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SEMINAR ON THROMBOLYSIS IN MYOCARDIAL INFARCTION—I

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Introduction. Coronary Thrombolysis: Second Chance Therapy—Maximizing the Advantage

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The major determinant of morbidity and mortality in coronary artery disease is the status of myocardial function. Thus, the thrust of our therapy has been directed toward maintenance of normal ventricular function and prevention of loss of heart muscle. Although numerous interventions have been designed to alter the balance of oxygen demand and oxygen supply to favorably affect ventricular performance, nothing has surpassed restoration of blood flow. In acute myocardial infarction, coronary thrombolysis occurs spontaneously in approximately 20% of patients in the early hours, and studies (1–3) have shown that lytic agents may produce lysis in an additional 40 to 70% of patients. The combination of thrombolytic therapy and spontaneous thrombolysis has achieved an early reperfusion rate of 70 to 90%. However, it is clear that "time means muscle," and strategies that have evolved relate to reducing the time from acute occlusion to thrombolysis. If thrombolysis occurs within 30 minutes of the acute event there is a high salvage rate of cardiac muscle (4); if it occurs within 90 minutes after the event substantial benefits have been demonstrated but after 3 hours the advantage diminishes (5,6).

Early thrombolysis gives an advantage in both short- and long-term mortality. The Italian GISSI trial (7) revealed a significant reduction in mortality—to 8.1% with intravenous streptokinase, as compared with 15.3% in control patients, when treatment was instituted within 1 hour of the onset of symptoms. When treatment was instituted within 3 hours, mortality was 8.5% in treated versus 11.9% in control patients. The advantage was minimal after 3 hours. Similarly, in the ISAM trial (5) after 21 days the mortality rate was 5.2% in those receiving intravenous streptokinase within 3 hours of the onset of symptoms, as compared with 6.5% in the placebo-treated group. As noted in this Seminar, at 7 months' follow-up the difference in mortality rates had narrowed to 10.9% in the streptokinase group and 11.1% in the placebo group (8). At 21 months, the mortality rates were 14.4% in the streptokinase group and 16.1% in the placebo group. These differences were not statistically significant.

Of particular note was the significantly higher reinfarction rate in the streptokinase-treated patients (8). This was also true in the GISSI study (7). Clearly, early reperfusion offered "a second chance," particularly in those treated very early, in whom there was muscle salvage and thus an opportunity to take advantage of this event and prevent recurrence—that is "maximizing the advantage." This Seminar may help us focus on ways to maximize the advantage of our second chance. The enthusiasm for percutaneous transluminal coronary angioplasty as an immediate therapy has gained great momentum (3,9) but without long-term randomized substantiation of its benefits. It would appear that individualization of therapy will prove beneficial.

Intravenous streptokinase will be the therapy of choice in many patients, because it can be administered early without major facilities available. Subsequent treatment, such as administration of intracoronary lytic agents, balloon angioplasty, coronary artery bypass surgery and combinations of these, may be utilized, depending on the specific situation. It is obvious from available studies (10,11) that there is time to individualize specific therapy in most patients, and that immediate angioplasty or surgery is not necessarily mandatory. In fact, recent studies have shown significant resolution of obstruction with lytic agents and spontaneous continued lytic activity in 15 to 30% of patients. This demonstrates the wisdom of short-term observation in selected patients and longer term observation in others.

Carefully utilized, recombinant tissue plasminogen ac-

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tivator will increase our effectiveness in coronary thrombolysis (12), providing a second chance to more patients, but at the "same time" increasing the need for diligence in individual patient therapy to "maximize this second chance." It is clear that, having gained the advantage, we cannot relax our careful surveillance of a given patient. Careful clinical follow-up with appropriate interventional therapy—be it medical, balloon angioplasty, laser therapy or coronary bypass surgery—will make the most of our advantage and should further reduce early and late morbidity and mortality in the very large segment of the population that is at risk for the ravages of acute myocardial infarction.

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