Prevalence of Carotid Plaque in a 63- to 65-Year-Old Norwegian Cohort From the General Population: The ACE (Akershus Cardiac Examination) 1950 Study

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Background—New data on extracranial carotid atherosclerosis are needed, as improved ultrasound techniques may detect more atherosclerosis, the definition of plaque has changed over the years, and better cardiovascular risk control in the population may have changed patterns of carotid arterial wall disease and actual prevalence of established cardiovascular disease. We investigated the prevalence of atherosclerotic carotid plaques and carotid intima–media thickness (cIMT) and their relation to cardiovascular risk factors in a middle-aged cohort from the general population.

Methods and Results—We performed carotid ultrasound in 3683 participants who were born in 1950 and included in a population-based Norwegian study. Carotid plaque and cIMT were assessed according to the Mannheim Carotid Intima–Media Thickness and Plaque Consensus, and a carotid plaque score was used to calculate atherosclerotic burden. The participants were aged 63 to 65 years, and 49% were women. The prevalence of established cardiovascular disease was low (10%), but 62% had hypertension, 53% had hypercholesterolemia, 11% had diabetes mellitus, and 23% were obese. Mean cIMT was 0.73±0.11 mm, and atherosclerotic carotid plaques were present in 87% of the participants (median plaque score: 2; interquartile range: 3). Most of the cardiovascular risk factors, with the exception of diabetes mellitus, obesity and waist–hip ratio, were independently associated with the plaque score. In contrast, only sex, hypertension, obesity, current smoking, and cerebrovascular disease were associated with cIMT.

Conclusions—We found very high prevalence of carotid plaque in this middle-aged population, and our data support a greater association between cardiovascular risk factors and plaque burden, compared with cIMT.

Clinical Trial Registration—URL: https://www.clinicaltrials.gov. Unique identifier: NCT01555411. (J Am Heart Assoc. 2018;7:e008562. DOI: 10.1161/JAHA.118.008562.)

Key Words: atherosclerosis, cardiovascular disease, carotid artery, carotid ultrasound

Atherosclerosis is a systemic disease that affects the vascular system and that develops gradually over years, initially as a thickening of the vessel wall and slowly developing into an atherosclerotic formation.1 B-mode ultrasound examination of the carotid artery is an effective and validated noninvasive method to assess the degree of atherosclerosis and subclinical disease. Both carotid intima–media thickness (cIMT) and carotid plaque have been used as surrogate markers of atherosclerosis and cardiovascular disease (CVD). Traditionally, cIMT is thought to represent the first structural change in the atherosclerotic process, likely to progress to an atheroma located in the carotid wall. Among all ultrasound measures, the total plaque area (the sum of all plaque areas) as a marker for plaque...
Clinical Perspective

What Is New?

- Carotid plaque was found in nearly 9 of 10 participants aged 63 to 65 years in this population-based study.
- Traditional cardiovascular risk factors were common in participants with carotid plaque, and we found a strong association between cardiovascular risk factors and carotid plaque burden.

What Are the Clinical Implications?

- When performing ultrasound examination of the carotid arteries in participants aged 63 to 65 years, carotid plaque will be a frequent finding.
- Our findings support previous data suggesting that assessment of carotid plaque burden may be more useful than measuring carotid intima–media thickness in cardiovascular risk stratification.

Medical History and Lifestyle Variables

Hypertension was defined as an average measurement of systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg in sitting position after 10 minutes of rest and/or use of antihypertensive medication. Diabetes mellitus was defined as HbA1c ≥6.5% and/or fasting plasma glucose ≥7.0 mmol/L and/or use of glucose-lowering medication. Obesity was defined according to the World Health Organization definition (body mass index [kg/m²] ≥30). Hypercholesterolemia was defined as total cholesterol ≥6.2 mmol/L and/or low-density lipoprotein ≥4.1 mmol/L and/or use of lipid-lowering medication. History of stroke or transient ischemic attack, CVD, smoking habits, and level of physical activity were self-reported. Higher education was defined as >12 years of formal education. Systemic Coronary Risk Evaluation (SCORE) was used to calculate the cardiovascular risk in the study population.

