CARDIAC disease is the single most important cause of death among patients receiving long-term dialysis therapy, accounting for 44 percent of overall mortality.1 Approximately 22 percent of these deaths from cardiac causes are attributed to acute myocardial infarction. For the period from 1993 through 1995, the adjusted overall death rate for patients on dialysis was 243 deaths per 1000 patient-years.1 The risks of death from cardiac causes and of death from all causes are higher among older patients, those with diabetic nephropathy, and those receiving peritoneal dialysis.1 Thus, there is an increasing burden of cardiac disease in patients on long-term dialysis, since the greatest increase in end-stage renal disease treated with dialysis has occurred in older patients and those with diabetic renal failure. The mortality rate from 1993 through 1995 for patients 65 years of age or more with diabetic end-stage renal disease was 368 deaths per 1000 patient-years, with cardiac disease accounting for 46 percent of overall mortality.2 In 1995 approximately 200,000 patients received dialysis in the United States; 18 percent of them received peritoneal dialysis, and 82 percent received hemodialysis.3

Despite the burden of cardiac disease among patients on dialysis, there are no published data on their long-term survival after acute myocardial infarction. The purpose of our study was to estimate the long-term survival of patients in the U.S. who were receiving dialysis and who had acute myocardial infarction. Using the U.S. Renal Data System data base4 of 627,983 patients (approximately three fourths of whom were on dialysis and one fourth of whom were renal-transplant recipients), we examined the outcome after a first acute myocardial infarction for 34,189 patients on long-term dialysis.

METHODS

All data were derived from the U.S. Renal Data System, which includes data on approximately 92 percent of all patients undergoing dialysis in the United States.5 The accuracy of these data has been validated previously.6

The study was a retrospective analysis of patients undergoing dialysis who were hospitalized for a first (index) acute myocardial infarction that occurred after the initiation of renal-replacement therapy from January 1977 to June 1995. The patients identified from the data base of 627,983 patients were those who had code 410, 410.X, 410.X0, or 410.X1 of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM).7 Eligible patients had received renal-replacement therapy for a total of at least 90 days and dialysis for at least 60 days before having an acute myocardial infarction. Demographic data on the patients included age, sex, race or ethnic group (Hispanic patients were not identified in the data base), calendar year of infarction, and primary renal diagnosis.

The effect of coexisting conditions was examined, since comorbidity significantly influences the survival of patients on dialysis.8,9 We used a previously developed comorbidity-profiling method based on ICD-9-CM diagnosis and procedure codes in Medicare Part A institutional inpatient claims. Coexisting conditions were identified by ICD-9-CM codes from hospitalizations that occurred before the index acute myocardial infarction. Coexisting conditions included congestive heart failure, other cardiac conditions (including valvular heart disease, implantation of a pacemaker, and arrhythmia), cancers other than skin cancer, peripheral vascular disease, cerebrovascular ischemia (which included cerebrovascular accident and transient ischemic attack), chronic obstructive pulmonary disease, gastrointestinal disease, gallbladder disease, and liver disease. Previous coronary revascu-
lization (coronary bypass surgery or coronary angioplasty) was analyzed separately in the Cox proportional-hazards model. In-hospital mortality and the number of deaths per 1000 patient-years were estimated. Survival time was calculated from the date of admission to the hospital for acute myocardial infarction to the date on which the data were censored or on which an end point (including in-hospital death) was reached. If a patient on dialysis had more than one infarction, the first was analyzed as the index event. The study end points were death from cardiac causes and death from any cause (including early in-hospital death). The data were censored if a patient underwent renal transplantation, was still alive at the end of the study, or was lost to follow-up.

Long-term survival and mortality were estimated by the life-table method. The log-rank test was used to compare cumulative survival in different groups. A Cox proportional-hazards model was used to evaluate the effect of independent predictors (demographic characteristics, coexisting illnesses, and duration of end-stage renal disease before acute myocardial infarction) on patients' survival. The reported P values in the Cox model are based on the Wald test. All reported P values are two-sided. Statistical analyses were performed with use of the SAS system for Windows, version 6.12 (SAS Institute, Cary, N.C.).

A parallel survival analysis of renal-transplant recipients with acute myocardial infarction was performed by the life-table method. The survival of patients on dialysis was compared with that of transplant recipients in a Cox model.

The Human Subject Research Committee of the Hennepin County Medical Center institutional review board approved this study.

RESULTS

There were 34,189 patients on dialysis who had acute myocardial infarction. The mean follow-up after myocardial infarction was 1.16 years (interquartile range [25th to 75th percentile], 0.05 to 1.59). There were 858 patients lost to follow-up.

