Impact of Carotid Plaque Screening on Smoking Cessation and Other Cardiovascular Risk Factors
A Randomized Controlled Trial
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Background: Screening of peripheral atherosclerosis is increasingly used, but few trials have examined its clinical impact. We aimed to assess whether carotid plaque screening helps smokers to improve their health behaviors and cardiovascular risk factors.

Methods: We randomly assigned 536 smokers aged 40 to 70 years to carotid plaque ultrasonographic screening (US group) vs no screening (control group) in addition to individual counseling and nicotine replacement therapy for all participants. Smokers with at least 1 plaque received pictures of their plaques with a 7-minute structured explanation. The outcomes included biochemically validated smoking cessation at 12 months (primary outcome) and changes in cardiovascular risk factor levels and Framingham risk score.

Results: At baseline, participants (mean age, 51.1 years; 45.0% women) smoked an average of 20 cigarettes per day with a median duration of 32 years. The US group had a high prevalence of carotid plaques (57.9%). At 12 months, smoking cessation rates were high, but did not differ between the US and control groups (24.9% vs 22.1%; P = .45). In the US group, cessation rates did not differ according to the presence or absence of plaques. Control of cardiovascular risk factors (ie, blood pressure and low-density lipoprotein cholesterol and hemoglobin A1c levels in diabetic patients) and mean absolute risk change in Framingham risk score did not differ between the groups. The mean absolute risk change in Framingham risk score was +0.6 in the US group vs +0.3 in the control group (P = .56).

Conclusion: In smokers, carotid plaque screening performed in addition to thorough smoking cessation counseling is not associated with increased rates of smoking cessation or control of cardiovascular risk factors.

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Many studies have found that measurements of peripheral atherosclerosis improves cardiovascular risk prediction, but few randomized controlled trials (RCTs) have examined the clinical impact of atherosclerosis screening. Evidence from observational studies suggests that screening for peripheral atherosclerosis and knowing its results might help motivate patients to optimize their health behaviors, such as adherence to drug regimens, change in lifestyle and increase in their perception of cardiovascular risk. However, the interpretation of these observational data is limited by the lack of comparison with a randomized control group. Two RCTs assessing the impact of atherosclerosis screening yielded conflicting results.

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Although atherosclerosis screening with carotid ultrasonography (US) or a computed tomographic scan of coronary artery calcification (CAC) has passed into law in Texas and is increasingly used in clinical practice, the role of screening for atherosclerosis in the clinical setting is still controversial. Given the limited RCT data, it is debated whether imaging should be considered only in certain subgroups of patients or extended to healthy adults, leading to controversial recommendations. Because many smokers stop smoking only after an acute cardiovascular event,
we hypothesized that patients’ knowledge of plaque screening results would enhance adherence to treatment regimens, motivation for lifestyle changes, and subsequent cardiovascular risk factor (CVRF) improvement. Pictures of atherosclerotic plaques might have a potential educational/motivational role by capturing a “teachable moment.” However, it is unknown whether carotid plaque screening represents a teachable moment similar to acute cardiovascular events. To assess whether screening for carotid plaques helps motivate smokers to stop smoking and improve their other CVRFs after a 12-month follow-up, we randomized 536 regular smokers to carotid plaque screening by means of US vs no screening (control group) in addition to a comprehensive smoking cessation program for all participants.

### METHODS

We conducted and reported this RCT according to CONSORT (Consolidated Standards of Reporting Trials) guidelines for trials assessing nonpharmacologic treatments.

### STUDY POPULATION

We recruited smokers from the general population in the French-speaking part of Switzerland by newspaper advertisements from November 1, 2007, through November 30, 2009. As previously described, eligible participants were women and men aged 40 to 70 years who smoked at least 10 cigarettes per day, with no periods of smoking abstinence of at least 3 months in the past year. We used questionnaires from a previous smoking cessation trial and excluded smokers with cardiovascular, life-threatening, or unstable psychiatric conditions, a high level of alcohol consumption (≥6 standard units each day during the past week), any cannabis consumption in the past 3 months, or any other drug abuse; use of nicotine replacement therapy (NRT) or other medications to quit smoking; a carotid US examination in the past year; or difficulty obtaining good US imaging of the carotids because of past radiotherapy or major neck surgery. Smokers attended baseline and follow-up visits at the University of Lausanne, which has a large experience in smoking cessation trials.

