Body mass index and the risk of giant cell arteritis—results from a prospective study

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Abstract

Objective. The aim of this study was to examine potential risk factors for GCA in a nested case-control study based on two prospective health surveys.

Methods. We used two population-based health surveys, the Malmö Preventive Medicine Program (MPMP) and the Malmö Diet Cancer Study (MDCS). Individuals who developed GCA after inclusion were identified by linking the MPMP and MDCS databases to several patient administrative registers. A structured review of the medical records of all identified cases was performed. Four controls for every confirmed case, matched for sex, year of birth and year of screening, were selected from the corresponding databases. Potential predictors of GCA were examined in conditional logistic regression models.

Results. Eighty-three patients (70% women, 64% biopsy positive, mean age at diagnosis 71 years) had a confirmed diagnosis of GCA after inclusion in the MPMP or MDCS. A higher BMI was associated with a significantly reduced risk of subsequent development of GCA [odds ratio (OR) 0.91/kg/m² (95% CI 0.84, 0.98)]. Smoking was not a risk factor for GCA overall [OR 1.36 (95% CI 0.77, 2.57)], although there was a trend towards an increased risk in female smokers [OR 2.14 (95% CI 0.97, 4.68)]. In multivariate analysis, adjusted for smoking and level of formal education, the inverse association between BMI and GCA remained significant (P = 0.027).

Conclusion. In this study, GCA was predicted by a lower BMI at baseline. Potential explanations include an effect of reduced adipose tissue on hormonal pathways regulating inflammation.

Key words: giant cell arteritis, body mass index, vasculitis, predictors.

Introduction

GCA is a form of vasculitis that affects mainly large and medium-sized arteries in persons >50 years of age. About 70% of patients are women [1, 2]. In patients with GCA, PMR is present in 40–60% of cases [1]. The highest reported incidence of GCA is found in Scandinavian countries and Minnesota (USA). In these populations, with partly similar ethnic backgrounds, annual rates of >20/100,000 people >50 years of age have been estimated [3, 4]. In Mediterranean countries the incidence is lower [5, 6] and Asian and Arab countries have the lowest reported incidence [7, 8]. The aetiology and pathogenesis of the disease are incompletely understood, but genetic factors have been implicated. HLA-DRB1*04 alleles have been associated with GCA in populations from France and Minnesota [9, 10], although in a study from Northern Italy, HLA-DRB1*04 was not associated with GCA [11]. There are limited data on predictors of GCA. In one previous case-control study of 49 women with GCA, a history of smoking, low BMI and several hormonal factors were associated with GCA [12]. Smoking [13–20] and a low level of formal education have been found to predict other chronic inflammatory disorders, including RA [13, 21–24]. The objective of this study was to examine
reproductive factors, smoking, level of education and BMI as potential risk factors for GCA in a nested case–control study based on two prospective health surveys.

Patients and methods

Cases and controls

This nested case–control study used information from the Malmö Diet Cancer Study (MDCS) and the Malmö Preventive Medicine Program (MPMP), two community-based health surveys performed in Malmö, Sweden, current population 300 000 [the population during the screening period (1974–96) was between 229 000 and 247 000]. This study was approved by the regional ethics committee for southern Sweden.

The MDCS included 30 447 subjects (12 121 men and 18 326 women) and was performed between 1991 and 1996. Details of recruitment and the cohort are described elsewhere [25]. The cohort included residents of Malmö, i.e. all women born 1923–50 and all men born 1923–45. The total source population of 74 138 persons corresponds to a participation rate of 40.8%. The only exclusion criteria were inadequate Swedish language skills and mental incapacity. Information on lifestyle factors, such as smoking, level of education, reproductive factors and previous and current health status, was obtained using a self-administered questionnaire. Data were collected on menopausal and menarche age, number of births and whether each child was breastfed and for how many months. Mean age at screening was 58 years in women and 59 years in men.

In the MPMP, 33 346 subjects (22 444 men and 10 902 women) were included between 1974 and 1992. Details of recruitment and the cohort are described elsewhere [2]. Every participant filled out a self-administered questionnaire on medical and personal history (including information on level of education, smoking and early menopause, but in contrast to the MDCS, there was no information on breastfeeding). The study had an overall response rate of 71%, with slight variation for different age groups (range 64–78%). During the first half of the period (1974–82), mostly men were invited, with mostly females during the second half (1981–92). The mean age at screening was 49 years in women and 44 years in men. In both surveys, height and weight were measured in light indoor clothing. Height was measured to the nearest centimetre and weight was recorded at intervals of 0.1 kg. BMI was calculated as weight (in kg)/height (in m)².

