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Lower Frequency of Comorbidities Prior to Onset of Giant Cell Arteritis: A Population-Based Study

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ABSTRACT. ***Objective.*** To assess the frequency of comorbidities and metabolic risk factors at and prior to giant cell arteritis (GCA) diagnosis.

Methods. This is a retrospective case control study of patients with incident GCA between January 1, 2000, and December 31, 2019, in Olmsted County, Minnesota. Two age- and sex-matched controls were identified, and each assigned an index date corresponding to an incidence date of GCA. Medical records were manually abstracted for comorbidities and laboratory data at incidence date, 5 years, and 10 years prior to incidence date. Twenty-five chronic conditions using International Classification of Diseases, 9th revision, diagnosis codes were also studied at incidence date and 5 years prior to incidence date.

Results. One hundred and twenty-nine patients with GCA (74% female) and 253 controls were identified. At incidence date, the prevalence of diabetes mellitus (DM) was lower among patients with GCA (5% vs 17%; $P = 0.001$). At 5 years prior to incidence date, patients were less likely to have DM (2% vs 13%; $P < 0.001$) and hypertension (27% vs 45%; $P = 0.002$) and had a lower mean number (SD) of comorbidities (0.7 [1.0] vs 1.3 [1.4]; $P < 0.001$) compared to controls. Moreover, patients had significantly lower median fasting blood glucose (FBG; 96 mg/dL vs 104 mg/dL; $P < 0.001$) and BMI (25.8 vs 27.7; $P = 0.02$) compared to controls. Multivariable logistic regression analysis revealed negative associations for FBG with GCA at 5 and 10 years prior to diagnosis/index date.

Conclusion. DM prevalence and median FBG and BMI were lower in patients with GCA up to 5 years prior to diagnosis, suggesting that metabolic factors influence the risk of GCA.

Key Indexing Terms: comorbidity, diabetes mellitus, epidemiology, giant cell arteritis, incidence, vasculitis

Giant cell arteritis (GCA) is the most common form of systemic vasculitis affecting the adult population over the age of 50 years, in both the United States and Europe.[1-4] Risk factors for the development of GCA are incompletely understood. Advancing age, female sex, and northern European origin are known to predispose patients to GCA.[5] Additionally, previous studies suggest that certain metabolic factors are linked to development of GCA. In Sweden, patients with incident GCA were found to have a lower prevalence of diabetes mellitus (DM) and a lower fasting blood glucose (FBG) many years before disease onset as compared to matched controls.[6] Moreover, a lower BMI was also identified as a risk factor for GCA in both Sweden and Iceland.[6-9] To date, these metabolic risk factors have not been evaluated in North American populations.

The frequency of comorbidities in patients with GCA may influence disease susceptibility and outcomes. Other rheumatologic conditions such as rheumatoid arthritis (RA) and systemic lupus erythematosus have been found to have increased

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prevalence of comorbid conditions at incidence.[10,11] Patients with GCA are also reported to have an increased rate of common comorbidities; however, this may largely be because of treatment with glucocorticoids.[12] The frequency of comorbidities in patients with GCA at disease onset as well as prior to disease onset/before treatment deserves further investigation.

This study aimed to evaluate the frequency of comorbidities and metabolic risk factors in patients with GCA at incidence as well as 5 and 10 years before clinical disease onset in comparison to age- and sex-matched controls from the same population. Further, the study aimed to identify the total number of associated comorbidities in patients with GCA at diagnosis as well as 5 years prior to diagnosis, as compared to controls.

METHODS

This is a retrospective case control study including patients with incident diagnosis of GCA in Olmsted County, Minnesota, during the period of January 1, 2000, through December 31, 2019, using the resources of the Rochester Epidemiology Project (REP). The REP is a record data linkage system that includes all the records for residents of Olmsted County, Minnesota, and provides access to all records including inpatient and outpatient for healthcare providers in Olmsted County, Minnesota, making the population of Olmsted County well-suited for population-based research.[13]

The patient cohort is described in detail elsewhere.[10] Briefly, patients were included in the study if they had a clinical diagnosis of GCA as deemed by the treating physician and confirmed by a rheumatologist. Patients fulfilled at least 1 of the following: (1) ≥ 3 1990 American College for Rheumatology classification criteria; (2) age ≥ 50 years with elevated inflammatory markers (erythrocyte sedimentation rate [ESR] ≥ 50 mm/h or C-reactive protein [CRP] ≥ 10 mg/L) and clinical signs of GCA; or (3) age ≥ 50 years with elevated inflammatory markers (ESR ≥ 50 mm/h or CRP ≥ 10 mg/L) and with radiographic evidence of large-vessel vasculitis. Imaging modalities used to diagnose large-vessel vasculitis included computed tomography (CT) angiography, magnetic resonance angiography, or positron emission tomography/CT.

