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Traditional Cardiovascular Disease Risk Factors in Dialysis Patients Compared with the General Population: The CHOICE Study

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Abstract. Although atherosclerotic cardiovascular disease (ASCVD) risk in end-stage renal disease (ESRD) is 5 to 30 times that of the general population, few data exist comparing ASCVD risk factors among new dialysis patients to the general population. This cross-sectional study of 1041 dialysis patients describes the prevalence of ASCVD risk factors at the beginning of ESRD compared with estimates of ASCVD risk factors in the adult US population derived from the Third National Health and Nutrition Examination (NHANES III). CHOICE Study participants had a high prevalence of diabetes (54%), hypertension (96%), left ventricular hypertrophy by electrocardiogram (EKG) criteria (22%), low physical activity (80%), hypertriglyceridemia (36%), and low HDL cholesterol (33%). CHOICE participants were more likely to be older, black, and male than NHANES III participants. After adjustment for age, race, gender, and ASCVD (defined as myocardial infarction, revascularization procedure, stroke, carotid endarterectomy, and amputation in CHOICE; and as myocardial infarction and stroke in NHANES III), the prevalence of diabetes, hypertension, left ventricular hypertrophy by EKG, low physical activity, low HDL cholesterol, and hypertriglyceridemia were still more common in CHOICE participants. Smoking, obesity, hypercholesterolemia, and high LDL cholesterol, however, were less common in CHOICE than NHANES III participants. The projected 5-yr ASCVD risk based on the Framingham Risk Equation among those older than 40 yr without ASCVD was higher in CHOICE Study participants (13%) than in the NHANES III participants (6%). In summary, many ASCVD risk factors are more prevalent in ESRD than in the general population and may explain some, but probably not all, of the increased ASCVD risk in ESRD.

Atherosclerotic cardiovascular disease (ASCVD) accounts for approximately half of deaths in end-stage renal disease (ESRD) and contributes to the extraordinarily high total annual mortality of 23% observed in such patients (1). The incidence of myocardial infarction (MI) and stroke in the dialysis population is 5- to 15-fold higher in ESRD (2), and cardiovascular mortality is 10- to 30-fold higher (3) than that seen in the general population (4–6), This increased risk is only partially explained by a high prevalence of ASCVD (2,4,7–9) and traditional ASCVD risk factors (10) at the initiation of dialysis (3,11,12).

The Special Report from the National Kidney Foundation Task Force on Cardiovascular Disease (13) called for further studies of ASCVD and its risk factors in ESRD patients. Most previous studies of ASCVD risk factors have investigated prevalent ESRD patients (14–17). Such studies may underestimate the presence and effect of risk factors because those with the highest degree of ASCVD risk tend to die sooner and are not included in a prevalent study population (*i.e.*, survival bias), an effect diminished but not eliminated by cross-sectional studies of incident dialysis patients.

Relatively few nationally representative studies (4,9,18–20) have described selected ASCVD risk factors among incident dialysis patients. Several other regional (21,22) and local (23,24) studies of incident patients have also been reported. None of these studies, however, compares ASCVD risk factor prevalence in the incident dialysis population with the general population.

This report presents the prevalence of ASCVD risk factors in the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study, a national study of incident dialysis patients (25), compared with estimates for the general population derived from the Third National Health and Nutrition Examination Survey (NHANES III). Because age, gender, race, and the presence of ASCVD are strongly associated both with ASCVD risk factors and ESRD, the NHANES estimates used for the comparison are adjusted to the age, gender, race, and ASCVD distribution of the CHOICE cohort. A second analysis uses the Framingham risk equation to estimate the 1- and 5-yr ASCVD risk among those without prevalent ASCVD and compares the derived ASCVD risk estimates from the CHOICE cohort with those of the NHANES III study population.

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Materials and Methods

Study Design and Research Population

This cross-sectional study is derived from the baseline data of CHOICE, a prospective cohort study of incident dialysis patients initiated in 1995 to investigate treatment choices and outcomes of dialysis care. Eligibility criteria for enrollment into CHOICE included initiation of chronic outpatient dialysis in the preceding 3 mo, ability to provide informed consent for participation, age older than 17 yr, and ability to speak English or Spanish. The Johns Hopkins University School of Medicine Institutional Review Board and the review boards for the clinical centers approved the study protocol.

From October 1995 to June 1998, 1041 participants from 19 states were enrolled at 81 dialysis clinics associated with Dialysis Clinic Inc. (DCI, Nashville, TN; $n = 923$), New Haven CAPD (New Haven, CT; $n = 86$), or Saint Raphael's Hospital (New Haven, CT; $n = 32$). A specimen bank was established to store blood samples from the DCI enrollees, and specimens were obtained for 898 (97.3%) of the DCI participants, allowing for measurement of complete lipid profiles in this subgroup. In addition, blood test results obtained from routine medical care were available for all 1041 participants. Enrollment occurred a median of 45 d after first dialysis (98% within 4 mo). Comorbidity data from the Medical Evidence Report (Form 2728 of the US Renal Data System [USRDS]) were used to compare characteristics of the CHOICE cohort to the characteristics of all incident dialysis patients in the United States in 1997 (the midpoint of recruitment). Although these data have been shown to underestimate the prevalence of comorbid conditions in incident dialysis patients (26), they provide an identical data source for comparisons between CHOICE and the US dialysis population.

Data Collection

CHOICE Clinical Data. Age, race, gender, physical activity, and tobacco use history were obtained via a questionnaire administered to the patient. Weight, height and pre- and postdialysis session BP were obtained from review of the patients' medical records. Prevalent ASCVD, diabetes, hypertension, and left ventricular hypertrophy (LVH) by electrocardiogram (EKG) criteria were determined at enrollment on the bases of review of all history and physical data, discharge summaries, progress notes, medication records, EKG, and problem lists from the dialysis clinic chart. All records were abstracted by two experienced dialysis research nurses at the CHOICE Comorbidity Assessment Center (New England Medical Center, Boston, MA). Mention of a condition (past or present) in the medical record was sufficient for positive coding.

