Ultrasonographic Manifestations of Common Carotid Atherosclerosis in Elderly Eastern Finnish Men
Prevalence and Associations With Cardiovascular Diseases and Risk Factors

Riitta Salonen, Markku Tervahauta, Jukka T. Salonen, Juha Pekkanen, Aulikki Nissinen, Martti J. Karvonen

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

cardiovascular diseases are very common in Finland, especially in middle-aged men. 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. The prevalence of asymptomatic carotid atherosclerosis in elderly populations is, however, not well known. Ultrasonographically assessed carotid atherosclerosis has predicted the risk of coronary events in middle-aged men. A previous population-based study reported an association between carotid atherosclerosis and signs of cerebral atherosclerosis, carotid claudication, 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.

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

Cardiovascular diseases are very common in Finland, especially in middle-aged men. 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.

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. 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. Carotid ultrasonography was carried out...
for 182 men. One man was not able to undergo ultrasonogra-
phy 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, electrocardiog-
raphy (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 intermit-
tent claudication.

Equipment
An ultrasonographic assessment of carotid arteries was
conducted by a physician (R.S.) and nurse Ulla Raisäinen.
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 scanhead functioning at a 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)
was 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
scannings by the physician (R.S.) who had performed them.
The reader had no knowledge of the medical history, medica-
tions, and symptoms of the subjects.

The PCVISION Plus Frame Grabber digitizer board (Im-
aging Technology Inc), installed in an IBM PC AT microcom-
puter, was used to digitize the longitudinal B-scan frames
chosen by the reader to represent the greatest IMT: distance
between the lumen-intima interface and the media-adventitia
interface. IMAGE-MEASURE morphometry software (Micro-
science Inc) was used to measure distances to derive IMT
measurements.

The sites of the thickest atherosclerotic lesion and the
projection showing the greatest IMT were located both at the
right and the left sides. When the site of the greatest IMT was
not obvious, IMT measurements were done at several sites and
the site with the greatest IMT was selected. IMT of the
posterior (far) wall was measured as the distance from the
leading edge of the first echogenic (bright) line to the leading
edge of the second echogenic line. The first line represents the
lumen-intima interface and the second line is produced by the
collagen-containing upper layer of the tunica adventitia close
to the media-adventitia interface.

Three measurements of IMT were carried out in the same
digitized image at the selected site of the greatest IMT in both
the right and left common carotid arteries at the far wall of the
artery. The mean of these six IMT measurements was used in
the present study. The measurements were not done at a
mineralized ("hard") plaque.

Classification of Severity of Atherosclerosis
In addition to the quantitative IMT measurements, the
physician also classified the subjects according to the config-
uration 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 inde-
pendent classifications, which concerned two different mani-
festations 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 ei-
ther (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 miner-
alization in either the right or left carotid artery system.

An atherosclerotic lesion 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 measure-
ment of mean 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 sub-
jects, previously not known by the reader, covered the identi-
ties 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 devia-
tion, 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 con-
cordant 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% con-
cordance.
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 measured 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 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 Cochrane-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).

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>70-74</td>
<td>1.4</td>
<td>0.7</td>
<td>0.7-5.3</td>
<td>87</td>
</tr>
<tr>
<td>75-79</td>
<td>1.5</td>
<td>0.6</td>
<td>0.7-4.0</td>
<td>59</td>
</tr>
<tr>
<td>80-89</td>
<td>1.6</td>
<td>0.8</td>
<td>0.7-3.5</td>
<td>36</td>
</tr>
<tr>
<td>All ages</td>
<td>1.5</td>
<td>0.7</td>
<td>0.7-5.3</td>
<td>182</td>
</tr>
</tbody>
</table>

Of 182 men, 170 (93%) had either a nonmineralized or a mineralized atherosclerotic lesion on either the right or the left side (Table 2). There was no relation with age. Eighty-two (45%) men had either an uneven wall surface or a protrusion, and another 11 men had at least a single mineralization. The prevalence of neither of these manifestations of carotid atherosclerosis differed significantly between the age groups.

