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Original Article

Rescue carotid stenting in tandem occlusions: 5 years' experience from a comprehensive stroke center

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الملخص

أهداف البحث: تقويم الشريان السباتي الإنقاذي أصبح مؤخرا علاجا إضافيا يتبع استخراج الخثرة الآلي في حالات الانسدادات المترادفة في الدورة الدموية الأمامية. ومع ذلك، هناك بيانات قليلة تدعم فوائد هذا العلاج في آسيا. افترضنا أن هذا العلاج مرتبط بتحسن النتائج السريرية بعد الإجراء.

طرق البحث: أجرينا تحليلا رجعيا للمرضى الذين خضعوا لتقويم الشريان السباتي الإنقاذي في حالات الانسدادات المترادفة للدورة الدموية الأمامية بين ديسمبر ٢٠٢٠ ومايو ٢٠٢٤ في مستشفانا. تم جمع البيانات السريرية والتصوير العصبي والإجرائية والمضاعفات. شملت النتائج الأولية معدل النتائج الجيدة (مقياس رانكين المعدل ≤ ٢) عند المتابعة بعد ٣ أشهر.

النتائج: تم تضمين تسعين مريضا مصابا بانسدادات مترادفة في الدورة الدموية الأمامية خضعوا لتقويم الشريان السباتي الإنقاذي في الدراسة. تم تحقيق إعادة التروية الناجحة (مقياس مختبر الجلطة الدماغي المعدل للتصوير الدماغي ≥ ٢ب) في جميع الحالات. في ٨٠ حالة تم استخدام نهج "من البعيد إلى القريب"، كان التشخيص-التوسيع بنسبة ٧٥.٦٪. حقق ثلاثة وخمسون مريضا (٥٨.٩٪) نتائج جيدة (مقياس رانكين المعدل ≤ ٢)، بينما أصيب ستة مرضى (٦.٧٪) بنزيف متصل بالبرنشيم من الدرجة الثانية وارتبط ذلك بالوفاة (مقياس رانكين المعدل ٦) بعد الإجراء.

الاستنتاجات: قد يرتبط وضع تقويم الشريان السباتي الإنقاذي في الانسدادات المترادفة بنتائج سريرية أفضل دون زيادة النزيف داخل القحف العرضي.

الكلمات المفتاحية: علاج السكتة الدماغية الحادة؛ تقويم الشريان السباتي النزيف داخل الدماغ علاج مضادات الصفائح الدموية؛ التصوير بالرنين المغناطيسي؛ إعادة التأهيل.

Abstract

Background and purpose: Rescue carotid stenting has recently been provided as an additional treatment followed by mechanical thrombectomy in patients with tandem occlusions of the anterior circulation. Nevertheless, few available data support the benefits of this treatment in Asia. We hypothesized that this treatment would be associated with improved postprocedural clinical outcomes.

Methods: We retrospectively analyzed patients who underwent rescue carotid stenting for tandem occlusions of the anterior circulation between December 2020 and May 2024 at our hospital. Clinical, neuroimaging, procedural, and complication data were collected. Primary outcomes

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included the rate of good outcomes with the modified Rankin Scale (mRS) ≤2 at 3-month follow-up.

Results: Ninety patients with tandem occlusions of the anterior circulation who underwent rescue carotid stenting were included, all of whom achieved successful recanalization. Among the 80 cases with the distal-to-proximal approach, diagnostic-Dotter was used in 85 %. Fifty-three patients (58.9 %) had good outcomes, and six patients (6.7 %) experienced parenchymal hemorrhage type II, which was associated with death (mRS 6) after the procedure.

Conclusion: Placement of rescue carotid stenting in tandem occlusions was associated with improved clinical outcomes, without increasing symptomatic intracranial hemorrhage.

