

Update on Mechanical Thrombectomy

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Received date: May 27, 2015; Accepted date: June 24, 2015; Published date: June 27, 2015

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Short Communication

Intra-arterial stroke therapy aims to restore perfusion of the distal arterial bed by recanalizing the primary arterial occlusive lesion [1]. Successful recanalization positively correlates with improved long-term functional outcomes [2-4]. The PROACT II trial published in 1999 demonstrated a clear benefit from administering prourokinase via a catheter-based approach directly into the occlusive lesion.

Ever since then several intra-arterial approaches have been used which moved from intra-arterial administration of a thrombolytic agent to a mechanical approach in which the occlusive clot is either fragmented and aspirated or retrieved en-bloc.

SWIFT [5] and TREVO 2 [6] published in 2012 were randomised controlled trials which demonstrated the superiority of second-generation retrieval devices (stentrievers) as compared to the Merci device (a first-generation device). The studies also raised hope that an improvement in the prognosis of acute ischaemic stroke was achievable.

Mechanical thrombectomy was shown not to be superior to intravenous rt-PA in three randomised controlled studies published in the New England Journal of Medicine in 2013. The results of MR RESCUE [7], SYNTHESIS Expansion [8] and IMS III [9] were perhaps unexpected and though the trials may have had potential design flaws, they led to clinical equipoise surrounding the use of mechanical thrombectomy in stroke treatment. Some of the studies might have failed to demonstrate the superiority of mechanical thrombectomy due to an inaccurate evaluation of arterial recanalization by TIMI score after endovascular treatment [10-12]. Experts also argued that since these studies utilised mainly first-generation devices and were found to be equally effective as intravenous thrombectomy, then one would expect that second generation devices would be superior to standard treatment. This was however just a hypothesis and well-designed randomised trials were needed to confirm this.

MR CLEAN [13] enrolled 500 patients from 16 centres in the Netherlands. Within the mechanical thrombectomy arm, eligible patients were treated with intra-venous thrombolysis and thrombectomy up to 6 hours from symptom onset and stentrievers were utilised in 81.5% of cases. In the second arm, patients were treated with standard care alone. There was an absolute difference of 13.5 percentage points in the rate of functional independence (mRS \leq 2) in favour of intervention (32.6% vs. 19.1%).

At the International Stroke Conference (ISC 2015) in Nashville three additional positive randomised controlled trials, namely ESCAPE [14], EXTEND-IA [15] and SWIFT PRIME [16] were presented.

ESCAPE [14] was a multi-centre collaboration trial which included 2 arms namely endovascular intervention and standard care versus standard care alone. Retrievable stents were used in 86% of cases

within the thrombectomy arm. The primary outcome was a shift analysis of the modified Rankin score (mRS) which favoured the thrombectomy group with an odds ratio of 2.6. Similarly the endovascular group achieved a better rate of functional independence at 90 days.

EXTEND IA [15] which was set in Australia was stopped after 70 patients (out of the 100 planned initially) had been enrolled because of significant benefit in the endovascular arm. Patients treated with Solitaire and t-PA achieved a much better functional outcome (a secondary outcome of the trial) at 90 days.

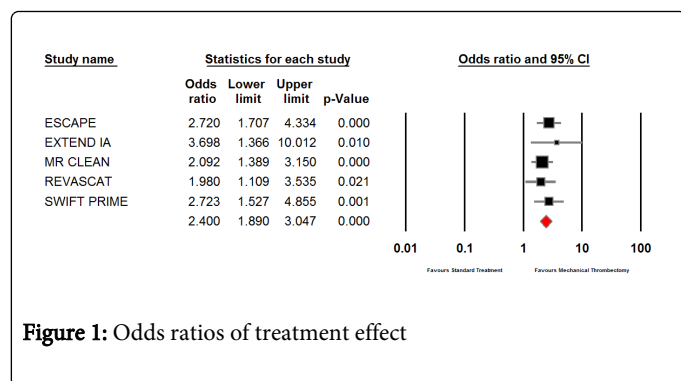
SWIFT PRIME [16] demonstrated a significant difference ($p=0.0002$) in the rate of functional independence (mRS \leq 2) at 90 days between patients treated with intervention and intravenous thrombolysis (60%) versus those treated with standard care alone (35%). The trial recruited 196 patients from 61 centres and intervention was performed using the Solitaire device.

