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Prevalence and Clinical Correlates of Coronary Artery Disease among New Dialysis Patients in the United States: A Cross-Sectional Study

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Abstract. Despite the high prevalence of coronary artery disease (CAD) among patients with end-stage renal disease (ESRD), few studies have identified clinical correlates using national data. The purpose of this study was to determine the prevalence and clinical associations of CAD in a national random sample of new ESRD in the United States in 1996/1997 ($n = 4025$). Data on demographic characteristics and comorbidities were obtained from the Dialysis Morbidity and Mortality Study, Wave 2. The principal outcome was CAD, defined as the presence of a previous history of CAD, myocardial infarction, or angina, coronary artery bypass surgery, coronary angioplasty, or abnormal coronary angiographic findings. Multivariate logistic regression analysis was used to assess the relationship of conventional factors and proposed uremic factors to the presence of CAD. CAD was present in 38% of patients. Of the total cohort, 17% had a history of myocardial infarction and 23% had angina. Several conventional risk factors, including advancing age, male gender, diabetes mellitus, and smoking, were significantly associated with CAD. Of the proposed uremic factors, lower serum albumin levels but higher residual renal function and higher hematocrit values were significantly associated with the presence of CAD. Vascular comorbid conditions, structural cardiac abnormalities, white race, and geographic location were also strongly correlated with the presence of CAD. This national study suggests that several conventional CAD risk factors may also be risk factors for CAD among the ESRD population. This study identifies nonconventional factors such as serum albumin levels, vascular comorbid conditions, and structural cardiac abnormalities as important disease correlates. Future longitudinal studies are required to explore the relative importance of the relationships observed here.

Cardiac disease is the leading cause of death among patients with end-stage renal disease (ESRD). It accounts for almost 50% of deaths among prevalent ESRD patients, according to several national registries (1,2). Coronary artery disease (CAD), which is the major factor in the pathogenesis of cardiac disease, is common among the ESRD population, with prevalence rates that are 5 to 20 times greater than those for the general population (3). In the general population, there has been a reduction in the mortality and morbidity rates for CAD through the implementation of effective risk factor-reduction programs and better interventions for patients with established CAD (4). No such trend has been observed for patients with ESRD (5).

The risk factors for CAD in the general population have been well characterized (6). The Framingham Study and other studies have identified a number of atherogenic risk factors, including increasing age, male gender, family history, hypertension, diabetes mellitus, smoking, and elevated serum cholesterol levels. More recently, homocysteine and lipoprotein(a) have been identified as additional coronary risk factors, necessitating a broadening of existing risk factor-reduction strategies (7,8). Many of these traditional risk factors are also present among patients with renal failure (9–11). However, it is unclear whether these conventional CAD risk factors are independently predictive of CAD among patients with renal failure. Few published studies have examined the relationship between conventional coronary risk factors and CAD in pre-ESRD or ESRD populations.

The excess prevalence of CAD among patients initiating dialysis has led to the hypothesis that the uremic environment might itself be atherogenic. Anemia, hypoalbuminemia, hyperphosphatemia, and metabolic acidosis may be responsible factors. Few studies have attempted to determine the independent effect of the uremic environment, with adjustment for conventional cardiac risk factors. To date, hyperphosphatemia, hyperparathyroidism, and elevated lipoprotein(a) and homocysteine levels have been demonstrated to be associated with CAD in prevalent ESRD patients (10–14). Furthermore, a recent cross-sectional study of >400 patients (257 with normal renal function and 160 with renal impairment) identified elevated lipoprotein(a) levels as a strong correlate of atherosclerotic disease in pre-ESRD patients (14). These studies, however, have been limited by small sample size, failure to adjust for important conventional and proposed uremic CAD risk factors, and failure to adjust for other potentially confounding variables.

The purpose of this study was to (*1*) describe the prevalence

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of CAD among new ESRD patients, as well as subgroups of patients, in 1996/1997, (*2*) describe the association of known conventional risk factors with the presence of CAD, (*3*) determine whether markers of uremia are associated with the presence of CAD, and (*4*) explore the relationships of other factors, including vascular and other comorbidities, structural cardiac abnormalities, race, geography, and pre-ESRD care, to the presence of CAD. The availability of data on these conventional and potential uremic factors for a large, randomly selected, national sample of new patients from the United States Renal Data System (USRDS) Dialysis Morbidity and Mortality Study (DMMS), Wave 2, provided us with a unique opportunity to further investigate these relationships. The importance of identifying and targeting potential uremic risk factors lies in the fact that these may contribute to the excess prevalence of CAD among new dialysis patients.

