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Risk of malignancy in patients with giant cell arteritis and polymyalgia rheumatica: A systematic review and meta-analysis

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ABSTRACT

Objective: To investigate the association between giant cell arteritis (GCA)/polymyalgia rheumatica (PMR) and malignancy risk.
Methods: We conducted a systematic review and meta-analysis of cohort studies that reported relative risk, hazard ratio, or standardized incidence ratio (SIRs) with 95% confidence comparing malignancy risk in patients with GCA/PMR versus non-GCA/PMR participants. Pooled risk ratios and 95% confidence intervals were calculated using a random-effect, generic inverse variance method.
Result: A total of six studies were identified and included in our data analysis. The pooled risk ratio of malignancy in patients with GCA/PMR was 1.14 (95% CI: 1.05–1.22). The risk was higher in the first 6–12 months after diagnosis with the pooled risk ratio of 2.16 (95% CI: 1.85–2.53). However, when we performed a sensitivity analysis that excluded one study with a potential selection bias, the pooled risk ratio decreased and did not achieve statistical significance.
Conclusion: Our study demonstrated a low but statistically significant increased malignancy risk among patients with GCA/PMR. However, when we excluded one study with potential selection bias, the new pooled risk ratio did not achieve statistical significance.

Introduction

Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR), two common chronic inflammatory rheumatologic disorders in adults aged over 50 years worldwide, are two closely related disorders that commonly occur together [1,2]. The hallmarks of these two diseases are systemic inflammation and a marked response to corticosteroid therapy.

An increased incidence of malignancy has been observed in several autoimmune inflammatory disorders, including idiopathic inflammatory myopathy, rheumatoid arthritis, and systemic lupus erythematosus. The mechanism behind this association remains unclear, but is believed to be related to dysregulation of the immune system [3–5]. Several case reports and case series have also suggested this increased risk in patients with GCA and PMR [6,7], but no definite association between GCA/PMR and malignancy has been established due to conflicting epidemiological studies. Thus, to further investigate this association, we conducted a systematic review and meta-analysis of cohort studies that compared the risk of malignancy in patients with GCA and/or PMR versus non-GCA/PMR participants.

Methods

Search strategy

Two investigators (P.U. and A.S.) independently searched published studies indexed in MEDLINE and EMBASE database from inception to January 2014 using the search strategy described in Appendix A. A manual search of references of selected retrieved articles was also performed. Conference abstract and unpublished studies were not included.

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Inclusion criteria

The inclusion criteria were as follows: (1) cohort studies (either prospective or retrospective) published as original studies reporting malignancy incidences in patients with GCA and/or PMR, (2) relative risk (RRs), hazard ratio (HRs), or standardized incidence ratio (SIRs) with 95% confidence intervals (CIs) were provided, and (3) non-GCA/PMR participants were used as a reference group.

Study eligibility was independently determined by each investigator noted above. Differing decisions were resolved by consensus. The quality of each study was also independently appraised by each investigator using the Newcastle–Ottawa quality assessment scale [8].

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/PMR, verification of malignancy, mean duration of follow-up, and adjusted effect estimates with 95% CI. The two investigators mentioned above independently performed this data extraction.

Statistical analysis

Data analysis was performed using Review Manager 5.2 software from the Cochrane Collaboration. Point estimates and standard errors were extracted from individual studies and were combined by the generic inverse variance method of DerSimonian and Laird [9]. 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. Statistical heterogeneity was calculated using Cochran's Q test. This statistic was complemented with the I^2 statistic, which quantifies the proportion of total variation across studies that is due to heterogeneity rather than chance. A value of I^2 of 0–25% represents insignificant heterogeneity, 25–50% low heterogeneity, 50–75% moderate heterogeneity, and 75–100% high heterogeneity [10].

Results

Our search strategy yielded 844 potentially relevant articles. Of them, 815 articles were excluded, as they were not cohort studies or were not conducted in patients with GCA/PMR. Rest of

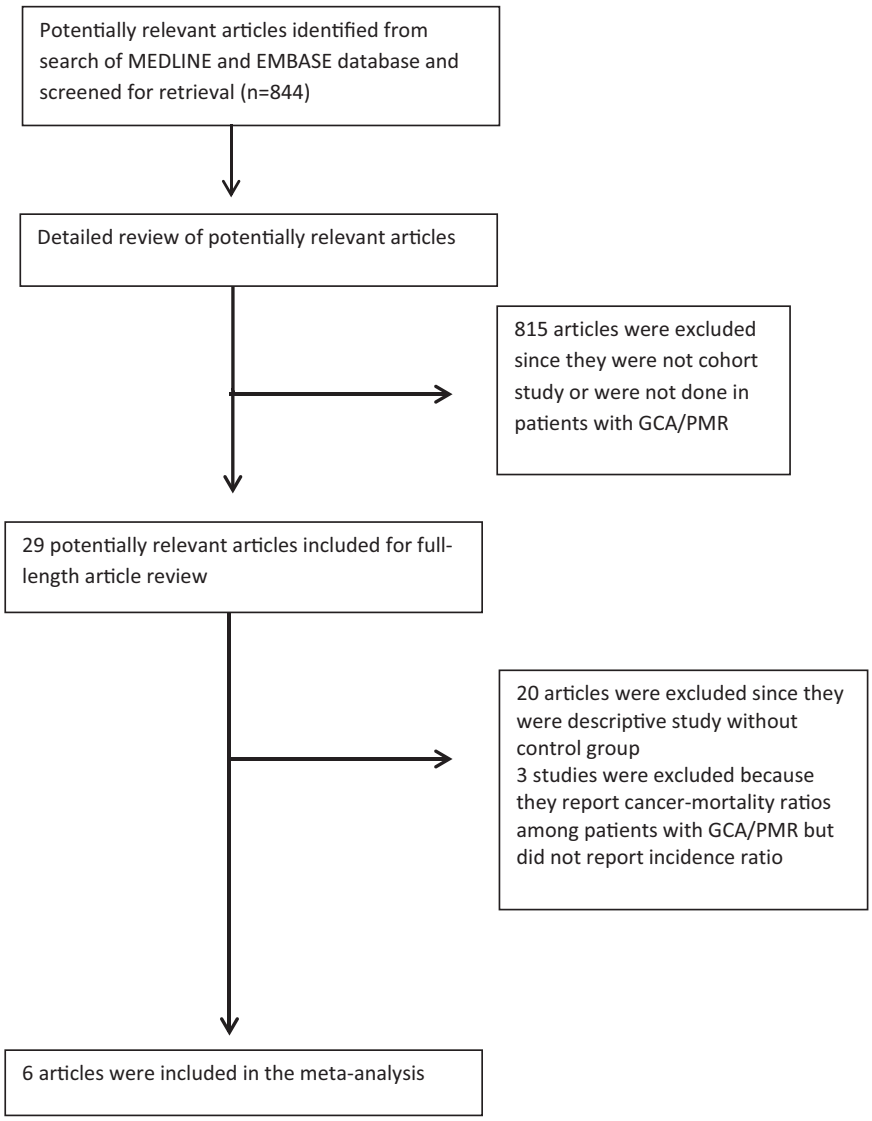

Fig. 1. An outline of our search methodology.