Aspiration Thrombectomy for Acute ST-Elevation Myocardial Infarction: Literature Review

Syed Mustajab Hasan, MD*, Mohammed Faluk, MD, Jay D. Patel, DO, Ramy Abdelmaseih, MD, Jay John Chacko, MD, Premranjan Singh, MD, FACC, FSCAI, and Jigar Patel, MD, FACC

Abstract: Over the years, aspiration thrombectomy for management of acute coronary syndrome was the center of discussion however due to multiple randomized control trials which did not provide sufficient evidence supporting use of this approach, this method is not routinely used. The benefit of this approach remains unknown, however, it is important to acknowledge the evolution of aspiration catheters and their potential in minimizing complications which were previously the set back of this approach. We provide a comprehensive review of the previous trials and how those catheters have since evolved significantly. (Curr Probl Cardiol 2021;46:100580.)

Introduction

As we all know, the underlying pathophysiology behind a ST-segment elevation myocardial infarction is due to coronary vessel occlusion with a plaque rupture leading to thrombus formation. Of the patients that undergo primary Percutaneous Coronary Intervention (PCI) in this setting, the rate of distal embolization may lead to worsening infarct, reduced systolic function and consequently, reduced survival rates. Over the past few years, thrombus removal via mechanical thrombectomy has been controversial in treatment of acute coronary

Curr Probl Cardiol 2021;46:100580
0146-2806/$ – see front matter
https://doi.org/10.1016/j.cpcardiol.2020.100580

syndrome. Recent randomized control trials did not provide sufficient evidence for the use of mechanical thrombectomy in patients with ST-elevation myocardial infarction however aspiration catheters have since then evolved. In this review article, we aim to highlight the benefits of the newer mechanical thrombectomy catheters in the setting of acute ST segment elevation myocardial infarction management.

Discussion

Manual and mechanical thrombus aspiration catheters are 2 modalities that have been used more recently, however, previous studies showed no comparable difference in mortality between patients with ST-Segment Elevation Myocardial Infarction (STEMI) treated with thrombus aspiration (TA) vs PCI alone while other studies showed that mechanical thrombus aspiration was associated to a worsening mortality rates. It is also important to point out that according to the studies mentioned and elaborated upon below, aspiration thrombectomy was also linked to a much higher risk of stroke.[1-6] Due to the aforementioned findings of no significant benefit and even potential complications, the routine use of thrombus aspiration before primary percutaneous coronary intervention with STEMI had been lowered to a class III recommendation as indicated by the 2015 American college of cardiology, American Heart Association and Society of Cardiovascular Angiography.

A review of prior studies would aid in better understanding of the role of thrombus aspiration and its future potential especially in light of the current mechanical evolution of aspiration catheters. Lets begin by looking at current evidence highlighting the lower incidence of death and major adverse cardiac events with thrombus aspiration. The TAPAS trial, which is a single center study which involved 1071 patients with acute ST-elevation myocardial infarction showed a trend for a decrease in major adverse cardiac events in addition to a survival benefit in patients with STEMI who were randomized to the thrombus aspiration group compared to patients who underwent PCI only. At 30 days, the numbers were as follows; Mortality: 2.1% compared to 4.0%; Risk Ratio 0.52; 95% confidence interval (CI), 0.26-1.07; $P = 0.07$. Reinfarction: 0.8% compared to 1.9% (10/531); Risk Ratio (RR) 0.40; 95% CI, 0.13-1.27, P value 0.11. Major adverse cardiac events; 6.8% compared to 9.4%, RR 0.72; 95% CI, 0.48-1.02, P value 0.12. The results of this trial showed the possible benefit of manual aspiration of thrombus as compared to conventional approach to PCI that entails balloon angioplasty as the initial step. This benefit applied to all patients regardless of demographic or clinical

presentation including age, sex, preprocedural TIMI flow etc. A 1-year follow up of this study further indicated that thrombus aspiration before stenting of the target lesion also improved clinical outcome when compared to PCI alone.[7,8]

In 2013, Khumbani et al concluded manual thrombus aspiration but not mechanical was beneficial in reducing 6-12 month incidence of major adverse cardiac events, all cause mortality, recurrent myocardial infarction and target vessel restenosis when compared with primary PCI alone. In this meta analysis, 25 clinical trials randomized acute myocardial infarction patient to aspiration (18 trails; 3936 patients) or mechanical thrombectomy (7 trials; 1598 patients) prior to PCI compared to conventional PCI alone. On one hand, comparison of aspiration thrombectomy vs primary PCI alone yielded results as follows; all cause mortality (2.7% compared to 3.9%; RR: 0.71; 95% CI: 0.51 to 0.99; $P = 0.049$). Composite major adverse cardiac events were significantly lower in the aspiration thrombectomy arm (10.8% compared to 14.0%; RR: 0.76; 95% CI: 0.63 to 0.92; $P = 0.006$). Of note, incidence of cerebrovascular complications were similar (0.7% compared to 0.4%; RR: 1.31; 95% CI: 0.30 to 5.79; $P = 0.72$).

