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Aspirin, Beta-Blocker, and Angiotensin-Converting Enzyme Inhibitor Therapy in Patients With End-Stage Renal Disease and an Acute Myocardial Infarction

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OBJECTIVES We sought to examine the use and impact of standard medical therapies in patients with end-stage renal disease (ESRD) faced with an acute myocardial infarction (AMI).

BACKGROUND The poor prognosis of patients in this high-risk population has become increasingly well recognized.

METHODS Using the ESRD database and the Cooperative Cardiovascular Project (CCP) database, we identified AMI patients who were receiving either peritoneal dialysis or hemodialysis before admission. The early administration of aspirin and beta-blockers was compared between ESRD and non-ESRD patients and the effect of these therapies on 30-day mortality was evaluated with logistic regression models.

RESULTS The cohort consisted of 145,740 patients without ESRD and 1,025 patients with ESRD. Aspirin (67.0% vs. 82.4%, $p < 0.001$), beta-blockers (43.2% vs. 50.8%, $p < 0.001$), and angiotensin-converting enzyme (ACE) inhibitors (38.5% vs. 60.3%, $p < 0.001$) were less likely to be administered to ESRD patients than to non-ESRD patients. The benefit of these therapies on 30-day mortality was similar among ESRD patients (aspirin: relative risk [RR] 0.64; 95% confidence interval [CI] 0.50 to 0.80; beta-blocker: RR 0.78; 95% CI 0.60 to 0.99; ACE inhibitor: RR 0.58; 95% CI 0.42 to 0.77) and non-ESRD patients (aspirin: RR 0.57; 95% CI 0.55 to 0.58; beta-blocker: RR 0.70; 95% CI 0.68 to 0.72; ACE inhibitor: RR 0.64; 95% CI 0.63 to 0.66).

CONCLUSIONS End-stage renal disease patients are far less likely than non-ESRD patients to be treated with aspirin, beta-blockers, and ACE inhibitors during an admission for AMI. The lower rates of usage for these medications, particularly aspirin, may contribute to the increased 30-day mortality. These findings demonstrate a marked opportunity to improve care in this population. (J Am Coll Cardiol 2003;42:201–8) © 2003 by the American College of Cardiology Foundation

Approximately 250,000 Medicare beneficiaries are enrolled in the end-stage renal disease (ESRD) program and receive either peritoneal dialysis or hemodialysis (1). Cardiovascular morbidity and mortality remain high among these patients in spite of advances in medical therapy. Approximately 60% of deaths reported in the ESRD database are attributed to either unexpected sudden deaths or arrhythmias. Herzog et al. (3) recently documented a 59% one-year mortality and a 70% five-year mortality after an AMI among patients receiving long-term dialysis. Other than patients with cardiogenic shock, no other patient population shares such a high mortality burden. Whether gaps in quality of care for this vulnerable population contribute to its high AMI mortality rate is not known.

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The rising dialysis rate, particularly among patients over age 65 years, should serve to focus attention on the patterns of care in these patients. Historically, these patients have not been represented in randomized AMI trials evaluating either medical or interventional strategies. Observational studies, although limited, have demonstrated a benefit of revascularization in this cohort in both acute and non-acute

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Abbreviations and Acronyms

ACE = angiotensin-converting enzyme
AMI = acute myocardial infarction
CCP = Cooperative Cardiovascular Project
CI = confidence interval
ESRD = end-stage renal disease
LDH = lactate dehydrogenase
RR = relative risk
SBP = systolic blood pressure
USRDS = U.S. Renal Data System

settings (4–7). In spite of the recognized mortality among ESRD patients with AMI, a large knowledge deficit persists. No study to date has specifically assessed the use and effectiveness of standard medical therapies in this cohort.

The Cooperative Cardiovascular Project (CCP) provides a unique opportunity to evaluate the patterns of care and the effectiveness of AMI therapies. This nationwide database of elderly patients includes a large number of patients with ESRD and describes contemporary care of patients with AMI (8). Our primary objective was to evaluate the use and potential benefits of medications in patients treated for ESRD compared with that observed in patients not receiving dialysis.

METHODS

Study sample. The patient cohort examined in this study was derived from the CCP national sample. The CCP database, collected as part of a national Medicare quality performance measurement and improvement initiative by the Centers for Medicare and Medicaid Services, contains detailed clinical data on 234,769 patients with a principal discharge diagnosis of AMI (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] 410) between January 1994 and February 1996 (8).

