Cost Effectiveness of Thrombolytic Therapy with Tissue Plasminogen Activator as Compared with Streptokinase for Acute Myocardial Infarction.

[Special Article]

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Outline

Graphics

Abstract ⊞

Background: Patients with acute myocardial infarction who were treated with accelerated tissue plasminogen activator (t-PA) (given over a period of 1 1/2 hours rather than the conventional 3 hours, and with two thirds of the dose given in the first 30 minutes) had a 30-day mortality that was 15 percent lower than that of patients treated with streptokinase in the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) study. This was equivalent to an absolute decrease of 1 percent in 30-day mortality. We sought to assess whether the use of t-PA, as compared with streptokinase, is cost effective.

Methods: Our primary, or base-case, analysis of cost effectiveness used data from the GUSTO study and life expectancy projected on the basis of the records of survivors of myocardial infarction in the Duke Cardiovascular Disease Database. In the primary analysis, we assumed that there were no additional treatment costs due to the use of t-PA after the first year and that the comparative survival benefit of t-PA was still evident one year after enrollment.

Results: One year after enrollment, patients who received t-PA had both higher costs ($2,845) and a higher survival rate (an increase of 1.1 percent, or 11 per 1000 patients treated) than streptokinase-treated patients. On the basis of the projected life expectancy of each treatment group, the incremental cost-effectiveness ratio -- with both future costs and benefits discounted at 5 percent per year -- was $32,678 per year of life saved. The use of t-PA was least cost effective in younger patients and most cost effective in older patients. At all ages, the use of t-PA in patients with anterior infarctions yielded more favorable cost-effectiveness values. In our secondary analyses, the cost-effectiveness values were most sensitive to a lowering of the projected long-term survival benefits of t-PA and to moderate or greater increases in the projected medical costs for patients in the t-PA group after the first year. In contrast, our results were not sensitive to even very unfavorable assumptions about the additional costs associated with the higher rate of disabling stroke that was noted in patients treated with t-PA in the GUSTO study.

Conclusions: The cost effectiveness of treatment with accelerated t-PA rather than streptokinase compares favorably with that of other therapies whose added medical benefit for dollars spent is judged by society to be worthwhile. (N Engl J Med 1995;332:1418-24.)

The value of thrombolytic therapy for patients with acute myocardial infarction has been firmly established. To identify the thrombolytic approach that most effectively produces sustained patency of the infarct-related artery and improves survival, the Global Utilization of

Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) investigators compared four different regimens: accelerated tissue plasminogen activator (t-PA), streptokinase with intravenous heparin, streptokinase with subcutaneous heparin, and a combination of t-PA and streptokinase [1]. ("Accelerated" refers to the administration of t-PA over a period of 1 1/2 hours -- with two thirds of the dose given in the first 30 minutes -- rather than the conventional period of 3 hours.) That study found a statistically significant relative decrease of 15 percent and an absolute decrease of 1 percent in 30-day mortality from all causes for treatment with accelerated t-PA as compared with the pooled streptokinase regimens (the mortality rates for which were not significantly different from one another). Furthermore, t-PA reduced the risk of death in each of the analyzed subgroups [1]. Some observers have questioned whether the improved survival rates seen in the GUSTO study are worth the substantial additional cost of t-PA.

We conducted a cost-effectiveness analysis to compare the value of t-PA treatment with that of streptokinase treatment on the basis of the information on mortality and use of resources from the GUSTO study and detailed data on the use of medical resources and the quality of life of a random subgroup of the GUSTO cohort residing in the United States.

Methods ⬩

Our analysis comparing accelerated t-PA with streptokinase used data from the GUSTO study: data on 1-year survival for all 41,021 patients enrolled in the study, data on the use of medical resources during the initial hospitalization for all 23,105 U.S. patients, and data on a prospective random sample of 2600 U.S. patients who underwent structured interviews by telephone 30 days, 6 months, and 12 months after enrollment on their use of medical resources and quality of life [1,2]. The particular costs and benefits examined in a cost-effectiveness analysis vary with the perspective of the study [3,4]. In medical economics, the analysis can be constructed to reflect the viewpoint of society as a whole, payers, health care providers, or patients. In the present study, we used a social perspective to identify relevant costs, although indirect costs (e.g., time lost from work) and nonmedical costs were not included. Effectiveness was measured in terms of additional life expectancy, and the effects of the treatments on the patients' quality of life were examined in a sensitivity analysis [5,6]. Both survival and costs were discounted continuously at an annual rate of 5 percent, as is consistent with conventional practice [6,7]. Extensive sensitivity analyses were performed. Cost-effectiveness ratios were expressed as the additional lifetime costs required to add one extra year of life with t-PA treatment as compared with streptokinase therapy. Higher cost-effectiveness ratios indicate lower cost effectiveness.

