A Case-Control Study of Baldness in Relation to Myocardial Infarction in Men

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Objective.—To examine the relationship between male pattern baldness and the risk of myocardial infarction in men under the age of 55 years.

Design and Participants.—A hospital-based, case-control study was conducted in eastern Massachusetts and Rhode Island. Cases were men admitted to a hospital for a first nonfatal myocardial infarction (n=665); controls were men admitted to the same hospitals with noncardiac diagnoses (n=772). Extent of baldness was assessed using the 12-point modified Hamilton Baldness Scale; other information was obtained by personal interview. Among the controls, the prevalence of any baldness was 34%, while the prevalence of baldness involving the vertex scalp was 23%.

Results.—After allowing for age, the relative risk estimate for frontal baldness compared with no hair loss was 0.9 (95% confidence interval, 0.6 to 1.3), for baldness involving the vertex scalp it was 1.4 (95% confidence interval, 1.2 to 1.9). Risk of myocardial infarction increased as the degree of vertex baldness increased (P<.01); for severe vertex baldness the relative risk was 3.4 (95% confidence interval, 1.7 to 7.0). The relationship between vertex baldness and myocardial infarction was consistent within strata defined by age and other risk factors for coronary artery disease.

Conclusion.—These data support the hypothesis that male pattern baldness involving the vertex scalp is associated with coronary artery disease in men under the age of 55 years.

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THE HYPOTHESIS has been raised that male pattern baldness (MPB) is a predictor of cardiovascular disease in men.1-3 Both baldness and coronary artery disease are more common in men than in women and circulating androgens, levels of which increase as high-density lipoprotein cholesterol levels decrease at puberty in men, are required for the expression of the inherited baldness trait.4

Minoxidil is a potent antihypertensive agent when taken systemically, and a number of serious side effects have been reported (eg, pericardial effusion, tachycardia, exacerbation of angina pectoris, and in laboratory animals, myocardial hemorrhage and papillary muscle necrosis).5-7 When applied topically, minoxidil stimulates thickening and pigmentation of the fine velus hairs on a proportion of the scalps of bald men. Because of this effect, the drug is used to treat MPB. If MPB is itself a predictor of cardiovascular disease, including myocardial infarction (MI), a higher incidence of MI or cardiovascular complications among topical minoxidil users relative to nonusers might be attributed to the drug when, in fact, MPB accounts for the difference. For this reason, it is important to ascertain whether baldness itself is an independent risk factor for cardiovascular disease. Reports in the literature examining the relationship of baldness to cardiovascular disease are insufficient to answer the question.

To test the hypothesis that MPB is related to the risk of first MI, we conducted a hospital-based, case-control study of incident MI among men under 55 years of age.

METHODS

Data Collection

The data were collected from January 1989 through May 1991 from men aged the age of 55 years who were admitted to 35 hospitals in eastern Massachusetts and Rhode Island. Each week, our office staff contacted the coronary care units of these hospitals to identify potential cases of first MI. The attending physician of each potential case was contacted by telephone to confirm the diagnosis of first MI and obtain permission to conduct an interview. Men admitted to the same hospitals for noncardiac diagnoses served as controls.

Data were collected by nurses, specially trained in interviewing techniques, using a structured questionnaire. Ninety percent of the data were collected by three nurses who each interviewed both cases and controls. The recorded data included descriptive factors (ie, age, race, weight, height, number of years of education, and occupation; past medical history; risk factors for MI [ie, history of physician-diagnosed and medically treated hypertension, angina, diabetes, and hypercholesterolemia]; history of MI in a first-degree relative; use of tobacco and alcohol; exercise; and personality score†); and medication use. The patient’s assessment of extent of baldness was recorded using both the Hamilton Baldness Scale (HBS) as modified by Norwood (Figure) and a continuous five-point scale (a score of 1 indicating no hair loss, and an extreme baldness). The interviewer’s assessment of extent of baldness according to the HBS was also recorded.

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The Hamilton Baldness Scale as modified by Norwood.

