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Validating recommendations for coronary angiography following acute myocardial infarction in the elderly: A matched analysis using propensity scores

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Abstract

We determined whether adherence to recommendations for coronary angiography more than 12 h after symptom onset but prior to hospital discharge after acute myocardial infarction (AMI) resulted in better survival. Using propensity scores, we created a matched retrospective sample of 19,568 Medicare patients hospitalized with AMI during 1994–1995 in the United States. Twenty-nine percent, 36%, and 34% of patients were judged necessary, appropriate, or uncertain, respectively, for angiography while 60% of those judged necessary received the procedure during the hospitalization. The 3-year survival benefit was largest for patients rated necessary [mean survival difference (95% CI): 17.6% (15.1, 20.1)] and smallest for those rated uncertain [8.8% (6.8, 10.7)]. Angiography recommendations appear to select patients who are likely to benefit from the procedure and the consequent interventions. Because of the magnitude of the benefit and of the number of patients involved, steps should be taken to replicate these findings.

Keywords: AMI; Coronary angiography; Practice guidelines; Clinical indication; Propensity score; Caliper matching

1. Introduction

The widespread and increasing use of guidelines and protocols has led researchers to investigate two questions: first, the extent to which current practices are consistent with these guidelines; and second, the extent to which adherence to guidelines leads to better outcomes for patients. Because of the importance of cardiovascular disease in terms of morbidity, mortality, and cost, many investigations have focused on this clinical condition. For example, several researchers have examined coronary angiography and revascularization procedures and demonstrated wide variability in use [1–6] and some instances of inappropriate use [7–11]. The correlation between adherence to treatment recommendations and outcomes has been studied less often, although one study of HMO enrollees in California [12] suggested improved survival among patients undergoing angiography who were rated necessary for the procedure.

In this study we assessed the link between adherence to recommendations for coronary angiography and survival using observational data from seven US states. Because guidelines increasingly incorporate a continuum of recommendations (e.g., the procedure is necessary, is appropriate but not necessary, is of uncertain benefit, or is inappropriate), we undertook to validate the accuracy of the explicit scale of appropriateness embedded in these guidelines. If there is no clear relationship with outcomes and the appropriateness scale, these scales should be discarded.

To achieve our goals, we studied a large national sample of Medicare beneficiaries treated after an acute myocardial infarction (AMI). We evaluated the appropriateness of coronary angiography more than 12 h after symptom onset but prior to hospital discharge and determined the extent to which use of the procedure in accordance with appropriate-

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ness ratings correlated with survival at 3 years from admission. We focused on coronary angiography because of wide variations in its use. Because our study is based on observational data, we adjusted for confounding by creating a matched sample using propensity scores.

2. Methods

2.1. Study population

We obtained our sample through the Cooperative Cardiovascular Project (CCP) [13] undertaken by the Health Care Financing Administration (HCFA). The sample included 64,140 fee-for-service Medicare beneficiaries aged 65–89 years who were discharged with a diagnosis of AMI from hospitals located in California, Florida, Massachusetts, New York, Ohio, Pennsylvania, and Texas during the period January 1, 1994 through June 30, 1995. These states were selected because they were known to differ in frequency of cardiac procedure use, are large, and are geographically diverse. We excluded 26,352 patients for the following reasons: (a) 1595 patients who may have been incorrectly coded as having an AMI (discharged alive with a length of stay less than 4 days); (b) 3011 who had incomplete data (resided outside the US; survival not obtained; medical records not available; transferred more than once); (c) 10,121 who were missing information needed to determine the appropriateness of angiography (the majority of whom were missing duration of symptom onset); and (d) 3126 who were not candidates for catheterization in the time frame of interest (2375 patients who underwent angiography within 12 h of symptom onset and 754 in a prior contiguous hospitalization). Because we studied long-term outcomes, we also excluded 12,796 patients with low likelihood of long-term survival [14] (patients with terminal illness, global brain damage, hepatic failure, metastatic cancer, and “do not resuscitate” orders; patients who died within 1 day of hospital admission). After applying the exclusion criteria, 37,788 patients were eligible for our study.

2.2. Data sources

We linked information from contiguous hospitalizations and, in the case of transfers, associated patients with the initial admitting hospital. Medical record data were abstracted at two Clinical Data Abstraction Centers under contract with HCFA. Information abstracted for each patient included cardiac history, comorbid conditions, AMI severity, medications, and results of tests. Sociodemographic information and Medicare eligibility were obtained using Medicare National Claims Standard Analytic Files. Use of coronary angioplasty and bypass surgery within 3 months of admission was determined from linked Medicare billing data. We determined patient mortality from the Health Insurance Master File. Characteristics of the hospital in which the patients were treated were obtained from three sources. The HCFA Provider of Service File and American Hospital Association databases were linked to our sample to obtain structural characteristics such as teaching affiliation and number of beds. We also conducted a telephone survey with hospital personnel to determine the availability of cardiac services, participation in clinical trials, and presence of resident training programs during the study period.

2.3. Appropriateness of angiography

We employed the RAND/UCLA methodology to revise [15] and refine [16,17] the RAND 1992 recommendations for angiography following AMI [18]. Briefly, the panel was comprised of five cardiologists, two cardiac surgeons, one general internist, and one family practitioner, each nominated by their professional organizations. Eight of the nine panelists participated in the 1992 RAND recommendations. After a literature review of the appropriateness of angiography [15], 890 clinical indications were specified for use of the procedure within 12 weeks of the infarction, 92 of which related to angiography during the initial hospitalization. Five variables were used to classify patients during the initial hospitalization: (1) duration of symptom onset ($<$6 h, 6–12 h, $>$12 h); (2) patient age ($<$75 years, $\geqslant$75 years); (3) prior use of thrombolytic therapy; (4) presence of contraindications to thrombolytic therapy; and (5) presence of a condition complicating the infarction (shock, persistent chest pain, persistent pulmonary edema, noninvasive evidence of mitral regurgitation or ventricular septal defect, left ventricular ejection fraction $<$35%, stress-induced ischemia, and recurrent ventricular tachycardia or fibrillation 24 h after the infarction) [19]. The 92 clinical indications were divided approximately equally across the three time frames describing the duration of symptom onset, with 28 indications falling into the greater than 12-h time frame. The updated RAND recommendations generally coincide with the American College of Cardiology and the American Heart Association (ACC/AHA) guidelines [20], although the ACC/AHA guidelines do not differentiate use by patient age.

A two-stage modified Delphi procedure was used to obtain the panelists’ judgements regarding the appropriateness and necessity of angiography. Appropriateness was categorized using a 4-point ordinal scale using a model-based estimate [16]: necessary (procedure is the best option available to the patient); appropriate, but not necessary (benefits greatly exceed risks); uncertain (benefits and risks about equal); and inappropriate (risks greatly exceed benefits). The model-based estimates were derived from an ordinal categorical model fitted to the panelists’ judgements and included both panelists and clinical indication random effects. Using these revised recommendations, we assigned patients in our cohort to one of 28 possible clinical subgroups based on abstracted medical record information.