Determining Costs ⬩

The costs of initial hospitalization (including charges for any transfers between hospitals) were calculated in two ways: from total cost estimates (variable costs plus fixed costs) from the Duke Transition One cost-accounting system, and from Medicare diagnosis-related-group (DRG) reimbursement rates Table 1. The Transition One system estimates hospital costs using a bottom-up approach that is based on resources consumed and unit prices for those resources [3]. Costs of the thrombolytic agents were also calculated in two ways: from the Drug Topics Red Book average of 1993 wholesale prices, [8] and from the average costs of the drugs in 16 randomly selected GUSTO hospitals (2 hospitals in each GUSTO geographic region) [1]. The Red Book average wholesale price of 1.5 million units of streptokinase was $320; the price of 100 mg of t-PA was $2,750. The average cost to the 16 GUSTO hospitals was $270 for 1.5 million units of streptokinase and $2,216 for 100 mg of t-PA. We assumed that pharmacy handling and

preparation costs and drug-administration costs would be equivalent for the two regimens. For follow-up hospitalization costs, we used Medicare DRG reimbursement rates for North Carolina Table 1. Reported hospitalizations and revascularization procedures were verified with the relevant institution. Physicians' fees for both initial and follow-up hospitalizations were drawn from the Medicare fee schedule for North Carolina Table 1.

Item	Hospital Cost	Physicians' Fees
	dollars	
Initial hospitalization*		
Day in ICU, no complications	1,380	126
Day in ICU, mild-to-moderate complications	2,070	187
Day in ICU, severe complications	2,760	248
Hospital day, not in ICU	475	54
Diagnostic cardiac catheterization†	1,670	400
Coronary angioplasty†	6,200	1,356
Coronary bypass surgery†	8,800	2,564
Use of intraaortic balloon pump	824	538
Use of temporary pacemaker	562	209
Pulmonary-artery catheterization	270	303
Cardioversion–defibrillation	112	134
Interhospital transfer	970	—
Emergency department visit	300	116
Rehospitalization‡		
Coronary bypass surgery with catheterization (106)	19,092	
Coronary bypass surgery without catheterization (107)	14,121	
Coronary angioplasty (112)	6,635	
Acute myocardial infarction, complicated (121)	5,384	
Fatal acute myocardial infarction (123)	4,745	
Cardiac catheterization with complex diagnosis other than myocardial infarction (124)	4,137	
Acute myocardial infarction, uncomplicated (122)	3,807	
Heart failure and shock (127)	3,440	
Cardiac catheterization without complex diagnosis (125)	2,676	
Angina pectoris (140)	2,098	
Chest pain (143)	1,744	
Diagnostic cardiac catheterization		400
Coronary angioplasty		1,356
Coronary bypass surgery		2,823
Initial hospital day		111
Subsequent hospital day		54
Initial clinic visit		96
Subsequent clinic visit		45

*Data on hospital costs are from the Duke Transition One cost-accounting system. Physicians' fees are from the Medicare fee schedule for North Carolina. ICU denotes intensive care unit.

†Costs shown are for procedures only.

‡Data on hospital costs are Medicare diagnosis-related-group (DRG) reimbursement rates

Table 1.-Costs Used in the Analysis

For the primary analysis, incremental costs included only cumulative hospital and physicians' costs for the first year after treatment. Because there were no empirical data on costs after one year, the primary analysis assumed no cost differences between the treatment groups after one year. All costs were expressed in 1993 dollars.

Estimating Survival ±|

To estimate survival rates after the end of follow-up in the GUSTO study, the primary analysis assumed that the hazard of death after one year did not depend on the thrombolytic agent received (i.e., that the survival curves of the two treatment groups were parallel) and that the patients' pattern of long-term survival was typical of the chronic, stable phase of coronary heart disease. To represent that pattern, we constructed a Cox proportional-hazards model based on the experience of 4379 patients in the Duke Cardiovascular Disease Database [9-12] with myocardial infarction between 1971 and 1992 who had either pathologic Q waves on a resting 12-lead electrocardiogram or a marked focal wall-motion abnormality seen on a left ventriculogram and who survived at least one year. This survival model was used to extend the 1-year survival data by an additional 14 years. For the model, we selected covariates that were available in the GUSTO data base, including age, sex, and location of infarction. Because, in the Duke data, approximately 20 percent of patients were alive at the last follow-up, we used a Gompertz function to extrapolate the tail of the survival curve [13].

Using this composite modeling approach, we generated lifetime survival curves for both treatment groups and calculated life expectancy as the area under each curve. The increase in life expectancy for the t-PA group was thus represented by the difference between the areas under the two curves. The survival curve for the t-PA group is presented in Figure 1.

