

SPECIAL ARTICLES

REGIONAL VARIATION ACROSS THE UNITED STATES IN THE MANAGEMENT OF ACUTE MYOCARDIAL INFARCTION

LOUISE PILOTE, M.D., M.P.H., ROBERT M. CALIFF, M.D., SHELLY SAPP, M.S., DAVE P. MILLER, M.S., DANIEL B. MARK, M.D., M.P.H., W. DOUGLAS WEAVER, M.D., JOEL M. GORE, M.D., PAUL W. ARMSTRONG, M.D., E. MAGNUS OHMAN, M.D., AND ERIC J. TOPOL, M.D.,
FOR THE GUSTO-1 INVESTIGATORS

Abstract Background. Differences in the management of acute myocardial infarction have been reported among countries, but few studies have investigated this issue in regions of the United States.

Methods. We compared the management of acute myocardial infarction among census regions across the United States, using data from the first Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries trial (GUSTO-1) comprising 21,772 patients, and from the American Hospital Association.

Results. We found substantial regional variation in the management of acute myocardial infarction in the United States. Beta-blockers (prescribed for a range of 55 to 81 percent of patients in the various regions), nitrates (prescribed for 61 to 77 percent), and angiotensin-converting-enzyme inhibitors (prescribed for 18 to 23 percent) were used most often in New England, whereas calcium-channel blockers (31 to 42 percent) and lidocaine (14 to 43 percent) were used least often there. Similarly, the proportion of patients undergoing various cardiac procedures

differed among regions (range for angiography, 52 to 81 percent of patients; angioplasty, 22 to 35 percent; and coronary-artery bypass surgery, 9 to 17 percent) and was lowest in New England. The regional use of cardiac procedures was closely related to their availability, except in New England. After the analysis was adjusted for clinical and hospital variables, patients in New England were found to be less likely to undergo angiography than patients in the other regions (odds ratio, 0.37; 95 percent confidence interval, 0.32 to 0.42). There was no apparent relation between the use of cardiac procedures and rates of recurrent infarction or death at 30 days or 1 year.

Conclusions. There is substantial regional variation in the use of cardiac medications and procedures to manage acute myocardial infarction in the United States. The use and availability of cardiac procedures are closely related. The management of acute myocardial infarction in New England is atypical in that the relatively limited availability of cardiac procedures does not account for their relatively low use in that region. (*N Engl J Med* 1995;333:565-72.)

EACH year, more than a million coronary angiography procedures, approximately 400,000 angioplasties, and 400,000 coronary-artery bypass operations are performed in the United States.¹ Coronary artery disease is highly prevalent, and its management often involves costly techniques. Thus, understanding the proper role of invasive diagnostic and therapeutic procedures is critical for the provision of high-quality, cost-effective care.

Several studies have reported differences among countries in the management of acute myocardial infarction and have assessed the effect of the intensity of care on clinical outcomes.²⁻⁵ Important differences have been found, including a much greater use of cardiac procedures in the United States than in other countries.⁵ We studied the extent of variation among regions of the United States in the management of acute myocardial infarction.

To evaluate differences in patterns of care among U.S. Census regions and to determine the principal factors responsible, we examined data from the first Global Utilization of Streptokinase and Tissue Plasmin-

ogen Activator for Occluded Coronary Arteries trial (GUSTO-1). This randomized clinical trial of thrombolytic strategies included more than 23,000 patients with confirmed acute myocardial infarction from the United States.⁶ That trial allowed practice patterns to be observed, because decisions about all medications except aspirin and thrombolytic agents and about all cardiac procedures were left to the discretion of the treating physicians.

METHODS

Study Population

All 6306 U.S. hospitals with acute care facilities were invited to participate in the study; 650 (10 percent) agreed to do so. The results of the primary study, conducted between December 1990 and February 1993, have been published previously.⁶ The study included patients with acute myocardial infarction presenting within six hours of the onset of chest pain who were eligible for thrombolytic therapy. No patients were excluded on the basis of age, the presence of cardiogenic shock, or previous coronary-artery bypass surgery.

The patients were randomly assigned to four different thrombolytic strategies: streptokinase with subcutaneous heparin, streptokinase with intravenous heparin, the administration of accelerated tissue plasminogen activator (t-PA) with intravenous heparin, and the combination of t-PA and streptokinase with intravenous heparin. Since randomization to the four treatment groups was balanced across regions of the United States, the analysis reported here does not take into account the treatment assignments. Except for treatment with thrombolytic agents, aspirin, and, where appropriate, beta-blockers, the management of myocardial infarction was left to the discretion of the treating physicians. Accordingly, we excluded 1292 patients who were randomly selected to undergo angiography at various intervals after their acute myocardial infarctions, because their cardiac procedures were dictated by the research proto-

From the Cleveland Clinic Foundation, Cleveland (L.P., S.S., D.P.M., E.J.T.); Duke University Medical Center, Durham, N.C. (R.M.C., D.B.M., E.M.O.); the University of Washington, Seattle (W.D.W.); University of Massachusetts Medical Center, Worcester (J.M.G.); and the University of Edmonton, Edmonton, Alta., Canada (P.W.A.). Address reprint requests to Dr. Topol at the Cleveland Clinic Foundation, Department of Cardiology, Desk F25, 9500 Euclid Ave., Cleveland, OH 44195.

Supported by a grant from the Heart and Stroke Foundation of Canada (to Dr. Pilote).

col.⁷ Another 41 patients were excluded because they had not had myocardial infarctions.

