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# Association of tobacco use and cessation with coronary atherosclerosis

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## Abstract

**Background and aims—**The impact of tobacco use and cessation on atherogenesis remains unclear. We aimed to study the association of tobacco use and prior cessation with the presence, extent and severity of atherosclerosis on coronary computed tomographic angiography (CTA).

**Methods—**We examined 1798 consecutive symptomatic patients without known coronary artery disease (CAD) referred for CTA, stratified by smoking status (never, current [within 30 days], or former [>30 days before CTA]). Plaque severity (none,<50%, ≥50% stenosis), composition (non-calcified [NCP], partially calcified [PCP], or calcified plaque [CP]), and segment involvement

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**Conflict of interest**

All authors declare that they have no conflict of interest and no relationship with industry related to this work. The opinions herein and assertions contained are the authors' alone, and do not constitute endorsement by the Department of the Army, Department of Defense or the United States Government. The content is solely the responsibility of the authors and does not represent the official views of Harvard Catalyst, Harvard University and its affiliated academic healthcare centers, or the National Institutes of Health.

**Author contributions**

All authors contributed significantly to the drafting of the manuscript, approve the work in its entirety, and meet criteria for authorship.

score (SIS) were visually graded. Multivariate analysis was performed, adjusting for CAD risk factors and cholesterol lowering medication use.

**Results—**The median age of patients was 50 years [IQR:42–58] (61% male), with 74% never smokers, 12% current smokers, and 14% former smokers (median quit duration=12 years [IQR:3–26]). Smoking exposure in former *versus* current smokers was 11 [IQR:5–25] and 10 [IQR:2–20] pack-years, respectively ($p$=0.01). Compared to never smokers, current smokers demonstrated an increased odds ratio of all plaque types (adjusted OR: any NCP=1.55 [95% CI 1.04–2.32], $p$=0.03; any PCP=1.61 [1.10–2.37], $p$=0.02; any CP=1.93 [1.32–2.81], $p$=0.001), non-obstructive CAD (aOR=1.47 [1.04, 2.07], $p$=0.03), obstructive CAD (aOR=1.81 [1.01–3.24], $p$=0.047), and SIS > 4 (aOR=1.60 [1.04–2.46], $p$=0.03). Compared to current smoking, prior smoking cessation (≥ 12 years) was associated with a decreased odds ratio of any NCP (aOR=0.42 [0.19–0.90], $p$=0.03), CP (aOR=0.43 [0.22–0.84], $p$=0.02), and obstructive CAD (aOR=0.40, [0.15–0.98], $p$=0.048).

**Conclusions—**Current smoking is independently associated with the presence and extent of coronary plaque, and a higher risk of non-obstructive and obstructive CAD compared to never smoking. Prior smoking cessation correlated with improvements in CTA-identified plaque measures.

### Keywords

Atherosclerosis; coronary computed tomographic angiography; smoking; tobacco; coronary artery disease

## Introduction

Cardiovascular disease (CVD) mortality has declined in recent decades owing to improvements in the management of CVD and its risk factors, including significant efforts to curb tobacco use (1). Still, the impact of smoking-related CVD on public health remains a global issue. In the United States, nearly 42 million (~1 in 5) adults are active smokers (2), contributing to the more than 16 million U.S. adults who live with a smoking-related disease (3). While smoking is well-known to increase the risk of major adverse cardiac events (MACE), the extent to which tobacco use and cessation impacts atherogenesis warrants further study.

Coronary computed tomographic angiography (CTA) is an established noninvasive technique used to visualize the presence, extent, severity and composition of atherosclerosis. Though prior studies have shown that the degree of coronary artery disease (CAD) can strongly predict future MACE (4), few studies have examined the relationship between smoking status and CTA-identified plaque (5, 6). Of these, the CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes) multinational registry observed a higher rate of MACE in current but not former smokers undergoing coronary CTA by comparison to never smokers (5). Yet, few studies have examined the dose-dependent impact of smoking on CTA-identified atherosclerosis or controlled for cholesterol lowering medication use among potential covariates. We aimed to examine the relationship between tobacco use and prior cessation on the presence, extent, composition and severity of CTA-identified coronary atherosclerosis.

## Patients and Methods

### Patient population

We examined 1,798 consecutive symptomatic patients without known CAD clinically referred for coronary CTA between May 2006 – February 2013 at Walter Reed National Military Medical Center. Patient demographics, medical history, and CTA results were collected prospectively as described previously (7). After CTA, comprehensive prescription, laboratory data and smoking status were independently queried using all available electronic medical records of the Department of Defense Military Healthcare System - a large, closed international health care network providing comprehensive health care, labs and medications. Independent data extraction was blinded to CTA findings in order to verify: smoking status, smoking history (pack-years), prior smoking cessation (quit duration), most recent cholesterol panel and statin or nonstatin cholesterol lowering medication use within 12 months prior to CTA.

