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ORIGINAL RESEARCH

An investigation of the cost and benefit of mechanical thrombectomy for endovascular treatment of acute ischemic stroke

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ABSTRACT

Introduction The use of mechanical thrombectomy for the treatment of acute ischemic stroke has significantly advanced over the past 5 years, with few available data. The aim of this study was to analyze the cost and benefit of mechanical thrombectomy devices utilized during endovascular therapy of ischemic stroke patients.

Methods A retrospective chart review of patients that underwent intra-arterial stroke interventions was conducted. Clinical, angiographic, all devices used, procedural and postprocedural event and outcome data were collected. Thrombectomy devices were categorized as Penumbra aspiration system thrombectomy (group P) or stent retriever (group S). Statistical analysis of outcomes and costs for each group was performed.

Results 171 patients underwent mechanical thrombectomy. The Penumbra aspiration system was able to primarily achieve recanalization in 41.7% and the stent retriever in 70.4% of the time ($p=0.006$). The average cost was \$11 159 and \$16 022 ($p=0.0002$) in groups P and S, respectively. Average time to recanalization for group P was 85.1 min and for group S, 51.6 min ($p<0.0001$). Procedural complications were more frequent with the stent retriever (11.1% vs 9.0%; $p=0.72$) as were periprocedural significant complications (14.8 v 3%; $p=0.04$). Successful recanalization rates (Thrombolysis in Cerebral Infarction score 2b-3) were the same in groups P and S (78.5 vs. 77.8%). Similar rates of good neurologic outcomes were seen in group P (36.4%) and group S (50.0%) ($p=0.19$).

Conclusions For the treatment of acute stroke patients, the use of aspiration appears to be the most cost effective method to achieve acceptable recanalization rates and low complication rates. Stent retriever with local aspiration, despite higher costs and complication rates, yielded better overall outcome.

INTRODUCTION

The National Institutes of Health estimates that stroke, the fourth leading cause of death and the leading cause of disability in the USA, consumes health care resources of approximately US\$70 billion threshold annually.¹⁻⁴ Early vessel recanalization in acute ischemic stroke has been shown to strongly correlate with improved clinical outcome and reduced mortality.^{5 6} Thrombectomy devices have recently been shown to be safe and effective up to 8 h after the onset of stroke symptoms.⁵⁻⁸

In addition to expanding the therapeutic time window for stroke treatment and broadening the treatment repertoire, mechanical approaches have been shown to produce higher recanalization rates than intravenous tissue plasminogen activator (tPA) or intra-arterial (IA) thrombolysis alone.^{6 9-12} The optimal treatment for acute ischemic stroke has continued to evolve and improve over the past decade, as evidenced by the evolution and iteration of mechanical stroke devices. However, limited data exist evaluating the practical application of these devices with regard to overall procedure device costs, time to vessel recanalization, and patient outcome.

The aim of this study was to highlight and analyze the cost and benefit of current stroke therapies; more specifically, the impact of various mechanical thrombectomy and adjuvant devices utilized during endovascular therapy of ischemic stroke patients.

METHODS

Under an institutional review board approved protocol, a retrospective chart review from May 2008 to October 2012 was performed from the electronic medical records of the Medical University of South Carolina of all stroke patients who were treated with endovascular therapy. Patients were evaluated for candidacy for IA therapy based on CT perfusion imaging, irrespective of time of symptom onset, as published previously.^{13 14} The study evaluated the primary thrombectomy device(s) used in each case as well as any additional devices that aided in achieving recanalization. All procedural diagnostic and intervention related materials and devices were recorded along with cost data. A cost analysis was performed on the devices used in recanalization.

Documented patient characteristics included age, gender, National Institutes of Health Stroke Scale score at presentation, time to presentation from last known normal, and modified Rankin Scale score (mRS) at 90 days or closest follow-up period to 90 days. mRS data were obtained from the stroke neurology or neurointerventional clinic records. Radiological and angiographic imaging was reviewed to document location of the vascular occlusion, recanalization time, Thrombolysis in Cerebral Infarction (TICI) flow pre- and postprocedure, and procedural complications. Device efficacy was ultimately

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evaluated based on restored flow postprocedure and occurrence of intraprocedural complications. Procedural related complications were documented and separated by device group. Clinically significant complications (including procedure related) such as symptomatic intracranial hemorrhage were also documented.

