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COST EFFECTIVENESS OF EARLY DISCHARGE AFTER UNCOMPLICATED ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Background Reducing the length of hospitalizations can reduce short-term costs, but there are few data on the long-term clinical and economic consequences of early discharge after uncomplicated myocardial infarction.

Methods Using data from the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-1) trial, we identified 22,361 patients with acute myocardial infarction who had an uncomplicated course for 72 hours after thrombolysis. Then, using a decision-analytic model, we examined the cost effectiveness of an additional day of hospitalization in this group. We defined incremental survival attributable to another day of monitored hospitalization, on the basis of the rate of resuscitation after cardiac arrest between 72 and 96 hours. Lifetime survival curves for each group in the decision-analytic model were estimated from one-year survival data from GUSTO-1.

Results Of the patients with an uncomplicated course within 72 hours after thrombolysis, 16 had ventricular arrhythmias during the next 24 hours; 13 of these patients (81 percent) survived for at least 24 hours. On average, another 0.006 year of life per patient could be saved by keeping patients with an uncomplicated course in the hospital another day. At a cost of \$624 for hospital and physicians' services, extending the hospital stay by another day would cost \$105,629 per year of life saved. In sensitivity analyses, it was found that a fourth day of hospitalization would be economically attractive only if its cost could be reduced by more than 50 percent or if a high-risk subgroup could be identified in which the estimated survival benefit would be doubled.

Conclusions Hospitalization of patients with uncomplicated myocardial infarction beyond three days after thrombolysis is economically unattractive by conventional standards. (N Engl J Med 2000;342:749-55.)

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CHANGES in health care delivery and efforts to curb medical costs have resulted in increased emphasis on reducing hospital stays after acute myocardial infarction. Although the potential reduction in cost achieved by a shorter stay in the hospital is easily shown, there is limited empirical information to indicate the length of stay that would minimize costs without compromising patients' outcomes.

Several investigations have suggested the feasibility and safety of discharge as early as three to five days after infarction.¹⁻³ In the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-1) trial, patients who had an uncomplicated course through day 4 after thrombolysis had a very low rate of death within 30 days.⁴ A randomized trial of early discharge would be needed to demonstrate conclusively the clinical and economic soundness of this change in the standard of care, but the extremely challenging logistics of such a trial make it unlikely that one will ever be conducted. Despite the absence of such evidence, many health care providers, for economic reasons, are developing guidelines based on the limited data available that would shorten the hospital stay after acute myocardial infarction. To assess comprehensively the clinical and economic implications of such a change, we used the GUSTO-1 data base to assess the cost effectiveness of prolonging hospitalization beyond 72 hours after thrombolysis in patients with uncomplicated acute myocardial infarction.

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METHODS

Patient Population and Study Data

Our study population was selected from the 41,021 patients enrolled in GUSTO-1. In that trial, patients were randomly assigned to one of four thrombolytic-treatment groups if they presented more than 20 minutes but less than 6 hours after the onset of symptoms of acute myocardial infarction, had ST-segment elevation of at least 0.1 mV in at least two limb leads or at least 0.2 mV in at least two contiguous precordial leads, and had no protocol-specified contraindications to enrollment.⁵

The date and time of any in-hospital occurrence of death, shock, reinfarction, stroke, congestive heart failure, recurrent ischemia, and urgent angiography and angioplasty were available from each patient's case-report form.⁵ If the form indicated that ventricular tachycardia or fibrillation had occurred after study entry, the date of cardioversion or defibrillation served as a surrogate for the date of arrhythmia. No data were available for events or complications, other than death, that occurred after discharge.

Statistical Analysis

Descriptive statistics (medians with 25th and 75th percentiles for continuous variables and percentages for discrete variables) were generated for base-line characteristics, length of stay, adverse events, and the length of time to an event.

Overview of the Cost-Effectiveness Analysis

We assessed the cost effectiveness of prolonging hospitalization for another day, assuming an uncomplicated course through the previous 72 hours. We defined an "uncomplicated" course as the absence of death, reinfarction, congestive heart failure, recurrent ischemia, shock, stroke, emergency angiography or angioplasty, bypass surgery, intraaortic balloon pumping, or cardioversion or defibrillation.⁴ Patients with an uncomplicated course who had evidence of angiographically important disease (at least 75 percent occlusion) in three vessels or the left main coronary artery (1143 patients) or had elective bypass surgery more than three days after thrombolysis (713 patients) were not considered candidates for early discharge and were excluded from our analysis. After we excluded patients for whom data on complications were insufficient, the final number of patients in the analysis was 38,911.