U.S. Census Regions

We divided the patients into subgroups according to the major regions defined by the U.S. Census: New England, Mid-Atlantic, South Atlantic, East North Central, East South Central, West North Central, West South Central, Mountain, and Pacific (see the Appendix). We grouped the East South Central and West South Central regions together as South Central because of the comparatively small numbers of patients from those regions.

Characteristics of the Patients

Prospectively collected information obtained from the case-report forms in the original study included the demographic and clinical characteristics of the patients at the time of enrollment and information on their hospital courses up to the time of discharge.⁶ Data on patients who were transferred to a second hospital were also collected up to the time of their discharge from that hospital. Deaths within 30 days and 1 year after the acute myocardial infarction were ascertained on the basis of postcards returned by the patients' families or through telephone contact or registered mail. Data on the quality of life were collected by interviewing a random one-eighth of the enrolled patients, as previously described.⁴

Characteristics of the Hospitals

Data on the hospitals, including whether they had facilities for coronary angiography and revascularization, were obtained from the 1993 data base of the American Hospital Association.⁹ The study sites were matched to this data base so that the data collected would be specific to the site. The matching was 95 percent complete. The 27 sites without matching files were contacted by telephone when data on the hospitals were missing. A total of 431 patients (2 percent of the overall group) remained for whom hospital data were missing. These patients were excluded only from the multiple regression analysis.

Statistical Analysis

To investigate regional variation in the use of cardiac procedures, we performed a stepwise logistic-regression analysis. The following demographic and clinical predictors were included in a clinical model:

recurrent ischemia, second infarction, shock, congestive heart failure, acute mitral regurgitation, arrhythmia, time to thrombolytic treatment, age, sex, family history of heart disease, hypercholesterolemia, diabetes, smoking, hypertension, infarct location, Killip class, previous angioplasty, and previous myocardial infarction. All the variables were dichotomous, except for age and time to thrombolytic treatment, which were included as continuous variables; Killip class, an ordinal variable that was included as a continuous variable; and infarct location, a categorical variable that was transformed into the dichotomous variables anterior and inferior.

A second model, the hospital-facilities model, was created by adding the information on hospital facilities to this clinical model. The availability of angiography, angioplasty, and bypass surgery was included in the form of patient-specific dichotomous variables. The effect of the eight regions was introduced into the second model by creating seven dummy variables, with the Mid-Atlantic region used as the reference group.

The logistic-regression models were developed from data on a random sample of 80 percent of the patients; the model was then validated with reference to the remaining 20 percent.⁹ After validation, the model was fitted to the entire data base to provide more exact estimates of measures. The validated models for the full set of data are reported here. Among the patients eligible for inclusion in the analysis, 12 percent had at least one missing demographic or hospital variable. We report results for the patients for whom data were complete; when we imputed data for the patients with missing variables, the results were similar.^{10,11}

RESULTS

Study Patients

A total of 21,772 U.S. patients were enrolled in the study after the exclusion of patients enrolled in the angiographic substudy. The geographic distribution was as follows: New England, 2318 patients (11 percent of the total); Mid-Atlantic, 3758 (17 percent); South Atlantic, 5296 (24 percent); East North Central, 3616 (17 percent); South Central, 1333 (6 percent); West North Central, 1551 (7 percent); Mountain, 1839 (8 percent); and Pacific, 2061 (9 percent). These patients were

Table 1. Demographic and Clinical Characteristics of the Study Patients, According to Region of the United States.

| CHARACTERISTIC* | NEW | MID- | SOUTH | EAST | SOUTH | WEST | MOUNTAIN | PACIFIC |
|--|-----------------------|------------------------|------------------------|--------------------------------|-----------------------|--------------------------------|----------|---------|
| | ENGLAND (N = 2318) | ATLANTIC (N = 3758) | ATLANTIC (N = 5296) | NORTH CENTRAL (N = 3616) | CENTRAL (N = 1333) | NORTH CENTRAL (N = 1551) | | |
| Demographic variables | | | | | | | | |
| Median age (yr) | 62 | 62 | 61 | 61 | 59 | 62 | 62 | 61 |
| Male sex (% of patients) | 72 | 72 | 72 | 71 | 77 | 71 | 74 | 75 |
| Clinical history (% of patients) | | | | | | | | |
| MI | 18 | 16 | 17 | 17 | 18 | 18 | 19 | 17 |
| Angina | 35 | 34 | 35 | 36 | 36 | 43 | 35 | 34 |
| Cardiac risk factors (% of patients) | | | | | | | | |
| Diabetes | 19 | 17 | 17 | 17 | 14 | 16 | 15 | 15 |
| Hypertension | 44 | 43 | 44 | 44 | 43 | 43 | 40 | 41 |
| Smoking | 41 | 41 | 45 | 45 | 51 | 41 | 40 | 41 |
| Family history of heart disease | 48 | 48 | 47 | 52 | 52 | 47 | 48 | 46 |
| Hypercholesterolemia | 37 | 39 | 39 | 34 | 34 | 45 | 36 | 41 |
| Characteristics of MI | | | | | | | | |
| Killip class 1 (% of patients) | 84 | 86 | 89 | 87 | 90 | 85 | 87 | 89 |
| Anterior location (% of patients) | 37 | 37 | 37 | 34 | 36 | 35 | 36 | 37 |
| Median peak creatine kinase (U/liter) | 1565 | 1576 | 1542 | 1587 | 1694 | 1430 | 1524 | 1414 |
| Median time to thrombolysis (hr) | 2.6 | 2.8 | 2.8 | 2.7 | 2.8 | 2.5 | 2.5 | 2.5 |
| Complications of MI (% of patients) | | | | | | | | |
| Recurrent ischemia | 27 | 27 | 22 | 20 | 11 | 29 | 20 | 18 |
| Shock | 7 | 7 | 8 | 7 | 5 | 7 | 9 | 6 |
| Congestive heart failure | 21 | 20 | 18 | 18 | 12 | 20 | 18 | 15 |
| Ventricular arrhythmia | 14 | 14 | 15 | 15 | 12 | 14 | 15 | 15 |
| Asystole or AV block | 17 | 15 | 16 | 16 | 14 | 19 | 16 | 15 |
| Atrial fibrillation | 10 | 10 | 10 | 10 | 10 | 13 | 11 | 10 |
| VSD, tamponade, or acute MR | 3 | 3 | 3 | 4 | 3 | 4 | 4 | 3 |