Keywords: Acute stroke therapy; Antiplatelet therapy; Carotid stenting; Intracerebral hemorrhage; MRI; Rehabilitation

Introduction

The anterior circulation accounts for approximately 70–80 % of all ischemic strokes[1], with about 15–25 % of these cases involving large vessel occlusion occurring as tandem occlusions.[2,3] Patients with these lesions typically experience poorer outcomes than those with isolated intracranial occlusion (morbidity and mortality rates of 70 % and 50 %, respectively).[4] Application of the "golden hour" recombinant tissue plasminogen activator (rTPA) solely to tandem occlusions might result in poorer outcomes in approximately 80 % of patients.[5] The limitation of the rTPA approach at occlusive sites is explained by thrombus size, severe extracranial stenosis, and weak antegrade flow.[6] Many randomized controlled trials have demonstrated the effectiveness of mechanical thrombectomy, the gold standard treatment for acute ischemic strokes due to large vessel occlusion of the anterior circulation. This treatment has recently been included in the AHA/ASA and ESO-ESMINT guidelines for early management of acute ischemic stroke.[7,8]

Despite the success observed in these trials, tandem occlusions were underrepresented, accounting for only 13–32 % of cases; consequently, robust, evidence-based recommendations for managing this specific lesion type remain lacking.[9] Tandem lesions-defined as severe stenosis or occlusion of the extracranial internal carotid artery on the same side as an intracranial occlusion-pose a significant challenge for endovascular therapy, making it more difficult to restore blood flow efficiently to the affected cerebral territory.[10] Many studies have demonstrated the roles of rescue carotid stenting with either proximal-to-distal or distal-to-proximal approaches in the successful recanalization of tandem occlusions[11,12]. Although rescue carotid stenting plays a critical role in successful recanalization, its use is influenced by neurointerventionalist expertise and hospital resources.[13,14] In Asian populations, despite the substantial prevalence of atherosclerotic disease, asymptomatic extracranial carotid artery stenosis is less common in this population than other populations. However, studies examining the efficacy and safety of rescue carotid stenting in this demographic are limited.[15–17]

Since 2020, our hospital in Vietnam has used recanalization strategies for tandem occlusions. However, the feasibility and safety of the proximal-to-distal approach in the Vietnamese population remain unclear. This study was aimed at evaluating the effects of rescue carotid stenting on clinical outcomes at 3 months in patients with tandem occlusions, with a focus on the proximal-to-distal approach, to provide insights into its feasibility and safety in the Vietnamese population.

Materials and Methods

Study design

This retrospective cohort study was conducted at our hospital in Can Tho City between December 2020 and May 2024. Data were extracted from the medical records of eligible patients. The study flowchart is presented in Figure 1.

Study process

The preprocedural anesthesia involved local or conscious sedation. A short 8F sheath was used to access the femoral artery. The coaxial system, including the 8F guiding catheter and the 5 F diagnostic catheter, was placed in the distal common carotid artery. On the basis of neurointerventionalists' experience, either a distal-to-proximal or a proximal-to-distal approach was used. With the distal-to-proximal approach, blood flow in the intracranial segments was first restored through mechanical thrombectomy, which was followed by rescue carotid stenting to maintain forward flow. Two techniques were used to pass an 8F guiding catheter over the extracranial lesion in this approach: (1) dilator-Dotter (coaxial system including an 8F guiding catheter and a tapered inner dilator) and (2) diagnostic-Dotter (coaxial system including an 8F guiding catheter and a 5 F diagnostic catheter). The proximal-to-distal approach reversed the order of the distal-to-proximal procedures. Additionally, an embolic protection device was used to prevent plaque debris during stenting, according to the characteristics of the extracranial lesion determined by the main neurointerventionalists. Successful reperfusion with endovascular therapy was defined as mTICI ≥ 2b. The loading dose of dual antiplatelet therapy (300 mg clopidogrel and 162 mg aspirin) was administered before the procedure.[18–20] After the procedure, neuroimaging (head CT scan or MRI) was conducted to determine contraindications to antiplatelet therapy. Hemorrhagic transformation was defined as a complication after intervention on follow-up imaging, according to ECASS II criteria, including four subtypes[21]: HI1, HI2, PH1, and PH2 (Figure 1). Poor outcomes were defined by mRS scores >3.

Patients' representatives provided written informed consent to the procedure. Our study followed the STROBE guidelines. The number needed to harm was used to quantify the number of patients who must be exposed to a particular treatment or intervention for one additional patient to experience harm.

