# Temporal Trends in the Treatment of Over 1.5 Million Patients With Myocardial Infarction in the U.S. from 1990 Through 1999

The National Registry of Myocardial Infarction 1, 2 and 3

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**OBJECTIVES** 

We sought to determine trends in the treatment of myocardial infarction from 1990 through 1999 in the U.S. and to relate these trends to current guidelines.

**BACKGROUND** 

Limited data are available to show how recent clinical trials and clinical guidelines have

impacted treatment of myocardial infarction.

**METHODS** 

Temporal trends in myocardial infarction treatment and outcome were assessed by using data from 1,514,292 patients in the National Registry of Myocardial Infarction (NRMI) 1, 2 and 3 from 1990 through 1999.

RESULTS D

During this interval, the use of intravenous thrombolytic therapy declined from 34.3% to 20.8%, but the use of primary angioplasty increased from 2.4% to 7.3% (both p=0.0001). The median "door-to-drug" time among thrombolytic therapy recipients fell from 61.8 to 37.8 min (p=0.0001), primarily owing to shorter "door-to-data" and "data-to-decision" times. The prevalence of non–Q wave infarctions increased from 45% in 1994 to 63% in 1999 (p=0.0001). From 1994 through 1999, there was increased usage of beta-blockers, aspirin and angiotensin-converting inhibitors, both during the first 24 h after admission and on hospital discharge (all p=0.0001). Between 1990 and 1999, the median duration of hospital stay fell from 8.3 to 4.3 days, and hospital mortality declined from 11.2% to 9.4% (both p=0.0001).

CONCLUSIONS

The NRMI data from 1990 through 1999 demonstrate that the recommendations of recent clinical trials and published guidelines are being implemented, resulting in more rapid administration of intravenous thrombolytic therapy, increasing use of primary angioplasty and more frequent use of adjunctive therapies known to reduce mortality, and may be contributing to the higher prevalence of non–Q wave infarctions, shorter hospital stays and lower hospital mortality. (J Am Coll Cardiol 2000;36:2056–63) © 2000 by the American College of Cardiology

The treatment of acute myocardial infarction (AMI) in the U.S. has undergone remarkable evolution over the decade of the 1990s. This evolution has primarily been driven by increasing awareness of therapies that have been shown by controlled, clinical trials to improve outcome (1) and that have subsequently been promoted by expert panels and formal published guidelines (2). However, a secondary, but powerful, motivation to change practice patterns has been economic pressure stemming from health care reform.

In July 1990, the National Registry of Myocardial Infarction (NRMI) was initiated to provide participating hospitals a means of tracking the characteristics, treatment and

outcome of their patients with AMI. The composite data from the 1,514,292 patients entered from 1990 through 1999 in the first three phases of NRMI (NRMI 1, 2 and 3) should provide insight into the evolving national practice patterns for treatment of AMI. This report describes trends in the presenting characteristics, treatment and outcome of patients with AMI from 1990 through 1999, as reflected by this large U.S. registry, and relates these trends to the recommendations of recent clinical trials and to heath care reform.

## METHODS

**Data collection.** The NRMI is an industry-sponsored, prospective, observational study (3). On entering NRMI, hospitals were asked to complete a form characterizing their facilities and services and then to record data from consecutive patients with AMI onto two-page case report forms, which were forwarded to an independent statistical center. Case report forms were less detailed for NRMI 1 (1990–

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Manuscript received November 2, 1999; revised manuscript received May 31, 2000, accepted July 14, 2000.

## Abbreviations and Acronyms

ACE = angiotensin-converting enzyme AMI = acute myocardial infarction

CABG = coronary artery bypass graft surgery

ECG = electrocardiogram or electrocardiographic

LBBB = left bundle branch block

IV = intravenous

NRMI = National Registry of Myocardial Infarction

PTCA = percutaneous transluminal coronary angioplasty

rt-PA = recombinant tissue-type plasminogen activator

1994) than for NRMI 2 (1994–1998) or NRMI 3 (1998 to present). Hospitals received quarterly reports summarizing local registry data, as well as parallel data from the state, nation and hospitals of similar bed size and invasive cardiovascular capability. To ensure quality control of registry data, registry coordinators were trained in data entry, utilizing a standardized manual of instructions and definitions. Case report forms were required to pass systematic range and internal consistency checking. Hospitals obtained approval of the registry data collection process as dictated by local policy.

Trend analysis. Data were grouped according to the calendar year of each patient's hospital arrival. Phase 1 of NRMI began in July 1990, so the initial period of data collection was six months in duration. For data variables common among NRMI 1, 2 and 3, trends over the period 1990–1999 were assessed. For variables contained only in the more detailed NRMI 2 and 3 data bases, trend analyses were confined to the period 1994–1999.

