

# Management of acute tandem occlusions: Stent-retriever thrombectomy with emergency stenting or angioplasty

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## Abstract

**Objective:** To compare outcomes following intracranial stent retriever-based intracranial thrombectomy (SRT) with emergency extracranial internal carotid artery (EICA) stenting or angioplasty alone in patients presenting with acute stroke due to tandem occlusions of the ICA.

**Methods:** Consecutive patients with acute anterior tandem occlusion who received an endovascular intervention within 6h of symptom onset between January 2013 and June 2016 were included in this prospective study. Demographic, radiological, procedural and clinical outcome data were compared between the stenting and the angioplasty alone groups.

**Results:** Of the 37 patients eligible for the study, 18 had angioplasty alone and 19 underwent stent placement. Successful recanalization rate was statistically significantly higher in the stenting group than in angioplasty alone group (74% vs. 39%) and although not statistically significant, more patients in the stenting group than in the angioplasty alone group had favourable outcomes (63% vs. 50%). There was no significant difference between groups in rates of symptomatic intracranial haemorrhage (SICH), cerebral herniation or mortality.

**Conclusion:** This study in a small sample size suggests that among patients with acute anterior tandem occlusion, SRT with EICA stenting tended to achieve higher recanalization and improved

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clinical outcomes at three months compared with SRT and angioplasty alone with a similar rate of SICH and mortality.

### Keywords

Acute tandem occlusion, extracranial carotid stenting, angioplasty, intracranial mechanical thrombectomy

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## Introduction

A tandem occlusion is an uncommon presentation of acute stroke that involves an occlusion of the extracranial internal carotid artery (EICA) and concomitant occlusion of either the intracranial ICA and/or middle cerebral artery (MCA).<sup>1,2</sup> The underlying pathophysiology involves either atherosclerotic disease in older patients, or a dissection of the proximal vasculature in younger patients, leading to complete occlusion and an embolus causing a distal tandem occlusion.<sup>2</sup> Due to the large clot burden and slow distal flow, systemic intravenous thrombolysis (IVT) alone often yields poor recanalization for acute tandem occlusion with recanalization rates ranging from 4.4 to 12.5%.<sup>4,5</sup> Although endovascular treatment has achieved high recanalization rates and favourable outcomes in patients with anterior large vessel occlusion including those with tandem occlusions, the proportion of patients with a good clinical outcome following acute anterior tandem occlusion is only approximately 25%.<sup>6-8</sup>

Recently, several case series have reported that emergency extracranial carotid artery stenting followed by intracranial stent-retriever thrombectomy (SRT) was effective and had an acceptable safety profile in the treatment of acute anterior tandem occlusions.<sup>9-11</sup> However, a major

concern of this procedure is that dual-antiplatelet loading following acute carotid artery stenting may potentially increase the risk of post-interventional symptomatic intracerebral haemorrhage (SICH) in a freshly re-perfused ischemic tissue, especially following IVT.<sup>11</sup>

To our knowledge, in the setting of acute tandem occlusions, few studies have compared outcomes following intracranial SRT with emergency EICA stenting or angioplasty alone. Therefore, the aim of this prospective study was to investigate the impact of SRT with EICA stenting or angioplasty alone on neurological outcomes in patients with acute ischemic stroke due to tandem occlusions.

## Patients and methods

Consecutive patients with acute ischemic stroke who received endovascular procedures and were registered in the Nanjing Stroke Registry Program between January 2013 and June 2016 were selected.<sup>12</sup> The study was approved by the ethics committees of the Central Research Institution at Jinling Hospital and informed consent was obtained from all patients or their surrogates.

