ONLINE FIRST

Impact of Carotid Plaque Screening on Smoking Cessation and Other Cardiovascular Risk Factors

A Randomized Controlled Trial

Nicolas Rodondi, MD, MAS; Tinh-Hai Collet, MD; David Nanchen, MD; Isabella Locatelli, PhD; Michèle Depairon, MD; Drahomir Aujesky, MD, MSc; Pascal Bovet, MD, MPH; Jacques Cornuz, MD, MPH

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 A_{1c} 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.

Trial Registration: clinicaltrials.gov Identifier: NCT00548665

Arch Intern Med. 2012;172(4):344-352.
Published online January 23, 2012.
doi:10.1001/archinternmed.2011.1326

Author Affiliations: Department of General Internal Medicine, University Hospital Inselspital, University of Bern, Bern, Switzerland (Drs Rodondi and Aujesky); and Department of Ambulatory Care and Community Medicine, University of Lausanne (Drs Rodondi, Collet, Nanchen, Locatelli, and Cornuz), and University Institute of Social and Preventive Medicine (Drs Locatelli and Bovet) and Service of Angiology (Dr Depairon), University of Lausanne and University Hospital Center, Lausanne, Switzerland.

MANY STUDIES HAVE found that measurements of peripheral atherosclerosis improves cardiovascular risk prediction,[1,2] but few randomized controlled trials (RCTs) have examined the clinical impact of atherosclerosis screening.[3] Evidence from observational studies suggests that screening for peripheral atherosclerosis and knowing its results might help motivate patients to optimize their health behaviors,[4,5] such as adherence to drug regimens,[6] change in lifestyle,[7,8] and increase in their perception of cardiovascular risk.[7,9] 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.[10,11]

For editorial comment see page 309

CME available online at www.jamaarchivescme.com and questions on page 308

Although atherosclerosis screening with carotid ultrasonography (US) or a computed tomographic scan of coronary artery calcification (CAC) has passed into law in Texas[12] and is increasingly used in clinical practice,[3,5] the role of screening for atherosclerosis in the clinical setting is still controversial.[12,13] Given the limited RCT data, it is debated whether imaging should be considered only in certain subgroups of patients[14] or extended to healthy adults,[15] leading to controversial recommendations.[14-16]

Because many smokers stop smoking only after an acute cardiovascular event,[17]

we hypothesized that patients' knowledge of plaque screening results would enhance adherence to treatment regimens,[5,18] motivation for lifestyle changes, and subsequent cardiovascular risk factor (CVRF) improvement. Pictures of atherosclerotic plaques might have a potential educational/motivational role[4,5] by capturing a "teachable moment." However, it is unknown whether carotid plaque screening represents a teachable moment similar to acute cardiovascular events.[17] 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)[19] 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.[20]

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,[21] 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.[22] We used questionnaires from a previous smoking cessation trial[23] 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.[23]

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).[24]

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.[8] Carotid plaques were defined as a focal widening of at least 50% relative to an adjacent segment, as recommended.[25,26] Although the choice of a best carotid measurement for risk prediction is controversial,[25] 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 ($\kappa = 0.89$; $P < .001$), similar to other studies.[26] 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.[8] 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,[21] 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[27] that was based on international guide-