*MI denotes myocardial infarction, AV atrioventricular, VSD ventricular septal defect, and MR mitral regurgitation.

treated at 596 participating hospitals (mean, 75 per region). In each region, the participating hospitals represented an average of 29 percent of the hospitals with coronary care units, 15 percent of those with intensive care units, and 13 percent of those with emergency departments.

Demographic and Clinical Characteristics

Overall, the demographic and clinical profile of the patients was similar across the United States (Table 1). The only notable differences were in the prevalence of current smoking (range among regions, 40 to 51 percent of the patients) and hypercholesterolemia (34 to 45 percent) and in the incidence of recurrent ischemia (11 to 29 percent).

Use of Cardiac Medications

The use of cardiac medications in the hospitals varied greatly across the United States (Table 2). New England had the highest percentages of patients for whom oral beta-blockers, nitrates, and angiotensin-converting-enzyme inhibitors were prescribed, whereas it had the lowest percentages using calcium-channel blockers, digitalis, and other positive inotropic agents. Prescriptions written at discharge followed a similar trend, with New England having the highest percentages of patients receiving beta-blockers, angiotensin-converting-enzyme inhibitors, and nitrates and the lowest percentages receiving calcium-channel blockers and digitalis.

Use of Cardiac Procedures

During hospitalization, 71 percent of all study patients underwent angiography, 30 percent underwent angioplasty, and 13 percent underwent coronary-artery bypass surgery. As with the use of medications, the use of cardiac procedures differed markedly among regions, and the pattern in New England was distinct from that of the other regions (Table 3). The propor-

tion of patients undergoing angiography ranged from 52 percent in New England to 81 percent in the South Central region. The use of angioplasty ranged from 22 percent in New England to 35 percent in the West North Central region, and that of coronary-artery bypass surgery ranged from 9 percent in New England to 17 percent in the South Central region. Among the patients who underwent angiography, however, there was very little regional variation in the proportions who subsequently underwent revascularization. Despite varying percentages of patients who underwent angiography, the extent of coronary vessel disease and the median left ventricular ejection fraction were similar across regions.

The use of other cardiac procedures in the acute care unit also differed regionally. Temporary transvenous pacemakers were used in 10 percent of all patients (range among regions, 7 to 14 percent), pulmonary-artery catheters in 19 percent (range, 15 to 22 percent), intraaortic balloon pumps in 6 percent (range, 3 to 7 percent), and mechanical ventilators in 17 percent (range, 14 to 20 percent).

Other Aspects of Care

The median stays in the hospital and the acute care unit did not differ substantially across the United States (range, seven to nine days and three to four days, respectively). The proportions of patients who were transferred to a second hospital ranged from 11 percent in the South Central region to 31 percent in the Mid-Atlantic and South Atlantic regions; in New England, this proportion was 25 percent. Information on the treatment of patients after an acute myocardial infarction was recorded until discharge, at both the initial and the transfer hospital.

Cardiac Care Facilities

Cardiac care facilities differed greatly across the United States among the hospitals participating in the

Table 2. Use of Cardiac Medications to Treat the Study Patients, According to Region of the United States.

| MEDICATION | NEW ENGLAND | MID-ATLANTIC | SOUTH ATLANTIC | EAST NORTH CENTRAL | SOUTH CENTRAL | WEST NORTH CENTRAL | MOUNTAIN | PACIFIC |
|---|-------------|--------------|----------------|--------------------|---------------|--------------------|------------|------------|
| | (N = 2318) | (N = 3758) | (N = 5296) | (N = 3616) | (N = 1333) | (N = 1551) | (N = 1839) | (N = 2061) |
| <i>percentage of patients</i> | | | | | | | | |
| In hospital | | | | | | | | |
| Beta-blocker | | | | | | | | |
| Oral | 81 | 77 | 74 | 70 | 70 | 72 | 55 | 73 |
| Intravenous | 51 | 55 | 54 | 54 | 52 | 55 | 70 | 56 |
| Lidocaine | 18 | 23 | 28 | 26 | 25 | 43 | 14 | 30 |
| Calcium-channel blocker | 31 | 35 | 36 | 42 | 42 | 36 | 39 | 42 |
| Positive inotropic agent | | | | | | | | |
| Digitalis | 14 | 16 | 18 | 17 | 20 | 17 | 18 | 17 |
| Other | 19 | 22 | 24 | 26 | 24 | 26 | 24 | 21 |
| Nitrate | | | | | | | | |
| Oral | 77 | 77 | 75 | 73 | 69 | 61 | 63 | 73 |
| Intravenous | 87 | 86 | 89 | 92 | 78 | 88 | 81 | 76 |
| Angiotensin-converting-enzyme inhibitor | 23 | 20 | 20 | 20 | 18 | 22 | 19 | 18 |
| At discharge | | | | | | | | |
| Beta-blocker | 71 | 64 | 57 | 54 | 49 | 57 | 47 | 53 |
| Calcium-channel blocker | 24 | 26 | 28 | 34 | 32 | 25 | 29 | 32 |
| Digitalis | 11 | 13 | 14 | 14 | 16 | 11 | 14 | 14 |
| Nitrate | 51 | 50 | 47 | 49 | 48 | 38 | 48 | 45 |
| Angiotensin-converting-enzyme inhibitor | 18 | 17 | 15 | 16 | 13 | 17 | 15 | 13 |

