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REVIEW

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Endovascular Treatment in Acute Ischemic Stroke: From Randomized Studies to Current Treatments

Akut İskemik İnmeli Hastalarda Endovasküler Tedavi: Randomize Kontrollü Çalışmalardan, Güncel Tedavi Önerilerine

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ABSTRACT

Rapid advances have been made in the treatment of acute ischemic stroke over the last 3 decades. Endovascular treatments have become the gold standard treatment in patients with large vessel occlusion, especially in the presence of penumbra, but due to the nature of ischemic stroke, it has become necessary to make treatment decisions in many controversial patient groups such as patients with distal occlusions and lpatients with arge core infarct. It is aimed to achieve good clinical results in more patients through national and international guidelines created all over the world. In this review written about the endovascular treatment of acute ischemic stroke, where there have been very rapid developments in recent years, large studies, meta-analyses and recommendations in international guidelines on this subject are summarized and recommendations are tried to be made for our country.

Keywords: Acute ischemic stroke, mechanical trombectomy, endovascular treatment.

ÖZ

Akut İskemik inmenin tedavisinde son 3 dekat boyunca hızlı gelişmeler kaydedilmiştir. Endovasküler tedaviler büyük damar oklüzyonu olan hastalarda özellikle penumbra varlığında altın standart tedavi olarak yer buldu, ancak iskemik inmenin doğası gereği daha distal oklüzyonlar, geniş infarkt alanı olan hastalar gibi birçok tartışmalı hasta grubunda tedavi kararları almak gerekliliği oluşmuştur. Tüm dünyada oluşturulan ulusal ve uluslararası rehberler aracılığı ile daha fazla hastada iyi klinik sonuçlara ulaşmak hedeflenmektedir. Son yıllarda çok hızlı gelişmelerin olduğu akut iskemik inmenin endovasküler tedavisi hakkında yazılan bu derleme ile, bu konuda yapılan büyük çalışmalar, metaanalizler ve uluslararası rehberlerdeki öneriler özetlenmiş ve ülkemiz için öneriler oluşturulmaya çalışılmıştır.

Anahtar Kelimeler: Akut iskemik inme, mekanik trombektomi, endovasküler tedavi.

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INTRODUCTION

Over the past three decades, rapid progress has been made in the treatment of acute ischemic stroke. In 2006, IV (intravenous) thrombolytic therapy was approved and started to be used in patients with acute ischemic stroke in Turkey. With the publication of the MR Clean study in 2014, mechanical thrombectomy has become the gold standard treatment for patients with large artery occlusion.[1] In our country too, mechanical thrombectomy is performed in many centres for the treatment of patients with acute ischemic stroke. In the last decade, many improvements have been made in the planning, patient selection, and implementation of endovascular treatment for acute ischemic stroke. Therefore, it has become necessary to prepare a guide for the planning of endovascular treatment of patients with acute ischemic stroke, taking into account the conditions of our country. The objective of this review is to provide recommendations regarding organization, patient selection, patient care and treatment planning for the endovascular treatment of patients with acute ischemic stroke. The selection of the authors for the review was made by the Interventional Neurology Working Group of the Turkish Neurological Society. Multicenter studies for each topic were summarised, recommendations in the AHA/ASA and ESO guidelines were referred to where available, and finally recommendations for our country were formulated.

ENDOVASCULAR TREATMENT OF ACUTE ISCHEMIC STROKE PATIENTS WITH LARGE VESSEL OCCLUSION IN THE FIRST 6 HOURS

Stroke is the major cause of disability worldwide and the second leading cause of mortality after ischemic heart disease. Early diagnosis and rapid treatment are essential to prevent and/or minimise morbidity and mortality in this condition that affects all social processes. This section summarizes the current recommendations for endovascular treatment of patients with large vessel occlusion in the first 6 hours following symptom onset according to current international guidelines.

Recombinant tissue plasminogen activator (rt-PA), which was approved by the FDA in the early 1990s and revolutionized the treatment of acute ischemic stroke, is currently recommended as a Class IA therapy in the guidelines.[2,3] However, the limited therapeutic window, poor efficacy in patients with high thrombus burden and contraindications such as recent surgery, coagulation abnormalities and a history of intracranial hemorrhage have led to the need for intra-arterial therapies. Mechanical thrombectomy (MT), as opposed to pharmacological fibrinolysis, is based on recanalisation of the occluded vessel by aspiration or retrievable stents.[4]

MAIN POINTS

- The gold standard treatment for acute ischemic stroke patients with large vessel occlusion is endovascular treatment.
- Patient selection is critical according to recommendations from clinical studies on endovascular treatment of patients with acute ischemic stroke.
- In the endovascular treatment of patients with acute ischemic stroke, not only technical success but also pre-hospital and emergency room organization and post-procedure follow-up are important.

Mechanical thrombectomy (MT) first introduced with MERCI (Concentric Medical, Mountain View, USA) followed by the Penumbra system (Penumbra, Alameda, USA).[5] These devices were evaluated in the Multi-MERCI and PENUMBRA trials.[6] The efficacy of the Penumbra System was demonstrated in a prospective single-arm study (Penumbra Pivotal Stroke Study, 2009) in 125 patients who were admitted within the first 8 hours. Successful recanalisation was 82% in Penumbra compared to 69% in Multi-MERCI. However, clinical outcomes were poor with only 25% having a 90-day mRS ≤ 2. The mortality rate (33%) and the rate of complications (12.8%) were high.[5]

Subsequently published randomised controlled trials such as SYNTHESIS, MR RESCUE and IMSIII have also failed to show the benefit of MT [5-7]. Following a series of trials in 2015, these devices led to the development of a second generation stent retriever that would change the standard of treatment in stroke patients with acute large vessel occlusion (BDO). Randomised controlled trials with the second generation of thrombectomy devices, including the first one MR CLEAN, ESCAPE, SWIFT PRIME, EXTEND-IA and REVASCAT, have all focused on the anterior system. ESCAPE had the longest inclusion framework, 12 hours from symptom onset. SWIFT PRIME, MR CLEAN and EXTEND-IA included patients up to six hours from symptom onset, whereas REVASCAT included patients up to 8 hours.[1,8-11] However, a HERMES meta-analysis was published to address the heterogeneity of these trials in subgroups (late admission to treatment, advanced age, mild mRS elevation before the procedure, and ineligibility for Intravenous (IV) thrombolytic (IVT)) and to demonstrate the efficacy of MT in different populations that were included. In this analysis, patients with anterior system BDO who were admitted within the first 12 hours were randomised to receive MT or standard treatment (ST). The primary outcome was reduced disability compared to mRS at day 90, and the secondary outcomes were functional independence, mortality and symptomatic hemorrhage at the 3rd month. Functional disability on day 90 was significantly lower in the MT group compared to the ST group (cOR 2.49, 95% CI 1.76-3.53; P<.0001). For one patient, the number needed to treat with MT to reduce disability by at least one level on the mRS was 2.6. There was no difference in the risk of 3rd month mortality, parenchymal hematoma, and symptomatic intracranial hemorrhage.[12] Another post-Hermes meta-analysis showed that MT was most beneficial when performed within 7 hours and 18 minutes. This reinforced the idea that time is of the essence and, similar to IVT, emphasis has been put on rapid recanalisation and reperfusion to achieve good functional independence in MT.[7,13]

All of these studies have shown that acute MT treatment of proximal occlusions of the anterior system within the first 6 hours after stroke onset is effective and safe, and it has been included in the guidelines as a treatment option at class IA evidence level for the treatment of acute ischemic stroke. In the updated 2019 AHA/ASA (American Heart Association/American Stroke Association) guidelines, MT with stent retriever is recommended in patients who meet the following criteria: preprocedural mRS 0-1; proximal vessel occlusion (ICA or MCA M1); ≥ 18 years of age; NIHSS ≥ 6; ASPECTS ≥ 6 in patients admitted within the first six hours. (Class-I, Level of Evidence A). It is recommended that MT be administered with IV alteplase in eligible patients (Class-I, Level of Evidence A).[3]

Population Intervention Comparator Outcome (PICO) questions of the European Stroke Organisation (ESO) and the European Society for Minimally Invasive Neurological Therapy (ESMINT) were answered by the ESO Guideline Committee, the ESMINT Guideline Committee, and the ESO and ESMINT Executive Committees. They were presented as recommendations or expert opinions with analyses of the available evidence and evidence-based recommendations.[14] This guideline also recommended best medical treatment (including IVT when indicated) in combination with MT, rather than best medical treatment alone, to improve functional outcome in adults with anterior BDO-related acute ischemic stroke occurring within the first six hours (Very high quality evidence, Strong recommendation).

