Association of Giant Cell Arteritis With Race

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IMPORTANCE Giant cell arteritis (GCA) is the most common vasculitis in adults and is associated with significant morbidity and mortality. Its incidence has been carefully studied in white populations, yet its relevance among other racial and ethnic groups is less well known.

OBJECTIVE To examine the incidence of biopsy-proven GCA (BP-GCA) in a tertiary care center–based population with a sizeable proportion of black patients.

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study identified all patients who underwent temporal artery biopsy (TAB) from July 1, 2007, through September 30, 2017, using the electronic medical record system at the Johns Hopkins Wilmer Eye Institute. Associations between self-reported race, sex, and age were explored and compared with all other patients attending the hospital over the same period. Data were analyzed from November 1, 2017, through July 31, 2018.

MAIN OUTCOMES AND MEASURES Estimated incidence rates of BP-GCA in black and white patients.

RESULTS Among 586 patients who underwent TAB (mean [SD] age, 70.5 [11.1] years; age range, 32-103 years; 423 [72.2%] women), 167 (28.5%) were black, 382 (65.2%) were white, and 37 (6.3%) were other or unknown. Of 573 individuals 50 years and older, 92 (16.1%) had BP-GCA; 14 were black (8.4% of all black patients undergoing testing) and 75 were white (19.6% of all white patients undergoing testing). Crude annual incidence rates for BP-GCA were 2.9 (95% CI, 1.3-5.5) per 100,000 for black and 4.2 (95% CI, 3.0-5.6) per 100,000 for white patients within the study population. Population-adjusted age- and sex-standardized incidence rates were 3.1 (95% CI, 1.0-5.2) and 3.6 (95% CI, 2.5-4.7) per 100,000 for black and white patients, respectively (difference, 0.5; 95% CI, −1.7 to 2.7; P = .70). The incidence rate ratio was 1.9 in women compared with men (95% CI, 1.1-3.4; P = .03) but was not significant in white compared with black patients (1.2; 95% CI, 0.6-2.4; P = .66).

CONCLUSIONS AND RELEVANCE In our cohort, BP-GCA occurred more commonly in women, but rates were similar between races. These findings do not appear to support the conclusion that GCA occurs more frequently in white compared with black patients.

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Giant cell arteritis (GCA) is a vasculitis of large and medium arteries that almost exclusively occurs in patients older than 50 years. Despite its clear association with advancing age, the exact etiology remains unclear. The treatment of GCA consists of immunosuppression, typically with corticosteroids. Untreated, GCA may lead to irreversible loss of vision, primarily owing to arteritic anterior ischemic optic neuropathy. Untreated, death may ensue from myocardial infarction, ischemic stroke, aortic aneurysm, and dissection, as well as complications of systemic therapy. Although color duplex ultrasonography of the temporal arteries and neuroimaging are increasingly used in the workup of GCA, temporal artery biopsy (TAB) remains the criterion standard for diagnosis.

Most epidemiological data on GCA are derived from predominantly white populations in Europe and North America. In Olmsted County, Minnesota, where a large part of the population is of Scandinavian descent, the annual incidence of GCA is 19.8 per 100,000 population 50 years and older. Giant cell arteritis in black patients is thought to be comparatively rare. In 1983, a 10-year study from Shelby County, Tennessee (in which the population at that time was 42% black), found the incidence of GCA in white patients to be 7 times greater than in black patients. Subsequent studies examining the frequency of GCA in other racial groups also suggest an almost negligible occurrence in black populations.

According to the 2010 US Census, more than 60% of the total population in Baltimore, Maryland, is black, providing a unique opportunity to study the incidence of GCA in a large cohort of black patients, which constituted the primary aim of our study. The secondary aim was to compare the incidence of GCA in black and white patients.

The histopathologic criteria used for the diagnosis of GCA can vary somewhat between centers. The criteria used in this study were based on a prior report from our institution.

Methods

Patients and Specimens

We performed a retrospective review to assess the medical records and histopathologic reports of all patients who underwent TAB at the Johns Hopkins Wilmer Eye Institute, Baltimore, Maryland, from July 1, 2017, through July 31, 2018. This study was approved by the institutional review board of the Johns Hopkins School of Medicine, which waived the need for informed consent because this was a retrospective medical record review with minimal risk. In addition, consent for review of medical records was not possible to obtain in individuals who were deceased or were no longer in the immediate area. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

The cohort included patients referred for TAB from within the Wilmer Eye Institute and those from other departments of the Johns Hopkins Health System, including all satellite sites. Biopsy results and demographic data, including age, sex, and self-reported race, were tabulated. Patients were considered to have biopsy-proven GCA (BP-GCA [ie, a positive TAB finding]) if histologic examination of the temporal artery revealed arteritis. Patients with biopsies of healed arteritis were counted as having BP-GCA. Indeterminate findings of biopsies were counted as negative. A single pathologist (C.G.E.) examined all the specimens during the study period, and we relied on the original diagnosis; specimens were not reexamined for the purpose of this study. The role of preoperative corticosteroid use was not assessed. Because GCA at younger than 50 years is a controversial entity, only patients 50 years and older were included for statistical analysis.