Consistent with National Cholesterol Education Program criteria, smoking status was defined as: never, current (cigarette or cigar use ≤ 30 days prior to CTA), or former smoker (use >30 days prior to CTA) (8). Hypertension was defined as a systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, and/or treatment with an antihypertensive medication (9). Diabetes mellitus was defined by a prior fasting blood glucose ≥ 126 mg/dL, 2-hour blood glucose ≥ 200 mg/dL during oral glucose tolerance testing, a hemoglobin A1c ≥ 6.5%, a random blood glucose ≥ 200 mg/dL, and/or use of insulin or an oral hypoglycemic agent (10). Dyslipidemia was defined as total cholesterol > 240 mg/dL, serum triglycerides > 150 mg/dL, high density lipoprotein cholesterol (HDL) < 40 mg/dL (male) or < 50 mg/dL (women), or treatment with a cholesterol lowering medication (8,11). Family history of early CAD was defined as clinical CAD involving a first-degree male relative less than 55 years old or first-degree female relative less than 65 years old.

Patients were excluded for unknown smoking status (n=51), or a history of known CAD defined as a prior myocardial infarction or coronary revascularization (n=64). The study was approved by local institutional review and compliant with Health Insurance Portability and Accountability Act guidelines.

### Coronary CTA

Coronary CTA was performed by 64-slice CT (Lightspeed VCT or Discovery CT750 HD; GE Healthcare, WI), with heart rate control and pre-scan sublingual nitroglycerin according to guidelines (12). An initial non-contrast CT was acquired for calcium scoring in a majority of patients (n=1574, 88%), and coronary artery calcium (CAC) scores were graded by the Agatston method (13). Contrast-enhanced coronary CTA was obtained by prospective ECG-triggering (n=1159, 64%) or retrospective ECG-gating with dose modulation (n=639, 36%) following a timing bolus. CTA acquisition variables were adjusted by the CTA provider in accordance with guidelines to minimize patient radiation exposure (12, 14). CTA scans were interpreted jointly (consensus) by a level 3-certified cardiologist and radiologist as part of routine clinical care (15). Using an 18-segment model, each coronary segment >1.5-mm

diameter was assessed for CAD presence and severity by visual grading defined as: normal (no plaque), non-obstructive (1-49% stenosis), obstructive (≥ 50%), or uninterpretable (≥ 1 uninterpretable segment). Consistent with prior research, we used an intention-to-diagnose approach where patients with ≥ 1 uninterpretable segment were categorized as having obstructive CAD (16). The number of coronary segments with any plaque was graded by the segment involvement score, as the sum of the number of segments with any plaque irrespective of the degree of luminal stenosis (17). In each segment with plaque, we performed a qualitative assessment of plaque composition defined as predominant non-calcified plaque (NCP), partially calcified plaque (PCP), or calcified plaque (CP) (15).

### Statistical analysis

Continuous variables with normal distributions are expressed as mean ± 1 standard deviation (SD) and compared with the Student's t test for two independent groups and 1-way analysis of variance between multiple groups. Continuous variables with non-normal distributions are expressed as median ± interquartile range (IQR) and compared with the Wilcoxon rank-sum test. Categorical variables are expressed as frequencies (%) and compared by the Pearson Chi-square test. Binary logistic regression was performed to obtain all odds ratios, with multivariate adjustment for age, gender, body mass index, diabetes, family history of early CAD, hypertension, and hyperlipidemia as a binary variable incorporating the use of a statin or non-statin cholesterol medication. To examine the dose-dependent effect of smoking on atherosclerotic plaque burden and composition, we performed adjusted odds ratios among smokers above the median exposure period (≥ 12 pack-years), with never smokers as a comparison group. Additionally, a 12-year period for quit duration was used to compare patients across the median value for prior smoking cessation, and considering evidence that the risk of coronary heart disease normalizes approximately 10–15 years after quitting (18, 19). Statistical analysis was performed using Stata (Version 13.1, Statacorp, TX), and a 2-tailed $p$-value < 0.05 was considered significant.