The cases were selected on the basis that they had been included in either the MPMP or the MDCS study before being diagnosed with GCA. They were identified by linking the MPMP and MDCS databases to the local outpatient clinic administrative register for Malmö University Hospital and the National Hospital Discharge Register [26]. Register data on diagnoses coded through 31 December 2008 were used. The medical records of the selected subjects were then structurally reviewed and cases were classified according to the 1990 ACR criteria for GCA [27]. In addition, data on visual manifestations, initial dose of corticosteroids and large vessel involvement (based on all vascular imaging studies performed up to the date of record review) were collected.

For every confirmed case of GCA, four controls who were alive and free of GCA when the index person was diagnosed with GCA were selected from the corresponding survey population (MDCS or MPMP). Controls were individually matched to cases for sex, year of birth and year of screening. Controls were randomly selected from those who fulfilled the matching criteria using specially designed software. Subjects with GCA were in the pool of possible controls until the time when they themselves became a case. For cases who were included in first the MPMP and later the MDCS before GCA diagnosis, the information from the MDCS was used. For such cases, controls were selected from the MDCS.

Variables

Information on lifestyle factors, such as smoking, level of education, reproductive factors and previous and current health status, was obtained using self-administered questionnaires at the time of the community-based health surveys. Patients who reported smoking at the screening date were compared with those who did not smoke. In the MPMP, individuals who responded yes to the question ‘have you ever in your life been a daily smoker for more than 6 months?’ were classified as ever smokers. In the MDCS, those who reported current smoking or former smoking in response to a multiple-choice question were classified as ever smokers.

In the MDCS, formal education was classified as follows: <8 years of elementary school, 9–10 years, 11–12 years, >12 years and university degree. In the MPMP, information was available on whether the individual had attended elementary school, secondary school or higher education. A low formal level of education was classified as no more than 8 years in the MDCS or elementary school only in the MPMP.

The total duration of breastfeeding (months) was calculated based on the questionnaire, available only in the MDCS. Non-responders were excluded from this analysis. Data on age at menopause were collected from the self-administered questionnaire from the MDCS. The women were stratified into two groups, early (<45 years) or normal to late (≥45 years) menopausal age. Since all cases and controls in the MDCS were ≥45 years of age when answering the questionnaire, those who had not yet reached menopause were classified in the later group. The MPMP questionnaire included a question specifically relating to early menopause (<45 years; yes or no).

Statistical analysis

Potential predictors of GCA were examined in conditional logistic regression models. Each case and the corresponding control were given a group number that was entered into the logistic regression models as a categorical variable. Analyses were performed first bivariately and then adjusted for the other risk factors in multivariate analysis. Risk factors for GCA were assessed in all
Cases and controls together as well as in women and men separately. Since the impact of early menopause on the risk of early onset GCA (i.e. closer to menopause) may be different from the impact on GCA developing in older women, this analysis was stratified by the median age at GCA onset. Odds ratios (ORs) per s.d. of BMI were calculated in men and women separately. The impact of BMI on the risk of GCA was also assessed by entering the quartile of BMI as a categorical variable in conditional logistic regression models in men and women separately, with the second quartile as the reference. Furthermore, the ORs for GCA were estimated for those who were overweight, overweight or obese, or obese, according to the WHO definition, compared with those with normal BMI. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS 20.0; IBM, Armonk, NY, USA) with $P < 0.05$ considered statistically significant.