For active GCA, histopathological criteria included marked thickening and edema of intima, which was present in all cases but not considered specific. The key feature was a mononuclear inflammatory infiltrate consisting predominantly of variable percentages of lymphocytes and macrophages, often with giant cells, involving multiple layers of the vessel wall. Disruption and/or loss of the internal elastic lamina, as highlighted by elastic fiber stains, was present in all cases but could be minimal in early lesions. Other features, including thrombosis and recanalization, mural necrosis, and a thickened and scarred media and adventitia, were often present but were not required for a diagnosis of active GCA. The key features used to diagnose healed GCA were significant fragmentation and/or loss of internal elastic lamina with associated thinning and fibrosis or scarring of the media, sometimes with capillary neovascularization. Adventitial scarring could also be present.

Racial and Ethnic Labels

Race and ethnicity are complex concepts that are nonetheless commonly used in epidemiology and medicine; for the purpose of this study, patient self-identified race and/or ethnicity labels were used as categorized in the electronic medical record system and the US Census. Herein, white refers to descendants from any of the white racial groups of Europe, the Middle East, or North Africa, and black refers to individuals of African descent. The Census Bureau used the terms black and African American interchangeably.

Statistical Analysis

Data were analyzed from November 1, 2017, through July 31, 2018. Histopathologic reports were reviewed by 3 investigators (A.M.G., A.R.C., and A.D.H.) who coded BP-GCA as a binary categorical outcome using standard criteria. For those pa-
patients undergoing biopsy, associations between groups were assessed using unpaired 2-tailed $t$ tests for continuous variables (ie, age) and $\chi^2$ tests for discrete variables (ie, race and sex). Results were stratified using Mantel-Haenszel methods to explore associations and possible interactions. A multivariable logistic regression model with age, sex, and race as covariates was used to assess factors associated with biopsy outcome. Stratified demographic data for all patients 50 years or older attending the hospital during the same period were obtained from the hospital electronic medical record system (Epic Systems Corporation).

Crude incidence rates were calculated using the number of incident cases as the numerator and patients of the corresponding sex and age groups seen at Johns Hopkins Health System during the same period as the denominator. Data were subsequently standardized to the US 2010 States Census population using the direct method. Poisson regression was applied to calculate incidence rate ratios to detect differences in sex and race between groups. All analyses were performed using Stata, version 14 (StataCorp). Two-sided $P < .05$ indicated significance.

### Results

During the 10-year study period, TAB was performed in 586 individuals, including 382 white (65.2%), 167 black (28.5%), and 7 Asian (1.2%) patients. Eight of 586 patients (1.4%) identified themselves as being Hispanic, a separate category from self-identified race. The racial and ethnic background of 22 patients (3.8%) was unknown or other.

Of 586 individuals undergoing TAB, 423 (72.2%) were women and 163 (27.8%) were men, and the mean (SD) age was 70.5 (11.1) years (range, 32-103 years). The mean (SD) age of patients selected for TAB was higher in white than black patients (71.5 [10.8] vs 68.9 [11.6] years), with a mean difference of 2.7 years (95% CI, 0.6-4.7 years; $P = .01$). Thirteen patients selected for TAB (2.2%) were younger than 50 years, and of those, 1 (a black patient in his mid-40s) had a positive biopsy result. However, because the concept of GCA in patients younger than 50 years is controversial, these patients were excluded from further analysis.

Of 573 individuals 50 years and older, a total of 92 (16.1%) had a positive biopsy finding; 14 were black (8.4% of all black patients undergoing testing), 75 were white (19.6% of all white patients undergoing testing), and 3 were listed as unknown or other. Indeterminate results were reported in 13 (2.3%) patients that included 2 black and 11 white patients. No patient who self-identified as Asian or Hispanic had BP-GCA or indeterminate biopsy findings.

The mean (SD) age of patients with BP-GCA was similar in white and black patients (75.4 [9.1] vs 74.1 [9.2] years), with a mean difference of 1.3 years (95% CI, −3.9 to 6.7; $P = .61$). Six patients (1.0%) with BP-GCA were aged 50 to 60 years; all were white, and both sexes were affected equally. The proportion of positive results was 26 of 160 (16.3%) for men and 66 of 413 (16.0%) for women (odds ratio [OR], 1.02; 95% CI, 0.6-1.7; $P = .94$). The likelihood of a positive result was higher for white than black patients (OR, 2.7; 95% CI, 1.5-4.8; $P = .001$).

Within the logistic regression analysis, the association between BP-GCA and white race persisted (OR, 2.5; 95% CI, 1.4-4.4; $P = .003$). Age was also found to be strongly associated with disease in patients undergoing biopsy, with a 4.4% (95% CI, 1.9%-6.9%; $P < .001$) increase in likelihood of BP-GCA for each year older than 50 years.

