ORIGINAL RESEARCH

Trends in Mortality Following Acute Myocardial Infarction Among Dialysis Patients in the United States Over 15 Years

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***Background*—**We sought to determine 15-year trends in mortality rates among dialysis patients with acute myocardial infarction (AMI) in the contemporary era.

***Methods and Results*—**Using the US Renal Data System database, we assembled 4 study cohorts of period-prevalent dialysis patients in 1993, 1998, 2003, and 2008 who were hospitalized for an index AMI in that calendar year. ST-segment elevation myocardial infarction (STEMI) and non-STEMI were identified, and in-hospital mortality was calculated. Cumulative probability of death during 2-year follow-up after AMI admission was estimated by the Kaplan–Meier method and adjusted for patient characteristics. A total of 42 933 dialysis patients with AMI were included. Between 1993 (n=4494) and 2008 (n=16 361), proportional increases occurred in patient groups aged ≥75 years (23% and 31%, respectively; $P<0.001$), of black race (25% and 31%, respectively; $P<0.001$), with end-stage renal disease due to diabetes (42% and 55%, respectively; $P<0.001$), and with non-STEMI (42.2% and 80.7%, respectively; $P<0.001$). For all patients with AMI, in-hospital mortality rates decreased (31.9% in 1993, 18.8% in 2008; $P<0.001$), as did unadjusted 2-year cumulative probability of death after AMI admission (76.5% in 1993, 71.5% in 2008; $P<0.001$). Between 1993 and 2008, among STEMI patients, in-hospital mortality (38.2% and 25.9%, $P<0.001$) and unadjusted 2-year cumulative probability of mortality (77.3% and 71.2%, $P<0.001$) decreased, but decreases did not occur among NSTEMI patients (14.2% and 14.9%, $P=0.47$, and 70.9% and 70.1%, $P=0.52$ respectively).

***Conclusions*—**In-hospital mortality and 2-year cumulative probability of death following AMI among dialysis patients decreased between 1993 and 2008 but only among STEMI patients, coincident with increased in-hospital percutaneous coronary intervention rates. Period-prevalent cases of non-STEMI markedly increased without interval change in survival. **(*J Am Heart Assoc*. 2015;4: e002460 doi: 10.1161/JAHA.115.002460)**

Key Words: end-stage renal disease • mortality • myocardial infarction • non–ST-segment elevation myocardial infarction • ST-segment elevation myocardial infarction

Acute myocardial infarction (AMI) is a catastrophic clinical event among dialysis patients and is associated with high in-hospital mortality rates and poor long-term survival.[1–4] More than 15 years have elapsed since the initial description of the dismal survival rates in this population based on data from the US Renal Data System (USRDS)[1]; the reported 1- and 2-year mortality rates were 55% and 71%, respectively, for the 1977–1984 cohort and 62% and 74%, respectively, for the 1990–1995 cohort. Several factors have been postulated to explain worse outcomes following AMI among dialysis patients relative to the general population, including challenges in establishing a timely diagnosis of AMI due to atypical presentations and clinical characteristics,[5,6] lower use and effectiveness of "conventional" evidence-based therapies,[3,4,7,8] and concern regarding therapeutic nihilism by the medical community toward these patients.

In the past 2 decades, noteworthy improvements in evidence-based therapies (including coronary reperfusion) have occurred in the general population, leading to considerable declines in AMI incidence and mortality in the modern treatment era.[9–11] Although improved outcomes in the general population cannot be automatically extrapolated to the population with end-stage renal disease (ESRD), some optimistic trends are apparent. Incident AMI rates among dialysis patients peaked in 2002 (80.8 and 78.5 per 1000 patient-years among hemodialysis and peritoneal dialysis patients, respectively) and

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Accompanying Figure S1 and Tables S1 through S3 are available at http://jaha.ahajournals.org/content/4/10/e002460/suppl/DC1

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have steadily declined since then (73.1 and 66.9 per 1000 patient-years, respectively, in 2011), probably reflecting the success of population-based preventive strategies.[12] Published evidence obtained from several large, high-profile registries has verified and emphasized the high prevalence of advanced chronic kidney disease (CKD) among AMI patients,[3] atypical clinical presentations with AMI,[5,13] poor short-term and long-term outcomes,[1] and the inverse correlation between worsening renal function and use of evidence-based therapies.[2,3,14,15] Increased emphasis on this high-risk population has likely served to heighten awareness among clinicians regarding specific issues of importance. Recently, a study from a single academic center in the Netherlands reported a substantial decrease in 30-day mortality among a cohort of 12 087 AMI patients with varying degrees of CKD between 1985 and 2008.[16] This temporal reduction in mortality was also noted among patients with stage 4 to 5 CKD, but findings were not generalizable because these patients made up merely 4% of the study population (and specific information regarding dialysis status was not available).