We used a decision-analytic model⁶ for the analysis, which was based, as much as possible, on empirical data from GUSTO-1 and the analysis of the cost effectiveness of alteplase in that trial.^{5,7} The base-case model reflected the starting assumptions and the variables included in the analysis (discussed below), all of which were subsequently subjected to sensitivity analyses. Cost effectiveness was expressed in terms of dollars per year of life saved. Discounting, the reverse of compounding, was used to adjust the life expectancy of patients during the follow-up period to the equivalent values at base line.⁸ A discount rate of 3 percent per year was used for the base case.

Main Assumptions in the Cost-Effectiveness Analysis

The following assumptions underlie the base-case analysis. First, among patients with an uncomplicated course through 72 hours, the rate of later cardiac events (including cardiac arrest) after thrombolysis in patients who are in the hospital is similar to that in patients who have been discharged. Second, discharge at 72 hours is feasible,¹ and testing and care not accomplished within 72 hours can effectively be shifted to the outpatient setting with no incremental costs beyond those of inpatient care. Third, the primary benefit of hospitalization beyond 72 hours for patients with an uncomplicated course is prompt resuscitation if cardiac arrest occurs. Thus, we assumed that discharged patients who had reinfarction, stroke, recurrent ischemia, heart failure, or other major complications that did not lead to cardiac arrest could return to the hospital promptly enough for any change in their long-term clinical outcomes or costs to be prevented. Fourth, inpatients who

are not monitored by an effective telemetry system fare no better than outpatients if cardiac arrest occurs. Thus, we examined the cost effectiveness of an extra monitored day as compared with discharge. Fifth, patients in a typical U.S. community who have cardiac arrest out of the hospital have a very low chance of being resuscitated.⁹ For the base case, we assumed a 30-day survival rate of 0 percent for out-of-hospital cardiac arrest. Sixth, patients who die in the hospital do so despite effective monitoring and therapy; these deaths are not preventable. And finally, patients could be discharged before any complications arose on day 4 that would cause clinicians to cancel plans for discharge.

Incremental Life Expectancy

To estimate the added years of life attributable to another monitored day of hospitalization, we used the GUSTO-1 data base and Kaplan-Meier estimates to define the rates of preventable and nonpreventable deaths that occurred in 24-hour periods after admission.¹⁰ An episode of ventricular arrhythmia treated by cardioversion or defibrillation, with survival for at least an additional 24 hours, was defined as a "preventable death," on the assumption that the patient would have died without such treatment. A nonpreventable death was defined as an in-hospital death from any cause that occurred during the same periods. To estimate the added years of life resulting from in-hospital resuscitation from an episode of ventricular arrhythmia, we used the empirical GUSTO-1 one-year survival data for patients with no complications.⁷ We estimated lifetime survival curves for patients who survived to 1 year as previously described, using subgroup-specific predictions from the Duke data base and a Cox proportional-hazards model to extend survival to 15 years with a Gompertz function, attached at 10 and 15 years, to extrapolate the tail of the survival curve. The area under the survival curves provided the life expectancy for each group.⁷

Incremental Costs

The costs of key hospital resources (e.g., room and monitoring) were derived from the GUSTO-1 cost-effectiveness analysis and the Duke Transition One cost-accounting system.⁷ Physicians' fees were derived from the Medicare fee schedule. All costs were expressed in 1997 U.S. dollars. The costs of each additional monitored day in the hospital were \$560 for the hospital and \$64 for the physician, and the lowest ratio of nurses to patients (1:6) was assumed. We estimated hospital costs for patients who had an uncomplicated course through the 72 hours after acute myocardial infarction but who were resuscitated after cardiac arrest between 72 and 96 hours (\$17,561) by averaging the costs for patients in our data base with this sequence of events after thrombolysis.

Sensitivity Analyses

In sensitivity analyses, we examined variations in all important variables in our base-case analysis, including the incidence of ventricular arrhythmias, the success of resuscitation during ventricular arrhythmias, the cost of a fourth day in the hospital, and the cost of care for patients who survived ventricular arrhythmias. For variables for which empirical estimates were available, the extremes of the 95 percent confidence intervals were used in the sensitivity analyses.

