Association of Family History With Cardiovascular Disease in Hypertensive Individuals in a Multiethnic Population

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Background—Hypertension alone is a poor predictor of the individual risk of cardiovascular disease. Hereditary factors of which hypertension is merely a marker may explain why some hypertensive individuals appear more susceptible to cardiovascular disease, and why some ethnicities have more often seemingly hypertension-related cardiovascular disease than others. We hypothesize that, in hypertensive individuals, a positive family history of cardiovascular disease identifies a high-risk subpopulation.

Methods and Results—Healthy Life in Urban Settings (HELIUS) is a cohort study among participants of Dutch, South-Asian Surinamese, African Surinamese, Ghanaian, Turkish, and Moroccan origin aged 70 years and younger. In participants with hypertension (n=6467), we used logistic regression to assess the association of family history of cardiovascular disease with prevalent stroke and nonstroke cardiovascular disease, adjusting for sex, age, education, and smoking. To detect ethnic differences, we tested for interaction between family history and ethnicity and stratified the analysis by ethnicity. A positive family history was associated with a higher prevalence of nonstroke cardiovascular disease (odds ratio [OR], 2.05; 95% CI, 1.65–2.54) and stroke (OR, 1.62; 95% CI, 1.19–2.20). The strongest association of family history with nonstroke cardiovascular disease was found among the Dutch (OR, 2.47; 95% CI, 1.37–4.44) and with stroke among the African Surinamese (OR, 2.17; 95% CI, 1.32–3.57). The interaction between family history and African Surinamese origin for stroke was statistically significant.

Conclusions—In multiethnic populations of hypertensive patients, a positive family history of cardiovascular disease may be used clinically to identify individuals at high risk for nonstroke cardiovascular disease regardless of ethnic origin and African Surinamese individuals at high risk for stroke. (*J Am Heart Assoc.* 2016;5:e004260 doi: 10.1161/JAHA.116.004260)

Key Words: cardiovascular diseases • cerebrovascular disease/stroke • HELIUS study • hypertension • race and ethnicity

Hypertension is considered the leading risk factor for cardiovascular disease (CVD), with myocardial infarction and stroke accounting for most cases.[1] Because of its high prevalence, hypertension is responsible for the majority of the cases of CVD.[2] However, data from longitudinal cohort studies are subject to confounding and cannot clearly show to what extent high blood pressure itself accounts for the observed risk and to what extent it is merely a marker that

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identifies high-risk patients. Data from randomized controlled trials of antihypertensive treatment are less subject to confounding, and therefore more reliable than those from longitudinal studies for estimation of the individual risk for CVD originating from hypertension alone. A Cochrane meta-analysis of 18 placebo-controlled trials for primary prevention showed that, in patients with untreated hypertension, the yearly incidence of either myocardial infarction or stroke is <1%.[3] This translates into a lifetime risk of either myocardial infarction or stroke of <20%, assuming risk increases linearly over the residual lifespan of subjects of similar age and country of origin as those in the trials.[4] In other words, over 80% of all untreated hypertensive individuals will experience no event in their lifetime. These data suggest that hypertension does not seem to be a strong risk factor for all individuals but it probably is for certain subpopulations. If we could identify the specific subpopulations in which hypertension itself results in an increased risk, we would be able to better target screening and adapt treatment decisions to the risk level.

Family history of CVD could be used as a tool to identify which hypertensive individuals are at particularly high risk. A positive family history of CVD is an independent predictor of

both myocardial infarction[5,6] and stroke.[7–9] Prognostic models for stroke that include both hypertension and family history have predictive value greater than models that include hypertension or family history alone.[8] Among individuals with hypertension, family history of CVD has been shown to be independently associated with mortality by ischemic heart disease[10] and family history of CVD mortality with incidence of overall CVD.[11] Therefore, a positive family history of CVD could reflect an underlying genetic predisposition related to CVD.[12]

In the current study, we investigated this possible role of family history in hypertensive individuals in a multiethnic population of relatively young age, since the incidence of hypertension-related CVD differs across ethnic groups,[13,14] even among persons with hypertension,[15,16] and since young individuals may be erroneously assigned a low risk of CVD. Therefore, better risk estimation in this specific group could lead to better identification of hypertensive individuals at high risk for CVD, especially in multiethnic populations.

