Original research

A novel angiographic classification for the endovascular recanalization of symptomatic nonacute extracranial vertebral artery occlusion

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ABSTRACT

Background There remains major uncertainty regarding the optimal therapy for symptomatic nonacute extracranial vertebral artery occlusion (EVAO). Endovascular recanalization for EVAO is technically challenging, and limited data are available. This research aimed to report a multicenter clinical experience of endovascular recanalization for symptomatic nonacute EVAO and establish a novel angiographic classification.

Methods From June 2011 to December 2019, 50 symptomatic nonacute EVAO patients treated with endovascular recanalization in three regional referral stroke centers were retrospectively analyzed. All patients were categorized into four groups based on the angiographic classification. The rates of technical success, periprocedural complications, any stroke or death within 1 month, and follow-up data were assessed.

Results The rates of technical success, periprocedural complications, and any stroke or death within 1 month were 86.0% (43/50), 12.0% (6/50), and 4.0% (2/50), respectively. The recanalization rates gradually decreased from Type A to Type D (100%, 94.7%, 80%, and 63.6%, respectively; P=0.007). The EVAO patients in the Type A group with tapered stump and short-segment occlusions showed excellent recanalization effects, with 100% technical success rates and no complications. Conversely, the lowest recanalization rate of 63.6% (7/11) and the highest periprocedural complication rate of 27.3% (3/11) were observed for the Type D group.

Conclusions Endovascular recanalization for symptomatic nonacute EVAO is technically feasible, especially Type A EVAO patients, which can provide an alternative treatment option for recurrent vertebrobasilar ischemia despite optimal medical therapy. The angiographic categorization established in this study is conducive to the selection of suitable patients prior to treatment decision.

INTRODUCTION

Extracranial vertebral artery occlusive disease is a frequent cause of posterior circulation ischemic stroke, which accounts for about 20%–32% of patients with posterior circulation transient ischemic attacks (TIAs) and strokes.1 2 Some studies have reported the effectiveness and safety of endovascular recanalization for acute extracranial vertebral artery occlusion (EVAO) in patients with acute tandem vertebrobasilar artery occlusions.3 4 However, the optimal therapy for symptomatic nonacute EVAO, including subacute to chronic occlusion beyond a 24-hour time window of ischemic onset, remains uncertain. In general, open surgery and endovascular recanalization are complementary and valuable alternatives for patients with recurrent stroke or TIA despite optimal medical therapy.5 6 The aim of treatment is to improve hemodynamics and/or to eliminate an embolusgenic source in the posterior circulation. Previous studies have reported that bypass surgery, vertebrecterectomy, or hybrid surgery can be considered a therapeutic option for posterior circulation infarction.5 6 Nevertheless, such procedures are not commonly performed because of the technical complexity and serious complications.7 With the development of endovascular intervention, few case reports have attempted to evaluate the feasibility of endovascular recanalization for nonacute EVAO.8 9 10 However, most of the reports involve only a single case, and case series are rare.

This research aimed to evaluate the technical feasibility and safety of endovascular recanalization for symptomatic nonacute EVAO and provide a guideline for the selection of patients prior to treatment decision. We retrospectively analyzed 50 nonacute EVAO patients who underwent endovascular recanalization at three large regional referral stroke centers, and established a novel angiographic categorization.

METHODS

Research data

The datasets generated and/or analyzed during this research are available from the corresponding author on reasonable request.