### STUDY PROTOCOL AND INTERVENTIONS

The institutional review board approved the protocol, and all participants gave written informed consent. Our primary outcome assessed whether US carotid plaque screening improved smoking cessation rates at 12 months. Our second outcome tested whether carotid plaque screening improved CVRF levels and overall 10-year cardiovascular risk based on the Framingham risk score (FRS).

Smokers were randomly assigned to the intervention (US) group undergoing carotid plaque screening or the control group without screening (Figure 1), in addition to a comprehensive smoking cessation program for all. Carotid B-mode US (system 5; Vingmed/General Electric) was performed by a trained observer blinded to clinical information, according to a standard protocol. Carotid plaques were defined as a local widening of at least 50% relative to an adjacent segment, as recommended. Although the choice of a best carotid measurement for risk prediction is controversial, the presence/absence of carotid plaques is a dichotomized variable that might be easily understood by patients and potentially useful to motivate a behavioral change. Intraobserver variability for carotid plaques among 20 randomly selected subjects showed 95% agreement between the first and second readings (κ = 0.89; P < .001), similar to other studies. Smokers with at least 1 carotid plaque received 2 pictures of their plaques followed by a 7-minute tutorial on the significance of atherosclerotic plaques, as previously tested. To ensure similar contact conditions, smokers without plaques and the control group received a 7-minute tutorial on smoking risks. Participants were asked to set a quit date within the week after US.

For both groups, participants underwent a comprehensive smoking cessation program for 1 year. As previously described, this program consisted of six 20-minute individual counseling sessions, 1 telephone call at 6 months, NRT patches tailored to individual needs, and brochures on smoking cessation. Interventions and visit schedules were standardized, and the study staff underwent a smoking cessation training for health care professionals that was based on international guide-
lines. We also collected data on smoking history (using a standardized questionnaire), comorbid conditions, educational level, and medication use.

RANDOMIZATION PROCEDURES

After attending the run-in visit, participants were randomly assigned to one of the 2 groups using a computer-generated randomization scheme in a 1:1 ratio without stratification or blocking (as recommended for non–fully blinded RCTs). The random assignments were concealed using sealed, opaque, sequentially numbered envelopes until all eligibility criteria had been assessed and informed consent had been obtained.

OUTCOMES

Based on standard criteria for smoking cessation RCTs, self-reported smoking cessation was biochemically confirmed by exhaled carbon monoxide levels (Micro Smokeryser; Bedfont Scientific Ltd) at each visit in addition to serum cotinine levels at 1 year using an enzyme-linked immunosorbent assay (Inspec II-Cotinine-EIA; Malhsan Diagnostika). We classified as current smokers those with carbon monoxide levels of at least 10 ppm or cotinine levels of at least 25 ng/mL (except if the participant was currently receiving NRT). The primary outcome was 1-week smoking abstinence (point prevalence) at 12 months. The secondary outcome was continuous abstinence from the quit date to study end. Smoking cessation ascertainment and tobacco counseling were performed by staff blinded to group allocation and US results, whereas participants could not be blinded, similar to previous screening studies, because the US result was the potential motivational tool. Participants’ physicians were also blinded to group assignments and US results.

