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Endovascular Therapy of Internal Carotid Artery Tandem Occlusions and Literature Review

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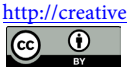

Abstract

Acute large vessel occlusion is a common cause of acute ischemic stroke (AIS), with high rates of disability and lethality. The incidence of tandem occlusion of the internal carotid artery accounts for about 20% of patients with large vessel occlusion of the anterior circulation in acute ischemic stroke. The low rate of recanalization by intravenous thrombolysis in AIS due to internal carotid artery tandem occlusion, the poor establishment of collateral circulation within a short time, and the complex pathogenesis often suggest a poor prognosis for patients. Mechanical thrombectomy (MT) is beneficial for the opening of intracranial large vessel occlusion with internal carotid artery tandem occlusion, there are many problems regarding the emergency management of carotid artery occlusion or stenosis after mechanical thrombectomy, and there are currently no standardized treatment recommendations; The sequential approach to the management of carotid tandem occlusion, the timing of carotid stenting, and the use of antiplatelet agents remain controversial. The current state of research on carotid tandem occlusion is analyzed in the literature to promote clinical understanding of endovascular treatment for patients with acute ischemic stroke due to carotid tandem occlusion.

Keywords

Stroke, Internal Carotid Artery, Tandem Occlusions, Endovascular Treatment

1. Concept and Diagnostic Approach to Tandem Lesions

Carotid tandem occlusion, defined as severe stenosis (≥90%) of the external segment internal carotid artery or occlusion accompanied by intracranial large

vessel occlusion, which results in acute ischemic stroke, is dominated by intravenous thrombolysis in the early stage, but the rate of recanalization after treatment is low and the overall outcome is suboptimal [1]. Additional studies point to the presence of severe stenosis (70% to 99% stenosis) or occlusion of the proximal part of the intracranial occluded vessel with concomitant ipsilateral internal carotid artery, middle cerebral artery (MCA), or anterior cerebral artery occlusion in the anterior circulation [2].

Computed tomographic angiography allows clear visualization of the site of the vascular lesion with a sensitivity of up to 95.5% for diagnosing tandem lesions and facilitates the identification of tandem lesions. However, its specificity is only 69.6%, which may overestimate the occurrence of tandem lesions [3].

Digital subtraction angiography (DSA) is the currently accepted "gold standard" for the diagnosis of large vessel disease. In tandem lesions, DSA not only defined the site and degree of stenosis of the diseased vessel, but also provides path images for endovascular treatment.

2. Etiology and Pathogenesis

According to the results of the international multicenter anterior circulation tandem lesion retrieval collaboration (Thrombectomy in Tandem Lesion, Titan) study, atherosclerosis accounts for approximately 70%, dissection for 20% to 30%, and embolization is much less common, approximately 10% [4].

The main etiologies of carotid tandem occlusion are large artery atherosclerosis and dissection. Acute ischemic stroke mainly results from carotid artery stenosis, which causes decreased cerebral perfusion blood flow and symptoms of neurological deficits [5]. Internal carotid artery occlusion is often associated with atherosclerotic plaque shedding and can progress to occlusive lesions as the blood circulation embolizes to the distal downstream, causing ischemia in different parts of the same vessel, and arterial thrombosis is associated with atherosclerosis. Some studies have shown that atherothrombosis is associated with intracranial tandem lesions [6]. Another cause of tandem carotid artery occlusion is carotid dissection, in which tearing of the intima leads to intramural hematoma formation, which causes arterial stenosis, occlusion, and aneurysmal changes, and is a common cause of stroke in young and middle-aged adults [7]. With the tearing of the intima of carotid vessels, blood enters the subintima, causing luminal stenosis or occlusion, causing distal cerebral tissue hypoperfusion, while the endothelial cells exposed to the blood activate the coagulation system, causing blood hypercoagulability and even thrombosis.

3. Endovascular Therapy Strategies for Acute Carotid Tandem Occlusion

Endovascular therapy as the first choice of treatment for patients with acute large vessel occlusion stroke (ALVOS) has improved the recanalization rate and improved clinical outcomes for patients with tandem lesions, and consensus has

been reached on endovascular therapy for patients with large vessel occlusion stroke. Because vessels occluded in series by the carotid artery often present with both intracranial distal embolization and extracranial proximal lesions, the clinical need to consider the sequence of treatment followed by retrograde treatment of the intracranial occluded vessel first, or antegrade treatment of the extracranial occluded vessel first.

