Healthcare Use and Direct Cost of Giant Cell Arteritis: A Population-based Study

Matthew J. Koster, Sara J. Achenbach, Cynthia S. Crowson, Hilal Maradit-Kremers, Eric L. Matteson, and Kenneth J. Warrington

ABSTRACT. ***Objective.*** To determine the healthcare use and direct medical cost of giant cell arteritis (GCA) in a population-based cohort.

Methods. A well-defined, retrospective population-based cohort of Olmsted County, Minnesota, USA, residents diagnosed with GCA from 1982–2009 was compared to a matched referent cohort from the same population. Standardized cost data (inflation-adjusted to 2014 US dollars) for 1987–2014 and outpatient use data for 1995–2014 were obtained. Use and costs were compared between cohorts through signed-rank paired tests, McNemar's tests, and quantile regression models.

Results. Significant annual differences in outpatient costs were observed for patients with GCA in each of the first 4 years (median differences: $2085, $437, $382, $388, respectively). In adjusted analyses, median incremental cost attributed to GCA over a 5-year period was $4662. Compared with matched referent subjects, patients with GCA had higher use of laboratory visit-days annually for each of the first 3 years following incidence/index date, and increased outpatient physician visits for years 0–1, 1–2, and 3–4. Patients with GCA had significantly more radiology visit-days in years 0–1, 3–4, and 4–5, and more ophthalmologic procedures/surgery in years 0–1, 1–2, 2–3, and 4–5 compared to non-GCA. Emergency medicine visits, musculoskeletal, and cardiovascular procedures/surgery were similar between GCA and non-GCA groups throughout the study period.

Conclusion. Direct medical outpatient costs were increased in the month preceding and in the first 4 years following GCA diagnosis. Higher use of outpatient physician, laboratory, and radiology visits, and ophthalmologic procedures among these patients accounts for the increased cost of care. (First Release May 1 2017; J Rheumatol 2017;44:1044–50; doi:10.3899/jrheum.161516)

Key Indexing Terms:
GIANT CELL ARTERITIS HEALTHCARE USE COST

Rheumatic diseases are chronic, disabling conditions that generate significant economic burden. In 2003, the total cost attributed to arthritis and other rheumatic conditions in the United States alone was estimated at $128 billion[1] and is expected to increase to $225 billion by the year 2020[2]. While healthcare use and costs have been studied extensively in rheumatoid arthritis (RA)[3] and systemic lupus erythematosus (SLE)[4], little information is available on the socioeconomic effect of systemic vasculitis.

Giant cell arteritis (GCA) is the most common primary systemic vasculitis among patients aged ≥ 50 years[5]. The overall estimated prevalence of GCA among this age group is 1 in 500[5]. Incidence is highest among populations of Northern European origin with estimates between 10–20/100,000 persons aged 50 years or older[6,7]. Compared with the general population, longterm mortality in patients with GCA is not significantly increased[6,8,9]. However, GCA is associated with significant comorbidities including vision loss, stroke, and aortic aneurysm/dissection. Additionally, glucocorticoid-associated adverse events including diabetes mellitus, hypertension, osteoporosis, fracture, infection, glaucoma, and cataracts have been reported in 68%–100% of patients with GCA[10,11,12]. Consequently, the combination of disease-specific and treatment-related comorbidities in patients with GCA places a substantial burden on healthcare use and medical care expenditures.

Information detailing the socioeconomic effect of GCA has been difficult to obtain because of the relative rarity of

From the Department of Internal Medicine, Division of Rheumatology; Department of Health Sciences Research, Division of Biomedical Statistics and Informatics; Department of Health Sciences Research, Division of Epidemiology, Mayo Clinic, Rochester, Minnesota, USA.

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M.J. Koster, MD, Department of Internal Medicine, Division of Rheumatology, Mayo Clinic; S.J. Achenbach, MS, Department of Health Sciences Research, Division of Biomedical Statistics and Informatics, Mayo Clinic; C.S. Crowson, MS, Department of Internal Medicine, Division of Rheumatology, and Department of Health Sciences Research, Division of Biomedical Statistics and Informatics, Mayo Clinic; H. Maradit-Kremers, MD, MSc, Department of Health Sciences Research, Division of Epidemiology, Mayo Clinic; E.L. Matteson, MD, MPH, Department of Internal Medicine, Division of Rheumatology, and Department of Health Sciences Research, Division of Epidemiology, Mayo Clinic; K.J. Warrington, MD, Department of Internal Medicine, Division of Rheumatology, Mayo Clinic.