Sensitivity Analyses ±|

Extensive sensitivity analyses were performed in order to find threshold values for variables in the model that would result in a cost-effectiveness ratio of more than $50,000 per year of life saved. We varied survival and costs in both the short and the long term for the t-PA group, the costs and adverse health consequences of the increased risk of disabling stroke associated with t-PA, and the utility weights we used to reflect the attitude of patients toward their current state of health.

Utility ±|

Utility (a number from 0 to 100 that summarizes the value patients attach to their current state of health) was measured in structured telephone interviews one year after treatment. Patients were asked, in a series of questions, how much of their current life expectancy -- assumed to be 10 years in their present state of health -- they would be willing to give up in order to live their remaining years in excellent health [14,15].

Subgroup Analysis ±|

We calculated the comparative cost-effectiveness value for treatment with t-PA instead of streptokinase for eight clinical subgroups defined by the patient's age (up to 40 years, 41 to 60

years, 61 to 75 years, or more than 75 years) and the location of the infarction (anterior or inferior). In a linear regression analysis, neither age nor the location of the infarction had an identifiable association with costs in the first year after treatment. Consequently, we used the cost differences from our primary analysis in calculating the cost-effectiveness values for the eight subgroups.

Statistical Analysis ⊥

Descriptive data are presented as percentages for discrete variables and as medians with 25th and 75th percentiles for continuous variables Table 2. Intention-to-treat analyses of base-line, six-month, and one-year data were performed with a chi-square test for discrete variables and by the Wilcoxon rank-sum test for continuous variables.

ITEM	STREPTOKINASE	t-PA	P VALUE
Initial hospitalization			
No. of patients	11,310	5908	
Cardiac catheterization (%)	72	73	0.51
PTCA (%)	31	31	0.86
CABG (%)	13	13	0.29
Pulmonary-artery catheterization (%)	20	18	0.002
Use of ventilator (%)	17	16	0.14
Use of intraaortic balloon pump (%)	6	6	0.21
Length of stay in ICU (days)	3.5 (2.5–5)	3.5 (2.5–5)	0.69
Total length of stay (days)	8 (6–11)	8 (6–11)	0.92
From discharge to 6 months			
No. of patients	1,187	580	
Cardiac catheterization (%)	14	17	0.26
PTCA (%)	10	12	0.41
CABG (%)	5	6	0.74
No. of rehospitalizations (%)			0.94
1	23	24	
2	6	7	
⩾3	3	3	
Hospital days	0 (0–2)	0 (0–2)	0.66
Total outpatient visits to physician	5 (3–7)	5 (3–7)	0.99
To cardiologist	2 (1–4)	2 (1–4)	0.43
To internist	0 (0–0)	0 (0–0)	0.05
To family or general practice physicians	1 (0–2)	1 (0–2)	0.60
To emergency department	0 (0–0)	0 (0–1)	0.26
From 6 months to 1 year after discharge			
No. of patients	1,135	553	
Cardiac catheterization (%)	5	5	0.73
PTCA (%)	2	3	0.03
CABG (%)	1	2	0.27
No. of rehospitalizations (%)			0.06
1	12	14	
2	2	4	
⩾3	1	1	
Follow-up hospital days†	0 (0–0)	0 (0–0)	0.03
Total outpatient visits to physician	3 (2–5)	3 (2–5)	0.37
To cardiologist	1 (0–2)	1 (0–2)	0.90
To internist	0 (0–0)	0 (0–0)	0.77
To family or general practice physicians	1 (0–2)	1 (0–2)	0.23
To emergency department	0 (0–0)	0 (0–0)	0.42

*Data on the initial hospitalization are for all U.S. subjects in the GUSTO study who were randomly assigned to t-PA or streptokinase. Data on the period from discharge to one year after discharge are for the random sample of the surviving members of this cohort who were interviewed by telephone at 30 days, 6 months, and 1 year. PTCA denotes percutaneous transluminal coronary angioplasty, CABG coronary-artery bypass surgery, and ICU intensive care unit.

Table 2.-Use of Medical Resources during the Initial Hospitalization and up to One Year after Discharge, According to Treatment

Results ⬆

Primary Analysis ⬆

Costs

Resource consumption within the first year was generally similar in the streptokinase and t-PA groups Table 2. There was a slightly higher use of pulmonary-artery catheters in the patients who received streptokinase during the initial hospitalization (20 percent, vs. 18 percent in the t-PA group; P = 0.002). There was a trend toward more percutaneous transluminal coronary angioplasty in the t-PA group (3 percent vs. 2 percent, P = 0.03) and more rehospitalization (19 percent vs. 15 percent, P = 0.06) from six months to one year after enrollment Table 2. At the time of initial hospital discharge, there was no difference between the two treatment groups in the rates of use of any of the major classes of cardiac medications. The estimated cumulative medical costs (hospital costs plus physicians' fees) at one year, exclusive of the cost of the thrombolytic agent, averaged $24,575 for patients treated with streptokinase and $24,990 for patients treated with t-PA. When the Red Book drug costs for the thrombolytic agent were added, the incremental, undiscounted costs for each patient who received t-PA were $2,845. The primary analysis assumed no increased costs for the t-PA group after the first year.

