Clin Neuroradiol
https://doi.org/10.1007/s00062-017-0645-1

REVIEW ARTICLE

Recommendations for Mechanical Thrombectomy in Patients with Acute Ischemic Stroke

A Clinical Guide by the Hellenic Stroke Organization

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Received: 13 October 2017 / Accepted: 25 October 2017

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Published online: 17 November 2017

Abstract This document presents the consensus recommendations of the Hellenic Stroke Organization which can be of assistance to the treating stroke physicians.

Keywords Acute stroke · Thrombectomy · Recommendations

Summary of Recommendations

1. *In patients with significant neurological symptoms due to an ischemic stroke with occlusion of a large vessel of the anterior cerebral circulation, we recommend endovascular treatment (EVT) with mechanical thrombectomy in the first 6 h after the onset of the symptoms (1A). Coexistence of ipsilateral extracranial carotid artery disease is not a contraindication (2B). Beyond the 6-h window, we recommend EVT for selected patients (1A). If no contraindications exist, we recommend that patients are firstly treated with intravenous thrombolysis with alteplase, provided that alteplase can be administered within 4.5 h after the onset of symptoms (1A).*
2. *Patients who are eligible for intravenous thrombolysis should receive alteplase, even if EVT is planned. The EVT should not delay the administration of alteplase, and vice versa, the administration of alteplase should not delay EVT. If the patient is a candidate for mechanical thrombectomy, we do not recommend waiting for clinical improvement after administration of alteplase (1A).*
3. *Patients who, based on the clinical setting, are candidates for EVT should be assessed with urgent intracranial computed tomography (CT) angiography or magnetic resonance angiography (1A). Furthermore, in patients who, based on the clinical setting, are candidates for EVT within the 6–24 h window, we recommended magnetic resonance imaging diffusion-weighted imaging (MRI-DWI) or perfusion CT to select the most suitable patients (1A).*
4. *In cases where intravenous thrombolysis with alteplase is contraindicated, we recommend mechanical thrombectomy as a first-line therapy for patients with acute occlusion of a large vessel of the anterior cerebral circulation (1B).*
5. *When there is an indication for mechanical thrombectomy, we recommend that EVT should be performed immediately without any delay, given that the time period from the onset of symptoms to recanalization is significantly correlated with the patient's clinical outcome (1A).*
6. *Mechanical thrombectomy should aim to achieve TICI (Thrombolysis in Cerebral Infarction) reperfusion grade 2b/3 (1A).*
7. *We recommend the use of stent-retriever devices or aspiration catheters to perform mechanical thrombectomy (1A).*
8. *Mechanical thrombectomy can be performed with the patient either under general anesthesia or conscious sedation. Due to the absence of strong evidence in favor of one of these approaches, the final decision should be made on clinical judgment (2B).*
9. *We recommend the establishment of specialized units that can provide urgent stroke diagnosis and treatment, as well as recruitment of sufficient, specialized and dedicated medical, nursing and paramedical personnel. These centers should offer 24/7 availability of intravenous thrombolysis with alteplase and EVT (1A).*
10. *In the case of acute occlusion of a large vessel of the anterior cerebral circulation in a patient that has an indication for EVT in a hospital that does not offer this treatment option, we recommend to transfer the patient immediately after intravenous thrombolysis to a center where mechanical thrombectomy can be performed (2B).*

Stroke has high incidence and prevalence rates in western societies reaching up to 300–350 new cases annually per 100,000 persons, rendering this syndrome as the third most frequent cause of death and the main cause of disability in the adult population. Among all stroke patients, approximately only one third will regain functionality up to a satisfying grade, one third will not survive the first year and one third will remain significantly disabled, a heavy burden for the patients themselves as well as for the care providers. It becomes clear that stroke constitutes a major public health issue with notable social and economic consequences. In this context, it is necessary to provide the best acute treatment to stroke patients in order to ameliorate the final outcome.

