UCSF UC San Francisco Previously Published Works

Title

Assessing the Relationship Between American Heart Association Atherosclerotic Cardiovascular Disease Risk Score and Coronary Artery Imaging Findings

Permalink

https://escholarship.org/uc/item/64b3k5ch

Journal

Journal of Computer Assisted Tomography, 42(6)

ISSN 0363-8715

Authors

Li, Ying Zhu, Guangming Ding, Victoria <u>et al.</u>

Publication Date

2018

DOI

10.1097/rct.00000000000823

Peer reviewed



HHS Public Access

Author manuscript

J Comput Assist Tomogr. Author manuscript; available in PMC 2021 May 13.

Published in final edited form as: *J Comput Assist Tomogr.* 2018 ; 42(6): 898–905. doi:10.1097/RCT.0000000000823.

Assessing the Relationship Between American Heart Association Atherosclerotic Cardiovascular Disease Risk Score and Coronary Artery Imaging Findings

Ying Li, MD, PhD^{*,†}, Guangming Zhu, MD, PhD^{*}, Victoria Ding, MS[‡], Bin Jiang, MD, PhD^{*}, Robyn L. Ball, PhD[†], Neera Ahuja, MD[§], Fatima Rodriguez, MD, MPH^{II}, Dominik Fleischmann, MD[¶], Manisha Desai, PhD[†], David Saloner, PhD[#], Luca Saba, MD^{**}, Max Wintermark, MD, MAS^{*}, Jason Hom, MD[§]

^{*}Department of Radiology, Neuroradiology Section, Stanford University School of Medicine, Palo Alto, CA

[†]Department of Neurology, PLA Army General Hospital, Beijing, China

[‡]Department of Medicine, Quantitative Sciences Unit

§Department of Medicine, Stanford University School of Medicine

^{II}Division of Cardiovascular Medicine, Stanford University

[¶]Department of Radiology, Cardiovascular Imaging Section, Stanford University School of Medicine, Palo Alto

*Department of Radiology, University of California San Francisco, San Francisco, CA

**Dipartimento di Radiologia, Azienda Ospedaliero Universitaria di Cagliari, Cagliari, Italy

Abstract

Objective: The aim of this study was to characterize the relationship between computed tomography angiography imaging characteristics of coronary artery and atherosclerotic cardiovascular disease (ASCVD) score.

Methods: We retrospectively identified all patients who underwent a coronary computed tomography angiography at our institution from December 2013 to July 2016, then we calculated the 10-year ASCVD score. We characterized the relationship between coronary artery imaging findings and ASCVD risk score.

Results: One hundred fifty-one patients met our inclusion criteria. Patients with a 10-year ASCVD score of 7.5% or greater had significantly more arterial segments showing stenosis (46.4%, P = 0.008) and significantly higher maximal plaque thickness (1.25 vs 0.53, P = 0.001).

Correspondence to: Max Wintermark, MD, MAS, Neuroradiology Section, Department of Radiology, Stanford University School of Medicine, 300 Pasteur Dr, Grant S047, Stanford, CA 94305 (max.wintermark@gmail.com). M.W. and J.H. are co-senior authors.

The authors declare no conflict of interest.

Supplemental digital contents are available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jcat.org).

However, among 56 patients with a 10-year ASCVD score of 7.5% or greater, 30 (53.6%) had no arterial stenosis. Furthermore, among the patients with a 10-year ASCVD score of less than 7.5%, 24 (25.3%) had some arterial stenosis.

Conclusions: There is some concordance but not a perfect overlap between 10-year ASCVD risk scores and coronary artery imaging findings.

Keywords

atherosclerotic cardiovascular disease score; computed tomography angiography; coronary artery

The guidelines for initiating statin treatment for the primary prevention of atherosclerotic cardiovascular disease (ASCVD) released by the American College of Cardiology and the American Heart Association (ACC/AHA) in November 2013 de-emphasize low-density lipoprotein cholesterol thresholds and instead focus on total ASCVD risk, as defined by the pooled cohort equations.¹ The Pooled Cohort Equations² formula estimates ASCVD risk, based on age, sex, race, diabetes mellitus, cholesterol values, smoking status, and blood pressure. According to the ACC/AHA guidelines, adults between 40 and 75 years old with a 10-year ASCVD risk score of 7.5% or higher should receive at least moderate-intensity statins.