Life Expectancy

Survival at 30 days was 92.7 percent in the streptokinase group and 93.7 percent in the t-PA group (P = 0.001), and 89.9 percent and 91.0 percent, respectively, after one year (P = 0.006). We projected a life expectancy from the time of enrollment in the GUSTO study of 15.27 years for patients treated with streptokinase and 15.41 years for patients treated with t-PA, or an undiscounted increase in life expectancy for the t-PA group of 0.14 year per patient (i.e., 14 additional years of life per 100 patients treated with t-PA).

Cost Effectiveness

With an increased life expectancy in the t-PA group of 0.14 year of life per patient, an increased cost of $2,845 per patient, and a discount rate of 5 percent, the comparative primary cost-effectiveness ratio for the use of t-PA instead of streptokinase was $32,678 per year of life saved. Substituting the average thrombolytic-drug costs to the hospitals in the GUSTO study for the Red Book wholesale prices in our primary analysis yielded a cost-effectiveness value of $27,115 per year of life saved. If we used Medicare DRG reimbursement rates for the initial hospitalization rather than the Duke Transition One costs, kept the Red Book prices for the thrombolytic agents, and left all other factors unchanged, the increase in costs for patients treated with t-PA was $3,154 and the cost-effectiveness ratio became $36,218 per year of life saved. Substituting the GUSTO prices for thrombolytic agents into this latter calculation reduced the additional cost of t-PA treatment to $2,670 and lowered the cost-effectiveness value to $30,655 per year of life saved.

Sensitivity Analyses ⬆

Differences in One-Year Survival

The 95 percent confidence interval for the 1.1 percent increase in one-year survival among patients in the t-PA group was 0.46 percent to 1.74 percent, a range that would produce cost-effectiveness ratios of $71,039 to $18,781 per year of life saved.

Differences in Long-Term Survival

The true life expectancy of the subjects could differ from the value predicted in our model of approximately 15 years. In addition, the survival curves may actually converge or diverge after one year. Either reducing the life expectancy or causing the survival curves to converge would reduce the additional years of life saved by t-PA treatment Figure 2. With a 5 percent discount rate, the cost-effectiveness ratio would rise above $50,000 if the number of years of life saved by t-PA treatment fell below 7 undiscounted years per 100 patients, and it would rise above $100,000 per year of life saved if the number of undiscounted years of life saved per 100 patients fell below 3.
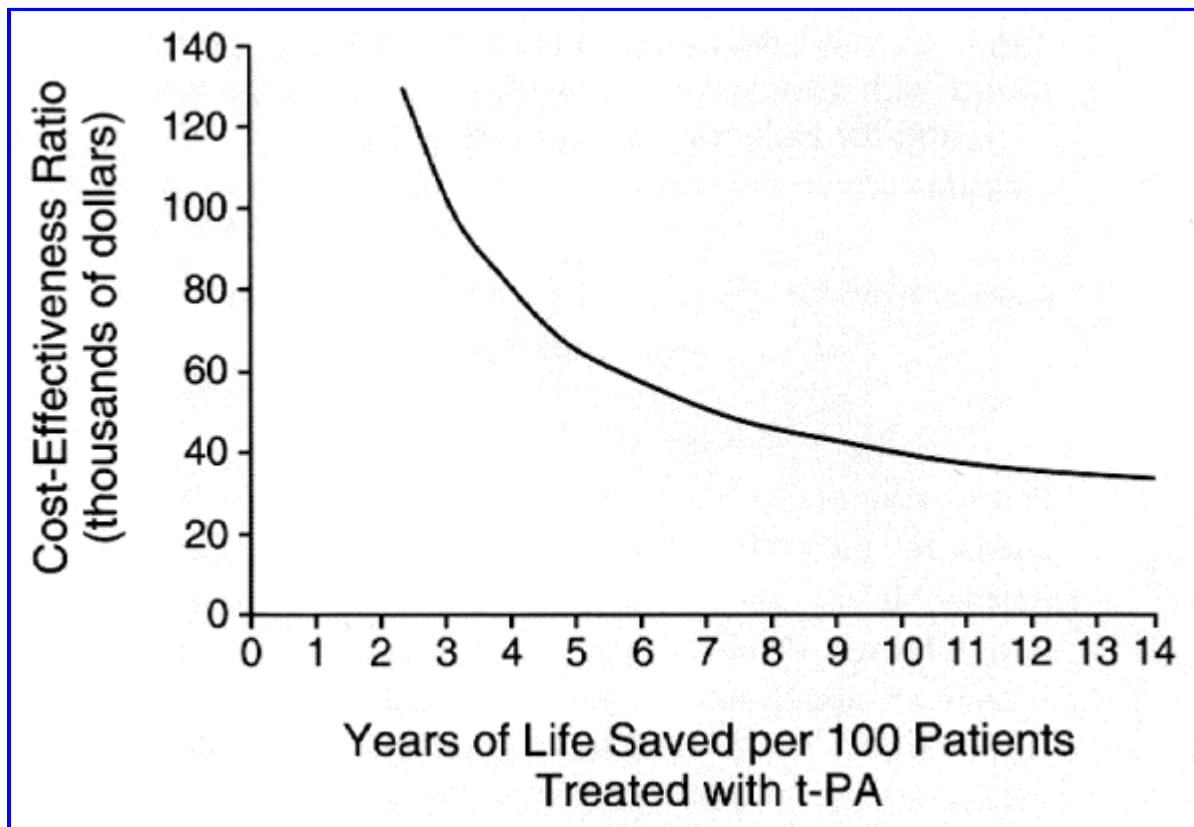