Address correspondence to Dr. M.J. Koster, 200 First St. SW, Rochester, Minnesota 55905, USA. E-mail: koster.matthew@mayo.edu

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this condition, scarcity of well-defined population-based cohorts, and the inability to evaluate outpatient cost and use from national databases. The aim of our study was to describe the healthcare use and direct medical cost of GCA in a well-defined population-based cohort.

MATERIALS AND METHODS

This study was approved by the Mayo Clinic Institutional Review Board (15-000270).

Study population. The study population consisted of a previously described inception cohort[11] of all Olmsted County, Minnesota, USA, residents first diagnosed with GCA, as defined by the 1990 American College of Rheumatology criteria, between January 1, 1982, and December 31, 2009. Each patient with GCA was individually matched with a referent subject without GCA for age, sex, and calendar year from the same population. Each referent subject was assigned an index date corresponding to the GCA incidence date of their matched patient with GCA. Comorbidities were assessed using electronic diagnostic index and billing codes[13]. An electronic adaptation of the Charlson Comorbidity Index (CCI)[14] was used to assess comorbidities during the period prior to GCA incidence date (or the index date of the referent subjects) through the end of the matched followup. Rheumatologic comorbidities were excluded from the calculation of the CCI.

Resource use data. Data on use of outpatient healthcare resources through the Mayo Clinic Cost Data Warehouse were available from January 1, 1995, through December 12, 2014. Standardized coding was present for all specific items and services provided and were in accordance with the Healthcare Common Procedure Coding System. All resources used during the study period were grouped together based on the corresponding *Current Procedural Terminology*, 4th edition, Berenson-Eggers Type of Service, and National Uniform Billing Committee codes. Coding was used to objectively assign services into the following categories: laboratory, radiology (plain radiographs, computed tomography, magnetic resonance imaging, ultrasound, nuclear medicine), emergency room visit, outpatient physician visit, musculoskeletal procedure/surgery, cardiovascular (CV) procedure/surgery, and ophthalmologic procedure/surgery. Because multiple line-item codes can be involved in the same service or procedure, visit-days were used to evaluate used services to prevent overestimation of services provided.

Cost data. Cost data from the Mayo Clinic Cost Data Warehouse were used to provide estimates of nationally representative unit costs. The database includes line-item detail on the date, type, and billed charge for all goods and services provided at each clinical encounter. Comprehensive cost data for patients with GCA and their matched referent subjects were available for all encounters at Mayo Clinic and its affiliated hospitals from January 1, 1987, through December 31, 2014. Unit-costing methodology was used to provide a standardized, inflation-adjusted estimate of cost (2014 US dollars) assigned to each service and procedure to reflect a national average cost. Total direct costs included all outpatient and inpatient healthcare costs incurred, with the exception of prescription drugs, nursing home care, physical therapy, durable medical equipment, and medical transportation.

Followup. Patients in both cohorts were followed until death, migration from Olmsted County, or December 31, 2014. When available, cost and use data were obtained beginning 12 months prior to the GCA incidence/index date. A maximum of 5 years following the incidence/index date was used for analysis and the followup of each matched pair was further truncated at the shortest length of followup for either member to ensure similar periods of observation for cases and controls. If less than 6 years of cost and use data were available, the observation period identified for the matched pair was included in the respective year(s) in the aggregate analysis. For example, a pair with incidence/index date in 1983 could contribute 1 year of cost (1987, Yr 5) but no use data; whereas, a pair with incidence/index date in 1993 could contribute up to 6 years (1992–1997, yrs –1 to 5) of cost and up to 3 years of healthcare use data (1995–1997, yrs 3–5).

Statistical analysis. Descriptive statistics (means, medians, percentages, etc.) were used to summarize the characteristics of patients with GCA and the referent subjects. Mean costs were reported after trimming the most extreme 5% of values to reduce the effect of outliers on the estimated means. Comparisons of patient characteristics between cohorts were performed using the chi-square and rank-sum tests. Use of selected healthcare services and costs were compared between GCA and non-GCA cohorts using signed-rank paired tests. Selected healthcare services with low yearly frequencies were analyzed categorically (e.g., 0 vs 1 or more) and comparisons between groups were performed using McNemar's tests.

A simple weighted quantile regression method[15], which examines specific percentiles of distribution in relation to covariates, was used to account for censoring, including both administrative censoring and losses to followup, as has been previously described[16]. Subjects with complete cost data histories were weighted in this analysis, corresponding to the probability of not having a censored cost data history for the entire 5 years of followup. Subjects who died during the followup period were considered to have complete, uncensored cost data, because these subjects would not acquire further medical costs. However, patients who were lost to followup because of emigration from Olmsted County may have incurred subsequent medical costs that were not available for study. The rationale for using a weighting method in the quantile regression allowed for the distinction between censoring of followup time and censoring of cost data[17].