Participants

Patients with acute ischemic stroke caused by tandem occlusions in the anterior circulation received rescue carotid stenting after mechanical thrombectomy in the intracranial segments. Tandem lesions of the anterior circulation were defined as occlusions of the extracranial carotid artery concomitant with the intracranial carotid artery or middle cerebral artery, as determined with digital subtraction angiography and confirmed by the main neurointerventionalists during endovascular treatment. The inclusion criteria were as follows: (1) age >18 years; (2) National Institutes of Health Stroke Scale (NIHSS) > 5 at admission; (3) onset-to-treatment time <24 h; and (4) Diffusion-Weighted Imaging Acute Stroke Prognosis Early CT Score (DWI-ASPECTS) ≥ 5. The exclusion criteria were as follows: (1) premorbid mRS >2 and (2) loss to follow-up after discharge.

Measures

The 3-month clinical outcome variables, which were accessed in follow-up examinations by experienced neurologists (Figure 1), were divided into two groups: good (defined as mRS ≤2) and poor (mRS >3) outcomes. The intraoperative outcomes included procedural time, the approach to tandem occlusions and intracranial thrombectomy, and the devices; the postoperative variables included neuroimaging characteristics (MRI or CT examination), postoperative complications associated with the procedure, length of hospital stay, and mortality. The outcome variables included age, sex, patient history, stroke onset time, MRI characteristics, and inpatient status. Data on medical records, pathology results, genetic test results, and patient statements (family history) were additionally obtained (Table 1).

Statistical analyses

For statistical analysis, we used R version 3.6.0, with the packages dplyr, MASS, sandwich, lmtest, and ggplot2. The dataset comprised 90 observations and included quantitative variables described with means and standard deviations for normally distributed data, or with medians and quartiles for non-normally distributed variables. Qualitative variables are presented as frequencies and percentages. Associations with independent variables were assessed with the chi-square test, whereas Fisher's exact test served as an alternative for small sample sizes or when the assumptions of the chi-square test were not met.

Variables with $p < 0.2$ in univariate tests were included in the multivariate model. The backward stepwise selection method was used for model selection, thus leading to the reporting of the final model. A multivariate Poisson regression model with robust methods was used to estimate the relative risk (RR), 95 % confidence interval (CI), and p-value. Model fit was assessed with AIC, BIC, and VIF metrics to evaluate the appropriateness of the model. Statistical significance was defined as $p < 0.05$.

Results

A total of 100 patients underwent rescue carotid stenting for tandem occlusion at our hospital between December 2020 and May 2024 (Figure 1). The demographic and clinical characteristics of eligible patients are listed in Table 1. The patients included 83 men, and the mean age (SD) was 64.2 (±11.1) years (range: 31−87 yearsOf the patients who experienced significantly poor outcomes (Table 2), 63 were smokers ($p = 0.002$) and 21 had dyslipidemia ($p = 0.004$). The median NIHSS score at admission was 14.9 ± 4.6, and NIHSS scores >14 were associated with poor outcomes ($p = 0.017$, Table 3). Furthermore, patients with onset-to-door times exceeding 3 h (53.3 %) had an elevated likelihood of poor outcomes at 3 months (RR = 2.21, 95 % CI 1.27−3.83, $p = 0.034$, Figure 2). Moreover, 51 (56.7 %) patients had tandem lesions on the left side, and the mean DWI-ASPECTS was 6.9 ± 1.1. The mean procedural time was 64.4 ± 33.3 min (range: 20−200 min). Although fewer patients underwent rescue carotid stenting lasting over 60 minutes (40 %) compared to those with procedures completed within 60 minutes (60 %), a significant difference in poor 3-month outcomes was observed between the two groups ($p = 0.004$, Table 3). Among 21 patients (23.3 %) with a complication after rescue carotid stenting, 18 had hemorrhagic transformation: seven with HI1, two with HI2, three with PH1, and six with PH2. All patients with