To assess the effects of variations in the cost of an additional day of hospitalization, we included in our sensitivity analysis the next-highest level of intensity of services (a nurse-to-patient ratio of 1:4 and a cost of \$866 per day). To assess the possible effects of increased costs due to an increased incidence of recurrent ischemia as a result of early discharge, we estimated that each extra recurrent ischemic event would incur incremental costs of \$1,114 for a visit to the emergency department and a 24-hour hospital stay. The remainder of the costs of care for such an episode would be identical in the two management strategies. In our sensitivity analyses, we used estimates of 10 percent and 30 percent for the percentages of patients who were discharged early and incurred this incremental cost.

To assess the potential economic effects of shifting some care from the inpatient to the outpatient setting, we added the costs of different levels of clinic visits and home health services from the

North Carolina Medicare fee schedule. We also evaluated the economic effect of follow-up telephone calls to patients who were discharged early. We estimated that two 15-minute follow-up calls by a registered nurse to each of such patients would cost approximately \$12 per patient.

RESULTS

Base Case

Among the patients in the GUSTO-1 trial, the hazard function for ventricular arrhythmia that required cardioversion or defibrillation was highest at enrollment and declined rapidly, with the risk after 48 hours becoming approximately constant (Fig. 1). Of the patients who had ventricular arrhythmia by day 4, 49 percent did not survive the initial hospitalization. For the patients in this group who survived during hospitalization, the one-year mortality rate was 9.5 percent, as compared with 2.3 percent for patients who survived during hospitalization and did not have ventricular arrhythmia by day 4. Beyond 72 hours, the incremental daily rates of death or major ventricular arrhythmia in patients with an uncomplicated course were relatively constant, regardless of how long the patients had been without complications (Table 1).

Of the patients with an uncomplicated course during the 72 hours after thrombolysis, 16 had ventricular arrhythmia during the next 24 hours; 13 of these patients (81 percent) survived for at least 24 hours. The base-line characteristics of the 16,550 patients with complications and the 22,361 patients with no complications within 72 hours after thrombolysis are shown in Table 2. The 16 patients with an uncomplicated course who had a major ventricular arrhythmia on day 4 were similar to the patients with complications in that they were older and more likely to have diabetes mellitus, prior angina, and prior myocardial infarction than the patients with an uncomplicated course who did not have ventricular arrhythmia on day 4.

Figure 2 shows the decision-analytic model and data used in the cost-effectiveness analysis of the base case. On average, an additional 0.006 year of life was gained by keeping patients with no complications in the hospital a fourth day. At an incremental cost of \$624 for an additional day of hospitalization, the resulting ratio of cost effectiveness was \$105,629 per year of life saved.

Sensitivity Analyses

If the incidence of ventricular arrhythmia on day 4 was at the upper limit of the 95 percent confidence interval of the Kaplan–Meier estimate (0.0013), the cost-effectiveness ratio was \$65,777 per year of life saved; if the incidence was at the lower limit (0.00046), the ratio was \$183,525 per year of life saved. The cost-effectiveness ratio was relatively insensitive to wide variations in the probability of death if ventricular arrhythmia occurred in hospitalized patients.

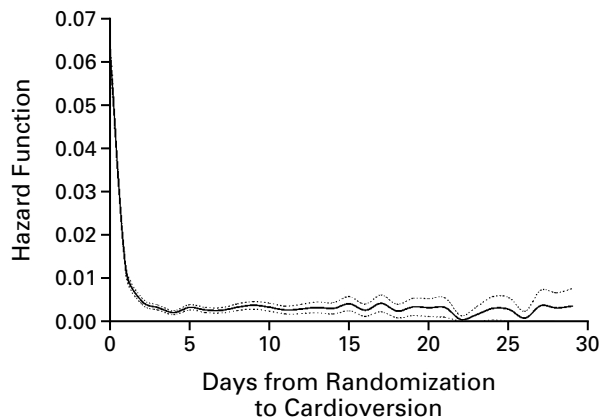


Figure 1. Hazard-Function Estimate for Cardioversion or Defibrillation in 41,021 Patients in the GUSTO-1 Trial Who Underwent Thrombolysis for Acute Myocardial Infarction.

Point estimates (solid line) are shown with 95 percent confidence intervals (dotted lines).

