

European Stroke Organisation (ESO)- European Society for Minimally Invasive Neurological Therapy (ESMINT) guidelines on mechanical thrombectomy in acute ischemic stroke

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ABSTRACT

Background Mechanical thrombectomy (MT) has become the cornerstone of acute ischemic stroke management in patients with large vessel occlusion (LVO). The aim of this guideline document is to assist physicians in their clinical decisions with regard to MT. **Methods** These guidelines were developed based on the standard operating procedure of the European Stroke Organisation, and followed the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach. An interdisciplinary working group identified 15 relevant questions, performed systematic reviews and meta-analyses of the literature, assessed the quality of the available evidence, and wrote evidence based recommendations. Expert opinion was provided if not enough evidence was available to provide recommendations based on the GRADE approach.

Results We found high quality evidence to recommend MT plus best medical management (BMM, including intravenous thrombolysis whenever indicated) to improve functional outcome in patients with LVO related acute ischemic stroke within 6 hours after symptom onset. We found moderate quality of evidence to recommend MT plus BMM in the 6–24 hour time window in patients meeting the eligibility criteria of published randomized trials. These guidelines further detail aspects of prehospital management, patient selection based on clinical and imaging characteristics, and treatment modalities.

Conclusions MT is the standard of care in patients with LVO related acute stroke. Appropriate patient selection and timely reperfusion are crucial. Further randomized trials are needed to inform clinical decision making with regard to the mothership and drip-and-ship approaches, anaesthesia modalities during MT, and to determine whether MT is beneficial in patients with low stroke severity or large infarct volume.

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Table 1 Synoptic table of PICO questions, evidence based recommendations, and expert opinions