On the other hand, mechanical thrombectomy vs conventional PCI yielded results at mean follow up of 6.2 months as follows; all cause mortality (4.5% compared to 3.9%; RR: 1.20; 95% CI: 0.64-2.23; $P = 0.57$). Major Adverse cardiac events (10.1% compared to 10.9%; RR: 1.10; 95% CI: 0.59 to 2.05; $P = 0.77$). This meta analysis indicated that aspiration thrombectomy was associated with a significant reduction in all cause mortality and MACE as opposed to mechanical thrombectomy which has no superiority to conventional PCI but was concerning due to the trend of higher incidence of stroke.[9]

Furthermore, evidence supports thrombus aspiration in maintaining or improving micro vascular integrity which leads to reduced infarct area as well as preventing thrombus embolization. In 2010, Sardella et al performed the single center EXPIRA trial of 175 patients (thrombectomy with export catheter in infarct related artery during primary percutaneous coronary intervention) in which the investigators compared postprocedural infarct size and myocardial perfusion using contrast enhanced MRI. The study yielded results as follows, postprocedural rates of Myocardial Blush Grade (MBG) ≥ 2 and ST-segment resolution $>70\%$ was higher in the group that underwent thrombus aspiration compared to the primary PCI group; 89% compared to 59% and 84% compared to 40% respectively. At the 3-month mark, the infarct size in the thrombus aspiration group decreased from $14 \pm 12\%$ to $9 \pm 4.5\%$; P value 0.001. On the other

hand, no improvement in infarct size was seen in the conventional PCI group. Additionally, patients who underwent thrombus aspiration had lower cardiac mortality compared to the conventional PCI group (0% vs 4.6% *P* ''value 0.02, log rank test). These findings illustrate the benefit of manual thrombus aspiration before stenting significantly improved myocardial perfusion, which consequently resulted in decreased cardiac death and major adverse cardiac events at 24 months.[10]

Thrombus aspiration has also been shown to improve efficiency of PCI procedures. In 2014, Fernandez-Rodriguez et al evidenced that the use of thrombus aspiration was associated with reduced number of stents per lesion, shorter stent lengths as well as larger stent sizes. Main results of this study showed a higher prevalence of angiographic success (78.8% compared to 68%, *P* value 0.015) and improved post procedural TIMI flow (TIMI flow 3: 85.9% compared to 78.3%, *P* value 0.04) in comparison to the nonthrombus aspiration group. Moreover, the rate of direct stenting was higher (58.7% compared to 45.5%, *P* value 0.009) and the number of stents placed was lower (1.3 $\pm$ 0.67 compared to 1.5 $\pm$ 0.84, *P* value 0.009). Of the stents placed, patients with thrombus aspiration also had stents that were larger (3.17 $\pm$ 0.43 compared to 2.93 $\pm$ 0.44 mm, *P* value 0.001) and shorter (24.1 $\pm$ 11.8 compared to 26.9 $\pm$.7 mm, *P* value 0.038) as compared to the nonthrombus aspiration group.[11]

As evidenced by the aforementioned literature, thrombus aspiration seems promising which raises the question, why is mechanical thrombectomy not the current standard of treatment of acute coronary syndrome? Lets further delve into the evidence that previously showed no clinical benefits of thrombus aspiration during PCI.