## Results

### Baseline characteristics

The median age of all patients was 50 years [IQR: 42–58 years] (61% male), including 74% never smokers, 14% former smokers, and 12% current smokers (Table 1). Former smokers were more likely to be older, with greater smoking exposure (pack-years), and had a higher prevalence of hypertension and diabetes. Conversely, current smokers were younger and more predominantly male. By comparison to never smokers, current smokers reported a higher frequency of any chest pain. Additionally, our study found a step-wise increase in triglyceride levels from never smokers, to former and current smokers ($p < 0.001$ between groups). Conversely, we identified a trend towards lower HDL in current smokers compared to former smokers and never smokers ($p=0.10$ between groups). While the rate of medication use was not significantly different between groups, a trend towards lower statin or non-statin cholesterol medication use was noted among current smokers ($p=0.10$ between groups).

### Current smoking associated with CAD presence, extent, and severity

Coronary CTA findings are demonstrated in Table 2 stratified by smoking status, with no significant difference in CTA settings between groups. By comparison to never smokers, former and current smokers demonstrated a significant difference in CAC scores and CAD severity. Unadjusted, this finding appears driven by a higher frequency of both non-obstructive and obstructive CAD in former smokers. Notably, the severity of CAD and CAC was similar among current and never smokers despite a significant age difference between these groups (median age: 44 years *vs.* 50 years, respectively, $p<0.001$). Though observational, this finding supports the hypothesis that smoking may accelerate vascular aging (20). When stratified by age tertile and smoking status, current smoking was associated with the highest prevalence of obstructive CAD (Fig. 1).

Considering baseline differences between groups noted in Table 1, we performed multivariate analyses to control for age, gender, CAD risk factors and cholesterol medication use. By comparison to never smokers, current but not former smoking was independently associated with an increased adjusted odds ratio of all plaque types, plaque extent (SIS > 4), and the presence of non-obstructive or obstructive CAD (Table 3).

### Dose-dependent effect of smoking on CAD

To examine the dose-dependent effect of smoking on atherosclerotic plaque burden and composition, we performed multivariate analysis in nonsmokers *versus* smokers stratified above the median exposure period. As shown in Fig. 2, patients with ≥ 12 pack-year exposure were more likely to have partially calcified or calcified plaque, and more extensive plaque, by comparison to never smokers. When stratified by pack-decades, smoking exposure had a dose-dependent association with the presence of all plaque types by adjusted comparison to never smokers (Supplemental Fig. 1).

### Prior smoking cessation is associated with reduced CAD severity

Adjusted odds ratio of CAD measures stratified by duration of prior smoking cessation are shown in Fig. 3, using current smokers as the reference group. Among former smokers, we included patients with known quit date information, categorized as cessation within 12 years prior to CTA (n=179) and quit duration ≥ 12 years (n=149). By this analysis, patients who quit ≥ 12 years previously had a lower likelihood of non-calcified plaque, calcified plaque and obstructive CAD than current smokers.

### Sensitivity analysis

Considering the potential impact of cholesterol medications on plaque analysis, we performed an additional sensitivity analysis excluding patients on a statin (n=604, 34%) or non-statin cholesterol lowering medication (n=159, 9%). The exclusion of patients on cholesterol lowering medications did not result in any significant differences in our primary analysis or associations between prior smoking cessation and plaque measures (Supplemental Tables 1 and 2).

## Discussion

Among patients without known CAD referred for CTA, the main findings of this study are: (i) current but not former smoking was associated with the presence, extent and severity of CAD *versus* never smoking; (ii) smoking demonstrated a dose-dependent association with plaque presence and extent by comparison to never smokers; and (iii) patients who quit smoking ≥ 12 years prior to CTA had a lower likelihood of non-calcified plaque, calcified plaque and obstructive CAD by comparison to current smokers.

To date, several studies have shown that tobacco smoke contributes free radical-induced oxidative stress on the vascular endothelium, triggering an inflammatory response, hypercoagulable state and alterations in lipid profiles (21, 22). Conversely, smoking cessation has been shown to reverse the risk of MACE, with normalization of pro-inflammatory and hypercoagulability states to that of nonsmokers (23). Yet, the extent to which tobacco use and cessation impacts atherosclerosis remains unclear.