-Apart from the above criteria, MT was presented as a weak recommendation in the case of mRS score >1, ASPECTS <6 or NIHSS score <6 before admission (Class-IIb, Level of Evidence BR) (3); ESO/ESMINT asked as separate PICOs and it was stated that it could be applied in the presence of examination findings causing disability such as aphasia or hemiparesis or in the case of deterioration despite IVT as an expert opinion instead of a recommendation due to very low evidence quality in patients with NIHSS <5. In the case of ASPECTS <6 or core volume >70 mL or >100 mL on non-contrast CT, it was stated that MT may be appropriate on an individual basis in selected cases as an expert opinion rather than a recommendation due to the very low quality of the evidence.[14]

Recommendation

Patients over 18 years of age with an mRS score of 0-1 and an admission NIHSS score of ≥ 6 who are admitted within the first six hours should be urgently taken under MT process if ASPECTS ≥ 6 and BDO (ICA or MCA M1) are detected. IVT should be initiated in eligible patients without delaying the pre-MT evaluation process.

ENDOVASCULAR TREATMENT IN AN ACUTE ISCHEMIC STROKE PATIENT BETWEEN 6-24 HOURS AFTER LAST TIME OF NORMAL APPEARANCE

Although the standard treatment window is considered to be 0-6 hours, it is known that the ischemic penumbra can survive for a longer period in some patients. Wake-up strokes and acute ischemic stroke patients admitted after six hours account for approximately 14-27% of all strokes.[15] This has highlighted the potential for late-admitted patients to benefit from MT.

Two RCTs published in 2018; DAWN and DEFUSE 3 trials demonstrated that MT was safe and effective within 6-24 hours and 6-16 hours in acute ischemic stroke.[15,17] Both trials were stopped early due to significantly good outcomes in the MT group.

DAWN Trial

In the DAWN study published in 2018[16], 206 patients were randomised on the basis of clinical and imaging mismatch within 6-24 hours. The rate of functional independence at the 3rd month was significantly higher in the MT group (49% vs 13%, P<.001). No difference was found in mortality and symptomatic intracranial hemorrhage (sICH). NNT (number of patients to be treated for one person to benefit): 2.8 (Table 1).

DEFUSE 3 Trial

In the DEFUSE 3 study published in 2018[17], 182 patients were randomised in the 6-16 hour interval with perfusion infarct mismatch criteria. Functional independence at the 3rd month was higher in the MT group (45% vs 17%, P<.001) and mortality was lower (14% vs 26%, P=.05). There was no significant difference for sICH. NNT: 3.6 (Table 1). Considering that the median infarct volumes in both trials were small (7-10 ml), it is inevitable that patients with small infarct area, late admission and selected with appropriate criteria will benefit clinically from MT.

MR CLEAN-LATE Trial

In the MR CLEAN-LATE Trial published in 2023 535 patients were randomised using criteria that assessed collateral flow within 6-24 hours. At the 3rd month, the mRS score improved significantly in the MT group. However, sICH was higher in the MT group (7% vs 2%, P<.05). No mortality difference was found (Table 1). In the two-year follow-up results of the MR CLEAN-LATE trial, it was found that the improvement in mRS score continued in favour of the MT group (median mRS 4-6), and mortality increased in the control group (34%-41%), although not to a significant extent.[19] The MR CLEAN-LATE trial and two-year follow-up results show that MT improves functional outcome in patients with evidence of collateral flow in the 6-24 hour time frame and that this effect is sustained for at least 2 years, but may increase the risk of symptomatic intracerebral hemorrhage.

Table 1: Specifications of DAWN,[16] DEFUSE 3[17] ve MR CLEAN-LATE[18] trials

	DAWN	DEFUSE 3	MR CLEAN-LATE
Number of Participants	206 (107/99)	182 (92/90)	535 (268/267)
Inclusion Criteria	6-24 hours Clinical deficit-infarct mismatch >80 y, NIHSS >10; infarct <21 ml or <80 y, NIHSS >10; infarct <31ml or <80 y, NIHSS >20; infarct 31-51ml	6-16 hours NIHSS > 7 Perfusion mismatch Infarct <70 ml and Mismatch ratio 15 >1,8 and Mismatch volume >ml	6-24 hours NIHSS score ≥2 Presence of collateral flow
Imaging	CT perfusion or MR diffusion (RAPID)	CT perfusion or MR diffusion (RAPID)	CT/CT angiography
mRS 0-2 on Day 90	49% / 13% P<.001	45% / 17% P<.001	%39 / 34% P=.35
Mortality	19% / 18% P=.99	%14 / 26% P=.05	24% / 30%
Symptomatic Intracranial Hemorrhage	%6 / 3% P=.50	7% / 4% P=.75	7% / 2% P<.05

Note: The numerical data refer to the MT and the medical group, respectively

Following the DAWN and DEFUSE 3 trials, international guidelines for the treatment of acute ischaemic stroke began to recommend MT in BDO patients admitted after 6 hours (Table 2).

Table 2. Endovascular treatment guideline recommendations for patients admitted between 6-24 hours

Guideline	Therapeutic Window	Recommendation Level	Patient Selection Criteria
AHA/ASA (2019)(3)	6-16 hours	Class I Evidence level A	DAWN / DEFUSE 3 criteria
	16-24 hours	Class IIa Evidence Level B-R	DAWN criteria
NICE (2019)(20)	6-24 hours	Is recommended	Identification of salvageable tissue (BTP/DWI-MRG)
ESO/ESMINT (2019) (21)	6-24 hours	Strong recommendation Mid-level evidence	DAWN / DEFUSE 3 criteria
Australia (2020) (22)	< 24 hours	Strong recommendation	Patient-centered decision
Japan (2021)	6-16 hours	Level A Mid-level evidence	On the basis of clinical and imaging data
	16-24 hours	Level B Mid-level evidence	
Canada (2022)(23)	6-24 hours	Strong recommendation High evidence level	ASPECT >5 ve good collateral / DEFUSE 3 / DAWN criteria

Recommendations

In acute stroke treatment, the focus is on tissue-based rather than time-based patient selection. Patients should be considered eligible for MT if they have salvageable tissue at 6-24 hours. Taking into account individual factors and imaging findings, MT can be performed in late-admitted stroke patients. Evidence from randomised trials suggests that functional improvement is achieved within 6-24 hours in appropriately selected patients.

- Referral schemes and algorithms should be in place for acute ischemic stroke patients.
- Patients with an NIHSS > 10 should be referred to a comprehensive stroke center as soon as possible
- Patients who fulfil the criteria for DAWN/DEFUSE 3 should be treated with MT
- In the absence of software programs, mismatch can be assessed with CT perfusion / DWI-MRI.
- If it is not possible to assess the mismatch, young patients with an ASPECT > 7 on admission and good collaterals should be considered for MT
- Pre-stroke mRS and comorbidities should be taken into account
- Care should be taken regarding the risk of reperfusion injury (sICH)

Endovascular Treatment of an Acute Ischemic Stroke Patient with Distal Medium Vessel Occlusion

Distal medium vessel occlusions (MeVO) account for 25-40% of acute ischemic strokes and there is still uncertainty regarding the indication for endovascular therapy (EVT).[20] The current AHA/ASA (American Stroke Association/American Heart Association) guideline states: "Although the benefit is uncertain, mechanical thrombectomy using retractable stents is reasonable in carefully selected patients with acute ischemic stroke who can be punctured within the first 6 hours and whose site of occlusion is MCA M2 or M3, ACA, vertebral artery, basilar artery, or posterior cerebral artery" (level IIb).[3] On the other hand, the ESO/ESMINT (European Stroke Organisation-European Society for Minimally Invasive Neurological Therapy) guideline states that "it is reasonable to perform MT in patients with M2 occlusion who meet the inclusion criteria of randomised trials". However, there is no recommendation for MCA-M3, ACA, PCA.[14] Despite intravenous thrombolysis (IVT) and medical treatment in clinic, we often see patients who develop a significant degree of disability as a result of MeVO.[21] Therefore, we wanted to review the most recent RCT data and the guideline recommendations together.