2.4. Statistical analysis

Because we collected detailed clinical information describing admission severity of the patient and characteristics of the hospital to which the patient was admitted, we assumed that treatment (angiography vs. no angiography) was randomly assigned with probabilities that depended on the observed covariates alone. We then employed a propensity score approach [21,22] to compare survival between those receiving angiography and those who did not within each category of appropriateness. The propensity score is a measure of the likelihood that a patient would have undergone angiography using the patient's covariate scores. For patients with a similar *propensity* to undergo coronary angiography, we compared outcomes among those who underwent angiography with those who did not, within each category of appropriateness. For notational convenience, we sometimes refer to a patient undergoing angiography as "cathed" and a patient not undergoing angiography as "noncathed."

2.4.1. Creating the matched sample

To estimate the propensity scores, we fitted a logistic regression model in which the outcome was the log-odds of undergoing angiography more than 12 h after symptom onset but prior to discharge. The model had the following general structure:

$$Q(\mathbf{X}) = \text{logit}(P(\text{Angiography}|\mathbf{X})) = \beta'\mathbf{X} \qquad (1)$$

Using the medical record, we combined information documenting duration of symptom onset at the time of admission and the time of coronary angiography to determine whether a patient received the procedure more than 12 h after onset. Specifically, if the patient (i) arrived at the hospital less than 6 h after symptom onset and was cathed more than 12 h after arrival, (ii) arrived between 6 and 12 h after symptom onset and was cathed more than 6 h after arrival, or (iii) arrived more than 12 h after symptom onset and was cathed prior to discharge, we coded Angiography as true for the patient and false otherwise. By design, we excluded patients who underwent angiography within 12 h of symptom onset [exclusion (d) in Study Population description].

The components of **X** in Model (1) consisted of patient (demographic, comorbidity, admission severity) and hospital characteristics as well as interactions among the covariates. Demographic variables included age, gender, race, and body mass. Comorbid disease was characterized by a series of binary variables that reflected whether the medical record indicated a history of a particular disease (angina, angioplasty, bypass surgery, cancer, cerebral vascular accident, chronic obstructive pulmonary disease, congestive heart failure, dementia, diabetes, hypertension, MI, peripheral vascular disease). We quantified admission severity using admission variables (patient mobility, respiration rate, mean arterial pressure, congestive heart failure, cardiac arrest, stroke, shock on arrival, duration of chest pain, presence of any contraindication to thrombolytic therapy.); laboratory measurements (creatinine, albumin, serum urea nitrogen, etc.); results based on diagnostic tests (conduction disturbance, cardiomegaly, S_3 gallop rhythm, etc.); whether they received thrombolysis, and complications of the MI [shock after arrival, persistent chest pain, persistent pulmonary edema, ejection fraction (based on MUGA or echocardiogram only), ischemia, recurrent ventricular tachycardia]. Characteristics of the initial admitting hospital included urban location, geographic state, number of beds, availability of cardiac services, participation in clinical trials, cardiology fellowship, and teaching affiliation.

In general, only results recorded at admission were utilized in Eq. (1). Two exceptions to this rule involved presence of some comorbid diseases and the severity of the AMI as measured by complicating factors. For several comorbidities, we used information from multiple medical records if available. For example, if a history of diabetes was recorded in at least one record, we assumed diabetes was present at admission. We used information beyond the first day of arrival but measured prior to the decision to perform angiography to characterize complications of the MI. For example, we determined whether the patient had persistent chest pain more than 24 h after arrival.

We assumed that missing observations were missing at random, implying that the mechanism by which data were missing is unrelated to information not contained in our observed data. For discrete-valued variables, we included a binary variable that represented "missing." In the case of continuous-valued variables, we created two variables: a binary variable indicating whether the variable was measured and if measured, a continuous variable indicating the value of the variable. We assessed the appropriateness of the regression model through graphical displays (empirical logit plots) and quantified model accuracy by the area under the Receiver Operator Characteristic (ROC) curve.

Once the model was estimated, we stratified the cohort by clinical indication, and within an indication, matched each patient who underwent angiography to a patient with closest [23] estimated propensity score who did not. We included in our analyses only those matches that were within 0.60 of the pooled standard error of $q(\mathbf{X})$ [24] where $q(\mathbf{X})$ is the estimated logit. Specifically, for each clinical indication (1, 2, . . ., 28), we first randomly ordered the cathed patients. For the first cathed patient, we found all noncathed patients, j, such that

$$|q(\mathbf{X}_1) - q(\mathbf{X}_j)| \le 0.60\ s_q \qquad (2)$$

where s_q is the square root of the variance of the estimated logits, $q(\mathbf{X})$. This method of defining the closeness of a match is referred to caliper matching and is the observational study analogue of randomization in a clinical trial. We selected the closest noncathed patient j meeting the restriction described in Eq. (2) and then removed the cathed and matched noncathed patient from the sample. If no noncathed patient could be found, we removed the cathed patient from the sample and classified the cathed patient as "unmatched." Once we completed matching in clinical indication i, we moved to the next indication and repeated the process. Fig. 1 summarizes our methods for identifying and creating the matched sample.