Inclusion criteria were as follows: patients older than 18 years of age; acute anterior tandem occlusion demonstrated on admission by cranial computed

tomography angiography (CTA) and confirmed by digital subtraction angiography (DSA); an endovascular procedure (i.e., EICA (stenting or angioplasty alone) with SRT performed within 6h of symptom onset; no cerebral haemorrhage and no early cerebral infarction involving more than one-third of the endangered territory on computed tomography (CT). Patients with intracranial occlusions treated with intra-arterial thrombolysis or with devices other than stent-like retrievers (e.g., angioplasty or microwire clot disruption) and those lost to follow up at 90 days were excluded from the study.

Endovascular procedures were routinely performed with the patient under conscious sedation. During the procedure, an 8F guide catheter was placed in the distal common carotid artery (CCA). Thereafter, the extracranial ICA occlusion was gently passed with a 0.014-inch microwire (Synchro; Stryker, Kalamazoo, Michigan) and then a 0.018/0.027micro-catheter (Rebar; ev3-Covidien Neurovascular, Irvine, California) was advanced past the occlusion. Angiography was performed through the micro-catheter to assess the ICA status and thrombus/occlusion in the intracranial circulation. The decision to perform carotid stenting and the type of stent used depended on the ICA status and/or the preference of the interventionalist. Open-cell stents (Precise [Cordis Corporation, Miami, Florida] and Acculink (Abbott Vascular, Temecula, CA) and closed-cell stents (Wallstent [Boston Scientific, Natick, MA]) were used. Intracranial thrombectomy was performed using the stent-retriever system (Solitaire; ev3-Covidien Neurovascular, Irvine).

Following EICA treatment, patients who received intravenous recombinant tissue plasminogen activator (rtPA) then received aspirin (100mg) and clopidogrel (75 mg) 24 hours later and continued to take these treatments daily for a minimum of three months. All other patients received aspirin

(300mg loading dose followed by 100mg daily for a minimum of six months) and clopidogrel (300mg loading dose followed by 75mg daily for a minimum of three months). Patients with disorders of consciousness were given anti-platelet medications by nasogastric tube. Follow-up neuroimaging was conducted and treatment was discontinued if there was evidence of cerebral haemorrhage.

The cerebral collateral circulation was assessed on initial angiography. The grading system of the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) for collateral flow was used where grade 0 or 1 was considered poor collateral circulation and grade of 2–4 was considered good collateral circulation.<sup>13,14</sup>

Angiography was usually performed after the initial thrombectomy to assess the recanalization of the target artery and reperfusion of distal cerebral tissue and to detect possible distal embolization in the MCA, anterior cerebral artery or their branches.

Recanalization status was assessed using the modified treatment in cerebral ischemia (mTICI) score.<sup>15</sup> Successful recanalization was defined as persistent mTICI 2b-3 score on an angiogram taken after at least 10 minutes.<sup>15</sup> Carotid re-vascularisation was considered adequate if residual stenosis was <30%. If recanalization was absent or incomplete, rescue thrombectomy was repeated up to three times.

Post-interventional brain CT or magnetic resonance imaging (MRI) scans were performed 24–36h after admission or whenever the clinical neurological status abruptly deteriorated. Further neuroimaging was performed at the discretion of the attending physicians.

The primary efficacy outcome was the modified Rankin scale (mRS) at three months, dichotomized as favourable

outcome (mRS 0-2) or unfavourable outcome (mRS 3-6)<sup>16</sup>. The mRS was a consensus evaluation made by two-trained independent study nurses blinded to the initial treatment and the score was based on a clinical investigation or structured telephone interview. Safety outcomes included the incidence of symptomatic and asymptomatic intracranial haemorrhage,<sup>17</sup> cerebral herniation and overall mortality at three months.

### Statistical analyses

Continuous variables were expressed as mean ± standard deviation (SD) or median and interquartile range (IQR), whereas categorical variables were described as percentages. Student's t-test, Fischer's exact test were used according to the studied variables characteristics. Statistical analyses were performed by Y.X. using SPSS software (version 19.0 for Windows®; (IBM SPSS, Armonk, NY: IBM Corp, USA). A two-sided analysis was used and a *P*-value <0.05 was considered to indicate statistical significance.