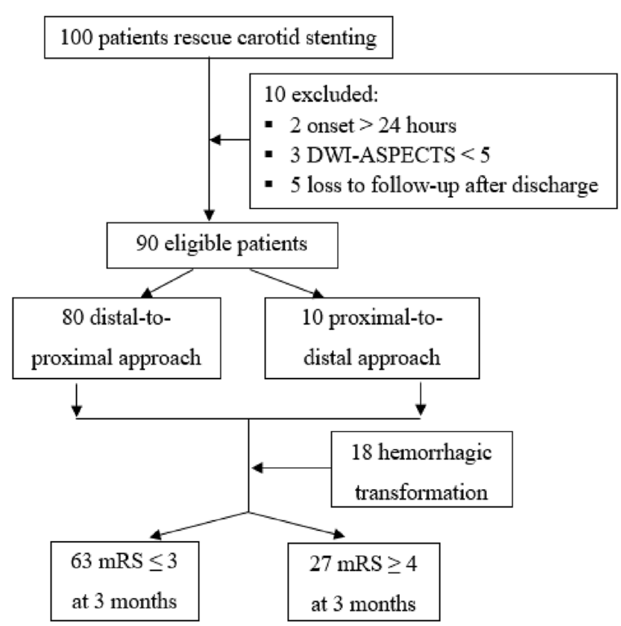

Figure 1: Flowchart of patient inclusion in the study. AIC: 104; BIC: 119; VIF<2.

Table 1: Definitions of outcome variables and analysis variables.

Variables	Variable definition	Variable classification	Method of data collection
Age	Patient age (years)	Quantitative variable	Medical report
History	Family history Personal history	Categorical variable	Medical report and patients' relatives
DWI-ASPECTS	0–10 scores	Quantitative variable	Medical report
Hemorrhagic transformation stage	HI1, HI2, PH1, PH2	Qualitative variable	Medical report
Procedure	Approaches, devices	Categorical variable	Medical report
Modified Rankin Scale (mRS)	0–6 scores	Quantitative variable	Medical report

Table 2: Baseline characteristics of patients with rescue carotid stenting.

Baseline characteristics	Rescue stenting (N = 90) n (%)
Pre-procedure	
Age in years[a]	64.2 (±11.1)
Male sex	83 (92.2)
Hypertension	70 (77.8)
Smoking	63 (70.0)
Dyslipidemia	21 (23.3)
Chronic kidney disease	6 (6.7)
Diabetes	16 (17.8)
Onset-to-door time in hours[b]	4 (2–6)
NIHSS[a]	14.9 (±4.6)
DWI-ASPECTS[a]	6.9 (±1.1)
Left side	51 (56.7)
Door-to-groin puncture time in min[b]	102.5 (80–120)
Procedure	
Procedural time in min[b]	60 (40–80)
Aspiration only	46 (51.1)
Proximal-to-distal approach	10 (11.1)
Stent length in mm[b]	40 (40–50)
Stent diameter in mm[b]	7 (7–7)
Second balloon length in mm (n = 39)[b]	16 (15–20)
Second balloon diameter in mm (n = 39)[b]	4 (4–5)
Diagnostic-Dotter technique	68 (85)
EPD	33 (36.7)
Post-procedure	
Sedation after procedure	59 (65.6)
Complications	21 (23.3)
Hemorrhagic transformation	18 (20.0)
Length of ICU stay in days[a]	4.7 (±4.8)
Length of hospital stay in days[b]	9 (7–14)
Stroke rehabilitation	77 (85.6)
Decompressive craniectomy	3 (3.3)

[a] Mean (±standard deviation).
[b] Median (first quartile–third quartile).

type PH2 had mRS scores of 6. Decompressive craniectomy was performed in 3.3 % of patients, including 2.2 % for type PH2 hemorrhage and 1.1 % for malignant edema. These conditions were associated with poor outcomes following rescue stenting (p = 0.025, Table 3). Beyond hemorrhagic transformation complications, no other potential complications (such as stroke recurrence, stent thrombosis, or access site complications) were recorded.

Table 3: Association between patient characteristics and clinical outcomes in mRS at 3 months.