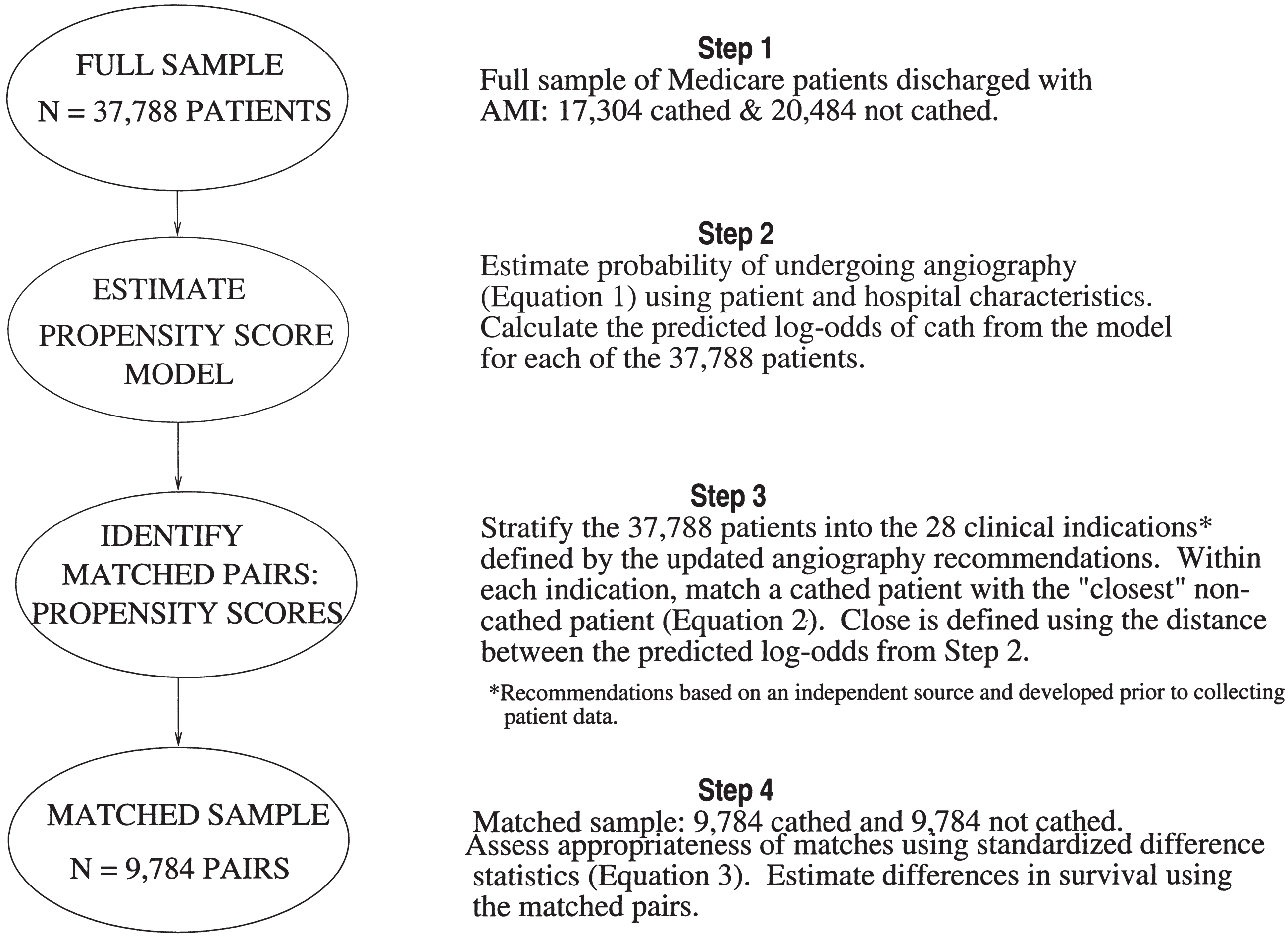

Fig. 1. Algorithm for creating matched sample.

2.4.2. Quantifying bias

We assessed the degree of imbalance within the matched pairs as well as between the matched and unmatched patients using the standardized difference, d_i, in covariate means [21]. For each covariate, we calculated

$$d_i = 100 \times (x_{ci} - x_{nci}) / \sqrt{\{(s^2_{ci} + s^2_{nci})/2\}}$$

where x_{ci} and x_{nci} are the sample means in the catheterized and noncatheterized groups of the ith covariate, respectively, and s^2_{ci} and s^2_{nci} are the corresponding sample variances. Small (<10%) absolute values of d_i support the assumption of balance [25] between treatment groups.

2.4.3. Relation between angiography recommendation and survival

We assessed all-cause mortality within the 3 years after hospital admission for all patients meeting our inclusion criteria. Using the matched pairs, we determined the association between angiography and survival using McNemar's test within each appropriateness category and constructed 95% confidence intervals (Cl) for the paired differences. To avoid ceiling effects, relative risk estimates and their corresponding 95% Cls were also calculated. Because patients were classified into mutually exclusive clinical indications, we computed the fraction of the total mortality difference associated with each indication. The total difference was calculated at $\Delta = \Sigma w_i y_i / \Sigma w_i$ where y_i is the paired difference in 3-year mortality, w_i is the inverse of the variance of the paired difference, and i denotes clinical indication so that the fraction of the effect associated with the ith indication

$$\frac{w_i y_i / \sum w_i}{\Delta}.$$

2.4.4. Use of subsequent therapies

Because any potential benefit of angiography would result from subsequent therapies, we determined rates of coronary artery bypass graft surgery (CABG) and percutaneous transluminal coronary angioplasty (PTCA) within 3 months of the initial admission for patients undergoing angiography. Discharge rates of aspirin, β-blockers, and ACE inhibitors for ideal candidates [26] were calculated within appropriateness categories, and Mantel–Haenszel tests [27] were conducted to test associations between drug use and angiography, controlling for appropriateness category.

2.4.5. Robustness of results

We assessed the robustness of our results in three specific ways. First, to examine the impact of unmeasured selection effects we varied the strength of the relationship of a hypothetical unmeasured binary covariate, U, with angiography and 3-year survival benefit, and computed upper bounds on the significance of McNemar's test [28]. Specifically, if U assumes values of 0 or 1, then we examined upper bounds on the P value for McNemar's test assuming that two patients with the same observed covariates but differed in U and in their odds of receiving the treatment by a fixed amount, denoted γ. We varied γ from a minimum of 1.0 (no difference) to 6.0 (huge differences) and identified the smallest value of γ at which our inferences would change.

Second, to examine whether the angiography benefits were related to availability of hospital cardiac services, we reestimated survival benefits after matching each cathed patient to a noncathed patient within clinical indication *and* hospital type. We classified hospitals into two categories: hospitals with the capability to perform coronary angiography and those without this capability. Patients initially admitted to hospitals without this capability would need to be transferred to a hospital with coronary angiography capabilities in order to receive the procedure.

Finally, we examined 2-day survival differences within appropriateness category using the matched sample. Because we would not expect a benefit to appear within this short time frame, large differences (>5%) may indicate a departure from our assumption that the probability of undergoing angiography depended on the observed covariates alone.

Table 1
Characteristics and unadjusted survival in full and matched study cohorts

	Characteristic, N(%)	
	Full	Matched
Number of patients	37,788	19,568
Age (years)		
65–69	8,271 (22)	4,504 (23)
70–74	9,735 (26)	6,599 (34)
75–79	8,730 (23)	3,958 (20)
80–84	7,121 (19)	3,393 (17)
85–89	3,931 (10)	1,114 (6)
Race		
White	34,091 (90)	17,593 (90)
Black	1,857 (5)	989 (5)
Other/unknown	1,840 (5)	986 (5)
Female	17,547 (46)	8,892 (45)
State		
California	5,179 (14)	2,815 (14)
Florida	6,454 (17)	3,439 (18)
Massachusetts	3,030 (8)	1,343 (7)
New York	6,439 (17)	3,266 (17)
Ohio	4,387 (12)	2,225 (11)
Pennsylvania	7,627 (20)	3,937 (20)
Texas	4,672 (12)	2,543 (13)
Angiography	17,304 (46)	9,784 (50)
Appropriateness category		
Necessary	10,218 (27)	5,760 (29)
Appropriate, not necessary	14,317 (38)	7,104 (36)
Uncertain	13,253 (35)	6,704 (34)
Survival		
1-Year	30,094 (80)	15,943 (82)
2-Year	26,973 (71)	14,490 (74)
3-Year	24,275 (64)	13,217 (68)

3. Results

3.1. Characteristics of the study population

The study cohort consisted of 37,788 patients, the majority of whom were white, slightly less than half were female, and 46% of whom underwent angiography during the initial episode of hospital care (Table 1). Twenty-nine percent, 36%, and 34% of patients were rated as necessary, appropriate but not necessary, or uncertain for angiography, respectively, in the matched cohort. Unadjusted survival at 3 years was 64% in the full cohort and 68% in the matched cohort.

