

Special Article

THE VOLUME OF PRIMARY ANGIOPLASTY PROCEDURES AND SURVIVAL AFTER ACUTE MYOCARDIAL INFARCTION

JOHN G. CANTO, M.D., M.S.P.H., NATHAN R. EVERY, M.D., M.P.H., DAVID J. MAGID, M.D., M.P.H., WILLIAM J. ROGERS, M.D., JUDITH A. MALMGREN, PH.D., PAUL D. FREDERICK, M.P.H., M.B.A., WILLIAM J. FRENCH, M.D., ALAN J. TIEFENBRUNN, M.D., VIJAY K. MISRA, M.D., CATARINA I. KIEFE, PH.D., M.D., AND HAL V. BARRON, M.D., FOR THE NATIONAL REGISTRY OF MYOCARDIAL INFARCTION 2 INVESTIGATORS*

ABSTRACT

Background There is an inverse relation between mortality from cardiovascular causes and the number of elective cardiac procedures (coronary angioplasty, stenting, or coronary bypass surgery) performed by individual practitioners or hospitals. However, it is not known whether patients with acute myocardial infarction fare better at centers where more patients undergo primary angioplasty or thrombolytic therapy than at centers with lower volumes.

Methods We analyzed data from the National Registry of Myocardial Infarction to determine the relation between the number of patients receiving reperfusion therapy (primary angioplasty or thrombolytic therapy) and subsequent in-hospital mortality. A total of 450 hospitals were divided into quartiles according to the volume of primary angioplasty. Multiple logistic-regression models were used to determine whether the volume of primary angioplasty procedures was an independent predictor of in-hospital mortality among patients undergoing this procedure. Similar analyses were performed for patients receiving thrombolytic therapy at 516 hospitals.

Results In-hospital mortality was 28 percent lower among patients who underwent primary angioplasty at hospitals with the highest volume than among those who underwent angioplasty at hospitals with the lowest volume (adjusted relative risk, 0.72; 95 percent confidence interval, 0.60 to 0.87; $P < 0.001$). This lower rate, which represented 2.0 fewer deaths per 100 patients treated, was independent of the total volume of patients with myocardial infarction at each hospital, year of admission, and use or nonuse of adjunctive pharmacologic therapies. There was no significant relation between the volume of thrombolytic interventions and in-hospital mortality among patients who received thrombolytic therapy (7.0 percent for patients in the highest-volume hospitals vs. 6.9 percent for those in the lowest-volume hospitals, $P = 0.36$).

Conclusions Among hospitals in the United States that have full interventional capabilities, a higher volume of angioplasty procedures is associated with a lower mortality rate among patients undergoing primary angioplasty, but there is no association between volume and mortality for thrombolytic therapy. (N Engl J Med 2000;342:1573-80.)

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MANY studies have documented an inverse relation between the rate of mortality from cardiovascular causes and the number of elective reperfusion procedures performed by individual practitioners or hospitals. Lower mortality rates have been associated with higher volumes of elective procedures in studies of percutaneous transluminal coronary angioplasty (PTCA),¹⁻⁴ coronary stenting,⁵ and coronary-artery bypass grafting.^{6,7} However, it is not known whether there is an inverse relation between mortality and primary angioplasty or thrombolytic therapy for acute myocardial infarction. Unlike the outcome of pharmacologic therapies, the outcome of invasive cardiac procedures depends on individual expertise, which in turn may depend on the volume of procedures performed. Also, the outcome for patients with myocardial infarction may be dependent on the early use of adjunctive medications, such as aspirin, heparin, or beta-blockers. It is possible that hospitals treating large numbers of patients with myocardial infarction have superior outcomes simply because accepted therapies are administered more frequently or more quickly than at hospitals with smaller numbers of such patients.

