortality was 62.16%. Patients who have experienced a brainstem hemorrhage may not benefit from surgical therapy, according to Fewel and Manno's research (20, 21). Surgical intervention was linked to 30-day mortality in Jang's research (6), however, Kearns et al. and Hara et al. argued that surgical intervention was effective (22, 23). This study's 30-day death rate of 62.16% was higher than earlier reports in the literature. We speculate that this may be due to differences in the study population, study design, etc. Surgical treatment for PHBH is a controversial issue, with some studies showing better outcomes with surgery and others showing no difference compared to conservative treatment. In light of this, the 30-day mortality rate for patients treated with surgery was compared to those not treated with surgery. The results showed a 30-day mortality rate of 59.37% for 64 patients treated with surgery and 80% for 10 patients not treated with surgery (**Table 6**). This suggests that surgical treatment may have a positive impact on 30-day mortality in PHBH patients, although further research is needed to confirm this. Nevertheless, we are optimistic about the surgical treatment of PHBH. With the popularization of observation equipment and the advancement of surgical techniques, the anatomical understanding of the safety zone of the brainstem has been improved, and some success has been achieved in removing the hematoma by selecting a suitable access route via the safety zone into the brainstem according to the location of the hematoma. We believe that the key factors influencing surgical choice are hematoma volume and hematoma type. In order to lower local and overall intracranial pressure and preserve CSF circulation, the surgical procedure should attempt to remove as much of the clot as feasible while causing the least amount of disturbance to the surrounding brain (24). Direct hematoma evacuation and successful decompression are two benefits of surgery. Nonetheless, there is a potential for increased risk from operation-induced tissue injury. According to our perspective, this operation is suitable for patients who have brain stem

TABLE 6 The 30-day mortality in patients with and without surgical treatment for PHBH.

Treatment	Number of cases (*n*)	Died within 30 days	Survived within 30 days	30-day Mortality Rate(%)
Surgery	$n = 64$	38	26	59.37
No Surgery	$n = 10$	8	2	80
Total	74	46	28	

compression and who are unable to endure the possibility of a fourth ventricle obstruction brought on by a hematoma that has extended into the fourth ventricle. The right patient selection is one of the most crucial aspects impacting the outcome of surgery, and in our experience, the criteria are as follows. GCS $\leq$ 7 points for hematoma volume $\geq$5 ml; GCS $\leq$ 5 points for hematoma volume 3–5 ml, conservative until the onset of disease more than 72 h, or complicated by acute hydrocephalus.

Currently, there is plenty of research on the prognosis and affecting variables of hypertensive supratentorial hemorrhage (25, 26). However, there is a lack of research on brainstem hemorrhages. According to Raison et al., the location of the hematoma, the severity of the hemorrhage, and the patient's state at the time of onset al.l affect the prognosis of PHBH patients. The mortality rate approaches 100% when the hematoma volume is more than 10 ml (27, 28). The results of our study showed a mortality rate of 100.% (19/0) in patients with a hematoma volume greater than 10 ml and a mortality rate of 75% (24/32) in patients with a hematoma volume of 5–10 ml. The results of the univariate analysis revealed a significant difference in the impact of hematoma volume on prognosis [OR = 2.25 (95% CI: 1.60, 3.17), $P < 0.0001$], indicating that hematoma volume may play a role in determining the prognosis of brainstem hemorrhage. According to multivariate logistic regression analysis, the hematoma volume was not only a risk factor for death in patients with brainstem hemorrhage [OR = 2.90 (95% CI: 1.58, 5.32), $P < 0.05$], but it was also an independent factor ($P = 0.0006$). The findings were in line with those that had previously been published in the literature (7). Other studies have suggested that GCS score can be an independent risk factor for death in PHBH. In the present study, univariate analysis showed that the GCS score was statistically significant for 30-day death in patients with brainstem hemorrhage ($P = 0.0039$), which is consistent with previous reports in the literature (29). Meng's study showed no statistically significant effect of GCS score on the prognosis of patients with brainstem hemorrhage ($P = 1.000$). However, our study doesn't support these findings. In their study, many confounding factors, including age, sex, prior medical history, GCS score, stereotactic aspiration surgery, and combined hydrocephalus were not adjusted for. This may have biased their findings. Previous studies have shown that approximately 39.5% of PHBH entered the ventricular system, and the incidence of hydrocephalus was as high as 30.3% when the hemorrhage was located close to the fourth ventricle and midbrain aqueduct, with a markedly elevated risk of death and a poor prognosis (2, 30). In our study, we found that the presence of hydrocephalus was associated with 30-day mortality ($P = 0.0094$), which is consistent with previous results described in the literature. The fact that men were much more impacted by brainstem hemorrhage than women was also confirmed; However, we could not find any evidence of a gender or age difference ($P = 0.592$ and $P = 0.256$, respectively), which was consistent with the literature (30).

There are several benefits to our study. Firstly, in addition to using the generalized linear model to assess the linear association between hematoma volume and 30-Day mortality, we also utilize the generalized additive model to elucidate the nonlinear relationship. GAM has clear advantages when dealing with non-linear relations; it can handle non-parametric smoothing; and it will fit a regression spline to the data. We shall learn more about the true connections between exposure and outcome with the aid of GAM. Secondly, because this was an observational study with potential confounding that could not be avoided, we strictly applied statistical correction to reduce residual confounding. Even though the prior study found a linear relationship between hematoma volume and 30-Day mortality, we were unable to find this connection in our study even after adjusting for age, sex, prior medical history, GCS score, stereotactic aspiration surgery, combined hydrocephalus, BMI, admission SBP, admission DBP, and other confounding factors that the prior study had not taken into account.

Limitation

This study has several restrictions. Firstly, the sample size of 74 patients in our study is relatively small, which may limit the statistical power of our analyses and the generalizability of our findings. The rarity of primary hypertensive brainstem hemorrhage may have contributed to the small sample size, as we had to rely on data from patients who were treated at our institution during a specific period. In addition, we did not perform a power analysis or an *a priori* sample size analysis, which may have further contributed to the small sample size. Secondly, the limitations of the retrospective cohort study design and the potential sources of bias and variance may have affected our analyses. We recognize that the retrospective design may have limited our ability to control for confounding variables and may have introduced selection bias or measurement bias. This study was limited to Chinese people, with certain regional and ethnic restrictions. In future studies, we will consider multi-center collaborations or expanding the scope of the study to include additional outcome measures or patient populations.

