

# Letter to the Editor (Matters arising from published papers)

Rheumatology 2021;60:e262–e263  
doi:10.1093/rheumatology/keab143  
Advance Access Publication 12 February 2021

## Comment on: Negative associations for fasting blood glucose, cholesterol and triglyceride levels with the development of giant cell arteritis: reply

DEAR EDITOR, We thank Dr Huang *et al.* for their letter [1], and their interest in our article [2] and for their comments on methodological issues in analyses of predictors of GCA.

We agree that residual confounding cannot be excluded, and that the exposures listed by Huang *et al.* are relevant in this context. Smoking was adjusted for. Unfortunately, data on other potential confounders such as physical activity, quantified alcohol consumption and diet were not available in this cohort. Use of statins and other lipid lowering drugs was low in Sweden at the time of inclusion. Information on household income was not available. However, additional analyses, adjusted for occupation (blue- vs white-collar work, based on self-reported job titles in the Swedish national census and standardized classification), as previously described [3] gave similar estimates of odds ratios for developing GCA: fasting blood glucose (FBG) 0.21 per (s.d.) (95% CI: 0.09, 0.53), cholesterol 0.76 per s.d. (95% CI: 0.31, 0.71) and triglycerides 0.47 per s.d. (95% CI: 0.26, 0.84).

As a follow-up to our findings on a negative association between body mass index (BMI) and GCA [4], we have previously investigated the relation between self-reported physical activity and subsequent GCA in a similar cohort, based on the Malmö Diet and Cancer Study. The results have been reported in abstract form [5]. We concluded that physical activity did not influence risk of GCA, and that a lower BMI predicted GCA in analysis adjusted for physical activity [5].

On the other hand, the metabolic features found to be associated with GCA in our recent study [2] may be path variables that are due to underlying differences in diet, physical activity etc. Regardless of this, metabolic regulation of inflammation, as outlined in the Discussion in our article, may explain the observed associations.

Our results differ from the studies that reported shared risk factors for GCA and cardiovascular disease, but are in agreement with those from a population-based cohort study from Iceland [6]. The situation is, thus, more complex than described by Huang *et al.* The choice of a negative control exposure in this type of analysis is not obvious.

Due to the limited sample size, sex-differences in the statistical significance should be interpreted with caution. All associations were in the same direction in women and men. BMI is a relatively crude measure, in particular in men, and may not adequately reflect the relevant metabolic features in all individuals.

The choice of current smoking rather than ever smoking for the adjustments was based on selection of covariates from the univariate analyses, where current smoking, but not ever smoking, had a significant negative association with GCA. However, when adjusting for ever smoking, the results did not differ significantly from the published models that included current smoking (odds ratio for developing GCA for FBG 0.49 per s.d. (95% CI: 0.27, 0.91), for cholesterol 0.62 per s.d. (95% CI: 0.44, 0.87) and for triglycerides 0.36 per s.d. (95% CI: 0.20, 0.64)).

In summary, results were similar in models adjusted for socio-economic status and ever smoking. Although other exposures may contribute to residual confounding in this context, FBG and blood lipids may also be path variables that contribute directly to GCA pathogenesis. Hypotheses of possible underlying mechanisms, including those on metabolic regulation of vascular inflammation described in our article [2], are important for further efforts to understand the origins of GCA. In this process, epidemiologic studies should be combined with analyses of biomarkers and experimental disease models.

**Disclosure statement:** The authors have declared no conflicts of interest.

**Funding:** No specific funding was received from any funding bodies in the public, commercial or not-for-profit sectors to carry out the work described in this manuscript.

## Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

**Karin Wadström<sup>1</sup>, Lennart Jacobsson<sup>1,2</sup>, Aladdin J. Mohammad<sup>3,4</sup>, Kenneth J. Warrington<sup>5</sup>, Eric L. Matteson<sup>5</sup> and Carl Turesson<sup>1,3</sup>**

<sup>1</sup>Rheumatology, Department of Clinical Sciences, Lund University, Malmö, <sup>2</sup>Department of Rheumatology & Inflammation Research, Institute of Medicine, Sahlgrenska

Academy, University of Gothenburg, Gothenburg,  
<sup>3</sup>Department of Rheumatology, Skåne University Hospital,  
Malmö, Sweden, <sup>4</sup>Department of Medicine, University of  
Cambridge, Cambridge, UK and <sup>5</sup>Division of Rheumatology,  
Mayo Clinic College of Medicine and Science, Rochester,  
MN, USA

Accepted 01 February 2021

Correspondence to: Karin Wadström, Department of  
Rheumatology, Skåne University Hospital, 205 02 Malmö,  
Sweden. E-mail: karin.wadstrom@med.lu.se

## References

- 1 Huang L-W, Weng J-H, Wei JC-C. Comment on: negative associations for fasting blood glucose, cholesterol and triglyceride levels with the development of giant cell arteritis. *Rheumatology* 2021;60:e258–59.
- 2 Wadström K, Jacobsson L, Mohammad AJ *et al*. Negative associations for fasting blood glucose, cholesterol and triglyceride levels with the development of giant cell arteritis. *Rheumatology* 2020;59:3229–36.
- 3 Bergstrom U, Jacobsson L, Nilsson J-Å, Berglund G, Turesson C. Pulmonary dysfunction, smoking, socioeconomic status and the risk of developing rheumatoid arthritis. *Rheumatology* 2011;50:2005–13.
- 4 Jakobsson K, Jacobsson L, Warrington K *et al*. Body mass index and the risk of giant cell arteritis—results from a prospective study. *Rheumatology* 2015;54:433–40.
- 5 Jakobsson K, Jacobsson L, Warrington K *et al*. The association between lower body mass index and increased risk of giant cell arteritis is not explained by differences in physical activity. *Arthritis Rheum* 2012;64 (Suppl 10):393.
- 6 Tomasson G, Bjornsson J, Zhang Y, Gudnason V, Merkel PA. Cardiovascular risk factors and incident giant cell arteritis: a population-based cohort study. *Scand J Rheumatol* 2019;48:213–7.