We restricted the study sample to patients age 65 years and older presenting directly to the index hospital with clinical evidence of AMI at the time of arrival. We defined AMI as either an elevation of the creatine kinase-MB fraction level (>5%), an elevation of lactate dehydrogenase (LDH) levels above normal with reversal of isoenzymes ($LDH_1 > LDH_2$), or the presence of at least two of the following criteria: chest pain during the prior 48 h, a twofold elevation in creatine kinase, and diagnostic electrocardiographic changes (ST-segment elevation or new Q waves). We excluded patients transferred from another acute-care facility, because their initial management could not be ascertained. Repeat admissions for AMI were also excluded from the analysis.

We predefined three subgroups based on the patient's eligibility for specific medical therapies. "Ideal aspirin candidates" included those patients without any absolute/relative contraindications to treatment with aspirin: history of allergic reaction to aspirin, history of internal bleeding or bleeding disorder, history of gastrointestinal ulcer, active bleeding upon arrival, hemoglobin <10 g/dl or hematocrit <30%, platelet count <100,000, comorbid conditions including cirrhosis/hepatic failure, leukemia/lymphoma, metastatic cancer/terminal illness, and immunosuppression. "Ideal beta-blocker candidates" included those patients without absolute/relative contraindications to beta-blockers: bradycardia (pulse <60 beats/min), hypotension (systolic blood pressure [SBP] <80 mm Hg), clinical evidence of cardiogenic shock upon arrival, asthma/chronic obstructive pulmonary disease, and advanced heart block (second- or third-degree atrioventricular block). "Ideal angiotensin-converting enzyme (ACE) inhibitor candidates" included patients with a documented left ventricular ejection fraction <40% who had no absolute/relative contraindications to ACE inhibitors, such as history of allergic reaction, of cardiogenic shock, or of hypotension during hospitalization, or serum creatinine >2.5 mg/dl (for non-ESRD patients only).

Data sources. The data elements collected as part of CCP have been reported previously and include more than 140 variables for each patient (8). Trained medical record reviewers abstracted patient demographics, past cardiac and noncardiac history, admission characteristics, diagnostic test results, and information on in-hospital events and procedures. The high reliability of the abstraction process has been reported (9).

Enrollment in the ESRD program was determined by matching patients in the CCP and the U.S. Renal Data System (USRDS). We were able to match personal identifier numbers for 98% of the patients in the CCP. Patients with a history of renal transplantation (a small proportion of the cohort) were excluded from the analysis because their natural course was not expected to parallel that of patients receiving either hemodialysis or peritoneal dialysis.

Dates of death in the Medicare Enrollment Database were derived both from the discharge dates of billing records indicating a discharge disposition of death and from the Master Beneficiary Record. The use of the Medicare Enrollment Database to establish the time of death has been validated (10).

Statistical analysis. The primary cohort was stratified by enrollment in the USRDS before the admission for the index AMI. We evaluated the bivariate association between ESRD enrollment and the patient demographic and clinical variables. The rates of usage for aspirin, beta-blocker, and ACE inhibitor therapy during the index hospitalization were compared between patients with ESRD and those not receiving dialysis. For categorical characteristics, comparisons were made using the chi-squared test. Comparisons of continuous parameters were made using the *t* test and the results were reported as means ± SD.

We used a logistic model to determine the association of in-hospital aspirin, beta-blocker, and ACE inhibitor therapy with 30-day mortality among patients with and without ESRD. Demographic characteristics, including age, race, and gender, were included in the model. Adjustment for

imbalances in other patient characteristics was performed by adding covariates from the previously published Global Utilization of Streptokinase and tPA for Occluded Coronary Arteries (GUSTO)-1 mortality model—SBP at admission, pulse, location of AMI, Killip class, height, weight, history of infarction, history of bypass surgery, smoking status, and the presence or absence of diabetes, hypertension, and cerebrovascular disease—to the logistic model (11). As a surrogate for myocardium at risk, we identified the number of leads with ST-segment elevation and calculated the sum of ST-segment elevation in all 12 leads of the initial electrocardiogram. The following variables were also incorporated into the model: duration of symptoms before hospital arrival, impaired mobility, the presence of chronic obstructive pulmonary disease, and left bundle branch block.

For all models, calibration was evaluated by comparing fitted probabilities of aspirin, beta-blocker, and ACE inhibitor use with observed use within deciles of probability (12). Discrimination was evaluated by calculating an area under the receiver operating characteristic curve for each model (13). Multicollinearity among the variables was tested using the Pearson coefficient. The statistical analyses were performed with the SAS 8.2 software package (SAS Institute, Cary, North Carolina). Odds ratios were converted to risk ratios using methods described by Zhang and Yu (14).

RESULTS

Baseline characteristics. The CCP database contains 234,769 abstracted medical records representing 210,996 unique individuals. We were able to identify 206,676 (98.0%) of these individuals for the purpose of determining those patients enrolled in the USRDS. Of these patients, 157,872 (76.3%) presented directly to the index hospital (n = 180,522) and had clinical evidence of AMI (n = 176,931) upon arrival. The exclusion of 10,826 patients younger than age 65 years, and 281 patients with a history of renal transplantation, produced the final cohort of 146,765 patients.