### Results

Of the 44 patients who had acute anterior tandem occlusion and underwent endovascular therapy seven cases were excluded from the study because their intracranial occlusion had been treated by intra-arterial thrombolysis (three patients), angioplasty alone (two patients) or micro-wire clot disruption (two patients). The median age of the 37 remaining patients was 61 years (IQR, 56-67) years and 27 (73%) were male (Table 1). The most probable cause of occlusion was atherosclerosis in 22 (60%) patients and dissection in 15 (41%) patients. Median NIHSS score was 15 (IQR, 12-20) on admission and 9 (IQR, 6-19) at 24 hours. Twenty-eight (76%) patients presented with a good collateral

**Table 1.** Demographic and clinical characteristics of the patients with acute stroke due to tandem occlusions of the carotid artery who received endovascular treatment.

Characteristic	All patients n=37
Age, years	61 (56–67)
Sex, male	27 (73)
Hypertension	22 (60)
Current smoker	12 (32)
History of ischemic stroke	4 (11)
History of TIA	3 (8)
Type of aortic arch:	
I	14 (38)
II	18 (49)
III	5 (14)
Occlusion type	
Atherosclerosis	22 (60)
Dissection	15 (41)
ASITN/SIR (2–4)	28 (76)
ASPECTS (baseline)	9 (7–10)
NIHSS score on admission	15 (12–20)
after 24h	9 (6–19)
Distal embolic events	8 (22)
Received intravenous rt-PA treatment	12 (32)
Number of stent retriever passes	2 (1–3)
Time from symptom onset to recanalization, min	353±77
Time from symptom onset to puncture, min	262±78
Time from puncture to final recanalization, min	86 (65–106)
mTICI (2b-3) (i.e., successful recanalization)	21 (57)
mRS ≤2 (i.e., favourable outcome)	21 (57)
Mortality	7 (19)
SICH	3 (8)
aSICH	10 (27)
Cerebral herniation	4 (11)

Values are shown as mean ± standard deviation, median (interquartile range) or *n* (%)

Abbreviations: NIHSS, National Institutes of Health stroke scale; TIA, transient ischemic attack; ASPECTS, Alberta stroke program early computed tomography score; ASITN/SIR, American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology collateral flow grading system;<sup>13,14</sup> rt-PA, recombinant tissue plasminogen activator; mTICI, modified treatment in cerebral ischemic score;<sup>15</sup> mRS, modified Rankin scale; SICH, symptomatic intracerebral haemorrhage; aSICH, asymptomatic ICH

status (i.e., ASITN/SIR 2-4) and median ASPECTS was 9 (IQR, 7-10). Twelve (32%) patients received intravenous rt-PA prior to endovascular treatment. Distal occlusion sites were as follows: MCA M1, 27/37 (73%); MCA M2, 8/37 (22%); terminal ICA in 2/37 (5%).

The median time from groin puncture to recanalization was 86 (IQR, 65-106) min. The overall mean time  $\pm$ SD from symptom onset to recanalization was  $353 \pm 77$  min.

Successful recanalization (i.e., mTICI 2b-3) and favourable outcome (mRS 0-2) at three months were achieved in 21 (57%) patients. Seven (19%) patients died within the three months following the procedure (three (8%) due to SICH and four (11%) due to cerebral herniation). Procedural related complications, such as distal embolization into different vascular

territories were observed in eight (22%) patients. No other procedural related complications (e.g., acute stent thrombosis, vessel rupture or dissection) were observed.

There were no differences between stenting and angioplasty alone groups in terms of demographic data, admission NIHSS score, baseline ASPECTS, collateral status, number of stent retriever passes, distal embolization, onset to recanalization time and puncture to final recanalization time (Table 2). Although, the successful recanalization rate was higher in the stenting group compared with the angioplasty alone group (74% vs. 39%,  $P=0.04$ ), there was no difference between groups in favourable outcome (mRS (0-2), 63% vs. 50%) (Table 3).