The distribution of patients across the 28 clinical indications is presented in Table 2, ordered by frequency of angiography within the two age subgroups. The physician panel that revised the appropriateness ratings [17] prior to the analysis of our study cohort did not rate any of the 28 subgroups as inappropriate nor did they rate any patient aged 75 years or older as necessary for angiography. Of patients experiencing complications, the majority had either persistent chest pain or persistent pulmonary edema. In general, patients under 75 years of age were more likely to undergo angiography—60% of all patients in this age group did. Of these patients, those receiving thrombolytic therapy and having persistent chest pain were the most likely to undergo angiography. In contrast, only 33% of patients aged 75 years or older underwent angiography. The indication in this older age group in which patients received angiography most frequently was also the subgroup for which younger patients were most likely to receive angiography, thrombolysis and persistent chest pain.

3.2. Propensity score analyses

Descriptive analyses indicated that patients not undergoing angiography were older, generally sicker, and were more likely to be admitted to small, rural, nonteaching hospitals without the capability to perform invasive procedures (Table 3, columns 2–4). Fig. 2 displays the predicted probabilities of undergoing angiography stratified by observed angiography status using a logistic regression model with 102 predictors (ROC area: 0.84). Based on this model, we matched 57% of the 17,304 cathed patients to noncathed patients using estimated propensity scores displayed in Fig. 2. The unmatched angiography patients were more likely to be admitted to large, teaching, urban hospitals with the capability to perform invasive cardiac procedures; were younger; were less sick; and had less comorbid disease compared to the an-

Table 2
Distribution of patients across clinical indicators

Clinical subgroup	% of cohort	% cathed	Treatment recomm.
Under 75 years of age			
Thrombolysis, MI complicated by persistent chest pain	4.1	75.7	N
Thrombolysis, MI complicated by shock	0.1	75.3	N
No Thrombolysis, MI complicated by persistent chest pain	11.9	66.7	N
Thrombolysis, MI complicated by recurrent VT/VF >24 h after MI	0.1	66.7	A
Thrombolysis, MI complicated by severe LV dysfunction	0.3	65.7	A
Thrombolysis, uncomplicated MI	3.9	65.5	U
Thrombolysis, MI complicated by persistent pulmonary edema	1.8	63.3	N
No Thrombolysis, uncomplicated MI	12.9	62.2	U
No Thrombolysis, MI complicated by shock	0.2	59.2	N
No Thrombolysis, MI complicated by recurrent VT/VF >24 h after MI	0.5	50.9	A
No Thrombolysis, MI complicated by stress-induced myocardial ischemia	1.8	48.9	A
No Thrombolysis, MI complicated by severe LV dysfunction	0.9	47.9	A
Thrombolysis, MI complicated by stress-induced myocardial ischemia	0.3	45.1	A
No Thrombolysis, MI complicated by persistent pulmonary edema	9.0	41.0	N
75 Years of age and older			
Thrombolysis, MI complicated by persistent chest pain	2.4	58.2	A
Thrombolysis, MI complicated by shock	0.2	50.8	A
Thrombolysis, uncomplicated MI	2.0	48.1	U
Thrombolysis, MI complicated by severe LV dysfunction	0.2	43.8	U
Thrombolysis, MI complicated by persistent pulmonary edema	1.3	41.9	U
No Thrombolysis, MI complicated by persistent chest pain	13.4	41.1	U
Thrombolysis, MI complicated by recurrent VT/VF >24 h after MI	0.1	37.5	U
No Thrombolysis, MI complicated by shock	0.3	35.1	A
No Thrombolysis, uncomplicated MI	13.0	34.3	U
No Thrombolysis, MI complicated by stress-induced myocardial ischemia	1.1	32.7	U
No Thrombolysis, MI complicated by recurrent VT/VF >24 h after MI	0.4	26.8	U
Thrombolysis, MI complicated by stress-induced myocardial ischemia	0.2	24.1	U
No Thrombolysis, MI complicated by severe LV dysfunction	1.2	21.3	U
No Thrombolysis, MI complicated by persistent pulmonary edema	16.4	20.0	A
Number of patients	37,788	45.8	

Percent of cohort denotes the percentage of the full cohort classified into the clinical stratum; % cathed denotes the percentage of patients within the subgroup undergoing angiography more than 12 h after symptom onset but prior to discharge. Indicators ordered in terms of frequency of angiography. VT = ventricular tachycardia; VF = ventricular fibrillation; LV = left ventricular. Rating: N = necessary, A = appropriate but not necessary, U = uncertain.

giography patients for whom we found matches (Table 3, columns 8–10). Prior to matching, the average predicted propensities to undergo angiography were 65% and 30% in the two groups; after matching, the propensities were within 4 percentage points (Table 3, columns 5–7).

While Table 3 displays the degree of imbalance for a subset of the covariates, Fig. 3 displays the distribution of the differences, d_i, for the main covariates included in the model (interactions are not included in the figure). After matching, all standardized differences in covariate means are less than 10% (Fig. 3: upper right histogram), reduced substantially from the prematching distribution (Fig. 3: upper left histogram). However, although the matched and unmatched cathed patients (Fig. 3: lower left histogram) are more comparable than the cathed and noncathed patients prior to matching, the unmatched cathed patients are different from those included in the matched sample. This implies that there may be a bias in our overall estimate of benefit due to discarding cathed patients.

3.3. Appropriateness of angiography and patient outcomes

We observed an absolute survival benefit associated with angiography in each appropriateness category (Table 4) using the matched sample. The benefit was largest for patients for whom angiography was deemed necessary and smallest for those for whom it was deemed uncertain. By 3 years, the survival rate among necessary patients who underwent angiography was 73% compared to 56% among necessary patients who did not receive the procedure; in contrast, the survival rates were 83% and 75%, respectively, among catheterized and noncatheterized patients who were judged uncertain. The relative risks (95% Cl) of 3-year survival for those undergoing angiography relative to those not receiving the procedure, adjusting for matching were: 1.51 (1.42, 1.61), 1.45 (1.38, 1.53), and 1.34 (1.25, 1.43) for necessary, appropriate, and uncertain patients, respectively.

More than 50% of the total 3-year benefit, $\Delta = -0.135$ [S.E. = 0.006], arose from patients not receiving thrombolytic therapy having infarctions complicated either by chest pain or by pulmonary edema (Fig. 4) while a small fraction (6%) of the benefit was attributed to patients with noninvasive evidence of LV dysfunction or inducible ischemia.