In the CHOICE study, ASCVD was defined as a history of MI, coronary artery bypass or angioplasty, carotid endarterectomy, stroke, peripheral bypass, peripheral angioplasty, or amputation. The definition of diabetes included both type 1 and type 2 diabetes. Current physical activity was determined by two questions: "At least once a week, do you engage in any regular exercise such as brisk walking, jogging, bicycling, *etc.*, long enough to work up a sweat?" and "If so, how many times per week?" Exercise to perspiration was estimated to be equivalent to a 5.0 metabolic equivalent task (MET) or greater activity (*e.g.*, stationary bicycling as a conditioning exercise is a 5.0 MET activity) (27–29). LVH on EKG was coded positive if the note "LVH by EKG criteria" was present in chart records or on an EKG report.

Age, race, and gender were available for all CHOICE participants. Diabetes, ASCVD, and hypertension status was available for 1038 (99.7%) of 1041 participants. Smoking, body mass index, physical activity, BP, and EKG were available, respectively, for 975 (94%), 971 (93%), 946 (91%), 943 (91%), and 653 (63%) of the cohort. When risk factors were analyzed separately, all participants with information were included. When risk factors were combined for analyses (e.g., Table 4), only participants with complete information on all variables were included in analyses.

Specimen Bank and Laboratory Assays. Nonfasting venous serum specimens are collected at the DCI dialysis facilities just before a dialysis session. Specimens are spun at 2500 to 3000 rpm and filtered on site within 45 min of phlebotomy and sent overnight to the DCI Central Laboratory (Nashville, TN), where they are stored at −80°C. More than 95% of samples are frozen within 48 h of venipuncture. The CHOICE cohort enrolled incident dialysis patients, but serologic parameters may be highly variable at the initiation of dialysis and may not reflect an individual's long-term level because of changes in dialysis dose and clinical status. To provide a more stable estimate of an individual's level of serologic markers, samples drawn at approximately 3 mo after enrollment were used. The median time from enrollment to collection was 2.8 mo, with 95% of samples obtained within 4.8 mo. The median time from first dialysis to serum collection was 4.4 mo, with 95% of samples obtained within 7 mo. Laboratories performing all assays were blinded to all clinical information, including age, race, gender, and comorbid conditions.

Colorimetric methods that used an Olympus (Hamburg, Germany) autoanalyzer were used to determine total cholesterol (coefficient of variation [CV], 5.3%), HDL cholesterol (CV, 9.6%), and triglyceride (CV, 12.3%) levels (all CV values were determined by blinded split samples; $n = 39$). The Friedewald formula was used to calculate LDL cholesterol for those with triglycerides <400 mg/dl. Apolipoprotein-A1 (CV, 12.3%) and apolipoprotein-B (CV, 9.5%) were measured via immunonephelometric methods with a Dade-Behring (Marburg, Germany) autoanalyzer. Of the 898 specimen bank participants with serum available, total cholesterol, triglycerides, and HDL cholesterol data were available for 862 individuals (96%). For calculation of the Framingham risk equation, the baseline total cholesterol obtained for routine care was used to fill in missing data for those not able to participate in the specimen bank ($n = 19$).

NHANES III Data. To obtain population-based estimates of ASCVD risk factors, we used data from NHANES III (30–33). The sample design used complex, multistage, clustered samples of civilian, noninstitutionalized populations. A total of 20,050 adults were interviewed and examined. Of these, we analyzed 19,753 who had complete data on age, gender, race, and history of MI and cerebrovascular accident (the NHANES definition of ASCVD). Of these, 19,395 had BP measured; 17,848 had self-reported diabetes, smoking, body mass index, physical activity, and congestive heart failure data; 8436 (those older than 40 only) had EKG evaluated for evidence of LVH; and 16,870 had cholesterol, triglycerides, and HDL cholesterol measured. To correspond to the CHOICE questionnaire, the frequencies of all 5.0 MET or greater activities were tabulated and combined.

Statistical Analyses

Statistical analyses were performed with STATA (version 6.0). Descriptive statistics that used means, medians, proportions, SE, and confidence intervals were performed on all variables where appropriate. For the CHOICE data, the exact binomial method was used to determine SE for proportions.

The standard NHANES III Mobile Examination Center survey weights were used for survey estimates in the general US population. The NHANES weights were then modified to provide ASCVD risk factor and SE estimates adjusted to the age decade, gender, race, and ASCVD distribution of the CHOICE cohort (see Appendix for method).

Table 1. Dialysis modality and Medical Evidence Report (Form 2728) characteristics of the CHOICE cohort (recruited 1995–1998), compared with all incident end-stage renal disease (ESRD) patients receiving dialysis

Characteristic	CHOICE Cohort (n = 1041)	1997 USRDS Incident Dialysis Patients (n = 79,102)
Form 2728 demographic data		
Mean age, years		60.2
Sex, %		
male	54	53
female	46	47
Race, %		
white	67	65
black	28	29
other	5	6
Form 2728 comorbidity data		
Cause of ESRD, %		
diabetes mellitus	47	42
hypertension	17	25
glomerulonephritis	16	9
other	20	23
hypertension, %	74	74
diabetes, %	40	41
insulin dependence, %	29	24
coronary artery disease, %	21	25
myocardial infarction, %	9	9
congestive heart failure, %	25	35
cardiac arrest, %	1.4	1.0
cardiac dysrhythmia, %	5	6.2
pericarditis, %	1.4	1.1
stroke or transitent ischemic attack, %	8	10
peripheral vascular disease, %	13	15
chronic obstructive lung disease, %	6	7
tobacco use, %	8	6
malignancy, %	4	5
Form 2728 Laboratory Data		
mean hematocrit (%)	28.6	28.6
mean serum albumin (g/dl)	3.4	3.2
mean serum creatinine (mg/dl)	8.8	8.1
mean serum blood urea nitrogen (mg/dl)	90	92
Modality, %		
hemodialysis	73	87[a]
peritoneal dialysis	27	13[a]

[a] Estimates are based on dialysis modality distribution in the prevalent US Renal Data System (USRDS) population.

