Oregon Health & Science University
School of Medicine

Scholarly Projects Final Report

Title *(Must match poster title; include key words in the title to improve electronic search capabilities.)*
Diagnostic Considerations of Giant Cell Arteritis in Veterans

Student Investigator's Name
Paul Sungwoo Kay

Date of Submission *(mm/dd/yyyy)*
03/16/2023

Graduation Year
2023

Project Course *(Indicate whether the project was conducted in the Scholarly Projects Curriculum; Physician Scientist Experience; Combined Degree Program [MD/MPH, MD/PhD]; or other course.)*
Scholarly Projects Curriculum

Co-Investigators *(Names, departments; institution if not OHSU)*
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Mentor's Name
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Mentor's Department
Neuro-ophthalmology

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Concentration Lead's Name
Lisa Silbert

Project/Research Question
The goal of this study is to identify differences in the criteria, risks, and outcomes of diagnosing giant cell arteritis in a veteran patient population compared to the general population.

Type of Project *(Best description of your project; e.g., research study, quality improvement project, engineering project, etc.)*
Research Study

Key words *(4-10 words describing key aspects of your project)*
Giant cell arteritis, vasculitis, veterans, temporal artery biopsy

Meeting Presentations
If your project was presented at a meeting besides the OHSU Capstone, please provide the meeting(s) name, location, date, and presentation format below (poster vs. podium presentation or other).
North American Neuro-Ophthalmology Society (NANOS), Orlando FL, 03/14/23, Poster Presentation

Publications *(Abstract, article, other)*
If your project was published, please provide reference(s) below in JAMA style.
NA

Submission to Archive
Final reports will be archived in a central library to benefit other students and colleagues. Describe any restrictions below (e.g., hold until publication of article on a specific date).
No restrictions.

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Next Steps
What are possible next steps that would build upon the results of this project? Could any data or tools resulting from the project have the potential to be used to answer new research questions by future medical students?
We would like to look at the possibility of a risk calculator to assess the weight of certain clinical variables on the likelihood of having a positive temporal artery biopsy.

Please follow the link below and complete the archival process for your Project in addition to submitting your final report.

https://ohsu.ca1.qualtrics.com/jfe/form/SV_3ls2z8V0goKiHZP

Student's Signature/Date *(Electronic signatures on this form are acceptable.)*
This report describes work that I conducted in the Scholarly Projects Curriculum or alternative academic program at the OHnSU School of Medicine. By typing my signature below, I attest to its authenticity and originality and agree to submit it to the Archive.

X
Studen

Mentor's Approval *(Signature/date)*

X
Mentor Name

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Report*: Information in the report should be consistent with the poster, but could include additional material. Insert text in the following sections targeting 1500-3000 words overall; include key figures and tables. Use Calibri 11-point font, single spaced and 1-inch margin; follow JAMA style conventions as detailed in the full instructions.*

Introduction *(≥250 words)*

Giant cell arteritis (GCA) formerly known as temporal arteritis, is the most prevalent form of primary systemic vasculitis in adults, characterized by debilitating symptoms such as severe headaches, scalp tenderness, and jaw claudication. However, studies on GCA have been limited in volume or subject to retrospective meta-analysis[1]. Although the overall etiology of GCA remains unknown, the most feared complication of untreated GCA is a sudden, irreversible loss of vision in one or both eyes due to ophthalmic artery occlusion. Immediate treatment with high-dose corticosteroids is therefore indicated upon suspicion of GCA and has been shown as a rapid and effective treatment even before a definitive diagnosis has been made. However, the clinical indications and accuracy of TABs in the diagnosis of GCA in a veteran population with increased rates of physical and mental comorbidities remain poorly understood. Many signs and symptoms, such as elevated ESR and CRP, indicating TAB in the general population may not be appropriate in this specific patient population and may be indicators of other health issues.

