Original Article

Endovascular Treatment for Acute Tandem Occlusion Stroke: Results from Case Series of 17 Patients

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Abstract

Background and Purpose: Tandem occlusive lesion, a major challenge for thrombectomy in acute anterior circulation strokes, is poorly represented in randomized trials. This study demonstrates the findings of thrombectomy in tandem occlusion and comparative analysis of two treatment groups (extracranial versus intracranial first subgroup). **Patients and Methods:** We enrolled and divided 17 patients with acute tandem ischemic stroke who received endovascular treatment into two groups. Group 1 with completed (100%) internal carotid artery (ICA) occlusion was treated by an extracranial stent, whereas Group 2 with severe (70%–99%) ICA occlusion was prioritized with intracranial thrombectomy. Data of clinical parameters, imaging and angiographic results, periprocedural complications, and results after 3 months were collected and analyzed. **Results:** The mean age of patients was 70.2 ± 8.8 years, and males accounted for 94.1%. The National Institutes of Health Stroke Scale and Alberta Stroke Program Early CT Score (ASPECTS) baseline were 16.6 ± 4.2 and 7.6 ± 1.1, respectively, with occlusive side was 52.9% on the right. Group 1 including ten cases (58.8%) was treated extracranial lesion with carotid stent before intracranial thrombectomy, and Group 2 with seven cases (41.2%) was prioritized intracranial thrombectomy. In total 17 procedures, there were ten stent retrievers (58.8%), four aspirations (23.5%), and three Solumbra (17.7%). No re-occlusion of carotid stent postoperation was recorded. The good revascularization (thrombolysis in cerebral infarction 2b-3) was archived in 82.4% of patients, while symptomatic hemorrhage was seen in 2 cases (11.8%). Three months after treatment, patients with favorable clinical outcome (Modified Rankin Scale ≤2) accounted for 47.1%. **Conclusion:** Our study determined a promising outcome with reasonable good recanalization and clinical recovery for endovascular intervention in tandem ischemic. In the subgroup of treatment, "extracranial stent first" had more complex disease with completed ICA occlusion which required longer procedure time may lead to worse outcome.

Keywords: Acute ischemic stroke, clinical outcome, endovascular treatment, tandem occlusion, thrombectomy

Introduction

Tandem occlusion is defined as the lesion involved not only the extracranial (cervical) part of the internal carotid artery (ICA) but also concomitant thromboembolism of its intracranial distal segment or middle cerebral artery (MCA frequently M1, M2).[1] It is considered as the poor prognosis factor in the scheme of acute ischemic stroke (AIS) treatment due to its high mortality and morbidity with low response to intravenous tissue plasminogen activator (IV r-tPA).[1,2] Endovascular treatment (EVT), on the other hand, has some advantages in recanalizing the large vessel occlusion (LVO), saving the cerebral penumbra parenchyma, and consequently leading to favorable clinical outcomes.[3,4] Even the feasibility of EVT in tandem cerebral occlusion treatment was indicated in several studies, the most effective strategy for both extracranial and intracranial lesions is still unclear.[5] In addition, in the tandem stenotic setting, the catheter is advanced with difficulty compared to embolic one due to a small lumen resulting mostly from plaque with little thrombus inside. Here, we share our initial experience on management of tandem occlusion in AIS by comparing two groups of EVT.

Patients and Methods

Patients

Patients, who suffered from an acute tandem stroke of anterior circulation during the period from January 2016 to June 2018, were treated at the Radiology Center of Bach Mai Hospital (BMH) – a major comprehensive stroke center in the North of Vietnam. This retrospective study was conducted on the data from the picture archiving and communication system

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and patients' notes, which were carefully written and stored in BMH. For further evaluation, we divided all patients in two groups of treatment: group 1 with completed (100%) ICA occlusion was treated by extracranial stent first and then combined with intracranial thrombectomy, whereas Group 2 with severe (70%–99%) ICA occlusion was received thrombectomy first. Clinical characteristics, imaging findings, operation results, and clinical outcomes were compared between groups.

