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Coronary artery disease in giant cell arteritis: A systematic review and meta-analysis

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ABSTRACT

Objective: To investigate the association between giant cell arteritis (GCA) and risk of coronary artery disease (CAD).
Methods: We conducted a systematic review and meta-analysis of observational studies that reported relative risks, hazard ratios, or standardized incidence ratios with 95% confidence interval comparing CAD risk in patients with GCA versus non-GCA controls. Pooled risk ratios and 95% confidence intervals were calculated using a random-effect, generic inverse variance of DerSimonian and Laird.
Result: Six studies with 10,868 patients with GCA and 245,323 controls were identified and included in our data analysis. The pooled risk ratio of CAD in patients with GCA was 1.51 and did not achieve statistical significance (95% CI: 0.88–2.61). The statistical heterogeneity was high with an I^2 of 97%.
Conclusion: In contrast to other chronic systemic inflammatory disorders, our meta-analysis did not show any statistically significant increased risk of CAD among patients with GCA.

Introduction

The association between chronic inflammation and premature atherosclerosis is well recognized [1,2]. Several studies have demonstrated the detrimental effect of inflammatory cytokines, oxidative stress, and activated leukocytes on endothelial function, resulting in the acceleration of atherosclerosis [3–6]. Chronic inflammation has also been shown to promote the coagulation cascade, impair the anti-coagulation pathway, and inhibit fibrinolysis resulting in a hypercoagulable state [7,8]. These factors may serve as the fundamental pathophysiology of the development of premature coronary artery disease (CAD). Moreover, an increased incidence of CAD has been observed in several chronic inflammatory disorders, such as rheumatoid arthritis, idiopathic inflammatory myopathy, systemic sclerosis, and systemic lupus erythematosus [9–12].

Giant cell arteritis (GCA) is a chronic inflammatory condition characterized by medium- and large-vessel granulomatous vasculitis, typically affecting adults older than 50 years of age [13]. Vascular complications of GCA include ischemic optic neuropathy, stroke, large-vessel stenosis, and aneurysm [14]. Patients with GCA may be at an increased risk of CAD as well. However, the data on CAD risk in these patients remain unclear due to conflicting epidemiological studies [15–17]. Thus, to further investigate this association, we conducted a systematic review and meta-analysis of case–control and cohort studies that compared the risk of CAD in patients with GCA versus non-GCA participants.

Methods

Search strategy

Two investigators (P.U. and M.J.K.) independently searched published studies indexed in MEDLINE and EMBASE database from inception to August 2014 as well as the American College of Rheumatology annual conference abstract database from 2006 to 2013 using the search strategy described in Appendix 1. A manual search of references of selected retrieved articles was also performed.

Inclusion criteria

The inclusion criteria were as follows: (1) cohort or case–control study (either prospective or retrospective) published as original study or abstract reporting CAD incidence in patients with GCA; (2) relative risk (RRs), odds ratio (ORs), hazard ratio (HRs) or

