



Original Article

# Antiplatelet therapy within 24 hours of tPA: lessons learned from patients requiring combined thrombectomy and stenting for acute ischemic stroke

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**Objective:** Although stroke guidelines recommend antiplatelets be started 24 hours after tissue plasminogen activator (tPA), select mechanical thrombectomy (MT) patients with luminal irregularities or underlying intracranial atherosclerotic disease may benefit from earlier antiplatelet administration.

**Methods:** We explore the safety of early (<24 hours) post-tPA antiplatelet use by retrospectively reviewing patients who underwent MT and stent placement for acute ischemic stroke from June 2015 to April 2018 at our institution.

**Results:** Six patients met inclusion criteria. Median presenting and pre-operative National Institutes of Health Stroke Scale scores were 14 (Interquartile Range [IQR] 5.5-17.3) and 16 (IQR 13.7-18.7), respectively. Five patients received standard intravenous (IV) tPA and one patient received intra-arterial tPA. Median time from symptom onset to IV tPA was 120 min (IQR 78-204 min). Median time between tPA and antiplatelet administration was 4.9 hours (IQR 3.0-6.7 hours). Clots were successfully removed from the internal carotid artery (ICA) or middle cerebral artery (MCA) in 5 patients, the anterior cerebral artery (ACA) in one patient, and the vertebrobasilar junction in one patient. All patients underwent MT before stenting and achieved thrombolysis in cerebral infarction 2B recanalization. Stents were placed in the ICA (n=4), common carotid artery (n=1), and basilar artery (n=1). The median time from stroke onset to endovascular access was 185 min (IQR 136-417 min). No patients experienced symptomatic post-procedure intracranial hemorrhage (ICH). Median modified Rankin Scale score on discharge was 3.5.

**Conclusions:** Antiplatelets within 24 hours of tPA did not result in symptomatic ICH in this series. The safety and efficacy of early antiplatelet administration after tPA in select patients following mechanical thrombectomy warrants further study.

**Keywords** Acute ischemic stroke, Emergent stenting, Mechanical thrombectomy, Intracranial hemorrhage, Antiplatelet

## INTRODUCTION

Acute ischemic stroke (AIS) is a life-threatening medical emergency that warrants immediate intervention. Current guidelines for the safe and effective treatment of AIS include administration of intravenous (IV) recombinant tissue plasminogen activator (tPA) for thrombolysis within 4.5 hours of symptom onset. This time-window was established by analysis of the NINDS, ECASS, ATLANTIS, EPITHET, and IST-3 randomized controlled trials (RCTs), which revealed improved functional stroke outcomes when tPA was delivered within 3-4.5 hours of stroke onset, and greater proportional and absolute benefits from earlier treatment.<sup>33)</sup> For AIS caused by a large vessel occlusion (LVO) in the proximal anterior circulation, the MR CLEAN, ESCAPE, SWIFT PRIME, EXTEND-IA, and REVASCAT RCTs showed that intra-arterial mechanical thrombectomy (MT) is safe and more effective than IV thrombolysis alone.<sup>33)</sup>

Intracranial hemorrhage (ICH) is a concern with LVO, with reported rates up to 6.4% overall in patients treated with IV thrombolysis and 11.2% for those treated with endovascular therapy.<sup>5)7)9)12)18)21)28)30)34)</sup> Although the risk of symptomatic ICH is significantly increased with MT likely due to a combination of endothelial damage and/or use of antithrombotic agents to prevent periprocedural thrombotic events,<sup>1)15)17)19)27)31)37)</sup> in selected LVO patients with high risk of re-occlusion due to incomplete revascularization, luminal irregularities, or underlying intracranial atherosclerotic disease (ICAD), early initiation of antiplatelet regimens may decrease the risk of further ischemic events. There is nonetheless concern for increased ICH risk in MT patients receiving peri-procedural antiplatelet therapy (with or without prior tPA) despite inconclusive data,<sup>32)39)</sup> and it is typically avoided until 24 hours post-procedure.