Study subjects

Patients were screened through the prospectively acquired endovascular stroke databases of three large regional referral stroke centers. The clinical, demographic, imaging procedural and follow-up data were collected. From June 2011 to December 2019, 50 symptomatic nonacute EVAO patients treated with endovascular recanalization were identified. Among them, 43 patients were male, with a mean age of 51.50±8.89 years (ranging from 45 to 76 years). After EVAO was diagnosed with CT angiography (CTA) according to the initial manifestation (stroke or TIA), all patients were subjected to optimal medical therapies (dual antiplatelet agents and risk factor modification). The duration of occlusion was defined as the time from EVAO...
diagnosis to endovascular therapy. All patients were clinically examined and followed up. If they still suffered from recurrent stroke or TIA due to hemodynamic compromise or suspected stump syndrome, endovascular treatment was considered. All patients had a mismatch between stroke severity (NIHSS) and MRI diffusion weighted imaging (MRI-DWI) infarct core (according to the clinical judgment of the treating physician). The clinical and radiographic findings indicated the occurrence of cerebral hemodynamic failure, such as watershed infarcts on MRI, low blood pressure, and/or worsening of symptoms in the upright position. All patients signed a written informed consent prior to endovascular therapy. The ethical approval for this research was obtained from the Institutional Review Board of Beijing Tiantan hospital, and the requirement for written informed consent to review patient medical records was waived.

**Inclusion and exclusion criteria**

The inclusion criteria were: nonacute proximal extracranial vertebral artery (V1 or proximal V2 segment) occlusion diagnosed and confirmed by CTA and digital subtraction angiography (DSA), respectively; recurrent posterior circulation stroke or TIA; visible occlusion stump and distal V2 segment, as reconstituted via muscular branches and thyrrocervical trunk branches; combined with a complete occlusion or hypoplasia of contralateral vertebral artery or normal contralateral vertebral artery, but the occluded side presented with vertebral artery stump syndrome, which means that the low blood flow in the stump may induce thrombosis and ultimately distal embolism; bilateral sides of the posterior communicating artery were aplastic or hypoplastic; at least one atherosclerosis risk factor (eg, smoking, hypertension, hyperlipidemia, diabetes mellitus, and coronary artery disease); and patients who did not opt for bypass surgery.

The exclusion criteria were: no atherosclerotic lesions, including suspected vasculitis, radiation angiopathy, or arterial dissection; concomitant with intracranial aneurysm or any bleeding disorder; large infarction core, as defined as a posterior circulation Alberta Stroke Program Early CT Score (pc-ASPECTS) based on MRI DWI<6 points; and combined with occlusion of the basilar artery or distal intracranial vertebral artery.

**Angiographic categorization of nonacute EVAO**

Nonacute EVAO patients were angiographically analyzed based on DSA. The occlusion stump morphology was classified as tapered or nontapered. The occlusion length was measured in a straight line from the occluded stump to the distal reconstituted V2 segment, and was grouped as ≤50 or >50mm. Angiographic evaluation was performed by two independent neuroradiologists, and disagreements were resolved through discussion.

According to the occlusion stump morphology and occlusion length, nonacute EVAO patients were categorized into four types as follows: Type A (figures 1A and 2A-C), the extracranial vertebral artery was occluded, with a tapered occlusion stump and occlusion length ≤50 mm; Type B (figures 1B and 2D-F), the extracranial vertebral artery was occluded, with a tapered occlusion stump and occlusion length >50 mm; Type C (figures 1C and 3 A-C), the extracranial vertebral artery was occluded, with a nontapered occlusion stump and occlusion length ≤50 mm; and Type D (figures 1D and 3 D-F) the extracranial vertebral artery was occluded, with a nontapered occlusion stump and occlusion length >50 mm.

**Figure 1** Schematic diagram for the angiographic categorization of patients with nonacute extracranial vertebral artery occlusion (EVAO). (A) the extracranial vertebral artery of type A EVAO is occluded, with a tapered occlusion stump and occlusion length ≤50 mm. (B) the extracranial vertebral artery of type B EVAO, is occluded, with a tapered occlusion stump and occlusion length >50 mm. (C) the extracranial vertebral artery of type C EVAO is occluded, with a nontapered occlusion stump and occlusion length ≤50 mm. (D) the extracranial vertebral artery of type D EVAO is occluded, with a nontapered occlusion stump and occlusion length >50 mm.

**Endovascular recanalization procedure**

The recanalization procedure was carried out under general anesthesia via the transfemoral route. In four patients, recanalization via the femoral artery failed. Considering the angle between the occluded stump and the subclavian artery, the operations were successfully conducted via the radial artery route.