With the introduction of the new ACC/AHA guidelines, the number of adults eligible for statin treatment went up to an estimated 28% to 48%,^{3–5} as compared with 8% to 17% under the previous set of recommendations.⁶ This expansion of statin treatment eligibility under the new ACC/AHA guidelines is supported by some studies that suggest statins are effective for reducing risk regardless of low-density lipoprotein cholesterol or total risk levels.^{7–9} However, the pooled cohort equations may overestimate ASCVD risk,^{10–12} and millions of adults in the United States may be exposed to unnecessary statin treatment costs and risks based on other analyses.^{5,13} Although statins are usually well tolerated, they may have adverse effects, including myalgias, especially in patients with multiple medical comorbidities.¹⁴ Statins interact with drugs that affect the cytochrome P450 enzyme group. ¹⁵ Statins are associated with a small but significantly increased risk of type 2 diabetes mellitus.^{14,16} Statins involve a gross domestic product–adjusted total cost of \$17 billion per year.¹⁷ Statin intolerance, particularly myalgias, is very common and is associated with high rates of statin discontinuation.^{18,19}

The 2013 ACC/AHA guidelines do not explicitly recommend including vascular imaging; however, a coronary artery calcium (CAC) score of equal to or greater than 300 Agatston units or equal to or greater than 75th percentile for age, sex, and ethnicity is referred to as a specific risk factor in patients for whom risk assessment is uncertain.¹ In the Multi-Ethnic Study of Atherosclerosis (MESA), addition of CAC score to a prediction model based on traditional risk factors significantly improved the classification of risk, allowing both upclassification and down-classification of risk based on CAC scores.²⁰ However, CAC score only reflects calcified atherosclerotic plaques and not fatty or other noncalcified plaques that are as likely or even more likely to be associated with luminal stenosis.²¹ Indeed, while zero CAC scores may have value as a prognostic marker of low risk, obstructive coronary artery disease (CAD)—including total coronary occlusion—is not uncommon even in the absence

of detectable calcification.²² Furthermore, some investigators assert that CAC does not actually add incremental prognostic value to other coronary computed tomography angiography (CTA) measurements.²³

This study's objective was to determine whether patients with a high 10-year ASCVD risk score have more advanced vascular imaging features of coronary artery atherosclerosis, including calcified and noncalcified plaques. For this purpose, we analyzed the relationship between CTA imaging characteristics of coronary artery atherosclerosis and the 10-year risk of ASCVD. Specifically, we wanted to examine how often the ASCVD risk score is concordant or discordant with coronary artery imaging findings.

MATERIALS AND METHODS

Study Population

We retrospectively identified all patients who underwent a coronary CTA at our institution from December 2013 to July 2016. Our study was approved by the institutional review board. We used the medical records to gather the clinical information required to calculate the 10-year ASCVD score using the pooled cohort equations from the 2013 ASA/AHA guidelines. We excluded patients for whom the 10-year ASCVD score could not be calculated (age outside the 40- to 79-year range, total cholesterol outside the 130- to 320-mg/dL range, high-density lipoprotein cholesterol outside the 20- to 100-mg/dL range, systolic blood pressure outside the 90- to 200-mm Hg range, no smoking status record). We also excluded patients who had a coronary artery stent placed or received a coronary artery bypass graft. We excluded patients for whom more than 6 months elapsed between the clinical visit/blood draw to measure the clinical variables and the coronary imaging study. Finally, if a patient underwent several coronary imaging studies, we selected the imaging features for the study that corresponded to the closest to the clinical visit/ blood draw for our analysis.

Coronary Artery Imaging Protocol

The CTA studies of the coronary arteries were obtained on 16- and 64-slice computed tomography scanners (GE Healthcare, Milwaukee, IL or Siemens Healthcare, Erlangen, Germany), spiral mode, 0.6- to 0.8-second gantry rotation acquisition parameters: 100 kVp/240 mA. Patient prepared with oral β -blocker or sublingual nitroglycerine to goal heart rate (HR) approximately 60 ± 5 beats/min (bpm). The image acquisition protocol was as follows: The calcium scoring imaging was achieved from non-contrast high-resolution CT, scan range: carina through the apex of the heart; slice thickness: 2.5 to 3 mm; imaging phrase: for single source, end diastole HR less than 63 bpm, end diastole and end systole HR greater than 64 bpm; for dual source, end diastole HR less than 79 bpm, end systole HR greater than 200 mL, intravenous injection duration 25 seconds or less than 6 mL/s; scan range: 2 cm above left anterior descending coronary artery through the apex of the heart; slice thickness: 0.625 to 0.75 mm; imaging phrase: for single source, end diastole HR greater than 66 bpm; for dual source of the systole HR greater than 65 bpm, end diastole and end systole HR less than 65 bpm, end diastole HR less than 66 bpm; for dual source, end

diastole HR <65 bpm, end diastole and end systole HR 66 to 75 bpm, end systole HR greater than 86 bpm.

Coronary Artery Imaging Review

The left coronary artery and right coronary artery were assessed separately. The left coronary artery was divided into 3 segments: left main coronary artery, left anterior descending branch, and left circumflex branch. We formatted images perpendicular to the lumen of each of these segments and visually assessed each segment for maximal degree of stenosis, maximal atherosclerotic/calcium plaque thickness, and the presence or absence of calcified plaque.

The Agatston CAC score was computed for each of the coronary arteries based on the size and density of the regions identified to contain calcium²⁴: 0 means no identifiable atherosclerotic plaque (a negative examination); 1 to 10 means minimal plaque burden; 11 to 100 means mild plaque burden; 101 to 400 means moderate plaque burden; and greater than 400 means extensive plaque burden.

Statistical Analysis

According to the guideline²⁵ and other studies' result, our study patients were divided into 2 groups based on the 10-year ASCVD score: less than 7.5% and 7.5% or greater. We also tested a more stringent cutoff value and repeated our analysis for patients with 10-year ASCVD score of less than 10% and 10% or greater.

