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EDITORIAL COMMENT

The Utility of Thrombus Aspiration for NSTEMI

Déjà Vu of Aspiration for Primary PCI*

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The presence of heavy thrombus burden at the time of percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI) is associated with an increased incidence of major adverse cardiovascular events (MACE) during follow-up (1). Distal embolization of thrombus can lodge in the smaller arterioles and capillaries downstream, leading to suboptimal angiographic results after PCI with reduced Thrombolysis In Myocardial Infarction (TIMI) flow and myocardial blush grade (2). The resulting microvascular obstruction (MO) prevents gadolinium from entering the downstream region of myocardium and is characterized by an area of signal void within the surrounding bright infarct on late gadolinium-enhancement cardiac magnetic resonance (CMR) T1 imaging. The hope has been that thrombus aspiration will prevent distal embolization and result in significant improvement of outcomes after PCI for AMI. However, the recent large TASTE (Thrombus Aspiration in Myocardial Infarction) trial involving 7,244 patients did not demonstrate a benefit for death (3). Meanwhile, a meta-analysis of randomized, controlled trials, including TASTE, suggests that aspiration thrombectomy compared with conventional primary PCI resulted in a significant reduction in reinfarction, stent thrombosis, and late mortality (4). Although thrombus presence at the time of PCI is higher in STEMI than in patients with non-STEMI (NSTEMI) (5), the question remains whether patients with thrombus present on angiography for NSTEMI will benefit from routine thrombus aspiration or should thrombus aspiration be used only in certain cases based on the clinical scenario. In the case of NSTEMI, aspiration devices are less commonly used, as seen in the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial, in which thrombus aspiration was used in only 2% of patients (6). Will the utility of thrombus aspiration for NSTEMI be a primary PCI déjà vu?

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In this issue of the *Journal*, Thiele et al. (7) present the findings of the TATORT-NSTEMI (Thrombus Aspiration in Thrombus Containing Culprit Lesions in Non-ST-Elevation Myocardial Infarction) trial in which the authors randomized 440 patients with angiographic evidence of a thrombus-containing lesion at the time of PCI to either adjuvant aspiration thrombectomy and PCI or PCI alone. Interestingly, the authors selected the extent of late MO in the percentage of left ventricular mass on CMR imaging performed 1 to 4 days after PCI as the primary endpoint for the study, with other CMR and angiographic parameters as well as clinical outcomes as the secondary study endpoints. The study found that adjuvant thrombus aspiration at the time of PCI did not significantly reduce the amount of late MO, reduce infarct size, or improve TIMI flow grade, myocardial blush, or other CMR or angiographic outcomes (7). Furthermore, clinical outcomes of death, reinfarction, target vessel revascularization, or new congestive heart failure were not significantly different at 6-month follow-up, although the study was not

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adequately powered to assess these outcomes (7). Given that the study enrolled 20 fewer patients than expected and the MO size by left ventricular mass in this study was quite small (1.7%), with an MO prevalence of 31%, the question is raised whether the primary outcome was properly powered as these values are lower than those predicted of 2% and 40%, respectively, in the initial trial design (8). This study raises several questions as to why MO was not significantly decreased with aspiration thrombectomy. 1) Is MO the best surrogate endpoint to select, or should hard endpoints have been used? 2) Does time to PCI affect MO and outcomes? 3) Does the lack of benefit of aspiration thrombectomy simply reflect smaller thrombus burden with NSTEMI compared with STEMI?

With regard to the first question, the choice of MO on CMR imaging may not be the best choice to reflect hard endpoints after PCI. Although several studies previously suggested that late MO was associated with poor prognosis after AMI (9), a recent systematic review and meta-analysis assessing the prognostic value of multiple CMR predictors of prognosis demonstrated that there is not enough evidence to support the use of MO for prognostication in patients with recent MI (10). With regard to the second question, the time to aspiration thrombectomy may play an important role. A recent meta-regression analysis of randomized controlled trials comparing adjuvant aspiration thrombectomy with conventional PCI suggested greater benefit for mortality with aspiration thrombectomy compared with conventional PCI with longer time from symptom onset to treatment (11). This concurs with results of De Vita et al. (12), who found decreasing benefit with conventional PCI over time but no such decrease for aspiration thrombectomy and PCI in the treatment of AMI. These data imply that perhaps the longer the thrombus has time to organize, the less effective aspiration thrombectomy can be, suggesting such extraction techniques would be less effective in the NSTEMI compared with a fresh thrombus in STEMI. In addition, the increased time to PCI with NSTEMI also may result in a greater incidence of distal embolization before PCI, abrogating the effectiveness of aspiration thrombectomy. Finally, thrombus burden in NSTEMI is often less than in STEMI, raising the question whether the decreased incidence and burden of thrombus with NSTEMI are inadequate to derive a significant benefit like that suggested in STEMI. The issue of direct stenting also was different between the groups but did not appear to affect MO. In the TATORT-NSTEMI trial, neither the degree of thrombus burden nor the use of direct stenting appeared to affect MO, whereas variables associated with MO were pre-PCI TIMI flow, diabetes mellitus, and culprit lesion in the left anterior descending or left circumflex artery (7). Thus, aspiration thrombectomy appears largely negative in all groups of NSTEMI patients and implies that, although not harmful, aspiration thrombectomy does not benefit those even with large thrombus burden.

Because of the cost of designing large multicenter, randomized, controlled trials, the use of surrogate endpoints rather than the hard endpoints of death and reinfarction is likely to continue. However, we have to be confident in the surrogate endpoint, so if the study results are negative, one must be willing to accept that the question has been sufficiently addressed. In the case of TATORT-NSTEMI trial, although late MO is not significantly reduced with thrombus aspiration, we are not certain that the same can be said for MACE. It is important to note that the upcoming TAPAS II (Thrombus Aspiration During Percutaneous Coronary Intervention in Acute Non-ST-Elevation Myocardial Infarction Study) has selected myocardial blush grade as the primary endpoint and also will likely be underpowered to assess clinical endpoints of death, reinfarction, or MACE (13). On the other hand, it may be impossible to examine this question in a clinical trial because aspiration thrombectomy will likely continue to be used in certain patients based on the variability of other confounders, such as thrombus size, thrombus age, and infarct size. Without any definitive data to support routine thrombus aspiration for all patients and all lesions, as with the STEMI indication, we should continue to perform procedures that we believe are in the best interest of our patients. Physicians may use it primarily in patients with large thrombus burden and with TIMI flow grade 0 to enable accurate stent placement. Before closing the door on aspiration thrombectomy, let's wait for the upcoming results from the TOTAL (A Trial of Routine Aspiration Thrombectomy With Percutaneous Coronary Intervention [PCI] Versus PCI Alone in Patients With ST-Segment Elevation Myocardial Infarction [STEMI] Undergoing Primary PCI), which will recruit >10,000 patients and should help provide a definitive answer as to whether aspiration thrombectomy provides clinical benefit in patients with AMI (14). Could, however, the utility of aspiration thrombectomy in NSTEMI be déjà vu?

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