Clinical Trials for Endovascular Treatment of MeVO

Firstly, MeVO needs to be clearly defined. DISTAL (EnDovascular therapy plus best medical treatment (BMT) versus BMT alone for MedIum VeSsel Occlusion sTroke - a prAgmatic, international, multicenter, randomised triaL) is defined as occlusion of the co-/non-dominant MCA M2, M3/M4, ACA A1/A2/A3 or PCA P1/P2/P3 segments. In the DISCOUNT (The Evaluation of Mechanical Thrombectomy in Acute Ischemic Stroke Related to a Distal Arterial Occlusion) trial, on the other hand, it was considered to be M3, ACA A1/A2/A3 or PCA P1/P2/P3 segment occlusion above the mid-height of the insula, predominantly distal M2. In the other trials, DISTALS (Distal Ischemic Stroke Treatment With Adjustable Low-profile Stentriever) and ESCAPE-MeVO (Endovascular treatment to improve outcomes for medium vessel occlusions), the definitions are close but show differences (Table 3).

In addition, the primary and secondary MeVO should also be mentioned. Primary MeVO results from the mechanism of the underlying large vessel occlusion, whereas secondary MeVO results from EVT-induced thrombus rupture or spontaneous thrombus migration in large vessel occlusion. In the majority of studies, the ratio of primary to secondary MeVO was 3.3:1.[5] It is widely believed that the low number of secondary MeVOs is due to the need to capture the condition that occurs during EVT and, more importantly, the need for detailed control imaging of MeVO that occurs spontaneously or with systemic thrombolysis. In a post-hoc analysis of two prospective cohort studies, 20-40% of all MeVOs were reported to be secondary MeVOs.[22] Secondary MeVO resulting from more proximal occlusions involves a larger ischaemic area. Although the data are limited, secondary MeVOs are an independent predictor of a poor outcome and are important in this regard. A recent systemic review and meta-analysis found EVT to be effective and safe in primary and secondary MEVO.[23]

Another important issue is the procedure to be followed in cases of MeVO that causes posterior circulation ischemia. The NIHSS may not fully reflect the severity of posterior circulation ischemia and may be lower than the NIHSS for anterior circulation ischemia. However, it may lead to ischemia of important sites, such as the primary visual cortex and thalamus, which may have a significant impact on quality of life. Nevertheless, EVT is avoided in these patients and thrombolytic therapy is administered when appropriate.[24] Besides, a multicentre trial reported successful revascularisation (87.5%) and a low intracerebral hemorrhage rate (4%) with EVT in the literature.[25] Another recent study similarly reported 81% revascularisation with EVT for PCA P2-P5 occlusion and 3% intracerebral hemorrhage.[26] Although these data are limited, the results are promising. Still, it should be noted that the risk of EVT complications in MeVO is likely to be higher than in patients with a large vessel occlusion, where a small vessel diameter increases the risk of iatrogenic vessel injury. In addition, it is extremely important for the success of recanalisation and the prevention of complications to determine the appropriate size and configuration of materials and techniques for EVT to be performed in these vessels.

Table 3. Endovascular treatment trials in MEVO patients

TRIALS	DISCOUNT	DISTAL	DISTALS	ESCAPE-MeVO
Number of Cases	488	526	168	530
Countries	France	Belgium, Finland, Germany, Spain, Switzerland, United Kingdom	Vessel distal diameter ≥1.5 mm (BTA or MRA)	M2, M3, M4 (MCA) AI, A2, A3 (ACA) PI, P2, P3 (PCA)
Occluded Area	Distal M2, M3 (MCA) AI, A2, A3 (ACA) PI, P2, P3 (PCA)	Co-/non-dominant M2, M3, M4 (MCA) AI, A2, A3 (ACA) PI, P2, P3 (PCA)	Vessel distal diameter ≥1.5 mm (BTA or MRA)	M2, M3, M4 (MCA) AI, A2, A3 (ACA) PI, P2, P3 (PCA)
Other imaging criteria	Absence of tandem occlusion of the carotid arteries	Hypoperfusion-hypodensity or diffusion-flair or diffusion-flair mismatch in patients with 6-24 hours	Absence of tandem occlusion of the carotid arteries Perfusion lesion volume ≥10cc Ischemic core lesion is 50% or less of the hypoperfused area	ASPECTS 8 Salvageable area demonstration in BT, DWI, PWI
NIHSS score ≥2	≥5	≥4 or disabilityn symptoms	2-24 or 4-24 in the presence of haemlanopia or aphasia	>5 or between 3-5 if disability symptoms are present
Age	≥18	≥18	18-85	≥18
Start period	Bt/Btp/MRG mismatch status for the	6th hour or ≤6 hours or 6-24 hours	≤24 hours	< 12 hours
Primary outcomes	90 days mRS 0-2	90 days mRS	Successful reperfusion (PWI) without symptomatic intracranial hemorrhage	90 days mRS
Materials used	Trevor, Catchview mini, pReset Lite, Tigertriever13; Max and Qaspiration catheters (size 3/4/5)	All certified products	Tigertriever 13	Solitaire X
Start and completion date	9.30.2021-12.30.2023	12.9.2021-December 2024	3.25.2022-January 2024	4.15.2022-12.31.2025

IMAGING in MeVO

Non-invasive imaging data is primarily used to detect MeVO. Non-contrast CT is effective in showing erythrocyte-rich thrombus with hyperdense spots. However, it is not always possible to see this finding in the clinic. Similarly, peripheral blooming artifact can be visible on MRI SWI sequence. Again, changes in intensity can be observed with localised low flow due to slowing of the flow in the MRI-FLAIR sequence. However, it is difficult to perform MRI everywhere in clinical practice. CTA and MRA are preferred for evaluating MCA-M2, ACA-A1, PCA-P1. However, the accuracy of the data is limited due to reduced resolution in more distal branches. Studies on new techniques for CTA and MRA (wavelet CTA and 7-T MRI) are still in progress. Another method is CT-P and MR-P, in which a wedge-shaped hypoperfusion can be observed in the anatomical irrigated area of the feeding vessel. Alternatively, to save time, patients can be taken directly to the angiography unit and MeVO can be evaluated during angiography. There is also a view that the direct admission of patients with a NIHSS ≥10 to the angio unit is effective in terms of the rapid establishment of the diagnosis and the initiation of treatment.[24] There are no clear data on assessing tissue perfusion for EVT in MeVO, and evidence-based imaging criteria for these patients are unclear. Nevertheless, several recent studies have demonstrated the beneficial effects of reperfusion even when salvageable tissue is minimal or absent.[27,28]

Thrombolytic + Thrombectomy Bridging Therapy in MeVO Patients

The data suggest that 50% of physicians have a preference for EVT alone for M3, A2 and P2 occlusions when the patient is ineligible for thrombolytic therapy. In patients who are eligible for thrombolytic therapy, EVT is preferred at 40% for A2 and P2 occlusions, whereas this rate is reduced to 18% for M3 occlusions.[29] In these patients, thrombolytic therapy prior to EVT is less favoured. Pharmacological fibrinolysis is more effective with a low thrombus burden such as MeVO[30]; however, IVT alone recanalises only 30-50% of apparent occlusions.[31] There is also a risk of thrombus fragmentation and the development of a secondary MeVO during EVT after IVT.[32] Although there are currently no clear criteria for the use of IVT, EVT treatments or their combination, high recanalisation success has been shown in the literature with IVT before EVT without an increased risk of hemorrhage. Analysing data from 258 MeVO patients in INTERRSeCT and PRovelT trials, recanalisation was more frequent in those receiving IVT before EVT in control CT-A than in those not (47% vs 21%, P:.003). The INSPIRE trial including 945 MeVOs reported similar data (66% vs 49%, P:.005).[14,33,34]