In a study of 6,814 adults without known CVD undergoing CAC scoring in the Multi-Ethnic Study of Atherosclerosis (MESA), McEvoy et al compared smoking status with inflammatory biomarkers and subclinical CAD (24). By comparison to never smoking, current smoking was associated with an increased hsCRP > 2 mg/dL (adjusted odds ratio = 1.7 [95% CI 1.5–2.1]) and subclinical CAD (aOR CAC >0 = 1.8 [95% CI 1.5–2.1]). Quitting smoking was independently associated with lower inflammation and atherosclerosis (aOR hsCRP>2 mg/dL = 0.91 [0.88–0.95]; aOR CAC>0 = 0.94 [0.90–0.97], respectively) for every 5-year cessation interval. Similarly, Kim et al. examined 7,104 asymptomatic Korean adults self-referred for screening coronary CTA, observing a higher prevalence of any plaque, non-calcified plaque, obstructive CAD, and CAC score > 100 by comparison to never-smokers (6). Adjusting for CVD risk factors, atherosclerosis increased in a dose-dependent fashion with increasing tobacco exposure in their study.

Among mechanisms that may contribute to atherosclerosis development in smokers, our study found a step-wise increase in triglyceride levels from never smokers (mean=117 mg/dL), to former smokers (136 mg/dL) and current smokers (143 mg/dL) ($p< 0.001$ between groups). Conversely, we identified a trend towards lower HDL in current smokers (mean=48 mg/dL) compared to former smokers (50 mg/dL) and never smokers (54 mg/dL) ($p=0.10$ between groups). While further studies are needed to examine the mechanisms of smoking-related atherogenesis, recent evidence suggests that alterations in endothelial progenitor cells, plasma microparticles and micro-RNA may offer potential targets to examine the impact of smoking on vascular injury and atherosclerosis (25–28).

Finally, our study adds to prior literature by providing an association of dose-dependent tobacco use and prior cessation across various plaque measures in a cohort of symptomatic patients clinically referred for coronary CTA. Though our study does not assess the relationship of smoking status, CAD severity and plaque composition with clinical outcomes, the international CONFIRM registry has previously observed a higher rate of MACE in current but not former smokers undergoing coronary CTA by comparison to never smokers (5). Considering available evidence, future studies are warranted to prospectively

examine the long-term impact of smoking and tobacco cessation on atherogenesis and major adverse cardiac events.

We recognize several inherent limitations to our study. This is a cross-sectional analysis performed at a single-center, limiting generalizability. Second, our accounting of smoking status relied on accurate patient self-reporting and provider documentation, and provided no confirmation of smoking status by serum or urine cotinine levels. Further, we did not have information on second hand smoke exposure, which has been shown to contribute to inflammation, endothelial dysfunction and the development of atherosclerosis (29, 30). Finally, while we adjusted for CVD risk factors and cholesterol medications, unobserved confounders including diet and exercise may contribute to variations in plaque burden. Consequently, our results must be interpreted as hypothesis generating and not proof of causality. Acknowledging these limitations, our study adds to prior data regarding the association of tobacco use and cessation across a broad range of CTA-identified atherosclerosis measures.

Current smoking is significantly and independently associated with the presence and extent of coronary atherosclerosis, as well as an increased risk of non-obstructive and obstructive CAD by comparison to never smoking. Additionally, our study supports a dose-dependent relationship between smoking and atherogenesis in symptomatic patients clinically referred for CTA. Furthermore, prior smoking cessation correlated with improved plaque measures and strengthens the importance of smoking cessation to minimize the risk of cardiovascular disease.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations

| | |
|---|---|
| **CAD** | coronary artery disease |
| **CP** | calcified plaque |
| **CTA** | computed tomographic angiography |
| **CVD** | cardiovascular disease |
| **MACE** | major adverse cardiac events |
| **NCP** | non-calcified plaque |

**PCP** partially calcified plaque

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## Highlights

- Current smokers demonstrated an increase in coronary artery disease (CAD) extent and severity *vs.* never smokers
- Ever smokers had a dose-dependent association with the presence and extent of CAD
- Smoking cessation correlated with improved plaque measures *vs.* current smoking