Baseline characteristics	Outcomes		p value
	Poor n (%)	Good n (%)	
Demographic factors			
Age ≥60	21 (77.8)	39 (61.9)	0.143[a]
Male	25 (92.6)	58 (92.1)	1.000[b]
Risk factors			
Smoking	25 (92.6)	38 (60.3)	0.002[a]
Hypertension	22 (81.5)	48 (76.2)	0.580[a]
Dyslipidemia	1 (3.7)	20 (31.8)	0.004[a]
Chronic kidney disease	2 (7.4)	4 (6.4)	1.000[b]
Diabetes	3 (11.1)	13 (20.6)	0.374[b]
Admission parameters			
Admission NIHSS >14	19 (70.4)	27 (42.9)	0.017[a]
Onset >3 h	19 (70.4)	29 (46.0)	0.034[a]
Left side	16 (59.3)	35 (55.6)	0.745[a]
DWI-ASPECTS <7	12 (44.4)	17 (27.0)	0.104[a]
Door-to-groin puncture >120 min	7 (25.9)	13 (20.6)	0.580[a]
Procedural parameters			
General anesthesia	27 (100)	59 (93.7)	0.312[b]
Procedural time >60 min	17 (63.0)	19 (30.2)	0.004[a]
Proximal-to-distal approach	5 (18.5)	5 (7.9)	0.159[b]
Mechanical thrombectomy	18 (66.7)	26 (41.3)	0.027[a]
Unused EPD	22 (81.5)	35 (55.6)	0.019 [a]
Closed-cell stents	18 (66.7)	42 (66.7)	1.000 [a]
Post-procedure factors			
Sedation after procedure	20 (74.1)	39 (61.9)	0.266[a]
Complication	12 (44.4)	9 (14.3)	0.002[a]
Hemorrhagic transformation	10 (37.0)	8 (12.7)	0.008[a]
Without antiplatelet therapy	6 (22.2)	0 (0)	<0.001[b]
Decompressive craniectomy	3 (11.1)	0 (0)	0.025[b]
Unrehabilitation	6 (22.2)	7 (11.1)	0.198[b]
Length of ICU stay >6 days	18 (66.7)	10 (15.9)	<0.001[a]
Length of hospital stay >14 days	14 (51.9)	9 (14.3)	<0.001[a]

[a] Chi-square test.
[b] Fisher's exact test.

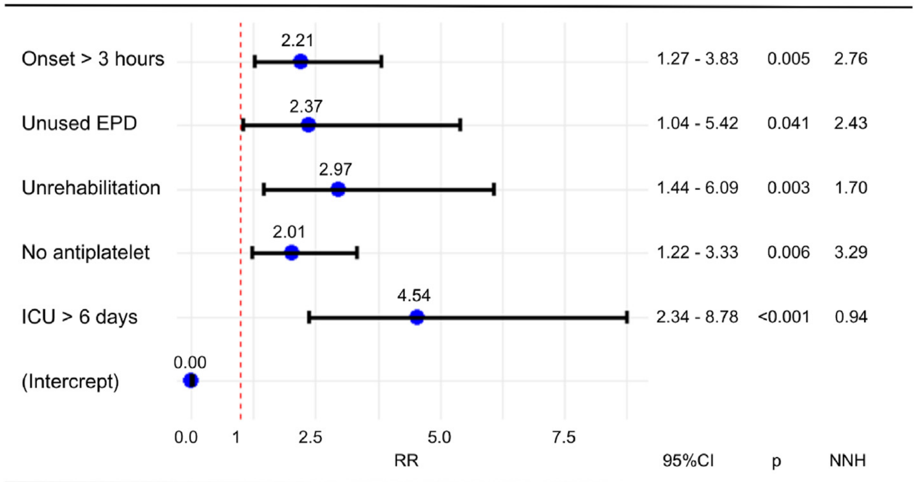

Figure 2: Multivariable Poisson regression analysis of factors associated with favorable outcomes.

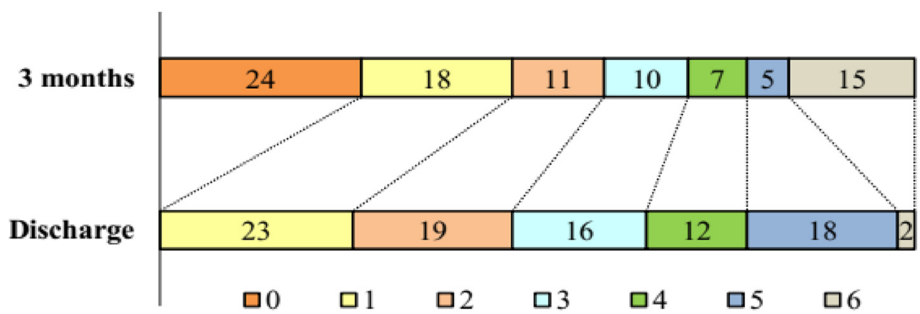

Figure 3: Distributions of the 3-month mRS in patients with rescue carotid stenting.