Among the cohort of 146,765 patients, 1,025 (0.70%) were enrolled in the USRDS. The mean age of patients enrolled in the USRDS was less than that of patients not receiving dialysis because enrollment in the USRDS entitles patients to Medicare coverage regardless of their age. Patient characteristics varied significantly based on enrollment in the USRDS (Table 1). Patients receiving dialysis had a higher prevalence of prior cardiovascular disease and were more likely to have comorbid conditions. They also had a higher incidence of heart failure, cardiogenic shock, and cardiac arrest. Dialysis patients were more likely to be admitted to larger institutions with coronary revascularization service on site and less likely to be cared for by cardiologists.

Application of medical therapy. Standard AMI therapies—aspirin and beta-blockers—were less likely to be used for patients receiving either peritoneal dialysis or hemodialysis (Fig. 1). Aspirin (62.0% vs. 78.9%, $p < 0.001$), beta-blockers (37.7% vs. 45.8%, $p < 0.001$), and ACE inhibitors (37.2% vs. 27.6%, $p < 0.001$) were less likely to be provided to patients receiving dialysis. There were 100,032 patients deemed ideal for aspirin, 100,445 patients ideal for beta-blockers, and 30,042 ideal for ACE inhibitors. The rates of usage for aspirin, beta-blockers, and ACE inhibitors were increased among these restricted cohorts. However, dialysis patients still remained less likely to receive any of the medical therapies.

30-day mortality. The 30-day mortality for patients receiving dialysis was higher than that for patients not receiving dialysis (29.0% vs. 18.3%, $p < 0.001$). Aspirin use was associated with lower 30-day mortality both in patients receiving dialysis (50% relative reduction; 21.1% vs. 41.8%, $p < 0.001$) and in those not receiving dialysis (63% relative reduction; 13.5% vs. 36.3%, $p < 0.001$) (Fig. 2). The restriction of the cohort to the 100,032 patients ideal for aspirin therapy yielded similar results. Beta-blocker use was associated with a 40% relative lower 30-day mortality among patients receiving dialysis (20.5% vs. 34.1%, $p < 0.001$) and a 56% relative lower mortality among patients not receiving dialysis (10.9% vs. 24.5%, $p < 0.001$) (Fig. 3). Among the patients considered ideal for beta-blockers, the reduction in mortality was also lower for patients receiving dialysis (34% lower; 20.7% vs. 31.2%, $p < 0.001$) than for those not receiving dialysis (53% lower; 10.4% vs. 22.0%, $p < 0.001$). Angiotensin-converting enzyme inhibitor use was associated with a 48% relative lower 30-day mortality among patients receiving dialysis (17.3% vs. 33.4%, $p < 0.001$) and a 27% relative lower mortality among patients not receiving dialysis (14.9% vs. 20.3%, $p < 0.001$) (Fig. 4). Among patients considered ideal for ACE inhibitors, the reduction in mortality was also higher for patients receiving dialysis (47% lower; 17.9% vs. 33.6%, $p = 0.007$) than for those not receiving dialysis (33% lower; 16.0% vs. 24.0%, $p < 0.001$).

After adjusting for baseline demographic and clinical risk factors, the administration of aspirin was associated with a similar mortality among patients receiving dialysis (relative risk [RR] 0.64; 95% confidence interval [CI] 0.50 to 0.80) and patients not receiving dialysis (RR 0.57; 95% CI 0.55 to 0.58) (Fig. 5). Among patients judged ideal for aspirin therapy, the benefit of aspirin therapy was similar in the dialysis group (RR 0.56; 95% CI 0.37 to 0.81) and the non-dialysis group (RR 0.54; 95% CI 0.52 to 0.56).

The association of beta-blockers with lower mortality was not as great as that with aspirin. Patients receiving dialysis had a 22% lower risk (RR 0.78; 95% CI 0.60 to 0.99) in mortality, whereas those not receiving dialysis had a 30% risk reduction (RR 0.70; 95% CI 0.68 to 0.72). The benefit of beta-blocker use was not statistically different between the dialysis and non-dialysis groups. Restricting the cohort to patients deemed ideal for beta-blocker use had no significant effect on the estimates in either the dialysis or non-dialysis subgroup.

