

## EDITORIAL COMMENT

# Ischemic Time

## The New Gold Standard for ST-Segment Elevation Myocardial Infarction Care\*

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In this issue of the *Journal*, Francone et al. (1) report an analysis of the relationship between time from the onset of symptoms to reperfusion (ischemic time) in ST-segment elevation myocardial infarction (STEMI) patients treated with primary percutaneous coronary intervention (PCI). These patients were evaluated with cardiac magnetic resonance imaging on day 3 for infarct size and infarct salvage, in addition to other indices of left ventricular size and function. Ischemic time quartiles were defined as 0 to 90 min, 90 to 150 min, 150 to 360 min, and >360 min. There was a dramatic increase of infarct size with ischemic time. Anterior infarcts were larger than nonanterior infarcts, but there was still significant ischemic time related salvage in patients with inferior infarcts. Microvascular obstruction was more prominent in patients with longer ischemic times and correlated with larger infarcts. The extent of myocardial salvage decreased significantly when the ischemic times were longer than 90 min. Additionally, end-diastolic and -systolic volumes decreased in patients with ischemic times <150 min, whereas in patients with ischemic times >150 min, these volumes increased over time. Similarly in patients with ischemic times <90 min, the ejection fractions improved over time, whereas they worsened in patients with ischemic times >360 min.

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Thirteen years ago, Boersma et al. (2) reported on the relationship of symptom onset to treatment delay on the absolute benefit of mortality reduction in patients with STEMI. This dramatic illustration of the golden hour of myocardial salvage in >50,000 patients was very similar in shape to the curve depicted in Figure 1C in Francone

et al. (1). De Luca et al. (3) also reported on the time dependence of survival with relation to ischemic time in patients treated with primary angioplasty. The infarct size curve in Figure 1A in Francone et al. (1) was very similar to the curve reported by De Luca et al. (3) in terms of rate of mortality. With the paper by Francone et al. (1), we now have hard physiologic evidence that ischemic times >90 min result in relatively little myocardial salvage.

As we begin to consider other treatment strategies that could potentially reduce ischemic times, we must also consider whether there are patient subsets that should have the most aggressive therapy, namely “high-risk patients.” De Luca et al. (4) found that survival was inversely proportional to ischemic time in high-risk patients but was not correlated with ischemic times in low-risk patients. Additionally, in patients with patent infarct-related arteries on initial angiography, there was a low mortality rate, which was not related to ischemic time. In high-risk patients and those with closed infarct related arteries, the survival curves of De Luca et al. (3) match the infarct size curves in Figure 1A in Francone et al. (1). In contrast, as illustrated in Figure 2 in Francone et al. (1), there was also an unequivocal relationship in patients with nonanterior (low-risk) infarcts with ischemic time. Patients with nonanterior infarct who were treated early had infarct sizes <10% on average, whereas those treated late had infarcts closer to 20% of the left ventricle. It is suggested, therefore, that patients with nonanterior infarct are definitely not low risk. The illustrations of ischemic time dependence on myocardial salvage in Figure 3 of Francone et al. (1) are quite dramatic. These images clearly demonstrate that lateral infarcts can be very similar in magnitude to anterior infarcts and should not be considered low risk.

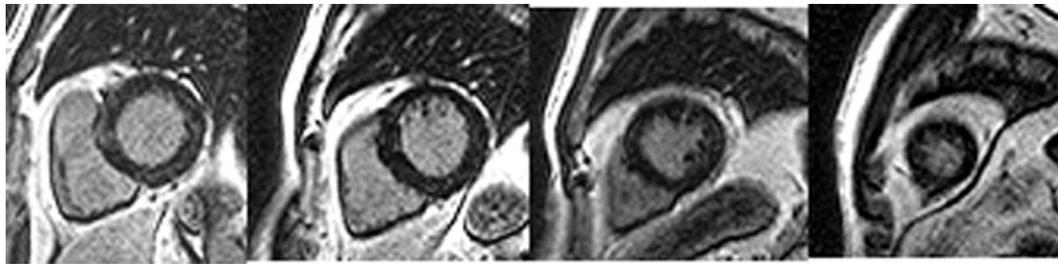
Because it routinely takes approximately 90 to 120 min from medical contact to PCI in most STEMI treatment centers in the U.S. (5), and most patients wait at least 90 min to call 911 or present to the emergency department (6), ischemic times of 180 to 210 min are presently considered optimal for primary PCI. If the findings by Francone et al. (1) are correct, ischemic times associated with primary PCI would result in limited infarct salvage in the majority of patients treated with that modality.