To test our hypothesis, we evaluated whether a positive family history of CVD is related to a higher prevalence of nonstroke CVD or stroke in a cross-sectional study of hypertensive individuals of different ethnic origins.

Methods

Study Population

Healthy Life in Urban Settings (HELIUS) is a cohort study on health among different ethnic groups living in Amsterdam, the Netherlands. The HELIUS study is described in detail elsewhere.[13] Briefly, baseline data collection took place in 2011–2015. Participants were randomly sampled from the municipal register, stratified by ethnicity, and included people aged 18 to 70 years of Dutch origin or belonging to one of the ethnic minority groups with a South-Asian Surinamese, African Surinamese, Ghanaian, Turkish, or Moroccan origin. Data were obtained by questionnaire, physical examination, and collection of biological samples. The study protocols were approved by the ethical review board of the Academic Medical Center of the University of Amsterdam, and all individuals provided written informed consent.

There were 22 165 individuals for whom both questionnaire data and physical measurements were available. We excluded individuals with unknown ethnic origin (n=48) or a Surinamese origin other than African of South Asian (n=500). From the remaining 21 617 participants, after multiple imputation (see Statistical Analysis), we selected 6467 individuals with hypertension, who were included in the analysis.

Definitions

Ethnic origin was defined based on the country of birth of the participant and of his or her parents as recorded in the municipal register of the city of Amsterdam.[13] Specifically, a participant is considered to be of non-Dutch ethnic origin if he or she fulfils either of these criteria: (1) he or she was born abroad and has at least one parent born abroad (first generation); or (2) he or she was born in the Netherlands but both his or her parents were born abroad (second generation).[17] The definition therefore accommodates participants of partially mixed ancestry by determining the predominant ethnicity based on the combination of the participant's and his or her parents' country of birth. The Surinamese group was further classified according to self-reported ethnic origin into "African," "South Asian," or other. Participants were considered of Dutch ethnicity if they and both parents were born in the Netherlands.

A positive family history of CVD was defined as a self-reported diagnosis of CVD in parents, siblings, or children that occurred at 60 years or younger. This definition is consistent with the one used in the most common risk scores used in clinical practice.[18,19] Information on family history of CVD was considered missing for patients who reported that they did not know their family history of CVD or who did not fill in the corresponding questionnaire item.

Blood pressure was measured as previously described.[20] Hypertension was defined as a systolic blood pressure ≥140 mm Hg or a diastolic blood pressure ≥90 mm Hg,[1] or the combined report of prior diagnosis of hypertension and current use of antihypertensive agents (Anatomical Therapeutic Chemical [ATC] codes C02, C03, C07, C08, and C09).[21]

Waist circumference was measured to the nearest 0.1 cm at the level midway between the lower rib margin and the iliac crest. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

Fasting blood samples were drawn and plasma samples were used to determine the concentration of glucose, low-density lipoprotein and high-density lipoprotein (HDL) cholesterol, and triglycerides (Roche Diagnostics, Tokyo, Japan). Diabetes mellitus was defined as fasting plasma glucose ≥7 mmol/L or reported use of glucose-lowering medications (ACT code A10). Dyslipidemia was defined as either reported use of lipid-lowering agents (ATC code C10) or cholesterol/HDL ratio ≥5.

Educational level was used as an indicator of socioeconomic position, as it has been found to be an indicator of the socioeconomic position most consistently associated with cardiovascular risk across ethnicities in a similar multiethnic sample from a European city.[22] It was defined as the highest qualification obtained in the Netherlands or in the country of

origin. The categories of educational level were: (1) never been to school or elementary schooling only; (2) lower vocational schooling or lower secondary schooling; (3) intermediate vocational schooling or intermediate/higher secondary schooling; and (4) higher vocational schooling or university. These categories were combined into low education (1st and 2nd category combined) and high education (3rd and 4th category combined).