Each patient was age- and sex-matched to 2 controls without GCA from the same population and each control was assigned an index date corresponding to the incidence date of GCA in the GCA cohort. Medical records for both patients and controls were manually reviewed, and information abstracted in a standardized form to include medical comorbidities as well as laboratory studies at incidence date and 5 years and 10 years prior to incident date. Subjects with < 1 year of diagnosis history were excluded from each analysis.

Moreover, 25 chronic conditions from either the Charlson, Elixhauser, or Rheumatic Disease Comorbidity Index were identified using International Classification of Diseases, 9th revision, diagnosis codes for both patients and controls.[11,12,14] Confirmation of comorbidity required ≥ 2 diagnosis codes at least 30 days apart and included a 2-year look-back period. Persons who did not have diagnosis codes according to this definition for a comorbidity were counted as not having the comorbidity. Comorbidities were studied at 2 different time intervals that included incidence/index date as well as 5 years prior.

Descriptive statistics (mean [SD] and median [IQR]) were used to summarize patient characteristics. Comparisons between the 2 groups were performed using chi-square, Fisher exact, or rank-sum tests. Analyses for association between lab outcomes and GCA were performed using logistic regression models adjusted for age, sex, smoking status (ever/never), and BMI. Analysis for association between risk factors and GCA complications within ± 6 months of diagnosis were performed. $P < 0.05$ was considered statistically significant for all analyses.

Analyses were performed using SAS version 9.4 (SAS Institute) and R 3.6.2 (R Foundation for Statistical Computing). The study was approved by institutional review boards (IRBs) of the Mayo Clinic (IRB 12-004025) and Olmsted Medical Center (IRB 024-OMC-12). Written informed consent was waived on the basis that this is a retrospective chart review with less than minimal risk.

RESULTS

The cohort included 129 patients with incident GCA with mean age of 77.1 (SD 8.1) years. Most of the patient population was non-Hispanic White (98%), and predominantly female (74%). Median time from symptom onset to GCA diagnosis was 1.1 months (IQR 0.7-2.3). Headache was the most prominent symptom (71%) followed by scalp tenderness (52%) and jaw claudication (48%). Polymyalgia rheumatica (PMR) symptoms were present in 38 (30%) patients. Temporal artery biopsy (TAB) was positive in 71% of the total patients and 77% of patients who had undergone biopsy. Large-vessel vasculitis on imaging was found in 15 patients accounting for 40% of patients in whom TAB was either negative or not done and representing 12% of the total sample. Twenty-two patients (17%) were diagnosed clinically (TAB and imaging either negative or not performed). The characteristics of the patient group are further outlined in Table 1.

Medical comorbidities at incidence/index date. Patients with GCA had a lower median (IQR) BMI (calculated as weight in kilograms divided by height in meters squared; kg/m^2) of 25.1 (23.0-28.4) compared to 27.7 (24.4-30.9) in controls ($P < 0.001$). Moreover, patients with GCA had significantly lower frequency of DM (5%) compared to controls (17%; $P = 0.001$).

More than half (57%) of the patients with GCA were never smokers, whereas 40% were former smokers; similarly, 56% and 40% of the controls were never or former smokers, respectively. There were no significant differences between the 2 groups ($P = 0.86$). There was no significant difference in the frequency of other comorbidities or the total number of comorbidities between patients and controls, as shown in Table 2.

Table 1. Characteristics of patients with incident diagnosis of GCA between 2000 and 2019 in Olmsted County, Minnesota.

	N = 129	(%)
Age at GCA diagnosis, yrs, mean (SD)	77.1 (8.1)	–
Female sex, n	96	74
Time from symptom onset to diagnosis, mos, median (IQR)	1.1 (0.7-2.3)	–
Headache	91/128	71
Scalp tenderness	64/124	52
Jaw claudication	61/126	48
Blurred vision	32/126	25
Transient vision loss	9/128	7
Polymyalgia rheumatica symptoms	38/128	30
Arm claudication	3/127	2
Leg claudication	2/127	2
Positive temporal artery biopsy	92/120	77
Imaging positive for large vessel involvement without positive biopsy	15/37	40

Values are n/N unless otherwise indicated. GCA: giant cell arteritis.