Secondary outcomes also included the following changes in CVRF levels after 12-month follow-up: low-density lipoprotein cholesterol (LDL-C) level, blood pressure, hemoglobin A1c (HbA1c) level in diabetic participants, high-sensitivity C-reactive protein (hs-CRP) level (smoking cessation has been suggested as a potential intervention for elevated hs-CRP levels), and overall 10-year coronary heart disease risk by FRS. We measured weight, height, blood pressure, and levels of HbA1c, glucose, and lipids after overnight fasting using standard methods. Plasma hs-CRP levels were measured by means of a high-sensitivity latex-enhanced immunonephelometric assay (nephelometer; Dade Behring GmbH). Other outcomes included change in physical activity measured by the International Physical Activity Questionnaire previously validated in 12 countries and change in cardiovascular drug regimen adherence by the Morisky medication adherence questionnaire, previously used in RCTs measuring drug regimen adherence. To detect potential psychological harms of screening, we assessed stress with the 4-item Perceived Stress Scale, quality of life by the 36-Item Short Form Health Survey, and depression scores using the Beck Depression Inventory.

STATISTICAL ANALYSIS

The primary analysis examined the unadjusted rates of 12-month smoking cessation with χ² tests using an intention-to-screen allocation of groups. We conducted sensitivity analyses, adjusting for factors that differed at baseline. In prespecified subgroup analyses, we stratified the US group by the presence or absence of carotid plaque (their presence being the presumable motivating factor) and compared those US group participants with vs those without plaque and those participants with plaque in the US group vs the control group. We performed the same analyses for the other outcomes (CVRF and FRS) using 2-sample t tests. To assess the sensitivity of our results to missing 12-month CVRFs (78 participants with follow-up by telephone or letter; smoking cessation still validated by carbon monoxide level measurements), we used multiple imputation that included all baseline characteristics (except collinear variables) and 12-month smoking cessation.

Our power calculations have been previously described. Briefly, we expected 10% 12-month smoking cessation rates in the control group, based on trials of NRT, and 20% rates in the US group. Using an α level of .05, a power of 80%, and an estimated 20% dropout rate, a difference would be observed with 263 smokers per group (with a total sample size of 530). No interim analyses were planned. For secondary outcomes, we could detect clinically meaningful CVRF changes with a power of more than 80% (changes in LDL-C level, <11.6 mg/dL [to convert to millimoles per liter, multiply by 0.0299]; in blood pressure, <5 mm Hg; in hs-CRP level, <1 mg/L [to convert to nanomoles per liter, multiply by 9.524]; and in FRS, <0.2% 10-year coronary heart disease risk).

RESULTS

We enrolled 536 smokers, including 267 randomly assigned to the carotid plaque screening group and 269 to the control group (Figure 1). A similar number of patients withdrew or were lost to follow-up among the randomized groups. Overall, 1 participant died in the US group and 2 in the control group; these deaths were unrelated to cardiovascular disease (suicide, drowning, and gastrointestinal tract bleeding). Fourteen participants were lost to follow-up, and 7 who had withdrawn their participation were classified as current smokers. The 3 deceased participants and 1 who had moved to an untraceable address were excluded from abstinence analyses, as recommended. At baseline, participants (mean age, 51.1 years; 45.0% women) smoked an average of 20 cigarettes per day, with a median duration of smoking of 31.7 years. (Table 1). Baseline characteristics did not differ markedly between the randomized groups (Table 1). The US group had a 57.9% prevalence of carotid plaques. Most participants (n = 461) intended to quit smoking within 30 days (86.0%), 65 (12.1%) intended to quit within 6 months, 8 (1.5%) were already trying to quit, and 2 (0.4%) were indeterminate.

At 12 months, biochemically validated smoking cessation rates were higher than 20%. Although there was a nonsignificant pattern of higher cessation rates at 1 and 6 months in the US group, the cessation rate did not differ at 12 months between both groups in intention-to-screen analysis for point prevalence abstinence (24.9% [95% CI, 19.7%-30.1%] vs 22.1% [95% CI, 17.1%-27.1%]; P = .45) and continuous smoking abstinence (20.4% [95% CI, 15.5%-25.2%] vs 20.2% [95% CI, 15.4%-25.0%]; P = .97) (Figure 2). Very few participants did not submit samples for biochemical verification of cessation, and the frequency of the few positive sample findings did not differ by group (Table 2).