3.4. Subsequent therapies

Among patients undergoing angiography prior to discharge, CABG within 3 months of the AMI was most fre-

Table 3
Characteristics of all patients, matched cathed and noncathed patients, and unmatched cathed patients

	All Patients			Matched Patients			All Cathed Patients		
Characteristic	Cathed	Not Cathed	d_i	Cathed	Not Cathed	d_i	Matched	Unmatched	d_i
No. of patients	17,304	20,484		9,784	9,784		9,784	7,520	
Prop. Score (%)	64.8	29.7	147.8	51.3	47.9	14.1	51.3	82.5	−131.5
Age (mean years)	73.2	77.4	−69.3	74.6	74.7	−2.2	74.6	71.3	53.3
At hospital arrival									
Duration of pain:									
<6 h	54.0	50.1	7.7	54.9	55.4	−1.0	54.9	52.8	4.2
6–12 h	9.6	8.9	2.4	9.5	9.3	0.8	9.5	9.6	−0.4
>12 h	21.1	14.5	17.5	17.8	17.4	0.9	17.8	25.5	−20.2
No pain	15.4	26.6	−27.8	17.9	17.9	−0.2	17.9	12.1	14.2
Shock	1.2	1.7	−4.5	1.4	1.5	−0.5	1.4	0.9	4.4
CHF	31.3	49.9	−38.7	38.6	40.2	−3.2	38.6	21.7	35.2
Thrombolytics									
Contraindicated	39.4	62.7	−48.1	47.3	48.2	−1.9	47.3	29.1	37.3
Received	22.7	12.0	28.4	18.7	18.7	−0.1	18.7	27.9	−24.6
During hospitalization, prior to decision to perform angiography									
Chest pain after arrival									
6–24 h	27.0	18.6	19.9	24.3	24.6	−0.7	24.3	30.5	−14.6
>24 h	35.5	24.0	25.4	30.5	33.3	−6.1	30.5	42.1	−25.5
Shock	3.1	3.1	−0.2	3.0	3.5	−3.1	3.0	3.3	−1.5
CHF	32.7	50.6	−37.1	39.5	41.7	−4.6	39.5	23.8	32.2
Cardiac arrest	3.3	4.6	−6.8	3.7	4.4	−3.7	3.7	2.8	4.5
Ejection fraction									
<35%	11.9	19.2	−20.3	15.4	16.3	−2.4	15.4	7.3	22.6
⩾35%	45.1	50.6	−11.0	50.1	50.2	−0.2	50.1	38.7	22.9
No test	43.0	30.2	26.8	34.5	33.5	2.0	34.5	54.1	−41.0
Missing	2.9	3.1	−1.2	3.1	3.1	0.2	3.1	2.5	3.6
Stress test									
Positive	6.6	6.5	0.6	8.2	7.6	2.6	8.2	4.6	14.8
Negative	6.9	12.5	−19.0	10.1	11.1	−3.5	10.1	2.8	24.8
No test	86.1	80.6	14.8	81.3	80.8	1.2	81.3	92.4	−29.9
Missing	0.3	0.4	−1.1	0.4	0.5	−1.4	0.4	0.3	2.3
Hospital characteristics									
Teaching Hospital	41.7	31.2	22.0	37.1	35.9	2.5	37.1	47.5	−21.7
Rural Hospital	7.1	14.9	−25.1	10.1	11.2	−3.7	10.1	3.2	22.2
No. of beds									
<100 beds	4.1	9.9	−22.9	6.2	7.0	−3.2	6.2	1.3	19.1
100–500	64.1	72.6	−18.3	68.6	69.3	−1.6	68.6	58.3	22.2
>500	31.8	17.5	33.5	25.2	23.7	3.7	25.2	40.4	−35.6
Cardiac services									
None	14.8	37.7	−54.0	23.3	25.6	−5.5	23.3	3.7	46.0
Cath-only	18.5	24.4	−14.4	22.5	24.3	−4.5	22.5	13.3	22.3
CABG/PTCA	60.6	30.3	63.7	47.5	42.9	9.8	47.5	77.5	−63.1
Missing	6.2	7.5	−5.4	6.7	7.2	−1.9	6.7	5.5	5.4

Subset of the 102 covariates included in the propensity score model. $d_i = 100(x_c - x_{nc})/\sqrt{\{(s^2_c + s^2_{nc})/2\}}$, where x_c and x_{nc} are the sample means in the cathed and noncathed groups, and s^2_c and s^2_{nc} are the corresponding sample variances. CHF = congestive heart failure. Contraindications to thrombolytic therapy considered present if any of the following was recorded: history of ulcer disease, history of internal bleeding, history of bleeding disorder, surgery within 2 months prior to admission, coumadin on admission, admission systolic blood pressure >180, admission diastolic blood pressure >110, or age >79 years. CABG/PTCA hospitals have capability to perform angioplasty or bypass surgery; Cath-only hospitals have capability to perform angiography but not angioplasty or bypass surgery; None denote hospitals that are not Cath-Only or CABG/PTCA hospitals.

quently performed in patients with clinical indications rated necessary (necessary = 32%, appropriate = 28%, uncertain = 23%; $P = .0001$). Although statistically significant ($P = .004$), angioplasty within 3 months varied much less among the appropriateness categories (necessary = 30%, appropriate = 32%, uncertain = 34%). Fifteen percent of patients underwent angiography within 3 months of their AMI (necessary = 32%, appropriate = 28%, uncertain = 39%; $P = .001$).

We observed a significant (Mantel–Haenszel $\chi^2 = 345$; $P = .001$) association of aspirin prescription and angiography, adjusting for appropriateness of the procedure (Fig. 5) among ideal candidates at discharge, although we did not detect significant associations for β-blocker ($\chi^2 = 0.5$; $P = .48$) or ACE Inhibitor ($\chi^2 = 1.8$; $P = .17$) prescription.

3.5. Robustness of results

In order to eliminate the estimated survival benefit of angiography among patients judged necessary for the procedure, an unobserved variable not entered into the propensity score model would have to increase the odds of angiogra-