RESULTS

The study population consisted of 147 subjects with GCA and 147 referent subjects without GCA matched for age, sex, and calendar year. The mean (± SD) age was similar in both the GCA and non-GCA cohorts. The followup of the matched pairs ended with death in 27 subjects with GCA and 28 without GCA. Subjects with GCA were more likely than non-GCA subjects to have peripheral vascular disease (41% vs 26%, $p = 0.005$), and were somewhat more likely to have cerebrovascular disease (42% vs 33%, $p = 0.09$) and peptic ulcer (24% vs 16%, $p = 0.08$) diagnosed prior to incidence/index date or at any time during the first 5 years of the matched followup. However, subjects with GCA were somewhat less likely than non-GCA subjects to have myocardial infarction (MI; 12% vs 20%, $p = 0.08$). The remaining comorbidities were similar in both cohorts (Table 1).

Healthcare use. The median [interquartile range (IQR)] number of outpatient physician and laboratory visit-days by year for patients with GCA and referent subjects are shown in Figure 1 (top panel). The proportion of patients with 1, 2, and 3 or more visit-days per year are shown for radiology (middle panel) and ophthalmologic visits (bottom panel) in Figure 1. During the year prior to the incidence/index date, patients with GCA had a higher median difference (MD) in outpatient physician (MD 3, IQR –2 to 7, $p < 0.001$) and laboratory (MD 2, IQR –1 to 5, $p < 0.001$) visit-days and in number of radiology (61% of patients with GCA have at least 2 visit-days vs 43% in non-GCA, $p = 0.024$) and ophthalmologic visit-days (54% of patients with GCA have at least 1 visit-day vs 35% in non-GCA, $p = 0.013$), compared with their matched referent subjects.

Following incidence/index date, patients with GCA had a higher median increase in outpatient physician visit-days during the first (MD 7, IQR 2–14, $p < 0.001$), second (MD

Table 1. Characteristics of patients with GCA and matched referent subjects. Values are n (%) unless otherwise specified.

Characteristics	GCA Subjects, n = 147	Non-GCA Subjects, n = 147	p
Female	118 (80)	118 (80)	1.00
Age, yrs, mean ± SD	77.2 ± 8.2	76.9 ± 8.5	0.85
Comorbidity type†			
Myocardial infarction	18 (12)	29 (20)	0.08
Congestive heart failure	40 (27)	43 (29)	0.70
Peripheral vascular disease	61 (41)	38 (26)	0.005
Cerebrovascular disease	62 (42)	48 (33)	0.09
Dementia	23 (16)	27 (18)	0.53
Chronic pulmonary disease	53 (36)	60 (41)	0.40
Peptic ulcer	35 (24)	23 (16)	0.08
Diabetes mellitus	27 (18)	35 (24)	0.25
Hemiplegia	5 (3)	7 (5)	0.56
Moderate/severe renal disease	26 (18)	30 (20)	0.55
Liver disease	10 (7)	15 (10)	0.30
Any cancer	70 (48)	76 (52)	0.48
Charlson Comorbidity Index*, mean ± SD	4.4 ± 3.8	4.4 ± 3.7	0.73

† Comorbidities diagnosed either prior to GCA incidence (or index date for the non-GCA subjects) or at any time during the first 5 years of the matched followup. * Rheumatologic comorbidities were excluded. GCA: giant cell arteritis.

1, IQR –1 to 8, p < 0.001), and fourth years (MD 2, IQR –2 to 6, p = 0.018), but the difference did not reach statistical significance in years 3 (MD 1, IQR –2 to 5, p = 0.08) and 5 (MD 1, IQR –4 to 5, p = 0.16). Laboratory visit-days were higher in patients with GCA compared with referent subjects during the first (MD 9, IQR 2–13, p < 0.001), second (MD 4, IQR –1 to 8, p < 0.001), and third years (MD 2, IQR –2 to 7, p = 0.022), but the difference did not reach statistical significance in years 4 (MD 1, IQR –2 to 6, p = 0.07) and 5 (MD 1, IQR –3 to 5, p = 0.33).

Radiologic visit-days were also higher among patients with GCA compared with referent subjects, with significantly higher frequencies in years 1 (70% of patients with GCA have at least 2 visit-days vs 49% in non-GCA, p = 0.006), 4 (54% of patients with GCA have at least 2 visit-days vs 36% in non-GCA, p = 0.028), and 5 (58% of patients with GCA have at least 2 visit-days vs 38% in non-GCA, p = 0.023). Comparisons of the frequency of radiologic visits did not reach statistical significance in years 2 (53% GCA vs 40% non-GCA for 2+ visit-days, p = 0.07) and 3 (60% GCA vs 46% non-GCA for 2+ visit-days, p = 0.06).