AIS patients with LVO and concomitant proximal high-grade “tandem” stenosis limiting access to distal lesions, or refractory intracranial stenoses, may require stent placement for successful revascularization.<sup>4)6)13)22)34)36)</sup> In these emergent cases antiplatelet therapy is initiated in the immediate peri-procedural period at our institution

to prevent stent occlusion secondary to local platelet activation. We herein evaluate the outcomes of antiplatelet use within 24 hours of tPA in this population, with this data having relevance to the potential safety of early antiplatelet administration in selected non-stent post-MT patients with high risk for re-occlusion due to incomplete revascularization or luminal irregularities.

## MATERIALS AND METHODS

This study was performed in compliance with Institutional Review Board (IRB) and Health Insurance Portability and Accountability Act regulations. Patient consent for procedures, data collection, and review was obtained based on institutional guidelines.

Retrospective review of a prospectively-maintained database of consecutive AIS patients undergoing MT at the University of California, San Diego Medical Center from June 2015 to April 2018 was conducted. Patients were included if they were treated with tPA within 4.5 hours of symptom onset, underwent acute MT with stent placement for refractory tandem occlusions or persistent stenosis, and had initiation of antiplatelet therapy (dual oral or rectal antiplatelets or eptifibatid drip with later transition to dual oral antiplatelets) within 24 hours of tPA administration.

Our institutional thrombolysis protocol is consistent with international guidelines and has been described previously.<sup>11)25)</sup> At the time of stroke code, patients were evaluated with activation of the neurointerventional team for thrombectomy. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) and all patients then underwent pre-procedure imaging: computed tomography (CT) or magnetic resonance imaging to rule out intracranial hemorrhage and CT angiography (CTA) or MR angiography (MRA) to assess for presence and location of vessel occlusion. All patients underwent diagnostic cerebral angiography (DCA) before and after intervention. Thrombectomy was performed using direct aspiration and/or stent retriever, and the thrombolysis in cerebral infarction

(TICI) scale was utilized to assess revascularization. Stent placement was performed after revascularization when possible. The institutional preference for antiplatelet administration in this patient subset evolved during the study period from primary loading of oral or rectal aspirin and clopidogrel after clearance post-operative head CT to initiation of intravenous eptifibatid before or immediately after stent placement with peri-procedural head CT, then transition to aspirin and clopidogrel. Antiplatelet-naïve patients received a loading dose of aspirin 650 mg and clopidogrel 150 mg, or eptifibatid 180 mcg/kg IV bolus then 2 mcg/kg/min IV maintenance. Patients with pre-existing antiplatelet therapy received adjusted dosages.

Via chart review, we identified the following patient characteristics: age, sex, NIHSS score, site of stenosis or occlusion and stent placement, TICI score, comorbidities, and post-operative complications. Symptomatic ICH was defined using ECASS criteria.<sup>29)</sup> Follow-up clinical outcomes were determined using the modified Rankin Scale (mRS). Medians and interquartile ranges (IQRs) of continuous variables are reported.

## RESULTS

A total of 6 patients (all men) met inclusion criteria.

Patient demographic, treatment, and outcome characteristics are displayed in Table 1. The median age was 55 years (IQR 53.3-62 years). Median presenting and pre-operative NIHSS scores were 14 (IQR 5.5-17.3) and 16 (IQR 13.7-18.7), respectively, with two patients experiencing post-tPA non-hemorrhagic neurologic progression. Five patients received standard pre-procedural IV recombinant tPA (0.9 mg/kg body weight), and one patient received 8 mg of intra-arterial (IA) tPA for a post-MT persistent distal middle cerebral artery (MCA) branch occlusion. The median time from stroke symptom onset to IV tPA administration was 120 min (IQR 78-204 min). Clots were successfully removed from the internal carotid artery (ICA) or MCA in 5 patients, the anterior cerebral artery (ACA) in one patient, and the vertebrobasilar junction in one patient. All patients underwent MT before stenting and achieved TICI 2B recanalization. Stents were placed in the ICA (n=4), common carotid artery (CCA; n=1), and basilar artery (BA; n=1). The median time from stroke onset to endovascular access was 185 min (IQR 136-417 min). Median time between tPA and antiplatelet initiation was 4.9 hours (IQR 3.0-6.7 hours). No patients experienced symptomatic ICH. One patient had delayed initiation of post-procedure antiplatelets due to contrast versus hemorrhage on post-operative head CT. Interval (6 hours) CTA demonstrated in-stent thrombosis and

