Sex and Topographic Differences in Associations Between Large-Artery Wall Thickness and Coronary Risk Profile in a French Working Cohort

The AXA Study

Jérôme Gariepy, Jean Salomon, Nicolas Denarié, Fatiha Laskri, Jean Louis Mégnien, Jaime Levenson, Alain Simon

Abstract—Previous reports have investigated associations between carotid intima-media thickness (IMT) and cardiovascular risk factors. Our objective was to investigate this question in greater depth by measuring both femoral and carotid IMT in relation to sex and multifactorial coronary risk. We investigated carotid and femoral artery IMT by using ultrasonography in 326 men and 462 women, 17 to 65 years old. We also evaluated body mass index, blood pressure, blood lipids, glucose, smoking, and Framingham coronary risk. In both vessels, IMT was lower in women than in men. Significant relations between carotid and femoral IMT existed with age and most risk factors in both sexes. After adjustment for age, carotid IMT was related to risk factors in both sexes except for diastolic blood pressure, HDL cholesterol, and smoking in women, whereas femoral IMT was related to triglycerides and smoking in both sexes, systolic blood pressure and blood glucose in men, and total and HDL cholesterol in women. Significant unadjusted and age-adjusted relations of Framingham risk existed with carotid and femoral IMT in both sexes, but slopes of these relations were greater (1) before than after age adjustment, (2) in men than in women at both sites, except the femoral artery after age adjustment, and (3) at the carotid than at the femoral site in both sexes before age adjustment. Carotid IMT in men appears to be a more powerful predictor than it is in women and femoral IMT in both sexes in reflecting multifactorial coronary risk burden, but these differences are partly conditional on age. (Arterioscler Thromb Vasc Biol. 1998;18:584-590.)

Key Words: arteries ■ risk factors ■ coronary disease ■ atherosclerosis ■ ultrasound

The early detection of preclinical arterial disease may increase our ability to predict the subsequent risk of cardiovascular complications and lead to optimal disease prevention strategies.1,2 There is growing evidence that the thickening of the arterial wall observable with B-mode ultrasonography represents one initial step of preclinical arterial disease.3 Even in the absence of discrete plaque, the combined thickness of the arterial intima and media, the so-called IMT, can be measured with considerable precision, particularly by coupling high-resolution, B-mode ultrasonography with an automated, computerized system of image analysis.4–6 Several studies of selected patients at risk for cardiovascular disease and a few population-based studies have provided evidence of an association between IMT, as measured in the extracranial carotid arteries, and cardiovascular risk factors.3,4,7–12 However, little attention has been given to the influence of risk factors on IMT as measured at sites other than the carotid artery, such as the femoral.8–11 A vessel considered to be as prone to atherogenesis as the carotid.12 The AXA Study is a prospective, worksite study designed to investigate the influence over time of traditional and new risk factors13,16 on carotid and femoral IMT as assessed ultrasonographically4,8 in a general population of male and female employees of the AXA Insurance Co working in the Ile de France area. Such an investigation is expected to provide additional insights into the mechanisms of large-artery wall thickening and its clinical relevance to the primary prevention of atherosclerotic disease. Two investigational steps have been scheduled in the study. The first one concerns the evaluation of risk factors and IMT at baseline, and the second step will be a follow-up of these measurements after 2 and 4 years, with the recording of morbid and fatal events after 4 years.