B-Mode Ultrasound Recordings of the Carotid Artery

Ultrasound images of the right and left extracranial arteries (common carotid artery, internal and external carotid artery) were recorded in both long- and short-axis views on a Vivid E9 machine (GE Healthcare) using a linear L9 array transducer for vascular imaging. The cIMT was measured in B-mode using a semiautomated IMT package for the Vivid E9 system. The measurements were conducted over a minimum of 10-mm length on both sides at the far wall in the common carotid artery, longitudinal and perpendicular to the ultrasound beam, in lateral view, at least 5 mm proximal of the bifurcation in an area with clearly defined lumen–intima and in a region free of plaque. The mean average cIMT was used (Figure 1).

A plaque was defined according to the latest version of the Mannheim Carotid Intima–Media Thickness and Plaque Consensus: a focal structure that protrudes into the arterial lumen of at least 0.5 mm or 50% of the surrounding cIMT value or that demonstrates a thickness of 1.5 mm measured form the media–adventitia interface.

The carotid artery was divided into 4 segments (common carotid artery, bifurcation, and internal and external carotid artery), and plaques were assessed in each segment. The diameter of the greatest plaque in each segment was measured. Plaque diameters ≥1.5, ≥2.5, and ≥3.5 mm were given 1, 2, and 3 points, respectively (Figure 2). The point scores for each of the 4 segments were summarized into a total plaque burden score, ranging from 0 to 24 points. Plaque assessment was performed blinded to medical history status and cardiovascular risk profile.

Carotid artery stenosis severity was assessed in accordance with Consensus Panel gray scale and Doppler US criteria; peak velocity <125 cm/s was considered normal.
125 to 230 cm/s showed 50% to 69% stenosis, and 
230 cm/s showed >70% stenosis.

The examinations were performed by 2 ultrasound tech-
nicians and 2 physicians, all trained in vascular ultrasound, 
and all underwent a joint training program before the start of 
the study. All analyses were performed offline on Echopac PC 
v12 (GE Vingmed) by the 2 physicians. Inter- and intrarater 
reliability tests were performed twice during the inclusion 
period, in which the 2 physicians measured plaque diameter 
twice for plaque score calculation on the same 25 randomly 
selected examinations. Both tests showed excellent results 
(Cronbach $\kappa = 0.999$).

Ethics

The study protocol was approved by the Regional Committees 
for Medical and Health Research Ethics in Norway (ref. 
number 2011/1475). All participants signed written informed 
consent before entering the study.

Statistical Analysis

Descriptive demographic and clinical measures are shown as 
mean±SD or as numbers and percentages. The cIMT is given as 
mean±SD, plaque score is shown as median and interquartile 
range, and prevalence is shown as percentages with 95% 
confidence intervals (score with continuity correction; Fleiss 
quadratic). The independent-samples Student $t$ test was used 
for comparisons between groups. Categorical variables were 
compared using the $\chi^2$ test. Distribution of plaque burden was 
assessed in relation to risk burden using percentiles. The 
impact of clinical variables on plaque score was analyzed using 
Poisson regression, because the plaque scores were approx-
imately Poisson distributed (Figure 3), whereas linear regres-
sion was used to assess the impact of clinical variables on cIMT, 
as cIMT was approximately normally distributed. Variables with 
$P \leq 0.1$ in univariate analyses were included in the multivariate 
analyses. The significance level was set at $P < 0.05$ in the 
multivariate analysis. All analyses were performed using IBM 
SPSS Statistics 23 software.

Results

After inviting 5827 participants, a total of 3706 were included 
in the ACE 1950 study (attendance rate 64%). One had 
missing values because of technical and anatomical difficul-
ties and 22 declined to take part in the ultrasound survey, 
leaving 3683 participants with complete carotid ultrasound 
examinations (Figure 4). The participants were aged 63 to 
65 years (mean: 63.9±0.7 years), and 1887 (51%) were male. 
Clinical characteristics are shown in Table 1.