To determine whether a higher volume of patients receiving reperfusion therapy is associated with better outcomes, we examined in-hospital mortality among patients with myocardial infarction who were treated

From the Department of Medicine, Division of Cardiovascular Diseases (J.G.C., W.J.R., V.K.M.), and the Center for Outcomes and Effectiveness Research and Education (J.G.C., C.I.K.), University of Alabama at Birmingham, Birmingham; the University of Washington Cardiovascular Outcomes Research Center, Seattle (N.R.E., J.A.M., P.D.E.); Health Services Research and Development, Veterans Affairs Puget Sound Health Care System, Seattle (N.R.E.); the Clinical Research Unit, Colorado Permanente Medical Group, Denver (D.J.M.); the Department of Preventive Medicine and Biometrics and the Division of Emergency Medicine, University of Colorado Health Sciences Center, Denver (D.J.M.); Harbor UCLA Medical Center, Torrance, Calif. (W.J.E.); Washington University School of Medicine, St. Louis (A.J.T.); and the University of California at San Francisco, San Francisco, and Genentech, South San Francisco, Calif. (H.V.B.). Address reprint requests to Dr. Canto at the University of Alabama at Birmingham, 363 BDB, 1808 7th Ave. S., Birmingham, AL 35294-0012.

*A complete list of the hospitals participating in the National Registry of Myocardial Infarction 2 can be obtained from Stat Probe, Lexington, Ky.

at hospitals with a range of experience in using emergency reperfusion therapies. We hypothesized that the mortality rate would be lower among patients undergoing primary angioplasty at hospitals with a high volume of angioplasty procedures than among patients undergoing primary angioplasty at low-volume hospitals. We also hypothesized that there would be no association between the mortality rate and volume for patients receiving thrombolytic therapy.

METHODS

Data Collection

The National Registry of Myocardial Infarction (NRMI) is a voluntary registry of cross-sectional data on patients hospitalized with confirmed myocardial infarction. Trained abstractors collected detailed data from the records of 772,586 patients admitted between June 1994 and March 1998 at 1470 participating hospitals. The characteristics of the registry, data-gathering procedures, and reliability have been reported elsewhere.⁸⁻¹⁰ For patients included in the NRMI, the diagnosis of myocardial infarction was based on at least one of the following findings: a value for serum total creatine kinase or serum creatine kinase MB that was two or more times the upper limit of the normal range; electrocardiographic evidence of acute myocardial infarction; enzymatic, scintigraphic, or autopsy evidence of myocardial infarction; or a diagnosis of myocardial infarction according to the *International Classification of Diseases, Ninth Revision, Clinical Modification* (code 410.X1).

Eligibility Criteria

Only hospitals capable of performing the entire spectrum of invasive cardiac procedures were included in the study. To minimize the bias associated with high rates of patient transfers, we excluded hospitals that did not have interventional capabilities or that did have interventional capabilities but without the on-site availability of cardiac surgery as a backup. Also, patients who had been transferred from other hospitals were excluded (34 to 39 percent of patients at the hospitals in the analysis of angioplasty and 29 to 42 percent of those at the hospitals in the analysis of thrombolytic therapy). In calculating the volume of angioplasty procedures for each hospital, we included all primary angioplasty procedures (even those performed in patients who had been transferred from other hospitals) to give maximal credit for the experience gained from performing angioplasty. The volume was calculated as the total number of patients who underwent primary angioplasty at each hospital divided by the total number of days for which the hospital reported data to the NRMI. Eligible hospitals were ranked according to volume, and the 25th, 50th, and 75th percentiles were used as cutoff points to define quartiles. Hospitals at which fewer than five primary angioplasty procedures were performed per year were excluded from the study. A similar analysis was performed to determine the quartiles for the volume of thrombolytic interventions among all eligible hospitals in the NRMI. A total of 422 hospitals were included in both the angioplasty group and the thrombolytic-therapy group.

Study Variables

The study variables included characteristics of the hospitals (urban or rural location, the number of beds, and whether or not the hospital was a teaching center) and demographic and clinical characteristics of the patients. Hospitals in nine U.S. Census regions were included in the study.¹¹ The hospitals were classified as urban if they were located in a county with at least one city that had a population of more than 50,000 or in a county with two cities that had a combined population of more than 50,000; all other hospitals were classified as rural. The total volume of patients with myocardial infarction was calculated as the total number of patients with myocardial infarction (regardless of whether they were transferred)

divided by the number of days for which a hospital reported data to the NRMI. For most of the study variables, missing data accounted for no more than 5 percent of the observations; the exceptions were the interval from the onset of symptoms to the patient's arrival at the hospital (12 percent of patients had missing data) and the interval from arrival at the hospital to the initial electrocardiographic study (10 percent).