Following these trials the European Society of Neuroradiology (ESNR) together with the European Stroke Organisation (ESO) and the European Society on Minimal Invasive Neurological Therapy (ESMINT) issued a consensus statement on the use of mechanical thrombectomy in acute ischaemic stroke. Although this consensus was not a guideline as such, it promoted the use of intra-arterial therapy and will act as a strong support for new guidelines for stroke therapy.

At the European Stroke Organisation (ESO 2015) meeting in Glasgow, REVASCAT [17], an additional positive randomised controlled trial on stroke treatment was presented. 206 patients were included in the trial performed in 4 centres in Spain. The thrombectomy arm utilised the Solitaire device and patients within this arm were also administered intravenous thrombolysis. Patients within the second arm of the trial were treated with standard medical care alone. The rates of functional independence at 90 days were 44% and 28% in the mechanical thrombectomy and standard care arms respectively with an odds ratio of 2.0 in favour of the former.

The publication of this positive data from 5 different randomised controlled trials confirms that endovascular treatment is highly beneficial and this should remove any scepticism surrounding the use of mechanical thrombectomy in acute stroke. It is also crucial to note the excellent functional outcomes achieved in these trials. 60% of acute stroke patients managed to achieve functional independence at 90 days in SWIFT PRIME [16] which promises a better prognosis for acute stroke patients.

The difference in the rates of functional independence in the 5 trials ranged from 13.5 to 31 percentage points which translates into a number needed to treat (NNT) as low as three patients for benefit [18]. The odds ratios of the treatment effect demonstrated in the recent randomised controlled studies are summarised in Figure 1. The overall odds ratio in favour of mechanical thrombectomy is 2.4 ($p=0.000$).



Importantly these studies also confirmed that there were no significant differences in the rates of mortality and symptomatic intracranial haemorrhage between patients treated with mechanical thrombectomy versus those treated with standard care alone. This also proves that mechanical thrombectomy is a safe procedure with a similar rate of adverse events to standard care.

Mechanical thrombectomy is often performed under local anaesthesia once an arterial occlusive lesion is confirmed. The occluding thrombus is entrapped between the stent struts and the vessel wall once the stent retriever is deployed. This allows an almost immediate restoration of blood flow. As opposed to conventional stents, stentriever allow thrombectomy to be performed as the stent is retracted back within the micro-catheter. The retrievable stents can also be applied repeatedly until satisfactory flow restoration is achieved.

Recommendations on Patient Selection*		
1	Intracranial vessel occlusion must be diagnosed with non-invasive imaging whenever possible before considering treatment with mechanical thrombectomy.	(Grade A, Level 1a, KSU Grade A)
2	If vessel imaging is not available at baseline, a NIHSS score of ≥ 9 within three, and ≥ 7 points within six hours may indicate the presence of large vessel occlusion.	(Grade B, Level 2a, KSU Grade B)
3	Patients with radiological signs of large infarcts (for ex. using the ASPECTS score) may be unsuitable for thrombectomy.	(Grade B, Level 2a, KSU Grade B)
4	Imaging techniques for determining infarct and penumbra sizes can be used for patient selection and correlate with functional outcome after mechanical thrombectomy.	(Grade B, Level 1b, KSU Grade B)
5	High age alone is not a reason to withhold mechanical thrombectomy as an adjunctive treatment.	(Grade A, Level 1a, KSU Grade A)

*Adapted from 'Consensus statement on mechanical thrombectomy in acute ischemic stroke' – ESO-Karolinska Stroke Update 2014 in collaboration with ESMINT and ESNR.

Table 1: Recommendations on patient selection

Patient selection [19] and timely intervention were shown to be crucial factors that influence functional outcome in acute stroke patients. The updated recommendations on patient selection for mechanical thrombectomy in acute ischaemic stroke are summarised in Table 1. The newer stent-based retriever devices were likely

responsible for the improved functional outcomes in the 5 trials as they are able to achieve a faster and more complete recanalization.

Many stroke centres were already performing mechanical thrombectomy prior to the publication of these trials. The new data that emerged supports this treatment and clinical equipoise does no longer exist. Stroke guidelines should therefore be modified to include mechanical thrombectomy as part of the multi-modal approach in acute ischaemic stroke treatment.

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