original article

Racial and ethnic differences in incident myocardial infarction in end-stage renal disease patients: The USRDS

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African Americans have a greater risk of cardiovascular disease (CVD) than Caucasians in early chronic kidney disease; however, limited data describe racial and ethnic differences in the risk of incident myocardial infarction (MI) among patients with end-stage renal disease (ESRD). We conducted a prospective, observational cohort study among 271 102 incident dialysis patients receiving renal replacement therapy enrolled in the United States Renal Data System (USRDS) for whom Medicare was the primary insurer between 1995 and 2000. The incidence and risk of any MI (non-fatal or fatal) estimated by Cox proportional hazards models was the primary outcome of interest. Of those with prevalent CVD at baseline (118 708), 14 849 had an incident non-fatal MI compared with 9926 events for those without prevalent CVD (152 394). Patients with prevalent CVD had higher crude rates of combined fatal and non-fatal MI (99.3/1000 person-years vs 42.9/1000 person-years) compared with those without prevalent CVD. Among those with prevalent CVD, African Americans (adjusted relative risk (aRR) = 0.65, 95% confidence interval (CI):0.62–0.68), Asian Americans (aRR = 0.74, 95% CI: 0.66–0.83), and Hispanics (aRR = 0.72, 95% CI: 0.68–0.77) were 26–35% less likely to have an incident MI compared to Caucasians. Similarly, among those without prevalent CVD, racial/ethnic minorities were 26–42% less likely to have an incident MI compared to Caucasians. We conclude that in a national setting where comparable access to dialysis and associated medical care, exist, racial/ethnic minorities were found to have a lower risk of non-fatal and fatal MI than Caucasians.

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Cardiovascular disease (CVD) is the primary cause of death in the general population and in patients with end-stage renal disease (ESRD).[1] Patients on dialysis are reported to have a 30-fold greater risk of CVD associated mortality than the general population.[2] Among individuals with chronic renal insufficiency, racial and ethnic (racial/ethnic) minorities have been found to have higher rates of CVD than Caucasians,[3] but limited data exist that compare racial and ethnic differences in incident myocardial infarction (MI) among those with ESRD. Utilizing data from the United States Renal Data System (USRDS), Trespalacios et al.[4] found that African Americans were less likely to have prevalent coronary heart disease than Caucasians, but racial/ethnic differences in admissions for acute coronary syndrome or MI were not assessed. Also, racial/ethnic differences in the risk of atherosclerotic disease (cardiovascular, stroke, peripheral vascular disease) were assessed recently, but risk of MI was not assessed separately.[5]

Initiated in 1972, the ESRD Medicare entitlement program has allowed for governmental reimbursement for initiation and continuation of dialysis across the United States. In that regard, the Medicare program was one of the first nationwide programs that offered a form of national health insurance coverage. We hypothesized that in the setting where medical insurance access is comparable, racial/ethnic differences in incident fatal and non-fatal MI would be minimized if access to care is the primary factor accounting for racial/ethnic disparities in incident MI. Using data from the USRDS, which records data from all patients who initiate dialysis in the United States, we sought to evaluate racial/ethnic differences in incident non-fatal and fatal MI in the setting where comparable insurance coverage for renal replacement therapy, physician reimbursement, and hospitalizations exists for all subjects.

RESULTS

Data were available for 506 922 ESRD patients who initiated renal replacement therapy between January 1, 1995 and

December 31, 2000. Of these, 201 870 (39.8%) patients were not eligible for Medicare insurance coverage within 90 days of starting renal replacement therapy and were excluded. Of the remaining patients, 33 950 (6.7%) were further excluded owing to an incomplete medical evidence form, before transplant or MI, or for not having Medicare coverage before December 31, 2000, which resulted in 271 102 patients identified for the current analysis. Of those identified, 118 708 (43.8%) had prevalent CVD, whereas 152 394 (56.2%) did not have prevalent CVD. Overall, 52.0% were male, 52.1% were Caucasian, 31.6% were African American, 3.0% were Asian American, and 11.5% were Hispanic. Diabetes (45.3%) was the primary cause of ESRD, followed by hypertension (28.1%) and glomerulonephritis (9.0%). On average, patients were anemic (hemoglobin 9.5 ± 1.8 g/dl), elderly (mean age 63.5 ± 15.3 years), slightly malnourished (albumin 3.2 ± 0.7 g/dl), and had low creatinine clearances (3.0 ± 6.0 ml/min) at the initiation of dialysis. Prevalent erythropoietin (EPO) use was observed in approximately a quarter of all patients (25.4%). Those of other race/ethnicity ($n = 4679$; 1.7%) were younger and more likely to have diabetes compared to the remaining groups.