Statistical Analysis

The hospital was the unit of analysis for assignment to a hospital-volume group. However, the patient was the unit of analysis for the evaluation of clinical variables and mortality. We present data for only those patients who received thrombolytic therapy or underwent primary angioplasty at eligible hospitals. An analysis that included all patients, whether or not they received reperfusion therapy, yielded no additional findings (data not shown). A linear association among the four quartiles was assessed with the use of the Mantel-Haenszel chi-square test for categorical variables, analysis of variance for continuous variables, and the nonparametric median (Brown-Mood) test for comparisons of median values.

Forward multiple logistic-regression models were developed to identify predictors of mortality. Because the cumulative risk of death was less than 10 percent, relative risks were estimated as odds ratios. Generalized-estimating-equation analyses, performed to account for clustering within hospitals, yielded no additional findings (data not shown). The first set of models was constructed to determine the relation between the volume of angioplasty procedures and mortality among patients who actually underwent primary angioplasty at hospitals that performed the procedure. The main independent variable was the quartile of volume, and the reference group was the group of hospitals with the lowest volume (first quartile). Variables sequentially added to the models included the location of the hospital (urban or rural) and the demographic characteristics, medical history, and clinical presentation of the patients.

Variables subsequently added to the models included cardiac medications administered within the first 24 hours after the patient's arrival at the hospital, the year the patient was admitted to the hospital (to account for temporal trends), and the total number of patients with myocardial infarction who were admitted to the hospital (to account for any additional influence of the volume of patients with myocardial infarction and of variability in the volume within quartiles).

A second set of models was constructed to determine the relation between the volume of thrombolytic interventions and mortality among patients who received thrombolytic therapy. We used the C statistic to determine the predictive value of each fully adjusted model. The C statistic ranges from 0 to 1, with higher numbers indicating greater predictive value.

RESULTS

Study Population

Table 1 shows the ranking of hospitals in the NRMI according to the number of patients who underwent primary angioplasty or received thrombolytic therapy. A total of 257,602 patients with myocardial infarction (33.3 percent of the entire NRMI cohort) were treated at a total of 450 hospitals (30.6 percent of all NRMI hospitals) in the angioplasty group, and a total of 277,156 patients with myocardial infarction (35.9 percent of the entire NRMI cohort) were treated at 516 hospitals (35.1 percent of all NRMI hospitals) for the thrombolytic-therapy group.

In general, there were few clinically relevant differences among patients according to the quartile of volume (Table 2). Notable differences included rel-

TABLE 1. HOSPITALS IN THE NATIONAL REGISTRY OF MYOCARDIAL INFARCTION, RANKED ACCORDING TO THE VOLUME OF REPERFUSION THERAPY, 1994–1998.*

QUARTILE	HOSPITALS	PATIENTS WITH MI	PATIENTS WHO UNDERWENT ANGIOPLASTY OR THROMBOLYSIS	VOLUME no./yr
		number		
Primary angioplasty				
1	113	42,362	2,825	5–11
2	112	56,145	5,245	12–20
3	113	67,460	9,303	21–33
4	112	91,635	19,162	>33
Total	450	257,602	36,535	—
Thrombolytic therapy				
1	129	38,964	3,929	5–15
2	129	48,003	8,385	16–28
3	129	74,380	14,694	29–45
4	129	115,809	28,658	>45
Total	516	277,156	55,666	—

*Hospitals were ranked according to the number of patients who underwent primary angioplasty or thrombolytic therapy at each hospital. The volume was calculated as the total number of patients who underwent primary angioplasty or thrombolysis at each hospital divided by the total number of days the hospital reported data to the registry. A minimal volume of five patients per year was required for a hospital to be included in the analysis. Quartiles were defined with the use of the 25th, 50th, and 75th percentiles as cutoff points. A total of 422 hospitals were included in both the angioplasty group and the thrombolytic-therapy group. MI denotes myocardial infarction.

actively higher proportions of white patients and patients with Q-wave infarctions at high-volume centers. Also, the median interval between the onset of symptoms and the patient’s arrival at the hospital was longer for patients treated at low-volume centers performing thrombolytic therapy than among those treated at high-volume thrombolytic-therapy centers.