There was no difference between groups in symptomatic intracranial haemorrhage

**Table 2.** Comparison of demographic and clinical characteristics between stenting and angioplasty alone groups in patients with acute stroke due to tandem occlusions of the carotid artery.

	Stenting Group <i>n</i> =19	Angioplasty alone Group <i>n</i> =18	Statistical Significance
Age, years	65 (53–67)	59 (56–67)	<i>ns</i>
Sex, male	14 (74)	13 (72)	<i>ns</i>
NIHSS score on admission	15 (12–19)	15 (12–23)	<i>ns</i>
Hypertension	9 (47)	13 (72)	<i>ns</i>
Current smoker	6 (32)	6 (50)	<i>ns</i>
Occlusion type			<i>ns</i>
Atherosclerosis	12 (63)	10 (56)	<i>ns</i>
Dissection	7 (37)	8 (44)	<i>ns</i>
ASPECTS	9 (8–10)	8 (6–10)	<i>ns</i>
ASITN/SIR (2–4)	14 (74)	14 (78)	<i>ns</i>
Received intravenous rt-PA	5 (26)	7 (39)	<i>ns</i>
Number of stent retriever passes	2 (1–2)	2 (1–3)	<i>ns</i>
Time from symptom onset to recanalization, min	$370 \pm 77$	$335 \pm 74$	<i>ns</i>
Time from symptom onset to puncture, min	$278 \pm 64$	$245 \pm 89$	<i>ns</i>
Time from puncture to final recanalization, min	82 (59–119)	92 (70–102)	<i>ns</i>
mTICI (2b-3) (i.e., successful recanalization)	14 (74)	7 (39)	0.04
Distal embolic events	3 (16)	5 (28)	<i>ns</i>

Values are shown as mean  $\pm$  standard deviation, median (interquartile range) or *n* (%)

Abbreviations: NIHSS, National Institutes of Health stroke scale; ASPECTS, Alberta stroke program early computed tomography score; ASITN/SIR, American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology collateral flow grading system;<sup>13,14</sup> rt-PA, recombinant tissue plasminogen activator; mTICI, modified treatment in cerebral ischemic score.<sup>5</sup>

**Table 3.** Efficacy and safety outcomes at three months for the stenting and angioplasty alone groups in patients with acute stroke due to tandem occlusions of the carotid artery.

	Stenting Group n=19	Angioplasty alone Group n=18	Statistical Significance
Efficacy outcome			
mRS (0-2)	12 (63)	9 (50)	ns
Safety outcome			
SICH	2 (11)	1 (6)	ns
aSICH	5 (26)	5 (28)	ns
Cerebral herniation	1 (5)	3 (17)	ns
Mortality	3 (16)	4 (22)	ns

Values are shown as n (%)

Abbreviations: mRS, modified Rankin scale; SICH, symptomatic intracerebral haemorrhage; aSICH, asymptomatic ICH.

(SICH), cerebral herniation or mortality rates (Table 3). Distal embolic events were observed in 3 (16%) of the stenting group and 5 (28%) of the angioplasty alone group.

Follow-up vascular imaging (i.e., at least one via CT angiography [CTA], magnetic resonance angiography [MRA], or digital subtraction angiography [DSA] within three months of the procedure) was obtained from 20 patients (11 in stenting group, 9 in angioplasty alone group). In the stenting group, one patient had severe in-stent asymptomatic restenosis (>70%) of the ICA and two patients had moderate stenosis of the distal MCA M1 segment with no restenosis of the ICA. In the angioplasty alone group, four patients had severe in-stent asymptomatic restenosis (>70%) and two patients had re-occlusion of the M2 segment of the MCA.