Individuals were considered smokers if they reported that they were currently smoking or when they had stopped smoking less than 5 years ago.[23]

Cardiovascular outcomes were based on questionnaire data. Nonstroke CVD was defined as self-reported myocardial infarction or self-reported angioplasty or bypass surgery in the coronary circulation or in the lower extremities. Stroke was defined as self-reported stroke, cerebral infarction, or cerebral hemorrhage.

Statistical Analysis

In the whole HELIUS sample, 3359 participants (15.5%) had missing data for at least one of the variables of interest in this analysis. For each variable, no more than 1.1% of observations were missing, with the only exception of family history of CVD, which was missing in 12.1% of the sample and, in particular, 19.8% of the Ghanaian participants. Before defining our variables and conducting the analysis, under the assumption that data were missing at random, we performed multiple imputation using the chained equations algorithm and generated 10 imputed data sets. Analysis results were pooled across all data sets using Rubin's rules.[24] We performed a sensitivity analysis by repeating all analyses with complete case analysis (N=18 032, of which 5202 had hypertension) comparing the effect sizes thus obtained with those obtained from the multiply imputed datasets and found that the results were similar.

We used logistic regression to examine the association of a positive family history of CVD with either nonstroke CVD or stroke as outcomes. First, we analyzed this association in the whole sample without considering ethnicity. Second, we analyzed the relationship separately for each ethnic group by calculating the significance level of the interaction between positive family history of CVD and ethnicity, using Dutch as a reference group, and showing the ethnicity-specific estimate of the association of family history of CVD with nonstroke CVD and stroke. The Dutch were chosen as a reference because they are the majority ethnic group in the Netherlands, and most non-Dutch minority groups are known to display a higher risk of CVD than the Dutch.[25,26] The results of logistic regressions are reported as odds ratios (ORs) with 95% CIs. In the regression analysis, we first used a univariate model with only family history as an independent variable (model 1), then adjusted the analysis for age and sex (model 2),

and additionally adjusted for smoking status and educational level (model 3). In a fourth model, we additionally adjusted for diabetes mellitus, dyslipidemia, and waist circumference (model 4). Because the covariates added in model 4 are strong determinants of the metabolic syndrome with relevant inheritable components,[27] they could reflect at least partly the same inherited predisposition identified by family history of CVD. Therefore, we expected moderate overadjustment to occur in model 4, possibly underestimating the effect size of the association between family history of CVD and the outcome variables.[28] We therefore consider model 3 our main analysis model.

Continuous data are reported as mean and SD and categorical data as frequency and proportions. To study differences in baseline characteristics, we used chi-square test for categorical variables and t test or ANOVA for continuous variables.

Two-sided P values $<.05$ were considered significant. Data were imputed and analyzed using R version 3.2.3 (The R Foundation for Statistical Computing, 2015).

Results

Demographic and clinical characteristics of the study population are presented in Table 1, by individuals with or without a positive family history of CVD. The mean age was 52.7 ($\pm$9.9) years, and 47.5% were male. There were 7.1% and 3.5% of individuals with a history of nonstroke CVD or stroke, respectively. Moroccans were the least represented ethnic group (10.2% of the sample) and African Surinamese the most represented (27.5% of the sample).

Of all individuals, 31% reported a positive family history of CVD. Individuals with a positive family history of CVD had a higher prevalence of almost all traditional risk factors: they were more likely to be treated for hypertension, to have diabetes mellitus or dyslipidemia, and to be smokers, as compared with individuals with a negative family history of CVD. However, the two groups did not differ in BMI or waist circumference. Individuals with a positive family history of CVD were more often highly educated and of Dutch, South-Asian Surinamese, and Turkish origin and less often of African Surinamese, Ghanaian, and Moroccan origin as compared with individuals with a negative family history of CVD.

