Abstract  We investigated the prevalence and associations with cardiovascular symptoms, signs, and risk factors of common carotid atherosclerosis using B-mode ultrasonography in a population sample of 182 eastern Finnish men aged 70 to 89 years. Men were examined in 1989 as a part of the 30-year follow-up examination of the eastern Finnish cohort of the Seven Countries Study. The mean maximal intima-media thickness (IMT) of the right and left common carotid arteries was 1.5 mm (range, 0.7 to 5.3 mm; standard deviation, 0.7 mm). Fifty-one percent of the subjects had nonmineralized atheroma and 91% had single or multiple mineralizations in any of the arterial segments imaged. Both mean maximal IMT and nonmineralized atheromas were associated significantly \((P<.05)\) with the presence of cerebral atherosclerosis, carotid murmurs, at least one nonpalpable peripheral arterial pulse, ischemic resting electrocardiographic abnormalities, and history of coronary heart disease but not with intermittent claudication at the 30-year follow-up. No significant associations were found between carotid mineralizations and clinical cardiovascular disease. Long-term elevations of serum cholesterol and long-term smoking, measured as the number of risk factor elevations in the six examinations, were associated with the presence of nonmineralized atheroma in the elderly (in 1989). Smoking and repeatedly detected hypertension, on the other hand, had an association with the presence of mineralizations in 1989. (Arterioscler Thromb. 1994;14:1631-1640.)

Key Words  •  atherosclerosis • B-mode ultrasound • population studies • cardiovascular disease • risk factors

Cardiovascular diseases are very common in Finland, especially in middle-aged men.1 The majority of cardiovascular diseases are of atherosclerotic origin. The occurrence of human atherosclerosis has traditionally been studied on the basis of either autopsies or invasive angiography. Therefore, it has not been possible to carry out studies in randomly selected population samples. High-resolution ultrasonography enables the noninvasive imaging and quantitative assessment of both early and advanced atherosclerotic lesions in superficial large and medium-sized arteries.

Ultrasonographic assessment of atherosclerosis has been applied in population samples in studies of occurrence and risk factors of early atherosclerosis.2-11 The prevalence of asymptomatic carotid atherosclerosis in elderly populations is, however, not well known.9,10 Ultrasonographically assessed carotid atherosclerosis has predicted the risk of coronary events in middle-aged men.5,11 A previous population-based study reported an association between carotid atherosclerosis and signs and symptoms of coronary heart disease (CHD) and cerebrovascular disease in the elderly.12 Prospective population studies indicate that the impact of the major coronary risk factors, smoking, elevated serum cholesterol concentration, and hypertension, is attenuated in the elderly.13 There are no previous reports from prospective studies on the association of risk factors assessed in middle age and later in life with the occurrence of carotid atherosclerosis in old age.

The purpose of the present study was to investigate the prevalence of different manifestations of B-mode ultrasonographically assessed cases of common carotid atherosclerosis and their associations with cardiovascular symptoms and signs assessed at the same time and with past and present levels of the major cardiovascular risk factors in elderly eastern Finnish men.

Methods

Study Population

In 1959, all 1711 men aged 40 to 59 years, living in two rural areas in eastern and southwestern Finland, were invited to take part in a prospective study of CHD and other atherosclerotic diseases, the Seven Countries Study.4,14 In this original study cohort 823 men were from eastern Finland and 888 men were from southwestern Finland. The 30-year follow-up examination of surviving men was performed in 1989, when the men were between 70 and 89 years of age. Of the 1711 men, 524 were alive in 1989 (233 from the east and 291 from the west). A total of 205 eastern Finnish men were examined in 1989, 184 of these at the local health center, which was the examination site.14 Carotid ultrasonography was carried out...
for 182 men. One man was not able to undergo ultrasonography because he had moved from the eastern to the western area and was examined at the southwestern examination site. Another man was too obese (body mass index, 37.6 kg/m²), and for that reason, only a small part of his common carotid arteries could be visualized. A third man was accidentally not invited to the ultrasound examination. One additional man underwent ultrasonography but not any of the other physical examinations in the health center and was examined at home. Thus, we investigated the prevalence of carotid atherosclerosis among 182 eastern Finnish men (mean age, 75.9 years), 78.1% of those alive in 1989. Of these 182 men, information was not available for two men on carotid auscultation, electrocardiography (ECG), and coronary symptoms; for three men on the status of peripheral arterial pulses; and for four men on clinical symptoms of cerebral atherosclerosis and history of intermittent claudication.