Most of the hospitals in both the angioplasty group and the thrombolytic-therapy group were located in urban areas (Table 2). Also, in both groups, high-volume hospitals were more likely than low-volume hospitals to be large facilities (with more than 350 beds), and low-volume hospitals in the thrombolytic-therapy group were more likely than high-volume hospitals to be teaching centers. However, there were no important differences in volume among teaching centers that performed primary angioplasty.

Pharmacologic Treatments and Cardiac Procedures

Patients who were eligible for acute reperfusion therapy and who were admitted to the centers with the highest volume of thrombolytic interventions (fourth quartile) were significantly more likely to receive reperfusion therapy of any type than were patients admitted to centers with the lowest volume (73.8 percent vs. 65.3 percent, $P < 0.001$) (Table 3). However, for eligible patients at hospitals performing angioplasty, there were no important trends in the

use of reperfusion therapy of any type according to the quartile of volume.

There were no important clinical differences among quartiles in the use of antiplatelet therapies, beta-blockers, or heparin within the first 24 hours after the patient’s arrival at the hospital, for either patients who received thrombolytic therapy or those who underwent primary angioplasty. However, in the group of patients who received thrombolytic therapy, the proportion who underwent cardiac catheterization, angioplasty, or bypass grafting was greater in the highest quartile than in the lowest quartile. The use of bypass grafting varied little according to volume among the hospitals performing angioplasty.

Interval between Arrival at the Hospital and Treatment

The interval between the patient’s arrival at the hospital and the initial electrocardiographic study varied little among the quartiles of hospitals for either form of reperfusion therapy (Table 4). However, the higher-volume hospitals in both the angioplasty group and the thrombolytic-therapy group were likely to administer such therapies sooner. The difference between the lowest and highest quartiles in the mean interval from the patient’s arrival at the hospital to the administration of reperfusion therapy was significantly greater for patients treated with primary angioplasty (28.2 minutes) than for those treated with thrombolysis (10.8 minutes).

In-Hospital Mortality

The crude mortality rate during hospitalization was 7.7 percent among patients admitted to hospitals in the lowest quartile of the angioplasty group and 5.7 percent among those admitted to hospitals in the highest quartile ($P < 0.001$) (Table 2). There was no significant association between the volume of thrombolytic interventions and in-hospital mortality among patients who received thrombolytic therapy (7.0 percent for the highest quartile and 6.9 percent for the lowest quartile, $P = 0.36$).

Among patients who actually underwent primary angioplasty, the mortality rate was significantly lower with each increasing quartile of volume, and was lowest among hospitals with the highest volume, even after adjustment for the early use of adjunctive medications known to influence mortality, the year of admission, and the total volume of patients with myocardial infarction ($P < 0.001$) (Table 5). Among patients who received thrombolytic therapy, there was no statistically significant association between the volume of such procedures and mortality ($P = 0.67$).

DISCUSSION

The primary finding in this large observational analysis was that in-hospital mortality was 28 percent lower among patients who underwent primary angioplasty at hospitals with the highest volume of such

TABLE 2. CHARACTERISTICS OF PATIENTS AND HOSPITALS AND OUTCOMES OF REPERFUSION THERAPY, ACCORDING TO THE QUARTILE OF VOLUME.*