Conclusion

Hematoma volume is an independent factor affecting 30-day mortality in patients with primary hypertensive brainstem hemorrhage. The severe and extensive neurological damage caused by primary hypertensive brainstem hemorrhage is highly unlikely to be fundamentally altered by a single protocol, and

new avenues need to be explored scientifically and continuously. Future studies could build on these findings by exploring the relationship between hematoma volume and mortality further, investigating other factors that may contribute to mortality in these patients, and exploring new treatment strategies. By doing so, we may be able to develop more effective approaches to the management of primary hypertensive brainstem hemorrhage and ultimately improve outcomes for these 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

The studies involving human participants were reviewed and approved by The Ethics Committee of The 908th Hospital of the Joint Logistic Support of the People's Liberation Army. 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

Author contributions ZY was involved in the study design; XZ was involved in data collection; ZY, QX, and ZZ were responsible for writing the article; YX, HL, and XY were engaged in data Analysis; LD and LZ conducted supervision; ZY approved the article. All authors contributed to the article and approved the submitted version.

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New aneurysm formation after endovascular embolization of a vertebral epidural AV fistula: a rare sequelae of NF AV fistulae

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Background: Neurofibromatosis type 1 (NF-1) is a dominant genetic disorder often accompanied by lesions of the neurovascular system. Patients with NF-1 are predisposed to unique vertebral artery fistula (AVF).

Case description: We report on a rare case of multiple neurovascular abnormalities in a 47-year-old man with neurofibromatosis. He was admitted due to a sudden headache and was found to have suffered a subarachnoid hemorrhage from a left vertebral arteriovenous fistula. He underwent two endovascular procedures complicated by a delayed extraspinal mass 7days after treatment. Angiography revealed a new vascular abnormality, and although we performed another embolization, it failed to respond to further embolization.

Conclusion: Vascular abnormalities in patients with NF-1 can be complex. Endovascular intervention remains feasible for NF-1 related AVF, however, partial occlusion of the fistula should be avoided to limit and iatrogenic damage to the blood vessels.

KEYWORDS

neurofibromatosis type 1 (NF1), vertebral arteriovenous fistulae, endovascular treatment, subarachnoid hemorrhage, aneurysm

Introduction

Neurofibromatosis type 1 (NF-1) is an autosomal dominant genetic disorder with widespread neuroectodermal and mesodermal dysplasia affecting the skin, nervous system, bone, and vascular system (1). Patients with NF-1 are predisposed to unique spinal epidural arteriovenous malformations (DAVF) (2). Vertebral arteriovenous fistulas (AVF) are rare type of epidural arteriovenous malformations usually located in the spine and widely accepted to require treatment (3). It is mainly caused by direct abnormal communication between branches of vertebral artery and spinal radiculomeningeal vein or epidural veins (3).

We discuss the clinical presentation and challenges of endovascular management of AVF in a case multiple NF-1 associated vascular lesions.

Case presentation

The patient was a 47-year-old man who was admitted to hospital following to a sudden headache 3 days prior. There was a previous history of resection of a tumor from the left side of the patient's neck 20-years before the current presentation.

Clinical examination revealed multiple neurofibromas and typical café-au-lait spots on the patient's skin (Figure 1A). Similar spots were also present on the skin of his immediate family members. The muscle strength of his limbs showed a progressive decline. On admission, only the left upper limb was affected, and the muscle strength was grade 1. By the third day, the muscle strength of both the left lower limb and the right upper limb had decreased to grade 1. He was otherwise fully conscious (GCS 15) with no other neurological deficits.

Computed tomography (CT) head showed subarachnoid hemorrhage (modified Fisher grade 2). The magnetic resonance imaging revealed space-occupying lesions deep in the right temporal lobe, flow voids in the craniovertebral junction (CVJ), and the left spinal canals from C3 to C4 (Figures 1G,H). CT angiography revealing a left cervical dural arteriovenous fistula, an aneurysm in the left internal carotid artery, multiple bone abnormalities in head and neck (Figures 1B–F). Digital subtraction angiography demonstrated the presence of multiple high-flow arteriovenous fistulae at the left CVJ (fistula A) and the C3–C4 level (fistula B), a direct shunt between the left vertebral artery and the epidural vein, forming a huge venous lake connected to the paravertebral venous plexus on the left (Figure 2A); the right vertebral arteriography exhibited a leftward retrograde flow of blood.

The patient was diagnosed with NF-1 accompanied by left AVF and subarachnoid hemorrhage. The compression of the spinal cord by the lacunae resulted in progressive quadriparesis, while the resulting high perimedullary venous pressures leading to the subarachnoid hemorrhage.

Treatment

Intervention was recommended to prevent further hemorrhage and arrest myelopathy. The complex architecture, extensive number lesions was felt increase difficulty and morbidty associated with open surgery. Previous reports in the literature of successful endovascular treatment of such AVFs, underpinned our choice of embolization as a safe treatment option for this patient.

The first treatment was performed 4 days after admission. Three detachable balloons were placed at the proximal end of fistula A，the venous lake of fistula B，and origin of the vertebral artery. One coil was added to support and fix the balloon in venous lake. Then, fistula A was completely occluded via the right vertebral artery using coils and Onyx (Supplementary Video 1). Post-operative angiography revealed the complete occlusion of fistula A and the beginning of the left vertebral artery. An anastomotic muscular branch backflow vertebral artery continued to supply blood to fistula B (Figures 2B–D). At 7 days, the carotid artery CT angiography showed the disappearance of abnormal blood vessels in the left neck (Figure 2E).

Eleven days post-procedure, a pulsating mass was observed at the left posterior auricular arear. Follow-up angiography revealed this to be a ruptured aneurysm from the distal muscular branch artery of the costocervical trunk (Supplementary Video 2). Further embolization of this aneurysm was performed using a gelatin sponge (Figures 3A–D).