Among those with prevalent CVD (Table 1), the majority were Caucasian (60.0%), followed by African Americans (25.6%), Hispanics (10.1%), Asian Americans (2.57%), and those of other race/ethnicity (1.69%). African Americans, Hispanics, and Asians were more likely to be female, were more likely to be less than 60 years of age, and were more likely to have diabetes than Caucasians. Those of other race/ethnicity (79.0%) contained the greatest proportion of those with diabetes as the underlying renal disease. EPO use before initiation of dialysis was less likely for African Americans and Hispanics compared with Caucasians and Asians, although baseline laboratory values were similar among all groups within the cohort.

Compared to those with prevalent CVD, those without prevalent CVD (Table 1) had greater proportions of African Americans (36.3%), Hispanics (12.6%), Asian Americans (3.41%), and those of other race/ethnicity (1.75%) than Caucasians (45.9%). Similar to what was found among those with prevalent CVD, diabetes was the primary cause of ESRD and greatest for those of other race/ethnicity, Hispanics, Asians, and African Americans (in that order) compared to Caucasians. Pre-dialysis EPO use was lowest for African Americans compared to other racial/ethnic groups, and African Americans were, on average, the youngest group to initiate renal replacement therapy. Hemoglobin levels were lower for those without prevalent CVD compared to those with prevalent CVD, and African Americans without prevalent CVD had the lowest hemoglobin level of all groups ($9.09 \pm 1.83\%$). On average, baseline serum creatinine levels were higher for racial/ethnic minority groups than Caucasians in both those with and without prevalent CVD, whereas African Americans started dialysis with the highest average baseline serum creatinine. Also, racial and ethnic minorities of both CVD groups had the lowest baseline serum albumin levels compared to Caucasians.

Unadjusted MI event rates were approximately two-fold greater among those with prevalent CVD compared to those without (Table 2), and highest among those less than 45 years of age (2.8-fold greater). Among those with prevalent CVD, greater non-fatal and combined MI event rates were observed for men, Caucasians, the elderly, those with hypertension as the primary cause of ESRD, and for those without pre-dialysis EPO use. Those 75 years and older, Caucasians, and those unable to ambulate had both the highest overall non-fatal and highest overall combined MI event rates. Similarly, among those without prevalent CVD, the elderly, Caucasians, those with diabetes, and those unable to ambulate were more likely to have both non-fatal and combined MI, although rates were similar between men and women and between those with and without predialysis EPO use.

We determined estimates of the adjusted relative risk (aRR) of incident non-fatal and combined MI separately for subgroups defined by prevalent CVD status (Table 3). Risk estimates were similar for models of non-fatal MI compared with combined MI; thus, results are shown only for the combined end point. All estimates were adjusted for age at the start of renal replacement therapy, gender, primary cause of ESRD, dialysis modality (hemodialysis, peritoneal dialysis, and transplant) and transplant waiting list status as well as available baseline laboratory values. Final models were restricted to 81 106 (prevalent) and 100 998 (non-prevalent CVD) subjects owing to missing laboratory values, although these restrictions changed the point estimates of the results minimally.

Among those with prevalent CVD, African Americans were estimated to have the lowest risk of combined MI (aRR = 0.65, 95% confidence interval (CI): (0.62, 0.68)) compared to Caucasians. Asian Americans with prevalent CVD had a 26% decreased risk (aRR = 0.74, 95% CI: (0.66, 0.83)), whereas Hispanics (aRR = 0.72, 95% CI: (0.68, 0.77)) had lower adjusted risk of incident non-fatal and fatal MI compared to Caucasians. With respect to other known risk factors, among those with prevalent CVD, increasing age, male gender, and renal failure owing to diabetic nephropathy were all independently associated with a greater risk of combined MI. Compared to patients on hemodialysis, those on peritoneal dialysis had a 2% lower risk of combined MI (aRR = 0.98, 95% CI: (0.93, 1.02)), whereas those on the wait list were 32% less likely to have an event compared to those not wait-listed on hemodialysis. Additionally, when other causes of cardiovascular death were added to the combined end-point, modest changes to the point estimates were found (data not shown).

Similarly, among those without prevalent CVD, African Americans had a 33% lower risk of combined MI (aRR = 0.67, 95% CI: (0.64, 0.71)) compared to Caucasians. Asian Americans without prevalent CVD had 28% lower risk (aRR = 0.72, 95% CI: (0.63, 0.81)), whereas Hispanics had a 35% lower adjusted risk of combined MI event (aRR = 0.65, 95% CI: (0.60, 0.70)), compared to Caucasians (Table 3).

