Blacks in the Coronary Artery Surgery Study: risk factors and coronary artery disease

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ABSTRACT In this paper we examine the relationship between risk factors and angiographically determined coronary artery disease for blacks and whites enrolled in the Coronary Artery Surgery Study (CASS). Analysis of data from the CASS registry indicated that blacks had a higher incidence of hypertension and current cigarette smoking than did whites in CASS and that chest pain was the major reason that both blacks and whites underwent coronary angiography for suspected or proven coronary disease. The CASS data also showed that, despite high levels of risk factors and chest pain, blacks had minimal or absent coronary disease. The results of this study raise several questions. First, to what extent are blacks in CASS representative of (1) blacks in the general population and (2) blacks undergoing coronary angiography? Additionally, are risk factors for coronary artery disease different for blacks than for whites? And finally, how does the physician effectively treat the black patient with high levels of risk factors and minimal coronary disease?


THE RELATIONSHIP between risk factors and coronary artery disease (CAD) has been the subject of numerous investigations.1–6 The established, independent risk factors for CAD include cigarette smoking, hypertension, hypercholesterolemia, low high-density lipoprotein cholesterol (HDL), diabetes mellitus, electrocardiographic abnormalities, age, sex, and type A behavior patterns.5 Other less well-established risk factors are obesity, physical inactivity, hypertriglyceridemia, hyperuricemia, psychosocial stress, and low socioeconomic status.6 It is important to realize that these risk factors have been established for white populations and may not be as relevant for black populations. It has been difficult to establish risk factors for blacks because there have been so few prospective or even retrospective studies of the incidence of CAD in blacks.7–8 Nevertheless, there is considerable information available on the prevalence of potential risk factors in black populations.9–15

The objectives of this article are (1) to examine the distribution of risk factors in blacks and whites in the Coronary Artery Surgery Study (CASS) patient population and (2) to examine the CASS population the relationship between race and the presence and extent of CAD.

Methods

Patients. Data analyzed for this study come from the CASS registry,16 which contains extensive demographic, clinical, and angiographic information on all consecutive individuals, who, having given informed consent for both angiography and data collection, underwent coronary angiography for suspected or proven CAD. Between July 1974 and May 1979, the CASS enrolled patients from 14 clinics in the United States and one in Canada. This analysis includes 23,581 of the 24,959 patients who were enrolled in CASS. Patients with previous bypass surgery and/or those of races other than black or white were not included in the analysis.

Study variables in CASS. Numerous demographic, clinical, and angiographic variables were recorded at baseline. Demographic variables included age, sex, race, employment status, and occupation. The observed race was recorded as "white," "black," or "other," with the choice of category being left to the interviewer. Employment status referred to the amount of time the patient was working at baseline; the categories included (1) full time, defined as 40 hr or more per week, (2) part time or less than 40 hr per week, (3) retired or stopped working when retirement age was reached, (4) quit or forced to quit before retirement age because of cardiac symptoms, with or without the recommendation of a physician, and (5) other or currently unemployed (by economic circumstances or choice), on temporary sick leave, or disabled secondary to noncardiac illness.

Occupation was categorized as (1) manual, defined as work that includes routine performance of heavy manual labor and/or physical exertion, (2) clerical, defined as any form of employment not regularly associated with heavy manual labor that does not involve stressful decision making responsibility, (3) professional, defined as work that requires advanced training and involves mental rather than physical tasks, as well as a definite
amount of stress and responsibility associated with decision making, (4) homemaker, defined as tasks associated with the management of a household, and (5) other, defined as any occupation that does not meet the above criteria.

Information concerning the three major risk factors was collected. Current smoking was defined as continued smoking within 3 months of entry into the study. Systolic and diastolic blood pressures were recorded on the initial physical examination at the time of study entry. Elevated blood pressure was defined as a systolic reading of 160 mm Hg or greater and/or a diastolic reading of 95 mm Hg or greater. For those receiving medications, blood pressure readings were taken while patients were on medications. Serum cholesterol level was measured at initial physical examination. Since the analysis of serum cholesterol was not a primary goal of the study and was recorded only if done clinically, no attempt was made to control the laboratory analysis at cooperating clinics aside from the standards imposed by the Joint Commission on the Accreditation of Hospitals. Consequently, not all patients in CASS had serum cholesterol analyzed. For those who did have the analysis, elevated serum cholesterol was defined as a reading of 260 mg/dl or higher.