**Definitions.** Myocardial infarction was defined by local hospital criteria, usually including a history suggestive of AMI accompanied by either total creatine kinase or creatine kinase, MB fraction greater than or equal to twice the upper limit of normal for the hospital's laboratory, or electrocardiographic (ECG) evidence of AMI, or, in the absence of these, alternative enzymatic, scintigraphic, echocardiographic or autopsy evidence of AMI—culminating in an

International Classification of Diseases (9th revision, clinical modification) discharge diagnosis code of 410.01 through 410.91 for AMI.

Hospitals were considered urban if located in a county with at least one city having a population >50,000 or two cities having a combined population >50,000. Treatment intervals for administration of thrombolytic therapy were defined according to the National Heart Attack Alert Program, where "door" indicates the time of patient presentation to the hospital; "data" represents the time of acquisition of the diagnostic ECG; "decision" means the time it was decided to administer thrombolytic therapy; and "drug" indicates the time thrombolytic therapy was initiated (4). Major bleeding included hemorrhagic episodes, other than intracranial bleeding, resulting in substantial hemodynamic compromise. Because many hospitals "dropped out" and "dropped into" the registry over time, "core hospitals" were identified; they contributed at least six patients during each six-month interval throughout NRMI 2 and 3 or the combined NRMI 1, 2 and 3 intervals. Core hospitals were identified separately for the NRMI 2 and 3 trend analysis and for the combined NRMI 1, 2, and 3 analyses.

Statistical analysis. For categoric data, the Mantel-Haenszel chi-square test was used as the measure of trend. For continuous data, one-way analysis of variance was used to test the null hypothesis that multiple population mean values are all equal. To test median values across multiple groups, p values were computed using the nonparametric Brown-Mood test. All statistical analyses were performed using a commercially available statistical package (SAS 6.12 [1996], SAS Institute, Cary, North Carolina). This report is based on data processed by the statistical center as of April 25, 2000.

#### **RESULTS**

Characteristics of participating hospitals (Table 1). A total of 1,249 hospitals contributed patients to NRMI 1;

Table 1. Characteristics of Participating Registry Hospitals

		Core Hospitals*				
	NRI	MI 1	NRMI	NRMI 2 and 3	NRMI 1, 2 and 3	
	First Period (July-Dec. 1990)	Last Period (JanJune 1994)	First Period (July-Dec. 1994)	Last Period (JanDec. 1999)	July 1994– Dec. 1999	July 1990- Dec. 1999
No. of hospitals	352	1052	1239	1432	572	58
No. of staffed beds (mean)	322	271	268	250	254	323
Medical school affiliation (%)	48.3	35.0	37.3	35.0	36.0	48.4
Member, Council of Teaching Hospitals (%)	11.9	8.2	9.9	7.7	6.1	10.2
Urban location (%)	88.4	74.3	79.4	76.2	73.3	86.2
Cardiac catheterization laboratory (%)	87.1	69.2	72.7	69.0	72.7	89.8
PTCA performed (%)	66.3	43.5	46.0	41.2	44.8	65.9
CABG performed (%)	61.6	27.1	39.5	36.7	38.1	62.4

<sup>\*</sup>Core hospitals were those hospitals contributing at least six patients during each complete six-month period of the registry.

CABG = coronary artery bypass graft surgery; NRMI = National Registry of Myocardial Infarction; PTCA = coronary angioplasty.

**Table 2.** Characteristics of the NRMI 2 and 3 Study Population

	Year						
	1994	1995	1996	1997	1998	1999	p Value*
	77,064	205,280	223,395	227,120	215,026	213,665	
Age (mean, years)	66.5	66.6	66.8	67.2	67.7	68.0	0.0001
Gender (% female)	37.7	37.7	38.1	38.3	38.8	39.3	0.0001
Race (% white)	86.3	86.5	86.3	85.9	85.4	85.7	0.0001
Weight (mean, kg)	78.0	78.3	78.5	78.6	79.3	79.4	0.0001
Payer status†(%)							
Commercial/PPO	22.8	22.8	21.6	20.5	32.7	37.7	0.0001
HMO	7.8	8.3	9.9	12.1	17.1	17.8	0.0001
Medicare	49.1	50.1	50.8	50.9	38.3	33.3	0.0001
Medicaid	3.0	3.0	2.9	2.7	2.6	2.6	0.0001
VA/CHAMPUS	0.9	0.9	0.8	0.7	0.4	0.4	0.0001
Self/other/unknown	16.5	15.0	14.0	13.1	9.0	8.1	0.0001
History (%)							
Myocardial infarction	24.5	24.6	24.6	24.6	24.0	24.1	0.0001
Angina	18.6	17.6	16.9	16.4	13.8	12.6	0.0001
Heart failure	11.9	12.3	13.1	13.6	15.2	15.8	0.0001
PTCA	7.0	7.5	8.2	8.8	9.7	10.4	0.0001
CABG	10.6	10.7	11.3	11.9	12.5	12.9	0.0001
Stroke	7.3	7.7	8.0	8.4	9.4	9.7	0.0001
Diabetes	25.1	25.6	26.2	27.0	28.3	28.9	0.0001
Hypertension	48.2	49.8	51.1	52.5	55.1	56.2	0.0001
Current smoking	28.0	28.3	28.3	27.1	26.7	25.9	0.0001
Family member with CAD	29.6	29.7	29.7	29.0	27.8	26.7	0.0001
Hypercholesterolemia	23.1	24.6	25.9	28.6	29.9	31.3	0.0001