Atherosclerotic carotid plaques were present in 87% of the 
participants. The median plaque score was 2 (interquartile 
range: 3). The most frequent plaque localization was carotid 
bulb, present in 83% of the participants. Plaque was more 
often present in men than women (92% versus 83%, $P < 0.001$). 
The prevalence of >50% carotid artery stenosis was 2.3% in 
the total cohort, with no significant sex differences (2.6% in
men versus 1.9% in women, \( P=0.228 \)). Ultrasound characteristics are shown in Table 2.

Increasing plaque scores were associated with increasing burden of traditional cardiovascular risk factors. An overview of the prevalence of cardiovascular risk factors in the different plaque categories is presented in Table 3. Participants with a plaque score in the fourth quarter (with a plaque score \( \geq 4 \)), compared with participants with scores in the first 3 quarters (with a plaque score \(<4\)), had a significantly higher prevalence of hypertension, hypercholesterolemia, diabetes mellitus, obesity, current smoking, CVD, and cerebrovascular disease. Furthermore, the proportion of high and very high 10-year risk of fatal CVD according to SCORE was significantly higher in the fourth quarter compared with the first 3 quarters. In addition, these participants also had significantly lower prevalence of higher education and physical activity.

The following variables were associated with higher plaque scores in both univariate and multivariate analysis: current smoking, hypertension, coronary heart disease, history of cerebrovascular disease, hypercholesterolemia, and physical inactivity. In contrast, female sex and higher education were associated with lower plaque scores (Table 4). The model explained 16% of the total variation of the plaque score (\( r^2=0.16 \)).

Mean cIMT was 0.73±0.11 mm. In univariate analyses, male sex, diabetes mellitus, hypertension, current smoking, obesity, waist–hip ratio, coronary heart disease, and history of cerebrovascular disease were associated with cIMT. In multivariate analysis, in descending order of impact, only sex, cerebrovascular disease, hypertension, obesity, and current smoking were independently associated with cIMT (Table 5). The model explained only 5% of the total variation of cIMT (\( r^2=0.05 \)).

**Discussion**

The early stages of carotid artery vessel pathology are highly visible in a general middle-aged population: Carotid plaques were present in 9 of 10 participants aged 63 to 65 years in
To our knowledge, no other studies have reported such high prevalence of carotid plaques in a population of this age group. The plaque score, as a measure of plaque burden, was associated with increased prevalence of cardiovascular risk factors, as expected. In addition, plaque score was associated with a greater number of cardiovascular risk factors and with higher explained variance than cIMT, supporting the notion that atherosclerotic plaque is a more advanced stage of vascular disease. Mean cIMT was just below the 75th percentile of the proposed age- and sex-specific reference interval for common cIMT in a general population. However, location, timing, and number of measurements, as well as the software algorithm, influence the cIMT results. This makes cIMT unsuitable for direct comparisons between studies and may explain higher cIMT values in our population, despite the cohort being rather healthy. Our findings reduce the value of cIMT in cardiovascular screening because almost all patients have detectable plaques.

Plaque burden increases with age. In previous studies, the prevalence of carotid plaques has varied significantly, ranging from 25% to 93%. In the present study, the definition of plaque was in accordance with the Mannheim Carotid Intima-Media Thickness and Plaque Consensus from 2004, in which cIMT ≥ 1.5 mm was considered as a plaque, whereas earlier studies used other definitions. In addition, the studies have included either older or younger patients, men only, or examination of only 1 artery. Population-based studies have shown a decrease in risk factors and cardiovascular mortality over past decades due to treatment of vascular risk in accordance with guidelines for this population-based study. Traditional cardiovascular risk factors were common in participants with plaque and were strongly associated with increasing plaque scores.

