

Editorial

Importance of Clinical Research in Percutaneous Coronary Interventions: the Case of Thrombectomy



Importancia de la investigación clínica en intervencionismo coronario: el ejemplo de la trombectomía

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In comparison with thrombolysis, primary angioplasty, was shown years ago to reduce mortality in patients with acute myocardial infarction, by more effectively recanalizing the vessel involved and reducing the complications of infarction.^{1,2} Subsequently, advances in technique and the devices used (as well as pharmacological developments) have contributed to the optimization of primary angioplasty outcomes. The use of stents (at first conventional bare metal stents and then drug-eluting stents) has reduced the rate of cardiac events, in particular those associated with re-occlusion of the treated vessel,^{3,4} and the use of the radial approach has reduced bleeding complications.^{4,5} All this evidence has been obtained from large, specifically-designed, randomized studies. Other elements, such as distal protection filters and devices for mechanical thromboaspiration, have shown no benefit, and therefore their use is currently not advised.

Manual thrombus aspiration devices are a simple way of reducing the thrombotic burden on the infarct-causing artery, with the aim of reducing distal embolization and ensuring adequate myocardial perfusion, thus potentially improving left ventricular function and prognosis in patients with acute myocardial infarction. Several randomized studies (mostly single-center and with a low number of patients) have shown that manual thromboaspiration improves myocardial perfusion outcomes (resolution of ST segment, myocardial blush, thrombolysis in myocardial infarction frame count) and reduces distal embolization.⁶ Moreover, the TAPAS study also showed a reduction in mortality in patients assigned to thromboaspiration⁷ (although this was not a primary outcome). All of these findings have led to an increased use of manual thromboaspiration devices during infarction, and to manual thrombectomy being given an important role in clinical practice guidelines on the treatment of myocardial infarction.⁸

However, the need to clarify the true role of routine manual thrombus aspiration and to identify which patients would derive the clearest benefit has prompted interventional cardiologists to

try to increase the level of evidence by using large randomized clinical trials with sufficient sample sizes to evaluate clinically relevant endpoints. In the TASTE trial, which had 7244 patients, thromboaspiration produced no improvement in mortality at 30 days (primary outcome) or at 1 year.⁹ Very recently, the TOTAL trial, which had 10 732 patients, also found that routine use of a manual thrombus aspiration device did not improve the 6-month prognosis in patients with acute myocardial infarction.¹⁰ These 2 large trials had concordant results, although they were methodologically very different (for example, postangiography randomization in TASTE and preangiography randomization in TOTAL, and time of onset of infarct < 24 hours in TASTE and < 12 hours in TOTAL). Both trials show, therefore, that there is no rationale for routine use of manual thrombus aspiration devices in myocardial infarction. A consideration with important practical implications is that the findings applied to all the subgroups assessed, including those who might have been expected to derive a greater benefit from manual thrombus aspiration devices, based on the time of onset of infarct, the thrombotic burden on the vessel, the coronary flow on initial angiography, and the location of the infarct. Neither of these trials identified any patient subgroups that derived a clinical benefit from the routine use of aspiration devices.^{9,10}

It is difficult to explain why thromboaspiration did not improve prognosis in patients with infarction, despite the improvement in outcomes related to myocardial perfusion. Probably, ventricular function and infarct size are related to numerous factors, only one of which is myocardial perfusion, as evaluated using electrocardiographic and angiographic parameters. In the INFUSE-AMI trial, intracoronary manual thrombus aspiration did not reduce infarct size or improve left ventricular contractility.¹¹

The meta-analysis published in *Revista Española de Cardiología*, by Spitzer et al¹² included the TASTE trial, which explains why, in contrast to other previously published meta-analyses, thrombectomy showed no clinical benefit.¹² By definition, meta-analyses include studies with different inclusion criteria and distinct endpoints, but they offer the possibility of evaluating the effect of a given therapeutic measure on events that are uncommon, but of great clinical importance. In fact, the evidence provided by meta-analyses contributes to sustaining the highest grade of scientific evidence (1A). In the meta-analysis by Spitzer et al,