\*The Mantel-Haenszel test assessed trends by serial time intervals over the duration of the registry. Time interval was six months in 1994 and 12 months thereafter. One-way analysis of variance was performed to compare group mean values for continuous fields (age, weight). †Payer categories were mutually exclusive in NRMI 2 and mutually inclusive in NRMI 3. In this table, the categories for NRMI 3 have been made mutually exclusive by prioritizing in the order of listing above. Thus, a patient with a Medicare HMO would be categorized in NRMI 3 as "HMO."

CAD = coronary artery disease; CHAMPUS = Civilian Health and Medical Program of the Uniformed Services; HMO = health maintenance organization; PPO = preferred provider organization; VA = Veterans Administration; other abbreviations as in Table 1.

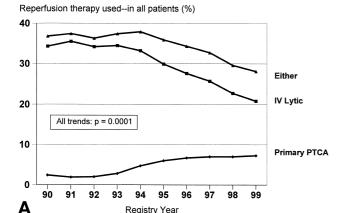
1,843 hospitals to NRMI 2 and 3; and 2,033 hospitals to NRMI 1, 2 and 3. However, the number of hospitals participating in the registry at any point in time was variable and ranged from 352 to 1,460. There were 58 "core" hospitals for the combined NRMI 1, 2 and 3 experience, and there were 572 core hospitals for the combined NRMI 2 and 3 experience. The average registry hospital had 250 to 300 beds and was nonteaching and urban and had capabilities for coronary arteriography, but less often percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft surgery (CABG).

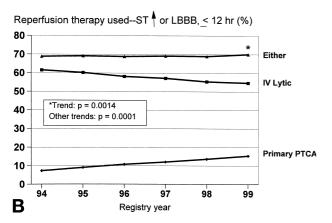
Patient characteristics. From 1990 through 1999, 352,742 patients were enrolled in NRMI 1, and 1,161,550 patients were enrolled in NRMI 2 and 3. The mean age of these 1,514,292 patients increased from 65.3 to 68.0 years from 1990 to 1999, and the proportion of females rose from 35.3% to 39.3% (both p = 0.0001). Separate analysis of the 1,161,550 patients enrolled in NRMI 2 and 3 between 1994 and 1999 showed similar trends for age and gender, along with an upward trend for weight (Table 2). In NRMI 2 and 3, payer status was ascertained and showed a sharp increase in prevalence of health maintenance organizations. Also noted was a reduction in the prevalence of previous angina, but an increase in previous heart failure, stroke, diabetes, hypertension, hypercholesterolemia or coronary revascularization.

Use of reperfusion therapy. Among the 1,514,292 patients in the combined NRMI 1, 2 and 3 data set, the proportion receiving either immediate thrombolytic therapy or primary PTCA fell from 36.8% in 1990 to 28.1% in 1999 (p = 0.0001) (Fig. 1A). During this interval, there was a significant fall in the use of intravenous (IV) thrombolytic therapy (from 34.3% to 20.8%, p = 0.0001), along with a sharp rise in the use of primary PTCA (from 2.4% to 7.3%, p = 0.0001).

Occurring simultaneously with the fall in the overall use of reperfusion therapy was a decrease in patients presenting with ST segment elevation or left bundle branch block (LBBB) within 12 h of symptom onset (from 36.4% in 1994 to 27.1% in 1999,  $p \leq 0.001$ ) and an increase in the prevalence of non–Q wave infarctions (from 45% in 1994 to 63% in 1999, p = 0.0001). The proportion of patients having troponin assays (documented only in NRMI 3) increased from 70.0% in 1998 to 84.3% in 1999 (p = 0.0001).