Demographic Characteristics

Fifty-six percent of the group were men, and 44 percent were women. Eight percent were 44 years of age or less, 37 percent were 45 to 64 years old, 35 percent were 65 to 74 years old, and 20 percent were 75 or more years old. Seventy-one percent were white, 25 percent black, 1 percent Native American, 2 percent Asian, and 1 percent of other ethnic groups. The cause of renal failure was diabetes in 34 percent, hypertension in 30 percent, and other conditions in 36 percent. Ten percent of acute myocardial infarctions occurred from 1977 through 1984, 30 percent from 1985 through 1989, and 60 percent from 1990 through 1995.

There were 3079 renal-transplant recipients with acute myocardial infarction. For these patients, the mean follow-up after myocardial infarction was 2.46 years. Seventy-two percent of the patients were men, and 28 percent were women. Thirty-four percent were 44 years of age or less, 55 percent were 45 to 64 years old, 10 percent were 65 to 74 years old, and 1 percent were 75 or more years old. Eighty-four percent were white, 14 percent were black, and 2 percent were of other races or ethnic groups. The cause of renal failure was diabetes in 31 percent, hypertension in 14 percent, and other conditions in 55 percent. Six percent of acute myocardial infarctions occurred from 1977 through 1984, 30 percent from 1985 through 1989, and 64 percent from 1990 through 1995.

We examined the temporal pattern of occurrence of acute myocardial infarction in relation to the duration of dialysis. There appeared to be an early hazard of myocardial infarction related to the initiation of dialysis, since 29 percent of infarctions occurred within one year and 52 percent within two years after the initiation of dialysis. In renal-transplant recipients, 15 percent of infarctions occurred within one year after transplantation and 29 percent within two years.

Mortality

Patients Undergoing Dialysis

The estimated in-hospital mortality for the entire cohort of patients on dialysis who had acute myocardial infarction was 26 percent. Twenty-one percent of patients under 65 years of age and 30 percent of those 65 or more years of age died in the hospital. Twenty-seven percent of all patients with diabetic end-stage renal disease and 30 percent of those 65 or more years of age died in the hospital.

Table 1 summarizes the rates of death from all caus-

---

### Table 1

<table>
<thead>
<tr>
<th>Age</th>
<th>Cause of Renal Failure</th>
<th>Rate of Death from Cardiac Causes Among Patients on Dialysis, According to Cause of Renal Failure, 1977 through 1995.*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Causes</td>
<td>Diabetes Mellitus Hypertension Other Causes</td>
</tr>
<tr>
<td></td>
<td>deaths/1000 patient-yr</td>
<td></td>
</tr>
<tr>
<td>Overall mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 yr</td>
<td>518.3±4.8</td>
<td>718.5±10.1</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>924.8±7.3</td>
<td>1091.2±16.5</td>
</tr>
<tr>
<td>Mortality from cardiac causes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 yr</td>
<td>296.9±3.6</td>
<td>421.4±7.7</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>532.1±5.5</td>
<td>626.5±12.5</td>
</tr>
</tbody>
</table>

*Rates are expressed as the numbers of deaths per 1000 patient-years ±SE.
POOR LONG-TERM SURVIVAL AFTER ACUTE MYOCARDIAL INFARCTION AMONG PATIENTS ON LONG-TERM DIALYSIS

from all causes and from heart disease according to renal diagnosis and the year of occurrence of acute myocardial infarction. Patients on dialysis who had diabetic end-stage renal disease had the highest mortality both overall and from cardiac causes. Surprisingly, the patients who had had acute myocardial infarctions most recently (between 1990 and 1995) had a higher overall rate of death from all causes than those who had had myocardial infarctions between 1977 and 1984 or between 1985 and 1989 (P<0.001). The trends were similar for death from cardiac causes.

The effects of independent predictors of overall mortality and mortality from cardiac causes were examined by the Cox proportional-hazards model. Table 3 summarizes independent predictors of overall mortality. The most powerful predictors of overall mortality were older age and the presence of diabetic end-stage renal disease. Coexisting noncardiac conditions (except gallbladder disease) independently increased the risk of death by 10 to 19 percent according to the Cox model. The duration of end-stage renal disease, however, did not independently affect survival. Thus, the time from the initiation of dialysis to the index acute myocardial infarction was not an independent predictor of survival. Previous coronary revascularization was associated with a 13 percent reduction in risk. Female sex was associated with a small survival advantage (relative risk of death, 0.96; 95 percent confidence interval, 0.94 to 0.99). Race was a more powerful predictor of survival, since nonwhite patients had better outcomes. As compared with whites, black patients had a relative risk of death of 0.82 (95 percent confidence interval, 0.80 to 0.85).