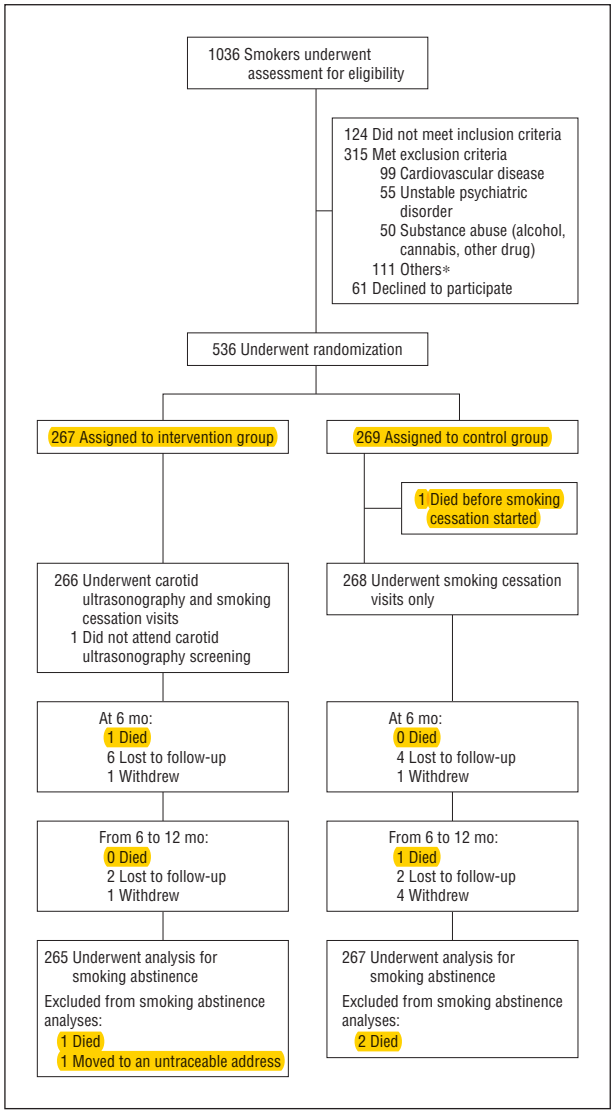

Figure 1. Flowchart of participants. Adapted from the CONSORT (Consolidated Standards of Reporting Trials) 2010 Statement flow diagram. *Other exclusion criteria were unstable nonpsychiatric condition (n=17), recent imaging of the carotid arteries (n=10), already receiving medication therapy for smoking cessation (n=12), request for medication other than nicotine replacement therapy (n=17), declined to attend follow-up visits (n=27), and participating in another study, leaving Switzerland for a longer period, or insufficient fluency in French (n=28).

lines. We also collected data on smoking history (using a standardized questionnaire[23]), 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).[28] 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,[29] self-reported smoking cessation was biochemically confirmed by exhaled carbon monoxide levels (Micro Smokerlyser; 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; Mahsan 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.[22,29,30] 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,[19] 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 A_{1c} (HbA_{1c}) 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[31]), and overall 10-year coronary heart disease risk by FRS.[24] We measured weight, height, blood pressure, and levels of HbA_{1c}, 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).[32] Other outcomes included change in physical activity measured by the International Physical Activity Questionnaire previously validated in 12 countries[33] and change in cardiovascular drug regimen adherence by the Morisky medication adherence questionnaire[34] previously used in RCTs measuring drug regimen adherence.[35] To detect potential psychological harms of screening,[11] we assessed stress with the 4-item Perceived Stress Scale,[36] quality of life by the 36-Item Short Form Health Survey,[37] and depression scores using the Beck Depression Inventory.[38]

STATISTICAL ANALYSIS

The primary analysis examined the unadjusted rates of 12-month smoking cessation with χ^2 tests using an intention-to-screen allocation of groups. We conducted sensitivity analyses, adjusting for factors that differed at baseline. In prespecified subgroup analyses,[21] 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.[39]