Among patients in NRMI 2 and 3 presenting with ST segment elevation or LBBB within 12 h of symptom onset, the proportion receiving immediate IV thrombolytic therapy or primary PTCA increased only slightly (from 68.8% to 70.0%, p = 0.0014), as the rise in the use of primary PTCA exceeded the fall in the use of IV thrombolytic therapy (Fig. 1B). Among patients treated in NRMI 2 and



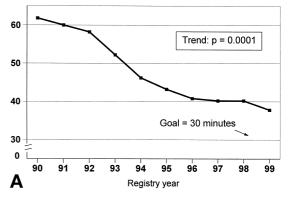


**Figure 1.** Use of reperfusion therapy in all patients and in those presenting with ST segment elevation or LBBB within 12 h of symptom onset. **A**, A total of 1,514,292 patients were enrolled in NRMI 1, 2 and 3. **B**, A total of 376,753 patients in NRMI 2 and 3 presented with ST segment elevation or LBBB within 12 h of symptom onset. Either = either IV lytic or primary PTCA; IV lytic = intravenous thrombolytic therapy.

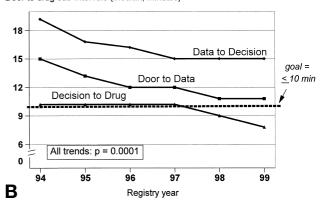
3 hospitals having the capability for both PTCA and CABG, the use of IV thrombolytic therapy fell from 59.1% in 1994 to 47.9% in 1999, whereas the use of primary PTCA increased from 11.8% to 24.4% (both p = 0.0001). Time to treatment. Among the 1,514,292 patients enrolled in NRMI 1, 2 and 3, the interval from symptom onset to hospital arrival fell only marginally between 1990 and 1999 (from a median of 2.2 to 2.0 h, p = 0.0001). Door-to-drug time was recorded only for recombinant tissue-type plasminogen activator (rt-PA) in NRMI 1. Among the 295,056 patients treated with rt-PA in NRMI 1, 2 and 3, the median interval from hospital arrival to initiating rt-PA (door-to-drug time) shortened significantly (Fig. 2A) (from 61.8 to 37.8 min, p = 0.0001). In NRMI 2 and 3, the door-to-drug time, as well as its component time intervals, was assessed for recipients of all IV thrombolytic agents. Among 266,177 such patients, the median door-to-drug time fell from 47 min in 1994 to 38 min in 1999, primarily due to shortening of the door-to-data interval (from 15.0 to 10.8 min) and a reduction in the data-to-decision interval (from 19.2 to 15.0 min, all p = 0.0001) (Fig. 2B).

The frequency of consulting another physician before

Door to drug interval (median, minutes)



Door to drug sub-intervals (median, minutes)

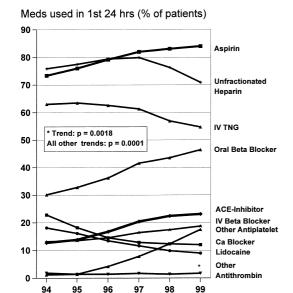


**Figure 2.** Door-to-drug intervals. **A,** Door-to-drug interval in 295,056 patients treated with rt-PA. Although the time to treatment shortened significantly, it did not achieve the goal of 30 min. **B,** Door-to-drug subintervals in 266,177 patients treated with all IV thrombolytic agents.

initiating thrombolytic therapy fell from 57.4% to 49.9% during NRMI 2 (p = 0.0001). Among thrombolytic recipients during this same time frame, the prevalence of emergency physicians as prescribers of the thrombolytic therapy increased from 50.7% to 65.7%, and the prevalence of cardiologists as the prescribing physician fell from 32.6% to 22.2% (both p = 0.0001)

**Medication use in first 24 h (Fig. 3).** During the first 24 h after presentation, the 1,161,550 patients in NRMI 2 and 3 showed upward trends in the use of aspirin, IV betablockers, oral beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, antiplatelet therapy other than aspirin (all p=0.0001) and antithrombin therapy other than heparin (p=0.0018). Also noted was less use of calcium channel blockers, IV lidocaine, IV nitroglycerin and unfractionated heparin (all p=0.0001). Among the 298,486 recipients of IV thrombolytic therapy in NRMI 2 and 3, similar upward trends were noted for aspirin (from 88.6% to 93.5%), IV beta-blockers (from 24.3% to 36.6%), oral beta-blockers (from 35.5% to 49.6%), either IV or oral beta-blockers (from 48.4 to 66.9%) and ACE inhibitors (from 7.5% to 18.9%) (all p=0.0001).

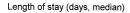
Noninvasive and invasive procedures. Among the 1,161,550 patients in NRMI 2 and 3, the performance of echocardiography during the hospital period was unchanged

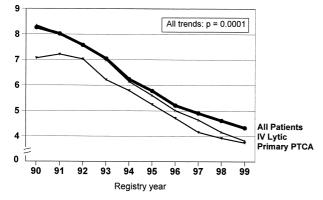


**Figure 3.** Medication (Meds) usage during first 24 h after hospital admission among 1,161,550 patients in NRMI 2 and 3. Ca blocker = calcium channel blocker; TNG = nitroglycerin.