After implanting the sheath introducer, heparin was given intravenously to maintain an activated clotting time of 200–300 s. An 8.0-Fr guiding catheter or Shuttle sheath was positioned in the right or left subclavian artery proximal to the ostium. As an intermediate support catheter, a 5.0-Fr diagnostic catheter (125 cm) was placed coaxially into the ostial stump. Coaxial assembly of a 0.014-inch microwire (Pilot series, Abbott Vascular, California, USA) and microcatheter were then performed carefully. If the 0.014-inch microwire could not pass the occluded segment, the occluded segment was probed by using a 0.018- or 0.035-inch guidewire. Once the guidewire traversed the stump, it was immediately removed. The microcatheter was then exchanged over a 0.014-inch microwire to navigate to and across the occlusion. The procedure was terminated if multiple attempts were done and the microcatheter/microwire system could not cross the occluded segments and the procedure time exceeded 30 min. A 2.0–20 mm diameter angioplasty balloon was advanced over the exchange microwire to cross the occlusion, and it was inflated to 6–8 atm to predilate the occlusion. Subsequently, a distal embolic protection device (Spider FX, EV3, Irvine, California, USA) was advanced over the exchange microwire and deployed distally if an adequate distal landing zone could be identified. The diameter and length of the occluded vertebral artery were measured after balloon angioplasty. The balloon-expandable
Ischemic stroke

Figure 2  Type A (A–C): (A) the right vertebral artery of type A EVAO is occluded with a tapered occlusion stump (arrow) following a selective right subclavian artery injection. (B) the distal V2 segment is reconstituted (arrow) via the thyrocervical trunk and muscular branches, but no opacification of the ≤50 mm segment is observed in both antegrade and retrograde views. (C) antegrade filling of the right vertebral artery occurs after stent reconstruction. The arrow shows the distal embolic protection device. Type B (D–F): (D) the left vertebral artery of type B EVAO is occluded with a tapered occlusion stump (arrow) following a selective left subclavian artery injection. (E) the distal V2 segment is reconstituted (arrow) via the thyrocervical trunk and muscular branches, but no opacification of the >50 mm segment is observed in both antegrade and retrograde views. (F) final angiogram shows good patency of the occluded vertebral artery.

Figure 3  Type C (A–C): (A) the left vertebral artery of type C EVAO is occluded with a nontapered occlusion stump (arrow) following a selective left subclavian artery injection. (B) the distal V2 segment is reconstituted (arrow) via the thyrocervical trunk and muscular branches, but no opacification of the ≤50 mm segment is observed in both antegrade and retrograde views. (C) final angiogram shows good patency of the occluded vertebral artery. Type D (D–F): (D) the right vertebral artery of type D EVAO is occluded with a nontapered occlusion stump (arrow) following a selective right subclavian artery injection. (E) the distal V2 segment is reconstituted (arrow) via the thyrocervical trunk and muscular branches, but no opacification of the >50 mm segment is observed in both antegrade and retrograde views. (F) final angiogram shows good patency of the occluded vertebral artery.

while the student’s t-test or Mann–Whitney U test was for continuous variables. Count data are presented as the frequency and composition ratio. If the variances differed greatly between groups, student’s t-test or the approximate χ² test was carried out. All statistical analyses were conducted using SPASS 20.0, and P<0.05 was considered significant.

RESULTS
Clinical features of nonacute EVAO patients
All 50 nonacute EVAO patients were treated with endovascular recanalization. Twenty-seven and 23 had left and right vertebral artery occlusions, respectively. The median duration of occlusion was 58.50 days (IQR=30.00–76.25), and the median time from last symptom onset to endovascular treatment was 14.00 days (IQR=12.00–17.25). Twenty-eight cases were combined with contralateral vertebral artery dysplasia, 20 cases with contralateral vertebral artery occlusion, and two patients had patent contralateral vertebral artery but their occluded sides presented with vertebral artery stump syndrome. Two patients combined with unilateral asymptomatic internal carotid artery stenosis, and the stenosis degree was 50%–70%. No interventional treatment was performed at the same time, and no patients were...
complicated with carotid artery occlusion. All 50 cases were categorized into four groups based on the angiographic classification. No remarkable differences in the demographic characteristics of EVAO patients were found among the four groups (see online supplemental table 1).