In general, the criteria to select patients for endovascular thrombectomy were as follows: (1) digital subtraction angiography confirmed tandem occlusion with embolism of the extracranial ICA in co-operation with the intracranial artery (T-ICA/MCA); (2) time from onset symptoms to recanalization within 6 h; (3) the National Institutes of Health Stroke Scale (NIHSS) score ≥6; (4) Modified Rankin Scale (MRS) score before stroke ≤2; (5) age ≥18 years; and (6) informed consent was given.

Endovascular treatment

Patients were given IV r-tPA before undergoing EVT if there was no contraindication, and general anesthesia was done for patients in unstable condition. The operation was performed in a monoplane angiographic machine from Phillips by experienced neuro-interventionists who had the certification of cerebral intervention and thrombectomy training. An 8F introducer was retrogradely placed into the femoral artery that allowed the guiding catheter (Neuron Max 088, Stryker or Corail 8F, Balt) to advance into the common carotid artery. At this point, after using a roadmap and try direct aspirations in the proximal ICA through the guiding catheter, the operators evaluated this lesion again. With the complete (100%) occlusion, we used "extracranial stent first" before thrombectomy (Group 1), meanwhile with severe stenosis (>90%) lesion, we chose "intracranial thrombectomy first" before considering extracranial stent (Group 2). In details, with Group 1, carotid stent (Wallstent, Boston/Protégé, Medtronic) following by dilated balloon was deployed immediately over the 300-cm microwire 0.014" (Floppy, Medtronic). Subsequently, the guiding catheter can cross the extracranial lesion leading to intracranial thrombectomy done by aspiration catheter (Sofia, Microvention/ACE, Penumbra), stent retriever (Solitaire 2, FR/Trevo Provue/Eric) or both depending on each specific case. Normally, the aspiration catheter was placed right before the thrombus proximal part while the stent retriever, in case of usage, was positioned with its proximal third overlapping the distal part of thrombus. Group 2, in the other hand, balloon angioplasty helped to widen the ICA for quick intracranial thrombectomy before coming back with consideration of the extracranial stent or not. As soon as a good recanalization (thrombolysis in cerebral infarction [TICI], 2b/3) was achieved or the time was over (>6 h from onset), the operation was finished with manual compression or closure devices applied to seal the puncture site of the femoral artery.

Anticoagulant medication

All patients received additional bolus dosage of 4000 UI heparin (2500 UI intra-arterial and 1500 UI intravenous) at the time of stenting to prevent thrombus inside. Until the next day, no more anticoagulation was given. After ruling out parenchymal hemorrhage on follow-up neuroimaging computed tomography/magnetic resonance imaging (CT/MRI) after 18 ± 6 h, dual antiplatelet therapy with 75-mg Plavix and 100-mg aspergic was prescribed orally or over the nasogastric tube for the next 3 months, followed by a permanent mono-antiplatelet therapy (MAPT) of 100-mg aspergic daily. If small hemorrhage was discovered without mass effect (HI-1, 2), MAPT could be applied. Otherwise, no anticoagulation was used until the next better scan.

Outcome measures

Neurological evaluation was followed up during hospitalization period as an early clinical improvement was defined as a reduction of NIHSS ≥4 points compared to the baseline NIHSS or NIHSS = 0 or 1 at 24 h postprocedure. A good clinical outcome is achieved when MRS score ≤2 within 90 days. The TICI scale was used immediately after the intervention to identify the recanalization result with successful one was featured as a TICI score ≥2b. All patients underwent CT/MRI scanning within 18 ± 6 h postoperation to identify hemorrhagic transformation or cerebral hemorrhage based on the Heidelberg Bleeding Classification. We also compared results between two groups of treatment to identify benefits from each technique.