Cases were segregated into two mechanical thrombectomy technological paradigms: Penumbra aspiration and stent retriever with local aspiration. These included cases in which thrombectomy was achieved solely with Penumbra aspiration system catheters (Penumbra Inc, Alameda, California, USA) and separators of any size and combination (group P). The technical details of the Penumbra aspiration system have recently been described in detail.¹⁵ The general treatment approach for Penumbra aspiration system catheter sizing was to choose the largest size catheter that would fit within the occluded vessel. If fragmentation of the clot occurred into downstream smaller vessels, additional small aspiration catheters were often required. If there was failure to recanalize, then additional adjunctive devices were utilized. Cases that required additional devices such as balloons, stents, or any other adjuvant devices in addition to the Penumbra aspiration system to successfully recanalize the vessel, were deemed a primary device recanalization failure. On Food and Drug Administration approval and release of the Solitaire device (ev3 Endovascular Inc, Plymouth, Minnesota, USA), all thrombectomy cases performed after April 2012 utilized the latest stent retriever devices (Trepo Pro, Stryker Neurovascular, Kalamazoo, Michigan, USA or Penumbra 3D separator, Penumbra Inc) to achieve recanalization (group S). In all stent retriever cases, the standardized methodology utilized a Penumbra 5Max aspiration catheter (Penumbra Inc), just proximal to the occlusion, and applying aspiration during removal of the stent retriever. If there was failure of recanalization after multiple stent retriever attempts, then aspiration with the 5Max and separator was performed or additional devices were introduced through the 5Max catheter which served as a distal access catheter. These cases and any other cases that required additional balloons or stents to primarily recanalize the vessel were deemed a primary device recanalization failure. If the patient had a carotid stenosis that required a stent to open the proximal vessel to then allow access to the downstream occlusion, they were placed into either the P or S group, depending on which device was subsequently used.

All devices utilized within the procedure, including femoral sheaths, IA tPA, guidewires, and catheters, were also documented and figured into the total cost of the procedure. If a procedural complication, such as a vessel dissection, was encountered, the device cost to treat the complication was also included in the overall cost analysis. In order to standardize price changes across different years, the advertized manufacturer suggested retail price as of 2012 was used in determining the overall procedure cost for all devices. Device cost was then computed with respect to each group, and analysis was performed to determine which methodology seemed to be most cost effective.

Statistics

Statistical analyses were performed using SAS V.9.2 (SAS Institute, Cary, North Carolina, USA). A population of 171 subjects was analyzed using descriptive statistics to characterize demographics and other clinical variables describing treatment, complications, and outcomes. Differences between the Penumbra and stent retriever device groups based on these variables were tested using the Student's *t* test for continuous measures and a χ^2 test for categorical measures. Differences between the device groups were tested using Fisher's exact test for

categorical measures with expected cell sizes <5 . All tests were two sided and assessed at a significance level of 0.05.

RESULTS

Patients

One hundred and seventy-one consecutive cases were investigated; 144 cases (84.2%) utilized the Penumbra aspiration devices. Penumbra aspiration catheters alone achieved primary recanalization in 41.7% of cases and the remainder required other devices to fully recanalize. Stent retriever devices (Solitaire, Trevo or Penumbra 3D separator) were successful as the primary device in recanalization in 70.1% ($p=0.006$) of cases, with the remainder requiring aspiration thrombectomy, stents, or balloon maceration. Thrombus location was documented for each of the 171 cases; 88.3% of all cases investigated involved anterior circulation occlusion while 11.7% of cases involved posterior circulation. Occlusion of the middle cerebral artery was the most common location (74.9%) followed by the internal carotid artery (12.9%) and basilar artery (9.9%). Of note, all but one posterior circulation occlusions were treated by aspiration thrombectomy (group P).

Outcomes

Successful revascularization, defined as a TICI score of 2b or 3, was nearly identical for both groups, with 78.5% for group P and 77.8% for group S ($p=0.9$). For complete revascularization alone, there was a significant difference, with group S achieving TICI 3 in 59.3% of cases compared with 28.5% for group P ($p=0.002$) (figure 1). There was a statistically significant difference in time required to revascularize (groin access to restoration of flow in the occluded vessel), 85.1 min for group P and 51.6 min for group S ($p<0.0001$). Procedural complications occurred in 9.0% of group P and 11.1% of group S cases ($p=0.72$). Clinical outcomes were not available for 13 patients. Clinically significant complications were seen in 3.5% for group P and 14.8% for group S ($p=0.04$). Clinical outcomes with good neurologic function at 90 days, as defined by mRS ≤ 2 , were not significantly different (36.4% in group P and 50.0% in group S) ($p=0.19$). However, the number of patients achieving mRS 0 was significantly greater in group S (26.9%) than in group P (8.3%) ($p=0.01$) (figure 2). When overall clinical outcomes were correlated with revascularization, there was significant improvement in rates of good neurologic outcomes (mRS 0–2) and rates of poor neurologic outcomes or death (mRS 5,6) in those where revascularization was successful (figure 3).