The 12-month change in blood pressure and levels of LDL-C, hemoglobin HbA1c, and hs-CRP did not differ between the 2 groups (Table 2). The mean change in 10-year FRS was +0.6% in the US group vs +0.3% in the control group (P = .56). Change in CVRF treatment did not differ except for antihypertensives in the US group (+2.1% vs 0% [P = .03]) but without a difference in controlled hyper-

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tension. The proportion of participants reporting potential harms did not differ between groups. No participant underwent carotid revascularization during the 1-year follow-up. 1 had coronary artery stenting for stable angina, and 3 had bypass procedures or dilation for lower extremity arteriopathy. Moreover, 1 participant had a cerebellar ischemic stroke and 1 had a myocardial infarction.

In the preplanned subgroup analysis among the US group, cessation rates did not significantly differ among participants with and without carotid plaques (point prevalence abstinence, 25.7% [95% CI, 18.7%-32.6%] vs 24.1% [95% CI, 16.2%-32.0%] if no plaques; P=.77), and changes in CVRFs were also similar (Table 3) except for a larger decrease in LDL-C levels in those with vs without plaques (−8.1 vs +3.9 mg/dL; P=.004), which persisted after removing participants who were treated or who initiated treatment with medications to lower lipid levels. Rates of controlled hypertension were slightly higher among those with plaques, which was likely related to the small increase in antihypertensive use. The rates of smoking cessation and 12-month CVRF change and control were similar in sensitivity analyses adjusting for the unbalanced distribution of some baseline characteristics or after multiple imputations for missing CVRFs.

Point prevalence abstinence was significantly associated with male sex (odds ratio, 1.68; 95% CI, 1.09-2.57).