**Table 2.** Estimated Cumulative Overall Mortality and Mortality from Cardiac Causes after Acute Myocardial Infarction among Patients with End-Stage Renal Disease, According to Cause of Renal Failure and Year of Occurrence of Acute Myocardial Infarction.*

<table>
<thead>
<tr>
<th>PATIENT GROUP</th>
<th>OVERALL MORTALITY AFTERAMI</th>
<th>CARDIAC MORTALITY AFTERAMI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 yr</td>
<td>2 yr</td>
</tr>
<tr>
<td>All patients</td>
<td>59.3±0.3</td>
<td>73.0±0.3</td>
</tr>
<tr>
<td>Year of AMI</td>
<td>1977–1984</td>
<td>55.4±0.9</td>
</tr>
<tr>
<td></td>
<td>1985–1989</td>
<td>56.0±0.5</td>
</tr>
<tr>
<td></td>
<td>1990–1995</td>
<td>61.7±0.3</td>
</tr>
<tr>
<td>Transplant recipients</td>
<td>All patients</td>
<td>24.1±0.8</td>
</tr>
<tr>
<td></td>
<td>Renal failure caused by diabetes</td>
<td>28.7±1.5</td>
</tr>
<tr>
<td></td>
<td>AMI in 1990–1995</td>
<td>24.1±1.0</td>
</tr>
</tbody>
</table>

* Rates are expressed as percentages ±SE. AMI denotes acute myocardial infarction.
Table 3 summarizes independent predictors of mortality from cardiac causes. Older age and the presence of diabetic end-stage renal disease were the most powerful predictors of mortality, and noncardiac coexisting conditions had a small effect. Previous congestive heart failure was associated with a relative risk of death from cardiac causes of 1.22 (95 percent confidence interval, 1.18 to 1.26). There was a reduced risk of death from cardiac causes after myocardial infarction for women (relative risk, 0.92; 95 percent confidence interval, 0.97 to 0.99). Race was a predictor of improved survival for all nonwhite patient groups. As compared with whites, black patients had a relative risk of death from cardiac causes of 0.81 (95 percent confidence interval, 0.78 to 0.84). Previous coronary revascularization was associated with a 10 percent reduction in risk.

The somewhat counterintuitive effect on survival of the time of occurrence of acute myocardial infarction is partly explained by the Cox model. According to the Cox model, patients who had more recent myocardial infarctions (those occurring between 1985 and 1989 or between 1990 and 1995) had better survival than those who had myocardial infarctions earlier (1977 to 1984). For patients with myocardial infarctions between 1990 and 1995, the relative risk of death from all causes was 0.87 (95 percent confidence interval, 0.83 to 0.90) and that of death from cardiac causes was 0.83 (95 percent confidence interval, 0.78 to 0.88). These results indicate that there has been a recent improvement in survival after adjustment is made for comorbidity.

Renal-Transplant Recipients

The estimated in-hospital mortality was 11.5 percent for the entire cohort of renal-transplant recipients. Table 2 includes selected mortality data for renal-transplant recipients with acute myocardial infarction.

Dialysis versus Transplantation

Large differences in mortality between patients on dialysis and renal-transplant recipients persisted after adjustment for demographic characteristics, cause of renal failure, duration of end-stage renal dis-

Table 4. Results of Cox Proportional-Hazards Model of Death from Cardiovascular Causes.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Relative Risk (95 Percent CI)*</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>45–64 yr</td>
<td>1.00 (0.97–1.04)</td>
<td>0.82</td>
</tr>
<tr>
<td>65–74 yr</td>
<td>1.02 (0.99–1.05)</td>
<td>0.18</td>
</tr>
<tr>
<td>&gt;75 yr</td>
<td>0.96 (0.93–1.00)</td>
<td>0.07</td>
</tr>
<tr>
<td>Prior revascularization</td>
<td>0.87 (0.82–0.93)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Year of acute myocardial infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1985–1989</td>
<td>0.86 (0.83–0.90)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1990–1995</td>
<td>0.87 (0.83–0.90)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*The reference group has the following characteristics: age <44 years, male sex, white race, other cause of end-stage renal disease, no coexisting illness or prior coronary revascularization, duration of end-stage renal disease <1 year, and acute myocardial infarction between 1977 and 1984. CI denotes confidence interval.
ease, calendar year of occurrence of acute myocardial infarction, and coexisting illnesses. The relative risk of death from all causes for patients undergoing dialysis as compared with renal-transplant recipients was 2.74 (95 percent confidence interval, 2.57 to 2.91). The relative risk of death from cardiac causes was 4.45 (95 percent confidence interval, 4.01 to 4.94). These results should be interpreted cautiously, because even after adjustment, patients undergoing dialysis and renal-transplant recipients may not be completely comparable.