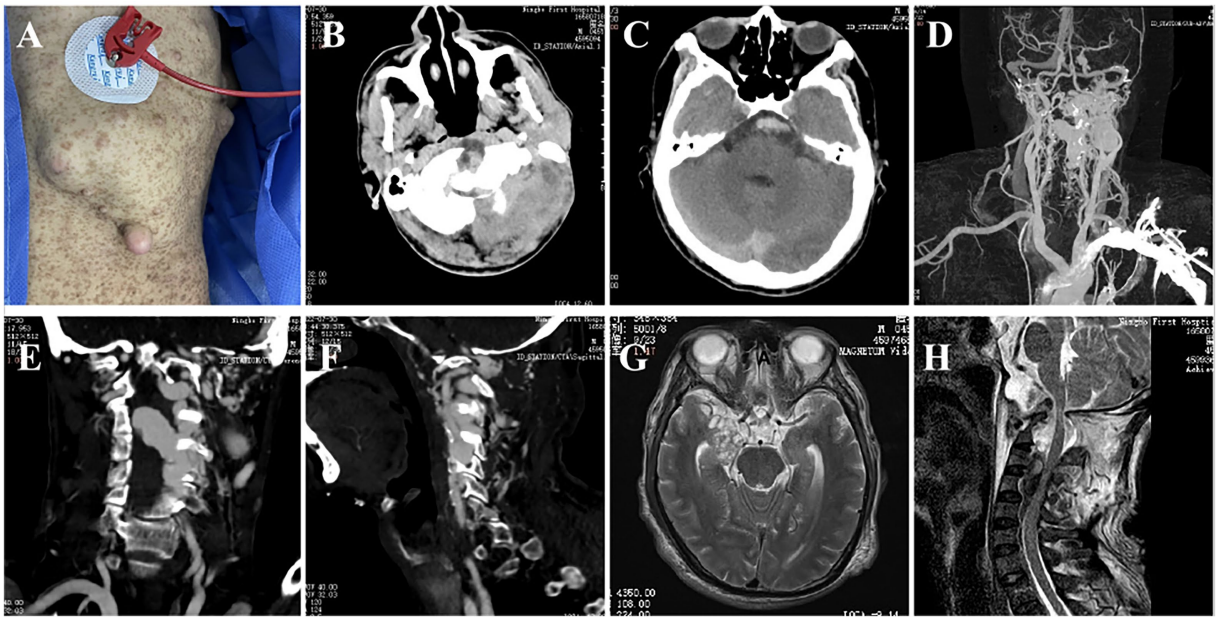

FIGURE 1
The patient's body surface features and imaging findings. **(A)** Multiple neurofibromas and typical café-au-lait spots; **(B)** Left skull bone destruction and occipital muscle swelling; **(C)** CTA showed subarachnoid hemorrhage; **(D–F)** CTA showed multiple vascular abnormalities in the left skull base and neck, and the thick venous lake compressed the spinal cord; **(G)** MRI showed the presence of an intracranial tumor; **(H)** Atlantoaxial dislocation, fluid void signal in the spinal canal and compression of the spinal cord.

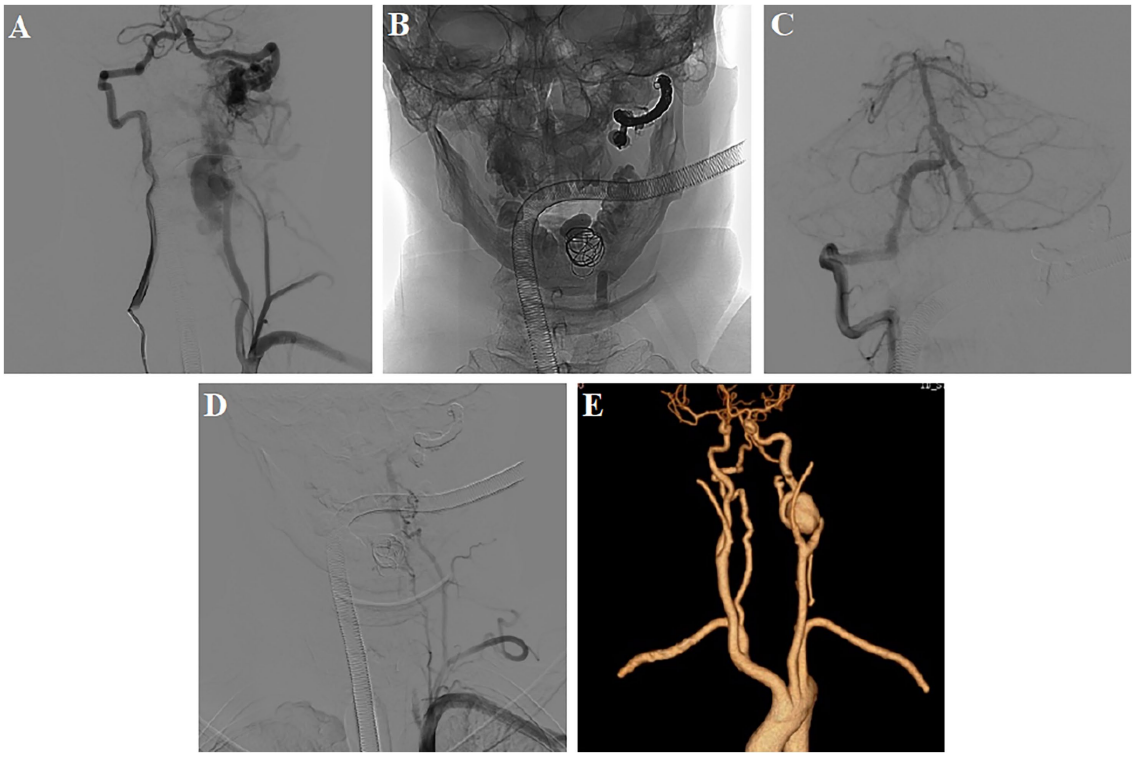

FIGURE 2
First postoperative DSA and CTA examination. **(A)** DSA demonstrated multiple high-flow arteriovenous fistulae at the left CVJ (fistula A) and the C3–C4 level (fistula B); **(B–D)** Balloon combined with a coil and Onyx embolization, leaving an anastomotic muscular branch backflow vertebral artery supplying blood to fistula B; **(E)** CTA showed the disappearance of abnormal blood vessels in the left neck.

Outcome and follow-up

The patient had left hemiplegia before treatment and recovered to grade 3 after first treatment. The mass was present without pulsation after second treatment. At 14 days, the mass in the left neck was further enlarged (Figure 3E). The patient declined further intervention following this and was kept under clinical and radiological surveillance with no further increases in the mass noted.

Discussion

Neurofibromatosis type 1, also termed von Recklinghausen's disease, is a genetic disorder following an autosomal dominant pattern. It arises from NF-1 gene mutations at the long arm of chromosome 17 (17q11.2) that induces developmental abnormalities of the vascular system, such as arterial occlusion, intracranial vascular dysplasia, moyamoya vasculopathy, and aneurysms (4).

Patients with NF-1 are predisposed to distinctive vertebral arterial fistulae (5). Typical manifestations include radiculopathy, neck pain, and neck mass, while AVF rupture cases are characterized by neck hematoma, SAH, and hypotension (2). The pathogenesis of NF-1-related AVF has not been fully understood. It is thought that fragility and defects of the arterial wall related to NF-1 can cause AVF (6). Swain et al. (7) proposed two possible mechanisms by which an AVF might arise in patients with NF-1: abnormalities of connective tissue, including dysplastic smooth muscle in the arterial wall. Alternatively, the abnormal arteriovenous communications are primarily congenital in nature and arise directly as a manifestation of mesodermal dysplasia association with NF-1 among young patients.

