Original research

Endovascular treatment for acute ischemic stroke in patients with tandem lesion in the anterior circulation: analysis from the METRICS study

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ABSTRACT

Background Acute ischemic stroke (AIS) due to anterior circulation tandem lesion (TL) remains a technical and clinical challenge for endovascular treatment (EVT). Conflicting results from observational studies and missing evidence from the randomized trials led us to report a recent real-world multicenter clinical experience and evaluate possible predictors of good outcome after EVT.

Methods We analyzed all AIS patients with TL enrolled in the prospective national study METRICS (Mechanical Thrombectomy Quality Indicators Study in Czech Stroke Centers). A good 3-month clinical outcome was scored as 0–2 points in modified Rankin Scale (mRS), achieved recanalization using the Thrombolysis In Cerebral Infarction (TICI) scale and symptomatic intracerebral hemorrhage (sICH) according to the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) criteria.

Results Of 1178 patients enrolled in METRICS, 194 (19.2%) (59.8% males, mean age 68.7±11.5 years) were treated for TL. They did not differ in mRS 0–2 (48.7% vs 46.7%; p=0.616), mortality (17.3% vs 22.7%; p=0.103) and sICH (4.7% vs 5.1%; p=0.809) from those with single occlusion (SO). More TL patients with prior intravenous thrombolysis (IVT) reached TICI 3 (70.3% vs 50.8%; p=0.012) and mRS 0–2 (55.4% vs 34.4%; p=0.007) than those without IVT. No difference was found in the rate of sICH (6.2% vs 1.6%; p=0.276). Multivariate logistic regression analysis showed prior IVT as a predictor of mRS 0–2 after adjustment for potential confounders (OR 3.818, 95% CI 1.614 to 9.030, p=0.002).

Conclusion Patients with TL did not differ from those with SO in outcomes after EVT. TL patients with prior IVT had more complete recanalization and mRS 0–2 and IVT was found to be a predictor of good outcome after EVT.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Previous randomized clinical trials (RCTs) conducted to compare endovascular treatment (EVT) alone with bridging therapy (intravenous thrombolysis (IVT)+EVT) showed conflicting results, despite similar inclusion criteria for all trials, and enrolled a non-significant number of acute ischemic stroke (AIS) patients with tandem lesion (TL). A recent large meta-analysis of three RCTs and six observational studies involving more than 3000 patients did not provide the number of patients with TL and further sub-analysis. The safety and benefit of prior IVT remains unclear in AIS patients with TL.

WHAT THIS STUDY ADDS

⇒ AIS patients treated with EVT for TL did not differ in 3-month clinical outcome from those with single occlusion of the intracranial artery. AIS patients with TL treated with bridging therapy for TL had more complete recanalizations and better 3-month clinical outcome compared to those treated with EVT alone. Prior IVT was found to be an independent predictor of good 3-month clinical outcome. IVT was not associated with a higher risk of bleeding complications including symptomatic ICH.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Prior IVT seems to be safe and beneficial in the treatment of AIS patients with EVT for TL. AIS patients with TL eligible for IVT would not be excluded.

INTRODUCTION

Acute ischemic stroke (AIS) due to anterior circulation (AC) tandem lesion (TL) occurs in 6–15% of all cases of AIS and in 10–20% of those with large vessel occlusion (LVO).[1–3] Endovascular treatment (EVT) of LVO in AIS is highly safe and effective, but treatment of TL may present both technical and clinical challenges; the optimal treatment strategy remains under discussion as sufficient evidence from randomized clinical trials (RCTs) is missing. Results from observational studies and data from patients' registries showed that EVT was safe and effective in the treatment of TL, including prior intravenous thrombolysis (IVT), and patients who

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underwent emergent carotid stenting had better outcomes and higher recanalization rates.[3–11]

Despite these reports, there is still no consensus on optimal antithrombotic treatment in patients with TL after emergent carotid angioplasty with stenting followed by mechnical thrombectomy (MT), especially in those treated with prior IVT; different antithrombotic treatment can be considered if carotid occlusion is caused by atheromatous plaques or arterial dissection. Furthermore, some previous results were controversial in regard to outcomes and safety of treatment.[12]

A lack of evidence from randomized trials, unclear guidelines and some conflicting results from observational studies led us to analyze AIS patients with TL who were enrolled in the national prospective METRICS study (Mechanical Thrombectomy Quality Indicators Study in Czech Stroke Centers),[13] and evaluate possible predictors of good clinical outcome after EVT.