One study [8], sixty tandem occlusion stroke patients were enrolled. Thirty-one (51.7%) patients received anterograde therapy, while 29 (48.3%) patients underwent the retrograde approach. Successful recanalisation (modified thrombolysis in cerebral infarction score 2b-3) occurred in 78.3% (47/60) of patients, and 50.0% (30/60) of patients achieved a modified Rankin scale score of 0-2 at 90 days. Patients undergoing the retrograde approach spent less time in distal occlusion recanalisation (125 (86 - 167) vs. 95 (74 - 122) minutes; P = 0.04) and achieved better functional outcomes at 90 days (69.0% (20/29) vs. 32.3% (10/31); P = 0.004) than patients who received anterograde therapy. The retrograde approach was associated with favourable clinical outcomes (odds ratio 0.21; 95% confidence interval 0.07 - 0.64; P = 0.006).

Wallocha *et al.* [9] found that advanced carotid artery stenting could improve collateral circulatory compensation and reduce distal displacement of proximal secondary thrombus, and the recanalization rates and clinical outcomes were not significantly different among different treatment modalities. Slawski *et al.* [10] showed that antegrade treatment resulted in high recanalization rates and favorable outcomes in patients with carotid tandem occlusions, which may be related to increased intracranial collateral flow, decreased distal embolization rate, and intracranial ischemic time after recanalization of extracranial carotid occluded vessels. Prior extracranial carotid balloon dilatation or closed-loop stent attachment may avoid unstable plaque detachment and reduce the risk of distal re-embolization associated with intraoperative procedures. In addition, after the proximal vessel is opened, it may increase the compensation of the intracranial collateral circulation and effectively curb the further expansion of the ischemic area, meanwhile, after the carotid angioplasty, it may be better to use the retriever device for distal vessel opening. It has been documented that after stenting of the proximal carotid artery, the proximal occluded vessel can be opened and the intracranial forward flow can be restored, resulting in recanalization of the distal embolic vessel or autolysis of the embolus in some patients [11].

However, some scholars do not support the view of antegrade treatment, considering that retrograde treatment may be a reasonable choice modality for patients with acute ischemic stroke caused by carotid artery tandem occlusion and can achieve intracranial target vessel recanalization as soon as possible.

Baik *et al.* [12] found that, among 37 cases of tandem occlusion of the included carotid arteries, 25 cases had mechanical thrombectomy of the intracranial artery followed by carotid artery stenting and 12 cases had carotid artery stenting followed by mechanical thrombectomy of the intracranial artery, and showed that patients who had mechanical thrombectomy of the intracranial ar-

tery followed by carotid artery stenting had significantly shorter recanalisation times and better outcomes.

Rangel-Castilla L. *et al.* [13] point out Tandem occlusions present treatment challenges, but high recanalization rates were possible in the present series using acute carotid artery stenting and mechanical thrombectomy concurrently. Proximal-to-distal and aspiration approaches were most commonly used because they were safe, efficacious, and feasible. Further study in the setting of a randomized controlled trial is needed to determine the best sequence for the treatment approach and the best technology for tandem occlusion.

Stampfl *et al.* [14] showed that anterograde treatment opened the occluded vessel for 20 min longer than retrograde treatment.

Cynthia B Zevallos *et al.* have shown that Carotid artery stenting and a retrograde approach had higher odds of successful reperfusion and good functional outcomes at 3 months than balloon angioplasty and an anterograde approach, respectively, in patients with tandem occlusions. A randomized controlled trial comparing these techniques with structured antithrombotic regimens and safety outcomes will offer definitive guidance in the optimal management of this complex disease [15]. Zhou Hang *et al.* found the recanalization sequence of balloon dilatation-thrombectomy-carotid artery stent and balloon dilatation-carotid artery stent-thrombectomy have no significant effect on the short-term prognosis of AIS patients. But the time required for the former puncture to the target vessel recanalization is shorter [16].