**DISCUSSION**

There are few data on long-term survival after acute myocardial infarction among patients on dialysis. Two preliminary reports suggested increased in-hospital mortality (29 percent and 33 percent) for these patients. In this study we have shown that acute myocardial infarction in patients on dialysis is a catastrophic event associated with dismal long-term survival. For the entire cohort of 34,189 patients on dialysis who had acute myocardial infarctions from 1977 to 1995, only 41 percent of patients survived for one year and 27 percent for two years. Even more striking was the poor survival of patients treated in the era of reperfusion. Patients who had acute myocardial infarctions from 1990 to 1995 had overall mortality rates of 61 percent at one year and 74 percent at two years. The two-year mortality from cardiac causes was about 50 percent in patients who had acute myocardial infarctions from 1977 to 1984 and 52 percent for those who had acute myocardial infarctions from 1990 to 1995. The high mortality from cardiac disease and even higher overall mortality probably reflect the effects of coexisting conditions, but it is unclear how much of the difference of approximately 20 percentage points between overall mortality and mortality from cardiac causes at two years is attributable to coexisting conditions. The persistently poor outcomes over time mask a small improvement in survival adjusted for comorbidity in the Cox model. There was a 13 percent reduction in the risk of death from all causes and a 17 percent reduction in the risk of death from cardiac causes in 1990 to 1995, as compared with 1977 to 1984. This masking is explainable by the increase in the proportion of older patients and patients with diabetes over time, which contributed to increased mortality.

The survival of patients on dialysis who had acute myocardial infarctions is considerably worse than would be expected on the basis of other published reports of patients without end-stage renal disease who had acute myocardial infarctions, including patients with other coexisting conditions. The most powerful independent predictors of overall mortality and mortality from cardiac causes in our study were older age and diabetic nephropathy, but even patients with end-stage renal disease that was not due to diabetes or hypertension had poor outcomes, with a 31 percent two-year survival (69 percent overall mortality). In diabetic patients without end-stage renal disease who had acute myocardial infarction, a one-year survival of 80 percent and a 19-month survival of 75 percent were reported in the era before reperfusion therapy became common.

In the Minnesota Heart Survey, the in-hospital case fatality rate in 1985 for patients with diabetes who had acute myocardial infarction was 18 percent in men and 16 percent in women. Over the period from 1970 to 1985, about three fourths of diabetic men and two thirds of diabetic women who were discharged after an acute myocardial infarction were still alive two years later. The Worcester Heart Attack Study, the overall in-hospital case fatality rate after myocardial infarction was 22 percent for diabetic patients for the period from 1975 to 1986. Approximately three fourths of diabetic men and two thirds of diabetic women discharged after an acute myocardial infarction were still alive two years later. In the Minnesota Heart Survey, the three-year survival rate after acute myocardial infarction ranged from 63.5 percent to 73.1 percent for men and from 60.6 percent to 66.9 percent for women from 1970 to 1985, with an additional reduction in mortality in 1990. In the present study, 60 percent of all patients on dialysis between 1990 and 1995 had acute myocardial infarctions. The substantial reduction in mortality from acute myocardial infarction over time that was observed in the Minnesota Heart Survey has not been mirrored in the population undergoing dialysis.

There appears to be greater mortality from cardiac causes and greater overall mortality among patients on dialysis who have acute myocardial infarctions than among another cohort of patients with end-stage renal disease, renal-transplant recipients who have myocardial infarctions. The two-year mortality from cardiac causes of 11.4 percent and overall mortality of 30.4 percent in the renal-transplant cohort are more favorable than the two-year mortality from cardiac causes of 51.8 percent and overall mortality of 73.0 percent among the patients undergoing dialysis. This difference in mortality is apparent at all times from 1 to 10 years.