Information on other risk factors was collected. This included early family history of CAD, defined as angina or myocardial infarction in parents, siblings, or aunts and uncles related by blood before the age of 55 years. History of diabetes, history of congestive heart failure, and history of hypertension were noted, as was the presence of an enlarged left ventricle or abnormal left ventricular contour on chest roentgenogram. Also, the existence of a prior myocardial infarction as reported by the patient and documented by medical record was noted. The Quetelet index of relative body weight or the ratio of weight divided by the square of height (kg/cm²) was calculated. Finally, the level of daily recreation and/or physical activity during the 3 months before enrollment was assessed.

In addition to assessment of risk factors, information related to clinical and angiographic indicators of CAD was obtained. The presence of chest pain was noted; the likelihood that the chest pain was angina was evaluated as definitely not, probably not, definite, or probable. The limitation of activity due to chest pain was measured by the Canadian Cardiovascular Society classification, and the presence of unstable angina was recorded. The predominant symptom of the disease was reported as angina, congestive heart failure, asymptomatic, arrhythmia, or other, and the functional impairment due to congestive heart failure was evaluated.

Also, several measures of the extent of CAD and left ventricular function were obtained. The number of diseased vessels, a measure of the extent of coronary disease based on interpretation of the coronary arteriogram, was calculated. The left ventricular wall motion score, a measure of segmental left ventricular function based on interpretation of the left ventriculogram filmed in the right anterior oblique projection, was also determined. The score comprised individual assessments from five defined regions and ranged from 5 (totally normal) to 30 (never observed, the whole heart aneurysmal). Finally, the presence of a 50% or greater stenosis in the left main coronary artery (LMCA) was indicated, as was the dominance of the coronary circulation.

Statistical methods. Risk factors are reported in percentages and means by sex and race. The chi-square test was used to test for statistical differences for categorical variables, and the t test was used to test for statistical differences for continuous variables.

Multivariate statistical methods were used to identify those risk factors that best predicted whether an individual had a 70% or greater stenosis in one or more of the three major coronary arteries. Stepwise linear discriminant analysis was used to distinguish the diseased from the nondiseased group. To determine whether race was a significant, independent predictor of CAD, at the first level all risk factors but race were allowed to compete for entry. Then, once variables with the most predictive power were selected, at the second level race was permitted to enter the model.

Results

Distribution of risk factors in CASS. The prevalence of risk factors in the CASS patient population is reported in table 1 by race and sex. With respect to demographic factors, the 573 blacks in CASS were younger and had a higher percentage of women than did their 22,781 white counterparts. The percentages of blacks and whites working full or part time were roughly the same, although a slightly lower percentage of blacks was retired, and a slightly higher percentage of blacks was forced to quit work because of CAD. The racial differences for occupation were much more apparent; two-thirds of black men in CASS were laborers, whereas only 40% of white men were employed in manual labor. Almost 30% of white men were employed in professional positions, whereas only 8.8% of black men were employed in such positions. The findings for women were also striking in that 26.7% of black women were employed as laborers, yet only 10.6% of white women were doing this kind of work. On a percentage basis, slightly more black than white women were employed in professional positions, yet a much higher percentage of white women were listed as homemakers.

In looking at the three major risk factors of current cigarette smoking, elevated blood pressure, and elevated serum cholesterol, it is apparent from table 1 that higher percentages of both black men and women were current smokers and had elevated blood pressure. Almost 50% of black men were current smokers, whereas 30.6% of white men were current smokers (p < .0001). However, white men were heavier smokers (p = .0002). A similar pattern held for black women, who were more likely to smoke but did not smoke as heavily as white women. Racial differences with respect to elevated blood pressure were also apparent; 24.5% of black men and 20.0% of black women were hypertensive, whereas 16.1% of white men and 16.0% of white women were found to be hypertensive. However, only the difference between black and white men was statistically significant. On the other hand, racial differences with respect to serum cholesterol were not statistically significant.