The present article reports the first findings of the initial step, ie, the evaluation of the clinical usefulness of IMT, based on a cross-sectional analysis of the relations between IMT and traditional cardiovascular risk factors and the estimated multifactorial risk of coronary events as assessed according to the Framingham model.17,18

Methods

Subjects
The present work is drawn from the AXA Study, a prospective, single-center, 4-year follow-up of healthy workers designed to...
investigate risk factors for and changes of the early stages of atherosclerosis. The investigation includes complete evaluation of cardiovascular risk factors and arterial status, as described below, at entry into the study (baseline) and 2 and 4 years later. The study population is composed of volunteers recruited from employees of an insurance company (AXA, Paris La Défense, France). The recruitment program was performed at a single, occupational health center responsible for the survey of 1900 employees. All employees free from cardiovascular disease, including stroke, transient ischemia, coronary heart disease, congestive heart failure, and intermittent claudication, as verified on the basis of a complete clinical examination and questioning by the occupational health practitioner (J.S.), were eligible for the study, within the limit of 50% of the surveyed population. This percentage was chosen because it offered sufficient statistical power for testing the objective of the study, i.e., the assessment of the relationships between cardiovascular risk factors and structural alterations of arteries, and because it was considered to be financially and practically feasible to administer at the workplace with optimal quality. During the recruitment period, which took place between September 1993 and September 1996, 830 subjects agreed to participate. Of these 830, only 788 subjects including 326 men and 462 women aged 17 to 65 years were enrolled in the study, because the ultrasound arterial investigation had not been performed in 42 subjects due to technical failure of the information handling equipment. This failure was due to lack of storage of recorded IMT images in the computer memory (see after) because the transient saturation of the memory mass system was unknown at the time. For each subject, all investigations were performed at the workplace site in the occupational medicine clinic during the course of one morning. Investigations included a multifactorial evaluation of cardiovascular risk factors and ultrasound arterial measurements. The study protocol was approved by the Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale du Centre Hospitalier Universitaire Créteil-Henri Mondor, and written consent was obtained from all participants. The present findings come from the cross-sectional analysis of data obtained during the first investigational step.

Cardiovascular Risk Factors

All traditional risk factors were carefully evaluated in each subject. Anthropometric measurements were taken by using standard techniques: body weight without heavy clothing by digital scales and height without shoes by fixed stadiometer. BMI was calculated as the ratio of weight to the square of height. Blood pressure was measured in the supine position as the average of three measurements taken at the same reading by means of an automated computerized program (Io ̄tec System, Io ̄data Processing) whose principles and detailed description have been provided elsewhere. The two parallel echogenic lines (double-line pattern), corresponding to the luminal-intimal and medial-adventitial interfaces defining the IMT, were obtained in the left carotid artery in all subjects, but because of poor interface visualization, the image obtained was not of sufficient quality in the right carotid artery of 1 subject, in the right femoral artery of 38 subjects, and in the left femoral artery of 34 subjects. The correct IMT image was “frozen” in end-diastole by ECG R-triggering, transferred to a computer (Apple Macintosh), digitized into 640×580 peak cells with 256 grey levels, and stored for off-line analysis. All off-line measurements of IMT were performed by the same reader (J.G., not the sonographer) by means of an automated computerized program (Īotec System, Īodata Processing) whose principles and detailed description have been provided elsewhere. Average IMT was calculated as the mean value of a great number of local IMT measures performed every 100 μm along at least 1 cm of longitudinal length of the artery. For each subject, a total IMT [(left + right)/2] was taken as a measure of current wall thickness of the common carotid and common femoral arteries. When this measure was missing on one side, the IMT estimate was based on the measurement of the site for which a value was available. In femoral arteries, total IMT was not obtained in 18 patients because IMT could not be measured on both sides. For quality-control assessment, random subsamples of IMT images of both common carotid and common femoral arteries were measured twice at a 6-month interval by the same reader (J.G.); mean absolute differences and correlation coefficients between repeated readings were, respectively, 0.0057 mm and .98 for carotid IMT (n=50) and 0.0049 mm and .97 for femoral IMT (n=50).