The only ASCVD events ascertained by NHANES III included MI and stroke. Therefore, the adjustment procedure for ASCVD described in the Appendix was predicated on the important assumption that the profile of risk factors in NHANES participants with a history of MI and stroke (which were ascertained) is similar to that of NHANES participants with a history of coronary artery bypass graft (CABG), percutaneous transluminal coronary angioplasty (PTCA), carotid endarterectomy, and peripheral vascular disease (which were not ascertained). Although this assumption is most likely not perfect, we believe that any differences that may exist would not result in significant errors in the adjustment procedure. Furthermore, such a bias would generally be conservative in nature and would tend to overestimate the adjusted NHANES estimates. This is because one would expect ASCVD risk factors to be slightly more prevalent in MI or stroke patients than in CABG, PTCA, carotid endarterectomy, or peripheral vascular disease patients.

All of the differences between NHANES and CHOICE were highly statistically significant. However, systematic differences in the methods used in the two studies may have accounted for some of the differences, and would not have been reflected in P values. We therefore chose not to present P values for these comparisons.

The Framingham risk equation (34) was used to estimate, at the individual level, the theoretical 8-yr cardiovascular risk for the NHANES III and CHOICE populations. The Framingham risk equa-

Table 2. Comparison of cardiovascular disease risk factor prevalence adjusted to the CHOICE distribution of age, race, gender, and prevalent cardiovascular disease[a]

CVD Risk Factors	CHOICE Cohort (n = 1041)	NHANES III Population (n = 19,537)	
	Estimates (SE)	Unadjusted NHANES III Estimates (SE)	Estimates Adjusted to CHOICE[b] (SE)
Demographics			
mean age (yr)[b]	57.8 (0.5)	43 (0.4)	57.3 (0.4)
gender (% male)[b]	54 (1.5)	48 (0.4)	54 (1.0)
race[b]			
white (%)	67 (1.5)	76 (1.2)	67 (1.8)
black (%)	28 (1.4)	11 (0.6)	28 (1.6)
other (%)	5 (0.7)	13 (0.9)	5 (0.5)
Comorbid conditions			
diabetes (%)	54 (1.5)	5 (0.2)	15 (0.8)
mean systolic BP (mmHg)	149 (0.6)	122 (0.4)	132 (0.5)
mean diastolic BP (mmHg)	79 (0.3)	74 (0.2)	76 (0.2)
hypertension (%)	96 (0.6)	23 (0.6)	44 (1.0)
blood pressure, JNC VI category			
optimal BP (%)	6 (0.7)	48 (0.9)	28 (1.1)
normal BP (%)	9 (0.9)	21 (0.5)	19 (0.8)
high normal (%)	16 (1.2)	13 (0.4)	19 (0.9)
stage 1 hypertension (%)	41 (1.6)	13 (0.5)	24 (1.0)
stage 2 hypertension (%)	23 (1.4)	4 (0.2)	8 (0.5)
stage 3 hypertension (%)	5 (0.7)	1 (0.1)	2 (0.3)
left ventricular hypertrophy on electrocardiogram (%)	22 (1.6)	1 (0.2)	3 (0.4)
Lifestyle factors			
mean BMI (kg/m^2)	27 (0.2)	26 (0.1)	28 (0.1)
obesity (% with BMI ≥30.0)	26 (1.4)	22 (0.7)	29 (1.0)
ever smoker (%)	61 (1.6)	53 (0.8)	63 (1.0)
current smoker (%)	15 (1.1)	28 (0.8)	28 (1.2)
physical activity (%) (≥5 METS, ≥3 times/wk)	14 (1.1)	33 (1.1)	31 (1.2)

[a] CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination; SE, standard error; BMI, body mass index; JCN VI, sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; MET, metabolic Equivalent Tasks.

[b] NHANES III estimates were adjusted to the age (by decade), gender, race and prevalent atherosclerotic cardiovascular disease distributions of the CHOICE cohort.

tion incorporates age, gender, total cholesterol, systolic BP, current smoking, LVH by EKG criteria, and glucose intolerance (defined as a diagnosis of diabetes, random glucose >120 mg/dl, or urine dipstick test positive for glucose) to estimate the 8-yr ASCVD risk in the Framingham cohort for those without a history of ASCVD (34,35). To obtain 1- and 5-yr cardiovascular risk estimates, we assumed a constant risk over the 8 yr, converting the calculated 8-yr risk into a 1-yr risk and 5-yr risk for each individual by means of the following formulas:

$$\text{1-yr risk} = [1 - e^{(0.125*(\ln(1-\text{8-yr risk})))}]$$

$$\text{5-yr risk} = [1 - e^{(0.625*(\ln(1-\text{8-yr risk})))}]$$

Results

Patient Characteristics

Table 1 shows that the age, gender, race, and dialysis modality distributions were similar to the US dialysis population reported in the USRDS (1). The proportion of those treated with peritoneal dialysis is higher than USRDS because CHOICE oversampled peritoneal dialysis patients. Diabetes and hypertension accounted for approximately two-thirds of ESRD, a figure similar to USRDS. However, the percentage of ESRD attributed to hypertension was lower than in USRDS. CHOICE Study participants were somewhat healthier than the national dialysis population, although for most conditions or serologic factors, the difference was not great. The largest difference was for prevalent congestive heart failure (25% in CHOICE, 35% in USRDS).