### Periprocedural outcomes

The rates of technical success, periprocedural complications, and any stroke or death during follow-up were 86.0% (43/50), 12.0% (6/50), and 4.0% (2/50), respectively. In the four classified groups, the recanalization rates gradually declined from Type A to Type D (100%, 94.7%, 80%, and 63.6%, respectively, \( P=0.007 \)). The rates of periprocedural complications in Types A, B, C, and D were 0%, 15.8%, 0%, and 27.3%, respectively (\( P=0.165 \)). See table 1 for the detailed clinical and angiographic outcomes.

One patient developed acute stent thrombosis after recanalization of the right vertebral artery and basilar artery embolism during the procedure, and was subsequently treated with recombinant tissue plasminogen activator and intra-arterial tirofiban. However, the patient suffered from postprocedural brainstem hemorrhage and died after 72 hours. Another patient developed left visual field hemianopia 2 days after successful recanalization. CTA revealed a patency of the left vertebral artery, and CT indicated low-density infarction in the right occipital lobe. Four patients underwent asymptomatic vascular dissection during the procedure. Among them, two cases failed to recanalize because the guidewire could not enter the distal V2 true lumen through occlusion, while in the other two cases, the operation was successful and the dissections were completely resolved after stent placement. No vascular perforation or hemorrhagic complication was observed.

### Follow-up outcomes

The median clinical follow-up period was 12 months (IQR = 7.25–24.00) for 49 patients, including 42 patients with successful recanalization and seven patients with failed recanalization attempts. The rate of any stroke or death was 4.1% (2/49) during the follow-up period. One patient (1/42) developed cerebral stem and ipsilateral cerebellar ischemic stroke at 6 months after successful recanalization. CTA showed stent restenosis, and the symptoms were alleviated after drug and rehabilitation treatment (mRS ≤1). Among the seven patients with unsuccessful recanalization, one patient (1/7) had recurrent posterior circulation stroke at 3 months after the operation, three patients had recurrent TIAs during the 6-month follow-up period, and the remaining three patients were stable. The median imaging follow-up period was 12 months (IQR = 6.00–24.00). Restenosis (>50% stenosis) occurred in 5/32 (15.6%) patients, as revealed by doppler ultrasonography (DUS), CTA, and/or conventional angiography follow-up examinations. One patient was symptomatic, while the remaining four were asymptomatic.

### DISCUSSION

Nonacute EVAO can cause posterior circulation ischemic symptoms or stroke through hemodynamic compromise or hypoperfusion-associated stump embolism. The natural course of EVAO occurred within a few months after recent episodes has not been determined to date. However, the prevalence of vertebral artery stump syndrome accounts for 1.4% of acute posterior circulation stroke, which exhibits significant associations with high stroke recurrence rate (25%) and worse prognosis. Therefore, active treatment is warranted for patients with symptomatic nonacute EVAO, especially within a few months after recurrent episodes.

Here, we reported a multicenter preliminary experience of endovascular recanalization for medically refractory EVAO, with the largest sample size on this topic to date. The findings revealed that endovascular recanalization was feasible, with an overall success rate of 86% and an incidence of periprocedural complications of 12%. The technical success rate showed a gradual decreasing trend from Type A to Type D (100%, 94.7%, 80%, and 63.6%, respectively, \( P=0.007 \)), indicating that this angiographic classification is conducive to the difficulty grading. When comparing two groups, Type A and Type D showed statistically significant differences (\( P=0.009 \)). Type A lesions, with tapered stump and short-segment occlusions, exhibited excellent recanalization effects (100% technical success and no complications), and the EVAO patients in this group could be the most suitable candidates for endovascular recanalization. Conversely, Type D lesions, with non-tapered stump and long-segment occlusions, had a low recanalization rate of 63.6% and a high complication rate of 27.3%. Hence, the benefits and risks of endovascular recanalization for this patient group need to be comprehensively weighed.