Statistical analysis

Descriptive data were represented as mean with standard deviation. In the invariable analysis, distributions in age, gender, and other parameters between different treatment groups were appraised by Fisher's exact test or independent sample *t*-test. Analyses were performed using SPSS software, Version 23 (SPSS, Chicago, IL, USA). $P < 0.05$ was identified as a statistically significant difference, and 95% confidence intervals (CI) were measured.

Results

Seventeen studied cases with ten in Group 1 and seven in Group 2 were done at our hospital. Mean age was 70.2 ± 8.8 with the male accounted for 94.1% (16/17 patients). Occlusion site was distributed equally in both sides, with nine cases (52.9%) on the right and eight cases (47.1%) on the left. All cases had proximal ICA occlusion in combination with T-ICA (35.3%), M1 (41.2%), and M2 (23.5%) with distribution of each group listed in Table 1. The NIHSS and ASPECTS on admission were 16.6 ± 4.2 and 7.6 ± 1.1, respectively. The average time from onset symptom to the hospitalization of the whole group, Group 1, and Group 2 was 112.9, 121.5, and 100.7 min, respectively. IV r-tPA was indicated in ten cases (58.8%) with three in Group 1 and seven in Group 2. Table 1 demonstrates the baseline demographic, clinical, and neuroimaging for the total and each group separately, whereas Table 2, in addition, makes

Table 1: Characteristic of tandem acute ischemic stroke patients in our study

Characteristics	Total (*n*=17)	Group 1 (*n*=10)	Group 2 (*n*=7)	Comparison of 2 groups
Age (median), years	70.2±8.8	70.5±10.7	69.9±6.1	
Range (95% CI)	58-85 (65.7-74.7)	58-85 (64.2-76.7)	60-80 (64.2-75.5)	*P*=0.9 (*t*-test)
Gender, male sex (%)	94.1	100	85.7	
NIHSS on admission	16.6±4.2	15.2	18.6	
Range (95% CI)	7-24 (14.4-18.7)	7-20 (12.9-17.6)	14-24 (15-22)	*P*=0.1 (*t*-test)
ASPECTS on admission	7.6±1.1	7.4±0.8	7.9±1.3	
Range (95% CI)	6-10 (7.1-8.1)	6-9 (6.9-7.9)	6-10 (6.6-9)	*P*=0.4 (*t*-test)
Occlusion side, *n* (%)				
Right	9 (52.9)	4 (40)	5 (71.4)	
Left	8 (47.1)	6 (60)	2 (28.6)	
Intracranial occlusion site, *n* (%)				
Distal ICA	6 (35.3)	3 (30)	3 (42.9)	
M1	7 (41.2)	5 (50)	2 (28.6)	
M2	4 (23.5)	2 (20)	2 (28.6)	
Time on admission (min)	112.9±43.9	121.5±44.7	100.7±43.1	
Range (95% CI)	60-220 (90.4-135.5)	80-220 (96.4-152.8)	60-180 (61-141)	*P*=0.35 (*t*-test)
IV r-tPA, *n* (%)	10 (58.8)	3 (30)	7 (100)	
Device used, *n* (%)				
Stent retriever	10 (58.8)	4 (40)	6 (85.7)	
Aspiration	4 (23.5)	4 (40)	0	
Solumbra	3 (17.7)	2 (20)	1 (14.3)	

NIHSS=National Institutes of Health Stroke Scale, IV r-tPA=Intravenous tissue plasminogen activator, ICA=Internal carotid artery, CI=Confidence interval, ASPECTS=Alberta Stroke Program Early CT Score