Figure 2.-Sensitivity Analysis of the Long-Term Increase in Survival in the t-PA Group as Compared with the Streptokinase Group. The y axis shows cost-effectiveness ratios expressed as dollars per additional year of life saved (all values are discounted). The x axis shows undiscounted years of life saved by the use of t-PA per 100 patients treated. In the primary analysis, t-PA saved 14 additional years of life per 100 patients treated and had a cost-effectiveness ratio of $32,678. If the t-PA and streptokinase survival curves converged over time, or if the life expectancy of the GUSTO cohort was less than that projected in our analysis, then the cost-effectiveness value would be greater and, therefore, less favorable

Discounting the value of future costs and benefits reduces their present value. If costs and increased years of life were not discounted at all, the primary cost-effectiveness ratio in our study would be $20,468 per year of life saved; if a discount rate of 10 percent was used, however, the cost-effectiveness ratio would rise to $47,337 per year of life saved.

Cost Differences in the First Year

Although the difference in associated costs between streptokinase and t-PA (exclusive of the cost of the drugs themselves) was not statistically significant, variations in the increased costs associated with t-PA treatment did affect the cost-effectiveness ratio Figure 3. A cost-effectiveness value of $50,000 is reached when the additional cost of t-PA treatment, including the cost of the thrombolytic agents, exceeds $4,350 per patient (53 percent higher than the cost calculated in the primary analysis). If the additional cost of t-PA use were $2,000, the cost-effectiveness ratio would be $27,736 per year of life saved. If the drug costs were those typical in Europe (approximately $1,000 for 100 mg of t-PA and $200 for 1.5 million units of streptokinase), the cost-effectiveness ratio would be $13,943 per year of life saved.
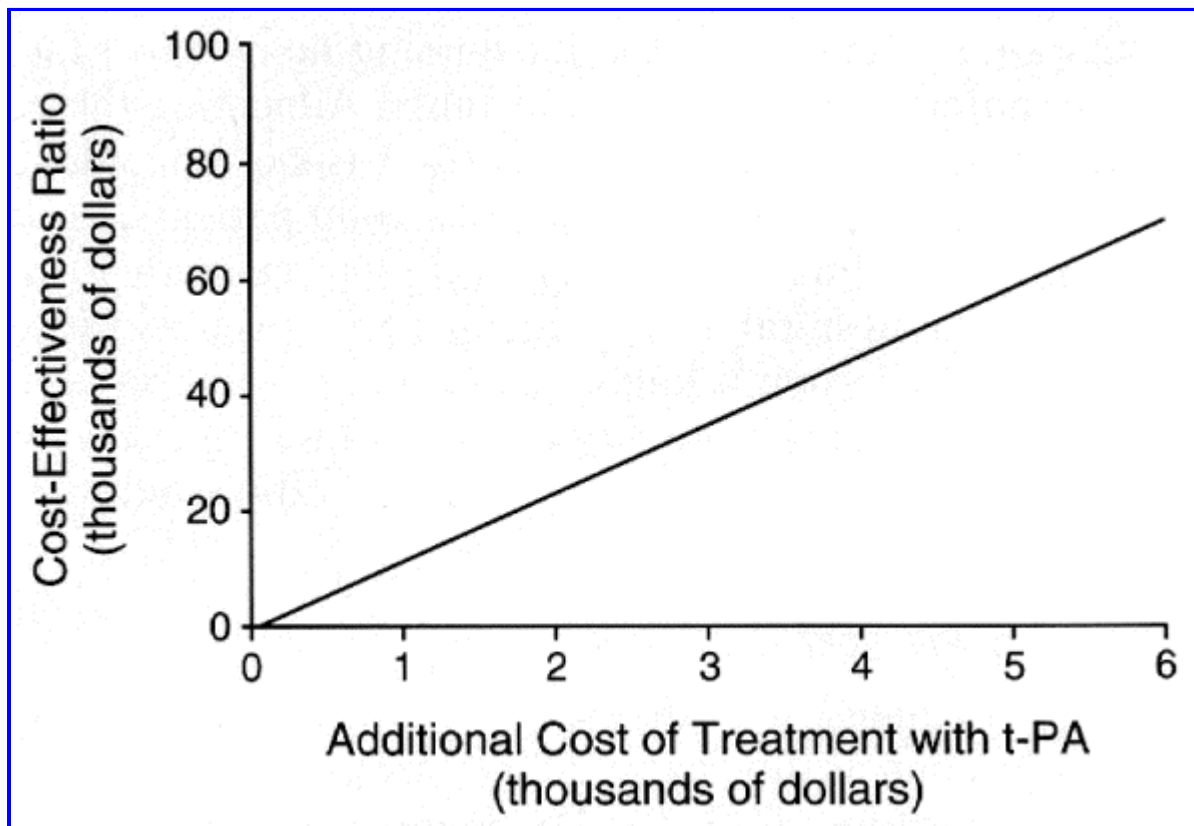