Our power calculations have been previously described.[21] Briefly, we expected 10% 12-month smoking cessation rates in the control group, based on trials of NRT,[40] 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 265 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 0.0259]; 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 patient 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.[29] 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[33,41,42] (**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 HbA_{1c}, 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-

Table 1. Baseline Characteristics According to Group Assignment[a]

Characteristic	All Participants (N=536)	US Group (n=267)	Control Group (n=269)	*P* Value[b]
Age, mean (SD), y	51.1 (7.3)	51.5 (7.6)	50.7 (7.1)	.19
Female sex, No. (%)	241 (45.0)	124 (46.4)	117 (43.5)	.49
Level of education, No. (%)				
Some high school	362 (67.5)	175 (65.5)	187 (69.5)	.23
High school graduate	58 (10.8)	35 (13.1)	23 (8.6)	
Postgraduate education	116 (21.6)	57 (21.3)	59 (21.9)	
Smoking history, median (IQR)				
No. of cigarettes/d	20 (20-30)	20 (20-30)	20 (20-30)	.77
Duration of smoking history, y	31.7 (27.0-37.5)	31.7 (26.4-38.0)	31.7 (27.6-36.9)	.93
No. of pack-years	35.7 (25.8-48.0)	35.0 (25.6-46.8)	36.1 (25.9-49.1)	.45
Age at initiation of smoking, y	17 (16-20)	17 (16-20)	17 (15-18)	.03
No. of previous attempts of smoking cessation	2 (1-3)	2 (1-3)	2 (1-3)	.94
Fagerström score[c]	5.0 (2.1)	4.9 (1.9)	5.2 (2.2)	.12
Other CVRFs				
Hypercholesterolemia, No. (%)[d]	267 (49.8)	128 (47.9)	139 (51.7)	.39
Hypertension, No. (%)[e]	149 (27.8)	87 (32.6)	62 (23.0)	.01
Diabetes mellitus, No. (%)[f]	18 (3.4)	10 (3.8)	8 (3.0)	.62
Body mass index, mean (SD)[g]	24.9 (4.1)	24.9 (4.1)	24.9 (4.1)	.91
Family history of early CHD, No. (%)[h]	70 (13.1)	26 (9.7)	44 (16.4)	.02
Framingham risk score, median (IQR)[i]	8.0 (3-16)	8.0 (4-16)	8.0 (3-16)	.96
Categories of Framingham risk score, No. (%)[i]				
<10%	276 (51.5)	136 (50.9)	140 (52.0)	.80
10%-20%	199 (37.1)	104 (39.0)	95 (35.3)	.38
>20%	61 (11.4)	27 (10.1)	34 (12.6)	.36
Cardiovascular preventive therapies, No. (%)				
Drugs to lower lipid levels	62 (11.6)	22 (8.2)	40 (14.9)	.02
Antihypertensives	81 (15.1)	45 (16.9)	36 (13.4)	.26
Antihyperglycemics	13 (2.4)	6 (2.2)	7 (2.6)	.79
Antiplatelet drugs	25 (4.7)	12 (4.5)	13 (4.8)	.85
Other variables, median (IQR)				
Physical activity, MET × min/wk[j]	3334 (1440-5436)	3360 (1554-5634)	3219 (1440-5238)	.34
Quality of life				
SF-36 physical component	53.6 (48.5-56.8)	53.7 (48.5-56.8)	53.5 (48.4-56.8)	.95
SF-36 mental component	49.0 (40.5-54.6)	49.0 (40.9-53.7)	49.0 (40.5-54.8)	.67
Cohen 4-item perceived stress scale	2 (1-3)	2 (1-3)	2 (1-3)	.77
Beck Depression Inventory[k]	5 (2-9)	5 (2-9)	5 (2-8)	.63