During recent years, a series of well-designed randomized trials were published convincingly showing that in selected stroke patients, the endovascular removal of the obstructing clot with the use of special devices (mechanical thrombec-

This article is a translation of an article previously published in Heart Vessels & Brain (April–June 2017):28–35 (http://83.212.32.147/internalmedicine/images/Guidelines/HSO_EVT_Guidelines_HVS2017.pdf) with kind permission of the authors. The article was translated by Dr. Evangelia Vemmou and Dr. Ilias Nikolakopoulos.

Table 1 Levels of evidence and grades of recommendations

Level of evidence
Level A: randomized trials without significant restrictions or conclusive evidence from observational studies
Level B: randomized trials with significant restrictions or strong evidence from observational studies
Level C: observational studies on patient series or expert opinions
Grade of recommendation
1: The recommendation is powerful as the benefit of the selection clearly outweighs the risk (or vice versa)
2: The recommendation is weak as it is not clear if the benefit of the selection outweighs the risk

tomy or endovascular thrombectomy, EVT) improves outcome.

This document presents the consensus recommendations of the Hellenic Stroke Organization which can be of assistance to the treating stroke physicians. We plan to revise this document every 2 years, or sooner if deemed necessary.

Methodology

The Hellenic Stroke Organization (HSO) is dedicated to promoting stroke medicine, prevention and education in Greece. The development and publication of clinical recommendations adapted to the Greek (Hellenic) stroke care system is an important tool to promote these aims and may serve as a useful clinical guide to practicing stroke physicians. In this context, in 2017 the HSO published two consensus clinical recommendations about a) antithrombotic management in patients with ischemic stroke [1] and b) intravenous thrombolysis in patients with acute ischemic stroke [2]. The present paper presents the HSO clinical recommendations about mechanical thrombectomy in patients with acute ischemic stroke.

The Board of Directors of the HSO considered several Greek stroke scientists as potential leaders of the working group and unanimously selected the first author given his extensive clinical expertise, significant research output and large teaching experience. After accepting the invitation, the leader assembled the core working group which consisted of experienced stroke scientists who prepared the first draft of the document. At the second stage, a larger group of Greek stroke scientists serving in Greece or abroad were invited to comment on and critically contribute to the first draft. The final draft was based on consensus after several rounds of constructive discussions and was agreed by all members of the working group. Due to restricted resources and given that the members of the working group serve in several countries in Europe as well as in the USA, we did not organize joint meetings. No funding or sponsorship or any kind of support was obtained to support the development of this document. This document has also been published in the Greek language in the April–June 2017 issue of the journal *Heart Vessels & Brain*.

The classification of the strength of recommendation and the level of evidence are presented in Table 1.

1. In patients with significant neurological symptoms due to an ischemic stroke with occlusion of a large vessel of the anterior cerebral circulation, we recommend endovascular treatment (EVT) with mechanical thrombectomy in the first 6 h after the onset of the symptoms (1A). Coexistence of ipsilateral extracranial carotid disease is not a contraindication (2B). Beyond the 6-h window, we recommend EVT for selected patients (1A). If no contraindications exist, we recommend that patients are first treated with intravenous thrombolysis with alteplase, provided that alteplase can be administered within 4.5 h after the onset of symptoms (1A). A total of six randomized trials (Table 2) recently showed improved functional outcome in patients treated with EVT with or without preceding intravenous thrombolysis compared to intravenous thrombolysis alone with alteplase or to conservative treatment. The proportion of patients who achieved a favorable clinical outcome (defined as a score 0–2 in the modified Rankin scale at 90 days) with EVT ranged between 33% and 72% [3–8]. These results were confirmed by the HERMES meta-analysis which included data from 1287 patients (634 in the thrombectomy arm, 653 in the control arm) and confirmed the therapeutic benefit of EVT (adjusted pooled odds ratio 2.49, 95% confidence interval CI 1.76–3.53; $p < 0.0001$) [9].