Materials and Methods

Study Design

Data were obtained from the DMMS, Wave 2, which is a special study of the United States Renal Data System. This study included a nationally representative sample of patients who were initiated on dialysis in 1996/1997. Twenty-five percent of dialysis facilities throughout the United States were sampled. From each of these, all patients who were beginning to undergo peritoneal dialysis and one-fifth of patients who were beginning to undergo hemodialysis (those with Social Security numbers ending in 2 or 9) were included. Therefore, peritoneal dialysis patients were oversampled by a factor of 5, to ensure comparable numbers. The modality type was assigned on day 60 of ESRD. The modality assignment for patients who were undergoing hemodialysis but were training for peritoneal dialysis on day 60 was deferred for 10 days. Patients excluded from the study included those <15 yr of age, patients who had received a renal transplant, and patients for whom information was not available on the outcome variables of interest.

The study start date for DMMS Wave 2 began 60 days after the initiation of chronic dialysis. Dialysis facility personnel obtained baseline data for all new patients, including data on demographic characteristics, causes of ESRD, Framingham Study-type risk factors, uremic risk factors, comorbidities, structural cardiac abnormalities, measures of secondary hyperparathyroidism, and elements of pre-ESRD care. The laboratory data used for the analyses were collected within a 3-mo period after the initiation of ESRD, with the exception of serum creatinine levels, which were measured before the first regular dialysis session. In addition, a self-administered patient questionnaire provided data on pre-ESRD care, quality of life, modality selection, and rehabilitation. Patients were prospectively monitored for 9 to 12 mo, and the data collection was complete in early 1998.

Data Analyses

For continuous variables, missing values were set to the mean of the overall sample. For categorical variables, missing values were considered not to be present. The means of continuous variables were compared with a *t* test. A χ^2 analysis was used to compare categorical variables.

The dependent variable of interest for our study was the presence or absence of CAD among new dialysis patients. CAD was defined as present in patients with one of the following indicators: history of CAD, myocardial infarction, or angina, previous angiography because of CAD, abnormal angiographic results, angioplasty, or coronary artery bypass grafting.

The independent variables were grouped into three models, for characterization of the relationship between conventional and uremic risk factors and the presence of CAD. The first multivariate model evaluated the effects of conventional cardiac risk factors, namely increasing age, gender, diabetes mellitus (defined as the cause of renal failure), BP, smoking (defined as ever smoked *versus* never smoked), serum cholesterol levels, and triglyceride levels. The relationship of BP to CAD was evaluated in the model by including systolic and diastolic BP measured before dialysis (an average of three readings recorded before the study start date) as independent covariates. We also included hypertension as a cause of ESRD in the model equation, as an index of chronicity. Data on homocysteine levels, lipoprotein(a) levels, and some other established, conventional, coronary risk factors (including a family history of CAD) were not available in the database. A second model, which evaluated the effects of proposed uremic factors on the presence of CAD, included baseline renal function measured as creatinine clearance (estimated by using the formula developed by the Modification of Diet in Renal Disease Study Group) (15), hematocrit values, serum albumin levels, measures of calcium and phosphate balance, parathyroid hormone, and serum bicarbonate levels as independent variables, with adjustment for all conventional risk factors. A final model was constructed to assess the effects of structural cardiac abnormalities (left ventricular hypertrophy and cardiomegaly), other comorbid conditions, and elements of pre-ESRD patient care on the presence of CAD, with adjustment for all other model covariates. The elements of pre-ESRD care included the use of erythropoietin before ESRD, late referral to a nephrologist (defined as referral <4 mo before ESRD *versus* greater), and the number of visits to a nephrologist/dietitian (>2 *versus* less), because we hypothesized that these might be correlated with the presence of CAD at the initiation of dialysis.

Multivariate logistic regression analysis determined the relationship of each covariate in each model to the outcome variable. For each model, the coefficient of determination (r^2) was computed. Subsequent analyses were performed to determine whether factors associated with CAD also varied with demographic or subgroup characteristics. Additional sensitivity analyses were performed to determine whether the relationships observed between proposed factors and outcomes were still apparent if a finer specification of CAD was used. For this finer specification, we included only patients with definite histories of myocardial infarction, abnormal coronary angiographic results/angioplasty, or coronary artery bypass grafting. All statistical analyses were performed using SAS version 6.12 software (SAS, Cary, NC).