### Table 1. Baseline Characteristics of the Study Population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n=3683)</th>
<th>Men (n=1887)</th>
<th>Women (n=1796)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>100</td>
<td>51</td>
<td>49</td>
</tr>
<tr>
<td>Hypertension</td>
<td>62</td>
<td>66</td>
<td>58</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>53</td>
<td>51</td>
<td>55</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>11</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>Obesity</td>
<td>23</td>
<td>24</td>
<td>21</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.92±0.10</td>
<td>0.97±0.07</td>
<td>0.85±0.08</td>
</tr>
<tr>
<td>Physical activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>5</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Exercise ≥2 d/wk</td>
<td>62</td>
<td>57</td>
<td>67</td>
</tr>
<tr>
<td>Higher education</td>
<td>46</td>
<td>50</td>
<td>42</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily smoker</td>
<td>14</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>Former</td>
<td>46</td>
<td>47</td>
<td>44</td>
</tr>
<tr>
<td>Never</td>
<td>35</td>
<td>33</td>
<td>37</td>
</tr>
<tr>
<td>History of coronary heart disease</td>
<td>7</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>History of cerebrovascular event</td>
<td>4</td>
<td>5.0</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Categorical variables are given as percentages, and normally distributed variables are given as mean±SD.

### Table 2. Ultrasound Characteristics of the Study Population

#### Ultrasound Measures

<table>
<thead>
<tr>
<th>Ultrasound Measures</th>
<th>Total (n=3683)</th>
<th>Men (n=1887)</th>
<th>Women (n=1796)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean cIMT right, mm</td>
<td>0.72±0.12</td>
<td>0.73±0.13</td>
<td>0.70±0.11</td>
</tr>
<tr>
<td>Mean cIMT left, mm</td>
<td>0.74±0.14</td>
<td>0.76±0.15</td>
<td>0.71±0.12</td>
</tr>
</tbody>
</table>

#### Plaque

<table>
<thead>
<tr>
<th>Median plaque score, IQR</th>
<th>2 (3)</th>
<th>3 (2)</th>
<th>2 (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>12.7 (11.6–13.8)</td>
<td>8.1 (6.9–9.4)</td>
<td>17.5 (15.7–19.3)</td>
</tr>
<tr>
<td>1–3</td>
<td>60.7 (59.2–62.4)</td>
<td>57.3 (55.1–59.6)</td>
<td>64.4 (62.2–66.6)</td>
</tr>
<tr>
<td>4–6</td>
<td>21.2 (19.2–20.4)</td>
<td>26.8 (24.6–28.9)</td>
<td>15.2 (13.6–16.9)</td>
</tr>
<tr>
<td>7–9</td>
<td>4.4 (3.7–5.1)</td>
<td>6.1 (5.1–7.3)</td>
<td>2.6 (2.0–3.6)</td>
</tr>
<tr>
<td>≥10</td>
<td>1.0 (0.7–1.4)</td>
<td>1.6 (1.1–2.3)</td>
<td>0.3 (0.1–0.7)</td>
</tr>
</tbody>
</table>

#### Degree of stenosis

<table>
<thead>
<tr>
<th>Degree of stenosis</th>
<th>Total occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–69</td>
<td>1.0 (0.1–0.4)</td>
</tr>
<tr>
<td>&gt;70</td>
<td>0.3 (0.1–0.4)</td>
</tr>
</tbody>
</table>

Categorical variables are given as percentages with 95% CI, and normally distributed variables are given as mean±SD. CI indicates confidence interval; cIMT, carotid intima-media thickness; IQR, interquartile range.
Table 3. Plaque Score in Groups in Relation to Cardiovascular Risk Factors