The prevalence of multiple mineralizations was higher in men with nonmineralized atheroma (72%) than in those with no soft atheroma (53%), χ² 7.19, P=.007. However, the association between the four-category classification of wall configuration, describing soft lesions, and the presence of mineralizations (none, single, multiple) was not statistically significant (Table 2). Mineralizations were most often located in the carotid bulb with carotid bifurcation, whereas nonmineralized atheromas were more dispersed along the whole common carotid arteries.

<table>
<thead>
<tr>
<th>Age (y) and Arterial Wall Configuration</th>
<th>Mineralization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smooth wall surface</td>
<td>None</td>
</tr>
<tr>
<td>70-74</td>
<td>3</td>
</tr>
<tr>
<td>Uneven wall surface</td>
<td>1</td>
</tr>
<tr>
<td>Protrusion</td>
<td>1</td>
</tr>
<tr>
<td>Large protrusion</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
</tr>
<tr>
<td>75-79</td>
<td>6</td>
</tr>
<tr>
<td>Smooth wall surface</td>
<td>0</td>
</tr>
<tr>
<td>Uneven wall surface</td>
<td>0</td>
</tr>
<tr>
<td>Protrusion</td>
<td>0</td>
</tr>
<tr>
<td>Large protrusion</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
</tr>
<tr>
<td>80-89</td>
<td>12</td>
</tr>
<tr>
<td>Smooth wall surface</td>
<td>1</td>
</tr>
<tr>
<td>Uneven wall surface</td>
<td>1</td>
</tr>
<tr>
<td>Protrusion</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
</tr>
</tbody>
</table>

Subjects were classified according to the more severe lesion in either right or left common carotid artery.

Table 1. Mean Maximal Common Carotid Intima-Media Thickness in Age Groups

Table 2. Number of Men According to the Presence of Mineralizations, Arterial Wall Configuration,* and Age
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
Cerebral symptoms present (n=10)
No cerebral symptoms (n=168)
Carotid murmur present (n=27)
No carotid murmur (n=153)
Ischemic ECG changes (n=66)
Free of CHD associated changes (n=114)
History of previous MI or angina pectoris (n=60)
No history of CHD (n=120)
Absent peripheral arterial pulse (n=39)
Palpable peripheral arterial pulses (n=140)
Intermittent claudication present (n=20)
No intermittent claudication (n=158)

![Bar graph showing 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.]

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 4. Associations of Serum Cholesterol Concentration (mmol/L), Smoking Status, and Pulse Pressure (mm Hg) Measured in Each Examination Year With the Presence of Nonmineralized Carotid Atheroma and Carotid Mineralizations in 1989

<table>
<thead>
<tr>
<th>Year of Risk Factor Measurement</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>P</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td>1959 Cholesterol</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>1964 Cholesterol</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>1969 Cholesterol</td>
<td>1.38 (1.08, 1.75)</td>
<td>1.20 (0.79, 1.35)</td>
<td>1.07 (0.84, 1.36)</td>
</tr>
<tr>
<td>1974 Cholesterol</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>1984 Cholesterol</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>1989 Cholesterol</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>1.01 (0.99, 1.03)</td>
<td>1.00 (0.96, 1.03)</td>
<td>1.00 (0.96, 1.03)</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, ie, 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 elderly 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.29 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,2,29 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 mm30 or as an IMT of ≥1.2 mm.3,29

Calcification of atherosclerotic plaque is widely regarded as a late manifestation of atherosclerosis.31 Ross and Glomset32 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.5,11

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.11 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.12 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.13 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 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.2,4,7,8,11 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.\textsuperscript{4,10,12,27} In the Rotterdam Elderly Study, persons over the age of 55 years with isolated systolic hypertension had a greater mean IMT in the common carotid arteries and more atherosclerotic plaques.\textsuperscript{10} In the earlier population studies in eastern Finnish middle-aged men, it was also shown that only the systolic blood pressure and the pulse pressure had a relation with both the mean maximal common carotid IMT\textsuperscript{4} and the presence of common carotid atheroma.\textsuperscript{32} 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.\textsuperscript{36} 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 1970s\textsuperscript{39} or the survival bias: a greater proportion of hypertensive than normotensive men have died before the present 30-year follow-up examination.\textsuperscript{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 nonprotruding 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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