Table 2. Demographic data and comorbidities using ICD-9 coding among GCA cases diagnosed between 2000 and 2019 and age- and sex-matched controls in Olmsted County, Minnesota.

	At Index Date		At 5 Years Prior to Index Date	
	Cases, n = 129	Controls, n = 253	Cases, n = 117	Controls, n = 226
Demographics				
Age, mean (SD)	77.1 (8.1)	77.0 (8.1)	72.1 (8.2)	71.5 (8.2)
Age range, yrs	53-93	53-93	48-88	48-88
Female sex	96 (74)	190 (75)	88 (75)	171 (76)
Non-Hispanic White	127 (98)	241 (95)	115 (98)	216 (96)
Comorbidities				
Cancer	7 (5)	15 (6)	8 (7)	12 (5)
Congestive heart failure	9 (7)	19 (8)	4 (3)	9 (4)
Dementia	1 (1)	3 (1)	0 (0)	1 (0)
Depression	6 (5)	9 (4)	2 (2)	10 (4)
Diabetes mellitus	7 (5)*	43 (17)*	2 (2)*	30 (13)*
Hypertension	54 (42)	115 (46)	32 (27)*	101 (45)*
Hypothyroidism	21 (16)	30 (12)	11 (9)	31 (14)
Liver disease	0 (0)	2 (1)	0 (0)	3 (1)
Metastatic cancer	0 (0)	4 (2)	0 (0)	2 (1)
Myocardial infarction	3 (2)	10 (4)	1 (1)	8 (4)
Psychoses	2 (2)	7 (3)	1 (1)	7 (3)
Chronic pulmonary disease	10 (8)	17 (7)	4 (3)	16 (7)
Peripheral vascular disease	13 (10)	14 (6)	3 (3)	5 (2)
Renal failure	4 (3)	9 (4)	1 (1)	6 (3)
Stroke	11 (9)	15 (6)	2 (2)	8 (4)
Valvular disease	13 (10)	14 (6)	6 (5)	11 (5)
Total comorbidities, mean (SD)	1.5 (1.7)	1.5 (1.6)	0.7 (1.0)*	1.3 (1.4)*

Values are n (%) unless otherwise indicated. * $P < 0.05$. GCA: giant cell arteritis; ICD: International Classification of Diseases, 9th revision.

Analysis of laboratory data showed that patients with GCA had a significantly lower median (IQR) hemoglobin 12.0 g/dL (11.2-13.1) compared to controls 13.4 g/dL (12.2-14.4). On the other hand, patients had a significantly higher median white blood cell (WBC) count 9.4 (7.7-11.3) × 10^9/L compared to controls 6.8 (5.5-8.2) × 10^9/L as well as significantly higher median platelet counts 352.5 (261.0-459.8) × 10^9/L compared to controls 223.0 (192.0-274.8) × 10^9/L (Table 3).

Medical comorbidities at 5 years prior to incidence/index date. At 5 years prior to diagnosis/index date, the frequency of DM was lower in patients with GCA (2%) compared to controls (13%; $P < 0.001$). Patients with GCA were also noted to have a lower frequency of hypertension (HTN; 32/117, 27%) compared to controls (101/226, 45%; $P = 0.002$; Table 2). The median (IQR) BMI was lower in patients with GCA (25.8 [23.1-29.9]) compared to controls (27.7 [24.0-31.7]; $P = 0.02$). Median body weight was lower in patients with GCA at 70.9 (61.5-81.0) kg, with a range of 46.2 kg to 109.5 kg, compared to controls (73.3 [62.4-86.9] kg), with a range of 43.5 kg to 145.4 kg, although not statistically significant ($P = 0.07$). Moreover, patients with GCA had an overall lower total mean (SD) number of comorbidities 0.7 (1.0) compared to controls 1.3 (1.4; $P < 0.001$) at 5 years prior to GCA onset.

Patients with GCA had a significantly lower median (IQR) FBG levels of 96.0 (90.0-102.5) mg/dL compared to 104.0 (93.8-117.3) mg/dL in controls ($P < 0.001$). On the other hand, patients with GCA had a significantly higher median total cholesterol (TC) of 211.0 (187.0-234.5) mg/dL, higher median high-density lipoprotein (HDL; 62.0 [52.0-74.5] mg/dL), and higher median low-density lipoprotein (LDL; 123.0 [97.0-139.5] mg/dL) compared to controls (201.0 [177.5- 221.0], 57.0 [45.0-67.0], and 112.5 [88-129.3] mg/dL, respectively; $P = 0.03$, 0.01, and 0.06, respectively).