The results of the logistic regression to estimate the association of a positive family history of CVD with the risk of either nonstroke CVD or stroke are shown in Table 2. We found that, after adjustment for age, sex, smoking status, and educational level (model 3), individuals with a positive family history of CVD had a significantly higher prevalence of both nonstroke CVD and stroke (OR, 2.05; 95% CI, 1.65–2.54 [$P<0.05$] and OR, 1.62; 95% CI, 1.19–2.20 [$P<0.05$],

Table 1. Characteristics of the Hypertensive Study Sample, by Family History of CVD

	Total Sample	Negative Family History	Positive Family History
	N=6467	n=4461 (69%)	n=2006 (31%)
Male	3070 (47.5)	2168 (48.6)	902 (45)*
Age, y	52.7±9.9	52.3±10.1	53.6±9.4*
Antihypertensive agents	3166 (49)	2043 (45.8)	1124 (56)*
Systolic BP, mm Hg	142.5±17.5	143.1±17.4	141.5±17.6*
Diastolic BP, mm Hg	86.0±10.3	86.3±10.3	85.3±10.2*
Without antihypertensive agents			
Systolic BP, mm Hg	149.3±13.9	149.6±14.1	148.5±13.3*
Diastolic BP, mm Hg	92.2±8.8	92.3±8.9	91.8±8.5*
BMI, kg/m^2	29.5±5.5	29.6±5.4	29.5±5.6
Waist circumference, cm	99.6±12.8	99.5±12.6	99.7±13.2
Diabetes mellitus	1287 (19.9)	844 (18.9)	443 (22.1)*
Dyslipidemia	2356 (36.4)	1441 (32.3)	915 (45.6)*
Lipid-lowering agents	1419 (21.9)	812 (18.2)	606 (30.2)*
HDL, mmol/L	1.31±0.39	1.33±0.40	1.27±0.38*
Triglycerides, mmol/L	1.33±0.85	1.27±0.83	1.40±0.87*
Without lipid-lowering agents			
HDL, mmol/L	1.45±0.44	1.47±0.45	1.40±0.42*
Triglycerides, mmol/L	1.14±0.77	1.10±0.76	1.23±0.78*
Smokers	1655 (25.6)	1056 (23.7)	600 (29.9)*
Educational level (high)	2698 (41.7)	1769 (39.6)	929 (46.3)*
Ethnicity			
Dutch	1026 (15.9)	633 (14.2)	393 (19.6)*
South-Asian Surinamese	1033 (16)	480 (10.8)	553 (27.6)*
African Surinamese	1776 (27.5)	1277 (28.6)	499 (24.9)*
Ghanaian	1180 (18.2)	1101 (24.7)	79 (3.9)*
Turkish	792 (12.3)	437 (9.8)	355 (17.7)*
Moroccan	660 (10.2)	533 (11.9)	127 (6.3)*
Nonstroke CVD	456 (7.1)	243 (5.4)	213 (10.6)*
Stroke	227 (3.5)	127 (2.8)	100 (5)*

Data are the average of 10 multiply imputed datasets. Continuous data are presented as mean±SD and categorical data are presented as number (percentage). BMI indicates body mass index; BP, blood pressure; CVD, cardiovascular disease; HDL, high-density lipoprotein.
*$P<0.05$ when compared with a negative family history.

respectively). Further adjustment by diabetes mellitus, dyslipidemia, and waist circumference in model 4 did not significantly attenuate the association (Table 2).

In the second part of our analysis, we analyzed the association of a positive family history of CVD with nonstroke CVD or stroke, stratified by ethnicity.

The demographic and clinical characteristics across ethnic backgrounds are shown in Table 3. Individuals with Ghanaian background had the lowest rate of positive family history of CVD (6.7%) and those with South-Asian Surinamese background had the highest (53.5%).

In every ethnic group, the distribution of vascular risk factors between individuals with positive and negative family history of CVD reflected that observed in the total sample. The only exceptions were HDL levels in individuals untreated with lipid-lowering medications, which among the Turks were lower among those with negative family history; and triglyceride levels in untreated individuals, which among the African Surinamese were higher among those with negative family history (data not shown).

