

Prevalence and Characteristics of a Family History of End-Stage Renal Disease among Adults in the United States Population: Reasons for Geographic and Racial Differences in Stroke (REGARDS) Renal Cohort Study

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This report describes the prevalence and characteristics of people with a family history of ESRD in a first-degree relative (FH-ESRD). This is a cross-sectional study of individuals in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort, a population-based sample of US residents who are 45 yr and older. FH-ESRD was ascertained at baseline among 12,030 participants of the cohort, and multivariate logistic regression was used to identify characteristics that were independently associated with FH-ESRD. FH-ESRD was reported by 9.5% of participants. Individual characteristics that were independently associated with FH-ESRD included black race (odds ratio [OR] 2.14; 95% confidence interval [CI] 1.82 to 2.53); female gender (OR 1.28; 95% CI 1.08 to 1.51); a history of diabetes (OR 1.22; 95% CI 1.02 to 1.47); a 1-SD change in the log of the C-reactive protein level (OR 1.10; 95% CI 1.01 to 1.19); and World Health Organization body mass index weight categories normal (OR 2.11; 95% CI 0.66 to 6.79), overweight (OR 2.64; 95% CI 0.82 to 8.42), and obese (OR 3.48; 95% CI 1.09 to 11.1) compared with underweight. Black but not white individuals with FH-ESRD were more likely to have an estimated GFR <60 ml/min per 1.73 m². There is a high prevalence of FH-ESRD among US adults, and the prevalence of FH-ESRD was higher among black individuals. Individuals with a positive family history were more likely to have diabetes and to be obese. If confirmed, then these findings suggest that individuals with FH-ESRD may benefit from interventions to improve the detection and treatment of chronic kidney disease risk factors such as diabetes and obesity.

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Family history of ESRD (FH-ESRD) is common among incident patients with ESRD. Ferguson *et al.* (1) were the first to note that a family history of a first- or second-degree relative with kidney disease was five times more common among black patients with ESRD. This single-center-based study was confirmed by a population-based study of incident patients with ESRD in the southeastern United States, where 23% of black individuals and 14% of white individuals reported a first- or second-degree relative with ESRD (2).

The prevalence of a FH-ESRD in the general population

without ESRD and the extent to which similar racial disparities exist has not been extensively examined, and little information is available about the prevalence of impaired kidney function among family members. A population-based telephone survey of 402 residents in a single southeastern state found that FH-ESRD was reported by 3.7% of respondents and that black individuals were six times more likely to report FH-ESRD compared with white individuals (3). Two small studies of voluntary participants in kidney disease screening programs found that 14% of individuals with FH-ESRD had a creatinine clearance <60 ml/min (4), and nearly 5% of first-degree relatives of black patients with hypertensive ESRD had a serum creatinine of ≥ 1.4 mg/dl (5).

The possibility that black individuals have a high prevalence FH-ESRD is particularly interesting in light of recent reports that the overall prevalence of chronic kidney disease (CKD) among black individuals in the US population is unexpectedly lower than that observed in white individuals (6–8). If racial disparities in the prevalence of FH-ESRD and associated kidney disease exist for the general population, then perhaps studying

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these families might assist in the understanding of this paradox and suggest interventions to reduce the occurrence of ESRD in these families. We address these issues by describing the prevalence and the characteristics of individuals with FH-ESRD and associated kidney function in a large, population-based sample of US adults who are 45 yr and older.

Materials and Methods

Study Design

Renal REGARDS is a population-based subcohort of the ongoing Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort study (9,10). The purpose of REGARDS is to identify factors that contribute to the excess stroke mortality among black individuals and in the southeastern United States. Upon completion of recruitment, the REGARDS cohort will consist of a representative sample of 30,000 individuals who are 45 yr and older with follow-up extending for up to 4 yr (10).

Participants

The REGARDS cohort was recruited from a national random probability sample of individuals who are 45 yr and older, 20% of whom reside in the coastal plain of North Carolina, South Carolina, and Georgia; 30% in the remainder of North Carolina, South Carolina, Georgia and the southeastern states of Tennessee, Mississippi, Alabama, Louisiana, and Arkansas; and 50% in the remaining 42 contiguous states (9). Recruitment is designed so that approximately one half of the participants will be black and one half will be white, and one half will be male and one half will be female. The sampling procedure was a stratified simple random sample that has been previously described (9). We started with a commercially available nationwide list of households stratified by age, race, gender, and geographic region. These lists are well-accepted sources for sampling frames and have been shown to be "an efficient method of identifying elderly respondents, and the estimates of health behaviors and health status were comparable with those obtained by random digit dialing techniques" (11). The likelihood of having a telephone and being included in these lists is generally >95% for the population that is 45 yr and older (12,13). As such, these lists represent accepted sampling frames. After a household contact was reached, the household members were enumerated and one individual who was 45 yr or older was randomly selected for interview.

