EDITORIAL COMMENT

Optimizing Outcomes in ST-Segment Elevation Myocardial Infarction*

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During the past two decades, major advances in the treatment of acute ST-segment elevation myocardial infarction (STEMI), including coronary care units and thrombolysis, have lowered the mortality after hospital presentation to approximately 5%. However, in recent years, there has been little further improvement in survival (1). Neither newer fibrinolytic agents nor attempts to combine a reduced-dose fibrinolytic agent with a glycoprotein (GP) IIb/IIIa inhibitor, which increase 60- to 90-min infarct-artery–related patency, have resulted in improved survival (2–4). Reasons for this apparent paradox may include poor myocardial perfusion through the microvasculature despite optimal epicardial coronary artery flow, continued myocardial cell death in ischemic border zones, or an inability to impact the high mortality associated with cardiogenic shock.

The authors are to be congratulated on completing this well-designed, randomized study in a large number of high-risk STEMI patients ineligible for standard reperfusion strategies. Unfortunately, their results add to the list of ineffective therapies for such patients. There were slight trends toward benefit with enoxaparin on recurrent myocardial infarction and angina, particularly in the least seriously ill patients, but these results were not statistically significant.

Limitations of the study, as pointed out by the authors, included a lower-than-expected event rate, thereby reducing the power of the study to detect an important difference, and a heterogeneous patient population (5). Other limitations included the possibility that the dose of unfractionated heparin was ineffectual (data on adequacy of anticoagulation was not provided) or that the dose of tirofiban was too low (6). Finally, although mortality is the traditional gold standard end point for myocardial infarction trials, other end points, such as infarct size, may better reflect the effects of therapy on long-term survival.

FUTURE THERAPIES FOR STEMI

To further reduce mortality associated with STEMI, new therapies will be needed to improve patency, myocardial perfusion, preserve ischemic myocardium, and reduce the mortality associated with shock. The benefits of reperfusion are greatest for patients who present early after symptom onset, emphasizing the need for patient awareness, early detection, and the potential benefit of administering reperfusion therapy in the field (7). The greater use of primary PCI and transfer strategies that combine pharmacologic and mechanical reperfusion (“facilitated PCI”) are under evaluation (8–10). Other approaches to increase early patency include transcatheter ultrasound to optimize lytic efficacy (11) and combinations of new antithrombin and antiplatelet agents (e.g., low molecular weight heparins, direct thrombin inhibitors, thienopyridines, and a P-selectin antagonist).

In addition to improving infarct-related artery patency, future strategies will also need to focus on improving myocardial perfusion through the microvasculature, which is an independent predictor of outcome (12). The platelet GP IIb/IIIa inhibitor abciximab improves coronary flow reserve (13), which may contribute to its benefit during primary PCI (14). Other approaches to reducing distal embolization during primary PCI that are under investigation include thrombectomy (15,16) and distal protection devices (17,18).

Even with successful reperfusion of both the epicardial artery and its microvasculature, further myocardial cell death may occur in adjacent ischemic territory. A number of treatments to reduce infarct size by preserving myocardial cell viability are under investigation. The theoretical benefit of glucose-potassium-insulin infusion first theorized by Sodi-Pallares in 1962 (19) and confirmed in a modern lytic

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trial (20) is being reassessed in the ongoing CREATE mega trial. However, many other pharmacologic approaches, including adenosine (21), neutrophil inhibition with an antibody to the CD 11/18 integrin (22), prostaglandin E-1 inhibition, inhibition of the sodium-hydrogen exchange pump (23), and complement C5 blockade (24), all have been unsuccessful. Two mechanical myocardial preservation strategies that show promise in pilot studies are hyperoxic blood perfusion in the infarct-related artery (25) and systemic hypothermia via an inferior vena cava heat-exchange catheter (26).

For patients who present with late and large infarctions, the options are limited, as demonstrated in the TETAMI trial. Furthermore, the residual viable myocardium may be insufficient to allow survival. Although a randomized trial demonstrated that emergent revascularization could improve the survival of patients with shock as compared with initial medical stabilization, the mortality in both groups was about 50% at 30 days (27). Ventricular-assist devices that can be rapidly inserted percutaneously may be beneficial in selected patients, and one such device is undergoing randomized assessment (28). Cardiac transplantation and myocardial regeneration (29) may also offer hope for some of these patients.

CONCLUSIONS

The advances in STEMI management over the past two decades have been remarkable. Nonetheless, the pace of mortality reduction has slowed. Future therapies that address the three “Ps” of patency, perfusion, and preservation, as well as novel therapies for cardiogenic shock, will be necessary to further improve survival. The benefit of delivering this specialized care in regional centers of excellence is obvious; however, the methodology to implement this approach is not (30,31).

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