The distribution of other risk factors was also investigated. From table 1, it is evident that a lower percentage of blacks reported an early family history of angina.
or myocardial infarction. Very high percentages of both black men and women reported a history of hypertension (56.8% and 65.7%, respectively). A higher prevalence of diabetes mellitus, a higher relative body weight, and a higher prevalence of congestive heart failure at baseline were also characteristics of blacks in CASS, although the last difference applied only to black women. On the other hand, white men had a higher rate of prior documented myocardial infarction (44.0% vs 38.2%; \( p = .03 \)) than did black men, yet there was no difference between rates for black and white women. A higher percentage of both black men and women had abnormal left ventricles on chest roentgenogram (\( p = .02 \) for both men and women). Finally, there appeared to be no significant differences in the level of recreational activity for blacks and whites.

**Clinical and angiographic findings in CASS.** Clinical and angiographic information concerning symptoms, limitation of activity, functional impairment, presence of CAD, and left ventricular dysfunction are presented in table 2. It was evident and expected that the presence of chest pain was the major reason why blacks and whites were studied angiographically. More specifically, angina was the predominant symptom in over 80% of both blacks and whites. However, only 62.8% of black men and 46.7% of black women had probable or definite angina, whereas 76.1% of white men and 64.3% of white women had probable or definite angina (\( p < .0001 \) for both men and women). Of those who had probable or definite angina, the severity of angina by sex did not differ appreciably according to race. Finally, the presence of unstable angina was similar in all four groups.

Of considerable interest were the results of coronary arteriography, also presented in table 2. Examination of the number of diseased vessels indicated that blacks of both sexes had considerably less CAD than did their
white counterparts (p < .0001 for men, p = .003 for women). In fact 47.0% of black men and 67.3% of black women had normal or minimally diseased coronary arteries, whereas only 19.7% of white men and 54.5% of white women had normal coronary arteries or minimal disease (zero-vessel category). Three-vessel disease was most prevalent in white men (32.8%) but was equally distributed in black and white women (11.5% vs 14.6%). It was also apparent that black men had a lower prevalence of LMCA disease than did white men; white men had over four times more LMCA disease than did black men (p < .0001), and white women had over two times that of black women, although the difference was not statistically significant. A higher percentage of blacks had normal left ventricles than did whites (p = .007 for men, p = .04 for women), although racial differences for more severely impaired left ventricles were not apparent. Finally, black men were more likely to have left-dominant coronary circulation than were white men (p = .03).

**Multivariate analysis.** To more fully examine the relationship between race and CAD, multivariate analysis was employed. The results of this analysis are reported in table 3; two types of F statistics are reported, the univariate F ratio and the F for when the variable entered the linear model. With the risk factors listed in table 1 (history of prior myocardial infarction and congestive heart failure were omitted), linear discriminant analysis was used to identify the predictors of CAD, which was defined as one or more diseased vessels. All variables with the exception of race were allowed to compete for entry, with the result that male sex, increasing age, elevated cholesterol, current or former smoking, history of diabetes, family history of CAD, nonlaborer occupation, sedentary recreational activity, lack of full or part time employment, and history of hypertension were associated with one or more diseased vessels. When all of these variables had entered the model, race was then allowed to enter. For the 17,726 individuals who had known data for variables used in the multivariate analysis, being black was asso-
TABLE 3
Results of stepwise linear discriminant analysis