Demographics, medical history, and imaging characteristics of the cohort were summarized by counts and percentages for categorical characteristics and by median and interquartile range (IQR) for continuous characteristics. Associations between risk groups and imaging characteristics were assessed by Fisher exact test for categorical variables and the Mann-Whitney *U* test or *t* tests for continuous variables, depending on whether the distribution was symmetric. The associations between 151 characteristics and risk score were assessed. All variables and their functional form (eg, chosen thresholds such as any stenosis and >50% stenosis) were selected for consideration a priori. All tests were 2-sided and conducted at the 0.05 level of significance. As the goal of our study was to characterize the association between clinical and imaging features, *P* values were not adjusted for multiple comparisons. Rather, we utilize the *P* values resulting from statistical testing as a descriptive statistic to quantify how likely a particular observed association is if there were truly no associations between risk score and the particular feature. Associations between ASCVD scores and imaging features were assessed using κ statistics.²⁶ All analyses were conducted in the R statistical computing framework, version 3.3.²⁷

RESULTS

Study Population

We retrospectively identified 1079 patients who underwent a coronary artery imaging study between December 2013 and June 2016. Of these, 151 patients met our inclusion criteria

(Fig. 1). The median interval between the blood draw and the coronary artery imaging study was -9.5 days (IQR, -48 to 5 days).

Patients with a 10-year ASCVD score of 7.5% or greater included significantly more males (34 [58.1%], P= 0.011), older patients (68 vs 51 years old, P< 0.001), patients with higher systolic blood pressure (133 vs 119, P< 0.001), and more patients receiving cholesterol-lowering medication (67.9% vs 42.1%, P= 0.002) and antihypertension agents (64.3% vs 42.1%, P= 0.008) (Table 1). This is expected as these are the parameters used to calculate the 10-year ASCVD score. Coronary artery calcium Agatston score was higher in 10-year ASCVD score of 7.5% or greater than those less than 7.5% (37 vs 0, P< 0.001). Significant differences in these characteristics were similarly observed for patients with a 10-year ASCVD score of 10% or greater (see Table, Supplemental Digital Content 1, http://links.lww.com/RCT/A74).

Imaging Findings

Patients with a 10-year ASCVD score of 7.5% or greater had significantly more arterial segments showing stenosis (46.4% vs 25.3%, P= 0.008). Significant stenosis (>50%) was rare in patients with a 10-year ASCVD score of less than 7.5% (4.2% vs 19.6%, P= 0.002). Maximal plaque thickness was significantly higher in patients with a 10-year ASCVD score of 7.5% or greater (1.25 vs 0.53, P= 0.001). Calcium plaques were less common in patients with a 10-year ASCVD score of less than 7.5% (35.8% vs 75%, P< 0.001) (Table 2). Similar observations were made for patients with a 10-year ASCVD score of 10% or greater (see Table, Supplemental Digital Content 2, http://links.lww.com/RCT/A75).

Concordance Between 10-Year ASCVD Score and Imaging Findings

Among the 56 patients with a 10-year ASCVD score of 7.5% or greater, 30 (53.6%) had no arterial stenosis, 29 (51.8%) had a maximal plaque thickness of less than 0.9 mm, 14 (25.0%) had no calcified plaque, and 33 (58.2%) had an Agatston score of less than 100 (Table 3). Among those patients, 14 (25%) had no any abnormal findings on CTAs. There was a significant overlap between patients showing no arterial stenosis, a maximal plaque thickness of less than 0.9 mm, and an Agatston score of less than 100 (26 [46.4%]). Only 14 (25%) (25%) of these patients showed, whereas most of them (42 patients, or 75%) had at least 1 tiny speck of arterial calcium (Fig. 2A).

Among the 95 patients with a 10-year ASCVD score of less than 7.5%, 24 (25.3%) had some arterial stenosis, 23 (24.2%) had a maximal plaque thickness of more than 0.9 mm, 34 (35.8%) had at least 1 calcified plaque, and 33 (21.2%) had an Agatston score of more than 100 (Table 3). There was a significant overlap between the patients showing some arterial stenosis, a maximal plaque thickness of more than 0.9 mm, at least 1 fatty plaque, and an Agatston score of 100 or greater (8 patients [8.4%]). Calcified plaques could be observed independently of the other features (14 patients [14.7%]) (Fig. 2B).

The imaging characteristics presented moderate or fair agreement with the ASCVD scores based on the κ statistics (Tables 3 and 4).

Among the 47 patients with a 10-year ASCVD score of 10% or greater, 23 (48.9%) had no arterial stenosis at all, 23 (48.9%) had a maximal plaque thickness of less than 0.9 mm, 11 (23.4%) had no calcified plaque, and 26 (55.3%) had an Agatston score of less than 100 (Table 4). Among those patients, 11 (23.4%) had no any abnormal findings on CTAs. There was a significant overlap between patients showing no arterial stenosis, a maximal plaque thickness of less than 0.9 mm, and an Agatston score of less than 100 (20 [42.5%]). Only 11 of these patients (23.4%) showed no calcium, whereas most of them (36 patients [76.6%]) had at least 1 tiny speck of arterial calcium (Fig. 2C).