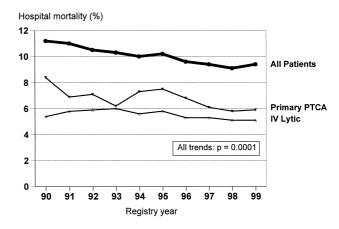
Registry year

from 1994 through 1999 (from 45.1% to 46.3%, p = 0.94), but stress testing decreased (from 11.6% to 8.5%, p = 0.0001). Among the 1,514, 292 patients in NRMI 1, 2 and 3, performance of coronary arteriography and CABG decreased from 1990 through 1999 (61.2% to 50.6% and 13.4% to 9.0%, respectively), whereas PTCA increased (from 23.5% to 26.1%) (all p = 0.0001). Among the more invasively equipped NRMI 1, 2 and 3 core hospitals, performance of coronary arteriography and PTCA increased (63.2% to 63.9% and 24.3% to 36.2%, respectively), but CABG decreased (from 14.0% to 11.8%) (all p = 0.0001). Hospital outcome. Among the 1,161,550 patients in NRMI 1, 2 and 3, the duration of hospital stay declined sharply (from a median of 8.3 days in 1990 to 4.3 days in 1999, p = 0.0001) (Fig. 4). The fall in length of hospital stay among patients receiving primary PTCA or IV throm-





**Figure 4.** Length of hospital stay among 1,514,292 patients in NRMI 1, 2 and 3. The length of stay shortened among all patients and in those receiving IV thrombolytic therapy or primary PTCA. IV lytic = intravenous thrombolytic therapy.

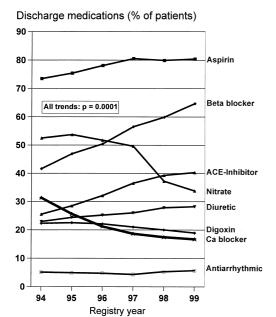


**Figure 5.** Hospital mortality among 1,514,292 patients in NRMI 1, 2 and 3. Hospital mortality declined among all patients and in those receiving IV thrombolytic therapy and primary PTCA. IV lytic = intravenous thrombolytic therapy.

bolytic therapy was similar to that of all patients. During this same interval, hospital mortality fell (from 11.2% in 1990 to 9.4% in 1999, p=0.0001) (Fig. 5). Hospital mortality also declined among patients receiving primary PTCA or IV thrombolytic therapy, but in the latter group, the decline was not quite as sharp as in the overall population. Among patients in NRMI 2 and 3 in whom the initial ECG findings were tabulated, similar mortality trends were noted between 1994 and 1999 for those presenting with findings of ST segment elevation or LBBB (n = 533,452) or for those presenting without such findings (n = 628,098) (10.6% to 9.8% and 9.9% to 9.1%, respectively, both p = 0.0001).

To account for a possible confounding influence of the shorter duration of hospital stay on mortality, trends for mortality during each day of hospital stay were examined. Among all patients, day 1 mortality fell from 3.1% in 1990 to 2.5% in 1999; day 2 mortality from 2.0% to 1.6%; and day 3 mortality from 1.6% to 1.4% (all p = 0.0001). More striking trends were noted among females and the elderly. For example, among the 339,290 female patients >70 years of age, day 1 mortality fell from 6.1% in 1990 to 4.3% in 1999; day 2 mortality from 4.8% to 2.7%; and day 3 mortality from 3.4% to 2.4% (all p = 0.0001).

Among the 1,161,550 patients in NRMI 2 and 3, a reduction was noted for cardiogenic shock (from 5.6% to 4.5%), sustained ventricular tachycardia or fibrillation (from 7.8% to 6.4%), reinfarction (from 3.3% to 1.8%), total stroke (from 1.5% to 1.1%) and cardiac rupture or electromechanical dissociation (from 0.9% to 0.6%). Major bleeding increased slightly (from 2.6% to 2.7%) (all p = 0.0001). **Discharge medications (Fig. 6).** Among the 805,341 patients in NRMI 2 and 3 who were discharged alive and not transferred out of the registry hospitals, upward trends were noted between 1994 and 1999 for discharge prescription of aspirin, beta-blockers, ACE inhibitors, antiarrhythmic agents and diuretic agents. Downward trends were observed for prescription of nitrates, calcium channel blockers and



**Figure 6.** Medications prescribed at hospital discharge. The most notable upward trends were in medications shown to improve survival, such as aspirin, beta-blockers and ACE inhibitors. Ca blocker = calcium channel blocker.

digoxin (all p=0.0001). Usage of lipid-lowering therapy, recorded only in NRMI 3, increased from 29.2% in 1998 to 36.2% in 1999 (p=0.0001).