The SWIFT PRIME [4] study included patients up to 4.5 h from the onset of the symptoms, whereas the MR CLEAN [5] and EXTEND-IA [3] studies included patients up to 6 h, REVASCAT [6] up to 8 h and ESCAPE [7] up to 12 h. Notably, only a small number of patients that were included in the trials were treated beyond the 6-h time window. Consequently, the positive results of the studies are valid and applicable mostly for patients who can be treated within the first 6 h from stroke onset. Most patients in the control groups received intravenous thrombolysis with alteplase, provided they could be treated within the time window of 4.5 h.

Recent studies demonstrated that the EVT in the presence of ipsilateral extracranial carotid artery disease is at least as efficient as EVT in patients without ipsilateral extracranial carotid artery disease [10–12]. The results of the DAWN study were recently announced at the 3rd European Stroke Organization Conference in Prague, where it was shown that EVT drastically improved the outcome of patients with ischemic stroke who were treated within the time window of 6–24 h based on MRI-DWI and perfusion CT imaging criteria. In particular, there was a 73% reduc-

Table 2 Summary of the recent randomized trials of mechanical thrombectomy

Trial	Number of patients	Study groups	Primary end point	Modified Rankin score 0–2 at 90 days	Symptomatic intracranial hemorrhage	Mortality
MR CLEAN [5]	500	a. Mechanical thrombectomy or/and intravenous thrombolysis b. Intravenous thrombolysis	Modified Rankin score at 90 days	32.6% vs. 19.1% ($p < 0.001$)	7.7% vs. 6.4% (NS)	21% vs. 22% (NS)
SWIFT-PRIME [4]	196	a. Intravenous thrombolysis and mechanical thrombectomy b. Intravenous thrombolysis	Modified Rankin score at 90 days	60% vs. 36% ($p < 0.001$)	1% vs. 3.4% ($p = 0.12$)	9% vs. 12% ($p = 0.50$)
EXTEND-IA [3]	70	a. Mechanical thrombectomy and intravenous thrombolysis b. Intravenous thrombolysis	Reperfusion at 24 h – Immediate neurological improvement (≥8 grades lowering of NIHSS ή NIHSS: 0–1)	72% vs. 39% ($p = 0.01$)	0% vs. 6% ($p = 0.49$)	9% vs. 20% ($p = 0.18$)
ESCAPE [7]	315	a. Mechanical thrombectomy and intravenous thrombolysis b. Intravenous thrombolysis	Modified Rankin score at 90 days	54% vs. 29% ($p < 0.001$)	3.6% vs. 2.7% ($p = 0.75$)	10.4% vs. 19% ($p = 0.4$)
REVASCAT [6]	206	a. Mechanical thrombectomy and intravenous thrombolysis b. Intravenous thrombolysis	Modified Rankin score at 90 days	43.7% vs. 28.1% ($p < 0.001$)	1.9% vs. 1.9% (p =1.00)	18.4% vs.15.5% ($p = 0.60$)
THRACE [8]	414	a. Intravenous thrombolysis and mechanical thrombectomy b. Intravenous thrombolysis	Proportion of patients with functional independency (modified Rankin score 0–2 at 90 days)	53% vs. 42% ($p = 0.028$)	2% vs. 2% ($p = 0.71$)	12% vs. 13% ($p = 0.70$)

NS not significant

tion of the relative risk for disability (OR 2.1, 95% CI: 1.20–3.12), without any difference in the safety outcomes between the two groups [13].

Patients with basilar artery occlusion were not included in the aforementioned recent EVT trials. There are insufficient data from randomized trials for this group of patients [14, 15]. Data from observational studies showed better outcome in patients if recanalization was achieved [16, 17]. Recanalization rates of >75% with the utilization of stent retrievers were reported [18].