**Equipment**

An ultrasonographic assessment of carotid arteries was carried out by a physician (R.S.) and nurse Ulla Raisänä. Each of them did approximately half of the scannings. The ultrasound examination of carotid arteries was performed while the subject was supine with his head turned away from the sonographer. We used a duplex ultrasound system ATL Ultramark 5 (Advanced Technology Laboratories) with a linear scanner functioning at 7.5-MHz scanning frequency in B-mode and a 5-MHz frequency in pulsed Doppler mode. The Doppler was used only to identify the vessels.

**Ultrasonographic Examination**

The B-mode scanning protocol involved the examination of the right and left common carotid arteries, including the lower portion of the carotid bulb below the carotid bifurcation. The lower part of the carotid bulb (up to the tip of the flow divider) is considered here as a part of the common carotid artery. Intima-media thickness (IMT) measurements were done in this segment below the top of the flow divider. Internal carotid arteries were not examined because they were not accessible in all subjects. Both longitudinal and cross-sectional images were viewed. The scanhead was in a perpendicular position in relation to the arterial walls. Three angles of interrogation were used: anterolateral, lateral, and posterolateral. The image was focused on the posterior (far) wall of common carotid arteries. The ultrasonographic examination including the preparation of the subject lasted on the average for 30 minutes. Scanning of the whole arterial segment examined was recorded on a videocassette recorder (VCR). The average duration of the recordings was 10 minutes.

**Measurement of Intima-Media Thickness**

The IMT was measured from VCR recordings of the scans by the physician (R.S.) who had performed them. The reader had no knowledge of the medical history, medications, and symptoms of the subjects.

The PCVISION Plus Frame Grabber digitizer board (Imaging Technology Inc), installed in an IBM PC AT microcomputer, was used to digitize the longitudinal B-scan frames chosen by the reader to represent the greatest IMT. The Pearson correlation between the original and repeated IMT (mean of right and left) was 0.996 (linear regression slope, 1.045; intercept, −0.042). The mean, standard deviation, minimum, and maximum were 1.50 mm, 0.65 mm, 0.74 mm, and 3.44 mm for the original and 1.52 mm, 0.69 mm, 0.74 mm, and 3.46 mm for the remeasurements, respectively. Of the reclassifications of the right common carotid arterial wall configuration, 49 of 50 (98%) were concordant (κ coefficient, 0.96). The respective numbers for the right and left carotid artery system.

**Classification of Severity of Atherosclerosis**

In addition to the quantitative IMT measurements, the physician also classified the subjects according to the configuration of the lumen-intima interface and the occurrence of mineralizations in both the near and far walls of common carotid arteries while she was viewing the videotapes.

Atherosclerotic lesions were scored according to two independent classifications, which concerned two different manifestations of atherosclerosis: the nonmineralized plaque and mineralizations. Nonmineralized plaque represents an earlier stage in the progression of the disease (Fig 1). First, the arterial wall configuration was classified into four categories, separately for the right and the left carotid arteries: (1) a smooth arterial wall surface, (2) an uneven arterial wall surface, (3) a protrusion to the lumen, and (4) a large protrusion (>25% of lumen diameter). For the present analysis, a person was defined to have an ultrasonographic nonmineralized atheroma when he had either (1) uneven arterial wall surface or a luminal protrusion or (2) a maximal IMT of ≥1.5 mm in either the right or the left carotid artery system.

The occurrence of mineralizations was classified separately for the right and the left carotid arteries as follows: (1) no mineralizations, (2) a single mineralization, and (3) multiple mineralizations. A mineralization was defined as the presence of an echogenic shadow. For the analysis, a person was defined as having a mineralization if he had a single or multiple mineralization in either the right or left carotid artery system.

Atherosclerotic lesions: the nonmineralized plaque was defined to be present if there was either a nonmineralized atheroma or a mineralization as defined above.