Results

The DMMS Wave 2 data set included data for 4024 patients who were initiated on dialysis in 1996/1997. After exclusion of patients <15 yr of age ($n = 99$), a total of 3925 patients were available for these analyses. The mean age of the study population was 58 ± 16 yr. Of these patients, 53% were male and 62% were white. The prevalence of CAD was 38% among new dialysis patients in 1996/1997 (Figure 1). Myocardial infarction was present in 14% and suspected for an additional 3%. A history of angina pectoris was recorded for 19% of the patients, and angina was suspected for an additional 4%. The prevalence of CAD varied according to gender and diabetic subgroup (Figure 2). The prevalence of CAD also varied according to race. Figure 3 illustrates the distribution of CAD among new dialysis patients according to race. White race exhibited the highest prevalence (43%), followed by Black and Native

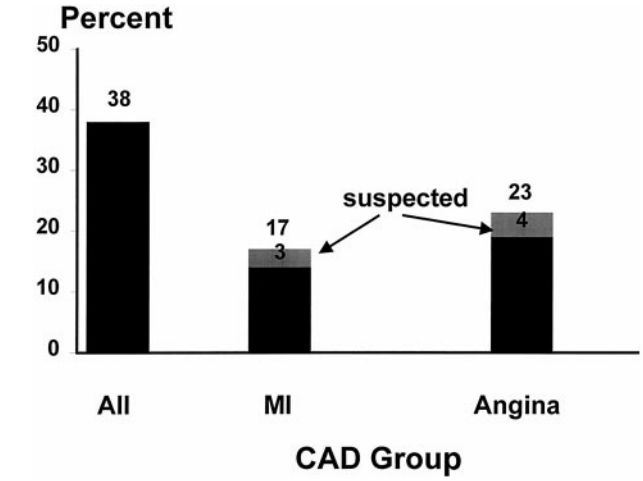

Figure 1. Prevalence of coronary artery disease (CAD) among new ESRD patients in the United States, 1996/1997. MI, myocardial infarction.

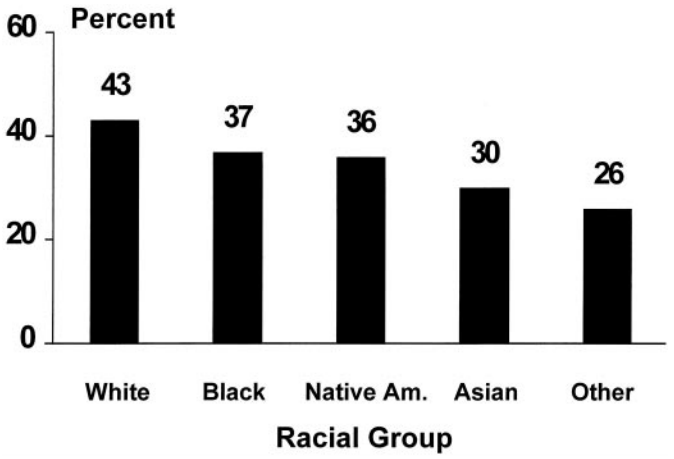

Figure 3. Prevalence of CAD according to race.

American racial groups (37 and 36%, respectively), whereas Asian and "Other" racial groups exhibited the lowest adjusted prevalence (30 and 26%, respectively). The association of race with CAD, adjusted for age, is shown in Figure 4. White patients were more likely to have CAD than non-white patients in all age groups, the magnitude of which increased with increasing age.

The distribution of demographic characteristics, comorbidities, structural cardiac abnormalities, pre-ESRD care, and laboratory parameters for the entire study population and for patients with and without CAD is presented in Table 1. Patients with CAD exhibited a greater prevalence of associated atherosclerotic conditions, including peripheral and cerebral vascular disease. Structural cardiac abnormalities (left ventricular hypertrophy and cardiomegaly) were also more prevalent among patients with CAD than among those without CAD. The mean serum creatinine concentration was lower (7.2 ± 2.7 *versus* 9.2 ± 4.0 mg/dl) and the creatinine clearance was higher (8.0 ± 2.9 *versus* 6.8 ± 2.8 ml/min) for patients with CAD, compared with those without CAD. Both serum total cholesterol levels and the HDL fraction were lower for patients with CAD. No significant differences were observed in the distribution of LDL cholesterol or triglyceride levels between groups.