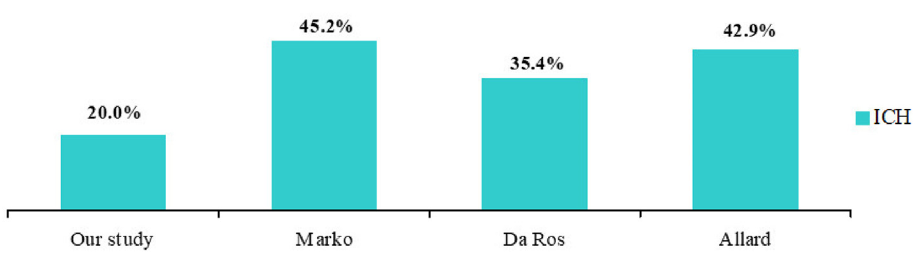

Figure 4: Postprocedural intracranial hemorrhage rates in the studies.

Overall, ICU lengths of stay longer than 6 days (RR = 4.54, 95 % CI 2.34–8.78, $p < 0.001$, Figure 2) and hospital stays longer than 14 days were significantly associated with poor outcomes ($p \leq 0.001$, Table 3).

Moreover, the rate of good outcomes (mRS ≤ 2) improved from 46.6 % at discharge to 58.8 % at 3 months; the number of deaths at 3 months increased by 13 cases compared to the number at discharge (Figure 3).

Discussion

Smoking and dyslipidemia are notable factors contributing to the progression of vascular damage and accelerating atherosclerosis.[22,23] These factors were found to increase the risk of poor outcomes after rescue carotid stenting (Table 3), in agreement with findings from a large prospective study on extracranial atherosclerotic stenosis.[24,25] Many studies have indicated positive results of endovascular therapy in the treatment of tandem occlusions. According to the AHA/ASA guidelines for the early management of acute ischemic stroke, mechanical thrombectomy offers additional benefits compared to medical treatment alone.[7] Beyond mechanical thrombectomy alone, additional recanalization therapies include extracranial angioplasty and carotid stenting, alone or combined.[10] In tandem occlusions, restoration of intracranial blood flow is more essential than that of extracranial blood flow. The use of appropriate approaches (proximal-to-distal and distal-to-proximal) in tandem occlusions is controversial. The distal-to-proximal approach comprises the dilator-Dotter and diagnostic-Dotter techniques. These techniques strengthen the coaxial system crossing over the occlusive carotid artery. In our study, diagnostic-Dotter (85 %) was used more frequently than dilator-Dotter, because its soft diagnostic catheter with a distal curve-tapered tip limits dissection and perforation during selection. However, the thrombi or debris in extracranial occlusion have a high risk of occluding the intracranial segments in the distal-to-proximal approach. Therefore, the embolic protection device has an important role in preventing procedural emboli from reaching other vasculature during the procedure. Moreover, Min et al.[16] have demonstrated that the distal-to-proximal approach provides benefits in achieving higher successful reperfusion rates and improved functional outcomes. Most meta-analyses have significantly favored stenting over mechanical thrombectomy with or without angioplasty for extracranial lesions[26] (OR, 1.43 [95 % CI, 1.07−1.91]).[10] Despite these positive findings, another systematic review found no significant difference in treatment efficacy between the two approaches.[27] Management of tandem occlusions without emergent stenting may address cervical lesions in a staged manner after the initial intracranial occlusion has been treated, for example by: (1) performing thrombectomy on the intracranial occlusion plus medical management (with anticoagulation or antiplatelet therapy) without immediately addressing the extracranial ICA, or (2) performing thrombectomy plus angioplasty, medical management, and delayed stenting. In our study, emergent stenting was required in all cases because of restenosis or even reocclusion of the extracranial lesion within 5 min after recanalization in the intracranial segments. Unsuccessful recanalization was associated with poor outcomes if emergent stenting was not performed.