**Reproducibility Study**

To estimate the intraobserver variability of the measurement of maximal IMT and classifications of lesion severity, a blinded rereading of a random sample of 50 VCR recordings (a subset of the present study subjects) was carried out approximately 3 years after the original readings. The IMT measurements and classifications were repeated by the same observer (R.S.), who had no knowledge of the previous values. Another person searched the recordings of the sampled subjects, previously not known by the reader, covered the identities of subjects on the video screen, and verified that the reader was blinded.

The Pearson correlation between the original and repeated IMT (mean of right and left) was 0.996 (linear regression slope, 1.045; intercept, −0.042). The mean, standard deviation, minimum, and maximum were 1.50 mm, 0.65 mm, 0.74 mm, and 3.44 mm for the original and 1.52 mm, 0.69 mm, 0.74 mm, and 3.46 mm for the remeasurements, respectively. Of the reclassifications of the right common carotid arterial wall configuration, 49 of 50 (98%) were concordant (κ coefficient, 0.96). The respective numbers for the left artery were 48 of 50 (96%; κ, 0.93). The classification of mineralizations was concordant for 48 of 50 (96%; κ, 0.91) for the right artery and 49 of 50 (98%; κ, 0.96) for the left artery. The presence of nonmineralized atheroma, the presence of mineralizations, and the presence of any lesion were reclassified with 100% concordance.
Classification of Cardiovascular Manifestations

Only those cardiovascular symptoms and signs assessed during the 30-year follow-up examination in 1989 were used in the present analyses. Resting ECGs were coded according to Minnesota coding rules. ST-segment changes were evaluated separately according to Punsar et al. CHD-associated resting ECG changes were considered present if there were major ECG abnormalities suggesting previous myocardial infarction (Minnesota code 1.1 alone or 1.2 combined with 5.1 or 5.2) or other CHD-associated abnormalities (Minnesota codes 1.2, 5.1-2, 7.1, 7.4, or 8.3 or horizontal or downward sloping ST-segment depression of ≥0.5 mm). History of CHD was considered present if there was definite history of myocardial infarction verified in a hospital during the last 5 years or definite or probable typical angina pectoris according to the Rose questionnaire.

Prevalence of cerebrovascular symptoms due to previous stroke and/or transient ischemic attack was judged by the examining physician. Ischemic cerebrovascular disease was considered present if there was stroke or transient ischemic attack in the medical history during the past 5 years and/or physical findings of earlier stroke. An auscultatory carotid murmur was considered present if heard on either side during the clinical examination. A peripheral arterial pulse was considered absent if at least one of either femoral, posterior tibial, or dorsalis pedis arteries was not palpable. Intermittent claudication was considered present if a participant reported pain, relieved when stopping, in either of the legs (calf/calves)
while walking at an ordinary pace on level ground or hurrying or walking uphill.

**Measurement of Risk Factors**

The present analysis considered both the predictive value of the risk factors measured in past examinations in 1959, 1964, 1969, 1974, and 1984 and the cross-sectional associations of risk factors measured at the 30-year follow-up examination in 1989. The procedures for the measurement of risk factors have been described in detail. Briefly, blood pressure was computed as the difference of systolic and diastolic pressures. Serum total cholesterol concentration was analyzed during 1959 to 1974 by the method of Abell et al as modified by Anderson and Keys and in 1984 and 1989 with an automatic analyzer. Smoking was assessed by personal interview always using the same questionnaire. Smoking was divided into three categories: never smokers, ex-smokers, and current smokers of cigarettes, cigars, or a pipe. Men who had quit smoking less than 1 year before the examination were regarded as current smokers.

**Statistical Analysis**

The dependence of carotid IMT on age was estimated by Pearson's linear correlation coefficients. In addition, one-way analysis of variance was used to test the statistical significance of both the variation of age-specific IMT means over age groups and of the linear trend of IMT means over age groups. The heterogeneity and trend in means were defined as statistically significant at two-sided P<.05.