Prevalence of ASCVD in the CHOICE cohort was determined for all ASCVD events (44%); MI (20%); MI or coronary revascularization (32%); stroke (11%); stroke and carotid endarterectomy (17%); and peripheral vascular disease, including bypass grafts, angioplasty, and amputation (26%).

Table 3. Comparison of lipid distribution adjusted to the CHOICE distribution of age, race, gender, and prevalent cardiovascular disease, stratified by lipid-lowering medication use[a]

Lipid	CHOICE Cohort		NHANES III Population	
	On Lipid-Lowering Medication (n = 169)	Not on Lipid-Lowering Medication (n = 872)	Not on Lipid-Lowering Medication (n = 19,194)	
	Estimates (SE)	Estimates (SE)	Unadjusted NHANES III estimates (SE)	Estimates adjusted to CHOICE[a] (SE)
On lipid-lowering medication (%)	16 (1.1)		2.8 (0.2)	8.4 (0.7)
Mean total cholesterol (mg/dl)	201 (4.1)	186 (1.7)	201 (0.7)	215 (1.3)
Total cholesterol, NCEP Category				
<200 (normal)	57 (4.3)	65 (1.8)	52 (0.9)	38 (1.4)
200–239 (borderline)	20 (3.5)	23 (1.5)	30 (0.8)	35 (1.1)
≥240 (high)	23 (3.7)	12 (1.2)	18 (0.6)	27 (1.3)
Mean LDL cholesterol (mg/dl)	111 (4.1)	106 (1.5)	126 (0.8)	136 (1.4)
High LDL cholesterol (% ≥160 mg/dl)	14 (3.2)	8.3 (1.1)	17 (0.8)	26 (1.7)
Mean apolipoprotein-B (mg/dl)	100 (2.8)	91 (1.1)	103 (0.8)	111 (1.0)
High apolipoprotein-B (% ≥140 mg/dl)	9 (2.5)	5 (0.8)	9 (0.6)	14 (1.1)
Mean HDL cholesterol (mg/dl)	43 (1.4)	43 (0.6)	51 (0.3)	50 (0.5)
Low HDL cholesterol (% <40 mg/dl)	48 (4.4)	45 (1.8)	23 (0.8)	28 (1.1)
Total HDL:cholesterol ratio	5.2 (0.2)	4.7 (0.1)	4.3 (0.04)	4.8 (0.06)
Mean apolipoprotein-A1 (mg/dl)	138 (3.2)	131 (1.1)	143 (1.0)	144 (1.0)
Mean triglycerides (mg/dl)	250 (14)	189 (5)	139 (2.0)	162 (2.7)
High triglycerides (% ≥200 mg/dl)	52 (4.4)	34 (1.7)	17 (0.6)	23 (0.9)
High triglycerides (≥200 mg/dl) and low HDL (<40 mg/dl) (%)	30 (4.0)	24 (1.6)	9 (0.4)	13 (0.9)

[a] NHANES, National Health and Nutrition Examination; SE, standard error.
[b] NHANES III estimates were adjusted to the age (by decade), gender, race, and prevalent atherosclerotic cardiovascular disease distributions of the CHOICE cohort.

ASCVD Risk Factors in the CHOICE Cohort

Table 2 lists the distribution of nonlipid ASCVD risk factors in CHOICE, compared with estimates from NHANES III. Notably, the prevalence of diabetes, hypertension, and LVH by EKG criteria was very high. Sixty-one percent of the cohort reported previous smoking, compared with 15% for current smoking, and only 14% reported physical activity resulting in perspiration at a frequency of three or more times per week.

Table 3 presents the distribution of lipids, stratified by lipid-lowering medication use. Sixteen percent of CHOICE participants were taking lipid-lowering medications (including HMG-CoA reductase inhibitors, fibric acids, nicotinic acid, or bile acid sequestrants). In the CHOICE cohort, total cholesterol, LDL cholesterol, apolipoprotein-B, and triglycerides were all significantly higher in those receiving compared with those not receiving lipid-lowering medication, and HDL cholesterol levels were similar in the two groups. Most participants not on lipid-lowering medications had normal or borderline high total cholesterol levels, whereas 42% had either low HDL cholesterol or high triglycerides and 24% had both.

Comparison between CHOICE and NHANES III

After adjustment of the NHANES III prevalence estimates to the age, race, gender, and ASCVD distribution of the CHOICE cohort, most nonlipid ASCVD risk factors were still more prevalent in CHOICE than the general population (Table 2). In CHOICE, diabetes, hypertension, LVH by EKG criteria, and physical activity differed greatly in the direction of greater ASCVD risk, compared with the adjusted NHANES III estimates. However, current smoking and obesity differed in the opposite direction, compared with the NHANES III adjusted estimates.

Table 3 also compares the lipid profile in CHOICE to the unadjusted and adjusted estimates among NHANES III participants not receiving lipid-lowering medications. CHOICE participants, regardless of lipid-lowering medication status, had lower total cholesterol, LDL cholesterol, apolipoprotein-B, HDL cholesterol, and apolipoprotein-A1 levels and higher triglyceride levels, compared with the adjusted NHANES III estimates.