Ophthalmologic procedure/surgery visit-days were higher among patients with GCA in years 1 (65% of patients with GCA have at least 1 visit-day vs 30% in non-GCA, p < 0.001), 2 (48% of patients with GCA have at least 1 visit-day vs 33% in non-GCA, p = 0.016), 3 (49% of patients with GCA have at least 1 visit-day vs 35% in non-GCA, p = 0.034), and 5 (51% of patients with GCA have at least 1 visit-day vs 34% in non-GCA, p = 0.040). Visit-days for musculoskeletal procedures/surgeries, CV procedures/surgeries, and emergency medical services were similar between both groups for the entire study period. Because of the sample size and variability of specific services received, comparisons of differences between individual line-item codes among matched subjects were not performed.

Cost. The total median (IQR) direct medical cost (inflated to 2014 US dollars) from the year preceding and up to 5 years following incidence/index date for both the patients with GCA and referent subjects are demonstrated in Figure 2. The MD for total (inpatient + outpatient) direct healthcare cost between patients with GCA and referent subjects for the entire year prior to incidence/index date did not reach statistical significance (MD $835, IQR –3255 to 5540, p = 0.12). However, when each month was separately evaluated, patients with GCA had a significantly higher total cost of healthcare (MD $417, IQR 132–1646, p < 0.001) in the month immediately preceding the incidence/index date. No differences in inpatient costs between GCA and non-GCA subjects were found throughout the entire study period.

MD in outpatient costs were significantly higher among patients with GCA annually from the year prior through 4 years following the incidence/index date (Table 2). The highest difference in cost observed between groups was demonstrated during the first year (MD $2085, IQR 571–4530, p < 0.001).

The incremental cost difference between the 2 groups for total (inpatient + outpatient; Table 3) and outpatient cost (Table 4) was examined using quantile regression models at different percentiles. Two models were examined. The first model adjusted costs based on age and sex. At the 10th percentile of costs, the incremental cost of care of GCA subjects over the 5-year period following diagnosis was $2679 (95% CI 968–4072) for combined inpatient and outpatient cost and $902 (95% CI 357–1648) for outpatient-specific cost of care. The GCA incremental cost increased steadily toward the upper range of cost distribution for outpatient costs, reaching $10,514 (95% CI 3456–14,947) at the 90th percentile of costs. The incremental cost of care for the combined inpatient and outpatient cost of care increased to $6351 (95% CI 422–10,486) at the 50th percentile of costs, but then declined in the 75th and 90th percentiles because of the markedly variable cost range of inpatient care seen in both groups. This model suggests that subjects with GCA at the 10th percentile of total costs incurred an additional $902 of outpatient cost compared to their age- and sex-matched peers, and those at the 90th percentile incurred an additional $10,514 of outpatient costs over a 5-year period. In addition to age and sex, the second model adjusted for comorbidities between matched GCA and non-GCA subject pairings using a weighted CCI and accounted for variability in inpatient care by adjusting for the number of inpatient days during the 5 years following incidence/index date. Following these adjustments, the incre-