Table 1 | Baseline demographics of USRDS Medicare cohort

	Overall	Caucasian	African American	Asian American	Hispanic	Other
Prevalent CVD						
Total	118 708	71 186 (60.0%)	30 452 (25.6%)	3051 (2.57%)	11 997 (10.1%)	2007 (1.69%)
Female	57 904 (48.8%)	31 604 (44.4%)	17 550 (57.6%)	1575 (51.6%)	6056 (50.5%)	1114 (55.5%)
Age group						
Less than 45 years	5996 (5.05%)	2297 (3.23%)	2713 (8.91%)	147 (4.82%)	706 (5.88%)	131 (6.53%)
45–59 years	20 606 (17.4%)	8807 (12.4%)	7540 (24.8%)	446 (14.6%)	3168 (26.4%)	643 (32.0%)
60–74 years	55 049 (46.4%)	33 366 (46.9%)	13 599 (44.7%)	1372 (45.0%)	5760 (48.0%)	945 (47.1%)
75 years and older	37 057 (31.2%)	26 716 (37.5%)	6600 (21.7%)	1086 (35.6%)	2363 (19.7%)	288 (14.4%)
Cause of ESRD						
Diabetes	62 712 (52.8%)	33 528 (47.1%)	16 720 (54.9%)	1832 (60.0%)	9036 (75.3%)	1586 (79.0%)
Hypertension	34 130 (28.8%)	21 649 (30.4%)	9784 (32.1%)	730 (23.9%)	1755 (14.6%)	211 (10.5%)
Glomerulonephritis	6996 (5.89%)	4908 (6.89%)	1329 (4.36%)	230 (7.54%)	444 (3.7%)	85 (4.24%)
Other	14 870 (12.5%)	11 101 (15.6%)	2619 (8.6%)	259 (8.49%)	762 (6.35%)	125 (6.23%)
Baseline lab values (N (%) or mean (s.d.))[a]						
Inability to ambulate	7413 (6.24%)	4328 (6.08%)	2085 (6.85%)	163 (5.34%)	726 (6.05%)	109 (5.43%)
EPO use predialysis	31 030 (26.1%)	19 910 (28.0%)	6929 (22.8%)	940 (30.8%)	2758 (23.0%)	489 (24.4%)
Age at start	68.1 (12.2)	70.4 (11.1)	64.3 (13.3)	69.3 (12.5)	64.7 (12.0)	62.6 (11.6)
Albumin (g/dl)	3.14 (0.63)	3.18 (0.61)	3.1 (0.63)	3.05 (0.64)	3.03 (0.63)	2.91 (0.64)
Hemoglobin (g/dl)	9.65 (1.68)	9.84 (1.62)	9.25 (1.75)	9.65 (1.75)	9.53 (1.68)	9.39 (1.65)
BUN (mg/dl)	91.1 (32.8)	93.0 (33.2)	88.1 (32.0)	91.4 (32.8)	87.6 (31.7)	87.7 (31.2)
Creatinine clearance (ml/min)	3.52 (6.41)	3.72 (6.66)	3.04 (5.98)	2.99 (5.48)	3.72 (6.16)	3.17 (5.78)
Serum creatinine (mg/dl)	6.99 (3.02)	6.53 (2.63)	7.98 (3.52)	7.38 (3.17)	7.08 (3.12)	7.17 (3.13)
Height (cm)	167.0 (12.9)	168.0 (12.7)	167.0 (12.9)	159.0 (11.6)	161.0 (12.8)	165.0 (12.8)