SUBJECTS AND METHODS

We analyzed all AIS patients enrolled in the nationwide prospective observational study METRICS in the year 2019; detailed information about the study protocol and study enrollment were published previously.[13] All participating centers provided prospectively collected detailed technical parameters and selected clinical data from all AIS patients treated with EVT in 2019. The obtained data from all participating centers were collected and analyzed anonymously. The study was approved by the multicenter ethics committee of University Hospital Olomouc (n. 24/9/2018). Individual informed consent of each enrolled patient was not required for this study analysis.

TL was defined as a proximal intracranial occlusion (intracranial occlusion of the internal carotid artery (ICA) or occlusion of M1-M2 segments of the middle cerebral artery (MCA)) and a cervical ICA occlusion or stenosis ≥70%.

Admission clinical status was evaluated using the National Institutes of Health Stroke Scale (NIHSS) by a neurologist. All patients underwent brain imaging including angiography of the brain. Eligible patients were treated with IVT. Cervical carotid angioplasty with or without a stent placement was performed according to the interventionalist's preference and based on individual conditions.

MT was performed using stent retrievers or thrombus aspiration, or a combination of both. The first step treatment option in individual patients was used according to a radiologist's decision. Achieved recanalization status was assessed according to the Thrombolysis In Cerebral Infarction (TICI) scale on the final angiogram.[14]

All patients with a stent placed into the ICA received intravenous acetylsalicylic acid (ASA) during EVT. In patients with bridging therapy, the dose of intravenous ASA was 250 mg.

Dual antiplatelet treatment (combination of 100 mg of ASA and 75 mg of clopidogrel) was started after endovascular treatment followed by switching to a single antiplatelet regimen after 3 months in patients with stent placement.

In all patients, the occurrence of intracerebral hemorrhage (ICH) was assessed on the follow-up CT or MRI after 24 hours. Symptomatic ICH (sICH) was defined as a local remote parenchymal hematoma (type 2) or subarachnoid hemorrhage associated with at least a four-point increase in the NIHSS score or leading to death.[10]

Neurological deficit was evaluated using the NIHSS after 24 hours and clinical outcome after 3 months using the modified Rankin Scale (mRS). A score of 0–2 points was considered a good outcome.

All complications (including technical) associated with EVT were recorded and collected from all affected patients. The following complications were analyzed: arterial dissection, arterial dissection with occlusion, arterial perforation, distal embolization, and groin complication, which was defined as any severe hemodynamically relevant bleeding requiring either surgical or endovascular treatment.

Statistical analysis

SPSS software (version 22.0; SPSS, Chicago, IL) was used for statistical analysis. Fisher's exact test, χ^2 test and Mann-Whitney U test were used for comparison of selected groups. Data normality was tested using the Shapiro-Wilk test. Univariate and multivariate logistic regression analysis (LRA) were used to evaluate prior IVT as a possible predictor for good clinical outcome after EVT in patients with TL. The multivariate model was adjusted for the following potential confounders: age, arterial hypertension, diabetes mellitus, atrial fibrillation, ischemic heart disease, admission NIHSS, achieved recanalization, complete recanalization, recanalization time (interval 'stroke onset – maximal achieved recanalization') and sICH. All tests used an α-level of 0.05 for significance.

RESULTS

Of 1375 MTs performed in the Czech Republic in the year 2019, 1178 (86%) patients were enrolled in the METRICS study and 194 (19.2%) of them (59.8% males, mean age 68.7±11.5 years) were treated for TL (table 1). Stenting of the ICA was performed in 153 (78.9%) patients; in the remaining 41 (21.1%) patients, angioplasty alone was used. Patients with TL were younger (68.7±11.5 vs 71.8±12.8 years; p<0.0001), more were males (59.8% vs 45.1%; p=0.0003), more of them frequently smoked (34.2% vs 20.2%; p<0.0001), and they did not differ in the key time intervals related to the logistics of the endovascular procedure from those with a single occlusion (SO) (table 1). Patients with TL did not differ in the 3-month clinical outcome (48.7% vs 46.7%; p=0.616), 3-month mortality (17.3% vs 22.7%; p=0.103), and in the rate of sICH (4.7% vs 5.1%; p=0.809) from those with SO.