RANDOMISED CONTROLLED TRIALS ASSESSING THE EFFECTIVENESS OF ENDOVASCULAR TREATMENT IN MEVO

In the ESCAPE-MeVO trial of 530 MeVO patients from 5 countries with acute ischaemic stroke within the first 12 hours, the majority of whom had occlusion of branches of the MCA, endovascular treatment was not found to be superior to standard treatment in terms of mRS scores and mortality at the 3rd month. In both groups, guideline-compliant patients received thrombolytic therapy.[35] Similarly, the DISTAL trial, which included 543 patients, found no superiority of endovascular treatment over standard treatment in terms of 3rd month mortality and disability. This study included patients with isolated occlusion of the middle or distal vessels (non-dominant or dominant M2 segment of the MCA; M3 or M4 segment of the MCA; A1, A2 or A3 segment of the anterior cerebral artery; or P1, P2 or P3 segment of the posterior cerebral artery) within 24 hours from the last normal appearance.[36]

The DISCOUNT study, another randomised trial of MeVOs, was planned to randomise 488 patients in France, but was discontinued after an interim analysis conducted after 163 patients had been enrolled due to safety concerns and because the standard treatment group had better functional outcomes at the 3rd month than the endovascular treatment group. Although clinical outcomes were better in the standard treatment group, mortality was reduced in the thrombectomy group and detailed analyses of the results of this trial are still in progress.[37] These three randomised controlled trials failed to show superiority of endovascular treatment over standard treatment in MeVO patients with acute ischemic stroke; however, the patient inclusion criteria of these trials were not the same and the randomised patients had lower NIHS scores and lower reperfusion rates than in other endovascular trials. Another study has shown that when endovascular treatment for patients with MeVO is decided on the basis of ASPECT scores, patients with good ASPECT scores will benefit from endovascular treatment.[38]

In this context, at least when deciding on endovascular treatment in patients with MeVO, it is necessary to select the patient who would benefit from it.

Recommendations

Based on current guidelines and randomised controlled trial data, EVT has not been shown to be superior to standard treatment in MEVO patients with acute ischemic stroke. However, in the first 6 hours and in patients with a high NIHS score and a good ASPECT score, EVT may be recommended at the clinician's decision. However, it is necessary to determine the appropriate size and configuration of materials and techniques taking into account the risk of iatrogenic vascular injury due to the small vessel diameter. The small diameter of the occluded vessel leads to some technical difficulties. Care should be taken when deciding whether to perform EVT, especially in the presence of tortuous intracranial and extracranial vessels.

Thrombolytic therapy prior to EVT is recommended in appropriate patients, if it is within the treatment window.

ENDOVASCULAR TREATMENT FOR POSTERIOR SYSTEM STROKE

Although basilar artery occlusion (BAO) accounts for 1% of all ischemic strokes and 5-10% of all intracranial large vessel occlusions, it is associated with significant morbidity and mortality.[39] As a result of randomised controlled trials, endovascular treatment (EVT) has become the standard treatment for anterior circulation stroke caused by large vessel occlusion and has been included in guidelines.[3,12] However, in the majority of these trials, BAO was either excluded or included in limited numbers. Despite observational data that support the efficacy of EVT in the posterior circulation, high-quality evidence from randomised controlled trials in BAO has been lacking until recently. The current American Heart Association/American Stroke Association guideline, with a lower class of recommendation and level of evidence (Class IIb; Level of Evidence C), states that EVT within the first 6 hours after stroke onset may be reasonable in selected patients with BAO, although the benefit is uncertain.[3] However, given the apparent benefit of EVT in the anterior circulation and the poor prognosis of BAO with limited treatment options, many centres are now practicing EVT for this condition.[40]

A 2006 meta-analysis of large case series compared intra-arterial thrombolysis with intravenous thrombolysis. Results regarding revascularisation and functional independence were similar in both groups.[41] In 2020, the BEST trial was published, the first randomised controlled trial to evaluate the effect of contemporary endovascular treatment with stent retrievers in the treatment of acute vertebrobasilar occlusion.[42] This trial failed to demonstrate a benefit of mechanical thrombectomy alone compared to standard medical therapy for the treatment of basilar artery occlusion from within 8 hours of the estimated time of occlusion. Similarly, in the subsequently published BASICS trial, there was no statistically significant difference in the primary outcome between the group of patients who received endovascular treatment for basilar artery occlusion initiated within 6 hours of stroke onset and those who received medical treatment.[43] However, the results of both studies were unable to exclude the benefit of endovascular intervention and paved the way for subsequent positive trials. The ATTENTION trial was a multicenter, prospective, randomised, open-label, blinded end-point, controlled study comparing EVT with best medical treatment in BAO patients admitted within 12 hours after symptom onset.[44] Patients treated with EVT had better results on the primary (90-day mRS score 0-3: 46% in the EVT group, 22.8% in the medical treatment group, (adjusted RR, 2.06 [95% CI, 1.46-2.91], P<.001, NNT 4) and secondary end-points (90 day mRS shift: (adjusted cOR, 2.87 [95% CI, 1.84-4.47], P<.00); 90 day mRS score 0-2: 33.2% in the EVT group, 10.5% in the medical therapy group, (adjusted RR, 3.17 ([95% CI, 1.84-5.46]; P<.001) when compared to the best medical treatment group. Patients treated with EVT were more likely to have a patent basilar artery on 24-hour imaging (adjusted RR, 2.58 [95% CI, 1.89-3.51]; P<.001). Despite the higher risk of symptomatic intracerebral hemorrhage (5.3% versus 0, adjusted risk difference 5.3% [95% CI, 2.3%-8.2%]; P=.001), 90-day mortality was lower in the EVT group (36.7% versus 55.3%, adjusted RR, 0.66 [95% CI, 0.52-0.82]; P<.001). In subgroup analyses, there was a trend towards effect modification in favour of the EVT group when pc-ASPECTS <8 (RR, 3.86 [95% CI, 0.98-15.24]; P=.04). There were no differences found in treatment effect according to age, NIHSS, start of randomisation, location of the occlusion and presence of intracranial atherosclerotic disease (ICAD). The BAOCHE trial was a multicenter, randomised, controlled study to evaluate the safety and efficacy of thrombectomy with the Solitaire stent retriever in BAO-related stroke treated within 6 to 24 hours after symptom onset.[45] 110 patients were randomised to EVT and 107 to best medical treatment (BMT). After an interim analysis in 212 patients, the study was discontinued due to the superiority of thrombectomy. Patients treated with EVT had better outcomes on the primary (90-day mRS 0-3) and secondary end-points (90-day mRS shift, 90-day mRS score 0-2) compared to the best medical treatment group. Rates of symptomatic intracranial hemorrhage were higher in the EVT group, but there was a trend toward lower mortality in the EVT group, and these results were consistent with the results of the ATTENTION trial. In conclusion, the BAOCHE trial demonstrated that in the absence of widespread infarction at onset, EVT is superior to best medical treatment in BAO patients admitted within 6-24 hour time frame and that EVT also has similar efficacy in BAOs with anterior circulation large vessel occlusions.

Although stent retriever thrombectomy was the preferred technique in BAOCHE, a combined technique was used in approximately half of the cases in the ATTENTION trial. Recent data support the use of a combination of stent retriever and aspiration technique for basilar artery occlusion.[46] Evidence also suggests that mechanical thrombectomy with first-pass aspiration or stent retriever may be safe and technically feasible for distal and medium posterior circulation occlusions, such as P2 or P3 segments of the posterior cerebral artery.[26]

EVT in BAO Patients Admitted with Low NIHSS Score

Patients with NIHSS <10 may have milder symptoms due to better collateral circulation, lower thrombus burden, partial occlusion of the basilar artery, or distal basilar thrombi, which may be more susceptible to IVT alone. The use of EVT in patients with a low NIHSS score is still controversial.[47] In this context, the ATTENTION trial findings suggest that the effect of EVT is limited in patients with mild clinical severity, which is consistent with the BASICS trial findings. All patients with BAO who are admitted with a low NIHSS should be carefully monitored due to the high risk of subsequent clinical deterioration in the absence of EVT.[48,49]

Posterior system thrombectomy in international guidelines: Although the benefit is unclear, the use of mechanical thrombectomy with a stent retriever may be reasonable in carefully selected patients with AIS who can be treated within 6 hours after onset of symptoms (groin puncture) and who have occlusions in the anterior cerebral arteries, vertebral arteries, basilar arteries, or posterior cerebral arteries.[50]

Recommendations

Based on current evidence, EVT is recommended for patients with AIS due to BAO who are admitted within 24 hours with a moderate or severe clinical presentation (NIHSS≥10) without extensive ischemic changes on imaging.

