Editorial

Optimizing reperfusion therapy in acute ST-elevation myocardial infarction by a pharmaco-invasive treatment approach in a well-organized network

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This editorial refers to ‘Safety and efficacy of a pharmaco-invasive reperfusion strategy in rural ST-elevation myocardial infarction patients with expected delays due to long-distance transfers’, by D.M. Larson et al., on page 1232

Importance of time and time delays in reperfusion therapy of acute ST-elevation myocardial infarction

Treatment of acute ST-elevation myocardial infarction (STEMI) has undergone important changes in the last few years. After implementation of primary percutaneous coronary intervention (pPCI; usually balloon dilatation followed by stent implantation) as the method of choice, previous pharmacological reperfusion strategies (fibrinolytic therapy) have rapidly lost their importance or have even been neglected in areas where it is believed that pPCI can be offered to all STEMI patients within the recommended time frame of 90 (to 120) min.

However, the real situation still is that a significant number of patients referred for pPCI, ranging from 20% to 80%, cannot be treated within this time frame. As time progresses, the benefits of mechanical reperfusion therapy decline, with negative influence on short- and long-term mortality. In this respect there is more concern with younger patients (<65 years) with anterior wall infarctions of short duration due to the hypothesis that the ‘golden hours’ of treatment (within the first 3–4 h after symptom onset) are critical to safe myocardium, while during the later course of myocardial infarction, the curve representing time after symptom onset and the magnitude of benefit ‘flattens’, and time is less of a critical determinant. However, time delays are not always important for patients referred for pPCI, and short and longer time delays have been shown to lead to similar mortality rates in mechanically reperfused patients, while success of fibrinolytic therapy is always time dependent.

Network organization

To avoid unacceptable time delays, STEMI guidelines as well as recent overviews have outlined the importance of organizing systems of care (networks) in order to shorten delay times from electrocardiogram (ECG) diagnosis (first medical contact) to first balloon dilatation in an experienced catheter laboratory by experienced personnel. An unexpected time delay from first medical contact to first balloon dilatation is not due to a lack of existing networks with respective treatment resources per se, but rather the absence of clear, systematic protocols for identifying treatment-eligible patients, and ensuring that therapies are available in a timely manner 24 h a day, 7 days a week, 365 days a year.

Impact of a pharmaco-invasive reperfusion strategy on clinical outcome

A pharmocological reperfusion strategy is offered pre-hospital and at present comprises fibrinolysis followed by early routine angiography and intervention especially in patients in whom pPCI cannot be offered in time (Figure 1). Such a pharmaco-invasive strategy provides a theoretical balance of risk and benefit, ensuring an open artery acutely, and, in the successfully reperfused patient,
accept long-distance transfers to catheter centres without optimal pre-treatment, or to transfer patients after initiation of fibrinolytic therapy to a nearby cardiac care unit without catheter facilities, and thereby to risk interhospital transfer with prolonged time delays until mechanical reperfusion, are still clinical practice in some areas worldwide, but should be avoided based on these insights.

Still unanswered questions

Interestingly, a recently published subgroup analysis of the TRANSFER-AMI trial revealed a strong heterogeneity in the treatment effects of a pharmaco-invasive strategy after fibrinolysis for STEMI, which was unexpectedly associated with beneficial outcome only in patients with a low-to-intermediate GRACE risk score, while the early invasive strategy was associated with worse outcome in high-risk patients. This seems irrational and adds to other unanswered questions including the optimal timing of PCI after initial fibrinolysis, which has been shown to be harmful when performed within 2 h of initiation of fibrinolytic therapy. The ongoing prospective, randomized STREAM trial in patients with acute STEMI of short duration will provide further information on the optimal treatment in a STEMI patient cohort, which is based on hypothetical consideration and registry data, believed to benefit in particular from a pharmaco-invasive strategy.

Conflict of interest: K.H. has received lecture fees from AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Eli Lilly, Pfizer, Sanov-Aventis, and The Medicines Company.

References


Figure I Studies comparing early routine percutaneous coronary intervention (PCI) vs. standard therapy after fibrinolytic therapy (with permission from Halvorsen and Huber, Thrombosis and Haemostasis 2011).