Clinical experience with the chronic total occlusion (CTO) of the coronary arteries has shown that stump morphology and occlusion length are two important predictors of successful recanalization for CTO. Therefore, the two simple and convenient angiographic parameters, namely, stump morphology and occlusion length, were used as indices of the proposed EVAO angiographic classification in this study. A tapered stump at the occlusion can facilitate guidewire entry into the occluded segment, while a nontapered or blunt stump increases the difficulty. This has also been well demonstrated in carotid CTO studies. In this cohort, the technical success rate of Type A and
B with tapered stump was 96.6%, and that of Type C and D with non-tapered stump was 71.4% (P=0.035), indicating that the occlusion stump morphology could reflect the difficulty of recanalization for EVAO lesions.

Although occlusion length has been shown to be an independent predictor for technical success in coronary CTO studies, Chen et al19 have indicated that the occlusion length may not be significant for estimating the technical success of carotid CTO recanalization. In the current series, the success rate of Type B lesions was higher than that of Type C lesions, even though the occlusion length of the former was longer than that of the latter. This suggests that the effect of occlusion length on technical success can be interfered by confounding factors such as stump morphology. However, in this study, long-segment lesions showed a tendency to increase perioperative complications. All periprocedural complications occurred in long-segment lesion groups (Types B and D). Theoretically, a longer occlusion is more likely to cause vascular dissection, and wiring across a long occlusion segment is not easy due to varying vessel courses, thereby resulting in a high risk of vessel damage. Hence, a larger sample size is warranted to identify the independent predictive value of occlusion length for technical success. Some other factors that may affect recanalization, such as the duration of the occlusion, tortuosity of the occlusion segment, stump angle, and presence of calcium, are not used as the parameters for EVAO angiographic classification. This is largely because the angiographic parameters selected for classification are mostly categorical, simple, and clinically applicable.

In this study, one patient developed acute in-stent thrombosis and basilar artery embolism after the distal embolic protection device was retracted during the operation. Iwata et al25 have attempted to reduce distal embolization during the endovascular revascularization of EVAO through the use of flow reversal, and many other clinicians have used different protecting devices, such as a distal balloon and Spider FX.21 However, it has been reported that the recanalization of a chronic long-segment EVAO can be performed safely without the use of protection devices.20 22 Thus, further controlled studies are required to confirm the efficacy of protection devices for endovascular recanalization of nonacute EVAO.

There have been concerns for stent restenosis in extracranial vertebral artery, with reports ranging from 10% to 43%.26 In this retrospective study, restenosis occurred in 5/32 (15.6%) patients and one patient was symptomatic and the other four were asymptomatic. This could be attributed to the fact that the majority of EVAO patients underwent CTA or DUS but did not undergo routine follow-up angiography.21 22 Compared with DSA, the specificity and sensitivity of ultrasound in the diagnosis of extracranial vertebral artery restenosis are satisfactory.27 In addition, the long-term follow-up imaging data of some EVAO patients were lacking, which might hinder the assessment of the overall restenosis rate. A recent study reported that contralateral disease could increase the risk of in-stent restenosis after vertebral artery ostium stenting.28 Further research is needed to evaluate the durability of endovascular recanalization.

There were several limitations in this study. First, this cohort study was retrospective with a modest sample size of patients. The angiographic parameters of classification proposed in this study were mainly based on multicenter preliminary experience, with the consideration of categorical and clinical applicability. Thus, a prospective study with larger sample size is needed to confirm our findings. Second, perfusion parameters were not adopted to screen our patients, as it was difficult to assess hypoperfusion in cases of posterior circulation occlusion. Lastly, a placebo control arm was not included in this research, and whether endovascular recanalization could be selected as an optimal medical therapy remained to be verified. It is necessary to determine the subgroups of EVAO patients that are most likely to benefit from endovascular recanalization prior to a controlled study.

CONCLUSIONS

Endovascular recanalization is technically feasible for symptomatic nonacute EVAO patients, especially Type A patients, which can provide an alternative treatment option for recurrent vertebralbasilar ischemia despite optimal medical therapy. The angiographic categorization established in this study is conducive to the selection of suitable patients prior to treatment decision.