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.

[a] Percentages have been rounded and might not total 100.

[b] Calculated as a 2-sided *t* test, a Pearson χ^2 test, or a rank sum test (when an IQR is reported).

[c] Indicates score for nicotine dependence (0 indicates low; 10, very high), expressed as mean (SD).

[d] Defined as a low-density lipoprotein cholesterol level greater than the Adult Treatment Panel III (ATP III) thresholds for drug therapy or current treatment.[24]

[e] Defined as a blood pressure level of at least 140/90 mm Hg, of at least 130/80 mm Hg if diabetes is present, or current treatment.[41]

[f] 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.[42]

[g] Calculated as weight in kilograms divided by height in meters squared.

[h] Indicates CHD in a male first-degree relative younger than 55 years or CHD in a female first-degree relative younger than 65 years.

[i] Framingham risk score according to ATP III guidelines and categories.[24]

[j] Indicates weighted estimate of total physical activity from all reported activities per week based on the International Physical Activity Questionnaire.[33]

[k] Score range, 0 to 63. A higher score indicates increased depressive symptoms.

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),

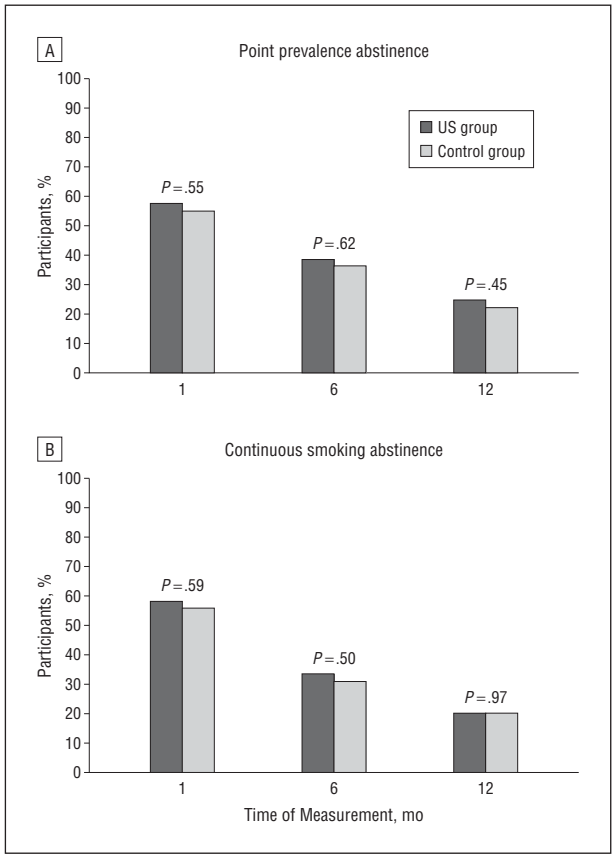

Figure 2. Smoking abstinence with biochemical confirmation according to randomized groups. Biochemical confirmation of smoking included exhaled carbon monoxide levels of at least 10 ppm and/or serum cotinine equivalent levels of at least 25 ng/mL. A, Comparison of screening vs control groups. Point prevalence abstinence: 57.7% vs 55.0% at 1 month, 38.6% vs 36.4% at 6 months, and 24.9% vs 22.1% at 12 months. B, Continuous smoking abstinence: 58.2% vs 55.8% at 1 month, 33.8% vs 30.9% at 6 months, and 20.4% vs 20.2% at 12 months. According to the Russel standard criteria,[29] consumption of 1 to 5 total cigarettes since the cessation date was counted as continuous smoking abstinence, explaining why the rate of continuous smoking abstinence was higher than point prevalence abstinence at 1 month when some participants had smoked less than 5 cigarettes in the past week. US indicates ultrasonography.

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.[13] In contrast to previous RCTs that were limited by a low number of participants with atherosclerosis[11] or the lack of biochemical validation of smoking cessation,[10,43] 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.[44] 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.[11] 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[5] 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[43] 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[45] 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,[10] 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

Table 2. Outcomes According to Group Assignment

Variable	US Group (n=267)	Control Group (n=269)	*P* Value
Point prevalence abstinence in the previous week, No. (%)			
Self-reported[a]	71 (26.8)	69 (25.8)	.80
Confirmed biochemically[a]	66 (24.9)	59 (22.1)	.45
No sample submitted	1 (0.4)	4 (1.5)	. . .
Positive sample finding[b]	4 (1.5)	6 (2.2)	. . .
Continuous smoking abstinence since cessation date, No. (%)[c]			
Self-reported	57 (21.5)	60 (22.5)	.79
Confirmed biochemically	54 (20.4)	54 (20.2)	.97
No sample submitted	0	1 (0.4)	. . .
Positive sample finding[b]	3 (1.1)	5 (1.9)	. . .
Change in CVRFs, mean (SE)			
LDL-C level, mg/dL[d]	−4.6 (2.3)	−5.8 (2.7)	.77
Systolic blood pressure, mm Hg[d]	2.5 (0.9)	3.4 (0.9)	.46
Diastolic blood pressure, mm Hg[d]	4.2 (0.7)	4.5 (0.7)	.74
HbA_{1c} level if diabetes mellitus present, %	0.3 (0.3)	0.1 (0.3)	.73
hs-CRP level, mg/L[e]	0.4 (0.4)	0.3 (0.4)	.90
Framingham risk score, %[f]	0.6 (0.3)	0.3 (0.4)	.56
Physical activity, MET × min/wk	−784 (205)	−793 (236)	.98
Change in control of CVRFs, No. (%)			
Controlled hypercholesterolemia[g]	17 (15.3)	20 (16.8)	.76
Controlled hypertension[h]	13 (17.6)	7 (13.2)	.51
Controlled diabetes[i]	0	0	NA
Change in cardiovascular preventive therapies, No. (%)[j]			
Drugs to lower lipid levels	13 (5.3)	9 (3.9)	.46
Antihypertensives	5 (2.1)	0	.03
Antidiabetics, including insulin	1 (0.4)	0	.33
Antiplatelet drugs	4 (1.6)	6 (2.6)	.47
Medication regimen adherence, mean (SD)[k]			
Baseline	0.7 (0.9)	0.8 (1.0)	.27
After 12 mo	0.6 (0.8)	0.7 (0.9)	
Potential harms, mean (SE)			
Change in quality of life			
SF-36 physical component	0.6 (0.4)	0.4 (0.5)	.80
SF-36 mental component	−0.2 (0.7)	−1.7 (0.8)	.16
Cohen 4-item perceived stress scale	0.0 (0.2)	0.3 (0.2)	.29
Beck Depression Inventory[l]	0.1 (0.3)	0.2 (0.3)	.81

Abbreviations: CVRF, cardiovascular risk factor; ellipses, values are not meaningful because the numbers used to calculate them are so small; HbA_{1c}, hemoglobin A_{1c}; hs-CRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; MET, metabolic equivalent task; NA, not applicable; SF-36, 36-Item Short Form Health Survey; US, ultrasonography.

SI conversion factors: To convert cholesterol to millimoles per liter, multiply by 0.0259; hs-CRP to nanomoles per liter, multiply by 9.524.

[a] As recommended,[29] 1 deceased participant and 1 who had moved to an untraceable address from the screening group and 2 deceased participants from the control group were excluded from smoking abstinence analyses.

[b] Defined as an exhaled carbon monoxide level of at least 10 ppm or a 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.

[c] Based on the Russel standard criteria,[29] consumption of 1 to 5 total cigarettes from the cessation date were counted as continuous abstinence.