We sought to determine trends in mortality rates among dialysis patients with AMI in the contemporary era, further categorized by type of AMI, namely, ST-segment elevation myocardial infarction (STEMI) or non-STEMI (NSTEMI).

Methods

Study Population and Study Period

Using the USRDS database, we identified period-prevalent dialysis patients in 1993, 1998, 2003, and 2008 whose first ESRD service date was at least 90 days before the beginning of the year (point-prevalent patients on January 1) or who reached day 91 of ESRD treatment during the year (incident patients) and were hospitalized with a first AMI in the prevalent year with Medicare as primary payer. We excluded patients whose age or sex was unknown and patients aged <20 years (calculated on the later of January 1 of the prevalent year or day 91 of ESRD). The baseline period was 12 months before the index hospitalization, during which comorbid conditions including prior coronary revascularization were identified. Follow-up began on the date of hospital admission with AMI and ended at the earliest occurrence of death, renal transplant, recovery of kidney function, loss to follow-up, or 2 years following AMI admission.

Identification of AMI, Medical Procedures, and Comorbid Conditions

AMI and specific type of AMI (NSTEMI or STEMI) were identified by International Classification of Diseases, ninth revision, clinical modification (ICD-9-CM) diagnosis codes from Medicare inpatient claims. We used ICD-9-CM procedure codes or Current Procedural Terminology codes to identify patients undergoing coronary revascularization with thrombolytics, percutaneous coronary intervention, or coronary artery bypass grafting during the index hospitalization. Timing of coronary revascularization relative to hospital admission was characterized as occurring during the first hospital day (defined as the admission day), during the first 2 hospital days (defined as the admission day and the next day), or at any time during the index hospitalization. In-hospital death was identified based on discharge status reported on the inpatient claims. Comorbid conditions (Table S1) were identified from relevant ICD-9-CM diagnosis codes on at least 1 Part A inpatient, skilled nursing facility or home health claim or on 2 Part A outpatient or Part B claims on different days during the baseline period.

Statistical Methodology

Baseline characteristics, type of AMI, timing of coronary revascularization, and in-hospital death were presented as percentages; differences across cohort years were assessed using chi-square tests. The cumulative probability of death during the follow-up period was estimated by the Kaplan–Meier method; differences were tested using the log-rank test. The cumulative probability of death was further adjusted for age, sex, race, ESRD duration, ESRD etiology, dialysis modality type at AMI admission, baseline coronary revascularization, and comorbid conditions using a model-based direct adjustment method with the 2008 cohort as the reference.[17] The differences in unadjusted and adjusted cumulative probability of death across cohort years at 1 and 2 years of follow-up were assessed using the bootstrap method. Visual inspection revealed that the proportionality of the risk of death over time across cohort years was questionable, and a piece-wise Cox regression model was used to address the time dependency of risk of death with cutoffs of ≤1 month and >1 to ≤24 months after AMI admission and included factors listed in Table 1. Analyses were performed for all AMI patients and for subgroups with NSTEMI and STEMI. Analyses were performed using SAS version 9.2 (SAS Institute).

Research conducted by the USRDS is classified as exempt under institutional review board regulations.

Results

Study Population and AMI Distribution in the Study Period

We identified 4494, 8081, 14 232, and 16 361 period-prevalent dialysis patients (n=43 168 patients) with AMI in

Table 1. Baseline Characteristics of Period-Prevalent Dialysis Patients With AMI in 1993, 1998, 2003, and 2008, Overall and by AMI Type