Recruitment began in February 2003, and additional measures of kidney function were collected beginning in May 2004 (10). Through December 2005, a total of 12,077 participants were recruited in this Renal REGARDS subcohort, which does not include the first 8600 REGARDS participants, for whom the kidney function data were not collected. We excluded from these analyses 47 individuals who reported that they had kidney failure and were on dialysis.

Data and Data Collection

Data collection methods have been published elsewhere (9). Data are obtained from each participant in a telephone interview followed by a subsequent in-home examination conducted by a health professional. Data that were used in these analyses were obtained during the telephone interview and included age; race; gender; self-report of previous stroke, myocardial infarction, and hyperlipidemia; smoking status; health insurance status; and assessment of socioeconomic status (primarily education and income). Reported health status was ascertained by asking, "In general, would you say that your health is excellent, very good, good, fair, or poor?"

Data that were obtained during the subsequent in-home examination included BP, height and weight, and abdominal circumference. The

following analytes were obtained from the REGARDS central laboratory: A complete blood count; C-reactive protein (CRP), measured using a validated, high-sensitivity, particle-enhanced immunonephelometric assay on the BNII nephelometer (N High Sensitivity CRP; Dade Behring, Deerfield, IL); cholesterol, HDL cholesterol, triglycerides, glucose, albumin and creatinine, measured by colorimetric reflectance spectrophotometry using the Ortho Vitros Clinical Chemistry System 950IRC instrument (Johnson & Johnson Clinical Diagnostics, Rochester, NY); and LDL cholesterol, calculated by the Friedewald equation for individuals with triglycerides <400 mg/dl.

As part of the telephone interview, self-reported family history of kidney failure was ascertained by asking respondents, "Has anyone in your immediate family ever been told that he or she had kidney failure? This would be someone who is on or had been on dialysis or someone who had a kidney transplant." Individuals who answered yes were asked the relationship of the individual(s) with kidney failure: "What relative or relatives had or has kidney failure?" Verbatim responses of as many relatives as recalled were reported. A positive history of ESRD in a first-degree relative was defined by (1) a yes answer to the first part of the family history question and (2) unprompted identification of at least one of the following relatives as having ESRD: Sibling, child, or parent.

Hypertension was defined as either self-reported use of antihypertensive medications or a systolic BP >140 mmHg or a diastolic BP >90 mmHg measured during the home examination, where systolic BP and diastolic BP were the average of two measures that were taken in the seated position. Diabetes was defined as taking insulin or oral hypoglycemics, or either a fasting (no intake 10 to 12 h before in-home visit) blood glucose ≥ 126 mg/dl or a nonfasting blood glucose ≥ 200 mg/dl. We defined hyperlipidemia as a "yes" answer to the telephone interview question, "Have you ever been told by a doctor that you have high cholesterol or an abnormal level of fats in your blood?"

The metabolic syndrome was defined using the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) criteria, which include waist circumference, triglyceride concentration, gender-specific HDL cholesterol, hypertension, and hyperglycemia (14).

GFR was estimated using the abbreviated Modification of Diet in Renal Disease (MDRD) equation and serum creatinine values calibrated to the Cleveland Clinic Foundation (CCF) laboratory because this laboratory's data were used to derive the MDRD equation (15). The REGARDS reference laboratory provided duplicate blood samples to the CCF for creatinine determination, and linear regression was used to calibrate the REGARDS data. The association between the CCF creatinine measurements, which were used to derive the MDRD equation, and those from the REGARDS reference laboratory is expressed by the following equation: CCF creatinine = 0.13633 + REGARDS creatinine \times 1.06062. Recalibrated serum creatinine values were computed for each participant and used to estimate GFR. We defined kidney disease as a GFR of <60 ml/min per 1.73 m².