VARIABLE	THROMBOLYTIC THERAPY				P VALUE†	PRIMARY ANGIOPLASTY				P VALUE†
	QUARTILE 1	QUARTILE 2	QUARTILE 3	QUARTILE 4		QUARTILE 1	QUARTILE 2	QUARTILE 3	QUARTILE 4	
No. of patients	3929	8385	14,694	28,658		2825	5245	9303	19,162	
Age (yr)					≤0.01					
Mean	62.8	61.9	62.0	62.0		61.7	61.6	61.7	62.0	
Median	62.9	61.8	62.2	62.1		61.8	62.0	61.9	62.2	
Female sex (%)	31.6	31.2	30.6	30.7		30.5	31.0	30.4	30.4	
White race (%)	81.1	80.4	85.3	90.1	≤0.01	82.5	84.1	87.3	90.5	≤0.01
Cardiac risk factors (% of patients)										
Diabetes mellitus	19.5	20.4	19.6	19.2		20.7	20.2	20.3	18.5	≤0.01
Hypertension	47.4	45.8	45.4	44.8		45.4	48.4	46.6	45.4	≤0.01
Current smoking	35.7	37.9	38.2	38.9	≤0.01	34.0	34.9	33.9	35.4	
Family history of coronary artery disease	30.9	33.0	34.6	36.0	≤0.01	31.5	33.4	33.3	32.6	
High serum cholesterol	28.7	30.5	30.5	28.9	≤0.01	27.2	29.3	30.9	31.6	≤0.01
Medical history (% of patients)										
Angina	11.6	13.2	13.4	12.8		16.9	14.3	14.6	13.8	≤0.01
Myocardial infarction	19.8	19.4	18.4	18.9		19.7	19.9	19.3	18.4	
Heart failure	5.0	3.9	3.9	3.9	≤0.01	4.0	4.4	4.3	3.7	
PTCA	8.3	8.9	8.9	8.7		13.3	13.4	13.7	13.5	≤0.01
CABG	9.1	8.4	8.0	8.1		7.4	7.3	8.6	8.3	
Stroke	3.4	3.4	3.2	3.3		5.4	5.7	5.8	4.8	≤0.01
Median interval between onset of symptoms and arrival at hospital (min)	105.0	100.2	94.8	93.0	≤0.01	109.8	111.0	108.0	105.0	
Mean systolic blood pressure (mm Hg)	141.6	140.0	140.3	139.4	≤0.01	136.8	137.6	138.8	139.0	≤0.01
Mean pulse (beats/min)	78.6	78.4	77.8	77.8		78.2	78.1	78.3	77.9	
Killip class (% of patients)										
I	85.8	86.6	87.5	87.5	≤0.01	84.9	83.8	84.9	85.7	≤0.01
II	9.9	9.6	9.3	8.7		9.0	9.0	8.6	8.8	
III	2.9	2.4	2.2	2.4		2.1	3.2	2.9	2.4	≤0.01
IV	1.4	1.4	0.9	1.4	≤0.01	4.0	4.0	3.5	3.0	≤0.01
Type of myocardial infarction (% of patients)										
Q wave	79.8	79.7	80.1	84.6	≤0.01	72.1	75.8	75.3	76.2	≤0.01
Anterior	34.1	35.6	34.6	33.8	≤0.01	36.5	39.1	36.5	36.1	≤0.01
Length of stay (days)										
Median	5.8	5.9	6.0	6.1		6.1	6.0	5.9	5.8	≤0.01
Mean	7.4	7.4	7.5	7.6		7.5	7.6	7.5	7.3	
Crude death rate (%)	6.9	7.0	6.6	7.0		7.7	7.5	7.0	5.7	≤0.01
Hospital characteristics (% of patients)										
Urban	95.0	93.8	95.5	97.8	≤0.01	93.4	93.5	95.2	94.7	≤0.01
>350 Beds	47.6	40.9	43.1	60.4	≤0.01	39.6	42.9	55.1	61.8	≤0.01
Teaching	32.8	21.2	18.3	11.8	≤0.01	20.6	26.8	18.5	19.9	≤0.01

*Percentages may not sum to 100 because of rounding. PTCA denotes percutaneous transluminal coronary angioplasty, and CABG coronary-artery bypass grafting.

†P values are for the comparisons among the quartiles.

procedures than among those who underwent angioplasty at hospitals with the lowest volume. This lower rate, which represented 2.0 fewer deaths per 100 patients, was independent of the total volume of cases of myocardial infarction, temporal trends, or early use of proven adjunctive therapies known to influence survival (such as aspirin, beta-blockers, and heparin). However, there was no significant relation between the

volume of thrombolytic interventions and in-hospital mortality among patients who received thrombolytic therapy. Finally, we found that high-volume centers tended to administer lifesaving reperfusion therapies faster than low-volume centers and that the difference was greater for patients who underwent primary angioplasty than for those who received thrombolytic therapy.

