ENDOVASCULAR APPROACHES TO ACUTE ISCHEMIC STROKE - INDIAN PERSPECTIVE

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Abstract

Aim: To review literature about endovascular approaches to acute ischemic stroke and provide Indian perspective about managing these cases.

Brief Summary: In acute ischemic stroke cases, intravenous thrombolysis (IVT) with altepase within 4.5 hours has been the standard of care. Due to certain limitations of IVT, in pooled patient-level data from 5 trials (HERMES [Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials], which included the 5 trials MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, and EXTEND-IA), mechanical thrombectomy (MT) is indicated for patients with acute ischemic stroke due to a large artery occlusion (LVO) in the anterior circulation who can be treated within 24 hours of the time last known to be well (ie, at neurologic baseline), regardless of whether they received intravenous alteplase for the same ischemic stroke event. The maximum benefit can be achieved within 6 hours of onset of symptoms. There are studies suggesting the benefit of MT in posterior circulation stroke as well as in distal arteries. We are going to review the methodology of endovascular techniques in brief alongwith Indian perspective on feasibility of this treatment approach in AIS.

Conclusion: Mechnicalthrombectomy is certainly an effective modality of treatment in large vessel occlusion in anterior circulation within 24 hours. More awareness regarding the approach in India, can reduce the stroke morbidity and mortality in many of the cases in future.

Introduction

The term “stroke” is applied to an acute focal (rarely global) neurological deficit resulting from decreased perfusion of the brain due to occlusion or rupture of the blood vessels supplying the brain. About 85% of strokes are ischemic in nature, due to in-situ thrombus superimposed on an atherosclerotic plaque or an embolism from a proximal source. According to ICMR statistics, 1,65,000 strokes occur each year, with nearly one stroke every 40 seconds and one stroke death every 4 minutes. Amongst the stroke survivors, many are afflicted with serious long-term disability.1-3

In comparison to west, most of the Indian studies addressing the incidence and prevalence rate (PR) of stroke are regional with relatively small sample size. Based on these studies the PR of stroke in India has been shown to vary from 40-470/ 100000 population 4. Crude IR varies from 33 –119.4 per 100000 populations in different studies in India. The Annual IR of stroke in India, as observed in the Kolkata, Mumbai, and Trivandrum studies are higher than that in Europe (61-111 per 100,000 per year) and Australia (99 per 100,000 per year)5.

The reperfusion either by Intravenous thrombolysis(IVT) or endovsacular approach should be the target in cases with AIS for salvaging the brain tissue. Though IVT is the suitable approach in most of the centres, it has the limitations of modest efficacy with early recanaliasation of 20 to 33%6 and narrow therapeutic window upto 4.5 hours.

Endovascular treatment

Indian experience

A study done in Karnataka ,India by vikramHuded et al7 on 45 patients who underwent endovascular treatment,the mean age at presentation was
49 years, median National Institutes of Health Stroke Scale (NIHSS) was 19 and the most common site was the middle cerebral artery (23 patients). Solitaire™ stentriever was used in 33 patients. The median pre-procedure Thrombolysis In Myocardial Infarction (TIMI) score was 0 and the median post-procedure TIMI score was 3.On follow-up at 3 months, the median Modified RankinnScale (mRS) was 0. Eight patients died during 3 months following stroke and they concluded that endovascular therapy is aviable options who either have contraindications to IVT or who fail IVT.

In a study done by Rakesh K singh et al8 in Mumbai, experience from 137 patients of anterior circulation (AC) and posterior circulation (PC) LVO(112 AC and 25 PC)was analysed.They concluded that MT is safe treatment and equally effective for both AC and PC LVO.

History and landmark trials

The first special device for clot removal in acute stroke was Mechanical Embolus Removal in Cerebral Ischemia (MERCI) retriever (Concentric Medical, Mountain View, California), a corkscrew-shaped device having a flexible nitinol wire in helical loops, approved by the USFDA in 2004. The MERCI trial was a pivotal single arm, prospective, multicenter trial in tPA ineligible patients presenting within 8 h. The recanalization rate was 46% with SICH rate of 8%.22 Multi MERCI trial was a similar study where IV rt-PA refractory patients were included. The recanalization rate was 57%, and the SICH incidence was 10%23.The rate of clinically significant device-related complications was 4.5%. Among patients in whom revascularization was achieved, there was a two-fold survival advantage and a significantly higher proportion of patients lived without significant disability. These studies proved the safety of mechanical thrombectomy in IV rt-PA ineligible patients and also in those who required a thrombectomy following administration of IV rt-PA.12