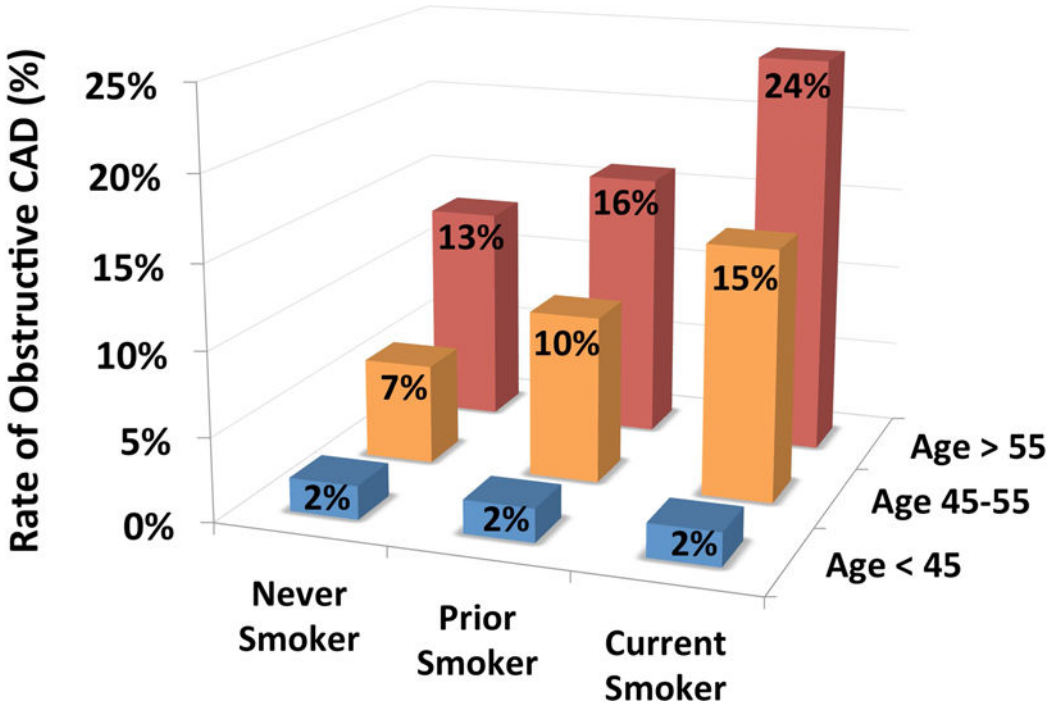


**Fig. 1. Rate of obstructive CAD stratified by smoking status and age tertile**

Demonstrates association of current smoking with the highest rate of obstructive CAD as a percentage of patients across age tertiles.