Table 2: Comparison with other studies

Studies, years	Total, *n*	Age (mean years)	Male, *n*	IV r-tPA, *n*	Initial NIHSS	onset-to-arrival time	Intracranial occlusion site			Extracranial first	Intracranial first
							ICA	M1	M2		
Our study, 2018	17	70	16	10	17	113	6	7	4	12	5
Chen, 2018	7	66	4	-	20	333	4	3	0	-	-
Yang D, 2018	60	64	51	-	17	166	-	-	-	31	29
R-Castilla, 2017	45	64	27	15	14	139	18	20	7	38	7
Mpotsaris, 2017	72	66	44	39	19	212	19	35	9	17	46
Sallustio, 2017	72	66	72	39	19	-	19	45	8	-	-
Grigoryan, 2016	100	64	64	40	18	438	31	53	10	-	-
Lockau, 2015	37	63	27	20	17	-	15	19	3	12	25
Arnholm, 2015	47	64	13	40	16	113	14	32	1	-	-

NIHSS=National Institutes of Health Stroke Scale, IV r-tPA=Intravenous tissue plasminogen activator, ICA=Internal carotid artery

a comparison between our and other international studies which were previously published.

Regarding the operation, general anesthesia was performed in 13/17 cases (76.5%) before the EVT while balloon guiding catheter (BGC) was only chosen in three cases. Stenting of the proximal ICA was placed successfully in all 11 cases (ten from Group 1 and one from Group 2) without overlapping stent in any case. For the intracranial thrombectomy, there were ten (58.8%) stent retriever, four (23.5%) aspiration, and three (17.7%) Solumbra techniques (both stent retriever + aspiration). Table 3 illustrates and shows the comparison of two groups concerning to the results of recanalization, procedural time, complication, imaging, and clinical improvement. The angiography time was 71.2 ± 32.9 min, with 82.2 ± 37.9 min in Group 1 and 55.4 ± 15.8 min in Group 2 but no statistically significant difference (P = 0.1) [Figure 1]. Successful recanalization (TICI, 2b-3) was achieved in 82.4% (14/17 patients): 80% in Group 1 and 85.7% in Group 2 (P = 0.64). For procedural complication, there was one case of A2 emboli, one case of M2 perforation, and another case of cardiac arrest. The rate of symptomatic intracranial hemorrhage at follow-up (16 ± 8 h) imaging was 11.8% (2 patients) – one with PH-2 in Group 1 and one with PH-1 in Group 2. The other two small hemorrhagic transformations of HI-1 were detected in Group 1. However, no re-occlusion of intracarotid stent was found.

Concerning the early clinical improvement (NIHSS reduced ≥4 in the 24 h postprocedure), there were nine patients (52.9%) with three from Group 1 and six from Group 2. After 3 months, the favorable clinical outcome (MRS ≤2) was achieved 47.1%

Table 3: Comparison between two groups of endovascular treatment

	All patients (n=17)	Group 1 (n=10)	Group 2 (n=7)	Comparison of 2 groups
Reperfusion, *n* (%)				
TICI 2a	3 (17.6)	2 (20)	1 (14.3)	P=0.64 (F-*test*)
TICI 2b	8 (47.1)	5 (50)	3 (42.9)	
TICI 3	6 (35.3)	3 (30)	3 (42.9)	
TICI 2b-3	14 (82.4)	8 (80)	6 (85.7)	
95% CI	58.8-100	53.8-100	55.6-100	
Angiography time (mins)	71.18±32.93	82.2±37.86’	55.43±15.8’	
Range (95% CI)	29-165 (54.2-88.1)	29-165 (60.2-106.9)	44-85 (41-70)	P=0.1** (t-*test*)
Procedural complications (%)	3 (17.6)	2 (20)	1 (14.3)	
95% CI	0-35.3	0-50	0-44	P=0.64 (F-*test*)
Early clinical improvement (%)	9 (52.9)	3 (30)	6 (85.75)	
95% CI	26-79	0-60	55.6-100	P=0.05 (F-*test*)
ASPECTS (16±8 h)	6.35±1.5	6.0±0.5	6.9±1.2	
Range (95% CI)	3-9 (5.6-7.1)	3-9 (4.8-7.2)	5-8 (5.7-8)	P=0.27** (t-*test*)
mRS after 3 months ≤2 (%)	8 (47.1)	3 (30)	5 (71.4)	
95% CI	23.5-70.6	0-60	33-100	P=0.12 (F-*test*)
ICH (%)				
Symptomatic	2 (11.8)	1 (10)	1 (14.3)	P=0.67 (t-*test*)
95% CI	0-29	0-33.3	0-49	
No symptomatic	2 (11.8)	2 (20)	0	