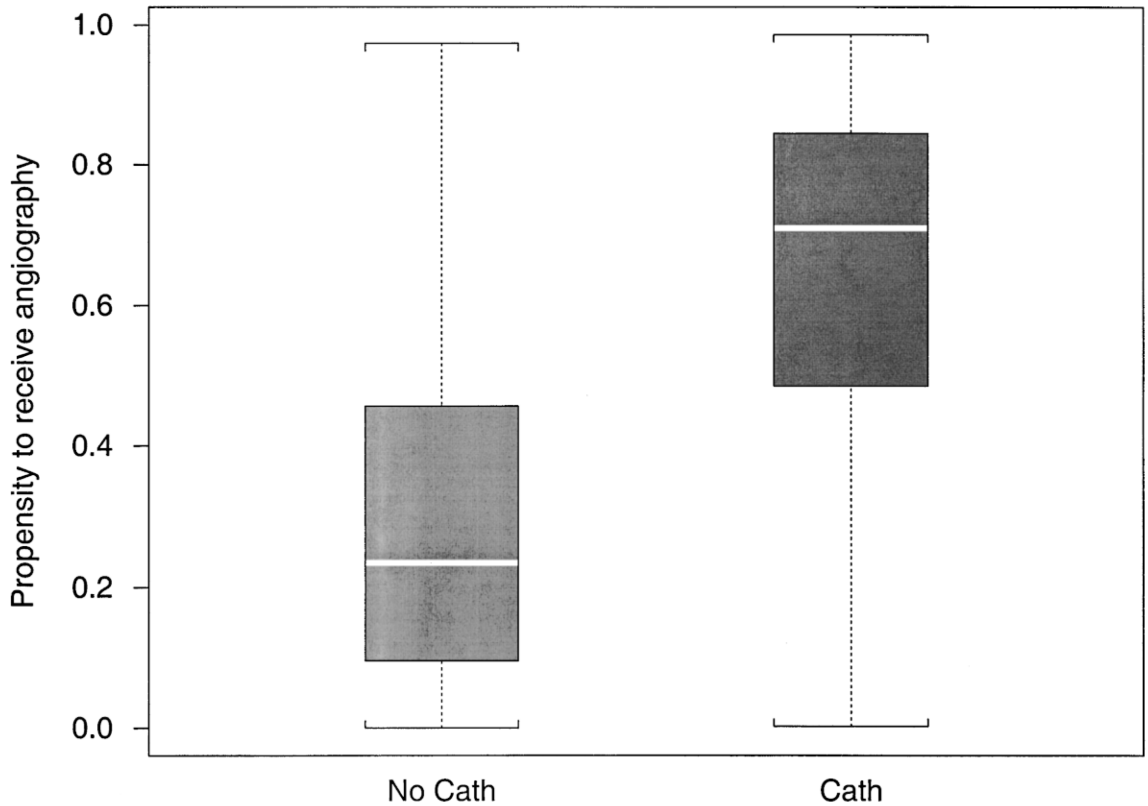

Fig. 2. Distribution of estimated probabilities of coronary angiography following AMI. Box plots of estimated probability of receiving coronary angiography based on a logistic regression model, stratified by observed angiography status. The horizontal white line represents the median estimated probability in each group. Results based on full sample (17,304 cathed patients and 20,484 noncathed patients) using a model containing 102 covariates (demographic, comorbid disease, admission severity, hospital characteristics, and interactions among these).

phy by more than twofold, adjusting for the 102 predictors already in our model. The corresponding odds ratios for appropriate and uncertain patients would need to be 2 and 1.5, respectively, to eliminate the observed survival benefit. The 3-year survival benefits were significant regardless of hospital type. Finally, survival differences at day 2 were less than 2% across all appropriateness categories (Table 4).

4. Discussion

This study provides data on two important questions related to the management of patients after an AMI. First, we observed a relationship between coronary angiography and improved survival for those patients undergoing catheterization more than 12 h after symptom onset. Second, the strength of this relationship correlated with the continuum of recommendations for this procedure in the expected directions. These results are important because the patient population was a large and generalizable one, consisting of over 40% of all Medicare beneficiaries with an AMI during the period of study. Our results, however, do not apply to the early use (e.g., within 12 h) of primary angioplasty.

We observed a significant increase in survival at 1, 2 and 3 years for patients judged necessary for angiography who had this procedure compared with those who did not. Clearly, the benefit of angiography cannot be attributed to angiography itself because a diagnostic procedure confers no benefit on survival. Rather, the benefit results from the constellation of subsequent or associated decisions such as revascularization undertaken as a result of knowing the coronary anatomy or drug therapy introduced because of appropriate medical management. Controlling for appropriateness category, we observed increased discharge prescription only for aspirin among ideal candidates who underwent angiography compared with those who did not. However, when considering all comers, and not those who are ideal candidates, there were significant increases in use of aspirin ($\chi^2 = 242$; $P = .001$) and β-blockers ($\chi^2 = 6$; $P = .01$) in cathed patients discharged alive compared to those patients not undergoing angiography. Either or both of these may have contributed to improved survival.

Several investigators have measured the impact of cardiac procedure rates on outcomes. Guadagnoli et al. [5] compared outcomes for all patients treated in a “high-rate” state (90-day angiography rate in Texas: 45%) with those in a “low-rate” state (90-day angiography rate in New York: 30%) and found no differences in 2-year mortality or health-related quality of life for Medicare beneficiaries treated during 1990. McClellan and colleagues [29] studied a similar population from a national perspective and demonstrated a small survival benefit at 4 years among patients whose treatment varied primarily because of distance to

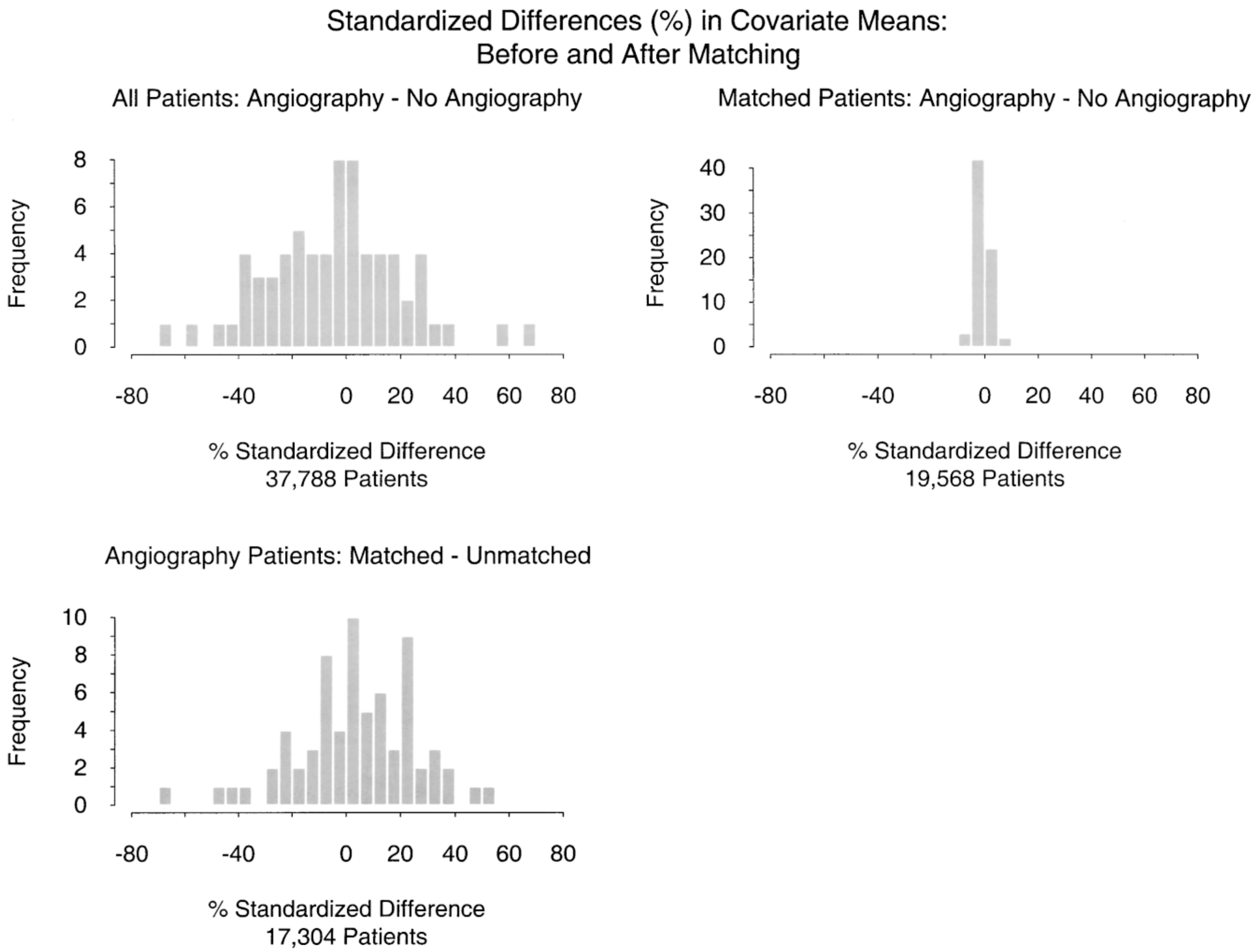

Fig. 3. Distribution of standardized differences in covariate means of full and matched samples. x-axis = percent differences, $d_i = 100(x_c - x_{nc})/\sqrt{\{s^2_c + s^2_{nc})/2\}}$, where x_c and x_{nc} are the sample means in the catheterized and noncatheterized groups, respectively, and s^2_c and s^2_{nc} are the corresponding sample variances. y-axis = frequency of covariates in propensity score model.

