

openheart Thrombus aspiration in STEMI revisited: impact on coronary microcirculation?

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In this issue of *Open Heart*, Hoole *et al*¹ present the *IMPACT* trial. The authors investigate the effect of thrombus aspiration (TA) on changes in microvascular function during primary percutaneous coronary intervention (PPCI) for ST elevation myocardial infarction (STEMI). However, no difference between the TA group and the control group receiving balloon angioplasty first line could be verified. This is a timely topic indeed, since the impact of TA on coronary microcirculation was an important rationale to suggest prognostic benefits in patients with STEMI in the past.

Early data from smaller and medium-sized randomised controlled trials (RCT) fuelled substantial enthusiasm about the concept of coronary thrombectomy with a view to reduce the thrombus burden, and avoid distal embolisation and consecutive 'no reflow' in PPCI.²⁻³ Of note, 'no reflow' following PPCI has been observed frequently in this patient cohort.⁴ This phenomenon has been closely associated with microvascular obstruction and increased myocardial infarct size, with worse adverse clinical outcome.⁵

Similarly, dislodged debris from the culprit lesion, consisting of conglomerates of platelets and neutrophil granulocytes, may congest the microvasculature and deteriorate the 'no reflow'.⁶ This is also a feature of the reperfusion injury (RI), which occurs after restoration of blood flow in the infarcted vessel.⁶ Notably, this RI has been estimated to account for up to 50% of the final infarct size, and efforts to mitigate the RI and 'no reflow' appear therefore as an appealing therapeutic approach.⁶

Unfortunately, more recent larger RCTs investigating manual thrombectomy in the setting of PPCI yielded rather disappointing results. Earlier this year, the largest RCT in this field was published.⁷ More than 10 000 patients referred for PPCI were randomised to receive TA or balloon angioplasty followed by

stenting.⁷ Neither the primary composite end point of cardiovascular death, cardiogenic shock, New York Heart Association (NYHA) class IV or recurrent myocardial infarction nor cardiovascular death after 6 months were improved by TA.⁷ Notably, 87% of patients had a significant thrombus burden.⁷ Some concern was raised over a slightly increased stroke rate in the TA group, however, very few events were observed in this patient cohort.⁷

Thrombectomy was also tested on top of intracoronary abciximab (glycoprotein, GPIIb/IIIa inhibition) administration in the INFUSE-AMI trial.⁸ While abciximab reduced the infarct size as assessed by cardiac MRI, this was not confirmed for thrombectomy.⁸ Several other strategies to reduce distal embolisation and microvascular obstruction were investigated, mostly in smaller pilot trials. Sezer *et al*⁹ suggested applying low-dose streptokinase after PPCI to open the microvasculature and improve microvascular function. They repeated coronary angiography 2 days after the index event, and reassessed the coronary flow reserve and the index of microvascular resistance. Importantly, all outcome measures of microvascular function were significantly improved in the streptokinase group as compared to the control group. After 6 months, there was no difference in left ventricular function between the study groups.⁹ However, this was a pilot study with a limited sample size of 40 patients, so no definitive conclusions could be drawn.⁹

The evaluation of the microvasculature by measuring the index of microvascular resistance and coronary flow are well established surrogate parameters to assess microvascular function, and are closely associated to outcome. Cuculi *et al*¹⁰ assessed microvascular resistance and coronary flow reserve as well as microvascular obstruction on cardiac MRI in patients undergoing primary PCI. The authors observed a severely dysfunctional microvasculature in those patients with



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evidence of microvascular obstruction.¹⁰ The same authors could demonstrate that an improvement in microcirculatory function within 24 h after PPCI is associated with improved left ventricular ejection fraction at 6 months.¹⁰ These results support the concept that distal embolisation and microvascular obstruction are relevant factors for long-term outcome after STEMI.