The multiple arteriovenous fistulae in the present case support the congenital theory while and recurrent vascular abnormalities after intervention was in keeping with fragility of dysplatic vessels. The patient had two fistulas located at the craniocervical junction (fistula A) and the C3–C4 level (fistula B). Cerebral angiography showed retrograde venous drainage to the skull base, suggesting high venous pressure as the cause of the subarachnoid hemorrhage. The large lake of veins compresses the spinal cord, leading to progressive loss of strength in the limbs. The most effective treatment of AVF is to seal the two fistulas separately. The large size of the venous lake, the ongoing cord compression from this lacuna limited the choice of embolic devices to balloons and coils to avoid exacerbating the mass effect from the AVF. Unfortunately, the high flow in the fistula dislodged the balloon beyond the fistula into the venous lake. The fistula remained patent with ongoing supply from the muscular branches of the costocervical trunk artery (but slightly increased resistance at the venous side). Attempts at occluding this branch with a microcatheter were unsuccessful. The flow across the fistula was however reduced at the end of the procedure. Angiography showed that this muscular branch was not only supplying blood to the fistula, but also had

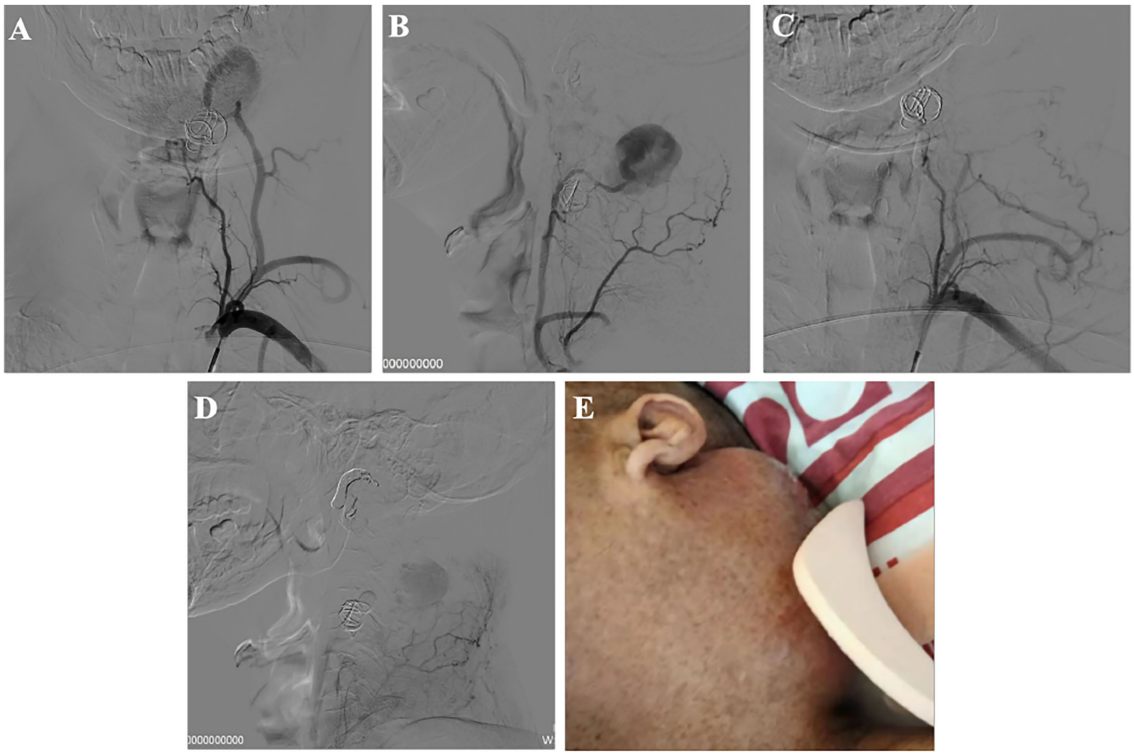

FIGURE 3
Recurrent vascular abnormality after the first operation and the second interventional treatment. **(A,B)** DSA showed muscular branch artery ruptured, forming a huge aneurysm; **(C,D)** After second treatment; **(E)** Left neck mass.

many branches to the neck muscles. Magnetic resonance examination showed that the muscle signal in this part of the patient was abnormal increasing concerns that occlusion of this blood vessel would likely result in ischemic necrosis. Even if Onyx is injected from this blood vessel, it cannot diffuse to the fistula to achieve embolization effect.

Aneurysmal formation on this preserved muscle branch so shortly after surgery is hypothesized to be related to abnormal vascular development and postoperative hemodynamic changes in NF-1 patients. This complication highlights some of the challenges associated with managing this patient group and provides insights to guide future therapeutic endeavors.

Conclusion

The vascular network of NF-1 related AVF is complex, and more may be prone to remodeling and *de novo* vascular lesions in patients with multiple fistulas. Endovascular embolization for NF-1 with AVF is feasible, but the fistula should be completely occluded during the treatment and any iatrogenic injury to the vessels.

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 the Ethics Committee of Ningbo First Hospital. 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

ZL and SZ made substantial contributions to design and drafted the manuscript. YZ, XL, and JZ collected data. YH revised the manuscript critically for important intellectual content. All authors contributed to the article and approved the submitted version.

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Conflict of interest

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2023.1132334/full#supplementary-material

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Hybrid surgery recanalization for high-level chronic internal carotid artery occlusion

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Objective: Although endovascular recanalization is considered a more effective treatment for chronic internal carotid artery occlusion (CICAO), the success rate of complex CICAO remains inadequate. We present hybrid surgery (carotid endarterectomy combined with carotid stenting) for complex CICAO and explore the influential factors and effects of hybrid surgery recanalization.

Methods: We retrospectively analyzed the clinical, imaging, and follow-up data of 22 patients with complex CICAO treated by hybrid surgery at the Zhongnan Hospital of Wuhan University from December 2016 to December 2020. We also summarize the technical points related to hybrid surgery recanalization.

Results: A total of 22 patients with complex CICAO underwent hybrid surgery recanalization. There were no postoperative deaths in all patients after hybrid surgery recanalization. Nineteen patients successfully underwent recanalization with a success rate of 86.4% and three cases with a failure rate of 13.6%. Patients were divided into success and failure groups. Significantly different radiographic classification of lesions was observed between the success group and the failure group ($P = 0.019$). The rates of CICAO with reverse ophthalmic artery blood flow in the internal carotid artery (ICA) preoperatively were 94.7% in the success group and 33.3% in the failure group ($P = 0.038$). Three cases of hybrid surgery recanalization failure were transferred for EC-IC bypass and had good neurological recovery. Postoperative average KPS scores of the 19 patients were improved compared to the preoperative ones ($P < 0.001$).

Conclusion: Hybrid surgery for complex CICAO is safe and effective with a high recanalization rate. The recanalization rate is related to whether the occluded segment surpasses the ophthalmic artery.