Because of short hospital stays, eligible patients were sometimes discharged before we could reach them and conduct an interview. In these instances, the patients were interviewed by telephone. Such men were mailed a copy of the HBS for use during the interview. In a few instances in which the patient was contacted in person by an interviewer but the interview could not be scheduled until after discharge (six cases, 19 controls), the interviewer's assessment of baldness was recorded when consent was obtained.

Cases

The cases were men 21 to 54 years of age who had been admitted to a hospital for a first MI and who had no prior history of rheumatic heart disease, cardiomyopathy, or cardiac surgery. Seven hundred thirty-four men were interviewed; this represents a participation rate among eligible cases of 84%. Four hundred ninety-five cases were interviewed in the hospital, and 229 were interviewed by telephone. Discharge summaries were reviewed for 708 (96%) of the cases; the diagnosis of a first MI was confirmed for 648 (92%). Patients were excluded from analysis for the following reasons: (1) history of prior MI (12 cases); (2) no discharge diagnosis of MI (12 cases); (3) a discharge diagnosis of MI but insufficient documentation to meet World Health Organization criteria for the diagnosis (ie, pathologic Q waves with evolution, elevated cardiac enzyme levels together with a typical history of chest pain, or elevated cardiac enzyme levels together with diagnostic electrocardiographic changes with evolution) (36 cases); and (4) history of prior treatment for baldness (nine cases). This left a total of 665 cases for analysis; the median age of the cases was 47 years.

Controls

The nurses interviewed as potential controls men from 20 to 54 years of age who had been admitted for noncardiac diagnoses to the general medical-surgical floors of the same hospitals as the cases. Men with a history of MI, rheumatic heart disease, cardiomyopathy, or cardiac surgery were excluded from the control series. Subjects with a history of angina without prior MI, however, were not excluded. Seven hundred eighty-one controls were interviewed; this represents a participation rate of 84% among eligible patients. Seven hundred fifty-eight controls were interviewed in the hospital, and 23 were interviewed by telephone. Controls were excluded from analysis for the following reasons: (1) history of a prior MI reported on the discharge summary (one patient); (2) history of prior treatment for baldness (seven patients); and (3) the subject's responses were judged by the interviewer to be unreliable (one patient). This left a total of 772 controls for analysis; the median age of the controls was 45 years. The reasons for hospital admission are as follows: (1) trauma or musculoskeletal conditions (289); (2) gastrointestinal disorders (218); (3) infectious diseases (125); (4) genitourinary diseases (62); and (5) other conditions (89).

Measures of Baldness

Extent of baldness among 772 controls as assessed by the patient is shown in Table 1. The prevalence of any baldness (category IIa or greater on the HBS) was 34%, and vertex baldness (categories III vertex, IV, and V through VII) was 23%. The latter figure is in quite good agreement with Norwood's report6 of the incidence of MPB using the same instrument to classify hair loss. Agreement between the patient's and interviewer's assessments of extent of baldness among the controls was good ($\kappa = 0.74$).
The distributions of selected risk factors for coronary artery disease and the patient's assessment of baldness according to type of interview (in-person or telephone) among the cases are shown in Table 2. The prevalence of baldness is similar among cases interviewed in person and by telephone; risk factors for coronary artery disease are also similarly distributed.

This suggests that the telephone interviews provide information regarding baldness and important confounding factors that is comparable to that obtained by in-person interview; therefore, we included patients interviewed by telephone in the analyses described here.

Statistical Analyses

The odds ratio was used to estimate the relative risk (RR) of MI for men with frontal and vertex baldness compared with men with no hair loss. Age-adjusted RR estimates were calculated using the Mantel-Haenszel procedure for data stratified by years of age (<45, 45-49, ≥50 years). Miethen's method was used to compute 95% confidence intervals (CIs). The prevalence of common risk factors for coronary artery disease among controls according to the patient's assessment of hair loss using the HBS is shown in Table 3. Except for age, body mass index, cigarette smoking, use of alcohol, amount of time spent in aerobic exercise each week, Framingham type A behavior score, number of years of education, and number of doctor visits in the past year, the confounding effect of age was further controlled using logistic regression models that included a continuous term for age. The results were not materially different from those obtained from models that used indicator terms for age, and only the latter are presented. Linear trends in RR estimates were evaluated by including continuous terms in logistic regression models.