<table>
<thead>
<tr>
<th>Step</th>
<th>Variable</th>
<th>Univariate F ratio</th>
<th>F ratio at point of entry</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1</td>
<td>Sex</td>
<td>2291.34</td>
<td>2291.34</td>
</tr>
<tr>
<td>2</td>
<td>Age</td>
<td>866.76</td>
<td>1158.66</td>
</tr>
<tr>
<td>3</td>
<td>Elevated cholesterol</td>
<td>193.64</td>
<td>304.96</td>
</tr>
<tr>
<td>4</td>
<td>Smoking status</td>
<td>236.49</td>
<td>275.47</td>
</tr>
<tr>
<td>5</td>
<td>Hx diabetes</td>
<td>42.92</td>
<td>51.36</td>
</tr>
<tr>
<td>6</td>
<td>Fam Hx angina, MI</td>
<td>5.35</td>
<td>47.67</td>
</tr>
<tr>
<td>7</td>
<td>Laborer</td>
<td>47.81</td>
<td>47.02</td>
</tr>
<tr>
<td>8</td>
<td>Recreational activity</td>
<td>4.41</td>
<td>27.81</td>
</tr>
<tr>
<td>9</td>
<td>Full or part time employment</td>
<td>94.10</td>
<td>18.59</td>
</tr>
<tr>
<td>10</td>
<td>Hx hypertension</td>
<td>3.05</td>
<td>10.49</td>
</tr>
<tr>
<td>11</td>
<td>Race^</td>
<td>122.27</td>
<td>59.54</td>
</tr>
</tbody>
</table>

Fam. Hx = family history; MI = myocardial infarction.

^Race entered at second level, where it was first considered, after all other variables were allowed to enter if statistically significant.

TABLE 4
Variables in linear discriminant analysis models for predicting the presence of significant coronary artery disease in blacks and whites

<table>
<thead>
<tr>
<th></th>
<th>Blacks</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Zero-vessel disease</td>
<td>One or more vessels</td>
</tr>
<tr>
<td></td>
<td>(n = 311)</td>
<td>(n = 260)</td>
</tr>
<tr>
<td>Age (mean)</td>
<td>46.0 ± 9.3 yr</td>
<td>51.8 ± 8.9 yr</td>
</tr>
<tr>
<td>Female</td>
<td>45.3%</td>
<td>26.2%</td>
</tr>
<tr>
<td>Cholesterol &gt;260 mg/dl (n)</td>
<td>12.4%</td>
<td>30.9%</td>
</tr>
<tr>
<td></td>
<td>(202)</td>
<td>(165)</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>37.3%</td>
<td>18.5%</td>
</tr>
<tr>
<td>Former</td>
<td>20.9%</td>
<td>29.2%</td>
</tr>
<tr>
<td>Current</td>
<td>41.8%</td>
<td>52.3%</td>
</tr>
<tr>
<td>Hx diabetes</td>
<td>11.6%</td>
<td>22.7%^</td>
</tr>
</tbody>
</table>

|                  | Whites                       |                     |
|                  | Zero-vessel disease          | One or more vessels |
|                  | (n = 6495)                   | (n = 16,473)        |
| Female           | 47.2%                        | 15.5%               |
| Age (mean)       | 49.9 ± 9.6 yr                | 54.2 ± 8.9 yr       |
| Cholesterol >260 mg/dl (n) | 17.4%          | 27.1%              |
|                  | (5021)                       | (16,473)           |
| Smoking status   |                              |                    |
| Never            | 37.0%                        | 19.6%              |
| Former           | 31.0%                        | 47.6%              |
| Current          | 32.1%                        | 32.8%              |
| Fam. Hx angina, MI | 44.3%                  | 43.3%^             |
| Hx diabetes      | 7.4%                         | 11.2%              |

Fam. Hx = family history; MI = myocardial infarction.
All comparisons p < .0001 except as follows: ^p = .001; ^p = .38, but significant in the multivariate model.

