Traditional Risk Factors and the Incidence of Sudden Coronary Death With and Without Coronary Thrombosis in Blacks

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Background—Blacks have a high rate of sudden coronary death (SCD). We determined the rate of SCD in men and women 30 to 69 years of age in a 6-year period recorded at a state Medical Examiner’s Office.

Methods and Results—In a subset of 327 whites and 130 blacks, hearts were systematically studied to determine the extent of coronary disease, presence and type of thrombus (acute rupture, acute erosion, stable plaque), and heart weight. These parameters were correlated with the presence of conventional risk factors. The estimated rate of SCD in blacks was similar to that in whites under the age of 40 years but increased compared with whites with advancing age, becoming 1.5 times the rate for whites in the 7th decade (95% of the increase in the 6th decade was due to sudden death with stable plaque). Among the autopsied group with severe coronary atherosclerosis, HDL cholesterol was higher and hypertension more prevalent in blacks, but there was no difference in the prevalence of healed infarcts, plaque burden, heart weight, acute thrombi, or rates of diabetes, cigarette smoking, and total cholesterol.

Conclusions—When compared with a control autopsy group of 568 deaths, multivariate analysis showed a significant association in blacks between stable plaque and left ventricular hypertrophy (risk ratio, 7.6), type 1 diabetes (risk ratio, 3.6), hypertension (risk ratio, 3.5), elevated total cholesterol (risk ratio, 3.1) and type 2 diabetes (risk ratio, 2.9). Because these risk factors are associated with SCD in blacks, they may be important targets for reducing the disparately high rate of SCD in blacks as compared with whites. (Circulation. 2002;105:419-424.)

Key Words: hypertrophy ■ risk factors ■ thrombosis ■ death, sudden
Methods

Rates of SCD

Computerized records of the Office of the Chief Medical Examiner in the State of Maryland, to which all unexplained sudden deaths in the state are referred, were retrospectively reviewed from 1994 to 1999. Unexpected SCD in the state of Maryland is determined by inspection, in which cases a coronary death is determined by scene investigation, or by complete autopsy. Sudden death was defined as symptoms commencing within 6 hours of death (witnessed arrest) or death occurring within 24 hours after the victim was last seen alive in his normal state of health; coronary death was defined as at least 1 epicardial coronary artery with ≥75% cross-sectional area lumen narrowing by atherosclerotic plaque or plaque with superimposed thrombus and no other cause of death. Of the 5139 designated SCD during the study period in the Office of the Chief Medical Examiner in the State of Maryland, complete autopsies were performed on 1593, for a rate of 31%. There was a total of 12 909 autopsies of noncoronary cardiovascular deaths during this period, with a 91% autopsy rate in these cases. Of the 1593 SCD autopsied cases, 457 were included in the current study (29%), and an additional 563 (35%) were studied by one of the coauthors but not included in the study. Of the 1593 autopsy cases of SCD, the autopsy rate varied with age: The autopsy rate was 78% in the 30- to 39-year age range, 54% in the 40- to 49-year age range, 24% in the 50- to 59-year age range, and 12% in the 60- to 69-year age range. The protocol for the study of sudden cardiac deaths seen in consultation from the medical examiner’s office was approved by the internal review board (Research Committee) of the Armed Forces Institute of Pathology.

For the first 5 years of this study, the total number of ischemic heart disease deaths according to vital statistics was 7662. According to data from the Office of the Medical Examiner, the percentage of these deaths that were sudden in men and women declined from nearly 100% in the 4th decade to 54% of white men, 76% of black men, 42% of white women, and 58% of black women in the 7th decade.

Case Selection for Detailed Examination of the Heart

From 1994 to 1999, hearts (cases and control subjects) from 1025 autopsied cases at the Office of the Chief Medical Examiner were examined in detail, with data on risk factors collected. The criteria for selection included availability of risk factor data and the diagnosis of the medical examiner on call to request diagnostic consultation. There were initially 1038 cases, from which 13 cases were discarded because of inadequate serum for risk factor determination. Basically, 2 to 3 days per week were selected as case entry days to the study, when one of the coauthors was available to perform the autopsies. In the 762 cases selected for detailed examination, the heart was weighed after removal of cavitary blood clots and the aorta (2.5 cm from the sinotubular junction). Heart weight was normalized for body weight as defined previously by Kitzman et al.12

Risk Factor Analysis

The postmortem evaluation of total cholesterol (TC), HDL cholesterol (HDL-C), glycohemoglobin for diabetes, and thiocyanate as a marker for cigarette smoking was performed as previously described.8 In every case, the available history was used as corroboration of autopsy determination of risk factors. Hypertension was considered present if either postmortem kidney evaluation was positive or if there was a clinical history. Type 1 diabetes was presumed if there was insulin dependence and body mass index <25 kg/m²; type 2 diabetes was based on glycosylated hemoglobin >8% in the absence of type 1 diabetes.