The ethnicity-specific associations of family history with nonstroke CVD and with stroke are shown in Table 4.

Table 2. Association of Positive Family History of CVD With Either Nonstroke CVD or Stroke Among Hypertensive Patients

Nonstroke CVD	
Events, No. (%)	456 (7.1)
Positive family history of CVD, OR (95% CI)	
Model 1	2.07 (1.67–2.55)*
Model 2	2.02 (1.63–2.50)*
Model 3	2.05 (1.65–2.54)*
Model 4	1.75 (1.41–2.18)*
Stroke	
Events, No. (%)	227 (3.5)
Positive family history of CVD, OR (95% CI)	
Model 1	1.78 (1.31–2.41)*
Model 2	1.70 (1.25–2.30)*
Model 3	1.62 (1.19–2.20)*
Model 4	1.38 (1.01–1.88)*

Model 1: unadjusted. Model 2: adjusted for age and sex. Model 3: model 2 + smoking status and educational level. Model 4: model 3 + diabetes mellitus, dyslipidemia, and waist circumference. CVD indicates cardiovascular disease; OR, odds ratio.
*$P<0.05$.

With regard to the first outcome, a positive family history of CVD was associated with a higher prevalence of nonstroke CVD in most ethnicities (model 3 in Table 4). Expressed in OR (95% CI), the point estimates for the association ranged from 1.16 (0.44–3.09) among the Moroccans to 2.47 (1.37–4.44) among the Dutch. Further adjustment for diabetes mellitus, dyslipidemia, and waist circumference in model 4 did not significantly alter the effect sizes or interethnic differences.

With regard to the second outcome, a positive family history of CVD was also associated with a higher prevalence of stroke in most ethnicities (model 3, Table 4). The OR (95% CI) for the association ranged from 0.88 (0.41–1.86) among the Dutch to 2.17 (1.32–3.57) among the African Surinamese. Further adjustment in model 4 did not significantly alter the effect sizes or interethnic differences.

To evaluate whether the differences between the ethnic groups in the association between family history of CVD and both outcomes were significant, the regression model included the interaction between family history and ethnicity. For the outcome nonstroke CVD, the interaction was not statistically significant. For the outcome stroke, the interaction was statistically significant in models 3 and 4, with the association between family history and stroke being stronger in the African Surinamese hypertensive participants than in the other ethnic groups ($P<0.05$). To further investigate this ethnic group, we used an interaction model to test for sex differences in this association among the African Surinamese (Table 5). While the interaction was not statistically

significant, the sex-specific ORs were higher in women (OR, 3.12 [95% CI, 1.61–5.64] for model 3) than in men (OR, 1.15 [95% CI, 0.43–3.06]).

Discussion

Our findings support the hypothesis that a positive family history of CVD independently identifies subgroups at higher risk for nonstroke CVD among patients with hypertension, and show that it specifically identifies hypertensive individuals at higher risk of stroke in women of the African Surinamese ethnic group.

Vascular disease among hypertensive individuals with a positive family history of CVD was found nearly twice as often than among hypertensive individuals with a negative family history, even after adjustment for notable environmental risk factors.

In the analysis on the sample stratified by ethnic groups, effect sizes in the fully adjusted model displayed large variations across ethnic groups. With regard to nonstroke CVD, the effect size of a positive family history of CVD was most pronounced for the Dutch and absent in the Moroccans. The other ethnicities were in between. Since the interaction term between family history of CVD and ethnicity for this outcome was not statistically significant, we cannot conclude that the Dutch had a higher risk for nonstroke CVD as compared with the other ethnic groups. With regard to stroke, the African Surinamese displayed the strongest association: in contrast to the other ethnic groups, African Surinamese hypertensive individuals with a positive family history of CVD are approximately twice as likely to report stroke as those with a negative family history of CVD. The interaction between family history of CVD and ethnicity for this outcome was statistically significant. While there was no statistically significant interaction between sex and family history of CVD in this ethnic group, the sex-specific effect sizes revealed that this result seems to be driven by individuals of female sex.