	All AMI					NSTEMI					STEMI				
	1993	1998	2003	2008	*P* Value	1993	1998	2003	2008	*P* Value	1993	1998	2003	2008	*P* Value
Sample size, n	4494	8081	14 232	16 361		1898	4502	9701	13 210		1658	2245	2331	1571	
Age category, y (%)					<0.001					<0.001					<0.001
20 to 44	7.0	5.3	4.9	5.0		6.4	5.3	4.8	4.9		7.9	5.8	5.8	5.7	
45 to 64	33.4	31.0	31.5	34.3		33.4	31.4	31.5	34.1		34.3	31.2	33.8	37.2	
65 to 74	36.7	35.0	31.1	29.6		37.0	35.5	31.4	29.5		35.7	34.5	30.9	28.3	
≥75	22.8	28.7	32.4	31.2		23.2	27.8	32.3	31.4		22.1	28.5	29.5	28.8	
Male, %	53.5	53.2	52.5	54.4	0.009	54.5	54.6	52.9	54.6	0.047	50.3	50.5	50.6	51.6	0.88
Race, %					<0.001					<0.001					<0.001
White	71.3	66.6	64.0	62.6		71.2	66.3	63.6	62.0		71.5	66.9	63.7	65.1	
Black	25.3	28.4	29.9	31.3		25.0	28.2	30.1	32.0		25.3	28.6	30.9	29.2	
Other	3.4	5.0	6.1	6.0		3.8	5.6	6.4	6.0		3.2	4.5	5.4	5.8	
ESRD primary cause, %					<0.001					<0.001					<0.001
Diabetes	41.5	48.5	52.9	54.9		42.9	49.8	53.0	55.3		40.0	46.6	52.1	53.1	
Hypertension	33.5	30.5	28.8	27.5		33.6	30.0	29.1	27.4		33.4	30.7	27.8	27.2	
Other	24.9	21.0	18.3	17.6		23.6	20.2	17.9	17.3		26.5	22.7	20.1	19.7	
ESRD duration, y (%)					<0.001					<0.001					<0.001
<1	35.8	30.4	28.9	25.0		37.8	30.6	29.4	25.2		33.9	30.7	27.1	25.1	
1 to <3	34.0	32.1	30.5	28.5		33.8	33.0	30.6	28.6		33.8	30.6	31.4	26.5	
3 to <5	15.1	19.6	19.3	20.7		14.9	19.8	19.0	20.8		15.4	19.8	20.1	20.9	
≥5	15.2	17.9	21.3	25.7		13.4	16.5	21.0	25.5		16.9	18.9	21.4	27.4	
Modality at AMI admission					<0.001					<0.001					<0.001
Hemodialysis	81.6	88.6	93.1	94.3		83.1	89.5	93.8	95.0		79.3	85.8	90.3	89.5	
Peritoneal dialysis	18.0	11.2	6.6	5.3		16.5	10.3	5.9	4.7		20.3	13.9	9.4	9.9	
Unknown	0.4	0.2	0.3	0.3		0.4	0.2	0.2	0.3		0.4	0.2	0.3	0.6	
Procedure and comorbidity at baseline															
Revascularization*	4.7	6.4	8.7	9.5	<0.001	5.4	6.8	8.9	9.4	<0.001	4.3	6.5	9.5	10.6	<0.001
CHF	53.0	58.1	60.9	61.6	<0.001	55.4	59.3	61.3	62.4	<0.001	48.7	53.3	55.0	52.5	0.032
Arrhythmia	29.8	37.2	40.0	42.0	<0.001	30.1	38.3	40.4	42.6	<0.001	27.0	32.5	32.9	34.1	<0.001
Myocardial infarction	18.4	24.1	27.6	26.3	<0.001	20.3	26.0	29.4	27.2	<0.001	16.9	20.7	23.7	21.3	0.001
Other cardiac disease	35.9	45.6	48.6	48.8	<0.001	34.7	46.5	49.1	49.3	<0.001	33.6	40.6	43.8	42.3	<0.001
CVA/TIA	17.9	22.0	25.7	26.6	<0.001	17.5	22.3	25.8	26.7	<0.001	17.7	21.2	23.8	23.9	<0.001

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1993, 1998, 2003, and 2008, respectively. A total of 235 patients (0.5%) appeared in 2 cohorts; therefore, this study included 42 933 unique dialysis patients with an index AMI in the selected cohort years. The distribution of NSTEMI and STEMI subgroups changed markedly during the study period (Figure 1). Between 1993 and 2008, the number of NSTEMI patients increased dramatically, and their proportion in the AMI cohort doubled (n=1898, 42.2% in 1993; n=13 201, 80.7% in 2008); however, the number of STEMI patients remained relatively unchanged, resulting in considerable progressive reduction in their proportions in the AMI cohort (n=1658, 36.9%, 1993; n=1571, 9.6%, 2008).