There was no significant difference in median hemoglobin, WBC count, or platelet counts in the 2 groups at this time frame.

Male patients were more likely to have GCA-related ischemic events (vision loss, limb ischemia, transient ischemic attacks, stroke, myocardial infarction, congestive heart failure, peripheral arterial disease) within the 6 months before/after the incident GCA date (Supplementary Table S1, available with the online version of this article). There were no differences in the underlying comorbidities at 5 years between patients with GCA with and without ischemic complications (Supplementary Table S1).

Medical comorbidities at 10 years prior to incidence/index date. At 10 years prior to GCA diagnosis/index date, the median body weight and median BMI in patients with GCA was numerically lower, although not meeting statistical significance ($P = 0.09$ and 0.06, respectively).

Patients with GCA were noted to have a significantly lower median (IQR) FBG (93.0 [88.8-101.3] mg/dL) compared to controls (98.0 [93.0-111.8] mg/dL]; $P < 0.001$) at 10 years prior to disease onset. Lipid profiles and other laboratory variables including hemoglobin, WBC counts, platelets, and serum creatinine were similar at this timepoint (Table 3).

Table 3. Vital signs recorded and laboratory data of GCA cases diagnosed between 2000 and 2019 in Olmsted County, Minnesota, and age- and sex-matched controls with comparison at incidence, 5 years, and 10 years prior, using chart review.

	At Index Date		At 5 Years Prior to Index Date		At 10 Years Prior to Index Date	
	Cases, n = 129 Median (IQR), n Available	Controls, n = 253 Median (IQR), n Available	Cases, n = 117 Median (IQR), n Available	Controls, n = 226 Median (IQR), n Available	Cases, n = 117 Median (IQR), n Available	Controls, n = 226 Median (IQR), n Available
Weight, kg	67.5 (57.3-79.2)*, 128	73.3 (62.3-83.4)*, 236	70.9 (61.5-81.0), 108	73.3 (62.4-86.9), 207	70.8 (61.7-81.4), 98	74.0 (64.0-85.9), 191
BMI, kg/m^2	25.1 (23.0-28.4)*, 128	27.7 (24.4-30.9)*, 236	25.8 (23.1-29.9)*, 108	27.7 (24.0-31.7)*, 207	26.0 (23.4-30.1), 98	27.8 (24.4-31.1), 191
Hemoglobin, g/dL	12.0 (11.2-13.1)*, 128	13.4 (12.2-14.4)*, 182	13.5 (12.8-14.1), 77	13.5 (12.6-14.3), 153	13.3 (12.7-14.2), 78	13.7 (12.8-14.6), 133
WBC, × 10^9/L	9.4 (7.7-11.3)*, 128	6.8 (5.5-8.2)*, 182	6.3 (5.3-8.1), 77	6.3 (5.4-7.7), 153	6.3 (5.6-7.6), 77	6.1 (5.2-7.1), 133
Platelets, × 10^9/L	352.5 (261.0-459.8)*, 128	223.0 (192.0-274.8)*, 182	225.0 (198.0-264.0), 77	225.0 (188.0-271.0), 153	236.5 (205.0-268.5), 78	227.0 (190.0-266.0), 133
TSH levels, mIU/L	2.0 (1.3-3.1), 91	2.0 (1.2-3.0), 156	2.1 (1.5-3.4), 60	1.9 (1.0-2.9), 122	2.3 (1.5-3.8), 55	2.0 (1.3-3.0), 115
FBG, mg/dL	104.0 (94.8-114.0), 92	103.0 (93.0-114.5), 179	96.0 (90.0-102.5)*, 79	104.0 (93.8-117.3)*, 156	93.0 (88.8-101.3)*, 72	98.0 (93.0-111.8)*, 138
Creatinine, mg/dL	0.9 (0.7-1.0)*, 117	1.0 (0.8-1.2)*, 216	0.9 (0.8-1.1), 80	1.0 (0.9-1.2), 168	0.9 (0.9-1.1), 80	1.0 (0.9-1.1), 147
TC, mg/dL	181.0 (154.5-207.5), 83	185.0 (157.0-213.0), 165	211.0 (187.0-234.5)*, 75	201.0 (177.5-221.0)*, 155	204.5 (181.3-231.5), 72	207.5 (182.5-239.0), 128
HDL, mg/dL	59.0 (48.0-70.0), 81	54.0 (44.0-66.0), 165	62.0 (52.0-74.5)*, 75	57.0 (45.0-67.0)*, 153	60.5 (49.3-72.0), 70	56.5 (45.0-71.0), 124
LDL, mg/dL	95.0 (77.0-121.0), 81	98.5 (78.0-119.8), 162	123.0 (97.0-139.5), 75	112.5 (88.0-129.3), 152	112.0 (98.0-138.5), 63	122.0 (91.0-141.0), 113
Triglycerides, mg/dL	101.0 (78.0-158.0), 81	121.0 (87.0-167.0), 165	107.0 (90.0-167.5), 75	132.0 (93.0-183.0), 153	109.0 (73.0-183.0), 71	127.0 (96.0-166.0), 125