Results

The total number of subjects with a registered diagnosis of GCA in the local outpatient clinic administrative register and the National Hospital Discharge Register after participation in the MPMP or MDCS was 119. Of these, six were actually diagnosed with and had been incorrectly registered with the diagnosis code for GCA. In eight cases the initial suspicion of a diagnosis of GCA was not sustained. In 22 cases there were insufficient data to support a diagnosis of GCA, including 10 for which the complete case records could not be retrieved. Thus we identified 83 individuals who had a confirmed diagnosis of GCA after enrolment in the MPMP or MDCS (Table 1). Of these, 56 were identified in the local hospital outpatient register and 54 within the National Hospital Discharge Register. Twenty-seven cases were identified in both registers. The median duration was 10.6 years (range 0.3–28.2) from enrolment in the health survey to GCA onset. Based on the total follow-up for the MDCS cohort through December 31 2008, the estimated incidence of GCA was 15/100,000 in persons >50 years of age (18/100,000 in women, 10/100,000 in men). The corresponding figure for the MPMP cohort was 7/100,000 (12/100,000 in women, 5/100,000 in men). Since a major proportion of the subjects, in particular in the MPMP, were close to 50 years of age at the start of the follow-up, incidence rates were expected to be lower than those seen in population-based studies of all individuals aged >50 years, which includes elderly individuals with a higher incidence. The estimated incidence among individuals aged 60–69 years was 10/100,000 (MDCS) and 11/100,000 (MPMP) in women and 7/100,000 (MDCS) and 6/100,000 (MPMP) in men. Corresponding estimates from Olmsted County, Minnesota (USA), are 15/100,000 in women and 9/100,000 in men [3].

BMI at screening was lower in the pre-GCA cases than in the controls (mean 24.3 kg/m$^2$ vs 25.6) (Table 2). In logistic regression analysis, a higher BMI was associated with a significantly reduced risk of subsequent development of GCA [OR 0.91/kg/m$^2$ (95% CI 0.84, 0.98)]. Results were similar in analyses restricted to biopsy-positive GCA [OR 0.89/kg/m$^2$ (95% CI 0.81, 0.97)].

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants, n</td>
<td>83</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>58 (70)</td>
</tr>
<tr>
<td>Age at GCA diagnosis, mean (s.d.)</td>
<td>71.0 (6.6) (56–83)</td>
</tr>
<tr>
<td>Recruited from the MPMP cohort, n</td>
<td>28</td>
</tr>
<tr>
<td>Recruited from the MDCS cohort, n</td>
<td>55</td>
</tr>
<tr>
<td>Included in both cohorts, n</td>
<td>24</td>
</tr>
<tr>
<td>Time from screening to GCA diagnosis, median (range), years</td>
<td>10.6 (0.3–28.2)</td>
</tr>
<tr>
<td>Biopsy positive*, n (%)</td>
<td>53 (64)</td>
</tr>
<tr>
<td>Fulfilled ACR criteria, n (%)</td>
<td>79 (95)</td>
</tr>
<tr>
<td>Visual impairment at diagnosis, n (%)</td>
<td>35 (41)</td>
</tr>
<tr>
<td>Large vessel involvement, n (%)</td>
<td>15 (18)</td>
</tr>
<tr>
<td>ESR at diagnosis, mean (s.d.), mm/h</td>
<td>83 (30)</td>
</tr>
<tr>
<td>Initial steroid dose, median (IQR), mg</td>
<td>prednisolone</td>
</tr>
</tbody>
</table>

*Seventy-seven cases underwent temporal artery biopsy. Seventy-one had a representative biopsy according to the pathology report. MPMP: Malmö Preventive Medicine Project; MDCS: Malmö Diet Cancer Study; IQR: interquartile range.

Individuals who were overweight or obese according to the WHO definition [28] (BMI >25 kg/m$^2$) had a lower risk for GCA [OR 0.42 (95% CI 0.23, 0.76)] compared with those with a normal BMI (18–25 kg/m$^2$). In particular, a significantly reduced risk was seen among those with obesity (BMI >30 kg/m$^2$) (Table 3). The negative association between BMI and GCA was significant among those who had a duration from screening above the median [10.6 years; OR 0.30 (95% CI 0.12, 0.77)]. A similar pattern could be observed in those with a duration from screening below the median [OR 0.50 (95% CI 0.23, 1.09)].

BMI was lower among women who subsequently developed GCA (Fig 1). In an analysis stratified by sex, we found a significant inverse association between BMI and GCA in women [OR 0.89/kg/m$^2$ (95% CI 0.81, 0.97)], but not in men [OR 0.97/kg/m$^2$ (95% CI 0.85, 1.11)]. Women with a BMI in the highest quartile had a lower risk of developing GCA compared with those with a BMI in the second quartile, who had a normal BMI (Table 4). There was no similar pattern in men (Table 4).