The association between ultrasonographically assessed carotid atherosclerotic lesions and clinical cardiovascular disease was tested for statistical significance with the SAS Cochran-Mantel-Haenszel statistic. The associations of cardiovascular disease manifestations with the mean maximal carotid IMT were estimated and tested for statistical significance by SAS multivariate logistic modeling.

**Results**

**Mean Carotid Wall Thickness and Prevalence of Atherosclerotic Lesions**

The mean of both the right and left common carotid arteries was 1.5 mm (Table 1). The Pearson correlation coefficient for the maximal IMT between the right and left side was 0.58. There was no statistically significant variation in the mean maximal carotid IMT over the three age groups (70 to 74, 75 to 79, and 80 to 89 years) even though there was a nonsignificant trend greater thickness at older ages. The correlation coefficient for mean maximal IMT and age was 0.10 (P=.175).
Relation of Carotid Atherosclerosis With Cerebral, Coronary, and Peripheral Artery Disease

The mean common carotid IMT was 47% (P = .003) greater in men with diagnosed cerebral atherosclerosis, 29% (P = .015) greater in those with carotid murmur, 17% (P = .009) greater in those with ischemic ECG abnormalities, and 12% (P = .028) greater in those with a history of previous myocardial infarction or typical angina pectoris than in men without corresponding findings (Table 3). Men in whom peripheral arterial pulse was absent had 21% greater carotid IMT than those with normal peripheral pulses (P = .0003, Table 3). The mean common carotid IMT was nonsignificantly greater in men with intermittent claudication than in others.

The age-adjusted prevalence of nonmineralized atheromas was significantly greater in men with either a history of myocardial infarction or typical angina pectoris (P = .001) than in others (Fig 2). The prevalence of nonmineralized atheromas was associated significantly also with cerebral atherosclerosis (P = .043), carotid murmur (P = .041), ischemic ECG abnormalities (P = .006), and the absence of peripheral pulse (P = .002) but not with intermittent claudication (P = .171) (Fig 2). The prevalence of multiple mineralizations did not associate significantly with any of the signs and symptoms of cardiovascular disease. However, men with cerebrovascular symptoms and absent peripheral pulse also tended to have multiple mineralizations more often.

Associations of Carotid Atherosclerosis With Coronary Risk Factors

The mean serum cholesterol concentration increased from 1959 (6.76 mmol/L) to 1969 (7.17 mmol/L) and then declined to 5.78 mmol/L in 1989 (Table 4). The trend in mean systolic blood pressure was less clear. The proportion of current smokers decreased monotonously from 57% in 1959 to 15% in 1989. The Pearson's correlation between the first (in 1959) and the last (in 1989) serum cholesterol measurements was 0.47, and that for systolic blood pressure was 0.38.

Associations of the major coronary risk factors (serum cholesterol, smoking, and pulse pressure) measured at earlier examinations (in either 1959, 1964, 1969, 1974, 1984, or 1989) with the presence of both nonmineralized atheroma and mineralizations in the 1989 examination were analyzed by constructing multivariate logistic models for each examination year separately (Table 4).

Of serum cholesterol concentrations measured at earlier examinations, those measured in 1959, in 1969, and in 1989 were each significant predictors of a nonmineralized atheroma in 1989, allowing for age and other risk factors measured in the same year.


Pulse pressure measured at all examinations except the last one (in 1989) was associated with multiple mineralizations but not with single mineralization or with nonmineralized atheroma in 1989. None of the annual systolic blood pressure measurements had any significant association with any of the atherosclerotic manifestations in 1989, and the associations for diastolic blood pressure values tended to be inverse.

To study the impact of cumulative (long-term) risk factor elevations earlier in life on the presence of common carotid lesions in the elderly, the associations of the numbers of elevated risk factor values in repetitive examinations (in 1959, 1964, 1969, 1974, 1984, and 1989) with nonmineralized and mineralized atheromas in 1989 were analyzed by multivariate logistic models (Table 5). In forced multivariate models including all three risk factors and age, only hypercholesterolemia and smoking were significant predictors of nonmineralized atheroma, and systolic hypertension was associated

