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Use of Tirofiban in Endovascular Thrombectomy: More Questions than Answers

Bonaventure Ip[1,2] · Hao Wang[3] · Simon Chun Ho Yu[4]

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Large vessel occlusion (LVO) strokes are mostly caused by cardioembolism, intracranial (ICAD) or extracranial atherosclerotic disease (ECAD). Although large artery atherosclerotic LVOs are less common than those caused by cardioembolism, endovascular therapy (EVT) for these conditions could be challenging. Immediate re-occlusion of ICAD/ECAD lesions is common due to thrombogenic plaques or elastic recoiling following thrombectomy and/or angioplasty [1]. Ongoing artery-to-artery embolism may also result in new tandem occlusions downstream to the lesion. As a result, emergent intra- or extracranial stenting is frequently considered to optimize antegrade flow [2]. These challenges prompt the need for a rapid-onset, potent, and safe periprocedural antiplatelet agent. In practice, tirofiban, a glycoprotein IIb/IIIb inhibitor, is commonly given in these scenarios. Yet, evidence regarding its efficacy, safety, and hemorrhagic risk with intravenous thrombolytic therapy (IVT) is relatively scarce.

The direct-MT trial offered a unique opportunity to answer the above questions as it consisted of an EVT alone arm and a bridging therapy (IVT + EVT) arm; and an Asian cohort which had a relatively high incidence of ICAD-related LVOs. In a post hoc analysis from the trial, Zhang et al. investigated the efficacy and safety of tirofiban use in EVT for patients who presented within a 4.5-h window [3]. The tirofiban group received a loading dose of 0.1–0.4 ug/kg/min over 30 min or 3–12 ug/kg intravenous bolus; followed by intravenous maintenance of 0.1 ug/kg/min for 24 h. Intravenous tirofiban was then discontinued after a 6-h overlap with dual oral antiplatelet therapy. Compared to the 459 (71.8%) patients without tirofiban, the 180 (28.2%) tirofiban recipients had similar rates of 90-day modified Rankin Scale distribution, successful final recanalization rate, outcome lesion volume on computer tomography (CT), and intracranial hemorrhage risk. No significant interaction between tirofiban and recombinant tissue plasminogen activator (rT-PA) was found. The overall rate of symptomatic intracerebral hemorrhage (sICH) was 4.4% (n = 34) according to the main trial [4]. The author thus concluded that tirofiban is a safe option for IVT-eligible patients with LVO undergoing EVT, though a lack of benefits was suggested.

One important message of the study was that tirofiban did not seem to aggravate the risk of safety outcomes when combined with IVT in patients with a good ASPECT score (median 9; IQR 7–10). The study results inferred that IVT should not preclude the use of tirofiban when deemed necessary to sustain recanalization, such as in cases of frequent re-occlusion or emergent stenting. However, the

✉ Simon Chun Ho Yu
simonyu@cuhk.edu.hk

Bonaventure Ip
ipyiuming@gmail.com

Hao Wang
neurology_hao@163.com

[1] Department of Medicine and Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, China

[2] Li Ka Shing Institute of Health Sciences, Faculty of Medicine, Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, China

[3] Department of Interventional Neurology, Linyi People's Hospital, Linyi, China

[4] Department of Imaging and Interventional Radiology, Prince of Wales Hospital, The Chinese University of Hong Kong, 30-32 Ngan Shing Street, Shatin, New Territories, Hong Kong, China

lack of benefit (or harm) with tirofiban should be interpreted with caution, as addressed by the authors. Firstly, the most significant limitations of the study were the non-randomization of tirofiban usage, and the unbalanced baseline characteristics in patients with or without tirofiban use. The tirofiban group had a higher proportion of large artery atherosclerotic LVOs (41.7% vs 7.2%) and emergent stenting (30.6% vs 7.0%); and lower proportion of prior antiplatelet use (11.6% vs 21.1%) and cardioembolism (32.8% vs 49.0%). Therefore, comparison could have been performed between two groups with vastly different risk factor profiles despite statistical adjustment. Secondly, the different perceived re-occlusion risk of ICAD lesions may have led to diverging decisions on tirofiban usage, thus confounding the indication of tirofiban. Thirdly, the unstandardized regimen of tirofiban in the study may also have confounded the comparisons. Lastly, the event rates of safety outcomes were low and the sample size may not be adequately powered to detect statistical significance.

Nevertheless, in conjunction with current literature, tirofiban does seem to be viable for LVO patients due to ICAD/ECAD if required [5], such as rescue stenting. Both randomized and observational data are urgently needed to address unanswered questions regarding tirofiban use, including the pairing with tenecteplase, a standardized regimen, post-tirofiban blood pressure control, as well as its use in late time window, large infarct cores, and posterior circulation lesions.

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Declarations

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