

State of endovascular therapy for acute ischaemic stroke

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Acute strokes result from an occlusion of intracranial vessels by either a thrombus or embolus. The aim of acute treatment of ischaemic strokes is removal of this occlusion and recanalization of the vessel. The modes of therapy available include the administration of intravenous tissue plasminogen activator (tPA) or endovascular therapy involving either intraarterial thrombolysis with recombinant tPA, mechanical clot disruption or clot retrieval.

There has been much debate over the effectiveness of the two treatment modalities in terms of rescuing the penumbra region and long term survival free of complications. Three randomized control trials were conducted to investigate this theory. Before these 3 trials, studies had suggested the superiority of endovascular therapy over intravenous tPA. But there was no mortality data from randomized studies and the long term outcome of the survivors was not known.

The three trials, namely Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy (MR RESCUE) trial, Local versus Systemic Thrombolysis for Acute Ischemic Stroke (SYNTHESIS Expansion) trial and Interventional Management of Stroke III (IMS III) were conducted independently at multiple centers around the world. We present below the conclusions drawn from these randomized control trials.

Patients Enrolled

MR RESCUE enrolled 127 patients between 2004 and 2011 at 22 different sites. Of these, however, 118 were taken into consideration. Patients had NIHSS scores in range 6-29 with infarcts of the anterior circulation. 58% of these patients were identified as having a favourable penumbra region.

IMS III enrolled 656 patients at 58 sites from 2006 to 2012. Patients had NIHSS scores greater than 8 and occlusion of the anterior or posterior circulation.

SYNTHESIS enrolled 362 patients at 22 different centers in

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the period 2008-2012. They included patients with occlusion of either anterior or posterior artery circulations and there was no limit for NIHSS score.

Type of Intervention

The exact modality of treatment employed varied between the 3 trials. While SYNTHESIS employed only endovascular therapy, within 4.5 hours, MR RESCUE and IMS III used both intravenous TPA (Tissue Plasminogen Activator) and endovascular therapy. Nearly 44% of the patients in MR RESCUE received intravenous TPA followed by endovascular intervention and the rest only endovascular therapy while all 656 patients in IMS III received both intravenous TPA and endovascular therapy. Intervention in MR RESCUE was within 8 hours and in IMS III within 3 to 4 hours.

The control treatment for both IMS III and SYNTHESIS was IV TPA while MR RESCUE employed standard care as control though 29.6% of these patients received IV TPA too. MR RESCUE trial also aimed at identifying if there was a relative benefit in patients with larger ischaemic penumbra compared to those with a large area of infarction. Thus, patients were divided into 'penumbra' and 'non-penumbra' groups prior to starting intervention.

Outcomes

Outcome was assessed by the percentage of recanalization and the rate of disability free survival at 90 days.

The IMS III trial assessed recanalization rates after 24 hours of intervention. The group receiving endovascular therapy showed 81% recanalization of ICA, 86% of the stem of MCA (M1) and 88% of a branch of MCA (M2). While the group receiving IV TPA showed 35% recanalization of ICA, 68% of the stem of MCA (M1) and 77% of a branch of MCA (M2). Long term effects were accessed after 90 days and showed that 40.8% of those who received endovascular therapy and 38.7% of those who received IV TPA were alive without any disabilities.

SYNTHESIS did not evaluate recanalization rates in patients however disability free survival at 90 days was 42% in the patients who had undergone endovascular therapy and 46.4% in those who underwent intravenous administration of TPA.

MR RESCUE trial evaluated recanalization rates 7 days after intervention. Recanalization rates were 71% in those who received endovascular therapy compared to 87% in those who received standard care. Long term assessment showed that 14% of those in penumbral group and 9% of those in non-penumbral group who underwent endovascular treatment were surviving without complications after a period of 90 days. In contrast, 23% of those in penumbral group and 10% of those in non-penumbral group who received IV TPA were living disability free after the same amount of time.

Conclusion

Treatment of acute ischaemic stroke can involve both IV TPA and endovascular therapy. However superiority of one of endovascular therapies over IV TPA cannot be established with certainty. Even though results from the IMS III trial show that recanalization rates with endovascular therapy are markedly higher than those with IV TPA, long term outcomes were similar in both groups. Findings of the other 2 trials were contradictory to this. MR RESCUE and SYNTHESIS prove that IV TPA is better than endovascular therapy in terms of short term and long term outcomes both.

It may be argued that the results of IMS III are more reliable as it had the greatest sample size and was done at more sites than the other two trials. However, IMS III did not solely employ endovascular therapy; IV TPA was administered prior to endovascular intervention. The

better results in IMS III may also be attributed to the earlier intervention compared to SYNTHESIS and MR RESCUE.

Should endovascular therapy be used instead of IV TPA in Pakistan?

With the current economic constraints in Pakistan and the low budget allotted to the health care sector, employing treatment modalities like intra arterial thrombolysis and mechanical disruption of clots may not be feasible.

The fact that its superiority over IV TPA in terms of efficacy is still questionable, further suggests that switching to endovascular therapy as a routine treatment for acute ischaemic stroke may not prove to be a wise decision. Weighing the pros and cons of endovascular therapy, the economic burden of importing thrombectomy devices and stent retrievers and training personnel to use these devices, makes it questionable if the switch from IV tPA to endovascular intervention will yield favourable results or not.

Suggested readings/References

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