Patients with TL had longer time intervals 'GP (groin puncture) – first passage of stent-retriever' (37±20 vs 23±12 min; p<0.0001) and 'GP – maximal achieved recanalization' (57±27 vs 39±22 min; p<0.0001) in comparison with SO patients.

TL patients with prior IVT had a higher rate of complete recanalization (TICI 3, 70.3% vs 50.8%; p=0.012) and a higher rate of good 3-month clinical outcome (mRS 0–2, 55.4% vs 34.4%; p=0.007) than those without IVT before EVT (table 2). No difference was found in the rate of sICH (6.2% vs 1.6%; p=0.276) and in the 'stroke onset – maximal achieved recanalization' time interval (254±94 vs 309±158 min; p=0.089) between both subgroups. Patients without prior IVT had more atrial fibrillation (38.1% vs 9.2%; p<0.0001) and ischemic heart disease (33.3% vs 16.0%; p=0.006) (table 2) and shorter time interval 'GP – first passage of stent retriever' (33±18 vs 39±20 min; p=0.013).

Univariate LRA showed age, admission NIHSS, hypertension, atrial fibrillation and prior IVT as independent predictors of good 3-month clinical outcome after EVT (table 3); sICH reached a borderline significance (p=0.05) (table 3).

The multivariate LRA model showed age, admission NIHSS, prior IVT, sICH and achieved recanalization (TICI ≥2b) as independent predictors of 3-month clinical outcome after EVT after adjustment for potential confounders (table 4).

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Table 1 Demographic, baseline clinical characteristics, selected key time intervals related to endovascular treatment, and clinical outcomes: comparison between TL and other patients

Parameter	TL	SO	P value
N, males (%)	194, 116 (59.8)	814, 367 (45.1)	0.0003
Age (mean±SD, years)	68.7±11.5	71.8±12.8	<0.0001
Admission NIHSS (median)	15	16	0.606
Arterial hypertension (%)	144 (74.2)	625 (76.8)	0.452
Atrial fibrillation (%)	36 (18.6)	355 (43.8)	<0.0001
Diabetes mellitus (%)	49 (25.3)	244 (30.0)	0.190
Ischemic heart disease (%)	42 (21.6)	229 (28.2)	0.066
Hyperlipidemia (%)	73 (37.6)	329 (40.4)	0.476
Smoking (%)	63 (34.2)	156 (20.2)	<0.0001
Prior ischemic stroke (%)	20 (10.3)	96 (11.8)	0.560
IV thrombolysis (%)	131 (67.5)	578 (71.0)	0.340
Secondary transport from SC to CSC (%)	79 (40.7)	298 (36.6)	0.322
Interval 'stroke onset – arrival to hospital performing MT' (median, mean±SD, min)	134, 159±109	123, 147±103	0.173
Interval 'hospital arrival – GP' (median, mean±SD, min)	53, 57±36	53, 57±37	0.962
Interval 'arrival to catheterization room – GP' (median, mean±SD, min)	14, 15±8	13, 15±9	0.523
Achieved recanalization (TICI ≥2b) (%)	166 (85.6)	679 (83.4)	0.464
Complete recanalization (TICI 3) (%)	103 (58.6)	460 (56.5)	0.389
General anesthesia (%)	46 (23.7)	137 (16.9)	0.027
Symptomatic ICH (%)	9 (4.7)	41 (5.1)	0.809
3-month mRS score 0–2 (%)	93 (48.7)	372 (46.7)	0.616
3-month mortality (%)	33 (17.3)	181 (22.7)	0.103

CSC, comprehensive stroke center; GP, groin puncture; ICH, intracerebral hemorrhage; IV, intravenous; mRS, modified Rankin Scale; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; SC, stroke center; SO, single occlusion; TICI, Thrombolysis In Cerebral Infarction scale; TL, tandem lesion.