[d] At 12 months, 76 values (US group, 34 participants; control group, 42) were missing for the lipid profile and 78 (US group, 35 participants; control group, 43) for blood pressure because of the absence of clinical examination and blood samples for participants who had a follow-up by telephone or by letter. Sensitivity analysis using multiple imputation of missing values was performed.

[e] At 12 months, 113 values (US group, 43 participants; control group, 70) were missing because of missing blood samples. Sensitivity analysis using multiple imputation of missing values was performed.

[f] Framingham risk score according to Adult Treatment Panel III (ATP III) guidelines and categories.[24]

[g] Indicates LDL-C level of less than the target from the ATP III guidelines[24] among those with hypercholesterolemia at baseline.

[h] Indicates 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[41] among those with hypertension at baseline.

[i] Indicates HbA_{1c} levels of less than 7.0%, according to American Diabetes Association guidelines, among the 18 participants with diabetes at baseline.

[j] Changes were calculated from the following values: US group, 243 participants; control group, 230.

[k] Adherence to a cardiovascular medication regimen among participants taking cardiovascular medication was measured with a self-reported 4-item scale[34] 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.

[l] Score range, 0 to 63. A higher score indicates increased depressive symptoms.

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

Variable	US Group With Plaque (A) (n=154)[a]	US Group Without Plaque (B) (n=112)[a]	Control Group (C) (n=269)	*P* Value for Group Comparison		
				A + B vs C	A vs B	A vs C
Point prevalence abstinence in the previous week, No. (%)						
Self-reported	42 (27.6)	29 (25.9)	69 (25.8)	.80	.75	.69
Confirmed biochemically	39 (25.7)	27 (24.1)	59 (22.1)	.44	.77	.41
No sample submitted	0	1 (0.9)	4 (1.5)	. . .	. . .	. . .
Positive sample finding[b]	3 (2.0)	1 (0.9)	6 (2.2)	. . .	. . .	. . .
Continuous smoking abstinence since cessation date, No. (%)[c]						
Self-reported	35 (23.0)	22 (19.6)	60 (22.5)	.79	.51	.90
Confirmed biochemically	32 (21.1)	22 (19.6)	54 (20.2)	.97	.78	.84
No sample submitted	0	0	1 (0.4)	. . .	. . .	. . .
Positive sample finding[b]	3 (2.0)	0	5 (1.9)	. . .	. . .	. . .
Change in CVRFs, mean (SE)						
LDL-C level, mg/dL[d]	−10.8 (3.5)	3.9 (3.5)	−5.8 (2.7)	.77	.004	.26
Systolic blood pressure, mm Hg[d]	2.4 (1.3)	2.5 (1.3)	3.4 (0.9)	.46	.95	.51
Diastolic blood pressure, mm Hg[d]	3.9 (0.9)	4.6 (1.0)	4.5 (0.7)	.74	.58	.57
HbA_{1c} level if diabetes mellitus present, %	0.1 (0.2)	0.7 (0.8)	0.1 (0.3)	.73	.36	.90
hs-CRP, mg/L[e]	0.9 (0.5)	−0.4 (0.6)	0.3 (0.4)	.90	.11	.36
Framingham risk score, %[f]	0.5 (0.4)	0.7 (0.5)	0.3 (0.4)	.56	.87	.67
Physical activity, MET × min/wk	−523 (256)	−1152 (335)	−793 (236)	.98	.13	.45
Change in control of CVRFs, No. (%)						
Controlled hypercholesterolemia[g]	15 (18.8)	2 (6.5)	20 (16.8)	.76	.09	.72
Controlled hypertension[h]	14 (26.9)	1 (4.5)	7 (13.2)	.51	.02	.08
Controlled diabetes[i]	0	0	0	NA	NA	NA
Change in cardiovascular preventive treatment, No. (%)[j]						
Drugs to lower lipid levels	10 (7.0)	3 (3.0)	9 (3.9)	.46	.17	.19
Antihypertensives	5 (3.5)	0	0	.03	.06	.004
Antidiabetics, including insulin	1 (0.7)	0	0	.33	.40	.20
Antiplatelet drugs	4 (2.8)	0	6 (2.6)	.47	.09	.91
Medication regimen adherence, mean (SD)[k]						
Baseline	0.7 (0.9)	0.9 (1.1)	0.8 (1.0)	.27	.70	.41
After 12 mo	0.6 (0.8)	0.8 (0.7)	0.7 (0.9)			
Potential harms, mean (SE)						
Change in quality of life						
SF-36 physical component	0.8 (0.6)	0.4 (0.7)	0.4 (0.5)	.80	.70	.69
SF-36 mental component	0.2 (0.9)	−0.8 (1.2)	−1.7 (0.8)	.16	.48	.12
Cohen 4-item perceived stress scale	−0.1 (0.2)	0.1 (0.4)	0.3 (0.2)	.29	.52	.19
Beck Depression Inventory[l]	0.1 (0.4)	0.2 (0.5)	0.2 (0.3)	.81	.83	.75

Abbreviations: CVRF, cardiovascular risk factor; ellipses, values are not meaningful because the numbers used to calculate them are so small; HbA_{1c}, hemoglobin A_{1c}; 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.

