Moving proximally through the intersection between the process and the content of care in ST-elevation myocardial infarction

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This editorial refers to 'Comparison of pre-hospital combination-fibrinolysis plus conventional care with pre-hospital combination-fibrinolysis plus facilitated percutaneous coronary intervention in acute myocardial infarction'¹ by H. Thiele et al., on page 1956.

'A physician can sometimes parry the scythe of death, but has no power over the sand in the hourglass.' HL Piozzi (1781)

Enhancing the care of patients with ST-elevation myocardial infarction continues to be a principal focus of the international cardiological community.¹ Although STEMI patients represent a minority of myocardial infarctions and only a modest proportion of overall deaths attributable to AMI, they constitute a rallying point for energizing major advances in both the process and the content of contemporary AMI care.² Controversy concerning reperfusion therapeutic strategies has revolved around the relative attributes of pharmacological vs. mechanical coronary interventions.³,⁴ Hence, a potentially attractive compromise would be to marry these two strategies by providing antecedent pharmacological reperfusion that subsequently facilitates percutaneous coronary intervention (PCI). Such a marriage rests on at least three fundamental tenets.

(i) Reperfusion at the earliest possible time after coronary occlusion maximizes myocardial preservation.

(ii) Subsequent success of percutaneous coronary mechanical intervention is enhanced, if some prior reperfusion has occurred.⁵

(iii) Current real world transfer times for primary PCI are unacceptably long.⁶

It remains unclear whether mechanical intervention is desirable in all STEMI patients receiving fibrinolysis, irrespective of the success of antecedent pharmacological therapy. Unquestionably, however, optimal outcomes in pharmacologically treated patients require prompt recognition of failed reperfusion and timely rescue PCI. In addition, those in whom recurrent ischaemia or re-infarction threaten may be better served by mechanical co-intervention.

Pharmacological regimens designed to enhance the success of PCI have heretofore ranged from full-dose fibrinolysis through combination half-dose lysis and platelet glycoprotein IIb/IIIa inhibitors to the use of IIb/IIIa inhibitors alone.

To date however, these strategies have had somewhat of a checkered career. The promise of enhanced reperfusion and safer therapy using the combination of half-dose fibrinolysis and IIb/IIIa inhibitors is unfulfilled, given the excess intracranial haemorrhage observed in patients over the age of 75 in both the ASSENT 3 and GUSTO V studies. The notion that early PCI would add value to fibrinolytic therapy despite negative past experience appears to have again been thwarted given the suspension of the ASSENT 4 PCI trial after enrolment of approximately one-third of its anticipated sample.⁷

In the minds of many health-care providers, pre-occupation with the contents of STEMI care has precluded appropriate focus on the process of timely delivery of reperfusion therapy and the recognition of the still substantial proportion of patients who go untreated despite clear indications.¹,²

Thiele et al.⁶ from Leipzig make a welcome and significant contribution to bridging the dynamic gap between the process of care delivery and its content thereby continuing the tradition of other seminal German contributors such as Rentrop, Neuhaus, Schröder, and Meier to the care of AMI. Drawing from the advantages of pre-hospital pharmacological reperfusion on one hand and timely mechanical co-intervention on the other, they demonstrated that facilitated PCI-enhanced reperfusion reduced infarct size (the primary 6-month endpoint) and tended to lower clinical complications. Leipzig, a city of approximately half-million people containing seven hospitals (three with PCI), was the origin of the 164 patients studied over ~3.5 years employing six mobile care units staffed with physicians. Patients were randomized pre-hospital either to half-dose reteplase and abciximab with aspirin and heparin followed by immediate catheterization or to a more conservative approach including rescue PCI using pre-defined criteria. Coronary angiography and discretionary PCI were...
recommended before discharge. Pharmacological therapy was provided within 30 min of ambulance arrival and ~90 min after symptom onset. For those patients randomized to PCI, the door-to-balloon time approximated to 63 min. Remarkably, 65% of patients were treated <2 h from symptom onset, exceeding the impressive 53% standard of ASSENT 3 PLUS. The pharmacological strategy used in this study worked: hence there was 69% TIMI-3 flow immediately prior to PCI, which improved to 93% following stenting of the culprit artery. In the pharmacological arm, 18% underwent rescue PCI and an additional 59 patients (73%) underwent PCI, 55 of whom were elective and four of whom were urgent, responding to recurrent angina. Facilitated PCI achieved an approximate of 50% reduction in infarct size, further corroborated by a commensurate lower end-systolic volume; however, there was no difference in global ejection fraction between groups. Notably, the frequency with which complete ST-segment recovery occurred was 80% in the facilitated PCI vs. 52% in the pharmacological alone arm.

Although the results from this small study provide encouragement to advocates of facilitated PCI, some caveats are noteworthy:

(i) Post hoc analysis revealed that at least six patients failed to achieve 50% ST resolution in the pharmacological alone arm, but did not receive protocol recommended rescue which would likely have improved their outcome.

(ii) Although only one disabling stroke was reported among 82 patients in the pharmacological alone arm, their median age was 60. We must stay mindful of the excess ICH in patients >75 years with such combination therapy.

We desperately need large-scale studies to adequately estimate both the benefit and the risk of facilitated PCI. Unfortunately two of the three large-scale trials planned to address this issue have been either discontinued or suspended and the third, the FINESSE Study, which has an arm identical to the Leipzig protocol, has been randomizing patients for >2.5 years, with the target enrolment well short of its goal of 3000 patients. The medical community needs to support such initiatives and the inclusion of pre-hospital treatment/randomization will be the key and provides potential incremental benefit as the Leipzig study suggests.

Required both a physician and delivery of an abciximab, bolus/infusion in the ambulance precludes wide applicability of the Leipzig strategy. Perhaps, simpler pre-hospital therapies delivered by well-trained paramedics using excellent information systems and risk modelling will become the next frontier for the investigation of STEMI patients. Oral clopidogrel, bolus fibrinolytic, and low molecular weight heparin all show promise. As health-care policy planners contemplate the value of such incremental additions to STEMI care, they should be comforted by understanding that these advances will also yield benefits applicable to the early triage of high-risk non-STE ACS patients, the survivors of sudden death, and those experiencing occlusion of another kind, i.e. stroke, where timely reperfusion is also a matter of life and death. By doing so, we may yet parry not only the scythe of death but also move proximally amidst the sand flowing through the hourglass.

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References