**Table 1.** Patient characteristics and outcomes

No.	Age	Sex	Initial NIHSS	Pre-op NIHSS	Etiology	tPA	Angio plasty	Stent Site	MT Site	OTT	OMT	TAT	TICI	HT	Discharge mRS	30d mRS	90d mRS
1	64	M	15	"	Stenosis	IV	Yes	R ICA	R ICA terminus, L A1/A2	0:57	2:19	10:49*	2B	0	4	NA	4
2	30	M	21	"	Dissection	IA	No	L ICA	L ICA terminus	3:35	0:49	1:53	2B	0	3	2	2
3	54	M	18	"	Dissection	IV	No	L ICA	L M1	1:18	2:15	3:01	2B	0	3	NA	NA
4	53	M	13	"	Stenosis	IV	No	R ICA	R M2	2:28	3:52	3:10	2B	0	2	2	NA
5	56	M	1	17	Dissection	IV	No	L CCA	L M2	2:00	7:59	6:41	2B	0	5	NA	NA
6	70	M	3	14	Stenosis	IV	Yes	BA	L VB junction	3:24	12:27	10:53	2B	0	6	6	6

\* Antiplatelet administration delayed by contrast extravasation versus hemorrhage on post-operative head CT.

NIHSS, National Institutes of Health Stroke Scale; tPA, tissue plasminogen activator [route of administration]; IV, intravenous; IA, intraarterial; MT, mechanical thrombectomy; ICA, internal carotid artery; CCA, common carotid artery; BA, basilar artery; VB, vertebrobasilar; OTT, Onset-to-tPA time (hour:minute); OMT, Onset-to-thrombectomy time (hour:minute); TAT, tPA-to-antiplatelet therapy time (hour:minute); TICI, thrombolysis in cerebral infarction; HT, hemorrhagic transformation; mRS, Modified Rankin Scale

the patient was loaded on aspirin and clopidogrel before undergoing mechanical thrombectomy and intra-arterial eptifibatide. One patient died from sepsis secondary to additional comorbidities. Median mRS on discharge was 3.5 (IQR 3-4.5). Follow-up data was only available for four patients.

## DISCUSSION

In this series of consecutive post-tPA/MT plus stenting patients receiving early antiplatelet therapy, there were zero instances of symptomatic ICH. In the absence of widely-accepted treatment guidelines for patients with tandem occlusions or refractory intracranial stenosis and AIS, there is ongoing debate for the role of acute stenting in this population due to the potentially increased risk of ICH with requisite antiplatelets,<sup>3)6)13)16)40)</sup> especially in patients that received prior tPA. Antiplatelet strategies by those advocating stenting in this setting typically involve pre- or peri-procedural dual oral antiplatelet or intravenous glycoprotein IIb/IIIa inhibitor loading followed by maintenance therapies,<sup>4)13)34)</sup> although holding antiplatelets for 24 hours after tPA despite stent placement has also been described.<sup>22)</sup> This latter approach likely derives from the current stroke guidelines that advise against the administration of antiplatelets within 24 hours of tPA,<sup>33)</sup> and are based on RCTs that demonstrated increased ICH risk without improved outcomes for the early administration of aspirin after tPA.<sup>41)</sup> However, these studies did not account for the increased thrombotic risk in patients undergoing MT or stent placement, a consideration highlighted by the in-stent thrombosis seen in the one patient in this study that had delayed initiation of post-procedural antiplatelets. While stent placement in our patient sample provided a compelling rationale for expedited post-tPA/MT antiplatelet initiation,<sup>10)16)</sup> this population is also an effective proxy for assessing the theoretical safety of early post-tPA/MT antiplatelet use in non-stented patients at high risk for re-occlusion (i.e., those with large vessel occlusions from ICAD versus embolic disease, elevated platelets, and residual embolic