In 2013, the randomized TASTE trial, which included 7244 patients, did not show any significant overall benefit after 30 days and 1 year. At the 30 day mark follow up, All cause mortality rate was 2.8% in the thrombus aspiration group compared to the 3.0% in the PCI only group (Hazard ratio [HR] with thrombus aspiration, 0.94; 95% CI 0.72-1.22, *P* value 0.63), rate of hospitalization because of reinfarction was 0.5% in the thrombus aspiration group and 0.9% in the PCI only group (HR 0.61, 95% CI 0.34-1.07, *P* value 0.09). Moreover, the rates of stent thrombosis, stroke, neurologic complications, perforation/tamponade, heart failure, or left ventricular dysfunction were similar. At the 1-year mark, all cause mortality was 5.3% in the thrombus aspiration group compared to 5.6% in the PCI only group (HR 0.94, 95% CI 0.78-1.15, *P* value 0.57).[3,12]

This study was followed by the TOTAL trial conducted in 2015 by Jolly et al. In this randomized control trial, the findings were similar to the previously mentioned TASTE trial demonstrating that routine manual

thrombus aspiration did not reduce MACE (6.9% in the TA group vs 7.0% in the PCI alone group (HR 0.99, 95% CI, 0.85-1.15, *P*= 0.86) and cardiovascular death (3.1% in the TA group compared to 3.5% in the PCI alone group, HR 0.90, 95% CI 0.73-1.12, *P* = 0.34), recurrent MI (2.0% compared to 1.8%, HR 1.07, 95% CI, 0.81-1.43, *P* = 0.62), Cardiogenic shock(1.8% compared to 2.0%, HR 0.92, 95% CI 0.69-1.22, *P* = 0.56), stent thrombosis (1.5% compared to 1.7%, HR 0.88, 95% CI 0.65-1.20, *P* = 0.42), TVR(4.5% compared to 4.3%, HR 1.03, 95% CI 0.85-1.24, *P* = 0.77), and NYHA class IV heart failure(1.9% compared to 1.8%, HR 1.09, 95% CI 0.82-1.45, *P* = 0.57) within the first 180 days were relatively comparable between the 2 groups. After the first year, the percentage of MACE (7.8% in the TA group compared to 7.8% in the PCI-alone group, HR, 1.00, 95% CI, 0.87-1.15, *P* = 0.99) and the cardiovascular deaths (3.6% compared to 3.8%; HR, 0.93, 95% CI, 0.76-1.14, *P* = 0.48), recurrent MI (2.5% compared to 2.3%, HR, 1.05, 95% CI, 0.82-1.36, *P* = 0.68), cardiogenic shock (1.9% compared to 2.1%, HR, 0.90, 95% CI, 0.68-1.19, *P* = 0.47), stent thrombosis (1.7% compared to 2.1%, HR, 0.82, 95% CI, 0.62-1.09, *P* = 0.18), TVR (5.5% compared to 5.1%, HR, 1.06, 95% CI, 0.90-1.26, *P* = 0.48), and NYHA class IV heart failure (2.1% vs 1.9%, HR, 1.10, 95% CI, 0.83-1.45; *P* = 0.50) were also comparable between the groups. Of note, there was also no difference between the 2 groups in regards to cardiovascular mortality at 30 days, 180 days, and 1-year follow-ups.[13,14]

In 2016, Sharma et al performed an angiographic substudy of the TOTAL trial o determine if manual aspiration improved micro vascular perfusion as measured by myocardial blush grade (MBG). Results of this substudy showed no improvement in TIMI flow grade or micro vascular perfusion when comparing PCI with TA to PCI alone.[15]

Prior evidence also indicated that thrombus aspiration did not improve myocardial reperfusion area. In 2013, Onuma et al conducted the TROFI trial, which was a randomized controlled trial to assess the effect of thrombus aspiration on flow area in STEMI patients. In this study, researches initially hypothesized that PCI with manual thrombectomy reduced thrombus burden which led to improvement in larger flow area as measured with optical frequency domain imaging (OFDI). However the results of the study revealed no difference between the 2 groups in stent area, minimum flow area, cardiac death, reinfarction, all cause death, stroke, or stent thrombosis.[16,17]

The mainstay of discussion and controversy however remains the increased risk of stroke associated with thrombus aspiration. This finding was discussed most in detail by the authors of the TOTAL trial. At the

30-day follow up, acute CVA occurred in 0.7% of the patients in the thrombus aspiration group compared to 0.3% of the patients who underwent PCI alone (HR 2.06, 95% CI, 1.13-3.75, $P = 0.02$). Moreover, this trend maintained at the 180 day and 1-year follow-up. Furthermore, a meta analysis in 2016 by El Dib et al reported that even though thrombus aspiration was associated with a potential minor decrease in mortality, authors noticed an increase stroke rate (0.8% compared to 0.5% (RR 1.56, 95% CI, 1.09-2.24, $P = 0.02$)