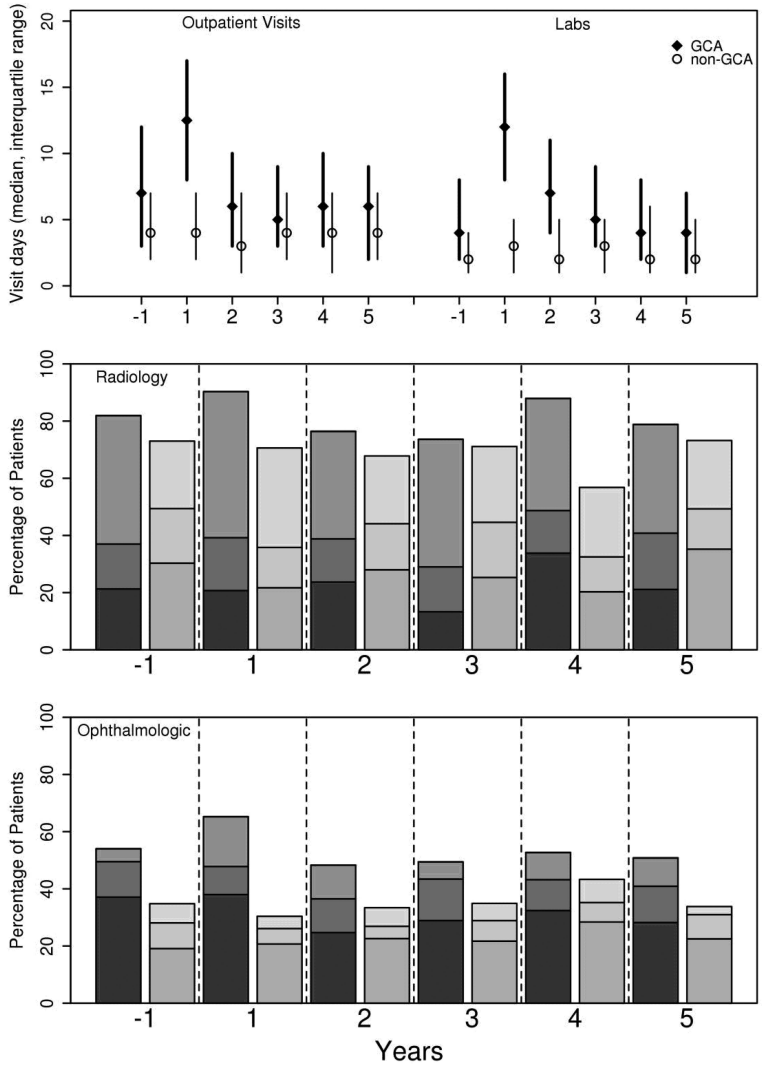

Figure 1. Top panel: Use of healthcare services by visit day for outpatient visits and labs. Middle panel: Percentage of patients with 1, 2, or 3+ radiology visit days (bottom, middle, and upper section of each bar, respectively). Bottom panel: Percentage of patients with 1, 2, or 3+ ophthalmologic visit days (bottom, middle, and upper section of each bar, respectively). Patients with GCA are darker bars and non-GCA referent subjects are lighter bars. GCA: giant cell arteritis.

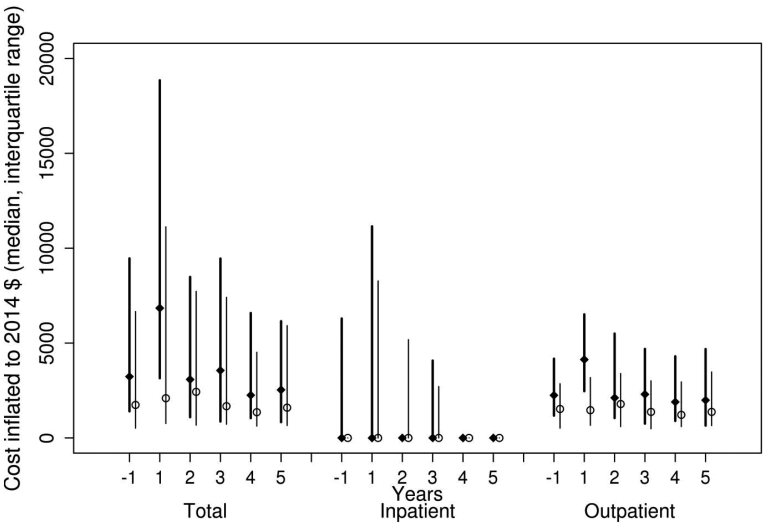

Figure 2. Direct medical costs by years of followup (inflation-adjusted to 2014 dollars) for patients with GCA (solid diamonds) and non-GCA referent subjects (open circles). GCA: giant cell arteritis.

Table 2. Excess healthcare outpatient cost related to GCA (inflation-adjusted to 2014 US dollars)*.

Time from Incidence Date, Yrs	No. GCA/ non-GCA Pairs	Median Difference (interquartile range)	Mean Difference (± SD)**	p*
–1 to 0	127	722 (–1144 to 2772)	756 (342)	0.01
0–1	133	2085 (571–4530)	2432 (412)	< 0.001
1–2	120	437 (–1365 to 3721)	1182 (370)	0.009
2–3	110	382 (–801 to 2615)	998 (361)	0.007
3–4	99	388 (–923 to 2997)	797 (365)	0.04
4–5	97	577 (–1488 to 2893)	493 (431)	0.11

* Signed-rank paired test. ** Because of cost variability, trimmed means were used to reduce effect of extreme outliers on estimated means. GCA: giant cell arteritis.

Table 3. Total (inpatient + outpatient) direct medical costs of care for subjects with GCA over a 5-year period. Values are the total incremental costs (95% CI) according to cost-percentiles for patients with GCA compared with referent subjects, inflation-adjusted to 2014 US dollars compared with referent subjects.