Patient Characteristics

Demographics of the study population changed notably from 1993 through 2008 (Table 1). Between 1993 and 2008, proportional increases occurred in patient groups aged ≥75 years (23% and 31%, respectively; $P<0.001$), of black race (25% and 31%, respectively; $P<0.001$), on hemodialysis at the time of AMI admission (82% and 94%, respectively; $P<0.001$), with ESRD due to diabetes (42% and 55%, respectively; $P<0.001$), and with dialysis duration >5 years (15% and 26%, respectively; $P<0.001$). Proportions of patients with history of AMI (18% in 1993, 26% in 2008; $P<0.001$) and prior coronary revascularization (4.7% in 1993, 9.5% in 2008; $P<0.001$) also significantly increased. Other cardiovascular diseases were significantly more prevalent in patients with AMI admissions in 2008 than for patients with admissions in 1993 (Table 1). Similar patterns of changes in patient

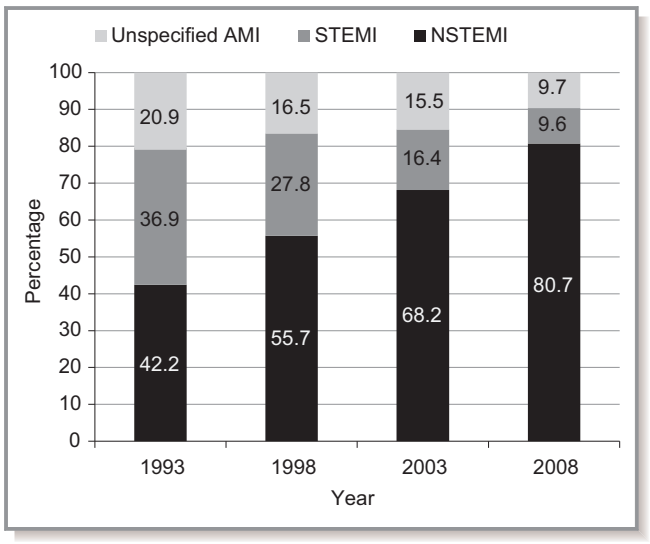

Figure 1. Period-prevalent dialysis patients with AMI in 1993, 1998, 2003, and 2008 by type of AMI. AMI indicates acute myocardial infarction; NSTEMI, non–ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction.

Table 1. Continued

	All AMI					NSTEMI					STEMI				
	1993	1998	2003	2008	*P* Value	1993	1998	2003	2008	*P* Value	1993	1998	2003	2008	*P* Value
PVD	41.3	48.1	50.7	52.7	<0.001	41.3	48.0	51.0	52.9	<0.001	41.3	46.8	47.9	47.7	<0.001
Cancer	7.4	8.3	9.0	9.2	<0.001	6.8	7.9	9.0	9.0	0.001	8.0	9.1	9.0	9.7	0.086
COPD	17.9	22.3	27.1	29.7	<0.001	18.4	22.3	27.9	30.3	<0.001	16.0	20.4	22.6	25.8	<0.001
GI disease	16.4	16.1	15.8	15.0	0.017	15.3	16.1	15.9	15.1	0.85	16.2	15.1	14.4	12.9	0.008
Liver disease	13.8	23.7	10.3	9.4	<0.001	13.2	24.1	10.1	9.6	<0.001	14.2	23.6	10.4	8.7	<0.001

AMI indicates acute myocardial infarction; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CVA/TIA, cerebrovascular accident/transient ischemic attack; ESRD, end-stage renal disease; GI, gastrointestinal; NSTEMI, non–ST-segment elevation myocardial infarction; PVD, peripheral vascular disease; STEMI, ST-segment elevation myocardial infarction.
*Included coronary artery bypass grafting and percutaneous coronary intervention.

characteristics were seen for NSTEMI and STEMI patients, but proportions of younger patients and patients on peritoneal dialysis were higher and prevalence of cardiovascular diseases was lower in STEMI than in NSTEMI patients (Table 1).

Trends in Mortality

In-hospital mortality among dialysis patients with AMI markedly decreased from 1993 to 2008 (31.9% and 18.8%, respectively; $P<0.001$) (Table 2). The unadjusted cumulative probability of all-cause death during 2-year follow-up after AMI decreased with each successive cohort year: 44.2%, 41.1%, 39.6%, and 35.7% at 30 days; 63.3%, 61.8%, 61.1%, and 56.6% at 1 year; and 76.5%, 75.6%, 74.8%, and 71.5% at 2 years for cohort years 1993, 1998, 2003, and 2008, respectively ($P<0.001$) (Figure 2A). Trends were similar for the adjusted cumulative probability of mortality (Figure S1A).