Among the 104 patients with a 10-year ASCVD score of less than 10%, 27 (26.0%) had some arterial stenosis, 26 (25.0%) had a maximal plaque thickness of more than 0.9 mm, and 40 (38.5%) had at least 1 calcified plaque (Table 4). There was a significant overlap between the patients showing some arterial stenosis, a maximal plaque thickness of more than 0.9 mm, at least 1 fatty plaque, and an Agatston score of 100 or greater (10 patients [9.6%]). Calcified plaques could be observed independently of the other features (17 patients [16.3%]) (Fig. 2D).

An Agatston score of 0 was present in 14 (25%) of the patients with a 10-year ASCVD score of 7.5% or greater and in 11 (23.4%) of the patients with a 10-year ASCVD score of 10% or greater. An Agatston score of less than 10 was present in 20 (35.7%) of the patients with a 10-year ASCVD score of 7.5% or greater and in 17 (36.2%) of the patients with a 10-year ASCVD score of 10% or greater.

DISCUSSION

The goal of our study was to assess the relationship between ASCVD risk score and vascular imaging features of coronary artery atherosclerosis. Not surprisingly, we found that patients with higher 10-year ASCVD risk score overall had more stenosis, increased wall thickness, more fatty plaques, and a higher Agatston score. However, we found a significant fraction of patients with high 10-year ASCVD risk scores who had minimal imaging abnormalities, as well as a significant fraction of patients with low 10-year ASCVD risk scores who, nonetheless, had significant imaging abnormalities; this discordance suggests that imaging can improve risk individualization and add value to scoring systems that rely solely on clinical information. Interestingly, we found that calcified plaques were the only imaging feature that was frequently observed in patients with both low and high 10-year ASCVD risk scores. Indeed, in the literature, the imaging biomarker that has been the most studied in terms of its association with the risk of vascular events is the CAC score, typically characterized using the Agatston methodology.²⁴

The relationship between zero CAC scores and obstructive CAD has been studied extensively; study populations have varied, with some investigators finding zero CAC scores strongly associated with no obstructive CAD and others finding a relatively high prevalence of obstructive CAD even in the absence of detectable calcium.^{22,23,28,29} A number of observational studies have documented strong associations between coronary calcium scores and the risk of incident cardiovascular events. A higher CAC score is associated with a higher cardiovascular risk; the adjusted risk of a coronary event was increased by a factor of

7.73 among participants with coronary calcium scores between 101 and 300 and by a factor of 9.67 among participants with scores greater than $300.^{30}$

There is increasing evidence that coronary calcium scores improve risk classification, particularly for intermediate-risk individuals.^{31,32} A study of 6809 individuals from the MESA cohort found coronary calcium scores were strong predictors of vascular events both in younger and older individuals. Comparing individuals with a CAC score of 0 with those with a CAC score of greater than 100, there was an increased incidence of CHD events from 1 to 21 per 1000 person-years.³³ In another 6698 individuals enrolled in MESA, coronary calcium scores were stronger predictors of cardiovascular and coronary events than carotid intima-media thickness; the areas under the curve to predict cardiovascular disease were 0.81 and 0.78, respectively.³⁴ Calcium scores reclassified 36% of intermediate-risk individuals, including 23% who were up-classified to high risk.²⁰ The overall net reclassification improvement was 14%, with an approximately equal proportion of correct up-reclassifications and correct down-reclassifications in the intermediate-risk group. Another study derived from MESA that focused on 4758 participants found that 77% of these patients were eligible for statins based on the new AHA/ASA guidelines. Among patients eligible for statins, 41% had a CAC score of 0 and developed only 5.2 ASCVD events/1000 person-years. If reclassified by imaging, approximately half of the patients would have been spared statin therapy.³⁵ Similarly, in the 2028 asymptomatic individuals in the Rotterdam Study, coronary calcium scores raised the C statistic for coronary events from 0.72 to 0.76³⁶; 52% of intermediate-risk individuals were reclassified, 22% as high risk, and the overall net reclassification improvement was 14%.36 Similar findings were obtained from another large, population-based cohort, the Heinz Nixdorf Recall Study, with more than 50% of intermediate-risk individuals reclassified.³⁷ Adding CAC score, the area under the curve of net reclassification improvement in that study was from 0.681 to 0.749.

However, there are several limitations to using a CAC score. Among these, the calcium score does not necessarily correlate well with the amount of CAD as defined on coronary CTA.³⁸

We acknowledge several limitations to our study. It is retrospective and cross-sectional in nature. The blood work and the carotid imaging were not obtained at the exact same time but within 6 months of each other. Patients who underwent a coronary CTA but did not have data to calculate the risk score were not included in the study, potentially compromising generalizability if these patients are systematically different from those included in the study. We do not anticipate this to be the case, assuming the patients missing these variables do not represent in any way more or less severe cases than those selected into our sample; however, their ASCVD score distributed as similar as other studies. Computed tomography angiograms of the coronary arteries of the patients enrolled in the study were ordered as part of clinical standard of care, which suggests that their vascular risk might be higher than that of the general population. This might result in the 10-year ASCVD risk scores observed in our sample being higher than those in the general population; however, it should not affect the comparison between 10-year ASCVD risk scores and imaging.