The absence of a statistically significant interaction between family history of CVD and ethnicity for the outcome nonstroke CVD, despite considerable differences in the ethnicity-specific ORs, could be due to limited power, since our cohort was rather young and had only few events per ethnic group. Indeed, a post hoc power calculation showed that, for the outcome stroke, the power for the ORs of family history of CVD observed in Dutch and African Surinamese in model 3 to be significantly different was about 60%, while, for the outcome nonstroke CVD and the ORs observed in Dutch and Moroccans, the power is only about 40%.

The differences in the effect size of the relationship between family history of CVD and the two outcomes across

Table 3. Characteristics of the Hypertensive Study Sample, Stratified by Ethnicity

N=6467	Dutch n=1026	South-Asian Surinamese n=1033	African Surinamese n=1776	Ghanaians n=1180	Turks n=792	Moroccans n=660
Male	612 (59.6)	505 (48.9)	694 (39.1)	507 (43)	430 (54.2)	322 (48.8)
Age, y	56.1±10.8	54.2±9.5	53.9±9.4	49.8±8.0	49.2±9.9	51.3±10.6
Antihypertensive agents	424 (41.4)	565 (54.7)	962 (54.2)	611 (51.8)	350 (44.2)	253 (38.3)
Systolic BP, mm Hg	138.4±16.1	144.0±18.1	142.8±17.2	145.1±17.7	140.8±17.3	141.5±17.2
Diastolic BP, mm Hg	83.6±9.8	85.3±9.6	86.6±9.9	89.4±10.6	84.6±10.4	82.5±9.9
Without antihypertensive agents						
Systolic BP, mm Hg	149.5±13.8	149.1±14.3	150.0±14.6	151.9±14.7	145.4±11.6	148.1±11.9
Diastolic BP, mm Hg	91.5±8.9	92.1±8.8	93.2±8.6	94.0±9.2	92.0±7.8	88.8±8.4
BMI, kg/m^2	27.8±4.8	28.1±4.7	29.6±5.8	29.6±4.9	32.1±5.8	31.0±5.2
Waist circumference, cm	99.5±13.1	97.8±11.4	98.4±13.9	97.4±11.2	104.6±12.8	103.4±11.7
Diabetes mellitus	96 (9.3)	350 (33.9)	323 (18.2)	165 (14)	169 (21.3)	184 (28)
Dyslipidemia	408 (39.8)	579 (56)	459 (25.9)	223 (18.9)	413 (52.1)	272 (41.2)
Lipid-lowering agents	210 (20.4)	407 (39.4)	307 (17.3)	155 (13.1)	192 (24.3)	148 (22.5)
HDL, mmol/L	1.32±0.38	1.23±0.36	1.42±0.42	1.56±0.43	1.16±0.31	1.21±0.31
Triglycerides, mmol/L	1.45±0.71	1.47±1.01	1.03±0.53	0.84±0.44	1.65±0.94	1.46±0.88
Without lipid-lowering agents						
HDL, mmol/L	1.49±0.44	1.29±0.36	1.52±0.44	1.63±0.46	1.21±0.33	1.27±0.37
Triglycerides, mmol/L	1.31±0.78	1.35±0.94	0.95±0.61	0.82±0.52	1.57±0.87	1.27±0.80
Smokers	322 (31.4)	294 (28.4)	592 (33.3)	84 (7.2)	268 (33.8)	95 (14.4)
Educational level (high)	698 (68)	397 (38.5)	905 (51)	310 (26.3)	189 (23.8)	199 (30.1)
Positive family history of CVD	393 (38.3)	553 (53.5)	499 (28.1)	79 (6.7)	355 (44.8)	127 (19.2)
Nonstroke CVD	65 (6.3)	122 (11.8)	80 (4.5)	62 (5.2)	93 (11.7)	35 (5.3)
Stroke	36 (3.5)	55 (5.4)	76 (4.3)	25 (2.2)	21 (2.7)	13 (1.9)

Data are the average of 10 multiply imputed datasets. Continuous data are presented as column mean±SD and categorical data as number (percentage). BMI indicates body mass index; BP, blood pressure; CVD, cardiovascular disease; HDL, high-density lipoprotein.

the 4 models are small. It can be noted that adjustment by age does not lead here to a strong reduction in the effect size of family history of CVD because our sample was relatively young, and the independent association of age with vascular events was therefore less evident.