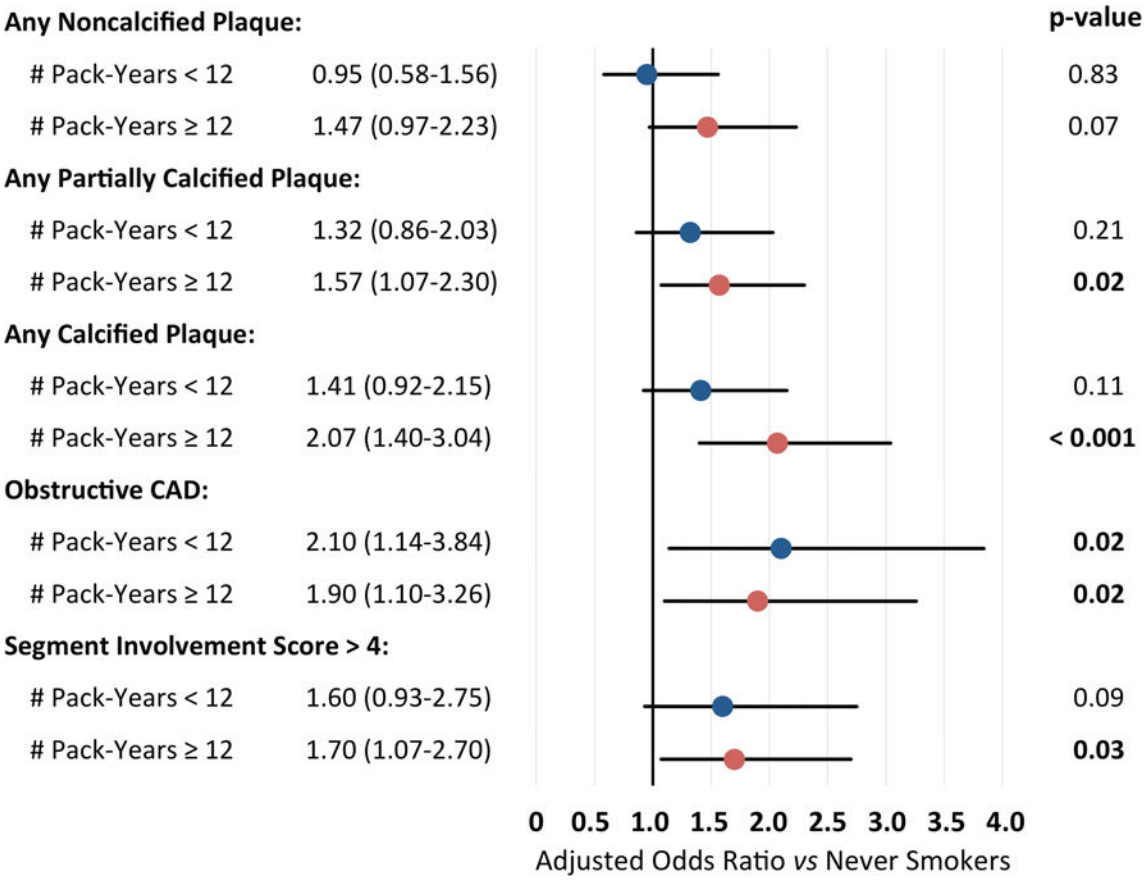


**Fig. 2. Association of smoking history with CAD measures**

Adjusted odds ratio of CAD measures by comparison to never smokers (n=1339), among patients with complete pack-year information and < 12 pack-year (n=179) or ≥ 12 pack-year smoking history (n=149). Demonstrates that patients with ≥ 12 pack-year exposure had a higher likelihood of all CAD measures *versus* never smoking. Adjusted for age, gender, BMI, diabetes, family history of early CAD, hypertension, hyperlipidemia, and use of a statin or non-statin cholesterol medication.

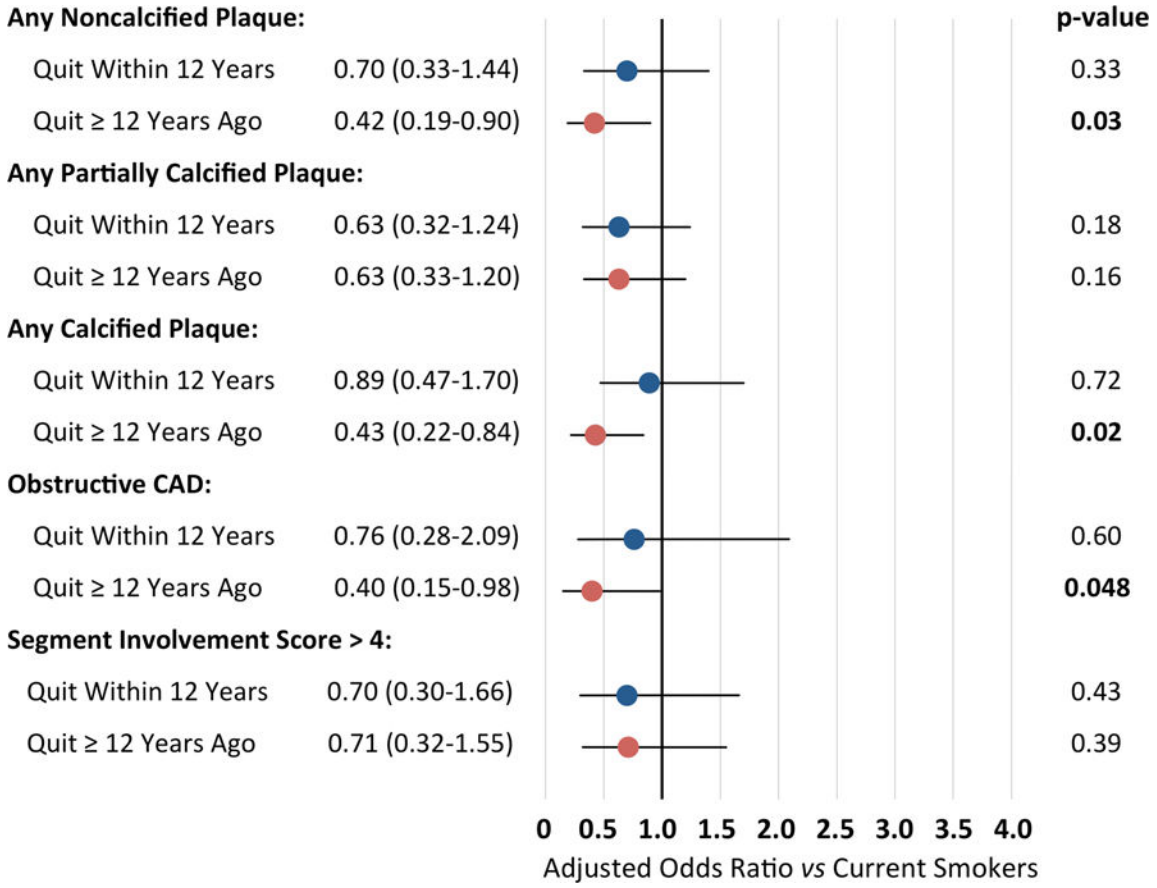


**Fig. 3. Association of prior smoking cessation with CAD measures**

Adjusted odds ratio of plaque type, severity and extent by comparison to current smokers (n=216), among patients who quit smoking within 12 years prior to CTA (n=90) and ≥ 12 years prior to CTA (n=94). Note that patients who quit ≥ 12 years previously had a lower likelihood of non-calcified plaque, calcified plaque and a lower likelihood of obstructive CAD. Analyses performed for patients with complete smoking cessation information, adjusted for age, gender, BMI, diabetes, family history of early CAD, hypertension, hyperlipidemia, and statin or non-statin cholesterol medications.