REFERENCES

Ischemic stroke

### Online supplementary table I: Baseline characteristics

<table>
<thead>
<tr>
<th>Variable names</th>
<th>Total (N=50)</th>
<th>Type A (N=10)</th>
<th>Type B (N=19)</th>
<th>Type C (N=10)</th>
<th>Type D (N=11)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, no. (%)</td>
<td>43(86.0)</td>
<td>8(80.0)</td>
<td>17(89.5)</td>
<td>8(80.0)</td>
<td>10(90.9)</td>
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<tr>
<td>Mean age, y</td>
<td>51.50±8.89</td>
<td>59.30±7.59</td>
<td>59.42±9.62</td>
<td>64.50±9.32</td>
<td>60.73±8.43</td>
<td>0.493</td>
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<td>Risk factors, no. (%)</td>
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<tr>
<td>Hypertension</td>
<td>41(82.0)</td>
<td>8(80.0)</td>
<td>15(78.9)</td>
<td>8(80.0)</td>
<td>10(90.9)</td>
<td>0.880</td>
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<td>Diabetes mellitus</td>
<td>20(40.0)</td>
<td>6(60.0)</td>
<td>8(42.1)</td>
<td>5(50.0)</td>
<td>1(9.1)</td>
<td>0.074</td>
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<td>Coronary heart disease</td>
<td>11(22.0)</td>
<td>2(20.0)</td>
<td>4(21.1)</td>
<td>5(50.0)</td>
<td>1(9.1)</td>
<td>0.212</td>
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<td>Dyslipidemia</td>
<td>20(40.0)</td>
<td>3(30.0)</td>
<td>8(42.1)</td>
<td>5(50.0)</td>
<td>4(36.4)</td>
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<td>Smoking history</td>
<td>33(66.0)</td>
<td>7(70.0)</td>
<td>15(78.9)</td>
<td>3(30.0)</td>
<td>8(72.7)</td>
<td>0.073</td>
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<td>Qualifying event, no. (%)</td>
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<td>Recurrent stroke</td>
<td>29(58.0)</td>
<td>7(70.0)</td>
<td>10(52.6)</td>
<td>4(40.0)</td>
<td>8(72.7)</td>
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<td>Recurrent TIA</td>
<td>21(42.0)</td>
<td>3(30.0)</td>
<td>9(47.4)</td>
<td>6(60.0)</td>
<td>3(27.3)</td>
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<td>Occlusive side</td>
<td></td>
<td></td>
<td></td>
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<td>Left VA</td>
<td>27(54.0)</td>
<td>5(50.0)</td>
<td>9(47.4)</td>
<td>5(50)</td>
<td>8(72.7)</td>
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<td>Occlusion to ER, days, median (IQR)</td>
<td>58.50(30.00-76.25)</td>
<td>60.00(42.50-67.75)</td>
<td>35.00(25.00-61.00)</td>
<td>61.50(51.25-130.00)</td>
<td>57.00(30.00-120.00)</td>
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<td>Last symptom to ER, days, median (IQR)</td>
<td>14.00(12.00-7.25)</td>
<td>14.50(12.00-5.75)</td>
<td>14.00(11.00-2.00)</td>
<td>13.50(11.75-16.25)</td>
<td>15.00(12.00-20.00)</td>
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<td>Pre MRS score, median (IQR)</td>
<td>2(1-3)</td>
<td>2(1-3)</td>
<td>2(1-3)</td>
<td>1(1-2)</td>
<td>2(1-3)</td>
<td>0.092</td>
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<td>Pre NIHSS score, median (IQR)</td>
<td>4(2-6)</td>
<td>4(2-8)</td>
<td>4(2-9)</td>
<td>4(2-6)</td>
<td>5(3-7)</td>
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<td>Distal Protection, no. (%)</td>
<td>45(90.0)</td>
<td>9(90.0)</td>
<td>18(94.7)</td>
<td>8(80.0)</td>
<td>10(90.9)</td>
<td>0.716</td>
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</tbody>
</table>
Abbreviations: ER, endovascular recanalization; IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; Pre, preprocedural; TIA, transient ischemic attack.