Estimation of 1- and 5-yr ASCVD Risk

Table 4 presents the hypothetical 1- and 5-yr ASCVD risk for all those older than 40 without ASCVD (NHANES III did not obtain EKG on those younger than 40 yr). Of the 459 CHOICE participants older than 40 without prevalent ASCVD, complete information was available for 253 individuals, primarily limited by the low number of individuals with an EKG

Table 4. Distribution of Framingham risk factors and projected 8-year Framingham cardiovascular disease (CVD) risk estimates among CHOICE and NHANES III participants >40 years old without prevalent cardiovascular disease

Framingham Risk Factors and Risk Projections	CHOICE, >40 years without CVD (n = 253)	NHANES III, >40 years without CVD (n = 11,298)
	Estimate (SE)[a]	Estimate (SE)
Framingham risk factors		
age (mean yr)	60 (0.8)	57 (0.4)
gender (% male)	49 (3.1)	45 (0.7)
mean total cholesterol (mg/dl)	191 (3.1)	217 (0.8)
mean systolic BP (mmHg)	151 (1.2)	129 (0.4)
current smoking (%)	15 (2.2)	23 (0.8)
left ventricular hypertrophy on EKG (%)	20 (2.5)	1 (0.2)
glucose intolerance (%)	68 (2.9)	12 (0.6)
1-year CVD risk projections (%)		
mean overall risk in those >40 years by age group (yr)	3.1 (0.1)	1.4 (0.03)
40–49 (n = 67)	1.4 (0.2)	0.5 (0.01)
50–59 (n = 61)	2.8 (0.3)	1.3 (0.03)
60–69 (n = 67)	4.0 (0.3)	2.1 (0.03)
>70 (n = 58)	4.5 (0.3)	2.9 (0.04)
5-year CVD risk projections (%):		
mean overall risk in those >40 years by age group (yr)	14 (0.6)	6.4 (0.1)
40–49 (n = 67)	6.5 (0.9)	2.3 (0.1)
50–59 (n = 61)	13 (1.1)	6.3 (0.2)
60–69 (n = 67)	18 (1.0)	10 (0.1)
>70 (n = 58)	20 (1.2)	13 (0.2)

[a] SE, standard error.

available (n = 289). To test for bias because of the low availability of EKG data, various factors were summarized in those with and without an EKG, as follows: age (60.0 *versus* 57.9 yr, P = 0.10), male gender (49 *versus* 49%, P = 0.93), systolic BP (153 *versus* 151 mmHg, P = 0.48), total cholesterol (191 *versus* 191 mg/dl, P = 0.94), glucose intolerance (68 *versus* 62%, P = 0.29), current smoking (15 *versus* 20%; P = 0.18), serum albumin (3.6 *versus* 3.6 g/dl; P = 0.94), hematocrit (32.1 *versus* 32.2%; P = 0.76), and serum creatinine (7.5 *versus* 7.6 mg/dl; P = 0.74). Furthermore, the projected 5-yr ASCVD risk after excluding the LVH on EKG term was 11.1% in those with an EKG compared with 10.5% in those without an EKG (P = 0.39), providing assurance that the two groups are sufficiently similar to warrant use of the available data.

The CHOICE participants analyzed in the Framingham equation analysis were slightly older than in NHANES III. Total cholesterol and smoking were higher in NHANES; and systolic BP, LVH on EKG, and diabetes were higher in CHOICE. The 5-yr projected ASCVD risk was approximately twice as high in CHOICE (13%) as in NHANES (6%). The age-stratified comparisons show a greater relative difference in the younger than the older age decades.

Discussion

This cross-sectional study extends the ASCVD risk factor information reported by previous national (4,18,19), regional (21,22), or local (23,24) studies of incident ESRD patients by analyzing a wider range of ASCVD risk factors in a geographically diverse and representative national cohort of incident dialysis patients and by making comparisons to the prevalence of risk factors in the general population.

Prevalence of Traditional ASCVD Risk Factors in CHOICE

This study found a high prevalence for many traditional ASCVD risk factors. The median age was high (60 yr), and 54% of the participants were male. Diabetes, hypertension, physical inactivity, hypertriglyceridemia, and low HDL cholesterol levels were highly prevalent.

Overall, we found a higher prevalence of traditional ASCVD risk factors in the CHOICE cohort than that reported by other national studies. Diabetes and smoking history were more prevalent in CHOICE than in the Case Mix Study (diabetes: 54 *versus* approximately 40%; and ever-smokers: 61 *versus* approximately 45%, respectively) (9). The Canadian study had slightly higher current smoking rates compared with CHOICE (22 *versus* 15%) but had a much lower diabetes prevalence (19 *versus* 54%) (4). Smoking history was also higher in CHOICE than the 40% seen in DMMS Wave 2 Study (20). Both predialysis-session mean systolic (149 mmHg) and diastolic (79 mmHg) BP were similar to DMMS Wave 2 Study (147 and 80

mmHg, respectively). Sixty-nine percent of the CHOICE cohort had a hypertensive predialysis BP.

The prevalence of LVH on EKG (22%) was lower than reported in the Case Mix Study (31%) but was similar that of the DMMS Wave 2 Study (20%) (20). However, both the DMMS Wave 2 Study and Case Mix Study included echocardiographic data in the definition of LVH, whereas CHOICE only used EKG criteria, which is known to underestimate the true prevalence of LVH. Foley *et al.* (36) found very high prevalence rates of LVH by echocardiogram (74%) in patients recruited within 1 yr of initiating dialysis.

Only 14% of participants reported physical activity to perspiration three or more times a week. This is consistent with studies by Painter *et al.* (37,38) and Painter (39), which found that ESRD patients have 63% of the exercise tolerance of age-matched sedentary non-ESRD patients. Although physical inactivity may contribute to the development of ESRD, it is certain that the high degree of comorbidity associated with ESRD itself promotes physical inactivity (the phenomenon of reverse causality). The precise relationship between exercise and ESRD can only be determined by a prospective study of persons with chronic renal insufficiency. None of the other studies of incident dialysis patients reported physical activity.

Total cholesterol and triglyceride levels in CHOICE were similar the DMMS Wave 2 Study (20), although we found lower total cholesterol and triglycerides in those not receiving lipid-lowering medication and higher levels among those receiving lipid-lowering medication. The mean HDL cholesterol level in CHOICE was much lower (43 mg/dl) than that reported in the DMMS Wave 2 Study (59 mg/dl) (20).