Statistical Analysis

An adjusted rate of SCD in the inspection cases was estimated by a sampling of autopsied cases because not all cases of sudden unexpected death presumed to be of cardiac origin by inspection prove to be of coronary origin by complete autopsy.7 For the purposes of this study, the rate of SCD was estimated as the sum of adjusted inspection cases and the autopsied cases. For each age decade (30 to 39, 40 to 49, 50 to 59, and 60 to 69 years), the rates of SCD were calculated for the following 4 groups: black men, white men, black women, and white women. The rate of SCD was determined for 100 000 population/y by means of population statistics from the census bureau for the state of Maryland (www.census.gov/population/estimate), which are given by age, race, and sex. For univariate analysis to compare risk factors among groups, χ² contingency tables for categorical and ANOVA means tables with Fisher’s post hoc test for continuous variables were used. Logistic regression was used to determine associations between risk factors and the presence of coronary disease. The dependent variables (stable plaque, plaque rupture, or plaque erosion versus control subjects) were analyzed with independent continuous (age, body mass index) and noncontinuous variables (smoking, hypertension, diabetes, elevated TC, top tertile, and decreased HDL-C, lowest tertile). All control subjects (cardiovascular deaths and noncardiovascular deaths) were included for univariate and multivariate analysis for risk factors other than hypertension and left ventricular hypertrophy. When hypertension was a variable for risk factor association, the analysis was repeated excluding the cardiomyopathy control subjects; when left ventricular hypertrophy was a variable for risk factor association, the analysis was repeated excluding both the cardiomyopathy and valve disease control subjects.

Results

Estimates of Overall Rates of SCD

The rate of severe coronary disease in the 762 natural deaths caused by cardiovascular diseases was 67% for whites and 47% for blacks. These population-adjusted rate of SCD
increased with advancing age (Figure 1). The rate for blacks was consistently higher in each group (Figure 1).

Rates of SCD by Presence or Absence of Thrombus

In the 457 cases of SCD, there were 327 whites and 130 blacks (Table 1). There was no racial difference in the rate of acute thrombi, but ruptures were more frequent in whites (Table 1). The frequency of acute thrombosis decreased with advancing age (60% in the 4th decade, 60% in the 5th decade, 45% in the 6th decade, and 30% in the 7th decade). When the percentage of the type of thrombus was applied to the rate of total SCD by race and sex, the rate of thrombus was similar in both races, but the rate of death with stable plaque was higher in blacks (Figures 2 and 3).

Racial Differences in Heart Weights, Plaque Burden, and Frequency of Healed Infarcts in SCD

When all cases of SCD were considered, there was no significant difference in adjusted mean heart weight by race (Table 1). When analyzed by age at the time of death, the adjusted heart weight of all cases of SCD increased from the 4th to the 7th decade (412±88 g, 450±86 g, 485±121 g, 527±111 g, respectively, P<0.0001). The overall mean plaque burden and incidence of healed infarcts were similar in whites and blacks (Table 1). There were no racial differences in plaque burden when assessed by decade (Figure 4) or when stable plaque was studied separately (231±81% in blacks, 226±82% in whites; P=0.7).

Risk Factor Profiles, SCD Versus Control Subjects: Whites and Blacks

Figures 5 and 6 demonstrate the univariate relation between risk factors and plaque types (stable plaque, plaque rupture, plaque erosion, and control subjects) stratified by race. Patterns of association between risk factors and mechanism were similar in blacks and whites. In both races, stable plaque was associated with hypertension and diabetes mellitus; acute thrombus with cigarette smoking; and plaque rupture with...
low HDL-C and high TC. TC was significantly elevated over control subjects in stable plaque only in blacks.

**Odds Ratios, SCD Versus Control Subjects: Whites and Blacks**

Odds ratios were calculated for the likelihood of elevation of each risk factor in each SCD group as compared with control subjects (Table 2). For stable plaque, left ventricular hypertrophy demonstrated the strongest association, with stable plaque in blacks and type 1 diabetes in whites. For stable plaque, hypertension was a significant risk factor in blacks but not whites, and elevated TC was a significant risk factor in blacks but not whites. For plaque rupture, elevated TC was the strongest risk factor in whites and blacks, with an especially high odds ratio in blacks (20:1). For plaque erosion, smoking was the strongest risk factor in blacks and whites, and in whites only, elevated TC was an independent risk factor for erosion.

