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Nonobstructive Coronary Artery Disease by Coronary CT Angiography Improves Risk Stratification and Allocation of Statin Therapy

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ABSTRACT

OBJECTIVES This study sought to determine prognostic value of nonobstructive coronary artery disease (CAD) for atherosclerotic cardiovascular disease (ASCVD) events and to determine whether incorporation of this information into the pooled cohort equation reclassifies recommendations for statin therapy as defined by the 2013 guidelines for cholesterol management of the American College of Cardiology and American Heart Association (ACC/AHA).

BACKGROUND Detection of nonobstructive CAD by coronary computed tomography angiography may improve risk stratification and permit individualized and more appropriate allocation of statin therapy.

METHODS This study determined the pooled hazard ratio of nonobstructive CAD for ASCVD events from published studies and incorporated this information into the ACC/AHA pooled cohort equation. The study calculated revised sex- and ethnicity-based 10-year ASCVD risk and determined boundaries corresponding to the original 7.5% risk for ASCVD events. It also assessed reclassification for statin eligibility by incorporating the results from meta-analysis to individual patients from a separate cohort.

RESULTS This study included 2 studies (2,295 subjects; 66% male; prevalence of nonobstructive CAD, 47%; median follow-up, 49 months; 67 ASCVD events). The hazard ratio of nonobstructive CAD for ASCVD events was 3.2 (95% confidence interval: 1.5 to 6.7). Incorporation of this information into the pooled cohort equation resulted in reclassification toward statin eligibility in individuals with nonobstructive CAD, with an original ASCVD score of 3.0% and 5.9% or higher in African-American women and men and a score of 4.4% and 4.6% or higher in Caucasian women and men, respectively. The absence of nonobstructive CAD resulted in reclassification toward statin ineligibility if the original ASCVD score was as 10.0% and 17.9% or lower in African-American women and men and 13.7% and 14.3% or lower in Caucasian women and men, respectively. Reclassification is observed in 14% of patients.

CONCLUSIONS Detection of nonobstructive CAD by coronary computed tomography angiography improves risk stratification and permits individualized and more appropriate allocation of statin therapy across sex and ethnicity groups. (J Am Coll Cardiol Img 2017;■:■–■) © 2017 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

ASCVD = atherosclerotic cardiovascular disease

CAC = coronary artery calcification

CAD = coronary artery disease

CTA = computed tomography angiography

The 2013 guidelines of the American College of Cardiology and American Heart Association (ACC/AHA) (1) introduced the 10-year event risk for atherosclerotic cardiovascular disease (ASCVD) as a benchmark for recommendations for statin therapy. These estimated event risks and thresholds were determined on the basis of the pooled cohort risk calculator of ASCVD, which uses the demographic and clinical risk factors from observational cohorts to calculate the 10-year event risk.

Following the release of the 2013 ACC/AHA guidelines, it has been demonstrated that these guidelines significantly improve the alignment of statin eligibility (defined as ≥7.5% 10-year ASCVD risk) and the presence of coronary artery disease (CAD); for example, Pursnani et al. (2) showed that alignment of the presence of coronary artery calcification (CAC) and statin eligibility in asymptomatic patients was improved from 23% to 63% as compared with the 2004 Adult Treatment Panel III guidelines of the National Cholesterol Education Program. Furthermore, studies suggest that assessment of CAD can reclassify statin eligibility in up to 50% of patients (3,4). For example, the absence of CAC identifies a large group (33%) of statin-eligible individuals who are at a similarly low risk as non-statin-eligible individuals (1.0% vs. 1.1% 10-year ASCVD risk, respectively) (2). Thus, although the newer guidelines improve detection of patients with CAD, cardiovascular imaging has demonstrated promising results to improve the statin allocation further.

Symptomatic patients undergo coronary computed tomography angiography (CTA) for the assessment of obstructive CAD but few (<15%) of these patients are diagnosed with obstructive CAD (5,6). However, the benefit of coronary CTA extends to the remaining 85% of patients because either CAD can be accurately excluded (30% to 40%) or nonobstructive CAD can be detected (approximately 50%) (5,7), both of which provide tremendous prognostic information beyond traditional risk assessment in both asymptomatic and symptomatic patients (8). Nevertheless, neither current primary prevention nor secondary prevention guidelines contain recommendations for medical therapy in patients with nonobstructive CAD beyond traditional cardiovascular risk factors. However, detailed knowledge of presence or absence of nonobstructive CAD may improve risk stratification and permit individualized and more appropriate allocation of statin therapy.

In this study, we used published data on the prognostic value of nonobstructive CAD to determine whether incorporation of this information into the pooled cohort equation reclassifies recommendations for statin therapy as defined by the 2013 ACC/AHA guidelines for cholesterol management. To do so, we performed a meta-analysis, used the results to modify the ASCVD risk calculator, and applied it to a separate population to assess the reclassification.

METHODS

SYSTEMATIC LITERATURE REVIEW AND DATA COLLECTION. A meta-analysis was conducted in adherence to the MOOSE (Meta-analysis of Observational Studies in Epidemiology) guidelines for meta-analyses and systematic reviews of observational studies (9). Two physician scientists (H.E. and R.A.P.T) searched PubMed for eligible studies using pre-defined selection criteria (**Figure 1**) and pre-defined search syntax for selection of studies that had assessed the prognostic value of coronary CTA published up to May 2016 (Online Appendix). No search restrictions were used, and references of included studies were manually checked to identify eligible studies missed by the primary search strategy. We included the eligible articles on the basis of the following criteria: study domain (patients with suspected CAD without a previous history of CAD); and index test (coronary CTA: obstructive CAD, nonobstructive CAD). If there was an overlap in study populations, the study with the largest population was included. We excluded animal studies, phantom studies, case reports (N < 10), and studies that did not report hazard ratios (HRs) for ASCVD events. Abstracts and unpublished studies were not included, and no contact was made with publication authors.

The characteristics of study subjects at baseline and outcomes were collected in consensus by 2 physician scientists (H.E. and R.A.P.T) for all selected studies. All the selected studies defined obstructive CAD as >50% luminal stenosis and nonobstructive CAD as any CAD with <50% luminal narrowing in at least 1 coronary artery segment. Study quality was assessed in consensus (H.E. and R.A.P.T) by using a modified version of the Quality In Prognosis Studies (QUIPS) tool (10). Our primary outcome of interest was ASCVD defined as cardiovascular death, nonfatal myocardial infarction, and stroke. The annualized ASCVD event risk in each study (if not reported) is calculated by using the median follow-up period. The average annual ASCVD risk of selected studies is calculated as mean of reported or calculated annualized event rates of the individual studies.

META-ANALYSIS: PROGNOSTIC VALUE OF NONOBSTRUCTIVE CORONARY ARTERY DISEASE. We identified studies that reported HRs of nonobstructive