Statistical Analyses

Means and proportions were used to describe the baseline characteristics, and *t* test and χ^2 tests were used to test differences between groups and for trends across groups. We used stepwise backward selection logistic regression models to identify characteristics that were independently associated with FH-ESRD (16). Each model initially included the following participant characteristics: Age, gender, race, GFR, comorbid conditions (hypertension, diabetes, stroke, and myocardial infarction), smoking status, reported health status, family income, health insurance status, educational attainment, serum albumin, hemo-

globin, and white blood cell count. We included categorical variables for both triglycerides and total cholesterol as well as a variable for a history of hypercholesterolemia. Each model controlled for region of residence. For three measures—abdominal girth, CRP, and body weight—we explored the association of FH-ESRD using both categorical and continuous measures. Because of the skewed distribution of the CRP values, a natural logarithmic transformation was used in all analyses. Analyses were done using SAS and Epi-Info (17,18).

Results

FH-ESRD, as defined by a first-degree relative with ESRD, was reported by 1145 (9.5%) of the 12,030 Renal REGARDS participants in the analysis. Among participants who did not report a first-degree relative with ESRD, 300 (2.5%) did report a second- degree or higher relative with a history of ESRD, 10,526 (96.7%) individuals reported no family history, and 59 (0.5%) did not know or were not sure about their family history. Thirty-nine individuals reported two generations of ESRD (three with a parent and a child, four with a sibling and a child, and 32 with a parent and a sibling) and no instances of three reported generations with ESRD. Among the 1184 reported first-degree relatives with ESRD, 9.3% ($n = 110$) were children of a participant, 48.2% ($n = 571$) were parents, and 42.5% ($n = 503$) were siblings.

A positive family history was reported by 6.4% of white and 14% of black participants (odds ratio [OR] 2.38; 95% confidence interval [CI] 2.11 to 2.71; Table 1). The mean (SD) age among individuals with and without a positive family history was 64.3 (9.1) and 65.4 (9.5) yr, respectively, and the prevalence of a positive FH-ESRD decreased with increasing age (Table 1). Individuals with a positive family history were more likely to be female and to report worse health status (Table 1).

Individuals with a positive FH-ESRD were more likely to have an elevated blood glucose and BP, whereas there was no difference among total, LDL, and HDL cholesterol levels between individuals who did and did not report a family member with ESRD (Table 2). FH-ESRD was reported by 7.9% of individuals with a professional education, 8.8% of those with more than a high school education, 10.7% of those with a high school diploma, and 11.8% of those with less than a high school education ($P = 0.00001$ for trend). FH-ESRD was reported by 7.4% of individuals in the highest quartile of reported income in comparison with 8.6% in the second, 9.7% in the third, and 12.3% in the lowest ($P < 0.0001$ for trend). Individuals with FH-ESRD were more likely to report that they did not have health insurance (8.3%) compared with individuals without a family history (6.4%; OR 1.32; 95% CI 1.05 to 1.66).

Table 1. Univariate associations of demographic characteristics, comorbidity, and FH-ESRD^a

Characteristic	No Family History (n [%])	Family History (n [%])	OR of FH-ESRD (95% CI)
Age (yr)			
45 to 54	1389 (89.6)	161 (10.4)	Reference ^b
55 to 64	4039 (89.6)	470 (10.4)	1.0 (0.83 to 1.21)
65 to 74	3548 (90.7)	365 (9.3)	0.89 (0.73 to 1.08)
75 to 84	1678 (92.6)	134 (7.4)	0.69 (0.54 to 0.88)
≥ 85	221 (94.4)	13 (5.6)	0.51 (0.28 to 0.91)
Race			
white	6643 (93.6)	453 (6.4)	Reference
black	4237 (86.0)	690 (14.0)	2.38 (2.11 to 2.71)
Gender			
male	4241 (92.1)	326 (7.9)	Reference
female	6641 (89.5)	782 (10.5)	1.38 (1.24 to 1.64)
Comorbid conditions			
hypertension	6190 (89.1)	756 (10.9)	1.49 (1.30 to 1.69)
diabetes	2034 (86.8)	308 (13.2)	1.61 (1.40 to 1.86)
stroke	665 (90.0)	74 (10.0)	1.06 (0.84 to 1.34)
MI	855 (90.2)	93 (9.8)	1.04 (0.83 to 1.30)
hyperlipidemia	5618 (89.9)	631 (10.1)	1.15 (1.02 to 1.30)
Health status			
excellent	1738 (93.0)	131 (7.1)	Reference ^c
very good	3413 (92.1)	291 (7.9)	1.13 (0.91 to 1.41)
good	3796 (89.5)	444 (10.5)	1.55 (1.26 to 1.91)
fair	1561 (88.2)	209 (11.8)	1.78 (1.40 to 2.25)
poor	353 (84.1)	67 (15.9)	2.52 (1.81 to 3.49)

^aCI, confidence interval; FH-ESRD, family history of ESRD; MI, myocardial infarction; OR, odds ratio.