**Discussion**

**Incidence of SCD: Blacks Versus Whites**

The current study demonstrates that the rate of SCD in black men and women is greater than in whites in the 6th and 7th decades. The rates of SCD caused by coronary thrombus are fairly similar in both races; the increase in blacks is due largely to an increase in deaths with stable plaque. The majority of SCD in blacks caused by stable plaque are associated with left ventricular hypertrophy and hypertension. The data suggest that blacks do not have an inherent increased risk for premature SCD before the age of 50 years, nor do they have an increased risk for the development of fatal coronary thrombosis.

**Left Ventricular Hypertrophy, Hypertension, and Blacks Dying With Stable Coronary Plaque**

Because of an increase in death caused by stable plaque, there is a relative increase in the incidence of sudden death in blacks compared with whites after the age of 50 years. When the data in the current study are analyzed, it is not apparent that the mechanism of sudden death differs fundamentally by race because the mean heart weight and frequency of cardiac scars are similar in blacks and whites dying with stable plaque. We have shown previously that thin-cap atheromas are less frequent in blacks than in whites, probably because acute ruptures represent a smaller proportion of SCD in blacks. The current study demonstrates that the actual rate of acute ruptures is similar in blacks and whites and that the smaller proportion of ruptures in blacks is secondary to an increase in the rate of SCD caused by stable plaque. The data in the current study showing no difference in plaque burden in SCD between blacks and
whites are consistent with angiographic studies, which have shown only modest increases in plaque burden in blacks compared with whites after acute myocardial infarction. The current study suggests that the reportedly high rates of SCD in blacks may be largely due to the high prevalence of hyper-tension. The high relative risk of blacks with hypertension and increased heart weight in patients dying with stable plaque complement findings of Liao et al., who have shown that among blacks hospitalized for acute coronary syndromes, left ventricular hypertrophy is a more important predictor of death than degree of coronary stenosis.

**Risk Factor Prevalence in SCD: Blacks and Whites**

In addition to hypertension and left ventricular hypertrophy, prior studies have shown that black patients with symptomatic coronary heart disease have a higher prevalence of diabetes and tobacco use. Although the current study shows that blacks dying with severe coronary atherosclerosis have a higher rate of diabetes versus whites when those dying with stable plaque or plaque rupture are considered, the increase is modest and not statistically significant. The lack of significant increase in dia-

**Risk Factors and Relation to Fatal Thrombus: Blacks and Whites**

The current data show an overall similarity of the risk factors profiles in blacks and whites when specific mechanisms of SCD are considered. The association between acute fatal plaque rupture and increased cholesterol is even more marked in blacks than in whites. The relatively high odds ratios for LDL lipoprotein levels and plaque rupture in blacks are reflected by the fact that HDL levels are elevated in all groups of blacks over whites, including control subjects, except for the group dying with plaque rupture. The association in blacks between plaque erosion and cigarette smoking is not as strong as in whites, suggesting that other factors may be more important in blacks for the pathogenesis of plaque erosion than in whites. Because TC is an independent risk factor for SCD caused by stable plaque in blacks and not in whites, the lowering of TC should be a major target of risk factor control in blacks.

**Limitations**

Because the autopsy rate was <25% in reported sudden death cases >50 years of age, the data in the older decades may be less likely to reflect the true rate of coronary deaths. However, the sample demonstrated that the rate of coronary disease in sudden unexpected natural deaths was lower in blacks than in whites, and the estimate of coronary deaths in the nonautopsied sample was adjusted to reflect this finding. Therefore, even though the true incidence of coronary disease in unexpected deaths in older men and women must remain an estimate because complete autopsies on all such cases is impossible, we believe that the current estimate is useful in comparing coronary deaths that are unexpected in whites and blacks. Further limitations include the fact that methods of determining risk factors were limited to a single collection at postmortem examination; duration of risk factor exposure was generally not available; and full information regarding risk factor modification (eg, aspirin and statin use) was not obtained. However, despite the relatively small numbers of patients in some strata and wide confidence intervals shown in Table 2, the detailed autopsy evaluation provides insights not possible in larger controlled studies based on death certificate data. Other limitations inherent in the study design are the case-control nature of the autopsy study, the fact that only a small portion of total deaths could be analyzed, resulting in selection bias, and the fact that generalizations to other populations are impossible. Also, control subjects included cardiovascular and noncardiovascular deaths because limiting control subjects to trauma deaths was not feasible.
Conclusions
Rates of SCD are similar in blacks and whites in the 4th decade; in later decades, there is an increasing gap, with a higher rate in black men and women. Excess deaths in blacks are largely due to an increase in deaths with stable plaque and left ventricular hypertrophy. Our data emphasize the importance of early diagnosis and proper control of hypertension and increased left ventricular mass, hypercholesterolemia, and diabetes, which probably would reduce the incidence of SCD in blacks.

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References
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