### Table 3. Mean (SD) Maximal Carotid Artery Intima-Media Thickness by Categories of Signs and Symptoms of CVD

<table>
<thead>
<tr>
<th>Signs and Symptoms of CVD</th>
<th>n</th>
<th>Mean IMT, mm</th>
<th>SD, mm</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral atherosclerosis present</td>
<td>10</td>
<td>2.10</td>
<td>0.87</td>
<td>.003</td>
</tr>
<tr>
<td>No cerebral atherosclerosis</td>
<td>168</td>
<td>1.43</td>
<td>0.67</td>
<td></td>
</tr>
<tr>
<td>Carotid murmur present</td>
<td>27</td>
<td>1.81</td>
<td>0.92</td>
<td>.015</td>
</tr>
<tr>
<td>No carotid murmur</td>
<td>153</td>
<td>1.40</td>
<td>0.64</td>
<td></td>
</tr>
<tr>
<td>Ischemic ECG changes</td>
<td>66</td>
<td>1.61</td>
<td>0.70</td>
<td>.009</td>
</tr>
<tr>
<td>Free of CHD-associated changes</td>
<td>114</td>
<td>1.38</td>
<td>0.69</td>
<td></td>
</tr>
<tr>
<td>History of previous MI or typical angina pectoris</td>
<td>60</td>
<td>1.58</td>
<td>0.63</td>
<td>.028</td>
</tr>
<tr>
<td>No history of CHD</td>
<td>120</td>
<td>1.41</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>Absent peripheral arterial pulse</td>
<td>39</td>
<td>1.82</td>
<td>0.85</td>
<td>.0003</td>
</tr>
<tr>
<td>Palpable peripheral arterial pulses</td>
<td>140</td>
<td>1.51</td>
<td>0.77</td>
<td></td>
</tr>
<tr>
<td>Intermittent claudication present</td>
<td>20</td>
<td>1.67</td>
<td>1.07</td>
<td>.437</td>
</tr>
<tr>
<td>No intermittent claudication</td>
<td>158</td>
<td>1.44</td>
<td>0.65</td>
<td></td>
</tr>
</tbody>
</table>

CVD indicates cardiovascular disease; IMT, intima-media thickness (mean value of six measurements altogether: three measurements on both left and right carotid artery walls); SD, standard deviation; ECG, electrocardiographic; CHD, coronary heart disease; and MI, myocardial infarction.
Fig 2. Bar graph shows age-adjusted prevalence (%) of ultrasonographically detected atherosclerotic lesions by clinical symptoms and signs of cardiovascular disease (CVD) among men aged 70 to 89 years. *P<.05 and †P<.01 for difference between categories of each sign or symptom. All differences in prevalence of mineralizations were statistically nonsignificant (P>.05) after adjusting for age. ECG indicates electrocardiographic; CHD, coronary heart disease; and MI, myocardial infarction.

only with multiple mineralizations in the elderly. On the average, for each time of elevation of serum cholesterol (>6.5 mmol/L) at any examination year, the risk of a nonmineralized atheroma in 1989 increased by 24% (95% confidence interval [CI], 7% to 43%; P=.005). Of the three risk factors, only smoking was associated with the presence of any mineralization in 1989 (46% risk elevation; 95% CI, 5% to 104%; P=.023) and systolic hypertension with multiple mineralizations (40% increased risk; 95% CI, 5% to 87%; P=.020).

Discussion

Because the resolution of B-mode (two-dimensional) ultrasonography is best for large superficial arteries, in the present study only the common carotid arteries, including the lower part of the carotid bulb (up to the tip of the flow divider), were examined using two-dimensional ultrasonography. It is obvious that atherosclerosis develops in different arterial systems at different ages, and atherosclerosis in different arterial beds may have different risk factors. Because of their easy access to ultrasound scanning, common carotid arteries are often used as indicators for general and coronary atherosclerosis.

B-mode ultrasonography is more sensitive in the detection and assessment of early atherosclerotic lesions than Doppler. It also can be more easily standardized between observers. Pulsed-wave Doppler enables the assessment of the internal and external carotid arteries, but its between- and within-observer reproducibility is inferior to B-mode.