Statistical Analysis

Values are expressed as mean±SD or, for categorical parameters, as percentage. Comparisons of risk factors between the sexes were performed by ANOVA. As the distribution of TGs, pack-years of smoking, and estimated Framingham risk values were skewed, a logarithmic transformation was applied. Mean levels of carotid and femoral IMT were compared between men and women by using multiple linear regression analysis adjusted for the possible confounding effect of age. The relations of carotid and femoral IMT with continuously distributed risk factors and estimated Framingham risk were evaluated by using several linear model procedures before and after adjustment for age. When relations of IMT with risk factors or Framingham risk were significant in both sexes, their slopes were compared by calculating the confidence interval for the difference between the slopes of the two regression lines in men and women. When relations of IMT with risk factors or Framingham risk were significant at both carotid and femoral sites in either sex, these relations were compared between sites by means of a general linear model relating risk factors, Framingham risk, and the difference between carotid IMT and femoral IMT. Statistical significance was considered at a value of P<.05. Results are presented separately for

**Selected Abbreviations and Acronyms**

- **BMI** = body mass index
- **CI** = confidence interval
- **DBP** = diastolic blood pressure
- **IMT** = intima-media thickness
- **SBP** = systolic blood pressure
- **TG** = triglyceride

--were defined as those having regularly smoked for the previous 3 months regardless of the amount smoked. Left ventricular hypertrophy (LVH) was measured by ECG and defined as present according to the criterion of Sokolow and Lyon: SV_1 + RV_1 or V_6 >5 mV, where S and R stand for amplitude.

Finally, the estimated multifactorial risk of coronary events at 10 years was calculated for each subject by entering into the equations of the Framingham risk model the following variables: age, sex, systolic blood pressure, total to HDL cholesterol ratio, current smoking coded as present or absent, diabetes coded as present or absent, and LVH coded as present or absent.

**Ultrasound Arterial Investigation**

All of the study subjects were investigated by the same sonographic physician (F.L.) at the workplace. Echographic investigations were performed with a real-time, B-mode ultrasound imager (Ultramark 4, Advanced Technologies Laboratories) using a 7.5-MHz probe. Imaging of the IMT was performed in the far wall of the right and left common carotid and common femoral arteries 2 to 3 cm proximal to the bifurcation, according to a standardized and careful procedure reported in detail elsewhere. The advanced technologies laboratories (Advanced Technologies Laboratories) using a 7.5-MHz probe. Imaging of the IMT was performed in the far wall of the right and left common carotid and common femoral arteries 2 to 3 cm proximal to the bifurcation, according to a standardized and careful procedure reported in detail elsewhere. The two parallel echogenic lines (double-line pattern), corresponding to the luminal-intimal and medial-adventitial interfaces defining the IMT, were obtained in the left carotid artery in all subjects, but because of poor interface visualization, the image obtained was not of sufficient quality in the right carotid artery of 1 subject, in the right femoral artery of 38 subjects, and in the left femoral artery of 34 subjects. The correct IMT image was “frozen” in end-diastole by ECG R-triggering, transferred to a computer (Apple Macintosh), digitized into 640×580 peak cells with 256 grey levels, and stored for off-line analysis. All off-line measurements of IMT were performed by the same reader (J.G., not the sonographer) by means of an automated computerized program (Īotec System, Īodata Processing) whose principles and detailed description have been provided elsewhere. Average IMT was calculated as the mean value of a great number of local IMT measures performed every 100 μm along at least 1 cm of longitudinal length of the artery. For each subject, a total IMT [(left + right)/2] was taken as a measure of current wall thickness of the common carotid and common femoral arteries. When this measure was missing on one side, the IMT estimate was based on the measurement of the site for which a value was available. In femoral arteries, total IMT was not obtained in 18 patients because IMT could not be measured on both sides. For quality-control assessment, random subsamples of IMT images of both common carotid and common femoral arteries were measured twice at a 6-month interval by the same reader (J.G.); mean absolute differences and correlation coefficients between repeated readings were, respectively, 0.0057 mm and .98 for carotid IMT (n=50) and 0.0049 mm and .97 for femoral IMT (n=50).