We have substantial evidence that early fibrinolysis followed by urgent PCI is safe and associated with a low risk of serious bleeding complications, as well as significant reductions in the incidence of recurrent ischemia (7–9). Pre-hospital fibrinolysis also has been associated with much shorter ischemic times and a 30% mortality reduction compared with in hospital fibrinolysis in >5,000 STEMI patients treated in Sweden (10).

Steg et al. (11) also demonstrated that in patients treated with pre-hospital fibrinolysis followed by PCI within 2 h of onset of symptoms, the 30-day mortality

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**Figure 1** Sequential Slices From Base to Apex of CMR Images With Contrast Enhancement Demonstrating No Significant Myocardial Necrosis

CMR = cardiac magnetic resonance.

was reduced from 5.2% to 2.2% compared with primary PCI. Additionally, the time to treatment was reduced by 16 min, and the incidence of shock on arrival to hospital was reduced from 3.6% to 0.0%. We have demonstrated a reduction in ischemic time of 55 min and improved Thrombolysis In Myocardial Infarction (TIMI) myocardial perfusion score in patients treated with a half-dose of pre-hospital reteplase plus emergent PCI compared with primary PCI (12). Denktas et al. (13) have reported that fibrinolytic acceleration of STEMI treatment coupled with urgent PCI (FAST-PCI) resulted in a reduction of 30-day mortality from 6.4% to 3.8% ( $p = 0.002$ ) compared with a primary PCI in a study of almost 3,000 patients. Despite this dramatic reduction in mortality, there was no increased risk of stroke or major bleeding with FAST-PCI (13).

A dramatic example of FAST-PCI follows. A 63-year-old chiropractor was awaiting a flight home from Houston to Ohio when he developed severe chest pain and lost consciousness, falling to the floor in the airport. Two bystanders initiated cardiopulmonary resuscitation and quickly cardioverted him by using an automatic external defibrillator. The Houston Fire Department Paramedics responded immediately, diagnosing the patient with an anterior STEMI using a pre-hospital 12-lead electrocardiogram. They transmitted this electrocardiogram to the STEMI center, where the anterior STEMI diagnosis was confirmed, and the patient was entered into a study that used pre-hospital aspirin, heparin, clopidogrel, and 10 U of reteplase followed by helicopter transport for urgent PCI. In route to the Memorial Hermann Heart and Vascular Institute, the patient's pain resolved, and on arrival to the catheterization laboratory his left anterior descending coronary artery had TIMI flow grade 3 with a critical proximal stenosis. The vessel was stented without complications, and he was discharged on day 4 after obtaining cardiac magnetic resonance imaging with gadolinium contrast (Fig. 1). The patient went from full cardiac arrest to an aborted anterior myocardial infarction with no evidence of myocardial necrosis by either tropo-

nin T cardiac marker assay or cardiac magnetic resonance imaging after FAST-PCI.

Francone et al. (1) are to be congratulated for a dramatic demonstration of the critical importance of ischemic time in the management of STEMI patients. Ischemic time, rather than medical contact to treatment time, should be the new gold standard for STEMI care. The STEMI treatment protocols and treatment systems need to be established, which can reduce the ischemic time to the golden hour we have discussed for so many years.

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**Key Words:** myocardial salvage ■ microvascular injury ■ cardiovascular magnetic resonance ■ time to reperfusion.