REVIEW ARTICLE

Richard P. Cambria, MD, Section Editor

The prevalence of abdominal aortic aneurysm is consistently high among patients with coronary artery disease

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Objective: **Emerging evidence suggests high prevalence of abdominal aortic aneurysm (AAA) among patients with coronary disease. Accurate characterization of the association between coronary disease and AAA and of the actual prevalence of AAA among patients with angiography-verified coronary artery disease (CAD) is needed to evaluate the possible benefits of systematic screening for AAA.**

Methods: **We searched for studies that reported the association between AAA and CAD or coronary heart disease (CHD; wider phenotype definition) in the general population (randomized controlled trials, prospective population cohorts) and those that reported the prevalence of AAA among patients with angiography-verified CAD through PubMed, Embase, and reference lists for the period between 1980 and 2014. Random-effects models were applied because of the high heterogeneity between included studies.**

Results: **Among the general population, 23 studies reported the association between CHD and the occurrence of subclinical AAA (positive ultrasound screening; meta-analyzed odds ratio of 2.38 with 95% confidence interval [CI] of 1.78-3.19; $P = 4.1 \times 10^{-9}$). According to four prospective studies, CHD is a strong predictor of future AAA events (fatal and nonfatal; meta-analyzed hazard ratio of 3.49 with 95% CI of 2.56-4.76; $P = 2.4 \times 10^{-15}$). Altogether, 10 studies reported the prevalence of AAA among patients with angiography-verified CAD or undergoing coronary artery bypass grafting. Among men, meta-analyzed prevalence was 9.5% (95% CI, 7.6%-11.7%). Among men undergoing coronary artery bypass grafting or with three-vessel disease, the prevalence was 11.4% (95% CI, 9.1%-13.9%). Among women, the prevalence was low (0.35%).**

Conclusions: **The risk of subclinical AAA and future AAA events is high among patients with coronary disease. Screening for AAA among CAD patients by cardiologists would be easy and inexpensive, with possible benefits to survival and risk evaluation. (J Vasc Surg 2015;62:232-40.)**

Abdominal aortic aneurysm (AAA) is a pathologic dilation of the abdominal aorta. It can lead to an aortic rupture, which in most cases is a lethal condition.[1] Aortic diameter of 30 mm or more is generally considered pathologic, and screening programs using this cutoff have been shown to reduce AAA-related mortality among older men.[1-3] Ruptures of AAAs affect predominantly men, and screening for AAA is not generally recommended among women.[4]

In the United Kingdom, a national program has been launched to screen all men aged 65 years.[5] In recently published guidelines, the U.S. Preventive Services Task Force recommends one-time screening for AAA by ultrasonography in men aged 65 to 75 years who have ever smoked but not among nonsmokers.[1] Although cost-effectiveness of large screening programs has been verified,[5,6] perhaps owing to simple lack of resources, screening of AAA is still not implemented on a general population level in most developed countries.

Coronary artery disease (CAD) is a risk factor for AAA.[7] In fact, a large proportion of patients treated emergently for AAA have CAD.[8] Currently, a small number of individual studies with heterogeneous study settings have reported exclusively the prevalence of AAA among patients with angiography-verified CAD.[9-14] Preliminary evidence also suggests that the severity of CAD is associated with prevalence of AAA.[9] Unfortunately, most of the previous individual studies are based on small populations of patients, and the results have been variable. Screening for AAA among CAD patients undergoing angiography is a compelling idea because of the low costs and availability of ultrasound for patients treated by cardiologists. Furthermore, accurate characterization of significant comorbidities may help improve risk stratification.[15,16]

We conducted a meta-analysis and a review of the results of all general population-based studies reporting the

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difference in the prevalence of AAA in patients with or without a history of coronary heart disease (CHD; a wider definition for the condition and with more uncertainty in the diagnostic criteria). Furthermore, we searched for studies that have reported the prevalence of AAA among patients with angiographically verified CAD to determine a reliable estimate of the prevalence (and possible heterogeneity in the estimate). Screening of patients with such unified selection criteria is the most reliable way of characterizing the association between the two conditions and aids in determining the possible benefit of systematic screening among these patients.