PICO question	Recommendations	Expert opinion
PICO 1: For adults with LVO related acute ischemic stroke within 6 hours of symptom onset, does MT plus BMM compared with BMM alone improve functional outcome?	In adults with anterior circulation LVO related acute ischemic stroke presenting within 6 hours after symptom onset, we recommend MT plus BMM, including IVT whenever indicated, over best BMM alone to improve functional outcome. Quality of evidence: High ⊕⊕⊕⊕ Strength of recommendation: Strong ↑↑	There is a consensus among the guideline group (11/11 votes) that patients with M2 occlusion fulfilled the inclusion criteria in most randomized trials and therefore MT is reasonable in this situation. There is a consensus among the panel (11/11 votes) that in analogy to anterior circulation LVO and with regard to the grim natural course of basilar artery occlusions, the therapeutic approach with IVT plus MT should strongly be considered.
PICO 2: For adults with LVO related acute ischemic stroke 6–24 hours from time last seen normal, does MT plus BMM compared with BMM alone improve functional outcome?	In adults with anterior circulation LVO related acute ischemic stroke presenting between 6 and 24 hours from time last known well and fulfilling the selection criteria of DEFUSE-3 or DAWN, we recommend MT plus BMM over BMM alone to improve functional outcome. Quality of evidence: Moderate ⊕⊕⊕ Strength of recommendation: Strong ↑↑	Patients should be treated with MT plus BMM up to approximately 7 hours and 18 min after stroke onset, without the need of perfusion imaging based selection. 10/11 experts agree that patients can be treated in the 6–12 hour time window if they fulfill the ESCAPE criteria, notably ASPECTS ≥6 and moderate to good collateral circulation. However, such patients should preferably be treated in the context of clinical studies. Also, concurrent software applications utilizing similar perfusion algorithms and rendering equivalent volumetry results as those used in the DAWN and DEFUSE-3 trials may be options, as well as simple volumetry on a high quality DWI scan for core volume when applying DAWN criteria. Therefore we advocate further research, inclusion of patients into late window trials, and implementation of institutional imaging standard operating procedures.
PICO 3: For adults with LVO related acute ischemic stroke, does IVT plus MT compared with MT alone improve functional outcome?	<ul style="list-style-type: none"> ▶ In LVO related ischemic stroke patients eligible for both treatments, we recommend IVT plus MT over MT alone. Both treatments should be performed as early as possible after hospital arrival. MT should not prevent the initiation of IVT, and IVT should not delay MT. Quality of evidence: Very low ⊕, Strength of recommendation: Strong ↑↑ <ul style="list-style-type: none"> ▶ In LVO related ischemic stroke patients not eligible for IVT, we recommend MT as standalone treatment. Quality of evidence: Low ⊕⊕, Strength of recommendation: Strong ↑↑	In LVO related ischemic stroke patients eligible for IVT before MT, 7/11 experts suggest the use of tenecteplase (0.25 mg/kg) over alteplase (0.9 mg/kg) if the decision on IVT is made after vessel occlusion status is known.
PICO 4: For adults with suspected acute stroke does the use of a prehospital scale compared with no prehospital scale: <ul style="list-style-type: none"> ▶ improve identification of patients eligible for MT? ▶ reduce time to reperfusion? 	In patients with suspected stroke, we cannot make a recommendation on the use of a prehospital scale for improving identification of patients eligible for MT. We suggest enrolling patients in a dedicated randomized controlled trial, whenever possible. Quality of evidence: Very low ⊕, Strength of recommendation: -	<ul style="list-style-type: none"> ▶ 11/11 experts concluded that there is currently not enough evidence to use a clinical scale in routine care to help triage potential thrombectomy candidates in the prehospital field. ▶ All patients suspected of having an acute stroke, irrespective of the time of onset, should undergo emergency imaging of the brain, including vascular imaging.
PICO 5: For adults identified as potential candidates for MT in the prehospital field, does the mothership model, compared with the drip-and-ship model, improve functional outcome?	We cannot make recommendations on whether for adults identified as potential candidates for MT in the prehospital field, the mothership or the drip-and-ship model should be applied to improve functional outcome. Quality of evidence: Very Low ⊕, Strength of recommendation: -	<ul style="list-style-type: none"> ▶ As there is lack of strong evidence for superiority of one organizational model, the choice of model should depend on local and regional service organization and patient characteristics (vote: 11/11 experts agree). ▶ The mothership model might be favored in metropolitan areas, with transportation time to a comprehensive stroke center of <30–45 min and the use of the drip-and-ship model when transportation times are longer (vote: 11/11 experts agree). ▶ As there is limited experience with the other two models (drip-and-drive, and mobile stroke unit) no expert opinion can be provided when to use these models (vote: 11/11 experts agree).
PICO 6: For patients aged 80 years or more with LVO related acute ischemic stroke, does MT plus BMM compared with BMM alone improve functional outcome?	<ul style="list-style-type: none"> ▶ We recommend that patients aged 80 years or more with LVO related acute ischemic stroke within 6 hours of symptom onset should be treated with MT plus BMM, including IVT whenever indicated. Application of an upper age limit for MT is not justified. Quality of evidence: Moderate ⊕⊕⊕, Strength of recommendation: Strong ↑↑ <ul style="list-style-type: none"> ▶ We suggest that patients aged 80 years or more with LVO related acute ischemic stroke between 6 and 24 hours from time last known well should be treated with MT plus BMM if they meet the eligibility criteria of the DEFUSE-3 or DAWN trials. Quality of evidence: Low ⊕⊕, Strength of recommendation: Weak ↑?	