Weight (kg)	73.5 (19.2)	73.7 (18.6)	76.1 (21.0)	59.9 (16.3)	69.1 (17.0)	72.8 (18.5)
No prevalent CVD						
Total	152 394	69 946 (45.9%)	55 330 (36.3%)	5191 (3.41%)	19 241 (12.6%)	2672 (1.75%)
Female	72 201 (47.4%)	31 692 (45.3%)	27 776 (50.2%)	2619 (50.5%)	8703 (45.2%)	1405 (52.6%)
Age group						
Less than 45 years	31 858 (20.9%)	11 104 (15.9%)	14 833 (26.8%)	994 (19.2%)	4362 (22.7%)	560 (21.0%)
45–59 years	36 633 (24.0%)	12 968 (18.5%)	15 628 (28.2%)	1166 (22.5%)	5882 (30.6%)	986 (36.9%)
60–74 years	54 546 (35.8%)	27 374 (39.1%)	17 604 (31.8%)	1909 (36.8%)	6775 (35.2%)	880 (32.9%)
75 years and older	29 357 (19.3%)	18 500 (26.4%)	7265 (13.1%)	1122 (21.6%)	2222 (11.6%)	246 (9.21%)
Cause of ESRD						
Diabetes	60 207 (39.5%)	24 651 (35.2%)	20 821 (37.6%)	2164 (41.7%)	10 820 (56.2%)	1745 (65.3%)
Hypertension	42 027 (27.6%)	16 633 (23.8%)	20 326 (36.7%)	1333 (25.7%)	3436 (17.9%)	296 (11.1%)
Glomerulonephritis	17 346 (11.4%)	9167 (13.1%)	4940 (8.93%)	889 (17.1%)	2045 (10.6%)	302 (11.3%)
Other	32 813 (21.5%)	19 495 (27.9%)	9242 (16.7%)	805 (15.5%)	2940 (15.3%)	329 (12.3%)
Baseline lab values (N (%) or mean (s.d.))[b]						
Inability to ambulate	4175 (2.74%)	1948 (2.79%)	1567 (2.83%)	100 (1.93%)	487 (2.53%)	72 (2.69%)
EPO use predialysis	37 921 (24.9%)	20 084 (28.7%)	11 444 (20.7%)	1576 (30.4%)	4212 (21.9%)	601 (22.5%)
Age at start	59.8 (16.4)	63.5 (16.0)	56.3 (16.2)	60.9 (16.6)	56.9 (15.6)	56.3 (14.4)
Albumin (g/dl)	3.2 (0.69)	3.26 (0.67)	3.15 (0.71)	3.2 (0.67)	3.15 (0.69)	3.01 (0.7)
Hemoglobin (g/dl)	9.44 (1.81)	9.76 (1.75)	9.09 (1.83)	9.5 (1.88)	9.35 (1.79)	9.28 (1.78)
BUN (mg/dl)	89.7 (34.0)	90.0 (33.8)	89.4 (34.3)	92.1 (34.9)	89.7 (33.5)	85.4 (32.1)
Creatinine clearance (ml/min)	2.56 (5.65)	2.9 (5.88)	2.15 (5.39)	2.22 (5.03)	2.63 (5.64)	2.34 (4.95)
Serum creatinine (mg/dl)	8.73 (4.05)	7.82 (3.36)	9.87 (4.54)	8.86 (4.0)	8.76 (4.07)	8.55 (3.82)
Height (cm)	167.0 (13.3)	168.0 (12.8)	168.0 (13.4)	160.0 (12.1)	163.0 (13.4)	165.0 (13.0)
Weight (kg)	73.9 (19.9)	73.9 (19.4)	76.5 (20.9)	60.5 (16.5)	70.2 (17.7)	74.4 (19.6)