As discussed above, the more recent large RCTs have failed to demonstrate a difference in clinical outcome between manual TA and first line balloon angioplasty in PPCI (table 1). Hoole and colleagues sought to investigate alterations in microvascular resistance during PPCI. Selected surrogate parameters might perhaps be more sensitive than hard clinical end points to detect any benefits favouring the principle of thrombectomy. The authors found that manipulation within the culprit vessel will lead to distal embolisation and affect the microvasculature, regardless of whether a thrombectomy device or a balloon inflation is used first. In patients with a relatively low index of microcirculatory resistance (IMR) <32 (where 12 or lower is considered as being normal) at baseline, the authors noted a significant increase of IMR after the first device was used.¹¹ This group may represent the patient subset with only modest thrombus burden and little distal embolisation per se, as these patients did have improved left ventricular function at follow-up. This finding might favour the idea of direct stenting or the use of mesh covered stents such as the MGuard device, rather than lesion preparation.^{12 13} In essence, patients with only modest thrombus burden might not benefit from TA at all, or TA might even be harmful in this subset of STEMI patients.

A limitation of the present study is its small sample size, which does not allow the detection of any differences in terms of clinical end points. There was a trend towards a superior left ventricular ejection fraction in the thrombectomy group, as well as an improved early and late microvascular obstruction (MVO), but again, the sample size was not sufficient to address such end points. Moreover, only patients with restored blood flow (\geq thrombolysis in myocardial infarction (TIMI) I) after wiring of the culprit vessel could be included. Patients with TIMI 0 flow and high thrombus burden after wiring were excluded. But these patients, in particular, might yield the greatest benefit from TA. Another limitation is the exclusive use of clopidogrel, while ticagrelor and prasugrel might also have had a favourable impact on spontaneous restoration of blood flow before PPCI and microvasculature.

Although the available data from most RCTs discourage the regular use of TA, it is important to keep a balanced perspective, given the fact that TA is only one intervention that is part of the complex PPCI approach. In general, only a handful of interventions that are commonly considered to be beneficial (eg, balloon angioplasty before stenting) translate into an improved clinical outcome. From our experience, patients with significant thrombus burden might still benefit.

In conclusion, the authors present an interesting study that failed to demonstrate any benefit on coronary microvascular function of TA over sole balloon angioplasty in PPCI. The results are in line with data from recent large RCTs. The growing data in this field do not support the routine use of TA in PPCI, which will rather be limited to certain indications with large thrombus burden.

Table 1 Selected randomised trials to investigate thrombectomy versus first line balloon angioplasty in patients undergoing PPCI

Study/year	Number of patients	Main conclusion
TOTAL 2015 ⁷	10 732	No difference in cardiovascular death, recurrent myocardial infarction, cardiogenic shock, or NYHA class IV heart failure within 180 days but increased risk of stroke at 30 days
TASTE 2014 ¹⁴	7244	No difference in death, or death, rehospitalisation for MI or ST after 12 months
TROFI 2013 ¹⁵	141	Similar flow and stent area, as assessed by OCT
EXPORT 2008 ¹⁶	249	No differences at 30 days in the rate of major adverse cardiac and cerebral events
NONSTOP 2004 ¹⁷	258	No difference in no-reflow or slow flow phenomena
PIHRATE 2010 ¹⁸	196	No difference in ST resolution 60 min after PPCI, no difference in mortality at 6 months
ITTI 2012 ¹⁹	100	No difference in 6-month MACE rate (death, reinfarction, target lesion revascularisation and stroke)
MUSTELA 2012 ²⁰	208	In patients with high thrombus load, TA yielded better postprocedural STR and reduced MVO at 3 months, but was not associated with a reduction in infarct size and transmural injury
INFUSE-AMI 2012 ⁸	452	In patients with large anterior STEMI undergoing PPCI with bivalirudin, infarct size at 30 days was significantly reduced by bolus intracoronary abciximab delivered to the infarct lesion site but not by manual aspiration thrombectomy
VAMPIRE 2008 ²	355	Reduced MACE rate after 8 months in the TA group
TAPAS 2008 ³	1,071	Improved ST-segment resolution and clinical outcome

MACE, major adverse cardiac event; MI, myocardial infarction; MOV, microvascular obstruction; NYHA, New York Heart Association; OCT, optical coherence tomography; PPCI, primary percutaneous coronary intervention; STEMI, ST elevation myocardial infarction; STR, ST-segment resolution; TA, thrombus aspiration.

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