Considering type of AMI (Table 2), in-hospital mortality among STEMI patients was high but declined markedly between 1993 and 2008 (38.2% in 1993, 25.9% in 2008; $P<0.001$); mortality among NSTEMI patients was lower but remained relatively unchanged (14.2% in 1993, 14.9% in 2008; $P=0.47$). Unadjusted 1-year cumulative probability of death also declined among STEMI patients (66.8% in 1993, 56.9% in 2008; $P<0.001$) (Figure 2B), as did 2-year cumulative probability (77.3% in 1993, 71.2% in 2008; $P<0.001$). Among NSTEMI patients, however, there were no significant differences in the unadjusted cumulative probabilities of death at 1 year (53.1% in 1993, 54.4% in 2008; $P=0.32$) (Figure 2C) and 2 years (70.9% in 1993, 70.1% in 2008; $P=0.52$) during the study period. Trends were similar for the adjusted 2-year cumulative probability of death among NSTEMI patients (Figure S1B) and STEMI patients (Figure S1C). Table S2 shows unadjusted and adjusted cumulative probability of death at 1 month, 1 year, and 2 years after AMI admission for each cohort year, overall, and by AMI type.

Interval Hazards of Mortality

Table 3 presents the adjusted hazards of mortality after AMI by interval of follow-up (≤1 month and >1 to ≤24 months following AMI). The greatest reduction in the hazard for mortality occurred in the first 30 days in the overall AMI cohort. With the 2008 cohort as reference, the adjusted hazard ratios for mortality in the first 30 days were 1.67 (95% CI 1.57 to 1.77) in 1993, 1.33 (95% CI 1.26 to 1.40) in 1998, and 1.20 (95% CI 1.15 to 1.25) in 2003 ($P<0.001$ for each) for the overall AMI cohort. A similar pattern was seen among STEMI patients. For NSTEMI patients, however, the adjusted hazard ratios for mortality within the first 30 days were

Table 2. In-Hospital Mortality and Timing of Coronary Revascularizations Relative to Admission for Each Year, All AMI and by Type of AMI

	Total, n	In-Hospital Mortality, n (%)	Timing of PCI Relative to Admission, n (%)			Timing of CABG Relative to Admission, n (%)		
			Day 1*	Days 1 and 2	Entire Stay	Day 1*	Days 1 and 2	Entire Stay
All AMI								
1993	4494	1432 (31.9)	54 (1.2)	85 (1.9)	241 (5.4)	13 (0.3)	18 (0.4)	85 (1.9)
1998	8081	2090 (25.9)	231 (2.9)	328 (4.1)	755 (9.3)	40 (0.5)	69 (0.9)	361 (4.5)
2003	14 232	3350 (23.5)	462 (3.2)	828 (5.8)	1911 (13.4)	28 (0.2)	78 (0.5)	519 (3.6)
2008	16 361	3072 (18.8)	871 (5.3)	1472 (9.0)	2871 (17.5)	47 (0.3)	88 (0.5)	599 (3.7)
NSTEMI								
1993	1898	270 (14.2)	—	17 (0.9)	96 (5.1)	—	—	—
1998	4502	667 (14.8)	60 (1.3)	109 (2.4)	375 (8.3)	12 (0.3)	28 (0.6)	219 (4.9)
2003	9701	1549 (16.0)	169 (1.7)	413 (4.3)	1244 (12.8)	—	32 (0.3)	339 (3.5)
2008	13 210	1962 (14.9)	386 (2.9)	904 (6.8)	2119 (16.0)	17 (0.1)	40 (0.3)	464 (3.5)
STEMI								
1993	1658	634 (38.2)	43 (2.6)	62 (3.7)	132 (8.0)	—	11 (0.7)	63 (3.8)
1998	2245	765 (34.1)	161 (7.2)	204 (9.1)	332 (14.8)	26 (1.2)	35 (1.6)	110 (4.9)
2003	2331	774 (33.2)	256 (11.0)	341 (14.6)	527 (22.6)	15 (0.6)	30 (1.3)	125 (5.4)
2008	1571	407 (25.9)	427 (27.2)	490 (31.2)	597 (38.0)	20 (1.3)	30 (1.9)	86 (5.5)

Values for ≤10 patients are suppressed and are designated by the — symbol. AMI indicates acute myocardial infarction; CABG, coronary artery bypass grafting; NSTEMI, non–ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.
*Defined as the day of admission for AMI.