SI conversion factors: To convert cholesterol to millimoles per liter, multiply by 0.0259; hs-CRP to nanomoles per liter, multiply by 9.524.

[a] One participant did not attend carotid plaque screening and was excluded from these subgroup analyses.

[b] Defined 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.

[c] Based on the Russel standard criteria,[29] consumption of 1 to 5 total cigarettes from the cessation date were counted as continuous abstinence.

[d] At 12 months, 75 missing values (US group with plaque, 16 participants; US group without plaque, 17; and control group, 42) for the lipid profile and 77 (US group with plaque, 17 participants; US group without plaque, 17; and control group, 43) for blood pressure owing to the absence of clinical examination and blood samples for participants who had a follow-up by telephone or by letter. Sensitivity analysis using multiple imputation of missing values was performed.

[e] At 12 months, 113 missing values (US group with plaque, 23 participants; US group without plaque, 19; and control group, 70) for hs-CRP because of missing blood samples. Sensitivity analysis using multiple imputation of missing values was performed.

[f] Framingham risk score according to Adult Treatment Panel III guidelines and categories.[24]

[g] Indicates LDL-C level of less than the target from the ATP III guidelines[24] among those with hypercholesterolemia at baseline.

[h] Indicates 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[41] among those with hypertension at baseline.

[i] Indicates HbA_{1c} levels of less than 7.0%, according to American Diabetes Association guidelines, among the 18 participants with diabetes at baseline.

[j] Changes were calculated from the following values: US groups, 243 participants; control group, 230.

[k] Adherence to a cardiovascular medication regimen among participants taking cardiovascular medication was measured with a self-reported 4-item scale[34] 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.

[l] Score range, 0 to 63. A higher score indicates increased depressive symptoms.

cal cardiovascular disease screening on patient behavior also provided information on screening results only once[10,11,43]; we also found that knowledge retention about atherosclerosis[8] remained very high at 12 months (94%) in our RCT. Carotid US screening was not repeated during follow-up, and we could not assess the potential motivational impact of plaque progression/regression. Because 21.1% of participants had missing hs-CRP

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 screening[11,43,44] 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 practice[5,18] 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 intense smoking counseling or to refine cardiovascular risk estimates to better target preventive medications.[4] Until such data become available, the benefit of atherosclerosis screening should be demonstrated in RCTs[4] before its use can be generally recommended.[48]

Accepted for Publication: November 7, 2011.
Published Online: January 23, 2012. doi:10.1001/archinternmed.2011.1326
Correspondence: Nicolas Rodondi, MD, MAS, Department of General Internal Medicine, University Hospital Inselspital, University of Bern, Bern 3010, Switzerland (Nicolas.Rodondi@insel.ch).
Author Contributions: *Study concept and design:* Rodondi, Aujesky, Bovet, and Cornuz. *Acquisition of data:* Rodondi, Collet, Nanchen, Depairon, and Cornuz. *Analysis and interpretation of data:* Rodondi, Collet, Nanchen, Locatelli, Depairon, Aujesky, Bovet, and Cornuz. *Drafting of the manuscript:* Rodondi. *Critical revision of the manuscript for important intellectual content:* Collet, Nanchen, Locatelli, Depairon, Aujesky, Bovet, and Cornuz. *Statistical analysis:* Rodondi, Collet, Nanchen, and Locatelli. *Obtained funding:* Rodondi, Bovet, and Cornuz. *Administrative, technical, and material support:* Rodondi, Collet, Depairon, Bovet, and Cornuz. *Study supervision:* Rodondi, Nanchen, and Depairon.
Financial Disclosure: None reported.

Funding/Support: This study was supported by research grant 3200B0-116097 from the Swiss National Science Foundation, by the Swiss Heart Foundation, by the Lausanne University Hospital Strategic Plan, and by grant FPT 08.002282 from the Swiss Tobacco Prevention Funds, Federal Office of Public Health.