In total, 35 (18%) periprocedural complications occurred in patients with TL. Peripheral embolism was the most frequent periprocedural complication and occurred in 21 (10.9%) TL patients, which was more frequent in comparison to those with SO (10.9% vs 6.5%; p=0.034). No difference was found in the rate of peripheral embolization between TL patients treated using balloon guiding catheter and standard guiding catheter (12.5% vs 11.3%). Similarly, arterial dissection, which occurred in 10 (5.0%) TL patients, was more frequent in comparison to SO patients (5.0% vs 0.9%; p=0.0003). The rate of groin bleeding did not differ between TL and SO patients (0.5% vs 1.1%; p=0.702). In three (1.5%) patients, the perforation occurred during the intervention procedure.

DISCUSSION

In this analysis, we present the results of EVT in AIS patients with TL, who were enrolled in the national multicenter prospective METRICS study. We found no difference in the rate of good 3-month clinical outcome, mortality and sICH after EVT between TL and SO patients. The main finding of our study is that patients treated with IVT before EVT had a higher rate of complete recanalization (TICI 3) and a higher rate of good 3-month clinical outcome in comparison to those without IVT (table 2). Recently published analysis from the TITAN (Thrombectomy in Tandem Lesions) registry and ETIS (Endovascular Treatment in Ischemic Stroke) registry showed that patients with TL and prior IVT had higher odds of favorable outcome (mRS 0–1) and successful intracranial recanalization (TICI 2b/3) after EVT.[9] However, three previous RCTs conducted to compare EVT alone with bridging therapy (IVT+EVT) showed conflicting results despite similar inclusion criteria for all trials.[15–17] Moreover, the number of patients with TL enrolled into these trials was non-significant. A recent large meta-analysis of three RCTs and six observational studies involving more than 3000 patients showed no difference in clinical outcome between those patients treated with EVT alone and those treated with bridging therapy,[18] but the number of patients with TL and further sub-analysis were not provided; thus, the main finding of this meta-analysis limits the interpretation for patients with TL.[18]

The higher rate of complete recanalization (TICI 3) found in patients with prior IVT in our analysis (table 2) might relate to the recent finding of a significantly smaller size of retrieved clots after bridging therapy in comparison to the size of clots retrieved after EVT alone,[19] and to the previous observations that thrombolysis was associated with significant changes in structural composition and in fibrin network architecture of the retrieved clot.[20] On the other hand, a sensitivity to thrombolytic agents might depend on original thrombus composition and its origin. In our study, patients treated with bridging therapy had atrial fibrillation less frequently in comparison to those treated with EVT alone (table 2); thus, we may speculate that a higher rate of complete recanalization might relate to a different origin and composition of thrombi, which might be more sensitive to alteplase, in some of those patients with TL.

We did not find a difference in the rate of sICH between patients with prior IVT and with EVT alone (table 2), and the overall rate of sICH (6.2%) was similar to the rates reported from the TITAN and ETIS registry (8.1%)[9] and from recent large meta-analysis.[18 21] Our findings, as well as those from previous reports, suggest that IVT before EVT seems to be safe,[18 22–24] even in patients with TL[9 12]; however, patients treated with EVT alone may have a lower risk ratio for any type of ICH compared to those treated with bridging therapy.[18]

In our analysis, prior IVT was found to be an independent predictor of 3-month good outcome after EVT for TL after adjustment for potential confounders (table 4). We found that patients without prior IVT more frequently had atrial fibrillation (38.1% vs 9.2%; p<0.0001) and ischemic heart disease (33.3% vs 16.0%; p=0.006) (table 2), and that these factors might contribute to poorer 3-month outcome in those without prior IVT.

Our patients with TL were younger, more frequently males, and smoked more often than patients with SO (table 1). We suggest that these findings might relate to a different etiology of arterial occlusions in some TL patients in comparison to those with SO, especially in the case of cervical carotid occlusion or severe stenosis, which might be atherothrombotic in origin (male smokers) or caused by a dissection (younger patients).

We did not find any difference in the logistic key time intervals between patients with SO and TL (table 1), but the time intervals related to the interventional procedure were longer in those with TL, as was predictable. No difference in all key time intervals, including the 'stroke onset – maximal achieved recanalization' interval, was observed between TL patients with bridging therapy and without prior IVT, except the time interval 'groin puncture – first passage of stent-retriever', which was shorter in those without IVT (table 2).