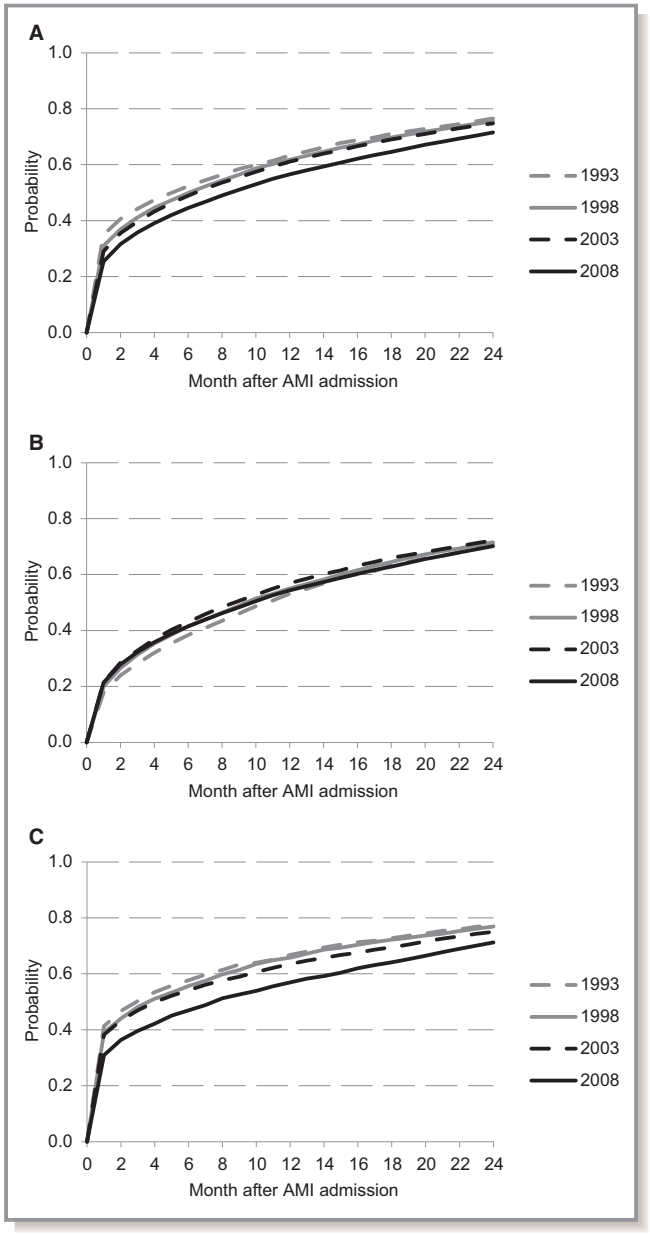

Figure 2. Unadjusted cumulative probability of death following hospitalization for AMI among period dialysis patients in 1993, 1998, 2003, and 2008, shown overall (A) and by AMI type: non-STEMI (B) or STEMI (C). AMI indicates acute myocardial infarction; STEMI, ST segment elevation myocardial infarction.

progressively worse from 1993 through 2008, although the comparisons were not statistically significant (Table 3).

Among all patients who survived the first 30 days after AMI admission, the hazard of mortality during months 2 to 24 was also reduced successively from 1993 to 2008, although the magnitude of reduction was not as great as within the first 30 days. With the 2008 cohort as the reference, the adjusted hazard ratios were 1.18 (95% CI 1.12 to 1.25) in 1993, 1.13 (95% CI 1.08 to 1.17) in 1998, and 1.10 (95% CI 1.06 to 1.14) in 2003 ($P<0.001$ for each) for the overall AMI cohort. Similar patterns were seen in patients with STEMI and NSTEMI, except that no statistically significant difference was noted between 2003 and 2008 among STEMI patients (Table 3). Table S3 presents the results for each covariate in the model.