Percentile	Model 1*	Model 2†
10th	2679 (968–4072)	1018 (82–1973)
25th	2909 (1135–5016)	1400 (–865 to 3167)
50th	6351 (422–10,486)	3576 (635–6140)
75th	5431 (–6156 to 19302)	6012 (2258–10,136)
90th	–7187 (–34,065 to 16,335)	7530 (–124 to 14,216)

* Adjusted for age and sex. † Adjusted for age, sex, weighted Charlson Comorbidity Index, and number of inpatient days. GCA: giant cell arteritis.

Table 4. Direct outpatient cost of care for subjects with GCA over a 5-year period. Values are the total incremental costs (95% CI) according to cost-percentiles for patients with GCA compared with referent subjects, inflation-adjusted to 2014 US dollars.

Percentile	Model 1*	Model 2†
10th	902 (357–1648)	890 (173–1594)
25th	1902 (566–2953)	2399 (1210–3382)
50th	4227 (1960–6162)	4662 (1903–7139)
75th	9393 (5570–11,614)	7668 (5845–9564)
90th	10,514 (3456–14,947)	7833 (3275–14,357)

* Adjusted for age and sex. † Adjusted for age, sex, weighted Charlson Comorbidity Index, and number of inpatient days. GCA: giant cell arteritis.

mental outpatient cost of GCA ranged from $890 at the 10th percentile of costs up to $7833 at the 90th percentile over a 5-year period (Table 4).

Further analysis was performed on the subset of matched pairs in which data were available from 1 year prior through 5 years following the incidence/index date for use (n = 52) and cost (n = 70). Use among those with 6 years of available data was similar in all domains to the larger aggregate analysis that included 6-year and partial followup (results not shown).

DISCUSSION

To our knowledge, our report is the first North American population-based study to evaluate use of outpatient services and direct medical costs of GCA from 1 year prior and up to 5 years following diagnosis. Our findings indicate that subjects with GCA incur substantially higher total cumulative direct medical cost in the month immediately preceding diagnosis and annually for the first 4 years following diagnosis compared with subjects without GCA.

The healthcare use and direct medical cost of other rheumatologic diseases including SLE[4] and RA[3] have been extensively evaluated, but the economic burden of GCA is largely unknown. Although considered a rare condition, the number of incident cases of GCA is expected to concurrently increase with the aging global population. A disease projection for GCA estimated that by 2050 more than 3 million people will have been diagnosed with GCA in North America, Europe, and Australasia[18]. It is estimated that by 2050 the cost of GCA-related complications would markedly increase, with about $70.6 billion of cumulative cost being spent on visual impairment for patients diagnosed with GCA from 2014–2050 in the United States alone[18].

Beyond disease projection models, limited information on GCA-associated cost is available. One study evaluated the socioeconomic effect of 5 systemic vasculitides including GCA in New York state using hospital admission data sources[19]. However, only costs attributed to inpatient care were reported, and a population-based comparator cohort was not included for incremental cost assessment[20]. While a marginally greater risk of hospitalization has been previously described in our cohort[21], our study did not identify a noticeably significant difference in the overall cost of inpatient care between subjects with GCA and non-GCA referent subjects. A potential explanation for this lack of increase is the large variability in inpatient cost among a relatively small patient sample size. These factors may prevent identification of small cost differentials between groups. Further, most of the care related to the diagnosis and management of GCA in the United States occurs in the outpatient setting.

The findings from our current study suggest that incre-

mental increases in outpatient direct medical cost of GCA are already evident in the year preceding diagnosis. A corresponding increase in outpatient physician, laboratory, and radiology visit-days over the same interval suggests that these costs are associated with establishing diagnosis. To our knowledge, no other study has evaluated healthcare use or cost in the time period leading up to the GCA incidence date. A recent database study by Babigumira, *et al* used a national sample of US administrative medical claims to estimate the cost of GCA limited to the year immediately following diagnosis[20]. Similar to our current study, Babigumira, *et al* found that the 1-year cost was significantly increased among patients with GCA. While inpatient, outpatient, and pharmacy costs were all higher among patients with GCA, the outpatient cost difference between patients with GCA and controls ($10,389) was 2-fold greater than the inpatient cost difference ($5139), further highlighting that most care for patients with GCA is provided in the outpatient setting.

A closer parallel to our GCA cohort is a study evaluating patients with isolated polymyalgia rheumatica (PMR) from the same Olmsted County population. In this cohort of patients with isolated PMR, the total yearly direct medical cost was similarly highest in the year of diagnosis[16]. Thereafter, cost of care decreased over time, but remained higher than those of comparator subjects. Use of outpatient visits and laboratory testing was higher in patients with PMR in the year following diagnosis, but thereafter became similar to that of controls. A longer duration of disease and higher number of associated complications may account for the persistent increase in healthcare use and cost among patients with GCA compared to those with PMR.