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Table 2 Demographic, baseline clinical characteristics, selected key time intervals related to endovascular treatment, and clinical outcomes: comparison between TL patients with and without prior IVT

Parameter	IVT	No IVT	P value
N, males (%)	131, 84 (64.1)	63, 32 (50.8)	0.076
Age (mean±SD, years)	68.4±10.9	69.2±12.8	0.688
Admission NIHSS (median)	15	17	0.063
Arterial hypertension (%)	99 (75.6)	45 (71.4)	0.537
Atrial fibrillation (%)	12 (9.2)	24 (38.1)	<0.0001
Diabetes mellitus (%)	37 (28.2)	12 (19.0)	0.167
Ischemic heart disease (%)	21 (16.0)	21 (33.3)	0.006
Hyperlipidemia (%)	50 (38.2)	23 (36.5)	0.823
Smoking (%)	44 (35.2)	19 (32.2)	0.689
Prior ischemic stroke (%)	7 (5.3)	13 (20.6)	0.001
Secondary transport from SC to CSC (%)	58 (44.3)	21 (33.3)	0.146
Interval 'stroke onset – arrival to hospital performing MT' (median, mean±SD, min)	133, 150±100	140, 177±125	0.284
Interval 'hospital arrival – GP' (median, mean±SD, min)	50, 54±37	59, 62±34	0.074
Interval 'arrival to catheterization room – GP' (median, mean±SD, min)	15, 15±8	12, 14±8	0.241
Interval 'stroke onset – maximal achieved recanalization' (median, mean±SD, min)	248, 254±94	251, 309±158	0.089
Achieved recanalization (TICI ≥2b) (%)	116 (88.5)	50 (79.4)	0.088
Complete recanalization (TICI 3) (%)	71 (70.3)	32 (50.8)	0.012
General anesthesia (%)	32 (24.4)	14 (22.2)	0.735
Symptomatic ICH (%)	8 (6.2)	1 (1.6)	0.276
3-month mRS score 0–2 (%)	72 (55.4)	21 (34.4)	0.007
3-month mortality (%)	19 (14.6)	14 (23.0)	0.155

CSC, comprehensive stroke center; GP, groin puncture; ICH, intracerebral hemorrhage; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; SC, stroke center; TICI, Thrombolysis In Cerebral Infarction scale; TL, tandem lesion.

A previous report showed that a heparin dose of 3000 IU administered during the EVT intervention for TL was a significant predictor of sICH,[25] while in our study patients did not receive heparin during the EVT.

The overall rate of periprocedural complications in our TL patients (18%) did not exceed the rate reported in those patients from the ETIS registry (17.2%).[10] Peripheral embolism to new

Table 3 Univariate logistic regression analysis for identification of independent predictors of good 3-month clinical outcome (mRS 0–2) in patients with TL

Variable	P value	OR	95% CI
Age	0.0003	0.950	0.924 to 0.976
NIHSS	0.0001	0.901	0.855 to 0.948
Diabetes mellitus	0.146	0.611	0.314 to 1.187
Hypertension	0.002	0.339	0.171 to 0.669
Atrial fibrillation	0.026	0.414	0.189 to 0.902
Hyperlipidemia	0.562	1.189	0.662 to 2.136
Smoking	0.104	1.670	0.899 to 3.101
IV thrombolysis	0.008	2.365	1.257 to 4.445
Symptomatic ICH	0.050	0.122	0.014 to 0.997
Achieved recanalization (TICI ≥2b)	0.062	2.245	0.958 to 5.254
Complete recanalization (TICI 3)	0.092	1.636	0.922 to 2.901
General anesthesia	0.636	0.852	0.437 to 1.656
Interval 'stroke onset – maximal achieved recanalization'	0.224	0.998	0.995 to 1.001
Secondary transport from SC to CSC	0.885	0.958	0.537 to 1.708

CSC, comprehensive stroke center; ICH, intracerebral hemorrhage; IV, intravenous; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SC, stroke center; TICI, Thrombolysis In Cerebral Infarction scale; TL, tandem lesion.