2. Patients who are eligible for intravenous thrombolysis should receive alteplase, even if EVT is planned and EVT should not delay the administration of alteplase, and vice versa, the administration of alteplase should not delay EVT. If the patient is a candidate for mechanical thrombectomy, we do not recommend waiting for clinical improvement after administration of alteplase (1A). In the aforementioned randomized trials of EVT, most patients were treated with intravenous thrombolytic therapy provided they presented within the 4.5-h time window [3–6]. Mechanical thrombectomy was performed immediately without waiting for clinical improvement after intravenous administration of alteplase. A meta-analysis of five studies demonstrated that the time between symptom onset and recanalization is directly correlated to better clinical outcome. In the group of patients who were eligible for EVT, clinical outcome worsened by one point in the modified Rankin scale score for every hour of delay to open the vessel [9, 19].

3. Patients who, based on the clinical setting, are candidates for EVT should be assessed with urgent intracranial CT angiography or MR angiography (1A). Furthermore, in patients who, based on the clinical setting, are candidates for EVT within the 6–24 h window, we recommended MRI-DWI or perfusion CT to select the most suitable patients (1A). In all six aforementioned randomized trials of EVT, patients were eligible for EVT only if an occlusion of a large intracranial arterial segment of the anterior cerebral circulation was diagnosed (internal carotid artery or middle cerebral artery). In this context, apart from the brain CT or MRI, a CT angiography or MR angiography was necessary.

Patients with the following characteristics can be considered as suitable candidates for intracranial vascular imaging based on the trial results:

- Modified Rankin scale score 0–1 before stroke
- National Institutes of Health Stroke Scale (NIHSS) score ≥6 at admission
- ASPECTS (Alberta stroke program early CT) score ≥6.

Patients not fulfilling all of the above criteria had little representation in the recent EVT trials, and hence, benefits for them cannot yet be considered as proven. In this context, for these patients the choice of performing EVT should be based on clinical judgment and individualized on a patient basis. There was a sufficient number of patients older than 80 years in these trials and this age limit should not be considered as a contraindication for EVT.

As previously mentioned, the DAWN study recently showed that EVT significantly improved the outcome of patients with ischemic stroke who were treated in the 6–24 h time window based on MRI-DWI and perfusion CT imaging criteria. Hence, MRI-DWI or perfusion CT should be performed in patients who are candidates for EVT and can be treated in the 6–24 h time window to look for a substantial mismatch.

4. In cases where intravenous thrombolysis with alteplase is contraindicated, we recommend mechanical thrombectomy as a first-line therapy for patients with acute occlusion of a large vessel of the anterior cerebral circulation (1B). With the exception of the SWIFT PRIME study, the aforementioned randomized trials also included patients with contraindications for intravenous thrombolysis. In a meta-analysis of this population (188 patients in 5 studies), the benefit of EVT compared to the control group was confirmed (OR 2.43, 95%CI: 1.30–4.55) [9].

5. When there are indications for mechanical thrombectomy, we recommend that EVT should be performed immediately without any delay, given that the time period from the onset of symptoms to recanalization is significantly correlated with the patient's clinical outcome (1A). In a meta-analysis of the aforementioned randomized trials, it was shown that for every hour of delay of recanalization, the probability of a good outcome was reduced by 19% (OR 0.8, 95% CI, 0.71–0.92) [19]. In this context, it is crucial to organize stroke centers in such a way to minimize any unnecessary delays [20, 21].

6. Mechanical thrombectomy should aim to achieve TICI reperfusion grade 2b/3 (1A). In the aforementioned recent EVT trials, successful reperfusion was defined as TICI score equal to 2b or 3. The use of stent retrievers led to reperfusion rates between 59% and 88%. These studies also showed that optimal reperfusion increased the probability of a good outcome. The highest reperfusion rates were reported in the SWIFT PRIME (88%) and EXTEND-IA (86%) studies and they reflect to the high rates of favorable clinical outcome that were observed in these trials (60% and 71%, respectively). The lowest reperfusion rate (59%) was documented in the MR CLEAN trial, in which favorable clinical outcome was reached only in 33% of patients [3–5]. Non-randomized trials published in 2016 displayed particularly high rates of TICI grade 3 when the stent retriever device was used in combination with a suction device [22].

