Should we transfer patients with acute myocardial infarction to a tertiary care hospital for primary angioplasty?

See page 823 for the article to which this Editorial refers

The advantages and disadvantages of primary angioplasty and pharmacological reperfusion are well-known. A meta-analysis of all randomized studies has shown a significant reduction in the incidence of death and reinfarction at 30 days, favouring primary angioplasty\cite{1}. Since most hospitals throughout the world do not have catheterization facilities or are not able to provide a 24-hour service, the obvious question arises whether one should routinely transfer patients with ST-segment elevation acute coronary syndromes to a tertiary care hospital for intervention. This question was addressed in the PRAGUE (PRimary Angioplasty in patients transferred from General community hospitals to specialized PTCA Units with or without Emergency thrombolysis) study in this issue\cite{2}.

In the PRAGUE study, 300 patients were randomized to in-hospital fibrinolysis with streptokinase, transfer to a tertiary care hospital with the same fibrinolytic regimen given during transport, or transfer to the hospital for primary angioplasty/stenting but without pre-treatment with streptokinase. The primary end-point of the study, the composite of death, reinfarction and stroke at 30 days, was observed in 8% of the patients randomized to primary angioplasty/stenting, in 15% of the patients randomized to the combined therapy and in 23% of the patients who were treated in the community hospitals ($P<0.02$ vs primary angioplasty). From these results the authors conclude that patients presenting with ST-segment elevations or new bundle branch block should get primary coronary angioplasty/stenting even if these procedures require transfer to a tertiary care hospital provided that the coronary interventions can be performed within 90 min.

Is this far-reaching recommendation acceptable to the cardiological community? The answer is no. Although the PRAGUE investigators should be congratulated for having successfully completed a very difficult study, at least from a logistical point of view, scrutinizing the results of the study indicates that the populations and treatments studied and the corresponding outcomes are not representative of what is generally being observed nowadays. First, the number of patients studied is small and selected from a much larger population of 1588 patients presenting with ST-segment elevations or bundle branch block to community hospitals. It is not totally clear why so many patients were excluded. The mortality, reinfarction and stroke rates observed in the fibrinolysis-alone arm of this study population are twice that observed with the same fibrinolytic in much larger trials. Also, in the other two arms of the study these end-points were more frequently observed than in most recent trials.

Secondly, the use of streptokinase as the fibrinolytic agent has put the pharmacological reperfusion-alone and combination arms at a disadvantage when compared with up-to-date mechanical reperfusion (angioplasty with stenting in 79% of the patients!). Although streptokinase is still the most frequently prescribed fibrinolytic, better agents are available. Although these agents are more expensive, cost constraints cannot be used as an argument here since fibrinolysis was compared with much more expensive treatment strategies. Thirdly, in spite of relatively short distances and investigators trying to keep the transfer time as short as possible, the delay between admission to the community hospital and the first balloon inflation at the tertiary care hospital was more than 90 min on average. These delays are likely to be much longer in the real world, outside the setting of a clinical trial.

The worst outcome with pre-intervention fibrinolysis as compared with primary angioplasty/stenting in

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this study also needs further discussion. A recent trial has shown that pre-intervention fibrinolytic therapy may confer an advantage. In the PACT trial, 606 patients with ST-segment elevation acute coronary syndromes were randomly assigned either an i.v. bolus of 50 mg alteplase or placebo followed by rescue angioplasty/stenting if TIMI grade 3 flow was not observed at 90 min[3].

Pre-treatment with alteplase was associated with more TIMI grade 3 flow and did not alter the efficacy and safety of the subsequent coronary intervention. Patients with early TIMI grade 3 flow had a better ejection fraction at 1-week follow-up. It is unclear why the PRAGUE study failed to show a benefit of this combined strategy. A rebound pro-aggregatory effect after stopping the infusion of streptokinase may be responsible for the very high in-stent rethrombosis rate (8-1%) in this group[4]. Also, the use of high extra doses unfractionated heparin may have played a role.

Intravenous GP IIb/IIIa antagonists were not given in this study. It is this new potent antiplatelet therapy that may completely change our strategy in the near future and make the results of this study somewhat irrelevant. Recent studies have shown that the combined use of a reduced dose of a fibrinolytic (alteplase or reteplase) and a GPIIb/IIIa antagonist (abciximab, eptifibatide) are associated with a high TIMI grade 3 flow rate (around 75%) and better reperfusion at the tissue level[5,6]. Moreover, as in the PACT trial[5], the SPEED (Strategies for Patency Enhancement in the Emergency Department) trial[6] has shown that this pre-treatment may facilitate subsequent coronary interventions. If the safety and efficacy of this new approach is confirmed in large trials (GUSTO IV-AMI—Global Use of Strategies to Open Occluded Coronary Arteries, and ASSENT 3—Assessment of the Safety and Efficacy of a New Thrombolytic) it is likely that most patients with ST-segment elevation acute coronary syndromes will receive the combined pharmacological treatment as soon as possible. Only a minority of these patients will require additional urgent mechanical interventions. If these interventions cannot be performed in-house urgent transfer is indicated. This can be performed safely as shown by the PRAGUE investigators. Routine transfer of all patients with ST-segment elevation or bundle branch block to a tertiary care hospital, however, would imply that many of these patients would not receive any reperfusion therapy for at least 90 min. This will become unacceptable when a pharmacological reperfusion is available that would result in more than 75% TIMI grade 3 flow at the end of this 90 min.

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References


Obesity, Cinderella of CHD risk factors

See page 808 for the article to which this Editorial refers

Obesity is a complex multifactorial chronic disease that develops from an interaction of genotype and the environment[1]. Body fat is commonly estimated by using the body mass index, which is the weight in kilograms divided by the square of the height in meters. Overweight is defined as a body mass index of 25–29·9 kg·m⁻² and obesity as a body mass index of

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