In recent years, Chinese scholars have proposed the BATS technique (BAT-Aspiration-Thrombectomy-Stenting), Introduced below:

Step 1. Through the proximal occlusion of internal carotid artery with BAT technology (BAT): Assisted by the bat (balloon assisted tracking technique) technique, a direct 8F guide catheter or a 6F long sheath was passed through the occlusion, rather than a distal aspiration catheter. Step 2. Direct thrombus aspiration from the carotid artery (Aspiration): after occlusion of the initial segment of the ICA by the 8F guide catheter, aspiration was initiated immediately, followed by a 6F distal aspiration catheter into the internal carotid artery at the initial segment, petrous segment, and cavernous sinus segment to clear the thrombus by segmental aspiration. Care is taken at this point to ensure that proximal flow is blocked, avoiding unnecessary fuming and contrast until pumping back to stabilize reverse flow. Backward aspiration segment by segment is recommended within a tortuous carotid artery segment to avoid damaging the vessel by forced forward pushing. Step 3. Mechanical thrombectomy in intracranial occlusion segments (Thrombectomy): a combination of long stent + distal aspiration catheter embolization technique is recommended to improve the rate of first pass recanalization. Avoidance of unnecessary forward contrast through the distal aspiration catheter is recommended before release of positioning of the retriever stent. The swim technique is recommended within M1, with aspiration in situ after stent retriever and retraction segment by segment continuing to clear

the thrombus. A 30 mm length or longer peg Retriever is recommended, ensuring coverage of the ICA terminus distal to the M1 bifurcation. Step 4. Proximal carotid artery stenting (Stenting): completion of proximal carotid artery stenting (CAS) is recommended after intracranial large vessel embolectomy has been completed. Use embolic protection device (EPD) whenever possible. Recommended the release of EPD through middle catheter, and under the protection of EPD, the direct delivery of stent system through high guide catheter or large lumen middle catheter, use the Trojan Horse technology to release carotid stent, if necessary balloon posterior expansion of stenosis segment, send again into middle catheter to recover the EPD and aspirate *in situ*. In a subset of tandem cases of proximal dissection, EPD protection may be omitted when using closed-loop braided stents.

There is no clear opinion on the treatment modality of mechanical thrombectomy for acute carotid tandem occlusion, but the proposal of the BATS technique, offers a promising solution for acute carotid tandem occlusion.

4. Is the Carotid Artery Stenting Procedure Performed Emergently?

It is also controversial whether emergent stenting should be performed for acute extracranial severe carotid lesions. The present single- and multicenter studies and the analysis of clinical trials suggest that urgent carotid artery stenting may be reasonable. Behme *et al.* [17] showed that emergent carotid stenting may be reasonable in patients with tandem carotid artery occlusion, and the study considered carotid stenosis in tandem lesions as symptomatic stenosis, which was proximal to balloon dilatation and stent implantation, making subsequent management of intracranial occlusion easier. Papanagiotou *et al.* [4] found that emergent stent implantation combined with antiplatelet aggregating drugs in patients with extracranial carotid artery disease had a high recanalization rate and good clinical outcome. Jadhav *et al.* [18] concluded that urgent stent implantation for extracranial carotid stenosis during endovascular thrombectomy in patients with intracranial occlusion is associated with a comparable safety profile to no stent implantation, whereas patients with carotid artery stenting in the acute phase have a better prognosis.

Anadani M, *et al.* [19] by conducting research on French prospective multicenter observational ETIS (Endovascular Treatment in Ischemic Stroke) and the international TITAN (Thrombectomy in Tandem Lesions) registries have shown that Patients treated with acute cervical ICA stenting for tandem occlusion strokes had higher odds of 90-day favorable outcome, despite higher odds of intracerebral hemorrhage; however, most of the intracerebral hemorrhages were asymptomatic.

Marnat G *et al.* found that endovascular treatment of carotid artery dissection tandem occlusions is safe and effective compared with isolated anterior circulation occlusion stroke therapy. Hence, a more conservative approach with stent

placement only in cases of circle of Willis insufficiency may be a reliable and safe strategy [20]. Kim B *et al.* [21] pointed CAS-EVT strategy seemed to be effective and safe in cases of tandem cICAO-LVO. CAS-EVT strategy was associated with recanalization success, resulting in better clinical outcome.

However, some scholars believe that carotid artery stenting is not recommended for patients with extracranial carotid artery lesions in the acute stage, mainly considering the risk posed by intracranial hemorrhage. Akpinar *et al.* [22] reported on 15 patients with tandem occlusion of the carotid artery treated with endovascular therapy, all of whom underwent balloon angioplasty alone to maintain extracranial carotid access to the occlusion, followed by mechanical thrombectomy of the distal occlusion, and delayed carotid stenting, and found that 80% of patients successfully achieved recanalization and 66.7% achieved good clinical outcomes, Also the authors suggested that it seems to be a safer procedure to perform carotid angioplasty assisted by mechanical thrombectomy without emergent stenting in patients with carotid tandem occlusion.