In addition to outpatient physician visits and laboratory and radiology testing, patients with GCA in our current study had a higher frequency of ophthalmologic surgeries/procedures in 4 of the 5 years following diagnosis. These increased services correspond with what is known about visual complications in GCA. Several studies demonstrate visual impairment in up to 20% of patients at or around the time of GCA diagnosis[22,23], later followed by an increased risk of developing glucocorticoid-associated ocular disease. Posterior subscapular cataracts, in particular, have been seen in up to 41% of patients with GCA taking chronic glucocorticoid therapy[10].

Interestingly, musculoskeletal procedure/surgery was not increased among patients with GCA compared with non-GCA subjects. Although osteoporotic fractures are a well-known and frequent complication of glucocorticoid therapy[10,24], a direct increased risk of fracture among patients with GCA to age- and sex-matched controls has not yet been quantified. CV procedure/surgery was also similar between groups. While a higher baseline prevalence of MI in the control subjects may have offset identification of an observed difference, a systematic review and metaanalysis has demonstrated that patients with GCA are not at a significantly increased risk of coronary artery disease compared with non-GCA subjects[25].

Our study has several strengths. First is the well-defined, population-based cohort of subjects with GCA with comparison subjects matched for age, sex, and calendar year. Second, the database uses standardized and uniform coding of line-item services, allowing for objective categorization. Further, the database provides an estimated economic cost for each recorded line-item including both the billed charge and true resource use, the latter of which was used to reflect the accurate cost of care. Finally, the value of each unit was adjusted to national cost norms providing an accurate and generalizable estimation of relevant economic cost.

Results from our study should be interpreted in light of some limitations. First, the pattern of used services may reflect regional or institutional practices and may differ compared with other areas. Both groups are from the same population, thus it is anticipated that the regional variations in healthcare use and cost would be experienced by both cohorts, mitigating the effect of practice patterns on the incremental cost of care observed. Second, review of the individual services and cost units did not allow classification of items based on active disease, chronic disease-related complications, or treatment-associated adverse events. Assessing such contributions in future studies would be of benefit.

A further limitation of our study is that some subjects were included for only part of the followup period. However, because followup of each matched pair was truncated at the shortest length of followup for either member, duration of observation was similar for both cases and referent subjects, negating the effect of partial contribution on the overall results. Indeed, comparison of patients with 6-year data did not differ for either cost or healthcare use with the larger aggregate group. While the longitudinal design of our study is a particular strength, it is possible that the costs of care may evolve over time as newer healthcare modalities became available (e.g., advanced imaging). Unfortunately, because of the limited sample size, stratified cost based on calendar year was not feasible. Last, the cost database used in our study does not include categories of cost related to outpatient prescription drugs, nursing home or assisted-living fees, durable medical equipment, or transportation services. Consequently, the effect of these items is unknown, though not anticipated to substantially contribute to the overall cost of care for GCA.

Although biologic agents were not used in our patient cohort, ongoing research is identifying a potential involvement for them in the treatment of GCA. While these medications are more expensive, they may lead to fewer disease or treatment-related complications. Therefore, future cost analysis of patient populations receiving such medications will need to be analyzed.

The direct cost of care for patients with GCA is higher

than non-GCA referent subjects beginning 1 month prior to diagnosis and extending 4 years following. A higher use of outpatient physician visits as well as laboratory, radiology, and ophthalmologic services appears to account for this difference. Further population-based studies evaluating use and cost in GCA are needed to confirm findings in larger samples and more diverse communities. Future research will need to address methods of cost-effective care models and the effect of targeted therapeutics in patients with GCA.