Discussion
These results from CASS indicate that both black men and black women studied angiographically have high levels of risk factors. In comparison to their white counterparts, black men had a higher prevalence of elevated blood pressure, were more likely to have been treated for hypertension and diabetes, and were more likely to be current cigarette smokers, although they did not smoke as heavily. Black women, when compared with white women, were also found to have a higher prevalence of age-adjusted elevated blood pressure and were also much more likely to have reported a history of hypertension or diabetes. However, when current cigarette smoking was adjusted for age, black and white women in CASS exhibited comparable rates of current smoking, although white women were heavier smokers. On the other hand, both white men and women had a greater family history of CAD. These data clearly indicate that in CASS, black men and women exhibited higher levels of modifiable risk factors than did white men and women. However, it is important to recognize that blacks were younger than whites in CASS and that this reduced their level of risk.

Whereas both blacks and whites presented with chest pain as their chief complaint, in almost half of black men and two-thirds of black women, no significant coronary disease could be found to account for this chest pain. This paradox of relative youth, high levels of risk, and evidence of minimal disease for blacks has been noted previously.10, 13, 14, 20 However,
most studies have used CAD mortality and morbidity as end points and have not used arteriographic indexes as measures of CAD. Pearson et al.11,21 used arteriographic measures of CAD in blacks and found the extent of disease to be similar in blacks and whites. After adjustment for relevant clinical characteristics as well as risk factors, Oberman and Cutter20 reported that whites were three times as likely to have disease in two or more vessels than were blacks.

Some have suggested the presence of protective factors that might explain this paradox.10 These protective factors include higher levels of HDL, higher work exercise levels, lower triglyceride levels, higher alcohol intake, lower prevalence of type A personality, and a genetic disposition that protects blacks from coronary atherosclerosis. Since HDL concentrations were not obtained and since alcohol consumption was not measured, it was not possible to evaluate their protective function in CASS. Although triglycerides were much lower for blacks in CASS than for whites, the fact that measurements were obtained in less than half of the blacks made it difficult to evaluate the usefulness of the association with risk of CAD. It is possible that blacks may have benefited from the physical activity associated with manual labor. Since measures of type A behavior and psychosocial stress were not available in CASS, it was not possible to evaluate their protective features for blacks.

Given the high levels of risk factors for blacks in CASS, it is difficult to explain the low levels of CAD. It is possible that increased risk due to hypertension and cigarette smoking resulted in death caused by stroke and cancer, which in turn may have precluded blacks from being studied for coronary atherosclerosis. Moreover, the risk factors relevant for whites may not be so for blacks, although in CASS the risk factors for the two groups were similar. Again, unmeasured factors may have protected blacks from their high levels of risk. The conclusion, however, is that in CASS, for whatever reasons, being black was associated with the absence of atherosclerotic disease.

It is possible that differential selection of patients for angiography at the 14 CASS clinical sites that enrolled blacks may have resulted in a biased sample of disease-free blacks. To determine whether this was the case, clinical sites that enrolled at least five black patients were ranked with respect to the percentage of normal (zero-vessel disease) black and white patients studied. The order of ranks for blacks and whites did not differ substantially. The site that had the highest percentage of white normals also had the highest percentage of black normals, whereas the institution that had the lowest percentage of white normals had the third lowest percentage of black normals. In each and every CASS clinic, blacks had a lower percentage with CAD. Additionally, stepwise linear discriminant analysis with the variables in table 3 and indicator variables for each clinic as possible predictors of disease in one or more vessels was performed. As expected, the populations at the individual clinics did differ in that seven CASS clinic indicator variables entered the model. However, race was still a significant predictor of coronary disease (F = 54.2) as it was in the analysis reported in table 3 (F = 59.5).

It is also possible that differential ascertainment of atherosclerosis among clinics because of technical differences in the recording, filming, and reading of films may account for black-white differences in CASS. This is an unlikely occurrence, given that CASS had an ongoing quality-assurance program for angiographic technical quality and interpretation.16,22,27 In this program, agreement between readers on the number of diseased vessels was 72.1% of 870 films. The films of 13 blacks were included in this program; quality-control readers were blinded to the original reading and patient information (including race). In 10 of 13 films (76.9%), the original and quality-control readers exhibited agreement on the number of diseased vessels.