Dorado *et al.* [23] recommended no emergent stent implantation in the acute phase of extracranial carotid lesions, consideration of the method would delay the intracranial reperfusion time, and the use of intra-arterial antithrombotic drugs would lead to a high incidence of intracranial hemorrhage. Heck and Brown [24] considered preemptive balloon angioplasty in case of carotid tandem occlusion and recommended stenting only in acute situations and when adequate patency of the vessel could not be obtained. Lescher *et al.* [25] studied 39 consecutive patients with carotid artery tandem occlusion and compared the recanalization rates and outcomes between patients with and without carotid stent implantation and found no significant differences in the recanalization rates and outcomes between the two groups.

Marko M *et al.* reported that Tandem cervical carotid occlusion in patients with acute large vessel stroke did not lower the odds of good functional outcome in our study. Functional outcomes were similar irrespective of the management of the cervical ICA occlusion (stenting vs not stenting) [26].

Acute stroke patients with tandem lesions (*i.e.*, an occlusion or high-grade stenosis of the extracranial internal carotid artery (ICA) and a combined major intracranial artery occlusion) are challenging to treat. Currently, there is no consensus on the best treatment strategy, and thus, treatment approaches are highly variable. Carotid stenting may be considered when considering high-grade stenosis of the carotid artery after intracranial artery embolization, decompensation of the circle of Willis, and threatened thrombus in the carotid artery lumen, in the hope of future studies with larger and reliable RCTs to guide the choice.

5. Timing of Antiplatelet Aggregation Drug Use

Antiplatelet aggregation regimens are also a major problem in endovascular treatment of carotid artery tandem occlusion, particularly after stenting of carotid arte-

ries in the acute phase. Therefore, the choice of timing for the administration of antiplatelet aggregation drugs is particularly critical. At present, the optimal antithrombotic regimen for the perioperative period in tandem lesions remains unclear. Studies have shown that additional antiplatelet aggregating drugs may increase the risk of intracranial hemorrhage if patients have already received bridging therapy with intravenous thrombolysis [27]. A retrospective study showed that carotid artery stenting combined with the use of antiplatelet aggregation drugs did not increase the incidence of intracranial hemorrhage, but this study has certain limitations and further prospective studies and randomized trials are needed to select an optimal timing of antiplatelet aggregation drug use versus treatment regimen [28].

The TITAN research group found Administration of antiplatelet therapy during endovascular therapy for anterior circulation tandem occlusions was safe and was associated with a lower 90-day mortality. Optimal antiplatelet therapy remains to be assessed, especially when emergent carotid artery stenting is performed. Further randomized controlled trials are needed [29].

We recommend that DynaCT images be reviewed in the immediate postoperative period without or with reduced use of antiplatelet agents postoperatively if there is extensive contrast extravasation or if there is intracranial hemorrhage.

6. Complications and Prognosis

Symptomatic intracranial hemorrhage is a serious complication of endovascular treatment, affecting patient outcomes. Studies have reported that the incidence of intracranial hemorrhage after emergent carotid stenting in patients with acute ischemic stroke associated with carotid tandem occlusion reaches 20%. Another study found that symptomatic intracranial hemorrhage after endovascular thrombectomy in patients with carotid tandem occlusion was associated with a higher risk of adverse outcome and mortality, and that a larger preoperative infarct core was an independent predictor of symptomatic intracranial hemorrhage, whereas intravenous thrombolysis, emergent carotid stenting, and early antiplatelet aggregation medication did not increase the risk of intracranial hemorrhage [30].

However, with the development of neurointerventional techniques, several subsequent studies have suggested that there is no significant difference between tandem lesions and single lesions in terms of recanalization rates, rates of symptomatic intracranial hemorrhage, and 90-d outcomes. We summarized the results of the published literature and found that the recanalization rate in patients with tandem lesions ranged from 75% to 90%, the rate of symptomatic intracranial hemorrhage ranged from 5% to 10%, the 90-d modified Rankin Scale score was 0 to 2 in 44% to 50% of patients, the 90-d case fatality rate also decreased to 13% to 16%, and there was no significant difference in healing between tandem lesions and isolated intracranial lesions after thrombectomy [20] [27] [31] [32].

7. Future Research Prospects

Endovascular treatment is a safe and effective procedure for the treatment of tandem lesions, but no specific protocol is currently available for the treatment of patients with carotid tandem occlusion, and further large clinical randomized controlled trials are needed in the future to demonstrate that rapid opening of tandem occluded vessels and reduction of symptomatic intracranial hemorrhage are the focus of research.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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