# PATCAR: a new standard of care to reduce the chance of death in heart attack victims

*"The Prehospital Administration of Thrombolytic Therapy with Urgent Culprit Artery Revascularization (PATCAR) trial was designed to evaluate half-dose fibrinolysis coupled with urgent coronary revascularization in patients with ST segment elevation myocardial infarction versus primary percutaneous coronary intervention."*

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Myocardial infarction is the leading cause of death in the USA. Approximately 800,000 people will have a new or recurrent infarction each year [101]. Early, complete and sustained reperfusion of the infarct-related artery improves survival in patients presenting with ST segment elevation myocardial infarction (STEMI) [1]. The rapidity of therapy in STEMI is a determinant of survival [2–5]. In contemporary registries, mortality doubles as the door to balloon time (DTB) time exceeds 2 h [3,6]. The symptom onset to treatment times for STEMI patients is still too long and far from desirable [2]. Data from the NRMI database show that although the DTB times of the nontransfer patients decreased from 111 to 79 min from 1994 to 2006, and the DTB of the transfer patients times decreased from 226 to 139 min, the percentage of transfer patients with DTB times less than 90 min is still 8.8% in 2006 [2]. The current use of primary percutaneous coronary intervention (PPCI) and hospital-administered fibrinolytic therapy will not be sufficient to reduce the ischemic time to less than 2 h. The use of a strategy of fibrinolytic acceleration of STEMI treatment coupled with urgent percutaneous coronary intervention (FAST-PCI) may offer a solution to the problem [7]. It is known from previous trials that the patients who received fibrinolytics have higher thrombolysis in myocardial infarction (TIMI) flow grades on angiography [8–10]. When the patients undergoing PPCI for STEMI have a TIMI-3 flow before the intervention their survival has also been shown to be better than those without. The TIMI-3 flow before PCI was an independent predictor of survival in the PAMI-trial patients [11].

According a meta-analysis by Morrison *et al.,* the prehospital fibrinolysis patients had decreased in-hospital mortality when compared with the in-hospital fibrinolysis patients [12]. The symptom onset to treatment time for prehospital fibrinolysis patients was 104 versus 164 min for the in-hospital fibrinolysis group [12]. In the Combined Angioplasty and Pharmacological Intervention Versus Thrombolysis Alone in Acute Myocardial Infarction study, the effectiveness and safety of full-dose weight-adjusted tenecteplase followed by immediate transfer for facilitated PCI in patients presenting with high-risk STEMI was tested [13]. Compared with tenecteplase alone, this strategy was associated with a significant reduction in the combined end point of death, reinfarction, recurrent unstable ischemia or stroke, at 30 days and at 6 months, and was not associated with an increase in major bleeding. These results suggested that a strategy of full-dose fibrinolysis followed by immediate transfer for PCI was safe and superior to fibrinolysis alone [13]. The Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction trial compared prehospital fibrinolysis versus PPCI for STEMI. The patients who were randomized within 2 h of symptom onset showed a strong trend towards lower mortality when they received prehospital fibrinolysis than those who had PPCI [14].

Most patients with STEMI are first seen at hospitals and other locations at which PPCI is not available [15]. Physicians at these locations must either transfer patients with STEMIs to capable hospitals for PPCI or else administer fibrinolytics at their hospitals. The problem with the PPCI approach is that it entails a transfer, which imposes significant and unpredictable delays, while problems with the fibrinolytic therapy approach include that it may be contraindicated, it may be the second-best therapy, and it may not work in a third of cases, thereby requiring transfer for rescue PCI [16].