Table 4 Predictors of good 3-month clinical outcome (mRS 0–2) in TL patients on multivariate logistic regression model adjusted for age, NIHSS, diabetes mellitus, hypertension, atrial fibrillation, hyperlipidemia, smoking, IV thrombolysis, symptomatic ICH, achieved recanalization, complete recanalization, general anesthesia, and interval 'stroke onset – maximal achieved recanalization'

Variable	P value	OR	95% CI
Age	0.001	0.931	0.894 to 0.969
NIHSS	0.002	0.902	0.845 to 0.961
Diabetes mellitus	0.097	0.470	0.192 to 1.146
Hypertension	0.097	0.465	0.188 to 1.147
Atrial fibrillation	0.554	1.388	0.468 to 4.115
Hyperlipidemia	0.120	1.909	0.844 to 4.314
Smoking	0.828	0.916	0.415 to 2.019
IV thrombolysis	0.002	3.818	1.614 to 9.030
Symptomatic ICH	0.010	0.054	0.005 to 0.502
Achieved recanalization (TICI ≥2b)	0.031	4.546	1.145 to 18.04
Complete recanalization (TICI 3)	0.226	1.641	0.735 to 3.660
General anesthesia	0.652	0.814	0.332 to 1.993
Secondary transport from SC to CSC	0.910	0.958	0.458 to 2.003

CSC, comprehensive stroke center; ICH, intracerebral hemorrhage; IV, intravenous; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SC, stroke center; TICI, Thrombolysis In Cerebral Infarction scale; TL, tandem lesion.

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territory was the most frequent periprocedural complication, which was similar to previous reports,[10] and the rate of embolism recorded in our TL patients (10.9%) was predictably higher than in patients with SO and in line with previous findings in EVT for TL.[10]

Our analysis has limitations. A major limitation is the fact that patients were not randomized for bridging therapy, but IVT was performed in each individual patient according to eligibility criteria, as our study documented a routine clinical practice. The strategy of EVT including carotid stenting and periprocedural antiplatelet regimen were not standardized or unified before the initiation or during the duration of the METRICS study[13]. No central blinded assessment of imaging findings was performed and all radiological findings were evaluated by experienced neuroradiologists and interventional radiologists in each of the participating centers. The ASPECT (Alberta Stroke Program Early CT) score was not included in our study analysis; however, its possible association with clinical outcome might be expected. We did not consider including the ASPECT score in our analysis as none of the participating centers used the ASPECT score for patient selection for EVT within the standard 6 hour therapeutic time window. Some centers collected 3-month clinical outcomes in some patients additionally and retrospectively. We cannot exclude definitely that some differences among centers may have had an impact on some of our results.

In conclusion, patients with TL treated with bridging therapy had a higher rate of complete recanalization (TICI 3) and a higher rate of good 3-month clinical outcome in comparison to those without prior IVT, and no difference was found in the rate of sICH. IVT was found to be an independent predictor of good 3-month clinical outcome in TL patients treated with EVT.

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REFERENCES

1 Rubiera M, Ribo M, Delgado-Mederos R, *et al*. Tandem internal carotid artery/middle cerebral artery occlusion: an independent predictor of poor outcome after systemic thrombolysis. *Stroke* 2006;37:2301–5.
2 Poppe AY, Jacquin G, Roy D, *et al*. Tandem carotid lesions in acute ischemic stroke: mechanisms, therapeutic challenges, and future directions. *AJNR Am J Neuroradiol* 2020;41:1142–8.
3 Jadhav AP, Zaidat OO, Liebeskind DS, *et al*. Emergent management of tandem lesions in acute ischemic stroke. *Stroke* 2019;50:428–33.
4 Sadeh-Gonik U, Tau N, Friehmann T, *et al*. Thrombectomy outcomes for acute stroke patients with anterior circulation tandem lesions: a clinical registry and an update of a systematic review with meta-analysis. *Eur J Neurol* 2018;25:693–700.
5 Li W, Chen Z, Dai Z, *et al*. Management of acute tandem occlusions: stent-retriever thrombectomy with emergency stenting or angioplasty. *J Int Med Res* 2018;46:2578–86.
6 Zhu F, Bracard S, Anxionnat R, *et al*. Impact of emergent cervical carotid stenting in tandem occlusion strokes treated by thrombectomy: a review of the TITAN collaboration. *Front Neurol* 2019;10:206.
7 Papanagiotou P, Haussen DC, Turjman F, *et al*. Carotid stenting with antithrombotic agents and intracranial thrombectomy leads to the highest recanalization rate in patients with acute stroke with tandem lesions. *JACC Cardiovasc Interv* 2018;11:1290–9.
8 Cirillo L, Romano DG, Vornetti G, *et al*. Acute ischemic stroke with cervical internal carotid artery steno-occlusive lesion: multicenter analysis of endovascular approaches. *BMC Neurol* 2021;21:362.
9 Anadani M, Marnat G, Consoli A. Endovascular therapy with or without intravenous thrombolysis in acute stroke with tandem occlusion. *J NeuroIntervent Surg* 2021:1–7.
10 Happi Ngankou E, Gory B, Marnat G, *et al*. Thrombectomy complications in large vessel occlusions: incidence, predictors, and clinical impact in the ETIS registry. *Stroke* 2021;52:e764–8.
11 Anadani M, Marnat G, Consoli A, *et al*. Endovascular therapy of anterior circulation tandem occlusions: pooled analysis from the TITAN and ETIS registries. *Stroke* 2021;52:3097–105.
12 Nolan NM, Regenhardt RW, Koch MJ, *et al*. Treatment approaches and outcomes for acute anterior circulation stroke patients with tandem lesions. *J Stroke Cerebrovasc Dis* 2021;30:105478.