TABLE 1. CUMULATIVE KAPLAN–MEIER ESTIMATES OF THE RATE OF DEATH OR VENTRICULAR TACHYCARDIA OR FIBRILLATION ACCORDING TO THE TIME AFTER THROMBOLYSIS, ASSUMING AN UNCOMPLICATED COURSE THROUGH 48, 72, OR 96 HOURS.

DAY AFTER INFARCTION	NO. OF HOURS WITH UNCOMPLICATED COURSE		
	48	72	96
	mean ± SE		
3	0.25±0.0003	—	—
4	0.42±0.0004	0.13±0.0002	—
5	0.65±0.0005	0.32±0.0004	0.17±0.0003
6	0.88±0.0006	0.54±0.0005	0.35±0.0004
7	1.03±0.0007	0.67±0.0006	0.48±0.0005
8	1.21±0.0008	0.85±0.0007	0.66±0.0006
9–30	2.67±0.0013	2.17±0.0013	1.92±0.0012

If the intensity of services for the additional hospital day was increased (a nurse-to-patient ratio of 1:4 instead of 1:6), the cost-effectiveness ratio increased to \$145,967 per year of life saved. The cost-effectiveness ratio was insensitive to wide variations in the cost of care for patients who survived ventricular arrhythmia.

When it was estimated that recurrent ischemia was 10 percent more frequent in patients discharged early and that the cost of additional evaluation was \$1,114 per patient, the cost-effectiveness ratio was \$103,982 per year of life saved; if the frequency was estimated to be 30 percent higher, the cost-effectiveness ratio was \$100,690. If the rate of sudden death was assumed to be 25 percent lower in patients with an ad-

TABLE 2. BASE-LINE CHARACTERISTICS OF THE PATIENTS WITH AN UNCOMPLICATED COURSE AND THE PATIENTS WITH A COMPLICATED COURSE WITHIN 72 HOURS AFTER THROMBOLYSIS.

CHARACTERISTIC	COMPLICATED COURSE (N=16,550)	UNCOMPLICATED COURSE	
		NO VENTRICULAR ARRHYTHMIA ON DAY 4 (N=22,345)	VENTRICULAR ARRHYTHMIA ON DAY 4 (N=16)
Age (yr)			
Median	64	60	68
Interquartile range	55–72	50–68	48–76
Male sex (%)	71	77	69
Diabetes mellitus (%)	17	13	19
Current smoking (%)	40	46	38
Hyperlipidemia (%)	34	33	40
Hypertension (%)	42	35	38
Prior angina (%)	41	33	44
Prior myocardial infarction (%)	20	13	44
Prior angioplasty or bypass surgery (%)	9	6	25
Weight (kg)			
Median	78	78	80
Interquartile range	69–88	70–88	60–95
Systolic blood pressure (mm Hg)			
Median	126	130	121
Interquartile range	110–142	115–145	105–147
Heart rate (beats/min)			
Median	76	72	79
Interquartile range	64–90	62–84	63–84
Location of infarction (%)			
Anterior	46	34	31
Inferior	51	62	69
Other	3	4	0
Time to treatment (hr)			
Median	3	3	2
Interquartile range	2–4	2–4	2–4

ditional day of hospitalization than in patients who were discharged early, the cost-effectiveness ratio was \$74,742 per year of life saved; if it was 10 percent lower, the ratio would be \$90,653.

A final sensitivity analysis showed that the cost-effectiveness ratio ranged from \$103,636 to \$82,712 per year of life saved, depending on the intensity, type, and frequency of extra follow-up care that was required for patients who were discharged early.

DISCUSSION

Ideally, patients are discharged from the hospital after acute myocardial infarction when the risk of complications is minimized and when issues of post-infarction education and rehabilitation have been addressed. However, because of economic pressures, many hospitals are now discharging patients 72 hours after thrombolysis, even though there are limited data to show that it is safe to do so. To examine the cost effectiveness of another monitored day of hospitalization, we identified from the GUSTO-1 data base

22,361 patients who had had acute myocardial infarction and an uncomplicated course for 72 hours after thrombolysis. The rate of preventable events in this cohort over the subsequent 24 hours was extremely low. For this reason, our cost-effectiveness analysis of the base case indicated that an extra day in the hospital was associated with a cost-effectiveness ratio of more than \$100,000 per year of life saved, which is not cost effective.