BUN, blood urea nitrogen; CVD, cardiovascular disease; EPO, erythropoietin; ESRD, end-stage renal disease; s.d., standard deviation; USRDS, United States Renal Data System.
[a]Prevalent CVD baseline lab missing values: inability to ambulate (0.03%), hemoglobin (12.2%), albumin (21.4%), BUN (5.89%), and EPO use (0.06%).
[b]No prevalent CVD baseline lab missing values: hemoglobin (13.0%), albumin (23.2%), BUN (7.36%), and EPO use (0.06%).

Compared to patients on hemodialysis, those on peritoneal dialysis without prevalent CVD had an insignificantly elevated relative risk of combined MI (aRR non-prevalent CVD 1.06, 95% CI: (0.99, 1.15)). Additionally, those on the waiting list were 32% less likely to have an event compared to those not wait-listed on hemodialysis, whereas those who received a transplant were 69% less likely to have an event compared to those on hemodialysis.

DISCUSSION

Among a national cohort of patients who had Medicare as their primary insurance, prevalent CVD was a significant risk

Table 2 | Non-fatal and combined MI event rates (95% CI)

	N, total	N, non-fatal MI	N, combined MI	Non-fatal MI rate (per 1000) (95% CI)	Combined MI rate (per 1000) (95% CI)[a]
Prevalent CVD					
Total	118 708	14 849	18 349	80.3 (79.0, 81.6)	99.3 (97.8, 100.7)
Gender					
Men	60 804	7782	9662	83.5 (81.7, 85.4)	103.7 (101.6, 105.8)
Women	57 904	7067	8687	77.1 (75.3, 78.9)	94.7 (92.8, 96.7)
Age group					
Less than 45 years	5996	385	483	31.0 (28.0, 34.2)	38.9 (35.5, 42.4)
45–59 years	20 606	2026	2573	54.0 (51.7, 56.4)	68.6 (66.0, 71.3)
60–74 years	55 049	7444	9180	84.9 (83.0, 86.9)	104.8 (102.6, 106.9)
75 years and older	37 057	4994	6113	105.6 (102.7, 108.5)	129.2 (126.0, 132.5)
Race					
Caucasian	71 186	9921	12 139	98.3 (96.4, 100.3)	120.3 (118.2, 122.5)
African American	30 452	3046	3775	55.5 (53.5, 57.5)	68.7 (66.6, 70.9)
Asian American	3051	360	473	72.4 (65.1, 80.0)	95.1 (86.5, 103.7)
Hispanic	11 997	1326	1698	64.7 (61.2, 68.2)	82.8 (78.9, 86.7)
Other	2007	193	261	54.6 (47.1, 62.5)	73.8 (64.8, 82.7)
Cause of ESRD					
Diabetes	62 712	7924	9901	80.3 (78.6, 82.1)	100.4 (98.4, 102.3)
Hypertension	34 130	4511	5522	86.0 (83.5, 88.5)	105.3 (102.5, 108.1)
Glomerulonephritis	6996	776	959	62.3 (58.0, 66.7)	77.0 (72.1, 81.8)
Other	14 870	1638	1967	77.0 (73.3, 80.7)	92.4 (88.3, 96.5)
Ability to ambulate	111 255	14 026	17 273	80.0 (78.7, 81.3)	98.5 (97.0, 100.0)
Inability to ambulate	7413	817	1070	87.2 (81.3, 93.2)	114.2 (107.3, 121.0)
No EPO predialysis	87 610	11 207	13 832	81.8 (80.3, 83.4)	101.0 (99.3, 102.7)
EPO predialysis	31 030	3638	4511	76.1 (73.6, 78.6)	94.3 (91.6, 97.1)
No Prevalent CVD					
Total	152 394	9926	12 475	34.2 (33.5, 34.8)	42.9 (42.2, 43.7)
Gender					
Men	80 193	5099	6485	33.5 (32.6, 34.4)	42.6 (41.6, 43.6)
Women	72 201	4827	5990	34.9 (33.9, 35.9)	43.3 (42.2, 44.4)
Age group					
Less than 45 years	31 858	761	968	10.6 (9.9, 11.4)	13.5 (12.7, 14.4)
45–59 years	36 633	1986	2523	27.1 (25.9, 28.3)	34.4 (33.0, 35.7)
60–74 years	54 546	4594	5726	45.4 (44.1, 46.7)	56.6 (55.1, 58.0)
75 years and older	29 357	2585	3258	58.4 (56.2, 60.7)	73.6 (71.1, 76.2)
Race					
Caucasian	69 946	5391	6687	43.8 (42.6, 44.9)	54.3 (53.0, 55.6)
African American	55 330	3015	3835	26.7 (25.7, 27.6)	33.9 (32.8, 35.0)
Asian American	5191	332	410	33.6 (30.1, 37.4)	41.5 (37.5, 45.6)
Hispanic	19 241	1051	1364	27.2 (25.6, 28.8)	35.3 (33.4, 37.1)
Other	2672	135	177	23.9 (20.1, 28.1)	31.4 (26.8, 36.0)
Cause of ESRD					
Diabetes	60 207	4848	6121	43.8 (42.6, 45.0)	55.3 (53.9, 56.7)
Hypertension	42 027	2903	3632	35.8 (34.6, 37.2)	44.8 (43.4, 46.3)
Glomerulonephritis	17 346	739	921	19.5 (18.2, 21.0)	24.4 (22.8, 25.9)
Other	32 813	1436	1801	23.6 (22.4, 24.8)	29.6 (28.2, 30.9)
Ability to ambulate	148 219	9661	12 125	34.0 (33.3, 34.7)	42.7 (41.9, 43.4)
Inability to ambulate	4175	265	350	41.8 (36.9, 46.9)	55.1 (49.4, 60.9)
No EPO predialysis	114 385	7426	9397	33.6 (32.8, 34.4)	42.5 (41.6, 43.4)
EPO predialysis	37 921	2498	3075	36.1 (34.7, 37.5)	44.4 (42.8, 46.0)

CVD, cardiovascular disease; EPO, erythropoietin; ESRD, end-stage renal disease; CI, class interval; MI, myocardial infarction.
Combined MI includes fatal and non-fatal MI events.
[a]CI, confidence interval.

Table 3 | Relative risk of combined non-fatal and fatal MI adjusted for baseline covariates[a]