From December 2010 onwards, there are six trials as MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, EXTEND-IA and THRACE, suggested benefit in approximately 53% cases with strokes with proximal anterior circulation with time ranging from 6 to 24 hours.12 There are studies with benefit of MT in posterior circulation and distal middle cerebral arteries, but needs further evidence for the proven efficacy.18 Two issues may limit the widespread clinical use of mechanical thrombectomy. First, only an estimated 10 percent of patients with acute ischemic stroke have a proximal large artery occlusion in the anterior circulation and present early enough to qualify for mechanical thrombectomy within 6 hours, while approximately 9 percent of patients presenting in the 6 to 24 hour time window may qualify for mechanical thrombectomy . Second, only a few stroke centers have sufficient resources and expertise to deliver this therapy. 20,21

Patient selection for endovascular approach

According to latest AHA/ASA guidelines 12 currently, the selected cohorts to be considered for endovascular treatment include the following:

1. Patient should be functionally independent (modified Rankin score (mRS) 0 to 1)
2. Patient should be an adult with significant stroke (age ≥ 18 years, NIHSS score of ≥ 6)
3. Computed tomography (CT) brain without evidence of large infarct suggested by Alberta Stroke Program Early CT Score (ASPECTS) of ≥ 6 with imaging proven causative occlusion of the internal carotid artery or proximal middle cerebral artery (MCA) M1 segment.
4. The technical goal of the thrombectomy procedure should be reperfusion to a modified thrombolysis in cerebral infarction (mTICI) 2b/3 angiographic result to maximize the probability of a good functional clinical outcome.
5. Treatment can be initiated (groin puncture) within 6 hours of symptom onset.

But guidelines also suggested benefit of MT in following scenarios

A. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended. (class 1, level of evidence A)
B. In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.(class IIa, Moderate quality of evidence)

The DAWN and DEFUSE 3 trial criteria were imaging based on clinical ASPECTS mismatch. For patients with ischemic stroke caused by a large artery occlusion in the proximal anterior circulation who are evaluated at stroke centers that do not use automated infarct volume determination, mechanical thrombectomy if treatment can be started within 6 to 24 hours of the time last known to be well and there is a clinical-ASPECTS mismatch, such as an NIHSS ≥10 and ASPECTS ≥6.

Posterior circulation stroke

Although the benefits are uncertain, mechanical thrombectomy may be a reasonable treatment option for patients with acute ischemic stroke caused by occlusion of the basilar artery, vertebral arteries, or posterior cerebral arteries when performed at centers with appropriate expertise . Mechanical thrombectomy is proven effective only for select patients with acute ischemic stroke caused by a proximal intracranial arterial occlusion in the anterior circulation; the trials that established the benefit of mechanical thrombectomy largely excluded patients with posterior circulation infarcts. Data from uncontrolled observational studies and registries suggest that endovascular therapy for basilar artery occlusion leads to a higher rate of good functional outcomes (approximately 30 to 40 percent) and lower mortality (approximately 30 percent) than expected when compared with outcomes among patients who did not receive endovascular therapy. By comparison, a systematic review identified 76 patients receiving intravenous thrombolysis with alteplase for basilar artery occlusion found that the rate of good functional outcome was approximately 22 percent, and mortality was approximately 50 percent. 18

ASPECTS (Alberta Stroke Program Early CT Score)

ASPECTS was developed to provide a simple and reliable method of assessing ischemic changes on head CT scan in order to identify acute stroke patients unlikely to make an independent recovery despite thrombolytic treatment. 9 The ASPECTS method has also been adopted to assess the extent of ischemia on diffusion-weighted MRI (DWI); the ability to detect early ischemic changes by ASPECTS was similar on noncontrast CT and DWI [23].

The ASPECTS value is calculated from two standard axial CT cuts; one at the level of the thalamus and basal ganglia, and one just rostral to the basal ganglia.

- The ASPECTS method divides the middle cerebral artery (MCA) territory into 10 regions of interest.
- Subcortical structures are allotted three points: one each for caudate, lentiform nucleus, and internal capsule.
- MCA cortex is allotted seven points:
  Four of these points come from the axial CT cut at the level of the basal ganglia, with one point for insular cortex and one point each for M1, M2, and M3 regions (anterior, lateral, and posterior MCA cortex).
  Three points come from the CT cut just rostral to the basal ganglia, with one point each for M4, M5, and M6 regions (anterior, lateral, and posterior MCA cortex).
- One point is subtracted for an area of early ischemic change, such as focal swelling or parenchymal hypoattenuation, for each of the defined regions.