As the therapeutic effect of EVT in BAO is similar to that in anterior circulation stroke, EVT should be performed in eligible BAO patients.

For patients with milder symptoms (NIHSS≤10), IVT may be a better option. However, the use of EVT in BAO patients with mild deficits should be evaluated in light of the patient's clinical presentation, age, and coexisting factors.

Endovascular Treatment of Acute Ischemic Stroke Patients with Tandem Occlusion

The non-availability of randomised clinical trials for anterior system tandem occlusions leaves unanswered the questions of which patients should undergo carotid artery stenting, whether the stenting approach should be anterograde or retrograde or whether stenting or endarterectomy should be performed in a separate session, whether bridging therapy should be performed, whether the risk of hemorrhage in these patients is increased if bridging therapy is performed, how medical treatment should be arranged in stented patients, and whether or not this medical treatment increases the risk of intracranial hemorrhage.

There has not been a randomized clinical trial conducted on this topic. A randomised clinical trial (NCT04261478) is planned for 2024. The American Heart Association/American Stroke Association guidelines accept mechanical thrombectomy for tandem occlusions as evidence level IIb.[3] In European guidelines, 9 out of 11 experts agreed that acute stenting of tandem occlusions should be performed when needed.[14]

Mechanical thrombectomy for large-vessel occlusions in the anterior system has revolutionized the treatment of large-vessel occlusions in the anterior system and has achieved better clinical outcome rates compared to the medical treatment group.[3] Due to the lack of standardization of the mechanical thrombectomy procedure, there are differences in the treatment approach of some subgroups, such as tandem occlusion.[51] Anterior system tandem occlusion is simultaneous occlusion of both extracranial (cervical ICA occlusion or carotid stenosis 70% or greater) and same-side intracranial (distal ICA and/or MCA M1-2 and/or ACA A1) major vessels.[52] It accounts for 10-20% of anterior system strokes. There were 17% cases of tandem occlusions in the ESCAPE trial, 18.6% in the REVASCAT trial and 32.3% in the MR CLEAN trial.[53] In untreated cases, morbidity has been reported to be up to 70% and mortality up to 50%.[54] In patients who received intravenous thrombolysis, poor clinical outcomes of up to 80% have been reported due to high thrombus burden and difficulty in delivering thrombolytic therapy to the site of occlusion.[55] In terms of etiology, it is found that 60-70% are atherosclerotic plaque, 20-30% are dissection, and less than 5% are carotid web and cardiac embolism.[56]

Acute stenting reduces the recurrence of stroke and prevents the growth of the infarct by improving cerebral blood perfusion. It may also help to open the occlusion in the intracranial localisation. On the other hand, acute stenting may increase the risk of stent thrombosis, hyperperfusion and intracranial hemorrhage. If the vascular structure is tortuous, it may be difficult to pass the catheter through the stent after carotid stenting.[52-56]

The advantage of the anterograde approach is that increased blood flow leads to increased collateral flow and may allow for easier recanalization of the distal occlusion, reduced risk of reocclusion, easier navigation with the roadmap, and plaque stabilization. Its disadvantage is that the distal recanalization time may be delayed. The advantage of the retrograde approach is the shorter time required for distal recanalization. Its disadvantage is the increased risk of distal embolism.[54-56]

The etiologic cause of an occlusion of the cervical ICA is important. Because trials have demonstrated that the clinical outcome between dissection and atherosclerosis groups with acute stenting was statistically better in the atherosclerosis group. The risk of spontaneous recanalization and recurrent stroke is lower in the dissection group. Therefore, if dissection is present as the etiologic factor, acute stenting should be performed in selected cases.[57-59] In meta-analyses conducted prior to the year 2020, there was no difference between the groups with and without acute stenting, whereas meta-analyses performed in the last few years have emphasized that the clinical outcome was better in the stenting group.[60] When the pooled data from the two studies were analyzed, patients in the stenting group had more successful recanalization, better clinical outcome at the 90th day, and a higher rate of any intracranial hemorrhage, but no significant difference in symptomatic or parenchymal hematoma type 2. In addition, when patients with and without bridging were compared,

the bridging group showed better clinical outcomes and higher rates of successful recanalization, and an increased risk of hemorrhage that did not reach statistical significance.[56,61,62] In a meta-analysis of 15 studies (n=1857 patients), bridging therapy was reported to have better clinical outcome, lower mortality, and a higher rate of successful recanalization, however there was no difference in symptomatic intracranial hemorrhage (sICH) between the two treatments.[63] In a multicenter, international, cross-sectional study (685 patients; 363 acutely stented, 260 non-stented), acute stenting in tandem occlusion was associated with improved functional outcomes and reperfusion rates without an increased risk of sICH and mortality.[64] In another study, 44 of 691 patients had ASPECTS 0-5 and 505 had ASPECTS 6-10. Low ASPECTS patients had lower 90-day mRS 0-2 and higher rates of symptomatic intracranial hemorrhage.[65] Of the 753 patients who received thrombolytic therapy, 124 were in the tenecteplase group and 629 were in the alteplase group. The rates of good clinical outcomes at the 90th day were similar between the two groups. A higher rate of successful recanalization was achieved in the tenecteplase group. Any intracranial hemorrhage was more common after the use of tenecteplase. However, the risks for sICH and parenchymal hematoma were similar. In patients with tandem occlusions, thrombolysis with tenecteplase appeared to be reasonably safe, especially with an increase in early recanalization rates.[66]

Recommendations

In cases planned for tandem occlusion and acute stenting, acute stenting can be safely performed if the CT ASPECT score on admission is greater than 6, the NIHSS score is less than 10, and the etiology is atherosclerotic.

Atherosclerotic patients with tandem occlusion should receive medical treatment after stenting, even if they are receiving thrombolytic therapy.

Especially in cases involving distal ICA occlusion, a large-diameter (8F-9F) guide catheter should be used to avoid obstruction of the guide catheter.

If the cervical ICA is repeatedly occluded in cases with a low ASPECT score and a high NIHSS, and if the angiographic image shows an unstable and irregular appearance of the plaque, acute stenting may also be performed.

If very severe vascular tortiosis is present and stenting is being considered, the retrograde approach should be an option, especially since it may be very difficult to move the aspiration catheter distally.

Endovascular Treatment for Patients with Large Core Infarct Area

In patients with acute and extensive anterior circulation ischemic stroke (ASPECTS score 2-5) due to large vessel occlusion, treatment with mechanical thrombectomy (MT) may improve clinical outcomes. Although patients with an ASPECTS score of ≥6 were initially considered eligible for endovascular treatment, recent studies have shown that patients with large infarcts with ASPECTS scores of 2-5 may also benefit from this treatment.

There are six large randomised controlled trials that have evaluated the efficacy of thrombectomy in patients with large infarcts. RESCUE-Japan LIMIT,[67] SELECT2,[68,69] ANGEL-ASPECT,[70] TENSION,[71,72] TESLA,[73] and LASTE[74] (Table 4), despite using different patient populations, ethnicities, and imaging criteria, demonstrated significant MT benefit in this group of patients. These studies have reported that positive clinical outcomes can be achieved even when treatment is initiated up to 24 hours after the last known well state.