At the base-case estimate of \$105,629 per year of life saved, prolonging hospitalization for patients who had an uncomplicated course during the 72 hours after thrombolysis is economically unattractive as compared with other common strategies for managing acute myocardial infarction.^{7,11,12} For example, substituting the use of alteplase for streptokinase in patients with acute myocardial infarction who are eligible for thrombolytic therapy costs about \$33,000 per year of life saved.⁷ The routine use of angioplasty in middle-aged men with acute myocardial infarction costs approximately \$52,000 per year of life saved.

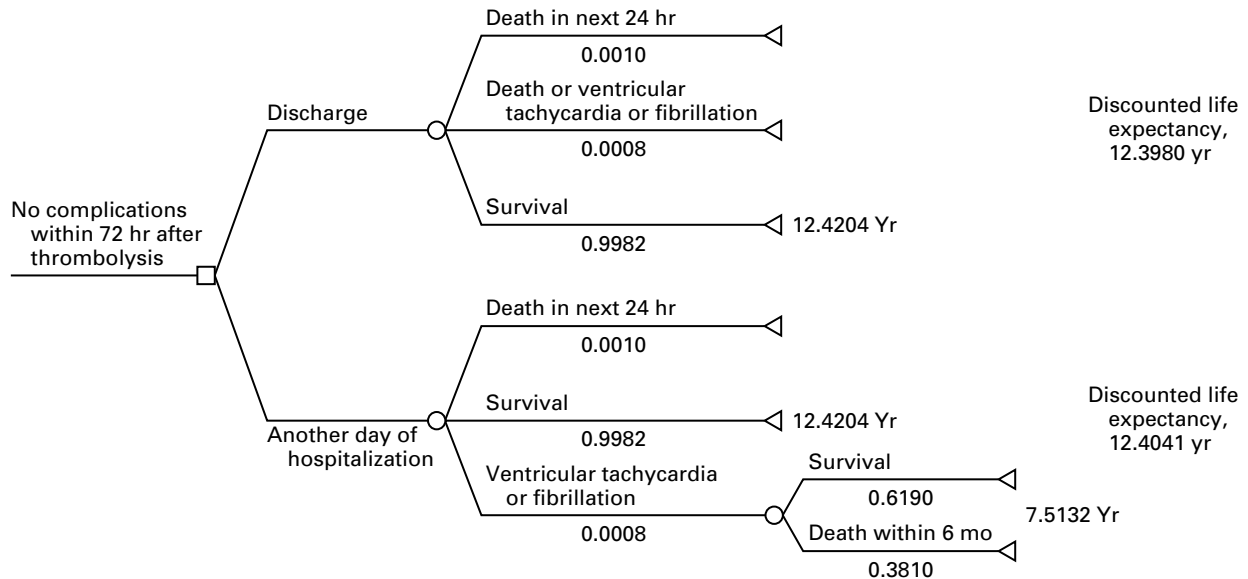


Figure 2. Decision-Analytic Model with Probabilities of Events, Survival after Events, and Life-Expectancy Estimates Used in the Cost-Effectiveness Analysis.

In the context of its value relative to that of other accepted or recommended societal efforts, an extra day of hospitalization for patients in this group is much more cost effective than the use of smoke detectors in homes (\$239,919 per year of life saved) but less cost effective than driver’s-side airbags (\$47,984 per year of life saved).¹²

If it could be determined which patients among those with an uncomplicated course are at higher risk for ventricular arrhythmia, prolonging admission for those patients would be more cost effective. However, because the rate of ventricular arrhythmia on day 4 in patients with an uncomplicated course during the first 72 hours is very low, the identification of such patients would be difficult. Although the subgroup of patients who had ventricular arrhythmia on day 4 was too small to permit definite conclusions to be drawn, we did find that these patients were older than the patients who did not have ventricular arrhythmia on day 4; that more of them were women; that they were more likely to have diabetes or prior coronary disease and to have undergone revascularization; and that they had a lower base-line systolic blood pressure and a higher heart rate.

Because the rate of ventricular arrhythmia on day 4 was a critical variable in our analysis, we compared our estimate of this low-frequency event with the rate in a similar, more recent trial of thrombolytic therapy in myocardial infarction. The GUSTO III trial used the same entry and exclusion criteria and the same basic case-report form as GUSTO-1 and thus provides comparable data.¹³ Of 7553 patients in the GUSTO III trial who had an uncomplicated course

for 72 hours after thrombolysis, 3 (0.04 percent) had ventricular arrhythmias on day 4, a rate even lower than that used in our base-case analysis. To refine our estimate of the rate of preventable death on day 4 and thus of the cost effectiveness of an additional day of hospitalization after 72 hours, we pooled the rates of ventricular arrhythmia on day 4 in the GUSTO-1 and GUSTO III trials and used the 95 percent confidence limits for the sensitivity analysis. The calculated cost-effectiveness ratio was \$122,247 per year of life saved.