Therefore, a normal CT scan has an ASPECTS value of 10 points, while diffuse ischemic change throughout the MCA territory gives a value of 0.

Endovascular techniques

There are two methods as stent retrievers or catheter aspiration.

1.Stent retrievers

These include the first-generation Merci Retriever and Penumbra System devices, and the second-generation Solitaire Flow Restoration Device and Trevo Retriever. The first-generation Merci and Penumbra devices may increase recanalization rates in carefully selected patients, but their clinical utility for improving outcomes after stroke is unproven . When compared directly with the Merci retriever in small randomized trials, the second-generation Solitaire and Trevoneurothrombectomy devices achieved significantly higher reperfusion rates and better patient outcomes. In light of these data and the positive thrombectomy trials discussed above, which preferentially used the second-generation devices, only the second-generation devices should be used to treat patients with acute ischemic stroke. 16,17,18

2. Catheter aspiration devices

This method employs a catheter to aspirate the thrombus as the first approach to performing thrombectomy; if aspiration alone does not achieve reperfusion after one or more passes, a stent retriever can be inserted through the catheter to complete the thrombectomy. Mounting evidence suggests that catheter aspiration devices can attain rates of revascularization and good functional outcome that are similar to the rates achieved with second-generation stent retrievers. 16,17,18

Monitored anaesthesia as conscious sedation is preferred over general anasethesia in cases for MT. But it has to be case based depending on the situation.

Systolic blood pressure to kept between 150 to 180 mmHg prior to reperfusion; SBP ≥150 mmHg may be useful for maintaining adequate collateral blood flow during the time the large artery remains occluded. 12,15Once reperfusion is achieved with mechanical thrombectomy, we suggest targeting SBP to <140 mmHg. However, the optimal blood pressure range with mechanical thrombectomy is not well-defined, and there are few data to guide periproceduralmanagement .

Complications related to MT

In the MR CLEAN trial, clinical signs of a new ischemic stroke in a different vascular territory within 90 days of treatment were more common in the intra-arterial group compared with no endovascular therapy (5.6 versus 0.4 percent). Device-related serious adverse events are uncommon but include access site hematoma and pseudoaneurysm, arterial perforation, and arterial dissection. Transient intraprocedural vasospasm is also uncommon but is sometimes noted.

Mechanical thrombectomy is not associated with increased rates of symptomatic intracranial hemorrhage or mortality. In meta-analysis of 5 trials, with pooled patient-level data for 1287 subjects, there was no significant difference between the intervention population and control population for 90-day symptomatic intracranial hemorrhage (4.4 versus 4.3 percent) or mortality (15 versus 19 percent). 10,11,14

Recommendations for Indian subcontinent

Many Indian hospitals lack the necessary infrastructure and organization required to triage and treat patients with stroke quickly and efficiently. Clinical stroke services are limited, often nonexistent in many parts of the country, distinctly so in the public sector health-care segment.

The existing treatment gaps in stroke care include a low rate (0.5%) of thrombolysis for stroke; and, non-availability of stroke physicians round the clock, stroke interventionalists, stroke care pathways,stroke units, stroke teams, sufficient community awareness programs, and efficient public emergency ambulance systems, which are all essential elements necessary to provide optimal stroke care to the community. It is imperative that adequate measures are implemented to meet the stroke epidemic in India. In future, if is feasible, inclusion of thrombolysis either intravenous or mechanical in Ayushman Bharat scheme might change whole scenario of stroke manangement in India.

Recommendations

1. Acute Stroke Team Composition- To cater to emergency patient in least possible time gap.
2. Capacity Building for Stroke Intervention- To create centres well equipped to handle the endovascular treatment and necessary machinery.
3. Need for Incorporating Vascular Neurology Training in Neurology Training Curricula- To decrease the threshold time of neurologists to decide about emergency stroke care management i.e subjecting thesuitable patients to endovascular treatment
4. “Fellowship” Program for Stroke Intervention in India- To dissipate the existing knowledge and timely update the advancement in the field of intervention stroke management.