RESULTS

The distribution of baldness among cases and controls, according to the patient's assessment using the HBS, is shown in Table 4. Age-adjusted and multivariate RR estimates were similar. Frontal baldness was not associated with increased risk of MI. Age-adjusted RR, 0.9). For mild or moderate vertex baldness, the age-adjusted RR estimates were approximately 1.2, while for extreme baldness the estimate was 3.4 (95% CI, 1.7 to 7.0). The trend of increasing risk of MI with increasing extent of vertex baldness was statistically significant (P<.01). For any vertex baldness (ie, mild, moderate, and severe combined), the age-adjusted RR was 1.4 (95% CI, 1.2 to 1.9). For baldness overall, the risk of MI was not related to age at onset of hair loss. Among men with moderate to severe vertex baldness, MI risk decreased as age of onset increased, but this trend was not significant (P>.50). Compared with men with no hair loss, the age-adjusted RR estimates for MI at the ages of less than 25 years, 25 to 34 years, and 35 years and older were 2.1 (95% CI, 1.2 to 3.5), 1.8 (95% CI, 0.9 to 3.6), and 0.9 (95% CI, 0.3 to 2.5), respectively.

The distribution of baldness among cases and controls according to the interviewer's assessment using the HBS is shown in Table 5. The extent of baldness was treated as "unknown" for 300 cases and four controls who were interviewed by telephone and for whom an interviewer's assessment was not recorded. The age-adjusted and multivariate RR estimates were again similar. Frontal baldness was not associated with increased risk of MI (age-adjusted RR, 1.0). For mild or moderate degrees of vertex baldness, the RR estimates were 1.4; for the most extreme category of vertex baldness, the estimate was 2.8 (95% CI, 1.6 to 4.8). For any vertex baldness, the age-adjusted RR was 1.4 (95% CI, 1.2 to 2.0). As in the data based on the patient's assessment of baldness, the risk of MI was not related to age at onset of hair loss overall. In addition, risk was not related to age at onset among men who were classified by an interviewer as having moderate to severe vertex baldness.

The distribution of cases and controls according to the patient's assessment of hair loss using the continuous five-point scale is shown in Table 6. The RR estimates increased with increasing extent of baldness.
The hypothesis that baldness may be a predictor of coronary artery disease is not new. More than 25 years ago, in a study of the relationship between baldness and obstructive lung disease, Buick et al. found higher rates of baldness among 40- to 50-year-olds than among men with obstructive lung disease, lung cancer, or among random samples selected from controls. The heart disease patients were not characterized further, however, and no statistical tests were reported. In a case-control study of risk factors for coronary heart disease, Cotton et al. reported a higher mean baldness score among 91 men with a history of MI (4 months to 10 years previously) than among 98 healthy male blood donors. After diastolic blood pressure and the presence of cornel acous, degree of baldness was the third best discriminator between cases and controls in these data. In a small study of the relationship between indexes of masculinity (plasma testosterone levels, muscle thickness, baldness, and density of terminal body hair), Halin et al. found no difference in the prevalence of baldness among 48 men treated in hospital for MI in the previous 4 years and 48 age-matched controls admitted to a hospital for surgical conditions. Using the same baldness scoring system as Halin et al., Cooke et al. observed higher rates of atherosclerosis to severe vertex baldness in men older than 40 years of age with coronary artery disease (defined as a past history of MI or treated angina pectoris) than among controls. While this study's results were reported as negative (P < 0.1), the prevalence of baldness was higher among men with coronary artery disease than among controls in four out of five age strata; among men aged 50 to 59 years, the odds ratio was 2.8 (P < 0.05), and for all ages combined the odds ratio was 2.6 (P < 0.001). After 17 years of follow-up of 464 men in Malmo, Sweden, Persson and Johansson reported higher rates of probable or definite coronary heart disease among men with baldness at enrollment (55.5%) than among men without baldness (19.7%). The number of men in this prospective study was small and neither the prevalence of baldness at entry nor the results of a test of significance of the difference in coronary heart disease incidence were reported. In an analysis of the 12-year follow-up data from the Olivetti Heart Study, Tavore et al. reported that the men with occipital baldness had higher levels of total cholesterol and diastolic blood pressure than did men with no baldness or baldness that was limited to the frontal scalp.
Our results support the hypothesis that MPB is associated with an increased risk of MI in men under the age of 55 years. In these data, the increase in risk was modest overall and limited to men with baldness involving the vertex scalp. The RR estimate for men with extreme vertex baldness compared with men with no baldness was approximately 3.0; for lesser degrees of hair loss, risk was lower. The association was present among men in each of three age categories and regardless of the presence of other risk factors for coronary artery disease (ie, smoking, hypertension, hypercholesterolemia, and family history of MI). There was no consistent evidence for an effect of age at onset of hair loss, however.