Obviously, the more expensive the additional day of hospitalization, the more economically unattractive it becomes. If hospitals could substantially lower the marginal cost of the additional day (so that it was more than 50 percent lower than our estimate of \$624 per day), keeping patients an extra day could approach the economically attractive threshold of less than \$50,000 per year of life saved. However, in a review of several clinical trials involving patients with acute coronary syndromes that contained empirical data on cost, we found that the mean daily cost of a hospital room was very similar to our base-case estimate.^{14,15}

Several of our assumptions could be challenged. First, we assumed that adverse nonfatal events that occurred after discharge had no effect on incremental life expectancy or costs. Because the GUSTO-1 trial did not collect follow-up data on outcomes other than death, we could not support this assumption with empirical data. The most common nonfatal complication in this population is recurrent ischemia. In sensitivity analyses, we examined the possibility that early discharge might make the rate of recurrent is-

chemia 10 to 30 percent higher among discharged patients than among those who were hospitalized an extra day and that there might be a resulting increase in incremental costs. These changes had no significant effect on our results.

Even if the rates of nonfatal adverse events were 30 percent higher in patients discharged at 72 hours, either the life-expectancy benefit from remaining in the hospital would have to be 0.013 life-year (2.1 times the base-case difference), or the additional short-term cost of care would have to be 47 percent of that used in the base case for patients who were discharged at 72 hours, for the cost-effectiveness ratio of an extra hospital day to reach \$50,000 or less per year of life saved. Furthermore, only a much higher rate of sudden death (more than 50 percent higher) in patients discharged rather than kept in the hospital on day 4 would bring the estimate of cost effectiveness near \$50,000 per year of life saved. The effectiveness of such a management strategy in preventing death is difficult to imagine in the context of current practice, in which even the most effective therapies have been shown to reduce the rate of death from all causes after myocardial infarction by only 25 to 30 percent.

Second, attempts to reduce costs through shorter hospitalizations must account for costs being shifted to the outpatient arena. We assumed that during a three-day stay, all risk stratification, teaching, and rehabilitation that are now considered part of standard care could be accomplished. Most centers probably cannot achieve this goal without substantially re-engineering their current practices of care. Data from small clinical studies support the safety and prognostic usefulness of stress testing as early as three to four days after uncomplicated myocardial infarction,^{1,16-19} but a concerted effort among clinicians and providers of support services would be needed for testing to be performed and results to be made available by the end of the third day of hospitalization. Our model assumed a long-term societal perspective in which all short-term inefficiencies involved in implementing a program of early discharge would be resolved. Thus, the cost effectiveness of an additional day in the hospital remains constant even if a proportion of eligible patients at a specific hospital could not be discharged after a 72-hour stay. Even small-to-moderate increases in outpatient costs after early discharge (for home health services, postinfarction education, follow-up calls, or clinically driven evaluation) would not greatly improve the economic attractiveness of longer hospitalization.

Our results apply to patients with an uncomplicated course who have undergone thrombolysis for acute myocardial infarction and meet the inclusion criteria for the GUSTO-I trial. These results may not be generalizable to other patients with myocardial infarction who were treated with thrombolytic or other reperfusion strategies or to those not treated with reperfu-

sion therapy, although some studies suggest that these groups rarely have complications within three to five days after treatment.^{2,20-22}

Finally, studies have shown that even with the current lengths of stay after infarction, clinicians could be more effective in instituting therapies that are clearly beneficial in secondary prevention (such as treatment with aspirin, beta-blockers, and angiotensin-converting-enzyme inhibitors); this lack of effectiveness may adversely affect outcomes.²³⁻²⁶ The ability to provide these services during shorter hospitalizations or in the outpatient setting must be ensured before early-discharge practices are endorsed or adopted.

In conclusion, in relation to other medical interventions, extending hospitalization beyond 72 hours after thrombolysis for patients with uncomplicated myocardial infarction is not cost effective. Continuous quality control and long-term follow-up of early-discharge plans are needed to ensure that short-term gains (in reduced costs due to shorter hospitalization) do not occur at the expense of long-term outcomes.

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