TICI=Thrombolysis in Cerebral Infarction, CI=Confidence interval, ICH=Intracerebral hemorrhage, mRS=Modified Rankin Scale, ASPECTS=Alberta Stroke Program Early CT Score, **P <0.5

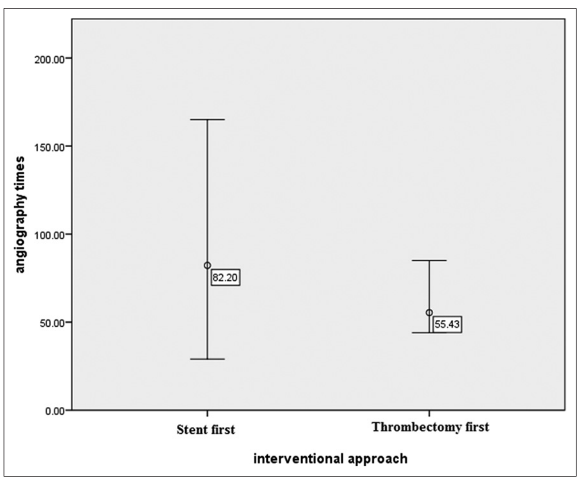

Figure 1: Angiography time in a comparison between Group 1 (stent first) and Group 2 (thrombectomy first)

in the whole group, with 30% in Group 1 and 71.4% in Group 2 but no statistically significant difference with P = 0.12. In particular, there was no mortality.

Discussion

In our series, there were 16/17 males (94.1%), similar to a study conducted by Rodrigues *et al*. (11/12 male patients).[6] This dominance in gender can be explained by men’s harmful living styles such as smoking or drinking which are the main reasons for atherosclerosis disease of carotid artery. The average age of patients in this report was 70.2 that is higher than most of other studies such as the mean age of the cases was 64.4 in a work reported by Grigoryan *et al*. and was 64.0 in a work done by Rangel-Castilla *et al*.[7,8] In the this study’s scale, occlusion site, the distribution of intracranial lesion in detail comparing to one done by Chen *et al*., was similar in M1 (41.2% vs. 42.9%) but lower in ICA (35.3% vs. 57.1%) and higher in M2 (23.5% vs. 0%).[9] The NIHSS on admission (16.6) was compatible to these data in the other studies such as 17.6 in Grigoryan’ study and 17 in Lockau and Yang’s works but still lower than those in the reports by some other authors like Chen *et al*. (20), Mpotsaris *et al*. (19), or Sallustio *et al*. (19).[7,9-13] In particular, the ASPECTS admission was similar as in a work done by Grigoryan *et al*. (7.6 vs. 7.5)[7] Regarding to time from onset to hospital admission, we shared the same result with Steglich-Arnholm *et al*. that was 113 min, but rate of using IV r-tPA in our series was lower than their one: 58.8% versus 85.1%.[14] Other studies had a lower indication of IV r-TPA before EVT reported by other authors like Mpotsaris *et al.* and Sallustio *et al*. (54.2%) or Grigoryan *et al*.(40%); the late hospital admission time of 212 and 438 min, respectively, could be claimed as the main reason.[7,11,13]

