Editorial

Thrombus aspiration in primary percutaneous coronary intervention: still a valid option with improved technique in selected patients!

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Provenance: This is a Guest Editorial commissioned by Section Editor Yue Liu, MD, (Department of Cardiology, the First Affiliated Hospital of Harbin Medical University, Harbin, China).

Comment on: Jolly SS, James S, Džavík V, *et al*. Thrombus Aspiration in ST-Segment-Elevation Myocardial Infarction: An Individual Patient Meta-Analysis: Thrombectomy Trialists Collaboration. Circulation 2017;135:143-52.

Submitted Mar 28, 2017. Accepted for publication May 11, 2017.
doi: 10.21037/cdt.2017.05.09
View this article at: http://dx.doi.org/10.21037/cdt.2017.05.09

Thrombus aspiration during primary percutaneous coronary intervention (pPCI) has been used to improve myocardial perfusion through a reduction of the thrombotic burden eventually resulting into better clinical outcomes (1,2). After the initial enthusiasm derived from the mortality reduction shown in early randomized and observational studies (3-7), disappointing results have been yielded in more recent larger scale trials testing the routine use of thrombus aspiration in pPCI (8-12). As a consequence, this technique has lost its initial appeal such that it is currently often neglected or even considered as a useless hassle by the interventional cardiologists.

The recent meta-analysis by Jolly *et al*. (13) conducted in more than 18,000 patients once again reinforces the evidence that overall there is no benefit in the routine use of thrombus aspiration during pPCI. However, it has the merit to shed light on the residual potential of this technique, which has probably been dismissed too quickly. First, there were no significant differences in the occurrence of cardiovascular events up to 1-year post-pPCI between patients treated conventionally versus those treated with routine adjunctive thrombus aspiration. Of interest, in the subgroup of patients with large angiographic thrombus burden (i.e., TIMI thrombus grade ≥3), thrombus aspiration was associated with a significant reduction in cardiovascular death [2.5% *vs.* 3.1%; hazard ratio 0.80, 95% confidence interval (CI), 0.65–0.98, P=0.03].

The strength of this meta-analysis relies in the collection of individual patient data. This approach allows the evaluation of specific patients' subgroups, such as those with high thrombus burden, although in the absence of adjustment for multiple comparisons all secondary analyses should only be considered as hypothesis-generating. On the other side, potential weakness might derive from some important differences in the study design and patients included among the trials considered (*Table 1*). This meta-analysis in fact assessed data from the three largest randomized trials on this topic, namely Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study (TAPAS) (4,5), Thrombus Aspiration in ST elevation Myocardial Infarction in Scandinavia (TASTE) (8,9) and Thrombectomy with PCI versus PCI Alone in Patients with STEMI (TOTAL) (11,12). While in TAPAS and TOTAL patients were randomized to thrombus aspiration or conventional PCI prior to coronary angiography, in TASTE the randomization was performed after angiography, potentially introducing heterogeneity in coronary anatomy between the studies. Moreover, thrombus grade was evaluated before wire crossing in TAPAS and TOTAL and after wiring in TASTE. This explains the 74% rate of patients with thrombus grade 4 or 5 in TOTAL trial, whereas this

Table 1 Main characteristics of the three trials included in the meta-analysis by Jolly *et al*.

Study/characteristic	TAPAS	TASTE	TOTAL
Year of publication	2008	2013	2015
Type of study/location	Single center/Netherlands	Multi-center/Sweden, Ireland, Denmark	Multi-center/Canada
Number of centers	1	31	87
Patients screened	1,161	12,005	Not reported
Percentage of patients included	92%	60%	Not reported
Follow-up (months)	12	12	12
Time from symptoms onset to intervention (hours)	0.5–12	0.5–24	0–12
Intervention	Routine thrombus aspiration with direct stenting when possible	Routine thrombus aspiration	Routine thrombus aspiration
Manual aspiration device	Export®	Export®, Pronto®, Eliminate®	Export®
Primary outcome	Myocardial blush grade 0–1	All-cause mortality at 30 days	Composite of death from cardiovascular causes, recurrent MI, cardiogenic shock or NYHA class IV at 180 days
Number of patients	1,071 (535 in the TA group/536 in the PCI alone group)	7244 (3,623 in the TA group/3,621 in the PCI alone group)	10,063 (5,033 in the TA group/5,030 in the PCI alone group)
Timing of randomization	Before angiogram	After angiogram	Before angiogram
Radial access (%)	Routinely femoral	66	68
Predilatation in TA group (%)	Not allowed	Allowed	6
Direct stenting facilitated by TA (%)	62	15	17
Bare-metal stent use (%)	92	48	52
Drug-eluting stent use (%)	0	49	45
Effective thrombus retrieval (%)	73	No data	70
Baseline TIMI flow, grade 0/1 TA/PCI alone (%)	55/60	77/77	66/67
GP IIb/IIIa inhibitor use TA/PCI alone (%)	93/90	17/15	38/41
Study outcomes (TA *vs.* PCI alone)			
Myocardial reperfusion	↑	No data	↑
1-year mortality	↓	=	=
1-year re-infarction	=	=	=
1-year stent thrombosis	=	=	=
1-year target-vessel revascularization	=	=	=
1-year heart failure	No data	No data	=