* $P < 0.05$. FBG: fasting blood glucose; GCA: giant cell arteritis; HDL: high density lipoprotein; LDL: low density lipoprotein; TSH: thyroid-stimulating hormone; TC: total cholesterol; WBC: white blood cell.

Multivariable logistic model for metabolic risk factors over 10 years. To further ascertain the identified metabolic factors, a multivariable logistic model was used for FBG, TC, LDL, and HDL to adjust for age, sex, smoking status, and BMI. There was a significant negative association between FBG and the development of GCA at 5 years prior to GCA incidence with an odds ratio (OR) per mg/dL of 0.97 (95% CI 0.94-0.98; $P < 0.001$). This association also reached significance at 10 years prior to the incidence of GCA with an OR of 0.98 (95% CI 0.95-0.99; $P = 0.02$; Table 4).

On the other hand, higher TC and LDL levels were associated with the development of GCA at 5 years prior to diagnosis with an OR per mg/dL of 1.01 (95% CI 1.00-1.02; $P = 0.04$) and 1.01 (95% CI 1.00-1.02; $P = 0.04$), respectively; there was no association with HDL values. The associations between TC, LDL, and HDL and GCA diagnosis were not identified at 10 years prior to diagnosis (Table 4).

DISCUSSION

In this study of incident cases of GCA over 2 decades in Olmsted County, Minnesota, patients with GCA had lower median BMI and lower frequency of DM compared to controls at the time of diagnosis. Interestingly, at 5 years prior to diagnosis, patients had a lower median BMI, lower median FBG, lower frequency of DM and HTN compared with controls. Even 10 years prior to diagnosis, patients with GCA had a lower median FBG. Moreover, the total number of comorbidities was also lower (ie, patients with incident GCA seem to be overall healthier than controls several years prior to diagnosis). Patients with GCA had higher median TC, HDL, and LDL compared to controls at 5 years prior to diagnosis.

Catabolic weight loss as a result of a systemic inflammatory state has been observed in rheumatic diseases and malignancy.[15,16] Although inflammatory-associated cachexia may contribute in part to lower BMI and median FBG at GCA diagnosis, these findings cannot be attributed to inflammation alone because persistent trends were observed up to 10 years prior to GCA diagnosis. This implies that the association of lower FBG and BMI is more likely genetically determined rather than an environmental factor or inflammation driven. Conversely, lower median hemoglobin and higher median platelet counts at incidence in patients with GCA compared to controls were not seen at 5 years and 10 years prior to incidence, signifying these observations result from a disease-associated inflammatory state. Further, the association of lower FBG and lower BMI with development of GCA has been observed across cohorts in different populations. Specifically, lower FBG and lower BMI have also been noted prior to GCA diagnosis in population-based studies in northern European countries.[6-9,17] The population of Olmsted

Table 4. Logistic model for risk factors (FBG, total cholesterol, LDL, and HDL) among incident patients with GCA diagnosed between 2000 and 2019 in Olmsted County, Minnesota, adjusted for age, sex, smoking status (ever/never), and BMI.

	5 Years Prior to GCA Diagnosis		
	OR	95% CI	*P*
FBG, mg/dL	0.97	0.94-0.98	< 0.001
TC, mg/dL	1.01	1.00-1.02	0.04
LDL, mg/dL	1.01	1.00-1.02	0.04
HDL, mg/dL	1.01	1.00-1.03	0.17
	10 Years Prior to GCA Diagnosis		
	OR	95% CI	*P*
FBG, mg/dL	0.98	0.95-0.99	0.02
TC, mg/dL	1.00	0.99-1.01	0.96
LDL, mg/dL	1.00	0.99-1.01	0.54
HDL, mg/dL	1.01	0.99-1.03	0.499

FBG: fasting blood glucose; GCA: giant cell arteritis; HDL: high density lipoprotein; LDL: low density lipoprotein; OR: odds ratio; TC: total cholesterol.