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13 Köcher M, Šaňák D, Zapletalová J, *et al*. Mechanical thrombectomy quality indicators study in Czech stroke centers: results of the metrics study. *J Stroke Cerebrovasc Dis* 2022;31:106308.
14 Higashida RT, Furlan AJ. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. *Stroke* 2003;34:109–37.
15 Yang P, Zhang Y, Zhang L, *et al*. Endovascular thrombectomy with or without intravenous alteplase in acute stroke. *N Engl J Med* 2020;382:1981–93.
16 Zi W, Qiu Z, Li F, *et al*. Effect of endovascular treatment alone vs intravenous alteplase plus endovascular treatment on functional independence in patients with acute ischemic stroke: the DEVT randomized clinical trial. *JAMA* 2021;325:234–43.
17 Suzuki K, Matsumaru Y, Takeuchi M, *et al*. Effect of mechanical thrombectomy without vs with intravenous thrombolysis on functional outcome among patients with acute ischemic stroke: the SKIP randomized clinical trial. *JAMA* 2021;325:244–53.
18 Zhang J, Chen S, Shi S, *et al*. Direct endovascular treatment versus bridging therapy in patients with acute ischemic stroke eligible for intravenous thrombolysis: systematic review and meta-analysis. *J NeuroIntervent Surg* 2022;14:321–5.
19 Rossi R, Molina S, Mereuta OM, *et al*. Does prior administration of rtPA influence acute ischemic stroke clot composition? Findings from the analysis of clots retrieved with mechanical thrombectomy from the RESTORE registry. *J Neurol* 2022;269:1913–20.
20 Stanford SN, Sabra A, D'Silva L, D'Silva L, *et al*. The changes in clot microstructure in patients with ischaemic stroke and the effects of therapeutic intervention: a prospective observational study. *BMC Neurol* 2015;15:35.
21 Hellegering J, Uyttenboogaart M, Bokkers RPH, *et al*. Treatment of the extracranial carotid artery in tandem lesions during endovascular treatment of acute ischemic stroke: a systematic review and meta-analysis. *Ann Transl Med* 2020;8:1278.
22 Mistry EA, Mistry AM, Nakawah MO, *et al*. Mechanical thrombectomy outcomes with and without intravenous thrombolysis in stroke patients: a meta-analysis. *Stroke* 2017;48:2450–6.
23 Gariel F, Lapergue B, Bourcier R, *et al*. Mechanical thrombectomy outcomes with or without intravenous thrombolysis. *Stroke* 2018;49:2383–90.
24 Katsanos AH, Malhotra K, Goyal N, *et al*. Intravenous thrombolysis prior to mechanical thrombectomy in large vessel occlusions. *Ann Neurol* 2019;86:395–406.
25 Da Ros V, Scaggiante J, Sallustio F, Ros D V, Scaggiante J. Lattanzi J, *et al*. Carotid stenting and mechanical thrombectomy in patients with acute ischemic stroke and tandem occlusions: antithrombotic treatment and functional outcome. *AJNR Am J Neuroradiol* 2020;41:2088–93.

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