TABLE 3. PHARMACOLOGIC TREATMENTS AND INVASIVE CARDIAC PROCEDURES ACCORDING TO THE QUARTILE OF VOLUME.*

VARIABLE	THROMBOLYTIC THERAPY				P VALUE†	PRIMARY ANGIOPLASTY				P VALUE‡
	QUARTILE 1	QUARTILE 2	QUARTILE 3	QUARTILE 4		QUARTILE 1	QUARTILE 2	QUARTILE 3	QUARTILE 4	
	Reperfusion therapy									
No. of eligible patients‡	11,724	14,492	23,028	36,292		15,061	18,607	23,590	31,039	
Thrombolytic therapy (%)	26.5	45.3	50.8	62.0	<0.01	59.2	51.8	47.0	27.1	<0.01
PTCA (%)	38.8	25.8	19.6	11.8	<0.01	10.3	16.0	22.0	37.9	<0.01
Any reperfusion (%)	65.3	71.1	70.4	73.8	<0.01	69.5	67.8	69.0	65.0	<0.01
Other medications within 24 hr										
No. of patients§	3,929	8,385	14,694	28,658		2,825	5,245	9,303	19,162	
Aspirin or an antiplatelet agent (%)	92.2	92.7	93.8	93.6	<0.01	88.1	88.6	89.4	90.9	<0.01
Beta-blocker (%)	52.5	55.5	54.7	55.0	<0.01	43.8	46.9	44.5	46.4	<0.01
Heparin (%)	97.0	96.8	97.7	97.6	<0.01	91.8	93.1	92.7	94.7	<0.01
Invasive procedures										
No. of patients§	3,929	8,385	14,694	28,658		2,825	5,245	9,303	19,162	
Catheterization (%)	75.5	77.5	78.7	80.2	<0.01	100	100	100	100	
PTCA (%)	39.7	41.6	41.1	42.1	<0.01	100	100	100	100	
CABG (%)	14.8	15.5	16.5	17.8	<0.01	8.5	9.1	8.0	8.8	

*PTCA denotes percutaneous transluminal coronary angioplasty, and CABG coronary-artery bypass grafting.

†P values are for the comparisons among the quartiles.

‡Patients were considered eligible for thrombolysis if the initial hospital electrocardiogram revealed an ST-segment elevation of more than 1 mm in two contiguous leads or left bundle-branch block, if the symptoms had developed no more than 12 hours earlier, and if there were no contraindications to thrombolytic therapy. Patients were considered eligible for primary angioplasty if the initial hospital electrocardiogram revealed an ST-segment elevation of more than 1 mm in two contiguous leads or left bundle-branch block and if the symptoms had developed no more than 12 hours earlier.

§Data are numbers of patients who received reperfusion therapy.

TABLE 4. INTERVAL BETWEEN ARRIVAL AT THE HOSPITAL AND EVALUATION AND TREATMENT, ACCORDING TO THE QUARTILE OF VOLUME.

VARIABLE	THROMBOLYTIC THERAPY*				PRIMARY ANGIOPLASTY			
	QUARTILE 1	QUARTILE 2	QUARTILE 3	QUARTILE 4	QUARTILE 1	QUARTILE 2	QUARTILE 3	QUARTILE 4
	No. of patients	3929	8385	14,694	28,658	2825	5245	9303
Arrival to electrocardiogram (min)								
Mean	12.6	12.0	11.4	14.4	14.4	13.8	12.6	10.8
Median	7.8	7.8	7.8	9.0	9.0	9.0	7.8	7.8
Arrival to thrombolytic therapy (min)								
Mean	74.4	67.8	67.2	63.6	—	—	—	—
Median	48.6	43.8	42.0	40.2	—	—	—	—
Arrival to angioplasty (min)								
Mean	—	—	—	—	198.6	196.8	189.6	170.4
Median	—	—	—	—	129.0	135.0	129.0	118.8

*P<0.001 for all comparisons of median and mean values among the quartiles.

There are many possible explanations for the inverse relation between the volume of angioplasty procedures and in-hospital mortality. Hospitals that have a high total volume of patients with myocardial infarction may have better outcomes because of institutional factors involved in the care of large numbers of such patients, and those centers are also likely to

have a high volume of primary angioplasty procedures. However, even after we adjusted for the total volume of patients with myocardial infarction at each hospital, the volume of procedures was still a significant, independent predictor of a better outcome.

Referral bias may be another explanation for the better outcomes at high-volume angioplasty centers.

TABLE 5. UNADJUSTED AND ADJUSTED RELATIVE RISK OF DEATH AMONG PATIENTS WHO UNDERWENT PRIMARY ANGIOPLASTY OR RECEIVED THROMBOLYTIC THERAPY, ACCORDING TO THE QUARTILE OF VOLUME.