The difference across ethnicities in the relationship between family history and future CVD might be explained by an underlying genetic predisposition, which is different for each ethnicity. It is well known that individuals of African background often have more severe organ damage from hypertension as compared with individuals of Caucasian background.[16,29,30] A positive family history also reflects a genetic background responsible for CVD, and because positive family history is associated with CVD even after adjustment for environmental confounders, this genetic background seems likely to be responsible for the increased risk for CVD. By dividing our cohort by ethnic background and positive family history, the genetic susceptibility becomes

more pronounced, resulting in the identification of hypertensive individuals at particular risk because of their genetic background.

Study Limitations

Our study has some limitations. First, in studies of an associative nature it is impossible to distinguish cause from consequence. Nevertheless, a genetic predisposition can be assumed to be present from birth. Accordingly, if a positive family history is associated with vascular disease, this could reflect a specific genetic background. While lifestyle factors shared in families could also play a role, they are still less likely than genetic factors to be shared by first-degree relatives.[31]

Second, self-reported family history of CVD may be inaccurate. Nevertheless, it has good discriminatory power: validation studies of the accuracy of offspring-reported

Table 4. Ethnicity-Specific Association of Positive Family History of CVD With Either Nonstroke CVD or Stroke Among Hypertensive Patients

	Dutch n=1026	South-Asian Surinamese n=1033	African Surinamese n=1776	Ghanaians n=1180	Turks n=792	Moroccans n=660
Nonstroke CVD						
Events, No. (%)	65 (6.3)	122 (11.8)	80 (4.5)	62 (5.2)	93 (11.7)	35 (5.3)
Positive family history of CVD, OR (95% CI)						
Model 1	2.65 (1.47–4.79)*	1.42 (0.94–2.16)	1.93 (1.19–3.14)*	1.45 (0.51–4.10)	1.73 (1.04–2.86)*	1.09 (0.42–2.83)
Model 2	2.61 (1.45–4.69)*	1.53 (1.00–2.36)*	2.02 (1.24–3.28)*	1.42 (0.50–4.05)	1.94 (1.17–3.22)*	1.09 (0.41–2.89)
Model 3	2.47 (1.37–4.44)*	1.60 (1.03–2.47)*	2.10 (1.29–3.42)*	1.54 (0.54–4.41)	1.86 (1.12–3.08)*	1.16 (0.44–3.09)
Model 4	2.24 (1.24–4.05)*	1.42 (0.91–2.22)	1.94 (1.17–3.22)*	1.33 (0.45–3.93)	1.87 (1.11–3.14)*	1.28 (0.48–3.42)
Stroke						
Events, No. (%)	36 (3.5)	55 (5.4)	76 (4.3)	25 (2.2)	21 (2.7)	13 (1.9)
Positive family history of CVD, OR (95% CI)						
Model 1	1.01 (0.47–2.13)	1.73 (0.95–3.15)	2.08 (1.27–3.41)*	1.60 (0.33–7.74)	1.21 (0.49–3.01)	0.97 (0.16–5.86)
Model 2	0.95 (0.45–2.02)	1.77 (0.97–3.24)	2.08 (1.27–3.42)*	1.57 (0.33–7.60)	1.24 (0.50–3.08)	0.96 (0.16–5.76)
Model 3	0.88 (0.41–1.86)	1.80 (0.98–3.32)	2.17 (1.32–3.57)*	1.63 (0.33–7.98)	1.14 (0.46–2.84)	1.00 (0.17–6.01)
Model 4	0.80 (0.38–1.71)	1.56 (0.84–2.88)	2.02 (1.21–3.36)*	1.46 (0.29–7.31)	1.15 (0.46–2.87)	1.11 (0.18–6.75)