It has previously been theorized that the number of complications such as stroke, vessel dissection, or contractile dysfunction occurring with thrombus aspiration varies with the different types of aspiration catheters. This is very important to take into consideration when comparing the aforementioned clinical trials as the use of different catheters likely affected the outcomes of the respective trials.[18,19] At the time of these publications, it was conceived that an improvement in equipment and technique would potentially reduce device related complications. To improve rate of complications, it was of utmost importance to first understand the pathophysiology behind these complications. Brown et al discussed potential mechanisms of how stroke may be caused with the use of mechanical thrombectomy with primary PCI. Firstly, many a times a thrombus is not completely aspirated which increases its risk of breaking and embolizing fragments into systemic vasculature. Second, during thrombus aspiration, if a thrombus is not fully aspirated with manual aspiration, the thrombus is at risk of entering systemic vasculature as well, this is due to noncontinuous suction during catheter withdrawal. It is also important to highlight the fact that prior studies showed the higher incidence of stroke was >30 days after procedure which shows that this complication may not actually be related to thrombus aspiration, but to other factors that have not yet been well understood.[20]

Since that time, catheter based thrombectomy has significantly involved. Recently, in an attempt to deliver the most efficient thrombus aspiration while concomitantly minimizing distal embolizing, the thrombus aspiration paradigm shifted from manual aspiration to mechanical thrombus aspiration with a catheter design to deliver continues vacuum power. This new system not only increased aspiration power 10 fold as measured by aspiration flow rate, but also provides larger lumen tips with circumferential aspiration to ensure complete thrombus aspiration which in turn minimizes the complications mentioned above.

This new mechanism of catheter based thrombus aspiration can potentially change the management of acute coronary syndrome.

Conclusion

Although prior research showing inconclusive and conflicting results regarding risks and benefits associated with aspiration thrombectomy, it is important to note that since those trials, aspiration catheters have evolved. These newer mechanical catheters as opposed to manual aspiration catheters addressed the theorized pathophysiology that was previously have thought to lead to the complications mentioned above and have been optimized. Future randomized control trials are needed to address the efficacy and safety of these catheters that may lead to aspiration thrombectomy becoming the mainstay in the management of acute coronary syndromes.

Disclaimer

This research was supported (in whole or in part) by HCA and/or an HCA affiliated entity. The views expressed in this publication represent those of the authors and do not necessarily represent the official views of HCA or any of its affiliated entities.

REFERENCES

1. Kumbhani DJ, Bavry AA, Desai MY, Bangalore S, Bhatt DL. Role of aspiration and mechanical thrombectomy in patients with acute myocardial infarction undergoing primary angioplasty: an updated meta-analysis of randomized trials. *J Am Coll Cardiol* 2013;62:1409–18. https://doi.org/10.1016/j.jacc.2013.04.025.
2. Sirker A, Mamas M, Kwok CS, et al. Outcomes from selective use of thrombectomy in patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: an analysis of the British Cardiovascular Intervention Society/National Institute for Cardiovascular Outcomes Research (BCIS-NICOR) registry, 2006-2013. *JACC Cardiovasc Interv* 2016;9:126–34. https://doi.org/10.1016/j.jcin.2015.10.047.
3. Lagerqvist B, Fröbert O, Olivecrona GK, Gudnason T, Maeng M, Alström P, Andersson J, Calais F, Carlsson J, Collste O, Götberg M, Hårdhammar P, Ioanes D, Kallryd A, Linder R, Lundin A, Odenstedt J, Omerovic E, Puskar V, Tödt T, Zelleroth E, Östlund O, James SK. Outcomes 1 year after thrombus aspiration for myocardial infarction. *N Engl J Med* 2014;371:1111–20. https://doi.org/10.1056/NEJMoa1405707.
4. Fröbert O, Lagerqvist B, Olivecrona GK, et al. Thrombus aspiration during ST-segment elevation myocardial infarction. *N Engl J Med* 2013;369:1587–97. https://doi.org/10.1056/NEJMoa1308789.
5. Bhindi R, Kajander OA, Jolly SS, et al. Culprit lesion thrombus burden after manual thrombectomy or percutaneous coronary intervention-alone in ST-segment elevation