In conclusion, our study shows that there is some concordance but not a perfect overlap between 10-year ASCVD risk scores and the imaging features of coronary atherosclerotic

disease. Our next step will be to determine the incidence of vascular events in patients with high 10-year ASCVD risk scores but normal or near-normal coronary arteries on computed tomography.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

REFERENCES

- Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63:2889–2934. [PubMed: 24239923]
- Goff DC, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63:2935–2959. [PubMed: 24239921]
- 3. 2013 ACC/AHA cholesterol guideline and implications for Healthy People 2020 cardiovascular disease prevention goals. J Am Heart Assoc. 2016; 5:e002124.
- Tran JN, Caglar T, Stockl KM, et al. Impact of the new ACC/AHA guidelines on the treatment of high blood cholesterol in a managed care setting. Am Health Drug Benefits. 2014;7:430–443. [PubMed: 25558305]
- Pandya A, Sy S, Cho S, et al. Cost-effectiveness of 10-year risk thresholds for initiation of statin therapy for primary prevention of cardiovascular disease. JAMA. 2015;314:142–150. [PubMed: 26172894]
- 6. 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;285:2486–2497. [PubMed: 11368702]
- 7. Psaty BM, Weiss NS. 2013 ACC/AHA guideline on the treatment of blood cholesterol: a fresh interpretation of old evidence. JAMA. 2014;311: 461–462. [PubMed: 24264722]
- Krumholz HM. The new cholesterol and blood pressure guidelines:perspective on the path forward. JAMA. 2014;311:1403–1405. [PubMed: 24682222]
- Robinson JG. Accumulating evidence for statins in primary prevention. JAMA. 2013;310:2405– 2406. [PubMed: 24276744]
- Pencina MJ, Navar-Boggan AM, D'Agostino RBSr, et al. Application of new cholesterol guidelines to a population-based sample. N Engl J Med. 2014;370:1422–1431. [PubMed: 24645848]
- Guallar E, Laine C. Controversy over clinical guidelines: listen to the evidence, not the noise. Ann Intern Med. 2014;160:361–362. [PubMed: 24473997]
- 12. Redberg RF, Katz MH. Statins for primary prevention: the debate is intense, but the data are weak. JAMA. 2016;316:1979–1981. [PubMed: 27838702]
- Yeboah J, Sillau S, Delaney JC, et al. Implications of the new American College of Cardiology/ American Heart Association cholesterol guidelines for primary atherosclerotic cardiovascular disease event prevention in a multi ethnic cohort: Multi-Ethnic Study of Atherosclerosis (MESA). Am Heart J. 2015;169:387–395.e383. [PubMed: 25728729]
- Ramkumar S, Raghunath A, Raghunath S. Statin therapy: review of safety and potential side effects. Acta Cardiol Sin. 2016;32:631–639. [PubMed: 27899849]
- Golomb BA, Evans MA. Statin adverse effects: a review of the literature and evidence for a mitochondrial mechanism. Am J Cardiovasc Drugs. 2008;8:373–418. [PubMed: 19159124]
- Sattar N, Preiss D, Murray HM, et al. Statins and risk of incident diabetes: a collaborative metaanalysis of randomised statin trials. Lancet. 2010;375: 735–742. [PubMed: 20167359]