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Values are expressed as mean±SD or, for categorical parameters, as percentage. Comparisons of risk factors between the sexes were performed by ANOVA. As the distribution of TGs, pack-years of smoking, and estimated Framingham risk values were skewed, a logarithmic transformation was applied. Mean levels of carotid and femoral IMT were compared between men and women by using multiple linear regression analysis adjusted for the possible confounding effect of age. The relations of carotid and femoral IMT with continuously distributed risk factors and estimated Framingham risk were evaluated by using several linear model procedures before and after adjustment for age. When relations of IMT with risk factors or Framingham risk were significant in both sexes, their slopes were compared by calculating the confidence interval for the difference between the slopes of the two regression lines in men and women. When relations of IMT with risk factors or Framingham risk were significant at both carotid and femoral sites in either sex, these relations were compared between sites by means of a general linear model relating risk factors, Framingham risk, and the difference between carotid IMT and femoral IMT. Statistical significance was considered at a value of P<.05. Results are presented separately for

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men and women. The statistical analysis was carried out on a computer (Apple Macintosh) with the use of JMP (SAS) and Excel (Microsoft) software.

Results

Table 1 shows that compared with men, women had no significant difference in age but significantly lower values of BMI, SBP, DBP, total cholesterol, TGs, and blood glucose, as well as lower prevalence of hypertension; HDL cholesterol was also higher in women than in men, but no differences in the prevalence of hypercholesterolemia, diabetes, current smoking, and ECG LVH existed between the sexes; as a result of these differences, the estimated Framingham risk of coronary disease was 66% lower in women than men (Table 1).

Figs 1 and 2 show the distribution of carotid and femoral IMT in men and women. IMT was significantly lower in women than in men in both arteries ($P<.001$), with an age-adjusted difference for carotid and femoral, respectively, of 0.040 mm (95% CI, 0.029 to 0.051) and 0.058 mm (95% CI, 0.045 to 0.070).

Relations Between IMT and Coronary Risk Profile

The unadjusted relations between IMT and risk factors are shown in Tables 2 and 3. Carotid IMT was significantly associated with age, BMI, SBP, DBP, total cholesterol, and blood glucose in both sexes, as well as with smoking in men and TGs in women. Femoral IMT was significantly associ-
ated with age, BMI, SBP, DBP, total cholesterol, blood glucose, and smoking in both sexes, as well as with HDL cholesterol (negatively) and TGs in women. Table 4 shows that unadjusted relations between carotid and femoral IMT and Framingham coronary risk were significant in both sexes. After adjustment for age, carotid IMT was significantly associated with BMI, SBP, total cholesterol, TGs, and blood glucose in both sexes, as well as with DBP, HDL cholesterol (negatively), and smoking in men (Table 2). Significant age-adjusted relations between femoral IMT and TGs and smoking in both sexes existed, as well as with SBP and blood glucose in men and total cholesterol and HDL cholesterol (negatively) in women (Table 3). Table 4 shows that age-adjusted relations of carotid and femoral IMT with Framingham coronary risk were significant in both sexes.

### Influence of Sex in Relations Between IMT and Coronary Risk Profile

Before adjustment for age, carotid IMT was related significantly with smoking in men but not in women and with TGs in women but not in men, and the slopes of relations of carotid IMT with age, BMI, and DBP were significantly greater in men than in women (Table 2). After adjustment for age, carotid IMT was related significantly with DBP, HDL cholesterol, and smoking in men but not in women, and the slope of the relation of carotid IMT and BMI was greater in men than in women (Table 2). Before adjustment for age, femoral IMT was related significantly with HDL cholesterol and TGs in women but not in men, and the slopes of the relations of femoral IMT with age, BMI, and smoking were greater in men than in women (Table 3). After adjustment for