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Table 1 Continued

PICO question	Recommendations	Expert opinion
PICO 7: For adults with LVO related acute ischemic stroke, does selection of MT candidates based on a particular ASPECTS or infarct core volume threshold compared with no specific threshold improve functional outcome?	<ul style="list-style-type: none"> ▶ We do not recommend an upper NIHSS score limit for decision making on MT. We recommend that patients with high stroke severity and LVO related acute ischemic stroke be treated with MT plus BMM, including IVT whenever indicated. These recommendations also apply for patients in the 6–24 hour time window, provided that they meet the inclusion criteria for the DAWN or DEFUSE-3 studies. <p>Quality of evidence: High ⊕⊕⊕⊕, Strength of recommendation: Strong ↑↑.</p> <ul style="list-style-type: none"> ▶ We recommend that patients with low stroke severity (NIHSS 0–5) and LVO related acute ischemic stroke within 24 hours from time last seen normal be included in randomized controlled trials comparing MT plus BMM vs BMM alone. <p>Quality of evidence: Very low ⊕, Strength of recommendation: -.</p>	<p>In patients with a low NIHSS score (0–5) who are not eligible for a dedicated randomized controlled trial, we suggest that treatment with MT in addition to IVT (or alone in case of contraindication to IVT) may be reasonable:</p> <ul style="list-style-type: none"> ▶ in patients with deficits that appear disabling (eg, significant motor deficit or aphasia or hemianopia) at presentation (vote: 9/11 experts) ▶ in the case of clinical worsening despite IVT (vote: 9/11 experts) ▶ we did not reach a majority vote to suggest MT in patients with deficits that appear non-disabling (eg, mild hypoesthesia) at presentation (vote: 5/11 experts)
PICO 8: For adults with LVO related acute ischemic stroke, does selection of MT candidates based on a particular ASPECTS or infarct core volume threshold compared with no specific threshold: <ul style="list-style-type: none"> ▶ improve identification of patients with a therapy effect of MT on functional outcome? ▶ decrease the risk of symptomatic intracerebral hemorrhage? 	<ul style="list-style-type: none"> ▶ In the 0–6 hour time window, we recommend MT plus BMM (including IVT whenever indicated) over BMM alone in LVO related anterior circulation stroke patients without evidence of extensive infarct core (eg, ASPECTS ≥6 on non-contrast CT scan or infarct core volume ≤70 mL). <p>Quality of evidence: High ⊕⊕⊕⊕, Strength of recommendation: Strong ↑↑.</p> <ul style="list-style-type: none"> ▶ In the 6–24 hour time window, we recommend MT plus BMM (including IVT whenever indicated) over BMM alone in LVO related anterior circulation stroke patients fulfilling the selection criteria of DEFUSE-3 or DAWN, including estimated volume of infarct core. <p>Quality of evidence: Moderate ⊕⊕⊕, Strength of recommendation: Strong ↑↑.</p> <ul style="list-style-type: none"> ▶ We recommend that anterior circulation stroke patients with extensive infarct core (eg, ASPECTS <6 on non-contrast CT scan or core volume >70 mL or >100 mL) be included in randomized controlled trials comparing MT plus BMM vs BMM alone. <p>Quality of evidence: Very low ⊕, Strength of recommendation: -.</p>	<p>If inclusion of the patient in a dedicated randomized controlled trial is not possible, we suggest that treatment with MT may be reasonable on an individual basis in selected cases with ASPECTS <6 or core volume >70 mL (11/11 experts agree). Patient selection criteria might include age, severity and type of neurological impairment, time since symptom onset, location of the ischemic lesion on plain CT scanner or MRI, and results of advanced imaging, notably perfusion–core mismatch.</p>
PICO 9: For adults with LVO related acute ischemic stroke, does selection of MT candidates based on advanced perfusion, core, or collateral imaging compared with no advanced imaging: <ul style="list-style-type: none"> ▶ improve identification of patients with a therapy effect of MT on functional outcome? ▶ decrease the risk of symptomatic intracerebral hemorrhage? 	<ul style="list-style-type: none"> ▶ In adult patients with anterior circulation LVO related acute ischemic stroke presenting from 0 to 6 hours from time last seen normal, advanced imaging is not necessary for patient selection. <p>Quality of evidence: Moderate ⊕⊕⊕, Strength of recommendation: Weak ↓?</p> <ul style="list-style-type: none"> ▶ In adult patients with anterior circulation LVO related acute ischemic stroke presenting beyond 6 hours from time last seen normal, advanced imaging selection is necessary. <p>Quality of evidence: Moderate ⊕⊕⊕, Strength of recommendation: Strong ↑↑.</p>	
PICO 10: For adults with LVO related acute ischemic stroke, does MT performed in a comprehensive stroke center compared with MT performed outside of a comprehensive stroke center: <ul style="list-style-type: none"> ▶ improve functional outcome? ▶ reduce time to reperfusion? ▶ reduce the rate of symptomatic intracerebral hemorrhage? 	<ul style="list-style-type: none"> ▶ In adult patients with LVO related acute ischemic stroke, we recommend treatment in a comprehensive stroke center. <p>Quality of evidence: Very low ⊕, Strength of recommendation: Strong ↑↑.</p>	
PICO 11: For adults with LVO related acute ischemic stroke, does reperfusion TICI grade 3 compared with reperfusion TICI grade 2b improve functional outcome?	<p>For adults with LVO related acute ischemic stroke, we recommend that interventionalists should attempt a TICI grade 3 with reperfusion, if achievable with reasonable safety.</p> <p>Quality of evidence: Low ⊕⊕, Strength of recommendation: Strong ↑↑.</p>	

