Findings consistent with subclinical vasculitis in patients with new onset polymyalgia: a systematic literature review and a meta-analysis of cohort data

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Introduction: The clinical manifestation of giant cell arteritis (GCA) includes cranial symptoms (new onset headache, vision impairment or jaw claudication), peripheral vascular claudication, constitutional symptoms, but also symptoms of polymyalgia rheumatica (PMR). Some GCA patients present with PMR symptoms only and thus may not be diagnosed with GCA. The aims of this systematic literature review and meta-analysis are first, to search for data on the prevalence of subclinical GCA (absence of cranial ischemic symptoms) in newly diagnosed PMR patients and second to describe the association of patient characteristics with the presence of subclinical GCA.

Methods: We systematically searched and subsequently screened PubMed, Embase.com and Web of Science databases and included studies of corticosteroid-naïve patients with polymyalgia who did not report cranial symptoms consistent with GCA. Authors of the publications identified in the literature review were asked to share individual patient data (IPD). Potential predictors of GCA were assessed in univariable mixed effects logistics regression models with vascular involvement (no/yes) as the outcome and with study modeled as a random effect. We imputed missing values in the data using multilevel joint modeling multiple imputation. Selected potential predictors were included in a multivariable model.

Results: Out of 3047 screened studies, 13 fulfilled the inclusion criteria. These studies, published from 1961-2019, reported on 543 PMR patients who were examined by TAB (n=175), US (n=110), PET or PET-CT (n=258). These diagnostic measures led to the diagnosis of 115 PMR patients with GCA. The prevalence of patients with findings compatible with GCA within these studies ranged from 0-92%, with a median prevalence of 20%. Information on patients' characteristics were largely missing, therefore we collected IPD from 243 patients in the seven published cohorts using PET for GCA diagnosis. The odds for candidate predictors of vascular involvement in the multivariable model were: Age (in years) OR 0.98 (0.93 - 1.03), female sex OR 1.46 (CI: 0.61 - 3.48), experiencing inflammatory back pain OR 5.89 (CI: 1.45 - 23.92), body temperature > 37°C OR 1.28 (CI: 0.52 - 3.15), experiencing weight loss OR 1.38 (CI: 0.62 - 3.11), scaled thrombocyte count (in 1e+09/ml) OR 1.30 (CI: 0.76 - 2.21), current smoking status OR 2.37 (CI: 0.26 - 21.91), experiencing lower limb pain OR 0.3 (CI: 0.1 - 0.88), increase in hemoglobin (per 1 g/dl) OR 0.8 (CI: 0.59 - 1.09), shoulder girdle pain OR 0.38 (CI: 0.04 - 3.17), pelvic girdle pain OR 0.71 (CI: 0.26 - 1.94), neck pain OR 0.36 (CI: 0.09 - 1.48), duration of morning stiffness OR 1.0 (CI: 0.99 - 1.00), C-reactive protein (CRP) level (in mg/l) OR 1.0 (CI: 0.99 - 1.01) and diabetes OR 0.3 (CI: 0.04 - 2.13).

Conclusions: Our meta-analysis shows a median prevalence of subclinical GCA in newly diagnosed PMR patients of 20%, which remained stable over the last 60 years irrespective of the diagnostic method used. Several promising predictor variables were found using the thus far largest IPD dataset on this topic. Further exploration of these variables in PMR patients and studying the association of subclinical GCA with long-term patients' outcomes is warranted.