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LETTERS TO THE EDITOR

Reperfusion in Acute Myocardial Infarction

Should the Guidelines Be Modified?

We have read with great interest the manuscript written by Dieker et al. (1) and the editorial by Jacobs and Hochberg (2) about the delays in the pre-hospital phase of acute myocardial infarction. We appreciate the research in this still-unresolved subject. In the last decade there have been important improvements in the mechanical reperfusion of acute myocardial infarction in terms of more potent antiplatelet therapy, better devices, development of system networks, and reduced in-hospital delays. However, as the authors state, there is still a pending issue with pre-hospital delays in those patients whose first medical contact is in a hospital without percutaneous coronary intervention capability. We believe that the guidelines should address in a more adequate manner the role and benefits of the pre-hospital thrombolysis in the first 2 or 3 h and take into account that it might be the preferable approach in certain scenarios. Previous randomized studies demonstrated that in the first 3 h the results of thrombolysis and primary angioplasty are comparable (3,4), but in the CAPTIM (Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction) trial after 5 years of follow-up (5) the patients included in the first 2 h showed a mortality of 5.8% with thrombolysis and 11.1% with primary angioplasty (hazard ratio: 0.50, 95% confidence interval: 0.25 to 0.97, p = 0.04). We believe that thrombolysis followed by catheterization in 24 h might be a reasonable option in certain circumstances, such as when it is presumed that it will not be possible to achieve reperfusion in the desirable interval—especially in the mentioned patients who need to be transferred to a different hospital. In our opinion, the pre-hospital phase of the management of acute myocardial infarction with primary angioplasty usually does not receive the same attention as whether there is a system of primary angioplasty. Programs of primary angioplasty are implemented—not unusually in certain countries with public medical systems—without an adequate system of transport, where the same ambulance is shared with other different, urgencies such as polytraumatisms or traffic accidents. We think that until this important and pending issue is solved, thrombolysis in the ambulance should be considered an even a better option in the guidelines than primary angioplasty in the mentioned cases.

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Pre-Hospital Thrombolysis Rather Than Primary Percutaneous Intervention Is the Treatment of Choice for Patients With ST-Segment Elevation Myocardial Infarction Presenting Early After the Onset of Symptoms

Dieker et al. (1) reported improved outcomes for patients with ST-segment elevation myocardial infarction (STEMI) who had direct referral to an intervention center after ambulance-based diagnosis and pre-hospital notification as compared to those referred through a nonintervention center. The results are not surprising. The investigators, however, fail to discuss an alternative treatment namely that of ambulance initiated pre-hospital thrombolysis (PHT) with pre-notification and transport to an intervention center followed by routine angiography and percutaneous intervention (PCI) if appropriate within 24 h of admission. Available evidence indicates that such an approach would yield superior results to those achieved in the field triage arm of their study.

There has only been 1 randomized study of PHT versus primary PCI with long-term outcomes (2). In this study, patients randomized to receive ambulance-administered PHT within 2 h of onset of symptoms had a substantially lower 5-year mortality than those randomized to primary PCI (5.8% vs. 11.1%, p = 0.04). Those randomized between 2 and 4 h of symptoms had similar 5-year mortality (14.5% vs. 14.4%). In support of these findings, the Viennese STEMI registry showed improved outcomes for thrombolysis administered within 2 h after the onset of symptoms as

compared to primary PCI in this time frame (3). Importantly, in this registry, only 14.6% of patients were able to receive primary PCI within 2 h of symptom onset, whereas 50.5% of patients were able to receive thrombolysis.

Irrespective of the method chosen, the aim of reperfusion is to salvage myocardium and improve outcomes. A wealth of data indicates that reperfusion within 2 h of symptom onset results in markedly better outcomes than reperfusion at later intervals. Even with effective public education campaigns, it is likely that only a small minority of patients can ever receive primary PCI within 2 h of the onset of symptoms, whereas a substantial proportion of patients can receive PHT and achieve reperfusion within this time frame. Rather than primary PCI for patients presenting early after the onset of symptoms, ambulance-administered thrombolysis followed by transport to a PCI capable hospital is the protocol that should be promoted.

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Reply

With interest we read the comments of Dr. Lozano and colleagues and Dr. Harper on the issue of reperfusion therapy for "pre-hospitally" diagnosed ST-segment elevation myocardial infarction patients presenting early after symptom onset. Although Dr. Harper suggests fibrinolysis with an early invasive strategy in all pre-hospital patients, Dr. Lozano and colleagues suggest this strategy under "certain circumstances." Our registry data show that with our strategy of pre-hospital diagnosis, catheter laboratory notification from the ambulance, and direct transportation to an intervention center with optimal in-hospital logistics, primary angioplasty can be performed within 90 min of diagnosis in more than 80% of patients. We acknowledge that pre-hospital and in-hospital infrastructure varies per country and region, which might affect the preferred reperfusion therapy.

The current guidelines state that primary angioplasty is the unequivocally preferred reperfusion strategy, if it can be performed within 90 min of presentation by an experienced team of personnel (1). The guidelines are based on the currently available evidence, including the CAPTIM (Comparison of Primary Angioplasty and Prehospital Fibrinolysis in Acute Myocardial Infarction Trial) results, and they do not make an exception for pre-hospital (or early) presenting patients. Dr. Harper's statement that an early pre-hospital fibrinolytic strategy is superior to primary angioplasty lacks sufficient scientific evidence and therefore is not supported by current guidelines. The remark that our results would have been better if a pre-hospital fibrinolytic strategy would have been used instead of primary angioplasty is presumptuous.

We agree with Dr. Lozano and colleagues that pre-hospital fibrinolysis with a routine early invasive strategy is the preferred reperfusion strategy under certain circumstances—namely if high-quality primary angioplasty performed in a timely fashion is not available. Our registry was initiated to monitor treatment delays in primary angioplasty. Before the initiation of primary angioplasty, pre-hospital fibrinolysis with a liberal rescue strategy has been successfully used for more than 1 decade, with two-thirds of patients being treated within 2 h of symptom onset. Our primary angioplasty data demonstrate that most patients are treated within the time window of the guideline. Moreover, we show that guideline adherence can be substantially improved if all patients are referred directly to an intervention center instead of through a nonintervention center.

We concur with both authors that the impact of (early) pre-hospital fibrinolysis with an early invasive strategy in patients at low risk of bleeding might be underestimated, and this strategy deserves further study. To date, the CAPTIM study is the only available randomized trial in the pre-hospital setting comparing both reperfusion strategies in the optimal setting. The suggested superiority of early fibrinolysis stems from a subgroup analysis of a prematurely discontinued, overall neutral trial, and these results should be interpreted with caution. The currently enrolling STREAM (Strategic Reperfusion Early After Myocardial Infarction) trial compares both reperfusion strategies in patients presenting within 3 h of symptom onset, and results are eagerly awaited. At least until then, timely high-quality primary angioplasty remains the treatment of preference.

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