Figure 3.-Sensitivity Analysis of the Cost Difference between Treatment with t-PA and Treatment with Streptokinase, Assuming No Cost Differences beyond the First Year after Treatment. The y axis shows cost-effectiveness ratios expressed as dollars per additional year of life saved. The x axis shows the increased cost per patient associated with treatment with t-PA. In the primary analysis, the increased cost per patient was $2,845

Cost Differences after One Year

In the primary analysis, we assumed no cost difference between t-PA and streptokinase beyond the first year after treatment. In a random subgroup of U.S. patients, we observed a mean increased cost per patient for the t-PA group between six months and one year of $508 (P = 0.38). Although it was not statistically significant, we used this figure to estimate the possible increase in long-term costs for subjects who survived one year after treatment. If we annualize this figure to $1,016 per year, discount future costs at 5 percent per year, and calculate on the basis of the average GUSTO patient's life expectancy (15 years), an additional $9,975 is added to

the costs associated with t-PA, yielding an incremental cost-effectiveness ratio of $147,333 per year of life saved. If the increased level of cost continues for only the second year after treatment, then the cost-effectiveness ratio would be approximately $44,000. If the higher costs continue through the third year of follow-up, the cost-effectiveness ratio would be approximately $55,300 per year of life saved.

Quality of Life

At one year, the mean utility weights measured in our interviews were 0.90 for both treatment groups. That is, patients were hypothetically willing to trade 10 years of life at their present state of health for 9 years of excellent health. Weighting increased survival in both groups by this factor yielded a cost-effectiveness ratio of $36,402 per quality-adjusted year of life saved.

Increased Risk of Stroke

In the first 30 days after treatment in the GUSTO study, t-PA produced a net increase of one disabling nonfatal stroke per 1000 patients treated, as compared with the rate with streptokinase [1]. If disabling nonfatal stroke is considered an end point equivalent to death in the hospital, then the increase in life expectancy estimated for the t-PA group in our model is reduced to 0.13 undiscounted year per patient, and the primary cost-effectiveness ratio increases to $35,538.

Costs for the care of survivors of stroke in the first year after treatment were included in our primary analysis. In a sensitivity analysis, we assumed that patients with stroke who were in a rehabilitation hospital or nursing home one year after treatment (12 percent of the stroke survivors) would incur the costs of such care (an average daily cost of $1,212 for care in a rehabilitation hospital and $155 for nursing home care) for the remainder of their life expectancy. Allocating these extra costs to the t-PA group on the basis of one additional disabling nonfatal stroke per 1000 patients, and counting disabling stroke as an end point equivalent to death in the hospital, produce a cost-effectiveness ratio of $36,238. If each additional disabling stroke in the t-PA group required nursing home care for an average of 15 years, then the cost-effectiveness ratio would be $42,400.

Subgroup Analyses ⬆

We calculated incremental cost-effectiveness ratios for eight clinical subgroups defined by age and location of the infarction Table 3. The number of years of life added by treatment with t-PA was greater for older patients than for younger patients and greater for anterior than for inferior infarction. For patients with anterior myocardial infarction, cost-effectiveness ratios were above $50,000 only for subjects 40 years of age or younger. For patients with inferior myocardial infarction, values were above $50,000 for subjects up to 60 years of age.