- Salami JA, Warraich H, Valero-Elizondo J, et al. National trends in statin use and expenditures in the US adult population from 2002 to 2013: insights from the Medical Expenditure Panel Survey. JAMA Cardiol. 2017; 2:56–65. [PubMed: 27842171]
- Harper CR, Jacobson TA. The broad spectrum of statin myopathy: from myalgia to rhabdomyolysis. Curr Opin Lipidol. 2007;18:401–408. [PubMed: 17620856]
- Harper CR, Jacobson TA. Evidence-based management of statin myopathy. Curr Atheroscler Rep. 2010;12:322–330. [PubMed: 20628837]
- Polonsky TS, McClelland RL, Jorgensen NW, et al. Coronary artery calcium score and risk classification for coronary heart disease prediction. JAMA. 2010;303:1610–1616. [PubMed: 20424251]
- Lehman SJ, Schlett CL, Bamberg F, et al. Assessment of coronary plaque progression in coronary computed tomography angiography using a semiquantitative score. JACC Cardiovasc Imaging. 2009;2:1262–1270. [PubMed: 19909929]
- Gottlieb I, Miller JM, Arbab-Zadeh A, et al. The absence of coronary calcification does not exclude obstructive coronary artery disease or the need for revascularization in patients referred for conventional coronary angiography. J Am Coll Cardiol. 2010;55:627–634. [PubMed: 20170786]
- 23. Villines TC, Hulten EA, Shaw LJ, et al. Prevalence and severity of coronary artery disease and adverse events among symptomatic patients with coronary artery calcification scores of zero undergoing coronary computed tomography angiography: results from the CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter) registry. J Am Coll Cardiol. 2011;58:2533–2540. [PubMed: 22079127]
- Agatston AS, Janowitz WR, Hildner FJ, et al. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol. 1990;15:827–832. [PubMed: 2407762]
- 25. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guidelineon the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129:S1–S45. [PubMed: 24222016]
- 26. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33:159–174. [PubMed: 843571]
- 27. Team RC. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2017.
- Mittal TK, Pottle A, Nicol E, et al. Prevalence of obstructive coronary artery disease and prognosis in patients with stable symptoms and a zero-coronary calcium score. Eur Heart J Cardiovasc Imaging. 2017;18:922–929. [PubMed: 28379388]
- Correia LCL, Esteves FP, Carvalhal M, et al. Zero calcium score as a filter for further testing in patients admitted to the coronary care unit with chest pain. Arq Bras Cardiol. 2017;109:97–102.
- Detrano R, Guerci AD, Carr JJ, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. N Engl J Med. 2008;358: 1336–1345. [PubMed: 18367736]
- Helfand M, Buckley DI, Freeman M, et al. Emerging risk factors for coronary heart disease: a summary of systematic reviews conducted for the U.S. Preventive Services Task Force. Ann Intern Med. 2009;151:496–507. [PubMed: 19805772]
- 32. Greenland P, Bonow RO, Brundage BH, et al. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography) developed in collaboration with the Society of Atherosclerosis Imaging and Prevention and the Society of Cardiovascular Computed Tomography. J Am Coll Cardiol. 2007;49:378–402. [PubMed: 17239724]
- 33. Tota-Maharaj R, Blaha MJ, Blankstein R, et al. Association of coronary artery calcium and coronary heart disease events in young and elderly participants in the multi-ethnic study of atherosclerosis: a secondary analysis of a prospective, population-based cohort. Mayo Clin Proc. 2014;89:1350–1359. [PubMed: 25236430]

- 34. Folsom AR, Kronmal RA, Detrano RC, et al. Coronary artery calcification compared with carotid intima-media thickness in the prediction of cardiovascular disease incidence: the Multi-Ethnic Study of Atherosclerosis (MESA). Arch Intern Med. 2008;168:1333–1339. [PubMed: 18574091]
- 35. Nasir K, Bittencourt MS, Blaha MJ, et al. Implications of coronary artery calcium testing among statin candidates according to American College of Cardiology/American Heart Association Cholesterol Management Guidelines: MESA (Multi-Ethnic Study of Atherosclerosis). J Am Coll Cardiol. 2015;66:1657–1668. [PubMed: 26449135]
- Elias-Smale SE, Proença RV, Koller MT, et al. Coronary calcium score improves classification of coronary heart disease risk in the elderly: the Rotterdam Study. J Am Coll Cardiol. 2010;56:1407– 1414. [PubMed: 20946998]
- Erbel R, Möhlenkamp S, Moebus S, et al. Coronary risk stratification, discrimination, and reclassification improvement based on quantification of subclinical coronary atherosclerosis: the Heinz Nixdorf Recall study. J Am Coll Cardiol. 2010;56:1397–1406. [PubMed: 20946997]
- de Agustín JA, Gómez de Diego JJ, Marcos-Alberca P, et al. Impact of calcium score on agreement between multidetector computed tomography and invasive coronary angiography. Rev Esp Cardiol (Engl Ed). 2017.



FIGURE 1. Patient inclusion decision tree for our study.



FIGURE 2.

Venn diagrams displaying (A) number of patients with *no* stenosis, *no* fatty plaque, and/or no calcium among those with ASCVD risk of 7.5% or greater (n = 56); (B) number of patients with any stenosis, maximum plaque thickness of 0.9 mm or greater, fatty plaque, and/or calcium among those with ASCVD risk of less than 7.5% (n = 95); (C) number of patients with no stenosis, no fatty plaque, and/or no calcium among those with ASCVD risk of 10% or greater (n = 47); and (D) number of patients with any stenosis, maximum plaque thickness of 0.9 mm or greater, fatty plaque, and/or calcium among those with ASCVD risk of less than 30% or greater (n = 47); and (D) number of patients with any stenosis, maximum plaque thickness of 0.9 mm or greater, fatty plaque, and/or calcium among those with ASCVD risk of less than 10% (n = 104). Figure 2 can be viewed online in color at www.jcat.org.