^b χ^2 for trend 25.01, $P < 0.00001$.

^c χ^2 for trend 49.0, $P < 0.00001$.

Table 2. Univariate associations of cardiovascular risk factors and FH-ESRD^a

Cardiovascular Risk Factors	No Family History (n [%])	Family History (n [%])	OR of FH-ESRD (95% CI)
LDL cholesterol (mg/dl)			
<100	4152 (90.8)	420 (9.2)	Reference
100 to 129	3258 (90.2)	354 (9.8)	1.07 (0.92 to 1.25)
130 to 159	1862 (91.6)	170 (8.4)	0.90 (0.75 to 1.09)
160 to 189	626 (88.5)	81 (11.5)	1.28(0.99 to 1.66)
≥190	226 (89.3)	27 (10.7)	1.18 (0.77 to 1.81)
HDL cholesterol (mg/dl)			
<40	1856 (90.5)	194 (9.5)	Reference
40 to 49	2652 (89.8)	300 (10.2)	1.08 (0.89 to 1.31)
50 to 59	2390 (91.0)	236 (9.0)	0.94 (0.77 to 1.14)
≥60	3363 (90.9)	338 (9.1)	0.96 (0.80 to 1.16)
Triglycerides (mg/dl)			
<150	7313 (90.3)	789 (9.7)	Reference
150 to 199	1525 (91.2)	148 (8.8)	0.90 (0.75 to 1.09)
200 to 499	1429 (91.7)	130 (8.3)	0.84 (0.69 to 1.03)
≥500	68 (87.2)	10 (12.8)	1.36 (0.66 to 2.75)
Glucose (mg/dl)			
≤25	9409 (91.1)	915 (8.9)	Reference ^c
126 to 150	616 (89.0)	76 (11.0)	1.27 (0.98 to 1.64)
151 to 175	260 (84.1)	49 (15.9)	1.94 (1.40 to 2.68)
176 to 200	162 (85.3)	28 (14.7)	1.78 (1.16 to 2.71)
≥200	283 (83.0)	58 (17.0)	2.11 (1.56 to 2.84)
Smoking			
never	4958 (90.3)	538 (9.7)	Reference
past	4303 (91.2)	418 (8.8)	0.90 (0.78 to 1.03)
current	1557 (89.6)	180 (10.4)	1.07 (0.89 to 1.28)
JNC 7 BP stage ^b			
normal BP	2876 (91.9)	253 (8.1)	Reference ^d
prehypertension	5433 (91.1)	533 (8.9)	1.12 (0.95 to 1.31)
hypertension, stage 1	1880 (88.5)	245 (11.5)	1.48 (1.23 to 1.79)
hypertension, stage 2	527 (85.0)	93 (15.0)	2.01 (1.54 to 2.61)

^aJNC 7, The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

^bNormal BP (systolic BP [SBP] <120 and diastolic BP [DBP] <80 mmHg); prehypertension (SBP 120 to 130 or DBP 80 to 90 mmHg); hypertension, stage 1 (SBP 140 to 159 or DBP 90 to 99 mmHg); and hypertension, stage 2 (SBP ≥160 or DBP ≥100 mmHg) (48).

^c χ^2 for trend 33.608, $P < 0.00001$.

^d χ^2 for trend 28.751, $P < 0.00001$.

Individuals with FH-ESRD were more likely to have the metabolic syndrome (Table 3). The prevalence of a positive FH-ESRD increased from 5.7% among individuals without any of the metabolic syndrome traits to 12.3% of individuals with all five traits ($P < 0.00001$ for trend; Table 3). The mean (SD) BMI among those with and without a family history was 31.3 (7.0) and 29.0 (6.2) kg/m², respectively ($P < 0.0001$). FH-ESRD was lowest among those with normal BMI (6.7%) and higher among those who were overweight 8.3% and those who were obese (12.5%) ($P < 0.00001$ for trend; Table 3).