Covariate	Prevalent CVD		No prevalent CVD	
	Relative risk (95% CI)	*P*-value	Relative risk (95% CI)	*P*-value
Gender (women vs men)	0.88 (0.84, 0.92)	<0.001	0.87 (0.82, 0.91)	<0.001
Age per 10 years	1.19 (1.17, 1.21)	<0.001	1.32 (1.30, 1.35)	<0.001
Race				
Caucasian	1.0	—	1.0	—
African American	0.65 (0.62, 0.68)	<0.001	0.67 (0.64, 0.71)	<0.001
Asian American	0.74 (0.66, 0.83)	<0.001	0.72 (0.63, 0.81)	<0.001
Hispanic	0.72 (0.68, 0.77)	<0.001	0.65 (0.60, 0.70)	<0.001
Other	0.65 (0.56, 0.75)	<0.001	0.58 (0.49, 0.70)	<0.001
Cause of ESRD				
Diabetes	1.0	—	1.0	—
Hypertension	0.88 (0.84, 0.92)	<0.001	0.72 (0.68, 0.76)	<0.001
Glomerulonephritis	0.75 (0.69, 0.81)	<0.001	0.49 (0.45, 0.53)	<0.001
Other	0.78 (0.73, 0.82)	<0.001	0.50 (0.47, 0.54)	<0.001
Modality				
Hemodialysis	1.0	—	1.0	—
Peritoneal dialysis	0.98 (0.92, 1.05)	0.588	1.06 (0.99, 1.15)	0.099
Transplant	0.47 (0.38, 0.59)	<0.001	0.41 (0.35, 0.48)	<0.001
Wait list	0.68 (0.59, 0.80)	<0.001	0.68 (0.60, 0.76)	<0.001
Baseline				
Hypertension	0.98 (0.93, 1.02)	0.309	0.94 (0.89, 0.99)	0.011
Peripheral vascular disease	1.21 (1.16, 1.26)	<0.001	1.27 (1.18, 1.37)	<0.001
Inability to ambulate	1.00 (0.93, 1.08)	0.961	1.05 (0.92, 1.20)	0.453
EPO use	0.89 (0.86, 0.93)	<0.001	0.94 (0.89, 0.99)	0.015
Albumin (g/dl)	0.93 (0.90, 0.96)	<0.001	0.89 (0.86, 0.92)	<0.001
Hemoglobin (g/dl)	1.04 (1.02, 1.05)	<0.001	1.03 (1.02, 1.05)	<0.001
BUN (mg/dl)	1.00 (1.00, 1.00)	0.828	1.00 (1.00, 1.00)	0.395
Creatinine clearance (ml/min)	1.00 (0.99, 1.00)	0.06	1.00 (0.99, 1.00)	0.128
Height per 10 cm	0.99 (0.97, 1.00)	0.129	0.99 (0.97, 1.01)	0.171
Weight per 10 kg	0.96 (0.95, 0.97)	<0.001	0.96 (0.95, 0.97)	<0.001

BUN, blood urea nitrogen; CI, class interval; CVD, cardiovascular disease; EPO, erythropoietin; ESRD, end-stage renal disease; MI, myocardial infarction.
[a]After restricted to patients without missing covariates, N=81 106 and 100 998 for prevalent CVD and no prevalent CVD respectively.

factor for recurrent MI, whereas belonging to a racial/ethnic minority group was associated with a lower risk of non-fatal and combined fatal and non-fatal MI compared with Caucasians. Racial/ethnic differences in risk were similar among those with and without prevalent CVD diagnosed at the time of initiation of dialysis.

Because African Americans are less likely to be diagnosed with cardiovascular events prospectively in the general population, we felt that it was important to also explore cardiac-related deaths as a combined outcome with non-fatal MI. Studies have shown that African Americans have been more likely to present with out of hospital cardiac arrests than Caucasians and less likely to have cardiac procedures ordered compared with Caucasians,[6–12] although this may be negligible in the dialysis population.[13] We found that for both non-fatal and combined MI, African Americans and other minority groups had a lower risk of incident MI events compared to Caucasians regardless of which combined end-point was examined.

Recently, limited studies have evaluated racial/ethnic differences in the risk of incident MI and MI-associated mortality in a national dialysis population. Trespalacios[4]

evaluated the risk of acute coronary syndrome in the USRDS Dialysis Morbidity and Mortality Study, Wave II, and found that African Americans were 46% less likely to have prevalent CVD; however, the risk of incident cardiac event was not reported separately by race or ethnicity. In a report that used combined data from CMS and the USRDS, Ganesh[14] evaluated all-cause mortality in hemodialysis and peritoneal dialysis patients, and found that Caucasians had a 1.25-fold greater risk of mortality than non-white subjects (aRR = 1.25, 95% CI: 1.22–1.29); however, individual racial and ethnic groups risk of cardiac-related mortality was not assessed. Finally, utilizing USRDS data, Parekh et al[5] also found that African Americans had a lower incidence of atherosclerosis events, results that are similar to ours except that their final outcome included all causes of atherosclerotic disease, such as coronary artery disease and peripheral vascular disease.[5]

Although the current study results are robust, results from studies evaluating racial and ethnic differences in incident MI in populations with earlier stages of chronic kidney disease before the initiation of dialysis have been inconsistent. In a meta-analysis that combined four community cohort studies, Weiner[3] reported that African Americans had a 1.8-fold

greater risk of a combined cardiac/stroke/death outcome than Caucasians, and that African Americans with chronic kidney disease had a greater risk of having an MI than white subjects. Conversely, using data from a large managed care system population with diabetes, Karter[15] reported that African Americans and other minority populations were less likely to have an incident MI, but were as likely to be diagnosed with congestive heart failure compared with Caucasians. In addition, we previously reported that diabetic African-American veterans and other minority populations were less likely to be diagnosed with prevalent CVD and had a slight survival advantage compared with Caucasians.[16] Differences in studies may be related to access to preventive health care before initiating renal replacement therapy, although further research is necessary in this regard. Alternatively, the disparity observed among ESRD patients may be contingent upon the ability of patients to survive the later stages of chronic kidney disease to initiate renal replacement therapy, and perhaps only the healthiest minority patients survive to initiate dialysis; thus, minorities may have a perceived lower incidence of MI than Caucasians owing to a healthy cohort effect.