O’Leary and coworkers have published findings concerning the prevalence of carotid atherosclerosis in elderly persons of the Framingham cohort. Duplex imaging ultrasonography was performed in 1189 subjects aged 66 to 93 years to assess patterns of extracranial carotid disease. The results suggested that no significant disease was found in 30%, mild disease in 62%, moderate disease in 5%, and severe disease or occlusion in 3% of subjects. The limited sensitivity of Doppler imaging could explain the high percentage of subjects with no carotid atherosclerosis in that study.

Bots and coworkers reported focal distal common carotid calcifications or acoustic shadowing only in 5% of 66 normotensive subjects and in 15% of 33 subjects with isolated systolic hypertension with a mean age of 72 years.

The mean maximal thickness of the intima-media complex of the common carotid arteries in the present study population was 1.5 mm, ranging from 0.7 to 5.3 mm. In KIHD (Kuopio Ischaemic Heart Disease Risk Factor Study), the mean of respective IMT was 0.9 mm and the range 0.5 to 4.1 mm in eastern Finnish men aged 42 to 60 years. The scanning procedure in both studies was done by similar methods.

In middle-aged men in the KIHD study, the mean maximal IMT rose sharply and significantly with increasing age. In the present study in men aged 70 to 89 years, the mean maximal common carotid IMT did not increase significantly with age. Taking these studies together suggests that the common carotid IMT elevates with increasing age from the age of 40 to 70 years;
<table>
<thead>
<tr>
<th>Year of Risk Factor Measurement</th>
<th>Mean or %</th>
<th>Nonmineralized Atheroma</th>
<th>Any Mineralization</th>
<th>Multiple Mineralizations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>1959 Cholesterol</td>
<td>6.76</td>
<td>1.30 (1.01, 1.66)</td>
<td>1.08 (0.71, 1.65)</td>
<td>1.06 (0.82, 1.35)</td>
</tr>
<tr>
<td></td>
<td>Current smoking</td>
<td>57%</td>
<td>1.35 (0.65, 2.82)</td>
<td>4.00 (1.02, 15.71)</td>
</tr>
<tr>
<td></td>
<td>Past smoking</td>
<td>25%</td>
<td>0.84 (0.37, 2.28)</td>
<td>0.80 (0.23, 2.78)</td>
</tr>
<tr>
<td></td>
<td>Pulse pressure</td>
<td>54.1</td>
<td>1.01 (0.98, 1.04)</td>
<td>1.05 (0.99, 1.11)</td>
</tr>
<tr>
<td>1964 Cholesterol</td>
<td>6.99</td>
<td>1.23 (0.95, 1.59)</td>
<td>1.42 (0.89, 2.27)</td>
<td>1.28 (0.96, 1.69)</td>
</tr>
<tr>
<td></td>
<td>Current smoking</td>
<td>54%</td>
<td>1.68 (0.80, 3.51)</td>
<td>3.27 (0.80, 13.33)</td>
</tr>
<tr>
<td></td>
<td>Past smoking</td>
<td>28%</td>
<td>1.42 (0.64, 3.16)</td>
<td>0.58 (0.16, 2.08)</td>
</tr>
<tr>
<td></td>
<td>Pulse pressure</td>
<td>53.1</td>
<td>1.01 (0.98, 1.04)</td>
<td>1.06 (1.00, 1.12)</td>
</tr>
<tr>
<td>1969 Cholesterol</td>
<td>7.17</td>
<td>1.38 (1.08, 1.75)</td>
<td>1.20 (0.79, 1.82)</td>
<td>1.07 (0.84, 1.36)</td>
</tr>
<tr>
<td></td>
<td>Current smoking</td>
<td>45%</td>
<td>2.12 (1.02, 4.42)</td>
<td>5.39 (1.03, 28.23)</td>
</tr>
<tr>
<td></td>
<td>Past smoking</td>
<td>39%</td>
<td>0.98 (0.47, 2.04)</td>
<td>0.59 (0.18, 1.98)</td>
</tr>
<tr>
<td></td>
<td>Pulse pressure</td>
<td>61.7</td>
<td>1.02 (0.99, 1.04)</td>
<td>1.03 (0.98, 1.07)</td>
</tr>
<tr>
<td>1974 Cholesterol</td>
<td>6.71</td>
<td>1.23 (0.93, 1.62)</td>
<td>1.35 (0.81, 2.25)</td>
<td>0.98 (0.73, 1.30)</td>
</tr>
<tr>
<td></td>
<td>Current smoking</td>
<td>33%</td>
<td>2.36 (1.09, 5.11)</td>
<td>5.35 (1.03, 27.76)</td>
</tr>
<tr>
<td></td>
<td>Past smoking</td>
<td>50%</td>
<td>1.27 (0.64, 2.54)</td>
<td>1.71 (0.56, 5.24)</td>
</tr>
<tr>
<td></td>
<td>Pulse pressure</td>
<td>59.4</td>
<td>1.01 (0.99, 1.03)</td>
<td>1.00 (0.96, 1.04)</td>
</tr>
<tr>
<td>1984 Cholesterol</td>
<td>6.34</td>
<td>1.16 (0.92, 1.47)</td>
<td>1.43 (0.94, 2.18)</td>
<td>0.98 (0.84, 1.36)</td>
</tr>
<tr>
<td></td>
<td>Current smoking</td>
<td>20%</td>
<td>2.40 (1.02, 5.66)</td>
<td>2.01 (0.37, 10.82)</td>
</tr>
<tr>
<td></td>
<td>Past smoking</td>
<td>56%</td>
<td>1.42 (0.72, 2.80)</td>
<td>1.20 (0.38, 3.79)</td>
</tr>
<tr>
<td></td>
<td>Pulse pressure</td>
<td>64.8</td>
<td>1.01 (0.99, 1.03)</td>
<td>0.99 (0.96, 1.03)</td>
</tr>
<tr>
<td>1989 Cholesterol</td>
<td>5.78</td>
<td>1.34 (1.01, 1.78)</td>
<td>1.29 (0.76, 2.14)</td>
<td>0.96 (0.73, 1.27)</td>
</tr>
<tr>
<td></td>
<td>Current smoking</td>
<td>15%</td>
<td>2.46 (0.94, 6.45)</td>
<td>1.21 (0.22, 6.58)</td>
</tr>
<tr>
<td></td>
<td>Past smoking</td>
<td>60%</td>
<td>1.99 (0.99, 4.00)</td>
<td>1.15 (0.37, 3.62)</td>
</tr>
<tr>
<td></td>
<td>Pulse pressure</td>
<td>71.5</td>
<td>1.01 (1.00, 1.03)</td>
<td>0.99 (0.97, 1.02)</td>
</tr>
</tbody>
</table>