Table 3. Use of Cardiac Procedures in the Treatment of the Study Patients, According to Region of the United States.

| VARIABLE | NEW ENGLAND (N = 2318) | MID-ATLANTIC (N = 3758) | SOUTH ATLANTIC (N = 5296) | EAST NORTH CENTRAL (N = 3616) | SOUTH CENTRAL (N = 1333) | WEST NORTH CENTRAL (N = 1551) | MOUNTAIN (N = 1839) | PACIFIC (N = 2061) |
|---|------------------------|-------------------------|---------------------------|-------------------------------|--------------------------|-------------------------------|---------------------|--------------------|
| Procedure (% of patients) | | | | | | | | |
| Angiography | 52 | 67 | 77 | 79 | 81 | 72 | 72 | 66 |
| Angioplasty | 22 | 26 | 33 | 33 | 34 | 35 | 34 | 24 |
| Coronary surgery | 9 | 12 | 14 | 14 | 17 | 14 | 13 | 12 |
| Characteristics of angiography | | | | | | | | |
| Elective (% of patients) | 73 | 77 | 87 | 84 | 88 | 75 | 81 | 86 |
| Diseased coronary vessels (% of patients) | | | | | | | | |
| None | 12 | 11 | 13 | 11 | 11 | 10 | 12 | 13 |
| One | 33 | 34 | 35 | 36 | 35 | 34 | 37 | 35 |
| Two | 31 | 31 | 29 | 30 | 31 | 28 | 28 | 29 |
| Three | 21 | 22 | 22 | 21 | 21 | 24 | 20 | 22 |
| Left main | 3 | 2 | 2 | 2 | 3 | 3 | 3 | 2 |
| Left ventricular ejection fraction (%)* | 50 | 50 | 51 | 50 | 50 | 51 | 53 | 55 |
| Procedure following angiography (% of patients) | | | | | | | | |
| Angioplasty | 43 | 39 | 43 | 42 | 42 | 48 | 47 | 37 |
| Coronary-artery bypass surgery | 18 | 18 | 18 | 18 | 21 | 19 | 18 | 18 |

*The values represent the median left ventricular ejection fractions.

study (Table 4). The use of cardiac procedures was directly related to the availability of cardiac care facilities, particularly those for angiography (Fig. 1). In general, cardiac procedures were least used and least available in New England, whereas they were most used and most available in the South Central region.

Clinical Outcomes

Regionally, mortality rates ranged from 5.4 to 7.2 percent in the hospital ($P=0.21$), from 5.8 to 7.7 percent at 30 days ($P=0.34$), and from 8.6 to 10.3 percent at 1 year ($P=0.24$), and rates of second infarctions in the hospital ranged from 3.1 to 4.5 percent ($P=0.35$) (Table 5). Other clinical outcomes, including function-

al status and the incidence of chest pain and dyspnea, were similar across the United States.⁴

Explaining Regional Variation in Management

Angiography was used as a marker of regional variation because after patients undergo this procedure, there is little further regional variation in rates of revascularization (Table 3). The expected rates of angiography generated by our clinical model were quite different from the observed rates but were quite constant across the country, in accordance with the homogeneous clinical profiles (Table 6). The expected rates generated by our hospital-facilities model were generally closer to the observed rates, except in New England, where the expected and observed rates still differed

Table 4. Availability of Cardiac Procedures and Characteristics of Study Hospitals, According to Region of the United States.

| VARIABLE | NEW ENGLAND (N = 2318) | MID-ATLANTIC (N = 3758) | SOUTH ATLANTIC (N = 5296) | EAST NORTH CENTRAL (N = 3616) | SOUTH CENTRAL (N = 1333) | WEST NORTH CENTRAL (N = 1551) | MOUNTAIN (N = 1839) | PACIFIC (N = 2061) |
|---|------------------------|-------------------------|---------------------------|-------------------------------|--------------------------|-------------------------------|---------------------|--------------------|
| No. of hospitals | 51 | 87 | 124 | 104 | 54 | 44 | 55 | 50 |
| Percentage of patients with access to treatment | | | | | | | | |
| Angiography | 68 | 64 | 81 | 92 | 91 | 78 | 73 | 76 |
| Angioplasty | 35 | 45 | 46 | 66 | 81 | 74 | 55 | 60 |
| Bypass surgery | 33 | 43 | 46 | 62 | 83 | 73 | 56 | 47 |
| Acute care | 32 | 58 | 72 | 60 | 61 | 56 | 35 | 38 |
| Median size (no. of beds) | | | | | | | | |
| All beds | 310 | 390 | 369 | 402 | 468 | 400 | 262 | 250 |
| Acute care beds | 9 | 10 | 12 | 12 | 12 | 10 | 10 | 10 |
| Type of ownership (% of hospitals)* | | | | | | | | |
| Government | 5 | 6 | 17 | 6 | 25 | 9 | 9 | 23 |
| Non-government | 95 | 93 | 75 | 93 | 57 | 87 | 79 | 74 |
| Investors | 1 | 2 | 9 | 0 | 19 | 4 | 12 | 3 |
| Rural location (% of hospitals) | 16 | 3 | 17 | 9 | 8 | 19 | 13 | 4 |
| Approved for residency (% of hospitals) | 49 | 67 | 40 | 56 | 42 | 56 | 44 | 39 |