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Table 1. Baseline Characteristics Stratified by ESRD Status on Admission

Characteristics	No ESRD (n = 145,740)	ESRD (n = 1,025)	p Value
Demographics			
Age (mean)	76.5 ± 7.4	74.0 ± 6.2	0.001
Age >75 yrs	56.0	41.3	0.001
Median age (25th, 75th)	75 (69, 81)	69 (62, 75)	
Female (%)	49.1	39.2	0.001
Caucasian	90.5	73.4	0.001
Risk factors			
Hypertension	61.8	80.9	0.001
Diabetes	30.5	46.6	0.001
Smoker	14.7	10.5	0.001
Cardiac history			
Myocardial infarction	29.3	36.8	0.001
Heart failure	21.2	39.8	0.001
PTCA	6.6	10.7	0.001
Bypass surgery	12.5	18.7	0.001
Noncardiac history			
Stroke	13.9	16.5	0.016
COPD	20.3	21.0	0.56
Dementia	5.8	4.7	0.12
Limited mobility	18.4	30.8	0.001
Nursing home resident	5.4	4.3	0.13
Clinical presentation			
Symptom onset <6 h	54.6	47.8	0.001
Shock on arrival	2.2	3.6	0.003
Early cardiac arrest	3.1	5.9	0.001
Height	66.0 ± 4.1	66.1 ± 4.1	0.34
Weight	161.7 ± 35.9	152.3 ± 32.1	0.001
Hypotension (SBP <90 mm Hg)	1.6	4.1	0.001
Bradycardia (HR <60 beats/min)	9.1	5.5	0.001
Killip class 1	50.9	33.4	0.001
Killip class 2	12.1	14.5	
Killip class 3	34.8	48.5	
Killip class 4	2.2	3.6	
Electrocardiographic features			
Atrial fibrillation	9.4	10.5	0.19
ST-segment elevation	37.4	31.3	0.001
ST-segment elevation ≥3 leads	33.5	27.9	0.001
Sum ST-segment elevation ≥6 mm	18.5	15.0	0.005
Anterior location	46.6	43.2	0.031
LBBB	6.5	7.4	0.26
Hospital characteristics			
Annual AMI volume	208 ± 177	255 ± 177	0.001
PTCA service available	41.0	54.2	0.001
Primary MD cardiologist	30.4	17.4	0.001

The highly significant p values derive predominantly from the large size of the patient cohort.

AMI = acute myocardial infarction; COPD = chronic obstructive pulmonary disease; ESRD = end-stage renal disease; HR = heart rate; LBBB = left bundle branch block; PTCA = percutaneous transluminal coronary angioplasty; SBP = systolic blood pressure.

The ACE inhibitors, in contrast to aspirin and beta-blockers, appeared to have a greater benefit among patients receiving dialysis (42% lower risk; RR 0.58, 95% CI 0.42 to 0.77) than among those not receiving dialysis (36% risk reduction; RR 0.64, 95% CI 0.63 to 0.66). This difference was not statistically significant. Similar estimates were identified among patients deemed ideal for ACE inhibitor therapy.

DISCUSSION

The prognostic significance of dialysis among elderly patients with AMI has received little attention in spite of the high mortality among this group. To the best of our knowledge, our analysis is the first large-scale study to date that has examined the medical therapy of dialysis patients with AMI and assessed the association of aspirin and beta-blocker use on 30-day mortality. Our findings indicate that aspirin, beta-blocker, and ACE inhibitor therapy exert a short-term survival benefit among patients with ESRD similar to that observed in patients not receiving dialysis. Yet, these medications are far less likely to be provided to patients receiving dialysis, even among those considered ideal for these medications, than to patients not receiving dialysis. Improving the quality of care through the increased

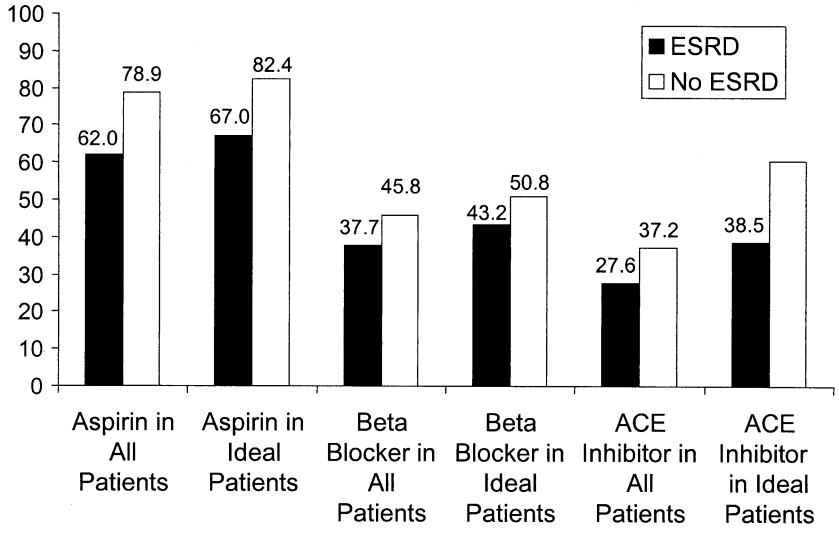

Figure 1. Aspirin, beta-blockers, and angiotensin-converting enzyme (ACE) inhibitors were less likely to be provided to patients with end-stage renal disease (ESRD) than those without ESRD. In an analysis of patients considered ideal for the individual therapies, the overall administration rates were higher, but patients with ESRD still remained less likely to receive the therapy than those without ESRD. The p value for each comparison between ESRD and non-ESRD patients was <0.001.

use of aspirin and beta-blockers could therefore reduce mortality among patients with ESRD presenting with AMI.