The mean (SD) albumin was 4.08 (0.32) g/dl and 4.12 (0.32) mg/L, respectively, among those with and without FH-ESRD, and the respective geometric mean CRP was 2.85 (3.21) and 2.21

(3.25) mg/L ($P < 0.001$). In contrast, the mean (SD) white blood count did not differ between the groups: 5.90 (1.87) $\times 10^9$ cells/L for those with FH-ESRD and 5.91 (1.99) $\times 10^9$ cells/L among without a FH-ESRD ($P = 0.84$).

The mean (SD) hemoglobin among those with FH-ESRD was 13.4 (1.4) g/dl and among those without a family history was 13.7 (1.4) g/dl. Participants with a hemoglobin >13 g/dl had an 8.2% prevalence of FH-ESRD. In comparison, 11.2% of individuals with hemoglobin between 12 and 13 g/dl, 11.8% between 11 and 12 g/dl, 14.9% between 10 and 11 g/dl, 13.9% between 9 and 10 g/dl, and 15.4% <9 g/dl reported FH-ESRD ($P < 0.00001$ for trend).

After accounting for other individual characteristics that

Table 3. Univariate associations of obesity, metabolic syndrome, and FH-ESRD^a

Metabolic Factors	No Family History (n [%])	Family History (n [%])	OR of FH-ESRD (95% CI)
Abdominal obesity ^b	4850 (88.1)	653 (11.9)	1.69 (1.49 to 1.92)
BMI ^{c,d}			
<18.5	146 (96.7)	5 (4.0)	0.48 (0.17 to 1.22)
normal	2700 (93.3)	194 (6.7)	Reference
overweight	3893 (91.7)	353 (8.3)	1.26 (1.05 to 1.52)
obese	3976 (87.5)	569 (12.5)	1.99 (1.67 to 2.37)
Elevated triglycerides (mg/dl)	3022 (91.3)	288 (8.7)	0.88 (0.76 to 1.02)
Low HDL cholesterol (mg/dl)	3213 (89.6)	375 (10.4)	1.19 (1.04 to 1.36)
ATP III metabolic syndrome traits ^b			
0	1487 (94.3)	90 (5.7)	Reference ^e
1	2594 (92.1)	222 (7.9)	1.41 (1.09 to 1.84)
2	2528 (90.9)	254 (9.1)	1.66 (1.29 to 2.15)
3	1962 (88.2)	262 (11.8)	2.21(1.71 to 2.85)
4	1123 (88.0)	153 (12.0)	2.25 (1.70 to 2.98)
5	406 (87.7)	57 (12.3)	2.32 (1.61 to 3.34)

^aATP III, Adult Treatment Panel III; BMI, body mass index.

^bAbdominal obesity was defined as a waist circumference in men >102 cm (>40 in) and in women >88 cm (>35 in); elevated triglycerides as >150 mg/dl; low HDL cholesterol in men as <40 mg/dl and in women as <50 mg/dl; hypertension as a history of high BP or mean BP >130/85 mmHg; and diabetes as a history of diabetes or fasting glucose >110 mg/dl. Metabolic syndrome defined as three or more traits.

^c χ^2 for trend 76.282, $P < 0.00001$.

^dNormal BMI 18.5 to 24.9 kg/m²; overweight 25 to 29.9 kg/m²; and obese ≥ 30 kg/m².

^e χ^2 for trend 47.612, $P < 0.00001$.

were included in multivariable logistic models, black, compared with white, individuals had a higher prevalence of FH-ESRD (OR 2.14; 95% CI 1.82 to 2.53). Other traits that were independently associated with FH-ESRD included female gender, diabetes, BMI, and an elevated log-transformed CRP (Table 4). By contrast, there was no association with age, previous stroke or myocardial infarction, hypertension, smoking, educational status, income, perceived health, health insurance, cholesterol and triglycerides, hemoglobin, albumin, or white blood cell count.

