Coronary Microvascular Obstruction — A Puzzle with Many Pieces

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Prompt referral for mechanical reperfusion by urgent primary percutaneous coronary intervention (PCI) represents a pivotal step in the current management of ST-segment elevation myocardial infarction (STEMI).1 Yet, in a sizable proportion of patients, this intervention reopens the obstructed epicardial coronary artery but does not achieve myocardial reperfusion because of coronary microvascular obstruction. Several studies have clearly shown that coronary microvascular obstruction has a negative effect on outcome, negating the potential benefit of primary PCI. Indeed, such obstruction is associated with an increased prevalence of early postinfarction complications, adverse left ventricular remodeling, late repeat hospital stays for heart failure, and death.

In humans, distal atherothrombotic embolization contributes to coronary microvascular obstruction.2 Thus, the removal of an intravascular thrombus during the procedure with the use of dedicated extraction catheters is an attractive strategy for reducing the burden of distal atherothrombotic embolization.3 The Thrombus Aspiration during Percutaneous Coronary Intervention in Acute Myocardial Infarction Study (TAPAS) — an earlier randomized trial of thrombus aspiration — suggested a clinical benefit of this intervention. Although the primary end point of the trial was the surrogate measure of myocardial blush grade (for which a significant benefit of aspiration thrombectomy was shown), the TAPAS investigators also reported an improvement in 1-year survival with thrombus aspiration.4 In contrast, the recent large Thrombus Aspiration in ST-Elevation Myocardial Infarction in Scandinavia (TASTE) trial showed no reduction in mortality at 30 days or 1 year with routine thrombectomy.5,6

Jolly and colleagues now report in the Journal the primary results of the Trial of Routine Aspiration Thrombectomy with PCI versus PCI Alone in Patients with STEMI (TOTAL).7 The hypothesis they tested was that in patients with STEMI who undergo primary PCI, a strategy of adjunctive routine manual thrombus aspiration would prove to be superior to conventional PCI with respect to a composite end point of cardiovascular death, recurrent myocardial infarction, cardiogenic shock, or class IV heart failure within 180 days. In this trial, routine manual thrombus aspiration, as compared with conventional PCI, did not reduce the primary end point and was associated with a significantly higher risk of stroke, the key safety outcome. The main strengths of this trial were the study design and the large sample size. The main limitation was that the higher rate of stroke, correctly reported by the authors, is difficult to interpret and is likely to be a chance finding for a couple of reasons. First, the study was underpowered to detect significantly different rates of stroke, and the number of events was relatively small. Second, the increase in stroke risk with thrombectomy was not confined to the periprocedural period, as would be expected if the procedure were causal, but continued to develop with time, as shown in Figure 1B in the article.

Although the findings of TOTAL are consistent with those of the TASTE trial and together suggest that the time has arrived to prepare a requiem for routine manual thrombectomy, neither study allows us to rule out the possibility...
that thrombus aspiration might be beneficial in high-risk patients. Indeed, the event rates in both trials were substantially lower than expected, a finding that suggests that the trials did not enroll high-risk patients. Interestingly, in both trials, the event rates in the placebo group were about half that initially considered for power calculation. Furthermore, in the TASTE trial, mortality was about one third of that observed in patients who were followed up in a parallel registry. The notion that thrombus aspiration might be beneficial in a subset of patients, such as high-risk patients excluded from the trials and those who were initially assigned to undergo conventional PCI and then crossed over to thrombectomy (about 1 in 10 in TOTAL), is supported by a recent meta-analysis, including the TASTE trial, which showed lower rates of late death, reinfarction, and stent thrombosis over to thrombectomy (about 1 in 10 in TOTAL), a finding that suggests that the trials did not enroll high-risk patients. Interestingly, in both trials were substantially lower than expected, a finding that suggests that the trials did not enroll high-risk patients. Indeed, the event rates in in patients in the thrombectomy group than in those in the PCI-alone group.6 In conclusion, the prevention and treatment of coronary microvascular obstruction remains an unmet need. Four interacting mechanisms cause microvascular obstruction in humans: distal embolization, ischemia-related injury, reperfusion-related injury, and individual susceptibility of the microcirculation to injury. It is likely that the relevance of these mechanisms differs among patients. Furthermore, preexisting coronary microvascular dysfunction is emerging as a causal factor for future acute coronary events and for a worse response to reperfusion therapies.9 Thus, an integrated and personalized approach addressing all mechanisms in different time windows is needed in order to reduce the strikingly increased risk conferred by coronary microvascular obstruction. Although door-to-balloon times have improved significantly over the past 10 years, in-hospital mortality for STEMI has remained virtually unchanged.10 The time has come to turn our attention to the development of treatments that address the continuum of STEMI care, from symptom onset through return to the community.

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Surgical Ablation of Atrial Fibrillation — When, Why, and How?

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In 1987, Dr. James L. Cox performed the first maze procedure for surgical ablation of atrial fibrillation.1 Previous efforts at surgical correction were not uniformly successful, and some procedures corrected cardiac rhythm but did not restore synchronized atrial contraction. Cox’s maze procedure, performed with a precise pattern of incisions and suturing of the right and left atria, proved highly successful in restoring sinus rhythm and, in many patients, reestablishing atrial transport function. There is, however, a lack of consensus regarding indications for surgical ablation of atrial fibrillation.

In patients with structural heart disease, atrial