Core hospitals. Except where noted, all of the temporal trends reported above for the total population of patients enrolled in NRMI 1 and 2, or NRMI 2 and 3 separately, were confirmed in independent analyses of patients enrolled at the core hospitals for these registries during the respective time frames (data not shown).

### **DISCUSSION**

The NRMI is the largest data base of AMI in the world, currently enrolling patients from over one-fourth of all acute-care hospitals in the U.S. This report shows that, from 1990 through 1999, practice patterns evolved generally in accordance with recommendations of recent clinical trials and published guidelines and resulted in more rapid implementation of thrombolytic therapy and greater use of appropriate adjunctive therapy. In parallel with ongoing national health care reform, there was an increase in health maintenance organizations as the primary payer for infarctrelated admissions and a sharp reduction in hospital stays. In accordance with physician preference, there was a steep increase in the use of primary PTCA and a decrease in the use of thrombolytic therapy. Finally, hospital mortality declined, both in patients receiving and in patients not receiving reperfusion interventions.

Changing patterns for utilization of reperfusion therapy. Because reperfusion therapy lowers the mortality of AMI, it should be implemented in every eligible patient (5). Surprisingly, the proportion of patients receiving an early

reperfusion intervention declined from 1990 through 1999 (Fig. 1A). In large part, this may have been due to a declining eligibility for reperfusion, rather than to an increasing failure to treat eligible patients. There was a fall in the proportion of patients presenting within 12 h with ST segment elevation or LBBB, the group known to benefit from thrombolytic therapy (6). The proportion of such subjects who were treated with either thrombolytic therapy or primary angioplasty remained relatively stable (Fig. 1B). However, as previously noted, over 25% of these patients did not have an early reperfusion intervention (7). The fact that the proportion of untreated eligible patients has remained stable since 1994, despite the growing utilization of primary PTCA, suggests that the latter intervention is being employed primarily in thrombolytic candidates, rather than as an "additional" means of reperfusing thrombolytic ineligible patients.

Factors determining time to treatment. Because AMI is a time-dependent process, the speed of implementation of thrombolytic therapy is critical in limiting myocardial injury and mortality (5,8). From 1990 through 1999, the door-to-drug interval fell significantly in the NRMI population (Fig. 2A), but did not achieve the goal of 30 min, as proposed by the National Heart Attack Alert Program (4). As previously reported, the major component of delay is the data-to-decision time (Fig. 2B), the interval during which "consultation" as to whether thrombolytic therapy should be administered is often sought between emergency department personnel and another physician, such as the patient's primary physician, an internist or a cardiologist (9). This consultative delay may increase both time to treatment and mortality (9).

To reduce the data-to-decision time, it has been recommended that hospitals empower emergency physicians to treat patients with typically presenting symptoms of AMI immediately, without consultation (4). This policy is being successfully implemented, at least in some NRMI hospitals, as evidenced by the decline in frequency of consultation before thrombolysis, the increasing proportion of emergency physicians as the ones ordering thrombolytic therapy and the fall in the data-to-decision interval from 1990 through 1999.

Relation of medication usage and procedures to evidence-based guidelines. Multiple, randomized, controlled clinical trials over the past two decades have investigated the impact of adjunctive pharmacotherapies and mechanical interventions on survival after AMI. The NRMI data show that practitioners have begun to incorporate many of the findings of these trials into practice. Medications shown to improve early- and long-term survival, including aspirin (8,10), beta-blockers (11) and ACE inhibitors (12), have increased in usage during the first 24 h of the hospital period (Fig. 3) and at hospital discharge (Fig. 6), whereas the use of agents with potentially deleterious effects, such as calcium channel blockers (13) and lidocaine (14) has declined. The use of "other antiplatelet therapy" has

increased in parallel with the increasing prevalence of early angioplasty. The use of most other agents has remained stable.

Despite the favorable trends in the utilization of pharmacologic therapy, there would appear to be potential for further improvement. Although NRMI did not assess eligibility for each of the adjunctive therapies, it is likely that, in recipients of thrombolytic therapy, the most recently cited rates of utilization were suboptimal for aspirin, betablockers and ACE inhibitors during the first 24 h (93.5%, 66.9% and 18.9%, respectively), especially because the rates of utilization for these agents was 97.4%, 80.8% and 53.9%, respectively, in the most recently reported large-scale clinical trial of thrombolytic therapy (15).