Comparison with the General Population (NHANES III)

To our knowledge, no previous studies have attempted to compare the ASCVD risk factor profile in incident ESRD patients with the general population. Direct comparisons are difficult to interpret because the age, race, gender, and, in particular, the prevalence of ASCVD differ greatly between the two populations. The higher ASCVD prevalence in ESRD inflates the prevalence of ASCVD risk factors, thus confounding a direct comparison of ASCVD risk factors between the two populations. We therefore adjusted population estimates obtained from NHANES III to mirror the age, gender, race, and ASCVD profiles of the CHOICE population (Table 2).

Many ASCVD risk factors were strikingly higher in CHOICE when compared with the adjusted NHANES III estimates, particularly diabetes, hypertension, LVH by EKG criteria, physical activity, low HDL cholesterol, and high triglycerides. These traditional risk factors have potential to explain some of the increased ASCVD risk in ESRD.

The CHOICE estimates for current smoking, total cholesterol, LDL cholesterol, and body mass index were lower in CHOICE than the adjusted NHANES III estimates, perhaps related to reverse causality (*i.e.*, the comorbidity and malnutrition associated with ESRD may lead to lower cholesterol levels and the decision to quit smoking, rather than *vice versa*).

The high prevalence of ASCVD risk factors in the CHOICE cohort also stands in contrast to Culleton *et al.* (40), who studied ASCVD risk factors among 664 individuals with mild chronic renal insufficiency (creatinine 136 to 265 μmol/L in men, 120 to 265 μmol/L in women). Although they found an increased prevalence of diabetes (approximately 10%), ASCVD (approximately 19%), hypertension (approximately 35%), and LVH on EKG (approximately 3.5%), relative to the general population, the prevalence for all these conditions in CHOICE is much higher. This suggests that ASCVD, hypertension, diabetes and congestive heart failure either predispose to the progression to ESRD, or are worsened by progression of chronic renal insufficiency, or are markers of a group of individuals at high risk of progression. It is likely that all three processes play a role in progression to ESRD.

Estimation of ASCVD Risk Attributable to Framingham Risk Factors

The very high prevalence of traditional risk factors in ESRD may explain some of the excess ASCVD risk seen in ESRD, although it is unlikely to explain all of it (10). In an effort to quantify ASCVD risk based on traditional risk factors alone, Sarnak *et al.* (41) applied the Framingham risk equation (34) to 1795 patients with chronic renal insufficiency. They found a weak negative correlation between the calculated ASCVD risk and baseline GFR, suggesting that the Framingham risk factors increase in prevalence as GFR declines. Cheung *et al.* (42), who also use the Framingham risk equation, report no significant difference between the calculated ASCVD risk among prevalent ESRD patients in the Hemodialysis (HEMO) study clinical trial compared with the general population, after age adjustment.

In this analysis, we compared the Framingham risk equation score among those older than 40 without ASCVD in the NHANES population to similar individuals in CHOICE. The hypothetical 1- and 5-yr *de novo* ASCVD risk in the CHOICE cohort was approximately two times that of the NHANES III population. After age stratification, the relative difference between the two groups was greatest in the youngest age groups. It is important to stress that these calculated projections reflect the estimated ASCVD risk that would result from this particular configuration of Framingham risk factors in the absence of ESRD. They are not estimates of the true *de novo* ASCVD risk among ESRD patients, for whom the actual ASCVD risk may be from 5 to 15 times higher.

It may be inferred from these projections that as a group, the Framingham risk factors explain some, but probably not all, of the extraordinarily high ASCVD risk seen in ESRD. Other studies of mortality in ESRD (9,14,16,43) have shown either U-shaped or inverse relationships between mortality and various traditional risk factors such as BP and cholesterol—opposite to what is seen in the general population. Age, diabetes, and LVH, however, are known to be risk factors for mortality in the ESRD population. Traditional ASCVD risk factors, particularly cholesterol and hypertension, may interact with other nontraditional risk factors such as inflammation, comorbidity, and malnutrition in the context of ESRD, thus altering

their overall association with incident ASCVD in this population.

Limitations of the Study

Although we consider this a study of "incident" ESRD patients, the median time from initiation of dialysis to enrollment was 45 d. The study likely was not able to capture the very ill ESRD patients who die early after initiation of dialysis. Every effort was made to include in the study all new dialysis patients at the 81 participating centers. However, Table 2 shows that CHOICE recruited somewhat healthier patients than the USRDS population, suggesting that our data may underestimate the true ASCVD risk factor prevalence in dialysis patients. We estimate that this effect is small, however, because most differences between the two populations were minor.

The comparisons between NHANES III and CHOICE data must be interpreted with the understanding that some portion of the differences in prevalence estimates between the two studies may be due simply to sampling design and the methods of data ascertainment, which were in some cases very different in the two studies.

Another limitation is that the calculated risk estimates that use the Framingham equation in NHANES III are overestimated to some degree as a result of the manner in which ASCVD was defined. Included in the NHANES "no-ASCVD" group are those who have had a CABG, PTCA, carotid endarterectomy or peripheral vascular disease, but who also never had an MI or cardiovascular accident. Such individuals, who were not excluded from the NHANES risk prediction analysis, will inflate the ASCVD risk scores for the NHANES III estimates in Table 4. However, we estimate that this effect is not large because the proportion of such individuals in the total NHANES III sample is low.

The CHOICE Study analyzed nonfasting specimens for the lipid analyses. The results should be interpreted with the understanding that the Friedewald equation, used to calculate LDL cholesterol levels, may underestimate the actual LDL cholesterol level. However, we also measured apolipoprotein-B, the primary lipoprotein in LDL cholesterol. The relative differences between CHOICE and NHANES are similar for apolipoprotein-B and the calculated LDL cholesterol levels, suggesting that any effect due to the use of nonfasting specimens is small.