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Table 1 Continued

PICO question	Recommendations	Expert opinion
PICO 12: For adults with LVO related acute ischemic stroke, does MT using direct aspiration compared with a stent retriever: ► improve functional outcome? increase the rate of complete reperfusion?	<ul style="list-style-type: none"> ► There is currently no evidence that contact aspiration alone improves functional outcome compared with BMM in patients undergoing MT. ► There is currently no evidence that contact aspiration alone increases the rate of reperfusion over thrombectomy using a stent retriever. ► Therefore, we suggest the use of a stent retriever over contact aspiration alone for MT in patients with acute ischemic stroke. Quality of evidence: Very low ⊕; Strength of recommendation: Weak ↑?	9/11 experts believe that ADAPT may be used as standard firstline treatment, followed by stent retriever thrombectomy as rescue therapy if needed. Besides, <ul style="list-style-type: none"> ► We did not reach a majority vote on that distal aspiration should be used only in combination with a stent retriever (3/11 experts) ► 8/11 experts believe that any MT procedure should be performed preferably in conjunction with a proximal balloon guide catheter.
PICO 13: For adults with LVO related acute ischemic stroke undergoing MT, does conscious sedation compared with general anesthesia improve functional outcome?	We cannot provide recommendations to use general anesthesia or conscious sedation in patients undergoing MT, due to a low quality of evidence and conflicting results between 3 small single center randomized clinical trials and the best available observational evidence. Therefore, we recommend the enrollment of patients in multicenter randomized controlled trials addressing this question. Quality of evidence: Very low ⊕, Strength of recommendation: -	We suggest that further randomized multicentric data with less bias should be generated. However, if inclusion of the patient in a randomized controlled trial is not possible, 11/11 experts suggest that local anesthesia or conscious sedation may be favored over general anesthesia, if the patient is able to undergo MT without general anesthesia. On the other hand, general anesthesia does not need to be avoided if indicated. The decision for or against general anesthesia should be made rapidly and delays to induction of general anesthesia should be minimized. We suggest that, according to the three randomized controlled trials, a specialized neuroanesthesiological or neurocritical care team should perform the general anesthesia procedure, whenever possible. Excessive blood pressure drops should be avoided (see PICO question 14). Adequate monitoring of vital parameters of patients under conscious sedation or local anesthesia is also advised.
PICO 14: For adults with LVO related acute ischemic stroke undergoing MT, does maintaining blood pressure to a particular target compared with an alternative target improve functional outcome?	<ul style="list-style-type: none"> ► We suggest to keep blood pressure below 180/105 mmHg during and 24 hours after MT. No specific blood pressure lowering drug can be recommended. Quality of evidence: Very low ⊕, Strength of recommendation: Weak ↑? <ul style="list-style-type: none"> ► During MT, systolic blood pressure drops should be avoided. Quality of evidence: Very low ⊕, Strength of recommendation: Strong ↓↓	11/11 experts think that the degree of reperfusion should be taken into account in the choice of a blood pressure target after MT, with a lower blood pressure target in case of complete reperfusion.
PICO 15: For adults with LVO related acute ischemic stroke and high grade ipsilateral extracranial carotid stenosis, does cervical stenting in addition to MT compared with MT alone improve functional outcome?	<ul style="list-style-type: none"> ► No recommendation can be provided regarding which treatment modality should be favored in patients with LVO related acute ischemic stroke and associated extracranial carotid artery stenosis or occlusion. We recommend the inclusion of such patients in dedicated randomized controlled trials. Quality of evidence: Very low ⊕, Strength of recommendation: -	9/11 experts suggest that if inclusion in a dedicated randomized controlled trial is not possible, patients with high grade stenosis or occlusion may be treated with intraprocedural stenting if unavoidably needed.

ADAPT, a direct aspiration first pass technique; ASPECTS, Alberta Stroke Program Early CT Score; BMM, best medical management; DAWN trial, Diffusion Weighted Imaging or Computerized Tomography Perfusion Assessment with Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention with Trevo; DEFUSE-3 trial, Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3; DWI, diffusion weighted imaging; ESCAPE, Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times; IVT, intravenous thrombolysis; LVO, large vessel occlusion; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; PICO, Population, Intervention, Comparison, Outcome; TICI, Thrombolysis in Cerebral Infarction.