About 13/17 patients (76.5%) underwent general anesthesia and accounted for 76.5% in comparison with 82% recorded by Rangel-Castilla *et al*., because most of the patients came in a severe condition due to LVO.[8] BGC was used in only three cases of Group 2. The reason was that in Vietnamese market, we only had small BGC-like Corail 8F (Balt), and its inner diameter is reasonable for stent deployment. Therefore, Neuron Max 088 (Stryker) was normally our first choice, especially in case of complicated lesion such as tandem stroke for further carotid stenting without changing of sheath if any. With intracranial thrombectomy, we prefer to perform stent retriever separately (10/17 cases) instead of combining with the others (4/17 aspiration alone and 3/17 Solumbra technique). This result was opposite to a record done by Range Castilla *et al*. which showed that the dominated rate came to aspiration alone as 15/45 and combination technique as 25/45.[8] Especially, the successful technique of proximal carotid stent achieved in 100% with 80% good recanalization in Group 1. This outcome was compatible with a report done by Rodrigues *et al*.: 100% technical success and 93.8% good recanalization.[6] Furthermore, no re-occlusion inside the carotid stent was recognized in the following image even without continuous anticoagulant after only 4000 UI of heparin during the procedure. This impressive result may lead to exclude or reduce anticoagulant dosage after carotid stenting until the follow-up imaging to prevent severe hemorrhagic event, but more studies are required for a clearer conclusion. A case with proximal carotid stent in combination with aspiration thrombectomy was seen [Figure 2].

The average time from groin puncture to recanalization in our series was 71.2 min, better than 81 min in a report by Rangel-Castilla *et al*.[8] We also achieved 82.4% of good recanalization in total 35.3% of TICI-3 (complete recanalization). This result, particularly, was higher than one published by Yang *et al*. (78.3%) but lower than that done by Rangel-Castilla *et al*. (87%), Grigoryan *et al.* (total

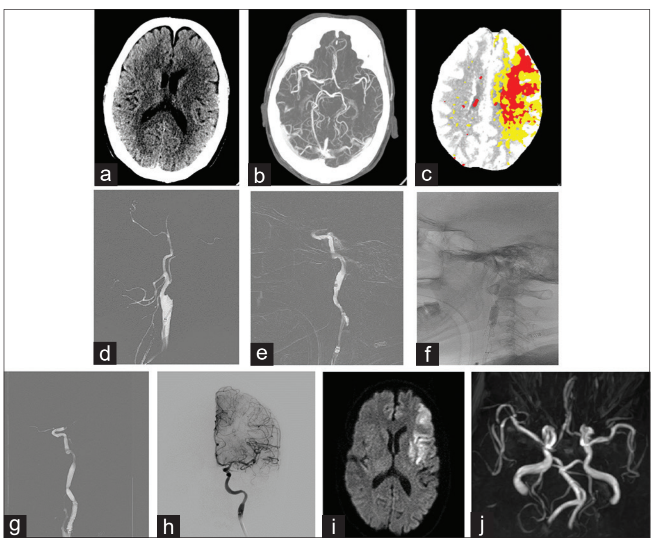

Figure 2: Tandem stroke patient treated with extracranial carotid stent + intracranial thrombectomy. A 59-year-old, 3rd-h stroke patient came to BMHU with the National Institutes of Health Stroke Scale 20. Imaging data (a-c) showed tandem occlusion of L-prox. internal carotid artery + M1, ASPECTS 7, collateral score 4, vcore/penumbra = 54/116 ml. Angiography then confirmed the diagnosis (d and e). Protégé carotid stent 8/20 deployed with dilatation of PowerCross Balloon 6/30 (f). An aspiration by Sofia plus to archived TICI 3 after crossing extracranial lesion with Neuron Max guiding catheter in C2 segment (g and h). Procedure lasted in 60 min. Magnetic resonance imaging follow-up revealed good recanalization from the internal carotid artery to the middle cerebral artery with small hemorrhage of HI-1 (i and j). Modified Rankin Scale after 3 months