Routine coronary arteriography and mechanical revascularization after infarction have not been found to improve the rates of survival or subsequent AMI in most (6,16–18), but not all, studies (19). In NRMI, the use of coronary arteriography declined from 1990 through 1999, but the use of PTCA increased. The decline in coronary arteriography was likely an artifact due to the influx into the registry of hospitals without the capability for invasive procedures. Indeed, among the stable cohort of NRMI 1, 2 and 3 core hospitals, the use of both coronary arteriography and PTCA increased from 1990 through 1999. The relatively high use of postinfarction coronary arteriography in the U.S., as reflected by NRMI, represents a singular departure from otherwise close adherence to the majority of clinical trial recommendations.

Exercise testing four to six days after infarction, either before or just after discharge, has been recommended as appropriate clinical practice (2). However, NRMI data show that predischarge stress testing is declining and is currently performed in <10% of patients. Reasons for the decline likely include the fact that patients are often discharged before stress testing can be scheduled or safely undertaken, and because many patients undergo coronary arteriography and revascularization before discharge.

Changing outcomes for AMI: Hospital stay, mortality and morbidity. The most impressive trend in the current report is the dramatic decline in hospital stay (Fig. 4). The progressive decline in length of stay may be related to the increasing use of appropriate pharmacologic and mechanical interventions to limit infarct size and recurrent ischemia. However, it is likely that the major impetus for early discharge has been health care reform, specifically the implementation of "critical pathways" and other quality control measures to improve efficiency and reduce the cost of hospital care (20). Although primary PTCA has been advocated as a means of significantly shortening hospital stay, as compared with thrombolytic therapy (21), the differences between length of stay between these two reperfusion modalities in the NRMI experience were rather small.

Hospital mortality declined slightly from 1990 through 1999 in NRMI. The magnitude of mortality decline over

time appeared to be somewhat less among those receiving IV thrombolytic therapy, a population generally considered to be at lower risk (22). Among the higher risk, nonthrombolytic recipients, the fall in mortality may have been related to increasing use of appropriate pharmacologic therapy. These hospital mortality data should be interpreted with caution, however. By definition, they do not account for patients after hospital discharge. Furthermore, they do not account for patients transferred from the NRMI hospital to another institution. The trends in hospital mortality may also have been impacted somewhat by the progressively shorter lengths of hospital stay. However, individual mortality trend analyses for each of the first three days of hospital stay showed significant declines from 1990 through 1999. The mortality data may also have been influenced by changing hospital definitions for AMI over time. With the adoption of newer serum markers, such as troponin I or T, a larger proportion of smaller and lower risk infarctions may have been entered into the registry over time.

**Study limitations.** The limitations of the NRMI have been enumerated previously (3), and primarily include the fact that 1) registry hospitals, though numerous, may not be representative of all U.S. hospitals; 2) there is no on-site validation of data collection forms; and 3) there is no follow-up after hospital discharge. However, a recent study has shown very close agreement between data collected by NRMI coordinators and data collected independently by chart abstractors for the Cooperative Cardiovascular Project in Medicare-eligible patients at hospitals participating in both studies (23). A limitation unique to the present report is the potential for the trend data to be distorted by the changing hospital composition of the registry. To address this concern, data were examined from core hospitals that consistently contributed to the registry over time. In almost all instances, there was close agreement between the overall registry data and data of the core hospitals. Another potential limitation is the fact that, although medication usage is tracked, NRMI does not attempt to assess clinical eligibility for each medication. Thus, failure to use certain medications may reflect contraindications to their use. However, assuming the characteristics of the population does not change substantially over time, the trend analyses still properly reflect the change in frequency of usage of the medications.

Conclusions. These data from the NRMI during the period 1990–1999 show that practitioners are initiating thrombolytic therapy faster, using primary PTCA and proven life-saving adjunctive pharmacotherapy more commonly and discharging patients sooner. There appears to be a declining hospital mortality for AMI. It is likely that many of these favorable trends resulted directly from participation in this registry, which provided participating hospitals with quarterly summaries of their individual hospital data, along with that of hospitals of like size and invasive capability.

Despite these favorable trends, it is evident that more work remains to be done. Over 25% of patients presenting

within the first 12 h of symptom onset with ST segment elevation or LBBB fail to receive a reperfusion intervention; door-to-drug time remains suboptimal, especially the data-to-decision subinterval; and there is the potential to further expand the use of potentially beneficial pharmacotherapy such as aspirin, beta-blockers and ACE inhibitors. Accordingly, the next phase of the registry (NRMI 4) will place increased emphasis on the identification and treatment of patients eligible for reperfusion, while continuing to emphasize rapid delivery of reperfusion interventions and appropriate use of adjunctive pharmacotherapy.

