Although 75% of patients in the AT group yielded macroscopic thrombus material, the associated microvascular obstruction assessed by magnetic resonance imaging within 4 days was not different from that of the control. The investigators conclude that adjunctive AT does not lead to an improvement of myocardial reperfusion and infarct size in patients with NSTEMI. This conclusion, however, is arguable because an important confounding factor was left out from the analysis, namely the time from symptom onset to PCI.

In the report from Thiele et al. (1), the time from symptom onset to PCI was extended to 72 h, much longer than the time limit used in previous AT trials (<12 h in most AT trials in STEMI, and <24 h in the earliest trial proving feasibility of AT in NSTEMI [2]). The duration from symptom onset to PCI is associated with the change in composition of thrombus material (3). As thrombi "age," the proportion of fresh thrombotic material decreases whereas organized material increases. Therefore, the effectiveness of AT in restoring brisk coronary flow will be reduced if done late. In addition, irreversible injury also progresses in the jeopardized, but salvageable, myocardium as critical ischemia continues. This timing difference in the effect of AT on myocardial reperfusion in STEMI patients has been shown in previous studies (4,5). In our previous study, the benefit of AT is most significant in STEMI patients treated within 4 to 8 h after symptom onset, compared with patients treated within 0 to 4 h or 8 to 12 h. It is possible that within 4 h from onset the thrombi are so soft that they may respond similarly to either conventional PCI or AT. On the other hand, when AT was done later than 8 h from onset, the thrombi are too organized to be removed completely. In addition, as there is minimal myocardium left to be salvaged late in the course, the benefit of AT will be mitigated. The changes in thrombus composition and loss of salvageable myocardium as time lapsed may thus result in an optimal "time window" for AT to be effective. We believe, therefore, the timing of AT after symptom onset should be considered and analyzed accordingly in all future AT studies.

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REPLY: Aspiration Thrombectomy

Timing Should Be Considered

We thank Dr. Hung and colleagues for their considerations on timing of thrombectomy. In the TATORT-NSTEMI (Thrombus Aspiration in Thrombus Containing Culprit Lesions in Non-ST-Elevation Myocardial Infarction) trial, the inclusion criterion was indeed last symptoms <72 h, which is longer than in previous ST-segment elevation myocardial infarction (STEMI) trials in which primary PCI is usually performed <12 h after symptom onset, although the recent TAPAS trial (Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study) had a 24-h inclusion criterion (1,2). However, in non-STEMI (NSTEMI), it is usually difficult to define the exact symptom onset and also the last symptom occurrence because symptoms are often stuttering. Therefore, the inclusion criterion of last symptoms has been chosen in multiple previous NSTEMI trials ranging from 24 to 72 h (3). Although the 72 h inclusion criterion in the TATORT-NSTEMI trial was in the upper range in comparison to other NSTEMI trials, the time from last symptoms to angiography (TATORT-NSTEMI: 10.5 h thrombectomy vs. 10.0 h control) was similar to previous trials ranging from 8 to 10 h in a timing trial (3) and even shorter in comparison to another trial with approximately 30 h until invasive angiography (4).

Thrombus age may play a role on thrombectomy success in STEMI patients. Currently, there is conflicting evidence that aspiration thrombectomy

may be beneficial in STEMI patients presenting early. In the INFUSE-AMI trial including only anterior STEMI patients presenting <4 h after symptom onset, there was no benefit of thrombectomy on infarct size or any other marker of reperfusion success (5). No data are available for NSTEMI showing a relation of symptom onset on thrombus age, which is also important in the light of different thrombus composition in NSTEMI versus STEMI. In a sensitivity analysis of the TATORT-NSTEMI trial, there was no difference in the primary endpoint of microvascular obstruction for patients presenting with last symptoms <4 h versus >4 h, supporting the overall results of the trial.

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