Ischemic Heart Disease

Myocardial Infarction

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[*Rev Cardiovasc Med.* 2001;2(3):174–176]
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Two important aspects of the diagnosis and management of myocardial infarction (MI) are reviewed: the effect of thrombolysis in elderly patients with MI and the ramifications of asymptomatic or unrecognized MI.

Lack of Benefit for Intravenous Thrombolysis in Patients with Myocardial Infarction Who Are Older than 75 Years

Thiemann DR, Coresh J, Schulman SP, et al.
Circulation. 2000;101:2239-2246.

To determine the results of thrombolytic therapy in the elderly, this retrospective analysis utilized the large Cooperative Cardiovascular Project (CCP) database of Medicare fee-for-service beneficiaries, aged 65 to 86, whose principal discharge diagnosis was acute myocardial infarction (MI). The analysis was limited to 7864 patients who were treated within 12 hours of symptoms and who had electrocardiographic ST-segment elevation in 2 or more contiguous leads (1.5 mm or greater in limb leads and 2 mm or greater in precordial leads). Those with contraindications to thrombolysis were excluded. Patients were divided into subgroups by age: 65 to 75 and 76 to 86. In the younger group, 74% received thrombolytics; in the older group, 60% received them. The remaining patients received aspirin and heparin. Of those receiving thrombolytics, approximately 75% were treated with tissue plasminogen activator (t-PA) and the remainder, with streptokinase.

Patients in the thrombolytic cohort were judged to be at lower risk for mortality within 30 days than were patients treated with aspirin and heparin alone. This was determined on the basis of lower rates of anterior MI, Killip class III MI, and comorbidity. This translated into predicted lower mortality rates, based on a logistic regression model, markedly favoring the thrombolytic group. Nonetheless, despite a lower projected mortality in patients treated with thrombolytics, compared with those treated with aspirin and heparin alone, unadjusted survival differed markedly according to age. Patients aged 65 to 75 who were treated with thrombolytics had a crude mortality of 6.8%, compared with 9.8% for patients not treated with these agents. Among patients older than 75 years, the ratio was reversed; crude mortality for those treated with thrombolytics was 18%, compared with 15.4% for patients not treated with thrombolytics. In the proportional hazards multivariate analysis of 30-day survival, the interaction between age and thrombolytic therapy was highly significant. For patients aged 65 to 75, thrombolytic therapy provided a consistent survival advantage; hazard ratios ranged from 0.76 (P = .02) to 0.88 (P = 0.29), depending on the statistical model. The converse was the case among patients aged 76 to 86, in whom thrombolytic therapy was associated with an increase in mortality, with a hazard ratio ranging from 1.29 (P = .01) to 1.38 (P = .003).

These results are somewhat surprising and certainly of concern. This was not a randomized trial, and all observational studies have their strengths and weaknesses. Nonetheless, this large study does provide a perspective of the results of thrombolytic therapy in clinical practice nationwide, as opposed to randomized trials that tend to enroll highly selected, healthier patients.[1] Previous trials and the Fibrinolytic Therapy Trialists' Collaborative Group meta-analysis[2] suggested that patients older than 75 showed a nonsignificant trend toward absolute benefit from thrombolytic therapy, although the magnitude was less than in younger patients.[3,4] The differences between the results of the randomized trials and this study are likely multifactorial but may relate to a healthier population in the trials as well as to the more standardized and consistent care experienced by a trial population (for example, in regard to post-thrombolytic anticoagulation). In some of the trials included in the Fibrinolytic Therapy Trialists' meta-analysis, however, many of the nonthrombolytic patients did not receive heparin or aspirin.

It would appear, therefore, that thrombolytics are helpful in the "young old" but potentially harmful in patients over age 75. Potential explanations include a greater risk of bleeding and intracranial hemorrhage, an increased rate of cardiac rupture, and perhaps a diminished benefit from thrombolytics because of more multivessel disease and lower rates of thrombolysis in MI (TIMI) III blood flow in the elderly. This study, while of interest and concern, does not justify the withholding of throm-

bolytics in all elderly patients who are 75 or older. Nonetheless, the study tends to strengthen the case for primary angioplasty or percutaneous coronary intervention in the elderly. In several trials, the benefit of primary angioplasty over thrombolysis was disproportionately greater in the elderly[5] and, in a large observational study from the CCP database (confined to patients 65 and older), 30-day and 1-year mortality rates were lower in patients managed with primary angioplasty versus thrombolytics.

In summary, the elderly are a heterogenous group (both chronologically and physiologically) who are frequently underrepresented in randomized trials. The CCP data emphasize the need for additional trials and observational studies that are specifically focused on the elderly and on subgroups within the elderly.

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Prevalence, Clinical Characteristics, and Mortality among Patients with Myocardial Infarction Presenting without Chest Pain

Canto JG, Shlipak MJ, Rogers WJ, et al.
JAMA. 2000;283:3223-3229.