A 2024 meta-analysis of these trials found that patients who underwent mechanical thrombectomy were more likely to achieve functional independence (i.e., mRS score 0-2) compared with those who received medical treatment alone (20% versus 8%; RR 9.5%, 95% CI 6.8%-12.2%). The number needed to treat (NNT) to achieve functional independence (mRS score 0-2) was 10.6 (95% CI 8.2-14.8). The NNT for a better functional outcome (a positive increase in the mRS ordinal score) was 4.7 (95% CI 3.7-6.6).[75] In the same way, meta-analyses of other randomized controlled trials evaluating the efficacy of MT in large ischemic infarcts have demonstrated similar benefits.[76,77]

Even in groups with extensive brain damage, such as patients with an ASPECTS score of 0-2, thrombectomy has been reported to significantly improve neurological outcome at 90 days (OR 1.62; 95% CI 1.29-2.04).[78]

In another meta-analysis that included four large randomized controlled trials (RESCUE-Japan LIMIT, SELECT2, ANGEL-ASPECT, and TESLA), MT was found to reduce permanent disability and provide better functional outcomes at three months. The rate of independent ambulation (mRS 0-3) was considerably higher in the MT group (RR 1.69; 95% CI 1.33-2.14). However, the difference regarding excellent functional outcome (mRS 0 to 1) was not significant (RR 1.46; 95% CI 0.91 to 2.33).[79]

Table 4. Clinical trials involving patients with large infarcts

Trial Name	Baseline Imaging	Time range	ASPECT	90th day Primer Outcome	Functional Independence		Symptomatic Hemorrhage		Mortality	
					EVT %	Medical %	EVT %	Med %	EVT %	Med %
RESCUE-Japan LIMIT	MRI (14% combined with CT)	<6	3-5	mRS 0-3	14	7	9	4	18	23
ANGEL-ASPECT	CT ve CTP (8% combined with MR)	<24	3-5	mRS Shift	30	11	6	2	21	20
SELECT	CT and CTP	<24	3-5	mRS Shift	20	7	1	1	38	41
TESLA	CT	<24	3-5	mRS	16	2	7	5	39	51
TENSION	CT (18% combined with MR)	<11	2-5	mRS Shift	14	8	4	1	35	33
LASTE	CT (16% combined with MR)	<6.5	0-5 (if >80 then 4.5)	mRS Shift	13	4	9	5	36	55

Although the risk of symptomatic intracranial hemorrhage after thrombectomy is generally low, hemorrhage was reported in approximately half of the patients who underwent thrombectomy in the RESCUE-Japan LIMIT[67] and ANGEL-ASPECT[70] trials. However, there was no significant difference regarding three-month mortality (RR 0.98; 95% CI 0.83-1.15).

In patients with large infarcts, MT has the potential to reduce disability and improve functional outcomes when performed with careful patient selection. Recent high quality studies have shown that MT is a safe and effective option in this group of patients and have provided guidance for clinical practice. Future research will further contribute to the guidelines by clarifying the long-term benefits of treatment in larger patient groups.

Recommendations

In centers where multimodal imaging is available, patients with large core infarcts can receive endovascular treatment provided that the presence of a penumbra can be demonstrated.

In centers where multimodal imaging is not available, endovascular treatment may be performed in young patients (<65 years) without premorbid sequelae, within the first 6 hours after the last normal appearance, and in selected patients with an ASPECT score >2, as decided by an interventional neurologist.

Emergency Department Management Prior to Endovascular Treatment of Acute Ischemic Stroke

Early diagnosis of stroke patients and their access to appropriate treatment as soon as possible is the first step in stroke management.[4,5] This highlights the importance of managing patients with AIS in emergency departments. In this context, there is a need for a specific protocol and organizational structure for the management of AIS cases in emergency departments.

In the emergency department, triage, rapid diagnosis, appropriate imaging, and assessing eligibility for treatment before endovascular therapy (EVT) is critical.[80,81] All the steps from the onset of the patient's symptoms to the time when the patient receives proper treatment are defined as the 8Ds of stroke (Detection - Dispatch - Delivery - Delivery - Door - Data - Decision - Drug/Device - Disposition).[82,83] The first step, Detection, refers to the rapid recognition of early signs of a stroke. Dispatch refers to calling 112 and activation of the emergency services network.[83,84] In the 3rd D, Delivery, i.e. the transfer phase, which means the transfer ofthe patient to an appropriate hospital before the emergency department, we see two organizational models: Mothership and Drip&Ship.[81,82] Transportation of the patient to the nearest primary stroke center and then to the nearest comprehensive stroke center is referred to as the Drip&Ship model whereas transportation of the patient to the nearest comprehensive stroke center bypassing a closer primary stroke center is referred to as the Mothership model.[84-86] In recent years, the superiority of these two organizational models over each other has been the subject of randomized control trials. In two meta-analyses conducted in 2020 and 2022, it was reported that the mothership model was associated with a better clinical outcome in patients with AIS who were eligible for EVT.[87,88] The European Stroke Organization ESO-ESMINT 2023 guideline states that there is no strong evidence of superiority between these two models and that the choice of model should be dependent on the local and regional service network and patient characteristics.[14] When we look at these two transfer models, we come across the "Door in Door out" (DIDO) time, which is a very important parameter for the Drip & Ship model. Reducing DIDO time, which refers to the time between the patient's hospital admission and discharge to the comprehensive stroke center to which he/she is transferred, has been associated with favorable clinical outcomes.[88,89]

Table 5. NIHSS Scale

1. Level of Consciousness
0: Fully awake and alert
1: Slightly stimulable or slightly inattentive
2: Highly stimulable, responding only to intense stimuli
3: No reaction, no response to any stimulus

1a. Responding to Questions
0: Answers questions correctly
1: Answers one of the questions incorrectly
2: Answers both questions incorrectly

1b. Executing Instructions
0: Executes both instructions
1: Executes only one of the instructions
2: Can not execute any instruction

2. Eye Movements
0: Normal
1: Partial paralysis (paresis)
2: Complete paralysis

3. Visual Range
0: Normal
1: Partial Loss
2: Complete loss in one eye or one area
3: Complete loss both eyes or the area

4. Facial Muscles
0: Normal
1: Mild facial paralysis
2: Moderate facial paralysis
3: Complete facial paralysis

5. Motor Strength (Arm)
Arm 1 (The Right Arm) and Arm 2 (The Left Arm) are assessed separately.
0: Normal; no drop at all
1: Mild weakness; no arm drop
2: Moderate weakness; the arm drops but does not contact the surface
3: Severe weakness; the arm drops and contacts the surface
4: No movement

6. Motor Strength (Leg)
Leg 1 (The Right Leg) and Leg 2 (The Left Leg) are assessed separately.
0: Normal; no drop at all
1: Mild weakness; no leg drop
2: Moderate weakness; the leg drops but does not contact the surface
3: Severe weakness; the leg drops and contacts the surface
4: No movement

7. Coordination (Ataxia)
0: Normal
1: Mild ataxia
2: Severe ataxia

8. Sensory Perception
0: Normal; no sensory loss at all
1: Mild to moderate sensory loss
2: Severe sensory loss or no sensory perception

9. Language (Aphasia)
0: Normal; no abnormal language
1: Mild to moderate aphasia; mild difficulty in understanding or generating
2: Moderate aphasia; significant difficulty in understanding or generating
3: Severe aphasia; major difficulty in understanding or generating, inability to communicate at all

10. Dysarthria (Speech Impairment)
0: Normal; no abnormalities in speech
1: Mild to moderate dysarthria; some intelligibility problems
2: Severe dysarthria; unintelligible speech or inability to speak at all

11. Neglect (Hemi-neglect)
0: Normal; no neglect
1: Partial neglect
2: Complete neglect (The patient completely neglects one side of the body)

The fourth D, door, is the patient's arrival at the emergency department, and emergency department management begins at this step.[80,81] There are a number of algorithms for rapid diagnosis of AIS in the emergency department and pre-emergency department and for the decision of referral to the appropriate hospital for treatment. The 2019 American Heart and Stroke Association (AHA/ ASA) guidelines for the early management of patients with AIS recommend the use of the National Institutes of Health Stroke Scale (NIHSS) with a Class I Level of Evidence B in emergency departments (3) (Table 5). In addition to these algorithms, algorithms that are commonly used, but whose benefits have been demonstrated primarily in the prehospital setting, are summarized in Table 6 [90-95]).