Mechanisms for these observed differences in the risk of MI and MI-related deaths by race/ethnicity are speculative at best. Khurana[17] reported that African-American women had similar coronary calcium scores compared to Caucasian women, even though African-American women in the study had a greater number of CVD risk factors than Caucasian women.[17] Conversely, Bild *et al.*[18] found no difference in coronary calcification among participants of the Coronary Artery Risk Development in Young Adults study,[18] whereas other investigators reported that African Americans had lower coronary calcium stores than white subjects in cross-sectional analyses.[19,20] The long-term risk of incident CVD, however, was not assessed. In a study that evaluated racial disparities in the rates of revascularization and cardiovascular procedures, Barnhart[21] found that African Americans were as likely to survive as Caucasians in the absence of cardiovascular revascularization. In addition, using data from the Myocardial Infarction Triage and Intervention registry, Maynard showed that when African Americans obtained coronary artery disease catheterization as frequently as Caucasians, African Americans had better survival.[12]

Factors thought to contribute to racial/ethnic disparities in the incidence of MI include lack of access to medical care,[22,23] low socio-economic status,[22,23] increased prevalence of risk factors such as smoking, hypertension, obesity, and diabetes,[3,23] lack of access to cardiovascular associated procedures or racial discrimination in referral for cardiac-related procedures,[24] or misclassification of CVD diagnoses. As African Americans and other minority groups are more likely to have chronic kidney disease, one could hypothesize that racial/ethnic minorities might be at greater risk for death before the initiation of dialysis, although this hypothesis was not evaluated in recent studies using Medicare data.[25] This assertion could be true in populations that do not have access to care but has shown not to be the case in populations with

access to care before initiation of dialysis such as the veterans.[16] In addition, differential receipt of a diagnosis of MI or cardiac-related procedures could explain some of the differences found in the current study; however, utilizing USRDS data, Daumit *et al.*[13] found that once dialysis was initiated, racial disparities in receipt of cardiac procedures was negligible. Although controversial, possible genetic or biologic differences in CVD susceptibility,[26] or other potential biologic differences such as differences in parathyroid hormone and calcium levels,[27] blood pressure control, or cytokine polymorphisms[28–31] may exist and could contribute to racial/ethnic differences in MI rates.

Although the current study is strengthened by the evaluation of a national cohort of incident dialysis patients, there are certain limitations that deserve discussion. Because of limitations of the USRDS database, this study could not evaluate the potential effect of differences in dialysis prescription, current medication use, ongoing nutritional status,[32] dialysis adequacy, dialysis compliance, current EPO use or hemoglobin level changes over time, smoking, or dyslipidemia, factors that are all known to affect the risk of CVD in the dialysis population. However, the study was able to adjust for baseline characteristics, which included an assessment of baseline nutritional status (albumin), anemia (hemoglobin), predialysis EPO use, and diagnosis of hypertension, all of which were not found to contribute significantly to racial/ethnic differences in the risk of combined MI. An additional limitation was that race and ethnicity were not known for a very small number of patients, 11 (0.01%); however, this number was so small that it did not have any effect on the final outcomes. Further, because the USRDS only records hospitalization data from those patients with Medicare as the primary insurance, there is limited ability to generalize the results to patients with private insurance. Finally, we were not able to adjust for factors that may be potentially related to health disparities, such as lack of access to medical care before initiation of dialysis, worse socio-economic status, and misclassification of CVD diagnosis before initiation of dialysis. However, similar results were found for those with and without prevalent CVD, adjusted for EPO use (potentially a surrogate marker for those with prior access to health care), which makes the contribution of these variables to a change in the overall findings less likely.

We conclude that ESRD patients with prevalent CVD have a much greater risk of incident non-fatal and combined MI, and that belonging to a racial and ethnic minority group is associated with lower rates of non-fatal and fatal MI compared to Caucasians, after adjustment for time on dialysis, dialysis modality, age, gender, placement on the transplant waiting list, and baseline characteristics. Further research is warranted to determine biologic or environmental factors that may play a role in CVD among ESRD patients.