Adjusting for age, race, and gender, the mean GFR among

individuals with and without FH-ESRD was 61.1 and 62.8 ml/min per 1.73 m², respectively ($P = 0.001$). Among black individuals, the estimated GFR among those with and without a family history was 63.9 and 66.2 ml/min per 1.73 m² ($P = 0.0006$) and for white individuals was 58.3 and 59.4 ml/min per 1.73 m² ($P = 0.16$). The odds of FH-ESRD increased among black individuals as GFR declined ($P < 0.0001$). For example, compared with a GFR >60 ml/min per 1.73 m², black individuals with a family history had a 27% greater odds of a GFR between 50 and 59 ml/min per 1.73 m² (OR 1.27; 95% CI 1.02 to 1.58), increasing to a three-fold larger odds (OR 3.24; 95% CI

Table 4. Multivariable associations of participant characteristics and FH-ESRD^a

Characteristic	Estimate (SE)	OR (95% CI)
Intercept	-2.6590 (0.1565)	—
Race (referent white)	0.3807 (0.0421)	2.14 (1.82 to 2.53)
Gender (referent male)	0.1223 (0.0435)	1.28 (1.08 to 1.51)
BMI category (referent underweight)		
normal	0.00634 (0.1666)	2.11 (0.66 to 6.79)
overweight	0.2283 (0.1591)	2.64 (0.82 to 8.42)
obese	0.5061 (0.1578)	3.48 (1.09 to 11.10)
Diabetes (referent no)	0.0996 (0.0469)	1.23 (1.03 to 1.48)
Log CRP	0.0775 (0.0367)	1.08 (1.01 to 1.16)
1-SD change in logCRP		1.096 (1.01 to 1.19)

^aThe initial model included the following terms: Race; GFR; age; gender; history of stroke, MI, hypercholesterolemia, diabetes, hypertension, and smoking; educational status; income; perceived health; health insurance; cholesterol and triglycerides; hemoglobin; C-reactive protein (CRP); albumin; white count; BMI; and region of the country.

1.27 to 8.0) for individuals with GFR between 10 and 19 ml/min per 1.73 m² (Table 5). A similar relationship was not noted for white individuals, although the small numbers of individuals with stage 3 GFR <30 ml/min per 1.73 m² may have obscured a relationship.

Discussion

The major finding of this report is that adults who are older than 45 yr in the US population report a high prevalence (9.5%) of having a first-degree relative with ESRD. FH-ESRD was independently associated with black race, female gender, diabetes, obesity, and higher CRP. Obesity was the strongest risk factor and was associated with a 3.5-fold higher odds of FH-ESRD. Furthermore, black individuals were twice as likely as white individuals to have FH-ESRD. Finally, black family members were more likely to have impaired kidney function, and the prevalence of a positive family history increased as GFR declined.

Our results are consistent with reports of a high prevalence of a positive family history of kidney disease among individuals with incident ESRD. A positive FH-ESRD has also been associated with increased prevalence of proteinuria (19–21); however, we are unable to confirm this association in the REGARDS population because these data are not available. Other participant characteristics that were associated with a family history, including diabetes (22), hypertension (23), anemia (24–26), the metabolic syndrome (27,28), and markers of inflammatory stress (29,30), have been previously associated with CKD and risk for progression to ESRD.

The independent association between obesity and a positive family history is consistent with the possibility that body weight, perhaps mediated by shared genetic (31,32), dietary (33), and socioeconomic (34) factors, may be associated with kidney disease in these individuals and their families. Kramer *et al.* (35) reported that participants in the Hypertension Detection and Follow-Up Program (HDFP) who had normal baseline kidney function and were overweight (OR 1.21; 95% CI 1.05 to 1.41) or obese (OR 1.40; 95% CI 1.20 to 1.63) were at increased risk for developing 1+ or greater proteinuria and/or a GFR of

<60 ml/min per 1.73 m² compared with normal weight individuals. Similarly, Gelber *et al.* (36) noted that overweight and obese participants in the Physicians' Health Study were more likely to experience a decline in GFR during an average of 14 yr of follow-up. They found that individuals in the highest quintile of BMI (>26.6 kg/m²) were more likely to develop a GFR <60 ml/min per 1.73 m² (OR 1.45; 95% CI 1.19 to 1.76). Hsu *et al.* (37) reported that among members of a large managed care organization, the risk for ESRD among overweight individuals (BMI between 25.0 and 29.9 kg/m²) was 1.87 times that of individuals with normal weight, and increasing levels of obesity were associated with increasing risk for ESRD, with a BMI between 30.0 and 34.9 kg/m² having a 3.57 times increased risk, those with BMI between 35.0 and 39.9 kg/m² having a 6.12 times increased risk, and those with a BMI ≥40 kg/m² having a 7.07 times increased risk that persisted after accounting for other risk factors. Iseki *et al.* (38) from Okinawa, Japan, reported that the risk for ESRD increased from 2.48 per 1000 in the lowest quartile of BMI (<21.0 kg/m²) to 5.81 per 1000 participants in the highest quartile of BMI (≥25.5 kg/m²). Finally, we recently reported that after controlling for age, race, gender, primary cause of ESRD, history of diabetes, history of hypertension, and estimated GFR at initiation of dialysis therapy, incident patients who had ESRD and reported a first- or second-degree family member were more likely to be overweight (OR 1.17; 95% CI 1.08 to 1.26), obese (OR 1.25; 95% CI 1.14 to 1.37), and morbidly obese (OR 1.40; 95% CI 1.27 to 1.55) (39). In contrast to these reports, Evans *et al.* (40) reported no association between BMI and risk for ESRD among members of a Scandinavian cohort.