These data include cases only men who survived their first MI. It seems unlikely that bald men are more often admitted to a hospital for MI than men without hair loss; physicians do not recognize MPB as a risk factor for MI and do not make diagnostic or treatment decisions based on this patient characteristic. We are unaware of any data showing survival following MI to vary according to the presence or absence of baldness, and we believe that such differential survival is improbable.

Information bias is unlikely to account for our findings. The data were collected by specially trained nurse-interviewers using a highly structured questionnaire, in an identical fashion for both cases and controls, and we excluded from analysis all men with a history of prior medical or surgical treatment with MPB. That we cannot exclude the possibility that our nurse-interviewers may have been aware of the study hypothesis and were potentially biased in assessing extent of baldness is a limitation of this study. The patients, however, were never told the hypothesis, so their self-assessments of extent of baldness should be unbiased. In addition, an association between baldness and the risk of MI was observed for each of the three measures of MPB studied: (1) the patient’s self-assessment using the HBS, (2) the interviewer’s assessment using the HBS, and (3) the patient’s self-assessment using a continuous five-point scale. Independent of the method used to assess extent of baldness, the risk of MI was significantly increased among men with substantial degrees of hair loss and did not differ materially according to the method of assessment.

We controlled for the potential confounding effects of the principal risk factors for coronary artery disease. The similarity in the age-adjusted and multivariate RR estimates is evidence against substantial additional confounding in these data, and the consistency of the association across strata defined by age and the major risk factors for coronary artery disease is also reassuring.

The mechanism responsible for the observed association is unclear. One possibility is that dihydrotestosterone (DHT), an active metabolite of testosterone produced in tissue by the action of 5a-reductase, is involved in the pathogenesis of both MPB and MI. The principal androgen responsible for MPB appears to be DHT.16 Men with an inherited deficiency of 5a-reductase have low levels of circulating DHT and do not become bald despite having normal or elevated serum testosterone levels. Dihydrotestosterone has been proposed as a factor that is possibly responsible for the sex difference in coronary artery disease incidence. Receptors specific for DHT are present in cardiac muscle and blood vessels of at least two species of subhuman primates.17 In castrated male monkeys, treatment of HTN caused high-density lipoprotein cholesterol levels to decrease.18 In humans, however, available data on the relationship between serum DHT level and lip-
ids do not suggest that DHT is likely to adversely affect lipid profiles. Among men without coronary disease, serum DHT level has been positively correlated with high-density lipoprotein cholesterol level.22 Also, elderly men who were invited for 3 months with topical DHT have been reported to experience moderate decreases in total and low-density lipoprotein cholesterol levels, and only slight decreases in high-density lipoprotein cholesterol levels.24,25 Another study, serum lipid levels did not change during 11 to 14 days of oral exposure to a 5α-reductase inhibitor despite significant decreases in DHT levels.24

Little has been reported on the relationship between DHT level and the risk of II in humans. Two epidemiologic studies of the relationship between sex hormones and coronary artery disease found slightly higher serum DHT levels in men following MI than among healthy controls.26,27 Although both studies were small and in neither was the difference statistically significant.

In conclusion, it is possible that baldness is an indicator of patterns of androgen metabolism that increase the risk of MI, but there is no clear-cut evidence to that effect. From a practical perspective, however, if the present findings are confirmed, the presence of baldness may serve as a useful indicator of increased risk of MI.

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