hospitals. The 90-day angiography rates were 28% in close hospitals and 18% in far hospitals. Tu et al. [30] compared survival for AMI patients treated during 1991 in Ontario (30-day angiography rate: 7%) with those in the US (30-day angiography rate: 35%) and found no differences in 1-year mortality rates. In each case, the authors employed the technique of instrumental variables, either implicitly or explicitly. The generalizability of their results, therefore, is applicable only to the subgroup of patients whose treatment varies with variation in the instrument, or "marginal" patients for the procedure [31]. For example, in the Texas–New York comparison, the marginal patient is one who would undergo angiography in Texas but who would not in New York. These investigators studied angiography within 90 days of the AMI using an unmatched cohort of all elderly AMI patients.

Table 4
Survival stratified according to recommendation category

%	Necessary (No. pairs = 2880)			Appropriate (No. pairs = 3553)			Uncertain (No. pairs = 3352)		
Survival	Cathed	Not cathed	Diff. (95% Cl)	Cathed	Not cathed	Diff. (95% Cl)	Cathed	Not cathed	Diff. (95% Cl)
2-day	99.7	98.2	1.5 (1.0, 2.0)	99.4	97.7	1.8 (1.2, 2.3)	99.9	99.5	0.4 (0.1, 0.7)
In-hospital	96.5	91.7	4.8 (3.6, 6.0)	93.8	90.3	3.5 (2.3, 4.8)	98.9	98.1	0.8 (0.3, 1.3)
1-year	85.3	72.8	12.5 (10.4, 14.7)	80.8	69.1	11.7 (9.7, 13.8)	92.3	88.7	3.6 (2.2, 4.9)
2-year	79.1	62.8	16.3 (13.9, 18.7)	73.9	59.1	14.8 (12.6, 17.0)	88.0	81.3	6.8 (5.0, 8.5)
3-year	73.2	55.6	17.6 (15.1, 20.1)	67.9	50.7	17.2 (14.9, 19.5)	83.4	74.6	8.8 (6.8, 10.7)

Diff. = percent of angiography patients surviving − percent of patients not undergoing angiography surviving. Positive differences indicate a benefit of angiography. Estimates based on the matched sample.

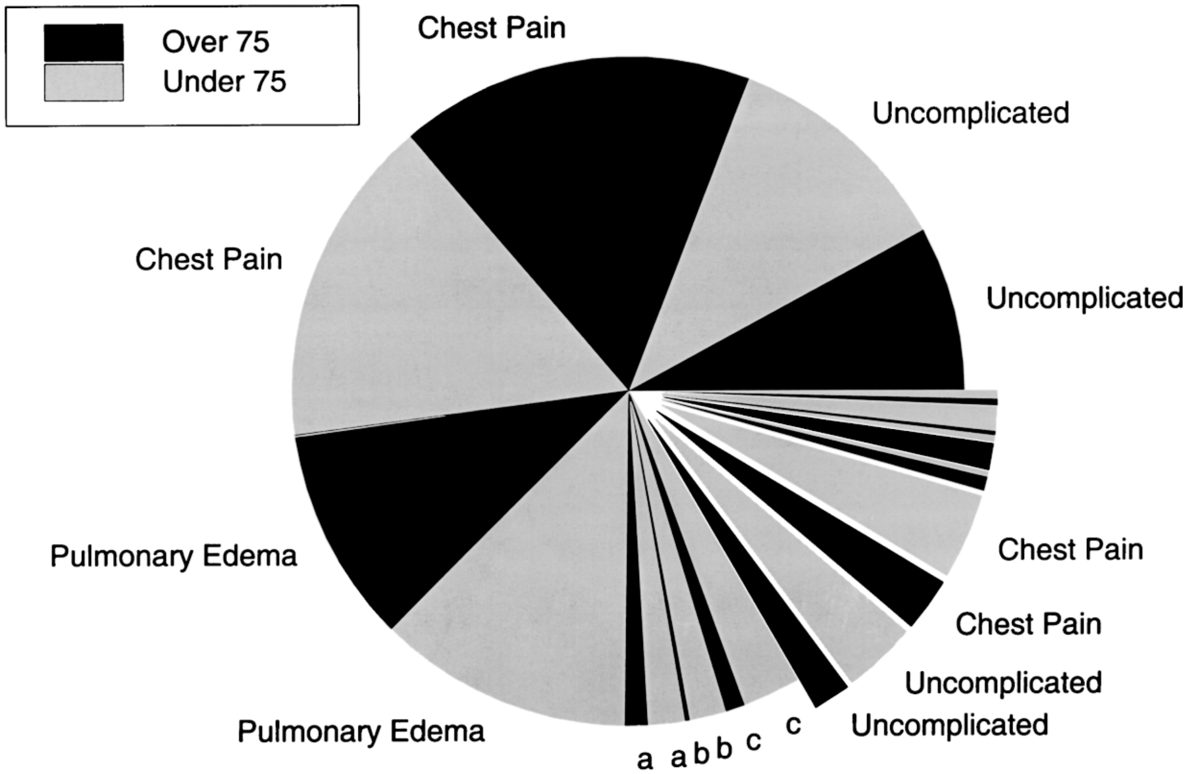

Fig. 4. Relative contribution of total 3-year benefit for each clinical indication. Pie graph represents that fraction of the total 3-year mortality benefit associated with each clinical indication estimated from the matched sample. The pieces moved away from the center of the pie correspond to indications in which thrombolytic therapy was received. The darker (lighter) shaded pieces represent those over 75 years of age (under 75 years of age). [a]LV<35%; [b]stress-induced myocardial ischemia; [c]recurrent ventricular tachycardia or fibrilliation.

More recently, Selby and colleagues [12] demonstrated that AMI patients judged necessary for angiography treated during 1990–1992 in hospitals performing a high volume of angiography procedures had better 3-year survival compared with similar patients treated in low-volume hospitals in one managed care system. Like the Selby study, our study examined impact in several patient subgroups defined by "clinical need" of the procedure. The marginal patients from the other studies [5,29,30] are likely to be similar to those in our "uncertain" or to an "inappropriate" category.

