

## INFARCT MANAGEMENT IN THE 21ST CENTURY

Intravenous thrombolytic therapy, usually administered with acetylsalicylic acid (ASA) and heparin, represents the dominant acute reperfusion therapy for acute ST-elevation or bundle-branch infarction worldwide. The patient should be instructed to chew 160 mg of ASA, whether or not he/she is taking ASA at baseline, as this decreases the mortality rate by just under 20%.

The use of thrombolytics with streptokinase decreases mortality by 20%. There is a dramatic benefit from the use of ASA and thrombolytic therapy in the management of acute ST-elevation or bundle-branch infarctions.

### Patency Rates

Newer thrombolytic agents, such as recombinant plasminogen activator (r-PA), and tenec-teplase (TNK), show marginal incremental benefits.

Overall patency rates at 90 minutes with drug therapy will range up to 60%

to 65%. Ninety-minute patency with streptokinase averages about 40%, t-PA 60%, and similarly, the results for TNK and r-PA average in the order of 60% as well. Direct angioplasty leaves a patency of 85% to 90% at 90 minutes. The incremental benefit of direct angioplasty, however, is marginal for the vast majority of patients suffering from myocardial infarctions (MIs). Patients with major MIs and unstable patients with low blood pressure (BP) and heart failure will do best with direct angioplasty, provided it is done within 60 minutes.

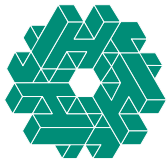
The recent GUSTO III trial demonstrated that r-PA (a derivative of t-PA with a longer half-life and reduced fibrin sensitivity) reduced mortality by 7.5% versus 7.2% with tissue plasminogen activator (t-PA) (n = 15,000).<sup>1</sup> The Kaplan-Meier event rates are summarized in Figure 1.

TNK, a t-PA derivative with a longer

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half-life given as a single bolus, has been recently introduced. It has more fibrin selectivity. It is given in a weight-adjusted dose and may have an advantage due to its favourable safety profile in the elderly. Again, the major benefit in safety may be related to weight adjustment and not to the drug itself.

In ASSENT-2, the mortality of close to 17,000 patients taking TNK and t-PA was comparable in the order of 6.2%.<sup>2</sup> A meta-analysis of bolus thrombolytic agents raises the concern of an increased risk of hemorrhagic stroke. More data are needed.

Newer thrombolytics have an advantage in ease of administration in one or two doses where infusions are not necessary. The opportunity to use these agents in the pre-hospital phase will be an exciting area. The number one determinant benefit is getting the agents on board as quickly as possible. It is evident that for every 60 minutes lost prior to starting a thrombolytic or opening an artery, one life per 100 patients treated is lost.

Newer combination therapies, such as half-dose t-PA and IIb/IIIa antagonists (i.e., abciximab) were evaluated in GUSTO-V.<sup>3</sup> A total of 16,588 patients with ST-elevation or bundle-branch infarction were randomized to abciximab

and half-dose r-PA versus r-PA. At 30 days, 499 (5.9%) of the patients in the r-PA group had died, compared with 468 (5.6%) deaths in the combined r-PA and abciximab group.

## Physician's Perspective

Thrombolytics and ASA have dramatically reduced mortality in acute ST-elevation or new bundle-branch MI. Starting any thrombolytic for the right reason, along with ASA, saves lives. There are marginal benefits to newer thrombolytic agents. Their advantage may be in ease of use. This may allow pre-hospitalization utilization of thrombolytics to a wider degree. While direct angioplasty opens arteries better, the incremental advantage is small and the

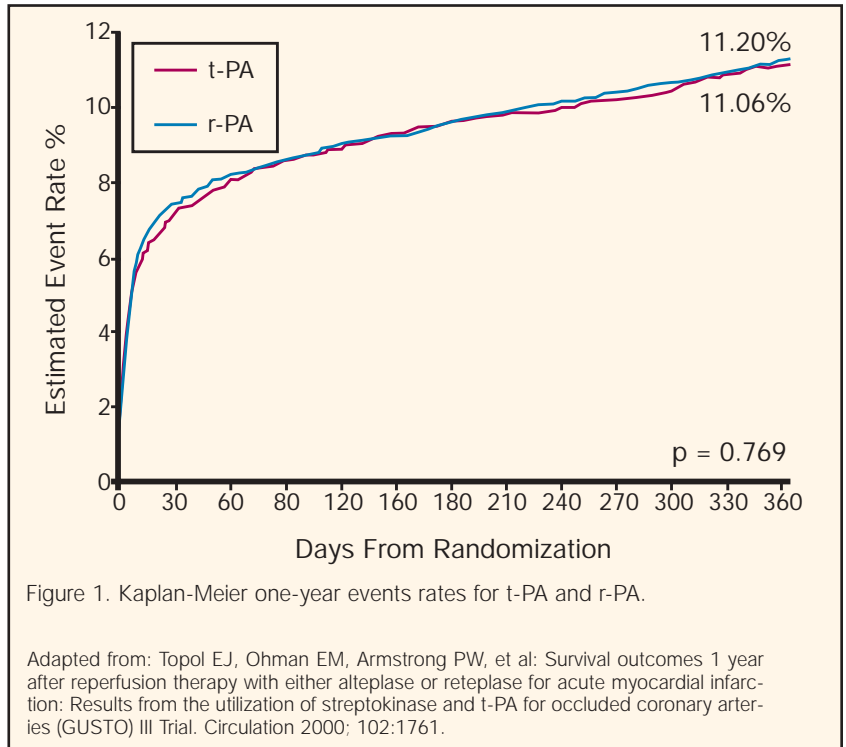


Figure 1. Kaplan-Meier one-year events rates for t-PA and r-PA.

Adapted from: Topol EJ, Ohman EM, Armstrong PW, et al: Survival outcomes 1 year after reperfusion therapy with either alteplase or reteplase for acute myocardial infarction: Results from the utilization of streptokinase and t-PA for occluded coronary arteries (GUSTO) III Trial. *Circulation* 2000; 102:1761.