MODEL*	RELATIVE RISK (95% CI)†		
	QUARTILE 2	QUARTILE 3	QUARTILE 4
Primary angioplasty			
Unadjusted	0.96 (0.81–1.14)	0.89 (0.76–1.04)	0.72 (0.62–0.84)
Adjusted for demographic characteristics	0.92 (0.76–1.10)	0.84 (0.71–1.00)	0.71 (0.61–0.83)
Adjusted for demographic characteristics and medical history	0.92 (0.77–1.10)	0.84 (0.71–1.00)	0.72 (0.61–0.84)
Adjusted for demographic characteristics, medical history, clinical presentation, and medications within 24 hr	0.87 (0.71–1.07)	0.84 (0.70–1.02)	0.74 (0.62–0.89)
Adjusted for demographic characteristics, medical history, clinical presentation, medications within 24 hr, year, and volume of patients with MI	0.87 (0.71–1.07)	0.83 (0.69–1.01)	0.72 (0.60–0.87)
Thrombolytic therapy			
Unadjusted	1.00 (0.86–1.16)	0.96 (0.83–1.10)	1.00 (0.88–1.14)
Adjusted for demographic characteristics	1.10 (0.94–1.29)	1.02 (0.88–1.19)	1.09 (0.94–1.25)
Adjusted for demographic characteristics and medical history	1.12 (0.95–1.32)	1.05 (0.90–1.22)	1.11 (0.96–1.28)
Adjusted for demographic characteristics, medical history, clinical presentation, and medications within 24 hr	1.24 (1.04–1.47)	1.18 (1.00–1.38)	1.22 (1.05–1.42)
Adjusted for demographic characteristics, medical history, clinical presentation, medications within 24 hr, year, and volume of patients with MI	1.23 (1.04–1.46)	1.16 (0.99–1.36)	1.18 (1.00–1.39)

*Demographic characteristics included age, sex, and urban or rural location of the hospital. Medical history included cardiac risk factors (hypertension, diabetes mellitus, current smoking, family history of coronary artery disease, and hypercholesterolemia) and previous cardiac disorders or treatment (myocardial infarction, angina, heart failure, coronary angioplasty, coronary bypass surgery, or stroke). Clinical presentation included Q-wave or non-Q-wave myocardial infarction, Killip class, presence or absence of anterior myocardial infarction, presence or absence of ST-segment elevation or left bundle-branch block on the initial electrocardiogram, and a delay of more than six hours between the onset of symptoms and arrival at the hospital. Medications within 24 hours included heparin, aspirin, nitroglycerin, beta-blockers, lidocaine, intravenous magnesium, angiotensin-converting-enzyme inhibitors, and calcium-channel blockers. The C statistic was 0.872 for the fully adjusted angioplasty model and 0.841 for the fully adjusted thrombolytic-therapy model.

†The relative risk is for the comparison with the first quartile. CI denotes confidence interval, and MI myocardial infarction.

Such a bias results when the reputation of a physician or hospital for superior outcomes leads to increased referrals, including referrals of patients with less serious disorders, who might have superior outcomes regardless of treatment. However, most of the baseline characteristics were similar among the quartiles, and the results did not change significantly after adjustment for known differences. In addition, referral bias was limited by the restriction of the analysis to hospitals with full interventional capabilities, where the proportion of patients transferred to other hospitals was negligible (<3 percent), and by the exclusion of patients transferred from other institutions. Therefore, differences in transfer rates are not likely to explain the observed differences in mortality between patients who underwent angioplasty at high-volume hospitals and those who underwent angioplasty at low-volume hospitals.

On the other hand, the lower mortality rate at high-volume angioplasty centers than at low-volume centers may be due in part to the finding that the inter-

val between the patient's arrival at the hospital and the administration of reperfusion therapy was significantly shorter at high-volume angioplasty centers than at low-volume centers. It is known that faster restoration of antegrade flow is associated with improved survival. The lower mortality rate at high-volume angioplasty centers may also be due to the fact that physicians who perform reperfusion procedures at high-volume centers, as well as other members of the cardiac-catheterization team at such centers, may have more opportunities to improve and perfect their technical skills through practice. Our findings suggest that the volume of angioplasty procedures may be a proxy for the process of care.