Our finding that mortality after acute myocardial infarction among patients on dialysis is lower for blacks than for whites is consistent with previously published data on the survival of patients on dialysis. In 1984 the one-year death rate of white patients on dialysis was higher than that of black patients by 13 deaths per 100 patient-years. By 1994 this difference had narrowed to 5 deaths per 100 patient-years. Bloem bergen et al. reported that white patients had a 29 percent higher risk of death than blacks and that whites were 34 percent more likely
to die of myocardial infarction. In the present study, the overall risk of death after myocardial infarction for patients on dialysis was 18 percent lower for blacks than for whites, and the risk of death from cardiac disease was 19 percent lower.

We found a small advantage in terms of survival after acute myocardial infarction associated with female sex, with a 4 percent reduction in overall mortality and an 8 percent reduction in mortality due to cardiac disease. Although female sex has usually been associated with higher mortality from acute myocardial infarction among patients without end-stage renal disease, a recent study disputes earlier reports of excess early mortality in women.24

Our data suggest that there is an early risk of acute myocardial infarction associated with the initiation of dialysis, with 29 percent of infarctions occurring within one year and 52 percent occurring within two years after the initiation of dialysis. Usually patients with end-stage renal disease are evaluated for risk of cardiac events only when they are being considered for renal transplantation. We suggest that an evaluation for cardiac risk be considered for such patients at the initiation of dialysis.

There are several limitations to our study. The primary source of the U.S. Renal Data System data was Medicare claims data, which may be subject to inaccuracies in the diagnosis of acute myocardial infarction. After comparing claims data with medical-chart (clinical) data in a study of 12,937 patients undergoing inpatient cardiac catheterization, Jollis et al.25 found an 88 percent rate of agreement between claims data and clinical data with respect to the ICD-9-CM code for acute myocardial infarction (410), with a specificity of 95 percent.26 We undoubtedly missed some patients with acute myocardial infarction, since Jollis et al. found that claims data had 76 percent sensitivity as compared with clinical data for the diagnosis of acute myocardial infarction.25

Two aspects of our methods may have led to an underestimation of mortality. Our survival analysis ignored out-of-hospital deaths from acute myocardial infarction and those occurring less than 60 days after the initiation of dialysis. The issue of "missed" or "uncounted" acute myocardial infarctions makes accurate estimation of the incidence of acute myocardial infarction difficult, but our data indicate that in 1995 there were at least 5000 first-time infarctions after the initiation of dialysis, with 1300 in-hospital deaths, in a population of 200,000 patients on dialysis. The total number of acute myocardial infarctions and resulting in-hospital deaths may be considerably larger, since in our study, survival analysis was restricted to the first (index) acute myocardial infarction. On the basis of data from the U.S. Renal Data System, approximately 4600 deaths per year (not restricted to in-hospital deaths) in 200,000 patients on dialysis are attributed to acute myocardial infarc-

tion.1 The principal weakness of the data base is that it provides few clinical data. Therefore, important prognostic factors, such as the left ventricular ejection fraction and hemodynamic data, were not available for our study.

The present study does not explain the persistence of poor survival rates after acute myocardial infarction over time, even in the reperfusion era. Preliminary data from an ongoing study suggest that thrombolytic therapy is underused in the treatment of patients on dialysis who have acute myocardial infarction,26 but there are no published data on the survival of patients on dialysis who receive reperfusion therapy for acute myocardial infarction.

We conclude that patients on dialysis who have acute myocardial infarction have high rates of death from cardiac causes and poor long-term survival. Our data provide support for the development of more aggressive strategies for the prevention and treatment of acute myocardial infarction in patients on dialysis.

Supported by a grant (1 RO1 DK 49540) from the National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Md.

The data reported here have been supplied by the U.S. Renal Data System. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the U.S. government.

REFERENCES


Gaylin DS, Held PJ, Port FK. The impact of comorbid and sociodemographic factors on access to renal transplantation. JAMA 1993;269:603-8.


Collins AJ, Hamon G, Umen A, Kjellstrand C, Keshaviah P. Changing risk factor demographics in end-stage renal disease patients entering hemo-
dialysis and the impact on long-term mortality. Am J Kidney Dis 1990;25:
422-32.
outcome after Q wave and non-Q wave myocardial infarction in a large
17. Smith JW, Marcus FI, Scrolem R. Prognosis of patients with diabetes
in prevalence of diabetes mellitus in patients with myocardial infarction and
effect of diabetes on survival: the Minnesota Heart Survey. Diabetes Care
19. Donahue RP, Goldberg RJ, Chen Z, Gore JM, Alpert JS. The influence
of sex and diabetes mellitus on survival following acute myocardial infarction:
hospitalized myocardial infarction patients between 1970 and 1985: the

Volume 339 Number 12  ·  805