*Percentages for each region do not all total 100 because of rounding.

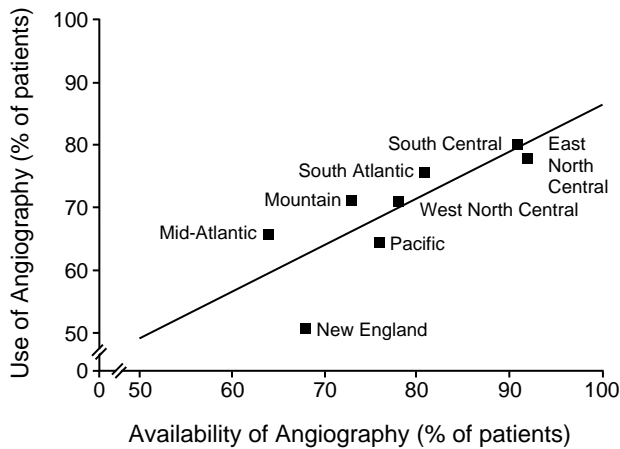


Figure 1. Positive Association between the Use and the Availability of Coronary Angiography in Regions of the United States. The outlier status of New England in this analysis is supported by the studentized-residual statistic, which is the distance of the observed value from the regression line, adjusted for the model's variability. The studentized residual for New England was greater than 4, whereas the remaining seven residuals were well within the expected bounds of -2 to 2.

considerably. This trend is also apparent in Figure 1, where the association between the availability of angiography and its use is quite strong for most regions except New England, which appears to be atypical.

Figure 2 shows the odds ratios and 95 percent confidence intervals for the factors influencing the use of angiography before discharge from the hospital. After adjustment for potentially confounding clinical and demographic variables, regional variation in the likelihood of undergoing angiography prevailed. The degree

of variation was less when hospital characteristics were added to the model, yielding the following odds ratios (and 95 percent confidence intervals) for the regions as compared with the Mid-Atlantic region (the reference category): South Atlantic, 1.6 (1.4 to 1.8); South Central, 1.5 (1.3 to 1.8); East North Central, 1.6 (1.4 to 1.8); West North Central, 1.0 (0.9 to 1.2); Mountain, 1.3 (1.1 to 1.5); and Pacific, 0.9 (0.8 to 1.0). However, patients treated in New England were much less likely to undergo angiography than patients treated in other regions (odds ratio, 0.37; 95 percent confidence interval, 0.32 to 0.42).

The association between treatment in New England and the decreased use of angiography was stronger than the associations found for most clinical and hospital characteristics except for the association of recurrent ischemia (odds ratio, 2.5; 95 percent confidence interval, 2.2 to 2.7) and on-site angiography facilities (odds ratio, 1.7; 95 percent confidence interval, 1.5 to 1.9). There was a strong interaction between treatment in New England and recurrent ischemia (odds ratio, 2.7; 95 percent confidence interval, 2.0 to 3.6). Patients with recurrent ischemia were very likely to undergo angiography in all census regions except New England, where the procedure was considerably less likely to be performed.

DISCUSSION

This study demonstrated marked regional variation in the management of acute myocardial infarction in the United States. The variation was found in the use of both medications and procedures. The discordance between the approach to management in New England and that in the other regions was a surprising finding;

Table 5. Clinical Outcomes of the Study Patients, According to Region of the United States.