88%, TICI-3: 40%), and Yi *et al*. (total 96.3%).[4,7,8,12] It resulted in our 52.9% early clinical improvement (NIHSS reduced ≥4 or to 0 or 1 in the next day) and 47.1% favorable outcome (MRS ≤2) after 3 months, which was equivalent to records by Mpotsaris *et al*. (46%) and Yang *et al*. (50%) higher than reports released by Sallustio *et al*. (32%) and Grigoryan *et al*. (42%) but lower than Rangel-Castilla *et al*. (73.3%) and Yi *et al*. (61.8%).[4,7,8,11-13] In contrast, our series did not identify any patients who died after 3 months while death rate was 32%, 20%, 15.4%, and 13% in other the reports published by Sallustio *et al.*, Grigoryan *et al.*, Yi *et al.*, and Mpotsaris *et al*., respectively.[4,7,11,13]

Symptomatic hemorrhage within 24-h procedure was seen in two cases (11.8%), which was higher than the other reports done by Steglich-Arnholm *et al*. (4%) and Mpotsaris *et al*. (5%) but lower than a work done by Sallustio *et al*. (12.5%).[11,13,14] A PH-2 hemorrhagic patient with severely mass effect from Group 1 underwent a surgery of cerebral hematomectomy and his MRS was 5 after 3 months. In addition, we experienced one case who suddenly revealed hypotension and bradycardia (to 0) because our effort in advancing the microcatheter hardly went through complete occlusive extracranial ICA. This action triggered the carotid sinus reactions leading to cardiac arrest condition. After the rapid resuscitation, all the vital sign came back to normal and we can continue our procedure. Another case of M2 perforation happened post three passes of stent retriever resolving automatically after 2 min without using balloon.

Sharing the same characteristics of age, gender, admission time, NIHSS, and ASPECTS baseline [Table 1 with $P > 0.05$, *t*-test] between two groups, our studies revealed that with carotid stent in the proximal ICA, the operating time was longer in Group 1 comparing to Group 2 even when there was no statistically significant difference between two groups (82.2 vs. 55.4 min, $P = 0.1$). This was quite similar to results obtained by Lockau *et al*. (110.8 vs. 43.1 min, $P < 0.001$), Yang *et al.* (125 vs. 95 min, $P < 0.001$), and Coelho *et al.* (overall mean difference of 1.76, 95% CI: 1.59–1.93).[10,12,15] In the era of stroke, the protocol is essential for improving, especially for focusing to shorten the time as much as possible. Moreover, even achieving an equivalent result of good recanalization (80% vs. 85.7%), the favorable outcome after 3 months was 30% to 71.4% with higher figures came logically to Group 2, but "no statistically significant difference" with $P = 0.12$, this may be due to the lower number of patients recruited in our study. We shared the same idea with Yang *et al.*, Wilson *et al.*, and Coelho *et al*.; in their analysis reviews, there was no superior benefit recognized in the "stent first" group compared to "thrombectomy first" group. However, in our nonrandomized studies, all these unfavorable results of Group 1 could be explained reasonably by its more severe condition of ICA disease (100% occlusion) compared to Group 2 (70%–99%) which led to longer time (for stent deployment) and then, consequently, to worse outcome. Therefore, this was the main reason that we still need more RCTS with high amount of patients to prove the recommendation and role of ICA stenting in acute stage.[15,16]

Our study had some limitations. First, it was conducted with no randomization in treatment decision for each group. Second, the small sample size was a critical factor affecting to the result. Finally, the number of qualified neuro-interventionists was still insufficient at BMH. In the future, not only the sharp increase in the number of EVT for AIS but also the better stroke care systems are needed, we hope that a prospective, multicenter registry, and randomized control trial will be implemented in Vietnam.

Conclusion

This study demonstrated a promising outcome with reasonably good recanalization and clinical recovery for EVT in the AIS of tandem occlusion even there was a challenge during the procedure. In the subgroup of treatment, "extracranial stent first" had more complex disease with completed ICA occlusion which required longer procedure time may lead to worse outcome. The continuous anticoagulants after stenting may be unnecessary until the next day of follow-up imaging to avoid symptomatic hemorrhage without the re-occlusion intracarotid stent.

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Conflicts of interest

There are no conflicts of interest.

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