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.

Received September 7, 2001. Accepted April 6, 2002.

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DOI: 10.1097/01.ASN.0000019641.41496.1E
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).
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

<table>
<thead>
<tr>
<th>CVD Risk Factors</th>
<th>CHOICE Cohort (n = 1041)</th>
<th>Unadjusted NHANES III Estimates (SE)</th>
<th>Estimates Adjusted to CHOICEb (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean age (yr)b</td>
<td>57.8 (0.5)</td>
<td>43 (0.4)</td>
<td>57.3 (0.4)</td>
</tr>
<tr>
<td>gender (% male)b</td>
<td>54 (1.5)</td>
<td>48 (0.4)</td>
<td>54 (1.0)</td>
</tr>
<tr>
<td>raceb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>white (%)</td>
<td>67 (1.5)</td>
<td>76 (1.2)</td>
<td>67 (1.8)</td>
</tr>
<tr>
<td>black (%)</td>
<td>28 (1.4)</td>
<td>11 (0.6)</td>
<td>28 (1.6)</td>
</tr>
<tr>
<td>other (%)</td>
<td>5 (0.7)</td>
<td>13 (0.9)</td>
<td>5 (0.5)</td>
</tr>
<tr>
<td>Comorbid conditions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diabetes (%)</td>
<td>54 (1.5)</td>
<td>5 (0.2)</td>
<td>15 (0.8)</td>
</tr>
<tr>
<td>mean systolic BP (mmHg)</td>
<td>149 (0.6)</td>
<td>122 (0.4)</td>
<td>132 (0.5)</td>
</tr>
<tr>
<td>mean diastolic BP (mmHg)</td>
<td>79 (0.3)</td>
<td>74 (0.2)</td>
<td>76 (0.2)</td>
</tr>
<tr>
<td>hypertension (%)</td>
<td>96 (0.6)</td>
<td>23 (0.6)</td>
<td>44 (1.0)</td>
</tr>
<tr>
<td>blood pressure, JNC VI category</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>optimal BP (%)</td>
<td>6 (0.7)</td>
<td>48 (0.9)</td>
<td>28 (1.1)</td>
</tr>
<tr>
<td>normal BP (%)</td>
<td>9 (0.9)</td>
<td>21 (0.5)</td>
<td>19 (0.8)</td>
</tr>
<tr>
<td>high normal (%)</td>
<td>16 (1.2)</td>
<td>13 (0.4)</td>
<td>19 (0.9)</td>
</tr>
<tr>
<td>stage 1 hypertension (%)</td>
<td>41 (1.6)</td>
<td>13 (0.5)</td>
<td>24 (1.0)</td>
</tr>
<tr>
<td>stage 2 hypertension (%)</td>
<td>23 (1.4)</td>
<td>4 (0.2)</td>
<td>8 (0.5)</td>
</tr>
<tr>
<td>stage 3 hypertension (%)</td>
<td>5 (0.7)</td>
<td>1 (0.1)</td>
<td>2 (0.3)</td>
</tr>
<tr>
<td>left ventricular hypertrophy on electrocardiogram (%)</td>
<td>22 (1.6)</td>
<td>1 (0.2)</td>
<td>3 (0.4)</td>
</tr>
<tr>
<td>Lifestyle factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean BMI (kg/m²)</td>
<td>27 (0.2)</td>
<td>26 (0.1)</td>
<td>28 (0.1)</td>
</tr>
<tr>
<td>obesity (% with BMI ≥30.0)</td>
<td>26 (1.4)</td>
<td>22 (0.7)</td>
<td>29 (1.0)</td>
</tr>
<tr>
<td>ever smoker (%)</td>
<td>61 (1.6)</td>
<td>53 (0.8)</td>
<td>63 (1.0)</td>
</tr>
<tr>
<td>current smoker (%)</td>
<td>15 (1.1)</td>
<td>28 (0.8)</td>
<td>28 (1.2)</td>
</tr>
<tr>
<td>physical activity (%) (≥5 METS, ≥3 times/wk)</td>
<td>14 (1.1)</td>
<td>33 (1.1)</td>
<td>31 (1.2)</td>
</tr>
</tbody>
</table>

a CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination; SE, standard error; BMI, body mass index; JNC 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.

The Risk Prediction Model

The Pooled Cohort Equations incorporate 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:

1-yr risk = \[1 - e^{0.125 \times (ln(1 - 8-yr \text{ risk})/2)}\]

5-yr risk = \[1 - e^{0.625 \times (ln(1 - 8-yr \text{ risk})/2)}\]

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 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 estimates for all those older than 40 without prevalent cardiovascular disease, stratified by lipid-lowering medication use at the time of ascertainment. The risk estimates were calculated using the Adult Treatment Panel III (ATP III) Algorithm. The estimation was based on the distribution of risk factors in the CHOICE cohort, adjusted for the age (by decade), gender, race, and prevalent atherosclerotic cardiovascular disease distributions of the CHOICE cohort.
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)
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 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.

None of the risk factor definitions in the Framingham equation included triglycerides. The Framingham scores are calculated using a logarithmic transformation of total cholesterol and 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.

Acknowledgments

We thank the patients, staff, and physicians who participated in the CHOICE Study at Dialysis Clinic, Inc.; New England Medical Center; New Haven CAPD; and Johns Hopkins University. We also acknowledge and thank the CHOICE-DCI Clinical Liaison Committee (Thomas Depner, M.D., H. Keith Johnson, M.D., K. Shashi Kant, Klemens Meyer, M.D., Richard Sherman, M.D., Edward Schroeder, M.D., Pradip Teradesai, M.D., John Van Stone, M.D., Alan Wasserstein, M.D., Lucius Wright, M.D., Jackson Yium, M.D., and Philip Zager, M.D.) and the New Haven CAPD Clinical Liaison Committee (Frederic Finkelstein, M.D., and Alan Kliger, M.D.) for their support of and involvement in the CHOICE Study. We also recognize and thank the CHOICE Scientific Advisory Committee (Paul Eggers, Ph.D., Sheldon Greenfield, M.D., H. Keith Johnson, M.D., Nathan Levin, M.D., Robin Luke, M.D., Richard Retting, Ph.D., and Paul Whelton, M.D., M.Sc.) for their scientific guidance and oversight of the CHOICE Study. Presented in part at the American Society of Nephrology Annual Meeting, October 2000. Published in part in abstract form as Longenecker JC, Coresh J, Powe NR, Levey AS, Fink NE, Klag MJ: Do traditional CVD risk factors explain race differences in CVD risk and the excess CVD risk in ESRD? The CHOICE Study. J Am Soc Nephrol 11:156A, 2000. CHOICE was supported by R01-HS-08365 (Agency for Healthcare Quality and Research, formerly the Agency for Health Care Policy and Research) from June 1995 to May 2000 and is currently supported by the National Institute of Diabetes, Digestive and Kidney Disorders, National Institutes of Health (NIDDK NIH; grant R01-DK-07024). Other NIDDK NIH grants include the following: R29-DK-48362 (J.C.); K24-DK-02856 (M.J.K.); and K24-DK-02643 (H.R.P.). Support was also received from the National Institute of Diabetes Digestive and Kidney Disorders, NIH (grant R01-DK-53869 to A.S.L.); and the National Heart, Lung and Blood Institute, National Institutes of Health (grant K08-HL-03896 to J.C.L.). Lipid assays were supported by the National Center for Research Resources (NIH grant M01-RR00052 to the Johns Hopkins University General Clinical Research Center).

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 \( \sum w_{ij} \) 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

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