Benefits of transfer primary angioplasty are durable, so why are we waiting?

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This editorial refers to 'Long-term outcomes of patients with acute myocardial infarction presenting to hospitals without catheterization laboratory and randomized to immediate thrombolysis or interhospital transport for primary percutaneous coronary intervention. Five years’ follow-up of the PRAGUE-2 trial' by P. Widimsky et al., on page 679

Myocardial infarction is an important public health problem worldwide. Rapid restoration of flow remains as the foundation for life-saving treatment of patients with ST-segment elevation myocardial infarction (STEMI). In Europe, it is heartening to note that the utilization of reperfusion therapies was increasing during the period from 2000–2001 to 2003–2004, based on the first and second Euro Heart Surveys of Acute Coronary Syndromes, respectively.1 Of 3750 patients enrolled from various geographical regions with dissimilar patient characteristics, using different study designs, patients transferred for primary angioplasty were less likely to experience this composite endpoint (relative risk (RR) = 0.58, 95% confidence interval (CI), 0.47–0.71; P < 0.001), with a favourable trend for mortality (RR = 0.81; P = 0.086). Notably, the occurrences of MI (RR = 0.32; P < 0.001) and stroke (RR = 0.44; P = 0.015) were significantly lower even though they received treatment ~70–103 min later. Although there is a short-term benefit, information on long-term outcome of this strategy is lacking. A subgroup analysis of DANAMI-2 showed that transfer for primary angioplasty was superior to immediate fibrinolysis among patients without diabetes, but may be detrimental to those with diabetes.4 Of 1572 patients, 173 (11%) suffered from diabetes. At 3 years, the risk of clinical re-infarction for patients treated with angioplasty compared with fibrinolysis was higher for patients with diabetes (RR = 2.57, 95% CI 1.48–4.46; P < 0.001), but lower for non-diabetic patients (RR = 0.52, 95% CI 0.36–0.74; P < 0.001).

Widimsky et al. are to be congratulated for providing further insight into long-term efficacy of the transfer strategy. Of 850 patients with STEMI to hospitals without cardiac catheterization facilities in the Czech Republic, those randomized to receiving immediate fibrinolysis were more likely to experience the 5-year primary endpoint, consisting of death, recurrent MI, or stroke, compared with those randomized to be transferred for primary angioplasty (hazard ratio, 1.35; 95% CI 1.02–1.70; P = 0.04). Although there was only a trend towards higher mortality for patients treated with fibrinolytic therapy (23 vs. 19%; P = 0.06), those treated with primary angioplasty were less likely to suffer from recurrent MI (12 vs. 19%; P = 0.009) and to receive revascularization procedures (34 vs. 51%; P < 0.001). Interestingly, from Figure 2, the two curves on the Kaplan–Meier plot appeared to diverge until the first year and the difference remained stable, suggesting that the benefit afforded by primary angioplasty continued for about a year and was maintained for the next 4 years.

Although the long-term results of the PRAGUE-2 trial were encouraging, the question remains whether they can be translated to daily practice. Unlike Europe where most of these studies were conducted in countries with highly organized emergency medical services, the third and fourth National Registries of Myocardial Infarction found that the median door-to-balloon time was 180 min, with 4.2% of the patients treated within 90 min, among 4278 patients transferred for primary angioplasty in the USA.5 Prolonging time to treatment diminishes the short- and long-term benefits of primary angioplasty.6 To reduce the adverse effects of delay, one sensible approach was to restore coronary flow early while waiting for definitive treatment. Indeed, facilitated angioplasty appeared to be particularly attractive for patients required to wait for the cardiac catheterization laboratories to be ready or to be transferred to another hospital. Those pre-treated with various
glycoprotein Ilb/IIa inhibitors and/or fibrinolytic agents were more likely to achieve restoration of normal coronary flow prior to angioplasty. After the procedure, the proportion of patients with normal antegrade flow was similar between patients who have and have not received these agents. Surprisingly, short-term mortality, re-infarction, urgent target revascularization, and bleeding complication rates were increased by 38, 78, 139, and 51%, respectively, among those who underwent facilitated angioplasty when compared with primary angioplasty. Likely, the excess in adverse events may be attributed partly to the prothrombotic milieu generated by fibrinolytic agents and, therefore, this therapeutic strategy is unlikely to be clinically effective.

Several factors may have accounted for the delay in treatment. Hospitals without cardiac catheterization laboratories should recognize their limitations when making treatment decisions for each patient. In particular, timeliness in transferring patients is of paramount importance. Numerous approaches have been suggested to reduce door-to-balloon time, focusing on logistical and organizational issues. Likely, these improvements will provide a better outcome for transfer patients as well. Currently, there is a call to optimize care for patients with acute STEMI in the USA by encouraging several stakeholders to demolish barriers so that primary angioplasty can become widely available and the procedure conducted by experienced operators in accredited institutions within the prescribed quality standards.

The wait for long-term data for transfer primary angioplasty may be over, but the wait for these patients receiving treatment must now be shortened. To deliver prompt, synchronous, coordinated, and premium care to this high-risk group of patients will require strong political will, judicious deployment of resources, and seamless integration of emergency medical services with hospitals.

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References