The Prehospital Administration of Thrombolytic Therapy with Urgent Culprit Artery Revascularization (PATCAR) trial was designed to evaluate half-dose fibrinolysis coupled with urgent coronary revascularization in patients with STEMI versus PPCI. The results of this

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pilot trial have been published recently [17]. The patients were divided into full-dose fibrinolysis and Coronary Care Unit management (group A), half-dose fibrinolysis and urgent PCI (group B), fibrinolytic ineligible (group C) and patients who were not transported by participating emergency medical services (group D). The group B patients had significantly better TIMI perfusion scores and TIMI flow grades and reduced ischemic times without an increase in the bleeding risk when compared with the PPCI group [17]. In the Alliance for Myocardial Infarction Care Optimization (AMICO) registry, the impact of FAST-PCI on the mortality, reinfarction and stroke rates among STEMI patients were compared with patients who had PPCI [7]. There were 2869 patients registered at the five different sites between 2001 and 2006. Of these, 1200 were treated by FAST-PCI. The remaining 1669 were treated with PPCI alone. There were fewer deaths, less reinfarction and a lower combined end point of death, reinfarction or stroke with the strategy of using reduced-dose prehospital fibrinolysis. AMICO registry results showed that FAST-PCI was superior to PPCI alone for STEMI victims [7]. These results contradict the meta-analysis of Keeley *et al.* [18]. Keeley *et al.* concluded that facilitated PCI (fibrinolytics or glycoprotein IIb/IIIa, administered just before or after hospital arrival) increased mortality and nonfatal myocardial infarction, as well as risks of bleeding and stroke. This meta-analysis included all the randomized trials regardless of the facilitator drug used, but the analysis was mainly driven by the ASSENT-4 trial [10]. The ASSENT-4 trial compared full-dose tenecteplase with PPCI in STEMI patients but was not designed to shorten the time to treatment. It was stopped early owing to excess stroke in the tenecteplase arm. The use of glycoprotein IIb/IIIa inhibitors was not permitted in the facilitated PCI group except for bailout situations, and the use of clopidogrel was limited to the stented patients at the time of cardiac catheterization [10]. The ASSENT-4 patients with TIMI 0–2 flow before PCI in the facilitated PCI group were also less likely to have TIMI-3 flow after the PCI [19]. This might be attributed to the prothrombotic environment after fibrinolytic therapy as well as the suboptimal antithrombin therapy in this trial.

The recently published FINESSE trial also did not answer the question of the effectiveness of very early fibrinolysis in the prehospital phase for STEMI patients [9]. In this trial 2452 patients with STEMI presenting less than 6 h after symptom onset, with 1–4 h estimated time to catheterization, were randomized to in-hospital half-dose double bolus reteplase (in patients <75 years of age) followed by PCI, or in-hospital abciximab bolus followed by PCI or in-lab abciximab and PCI. The median time to balloon was 2.2 h in all patients and the symptom onset to first bolus of reteplase was 165 min. Only 60% of the FINESSE patients were treated within 3 h of symptom onset and in those patients there was a trend towards more clinical benefit with reteplase and abciximab combination treatment.

The current mortality of STEMI patients in the USA is approximately 8% when all the hospitals are taken into account [101]. This is simply unacceptable with the availability of current medications and technology. The AMICO registry showed that it was possible to decrease the mortality of STEMI patients from 6.4 to 3.8%, without an increase in bleeding complications, with the use of reduced-dose fibrinolysis in the prehospital setting and urgent culprit artery revascularization [7]. In this registry there was also an increase in the infarct-related artery patency, and decrease in the presence of shock on arrival to the cardiac catheterization laboratory with prehospital fibrinolysis. This strategy for STEMI treatment should be tested with an appropriately powered randomized trial.

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In the future, the emergency medical services crews in the field will initiate the treatment of patients with STEMI at first medical contact. This treatment will involve multiple pharmaceutical agents, including fibrinolytic agents, dual antiplatelet therapy and anticoagulants. In most cases, a patient transport or transfer to a PCI-capable center will then occur, bypassing all of the closest hospital facilities that are not PCI centers. We believe the mortality of STEMI will decrease using this approach.

**Financial & competing interests disclosure**

*Ali E Denktas was partially supported by an unrestricted grant from PDL biopharma for the AMICO Trial. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.*

*No writing assistance was utilized in the production of this manuscript.*

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