## Discussion

Endovascular therapy for acute tandem occlusion is considered complicated and challenging.<sup>18</sup> Indeed, its long procedure times and complexity combined with mandatory dual antiplatelet therapy after stent placement are regarded as hazardous in the

acute setting.<sup>19</sup> In this present study, 21 (57%) patients achieved a favourable outcome at three months, seven (19%) patients died and SICH occurred in three (8%) patients. These findings are in agreement with results from previous studies and suggest that endovascular therapy for acute anterior tandem occlusion may be feasible and efficacious with an acceptable safety profile.<sup>20,21</sup> In common with systemic intravenous thrombolysis, the effect of endovascular therapy is highly time-critical.<sup>22</sup> While the use of additional devices such as stents can prolong recanalization time,<sup>23</sup> in this study there was no difference between treatment groups in procedural times. Similar findings have been obtained by other studies.<sup>21</sup> Nevertheless, the best management of acute carotid tandem occlusions (i.e., emergency carotid stenting or angioplasty alone) remains controversial.

Clearing the pathway by emergency extracranial carotid stenting may facilitate an intracranial thrombectomy procedure, but the potential risk of haemorrhagic transformation following concomitant dual antiplatelet therapy with SRT has to be weighed against the risk of restenosis from balloon angioplasty alone.<sup>24</sup> In this present study, there was no statistically

significant difference in the rate of SICH between the stenting and angioplasty alone groups (11% vs 6%), and the overall rate (8%) was similar to that found in a meta-analysis of eight studies involving tandem patients treated with acute ICA stenting (7 % [95 % CI, 2–13]).<sup>25</sup> Furthermore, there was no difference between the stenting and angioplasty alone groups in the occurrence of aSICH (26% vs. 28%). In addition, the rate of cerebral herniation caused by malignant oedema was lower in the stenting group (5%) than in the angioplasty alone group (17%) leading to a lower mortality rate in the stenting group (16%) compared with the angioplasty alone group (22%). These results may have occurred as a result of the high rate of successful recanalization in the stenting group (74%) compared with the angioplasty alone group (39%).

Unstable stenotic lesions in the symptomatic carotid artery are a major source of intracranial embolism in the carotid T or MCA and are the cause of long-term risk of recurrent ischemic events.<sup>26</sup> In a recent pooled analysis, researchers found a high risk (12%) of recurrent ipsilateral ischemic events at 14 days in patients with symptomatic carotid stenosis.<sup>27</sup> In this present study, follow-up vascular imaging was obtained from 20 patients (11 in stenting group, nine in angioplasty alone group). Although this was a small sub-group of patients, data showed that compared with angioplasty alone (44%), the risk of restenosis was lower in the stenting group (9%). However, these findings did not translate into a statistically significant difference between groups in the overall rate of favourable outcome at three months (stenting, 63% vs. angioplasty alone, 50%). Interestingly, the time of symptom onset to groin puncture was longer in the stenting group compared with the angioplasty alone group; long delays in stroke onset to groin puncture have been correlated to poor

outcomes after endovascular stroke treatment.<sup>28</sup>

The study had several limitations. For example, data were collected from a small cohort of patients at a single centre. However, tandem occlusions are a rare presentation of acute stroke.<sup>2</sup> In addition, the aetiology of the tandem occlusions was heterogeneous (i.e., 60% atherosclerosis, 41% dissections). Nevertheless, there was no difference between the two groups in the numbers of patients in the different occlusion types. Another limitation was that the decision to perform carotid stenting and the type of stent used was based on the individual experiences of the neurologist and interventionalist which may have led to some unintentional bias. Therefore, further multicentre studies with large sample sizes are required to confirm our results.

In conclusion, our study suggests that among patients with acute anterior tandem occlusion, SRT with EICA stenting tended to achieve higher recanalization and improved clinical outcomes at three months compared with SRT and angioplasty alone with a similar rate of SICH and mortality. In addition, follow-up vascular imaging showed that the risk of restenosis appeared to be lower in the stenting group compared with the angioplasty alone group.

#### **Declaration of conflicting interests**

The authors declare that there are no conflicts of interest.

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