Model 1: unadjusted. Model 2: adjusted for age and sex. Model 3: model 2 + smoking status and educational level. Model 4: model 3 + diabetes mellitus, dyslipidemia, and waist circumference. CVD indicates cardiovascular disease; OR, odds ratio. Interaction family history of CVD—ethnicity for nonstroke CVD: not statistically significant. Interaction family history of CVD—ethnicity for stroke: statistically significant for African Surinamese ($P<0.05$) in models 3 and 4.
*$P<0.05$.

parental events found likelihood ratios >8.0 for parental heart attack and stroke in medical records[32] and >10.0 for stroke self-reported by the parents themselves.[33] Moreover, we were able to gather specific information on which event had occurred, in which family member, and at what age; and questionnaires in HELIUS were completed with the help of a trained interviewer in a considerable proportion of the

Table 5. Sex-Specific Association of Positive Family History of CVD With Stroke Among Hypertensive Patients of African Surinamese Ethnicity

	African Surinamese Men (n=694)	African Surinamese Women (n=1082)
Stroke		
Events, No. (%)	29 (4.2)	47 (4.3)
Positive family history of CVD, OR (95% CI)		
Model 1	1.12 (0.42–3.01)	2.92 (1.59–5.36)
Model 2	1.15 (0.43–3.08)	2.89 (1.57–5.32)*
Model 3	1.15 (0.43–3.06)	3.12 (1.68–5.80)*
Model 4	0.96 (0.34–2.66)	3.06 (1.59–5.87)*

Model 1: unadjusted. Model 2: adjusted for age and sex. Model 3: model 2 + smoking status and educational level. Model 4: model 3 + diabetes mellitus, dyslipidemia, and waist circumference. Interaction family history—sex: not statistically significant. CVD indicates cardiovascular disease; OR, odds ratio.
*$P<0.05$.

minority ethnicities, ranging from 27% of the Surinamese to 40% of the Ghanaians. Nevertheless, the high number of missing values among the Ghanaians might also reflect greater inaccuracy among this population. However, individuals who did not recall their family history might have had a positive family history, so that the number of individuals with a positive family history was probably underestimated. In contrast, it is less likely that cases of positive family history are misclassified, because of the specific nature of the questions asked. We do not believe that our variable on this issue is less reliable than any other similar study.

Third, the HELIUS cohort was relatively young, including individuals aged 18 to 70 years. In our selection of hypertensive participants, the average age was 52.7 years. Since several participants who will develop CVD may not yet have developed it at the time of the inclusion, early-onset CVD might be overrepresented as compared with older-age CVD. Since early-onset CVD is more strongly associated with genetic predispositions than late-onset CVD,[6] we may have overestimated the impact of the genetic predisposition reflected by a positive family history of CVD.

Fourth, ethnic minority groups in the Netherlands have a higher case fatality rate than those of Dutch origin for both stroke[34] and nonstroke CVD.[35] If fatal cases among hypertensive individuals of minority ethnic groups were associated with positive family history of CVD, the absence of those

cases from the sample may have introduced sampling bias. Interethnic differences may therefore be different if those cases could be included.

Fifth, the HELIUS study was conducted in Amsterdam, the Netherlands, and only included the most common ethnic groups of this city.[13] While these ethnic groups are also important minority groups in several other European countries,[13] they do not include other ethnic groups important on a global level, such as those from Southern America and Eastern Asia.

Conclusions

A positive family history of CVD in African Surinamese hypertensive individuals is associated with a higher risk of stroke. Therefore, clinicians working with multiethnic hypertensive populations may consider preventive measures or more intense screening in individuals of this ethnicity with a positive family history of CVD if a predictive value of family history for nonstroke and stroke CVD in similar populations and ethnicities is confirmed by longitudinal studies.

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