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**Table 1**

Baseline characteristics.

| | All patients (n=1,798) | Never smoked (n=1339, 74%) | Former smoker (n=243, 14%) | Current smoker (n=216, 12%) | *p*-value |
|---|---|---|---|---|---|
| Age, years | 50 [IQR: 42–58] | 50 [IQR: 42–58] | 53 [IQR: 45–61] | 44 [IQR: 35–55] | < 0.001 |
| Male, n (%) | 1103 (61%) | 784 (59%) | 150 (62%) | 169 (78%) | < 0.001 |
| Body mass index, kg/m$^2$ | 29 ± 5 | 28 ± 5 | 30 ± 5 | 28 ± 5 | 0.57 |
| Smoking duration, pack-years | – | – | 11 [IQR: 5–25] | 10 [IQR: 2–20] | 0.01 |
| Time since last cigarette, years | – | – | 12 [IQR: 3–26] | (Less than 30 days) | — |
| Hypertension, n (%) | 851 (47%) | 627 (47%) | 139 (57%) | 85 (39%) | 0.003 |
| Hyperlipidemia, n (%) | 818 (45%) | 599 (45%) | 127 (52%) | 92 (43%) | 0.21 |
| Diabetes mellitus, n (%) | 178 (10%) | 123 (9%) | 38 (16%) | 17 (8%) | 0.008 |
| Family history of CAD, n (%) | 416 (23%) | 300 (22%) | 59 (24%) | 57 (26%) | 0.86 |
| Any chest pain, n (%) | 1274 (71%) | 922 (69%) | 177 (73%) | 175 (81%) | 0.001 |
| - Non-anginal chest pain | 181 (10%) | 147 (11%) | 19 (8%) | 15 (7%) | |
| - Atypical chest pain | 944 (53%) | 664 (50%) | 146 (60%) | 134 (62%) | 0.001 |
| - Typical chest pain | 149 (8%) | 111 (8%) | 12 (5%) | 26 (12%) | |
| Dyspnea, n (%) | 487 (27%) | 346 (26%) | 80 (33%) | 61 (28%) | 0.15 |
| Statin use, n (%) | 604 (34%) | 458 (34%) | 87 (36%) | 59 (27%) | 0.10 |
| Non-statin cholesterol med, n (%) | 159 (9%) | 113 (8%) | 30 (12%) | 16 (7%) | 0.10 |
| Aspirin use, n (%) | 613 (34%) | 445 (33%) | 94 (39%) | 74 (34%) | 0.27 |
| Total cholesterol, mg/dL [a] | 189 ± 38 [n=1721] | 190 ± 38 [n=1287] | 189 ± 39 [n=233] | 189 ± 37 [n=201] | 0.70 |
| LDL-C, mg/dL[a] | 114 ± 34 [n=1718] | 114 ± 34 [n=1286] | 113 ± 34 [n=233] | 115 ± 33 [n=199] | 0.86 |
| HDL-C, mg/dL[a] | 53 ± 17 [n=1720] | 54 ± 17 [n=1287] | 50 ± 15 [n=233] | 48 ± 15 [n=200] | 0.10 |
| Triglycerides, mg/dL[a] | 122 ± 72 [n=808] | 117 ± 67 [n=641] | 136 ± 75 [n=93] | 143 ± 100 [n=74] | < 0.001 |
| Systolic BP, mmHg[a] | 122 ± 16 [n=1697] | 122 ± 16 [n=1266] | 125 ± 16 [n=228] | 124 ± 16 [n=203] | 0.84 |
| Diastolic BP, mmHg[a] | 74 ± 11 [n=1696] | 73 ± 11 [n=1265] | 75 ± 11 [n=228] | 76 ± 10 [n=203] | 0.24 |

[a]Among patients with cholesterol and blood pressure values recorded within 12 months prior to coronary CTA [n = # of patients].

All values are expressed as mean ± SD, median [interquartile range], or frequency (%).

