

Thrombolytic Therapy for Acute Myocardial Infarction in the Elderly

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Acute myocardial infarction (MI) is a leading cause of morbidity and mortality in developed countries. Patients ≥ 75 years constitute up to 30% of the acute MI population and are associated with a 50% in-hospital mortality.¹ Thrombolytic therapy was shown in a meta-analysis of 9 largest randomized controlled trials to reduce 35-day mortality.² However, the benefit was observed mainly among patients < 75 years old. For patients ≥ 75 years, the 35-day mortality was 24.3% in those treated with thrombolytic therapy and 25.3% in the placebo group, a difference not reaching statistical significance. Two recent observational studies indicate that thrombolytic therapy may not be beneficial to the elderly. Berger et al showed no survival benefit at 30 days in patients ≥ 65 years when thrombolytic therapy was compared with no therapy (OR 1.01; 95% CI 0.94 to 1.09) while one-year mortality was lowered (OR 0.84; 95% CI 0.79 to 0.89). When analyzed according to the agent given, treatment with tissue plasminogen activator (tPA) was associated with a significant reduction in one-year mortality while mortality reduction was nonsignificant with streptokinase.³ In Thiemann's study, thrombolytic therapy was associated with a 38% relative increase in mortality among patients age 76 to 86 years, which translated into 4 more deaths for every 100 patients treated.⁴ These studies provoked debates in the cardiology community. White quoted new data analysis from the Fibrinolytic Therapy Trialists' (FTT) Secretariat on elderly patients treated with fibrinolytic therapy. For those meeting eligible criteria (ie, presentation within 12 hours with ST elevation or bundle branch block), the mortality rate was reduced from 29.4% to 26.0% ($p=0.03$) among patients over the age of 75 years. There were 34 lives saved per 1,000 patients treated.⁵

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The potential detrimental effect of thrombolytic therapy for the elderly may be explained by the following mechanisms. The excess bleeding risk in the elderly may outweigh the benefit of reperfusion. Age over 65 years is an independent risk factor for intracranial haemorrhage,⁶ which carries a mortality of over 50% in patients receiving thrombolytic therapy. Other bleeding complications requiring transfusion are also more common in the elderly. Cardiac rupture is another hazard that occurs more often in the aged. There is an age-related increase in sudden death from cardiac rupture as reported by the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI)-2 investigators.⁷ Lastly, elderly patients have a poorer LV functional recovery despite successful reperfusion as evidenced by clinical⁸ and animal studies.^{9,10}

There are also conflicting data on the choice of thrombolytic agent for the elderly. The GISSI-1 trial showed a trend of mortality reduction with streptokinase versus control in patients > 75 years.¹¹ In the Second International Study of Infarct Survival (ISIS-2), a significant reduction in mortality was observed for patients > 75 years receiving streptokinase.¹² However, all but those > 85 years had a lower mortality with accelerated tPA compared with streptokinase in the Global Utilization of Streptokinase and TPA for Occluded coronary arteries (GUSTO-1) trial.¹³ In Berger's observational study, significant mortality reduction at 1 year was seen with tPA but not streptokinase compared with no reperfusion therapy in patients older than 65 years.³

Although limited by selection bias even after adjustments are made, observational studies provide valuable insight into the outcome of the use of therapies out of randomized trial setting. In general, overall results of clinical trials should be applied to all subgroups unless there are differences among the subgroups. Given the discrepancy between results of randomized trials and observational studies and the potential differences

between elderly and younger patients in the response to thrombolytic therapy, the subgroup of elderly patients warrants randomized controlled trials for defining the optimal reperfusion therapy for acute MI. Before the availability of new data, each elderly patient with acute MI must be assessed individually. The absolute and relative contraindications of thrombolytic therapy should be observed strictly in order to minimize the adverse effects. The general status and co-morbidities should also be addressed before decision making. The elderly patient who is chronologically old but biologically young may be a better candidate for thrombolytic therapy.

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