Conclusions

Tremendous progress in the endovascular management of AIS with large vessel occlusion has resulted in a paradigm shift in the way this disease is being managed in the recent times. An improved patient selection using the clinical and imaging criteria along with technical and technological advancements in mechanical thrombectomy have resulted in a significantly improved outcome in stroke patients. It is pertinent to design the management strategies including treatment and prevention best suited to Indian infrastructure and economy; to design protocols and blue prints for ensuring best management to most patients, regardless of the socioeconomic and geographic barriers across the country.

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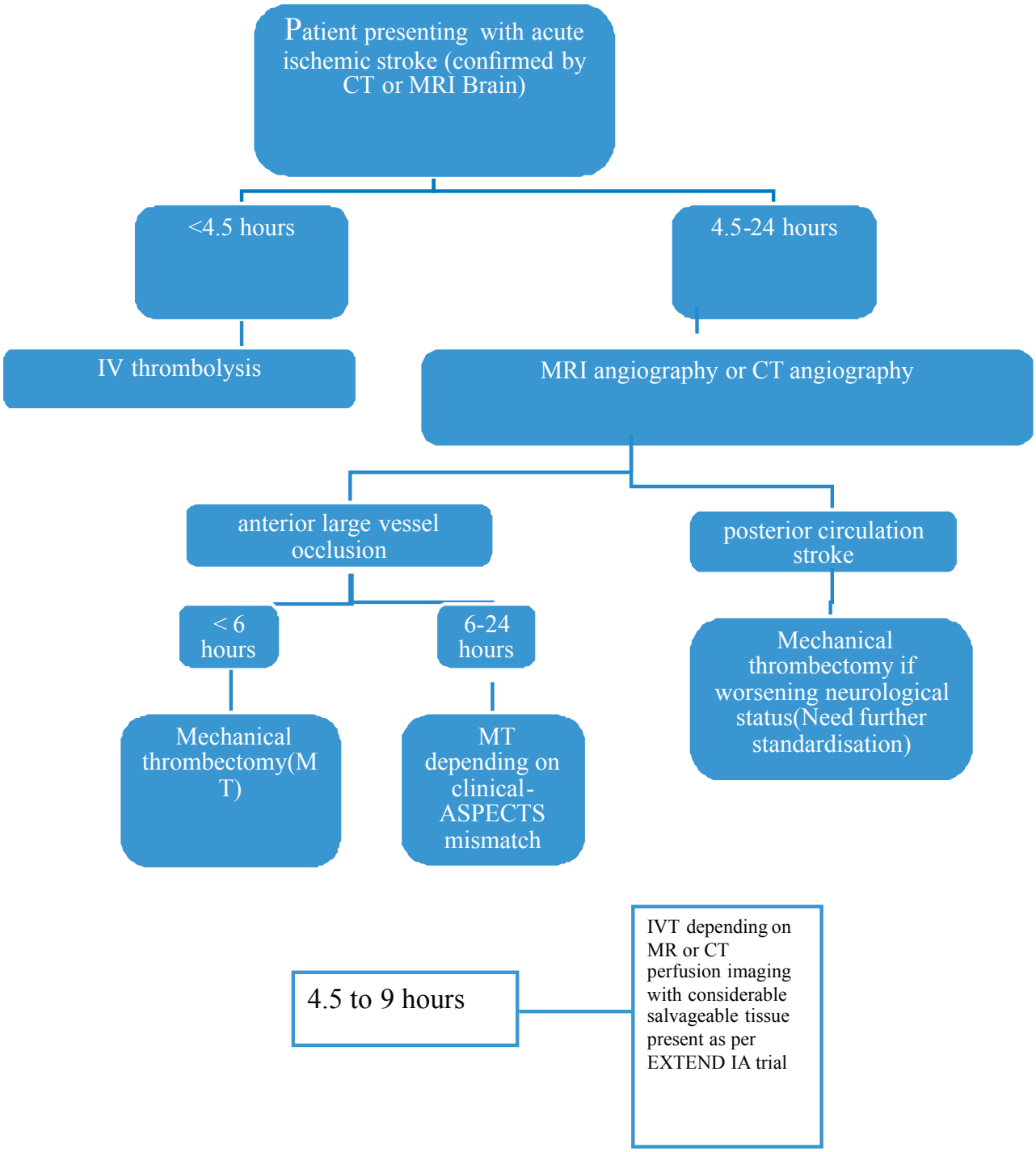
Quick guide for acute ischemic stroke



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