### Table 1. Baseline Characteristics According to Group Assignment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Participants (N=536)</th>
<th>US Group (n=267)</th>
<th>Control Group (n=269)</th>
<th>P Value&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>51.1 (7.3)</td>
<td>51.5 (7.6)</td>
<td>50.7 (7.1)</td>
<td>.19</td>
</tr>
<tr>
<td>Female sex, No. (%)</td>
<td>241 (45.0)</td>
<td>124 (46.4)</td>
<td>117 (43.5)</td>
<td>.49</td>
</tr>
<tr>
<td>Level of education, No. (%)</td>
<td>Some high school 362 (67.5)</td>
<td>175 (65.5)</td>
<td>187 (69.5)</td>
<td>.23</td>
</tr>
<tr>
<td>High school graduate</td>
<td>58 (10.8)</td>
<td>35 (13.1)</td>
<td>23 (8.6)</td>
<td>.23</td>
</tr>
<tr>
<td>Postgraduate education</td>
<td>116 (21.6)</td>
<td>57 (21.3)</td>
<td>59 (21.9)</td>
<td></td>
</tr>
<tr>
<td>Smoking history, median (IQR)</td>
<td>No. of cigarettes/d 20 (20-30)</td>
<td>20 (20-30)</td>
<td>20 (20-30)</td>
<td>.77</td>
</tr>
<tr>
<td>No. of cigarettes/d</td>
<td>20 (20-30)</td>
<td>20 (20-30)</td>
<td>20 (20-30)</td>
<td></td>
</tr>
<tr>
<td>Duration of smoking history, y</td>
<td>31.7 (27.0-37.5)</td>
<td>31.7 (26.4-38.0)</td>
<td>31.7 (27.6-36.9)</td>
<td>.93</td>
</tr>
<tr>
<td>No. of pack-years</td>
<td>35.7 (25.8-48.0)</td>
<td>35.0 (25.6-46.8)</td>
<td>36.1 (25.9-49.1)</td>
<td>.45</td>
</tr>
<tr>
<td>Age at initiation of smoking, y</td>
<td>17 (16-20)</td>
<td>17 (16-20)</td>
<td>17 (15-18)</td>
<td>.03</td>
</tr>
<tr>
<td>No. of previous attempts of smoking cessation</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
<td>.94</td>
</tr>
<tr>
<td>Fagerström score&lt;sup&gt;d&lt;/sup&gt;</td>
<td>5.0 (2.1)</td>
<td>4.9 (1.9)</td>
<td>5.2 (2.2)</td>
<td>.12</td>
</tr>
<tr>
<td>Other CVRFs</td>
<td>Hypercholesterolemia, No. (%)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>267 (49.8)</td>
<td>128 (47.9)</td>
<td>139 (51.7)</td>
</tr>
<tr>
<td>Hypertension, No. (%)&lt;sup&gt;e&lt;/sup&gt;</td>
<td>149 (27.8)</td>
<td>87 (32.6)</td>
<td>62 (23.0)</td>
<td>.01</td>
</tr>
<tr>
<td>Diabetes mellitus, No. (%)&lt;sup&gt;f&lt;/sup&gt;</td>
<td>18 (3.4)</td>
<td>10 (3.8)</td>
<td>8 (3.0)</td>
<td>.62</td>
</tr>
<tr>
<td>Body mass index, mean (SD)&lt;sup&gt;g&lt;/sup&gt;</td>
<td>24.9 (4.1)</td>
<td>24.9 (4.1)</td>
<td>24.9 (4.1)</td>
<td>.91</td>
</tr>
<tr>
<td>Family history of early CHD, No. (%)&lt;sup&gt;h&lt;/sup&gt;</td>
<td>70 (13.1)</td>
<td>26 (9.7)</td>
<td>44 (16.4)</td>
<td>.02</td>
</tr>
<tr>
<td>Framingham risk score, median (IQR)&lt;sup&gt;i&lt;/sup&gt;</td>
<td>8.0 (3-16)</td>
<td>8.0 (4-16)</td>
<td>8.0 (3-16)</td>
<td>.96</td>
</tr>
<tr>
<td>Categories of Framingham risk score, No. (%)&lt;sup&gt;j&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10%</td>
<td>276 (51.5)</td>
<td>136 (50.9)</td>
<td>140 (52.0)</td>
<td>.80</td>
</tr>
<tr>
<td>10%-20%</td>
<td>199 (37.1)</td>
<td>104 (39.0)</td>
<td>95 (35.3)</td>
<td>.38</td>
</tr>
<tr>
<td>&gt;20%</td>
<td>61 (11.4)</td>
<td>27 (10.1)</td>
<td>34 (12.6)</td>
<td>.36</td>
</tr>
<tr>
<td>Cardiovascular preventive therapies, No. (%)</td>
<td>Drugs to lower lipid levels 62 (11.6)</td>
<td>22 (8.2)</td>
<td>40 (14.9)</td>
<td>.02</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>81 (15.1)</td>
<td>45 (16.9)</td>
<td>36 (13.4)</td>
<td>.26</td>
</tr>
<tr>
<td>Antihyperglycemics</td>
<td>13 (2.4)</td>
<td>6 (2.2)</td>
<td>7 (2.6)</td>
<td>.79</td>
</tr>
<tr>
<td>Antiplatelet drugs</td>
<td>25 (4.7)</td>
<td>12 (4.5)</td>
<td>13 (4.8)</td>
<td>.85</td>
</tr>
<tr>
<td>Other variables, median (IQR)</td>
<td>Physical activity, MET × min/wk&lt;sup&gt;i&lt;/sup&gt;</td>
<td>3334 (1440-5436)</td>
<td>3360 (1554-5634)</td>
<td>3219 (1440-5238)</td>
</tr>
<tr>
<td>Quality of life</td>
<td>SF-36 physical component</td>
<td>53.6 (48.5-56.8)</td>
<td>53.7 (48.5-56.8)</td>
<td>53.5 (48.4-56.8)</td>
</tr>
<tr>
<td>SF-36 mental component</td>
<td>49.0 (40.5-54.6)</td>
<td>49.0 (40.9-53.7)</td>
<td>49.2 (40.5-54.8)</td>
<td>.67</td>
</tr>
<tr>
<td>Cohen 4-item perceived stress scale</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
<td>.77</td>
</tr>
<tr>
<td>Beck Depression Inventory&lt;sup&gt;k&lt;/sup&gt;</td>
<td>5 (2-9)</td>
<td>5 (2-9)</td>
<td>5 (2-8)</td>
<td>.63</td>
</tr>
</tbody>
</table>

Abbreviations: CHD, coronary heart disease; CVRF, cardiovascular risk factor; IQR, interquartile range; MET, metabolic equivalent task; SF-36, 36-Item Short Form Health Survey; US, ultrasonography.

