EDITORIAL COMMENT

Acute Myocardial Infarction: Are Diabetics Different?*

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Before considering whether diabetic patients undergoing myocardial infarction (MI) should be treated differently, let us consider diabetic patients with coronary artery disease and those who undergo interventional procedures. There is ample evidence from Framingham and elsewhere that diabetes carries a high risk for cardiac mortality (1). This is due to the premature development of atherosclerosis often associated with more diffuse coronary disease (2) and worse left ventricular function (3). The progression of coronary artery disease in diabetics has long been recognized and may be related to increased insulin-like growth factor, platelet-derived growth factor, insulin, and other substances that may promote atherogenesis (4), endothelial dysfunction, enhanced platelet aggregation and thrombus formation (5). The relationship of serum glucose level is unclear; however, hemoglobin A1C levels do seem to predict cardiovascular events (6). Recently the role of oxidative stress on platelet function has been explored (7).

Coronary angioplasty in diabetics has been a subject of interest since the technique was developed. The success rate of angioplasty increased and the complication rates fell in the two National Heart, Lung and Blood Institute registries comparing results from the late 1970s to the mid 1980s. This occurred despite an increasing number of diabetic patients in the latter cohort (8). Improved equipment and operator experience undoubtedly accounted for the improvement in this series as well as others (9,10).

The outcome of 1,133 diabetic patients treated at Emory University Hospital (Atlanta, Georgia) over a 10-year period was reviewed (11). The procedural success rates were similar between diabetic and nondiabetic patients, although a trend for an increased death and MI rate was present in insulin-requiring diabetics. The registry of the Society for Cardiac Angiography and Interventions (12) analyzing 10,622 patients found that diabetes had no independent association with adverse outcome. A similar finding was present in a study by the Multi-Hospital Eastern Atlantic Restenosis Trial investigators (13). Most of the patients in these series had single-vessel disease. Ellis et al. (9) found that among patients with multivessel disease, lesion classification and diabetes were the only independent variables of procedure outcome, with ischemic complications occurring in 15.4% of the diabetic patients and 5.8% of the nondiabetic patients. However, in an analysis of 8,207 patients treated at Emory University Hospital and the San Francisco Heart Institute in the mid 1980s, diabetes did not predict the occurrence of acute closure (10). It should be pointed out, however, that once acute closure occurred, diabetes was a significant predictor of mortality (38.5% in diabetics compared with 11% in nondiabetics, p = 0.024).

Restenosis and long-term outcome is also impacted by the presence of diabetes. Conventional angioplasty has consistently shown a statistically higher restenosis rate among patients with diabetes (14,15). Long-term survival of patients undergoing multivessel coronary angioplasty has been brought into question by the findings of a large series from Emory (16) as well as long-term findings of the Bypass Angioplasty Revascularization Investigation (BARI) and Emory Angioplasty versus Surgery Trial (EAST) trials (17,18). The recent advances in interventional cardiology, including stenting and potent antiplatelet therapy, may alter these findings (19,20).

The article by Hasdai et al. (21) takes as its initial premise that the outcome of acute MI therapy with thrombolysis is associated with a significantly worse outcome in diabetics than in nondiabetics, as shown in the Global Use of Strategies to Open Occluded Arteries in Acute Coronary Syndromes (GUSTO-1) trial. The current article in this issue of the Journal (21), examines the angiographic sub-study of patients undergoing thrombolysis or primary angioplasty in the GUSTO-IIb study. This study compared the acute and early outcomes of 177 diabetics with the outcomes of 961 nondiabetics who were randomized between thrombolysis and primary angioplasty. The study was convincing in showing a reduction in death, reinfarction or disabling stroke in the nondiabetic group. The authors contend that a similar trend was present for the diabetics; however, this did not reach statistical significance. It is mildly reassuring that among diabetics, this composite end-point was somewhat lower at 30 days in the angioplasty group (11 of 99) as compared with the thrombolysis group (13 of 78). Of concern, however, is the fact that the in-hospital mortality, although not showing a significant difference, was 5.1% in the thrombolysis group, which paralleled the nondiabetic results, but was 9.1% in the angioplasty group. The authors also note that mortality remained higher for the angioplasty group at six months, although there was no significant difference at one year. The

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angiographic study documented that Thrombolysis in Myocardial Infarction (TIMI) 3 flow among patients undergoing angioplasty was achieved in a similar percentage of diabetic and nondiabetic patients (73.1% vs. 78.1%). Although these figures indicate that the diabetic patients had comparable success with primary angioplasty, the results in both groups are disappointing. It would be hoped that TIMI 3 flow rates could be achieved perhaps approaching those seen in other primary angioplasty versus thrombolysis trials (22,23). It should be pointed out, however, that different core laboratory assessments of TIMI 3 flow may artificially exaggerate the differences.

One might speculate as to the reason why well accepted differences in long-term outcome in diabetic patients might not be reflected in the acute outcome of primary infarct angioplasty. The long-term outcome of patients depends in great measure on the magnitude of the disease state and the systemic factors that predispose the patient to progression of disease as well as restenosis. These factors clearly impact long-term survival of diabetic patients; current investigations into effective secondary preventive measures, including the value of tight glycemic control, are the subject of a great deal of ongoing research. The outcome of acute infarct angioplasty, however, depends in great measure on the ability to interrupt the infarction. In the time frame covered by the present study, one would not expect disease progression or restenosis to play a role, but factors such as more extensive disease in the diabetic patients could have influenced the postprocedure mortality. The use of the composite end point, although very popular in current clinical trials, does not give a complete picture. Whereas reinfarction in the diabetic group was significantly greater in the thrombolysis cohort, mortality trended in the opposite direction. These events should not be equated and one may also speculate that they are influenced by different aspects of the diabetic condition. Reinfarction may be driven by the prothrombotic features present in diabetic patients, while the early mortality may be linked to more extensive disease commonly present.

How can the outcomes of therapy for acute infarction be further improved? In the GUSTO IIb study, stenting and GPIIb/IIIa receptor blocking agents were rarely utilized. The impact of IIb/IIIa agents in diabetic patients has been dramatic in reducing periprocedural MI (19), although no documentation of early mortality improvement has been claimed. Likewise, coronary stenting (23) has been effective in reducing recurrent ischemia and reintervention although not improving periprocedural mortality.

One must agree with the conclusion that primary angioplasty should not be denied in diabetic patients. After all, primary angioplasty is basically an emergency procedure designed to save lives, while preventing recurrent ischemia and late restenosis are secondary objectives. Additional measures currently available and yet to be developed are needed to improve both short- and long-term survival in diabetic patients.