KEYWORDS

chronic internal carotid artery occlusion, hybrid surgery, carotid endarterectomy (CEA), carotid artery stent (CAS), recanalization

Introduction

Chronic internal carotid artery occlusion (CICAO) is characterized by progressive bilateral or unilateral occlusion of the internal carotid artery for more than 4 weeks, which carries higher recurrence rates of stroke, disability, and mortality (1). The main treatment modalities include medical therapy (antiplatelet and anticoagulant), extracranial–intracranial (EC-IC) bypass, carotid endarterectomy (CEA), and endovascular revascularization. The overall risk of stroke from CICAO is ~5–7% per year despite receiving the best available medical therapy (2–4). A carotid occlusion surgery study (COSS) in

2011 (5) indicated that EC-IC bypass surgery could improve the hemodynamic indicators of patients to some extent but could not effectively reduce the stroke recurrence rate. Furthermore, studies have shown that CEA is only suitable for short-segment occlusion limited to the neck (the success rate of opening occlusions was only 18.5–40.2%, and the postoperative restenosis rate was as high as 30.7–76.6%) (6, 7). With the development of endovascular intervention techniques and changes in the materials used, endovascular revascularization for CICAO is gradually being promoted. In 2018, Hasan et al. proposed a high success rate of open intravascular intervention of type A and B CICAO but a low success rate for cumulative carotid bifurcation of type C and D CICAO of the ophthalmic artery (8, 9).

The application of hybrid surgery (CEA combined with internal carotid artery stent implantation (CAS) in the same period) for the recanalization of CICAO has been reported in recent years and has achieved good outcomes (10–12). However, factors that affect the rate of revascularization and improvement of the daily living ability of patients have yet to be fully reported. This study aimed to explore the effects of hybrid surgery for complex CICAO (type C and D CICAO), describe the relevant technical points, and analyze factors that affect the recanalization rate.

Materials and methods

Patient and data collection

Ethics approval was waived by the local Ethics Committee of Wuhan University in view of the retrospective nature of the study, and all the procedures that were performed were part of routine care. We retrospectively analyzed the clinical, imaging, and follow-up data of CICAO patients treated by hybrid surgery from December 2016 to December 2020 (Figure 1). CICAO was defined as a duration of ≥4 weeks between diagnosis and treatment. The inclusion criteria were as follows: (i) those with complete occlusion of one side of the internal carotid artery (i.e., the occluded segment is larger than the cervical segment and the duration of ICA occlusion is more than 4 weeks); (ii) those with related clinical neurological symptoms; (iii) those with internal carotid artery occlusion who underwent hybrid surgery for recanalization, excluding those of simple CEA and CAS recanalization; and (iv) based on the newly suggested radiographic classification proposed by Hasan et al. (8), Type C CICAO with no ICA stump and patent lumen distally with collateral filling, from branches of the ECA, Pcom, and/or ACA, and Type D CICAO with no ICA stump and occluded lumen distally until the ICA bifurcation.

Exclusion criteria were listed as follows: (i) acute or subacute CICAO; (ii) other cerebrovascular diseases (Moyamoya disease, intracranial aneurysms, and cerebrovascular malformations) were excluded; (iii) the presence of severe systemic diseases in the heart, liver, kidney, lung, or other vital organs; (iv) inability to tolerate general anesthesia for surgery; and (v) patients who underwent other treatment modalities including pharmacological treatment, simple CEA or CAS recanalization, and intracranial and extracranial revascularization.

Demographic and baseline data included age, sex, smoking, past medical history (diabetes, hypertension, and heart disease), and duration of occlusion. The Karnofsky Performance Scale (KPS) scores on admission and duration from the last neurological event to surgery were also collected. Two neurosurgeons assessed all the images. The occlusion length, reverse ocular artery blood flow in ICA preoperatively, and collateral circulation measured by digital subtraction angiography (DSA) and cerebral blood perfusion (CTP) were collected and analyzed.

Preoperative preparations

Preoperative imaging and laboratory examinations were performed to eliminate surgical contraindications and evaluate the success rate and safety of the operation. All patients underwent neck vascular ultrasonography (US), a transcranial Doppler (TCD) study, magnetic resonance imaging (MRI), cerebrovascular DSA, computed tomography for the assessment of CTP or MRI for the evaluation of cerebral blood perfusion (PWI), cardiac US, and other related imaging examinations preoperatively and at 6 months postoperatively. All patients completed high-resolution MRI (HRMRI) for plaque examination and analysis.

Patients were prescribed oral aspirin (100 mg/day), clopidogrel sulfate (75 mg/day), and an atorvastatin calcium tablet (20 mg/night) for at least 1 week. If the patient showed resistance to clopidogrel hydrogen sulfate based on the chromogram and platelet aggregation rate, it was replaced with an oral ticagrelor tablet (90 mg/day for 2–3 days), and the platelet aggregation rate was rechecked to ensure that the inhibition rate was <50%.

Operative process

After successful general anesthesia and electrophysiological monitoring, the patient was placed in the supine position. After a successful femoral artery puncture using the right inguinal Seldinger technique, an 8-Fr artery sheath was placed, and the lesion location, occlusion length, occlusion type, and occlusion compensation were re-examined using angiography. After systemic heparinization, the guiding catheter was placed below the carotid artery bifurcation and adequately fixed.

The anterior approach to the sternocleidomastoid muscle on the side of the lesion was used after fixation was confirmed. The incision length was adjusted according to the bifurcation of the carotid artery. An incision of the skin, subcutaneous tissue, platysma muscle, and other layers was made to expose the sternocleidomastoid muscle. The sternocleidomastoid muscle was opened and fixed with a dilator to expose the carotid triangle. The carotid sheath was opened, and the common carotid artery, internal carotid artery, external carotid artery, superior thyroid artery, and sublingual nerve were marked with colored bands and fixed. Under the microscope, the blood vessels were subsequently blocked. An incision was made along the midline of the internal carotid artery before and after the bifurcation of the carotid artery. Plaques and inner intima were separated along with the interval between inner and middle intima. The inner intima of the carotid artery was severed at the interface of plaque segmentation. The segment of the internal carotid artery against the heart was segregated up and

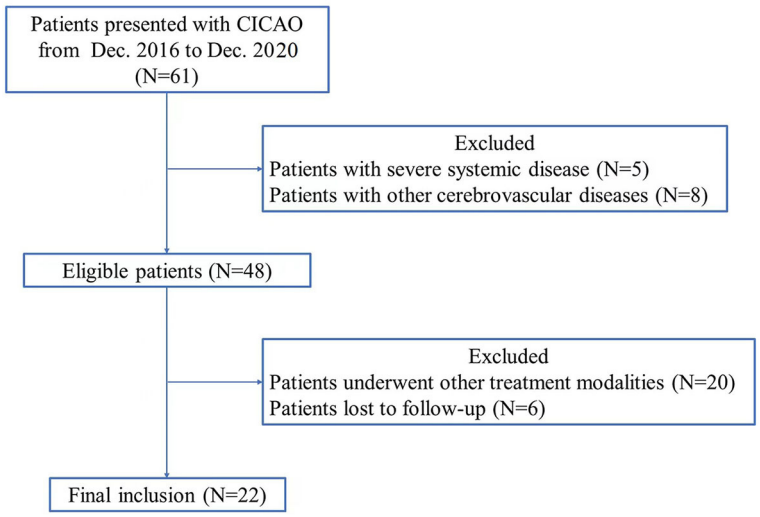

FIGURE 1
Flowchart of patient inclusion and exclusion.

dragged out as much as possible by intima stripers. Moreover, heparin saline wash was repeatedly used to clean the floats and tiny plaque from the blood vessels after closing the 6-0 vascular suture.