Although smoking was slightly more common among pre-GCA cases (Table 2), we found no significant association between current smoking at screening and subsequent GCA [OR 1.36 (95% CI 0.77, 2.57); Table 3]. In an analysis stratified by sex, the women who were smokers had an estimated doubled risk of developing GCA, but this difference did not reach significance [OR 2.14 (95% CI 0.97, 4.68)]. There was an interaction between smoking history and sex of borderline statistical significance [OR for the interaction term for female sex...
and current smoking 3.80 (95% CI 0.95, 15.15). In contrast, ever smoking was not associated with GCA development, either in men [OR 0.61 (95% CI 0.22, 1.68)] or in women [OR 1.07 (95% CI 0.55, 2.07)].

There was no significant association between a history of early menopause (before age 46) and GCA [OR 1.76 (95% CI 0.71, 4.39)], with similar patterns in analysis of cases with age at GCA onset above the median [i.e. > 72 years; OR 1.85 (95% CI 0.52, 6.54)] or below the median [OR 1.67 (95% CI 0.45, 6.25)]. Likewise, duration of breastfeeding also did not predict GCA (Table 3). Forty-six per cent of the cases and 52% of the controls reported that they had completed elementary school only or ≤ 8 years of school. A low level of formal education did not predict GCA (Table 3).

The impact of BMI was similar among those recruited from the MDCS [n = 55; OR 0.91/kg/m² (95% CI 0.84, 0.99)] and those recruited from the MPMP [n = 28; OR 0.90/kg/m² (95% CI 0.78, 1.03)]. Current smoking, a low level of formal education and early menopause were not significant predictors of GCA in separate analyses of the MPMP and MDCS cohorts (data not shown).

To adjust for potential confounders, multivariate analyses were used, adjusted for smoking and level of formal education. Even after adjustment the association between higher BMI and reduced risk of GCA remained significant [OR 0.91/kg/m² (95% CI 0.85, 0.99); Table 5]. A similar pattern was seen in women when studied separately (Table 5). In multivariate analysis, women who were smokers tended to have an increased risk of GCA (Table 5). Smoking was not a predictor in men in

### Table 2
Characteristics of the GCA cohort cases prior to diagnosis of GCA and controls

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>83</td>
<td>58</td>
<td>25</td>
</tr>
<tr>
<td>Cases</td>
<td>332</td>
<td>232</td>
<td>100</td>
</tr>
<tr>
<td>Age at screening, mean (s.d.), years</td>
<td>59.5 (8.8)</td>
<td>61.0 (8.7)</td>
<td>55.9 (8.2)</td>
</tr>
<tr>
<td>Current smoking at screening, n/N (%)</td>
<td>24/81 (30)</td>
<td>18/56 (32)</td>
<td>6/25 (24)</td>
</tr>
<tr>
<td>Ever smoking, n/N (%)</td>
<td>43/81 (53)</td>
<td>29/56 (52)</td>
<td>14/25 (56)</td>
</tr>
<tr>
<td>Low level of formal education, n/N (%)</td>
<td>32/70 (46)</td>
<td>24/54 (44)</td>
<td>8/16 (50)</td>
</tr>
<tr>
<td>BMI, mean (s.d.), kg/m²</td>
<td>24.3 (3.9)</td>
<td>23.9 (3.4)</td>
<td>25.3 (4.8)</td>
</tr>
<tr>
<td>Early menopause (age &lt; 45 years), n/N (%)</td>
<td>10/50 (20)</td>
<td>10/50 (20)</td>
<td>NA</td>
</tr>
<tr>
<td>Total number of months of breastfeeding, mean (s.d.)</td>
<td>11.3 (7.7)</td>
<td>11.3 (7.7)</td>
<td>NA</td>
</tr>
</tbody>
</table>

No more than 8 years in the MDCS cohort, elementary school only in the MPMP cohort. **Women in the MDCS cohort only.**

### Table 3
Potential predictors of GCA in bivariate analyses using conditional logistic regression models, for all and stratified by sex