<table>
<thead>
<tr>
<th></th>
<th>Percentiles</th>
<th>Quarters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>10 25 50 75 90 95 1–3 4 P Value</td>
</tr>
<tr>
<td>Plaque score</td>
<td>0 1 2 4 5 7</td>
<td>&lt;4 4</td>
</tr>
<tr>
<td>Plaque score in groups</td>
<td>0 1 2 3 4 5</td>
<td>6–7 3–4 5</td>
</tr>
<tr>
<td>Mean cIMT (mm)</td>
<td>0.73 ± 0.11</td>
<td>0.68 ± 0.10 0.71 ± 0.10 0.72 ± 0.11 0.74 ± 0.11 0.77 ± 0.12 0.80 ± 0.12 0.71 ± 0.10 0.78 ± 0.12 &lt;0.001</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>48.8</td>
<td>67.2 58.0 52.8 40.4 33.6 28.9 54.4 33.3 &lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>62.0</td>
<td>47.5 52.9 60.9 67.7 71.4 78.0 57.3 75.0 &lt;0.001</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>52.6</td>
<td>39.8 47.8 51.9 55.2 63.6 66.9 49.6 60.9 &lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>10.4</td>
<td>6.6 7.7 8.8 12.7 13.3 16.7 9.0 14.2 &lt;0.001</td>
</tr>
<tr>
<td>Obesity</td>
<td>22.6</td>
<td>20.1 21.0 21.0 24.5 25.3 26.7 21.8 25 0.047</td>
</tr>
<tr>
<td>Higher education</td>
<td>46.3</td>
<td>53.0 48.1 48.7 43.2 42.9 38.4 48.3 40.7 &lt;0.001</td>
</tr>
<tr>
<td>Physical activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>5.0</td>
<td>3.4 2.5 5.4 5.2 8.5 9.6 4.1 7.5 &lt;0.001</td>
</tr>
<tr>
<td>Exercise ≥2 d/wk</td>
<td>61.8</td>
<td>66.0 65.0 61.6 61.5 58.9 52.2 63.7 56.5 &lt;0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily</td>
<td>14.4</td>
<td>1.1 1.0 0.2 0.2 0.0 0.5 0.6 0.1 0.086</td>
</tr>
<tr>
<td>Former</td>
<td>45.8</td>
<td>44.3 44.9 44.6 48.5 46.9 44.1 45.7 46.2 0.82</td>
</tr>
<tr>
<td>Never</td>
<td>34.9</td>
<td>45.0 42.8 37.9 30.2 24.5 17.6 39.5 23.5 &lt;0.001</td>
</tr>
<tr>
<td>History of coronary heart disease</td>
<td>7.1</td>
<td>2.4 2.2 5.2 9.4 10.8 19.8 4.7 13.7 &lt;0.001</td>
</tr>
<tr>
<td>History of cerebrovascular event</td>
<td>3.8</td>
<td>1.7 2.3 3.4 3.9 7.5 7.9 2.9 6.2 &lt;0.001</td>
</tr>
<tr>
<td>Score</td>
<td>3.6 ± 2.4</td>
<td>2.8 ± 1.5 3.3 ± 1.8 3.7 ± 2.2 4.2 ± 2.7 4.6 ± 2.8 5.1 ± 2.9 3.5 ± 2.1 4.8 ± 2.9 &lt;0.001</td>
</tr>
<tr>
<td>Low risk</td>
<td>0.5</td>
<td>1.1 1.0 0.2 0.2 0.0 0.5 0.6 0.1 0.086</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>77.5</td>
<td>91.3 84.0 78.9 71.9 66.7 59.7 81.6 63.2 &lt;0.001</td>
</tr>
<tr>
<td>High risk</td>
<td>19.6</td>
<td>7.1 14.4 18.8 24.8 28.3 33.5 16.4 31.5 &lt;0.001</td>
</tr>
<tr>
<td>Very high risk</td>
<td>2.4</td>
<td>0.4 0.6 2.1 3.3 5.0 6.8 1.5 5.2 &lt;0.001</td>
</tr>
</tbody>
</table>