### TABLE 2. Relationships Between Common Carotid Artery IMT and Cardiovascular Risk Factors in Men and Women

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Men (n=326)</th>
<th>Age Adjusted</th>
<th>Women (n=462)</th>
<th>Age Adjusted</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>7 [6, 9]§</td>
<td>···</td>
<td>6 [5, 6]§</td>
<td>···</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>12 [8, 16]§</td>
<td>7 [4, 11]§</td>
<td>6 [5, 8]§</td>
<td>3 [2, 5]§</td>
<td>&lt;.01 &lt;.05</td>
</tr>
<tr>
<td>Blood pressure, per 10 mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>24 [15, 33]§</td>
<td>11 [3, 19]‡</td>
<td>16 [11, 22]§</td>
<td>6 [1, 11]†</td>
<td>NS NS</td>
</tr>
<tr>
<td>Diastolic</td>
<td>29 [18, 40]§</td>
<td>17 [8, 26]‡</td>
<td>14 [7, 21]§</td>
<td>5, NS</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Blood lipids, mmol/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>26 [14, 38]§</td>
<td>12 [2, 23]†</td>
<td>26 [19, 33]§</td>
<td>9 [2, 15]†</td>
<td>NS NS</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>−34, NS</td>
<td>−36 [−66, −5]‡</td>
<td>−9, NS</td>
<td>−12, NS</td>
<td>··· NS</td>
</tr>
<tr>
<td>TGs</td>
<td>11, NS</td>
<td>10 [0, 20]†</td>
<td>18 [6, 29]‡</td>
<td>12 [3, 21]‡</td>
<td>··· NS</td>
</tr>
<tr>
<td>Blood glucose, mmol/L</td>
<td>38 [22, 55]§</td>
<td>21 [6, 35]‡</td>
<td>38 [27, 49]§</td>
<td>17 [7, 26]§</td>
<td>NS NS</td>
</tr>
<tr>
<td>Lifelong dose, per 10 pack-years</td>
<td>23 [14, 32]§</td>
<td>11 [3, 18]‡</td>
<td>5, NS</td>
<td>1, NS</td>
<td>··· NS</td>
</tr>
</tbody>
</table>

Values are unadjusted or age-adjusted changes in IMT (in microns and [95% confidence interval]) by an increase of one unit (except for blood pressure and smoking) of the level of risk factors. n indicates number of subjects.

*Comparison by sex of slopes of IMT–risk factors relations performed only for relations significant in both sexes.

†P<.05, ‡P<.01, §P<.001.

### TABLE 3. Relations Between Common Femoral Artery IMT and Cardiovascular Risk Factors in Men and Women

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Men (n=318)</th>
<th>Age Adjusted</th>
<th>Women (n=452)</th>
<th>Age Adjusted</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>5 [4, 7]§</td>
<td>···</td>
<td>3 [2, 4]§</td>
<td>···</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>7 [3, 11]§</td>
<td>3, NS</td>
<td>2 [1, 4]‡</td>
<td>1, NS</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Blood pressure, per 10 mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>18 [9, 27]§</td>
<td>9 [1, 18]†</td>
<td>8 [3, 14]‡</td>
<td>3, NS</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic</td>
<td>15 [4, 26]‡</td>
<td>6, NS</td>
<td>8 [1, 15]†</td>
<td>4, NS</td>
<td>NS</td>
</tr>
<tr>
<td>Blood lipids, mmol/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>16 [4, 28]‡</td>
<td>6, NS</td>
<td>20 [13, 27]§</td>
<td>12 [4, 19]†</td>
<td>NS</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>−22, NS</td>
<td>−22, NS</td>
<td>−9 [−36, 0]†</td>
<td>−19 [−36, −3]‡</td>
<td>··· NS</td>
</tr>
<tr>
<td>TGs</td>
<td>12, NS</td>
<td>12 [1, 22]†</td>
<td>24 [13, 36]§</td>
<td>22 [11, 32]§</td>
<td>··· NS</td>
</tr>
<tr>
<td>Blood glucose, mmol/L</td>
<td>27 [11, 44]§</td>
<td>15 [0, 30]†</td>
<td>20 [8, 31]§</td>
<td>8, NS</td>
<td>NS</td>
</tr>
<tr>
<td>Lifelong dose, per 10 pack-years</td>
<td>31 [22, 39]§</td>
<td>23 [14, 31]§</td>
<td>15 [8, 23]§</td>
<td>13 [5, 20]§</td>
<td>&lt;.01 NS</td>
</tr>
</tbody>
</table>

Values are unadjusted or age-adjusted changes in IMT (in microns [95% confidence interval]) by an increase of one unit (except for blood pressure and smoking) of the level of risk factors. n indicates number of subjects.