The relationship of conventional risk factors to the presence of CAD is shown in Table 2. Increasing age, male gender, diabetes mellitus, and smoking were all strongly associated with the presence of CAD among new patients. For every 10-yr increase in age, the adjusted odds ratio (AOR) for CAD increased by 69%. Patients with diabetes mellitus as a cause of ESRD were twice as likely to have CAD than were nondiabetic patients. Patients who had smoked at any time in their lives were almost 50% more likely to have CAD than were those who had never smoked. Neither hypertension as a cause of ESRD nor systolic BP measured before dialysis was associated with the presence of CAD. In contrast, diastolic BP recorded

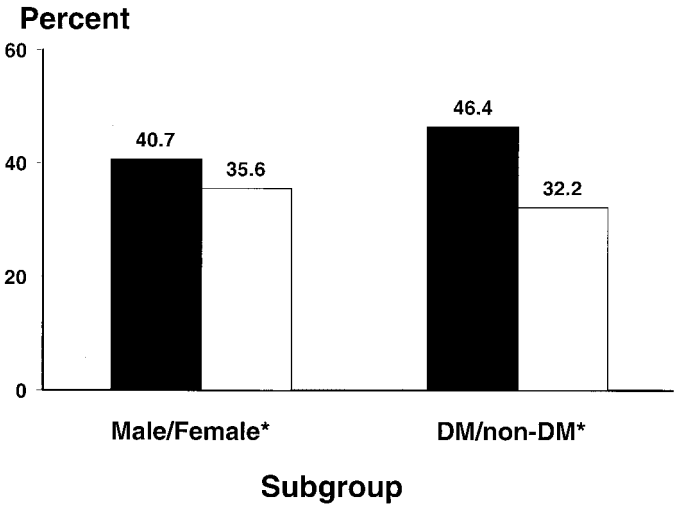

Figure 2. Prevalence of CAD according to gender and the presence of diabetes mellitus (DM). *, $P < 0.001$ for each pair, by χ^2 test.

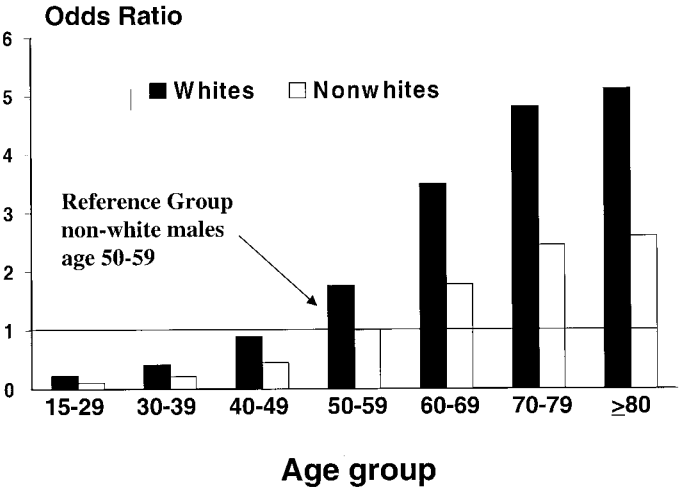

Figure 4. Odds ratios for CAD according to age and race, adjusted for gender and the presence of diabetes mellitus. ($P < 0.0001$ for all age groups compared with references 50–59.)

Table 1. Demographic and clinical characteristics of new ESRD patients ($n = 3925$), with and without CAD[a]