Table 6. Algorithms for Rapid Stroke Diagnosis in the Prehospital Setting

FAST-ED	Face-Arm-Speech-Eye Deviation-Denial/Neglect	58% sensitivity 87% specificity
CPSSS	Cincinnati Prehospital Stroke Severity Scale	89% sensitivity 73% specificity
RACE	The Rapid Arterial oCclusion Evaluation	85% sensitivity 68% specificity
LAMS	Los Angeles Motor Scale	81% sensitivity 89% specificity
VAN	Vision-Aphasia-Neglect	100% sensitivity 90% specificity

The fifth D, Data, means performing appropriate tests quickly after the patient arrives in the emergency department. The AHA/ASA guideline recommends that all patients presenting to the emergency department with suspected acute stroke receive Class I Evidence Level A brain imaging prior to any treatment.[3] It is recommended that an organization be established within the hospital for the rapid imaging of the brain in patients who may be candidates for intravenous (iv) thrombolytic therapy or EVT. Again, non-contrast computed tomography (CT) of the brain is recommended to rule out intracerebral hemorrhage with a Class I Level of Evidence A, and CT angiography or magnetic resonance imaging (MRI) angiography is recommended in cases where large vessel occlusion is suspected.[3] Furthermore, CT angiography has been reported to be more useful than MRI angiography for detecting large vessel occlusions. It is recommended not to expect serum creatinine levels prior to CT angiography unless the patient has renal insufficiency (Class IIa Evidence B). In addition, Diffusion, Flair MRI, and perfusion imaging modalities are recommended for wake-up strokes and/or strokes with uncertain onset.[3] Similarly, the 2023 ESO-ESMINT guideline recommends brain CT and CT angiography for all patients presenting to the emergency department within the first 6 hours with suspected large vessel occlusion. Advanced imaging is recommended for patients who are between 6-24 hours range.[14]

The AHA/ASA guideline recommends, with Class I evidence level B, that MRI is not necessary to rule out cerebral microhemorrhages in patients admitted to the emergency department within the first 4.5 hours who are candidates for IV thrombolytic therapy, and that treatment should be administered rapidly without wasting time with additional imaging.[3] Again, according to the AHA/ASA guideline, among the additional tests required to be performed in the emergency department other than imaging tests, only blood glucose measurement is recommended to be performed in all patients with AIS before IV thrombolytic therapy at Class I Evidence level B. Because hypoglycemia and hyperglycemia can mimic stroke, blood glucose assessment should be performed prior to treatment. Levels below 60 mg/dL should be treated (Class I Evidence C).[14] Previous randomised controlled clinical trials have demonstrated that hyperglycemia is associated with poor clinical outcomes.[96-98] Therefore, in patients with AIS (Class IIa Evidence C), the AHA/ASA guideline recommends that blood glucose be maintained in the range of 140-180 mg/dL and closely monitored for the first 24 hours.[3] Platelet count and coagulation parameters are only required if coagulopathy is suspected.[3] Additionally, electrocardiogram and troponin assessment are recommended in patients with AIS, but should not delay IV thrombolytic therapy and EVT procedures.[3]

Thereafter, clinical stabilization should be rapidly achieved in patients deemed eligible for EVT. Airway patency should be maintained. Oxygen and, if necessary, ventilatory support should be provided in the event of hypoxia (Class I Evidence C).[3,95] If hypoxia is not present in the patient (oxygen saturation > 94%), it is not recommended that additional oxygen support be provided.[3] The emergency department should also perform cardiac and blood pressure monitoring.[96] According to the AHA/ASA guidelines, hypotension and hypovolemia should be corrected to maintain systemic perfusion (Class I Evidence C), and in the case of hypertension, if the patient is to receive IV trombolytic therapy, blood pressure should be carefully lowered to systolic<185 mmHg, diastolic<110 mmHg and maintained at these levels for the first 24 hours after treatment (Class I Evidence B). In EVT patients not receiving IV thrombolytic therapy, it has been reported that it may be appropriate to achieve a pre-procedural blood pressure ≤185/110 mmHg (Class IIa Evidence B).[15] If hyperthermia (>38°C) is present, intervention and cooling should be performed in the emergency department. However, it is not clear whether hypothermia is beneficial in the treatment of AIS.[3]

Continuing with the 8 D's of acute stroke management,Decision, the 6th D, means deciding together with the patient and his family what the most appropriate treatment is based on all the examinations. The seventh step, Drug/Device, or treatment, refers to applying the appropriate treatment to the patient; the eighth D, Disposition, refers to taking the patient to the stroke unit or intensive care unit and continuing follow-up there.[82,83]

Recommendations

For endovascular treatment of acute ischemic stroke patients, brain CT and CT angiography or MRI and MR angiography are sufficient as imaging methods in the first 6 hours. Depending on the clinical condition of the patient, multimodal imaging may be required in the following hours.

Depending on the status and capacity of the stroke centers, either the Drip-and-Ship model or the Mother Ship model, or both, can be used in their regions.

Stroke centers should use metrics in accordance with international guidelines to reduce the time from the time of the event to the time of recanalization and should take measures to correct the measurements in these metrics.

Materials and Techniques Used for Endovascular Therapy in a Patient with Acute Ischemic Stroke

The choice of materials and techniques used to treat acute ischemic stroke in adults is critical in determining procedural success and clinical outcome. To summarise the clinical trials on this topic;

ASTER Trial: In patients with acute anterior system ischemic stroke due to large vessel occlusion who underwent thrombectomy, the direct aspiration thrombectomy technique did not significantly improve the near-total or total reperfusion rate (mTICI 2b/3) at the end of the procedure compared to the retrievable stent technique.[99]

COMPASS Trial: In patients with acute anterior system ischemic stroke due to large vessel occlusion who underwent thrombectomy, there was no significant difference in modified Rankin Scale (mRS) at the 90th day when the direct aspiration thrombectomy technique was compared with the retrievable stent technique. This trial supports the use of direct aspiration as an alternative to retrievable stents as a first-line treatment for acute ischemic stroke thrombectomy.[100]

ASTER2 Trial: In patients with acute ischemic stroke due to large vessel occlusion, the first thrombectomy technique using a combination of direct aspiration thrombectomy and a retrievable stent did not significantly improve the near-total or total reperfusion rate (eTICI 2c/3) at the end of the endovascular procedure compared to the technique using a retrievable stent alone.[101]

SFERA Trial: Transradial access was not worse than femoral access in terms of recanalization in patients with acute ischemic stroke due to large vessel occlusion.[102]

PROTECT-MT Trial: Compared to balloon-less guide catheters in patients undergoing endovascular thrombectomy for intracranial large vessel occlusion, the use of balloon guide catheters was associated with worse functional recovery.[103]

Europe and America Guide Recommendations

Guidelines for healthcare professionals published by the American Heart Association/American Stroke Association for the early treatment of acute ischemic strok.[3]

If patients meet all of the following criteria, mechanical thrombectomy with a retrievable stent should be used: (1) pre-stroke mRS score 0-1, (2) occlusion of the internal carotid artery or MCA segment 1 (M1), (3) age ≥18 years, (4) NIHSS score ≥6, (5) ASPECTS ≥6, and (6) treatment can be initiated within 6 hours from symptom onset (groin puncture) (Strong recommendation, strong evidence).

If patients meet all of the following criteria, direct aspiration thrombectomy as first-pass mechanical thrombectomy is recommended as an alternative to retrievable stent thrombectomy: (1) pre-stroke mRS score 0-1; (2) occlusion of the internal carotid artery or M1; (3) age ≥18 years; (4) NIHSS score ≥6; (5) ASPECTS ≥6; and (6) treatment can be initiated within 6 hours from symptom onset (groin puncture) (Strong recommendation, moderate evidence).

Although the benefits are uncertain, it may be reasonable to use mechanical thrombectomy with retrievable stents in carefully selected patients with acute ischemic stroke who can be treated within 6 hours from symptom onset (groin puncture) and who have an occlusion in MCA segment 2 (M2) or MCA segment 3 (M3) (Weak recommendation, moderate evidence).

It may be beneficial to use a balloon guide catheter in combination with a retrievable stent instead of a balloon-less guide catheter (Moderate level recommendation, limited data).

Use of large-diameter distal access catheters with retrievable stents may be advantageous (Moderate level recommendation, limited data).

European Stroke Organization - European Society for Minimally Invasive Neurological Therapy Guidelines for Mechanical Thrombectomy in Acute Ischemic Stroke

There is no evidence that direct aspiration is superior to retrievable stent thrombectomy in terms of increasing reperfusion rates.[18] Therefore, the use of retrievable stents for mechanical thrombectomy in patients with acute ischemic stroke is recommended over direct aspiration. (Very low level evidence and poor recommendation)

Recommendations

Retrievable stents are recommended for patients with acute ischemic stroke in the anterior system due to a large vessel occlusion who are scheduled to undergo a thrombectomy.