Antiplatelet therapy was crucial in supporting endovascular treatment, by decreasing the risk of stent thrombosis, and improving outcomes. Patients not receiving antiplatelet therapy post-recanalization had significantly poorer outcomes (RR = 2.01, 95 % CI: 1.22−3.33, p = 0.006). However, use of this treatment in patients with hemorrhagic complications (e.g., PH2) remains challenging because of contraindications (Figure 2). Although these cases had type PH2 hemorrhagic transformation in the postprocedural CT scan, which contraindicated antiplatelet therapy, this therapy was used in the other types to prevent stent thrombosis. One case had malignant edema with a new infarct caused by the long procedural time (150 min) that increased the risk of thrombus formation.

The mechanisms involved in hemorrhagic transformation can be considered from multiple perspectives, such as histological changes, vascular occlusion, collateral circulation, blood−brain barrier disruption, and infarct size. Two main factors in hemorrhagic transformation have been described: an imbalance between the formation of oxygenated free radicals and reperfusion injury, which causes vascular damage through various mechanisms, such as inhibition of protein synthesis, platelet activation, leukocyte infiltration, disruptions of the basal cell layer, and apoptosis in the central nervous system. Consequently, the basal cell layer and endothelial tight junctions are destroyed. Among the molecules involved, MMP-9 has been shown to play an important role in the destruction of the basal cell layer containing type IV collagen. Angioedema, in contrast to cytotoxic edema, is caused by the diffusion of macromolecules and secretions into the extracellular space, because of destruction of the basal cell layer. Angioedema can damage adjacent tissues and cause irreversible myelin damage.[28] In our study, 16 cases of hemorrhagic transformation were recorded, which included many cases of hemorrhagic infarction type 1 (HI1) (seven cases) and parenchymal hemorrhage type 2 (PH2) (six cases); however, only two PH2 cases underwent decompressive craniectomy. All PH2 cases involved antiplatelet drug discontinuation and led to death (mRS 6). Our findings for type PH2 were consistent with those from other studies.[10,12−14]

The rate of any intracranial hemorrhage was lower than reported in other studies, possibly for the following reasons (Figure 4): (1) maintenance of systolic blood pressure of 110−120 mmHg after the procedure; (2) reliance of the recanalization procedure on the DWI-ASPECTS on MRI, which had higher sensitivity than CT, in addition to clinical assessment; and (3) use of a double antiplatelet loading dose (two tablets of 81 mg aspirin and one tablet of 300 mg clopidogrel).

Our study's strengths included treatment protocol homogeneity, experienced neurointerventionalists, and high follow-up rates. However, our study's retrospective design limited its ability to establish causality and to control for confounding variables. The lack of a control group without rescue carotid stenting restricted comparative analysis and generalizability of the findings. Additionally, the single-center setting might potentially have introduced bias associated with local protocols and operator expertise. Although the homogeneity of treatment and high levels of neurointerventionalist experience are study strengths, they might limit the applicability of our findings to less specialized centers.

Furthermore, procedural decisions, such as the use of embolic protection devices and antiplatelet regimens, might not be standardized across institutions, thereby complicating broader implementation. The small sample size for certain subgroups, such as those with prolonged procedural times or specific complications, additionally limits the statistical power to draw robust conclusions.

Conclusions

In summary, carotid stenting is an effective rescue choice for improving clinical outcome rates. Further studies are needed before this treatment can be considered standard for tandem occlusions.

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Conflict of interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics statement

Our study was registered at ClinicalTrials.gov under ID NCT06397638. The study involving human participants was reviewed and approved by the Ethics Council for biomedical research at our hospital (11923/QD-S.I.S) and the Ethical Board of the University of Medicine and Pharmacy at Ho Chi Minh City (number 1087/HDDD-DHYD on November 2, 2023).

Ethics approval

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Informed consent

Informed consent was obtained from all patient representatives after provision of a detailed explanation of the procedures.

Author contributions

TML, DNT, and GLN conceptualized the study. TML, DNT, GLN, HNN, and TTN performed data curation. TML, DNT, HNN, and GNL conducted formal analysis. TML and GLN conducted investigation. GLN, DNT, NHN, LMBT, and TML performed the methods. GLN and TML performed project administration. TML and GLN provided resources. TML, HNN, and TTN were responsible for the software. GLN and TML supervised the study. GLN and TML validated the study. GLN and TML performed visualization. NHN, DNT, GLN, LMBT, and TML contributed to writing the original draft. NHN, DNT, GLN, LMBT, and TML contributed to writing review and editing.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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