*Comparison by sex of slopes of IMT–risk factors relations performed only for relations significant in both sexes.

†P<.05, ‡P<.01, §P<.001.
age, femoral IMT was related significantly with SBP and blood glucose in men but not in women and with total and HDL cholesterol in women but not in men (Table 3). Last, Table 4 shows that the slopes of unadjusted and age-adjusted relations between Framingham coronary risk and carotid IMT were greater in men than in women, just like the slope of the unadjusted relation between Framingham risk and femoral IMT.

### Influence of Topography on Relations Between IMT and Coronary Risk Profile

In men, before adjustment for age, the slopes of the relations between IMT and age and BMI (Tables 2 and 3) were significantly greater at the carotid site than at the femoral site ($P<.05$). In men after adjustment for age, significant relations of IMT with BMI, DBP, and total and HDL cholesterol existed at the carotid site but not at the femoral site, and the slope of the relation of IMT with smoking was lower ($P<.05$) at the femoral site than at the carotid site (Tables 2 and 3).

In women, before adjustment for age, significant relations of IMT with HDL cholesterol and smoking existed at the femoral site but not at the carotid site (Tables 2 and 3), and the slopes of the relations between IMT and age and BMI (Tables 2 and 3) were significantly greater at the carotid site than at the femoral site ($P<.001$). In women after adjustment for age, significant relations of IMT with HDL cholesterol and smoking existed at the femoral site but not at the carotid site, whereas significant relations of IMT with BMI, SBP, and glucose existed at the carotid site but not at the femoral site (Tables 2 and 3). Table 4 shows that in both sexes, the slopes of the unadjusted relations between Framingham coronary risk and IMT were greater at the carotid site than at the femoral site.

### Discussion

Previous studies have shown associations between carotid IMT and cardiovascular risk factors.3,4,7-12,20 Our objective was to examine in depth the relations between IMT and coronary risk profile by (1) assessing not only carotid IMT but also femoral IMT, which has been comparatively less investigated, and (2) considering the relation of IMT with Framingham coronary risk, which integrates the effects of multiple traditional risk factors.17 Our study subjects are fairly representative of clerical workers in the Ile de France area. Our B-mode IMT measurement is precise, thanks to the standardization of image recording according to telediastole, the automated, computerized measurement without reader dependence, and the calculation of average IMT as the mean of a great number of local IMT measurements.4,8,20 Because we found that carotid and femoral IMT values were higher in men than in women, we assessed the relations of IMT with coronary risk profile separately in men and women.

### Relations Between IMT and Coronary Risk Profile

As expected, carotid and femoral IMT values were associated with age.3,4,7-12,20 More novel are the associations found in both sexes between femoral IMT and risk factors, except HDL cholesterol and TGs in men and HDL cholesterol and smoking in women.23-30 More novel are the associations found in both sexes between femoral IMT and risk factors, except HDL cholesterol and TGs in men. Framingham risk was also associated with carotid and femoral IMT in men and women, suggesting potential value of the IMT in risk prediction. The reassessment of relations of IMT with risk factors and Framingham risk, after elimination of the confounding effect of age, attenuated the strength of these relations either by abolishing their significance (carotid IMT with DBP in women; femoral IMT with DBP and total cholesterol in men; and femoral IMT with BMI, blood pressure, and blood glucose in women) or by decreasing their slopes. Thus, the age-adjusted slopes of relations between Framingham risk and carotid and femoral IMT in both sexes were decreased by ~60% compared with unadjusted values.