This observational study of almost 435,000 patients with confirmed MI evaluated the frequency of presentation without chest pain as well as management and outcomes according to whether patients presented with or without chest pain. Patients were selected from the National Registry of Myocardial Infarction 2 database (June 1994 to March 1998), representing 1674 US hospitals.

Of all patients with confirmed MI, 33% did not have chest pain on presentation to the hospital. As a group, patients without chest pain were older, more frequently female, and more likely to have diabetes mellitus or prior congestive heart failure than were those with chest pain. Of note: the mean time from symptom onset to presentation was 7.9 hours, compared with 5.3 hours in patients with chest pain, and this difference was significant. Not unexpectedly, patients without chest pain were less likely to receive a diagnosis of MI on admission and less likely to be treated with acute reperfusion therapy, ß-blockers, aspirin, or heparin. Moreover, among patients treated with acute reperfusion therapy, the time interval from hospital arrival to treatment was substantially increased in comparison with patients presenting with chest pain. Mortality was extremely high—23.3%—compared with 9.3% among patients with chest pain (adjusted odds ratio for mortality, 2.21% [95% confidence intervals, 2.17% to 2.26%]). The magnitude of this mortality difference is highlighted by its persistence, even after adjusting for differences in age, comorbidity, and severity of presentations.

This registry study is subject to the limitation of all observational analyses but does raise several important issues.

First, it must be appreciated that atypical presentations of MI are common, particularly among the elderly. Such symptoms as dyspnea or congestive heart failure, atypical locations of pain or discomfort, central nervous system manifestations, syncope, weakness, and indigestion are well-documented "masquerades" of MI.[1] The lesson to be learned is that a heightened index of suspicion should be maintained. Many of these patients may have MI with ST-segment elevation on the electrocardiogram and, therefore, could benefit from reperfusion therapy.[2] Results of randomized trials, which usually require the presence of chest pain as an entry criterion, may not apply to this high-risk subgroup, among whom diagnostic and therapeutic strategies have the potential to markedly improve survival.[3,4] Second, a well-established tenet of reperfusion therapy is that "time is muscle" and that outcomes are strongly correlated with the delays between symptom onset and initiation of therapy.[3,6] There are many components to the time delay, and the segment most amenable to improvement is the "door-to-needle" or "door-to-balloon" times following admission to the emergency department.[5] The delay between the onset of symptoms and the patient's first attempt to obtain medical care (prehospital delay) remains a substantial and frustrating component in attempts to reduce the mortality of MI.[7] Community interventions to reduce prehospital delay are an attractive target, and a logical component of such efforts would be to increase patient sensitivity to the importance of both typical and atypical symptoms and the potential differences in presenting symptoms between men and women. Unfortunately, despite several attempts at community intervention using the mass media,

community organizations, and both professional and public education, the results have been, in general, disappointing.[8-12] Several studies have identified prehospital delays ranging from 150 to 420 minutes.[8-] Four studies (in Sweden, Switzerland, Australia, and Chicago) demonstrated mixed results, with little change in the use of emergency medical services (EMS) and relatively small changes in the time to treatment among patients with confirmed MI, despite an intensive community campaign.[8,11-13] A recent trial conducted in 20 US cities in 10 states showed an increase in the use of EMS but little change in prehospital delay.[7] The authors concluded that new strategies are needed to bring rapid and effective care to patients in the community who have acute MI.

A third issue relates to the entity of "clinically unrecognized MI," in which patients who have survived an MI escape detection until an electrocardiogram is performed subsequently, during a screening examination or for another clinical purpose. Past studies have suggested that 25% to 40% of MIs are clinically unrecognized.[14-18] It is somewhat disconcerting to note that in a recent study using the Cardiovascular Health Study database of individuals 65 and older, the majority of whom were free of cardiovascular disease at study entry, a previous MI was clinically unrecognized in 22.3% of patients.[15] Independent predictors of "silent" MI were an absence of both prior angina and prior congestive heart failure. Moreover, the subsequent survival of patients with and without clinically recognized MI was similar. The clinical implications are profound. There is a great deal we do not understand about symptoms and the pathophysiology of MI. Cost-effective screening mechanisms need to be identified, and the most effective method of risk stratification of such patients needs to be verified.

In "The Winter's Tale", William Shakespeare stated: "I have tremor cordis on me: my heart dances." What we have to realize is that the dancing heart beats to many different rhythms, and furthering our understanding of the symptomatology of the infarcting heart has enormous implications for management. There is much we still have to learn. ■

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Congestive Heart Failure

BNP as Treatment Marker

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[*Rev Cardiovasc Med.* 2001;2(3):174–176]
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For patients with heart failure, agents that confer survival benefits, such as angiotensin-converting enzyme (ACE) inhibitors, ß-adrenergic blockers, and aldosterone antagonists, target neurohormonal activation. In clinical trials, the dosing method for these therapies has been to titrate up to a target dose, unless it