RR denotes relative risk and CI, confidence interval, based on multivariate logistic regression models, a separate model for each examination year. In each model, four risk factor variables and age were entered in original units (as continuous).
thereafter, the increase levels off or at least decelerates. The lack of a relation at older ages could be due to selective survival of the subjects, i.e., those with greater IMT at younger ages had died earlier or were unable to participate in the ultrasound examination.

In the present study, there was only a weak association between the presence of nonmineralized atheromas and mineralizations. In the earlier population study in middle-aged men, small and large atheromas had different risk factor profiles, elevated serum low-density lipoprotein cholesterol being more closely associated with early atherosclerotic changes such as intima-media thickening and smoking with both early and advanced lesions including mineralizations and large nonmineralized atheromas. The prevalence of both nonmineralized atheromas and mineralizations was very high in the present study population. The prevalence was much higher than we observed in middle-aged men, especially considering the high cutoff limit (1.5 mm) for an elevated IMT to be defined as a plaque. In previous studies, plaques have been defined as protrusions with an IMT of ≥1.3 mm or ≥1.2 mm. Calcification of atherosclerotic plaque is widely regarded as a late manifestation of atherosclerosis. Ross and Glomset classify calcifications as complicated lesions, the final stage of atherosclerotic disease. Thus, nonmineralized atheromas are most likely an earlier manifestation of atherosclerosis than mineralizations. However, in middle-aged men large protrusive atheromas were the strongest predictor of a myocardial infarction, whereas small plaques, including mineralizations, had a weaker association with the risk of myocardial infarction. In the present study there was a significant association between cardiovascular disease signs and symptoms and the common carotid wall thickness. This provides further support for the observations from autopsy studies, comparisons of carotid ultrasonography and coronary angiography, and prediction of coronary events by carotid ultrasonography implying that there is a strong relation between carotid and coronary atherosclerosis. Even though coronary atherosclerosis starts to develop at a younger age, it appears to coincide with later carotid atherosclerosis. Previous studies have also indicated that coronary and common carotid atherosclerosis have largely the same risk factors. Similar to the present study, ultrasonographically assessed carotid atherosclerosis was associated closely with atherosclerosis in the lower extremities and with any cardiovascular disease in the Rotterdam Elderly Study. On the basis of our findings and those of the Dutch study, common carotid atherosclerosis can be regarded as a measure of generalized atherosclerosis.

