Pre-hospital diagnosis of myocardial infarction: an opportunity to improve outcomes?

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This editorial refers to 'Clinical impact of direct referral to primary percutaneous coronary intervention following pre-hospital diagnosis of ST-elevation myocardial infarction' by P. Ortolani et al., on page 1550

Ortolani et al. report on the potential impact of pre-hospital diagnosis of ST-elevation myocardial infarction (STEMI). The authors compared the different routes of referral taken by patients who were transferred for primary percutaneous coronary intervention (PCI). A total of 658 STEMI patients were studied and three predefined referral routes were compared: pre-hospital diagnosis and direct transportation (for patients within 90 min drive of the PCI centre, \( n = 166 \)), diagnosis at the interventional hospital emergency department (\( n = 316 \)), or diagnosis at local hospitals before transportation (\( n = 176 \)). The main finding of the study was that patients who had a pre-hospital paramedic and doctor with telemedicine transmission of STEMI and direct transfer for primary PCI had a significant reduction in 'treatment time’ (from onset of symptoms to first balloon dilatation).

Independent predictors of in-hospital all-cause mortality in the entire population were age, cardiogenic shock, post-procedural TIMI 2–3 flow, and lack of administration of glycoprotein IIb/IIIa inhibitors. Those with a pre-hospital diagnosis had the shortest median treatment time: 146 min compared with 191 min for those presenting to the emergency department within the PCI centre, and 236 min for referral made via a local hospital (\( P = 0.001 \)). Yet, this reduced time from STEMI onset to balloon dilatation did not translate into a statistically significant improvement in clinical outcome. Those managed pre-hospital, however, had an overall in-hospital mortality of approximately one-third less than that for each of the other two routes, although they were older; they had a significantly higher incidence of cardiogenic shock and did not receive glycoprotein IIb/IIIa inhibitors prior to the cardiac catheterization laboratory.

As with all non-randomized, retrospective studies, there are several potential sources of bias. The patients entered were subjected to several confounders. The number of patients attending the PCI emergency department was almost double the number of patients seen by the ambulance personnel for a pre-hospital diagnosis (316 vs. 166). It is not clear which patients tended to present for pre-hospital diagnosis, or why they presented in this manner. All the patients who attended an emergency department for diagnosis had a substantially longer delay from pain to ECG (median delay 75 min pre-hospital vs. 120 min in the PCI centre and 117 min in a local hospital; \( P = 0.001 \)). Proportionally, more patients with STEMI referred from the local hospitals had anterior infarction, although the authors comment that high-risk STEMI s were routinely referred for primary PCI. In addition, the group who were diagnosed pre-hospital only received aspirin at the time of diagnosis. This represents minimal therapy, especially when a physician also staffed the ambulance in addition to the paramedics. Furthermore, of those seen pre-hospital and prior to PCI significantly more patients had TIMI 0–1 flow. There was no defined pre-PCI treatment protocol for the entire study group. Pre-PCI clopidogrel was not given. There is a substantial window of opportunity to improve the outcome for patients diagnosed pre-hospital by introducing more aggressive pharmacotherapy at the time of diagnosis. It should also be noted that the in-hospital mortality was for patients who survived to reach the catheter laboratory and subsequently have a primary PCI. Nevertheless, the overall predictors of mortality reported in this study are in keeping with what would be expected.

It is interesting that in a 'real-world' setting, a substantial proportion of patients do not meet current European guidelines that PCI should be performed within 90 min of first medical contact (median ECG-to-balloon time was 97 min for those diagnosed at a local hospital). This finding is pertinent as treatment delay was shown to be a statistically significant univariate predictor of mortality (Table 4). The importance of minimizing treatment delay in primary PCI was further emphasized in a recently published study. In this meta-analysis of randomized controlled trials, minimization of in-hospital delay until primary PCI to <35 min provided the most substantial 30-day mortality benefit compared with in-hospital fibrinolysis. Prolonged door-to-balloon times have also been shown to be predictive of late mortality in STEMI patients. It is worth reconsidering transport strategies, or indeed treatment strategies to deliver timelier reperfusion to these patients, where current treatment standards are not achieved.
The results described in patients with cardiogenic shock appear to be very impressive. Using a standard definition of cardiogenic shock (confirmed in the catheter laboratory), the authors found that these patients benefitted substantially from pre-hospital diagnosis. In the small cardiogenic shock subgroup \((n = 80)\), pre-hospital diagnosis was associated with a two-thirds reduction in in-hospital mortality (from 48.1 and 37.5\% for the other referral routes to 13.8\% for those diagnosed pre-hospital; \(P = 0.019\)). Furthermore, mortality was only 6.2\% in shock patients who underwent PCI within the first 2 h. The outcome data for the cardiogenic shock patients diagnosed pre-hospital are certainly out of keeping with what would be expected from other larger studies.

In the SHOCK investigators’ study, 30-day mortality was 46.7\% in those who underwent early revascularization, although a significant treatment effect was noted in those who were randomized to revascularization within 6 h of their MI.\(^7\) In the large ALKK registry, total in-hospital mortality was 46.1\% for patients with cardiogenic shock, although increasing time from symptom onset to PCI was an independent predictor of mortality.\(^6\) The NRMI investigators noted an in-hospital mortality of 47.9\% for all patients with cardiogenic shock who were treated in 2004 (54.4\% of patients had primary PCI, and performing primary PCI was associated with a particularly lower in-hospital mortality in patients \(<75\) years old).\(^7\) Furthermore, it has recently been shown that those who present with cardiogenic shock early have the worst outcomes compared with those who develop the complication later:\(^8\) in-hospital mortality was reported to be 75\% for those presenting in cardiogenic shock vs. 56\% for those with delayed cardiogenic shock.

Ortolani et al.,\(^1\) only report on the patients who underwent primary PCI with the diagnosis of cardiogenic shock confirmed when the patient arrived in the catheter laboratory. It is certainly possible that some patients who presented with STEMI to the paramedics in cardiogenic shock died before they could have a primary PCI. In such a small cohort of patients, a small number of out-of-hospital deaths have the potential to greatly influence the results. It is possible that the pre-hospital diagnosed cardiogenic shock patients represent self-selected survivors (thus explaining the remarkably low in-hospital mortality of only 13.8\%). These results should therefore be interpreted with caution.

**Conclusions**

In this study, patients with STEMI who are treated with primary PCI suffer substantial delays until reperfusion is achieved in ‘real-world’ settings.\(^1\)\(^,\)\(^7\) There are opportunities for treating STEMI patients aggressively in the pre-hospital setting\(^10\) and the delivery of earlier reperfusion therapy is imperative to optimize outcomes and particularly to reduce mortality. The authors should be commended for aiming to transfer STEMI patients for primary PCI with minimal delay. However, many important issues still need to be addressed. The optimal pre-PCI pharmacological treatment strategy has not been defined and appears to have the potential to improve outcomes. The potential for earlier treatment for those in cardiogenic shock is worthy of further investigation in a larger group of patients, although the mortality will still be substantial, particularly among those with shock at initial presentation. This is particularly important where delays until PCI are likely to be significant and we await the results of larger randomized studies. Time is muscle and every effort should be made to provide reperfusion for STEMI patients with a minimum of delay.

**Conflict of interest:** none declared.

**References**


