DR. DAVID SEIFFGE (Orcid ID : 0000-0003-3890-3849)

Article type : Commentary

Corresponding author email id: david.seiffge@insel.ch

Minor stroke, major questions: how to treat patients with large vessel occlusion and minor symptoms?

Authors:
David J Seiffge[1] and Johannes Kaesmacher[2]
1 Department of Neurology, Inselspital University Hospital and University of Bern, Switzerland
2 Institute of Diagnostic and Interventional neuroradiology, Inselspital, University Hospital Bern Switzerland

Occlusion of a large intracranial artery (e.g. M1 or proximal M2 segment of the middle cerebral artery, internal carotid artery) deprives vital parts of the brain from blood flow and patients usually experience significant neurological deficits upon hospital presentation. If blood flow is not restored, steady progression and growths of the infarct core in the penumbra[1] will cause severe and irreversible damage. Only a few years ago – some of us will still remember that time before mechanical thrombectomy (MT) became standard of care - we sadly had to discuss indication for decompressive hemicraniectomy to save patients' life from malignant infarction[2] far too often. Since 2015, MT for large vessel occlusion has revolutionized treatment of stroke reperfusion therapy and it is rare that we need to discuss decompressive hemicraniectomy. In patients with severe neurological deficits and large vessel occlusion the decision to use MT is easy and straight forward having in mind its overwhelming benefits[3].

A subset of patients with large vessel occlusion actually presents only with minor symptoms (usually defined as a National Institute of Health Stroke Severity Score, NIHSS <5). This

phenomenon is caused by heterogeneous reasons including good collateral status supplying the penumbra or residual blood flow across a sub-occlusive thrombus. Many of these patients qualify for intravenous thrombolysis and will receive this therapy. However, secondary deterioration due to a lack of reperfusion of the occluded large vessel is frequent and may result in significant morbidity[4, 5]. Patients with large vessel occlusion and minor stroke symptoms (NIHSS<5) have been excluded from most pivotal randomized controlled trials and current guidelines are uncertain about whether or not these patients should receive MT[3].

In this issue of the European Journal of Neurology, Fein and colleagues[6] present novel data to elucidate this burning question of great clinical relevance. The authors combined data from two different prospective cohort studies: Patients with minor stroke and large vessel occlusion who received mechanical thrombectomy were recruited from the prospective German Stroke Registry-Endovascular Treatment (GSR-ET). As comparison group, patients who only received intravenous thrombolysis were extracted from the well-known SITS international thrombolysis registry. The authors performed propensity matching to compare 272 patients with intravenous thrombolysis only with 272 patients who received MT and intravenous thrombolysis. Good functional outcome (modified Rankin scale score of 0-2 at 3 months) was achieved in 77.0% of patients with MTand intravenous thrombolysis compared to 82.9% of patients with intravenous thrombolysis alone (p=0.119). Mortality and intracranial haemorrhage were also not different between both treatment regimens. A second propensity score matching analysis was conducted including patients from GSR-ET regardless whether they received intravenous thrombolysis or not. This larger cohort (624 patients in each group) found that patients receiving MT (rate of intravenous thrombolysis: 56.7%) had lower chance of good outcome (68.2%) compared to patients who received intravenous thrombolysis only from SITS (80.9% good clinical outcome, OR 2.16, 95% CI 1.43-3.28).

The study of Fein and colleagues has several strengths: both datasets originate from large, multi-centre prospective cohort studies in high-income countries offering the full spectrum of current stroke care. They are very likely to reflect current treatment standards at experienced stroke centres across Europe. Limitations inherent to the observational, matched, non-randomized design of this study have been addressed by careful statistical matching. However, this non-randomized comparison is the major limitation as it is very likely, that confounders have contributed to the result and propensity score matching cannot control for unknown and/or unmeasured confounders.

The study of Fein and colleagues shades light on this important topic and challenges the use of MT beyond current evidence from randomized controlled trials[6]. MT is often used in this clinical scenario despite the absence of high-level evidence from randomized controlled trials. The results from Fein and colleagues should encourage recruitment in ongoing trials (MOSTE NCT03796468; ENDOLOW NCT04167527) to maximize their validity and generalizability. Even the best observational study – and Fein and colleagues provide a carefully designed and well conducted example – are no replacement for evidence from randomized controlled trials[7].

Word count: 660/800

7/8 references

References:

1. Dirnagl U, Iadecola C, Moskowitz MA. Pathobiology of ischaemic stroke: an integrated view. *Trends in neurosciences*. Sep 1999;22(9):391-7. doi:10.1016/s0166-2236(99)01401-0

2. van der Worp HB, Hofmeijer J, Jüttler E, et al. European Stroke Organisation (ESO) guidelines on the management of space-occupying brain infarction. *Eur Stroke J*. Jun 2021;6(2):Xc-cx. doi:10.1177/23969873211014112

3. Turc G, Bhogal P, Fischer U, et al. European Stroke Organisation (ESO) - European Society for Minimally Invasive Neurological Therapy (ESMINT) Guidelines on Mechanical Thrombectomy in Acute Ischaemic StrokeEndorsed by Stroke Alliance for Europe (SAFE). *Eur Stroke J*. Mar 2019;4(1):6-12. doi:10.1177/2396987319832140

4. Boulenoir N, Turc G, Henon H, et al. Early neurological deterioration following thrombolysis for minor stroke with isolated internal carotid artery occlusion. *European journal of neurology : the official journal of the European Federation of Neurological Societies*. Feb 2021;28(2):479-490. doi:10.1111/ene.14541

5. Seners P, Perrin C, Lapergue B, et al. Bridging Therapy or IV Thrombolysis in Minor Stroke with Large Vessel Occlusion. *Annals of neurology*. Jul 2020;88(1):160-169. doi:10.1002/ana.25756

6. Feil K, Matusevicius M, Herzberg M, et al. Minor stroke in large vessel occlusion: Matched analysis of German Stroke Registry thrombectomy patients with Safe Implementation of Treatment in Stroke registry thrombolysis patients. *European journal of neurology : the official journal of the European Federation of Neurological Societies*. Feb 4 2022;doi:10.1111/ene.15272

7. Collins R, Bowman L, Landray M, Peto R. The Magic of Randomization versus the Myth of Real-World Evidence. *N Engl J Med*. Feb 13 2020;382(7):674-678. doi:10.1056/NEJMsb1901642

-

MANAGE-PD

Tool for Making Informed Decisions to **Aid Timely Management of Parkinson's Disease**

MANAGE-PD allows you to:

- Identify PD patients inadequately controlled on oral medications
- Determine which patients with PD may be adequately controlled on their current treatment regimen or may require changes to their treatment regimen

Scan the QR code to access to the web

Click here to access to the web

MANAGE-PD is an AbbVie Inc. registered Medical Device. It is a collaborative research and development effort between AbbVie Medical Affairs and Health Economics and Outcomes, the Parkinson's Foundation and an international panel of Movement Disorder Specialists.

PD: Parkinson´s Disease

Parkinson's Foundation

Veeva Code: ABBV-AA-00335-FM Approved: January 2022

abbvie