BP, blood pressure; CAD, coronary artery disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

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**Table 2**

CTA characteristics.

| | All patients (n=1,798) | Never smoked (n=1339, 74%) | Former smoker (n=243, 14%) | Current smoker (n=216, 12%) | *p*-value |
|---|---|---|---|---|---|
| Pre-scan heart rate, bpm | 57 ± 7 | 57 ± 7 | 57 ± 7 | 57 ± 6 | 0.23 |
| Tube current, mA | 539 ± 73 | 534 ± 73 | 562 ± 72 | 550 ± 74 | 0.97 |
| Tube potential, kV | 113 ± 12 | 112 ± 12 | 115 ± 12 | 113 ± 13 | 0.69 |
| Scan type | | | | | |
| - Prospective triggered | 1159 (64%) | 860 (64%) | 161 (66%) | 138 (64%) | 0.82 |
| - Retrospective gating | 639 (36%) | 479 (36%) | 82 (34%) | 78 (36%) | |
| CTA radiation dose, mSv[a] | 3.9 ± 3.7 | 3.8 ± 3.6 | 4.6 ± 4.1 | 3.7 ± 3.3 | 0.15 |
| CAD severity | | | | | |
| - No CAD | 995 (55%) | 758 (57%) | 117 (48%) | 120 (56%) | |
| - CAD 1–49% stenosis | 604 (34%) | 438 (33%) | 95 (39%) | 72 (33%) | 0.04 |
| - CAC ≥ 50% stenosis | 139 (8%) | 97 (7%) | 26 (11%) | 20 (9%) | |
| - ≥ 1 uninterpretable segment | 60 (3%) | 46 (3%) | 5 (2%) | 4 (2%) | |
| Segment involvement score > 4 | 239 (13%) | 163 (12%) | 49 (20%) | 27 (13%) | 0.003 |
| CAC score obtained (# of patients) | 1574 (88%) | 1165 (87%) | 219 (90%) | 190 (88%) | 0.93 |
| - CAC = 0 Agatston units | 915/1574 (58%) | 699/1165 (60%) | 106/219 (48%) | 110/190 (58%) | |
| - CAC = 1–99 | 414/1574 (26%) | 296/1165 (25%) | 66/219 (30%) | 52/190 (27%) | 0.03 |
| - CAC = 100–399 | 157/1574 (10%) | 106/1165 (9%) | 34/219 (16%) | 17/190 (9%) | |
| - CAC ≥ 400 | 88/1574 (6%) | 64/1165 (5%) | 13/219 (6%) | 11/190 (6%) | |

[a]Includes effective radiation for CTA only (excluding scout topogram, timing bolus and CAC scan).

CAC, coronary artery calcium; CAD, coronary artery disease; CTA, computed tomographic angiography.

**Table 3**

Smoking association with plaque present, extent and severity. Adjusted for risk factors and medications.

| | Never smoked (n=1339) | Former smoker (n=243) | | | Current smoker (n=216) | | |
|---|---|---|---|---|---|---|---|
| | | Adjusted OR[a] | 95% CI | *p*-value | Adjusted OR[a] | 95% CI | *p*-value |
| Any non-calcified plaque | **Reference** | 1.35 | [0.94, 1.94] | 0.11 | 1.55 | [1.04, 2.32] | 0.03 |
| Any partially calcified plaque | | 1.19 | [0.84, 1.68] | 0.33 | 1.61 | [1.10, 2.37] | 0.02 |
| Any calcified plaque | | 1.24 | [0.87, 1.76] | 0.23 | 1.93 | [1.32, 2.81] | 0.001 |
| Segment involvement score > 4 | | 1.35 | [0.94, 1.95] | 0.11 | 1.57 | [1.03, 2.42] | 0.04 |
| Normal CTA | | 1.00 | [0.72, 1.40] | 0.98 | 0.64 | [0.45, 0.90] | 0.01 |
| Non-obstructive CAD (< 50%) | | 1.02 | [0.74, 1.39] | 0.93 | 1.47 | [1.04, 2.07] | 0.03 |
| Obstructive CAD (≥ 50%) | | 1.18 | [0.70, 1.98] | 0.53 | 1.81 | [1.01, 3.24] | 0.047 |

[a]All odds ratios obtained by binary logistic regression adjusted for age, gender, body mass index, diabetes, family history of early CAD, hypertension, hyperlipidemia, and use of a statin or nonstatin cholesterol medication.

CAD, coronary artery disease; CI, confidence interval; CP, calcified plaque; CTA, coronary computed tomographic angiography; NCP, non-calcified plaque; OR, odds ratio; PCP, partially calcified plaque.

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