Characteristic	Study Population (% or mean ± SD)	Missing Data (%)	CAD Present (% or mean ± SD)	CAD Absent (% or mean ± SD)
CAD	38	3.5		
Conventional factors				
mean age (yr)[*]	58 ± 16	0	65 ± 2	53 ± 5
male gender (*versus* female)[**]	53	0	56	51
diabetes mellitus (cause of ESRD)[**]	43	0	52	37
hypertension (cause of ESRD)[***]	26	0	24	27
predialysis systolic BP (mmHg)	147 ± 21	2.2	146 ± 22	147 ± 21
predialysis diastolic BP (mmHg)[*]	80 ± 12	2.3	76 ± 12	81 ± 12
smoker[b,**]	40	7.2	46	37
total cholesterol (mg/dl)[**]	194 ± 55	10	191 ± 54	196 ± 56
LDL cholesterol (mg/dl)	151 ± 94	83	147 ± 91	153 ± 96
HDL cholesterol (mg/dl)	59 ± 69	83	53 ± 58	63 ± 75
triglyceride (mg/dl)	199 ± 144	22.8	200 ± 14	198 ± 15
Uremic factors				
hematocrit[*]	30.? ± 6.6	3.8	31 ± 6	30 ± 6
serum albumin (g/dl)[*]	3.46 ± 0.57	10	3.38 ± 0.55	3.51 ± 0.58
serum phosphate (mg/dl)[*]	5.5 ± 1.9	5.4	5.3 ± 1.8	5.7 ± 1.9
serum calcium (mg/dl)	8.7 ± 1.0	5.2	8.7 ± 0.9	8.7 ± 1.1
serum PTH (ng/ml)[*]	316 ± 371	21.5	278 ± 330	339 ± 393
serum bicarbonate (mg/dl)[*]	22 ± 4.7	10.8	22.4 ± 4.7	21.8 ± 4.8
serum creatinine (mg/dl)[c,*]	8.4 ± 3.7	7.3	7.2 ± 2.7	9.2 ± 4.0
creatinine clearance (ml/min)[d,*]	7 ± 2.9	16.1	8 ± 2.9	6.8 ± 2.8
Structural cardiac abnormalities				
left ventricular hypertrophy[e,**]	20	20	29	14
cardiomegaly[f,**]	26	15.5	39	18
Vascular/other comorbidities				
peripheral vascular disease[g,**]	21	4.6	38	11
cerebrovascular disease[**]	12	3	19	8
pericarditis[**]	2.8	3	4	2
Pre-ESRD care				
late referral (referral <4 mo before ESRD)	23	35	22	24
visits to nephrologist (>2 *versus* less)	42	35	41	42
visits to dietitian (>2 *versus* less)	35	35	34	36
erythropoietin use before ESRD (yes *versus* no)	16	37	16	17

[a] CAD, coronary artery disease; ESRD, end-stage renal disease; PTH, parathyroid hormone; *, $P < 0.001$; **, $P < 0.01$. ***, $P < 0.05$.
[b] Present or past smokers.
[c] Recorded before the first dialysis session.
[d] Before first dialysis session, per the Modification of Diet in Renal Disease study formula (15).
[e] Includes patients with history of left ventricular hypertrophy by electrocardiogram or echocardiogram.
[f] Defined as an enlarged heart by chest radiograph.
[g] Includes history of peripheral vascular disease amputation, intermittent claudication, or absent pulses.

before dialysis was inversely related to the presence of CAD. For every 10-mmHg increase in diastolic BP, the AOR for the presence of CAD decreased by 16%. In this analysis of conventional factors, neither serum cholesterol levels nor triglyceride levels were associated with the presence of CAD.

The independent relationships between uremic risk factors and the presence of CAD, with adjustment for conventional risk factors, are illustrated in Table 3. Higher serum albumin levels were associated with a lower likelihood of CAD among new ESRD patients (AOR = 0.76, $P = 0.0001$). In contrast, higher hematocrit values were associated with a greater likelihood of CAD, such that the AOR for CAD increased by 2% with every 1-unit increase in hematocrit. Similarly, a greater likelihood of CAD was observed for every 1-ml/min higher level of residual renal function (AOR = 1.07, $P = 0.0001$). Serum calcium, phosphorus, calcium-phosphate product, parathyroid hormone, and serum bicarbonate levels were not associated with CAD in this analysis.

The final model, with adjustment for factors in previous models, investigated the relationship of vascular and other

Table 2. Conventional factors associated with CAD among new patients with ESRD (model 1, $r^2 = 17\%$)

Variable	AOR[a]	*P* Value
Age (per 10 yr)	1.69	0.0001
Male gender (*versus* female)	1.32	0.0004
Predialysis diastolic BP (per 10 mmHg)	0.84	0.0001
Diabetes mellitus (*versus* all other causes)	2.08	0.0001
Smoking (*versus* never)	1.44	0.0001

[a] AOR, adjusted odds ratio. Adjusted for conventional risk factors, including hypertension (measured as a cause of ESRD), predialysis systolic BP, serum cholesterol and triglyceride levels, and the factors listed.

comorbidities, structural cardiac disease states, geography, and aspects of pre-ESRD patient care to the presence of CAD (Table 4). This model explained 26% of the total variability (r^2) in the presence of CAD. Vascular comorbidities and structural cardiac defects were strongly correlated with CAD. White race was also associated with a greater prevalence of CAD (AOR = 1.85, $P = 0.0001$) at the time of dialysis initiation. The presence of CAD among new dialysis patients also varied according to geographic location. New patients who were initiated on dialysis in network 5 (Washington DC, Maryland, Virginia, and West Virginia) were more likely to have CAD than the national average, whereas patients who underwent their first treatments in network 12 (Iowa, Missouri, Kansas, and Nebraska) were less likely to have CAD. Neither early nephrology referral, erythropoietin use, nor dietetic care during the pre-ESRD period was associated with the presence of CAD among new patients with ESRD.