From the perspective of the guiding catheter, an appropriate thread was chosen, and a tube was inserted through the distal internal carotid artery occlusion. Angiography was performed again to ensure that the vascular cavity was reached. The internal carotid artery stent was properly expanded to open the distal occlusion of the blood vessels. The final imaging study was used to determine the patency of the occluded segment and intracranial blood perfusion. Blood pressure was reduced moderately after opening the occlusion to avoid hyperperfusion. The blood vessels and muscles of the neck were sutured successively, and the skin was sutured subcutaneously without placing a drainage tube (Figure 2 for a typical case).

Postoperative management

Blood pressure was strictly controlled for at least 1 week after vascular opening to be 10–20% lower than the baseline blood pressure (i.e., the mean blood pressure at 3 days preoperatively). Patients' cognitive function, pupils, physical activity, and mental state were observed, and moderate fluid replacement was provided. Brain MRI combined with diffusion-weighted imaging (DWI), a neck vascular US, a TCD study, and indicators of myocardial infarction were reviewed within 1 week postoperatively.

Follow-up management

At 1 month, 3 months, 6 months, 1 year, 1.5 years, and 2 years postoperatively, we reviewed patients' general blood test results, biochemistry findings, blood coagulation, platelet aggregation rate, US examination of the neck vessels, TCD results, and other examinations; determined the KPS scores; and recorded the time of recurrent stroke. Total cerebral angiography and brain MRI + DWI were re-examined at 6 months, 1 year, and 2 years postoperatively.

Statistical analysis

All normally distributed continuous variables were reported as mean ± standard deviation (SD), and categorical data were reported as percentages or frequencies for descriptive characteristics. We assessed the differences between the two groups using the *t*-tests or Mann–Whitney *U*-test for continuous variables and the χ^2 or Fisher's exact tests for continuous and categorical variables. The statistical significance level was set at a *p*-value of $\leq$0.05, and all data were analyzed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, New York, USA) for statistical analysis.

Results

Patient demographics and outcomes

A total of 22 patients (15 men and 7 women) were finally included in the study, ranging in age from 42 to 77 years (average age, 62.91 ± 8.34 years). Patients were categorized into two groups (success group and failure group) based on recanalization or not. Of all 22 patients, 19 were successfully recanalized with a success rate of 86.36% and 3 were not (Table 1). Three cases of hybrid surgery recanalization failure were transferred for EC-IC bypass and had good neurological recovery. Age, sex, smoking, diabetes, hypertension, heart disease, and duration of occlusion did not differ significantly between the success and failure groups ($P > 0.05$; Table 1). All the patients had an atherosclerotic plaque in the imaging analysis, which was confirmed by preoperative US and HRMRI. Preoperative and intraoperative DSA shows that occlusion