REFERENCES

1. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr; Cardiovascular Health Study Collaborative Research Group. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. *N Engl J Med*. 1999;340(1):14-22.
2. Polonsky TS, McClelland RL, Jorgensen NW, et al. Coronary artery calcium score and risk classification for coronary heart disease prediction. *JAMA*. 2010;303(16):1610-1616.
3. Douglas PS, Taylor A, Bild D, et al. Outcomes research in cardiovascular imaging: report of a workshop sponsored by the National Heart, Lung, and Blood Institute. *Circ Cardiovasc Imaging*. 2009;2(4):339-348.
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.
5. Greenland P. Improving risk of coronary heart disease: can a picture make the difference? *JAMA*. 2003;289(17):2270-2272.
6. Kalia NK, Miller LG, Nasir K, Blumenthal RS, Agrawal N, Budoff MJ. Visualizing coronary calcium is associated with improvements in adherence to statin therapy. *Atherosclerosis*. 2006;185(2):394-399.
7. Korcarz CE, DeCara JM, Hirsch AT, et al. Ultrasound detection of increased carotid intima-media thickness and carotid plaque in an office practice setting: does it affect physician behavior or patient motivation? *J Am Soc Echocardiogr*. 2008;21(10):1156-1162.
8. Rodondi N, Auer R, Devine PJ, O'Malley PG, Hayoz D, Cornuz J. The impact of carotid plaque screening on motivation for smoking cessation. *Nicotine Tob Res*. 2008;10(3):541-546.
9. Sandwell JC, Wingard DL, Laughlin GA, Barrett-Connor E. Electron beam computed tomography screening and heart disease risk factor modification. *Prev Cardiol*. 2006;9(3):133-137.
10. Bovet P, Perret F, Cornuz J, Quilindo J, Paccaud F. Improved smoking cessation in smokers given ultrasound photographs of their own atherosclerotic plaques. *Prev Med*. 2002;34(2):215-220.
11. O'Malley PG, Feuerstein IM, Taylor AJ. Impact of electron beam tomography, with or without case management, on motivation, behavioral change, and cardiovascular risk profile: a randomized controlled trial. *JAMA*. 2003;289(17):2215-2223.
12. Khera A. Texas atherosclerosis imaging bill: quiet origins, broad implications. *Arch Intern Med*. 2011;171(4):281-283.
13. Rodondi N, Auer R, de Bosset Sulzer V, Ghali WA, Cornuz J. Atherosclerosis screening by noninvasive imaging for cardiovascular prevention: a systematic review [published online September 1, 2011]. *J Gen Intern Med*. doi:10.1007/s11606-011-1833-3.
14. Greenland P, Alpert JS, Beller GA, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2010;122(25):e584-e636. doi:10.1161/CIR.0b013e3182051b4c.
15. Naghavi M, Falk E, Hecht HS, et al; SHAPE Task Force. From vulnerable plaque to vulnerable patient, part III: executive summary of the Screening for Heart Attack Prevention and Education (SHAPE) Task Force report. *Am J Cardiol*. 2006;98(2)(suppl 1):2H-15H.
16. US Preventive Services Task Force. Using nontraditional risk factors in coronary heart disease risk assessment: US Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2009;151(7):474-482.
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.
18. Determining the role of subclinical disease testing in patients at intermediate risk: report of the Working Group 2004. National Heart, Lung, and Blood Institute Web site. http://www.nhlbi.nih.gov/meetings/workshops. Accessed June 28, 2011.
19. Young LH, Wackers FJ, Chyun DA, et al; DIAD Investigators. Cardiac outcomes after screening for asymptomatic coronary artery disease in patients with type 2 diabetes: the DIAD study: a randomized controlled trial. *JAMA*. 2009;301(15):1547-1555.
20. Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P; CONSORT Group. Methods