The use of an aspiration catheter with a retrievable stent may be appropriate in patients with acute ischemic stroke in the anterior system due to large vessel occlusion who underwent thrombectomy.

The use of a balloon guide catheter may be beneficial in patients with acute anterior system ischemic stroke due to large vessel occlusion and who underwent thrombectomy.

Follow-up of Acute Ischemic Stroke Patients After Endovascular Treatment

Research suggests that appropriate monitoring and structured care processes can improve the effectiveness of endovascular therapy (EVT) in patients with acute ischemic stroke. These approaches are designed to improve functional outcomes by reducing complications .[104]

The most important points that need to be considered in this process are:

1. Neuro-Intensive Care and Stroke Unit Follow-Up

First 24-48 hours:

Neurologic examination: Close monitoring of neurological status after EVT is critical. Serial examinations are performed to detect any new neurological events.[105]

Blood pressure management:

The blood pressure should be carefully controlled in order to maintain reperfusion and to reduce the risk of hemorrhage. Current clinical guidelines from the AHA/ASA and the European Stroke Organization recommend that blood pressure be maintained at <185/105 mm Hg and that SBP drops of <130 mm Hg be avoided.[3,106] Trials such as OPTIMAL-BP and BEST-II have shown that lower blood pressure goals do not confer a clear benefit on functional independence, but the detrimental effects are also minimal.[107,108]

In patients who are unable to recanalize, moderate hypertension protects the ischemic penumbra, and it is reasonable to allow the systolic blood pressure to be raised to 220 mm Hg to prevent hypotension or to support the hemodynamics with vasopressor therapy.[109]

Monitoring of the vital parameters:
Fever may increase neuronal damage by triggering the ischemic cascade. Normothermia should be ensured with the use of antipyretic medications and non-pharmacologic methods. In patients who require respiratory support, decisions regarding airway management, such as early extubation or tracheostomy, should be made with caution.

Brain imaging:
To detect complications such as intracranial hemorrhage after EVT or thrombosis after stent placement, CT or MR brain imaging should be performed within 24-48 hours.

Multimodal neuromonitoring in stroke:
It is a combination of technologies and methods used for real-time assessment of brain function and metabolic status (Table 7). This approach allows dynamic monitoring of the neurological status of stroke patients. It also helps to optimize treatment management .[110,111]

Medical Conditions Related to Large Vessel Occlusion (BDO)
Dysphagia: Dysphagia is common in patients with acute stroke and poses a risk of aspiration and pneumonia. These patients should be withheld from oral feeding until swallowing is safe, and enteral nutrition should be the preferred option.[112,113]

Deep Vein Thrombosis Prophylaxis: Intermittent pneumatic compression is recommended for patients with limited mobility. However, pharmacological prophylaxis may increase the risk of intracranial hemorrhage. Risk factors include previous venous thromboembolism, cancer, disability, and volume of ischemia. Pharmacologic prophylaxis may be aided by using heparin or enoxaparin.[114,116]

Antithrombotic Therapy and Medication Management
Anticoagulant/antiplatelet therapy: Initiation of antiplatelet or anticoagulant therapy following EVT is necessary to reduce the risk of reocclusion. In general, the use of antiplatelet therapy is associated with a small increase in the risk of symptomatic intracerebral hemorrhage after mechanical thrombectomy, but the net clinical benefit to the patient is increased. Provided that patients have not received IV thrombolytic therapy and the infarct volume is not large, there is no contraindication to the use of antiplatelets. In particular, in cases in which stenting is required because of a tandem lesion or an intracranial stenosis, antiaggregant therapy needs to be initiated.[117] As a result, a treatment plan should be in place that is sensitive to the individual's risk factors and comorbidities.

Blood glucose regulation: Blood glucose regulation is critical for preventing the negative effects of hypoglycemia and hyperglycemia .[116,118,119] The SHINE study demonstrated that keeping blood glucose levels between 140 and 180 mg/dL was sufficient.[120]

Complication Management
Due to the natural course of the stroke, the intensive care follow-up, or the technical devices used in the procedure, complications may occur after EVT. These complications can be managed by close neurological monitoring, blood pressure and blood glucose monitoring, and appropriate medical and surgical treatment. While the goal of acute interventions after acute ischemic stroke is to restore blood flow to the ischemic penumbra, secondary systemic physiologic disturbances such as hypotension, hyperthermia, or hyperglycemia that may enlarge the penumbra should be prevented or corrected.[104,105] (Table 8)

Functional and Neurological Rehabilitation Plan
Rehabilitation programs that are initiated in the early stages will accelerate the functional recovery of patients and increase their independence for the long term.[102] Multidisciplinary approaches such as physiotherapy, speech therapy and occupational therapy would be helpful in this process.[120,123]

Table 7. Multimodal Neuromonitoring in Neurointensive Care

Technology	Indication	Recommendation Strength Level	Quality of Evidence	Prevalence in Clinical Practice
Intracranial pressure monitoring	For patients at risk for increased intracranial pressure based on clinical or imaging data	Strong	Moderate	High
	Management of patients at risk for herniation	Strong	High	High
Cerebral autoregulation	Cerebral perfusion pressure management goals and prognosis determination; pressure reactivity is a commonly used method	Strong	Moderate	Developing
Electroencephalogram	For patients with persistent and unexplained altered mental status, convulsive status epilepticus (unable to return to normal within 60 minutes), treatment-resistant status epilepticus, comatose patients after therapeutic hypothermia and after cardiac arrest during the first 24 hours following rewarming.	Strong	Low	High
	For patients with aneurysmal subarachnoid hemorrhage who have an unreliable neurological examination and a delayed risk of cerebral ischemia.	Weak	Low	Low
Jugular venous oximetry	For patients who are at risk of cerebral ischemia and/or hypoxia	Weak	Low	Low
Brain Tissue Oxygenation Monitoring	For patients who are at risk of cerebral ischemia and/or hypoxia	Weak	Low	Low
Cerebral microdialysis	For patients who are at risk of cerebral ischemia, hypoxia, energy deficiency and glucose deprivation	Weak	Low	Low
Thermal diffusion flowmeter	For patients who are at risk of local cerebral ischemia	Weak	Low	Low

Table 8. Complications following endovascular thrombectomy

Localization	Complication	Management
Regarding the site of entry	Inguinal hematoma and femoral access site hemorrhage	Manual pressure, ultrasonography for assessment of pseudoaneurysm
	Femoral artery pseudoaneurysm	Ultrasound-guided compression, thrombin injection, possible surgical repair
	Femoral artery dissection	Observation is usually required, stenting is rarely required
	Femoral artery occlusion	Endovascular or open surgery for revascularization
	Retroperitoneal hematoma	Manual pressure at the site of arterial access, emergency blood type matching and usually transfusion, CT and CT angiography.
Extracranial	Distal hand ischemia (for radial access)	Vascular surgery consultation
	Cervical artery dissection	Usually observation, antiplatelet therapy; rarely carotid or vertebral stenting
Intracranial	Vasospasm	Usually observation; often use of intracerebral vasodilating medication (verapamil, nicardipine, milrinone, nimodipine)
	Vascular perforation	Neuroendovascular unit management, post-procedural CT imaging, management of hemorrhagic complications in the intensive care unit
	New site embolisation	Neuroendovascular unit management (including single thrombectomy or intracerebral thrombolytics)
	Cerebral edema	Treatment after large infarcts: the head should be elevated by 30 degrees, the serum sodium level should be monitored on a regular basis, hyperosmolar agents, mannitol and hypertonic saline should be actively used. In the event of sudden clinical decompensation, transient hyperventilation and surgical decompression may be required; however, continuous hyperventilation should be avoided.

Recommendations

After EVT, the patient needs to be cared for in a specialized stroke unit or in an intensive care unit under the care of experienced physicians.

The follow-up of the patient after EVT should be performed by a stroke neurologist, if possible, and if not, at least by a neurologist with experience in the follow-up of stroke patients.

The patient's follow-up after EVT, blood pressure, blood glucose, and antithrombotic treatment management should be performed according to the written protocols of each stroke center. These protocols should be developed in accordance with international guidelines.

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