Our data allow us only to speculate on the basis for the associations between younger age and female gender and a positive family history. It is possible that this age association may reflect differential survival among individuals with and without FH-ESRD or that older relatives may not have had access to renal replacement therapy during their lifespan. It is possible that increased prevalence of FH-ESRD among women may reflect better recall of family relationships and associated illness. Furthermore, it is possible that familial aggregation be

Table 5. Age- and gender-adjusted multivariable association of measures of renal function and FH-ESRD, shown by race strata

GFR	Black			White		
	FH-ESRD (n [%])	No FH-ESRD (n [%])	OR ^a	FH-ESRD (n [%])	No FH-ESRD (n [%])	OR ^b
>60	399 (61.9)	2745 (69.3)	Reference	221 (51.4)	3296 (51.8)	Reference
50 to 59	135 (20.9)	732 (18.5)	1.27 (1.02 to 1.58)	132 (30.7)	1932 (30.4)	1.02 (0.81 to 1.28)
40 to 49	61 (9.5)	305 (7.7)	1.38 (1.01 to 1.86)	49 (11.4)	784 (12.3)	0.93 (0.67 to 1.30)
30 to 39	23 (3.6)	124 (3.1)	1.28 (0.79 to 2.06)	24 (5.6)	270 (4.2)	1.33 (0.83 to 2.09)
20 to 29	19 (2.9)	36 (0.9)	3.63 (1.98 to 6.6)	2 (0.5)	73 (1.2)	0.75 (0.23 to 2.14) ^c
10 to 19	8 (0.7)	17 (0.4)	3.24 (1.27 to 8.0)	2 (0.5)	7 (0.1)	

^aχ² for linear trend 25.1, df = 5; P < 0.00001.

^bχ² for linear trend 0.066, df = 4; P = 0.7978.

^cTwo cells combined.

matrilineal, consistent with mitochondrial mutations and increased risk for hypertension (41) and insulin resistance in offspring of individuals with type 2 diabetes (42) and among black individuals with hypertensive ESRD (43). The independent association between CRP levels and FH-ESRD may reflect that CRP is a component of the metabolic syndrome or that elevated CRP levels are observed in patients with type 2 diabetes and with subclinical and clinical cardiovascular disease (44) and progressive kidney disease (29,30).

The clinical relevance of our observations is that FH-ESRD is a prevalent risk factor that identifies individuals who are at risk for CKD and ESRD and might benefit from interventions to improve the detection and management of risk factors for progressive CKD. Reports from the ESRD Network system and the Kidney Early Evaluation Program program demonstrate that members of at-risk families can be systematically identified (45) and screened (46) for kidney disease. Furthermore, the recently announced Family Reunion initiative by the National Kidney Disease Education Programs (47) is an example of family-based interventions that could include efforts to increase the early detection and guideline-based treatment of kidney disease among high-risk families.

There are limitations to our report. We cannot confirm the validity of FH-ESRD, and we did not obtain information on the number of first-degree relatives. This raises the possibility that individuals with large families are more likely both to be aware of a first-degree family member with ESRD and to be exposed to other environmental or behavioral risk factors. These limitations are offset first by the fact that a self-reported family history identified individuals who were different from other participants with respect to risk factors that are associated with CKD and second by requiring an unprompted identification of a parent, a sibling, or a child as the family member with ESRD to define a positive family history, which may have reduced recall error.

Conclusion

FH-ESRD is not uncommon among older Americans, and, after controlling for kidney function, these individuals are more likely to be black, to be obese, and to have diabetes. These observations suggest that families of patients with ESRD might benefit from targeted efforts to improve the detection and treatment of early CKD.

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Disclosures

None.

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