| VARIABLE* | NEW ENGLAND (N = 2318) | MID-ATLANTIC (N = 3758) | SOUTH ATLANTIC (N = 5296) | EAST NORTH CENTRAL (N = 3616) | SOUTH CENTRAL (N = 1333) | WEST NORTH CENTRAL (N = 1551) | MOUNTAIN (N = 1839) | PACIFIC (N = 2061) |
|---|------------------------|-------------------------|---------------------------|-------------------------------|--------------------------|-------------------------------|---------------------|--------------------|
| Events in the hospital | | | | | | | | |
| Reinfarction | | | | | | | | |
| % of Patients | 4.1 | 4.1 | 3.8 | 3.7 | 3.9 | 4.5 | 3.3 | 3.1 |
| 95% CI | 3.3-4.9 | 3.5-4.7 | 3.3-4.3 | 3.1-4.3 | 2.9-4.9 | 3.5-5.5 | 2.5-4.1 | 2.4-3.8 |
| Stroke | | | | | | | | |
| % of Patients | 1.5 | 1.4 | 1.6 | 1.6 | 1.6 | 1.8 | 1.2 | 1.5 |
| 95% CI | 1.0-2.0 | 1.0-1.8 | 1.2-2.0 | 1.2-2.0 | 0.9-2.3 | 1.1-2.5 | 0.7-1.7 | 1.0-2.0 |
| Death | | | | | | | | |
| % of Patients | 6.7 | 7.1 | 7.0 | 6.9 | 5.4 | 7.2 | 6.0 | 5.8 |
| 95% CI | 5.7-7.7 | 6.3-7.9 | 6.3-7.7 | 6.1-7.7 | 4.2-6.6 | 5.9-8.5 | 4.9-7.1 | 4.8-6.8 |
| Death within 30 days | | | | | | | | |
| % of Patients | 6.7 | 7.3 | 7.3 | 7.2 | 5.8 | 7.7 | 6.8 | 6.2 |
| 95% CI | 5.7-7.7 | 6.5-8.1 | 6.6-8.0 | 6.4-8.0 | 4.5-7.1 | 6.4-9.0 | 5.6-8.0 | 5.2-7.2 |
| Death by 1 year | | | | | | | | |
| % of Patients | 10.1 | 10.0 | 10.2 | 10.3 | 8.6 | 9.6 | 8.9 | 8.7 |
| 95% CI | 8.9-11.3 | 9.0-11.0 | 9.4-11.0 | 9.3-11.3 | 7.1-10.1 | 8.1-11.1 | 7.6-10.2 | 7.5-9.9 |
| Functional status at 1 yr† | | | | | | | | |
| Duke activity status index‡ | 32 (23, 50) | 37 (24, 51) | 32 (19, 46) | 36 (23, 50) | 37 (22, 51) | 35 (24, 46) | 37 (23, 51) | 35 (20, 50) |
| Any exertional chest pain (% of patients) | 19 | 20 | 26 | 23 | 19 | 18 | 21 | 16 |
| Any exertional dyspnea (% of patients) | 29 | 23 | 33 | 28 | 27 | 28 | 29 | 30 |

*CI denotes confidence interval.

†Functional status and symptoms were measured in the following numbers of patients: New England, 227; Mid-Atlantic, 383; South Atlantic, 544; East North Central, 389; South Central, 160; West North Central, 187; Mountain, 214; and Pacific, 172. Chest pain and dyspnea were assessed by interviewing the patients with the Rose questionnaires.⁴

‡Values shown are median scores, followed in parentheses by the 25th and 75th percentiles. Scores are expressed on a scale ranging from 0 (worst) to 52 (best).

New England had a lower rate of use of procedures and a more evidence-based use of medications.¹²⁻¹⁴

Regional variation in the use of cardiac procedures was not explained by differences in patient profiles or in the incidence of complications related to myocardial infarction. However, we found a strong relation between the availability of angiography in a region and the number of procedures performed there. This association was less strong in New England than in the other regions, suggesting that there are other important explanations for the different way of managing acute myocardial infarction in New England.

The use of cardiac medications during hospitalization and at discharge varied greatly across the United States. New England had the highest percentage of patients for whom medications shown to decrease mortality after an acute myocardial infarction were prescribed, as compared with other regions, and the lowest percentage of patients for whom medications shown to have no benefit or even a detrimental effect were prescribed. In keeping with the findings of Rogers and coworkers,¹⁵ beta-blockers were underused in most other regions, whereas calcium-channel blockers and prophylactic lidocaine were overused.

There have been previous reports of regional variation in medical practice,¹⁶⁻¹⁹ and an association between the availability of cardiac care services and the use of cardiac procedures has been noted,^{20,21} as it was in our study. Every and coworkers found that patients with acute myocardial infarction who were admitted to hospitals with angiography facilities were about three times more likely to undergo angiography than patients admitted to hospitals without such facilities.²⁰ Blustein showed a similar association in New York State.²¹ In our study, the same association between the availability and the use of cardiac procedures was observed, but it did not entirely explain the regional variation and certainly did not explain the more conservative approach in New England.

A number of hypotheses could explain the observed

Table 6. Expected and Observed Rates of Angiography, According to Region of the United States.

| REGION | OBSERVED RATE | EXPECTED RATE | |
|--------------------|---------------|-----------------|----------------------------|
| | | CLINICAL MODEL* | HOSPITAL-FACILITIES MODEL† |
| percent | | | |
| New England | 52 | 73 | 70 |
| Mid-Atlantic | 68 | 72 | 70 |
| South Atlantic | 78 | 72 | 72 |
| East North Central | 80 | 72 | 75 |
| South Central | 81 | 73 | 77 |
| West North Central | 72 | 73 | 75 |
| Mountain | 73 | 72 | 71 |
| Pacific | 67 | 72 | 72 |

*This model included demographic and clinical variables predictive of myocardial infarction.

†This model included variables related to hospital facilities in addition to the demographic and clinical variables.