GROUP OF PATIENTS*	INCREASED LIFE EXPECTANCY WITH t-PA		COST-EFFEC- TIVENESS RATIO†
	UNDISCOUNTED	DISCOUNTED	
	yr of life saved		*dollars*
Primary analysis	0.14	0.09	32,678
Inferior MI, age ⩽40	0.03	0.01	203,071
Anterior MI, age ⩽40	0.04	0.02	123,609
Inferior MI, age 41–60	0.07	0.04	74,816
Anterior MI, age 41–60	0.10	0.06	49,877
Inferior MI, age 61–75	0.16	0.10	27,873
Anterior MI, age 61–75	0.20	0.14	20,601
Inferior MI, age >75	0.26	0.17	16,246
Anterior MI, age >75	0.29	0.21	13,410

*MI denotes myocardial infarction. All patients in each treatment group were included in the primary analysis.

†Cost-effectiveness ratios show the cost in dollars per year of life saved (both discounted at 5 percent); these calculations were based on the assumption that patients treated with t-PA had costs in the first year that were $2,845 higher than those for patients treated with streptokinase.

Table 3.-Cost-Effectiveness Ratios for t-PA as Compared with Streptokinase in the Primary Analysis and for Selected Subgroups of Patients

Discussion ±

The substitution of accelerated t-PA for streptokinase in the treatment of acute myocardial infarction yields increased health benefits at a cost comparable to those of other expensive therapies routinely considered worthwhile. Benchmarks against which the average comparative cost-effectiveness ratio of t-PA ($32,678 per year of life saved) can be measured include that of coronary bypass surgery as compared with medical therapy for left main coronary artery disease ($7,000 per year of life saved), that of medical therapy as compared with no therapy for severe hypertension ($20,000 per year of life saved), and that of hemodialysis as compared with no dialysis for chronic renal failure ($35,000 per year of life saved) [16]. The upper limit for an acceptable cost-effectiveness ratio remains controversial, but values of more than $100,000 per year of life saved are generally considered too high. Most previous economic analyses of thrombolytic therapy have compared therapy with no therapy rather than comparing different agents [16-18]. Several earlier attempts to examine the incremental cost effectiveness of t-PA relative to streptokinase have made assumptions that are inappropriate in the light of the findings

of the GUSTO study [1,19,20]. However, Naylor et al. found that treatment with t-PA was cost effective, providing that the drug's beneficial effect on survival, as compared with streptokinase, was sustained for five years [21].

Sensitivity Analyses ±⌐

Our sensitivity analysis examined the effects of altering the key assumptions of the cost-effectiveness analysis, such as our estimate of 14 years of life saved per 100 patients treated with t-PA. This estimate was based on our survival model, on the increase in one-year survival observed in patients treated with t-PA as compared with those treated with streptokinase, and on an assumption that the survival curves for the two treatment groups would remain parallel after one year. The assumption that the survival curves will remain parallel is supported by the findings of other studies indicating that the benefit of thrombolysis is sustained through five years of follow-up [22-25]. In our sensitivity analysis of the assumed increase in survival, a threshold cost-effectiveness ratio of $50,000 per year of life saved was not exceeded until the increased survival for the t-PA group fell below 7 years of life added per 100 patients treated; a threshold value of $100,000 per year of life saved was not reached until the added years of life per 100 patients treated fell below 3.

Our results were not sensitive to changes in our estimates of costs. Only when the assumed increase in costs attributable to treatment with t-PA during the first year was 1.5 times greater than the value used in our study did the resulting cost-effectiveness ratio exceed $50,000 per year of life saved. If the patients who received t-PA were assumed to have continuing additional costs of about $1,100 per year (a figure projected from the nonsignificant cost difference observed in the second six months of follow-up) past the second follow-up year, the cost-effectiveness ratio became greater than $50,000. However, there is no basis in the empirical data from the GUSTO study for expecting such long-term cost differences between the two treatments.

Importance of Disabling Strokes ±⌐

One important question is the extent to which the additional hemorrhagic strokes produced by t-PA may cancel out some of the observed increase in survival, thereby making t-PA less attractive and less cost effective [1]. However, even the most unfavorable assumptions about nonfatal disabling stroke -- that patients with stroke had no increase in survival due to t-PA and that each patient would require 15 years of institutional care -- increased the cost-effectiveness ratio only moderately (to $42,400), because these costs were incurred by only 1 patient per 1000 receiving t-PA.