Author Manuscript

-
%
Ň
2
(~
Ľ
~
Ч
9
.5
Ξ.
E
3
5
Ē
· O
.5
Ц
4)
ц
0
S S
\mathbf{v}
4
S
24
\sim
Ц
>
5)
$\tilde{\mathbf{x}}$
5
\triangleleft
5
aı
, õ
X
- T
Ó
Ξ
~
\sim
<u> </u>
Ч
n
а
al
÷.
é
5
\cap
\sim
ς.
),(
51), (
51), (
151), (
= 151), (
1 = 151, (
(n = 151), (
t (n = 151), t
rt (n = 151), t
lort $(n = 151)$, (
hort $(n = 151)$, (
Solvert $(n = 151)$, (
Cohort $(n = 151)$, (
/ Cohort $(n = 151)$, (
ly Cohort (n = 151), (
tidy Cohort ($n = 151$), (
tudy Cohort $(n = 151)$, (
Study Cohort $(n = 151)$, (
F Study Cohort (n = 151), C
of Study Cohort (n = 151), (
of Study Cohort (n = 151), (
y of Study Cohort $(n = 151)$, (
ory of Study Cohort (n = 151), (
tory of Study Cohort (n = 151), (
story of Study Cohort (n = 151), (
History of Study Cohort (n = 151), (
History of Study Cohort (n = 151), (
I History of Study Cohort (n = 151), (
al History of Study Cohort (n = 151), (
ical History of Study Cohort (n = 151), (
dical History of Study Cohort (n = 151), (
edical History of Study Cohort (n = 151), (
Aedical History of Study Cohort (n = 151), (
Medical History of Study Cohort (n = 151), (
d Medical History of Study Cohort (n = 151), (
nd Medical History of Study Cohort $(n = 151)$, (
and Medical History of Study Cohort (n = 151), (
s and Medical History of Study Cohort ($n = 151$), (
cs and Medical History of Study Cohort $(n = 151)$, (
uics and Medical History of Study Cohort ($n = 151$), (
hics and Medical History of Study Cohort (n = 151), (
thics and Medical History of Study Cohort $(n = 151)$, (
raphics and Medical History of Study Cohort (n = 151), (
graphics and Medical History of Study Cohort $(n = 151)$, (
ographics and Medical History of Study Cohort (n = 151), (
nographics and Medical History of Study Cohort (n = 151), (
mographics and Medical History of Study Cohort $(n = 151)$, (
bemographics and Medical History of Study Cohort (n = 151), (

	Overall	10-y ASCVD Risk <7.5%	10-y ASCVD Risk 7.5%+	P^*
Total no. patients	151	95	56	
Female sex, n (%)	85 (56.3)	61 (64.2)	24 (42.9)	0.011
Age, median (IQR), y	56.00 (49.00, 65.00)	51.00(46.00, 56.00)	68.00 (61.75, 74.00)	<0.001
Race, n (%)				0.873
African American	5 (3.3)	3 (3.2)	2 (3.6)	
Asian/Pacific Islander	21 (13.9)	14 (14.7)	7 (12.5)	
Hispanic/Latino	23 (15.2)	16 (16.8)	7 (12.5)	
White	102 (67.5)	62 (65.3)	40 (71.4)	
Active smoker, n (%)	10 (6.6)	6 (6.3)	4 (7.1)	>0.999
History of smoking, n (%)	12 (7.9)	7 (7.4)	5 (8.9)	0.762
Smoking, median (IQR), packs/y	10.00 (1.19, 21.38)	$6.50\ (1.00,\ 26.75)$	12.50 (10.00, 17.62)	0.319
Systolic blood pressure, median (IQR), mm Hg	126.00 (115.50, 137.00)	119.00 (113.50, 129.50)	133.00 (123.00, 145.25)	<0.001
Antihypertension medication, n (%)	76 (50.3)	40 (42.1)	36 (64.3)	0.008
Total cholesterol, mg/dL, median (IQR)	176.00 (155.00, 206.50)	178.00 (156.50, 206.50)	173.00 (152.75, 207.75)	0.770
High-density lipoprotein, mg/dL, median (IQR)	53.00 (45.00, 64.50)	53.00 (45.00, 65.50)	54.00 (44.75, 64.00)	0.960
Cholesterol-lowering medication, n (%)	78 (51.7)	40 (42.1)	38 (67.9)	0.002
History of diabetes, n (%)	28 (18.5)	16 (16.8)	12 (21.4)	0.484
HbA1c, (%) median (IQR)	6.40 (5.95, 6.85)	6.40 (5.85, 7.03)	6.70 (6.35, 6.75)	0.828
Diabetes treatment, n (%)	26 (17.2)	15 (15.8)	11 (19.6)	0.545

TABLE 2.

Imaging Characteristics of Study Cohort (n = 151), Overall and by 10-Year ASCVD Risk Score Dichotomized at 7.5%