Trends in Coronary Revascularization

Finally, because in-hospital and short-term mortality after AMI admission declined greatly from 1993 to 2008, we evaluated use of early coronary revascularization during the AMI hospitalization. In-hospital use of percutaneous coronary intervention increased steadily between 1993 and 2008 (Table 2) but was higher among patients with STEMI (8% in 1993, 38% in 2008; $P<0.001$) than among NSTEMI patients (5% in 1993, 16% in 2008; $P<0.001$). In 2008, 597 (38%) STEMI and 2119 (16%) NSTEMI patients underwent in-hospital percutaneous coronary intervention; 427 (27.2%) and 386 (2.9%) procedures, respectively, occurred during the first hospital day, and 490 (31.2%) and 904 (6.8%) procedures occurred within the first 2 days. Rates of in-hospital coronary artery bypass grafting were low and did not change substantially in 15 years (1.9% of all AMI patients in 1993; 5.5% of STEMI patients in 2008). Use of thrombolytics during the AMI hospitalization was minimal; the highest rate was 1.5% among STEMI patients in 2008.

Discussion

This study is the first to report declining in-hospital and 2-year mortality among dialysis patients with AMI in the United States. These observations parallel trends in the general population[10,11] and offer a source of optimism in a population in which AMI has traditionally been associated with dismal survival. It is of interest that the decline in mortality was noted only among dialysis patients with STEMI. Survival of NSTEMI dialysis patients has not materially improved in the contemporary era; however, a substantial coincident increase (quadrupling) in prevalent dialysis patients with AMI occurred between 1993 and 2008, driven solely by a marked increase in use of diagnostic codes for NSTEMI.

Implications and Putative Explanations for Observed Mortality Trends

Our study complements the findings of Nauta et al[16] by extending the observation pertaining to improvement in AMI survival (noted among advanced CKD patients in that study) to dialysis patients. These findings likely reflect the effectiveness of evidence-based practices extrapolated from the general population, particularly among STEMI patients on dialysis. The greater relative reduction in mortality among STEMI, relative to NSTEMI, dialysis patients is in accordance

Table 3. Adjusted Hazard Ratios of Death After AMI by Interval of Follow-up (≤1 Month, >1 to ≤24 Months)

	Months After AMI			
	≤1 Month		>1 to ≤24 Months	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
All AMI				
1993	1.67 (1.57 to 1.77)	<0.001	1.18 (1.12 to 1.25)	<0.001
1998	1.33 (1.26 to 1.40)	<0.001	1.13 (1.08 to 1.17)	<0.001
2003	1.20 (1.15 to 1.25)	<0.001	1.10 (1.06 to 1.14)	<0.001
2008	Reference		Reference	
NSTEMI				
1993	0.90 (0.80 to 1.01)	0.09	1.15 (1.08 to 1.24)	<0.001
1998	0.97 (0.89 to 1.04)	0.38	1.10 (1.05 to 1.15)	<0.001
2003	1.02 (0.96 to 1.08)	0.59	1.09 (1.05 to 1.13)	<0.001
2008	Reference		Reference	
STEMI				
1993	1.58 (1.40 to 1.79)	<0.001	1.25 (1.11 to 1.40)	<0.001
1998	1.35 (1.21 to 1.51)	<0.001	1.17 (1.06 to 1.30)	0.003
2003	1.30 (1.17 to 1.46)	<0.001	1.06 (0.95 to 1.17)	0.31
2008	Reference		Reference	

Results using cutoffs of ≤1 month and >1 to ≤24 months. Covariates in the model included all factors listed in Table 1. AMI indicates acute myocardial infarction; HR, hazard ratio; NSTEMI, non–ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction.

with observations in the general population,[10] again likely reflecting evolving clinical practice patterns. As outlined, it is also likely that heightened awareness of the unique clinical concerns related to this population among clinicians contributed to decreased mortality. It bears emphasis, however, that in-hospital mortality was almost 3-fold higher among STEMI versus NSTEMI patients in 1998, and although it has improved in the most contemporary cohort, in-hospital mortality for STEMI patients continues to remain almost 2-fold higher.

A potentially intriguing question is whether fundamental differences in the pathophysiology and clinical presentations of STEMI and NSTEMI among dialysis patients account for marked differences in prevalence and mortality. An increase in NSTEMI incidence has been reported in the general population,[9] but the increase is not as dramatic as that among dialysis patients in this study. Several factors could explain this trend. Establishing an accurate diagnosis of NSTEMI in dialysis patients can be problematic because troponin increases and nonspecific electrocardiographic abnormalities are common and typical symptoms of acute coronary syndrome are less frequent,[5] but prevalence of obstructive coronary artery disease is high. Consequently, differentiating type 1 (or spontaneous) AMI from type 2 AMI (caused by supply/demand mismatch), particularly in the context of chronic baseline troponin elevation, can be difficult.[18] These diagnostic challenges, compounded by the transition of the preferred biomarker from creatinine kinase to higher sensitivity troponin assays, could potentially contribute to the remarkable uptick in diagnostic codes for NSTEMI between 1993 and 2008. In that regard, it is equally remarkable that the prevalence of diagnostic codes for STEMI has remained quite constant over nearly 2 decades, likely because establishing a diagnosis relies more heavily on specific electrocardiographic criteria rather than simply on biomarker criteria.