Subgroup Analyses ±⌐

As is true of the main GUSTO study, our subgroup analyses should be interpreted cautiously [1]. For most of the eight subgroups we studied, defined on the basis of age and location of the infarction, the cost-effectiveness ratio was below our benchmark figure of $50,000 per year of life saved. The cost-effectiveness ratios were least favorable for patients 40 years of age or younger and for patients 60 years of age or younger with inferior-wall infarctions, since these groups had the lowest one-year mortality rates and the smallest increases in survival due to treatment with t-PA [26]. In our study, we calculated the life expectancies of treated subgroups on the basis of our survival model, rather than on short-term empirical data for each subgroup. This technique provided more stable and consistent estimates than the alternative approach and also allowed us to control for the fact that anterior myocardial infarction was more frequent in older

patients.

Conclusions ⊡

The routine substitution of accelerated t-PA for streptokinase in the treatment of the approximately 250,000 eligible patients who have acute myocardial infarction in the United States each year would be cost effective by customary criteria. It would cost the nation approximately $500 million each year but would also provide 3.5 million additional years of life for patients after myocardial infarction. Our analysis can inform the decision about whether this should become the standard of care in the United States, but society itself must make the choice.

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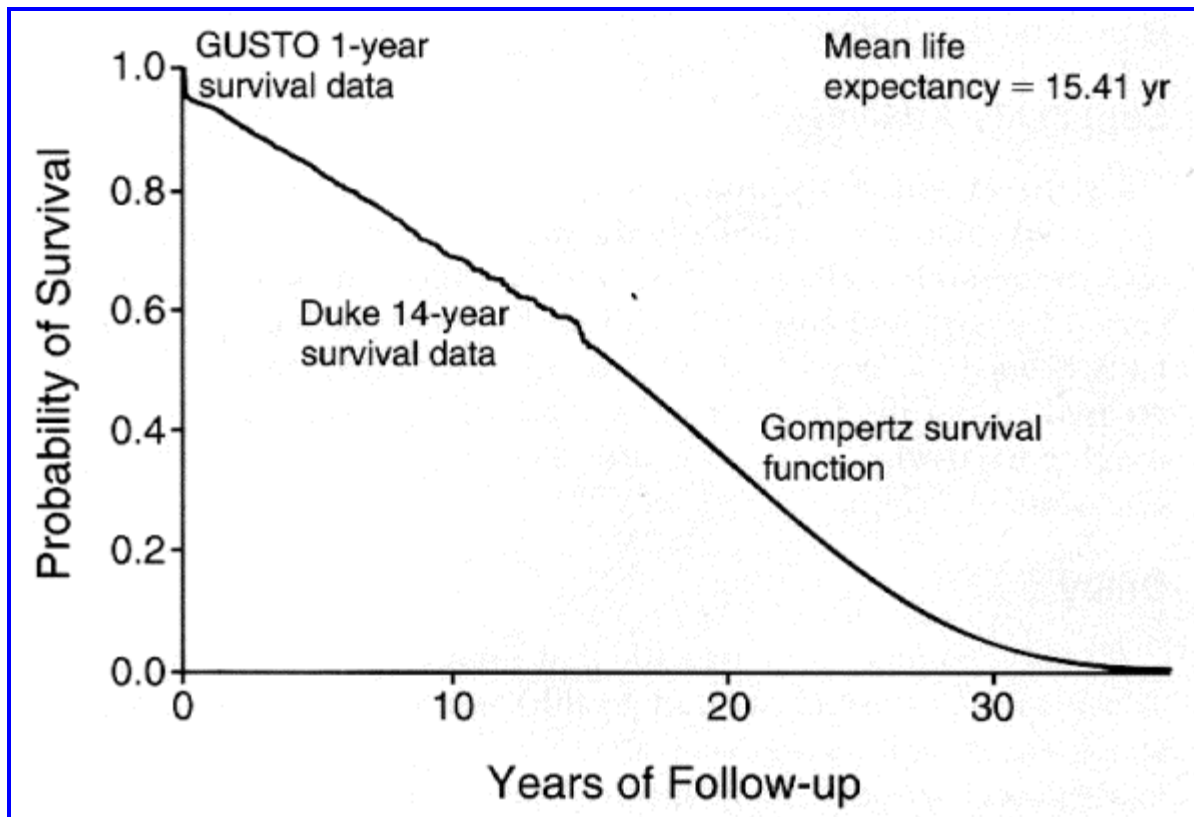
Figure 1.-Probability of Survival among Patients Treated with t-PA. A survival function of this type was used to estimate life expectancy for each treatment group. The curve consists of three parts: the survival pattern in the first year after treatment in the GUSTO study, data for an additional 14 years on survivors of myocardial infarction in the Duke Cardiovascular Disease Database, and a Gompertz parametric survival function adjusted to agree with the empirical survival data at the 10-year and 15-year follow-up points