EDITORIAL COMMENT

The Effectiveness of Primary PTCA: Does Patient Risk Matter?*

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Ever since the introduction of primary angioplasty as a method for reperfusion in the setting of acute myocardial infarction in 1982, controversy has surrounded its appropriate use. Taken as a group, modest-sized randomized clinical trials comparing primary angioplasty with thrombolytic therapy in acute myocardial infarction (AMI) patients eligible for either therapy have shown clinically meaningful and statistically significant reduction in death or recurrent myocardial infarction (MI) in patients treated with primary percutaneous transluminal coronary angioplasty (PTCA) (1–4). Although substantial growth has occurred in the use of this procedure in patients presenting with AMI and ST-segment elevation left bundle branch block controversy remains about the optimal use of primary angioplasty.

Although it is clear that in expert hands and in expert centers, primary PTCA appears to be the treatment of choice, use outside of these expert centers may not replicate these excellent results. Nonrandomized comparisons of primary PTCA and thrombolytic therapy in the Myocardial Infarction Triage and Intervention (MITI) Registry, National Registry of Myocardial Infarction (NRMI) and Cooperative Cardiovascular Project (CCP) databases have failed to confirm improved outcome in community patients treated with primary PTCA in comparison with thrombolytic therapy (5–8). We have observed higher mortality and morbidity rates in community primary PTCA patients than in those treated in the randomized trials. In general, community-based primary PTCA has been performed with slower treatment times and in lower-volume centers than primary PTCA performed in the randomized trials. In contrast, morbidity and mortality rates in thrombolytic-treated patients in the observational studies have also been somewhat lower than in the randomized trial, perhaps because of lower complication rates, particularly of intracranial bleeding (5,8).

In contrast to these observational studies, the present observational comparison reported by Zahn et al. (9) in this issue of the Journal using the Maximal Individual Therapy in AMI (MITRA) and Myocardial Infarction Registry (MIR) databases shows substantially improved outcomes in patients treated with primary PTCA in comparison to an otherwise similar thrombolytic cohort of patients (9). The investigators observed a 42% reduction in hospital mortality in primary PTCA patients after adjusting for baseline differences in the two patient groups. These differences are consistent with the outcome in a group of previously reported randomized trials.

One notable finding of this study is that the relative benefit of PTCA varied little from subgroup to subgroup, with odds ratios averaging 0.5 to 0.7. This uniformity further reinforces the concept of primary PTCA as a superior method of reperfusion. This finding, however, should not be used to predict benefit of intervention in an individual patient. As with many therapies, the absolute benefit of intervention over medications in acute MI is much greater in patients at higher risk. For example, subgroup analyses predict that only three very elderly patients (>84 years) require treatment with PTCA to result in one life saved. In contrast, 76 young patients (<55 years) must be treated to achieve the same benefit, with no statistically significant advantage over thrombolysis observed.

Unconditional endorsement of the results of this study is marred by limitations inherent in nonrandomized trials. As a prime example, approximately 88% of the primary angioplasty group received all their inpatient care at an angioplasty-equipped hospital, whereas approximately 92% of the thrombolytic group received all their care at a hospital lacking angioplasty facilities. Was the cardiac care provided at these two types of facilities comparable? The investigators note that cardiologists were more readily available in the angioplasty-equipped hospitals. Moreover, the statistically higher use of beta-blockers and angiotensin-converting enzyme inhibitors in the primary angioplasty group could be viewed as a surrogate for superior care. Although some of these potential differences in treatment can be adequately identified and compensated for in multivariate analyses, others cannot. Therefore, in addition to comparing angioplasty versus thrombolytics, the overall study also compared care provided by presumably larger and more experienced centers with smaller, less specialized centers. The true relative contribution of each of these to the impressive differences observed between groups is unknown. It is reassuring that a statistically significant mortality benefit for primary PTCA remained in the subgroup of patients treated at angioplasty-equipped hospitals, but we do not know whether these intervention and thrombolytic subgroups were comparable.