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thrombectomy showed no benefit for mortality, the rate of stent thrombosis, or other clinical events; these results concur with those of the TOTAL trial, which was not available when this meta-analysis was done. Also, similar to the TASTE trial, in this meta-analysis, routine thrombectomy was not associated with an increased incidence of stroke. In the TOTAL trial, however, patients assigned to thrombectomy had a significantly higher incidence of stroke. This information is naturally the subject of meticulous analysis with the aim of clarifying the possible influence of thrombectomy on the incidence of stroke. Either way, it is a clinically relevant finding, given that this was the safety endpoint of routine thromboaspiration in that trial.

What is the role, then, of manual thrombus aspiration devices in the current treatment of infarction? Manual thrombus aspiration devices will undoubtedly continue to have a place in the treatment of infarction, although not as a routine treatment but probably in 2 situations. Firstly, as "rescue" treatment, that is, when the use of regular devices does not achieve adequate recanalization of the vessel due to persistence of intracoronary thrombus. In the TOTAL study, which applied strict criteria for thromboaspiration in the group assigned to no thromboaspiration, the rate of thromboaspiration was 8.5%, performed mostly because of unacceptable angiographic outcomes with balloon angioplasty alone.¹⁰ Secondly, in the hands of interventional cardiologists experienced in primary angioplasty, we must maintain the treatment option of using manual thrombus aspiration devices as initial treatment in patients with an anticipated high risk of distal embolization or no reflow after balloon dilatation or direct coronary stent implantation. In the TASTE study, which carried out randomization following coronary angiography, 7244 patients were randomized, but during the enrolment period of the study, 4697 patients did not undergo randomization following angiography, of whom 1162 (almost 25% of those not randomized) were treated with thrombectomy following angiography.⁹ Thrombectomy has consistently been demonstrated to reduce distal embolisation and improve myocardial perfusion.⁶ Furthermore, none of the studies showed that the use of a manual thrombus aspiration device was associated with an increased rate of coronary complications, such as dissections or perforations.^{6,7,9,10,12} As already mentioned, the increased rate of stroke in patients assigned to thromboaspiration in the TOTAL study, a finding not observed in TASTE or other previous studies, should be the subject of a more detailed future analysis.

According to the latest available data from the registry of the European Society of Cardiology Department of Hemodynamics and Interventional Cardiology, thromboaspiration was used in 67% of primary angioplasties.¹³ Undoubtedly, this rate must be reduced in future to between 10% (the crossover rate from TOTAL) and 25% (the rate of use in nonrandomized patients in TASTE).^{9,10}

The example of manual thrombus aspiration devices during infarction clearly illustrates the need to carry out well-designed randomized clinical trials (regarding clinical endpoints) if we want to incorporate into our daily practice new devices that are clearly different to those we are currently using. This should also be done with other devices currently used in the treatment of myocardial infarction. In the case of self-expanding stents, there has only been, until now, 1 randomized study, with 80 patients, in which the primary endpoint was the percentage of struts with malapposition at 3 days postimplantation.¹⁴ With mesh stents, designed to reduce distal embolization, the MASTER randomized trial, which had 433 patients, showed a significant improvement in the primary endpoint of ST-segment resolution; furthermore, patients assigned to stenting in that trial had a significant reduction in mortality, but this was not the primary endpoint

and the sample size was not sufficiently large to evaluate clinical outcomes.¹⁵ In the case of bioresorbable scaffolds, randomized studies will be needed to show that these devices are at least equal to metallic drug-eluting stents in terms of safety in myocardial infarction, particularly regarding the rate of scaffold thrombosis.¹⁶

Currently, the available devices for percutaneous treatment of coronary disease have excellent clinical effectiveness and safety; the good outcomes obtained in some nonclinical endpoints does not indicate that they should be replaced by the new devices, but rather that these new devices need to be shown to offer clinical outcomes at least similar to those of the current devices.

CONFLICTS OF INTEREST

R. Moreno has received fees from Medtronic Inc. for conferences.

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