fragments/stenosis at the thrombectomy site).<sup>2)26)</sup>

Current data on the impact of antiplatelet use in the peri-thrombolysis/peri-thrombectomy period remains incomplete. While preexisting antiplatelet and anticoagulant use has been found to increase the risk for symptomatic ICH in patients with AIS, these effects appear to be independent of tPA administration or performance of a MT.<sup>14)15)23)24)38)</sup> Moreover, prior antiplatelet treatment may actually improve long-term post-stroke outcomes.<sup>38)</sup> A study by Broeg-Morway et al. provides additional relevant data, as it compared the outcomes of patients who received tPA and underwent endovascular intervention for AIS with and without aspirin, finding that antiplatelet therapy did not increase the risk of bleeding complications or poor clinical outcome in this cohort.<sup>8)</sup> Although endovascular recanalization procedures varied (e.g. IA thrombolysis, MT, and/or stent placement), and patients meeting our inclusion criteria were not separately described, this study provides evidence for the safety of early post-tPA antiplatelet use in AIS patients treated endovascularly.

Other series with mixed populations report no effect or a protective effect of tPA on the rate of symptomatic ICH post MT/stenting for AIS,<sup>4)40)</sup> despite a potentially increased risk of symptomatic ICH with stenting in general in AIS patients undergoing endovascular therapies.<sup>13)</sup> Han et al. also report a series of AIS patients receiving an emergent loading dose of antiplatelets (aspirin 300 mg and clopidogrel 300 mg) with acute stenting after tPA, finding a low rate of rate of hemorrhagic transformation (1/12 or 8.3%) with this protocol.<sup>20)</sup> Our data contribute to this literature, supporting the potential safety of early antiplatelet administration after tPA in selected AIS patients.

Limitations of our study include its small sample size and observational design. While our data are underpowered to definitely determine the impact of antiplatelet therapy on recanalization rates or ICH after tPA/MT, it highlights an important gap in the literature and current stroke treatment guidelines. These data support future RCTs comparing the outcomes of post-tPA/MT patients at high risk for re-occlusion with or without early an-

tiplatelet administration. Critical in the design of such trials will be multivariate analyses accounting for demographic and procedural confounders, as well as sustained patient follow-up to determine long-term clinical results.

## CONCLUSIONS

In this single-institution case series, symptomatic ICH was not seen after antiplatelet administration within 24 hours of tPA in patients undergoing MT and stent placement for AIS. These data warrant further exploration of the safety of early antiplatelet administration in post-tPA/MT patients deemed high risk for re-occlusion.

## Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

## REFERENCES

1. Abraham P, Scott Pannell J, Santiago-Dieppa DR, Cheung V, Steinberg J, Wali A, et al. Vessel wall signal enhancement on 3-T MRI in acute stroke patients after stent retriever thrombectomy. *Neurosurg Focus*. 2017 Apr;42(4):E20.
2. Bang OY, Kim BM, Seo WK, Jeon P. Endovascular therapy for acute ischemic stroke of intracranial atherosclerotic origin-neuroimaging perspectives. *Front Neurol*. 2019 Mar;10:269.
3. Behme D, Molina CA, Selim MH, Ribo M. Emergent carotid stenting after thrombectomy in patients with tandem lesions. *Stroke*. 2017 Apr;48(4):1126-8.
4. Behme D, Mpotsaris A, Zeyen P, Psychogios MN, Kowoll A, Maurer CJ, et al. Emergency stenting of the extracranial internal carotid artery in combination with anterior circulation thrombectomy in acute ischemic stroke: a retrospective multicenter study. *AJNR Am J Neuroradiol*. 2015 Dec;36(12):2340-5.
5. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. 2015 Jan;372(1):11-20.
6. Brekenfeld C, Schroth G, Mattle HP, Do DD, Remonda L, Mordasini P, et al. Stent placement in acute cerebral artery occlusion: use of a self-expandable intracranial stent for acute stroke treatment. *Stroke*. 2009 Mar;40(3):847-52.
7. Broderick JP, Palesch YY, Demchuk AM, Yeatts SD, Khatri P, Hill MD, et al. Endovascular therapy after intravenous t-PA versus t-PA alone for stroke. *N Engl J Med*. 2013 Mar;368(10):893-903.
8. Broeg-Morvay A, Mordasini P, Slezak A, Liesirova K, Meisterernst J, Schroth G, et al. Does antiplatelet therapy during bridging thrombolysis increase rates of intracerebral hemorrhage in stroke patients? *PLoS One*. 2017 Jan;12(1):e0170045.
9. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. 2015 Mar;372(11):1009-18.
10. Chaturvedi S, Yadav JS. The role of antiplatelet therapy in carotid stenting for ischemic stroke prevention. *Stroke*. 2006 Jun;37(6):1572-7.
11. Cheung VJ, Wali AR, Santiago-Dieppa DR, Rennert RC, Brandel MG, Steinberg JA, et al. Improving door to Groin puncture time for mechanical thrombectomy via iterative quality protocol interventions. *Cureus*. 2018 Mar;10(3):e2300.
12. Ciccone A, Valvassori L, Nichelatti M, Sgoifo A, Ponzio M, Sterzi R, et al. Endovascular treatment for acute ischemic stroke. *N Engl J Med*. 2013 Mar;368(10):904-13.
13. Dorado L, Castaño C, Millán M, Aleu A, de la Ossa NP, Gomis M, et al. Hemorrhagic risk of emergent endovascular treatment plus stenting in patients with acute ischemic stroke. *J Stroke Cerebrovasc Dis*. 2013 Nov;22(8):1326-31.
14. Dowlathshahi D, Hakim A, Fang J, Sharma M; Investigators of the Registry of the Canadian Stroke Network. Pre admission antithrombotics are associated with improved outcomes following ischaemic stroke: a cohort from the Registry of the Canadian Stroke Network. *Int J Stroke*. 2009 Oct;4(5):328-34.
15. Enomoto Y, Yoshimura S, Egashira Y, Yamagami H, Sakai N; Committee of Endovascular Salvage for Cerebral Ultra-acute Embolism (RESCUE)-Japan Study Group. The risk of intracranial hemorrhage in Japanese patients with acute large vessel occlusion; subanalysis of the RESCUE-Japan registry. *J Stroke Cerebrovasc Dis*. 2016 May;25(5):1076-80.
16. Enomoto Y, Yoshimura S. Antiplatelet therapy for carotid artery stenting. *Interv Neurol*. 2013 Sep;1(3-4):151-63.
17. Eugène F, Gauvrit JY, Ferré JC, Gentric JC, Besseghir A, Ronzière T, et al. One-year MR angiographic and clinical follow-up after intracranial mechanical thrombectomy using a stent retriever device. *AJNR Am J Neuroradiol*. 2015 Jan;36(1):126-32.

18. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med.* 2015 Mar;372(11):1019-30.
19. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet.* 2016 Apr;387(10029):1723-31.
20. Han YF, Dai QL, Chen XL, Xiong YY, Yin Q, Xu GL, et al. Emergent loading dose of antiplatelets for stenting after IV rt-PA in acute ischemic stroke: a feasibility study. *Int J Neurosci.* 2018 Apr;128(4):311-7.
21. Lees KR, Bluhmki E, von Kummer R, Brodt TG, Toni D, Grotta JC, et al. Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. *Lancet.* 2010 May;375(9727):1695-703.
22. Li W, Chen Z, Dai Z, Liu R, Yin Q, Wang H, et al. Management of acute tandem occlusions: Stent-retriever thrombectomy with emergency stenting or angioplasty. *J Int Med Res.* 2018 Jul;46(7):2578-86.
23. Luo S, Zhuang M, Zeng W, Tao J. Intravenous thrombolysis for acute ischemic stroke in patients receiving antiplatelet therapy: a systematic review and meta-analysis of 19 studies. *J Am Heart Assoc.* 2016 May;5(5):e003242.
24. Meurer WJ, Kwok H, Skolarus LE, Adelman EE, Kade AM, Kalbfleisch J, et al. Does preexisting antiplatelet treatment influence postthrombolysis intracranial hemorrhage in community-treated ischemic stroke patients? An observational study. *Acad Emerg Med.* 2013 Feb;20(2):146-54.
25. Mokin M, Ansari SA, McTaggart RA, Bulsara KR, Goyal M, Chen M, et al. Indications for thrombectomy in acute ischemic stroke from emergent large vessel occlusion (ELVO): report of the SNIS Standards and Guidelines Committee. *J Neurointerv Surg.* 2019 Mar;11(3):215-20.
26. Mosimann PJ, Kaesmacher J, Gautschi D, Bellwald S, Panos L, Piechowiak E, et al. Predictors of unexpected early reocclusion after successful mechanical thrombectomy in acute ischemic stroke patients. *Stroke.* 2018 Nov;49(11):2643-51.
27. Nahab F, Walker GA, Dion JE, Smith WS. Safety of periprocedural heparin in acute ischemic stroke endovascular therapy: the multi MERCI trial. *J Stroke Cerebrovasc Dis.* 2012 Nov;21(8):790-3.
28. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med.* 1995 Dec;333(24):1581-8.
29. Neuberger U, Möhlenbruch MA, Herweh C, Ulfert C, Bendszus M, Pfaff J. Classification of bleeding events: Comparison of ECASS III (European Cooperative Acute Stroke Study) and the new Heidelberg bleeding classification. *Stroke.* 2017 Jul;48(7):1983-5.
30. Nogueira RG, Lutsep HL, Gupta R, Jovin TG, Albers GW, Walker GA, et al. Trevo versus Merci retrievers for thrombectomy revascularisation of large vessel occlusions in acute ischaemic stroke (TREVO 2): a randomised trial. *Lancet.* 2012 Oct;380(9849):1231-40.
31. Nogueira RG, Smith WS; MERCI and Multi MERCI Writing Committee. Safety and efficacy of endovascular thrombectomy in patients with abnormal hemostasis: pooled analysis of the MERCI and multi MERCI trials. *Stroke.* 2009 Feb;40(2):516-22.
32. Pandhi A, Tsvigoulis G, Krishnan R, Ishfaq MF, Singh S, Hoit D, et al. Antiplatelet pretreatment and outcomes following mechanical thrombectomy for emergent large vessel occlusion strokes. *J Neurointerv Surg.* 2018 Sep;10(9):828-33.
33. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. *Stroke.* 2018 Mar;49(3):e46-110.
34. Rangel-Castilla L, Rajah GB, Shakir HJ, Shallwani H, Gandhi S, Davies JM, et al. Management of acute ischemic stroke due to tandem occlusion: should endovascular recanalization of the extracranial or intracranial occlusive lesion be done first? *Neurosurg Focus.* 2017 Apr;42(4):E16.
35. Saver JL, Jahan R, Levy EI, Jovin TG, Baxter B, Nogueira RG, et al. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. *Lancet.* 2012 Oct;380(9849):1241-9.
36. Sivan-Hoffmann R, Gory B, Armoiry X, Goyal M, Riva R, Labeyrie PE, et al. Stent-retriever thrombectomy for acute anterior ischemic stroke with tandem occlusion: a systematic review and meta-analysis. *Eur Radiol.* 2017 Jan;27(1):247-54.
37. Teng D, Pannell JS, Rennert RC, Li J, Li YS, Wong VW, et al. Endothelial trauma from mechanical thrombectomy in acute stroke: in vitro live-cell platform with animal validation. *Stroke.* 2015 Apr;46(4):1099-106.
38. Uyttenboogaart M, Koch MW, Koopman K, Vroomen PC, De Keyser J, Luijckx GJ. Safety of antiplatelet therapy prior to intravenous thrombolysis in acute ischemic stroke. *Arch Neurol.* 2008 May;65(5):607-11.
39. van de Graaf RA, Chalos V, del Zoppo GJ, van der Lugt A, Dippel DWJ, Roozenbeek B. Periprocedural antithrombotic treatment during acute mechanical thrombectomy for ischemic stroke: a systematic review. *Front Neurol.* 2018 Apr;9:238.

40. Zhu F, Bracard S, Anxionnat R, Derelle AL, Tonnelet R, Liao L, et al. Impact of emergent cervical carotid stenting in tandem occlusion strokes treated by thrombectomy: a review of the TITAN collaboration. *Front Neurol.* 2019 Mar;10:206.
41. Zinkstok SM, Roos YB; ARTIS investigators. Early administration of aspirin in patients treated with alteplase for acute ischaemic stroke: a randomised controlled trial. *Lancet.* 2012 Aug;380(9843):731-7.