

Prevalence and Prognosis of Nonobstructive Coronary Artery Disease in Patients Undergoing Coronary Angiography or Coronary Computed Tomography Angiography: A Meta-Analysis



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Abstract

Objective: To evaluate the prevalence, clinical characteristics, and risk of cardiac events in patients with nonobstructive coronary artery disease (CAD).

Patients and Methods: We searched PubMed, EMBASE, and the Cochrane Library from January 1, 1990, to November 31, 2015. Studies were included if they reported prevalence or prognosis of patients with nonobstructive CAD ($\leq 50\%$ stenosis) among patients with known or suspected CAD. Patients with nonobstructive CAD were further grouped as those with no angiographic CAD (0% or $\leq 20\%$) and those with mild CAD ($>0\%$ or $>20\%$ to $\leq 50\%$). Data were pooled using random effects modeling, and annualized event rates were assessed.

Results: Fifty-four studies with 1,395,190 participants were included. The prevalence of patients with nonobstructive CAD was 67% (95% CI, 63%-71%) among patients with stable angina and 13% (95% CI, 11%-16%) among patients with non-ST-segment elevation acute coronary syndrome. The prevalence varied depending on sex, clinical setting, and risk profile of the population investigated. The risk of hard cardiac events (cardiac death or myocardial infarction) in patients with mild CAD was lower than that in patients with obstructive CAD (risk ratio, 0.28; 95% CI, 0.20-0.38) but higher than that in those with no angiographic CAD (risk ratio, 1.85; 95% CI, 1.52-2.26). The annualized event rates of hard cardiac events in patients with no angiographic CAD, mild CAD, and obstructive CAD were 0.3% (95% CI, 0.1%-0.4%), 0.7% (95% CI, 0.5%-1.0%), and 2.7% (95% CI, 1.7%-3.7%), respectively, among patients with stable angina and 1.2% (95% CI, 0.02%-2.3%), 4.1% (95% CI, 3.3%-4.9%), and 17.0% (95% CI, 8.4%-25.7%) among patients with non-ST-segment elevation acute coronary syndrome. The correlation between CAD severity and prognosis is consistent regardless of clinical presentation of all-cause death, myocardial infarction, total cardiovascular events, and revascularization.

Conclusion: Nonobstructive CAD is associated with a favorable prognosis compared with obstructive CAD, but it is not benign. The high prevalence and impaired prognosis of this population warrants further efforts to improve the risk stratification and management of patients with nonobstructive CAD.

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Contemporary management strategies of coronary artery disease (CAD) are largely based on the evidence from patients with obstructive epicardial coronary stenoses. A coronary stenosis less than 50% is generally perceived to produce no ischemia and characterized as nonobstructive disease. Until recently, the prognosis of patients with nonobstructive CAD was thought to be benign, and given the limited evidence, there

are no professional guidelines on the management of these patients. However, the perception of the benign nature of nonobstructive CAD is challenged by the view that the vulnerability of plaques, rather than the extent of luminal narrowing, dominates the pathophysiology of future coronary events.^{1,2}

Although patients with nonobstructive CAD have been the focus of many studies, knowledge about prognosis of these patients



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is limited. Findings from early retrospective angiographic studies^{3,4} suggested that about two-thirds of acute myocardial infarction (MI) evolved from mild to moderate stenosis. In contrast, growing evidence in recent years indicates that CAD severity, identified by either coronary angiography (CA) or coronary computed tomography angiography (CCTA), is positively correlated with risk of events.⁵⁻⁷ However, very few of these individual studies were adequately powered to detect an effect on hard clinical outcomes (eg, death and MI). In the few recent large registries⁵⁻⁷ that focused on the relationship between CAD severity and risk of hard clinical events, substantial variability exists regarding research population (overrepresented by men or women), diagnostic modality (CA or CCTA), and definition of nonobstructive CAD. In addition, comparisons of nonobstructive CAD with obstructive CAD were rarely provided by these studies. Ascertaining the precise prevalence, clinical characteristics, and prognostic value of cardiac events associated with nonobstructive CAD is of critical importance to determining the appropriate management strategy for these patients, yet to date this information remains largely unclear. Accordingly, we conducted a systematic review and meta-analysis to evaluate the prevalence, clinical characteristics, and risk of cardiac events in patients with nonobstructive CAD compared with those with obstructive CAD and with those with no angiographic CAD among patients referred to CA or CCTA for suspected or known CAD as well as to identify sources of potential heterogeneity of existing data.

PATIENTS AND METHODS

Search Strategy

The guideline of the MOOSE (Meta-analysis of Observational Studies in Epidemiology)⁸ was followed for the conduct of the present systematic review and meta-analysis. We searched PubMed, EMBASE, and the Cochrane Library for the current literature. Detailed search strategies are given in [Supplemental Methods](#) (available online at <http://www.mayoclinicproceedings.org>). The last search was performed on November 1, 2015. Reference lists from these identified reports and reviews were manually screened to identify additional

relevant studies. To minimize the heterogeneity due to the rapidly advancing diagnostic techniques and treatment strategies, we included only studies published from January 1, 1990. The search was limited to studies in human adults published in peer-reviewed journals. Studies in abstract form without a published manuscript were excluded. No language restriction was applied.

Study Selection

Two investigators (Z.J.W. and L.L.Z.) screened the titles and abstracts of all retrieved literature independently and in duplicate. Then, full-text reports considered relevant were assessed for eligibility for inclusion. Disagreement was resolved by discussion and consulting a third investigator (Y.J.Z.). Studies were considered eligible for this review if (1) they investigated patients with known or suspected CAD with either CA or CCTA and involved more than 100 patients; (2) the data on the prevalence or clinical events were available according to the absence or presence of obstructive CAD. We excluded studies of acute ST-segment elevation myocardial infarction. Studies in which the study population included both patients with non-ST-segment elevation acute coronary syndrome (NSTEMI) and patients with ST-segment elevation myocardial infarction were included if data relevant to NSTEMI were reported separately.

Data Extraction

Two investigators (Z.J.W. and L.L.Z.) extracted the data from the full reports of the included studies independently and in duplicate. The data sought included first author, journal, publication year, study population, baseline clinical characteristics, prevalence, and outcomes of patients according to the presence and absence of obstructive CAD. Authors of the articles were individually contacted by e-mail when the data were unclear or to obtain additional data. Discrepancies between the 2 investigators were resolved by consensus. We assessed the quality of individual studies for the purpose of our primary end point of interest by using the Newcastle-Ottawa Quality Assessment for Cohort Studies.⁹

We defined *obstructive CAD* as more than 50% stenosis in at least 1 major epicardial coronary artery because it is the most commonly

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