	;			
	Overall	ASUVD KISK %	ASCVD KISK 7.5%+	-
Total no. patients	151	95	56	
Maximum plaque thickness, mean (SD), mm	0.80 (1.24)	0.53 (1.05)	1.25 (1.42)	0.001
Minimum luminal diameter, mean (SD), mm	2.49 (0.72)	2.62 (0.68)	2.28 (0.73)	0.004
No. patients with any stenosis, n (%)	50 (33.1)	24 (25.3)	26 (46.4)	0.008
No. arterial segments showing stenosis				
0	101 (66.9)	71 (74.7)	30 (53.6)	
1	31 (20.5)	17 (17.9)	14 (25.0)	
2	5 (3.3)	1 (1.1)	4 (7.1)	
3	11 (7.3)	4 (4.2)	7 (12.5)	
4	3 (2.0)	2 (2.1)	1 (1.8)	
No. patients with $>50\%$ stenosis, n (%)	15 (9.9)	4 (4.2)	11 (19.6)	0.002
No. arterial segments with >50% stenosis				
0	136 (90.1)	91 (95.8)	45 (80.4)	
1	11 (7.3)	2 (2.1)	9 (16.1)	
2	2 (1.3)	1 (1.1)	1 (1.8)	
3	2 (1.3)	1 (1.1)	1 (1.8)	
No. patients with $>75\%$ stenosis (%)	1 (0.7)	1 (1.1)	0 (0.0)	0.441
No. patients with any calcium, n (%)	76 (50.3)	34 (35.8)	42 (75.0)	<0.001
No. arterial segments showing calcified plaque				
0	75 (49.7)	61 (64.2)	14 (25.0)	
Ι	35 (23.2)	20 (21.1)	15 (26.8)	
2	13 (8.6)	6 (6.3)	7 (12.5)	
З	15 (9.9)	4 (4.2)	11 (19.6)	
4	13 (8.6)	4 (4.2)	9 (16.1)	
Segments with calcium, median (IQR)	1 (0, 2)	0 (0, 1)	1 (0.75, 3)	<0.001
Total Agatston score category				
0	74 (49.0)	60 (63.2)	14 (25.0)	
1–10	19 (12.6)	13 (13.7)	6 (10.7)	

Autho	
or Mar	
uscript	

Author Manuscript

Author Manuscript

	Overall	ASCVD Risk <7.5%	ASCVD Risk 7.5%+	P^*
11–100	26 (17.2)	13 (13.7)	13 (23.2)	
101-400	15 (9.9)	4 (4.2)	11 (19.6)	
>400	17 (11.3)	5 (5.3)	12 (21.4)	
Total Agatston score, median (IQR)	1 (0, 68)	0 (0, 7)	37 (1, 270)	<0.001
$_{*}^{*}$ P values obtained from the Chisquare or Fisher's e	sxact test for o	ategorical variables and	from t-tests for continuou	s variables.

TABLE 3.

Characteristics
60
Imagin
and
<u></u>
59
۲.
at
q
chotomize
<u> </u>
Ľ
sk Score
5
7
Ð
S
4
Yeaı
0
-
of
erlap
0 Ví

	ASCVD Risk <7.5% (n = 95)	ASCVD Risk 7.5% $(n = 56)$	Overall (n = 151)	Cohen r
Plaque				0.245
Maximum plaque thickness <0.9 mm	72	29	101	
Maximum plaque thickness 0.9 mm	23	27	50	
Stenosis				0.216
Maximum stenosis $= 0\%$	71	30	101	
Maximum stenosis >0%	24	26	50	
Stenosis dichotomized at 5%				0.240
Maximum stenosis 5%	73	30	103	
Maximum stenosis >5%	22	26	48	
Stenosis dichotomized at 10%				0.263
Maximum stenosis 10%	75	30	105	
Maximum stenosis >10%	20	26	46	
Calcium				0.365 *
No calcium	61	14	75	
Any calcium	34	42	76	
Single-artery calcium	20	15	35	
Multiartery calcium	14	27	41	
Total Agatston				
Agatston = 0	60	14	74	0.354
Agatston >0	35	42	77	
Agatston 10	73	20	93	0.408
Agatston > 10	22	36	58	
Agatston 100	86	33	119	0.346
Agatston > 100	6	23	32	
Agatston 400	06	44	134	0.189
Agatston >400	5	12	17	
* <i>P</i> value < 0.05.				

TABLE 4.

Characteristics
l Imaging
) and
10%
d at
Dichotomize
ore (
Sc
Risk
Ŋ
ASC
Year .
10-1
of
Overlap
-

	ASCVD Risk <10% $(n = 104)$	ASCVD Risk 10% (n = 47)	Overall (n = 151)	Cohen r
Plaque				0.256
Maximum plaque thickness <0.9 mm	78	23	101	
Maximum plaque thickness 0.9 mm	26	24	50	
Stenosis				0.226
Maximum stenosis $= 0\%$	77	24	101	
Maximum stenosis >0%	27	23	50	
Stenosis dichotomized at 5%				0.248
Maximum stenosis 5%	79	24	103	
Maximum stenosis >5%	25	23	48	
Stenosis dichotomized at 10%				0.270
Maximum stenosis 10%	81	24	105	
Maximum stenosis >10%	23	23	46	
Calcium				0.326
No calcium	64	11	75	
Any calcium	40	36	76	
Single-artery calcium	22	13	35	
Multiartery calcium	18	23	41	
Total Agatston Agatston = 0	63	11	74	0.316
Agatston >0	41	36	77	
Agatston 10	76	17	93	0.347
Agatston > 10	28	30	58	
Agatston 100	93	26	119	0.374
Agatston >100	11	21	32	
Agatston 400	26	37	134	0.176
Agatston >400	7	10	17	

J Comput Assist Tomogr. Author manuscript; available in PMC 2021 May 13.

 * *P* value < 0.05.