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI, per kg/m²</td>
<td>0.91</td>
<td>0.89</td>
<td>0.97</td>
</tr>
<tr>
<td>BMI 18–24.9 (normal)</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>25–29.9 (overweight)</td>
<td>0.57</td>
<td>0.45</td>
<td>1.36</td>
</tr>
<tr>
<td>≥ 30 (obese)</td>
<td>0.18</td>
<td>0.11</td>
<td>0.72</td>
</tr>
<tr>
<td>Current smoking (yes vs no)</td>
<td>1.76</td>
<td>1.76</td>
<td>NA</td>
</tr>
<tr>
<td>Low level of formal education (yes vs no)</td>
<td>1.00</td>
<td>1.00</td>
<td>NA</td>
</tr>
<tr>
<td>Early menopause (yes vs no)</td>
<td>1.00</td>
<td>1.00</td>
<td>NA</td>
</tr>
<tr>
<td>Breastfeeding (per month)</td>
<td>1.00</td>
<td>1.00</td>
<td>NA</td>
</tr>
</tbody>
</table>

OR: odds ratio; NA: not applicable.
FIG. 1 BMI in pre-GCA cases and controls, for all and stratified by sex

Values given as mean (95% CI).

**TABLE 4** BMI per quartile as a potential predictor of GCA in bivariate analyses using conditional logistic regression models stratified by sex

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI per quartile</strong></td>
<td><strong>OR</strong> 95% CI</td>
<td><strong>OR</strong> 95% CI</td>
</tr>
<tr>
<td>Quartile 1</td>
<td>0.87 0.36-2.07</td>
<td>1.29 0.32-5.14</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>1.25 0.52-3.01</td>
<td>0.71 0.16-3.06</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>0.17 0.05-0.55</td>
<td>1.22 0.32-4.67</td>
</tr>
</tbody>
</table>

Quartile 1: men 18.6–22.8 kg/m², women 17.4–22.1 kg/m²; quartile 2: men 22.8–25.4 kg/m², women 22.1–24.2 kg/m²; quartile 3: men 25.4–27.6 kg/m², women 24.2–27.5 kg/m²; quartile 4: men 27.6–42.0 kg/m², women 27.5–46.1 kg/m². OR: odds ratio.

**TABLE 5** Potential predictors of GCA in multivariate analyses adjusted for all included variables

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI, per kg/m²</strong></td>
<td><strong>OR</strong> 95% CI</td>
<td><strong>OR</strong> 95% CI</td>
<td><strong>OR</strong> 95% CI</td>
</tr>
<tr>
<td></td>
<td>0.91 0.85, 0.99</td>
<td>0.91 0.83, 0.99</td>
<td>0.96 0.82, 1.11</td>
</tr>
<tr>
<td><strong>Current smoking (yes vs no)</strong></td>
<td>1.54 0.74, 3.18</td>
<td>2.06 0.90, 4.72</td>
<td>0.54 0.09, 3.18</td>
</tr>
<tr>
<td><strong>Low level of formal education (yes vs no)</strong></td>
<td>0.80 0.42, 1.52</td>
<td>0.69 0.33, 1.45</td>
<td>1.29 0.34, 4.91</td>
</tr>
</tbody>
</table>

OR: odds ratio.
multivariate analysis (Table 5). Furthermore, there was no interaction between BMI and current smoking at screening ($P = 0.23$).

**Discussion**

In this nested case–control study we found that lower BMI was associated with an increased risk of GCA. Although not reaching statistical significance, current smoking appeared to increase the risk for GCA in women. Duration of previous breastfeeding or low level of formal education did not predict the development of GCA.

Our results on BMI are in agreement with the study by Larsson et al. [12] from Gothenburg, which was a case–control study with retrospective assessment of exposures in 49 women with biopsy-positive GCA. In contrast, in a survey of a population-based incidence cohort of PMR, there was no difference in BMI between PMR cases and non-PMR controls from the corresponding catchment area, and BMI did not predict the development of GCA among patients with PMR [29].

Another case–control study, by Kermani et al. [30], indicated that GCA patients had significantly fewer malignancies prior to the index date compared with controls. In their discussion, the authors highlighted that high BMI is a known risk factor for several cancers [31]. Our results of low BMI as a risk factor for GCA could partly explain their finding of fewer malignancies in GCA patients.

In previous studies, smoking has been shown to be a risk factor for developing GCA, in particular in women [12, 32], which is compatible with our results. In contrast, in a population-based study there was no significant association between GCA and current or ever smoking [30]. In contrast to smoking at screening, ever smoking did not tend to be associated with GCA development in our study, indicating that individuals who stop smoking may reduce their risk of GCA. Still, these data must be interpreted with caution, given the limited sample size.