TA, thrombus aspiration; PCI, percutaneous coronary intervention.

rate was only 32% in TASTE. Other differences might concern the data collection (e.g., cerebrovascular accidents were not recorded in TAPAS, and no distinction reported between stroke or TIA in TASTE) and adjudication of clinical endpoints (independent adjudication in TAPAS and TASTE, monitoring as part of an institutional registry in TASTE). In addition, some differences between the two pooled groups of patients are worth mentioning. First, patients treated with thrombus aspiration showed a longer interval from symptom onset to hospital arrival (190 *vs.* 185.5 min; P=0.025). While this difference might seem to be trivial, on a larger scale pain-to-needle time is still considered as one of the major determinants of prognosis in STEMI patients (14). Furthermore, in the thrombus aspiration group a higher frequency of direct stenting (39.5% *vs.* 21.1%, P<0.001) and lower use of glycoprotein IIb/IIIa inhibitors (32.3% *vs.* 35.1%, P<0.001) was recorded. Thrombus aspiration has been consistently shown to affect procedural strategies in terms of balloon dilatation and stent selection (4,6,8,15,16). In particular, it is associated with higher rate of direct stenting, lower rate of post-dilatation, with the implantation of less stents but of larger size as compared with conventional PCI (15,16). Whether these technical differences in PCI might have a substantial impact on clinical outcome is still controversial (17,18). As to the use of glycoprotein IIb/IIIa, previous evidence suggested that thrombus aspiration is of particular benefit in patients treated with glycoprotein IIb/IIIa inhibitors (19). Such synergistic effect was also confirmed by Pyxaras *et al.* (20), where the combination of manual thrombus aspiration with intravenous abciximab resulted into a significantly lower incidence of adverse cardiovascular events at 1 year compared with the single strategies. In a small randomized study, IC tirofiban combined with thrombus aspiration in STEMI patients undergoing pPCI, was associated with improved angiographic and clinical outcomes compared with thrombus aspiration alone or conventional PCI (21). Finally, similar evidence derives from the Intracoronary Abciximab Infusion and Aspiration Thrombectomy in Patients Undergoing Percutaneous Coronary Intervention for Anterior ST Segment Elevation Myocardial Infarction (INFUSE-AMI) trial (22) that showed in a post hoc analysis how median infarct size was lowest in the intracoronary abciximab plus aspiration group.

The clinical benefit shown with thrombus aspiration in terms of decreased cardiovascular death in the subgroup of patients with large angiographic thrombus burden was partly offset by an increased rate of stroke or transient ischemic attack (TIA) (0.9% *vs.* 0.5%; odds ratio 1.56, 95% CI, 1.02–2.42; P=0.04). The latter could be attributed to technical issues both operator- and device-related. These include catheter-induced embolization of the thrombus into the systemic vasculature, aggressive guiding catheter manipulation required to advance the aspiration catheter and displacing aortic atheroma, and longer procedure time resulting from the aspiration procedure (23). The risk of systemic embolization can be reduced with improved technique. For instance, a thrombus that cannot be fully aspirated is at risk of fracturing and shedding fragments or entering still intact into the systemic vasculature, particularly if suction is not maintained in the aspiration catheter, and the guiding catheter is not engaged in the artery as the aspiration catheter is withdrawn (24). Technical tips such as advancing the guiding catheter tip in the coronary artery and maintaining negative pressure on the aspiration catheter as it is withdrawn, or allow a retrograde blood spill-over from the guiding catheter after the aspiration catheter is removed are small technical measures but important to improve the safety of this procedure.

Interestingly, all three trials included in the meta-analysis only evaluated manual thrombus aspiration. While more complex (i.e., mechanical) devices might be more effective in extracting atherothrombotic particles from the coronary arteries, they are bulkier and require selected coronary anatomies. No consistent clinical benefit has been shown with these devices over PCI alone (19), however, potential benefits from these apparently more effective thrombectomy devices need to be tested in adequately powered ad hoc prospective studies.

Overall, the lesson derived from the meta-analysis by Jolly *et al.*, and in general from the literature produced over the last 10 years, is that performing thrombus aspiration routinely during pPCI does not result into substantial clinical benefit and in some situations, might be potentially harmful. However, thrombus aspiration if carefully performed may still be considered as a valuable technique in selected patients with large angiographic thrombotic burden.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest

to declare.

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Cite this article as: Mangiacapra F, Sticchi A, Barbato E. Thrombus aspiration in primary percutaneous coronary intervention: still a valid option with improved technique in selected patients! Cardiovasc Diagn Ther 2017;7(Suppl 2):S110-S114. doi: 10.21037/cdt.2017.05.09