In our study, we observed underuse of angiography, with only 60% of patients judged necessary undergoing this procedure. Because only 17% of our cohort received thrombolytic therapy, many patients may have had persistent occlusions of infarct-related arteries and thus would have benefited from angiography and subsequent revascularization procedures. Moreover, we found a smaller benefit for those in the uncertain category relative to necessary patients. Most of the patients with uncertain ratings—representing about one third of our full cohort—had uncomplicated AMIs (ACC/AHA Class IIb). Randomized trials have not demonstrated such a survival benefit with routine use of angiography for AMI patients without ischemic complications [32,33].

The findings from previous studies coupled with our own suggest that although areas with high volumes of cardiac procedure provide more cardiac services, the procedures appear not to be targeted toward those who may have the most to benefit. This observation may explain the lack of significant differences in survival benefits between high-use and low-use areas.

Our study has several limitations. Our analysis was based on an observational data set, and we had to adjust for possible differences in the characteristics of patients who did and did not undergo angiography. There are three potential sources of bias that may impact on our conclusions: nonignorable treatment assignment, incomplete matching, and inexact matching. The bias resulting from departures from ignorability cannot be estimated directly from a single study, although we attempted to examine the sensitivity of our conclusions to the size of this bias. Several sensitivity analyses indicate that our results are insensitive to unobserved differences in case mix. The missing covariate would have to substantially increase both the likelihood of catheterization and death by more than twofold to eliminate the effect. Moreover, the effect of the unobserved confounder would have to be independent of the variables included in the propensity score model. Survival differences at day 2 were negligible (Table 4), lending some support to the assumption ignorable treatment assignment.

We utilized a propensity score approach to reduce the biases that may result from incomplete and inexact matching.

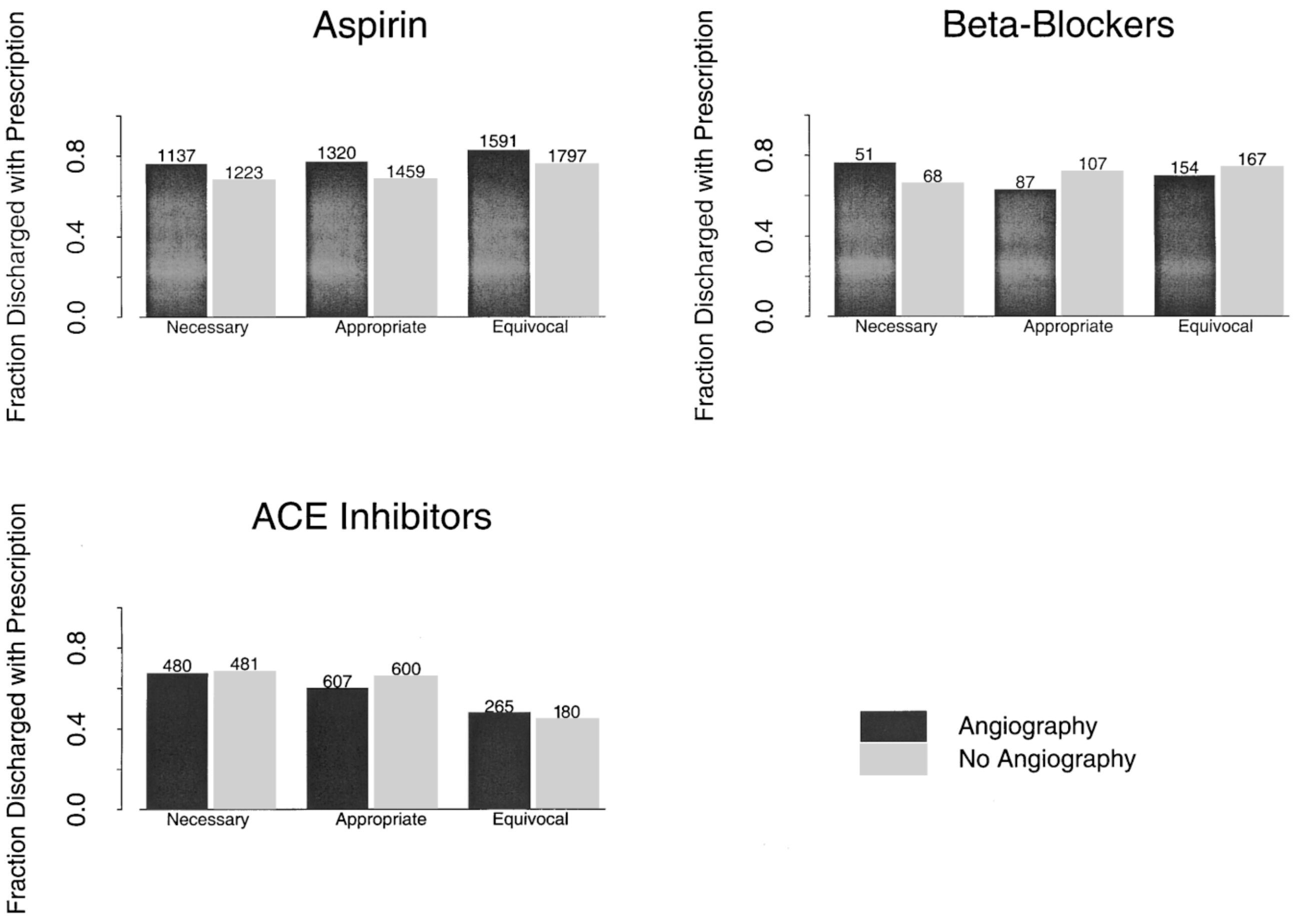

Fig. 5. Discharge medications and appropriateness of angiography. Fraction of ideal candidates from matched sample discharged on aspirin, β-blockers, and ACE inhibitors stratified by appropriateness category and angiography use. The number of patients known to be ideal for each medication is listed above each bar.

The approach is preferred to standard regression-adjustment approaches when there are many confounders and when the distributions of the confounders between treatment groups differ. The propensity score approach, a technique that has been employed in other recent medical studies [34–35], reduces the collection of many confounding variables to a single variable that permits easy comparisons of group differences. Although we were successful in reducing the bias that may have resulted from inexact matching on observed covariates, we were only able to adequately match 57% of all patients who underwent angiography. The unmatched angiography patients were generally younger and healthier than the matched angiography patients and if included in the comparisons would have biased the effect of angiography towards a larger benefit. Although the exclusion of the unmatched patients may have introduced a bias, their inclusion would have also compromised the comparability of the final matched groups. Because it is difficult to completely rule out all these biases, it is important for others to validate our findings.

In conclusion, coronary angiography following AMI was associated with increased survival for a relatively contemporary cohort of Medicare beneficiaries who had an AMI. The benefit was present in all categories of appropriateness that applied to these patients. Because of the magnitude of the benefit, the recent experiences of the patients, and the size of the group involved, the data suggest that not only is underuse of this procedure after AMI prevalent but may explain the lack of long-term survival differences between high-use regions and low-use regions. Because we were unable to match all patients who underwent coronary angiography, research should be undertaken to replicate our findings.

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