METHODS

This meta-analysis included cross-sectional studies, randomized controlled trials, prospective cohort studies, and nested case-control studies, which reported data of the univariate association (or applicable prevalence numbers) between CHD (as reported in most publications) and AAA. In addition, we searched for studies reporting the prevalence of AAA among patients with angiographically verified CAD or undergoing coronary artery bypass grafting (CABG). A study flow chart is presented in Fig 1. This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Appendix, online only) guidelines.

Search strategy. We assessed all publications that reported the prevalence of AAA among worldwide patient populations. We searched the electronic databases of PubMed and Embase for relevant papers published from 1980 through November 2014. The search terms were "abdominal aortic aneurysm" combined with "prevalence" or "coronary artery disease" or "coronary heart disease" or "screening" or "myocardial infarction" or "risk factor." A manual search was performed by checking the reference lists of original reports and review articles, retrieved through the electronic searches, to identify studies not yet included in the computerized databases.

Inclusion and exclusion criteria. The inclusion criteria were (1) studies in the mentioned three databases with full text; (2) studies conducted in general populations (prospective cohort studies, cross-sectional studies, randomized controlled trials, or nested case-control studies) reporting the prevalence of AAA at baseline or AAA events during follow-up among subjects with or without CHD or CAD or vice versa; and (3) studies conducted among patients with angiographically verified coronary stenosis ≥50% narrowing of at least one epicardial artery or undergoing CABG with sufficient information to estimate the pooled prevalence of AAA.

The exclusion criteria were (1) studies without specific sample origins; (2) studies with overlapping sample collection from the same origin; (3) studies not reporting data after sex stratification (for studies reporting screening among coronary angiography-verified CAD); and (4) studies that failed to present data clearly enough or with obvious paradoxical data.

Data extraction. All potentially relevant papers were reviewed independently by two investigators through assessing the eligibility of each article and abstracting data with standardized data abstraction forms. Disagreements were resolved through discussion. The following information, although some studies did not contain all of it, was extracted from the literature: first author's name; publication date; country; design; age; gender; number invited; number screened; definition of AAA; risk factors; and prevalence rate by different stratified factors, including areas difference, age, gender, and diameter of aneurysms.

Data analysis. The primary outcomes of this meta-analysis were the association (defined by unadjusted risk ratio) between subjects with or without CHD and the prevalence rate of AAA among patients with significant CAD on angiography. To examine possible sources of bias, stratified analyses were conducted for the studies. We investigated the effect of potentially distorting factors, including gender and severity of CAD.

Publication bias was assessed for the included studies by visually inspecting funnel plots and applying the Egger test and the test of Thompson and Sharp because heterogeneity between studies was high (based on a weighted linear regression of the treatment effect on its standard error using the method of moments estimator for the additive between-study variance component). Even distribution in the funnel plot suggests that there is no publication bias due to lack of publication of negative results or overpresentation of positive results. Risk factor associations were expressed as odds ratios (ORs) to obtain consistency across studies. All analyses were conducted using R, which is open source software.

A random-effects model was chosen for all data analyses as this model better addresses heterogeneity between studies (observed high in most analyses with $I^2 > 50\%$) and study populations and was less influenced by extreme variations in sample size. If heterogeneity was observed lower than 50% by I^2 index, a fixed-effects model was used. Heterogeneity among study prevalence estimates was assessed by means of the Q statistic, with magnitude of heterogeneity evaluated with the I^2 index.

RESULTS

The association between AAA and CHD in general population-based screenings and nested case-control studies. After removing all redundant publications, we found 27 publications reporting unadjusted ORs, hazard ratios (HRs), or prevalence numbers from which corresponding ORs could be derived for evaluating the association between CHD and AAA. Altogether, 23 publications addressed the prevalence of CHD among subjects with or without new AAA discovered on ultrasound screening at baseline (ie, subclinical AAA) (Table I). In a meta-analysis using a random-effects model, we found that CHD was associated with a higher occurrence rate of subclinical AAA (OR, 2.38; 95% confidence interval [CI], 1.78-3.19; $P = 4.1 \times 10^{-9}$). The between-study heterogeneity was high ($I^2 = 98.4\%$ [98.1%; 98.7%]) (Fig 2).