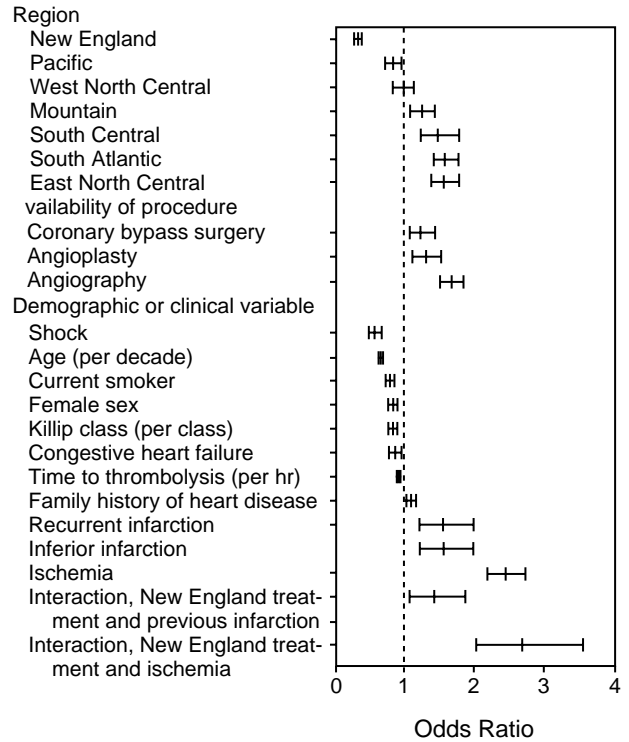


Figure 2. Odds Ratios and 95 Percent Confidence Intervals for Various Factors That Influenced the Use of Angiography before Hospital Discharge in 21,772 Study Patients with Acute Myocardial Infarction.

The Mid-Atlantic region was used as the reference category for the regional comparison. Odds ratios to the left of the dashed line indicate that angiography is less likely, and those to the right of the line that it is more likely.

variation in the management of acute myocardial infarction. First, medical uncertainty accounts for some of the variation. Despite the publication of several clinical trials and practice guidelines on the management of myocardial infarction after thrombolysis, physicians may remain uncertain about the applicability of a study or guideline to their patients.^{22,23} The interpretation and applications of such information may be affected by the presence or absence of leading medical centers in a given region or by the ratio of specialists to generalists.²⁴ Second, physicians' attitudes and patterns of testing and the preferences of patients may differ from region to region and may affect the selection of treatment.¹⁸ Third, inappropriate use of cardiac procedures may cause some of the variation.^{25,26} Finally, nonclinical factors, such as the insurance status of patients and state regulations, may influence the decision-making process.²⁷ Although the prevalence of managed care could potentially explain the lower rates of cardiac procedures in New England, this hypothesis would be inconsistent with the higher rates of procedures in the Pacific region, where managed care is particularly prevalent.

The management of acute myocardial infarction in New England appears to be at a halfway point between the less invasive approach previously reported in Cana-

da and the more invasive approach in the United States as a whole.^{2,4} The rates of angiography, angioplasty, and surgery among all the Canadian patients in the GUSTO-1 study were much lower than any of the regional rates in the United States. Marked differences in the approach to management did not result in marked differences in mortality and rates of reinfarction, although the study by Mark and coworkers suggested that adjusted one-year mortality was higher in Canada, and quality of life and functional status lower.⁴ Too conservative an approach may result in worse outcomes, but an aggressive approach will be more expensive and may not yield benefits commensurate with the extra costs. Identifying the proper balance between extra clinical benefits and extra costs is thus of great importance.

The present study was limited by our ability to demonstrate a direct relation between variation in procedure rates and clinical outcomes. First, this study had limited power to detect short-term differences in mortality and functional status among the eight regions. Thirty-day mortality in New England was 6.7 percent, as compared with a mean of 7.0 percent for the other seven regions. The power of our study to detect a difference in mortality of one percentage point was only 42 percent, and its power to detect a difference of two percentage points was 92 percent. Second, 1 year is too short a time in which to observe differences in outcomes as a function of revascularization; New England's change in rank with regard to mortality — from third lowest after 30 days to third highest after 1 year — may, however, be a meaningful trend. Indeed, in randomized trials comparing coronary-artery surgery with medical therapy, the survival curves do not favor surgery until after the first year.²⁸ Finally, we lacked information on the patients' clinical courses and on the frequency of revascularization procedures between discharge and the 30-day and 1-year follow-up points that might have influenced the outcomes.

Another limitation of the study was that not all hospitals in each region participated. The question of selection remains an issue; 72 percent of hospital sites overall had angiography available on the premises, but only 61 percent of sites in New England had such facilities. Similarly, facilities for angiography were available in 28 percent of the sites in the data base of the American Hospital Association but in only 23 percent of those in New England. Sites where angiography was available were oversampled, probably because patients with myocardial infarction are more likely to be treated there first; however, the general regional trend was very similar between the GUSTO-1 sites and those in the American Hospital Association data base.

In conclusion, we have demonstrated substantial regional variation in the management of acute myocardial infarction across the United States. A more evidence-based approach to the use of medications was apparent in New England. The regional variation in the use of cardiac procedures was not due to clinical differences among regions but was instead mostly related to the availability of these procedures. With respect

to the management of acute myocardial infarction, New England was atypical, in that the somewhat lower availability of procedures in that region did not account for their substantially more limited use.

We are indebted to Dawn Dykstra for assistance with data management, to Vesna Savor for clerical assistance, and to the GUSTO steering committee for reviewing the manuscript.

APPENDIX

The U.S. Census regions described in this article are as follows: *New England* — Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, and Connecticut; *Mid-Atlantic* — New York, New Jersey, and Pennsylvania; *South Atlantic* — Delaware, Maryland, District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Georgia, and Florida; *East North Central* — Ohio, Indiana, Illinois, Michigan, and Wisconsin; *East South Central* — Kentucky, Tennessee, Alabama, and Mississippi; *West North Central* — Minnesota, Iowa, Missouri, North Dakota, South Dakota, Nebraska, and Kansas; *West South Central* — Arkansas, Louisiana, Oklahoma, and Texas; *Mountain* — Montana, Idaho, Wyoming, Colorado, New Mexico, Arizona, Utah, and Nevada; and *Pacific* — Washington, Oregon, California, Alaska, and Hawaii.