These results likely represent several phenomena that together may result in improved outcome in community...
patients treated with primary PTCA. First, in contrast to previously reported observational studies (1988 to 1995), the MITRA and MIR databases represent a more contemporary standard of care (1994 and 1998). During most of this period, both coronary stents and glycoprotein-IIb/IIIa inhibitors were available and likely are associated with improved outcome in primary PTCA patients. There also appears to be a temporal trend toward improvement in primary PTCA outcome over time. The MITRA and MIR databases were evaluated in a previous publication by Zahn et al. (10) and showed substantial annual improvement in primary PTCA outcomes, while outcomes in thrombolytic therapy patients remained unchanged over the four-year reporting period. In addition to improvements in the primary PTCA procedure itself, there have been improvements in “door-to-balloon” times observed in several cohorts of primary PTCA patients (6,11). These improvements in door-to-balloon time likely represent a maturation of primary PTCA procedures, particularly in hospitals that have recently introduced primary PTCA. Standardized protocols as well as Continuous Quality Improvement (CQI) techniques have been shown to decrease door-to-balloon times in primary PTCA patients and may also improve outcomes (12).

A more important factor not addressed in the present study is the relationship between volume of primary PTCA procedures and outcome. The European model of cardiovascular care is generally a smaller number of very high-volume interventional and surgical centers. In this study, the proportion of hospitals with primary PTCA facilities was 18.5% compared with >40% in NRMI hospitals. Although not reported, it is likely that primary PTCA was performed in high-volume centers. In a recently reported study evaluating primary PTCA volume and outcome in the NRMI, Magid et al. (13) found that improved primary PTCA mortality and morbidity levels in comparison with thrombolytic therapy were observed in high- (>49 procedures/year) and medium-volume (17 to 48 procedures/year) primary PTCA centers. Lower-volume centers could not replicate the <4% mortality observed in the higher-volume centers.

So what are practitioners to do in 2001? Based on a number of prospective trials, it appears clear to us that, on average, moderate-to-high-risk patients presenting early in the course of an evolving infarction do better with primary PTCA than with thrombolytic drugs—provided the patient is treated expeditiously by an experienced operator in a high-volume center. The proper course of action for the large majority of patients who are not fortunate enough to present at the optimal time of day to such a facility is less clear. Should acute infarct patients presenting to smaller centers be treated immediately with thrombolytics, or should they be quickly transferred for primary PTCA? Unfortunately, the study by Zahn et al. (9) provides little guidance to this common dilemma. Only 3.3% of eligible patients were transferred for PTCA. Moreover, it is likely that frequent transfers in this study would have significantly delayed the median time to intervention and might have narrowed the mortality gap between the two groups.

Programs that choose to pursue after-hour or transfer-based interventions for AMI must develop ongoing quality-assurance programs to document compliance with established guidelines, most notably a “door-to-balloon” time of under 90 min (14). Furthermore, it is unlikely that building/staffing additional primary PTCA facilities would have a substantial impact on AMI outcomes in general, as it is unlikely that these centers can capture the numbers of patients necessary for excellent outcomes. Finally, it remains equally clear that treatment with thrombolytic agents provides an acceptable alternative to primary PTCA in many clinical settings.

What may hold greater promise for the highest standards of treatment for all patients is innovation within the pharmacologic treatment of AMI. It is unlikely that the newest generation of thrombolytic agents used alone will attain Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow rates seen in primary PTCA (>90%). The combination of lower-dose thrombolytic agents with glycoprotein-IIb/IIIa platelet antagonists holds promise in improving patency and outcome in pharmacologic-treated patients (15). A strategy of facilitated percutaneous coronary intervention with a thrombolytic agent followed by PTCA might also be a reasonable strategy in those patients treated initially at centers without primary PTCA.

Finally, the good news with all of this innovation is the continued reductions in morbidity and mortality in patients presenting with AMI. Although an optimal strategy for all patients has yet to be determined, it is likely that some combination of therapies performed quickly will result in continued improvements in outcome.

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**REFERENCES**