### Influence of Sex on Relations Between IMT and Coronary Risk Profile

Compared with men, in women the unadjusted and/or age-adjusted relations of carotid IMT with some risk factors and Framingham risk were either insignificant (IMT with DBP, HDL cholesterol, and smoking) or had a lower slope (IMT with age, BMI, and Framingham risk). The weaker relation of carotid IMT and BMI in women than in men is particularly clear-cut and raises questions about the nature of its mechanisms. The involvement of female sex hormones in the relative protection from cardiovascular disease may play a role.15 Also, susceptibility to upper-body fat accumulation, which occurs more frequently in men, has been shown to be more strongly associated with metabolic and cardiovascular disease than is lower-body obesity, which is more common in women.32 Moreover, sex differences in visceral fat lipolysis and metabolic complications of obesity may contribute to sex differences in vascular disturbances accompanying overweight.15 The greater strength of the relations of carotid IMT with the aforementioned risk factors and overall with the Framingham risk in men compared with women suggests a greater ability of carotid IMT to reflect the absolute coronary

### Table 4. Relations Between Framingham Coronary Risk and Carotid and Femoral IMT in Men and Women

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Unadjusted</th>
<th>Age Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Carotid IMT (C)</strong></td>
<td>3.2 [2.7, 3.7]*</td>
<td>1.3 [0.8, 1.8]*</td>
</tr>
<tr>
<td>Femoral IMT (F)</td>
<td>2.3 [1.8, 2.9]*</td>
<td>0.8 [0.3, 1.3]*</td>
</tr>
<tr>
<td>$P (C vs F)$</td>
<td>&lt;.05</td>
<td>NS</td>
</tr>
</tbody>
</table>

Results are given as absolute changes in Framingham risk at 10 years [95% confidence interval] by an increase of 100 μm of IMT.

*P<.001.
risk in men. However, the sex difference in the relation between Framingham risk and carotid IMT was modified when the change in Framingham risk was expressed as relative risk, ie, the percentage of the average Framingham risk measured in each sex. So after adjustment for age, the increase in relative risk by a unit increase in carotid IMT may be estimated as 17% in men and 23% in women. At the femoral site, unadjusted relations of IMT with risk factors and Framingham risk showed similar trends in both sexes, but relations with HDL cholesterol and TGs were significant in women but not in men, and the slopes of the relations with age, BMI, smoking, and Framingham risk were lower in women than in men. The age-adjusted sex differences were more heterogeneous, consisting of significant relations between femoral IMT and SBP and blood glucose in men but not in women and significant relations between femoral IMT and total and HDL cholesterol in women but not in men. Moreover, the age-adjusted increase in Framingham risk per unit increase in femoral IMT was not different between men and women, possibly because the sex differences in the relations between femoral IMT and risk factors counteracted each other when multiple risk factors were analyzed together. Also, the sex difference in the relation of Framingham risk and femoral IMT was conditional on relative risk. Thus, the age-adjusted increase in Framingham relative risk by unit increase in femoral IMT may be estimated at 10% in men and at 23% in women.

**Topographic Influence on Relations Between IMT and Coronary Risk Profile**

In men, carotid IMT compared with femoral IMT was related more strongly to aging and risk factors except smoking, which showed an opposite association. It is noteworthy that the stronger relation of IMT and BMI in men at the carotid site compared with the femoral site overall after adjustment for age. The mechanism of the topographic differences in the relations of IMT and BMI on coronary risk profile have not been elucidated. A different sensitivity of carotid and femoral arteries to the atherogenic effects of risk factors has been previously shown and may be explained in part by the differences in hydrostatic pressure and flow patterns between the two arteries. In conclusion, our findings indicate undeniable superiority of the carotid IMT in predicting absolute coronary risk in men compared with women and to femoral IMT in both sexes. Nevertheless, in men the superiority of carotid IMT is conditional on age and relative risk, and in women the relative contributions of carotid and femoral IMT in risk assessment are more balanced.

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