Categorical variables are given as percentages, and normally distributed variables are given as mean ± SD. cIMT indicates carotid intima–media thickness.
Table 4. Poisson Regression, Plaque Score in Relation to Cardiovascular Risk Factors and Lifestyle Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate Exp(B)</th>
<th>95% CI</th>
<th>P Value</th>
<th>Multivariate Exp(B)</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current smoking</td>
<td>1.741</td>
<td>(1.643–1.845)</td>
<td>&lt;0.001</td>
<td>1.512</td>
<td>(1.436–1.591)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>0.697</td>
<td>(0.669–0.725)</td>
<td>&lt;0.001</td>
<td>0.743</td>
<td>(0.703–0.786)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>1.667</td>
<td>(1.565–1.775)</td>
<td>&lt;0.001</td>
<td>1.323</td>
<td>(1.237–1.237)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.386</td>
<td>(1.328–1.447)</td>
<td>&lt;0.001</td>
<td>1.300</td>
<td>(1.243–1.359)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>1.430</td>
<td>(1.309–1.563)</td>
<td>&lt;0.001</td>
<td>1.254</td>
<td>(1.146–1.373)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>1.421</td>
<td>(1.198–1.556)</td>
<td>&lt;0.001</td>
<td>1.180</td>
<td>(1.087–1.281)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>1.251</td>
<td>(1.201–1.301)</td>
<td>&lt;0.001</td>
<td>1.144</td>
<td>(1.096–1.195)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Education</td>
<td>0.880</td>
<td>(0.845–0.916)</td>
<td>&lt;0.001</td>
<td>0.947</td>
<td>(0.908–0.987)</td>
<td>0.010</td>
</tr>
<tr>
<td>Waist–hip ratio</td>
<td>5.559</td>
<td>(4.516–6.843)</td>
<td>&lt;0.001</td>
<td>1.175</td>
<td>(0.863–1.599)</td>
<td>0.305</td>
</tr>
<tr>
<td>Obesity</td>
<td>1.083</td>
<td>(1.034–1.135)</td>
<td>0.001</td>
<td>0.979</td>
<td>(0.929–1.032)</td>
<td>0.453</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.260</td>
<td>(1.187–1.338)</td>
<td>&lt;0.001</td>
<td>1.009</td>
<td>(0.945–1.077)</td>
<td>0.797</td>
</tr>
</tbody>
</table>

Table 5. cIMT in Relation to Cardiovascular Risk Factors and Lifestyle Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate B</th>
<th>95% CI</th>
<th>P Value</th>
<th>Multivariate B</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (female)</td>
<td>−0.040</td>
<td>(−0.048 to −0.033)</td>
<td>&lt;0.001</td>
<td>−0.033</td>
<td>(−0.043–0.02)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.027</td>
<td>(0.019–0.034)</td>
<td>&lt;0.001</td>
<td>0.020</td>
<td>(0.013–0.028)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obesity</td>
<td>0.025</td>
<td>(0.017–0.034)</td>
<td>&lt;0.001</td>
<td>0.016</td>
<td>(0.007–0.026)</td>
<td>0.001</td>
</tr>
<tr>
<td>Current smoking</td>
<td>0.007</td>
<td>(0.004–0.010)</td>
<td>&lt;0.001</td>
<td>0.013</td>
<td>(0.003–0.023)</td>
<td>0.013</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>0.034</td>
<td>(0.011–0.039)</td>
<td>&lt;0.001</td>
<td>0.023</td>
<td>(0.005–0.042)</td>
<td>0.015</td>
</tr>
<tr>
<td>Waist–hip ratio</td>
<td>0.198</td>
<td>(0.161–0.236)</td>
<td>&lt;0.001</td>
<td>0.039</td>
<td>(−0.015 to 0.093)</td>
<td>0.154</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>0.016</td>
<td>(−0.001 to 0.033)</td>
<td>&lt;0.001</td>
<td>0.067</td>
<td>(−0.012 to 0.021)</td>
<td>0.595</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>0.025</td>
<td>(0.011–0.039)</td>
<td>0.001</td>
<td>0.004</td>
<td>(−0.010 to 0.018)</td>
<td>0.657</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.020</td>
<td>(0.008–0.032)</td>
<td>0.001</td>
<td>0.000</td>
<td>(−0.012 to 0.012)</td>
<td>0.989</td>
</tr>
<tr>
<td>Education</td>
<td>−0.002</td>
<td>(−0.004 to 0.001)</td>
<td>0.171</td>
<td>…</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>0.004</td>
<td>(−0.003 to 0.012)</td>
<td>0.256</td>
<td>…</td>
<td>…</td>
<td>…</td>
</tr>
</tbody>
</table>

Univariate and multivariate analysis. Variables with P<0.1 were included in the multivariate analysis. CI indicates confidence interval; cIMT, carotid intima–media thickness.

