WEST: new data on the integration of early thrombolysis and mechanical intervention in the early management of STEMI

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This editorial refers to: A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after ST-elevation myocardial infarction: the WEST (Which Early ST-elevation myocardial infarction Therapy) Study1† by WEST Steering Committee, on page 1530.

The choice between reperfusion strategies to manage ST-segment elevation acute myocardial infarction is a topic of immense interest, given the frequency of STEMI, its short-term mortality, and the potential impact on organization of acute cardiac care. There is general agreement that primary PCI, performed in timely fashion in an experienced centre, is an excellent and probably the best strategy. However, in many regions of the world, this cannot be implemented. Therefore, intravenous thrombolysis remains the default strategy. Several studies have therefore explored two avenues to improve the results of intravenous thrombolysis: the first is to attempt to provide earlier treatment by using pre-hospital thrombolysis (PHT). In general, PHT is associated with a reduction in 45–60 min in the delay to treatment and this is associated with a reduction in mortality.2 The second avenue is to combine PHT with subsequent mechanical intervention. In the CAPTIM randomized trial, pre-hospital lysis and systematic transfer to an interventional centre was associated with excellent results,3 very similar to those obtained by primary PCI. In addition, there is data to support the concept that for patients seen very early (within the first 2–3 h after symptom onset), pre-hospital lysis may even be superior to primary PCI, with a lower mortality and incidence of cardiogenic shock.4 In that time window, the advantages of primary PCI (high efficacy for recanalization of the infarct vessel, lack of bleeding risk) may be offset by the delays inherent to its implementation, while PHT is ‘at its best’ when targeting ‘fresh clots’ and in the time window compatible for myocardial salvage.5 This and other observations have led to the concept of ‘buying time’ for implementing primary PCI using intravenous thrombolysis en route to the catheterization laboratory: the facilitated primary PCI strategy. This attractive strategy which seemed to combine the best of both worlds was recently tested in the ASSENT-4 PCI trial and proved inferior to routine primary PCI.6 There are several hypotheses to explain this failure such as:

(i) The activation of platelets by thrombolysis followed by subsequent intervention without effective antiplatelet coverage by intravenous GpIIb/IIIa antagonists, given the concerns for major bleeding when the latter are combined with full dose lytics.

(ii) The fact that only a minority of patients were enrolled in the pre-hospital or ambulance setting, or in the first 2 h, i.e. when and where facilitated PCI would be expected to yield its greatest benefits. However, post hoc subset analyses did not indicate even trends for greater efficacy in these subsets.

However, pending completion of the ongoing FINESSE trial, there is currently no clear explanation other than the outstanding results of primary PCI, which are hard to beat or even equal.

Canadian investigators are reporting the results of the WEST trial,7 a pilot randomized trial of approximately 300 patients with STEMI, comparing three strategies: pre-hospital lysis and usual care, pre-hospital lysis and provisional rescue PCI in case of failure to achieve ST-segment resolution and mandatory invasive management within 24 h in other cases; and primary PCI. There are two interesting features to this trial, which makes it complementary to ASSENT-4 PCI: the average time from symptom to randomization was short (approximately within 2 h) and patients received state-of-the-art anti-thrombotic therapy (with patients undergoing PCI after lytics receiving clopidogrel and in many instances GpIIb/IIIa blockers). Finally, in this design, patients in the facilitated PCI arm underwent PCI early but not immediately after lysis, a strategy which has two important advantages: first, it would be logistically...
much easier to implement on a wide-scale than a strategy of immediate PCI following lysis. Second, it allows to provide potent anti-thrombotic (and particularly anti-platelet) therapy prior to PCI and therefore perform mechanical intervention in a potentially safer context. The main findings from WEST are that times to treatment were short because of the use of pre-hospital randomization. Mortality was very low in all groups, reflecting recruitment of a 'not high-risk' patient population, (despite using criteria similar to the DANAMI-2 trial), but most of all, reflecting the short time to effective therapy. Interestingly, mortality was lowest and very similar in the two groups which underwent intervention: lytic-facilitated PCI and primary PCI (1%), although the small size of the study precludes any serious direct comparison of mortality between the strategies, as the very wide confidence intervals demonstrate. This does not mean true non-inferiority and much less equivalence between strategies, but indicates the value of further comparisons between primary PCI and a strategy of early pre-hospital lysis coupled with regimented rescue PCI and routine coronary intervention within 24 h.

Finally, there was a trend for more shock and congestive heart failure in the group of patients treated with primary PCI, supported by higher peak CK, discharge ECG QRS scores, and NT-proBNP values at days 3 and 30.

This study is important from several standpoints:

(i) It demonstrates once more the benefits of pre-hospital decisions of reperfusion (beyond pre-hospital lysis): delays to therapy were always shorter (even in the primary PCI arm) when a decision was made in the pre-hospital setting (as compared with in-hospital).

(ii) It highlights that when mortality is very low (as is the case here with a hospital mortality in the range of 1%), other non-fatal endpoints may become important factors in strategy selection. In that respect, it is uncertain whether re-infarction is more appropriate or important than other endpoints, such as cardiogenic shock. The use of the latter would be expected to favour pre-hospital lysis (as previous randomized trials and registries have suggested low rates of shock when pre-hospital lysis was used, even lower than with primary PCI), whereas the use of re-infarction would be expected to favour primary PCI.

(iii) It allows to estimate event rates in the three strategies and this will be very useful for designing future trials.

The WEST trial suggests that there may be room for a combination of pharmacologic and mechanical intervention in the management of STEMI, provided lysis can be implemented very early (ideally in the pre-hospital setting) and mechanical intervention can be preceded by state-of-the-art anti-thrombin and anti-platelet therapy. The optimal timing of mechanical intervention may be slightly delayed when compared to what was performed in the ASSENT-4 PCI trial, which would be in fact more convenient. Further information will be provided by the ongoing CARESS in AMI trial, which also explores the benefit of mechanical intervention after thrombolysis. Our Canadian colleagues need to be congratulated for conducting this important trial which improves our understanding of the optimal integration of reperfusion strategies for the management of STEMI and shows that thrombolysis, when used timely, may remain an important partner in the early management of STEMI.

Conflict of interest: none declared.

References