REFERENCES

1. Yelin E, Murphy L, Cisternas MG, Foreman AJ, Pasta DJ, Helmick CG. Medical care expenditures and earnings losses among persons with arthritis and other rheumatic conditions in 2003, and comparisons with 1997. Arthritis Rheum 2007;56:1397-407.
2. Centers for Disease Control and Prevention. Chronic Disease Cost Calculator Version 2. [Internet. Accessed March 31, 2017.] Available from: www.cdc.gov/chronicdisease/calculator
3. Furneri G, Mantovani LG, Belisari A, Mosca M, Cristiani M, Bellelli S, et al. Systematic literature review on economic implications and pharmacoeconomic issues of rheumatoid arthritis. Clin Exp Rheumatol 2012;30 Suppl 73:S72-84.
4. Panopalis P, Clarke AE, Yelin E. The economic burden of systemic lupus erythematosus. Best Pract Res Clin Rheumatol 2012; 26:695-704.
5. Lawrence RC, Helmick CG, Arnett FC, Deyo RA, Felson DT, Giannini EH, et al. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. Arthritis Rheum 1998;41:778-99.
6. Mohammad AJ, Nilsson JÅ, Jacobsson LT, Merkel PA, Turesson C. Incidence and mortality rates of biopsy-proven giant cell arteritis in southern Sweden. Ann Rheumatic Dis 2015;74:993-7.
7. Gonzalez-Gay MA, Martinez-Dubois C, Agudo M, Pompei O, Blanco R, Llorca J. Giant cell arteritis: epidemiology, diagnosis, and management. Curr Rheumatol Rep 2010;12:436-42.
8. Matteson EL, Gold KN, Bloch DA, Hunder GG. Long-term survival of patients with giant cell arteritis in the American College of Rheumatology giant cell arteritis classification criteria cohort. Am J Med 1996;100:193-6.
9. González-Gay MA, Blanco R, Abraira V, García-Porrúa C, Ibáñez D, García-Pais MJ, et al. Giant cell arteritis in Lugo, Spain, is associated with low longterm mortality. J Rheumatol 1997; 24:2171-6.
10. Proven A, Gabriel SE, Orces C, O'Fallon WM, Hunder GG. Glucocorticoid therapy in giant cell arteritis: duration and adverse outcomes. Arthritis Rheum 2003;49:703-8.
11. Lundberg I, Hedfors E. Restricted dose and duration of corticosteroid treatment in patients with polymyalgia rheumatica and temporal arteritis. J Rheumatol 1990;17:1340-5.
12. Alba MA, García-Martínez A, Prieto-González S, Tavera-Bahillo I, Corbera-Bellalta M, Planas-Rigol E, et al. Relapses in patients with giant cell arteritis: prevalence, characteristics, and associated clinical findings in a longitudinally followed cohort of 106 patients. Medicine 2014;93:194-201.
13. Maradit Kremers H, Crowson CS, Gabriel SE. Rochester Epidemiology Project: a unique resource for research in the rheumatic diseases. Rheum Dis Clin North Am 2004;30:819-34.
14. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-83.
15. Bang H, Tsiatis AA. Median regression with censored cost data. Biometrics 2002;58:643-9.
16. Kremers HM, Reinalda MS, Crowson CS, Zinsmeister AR, Hunder GG, Gabriel SE. Direct medical costs of polymyalgia rheumatica. Arthritis Rheum 2005;53:578-84.
17. Lin DY, Feuer EJ, Etzioni R, Wax Y. Estimating medical costs from incomplete follow-up data. Biometrics 1997;53:419-34.
18. De Smit E, Palmer AJ, Hewitt AW. Projected worldwide disease burden from giant cell arteritis by 2050. J Rheumatol 2015; 42:119-25.
19. Cotch MF, Hoffman GS. The prevalence, epidemiology and cost of hospitalizations for vasculitis in New York State 1986 to 1990 [abstract]. Arthritis Rheum 1995;38:S225.
20. Babigumira JB, Li M, Boudreau DM, Best JH, Garrison LP Jr. Estimating the cost of illness of giant cell arteritis in the United States. Rheumatol Ther 2017 Jan 13 (E-pub ahead of print).
21. Michet CJ 3rd, Achenbach SJ, Crowson CS, Matteson EL. Hospitalization rates and utilization among patients with giant cell arteritis: a population-based study from 1987 to 2012. Semin Arthritis Rheum 2015;45:70-4.
22. Salvarani C, Cimino L, Macchioni P, Consonni D, Cantini F, Bajocchi G, et al. Risk factors for visual loss in an Italian population-based cohort of patients with giant cell arteritis. Arthritis Rheum 2005;53:293-7.
23. González-Gay MA, García-Porrúa C, Llorca J, Hajeer AH, Brañas F, Dababneh A, et al. Visual manifestations of giant cell arteritis. Trends and clinical spectrum in 161 patients. Medicine 2000;79:283-92.
24. Chandran A, Udayakumar PD, Kermani TA, Warrington KJ, Crowson CS, Matteson EL. Glucocorticoid usage in giant cell arteritis over six decades (1950 to 2009). Clin Exp Rheumatol 2015;33 Suppl 89:98-102.
25. Ungprasert P, Koster MJ, Warrington KJ. Coronary artery disease in giant cell arteritis: a systematic review and meta-analysis. Semin Arthritis Rheum 2015;44:586-91.