<sup>a</sup>Percentages have been rounded and might not total 100.

<sup>b</sup>Calculated as a 2-sided t test, a Pearson χ² test, or a rank sum test (when an IQR is reported).

<sup>c</sup>Indicates score for nicotine dependence (0 indicates low; 10, very high), expressed as mean (SD).

<sup>d</sup>Defined as low-density lipoprotein cholesterol level greater than the Adult Treatment Panel III (ATP III) thresholds for drug therapy or current treatment.

<sup>e</sup>Defined as a blood pressure level of at least 140/90 mm Hg, or of at least 130/80 mm Hg if diabetes is present, or current treatment.

<sup>f</sup>Defined as a fasting plasma glucose level of at least 126 mg/dL (to convert to millimoles per liter, multiply by 0.0555), a self-reported medical diagnosis, or the use of any hypoglycemic medication.

<sup>g</sup>Calculated as weight in kilograms divided by height in meters squared.

<sup>h</sup>Indicates CHD in a male first-degree relative younger than 55 years or CHD in a female first-degree relative younger than 65 years.

<sup>i</sup>Framingham risk score according to ATP III guidelines and categories.

<sup>j</sup>Indicates weighted estimate of total physical activity from all reported activities per week based on the International Physical Activity Questionnaire.

<sup>k</sup>Score range, 0 to 63. A higher score indicates increased depressive symptoms.
older age (1.87 for a 10-year increase; 95% CI, 1.22-1.88), lower number of cigarettes per day (0.76 for 10 more cigarettes; 95% CI, 0.60-0.96), and lower duration of smoking history (0.57 for a 10-year increase; 95% CI, 0.38-0.83) in multivariate analysis adjusting for randomized group assignment and baseline characteristics selected by backward deletion using \( P \leq .20 \).

**COMMENT**

In this RCT of 536 middle-aged smokers, carotid plaque screening by means of US was not associated with increased smoking cessation or better control of CVRFs after 12 months when added to comprehensive individual counseling and use of NRT products. In both groups, smoking cessation rates were more than 20% at 12 months. Furthermore, in the US group, smoking cessation rates did not differ according to the presence or absence of carotid plaques.

Our study adds important information to the few trials that have assessed the impact of atherosclerosis screening. In contrast to previous RCTs that were limited by a low number of participants with atherosclerosis or the lack of biochemical validation of smoking cessation, our RCT included the largest sample of smokers and smoking cessation was assessed objectively. A recent meta-analysis has found limited evidence of an effect of cardiovascular imaging on health behavior in primary prevention and called for higher-quality studies because most previous RCTs were relatively small (most trials with <200 participants) and included few smokers and because several did not record medications used during follow-up. Our results are consistent with a previous RCT that found no difference in CVRF control among 450 military personnel aged 39 to 45 years who underwent CAC screening vs no screening. However, the prevalence of smoking and other modifiable risk factors was low in that RCT, and only 15% of their participants had abnormal CAC scores compared with our higher-risk population with a 57.9% prevalence of carotid plaques. Our results were also consistent with the findings of a previous study that detected no difference for 4-year smoking cessation rates (\( P = .64 \)) and physical activity (\( P = .77 \)) among 2137 volunteers randomized to CAC screening vs no scanning. However, the previous study included a small number of smokers (111 participants [5.2%]), and participants underwent only a single counseling session on CVRFs compared with 6 sessions during the 12 months in our study. Although CVRFs partially improved in their CAC group compared with the no-scanning group, the absolute changes were very small (systolic blood pressure difference, −2 mm Hg; LDL-C level difference, −6 mg/dL). Potential explanations for these differences were that these changes occurred in highly educated participants (postgraduate education, 91% vs 21.9% in our RCT) and were concurrent with the introduction of antihypertensives (\( P = .02 \); 18%-24% vs 0%-2.1% in our RCT) and medication to lower lipid levels (\( P = .06 \); 25%-29% vs 3.9%-5.3% in our RCT). Whether these modest changes would reduce cardiovascular events remains to be demonstrated because myocardial infarction rates did not differ between participants who received scanning and those who did not.