County, Minnesota, resembles the population of northern European countries, being a majority White population, and both were found to have similar disease trends.[18,19] Further, the 2 populations share a common ancestry, which reinforces a potential genetic association of observed findings.

The observation of lower prevalence of DM among patients with GCA has been previously noted in a previous metaanalysis of GCA cohorts.[20] On the other hand, Medicare-based claim data suggested the opposite.[21] The lower prevalence of DM might explain the prior reported lower incidence of atherosclerosis in patients with GCA.[22] On the other hand, in a UK national database study, Li et al reported increased preexisting vascular disease including HTN and dyslipidemia among patients with GCA compared to controls, whereas rates of DM were similar.[23] The differences in the findings by Li et al, compared to those of the current study and others, could be attributed to the study methodology with reliance on database search for identification of both patients and comorbidities, compared to the manual chart review used in this study. Indeed, in a previous report on chronic obstructive pulmonary disease, a significant difference was seen in frequency of comorbidities based on claims data compared to chart review.[24]

The underlying mechanisms for our findings and those of the Swedish group are unclear; however, a possible explanation can stem from the role of glucose metabolism in immune system regulation. Glucose is the primary source of energy for T cells, and may regulate T cell function and differentiation.[25] T cell dysregulation can also be an end product of macrophage dysregulation, which can be induced by glucose metabolism through programmed death ligand-1 (PD-L1) expression.[26,27] PD-L1 regulates the immune response through a negative feedback mechanism leading to downregulation of the effector T cell response and thus protecting from immune damage.[28] Macrophages derived from patients with GCA have fundamentally low PD-L1 expression. Further studies are needed to investigate the role of these metabolic findings in the pathogenesis of GCA.

At GCA incidence, only DM was identified as an inverse risk factor (protective) for GCA, whereas at 5 years prior to incidence, DM and HTN were both identified as an inverse risk factor (protective) for GCA. Interestingly, the total number of comorbidities 5 years prior to diagnosis was lower in patients with GCA compared to controls but was similar at time of GCA incidence/index date, which differs from other autoimmune diseases, particularly RA, where an increased number of comorbidities at incidence is noted.[29] In particular, obesity and DM have been identified as risk factors for RA development, which does not appear to be the case with GCA.[30,31]

Interestingly, in a previous study from Lugo, Spain, 17 of 210 patients with biopsy-proven GCA had DM at onset, reinforcing the lower frequency of DM among patients with GCA.[32] The relatively low prevalence of DM and other traditional risk factors for atherosclerosis in the Lugo GCA cohort may have contributed to lower mortality. Moreover, in the Spanish cohort, patients with underlying HTN were found to be more prone to ischemic complications.[32] However, in the current study, there was no significant association between comorbidities and ischemic complications although male patients were more prone to ischemic complications.

Changes in the lipid profile were observed between patients with GCA and controls with the median TC, HDL, and LDL higher in patients with GCA compared to controls 5 years prior to diagnosis. This is in contrast with a Swedish population study that found decreased levels of TC and LDL prior to GCA diagnosis compared to controls who did not develop GCA.[6] The findings in the current report align with results also seen in the UK EPIC-Norfolk Study, which noted an increased TC and LDL in patients who developed GCA and PMR later in life compared to normal controls.[33] The observed variation in the lipid profile needs further confirmation to understand its role, if any, in disease pathogenesis.

The strengths of this study include the population-based setting, with the ability to identify both patients and controls in the inpatient and outpatient setting and ascertain their clinical and laboratory values through direct medical record chart review. The resources of the REP and the nature of the population in Olmsted County made it possible to study patients up to 10 years prior to their diagnosis with GCA. Last, the ascertainment of GCA diagnosis by manual chart review to ensure the diagnosis of GCA is a strength. Regarding the limitations of the study, the diagnostic coding data were not available for the patients and controls at 10 years prior to the diagnosis/index date because of changes in coding systems over time. Other limitations inherent in the study design were being retrospective in nature, missing laboratory data for some patients, and the potential of unknown confounders that were not captured in the medical records.

In conclusion, patients with GCA have lower frequency of DM and lower BMI and FBG up to 5 years prior to GCA diagnosis. Moreover, patients with GCA seem to be healthier than

controls 5 years prior to GCA diagnosis given the lower mean number of comorbidities. Further studies are needed to investigate the role of these metabolic observations and identify their role in the disease pathogenesis.

ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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