The relationships of conventional factors, proposed uremic factors, and all other factors to CAD were also explored by using the more specific measure of CAD (*i.e.*, patients with a definite history of myocardial infarction, abnormal coronary angiographic findings, coronary angioplasty, or coronary artery bypass grafting). In these analyses, the strength and magnitude of the associations observed were similar to those from previous models.

Discussion

This study of United States Renal Data System DMMS Wave 2 data provides evidence that the prevalence of CAD among patients who were initiated on dialysis in 1996/1997 was high, *i.e.*, 38%. Published data from the Case Mix Severity Study, describing comorbid conditions of new patients in 1986/1987, demonstrated a similar prevalence of 40% (16). This finding suggests that the burden of disease has not changed substantially among incident ESRD patients in the past 10 yr. The high prevalence of CAD among patients with ESRD in the United States has been described as a national epidemic. Because available data on the risk factors for CAD among patients with renal failure are scant, a task force convened by the National Kidney Foundation has recommended additional research on this subject through the use of observational studies (17). Our study further explores the relationship of conventional and nonconventional factors to CAD, using national data.

Our analyses suggest that several conventional risk factors, including increasing age, male gender, diabetes mellitus, and smoking, may be risk factors for CAD among patients with chronic renal disease, as in the general population. We did not, however, find evidence to invoke serum cholesterol levels and triglyceride levels as significant CAD correlates.

Age and gender are important, although nonmodifiable, pre-

Table 3. Uremic factors associated with CAD among new patients with ESRD (model 2, $r^2 = 18\%$)

Variable	AOR[a]	*P* Value
Hematocrit (per 1%)	1.02	0.002
Creatinine clearance (per 1 ml/min)	1.07	0.0001
Serum albumin (per 1 g/dl)	0.76	0.0001

[a] Uremic model adjusted for all factors in Table 2, the factors listed, and the nonsignificant covariates of serum bicarbonate, calcium phosphate, calcium-phosphate product, and parathyroid hormone.

Table 4. All factors associated with CAD among new patients with ESRD (full model, $r^2 = 26\%$)

Variable	AOR[a]	*P* Value
Conventional		
age (per 10 yr)	1.54	0.0001
male gender (*versus* female)	1.21	0.03
diabetes mellitus (*versus* all others)	1.61	0.0001
predialysis diastolic BP (per 10 mmHg)	0.90	0.004
smoker	1.22	0.02
Uremic		
creatinine clearance (per 1 ml/min)	1.06	0.0001
hematocrit (per 1%)	1.02	0.009
serum albumin levels (per 1 g/dl)	0.85	0.01
Race		
white (*versus* non-white)	1.85	0.0001
Geographic region		
network 5[b] (*versus* United States)	1.40	0.02
network 12[c] (*versus* United States)	0.72	0.07
Vascular/other comorbidities		
peripheral vascular disease	2.82	0.0001
cerebrovascular disease	1.89	0.0001
pericarditis	1.58	0.05
Structural cardiac abnormalities		
left ventricular hypertrophy	1.85	0.0001
cardiomegaly	1.96	0.0001

[a] Adjusted for conventional and proposed uremic factors, all 18 dialysis network areas, and elements of pre-ESRD care (including late referral to a nephrologist, frequency of visits to a dietitian and the nephrologist, and erythropoietin use in the pre-ESRD period).
[b] Network 5 includes Washington, DC; Maryland; Virginia; and West Virginia.
[c] Network 12 includes Iowa, Missouri, Kansas, and Nebraska.

dictors of CAD in the general population (6,7). Data from several renal registries have demonstrated the association of age with CAD in univariate analyses (2,3,5). We observed 54% greater odds of having CAD for every 10-yr increase in age in the adjusted analysis. Similarly, male gender was strongly associated with the presence of CAD among new ESRD patients (AOR = 1.21, $P = 0.03$). This observation is in agreement with the findings of Bloembergen *et al.* (18) and Parfrey *et al.* (11), who also demonstrated a strong positive association of male gender with the presence of CAD.