For smoking cessation, a recent Cochrane review found little evidence of increased smoking cessation rates by providing feedback on the biomedical effects of smoking except a significant benefit of lung age feedback after spirometry (relative risk, 2.12; 95% CI, 1.24-3.62) and US plaque screening in an RCT conducted in the Seychelles islands. In the study by Bovet et al. smokers who were provided with pictures of their own atherosclerotic plaque had a higher smoking cessation rate (17.6% in the screening group [22.2% in those who had plaque] vs 6.3% in the group without screening). However, that study included mostly light smokers (mean, 10 cigarettes per day), biochemical validation of smoking cessation was not performed, NRT was not provided, and smokers were provided with one brief smoking counseling session. Compared with previous studies, smoking abstinence at 6 months was far higher in the control group of our RCT (36.4% vs 6%), likely owing to the intensive program of smoking cessation counseling; we obtained similar high rates of smoking cessation among the control group in another RCT using...
the same program.23 We therefore cannot exclude carotid US as having no effect on smoking cessation because of the high intensity of our smoking cessation program per se. Whether plaque screening would have an effect on smoking cessation if counseling was less intensive (eg, in primary care settings) remains to be examined.

Our study has several limitations. We included only smokers motivated to quit, and volunteers are generally healthier than random smokers, potentially explaining the high cessation rates in our study. Imaging results were discussed only once, which might have limited the impact. However, previous trials of the effect of subclini-
Table 3. Outcomes Stratified by Group Assignment and the Presence or Absence of Carotid Plaques

<table>
<thead>
<tr>
<th>Variable</th>
<th>US Group With Plaque (A) (n=154)</th>
<th>US Group Without Plaque (B) (n=112)</th>
<th>Control Group (C) (n=269)</th>
<th>P Value for Group Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in cardiovascular preventive treatment, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drugs to lower lipid levels</td>
<td>10 (7.0)</td>
<td>3 (3.0)</td>
<td>9 (3.9)</td>
<td>.46</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>5 (3.5)</td>
<td>0</td>
<td>0</td>
<td>.03</td>
</tr>
<tr>
<td>Antidiabetics, including insulin</td>
<td>1 (0.7)</td>
<td>0</td>
<td>0</td>
<td>.33</td>
</tr>
<tr>
<td>Antiplatelet drugs</td>
<td>4 (2.8)</td>
<td>0</td>
<td>6 (2.6)</td>
<td>.47</td>
</tr>
<tr>
<td>Medication regimen adherence, mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>0.7 (0.9)</td>
<td>0.9 (1.1)</td>
<td>0.8 (1.0)</td>
<td>.27</td>
</tr>
<tr>
<td>After 12 mo</td>
<td>0.6 (0.8)</td>
<td>0.8 (0.7)</td>
<td>0.7 (0.9)</td>
<td></td>
</tr>
<tr>
<td>Potential harms, mean (SE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in quality of life</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF-36 physical component</td>
<td>0.8 (0.6)</td>
<td>0.4 (0.7)</td>
<td>0.4 (0.5)</td>
<td>.80</td>
</tr>
<tr>
<td>SF-36 mental component</td>
<td>0.2 (0.9)</td>
<td>−0.8 (1.2)</td>
<td>−1.7 (0.8)</td>
<td>.16</td>
</tr>
<tr>
<td>Cohen 4-item perceived stress scale</td>
<td>−0.1 (0.2)</td>
<td>0.1 (0.4)</td>
<td>0.3 (0.2)</td>
<td>.29</td>
</tr>
<tr>
<td>Beck Depression Inventory</td>
<td>0.1 (0.4)</td>
<td>0.2 (0.5)</td>
<td>0.2 (0.3)</td>
<td>.81</td>
</tr>
</tbody>
</table>