Though the volume of angioplasty procedures was associated with in-hospital mortality, there was no relation between the volume of thrombolytic interventions and in-hospital mortality. In this analysis, a higher volume of thrombolytic interventions was associated with a slightly shorter interval between the patient's arrival at the hospital and the administra-

tion of thrombolytic therapy, but this difference did not translate into an improved in-hospital mortality rate. This finding is not surprising, considering that the resources and expertise required for the proper administration of a thrombolytic drug are less extensive than those required for the proper performance of angioplasty.

Numerous investigators have reported on the relation between the volume of procedures and the outcome of elective coronary angioplasty and elective coronary bypass surgery. Two recent retrospective cohort studies have examined the association between the total volume of patients with myocardial infarction and outcome, using data from the Cooperative Cardiovascular Project. Thiemann et al.¹² studied the relation between the volume of Medicare patients with myocardial infarction treated at each hospital and survival. These investigators found that patients admitted to low-volume centers had a 17 percent higher risk of death than patients admitted to high-volume centers. The crude difference in mortality at 30 days between the lowest-volume and highest-volume hospitals was 2.3 deaths per 100 patients. Chen et al.¹³ reported that among Medicare patients with myocardial infarction, admission to hospitals ranked high on the list of "America's Best Hospitals" in cardiology, published annually by *U.S. News & World Report*, was associated with a lower 30-day mortality rate than admission to other hospitals, mainly because of the higher rates of use of aspirin and beta-blockers at the top-ranked hospitals.

Both groups of investigators underscored the potential contribution of the total volume of patients with myocardial infarction and the use or nonuse of adjunctive therapies to mortality after myocardial infarction. In an analysis adjusted for these factors, we found an independent association between a higher volume of angioplasty procedures and lower mortality among patients who underwent primary angioplasty. In the future, the wider availability of intracoronary stents and platelet glycoprotein IIb/IIIa receptor inhibitors may make coronary angioplasty easier to perform. However, in a study of patients undergoing intracoronary stent placement, the investigators reported that experience remained one of the most important predictors of a favorable outcome.⁵ An accompanying editorial concluded that the volume of procedures required for competency to perform angioplasty is also a valid criterion for competency in placing coronary stents.¹⁴

Our finding that volume was related to outcome for primary angioplasty but not for thrombolysis may have important implications for policy. Our data suggest that primary angioplasty should be considered as an alternative form of acute reperfusion therapy only at hospitals where the volume of procedures is sufficiently large for physicians to develop and maintain their skills. Furthermore, centers with low volumes of

angioplasty procedures should take this factor into account in developing angioplasty programs and establish institutional mechanisms to ensure prompt reperfusion therapy in patients with myocardial infarction. Hospitals with low volumes of angioplasty procedures may be able to improve the outcomes of their patients and approach the results of higher-volume centers if they improve the process of care — for example, by reducing the interval between the patient's arrival at the hospital and the performance of angioplasty. However, all centers must be careful to develop clear-cut reperfusion protocols in order to minimize indecision in choosing between alternative treatments.

Our study may be limited by its observational design and the possibility of residual confounding, although its strengths include a large sample and the use of a wide array of clinical variables in adjusting for differences in clinical characteristics and important potential confounders. For self-reported data, there are always issues involving incomplete responses and the reliability of data abstracted from medical records. These issues would be expected to weaken any association between volume and outcome. In addition, no data were available on the number of elective and emergency procedures performed by individual operators, the number of interventional cardiologists who performed primary angioplasty at each center, and mortality at 30 days. Our findings may be generalizable to all U.S. hospitals that provide angioplasty and thrombolytic therapy, and the patients in our study were of all ages and had all types of insurance. Nevertheless, our results must be interpreted with caution.

We conclude that patients with acute myocardial infarction who are treated at high-volume angioplasty centers have a lower mortality rate than patients treated at low-volume centers and that high-volume centers perform primary angioplasty faster. There is no association between volume and mortality among patients treated with thrombolysis. Our findings support the statement of the American College of Cardiology and the American Heart Association that "primary PTCA should be used as an alternative to thrombolytic therapy only if performed in a timely fashion by individuals skilled in the procedure and supported by experienced personnel in high-volume centers."¹⁵

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