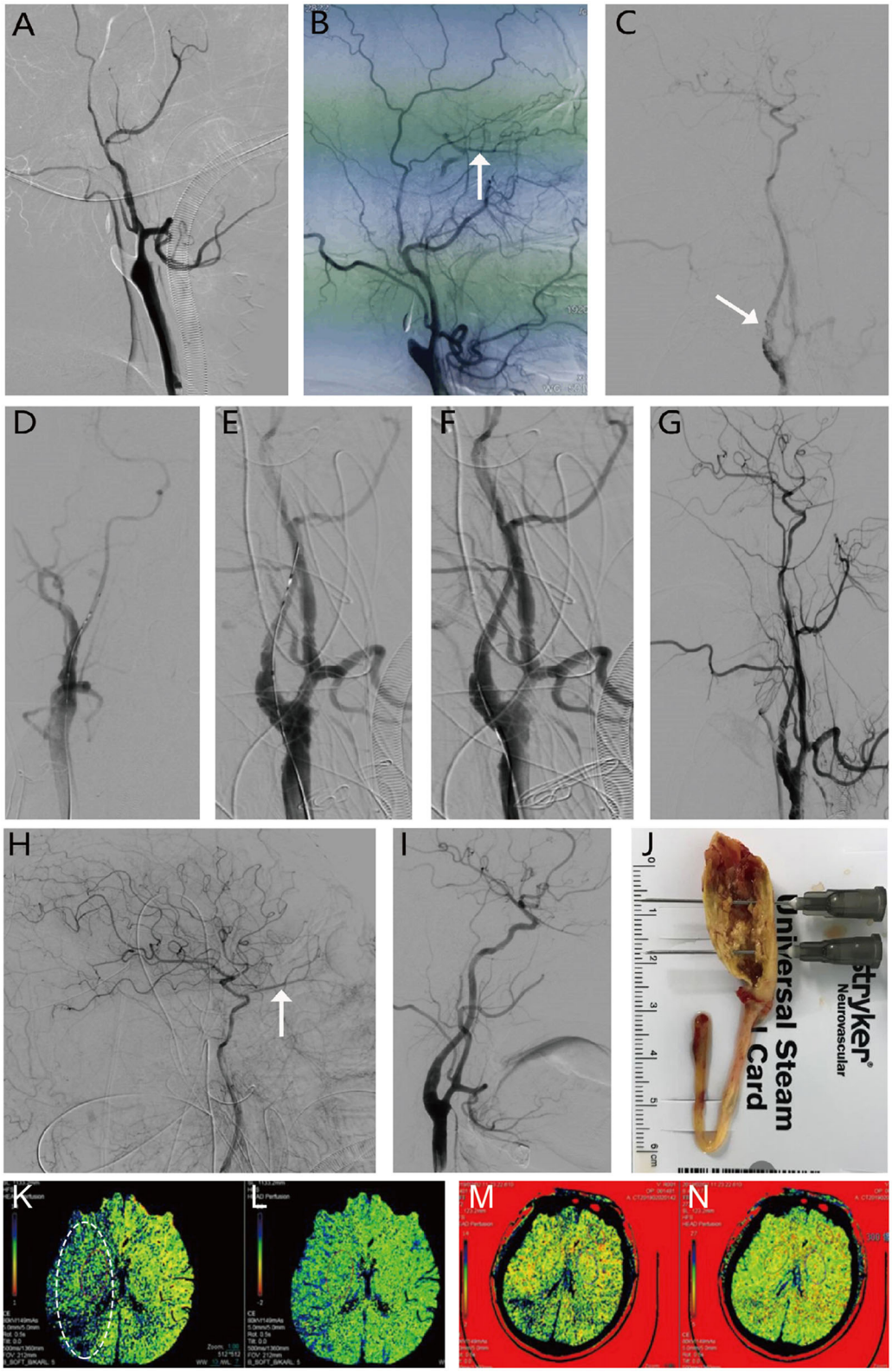

FIGURE 2
Procedure of open carotid endarterectomy (CEA) + internal carotid artery stent implantation (CAS) for right internal carotid artery occlusion. **(A, B)** Show occlusion of the right internal carotid artery, with (white arrow) indicating the backward opening of the ophthalmic artery, and the external carotid artery supplying blood to the internal carotid artery. **(C)** Shows that the internal carotid artery was open after CEA, but proximal stenosis is present (dashed white arrow) with poor intracranial perfusion. **(D, E)** Illustrate the procedure for CAS. **(F–H)** Show that after stent implantation, local stenosis is relieved, intracranial blood perfusion is significantly improved, and positive blood flow (white arrow) is restored to the ophthalmic artery. **(I)** Shows results of digital subtraction angiography at 6 months postoperatively. Further recovery of the vascular structure is observed without stenosis. **(J)** Shows intraoperative CEA with the removal of the internal carotid artery plaque and polarized thrombus, measuring ~10 cm. **(K–N)** Preoperative and postoperative perfusion CT. Compared with MTT in (**K**, white circle) and delayed TTP in **(L)** preoperatively, postoperative perfusion CT showed improvements in the **(M)** mean transit time (MTT) and **(N)** time to peak (TTP) after recanalization.

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TABLE 1 Preoperative and postoperative factors related to the recanalization rate.

Factors	Success group ($n = 19$)	Failure group ($n = 3$)	*P*-value
Age	62.5 ± 8.9	65.3 ± 3.2	0.6
Sex			>0.999
Male	13 (68.4%)	2 (66.7%)	
Female	6 (31.6%)	1 (33.3%)	
Smoking	12 (63.2%)	2 (66.7%)	>0.999
Past medical history			
Diabetes	11 (57.9%)	1 (33.3%)	0.571
Hypertension	10 (45.5%)	2 (66.7%)	>0.999
Heart disease	5 (26.3%)	1 (33.3%)	>0.999
Duration of occlusion			>0.999
<6 months	7 (36.8%)	1 (33.3%)	
≥6 months	12 (63.2%)	2 (66.7%)	
Length of occlusion			>0.999
<5 cm	8 (42.1%)	1 (33.3%)	
≥5 cm	11 (57.9%)	2 (66.7%)	
Reverse ophthalmic artery blood flow in ICA			0.038*
Yes	18 (94.7%)	1 (33.3%)	
No	1 (5.3%)	2 (66.7%)	
Postoperative complications			
Ischemic events	1 (5.3%)	0	
Hyperperfusion	1 (5.3%)	0	
Carotid-cavernous fistula	2 (10.5%)	1 (33.3%)	
Death	0	0	

*$p \leq 05$, which is statistically different.

length was less significant in the failure than in the success group ($P > 0.999$). Significantly different classification of lesions was observed between groups.

Interestingly, reverse ocular artery blood flow in ICA was found in 19 patients (86.4%), with 18 successful recanalizations and 1 failure. The success rates of CICAO with or without reverse ophthalmic artery blood flow in ICA were 94.7 and 33.3% in the success group and the failure group, respectively ($P = 0.038$). Notably, three patients had occlusions without reverse ophthalmic artery blood flow in ICA that exceeded the distal part of the ophthalmic artery and one underwent successful recanalization. The recanalization rate of this sub-group was 33.33%.

The postoperative complications and outcomes are shown in Table 1 and Figure 2. After successful recanalization, ischemic events occurred in one patient. One patient developed hyperperfusion syndrome. Three patients developed a carotid-cavernous fistula after the CEA procedure. After the proper treatment, both patients recovered completely. The average KPS scores of the 19 patients were 62.63 ± 8.72 preoperatively and 84.74 ± 5.67 postoperatively ($P < 0.01$; Figure 3).

Discussion

Previous studies have shown that there are many factors that could influence the recanalization rate of CICAO. The morphology of the lesion also needs to be considered; according to the Hasan et al. classification, types A/B, C, and D occlusions have 95–100%, 45–50%, and 25–30% of recanalization success rates, respectively (8). Types A and B have higher recanalization rates and lower complication rates compared to type C and type D. Visualization of the initial segment of the ICA at the common carotid artery bifurcation, combined with the presence of supraclinoid filling, makes CAS suitable for occlusion types A and B (13). To seek better treatment, Pinter et al. (10), Shih et al. (14), and Zhang et al. (15) attempted to apply hybrid surgery to the treatment of CICAO and achieved success. In 2013, Shih et al. addressed that the occluded internal carotid artery was successfully opened for three patients through hybrid surgery with CEA + CAS (14). Subsequently, some centers have performed relevant clinical research and achieved particular success (6, 11, 16). Hybrid surgery was proven to be a feasible and efficient treatment and increased the success rate of recanalization in patients with CICAO (12). In the present study, we found that hybrid surgery has apparent advantages in recanalizing chronic internal carotid artery occlusion with a high recanalization rate, and reverse ophthalmic artery blood flow in ICA preoperatively is a predictor of successful recanalization.

Our study shows that hybrid surgery has apparent advantages in treating CICAO with ineffective endovascular treatment. Among the 22 patients in this study, 19 had a successful opening of the internal carotid artery occlusion, and the recurrence rate of occlusion was 86.4%, which was higher than in previous studies (15, 16). After surgery, one patient developed a small frontal infarction; infarction incidence was only 5.3% with no death. We suggest that implementing CEA first in the recanalization of the internal carotid artery occlusion and excision of the plaque and polarized thrombus of the internal carotid artery occlusion as much as possible are necessary to provide a proper operative channel for performing CAS by shortening the distance between the distal step in the opening, and surgeons are more likely to find the actual cavity and the success rate of opening can be improved, especially for type C internal carotid artery occlusion in Hasan classification. Hybrid surgery can also effectively remove the plaque and its components in the neck, reduce the incidence of intra- and postoperative infarctions, and reduce the restenosis rate.