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## **REFERENCES**

- Yusuf S, Sleight P, Held P, McMahon S. Routine medical management of acute myocardial infarction: lessons from overviews of recent randomized controlled trials. Circulation 1990;82 Suppl II:II-117-34.
- Ryan TJ, Anderson JL, Antman EM, et al. ACC/AHA guidelines for the management of patients with acute myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). J Am Coll Cardiol 1996;28:1328–428.
- Rogers WJ, Bowlby LJ, Chandra NC, et al., for the Participants in the National Registry of Myocardial Infarction. Treatment of myocardial infarction in the United States (1990 to 1993): observations from the National Registry of Myocardial Infarction. Circulation 1994;90: 2103–14.
- National Heart Attack Alert Program Coordinating Committee 60
   Minutes to Treatment Working Group. Emergency department: rapid
   identification and treatment of patients with acute myocardial infarction. Ann Emerg Med 1994;23:311–29.
- Gruppo Italiano per lo Studio della Streptochinasa Nell'Infarto Miocardico (GISSI). Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Lancet 1986;1:397–402.
- The TIMI IIIB Investigators. Effects of tissue plasminogen activator and a comparison of early invasive and conservative strategies in unstable angina and non-Q-wave myocardial infarction: results of the TIMI IIIB trial. Circulation 1994;89:1545-56.
- Barron HV, Bowlby LJ, Breen T, et al., for the National Registry of Myocardial Infarction 2 Investigators. Use of reperfusion therapy for acute myocardial infarction in the United States: data from the National Registry of Myocardial Infarction 2. Circulation 1998;97: 1150-6.
- 8. Second International Study of Infarct Survival Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. Lancet 1988;2:349–60.

- Al-Mubarak N, Rogers WJ, Lambrew CT, Bowlby LJ, French WJ, the Second National Registry of Myocardial Infarction (NRMI 2) Investigators. Consultation before thrombolytic therapy in acute myocardial infarction. Am J Cardiol 1998;83:89–93.
- Fuster V, Dyken ML, Vokonas PS, Hennekens C. Aspirin as a therapeutic agent in cardiovascular disease. Circulation 1993;87:659–75.
- Yusuf S, Peto R, Lewis J, Collins R, Sleight P. Beta blockade during and after myocardial infarction: an overview of the randomized trials. Prog Cardiovasc Dis 1985;27:335–71.
- ACE Inhibitor Myocardial Infarction Collaborative Group. Indications for ACE inhibitors in the early treatment of acute myocardial infarction. Circulation 1998;97:2202–12.
- Furberg CD, Psaty BM, Meyer JV. Nifedipine: dose-related increase in mortality in patients with coronary heart disease. Circulation 1995:92:1326-31.
- MacMahon S, Collins R, Peto R, Koster RW, Yusuf S. Effects of prophylactic lidocaine in suspected acute myocardial infarction: an overview of results from the randomized, controlled trials. JAMA 1999;260:1910-6.
- 15. Assessment of the Safety and Efficacy of a New Thrombolytic (ASSENT-2) Investigators. Single-bolus tenecteplase compared with front-loaded alteplase in acute myocardial infarction: the ASSENT-2 double-blind randomised trial. Lancet 1999;354:716–22.
- 16. The TIMI Study Group. Comparison of invasive and conservative strategies after treatment with intravenous tissue plasminogen activator in acute myocardial infarction: results of the Thrombolysis in Myocardial Infarction (TIMI) phase II trial. N Engl J Med 1989;320:618–27.
- Should We Intervene Following Thrombolysis (SWIFT)? Trial Study Group. SWIFT trial of delayed elective intervention vs. conservative treatment after thrombolysis with anistreplase in acute myocardial infarction. BMJ 1991;302:555–60.
- 18. Boden WE, O'Rourke RA, Crawford MH, et al., for the Veterans Affairs Non–Q-Wave Infarction Strategies in Hospital (VANQWISH) Trial Investigators. Outcomes in patients with acute non–Q-wave myocardial infarction randomly assigned to an invasive as compared with a conservative management strategy. N Engl J Med 1998;338: 1785–92.
- FRISC II Investigators. Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. Lancet 1999;354:708–15.
- Pearson SD, Goulart-Fisher D, Lee TH. Critical pathways as a strategy for improving care: problems and potential. Ann Intern Med 1995;123:941–8.
- 21. Stone GW, Grines CL, Browne KF, et al. Implications of recurrent ischemia after reperfusion therapy in acute myocardial infarction: a comparison of thrombolytic therapy and primary angioplasty. J Am Coll Cardiol 1995;26:66–72.
- Cragg DR, Friedman HZ, Bonema JD, et al. Outcome of patients with acute myocardial infarction who are ineligible for thrombolytic therapy. Ann Intern Med 1991;115:173–7.
- Every NR, Frederick PD, Robinson M, Sugarman J, Bowlby L, Barron HV. A comparison of the National Registry of Myocardial Infarction 2 with the Cooperative Cardiovascular Project. J Am Coll Cardiol 1998;33:1886-94.