Implications and Significance of Short-Term Mortality Reduction in STEMI Patients

This study also demonstrated that most of the recent improvement in survival for dialysis patients with AMI was attributable to reduction in short-term mortality rates among STEMI patients. Conceivably, acute thrombotic occlusion in a culprit vessel among STEMI patients predisposes to higher success with revascularization strategies relative to NSTEMI patients, thus contributing to reduced short-term mortality among STEMI patients, coincident with higher percutaneous coronary intervention rates. It is tempting to ascribe the improved short-term survival to early coronary reperfusion because we found a significant increase in early coronary revascularization rates with percutaneous coronary

intervention among STEMI patients (Table 2); however, this observation must be considered strictly hypothesis generating and interpreted with caution. Moreover, based on claims data, the timing of revascularization can be determined for the calendar day of hospitalization only, not by number of hours elapsed since admission.

The benefit of early coronary revascularization among dialysis patients with AMI has been a matter of controversy and debate in the literature. Using a large cohort of 23 262 Swedish patients from 2003 through 2006, Szummer et al reported reduced overall 1-year mortality rates among NSTEMI patients undergoing an early invasive strategy; however, they noted no significant survival advantage among stage 5 CKD/dialysis patients (n=278).[14] Huang et al performed a meta-analysis involving 23 234 acute coronary syndrome patients with CKD because they contended that the study by Szummer et al was underpowered to detect differences in outcome among patients with advanced CKD.[19] Huang et al demonstrated an upfront benefit from early coronary revascularization at all stages of CKD (including ESRD) that persisted at 3 years. The observational data from this study involving a large number of dialysis patients support the notion that early coronary revascularization therapy is appropriate, particularly for STEMI patients.

Improved use of evidence-based medical therapy may also have contributed to improvement in mortality. Coincident with the decrease in AMI mortality in our study, the USRDS reported a sea change in the use of evidence-based medications that could potentially improve survival in dialysis patients.[12] In particular, the 2013 USRDS annual data report stated that beta blockers were prescribed to an impressive 78% of hemodialysis and 81% of peritoneal dialysis patients with AMI. Among hemodialysis and peritoneal dialysis patients, use of statins (64.1% and 69.2%, respectively) and clopidogrel (49.5% and 54.2%, respectively) also increased; these medications could also potentially influence short-term mortality rates in the context of AMI.

Study Limitations

This observational study using administrative data has important limitations. These include the potential for selection bias and unmeasured confounders and the lack of important clinical variables such as angiographic data and echocardiographic data, including left ventricular ejection fraction and infarct size. The complexity of clinical decision making regarding coronary revascularization among ESRD patients[20] factoring in the coronary anatomy, coronary calcification, high risk of bleeding, evaluation for transplant, and other variables cannot be fully accounted for by administrative data alone, which are also subject to appropriate coding during the index hospitalization. Similarly, the influence of other clinical factors affecting AMI mortality, such as evolving patterns in anticoagulant and antiplatelet agent use and effect of residual renal function and early initiation of dialysis, cannot be measured using these administrative data. The marked uptick in diagnostic codes for NSTEMI likely reflects overdiagnosis of a clinical condition that is heavily influenced by troponin levels in the contemporary era. Although this makes assessing the true prevalence of NSTEMI problematic, this observation also reflects a clinical reality that highlights the need for close attention to the dramatic increase and potential overuse of the diagnostic code for NSTEMI in this high-risk population and attendant unintended clinical and economic ramifications.

In conclusion, progressive improvement in survival among dialysis patients with AMI occurred over the past 15 years but was limited to short-term mortality reduction among STEMI patients. These trends probably reflect diffusion of evidence-based guidelines derived from the general population to this high-risk group. In addition, a marked interval increase occurred in the use of the diagnostic code for NSTEMI among dialysis patients and could, in part, reflect the increasing use of more sensitive cardiac biomarkers (ie, cardiac troponins). Sustained and systematic efforts targeting dialysis patients with AMI remain warranted because, despite promising trends, both short-term and long-term mortality rates remain extremely high in this population.

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Disclosures

None.

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