myocardial infarction: the optical coherence tomography sub-study of the TOTAL (thrombectomy versus PCI alone) trial. *Eur Heart J* 2015;36:1892–900. https://doi.org/10.1093/eurheartj/ehv176.
6. Jolly SS, Cairns J, Yusuf S, et al. Design and rationale of the TOTAL trial: a randomized trial of routine aspiration thrombectomy with percutaneous coronary intervention (PCI) versus PCI alone in patients with ST-elevation myocardial infarction undergoing primary PCI. *Am Heart J* 2014;167:315–21. https://doi.org/10.1016/j.ahj.2013.12.002. e1.
7. Vlaar PJ, Svilaas T, van der Horst IC, et al. Cardiac death and reinfarction after 1 year in the thrombus aspiration during percutaneous coronary intervention in acute myocardial infarction study (TAPAS): a 1-year follow-up study. *Lancet* 2008;371:1915–20. https://doi.org/10.1016/S0140-6736(08)60833-8.
8. Svilaas T, van der Horst IC, Zijlstra F. Thrombus aspiration during percutaneous coronary intervention in acute myocardial infarction study (TAPAS)—study design. *Am Heart J* 2006;151:597.e1–7. https://doi.org/10.1016/j.ahj.2005.11.010.
9. Kumbhani DJ, Bavry AA, Desai MY, Bangalore S, Bhatt DL. Role of aspiration and mechanical thrombectomy in patients with acute myocardial infarction undergoing primary angioplasty: an updated meta-analysis of randomized trials. *J Am Coll Cardiol* 2013;62:1409–18. https://doi.org/10.1016/j.jacc.2013.04.025.
10. Sardella G, Mancone M, Bucciarelli-Ducci C, et al. Thrombus aspiration during primary percutaneous coronary intervention improves myocardial reperfusion and reduces infarct size: the EXPIRA (thrombectomy with export catheter in infarct-related artery during primary percutaneous coronary intervention) prospective, randomized trial. *J Am Coll Cardiol* 2009;53:309–15. https://doi.org/10.1016/j.jacc.2008.10.017.
11. Fernández-Rodríguez D, Alvarez-Contreras L, Martín-Yuste V, et al. Does manual thrombus aspiration help optimize stent implantation in ST-segment elevation myocardial infarction? *World J Cardiol* 2014;6:1030–7. https://doi.org/10.4330/wjc.v6.i9.1030.
12. Wachtell K, Lagerqvist B, Olivecrona GK, James SK, Fröbert O. Novel trial designs: lessons learned from thrombus aspiration during ST-segment elevation myocardial infarction in scandinavia (TASTE) trial. *Curr Cardiol Rep* 2016;18:11. https://doi.org/10.1007/s11886-015-0677-6.
13. Jolly SS, Cairns JA, Yusuf S, et al. Outcomes after thrombus aspiration for ST elevation myocardial infarction: 1-year follow-up of the prospective randomised TOTAL trial. *Lancet* 2016;387:127–35. https://doi.org/10.1016/S0140-6736(15)00448-1.
14. Jolly SS, Cairns JA, Yusuf S, et al. Randomized trial of primary PCI with or without routine manual thrombectomy. *N Engl J Med* 2015;372:1389–98. https://doi.org/10.1056/NEJMoa1415098.
15. Sharma V, Jolly SS, Hamid T, et al. Myocardial blush and microvascular reperfusion following manual thrombectomy during percutaneous coronary intervention for ST elevation myocardial infarction: insights from the TOTAL trial. *Eur Heart J* 2016;37:1891–8. https://doi.org/10.1093/eurheartj/ehw157.
16. Onuma Y, Thuesen L, van Geuns RJ, et al. Randomized study to assess the effect of thrombus aspiration on flow area in patients with ST-elevation myocardial infarction:

an optical frequency domain imaging study—TROFI trial. *Eur Heart J* 2013;34:1050–60. https://doi.org/10.1093/eurheartj/ehs456.
17. García-García HM, Muramatsu T, Nakatani S, et al. Serial optical frequency domain imaging in STEMI patients: the follow-up report of TROFI study. *Eur Heart J Cardiovasc Imaging* 2014;15:987–95. https://doi.org/10.1093/ehjci/jeu042.
18. Fröbert O, Calais F, James SK, Lagerqvist B. ST-elevation myocardial infarction, thrombus aspiration, and different invasive strategies. A TASTE trial substudy. *J Am Heart Assoc* 2015;4:e001755. https://doi.org/10.1161/JAHA.114.001755.
19. Schiele F, Ecarnot F. Does thrombo-aspiration still have a place in the treatment of myocardial infarction? *BMC Cardiovasc Disord* 2016;16:97. https://doi.org/10.1186/s12872-016-0291-6.
20. Brown ED, Blankenship JC. A mechanism for stroke complicating thrombus aspiration. *Catheter Cardiovasc Interv* 2017;89:93–6. https://doi.org/10.1002/ccd.26682.