Abbreviations: CVRF, cardiovascular risk factor; ellipses, values are not meaningful because the numbers used to calculate them are so small; HbA1c, hemoglobin A1c; hs-CRP, high-sensitivity C-reactive protein; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; MET, metabolic equivalent task; NA, not applicable; SF-36, 36-item Short Form Health Survey; US, ultrasonography.

aDefined as exhaled carbon monoxide level of at least 10 ppm or serum cotinine level of at least 25 ng/mL despite self-reported smoking abstinence; such participants with a positive sample finding were counted as current smokers.

bOne participant did not attend carotid plaque screening and was excluded from these subgroup analyses.

cIndicates blood pressure of less than 140/90 mm Hg or of less than 130/80 mm Hg if diabetes was present according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure guidelines among those with hypertension at baseline.

dFramingham risk score according to Adult Treatment Panel III guidelines and categories.

eIndicates LDL-C level of less than the target from the ATP III guidelines among those with hypercholesterolemia at baseline.

fIndicates HbA1c levels of less than 7.0%, according to American Diabetes Association guidelines, among the 18 participants with diabetes at baseline.

gIndicates LDL-C level of less than the target from the ATP III guidelines24 among those with hypercholesterolemia at baseline.

hIndicates blood pressure of less than 140/90 mm Hg or of less than 130/80 mm Hg if diabetes was present according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure guidelines among those with hypertension at baseline.

iIndicates HbA1c levels of less than 7.0%, according to American Diabetes Association guidelines, among the 18 participants with diabetes at baseline.

jChanges were calculated from the following values: US groups, 243 participants; control group, 230.

kAdherence to a cardiovascular medication regimen among participants taking cardiovascular medication was measured with a self-reported 4-item scale in which 0 indicated high adherence levels and 4, low adherence levels. Use of the Morisky medication adherence questionnaire is protected by US copyright laws.
measurements at 12 months, we used multiple imputation to assess the sensitivity of our results to these missing data and found similar results. The significantly larger decrease in LDL-C levels in participants with plaques vs those without plaques should be interpreted with caution. This difference persisted after removing participants treated with medications to lower lipid levels and may be related to better diet or better drug regimen adherence or may have occurred by chance in the context of multiple analyses. We did not examine clinical cardiovascular events because such analysis would have likely required more than 10,000 study subjects.18

Our RCT has several strengths. Despite the fact that many smokers discontinue RCTs in case of smoking relapse, we had remarkably few dropouts (3.9%) compared with previous smoking cessation RCTs.22,30,46 Our dropout rate was also lower than those in several previous large studies of atherosclerosis screening11,43,44 and lower than planned in our power calculations (20%). Compared with previous similar RCTs,10,11 we included a higher-risk population with a high prevalence of CVRFs and carotid plaques (57.9%) and performed a biochemical validation of smoking cessation.

In summary, our RCT demonstrates that the addition of carotid plaque screening to a thorough smoking cessation program is not associated with improved smoking cessation or better control of CVRFs. These findings are important, given the increasing use of such screening in clinical practice3,18 and the growing trend of insurance company reimbursement for this screening.12 Future trials should examine the effect of atherosclerosis screening on cardiovascular events,3 although some have argued that such large and expensive trials may not be undertaken.15,47 Moreover, it should be evaluated whether atherosclerosis screening may be helpful among smokers who undergo less intensive smoking counseling or to refine cardiovascular risk estimates to better target preventive medications.9 Until such data become available, the benefit of atherosclerosis screening should be demonstrated in RCTs before its use can be generally recommended.85

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REFERENCES


4. O’Malley PG. The proof of atherosclerosis imaging is in the evidence: where are the studies [comment]? Arch Intern Med. 2011;171(11):976.


17. Smith PM, Burgess E. Smoking cessation initiated during hospital stay for patients with coronary artery disease: a randomized controlled trial. CMAJ. 2009;180(13):1297-1303.