Although there did not appear to be differential institutional selection for blacks with respect to disease, the contention that this is a biased sample of blacks cannot be disproved. In at least one sense, the blacks in CASS were exceptional; data from the National Center for Health Statistics indicate that the ratio of cardiac catheterization among whites to blacks is 1.7 (1.93 per 1000 vs 1.15 per 1000).24 It is evident that blacks are less likely to be included in data registries of patients who have undergone coronary arteriography. For example, blacks constituted only 2.4% of the CASS patient population and only 4.2% of the University of Alabama registry.26 In CASS, one clinic enrolled no black patients, and in four clinics blacks constituted 1% or less of the enrollees. In the remaining 10 clinics, the percentages of blacks ranged from 1.6% to 7.7%.

Yet, in other ways, the blacks in CASS may not be different from other blacks. A comparison of the distribution of the three major risk factors for blacks in CASS and the Second National Health and Nutrition Examination Survey19 (NHANES) indicates that these two groups were very similar with respect to risk for CAD. In addition, the occupational distribution of blacks in CASS, characterized by a high percentage of male laborers and working mothers, is probably similar to that of U.S. blacks of the same age. It is likely
that blacks in CASS had health insurance to cover the cost of angiography. Unfortunately, income and health insurance data were not obtained in CASS, so it was not possible to evaluate the influence of these factors in defining the black population in CASS.

In examining the relationship between risk factors and CAD in CASS, Vlietstra et al. have raised a number of important issues that should be considered in the current context. First, it is important to realize that the indicator of CAD employed in this study is angiographic as opposed to clinical. Second, the data on risk factors were obtained shortly before angiography and might not truly reflect the patient’s condition in the months and years before angiography. For example, laboratory values (serum cholesterol) and clinical history data were taken only at one point in time and may not be representative of the patient’s level of risk. However, the estimates of risk level do accurately represent the data available to physicians evaluating the likelihood of CAD in patients with chest pain. Third, there was no standardization of cholesterol readings, and in a sizeable percentage of patients cholesterol readings were not obtained. Additional discriminant analyses of the relationship between risk factors and CAD indicated that the most important risk factors did not change for either blacks or whites when cholesterol was not included in the analyses. Fourth, as has been mentioned, other important risk factors such as type A personality and HDL were not evaluated. Fifth, it is important to realize that this was a select group of patients who had chest pain and underwent angiography for its evaluation. Finally, we may have missed blacks as well as whites with CAD, who, because of other manifestations of the disease (e.g., myocardial infarction and sudden death) or because of death from other conditions (e.g., stroke or cancer), were not available for angiography.

It is relevant to consider the clinical importance of some of the findings of this study. First, further efforts must be made to reduce cigarette smoking and to control hypertension in the black population. There is evidence from NHANES that from 1971 to 1980 blacks did reduce cigarette smoking and were better able to control their hypertension. The results from NHANES are encouraging, but the fact that six of 10 black women and seven of 10 black men have one or more risk factors indicates that innovative efforts are required to make these numbers more favorable. Second, it is apparent that the diagnosis and treatment of the black patient with chest pain can be problematic in that many blacks have chest pain despite having normal coronary arteries. The finding of normal coronary arteries may lend a false sense of reassurance to both doctor and patient. Understanding of the etiology of chest pain in blacks is required. Some have hypothesized that there may be a differential incidence of coronary vasospasm in blacks, although no studies to date have reported this. Others have noted the existence of blacks with angina pectoris, marked left ventricular hypertrophy, and normal coronary arteries and have emphasized aggressive control of hypertension as the key to effective treatment. Studies of predominantly black populations from different regions of the country are needed to clarify these findings from CASS, as well as those from other large clinical trials. Such studies would provide much needed knowledge of the epidemiology and effective treatment of coronary disease in blacks.

Appendix

Cooperating Clinical Sites


Central Electrocardiographic Laboratory
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Coordinating Center
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Chairman of the Steering Committee
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National Heart, Lung, and Blood Institute
Eugene R. Passamani, M.D., Thomas Robertson, M.D., Charles Hollingsworth, Dr. P.H., and Peter Frommer, M.D.

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