MATERIALS AND METHODS
Data source
Data for the analyses were obtained from the 2003 USRDS database release. Details regarding the structure and data collection methods

have been reported elsewhere.[33] Briefly, the USRDS records demographic and clinical information on all patients with ESRD for whom renal replacement therapy was initiated and who have survived more than 90 days from the start of therapy. Baseline data were abstracted from the ESRD Medical Evidence Reports (Centers for Medicare and Medicaid Services Form 2728), the United Network for Organ Services transplant records, ESRD Network Census reports, and death notification reports. Among those patients for whom Medicare was the primary or secondary insurance provider, hospitalization data were obtained from Medicare billing records.

Study population
All incident dialysis patients greater than 18 years of age but less than 110 years who were enrolled in the USRDS between January 1, 1995 and 31 December 2000 for whom Medicare was the primary insurance were considered for this analysis. Medicaid patients were included in the cohort as well, as Medicaid and Medicare patients are listed together as a single choice in the USRDS insurance payer variable. Because USRDS data were incomplete for patients after 31 December 2000 owing to billing issues, data were censored after this date. Patients with an indication of renal transplantation or death before initiation of renal replacement therapy were excluded. Patients were considered at risk 90 days after initiation of renal replacement therapy until the first of the following: death, lost-to-follow-up, loss of Medicare as primary insurance coverage, end of study (31 December 2000), or 3 years after the date of transplant. Owing to the non-uniformity of transplantation data and the potential loss of Medicare data for those <65 years after 3 years of a successful transplantation, all transplant patients were censored 3 years after the transplantation date.

Determination of MI
An incident MI was characterized as being non-fatal (hospitalization) or fatal (death owing to MI). Using hospitalization data obtained from the USRDS billing records hospital standard analysis file (HOSP1.SAF and HOSP2.SAF), a non-fatal MI was defined as a primary or secondary *International Classification of Diseases, Ninth Revision* (ICD-9) code[34] consistent with MI (410.xx). The first date of hospitalization was considered the first date of non-fatal MI. Using the cause of death codes from the patients' standard analysis file, fatal MI was defined as any cause of death that was secondary to an MI, and included all codes for 'MI, acute'. Incident non-fatal and fatal MI events (combined MI) were combined for the final outcome.

Exposures
The primary risk factor of interest identified *a priori* was race or ethnicity. Patients were classified by race/ethnicity into the categories Caucasian, African American, Asian American, Hispanic and other, which were based on data from the USRDS standard analysis file and medical evidence form (Form 2728) obtained at the initiation of renal replacement therapy. Those included in the 'other' racial category were of Native American ethnicity or any other race/ethnicity not included above. Secondary predictors of interest included gender, age, primary cause of ESRD, renal replacement modality (peritoneal dialysis, hemodialysis, or transplant), and placement on the transplant waiting list. Other covariates of interest abstracted from the medical evidence form included the following baseline covariates: ability to ambulate, EPO use before renal replacement therapy, albumin (g/dl), hemoglobin (g/dl), blood urea

nitrogen (BUN) (mg/dl), creatinine (mg/dl), height (cm), and weight (kg). Baseline laboratory data were only considered for patients who had a laboratory test value recorded within 1 year of initiating renal replacement therapy. Prevalent CVD was defined by any indication of ischemic heart disease, MI, cardiac arrest, or congestive heart failure at baseline on the Medical Evidence Form 2728.

Statistical analysis
Incidence rates for non-fatal and combined MI were calculated as the observed number of events per total patient time at risk. Owing to a potential disparity in reporting of non-fatal MI among minorities and the inability to distinguish between patients with and without an MI resulting in immediate death, both non-fatal and combined non-fatal and fatal MI outcomes were investigated.[7–9] Non-fatal and combined MI event rates were calculated by the total number of events divided by the number of person-years at risk; confidence intervals were determined using a normal approximation and square-root transformation.[35] Patients were considered at risk at the start of Medicare coverage within 90 days of initiation of renal replacement therapy to the time of censoring. Cox proportional hazards models[36] using time-dependent covariates and robust variance estimation were used to analyze the association between race/ethnicity and the risk of incident MI separately for subgroups defined by prevalent CVD. Treatment status (hemodialysis, peritoneal dialysis, and transplant) and placement on the transplant waiting list were modeled as time-dependent covariates. Transplantation, however, was analyzed according to an 'intention-to-treat' principle. Thus, transplanted patients were analyzed in the transplantation group throughout the remainder of follow-up regardless of subsequent changes in transplantation status. Because of potential confounding and because those with prevalent CVD are known to be at risk for a subsequent cardiac event in the general population, we conducted separate analyses for those with and without prevalent CVD. All statistical analyses were performed using SAS version 8.2 (SAS Institute Inc., Cary, NC,USA) and S-Plus version 6.1 (Insightful Inc., Seattle, WA, USA).

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