Larsson et al. [12] found that a history of early menopause (before age 43) and longer duration of breastfeeding were strong predictors of developing GCA before the age of 70 years. Although our study sample was larger, we did not confirm these findings. Potential explanations for the discrepancies between our study and the study by Larsson et al. [12] include differences in the assessment of exposure (prospective vs retrospective) and the fact that our patients were older on average at GCA diagnosis (mean 72 years vs 64). However, in a subanalysis of the cases in our study who were <72 years of age at GCA diagnosis, the impact of early menopause on the risk of GCA was no greater than in the total sample.

In contrast to previous studies of predictors of RA [13, 21–24, 33, 34], there was no association between GCA and a low level of formal education and no inverse association with long-term breastfeeding. The lack of association with formal education is in agreement with a recent nationwide study of patients hospitalized with GCA in Sweden [35]. Taken together, these observations suggest that distinct and different patterns of exposure predict the development of RA and GCA.

There are several potential explanations for the association between lower BMI and subsequent GCA. First, adipose tissue might be directly protective for developing GCA through its effect on oestrogen synthesis and related anti-inflammatory pathways [36–39] or the production of hormones like adiponectin and inflammation-related cytokines, chemokines and acute phase proteins that may affect present or future inflammatory processes [40]. Obesity has also been associated with hyperactivity of the hypothalamic–pituitary–adrenal axis [41]. Increased release of endogenous corticosteroids could have anti-inflammatory effects and prevent disorders such as GCA.

Second, it might be possible that a low BMI is a variable for other risk factors such as smoking or pre-existing inflammatory response. Smoking is associated with a lower BMI [42–45]. If data on longitudinal smoking exposure up to the time of GCA diagnosis had been available in the present study, smoking exposure might have emerged as a stronger risk factor. Smoking has anti-oestrogenic effects in women [46], which may have an impact on inflammation, as discussed above.

Another potential pre-existing risk factor could be a higher predisease inflammatory response, which may result in a lower BMI before screening. This would be relevant to the very early inflammatory process, since the median time from screening to GCA diagnosis was >10 years. The inverse association with overweight was only statistically significant among those cases for which the time span from screening to diagnosis of GCA was above the median. This suggests that our observations are not due to inflammation-driven weight loss immediately preceding the clinical onset of GCA.

Third, the association between a low BMI and the development of GCA could be explained by a separate confounder independently predicting both conditions, either genetic or environmental. The association between BMI and the risk of GCA remained significant in multivariate analysis, adjusted for the level of formal education and smoking, suggesting that the impact of BMI is not explained by these factors. Still, we cannot exclude the possibility that undetected and unmeasured confounding by other exposures could influence our results.

Limitations of the study are mainly related to the relatively small number of cases. The relatively low participation rate in the MDCS may slightly hamper the ability to generalize our results to the source population. Lifestyle factors, such as smoking, can also change over time, making it more difficult to identify associations with GCA. Furthermore, since some of the risk factors studied here (smoking, BMI) are associated with mortality, and some longevity is necessary for developing GCA, the competing effect of mortality may have affected our results.

The strengths of this study include the community-based approach, the well-defined catchment area of the source population and the comprehensive effort to identify incident GCA using multiple sources. The estimated incidence rates in the present samples are slightly lower than the previously reported rates of 20–30/100,000 in
individuals >50 years of age [3, 4], but it should be kept in mind that due to the study design, subjects >50 years of age in the MPMP and MDCS cohorts were younger than a standard population of people >50 years of age. The incidence of GCA in individuals aged 60–69 years was ~30% lower compared with a population-based study from Minnesota [3]. Taken together, this suggests that a major proportion of incident GCA cases in the cohorts were included in this study, although cases who were managed in primary care exclusively might not be identified. Furthermore, those who moved to another area in Sweden and were diagnosed with GCA without hospitalization would not be captured. A further strength of this study is that data on predictors were collected before disease onset, which means that recall bias or the effect of GCA on lifestyle did not influence our results. This study therefore adds important information to previous retrospective case-control studies.

In conclusion, lower BMI is an independent risk factor for developing GCA. Smoking may also be a risk factor for GCA, in particular among women. To improve our understanding of early disease pathways and factors regulating inflammation and the development of GCA, further studies are needed.

### Rheumatology key messages

- GCA was predicted by a lower BMI prior to disease onset.
- Smoking may be a predictor of GCA in women.

### Acknowledgements

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

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