Summary

The prevalence of traditional ASCVD risk factors among incident ESRD patients is very high. Even after adjustment for age, gender, race, and a high prevalence of ASCVD, most, but not all, ASCVD risk factors are more prevalent in the ESRD population compared with the general population and may account for some of the increased ASCVD risk seen in ESRD. Prospective studies in ESRD are needed to further define the relationship between traditional ASCVD risk factors and incident ASCVD, and clinical trials are needed to determine if reduction of risk factors will indeed decrease the incidence of ASCVD in ESRD.

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Appendix

Derivation of Adjusted NHANES Weights

The following equation was used to adjust the NHANES weights to the age (by decade), race, gender, and ASCVD distribution of the CHOICE cohort:

$$w_{new} = w_{ij} \times \frac{c_i}{\sum_j w_{ij}}$$

Where w_{new} is NHANES population weight adjusted to the CHOICE population by age decade, race, gender, and ASCVD status; w_{ij} is NHANES weight for each individual *j* in stratum *i*; c_i is CHOICE proportion within each stratum *i* defined by age decade, race, gender, and ASCVD status; and Σw_{ij} is the summation of the NHANES weights within each stratum *i* defined by age decade, race, gender, and ASCVD status (the c_i term is divided by this summation term such that the w_{new} weights sum to 1.0).

References

1. United States Renal Data System: *USRDS 1999 Annual Data Report.* Bethesda, MD: National Institutes of Health, NIDDK, 1999

2. Parfrey PS, Foley RN, Harnett JD, Kent GM, Murray D, Barre PE: Outcome and risk factors of ischemic heart disease in chronic uremia. *Kidney Int* 49: 1428–1434, 1996
3. Sarnak MJ, Levey AS: Cardiovascular disease and chronic renal disease: A new paradigm. *Am J Kidney Dis* 35: S117–S131, 2000
4. Churchill D, Taylor D, Cook R, LaPlante P, Barre P, Cartier P, Fay W, Goldstein M, Jindal K, Mandin H, McKenzie J, Muirhead N, Parfrey P, Posen G, Slaughter D, Ulan R, Werb R: Canadian hemodialysis morbidity study. *Am J Kidney Dis* 19: 214–234, 1992
5. Rostand SG, Kirk KA, Rutsky EA: Relationship of coronary risk factors to hemodialysis-associated ischemic heart disease. *Kidney Int* 22: 304–308, 1982
6. Lindner A, Charra B, Sherrard DJ, Scribner BH: Accelerated atherosclerosis in prolonged maintenance hemodialysis. *N Engl J Med* 290: 697–701, 1974
7. Herzog CA, Ma JZ, Collins AJ: Poor long-term survival after acute myocardial infarction among patients on long-term dialysis [see comments]. *N Engl J Med* 339: 799–805, 1998
8. Parfrey PS, Harnett JD, Barre PE: The natural history of myocardial disease in dialysis patients. *J Am Soc Nephrol* 2: 2–12, 1991
9. Furth S, Hermann J, Powe N: Cardiovascular risk factors, comorbidity and survival outcomes in black and white dialysis patients. *Semin Dial* 11: 102–105, 1998
10. Foley RN, Parfrey PS, Sarnac MJ: Clinical epidemiology of cardiovascular disease in chronic renal disease. *Am J Kidney Dis* 32: S112–S119, 1998
11. Coresh J, Longenecker JC, Miller ER, Young HJ, Klag MJ: Epidemiology of cardiovascular risk factors in chronic renal disease. *J Am Soc Nephrol* 9: S24–S30, 1998
12. Levey AS: Controlling the epidemic of cardiovascular disease in chronic renal disease: Where do we start? *Am J Kidney Dis* 32: S5–S13, 1998
13. Special Report From the National Kidney Foundation Task Force on Cardiovascular Disease: Controlling the epidemic of cardiovascular disease in chronic renal disease: What do we know? What do we need to know? Where do we go from here? *Am J Kidney Dis* 32: S1–S199, 1998
14. Lowrie E, Lew N: Death risk in hemodialysis patients: The predictive value of commonly measured variables and an evaluation of death rate differences between facilities. *Am J Kidney Dis* 15: 458–482, 1990
15. Zager PG, Nikolic J, Brown RH, Campbell MA, Hunt WC, Peterson D, Van Stone J, Levey A, Meyer KB, Klag MJ, Johnson HK, Clark E, Sadler JH, Teredesai P: "U" curve association of blood pressure and mortality in hemodialysis patients. Medical Directors of Dialysis Clinic, Inc. [published erratum appears in *Kidney Int* 1998;54:1417]. *Kidney Int* 54: 561–569, 1998
16. Degoulet P, Legrain M, Reach I, Aime F, Devries C, Rojas P, Jacobs C: Mortality risk factors in patients treated by chronic hemodialysis: Report of the Diaphane Collaborative Study. *Nephron* 31: 103–110, 1982
17. Parfrey PS, Griffiths SM, Harnett JD, Taylor R, King A, Hand J, Barre PE: Outcome of congestive heart failure, dilated cardiomyopathy, hypertrophic hyperkinetic disease, and ischemic heart disease in dialysis patients. *Am J Nephrol* 10: 213–221, 1990
18. United States Renal Data System: Special Study of Case Mix Severity IV: Comorbid conditions and correlations with mortality risk among 3,399 incident hemodialysis patients. *Am J Kidney Dis* 20: 32–38, 1992
19. United States Renal Data System: IV. The USRDS Dialysis Morbidity and Mortality Study: Wave 2. United States Renal Data System. *Am J Kidney Dis* 30: S67–S85, 1997
20. Stack AG, Bloembergen WE: Prevalence and clinical correlates of coronary artery disease among new dialysis patients in the United States: A cross-sectional study. *J Am Soc Nephrol* 12: 1516–1523, 2001
21. Wolfe RA, Port FK, Hawthorne VM, Guire KE: A comparison of survival among dialytic therapies of choice: In-center hemodialysis versus continuous ambulatory peritoneal dialysis at home. *Am J Kidney Dis* 15: 433–440, 1990
22. Collins AJ, Ma JZ, Umen A, Keshaviah P: Urea index and other predictors of hemodialysis patient survival [published erratum appears in *Am J Kidney Dis* 1994;24:157]. *Am J Kidney Dis* 23: 272–282, 1994
23. Hylander B, Lundblad H, Kjellstrand CM: Changing patient characteristics in chronic hemodialysis. *Scand J Urol Nephrol* 25: 59–63, 1991
24. Mailloux LU, Napolitano B, Bellucci AG, Mossey RT, Vernace MA, Wilkes BM: The impact of co-morbid risk factors at the start of dialysis upon the survival of ESRD patients. *ASAIO J* 42: 164–169, 1996
25. Powe N, Klag M, Sadler J, Anderson G, Bass E, Briggs W, Fink N, Levey A, Levin N, Meyer B: Choices for healthy outcomes in caring for end-stage renal disease. *Semin Dial* 9: 9–11, 1996
26. Longenecker JC, Coresh J, Klag MJ, Levey AS, Martin AA, Fink NE, Powe NR: Validation of comorbid conditions on the end-stage renal disease medical evidence report: The CHOICE study—Choices for Healthy Outcomes in Caring for ESRD. *J Am Soc Nephrol* 11: 520–529, 2000
27. Paffenbarger RS, Jr., Blair SN, Lee IM, Hyde RT: Measurement of physical activity to assess health effects in free-living populations. *Med Sci Sports Exerc* 25: 60–70, 1993
28. Paffenbarger RS, Jr., Wing AL, Hyde RT: Physical activity as an index of heart attack risk in college alumni. *Am J Epidemiol* 108: 161–175, 1978
29. Ainsworth BE, Haskell WL, Leon AS, Jacobs DR Jr, Montoye HJ, Sallis JF, Paffenbarger RS Jr: Compendium of physical activities: Classification of energy costs of human physical activities. *Med Sci Sports Exerc* 25: 71–80, 1993
30. US Department of Health and Human Services: National Center for Health Statistics, Third National Health and Nutrition Examination Survey, 1988–1994. *NHANES III Laboratory Data File.* CD-ROM series 11. Public use data file documentation no. 76200. Hyattsville, MD: Centers for Disease Control and Prevention. Available from National Technical Information Service, Springfield, VA, 1996
31. US Department of Health and Human Services: National Center for Health Statistics. Third National Health and Nutrition Examination Survey, 1988–1994. *NHANES III Examination Data File.* CD-ROM series 11. Public use data file documentation no. 76200. Hyattsville, MD: Centers for Disease Control and Prevention. Available from National Technical Information Service, Springfield, VA, 1996
32. US Department of Health and Human Services: National Center for Health Statistics. Third National Health and Nutrition Examination Survey, 1988–1994. *NHANES III Electrocardiography Data File.* CD-ROM series 11. Public use data file documentation no. 76200. Hyattsville, MD: Centers for Disease Control and Prevention. Available from National Technical Information Service, Springfield, VA, 1996