Nearly 300,000 Americans have ESRD, and cardiovascular disease remains the leading cause of mortality among this group. Unfortunately, there is a paucity of literature regarding cardiovascular disease, particularly AMI, in this patient cohort. Randomized clinical trials have typically excluded high-risk subgroups, particularly patients with elevated serum creatinine, not to mention those receiving dialysis. Consequently, much of our knowledge of this population stems from observational studies (3,7,15).

The association of renal dysfunction and poor outcome after an AMI has been well documented. A previous analysis of the CCP by Chertow et al. (7) investigated the role of revascularization strategies in patients with AMI and ESRD. In comparison to medical therapy, there was a trend toward improved survival with coronary artery bypass surgery (RR 0.6; 95% CI 0.3 to 1.1; p = 0.09) and no significant impact on mortality with coronary angioplasty (RR 1.2; 95% CI 0.8 to 1.8; p = 0.5). In contrast to the current analysis, the diagnosis of ESRD was based solely on a high serum creatinine; the investigators could not identify whether the patient had been receiving dialysis before the admission for AMI. In addition, no information was provided regarding the use of standard medical therapies such

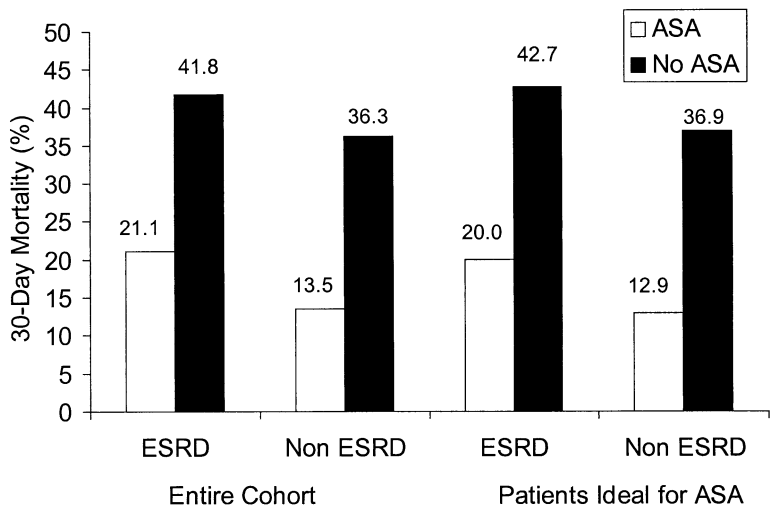

Figure 2. Thirty-day mortality was dramatically reduced by the administration of aspirin (ASA) during the hospitalization. The p value for each mortality comparison between patients taking ASA and those not receiving ASA was <0.001. The relative risk reduction in mortality was significantly greater for patients without end-stage renal disease (ESRD) than for those with ESRD in the entire cohort (63% vs. 50%, p = 0.01). After restricting the cohort to patients ideal for ASA, the reduction in mortality provided by aspirin therapy remained greater in the non-ESRD group, although it was no longer statistically significant (65% vs. 53%, p = 0.10).