Cost analysis

The mean cost across the groups was \$11 926.45, with a minimum procedural cost of \$3296.00 and a maximum cost of

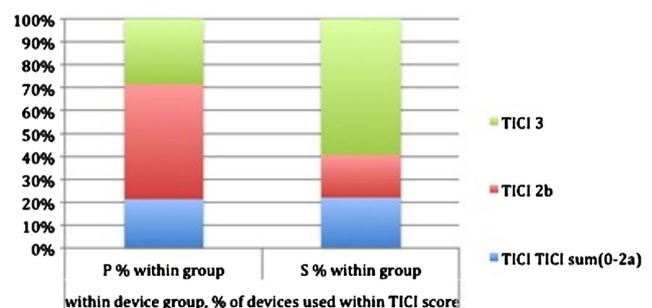


Figure 1 Percentage of patients within P and S groups achieving TICI 0-2, 2b, and 3.

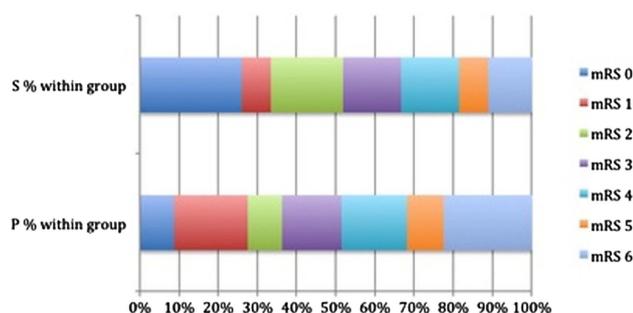


Figure 2 Percentage of patients within P and S groups achieving mRS of 0, 1, 2, 3, 4, 5, and 6.

\$60 872.91. Group P averaged \$11 158.62 per subject, with cost ranging from \$3296.00 to \$60 872.91. In cases where the Penumbra aspiration system was successful as the primary device that achieved revascularization, the cost was \$8727.06. Group S had a mean cost of \$16 021.53, with values ranging from \$9601.85 to \$35 724.00. In cases where a stent retriever was successful as the primary device that achieved revascularization, the cost was \$14 483.41.

DISCUSSION

This study found that utilization of direct aspiration to revascularize occluded vessels in patients with acute ischemic stroke could be done with a significantly lower cost with similar acceptable degrees of recanalization (TICI 2b and 3). However, the time to achieve revascularization was significantly longer and was only successful as the primary device to achieve recanalization 41.7% of the time. Superior (mRS 0) neurologic outcomes as well as the proportion of patients achieving complete recanalization (TICI 3) were significantly higher in those patients treated with stent retrievers, with local aspiration. Although clinically significant complications were significantly higher with the stent retriever group, good neurologic outcomes remained high within this group.

Angiographic imaging data were used to assess postprocedural flow restoration for the cases. The group using the Penumbra (group P) and the group using stent retrievers (group S) achieved similar TICI 2B or 3 scores in approximately 78% of their cases. However, there were significantly more cases achieving TICI 3 flow with stent retrievers. This finding is similar to that recently reported in an in vitro model in which better recanalization rates were found with Solitaire over Penumbra aspiration.¹⁶ The mechanism observed by the authors was generation of more and larger downstream particles produced by the debulking process from the Penumbra aspiration system. This was related to the use of the separator to debulk and fragment

the thrombus to a size small enough to fit through the aspiration catheter. The subsequent activity of the separator to then clear the end of the aspiration catheter can momentarily depress aspiration capability and result in many fragments being showered downstream.

Good clinical outcome, defined as mRS ≤ 2 , was also achieved at similar rates by the majority of patients in both groups. However, there were significantly more patients treated with stent retrievers, with local aspiration that achieved mRS 0. This likely relates directly to the increased number of patients achieving TICI 3 recanalization. The above proposed mechanism of fewer and smaller downstream emboli produced during the procedure likely also contributes to the improved clinical outcomes. When outcome was stratified by final revascularization status, there were significantly more patients with good clinical outcomes when the target vessel was recanalized (44.0%) than when recanalization failed (18.2%), similar to those in the Multi-MERCI (Mechanical Embolus Removal in Cerebral Ischemia) trial.¹⁷

Procedural complications were similar among the groups but clinically significant complications were significantly less in group P. In the stent retriever group, 14.8% of cases experienced a clinically significant complication during or after the procedure. These included symptomatic intracranial hemorrhage, vessel dissection, or perforation. One possible explanation for the complication rate in this group likely relates to the stent-like mechanism where the device exhibits outward radial force to create a channel through the thrombus and displace the thrombus along the vessel wall. During removal of the device there is subsequent traction of the device against the wall of the vessel. This has been shown to result in increased frequency of endothelial and vessel injury.¹⁸ This could also be related to the method utilized for device removal, although the method we employ using direct stent retriever retraction into a large aspiration catheter at the proximal edge of the clot should intuitively minimize vascular traction injury. The small sample size of group S should be noted also, and a more accurate representation of complications with respect to the group would be provided with a larger number of cases.