primary prevention and improved acute treatments. The amount of atherosclerosis largely depends on the underlying burden of cardiovascular risk factors, and the increase in cardiovascular risk factor control could, in theory, have resulted in less atherosclerosis. There is no reason to believe that the ACE 1950 study population has a higher vascular burden than other population studies. This is supported by a high proportion of diagnosed and treated hypertension at low rate of current smoking, a mean SCORE risk of 3.6%, and a higher proportion of diagnosed and treated hypertension at study inclusion. Furthermore, the low prevalence of high-grade stenosis in our study corresponds with previous studies, suggesting a similar rather than a greater atherosclerotic burden. Despite this, our results showed the presence of plaque in 9 of 10 participants. The most reasonable explanations are the change in definition of plaque and improved ultrasonography techniques and image quality, as many previous population-based studies of B-mode ultrasound screening of carotid arteries were carried out >2 decades ago.

Despite the fact that B-mode ultrasound of the carotid arteries is effective for detecting early vascular changes, it is not used routinely in cardiovascular risk assessment. Use in clinical practice is complicated by lack of standardization regarding the definition and measurement of cIMT and its high variability, and recommended use of cIMT measurements was recently withdrawn from clinical guidelines. Furthermore, a meta-analysis from 2012 concluded that the addition of cIMT measurements to the Framingham risk score was associated with a small and probably not clinically relevant improvement in risk prediction of first-time myocardial infarction or...
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stroke.29 Carotid plaque, however, compared with cIMT, has significantly higher prognostic accuracy in predicting future cardiovascular events and is recommended for risk assessment.28,30 Increased plaque score in high-risk populations predicts coronary lesions,31 and presence of plaque increases the risk of stroke \( \approx 1.5 \)-fold, independent of plaque location.4 The same study reported a dose-dependent association between carotid plaques and stroke risk.5 Our findings support the strong association between cardiovascular risk factors and degree of subclinical disease measured by plaque burden rather than cIMT. Consequently, we suggest that assessment of carotid plaque burden could be a useful tool in future cardiovascular screening and risk stratification, especially in populations with several risk factors, with the potential for improved risk control and primary CVD prevention.

The ultrasound procedure used in the ACE 1950 study was feasible to perform and interpret. The methodology of setting scores was easy to apply and had excellent interrater reliability. It takes only a few minutes to perform the procedure, which is suitable for use in clinical practice and as a screening tool by trained physicians, unlike measuring total plaque area, which is time consuming and probably more operator dependent. Guidelines for primary prevention include risk assessment, and measure of plaque burden may be included. Nevertheless, it remains to determined whether a higher plaque score, as a measure of plaque burden, in asymptomatic individuals is associated with an increased risk of future cardiovascular events.

Carotid plaque was more prevalent in men than in women, corresponding with other studies.17,32 It is well documented that women in the reproductive age group are protected from developing coronary heart disease compared with men of similar age.33 The effect is independent of cardiovascular risk factors and may be due to differences in vascular biology, including endothelial function, the production of nitric oxide,34 and protective properties of estrogen.33 Historically, men have had higher smoking consumption,35 but this was not the case in the ACE 1950 cohort; however, hypertension, obesity, and diabetes mellitus were significantly more prevalent in men.

Strengths and Limitations

Self-reported information regarding lifestyle variables and medical history such as history of stroke and CVD are associated with some uncertainties. Furthermore, nonresponder bias must be taken into account; however, a response rate of 64% is considered respectable in population-based studies and is in line with other Norwegian population-based studies,36,37 especially considering that most participants had full-time jobs and had to take a day off to participate. Furthermore, the lowest response rate was found in the municipalities located farthest away from the 2 centers. The strengths of this study are the large number of participants, trained investigators, and examination of the carotid artery on both sides. Demographically, the population is considered to represent a cross-section of the Norwegian population.

Conclusion

Carotid plaque was found in 87% of this cohort aged 63 to 65 years from the general population. Plaque burden showed greater association with traditional risk factors than cIMT. Future studies are needed to investigate the predictive ability of the plaque score for incident CVD.

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Disclosures

None.

References