7. We recommend the use of stent retriever devices or aspiration catheters to perform mechanical thrombectomy (1A). Stent retrievers were used in all patients in the EXTEND-IA, SWIFT-PRIME and REVASCAT trials and in 81.5% and 86.1% of patients in the MR CLEAN and ESCAPE trials, respectively [3–6, 23]. Recently, the ASTER trial reported no difference in the rate of reperfusion between the stent retriever and the contact aspiration arms [24].

8. Mechanical thrombectomy can be performed with the patient either under general anesthesia or conscious sedation. Due to the absence of strong evidence in favor of one of these approaches, the final decision should be made upon clinical judgment (2B). An advantage of conscious sedation is that, compared to general anesthesia, EVTcan be initiated directly without any time delay due to endotracheal intubation. Moreover, arterial pressure and therefore, collateral circulation can be maintained more efficiently at appropriate levels. The disadvantage of conscious sedation is the capacity of the patient to move. In a retrospective subgroup analysis of the MR CLEAN trial, it was shown that the benefit of thrombectomy might not exist if the procedure was performed with the patient under general anesthesia; however, this particular study had limitations [25]. On the contrary, two more recent randomized single center trials showed no difference in clinical

outcome between the two methods [25–27]. Randomized multicenter trials are warranted to clarify which is the optimal approach.

9. We recommend the establishment of specialized units that can provide urgent stroke diagnosis and treatment, as well as recruitment of sufficient, specialized and dedicated medical, nursing and paramedical personnel. These centers should offer 24/7 availability of intravenous thrombolysis with alteplase and EVT (1A). Hospitalization of stroke patients in organized dedicated stroke units is associated with improved clinical outcomes compared to standard ward care, irrespective of patient age, gender, stroke type or stroke severity. Current endovascular reperfusion therapies lead to high rates of recanalization and favorable clinical outcome and low rates of complications, corresponding to a number needed to treat (NNT) of 3–4 to avoid permanent disability [9].

After the convincing results of the recent EVT trials, it seems mandatory to establish well-organized stroke centers that can offer EVT on a 24/7 basis and can treat large numbers of patients [28]. These stroke centers should be based on multidisciplinary and multispecialty teams consisting of a) properly trained nursing and paramedical personnel, b) stroke physicians and c) stroke interventionalists, who are typically interventional neuroradiologists well-trained in acute stroke or alternatively other physicians who have been sufficiently trained in carrying out endovascular procedures and in particular EVT.

10. In cases of acute occlusion of a large vessel of the anterior cerebral circulation in a patient that has indications for EVT in a hospital that does not provide this treatment option, we recommend to transfer the patient immediately after intravenous thrombolysis to a center where mechanical thrombectomy can be performed (2B). The randomized trials of EVT also included patients initially diagnosed at hospitals without facilities to perform EVT who were subsequently transferred to EVT centers. The transferring process should be based on a well-organized protocol to ensure the rapid transfer of the patient with the maximum possible safety and support.

Acknowledgements We would like to thank Dr. Evangelia Vemmou and Dr. Ilias Nikolakopoulos for their editorial support.

Conflict of interest P. Papanagiotou: local principal investigator, SWIFT PRIME study; consultant services, Penumbra and Johnson&Johnson. T. Rizos received consulting fees, speakers fees and travel support from BMS Pfizer, Boehringer Ingelheim, Bayer HealthCare and Daiichi Sankyo, outside the submitted work. G. Ntaios, V. Papavasileiou, K. Psychogios, M. Psychogios, A. Mpotsaris, K. Spengos, M. Gravanis, S. Vassilopoulou, C. Gkogkas, P. Zampakis, P. Zis, A. Karantanas, M. Karygiannis, G. Karydas, E. Korompoki, K. Makaritsis, K. Marmagkiolis, H. Milionis, D. Mitsikostas, D. Nikas, A. Plomaritoglou, M. Politi, N. Ptochis, C. Savopoulos, K. Takis, N. Tsamopoulos, D. Tsetis, A. Hatzidakis, A. Chatziioannou, A. Hatzitolios and K. Vemmos declare that they have no competing interests.

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