and processes of the CONSORT Group: example of an extension for trials assessing nonpharmacologic treatments. *Ann Intern Med*. 2008;148(4):W60-W66.
21. Rodondi N, Bovet P, Hayoz D, Cornuz J. The Impact of CAROtid plaque Screening on Smoking (CAROSS) cessation and control of other cardiovascular risk factors: rationale and design of a randomized controlled trial. *Contemp Clin Trials*. 2008;29(5):767-773.
22. Jorenby DE, Hays JT, Rigotti NA, et al; Varenicline Phase 3 Study Group. Efficacy of varenicline, an $\alpha 4\beta 2$ nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation: a randomized controlled trial. *JAMA*. 2006;296(1):56-63.
23. Bize R, Willi C, Chiolero A, et al. Participation in a population-based physical activity programme as an aid for smoking cessation: a randomised trial. *Tob Control*. 2010;19(6):488-494.
24. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA*. 2001; 285(19):2486-2497.
25. Redberg RF, Vogel RA, Criqui MH, Herrington DM, Lima JA, Roman MJ. 34th Bethesda Conference: Task Force 3: what is the spectrum of current and emerging techniques for the noninvasive measurement of atherosclerosis? *J Am Coll Cardiol*. 2003;41(11):1886-1898.
26. van der Meer IM, Bots ML, Hofman A, del Sol AI, van der Kuip DA, Witteman JC. Predictive value of noninvasive measures of atherosclerosis for incident myocardial infarction: the Rotterdam Study. *Circulation*. 2004;109(9):1089-1094.
27. Humair JP, Cornuz J. A new curriculum using active learning methods and standardized patients to train residents in smoking cessation. *J Gen Intern Med*. 2003; 18(12):1023-1027.
28. Schulz KF, Grimes DA. Unequal group sizes in randomised trials: guarding against guessing. *Lancet*. 2002;359(9310):966-970.
29. West R, Hajek P, Stead L, Stapleton J. Outcome criteria in smoking cessation trials: proposal for a common standard. *Addiction*. 2005;100(3):299-303.
30. Volpp KG, Troxel AB, Pauly MV, et al. A randomized, controlled trial of financial incentives for smoking cessation. *N Engl J Med*. 2009;360(7):699-709.
31. Blake GJ, Ridker PM. Inflammatory bio-markers and cardiovascular risk prediction. *J Intern Med*. 2002;252(4):283-294.
32. Rifai N, Tracy RP, Ridker PM. Clinical efficacy of an automated high-sensitivity C-reactive protein assay. *Clin Chem*. 1999;45(12):2136-2141.
33. Craig CL, Marshall AL, Sjöström M, et al. International Physical Activity Questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc*. 2003;35(8):1381-1395.
34. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care*. 1986;24(1):67-74.
35. Levy RW, Rayner CR, Fairley CK, et al; Melbourne Adherence Group. Multidisciplinary HIV adherence intervention: a randomized study. *AIDS Patient Care STDS*. 2004;18(12):728-735.
36. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav*. 1983;24(4):385-396.
37. Ware JE Jr, Gandek B. Overview of the SF-36 Health Survey and the International Quality of Life Assessment (IQOLA) Project. *J Clin Epidemiol*. 1998;51 (11):903-912.
38. Hurt RD, Sachs DP, Glover ED, et al. A comparison of sustained-release bupropion and placebo for smoking cessation. *N Engl J Med*. 1997;337(17):1195-1202.
39. Moons KG, Donders RA, Stijnen T, Harrell FE Jr. Using the outcome for imputation of missing predictor values was preferred. *J Clin Epidemiol*. 2006;59 (10):1092-1101.
40. Silagy C, Lancaster T, Stead L, Mant D, Fowler G. Nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev*. 2004;(3):CD000146.
41. Chobanian AV, Bakris GL, Black HR, et al; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003;289(19):2560-2572.
42. Rodondi N, Newman AB, Vittinghoff E, et al. Subclinical hypothyroidism and the risk of heart failure, other cardiovascular events, and death. *Arch Intern Med*. 2005;165(21):2460-2466.
43. Rozanski A, Gransar H, Shaw LJ, et al. Impact of coronary artery calcium scanning on coronary risk factors and downstream testing: the EISNER (Early Identification of Subclinical Atherosclerosis by Noninvasive Imaging Research) prospective randomized trial. *J Am Coll Cardiol*. 2011;57(15):1622-1632.
44. Hackam DG, Shojania KG, Spence JD, et al. Influence of noninvasive cardiovascular imaging in primary prevention: systematic review and meta-analysis of randomized trials. *Arch Intern Med*. 2011;171(11):977-982.
45. Bize R, Burnand B, Mueller Y, Rège Walther M, Cornuz J. Biomedical risk assessment as an aid for smoking cessation. *Cochrane Database Syst Rev*. 2009; (2):CD004705.
46. Schnoll RA, Patterson F, Wileyto EP, et al. Effectiveness of extended-duration transdermal nicotine therapy: a randomized trial. *Ann Intern Med*. 2010;152 (3):144-151.
47. Cohn JN, Duprez DA. Time to foster a rational approach to preventing cardiovascular morbid events. *J Am Coll Cardiol*. 2008;52(5):327-329.
48. Redberg RF, Walsh J. Pay now, benefits may follow: the case of cardiac computed tomographic angiography. *N Engl J Med*. 2008;359(22):2309-2311.

Images From Our Readers

Snow-capped mountains at Mono Lake, California.

Courtesy of: Praveen Cheripalli, MD, Hospital Medicine, Shands Jacksonville Medical Center, Jacksonville, Florida.