33. US Department of Health and Human Services: National Center for Health Statistics. Third National Health and Nutrition Examination Survey, 1988–1994. *NHANES III Household Adult Data File*. CD-ROM series 11. Public use data file documentation number 76200. Hyattsville, MD: Centers for Disease Control and Prevention. Available from National Technical Information Service, Springfield, VA, 1996
34. Kannel WB, McGee D, Gordon T: A general cardiovascular risk profile: The Framingham Study. *Am J Cardiol* 38: 46–51, 1976
35. Brittain E: Probability of coronary heart disease developing. *West J Med* 136: 86–89, 1982
36. Foley RN, Parfrey PS, Harnett JD, Kent GM, Martin CJ, Murray DC, Barre PE: Clinical and echocardiographic disease in patients starting end-stage renal disease therapy. *Kidney Int* 47: 186–192, 1995
37. Painter P, Messer-Rehak D, Hanson P, Zimmerman SW, Glass NR: Exercise capacity in hemodialysis: CAPD and renal transplant patients. *Nephron* 42: 47–51, 1986
38. Painter P, Zimmerman SW: Exercise in end-stage renal disease. *Am J Kidney Dis* 7: 386–394, 1986
39. Painter P: The importance of exercise training in rehabilitation of patients with end-stage renal disease. *Am J Kidney Dis* 24: S2–S9, 1994
40. Culleton BF, Larson MG, Wilson PW, Evans JC, Parfrey PS, Levy D: Cardiovascular disease and mortality in a community-based cohort with mild renal insufficiency. *Kidney Int* 56: 2214–2219, 1999
41. Sarnak MJ, Coronado BE, Greene T, Wang SR, Kusek JW, Levey AS: Cardiovascular disease risk factors in chronic renal insufficiency. *Clin Nephrol* 2002, in press
42. Cheung AK, Sarnak MJ, Yan G, Dwyer JT, Heyka RJ, Rocco MV, Teehan BP, Levey AS, and the Hemodialysis (HEMO) Study: Atherosclerotic cardiovascular disease risks in chronic hemodialysis patients. *Kidney Int* 58: 353–362, 2000
43. Avram MM, Mittman N, Bonomini L, Chattopadhyay J, Fein P: Markers for survival in dialysis: A seven-year prospective study. *Am J Kidney Dis* 26: 209–219, 1995