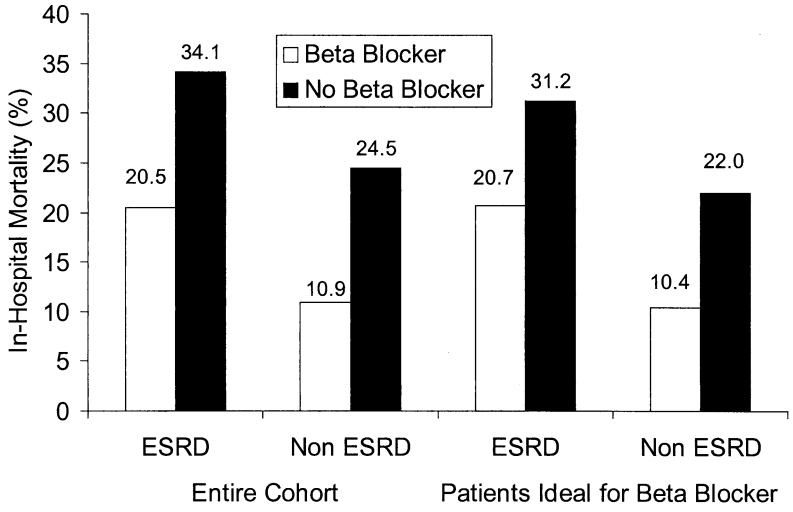

Figure 3. Thirty-day mortality was dramatically reduced by the administration of beta-blockers during the hospitalization. The p value for each mortality comparison between patients taking beta-blockers and those not receiving beta-blockers was <0.001. The relative reduction in mortality was significantly greater for patients without end-stage renal disease (ESRD) than for those with ESRD (56% vs. 40%, p = 0.02). After restricting the cohort to patients ideal for beta-blockers, the relative reduction in mortality provided by beta-blocker therapy was still significantly greater in the non-ESRD group (53% vs. 34%, p = 0.03).

as aspirin and beta-blockers. More recently, Shlipak et al. (15) demonstrated a correlation between increasing serum creatinine and one-year mortality after AMI. Unfortunately, patients with severe renal dysfunction (serum creatinine >4.0 mg/dl) were excluded from that analysis. Using the USRDS database, Herzog et al. (3) documented a strikingly high mortality of 59.3% at one year among dialysis patients who suffered an AMI. The relative risk of mortality was increased among patients 65 to 74 years of age (RR 1.78; 95% CI 1.69 to 1.88) and more than doubled in patients age 75 years and older (RR 2.09; 95% CI 1.98 to 2.21). Data regarding medical therapies were not available in the USRDS database at that time.

The efficacy of aspirin, beta-blockers, and ACE inhibitors among patients with AMI has been established in prior clinical trials. Early aspirin use reduced 35-day mortality by 23% in a meta-analysis of secondary prevention after AMI (16). The early use of beta-blockers produced a more modest impact on short-term mortality, ranging from 0% to 15% (17–19). The benefit of early beta-blocker administration became more apparent over time, with a 36% relative reduction in three-month mortality in the Göteborg trial (20). A meta-analysis of the trials of ACE inhibitors in AMI demonstrated a 7% relative reduction in 30-day mortality (21).

Patients in our cohort both with and without ESRD experienced a greater benefit with aspirin, beta-blockers, and ACE inhibitors than patients in the aforementioned

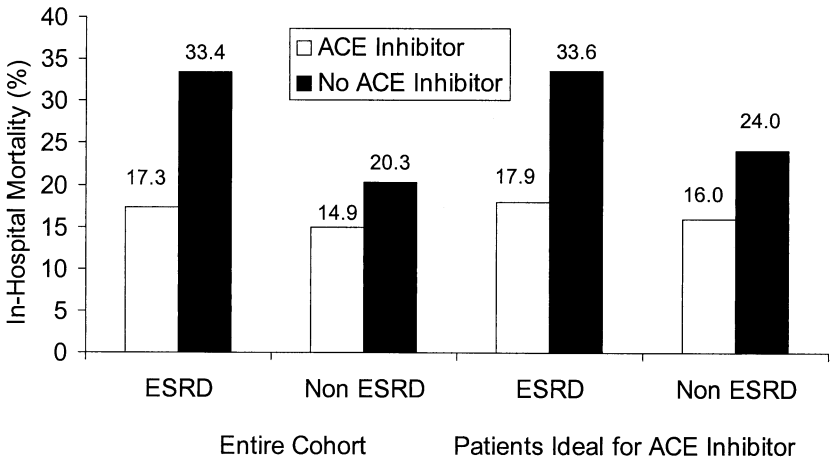

Figure 4. Thirty-day mortality was reduced by the administration of angiotensin-converting enzyme (ACE) inhibitors during the hospitalization. The p value for each mortality comparison between patients taking ACE inhibitors and those not receiving them was <0.001. The relative reduction in mortality was significantly greater for patients with end-stage renal disease (ESRD) than for those without ESRD (48% vs. 27%, p = 0.02). After restricting the cohort to patients ideal for ACE inhibitors, the relative reduction in mortality provided by ACE inhibitor therapy was still significantly greater in the ESRD group (47% vs. 33%, p = 0.43).