The crude incidence rate for BP-GCA was 2.9 (95% CI, 1.3-5.5) for black patients and 4.2 (95% CI, 3.0-5.6) for white patients per 100 000 population per year. Population-adjusted age- and sex-standardized rates per 100 000 population were 3.1 (95% CI, 1.0-5.2) for black patients and 3.6 (95% CI, 2.5-4.7) for white patients (difference, 0.5; 95% CI, −1.7 to 2.7; $P = .70$). Adjusted rates per 100 000 population were 2.3 (95% CI, 1.2-3.5) for men and 4.4 (95% CI, 2.9-5.8) for women. Our overall age- and sex-adjusted incidence rate of BP-GCA was 3.5 (95% CI, 2.5-4.5) per 100 000 population per year (Table). Overall, BP-GCA was found to occur more frequently in women than in men (incidence rate ratio, 1.9; 95% CI, 1.1-3.4; $P = .03$) and at similar levels in white and black patients (incidence rate ratio, 1.2; 95% CI, 0.6-2.4; $P = .66$).

### Discussion

In our 10-year retrospective study of GCA at the Johns Hopkins Wilmer Eye Institute, we reviewed the medical records of 586 patients who had TABs, 93 of whom had positive findings. To our knowledge, the only other North American study of GCA incidence with a comparable sample size to ours evaluated patients...
from Olmsted County, Minnesota, where the population is predominantly white; that study identified 173 incident cases of GCA during a 50-year study period. Our study is the largest, to our knowledge, to examine GCA incidence in a population that includes a sizeable proportion of black patients.

A large amount of the epidemiological data on GCA has been derived from Northern Europe. These data sets have established GCA as a disease that is relatively more common in white populations. Most studies from North America are consistent with this notion, with the notable exception of an 11-year retrospective study from the Texas Gulf Coast, in which 13 of 27 patients with GCA were black women. The only other study in the United States evaluating the incidence of GCA in a population with a relatively large proportion of black patients (42%) was from Shelby County, Tennessee. That study was conducted in 1983 and showed the incidence of GCA to be 7 times greater in white than in black patients; however, this study included only 26 cases of GCA (from 1971 until 1980) in total. A 12-year retrospective study examining the incidence of GCA in Hispanic patients included 121 patients, 20 (16.5%) of whom showed histologic evidence of arteritis; of those 121 patients, 6 were black, none of whom had a positive biopsy result. A 17-year retrospective study focusing on the incidence of GCA in Asian patients included 127 patients; of 38 patients (29.9%) who had BP-GCA, 1 was African American. These studies have suggested a low incidence of GCA in black patients, although their conclusions were drawn from relatively small sample sizes. Nevertheless, the notion that GCA rarely affects black individuals is widely accepted.

The mean age and sex ratios in our study are in keeping with other published data. The youngest patient with a positive biopsy result in our study was in his mid-40s, mirroring the outliers in the Shelby County study (2 black women aged 47 and 53 years). However, because GCA at younger than 50 years is a controversial entity, this patient was excluded from further analysis. Our findings are notable in that they appear to contradict the commonly held belief that GCA is rare in black compared with white patients. Based on previous epidemiological data, many physicians may have a higher threshold for TAB in black patients, but our findings suggest this should not be the case.

Limitations

Unless all patients in a defined study population undergo testing, the true incidence and prevalence of a disease can only ever be estimated. In our study, we evaluated patients seen and selected in our institution for TAB based on their clinical presentation. Although the Johns Hopkins Health System is the major health care system in Maryland, several other large hospitals exist in this region. The patient population at the Johns Hopkins Health System is mixed, reflective of Baltimore and surrounding regions. However, the patient population is predominantly white (approximately 60%), not precisely mirroring the census population of the city of Baltimore (63% black). We did not intentionally use different clinical criteria or thresholds when offering or performing TAB across different racial groups. Despite that effort, within our cohort, we found that white patients had a higher pretest probability of disease, with 19.6% of those tested having BP-GCA compared with 8.4% of black patients. This finding may suggest better surveillance of the black population or a stronger link between symptoms and disease in the white population. Further limitations of this study include the fact that we did not reexamine biopsy specimens but instead relied on the pathologist’s initial diagnosis. In addition, we did not assess preoperative corticosteroid use and whether or not this had any effect on biopsy results. We did, however, exclude any biopsies with indeterminate results.

Our overall age- and sex-adjusted incidence rate of BP-GCA of 3.5 (95% CI, 2.5-4.5) per 100 000 population per year is similar to that identified in Shelby County, Tennessee, although lower than that shown in other North American studies with markedly fewer black patients. The Wilmer Eye Institute is the primary source of TABs at the Johns Hopkins Health System, and we searched the pathology archive to ensure that all biopsies were captured. However, we cannot account for the unknown number of patients with suspected GCA who may have refused biopsy.

Conclusions

This retrospective cohort study examined the incidence of BP-GCA in black compared with white patients. Whereas previous reports have suggested that GCA is several times more common in white than in black patients, in our study, a difference by race could not be identified. We therefore recommend that the same clinical thresholds for diagnosing and managing GCA be applied to black and white patients.
REFERENCES