Hypertension is a major risk factor for the development of CAD in the general population (19). For patients with ESRD, previous studies demonstrated an increased risk of CAD with increasing diastolic BP (10,11). In this cross-sectional study, higher diastolic BP was associated with lower, not greater, likelihood of CAD, with adjustment for several conventional factors. One possible explanation for this negative association is that patients with CAD, compared with those without CAD, are more likely to have lower BP resulting from coexisting heart failure. It has also been suggested that isolated BP measurements obtained at single time points often do not discriminate between patients with longstanding hypertension and those without and thus may not be good measures of exposure (20,21). To address this concern, we included a measure to reflect longstanding hypertension (defined as hypertension as a cause of ESRD). Although this measure of hypertension was related to the presence of CAD in the univariate analysis, the final multivariate model, with adjustment for several other factors, did not identify chronic hypertension as a significant CAD correlate.

Our study corroborates the observations of other investigators with respect to the role of diabetes mellitus as a strong CAD correlate (3,10,11). Diabetic patients beginning dialysis were 50% more likely to have CAD than were nondiabetic patients, with adjustment for all other conventional risk factors in addition to several other measured factors. Because CAD among diabetic patients may be clinically silent and thus not detected using our clinical definition of CAD, the true effects of diabetic status on the presence of CAD may be underestimated in this population (22).

Although smoking is a major modifiable risk factor for the development of CAD in the general population, its role in the pathogenesis of CAD among patients initiating renal replacement therapy has been less well studied. A single case-control study by Kawagishi *et al.* (23) identified cigarette smoking as being strongly associated with the presence of carotid artery intima media thickness, a surrogate marker of atherosclerosis. In contrast, in a prospective cohort study by Parfrey *et al.* (11), smoking was associated neither with the presence of CAD in baseline examinations nor with the development of new CAD during follow-up. We observed that smokers had 22% greater likelihood of having CAD than nonsmokers, with adjustment for several other factors. Because smoking is a modifiable risk factor, measures to reduce its prevalence among this patient population represent an important prevention strategy.

We did not observe an association between cholesterol levels or triglyceride levels and CAD among new patients with ESRD. Data on serum cholesterol levels were available for 90% of the study population, and data on triglyceride levels were available for >77%. Rostand *et al.* (24) observed higher levels of total cholesterol, triglycerides, and HDL cholesterol and higher total cholesterol/HDL cholesterol ratios for chronic dialysis patients with significant CAD, compared with those without CAD. Similarly, longitudinal studies have identified increased total serum cholesterol, LDL cholesterol, and apolipoprotein B levels as predictors of atherosclerotic events among pre-ESRD and ESRD patients (25–27). The lack of an association between these isolated measurements of serum lipids and CAD does not exclude the possibility that lipids are, at some time in the course of renal insufficiency, important in CAD development.

It has been hypothesized that the effects of uremia contribute to the high prevalence of CAD. Our multivariate model found only the association with serum albumin levels to be supportive of this hypothesis. Higher serum albumin levels were significantly associated with less CAD. This relationship between hypoalbuminemia and the development of CAD was observed previously (11,28). Hypoalbuminemia has also been demonstrated to be associated with congestive heart failure (CHF) (29). Because patients with CAD are more likely to have CHF, the issue of confounding variables arises. In our study, CHF was more common among patients with CAD, compared with those without CAD (data not shown). In a separate analysis, which also included CHF as an independent covariate, the association between albumin levels and CAD no longer remained. This suggests that the presence of coexisting CHF among patients with CAD may explain the relationship between lower albumin levels and more CAD.

Higher hematocrit values and greater residual renal function were associated with more CAD (AOR = 1.02, $P = 0.007$; and 1.06 per 1-ml/min higher creatinine clearance, $P = 0.0001$, respectively), not less CAD. We speculated that these observations might be attributable to the fact that patients with CAD, compared with those without CAD, were initiated on dialysis earlier in the course of renal insufficiency and thus were more likely to be treated with erythropoietin. A comparison of residual renal function among patients with and without CAD revealed higher levels in the CAD group (8.0 ± 2.9 *versus* 6.8 ± 2.8 ml/min, $P = 0.0001$), suggesting that patients with CAD were indeed initiated on earlier in the course of renal insufficiency. Although we suspected greater use of erythropoietin in the CAD group, we did not find evidence to support this. Therefore, the earlier initiation of dialysis for patients with CAD may explain these unexpected associations of higher hematocrit values and greater residual renal function with CAD.