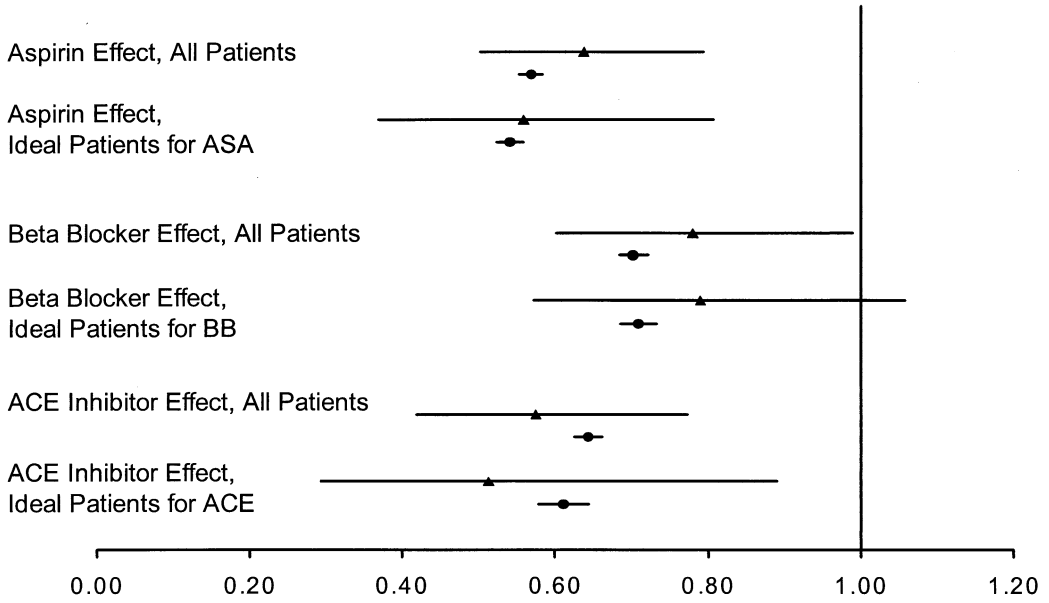

Figure 5. Effects are illustrated for the entire cohort as well as patients deemed ideal for each of the therapies. The mortality models showed good discrimination; the area under the receiver operating characteristic curve ranged from 0.75 to 0.78 for the 30-day mortality models. In assessing the goodness of fit in both models, there was less than a 10% difference between observed and expected mortality within each decile of probability for each model. The Pearson coefficient was <0.30 between the treatment variables and all other covariates. **Triangles** = patients with end-stage renal disease (ESRD); **circles** = patients without ESRD. ACE = angiotensin-converting enzyme; ASA = aspirin; BB = beta-blocker.

trials. This may reflect the fact that our patient population was sampled from Medicare beneficiaries, an inherently older group with more comorbidity and potentially more advanced cardiovascular disease than patients enrolled in the randomized clinical trials. Another explanation may lie in the fact that the CCP sampling time occurred more than a decade later than the other trials, and patterns of care may have changed.

We observed a similar absolute reduction in mortality with aspirin, beta-blocker, and ACE inhibitor therapy when comparing the dialysis and non-dialysis subgroups. Aspirin was associated with a 20.7% absolute reduction in 30-day mortality in dialysis patients and a 22.8% reduction in non-dialysis patients. The routine use of aspirin could therefore lead to one life saved for every five patients treated. Similarly, beta-blocker use was associated with a 13.6% absolute reduction in mortality in both the dialysis and non-dialysis patients. Consequently, one life could be saved for each seven patients treated with beta-blockers. The ACE inhibitor use was associated with a 16.1% absolute reduction in 30-day mortality in dialysis patients and a 5.4% reduction in non-dialysis patients. This translates into the potential to save one life for every six dialysis patients treated with an ACE inhibitor.

There are plausible reasons to suspect that aspirin, beta-blockers, and ACE inhibitors may be less effective in patients with ESRD than in those without renal insufficiency. Our data indicate that patients with ESRD have a greater burden of cardiovascular disease as well as other comorbid conditions. The presence of these associated conditions could reduce the impact of these standard medical therapies. Alternatively, patients with ESRD may have more contraindications to these medications, and thus, the risks of their use in patients with ESRD could outweigh the benefits. However, we found a benefit of aspirin, beta-blockers, and ACE inhibitors in patients with ESRD even before excluding patients who were not ideal for these therapies. The fact that these patients achieved the same benefit as those not receiving dialysis provides a strong justification for the administration of these medications. The lower use of both these therapies among dialysis patients, as demonstrated in our findings, represents a focus for improvement in quality of care. Future initiatives, both within the USRDS and at the local hospital level, should incorporate processes that guarantee a higher rate of usage of these medical therapies among dialysis patients.

Study limitations. Several issues should be considered in interpreting our study. Because this was an observational study based on a retrospective chart analysis, unmeasured factors in the CCP could have influenced our findings. To address this issue, we used methods that minimize the problems inherent in drawing inferences from observational data (22). Although statistical modeling techniques cannot completely control for this potential bias, the large number of variables available in the CCP allowed adjustment for many patient characteristics. Given the magnitude of survival benefit associated with aspirin, beta blockers, and ACE inhibitors in the ESRD population, these residual confounding factors would probably have a minimal impact on our results. Second, our results are based on data that were collected between 1994 and 1996, and improvements in health care delivery since that time may have served to

increase the use of aspirin, beta-blockers, and ACE inhibitors among patients with ESRD. Nevertheless, this study provides the first comprehensive analysis of AMI therapies among patients with ESRD.