In this case group, the average KPS score of 19 patients who underwent opening of the occlusion before surgery is 62.63 ± 8.72, and the average KPS score 6 months after surgery is 84.74 ± 5.67, with a bilateral comparison *P*-value of <0.001. There are statistical differences in the preoperative and postoperative KPS scores, suggesting that recanalization of the internal carotid artery occlusion could improve patients' living ability and cognitive function. Most scholars suggest that internal carotid artery recanalization, as a secondary prevention surgery, can reduce the recurrence rate of stroke, reducing the death and disability rate. However, it is unclear whether recanalization can improve a patient's quality of life. This study compares and analyzes the preoperative and postoperative

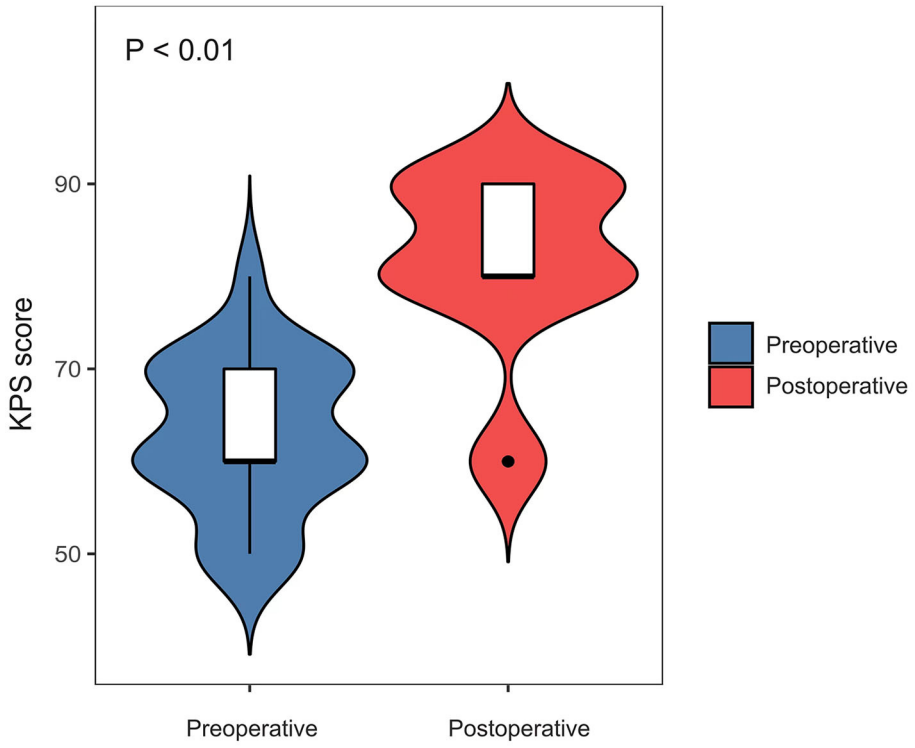

FIGURE 3
Comparison of preoperative vs. postoperative changes for a KPS score in the success group.

KPS scores and clarifies the role of recanalization of internal carotid artery occlusion in improving patients' living ability and cognitive function.

Previous studies found that prior neurological events, stump morphology, distal ICA reconstitution via contralateral injection, and distal ICA reconstitution at communicating or ophthalmic segments influence successful recanalization. Our results indicate that the reverse ocular artery blood flow in ICA preoperatively is a predictor of successful recanalization. If the occlusion does not exceed the distal part of the ophthalmic artery, the reverse ocular artery blood flow in ICA can be observed in preoperative or intraoperative DSA. In this event, the possibility of successful recanalization is higher than that exceeded the distal part of the ophthalmic artery. Among the 22 patients, 3 had occlusions that exceeded the distal part of the ophthalmic artery, and 1 underwent recanalization; thus, the recanalization rate of this group was 33.33%. Among the 22 patients, 19 had occlusions that did not exceed the distal part of the ophthalmic artery, and one did not undergo open CEA; thus, the recanalization rate of occlusion for this group was 94.74%. The recanalization rate was statistically significantly different between the groups of the abovementioned patients ($P = 0.038$). Other studies have shown that the occlusion length, involved segment, occlusion time, patient age, etc. are related to the recanalization rate (9, 14). However, no statistical difference in the recanalization rate was found on gender, age, occlusion period, and length in our study.

Limitations

Admittedly, our research also has some defects. First, this study is a retrospective study and not a randomized controlled study, which may lead to bias in patient selection and registration. Second, the number of cases in our study is smaller, which lacks comparative studies and short follow-up duration. Therefore, a larger sample size would have been needed to mitigate these effects. Finally, there may be some bias due to the different treatment timing of the symptomatic chronic occlusion of the carotid artery.

Conclusion

Hybrid surgery for complex CICAO is safe and effective with a high recanalization rate. Recanalization of an internal carotid artery occlusion can improve patients' living ability and cognitive function. The recanalization rate of occlusions correlates with the occluded segment; thus, determining whether the occluded segment accumulates above the ophthalmic artery can be important in the preoperative evaluation of whether the artery can be opened.

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

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. The patients/participants provided their written informed consent to participate in this study.

Author contributions

WZ and JC were involved in the study design. TZ and YC were involved in writing the original draft and modifying the manuscript. LW and YM were involved in data curation. YF and GL were involved in the formal analysis. All authors have read and approved the final study protocol.

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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.

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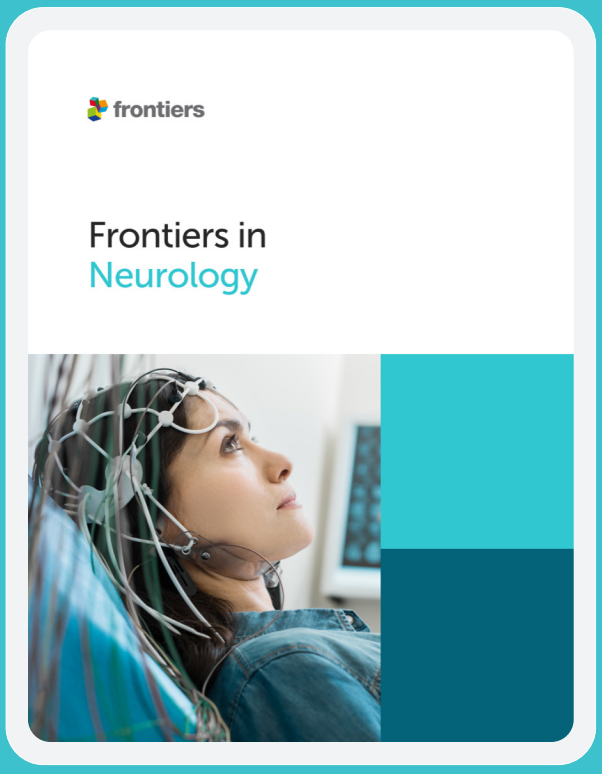

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