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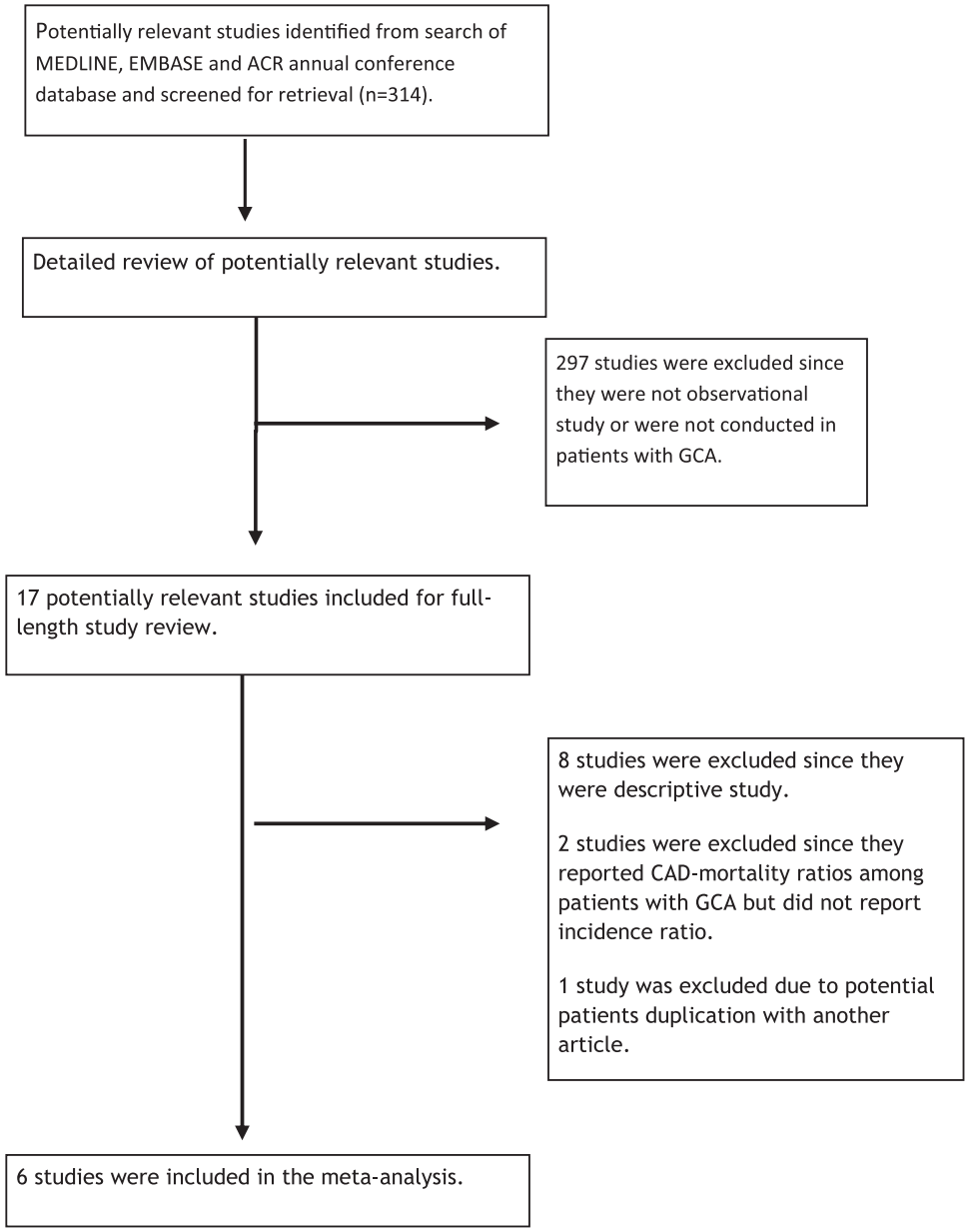

Fig. 1. Outline of our search methodology.

standardized incidence ratio (SIRs), with 95% confidence intervals (CIs) were provided; and (3) non-GCA participants and participants without CAD were used as a reference group for cohort study and case–control study, respectively.

Study eligibility was independently determined by each investigator noted above. Differing decisions were resolved by consensus. The quality of the included studies was independently appraised by each investigator using the Newcastle–Ottawa quality assessment scale. Using this scale, each study is assessed on eight items that are categorized into three groups including (1) the selection of the study groups, (2) the comparability of the groups, and (3) the ascertainment of the exposure or outcome of interest for case–control or cohort studies, respectively [18].

Data extraction

A standardized data collection form was used to extract the following information: last name of the first author, title of the article, year of publication, country where the study was conducted, year of publication, study size, study population, criteria used for the diagnosis of GCA, definition and method of verification of coronary artery disease, mean duration of follow-up, and adjusted effect estimates with 95% CI. This data extraction was independently performed by the two investigators. Any differences in data extraction were resolved by consensus.

Statistical analysis

Data analysis was performed using Review Manager 5.3 software from the Cochrane Collaboration. Adjusted point estimates and standard errors were extracted from individual studies and were combined by the generic inverse variance method of DerSimonian and Laird [19]. Given the high likelihood of between-study variance with the different study designs and populations, we used a random-effect model rather than a fixed-effect model. Cochran's Q test was used to determine the statistical heterogeneity of this study. This test was complemented with the I^2 statistic, which quantifies the proportion of total variation across