Conclusions. The extraordinarily high mortality of ESRD patients should serve to focus greater attention on their medical care. Our findings suggest there is an opportunity to improve the quality of care and, consequently, the survival among patients with ESRD. Aspirin, beta-blockers, and ACE inhibitors should be administered to dialysis patients without absolute contraindications to these therapies, and the medications should be provided early in the course of infarction. The data show a clear benefit of these medications among dialysis patients at 30 days.

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REFERENCES

1. US Renal Data System. 2002 Annual Data Report/Atlas. Chapter 1. Incidence and prevalence. http://www.usrds.org. Accessed on June 12, 2003.
2. United States Renal Data System. 2002 Annual Data Report/Atlas. Chapter 10. Cardiovascular special studies. http://www.usrds.org. Accessed on June 12, 2003.
3. Herzog CA, Ma JZ, Collins AJ. Poor long-term survival after acute myocardial infarction among patients on long-term dialysis. N Engl J Med 1998;339:799–805.
4. Castelli P, Condemi AM, Munari M. Immediate and long-term results of coronary revascularization in patients undergoing chronic hemodialysis. Eur J Cardiothorac Surg 1999;15:51–4.
5. Koyonagi T, Nishida H, Kitamura M, et al. Comparison of clinical outcomes of coronary artery bypass grafting and percutaneous transluminal coronary angioplasty in renal dialysis patients. Ann Thorac Surg 1996;61:1793–6.
6. Rinehart AL, Herzog CA, Collins AJ, Flack JM, Ma JZ, Opsahl JA. A comparison of coronary angioplasty and coronary artery bypass grafting outcomes in chronic dialysis patients. Am J Kidney Dis 1995;25:281–90.
7. Chertow GM, Normand ST, Silva LR, McNeil BJ. Survival after acute myocardial infarction in patients with end-stage renal disease: results from the Cooperative Cardiovascular Project. Am J Kidney Dis 2000;35:1044–51.
8. Marciniak TA, Ellerbeck EF, Radford MJ, et al. Improving the quality of care for Medicare patients with acute myocardial infarction: results from the Cooperative Cardiovascular Project. JAMA 1998;279:1351–7.
9. Huff ED. Comprehensive reliability assessment and comparison of quality indicators and their components. J Clin Epidemiol 1997;50:1395–404.
10. Fleming C, Fisher ES, Chang CH, Bubolz TA, Malenka DJ. Study outcomes and hospital utilization in the elderly: the advantages of a merged data base for Medicare and Veterans Affairs hospitals. Med Care 1992;30:377–91.
11. The GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. N Engl J Med 1993;329:673–82.
12. Hosmer DW, Lemeshow S. Applied Logistic Regression. New York, NY: Wiley, 1989.
13. Hanley J, McNeil BJ. The meaning and use of the area under the receiver operating characteristic (ROC) curve. Radiology 1992;143:29–36.
14. Zhang J, Yu K. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA 1998;280:1690–1.
15. Shlipak MG, Heidenreich PA, Naguchi H, Chertow GM, Browner WS, McClellan MB. Association of renal insufficiency with treatment and outcomes after acute myocardial infarction in elderly patients. Ann Intern Med 2002;137:555–62.
16. Antiplatelet Trialists' Collaboration. Secondary prevention of vascular disease by prolonged antiplatelet treatment. BMJ (Clin Res Ed) 1988;296:320–31.
17. MIAMI Trial Investigators. Metoprolol in acute myocardial infarction (MIAMI). A randomised placebo-controlled international trial. Eur Heart J 1985;6:199–226.
18. ISIS-1 Trial Investigators. Mechanisms for the early mortality reduction produced by beta-blockade started early in acute myocardial infarction: ISIS-1. Lancet 1988;1:921–3.
19. TIMI-2 Investigators. Thrombolysis In Myocardial Infarction (TIMI) phase II trial. N Engl J Med 1989;321:612.
20. Hjalmarson A, Elmfeldt D, Herlitz J, et al. Effect on mortality of metoprolol in acute myocardial infarction. A double-blind randomised trial. Lancet 1981;2:823–7.
21. ACE Inhibitor Myocardial Infarction Collaborative Group. Indications for ACE inhibitors in the early treatment of acute myocardial infarction. Systematic overview of individual data from 100,000 patients in randomized trials. Circulation 1998;97:2202–12.
22. Horwitz RI, Viscoli CM, Clemens JD, Sadock RT. Developing improved observational methods for evaluating therapeutic effectiveness. Am J Med 1990;89:630–8.