The group using Penumbra aspiration only (group P) displayed both the lowest mean cost with similar variability in cost (SD of \$6028.67 compared with \$6544.67 for group S). This was predominantly related to a complex anatomical or target lesion that required a multitude of additional devices besides the Penumbra to revascularize. Further, this occurred in a relatively large number ($\approx 60\%$) of aspiration cases. The device in group S had a higher mean cost at \$16 021.53. The cost range on these procedures was similar to those with the Penumbra. This is most likely related to the higher primary device success rate and requirement for fewer or cheaper adjunctive devices in the case of failure. Again, a much larger sample size is needed in order to fully elucidate the cost data for this group.

The technique we employ, using an aspiration catheter at the level of the clot for removal of the stent retriever rather than a proximal balloon guide catheter, does contribute to the cost as the aspiration catheter has a cost of \$1500 compared with the balloon guide catheter of \$895. However, this difference in cost does not result in a significant alteration of the overall procedure cost. The technique of local aspiration during stent retriever removal was driven by the theoretical benefits of reduced embolism to new territory that has been as high as 9% in the SWIFT (Solitaire with the Intention for Thrombectomy) trial and validated in an in vitro model.^{16 19} Further, in the event of failure to recanalize with a stent retriever, the large bore local aspiration catheter can then be used for direct aspiration

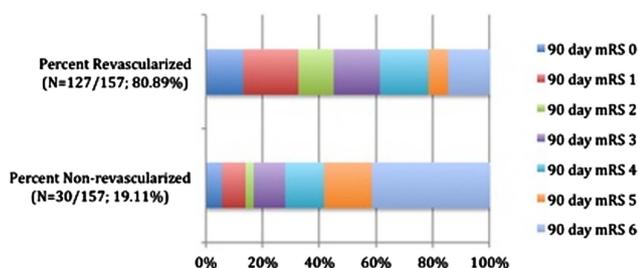


Figure 3 Percentage of patients within revascularized and non-revascularized groups achieving mRS of 0, 1, 2, 3, 4, 5, and 6.

thrombectomy or function as a conduit to deliver other assist devices, such as balloons or stents. This increases the speed with which devices can be exchanged as the carotid siphon does not need to be navigated with each new device. Distal intracranial access also likely improves safety, as the amount of vessel displacement during stent retriever removal is minimized and the likelihood of guide catheter complications is lower.²⁰

Several limitations in both device cost and efficacy exist in this study. First, all patients that underwent endovascular stroke therapy were considered for this study, regardless of time of symptom onset. However, our outcomes have been previously published and are within the acceptable range reported in the literature.¹³

The broad applicability of these study results are limited by the single center retrospective design. Most devices used in the cases were subject to unit cost inflation from 2009 to 2010 and, as a result and for the purposes of this study, the device cost was standardized using 2012 price values. Devices that were used in 2009 but did not continue into later years were assigned the unit cost according to the inventory in 2009. Intra-arterial tPA also experienced a significant shift in price as a result of a change in packaging. Prior to October 2009, tPA was dispensed in 50 mg vials and the unit cost, over \$2000, was charged regardless of how little or how much was used. After that date, 2 mg vials became available at a unit cost of \$87.00. For the purposes of this study, the cost of tPA was standardized from 2009 to 2012 at \$87.00 per 2 mg used. Most importantly, the sample size of the newer technology stent retriever group was relatively small. However, the standardized approach with this technique and high success rate with the primary device is not likely to change the overall cost due to the low probability of using a second device. There is a greater possibility that there could be a change in group S; however, this group already had significantly higher costs compared with the other groups. A larger group S would be more likely to positively affect our clinical and angiographic outcomes beyond the already reported improved outcomes, although these values remain within those reported in the literature.

In conclusion, for treatment of acute stroke patients, the use of aspiration as an initial approach is a significantly less expensive method to achieve acceptable recanalization rates with low complication rates; however, this technique alone is often unsuccessful. Stent retriever cases, while having a notably higher rate of complete recanalization, does cost significantly more and was associated with a higher clinically significant complication rate, although improved overall outcomes. This suggests that the most cost effective approach to a large vessel occlusion might be to attempt a brief direct aspiration with a large bore catheter (without the separator) first and if this fails then proceed with other devices, such as a stent retriever.

Contributors Each author listed should receive authorship credit based on material contribution to this article, revision of this article and final approval of this article for submission to this journal.

Ethics approval The study was approved by the institutional review board.

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

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