REFERENCES

1. Resnekov L, Chediak J, Hirsh J, Lewis HD Jr. Antithrombotic agents in coronary artery disease. *Chest* 1989;95:Suppl:52S-72S.
2. Pilote L, Racine N, Hlatky MA. Differences in the treatment of myocardial infarction in the United States and Canada: a comparison of two university hospitals. *Arch Intern Med* 1994;154:1090-6.
3. Rouleau JL, Moyé LA, Pfeffer MA, et al. A comparison of management patterns after acute myocardial infarction in Canada and the United States. *N Engl J Med* 1993;328:779-84.
4. Mark DB, Naylor CD, Hlatky MA, et al. Use of medical resources and quality of life after acute myocardial infarction in Canada and the United States. *N Engl J Med* 1994;331:1130-5.
5. Van de Werf F, Topol EJ, Lee KL, et al. Variations in patient management and outcomes for acute myocardial infarction in the United States and other countries: results from the GUSTO trial. *JAMA* 1995;273:1586-91.
6. The GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. *N Engl J Med* 1993;329:673-82.
7. The GUSTO Angiographic Investigators. The effects of tissue plasminogen activator, streptokinase, or both on coronary-artery patency, ventricular function, and survival after acute myocardial infarction. *N Engl J Med* 1993;329:1615-22.
8. American Hospital Association guide to the health care field. Chicago: American Hospital Association, 1993.
9. Neter J, Wasserman W, Kutner MH. Applied linear statistical models. 3rd ed. Homewood, Ill.: Richard D. Irwin, 1990:466-70.
10. Lee KL, Woodlief LH, Topol EJ, et al. Predictors of 30-day mortality in the era of reperfusion for acute myocardial infarction: results from an international trial of 41,021 patients. *Circulation* 1995;91:1659-68.
11. Little RJA. Regression with missing X's: a review. *J Am Stat Assoc* 1992;87:1227-37.
12. Teo KK, Yusuf S, Furberg CD. Effects of prophylactic antiarrhythmic drug therapy in acute myocardial infarction: an overview of results from randomized controlled trials. *JAMA* 1993;270:1589-95.
13. Lamas GA, Pfeffer MA, Hamm P, Wertheimer J, Rouleau J-L, Braunwald E. Do the results of randomized clinical trials of cardiovascular drugs influence medical practice? *N Engl J Med* 1992;327:241-7.
14. 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-117-II-134.
15. Rogers WR, Bowlby LJ, Chandra NC, et al. Treatment of myocardial infarction in the United States (1990 to 1993): observations from the National Registry of Myocardial Infarction. *Circulation* 1994;90:2103-14.
16. Topol EJ, Ellis SG, Cosgrove DM, et al. Analysis of coronary angioplasty practice in the United States with an insurance-claims data base. *Circulation* 1993;87:1489-97.
17. The Cardiology Working Group. Cardiology and the quality of medical practice. *JAMA* 1991;265:482-5.
18. Winters WL Jr. Cardiology and the quality of medical practice: a response. *JAMA* 1991;265:496-8.
19. Jollis JG, Ancukiewicz M, DeLong ER, Pryor DB, Muhlbauer LH, Mark DB. Discordance of databases designed for claims payment versus clinical information systems: implications for outcomes research. *Ann Intern Med* 1993;119:844-50.

20. Every NR, Larson EB, Litwin PE, et al. The association between on-site cardiac catheterization facilities and the use of coronary angiography after acute myocardial infarction. *N Engl J Med* 1993;329:546-51.
 21. Blustein J. High-technology cardiac procedures: the impact of service availability on service use in New York State. *JAMA* 1993;270:344-9.
 22. Rogers WJ, Baim DS, Gore JM, et al. Comparison of immediate invasive, delayed invasive, and conservative strategies after tissue-type plasminogen activator: results of the Thrombolysis in Myocardial Infarction (TIMI) Phase II-A trial. *Circulation* 1990;81:1457-76.
 23. Barbash GI, Roth A, Hod H, et al. Randomized controlled trial of late in-hospital angiography and angioplasty versus conservative management after treatment with recombinant tissue-type plasminogen activator in acute myocardial infarction. *Am J Cardiol* 1990;66:538-45.
 24. Ayanian JZ, Hauptman PJ, Guadagnoli E, Antman EM, Pashos CL, McNeil BJ. Knowledge and practices of generalist and specialist physicians regarding drug therapy for acute myocardial infarction. *N Engl J Med* 1994;331:1136-42.
 25. Leape LL, Park RE, Solomon DH, Chassin MR, Koseoff J, Brook RH. Does inappropriate use explain small-area variations in the use of health care services? *JAMA* 1990;263:669-72.
 26. Wennberg JE. The paradox of appropriate care. *JAMA* 1987;258:2568-9.
 27. Wenneker MB, Weissman JS, Epstein AM. The association of payer with utilization of cardiac procedures in Massachusetts. *JAMA* 1990;264:1255-60.
 28. Yusuf S, Zucker D, Peduzzi P, et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet* 1994;344:563-70.
-