Coronary ischemic syndromes may result from abnormalities of left ventricular function (30,31). In this analysis, abnormalities of left ventricular function, namely left ventricular hypertrophy and cardiomegaly, were independently associated with the presence of CAD among a national sample of new dialysis patients. We corroborate the findings of Parfrey *et al.* (11) from a cohort study of 432 patients. A five- to sixfold greater risk of new ischemic heart disease was observed for patients with concentric left ventricular hypertrophy and left

ventricular dilation, compared with patients without those conditions (11). We also observed that patients with documented cerebral and peripheral vascular disease were more likely to have CAD than were those without such disease. This finding has been confirmed in autopsy studies, in which atherosclerosis of the coronary vasculature was strongly correlated with disease of the carotid arteries (32). In fact, a recent prospective study by Hodis *et al.* (33) found that carotid artery intima media thickness predicted coronary events beyond those predicted by coronary artery measures of atherosclerosis. Screening for CAD among these at-risk patients may permit earlier detection, facilitate more timely intervention strategies, and lead to improved survival rates.

Racial differences in the prevalence of CAD have been described previously (11,22). In this study, with adjustment for several factors in the multivariate analysis, White patients were almost twice as likely to have CAD as non-White patients. It is unclear why these differences exist, but potential explanations include differences in access to health care, differences in socioeconomic status, and differences in referral patterns among racial groups (34). In the general population, White patients are more likely to receive medical attention for the treatment of CAD compared with Black patients (35). The recent observations of Daumit *et al.* (36) indicate that the same trend may be noted for patients with advanced renal insufficiency. In a 7-yr longitudinal study of almost 5000 patients, white patients who reached ESRD were 3 times more likely to have undergone an invasive coronary procedure than were their Black counterparts.

This study also provides evidence for geographic variations in the prevalence of CAD among new patients with ESRD in the United States. Of the 18 ESRD network areas, patients from ESRD network 5 exhibited a higher prevalence of CAD, whereas those from ESRD network 12 exhibited a lower prevalence of CAD, compared with the national average. Studies from the United States have demonstrated that the CAD mortality rates for the general population vary with longitude (37). It is likely that these geographic differences in cardiac mortality rates are related to geographic differences in the underlying CAD prevalence. The reasons for these differences in CAD prevalence in different ESRD network areas are not entirely clear, but differences in the prevalence of underlying risk factors, access to health care (primary and secondary prevention treatments), and climatic factors are likely possibilities (38).

Although we speculated that certain elements of pre-ESRD care might be associated with CAD presence at dialysis initiation, our final analysis did not indicate these elements as important clinical correlates. The lack of association between these pre-ESRD measures and CAD may be a function of the cross-sectional study design; however, it is also likely that many of these aspects of pre-ESRD care were implemented at a time when the underlying disease was at an advanced stage.

Although this study has major strengths, some weaknesses are also inherent. The cross-sectional study design does not permit a thorough evaluation of the complex relationships between many of the proposed factors and the presence of CAD. For example, we cannot adequately elucidate the relationship between renal function decline or hematocrit levels and the occurrence of CAD in this study, because the temporal association between exposure and outcomes cannot be addressed. An additional criticism might be related to the lack of specificity of our definition of CAD, which was used to identify all new ESRD patients with CAD. To enhance specificity, we restricted the analysis to a subset of patients for whom CAD was defined on the basis of a history of a myocardial infarction or an interventional coronary procedure, and we obtained similar results. We also acknowledge the lack of data on recently proposed CAD risk factors, including homocysteine levels, lipoprotein(a) levels, and markers of inflammation; accumulating evidence suggests that these may have important mechanistic roles in the development of atheroma in patients with chronic renal failure.

This national study confirms the findings of similar prevalence of CAD among incident and prevalent patients, suggesting that the mechanisms that predispose patients to ischemia are already operative during the pre-ESRD period. It suggests that increasing age, male gender, diabetes mellitus, and smoking may be risk factors for CAD among new patients with ESRD, as in the general population. It also identifies vascular comorbidities and structural cardiac abnormalities as strong CAD correlates. Because several of the factors identified are potentially modifiable, effective targeting and reduction of these factors may reduce the prevalence of CAD in new ESRD patients. Furthermore, the role of screening for CAD among patients with documented vascular disease and structural cardiac conditions warrants further consideration. We suggest that greater attention should be focused on the pre-ESRD population and that future research efforts should be directed at elucidating the natural history of CAD in this group.

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