Previous analyses in the present study cohort have indicated that serum cholesterol concentration measured in early middle age predicts later coronary deaths better than cholesterol levels measured in the elderly. Serum cholesterol concentration was measured 5, 15, 20, 25, and 30 years before the present examination of the study cohort. Consistent with this observation was our finding that the measurements of serum cholesterol levels both 30 years and 20 years before the present examination and the number of cholesterol elevations in the six examinations predicted the presence of nonmineralized atheromas in the elderly despite a less than perfect tracking of cholesterol over time. Our present data appear to suggest that exposure to elevated serum cholesterol levels both earlier in life as well as in middle age and even in the elderly contributes to the development of atherosclerotic lesions.

The impact of previous and current smoking on both the mean maximal common carotid IMT and the presence of atheromas was weaker than in most previous studies. Interestingly, although the presence of mineralizations was predicted best by smoking status 15 to 30 years earlier, the presence of nonmineralized atheromas was predicted best by smoking status only 5 to 20 years before the assessment of carotid atheroscle-
rosis. However, there were no statistically significant differences between relative risks for specific years. It could be speculated that nonmineralized atheromas are a more immediate consequence of smoking, whereas long-term exposure to cigarette smoking is required for the development of mineralizations.

In most previous population studies elevated systolic blood pressure has been associated with various manifestations of common carotid atherosclerosis.4,10,12,27 In the Rotterdam Elderly Study, persons over the age of 55 years with isolated systolic hypertension had a greater majority of our elderly subjects had mineralizations. The lack of a significant association of systolic blood pressure and pulse pressure had a relation with both the mean maximal common carotid IMT4 and the presence of common carotid atheroma.10 The lack of a positive association between diastolic blood pressure and atherosclerosis could be explained by the diastolic pressure–reducing effect of arterial stiffening, as suggested by Witteman and coworkers.38 In the present study, an index of long-term exposure to hypertension was associated with mineralized atherosclerotic lesions in the elderly. The lack of a significant association of systolic blood pressure and pulse pressure with the presence of nonmineralized atheroma may be explained by either the effective antihypertensive treatment campaign that took place in the study area, North Karelia, since the early 1970s39 or the survival bias: a greater proportion of hypertensive than normotensive men have died before the present 30-year follow-up examination.13

The present data indicate that almost all eastern Finnish men aged 70 to 89 years have ultrasonographically detectable atherosclerotic lesions in the common carotid arteries. Also, in this age group the severity of common carotid atherosclerosis does not appear to increase with age. While more than half the present study subjects had nonmineralized atheromas, the majority of our elderly subjects had mineralizations. The high prevalence of mineralizations in survivors into old age suggests that nonpromoting arterial mineralizations may not have a strong influence on prognosis. The high occurrence of mineralizations in the elderly also implies that the classification of mineralizations may not be as useful clinically as the assessment of protruding nonmineralized atheromas.

The present study provides further confirmation for the finding that for men, serum cholesterol level is more important than systolic blood pressure as a risk factor for nonmineralized atherosclerotic lesions. Our findings also suggest that serum cholesterol levels in early middle age and in the elderly are equally strong determinants of nonmineralized atherosclerotic lesions in the elderly. According to our study, serum cholesterol level in either the middle aged or in the elderly has no association with arterial mineralizations in elderly men, whereas smoking as well as systolic and pulse pressures appear to associate with the development of arterial mineralizations.

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