The United States Veterans Health Administration (VHA) holds the nation's largest electronic medical database. Veterans comprise 7% of the American population, including 24% of the population over 75 years old[2]. Building upon a clinical study of one VHA site cohort[3], we used this database to identify differences in demographics, risk factors, associated systemic conditions, and biopsy yield within the entire veteran population using novel methodology.

Methods *(≥250 words)*

This retrospective cohort study included 24,857 individuals with codes for GCA or temporal artery biopsy (TAB) since 1/1/2001 within the VA Informatics and Computing Infrastructure (VINCI) database. Patients with diagnosis codes for GCA given within 14-60 days after completion of TAB were considered positive for the disease. Unadjusted odds ratios were used as the measure of association between TAB results and clinical variables, including demographic (e.g., age at diagnosis, geographic region, and gender) and 18 medical comorbidities seen in GCA patients.

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Results *(≥500 words)*

	All with TAB	Positive	Negative	Odds Ratio	Significance
n	10,416	2285 (21.9%)	8131 (78.1%)	--	--
Female	737	138 (18.7%)	599 (81.3%)	0.80 (0.66-0.96)	--
Male	9679	2147 (22.2%)	7532 (77.8%)	--	P=0.3
Age at procedure Mean (95% CI)	71.0 (70.8, 71.2) N=10,416	72.8 (72.5, 73.2) N=2,430	70.4 (70.2, 70.6) N=7,986	1.03 (1.02-1.03)	P<.001

Table 1. Of 10,416 patients with a documented TAB procedure, 2285 were positive (21.9%). Mean age at diagnosis was 72.8 (95% CI [72.5, 73.2]) years, with highest prevalence between 70-79 (828 patients, 36.4%). Mean age at diagnosis was higher in males (73.2, 95% CI [72.8-73.6]) versus females (68.1 [66.3-69.9]), and odds of positive TAB were lower in females than males (0.80, 96% CI [0.66-0.96]).

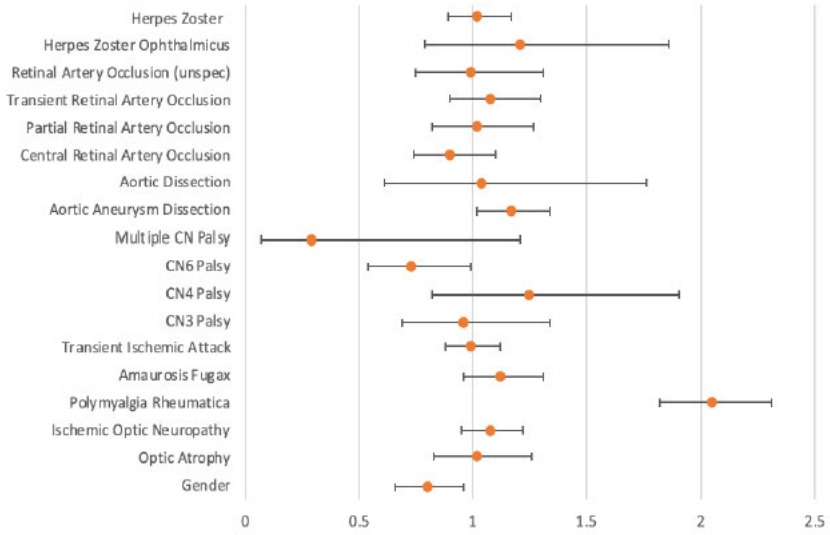

Figure 1. Odds of GCA were higher in patients with polymyalgia rheumatica (OR 2.05 [1.82-2.31]) and aortic aneurysm dissection (OR 1.17 [1.02-1.34]).

	All with TAB	Positive	Negative	Odds Ratio	Significance
ESR Mean (95% CI)	55 (54, 56) N=6378	63 (61, 64) 1618	52 (51, 53) 4760	1.60 (1.41, 1.82)	P<.001
CRP Mean (95% CI	23.4 (22.1, 24.6) N=5443	28.1 (25.4, 30.9) N=1402	21.7 (20.3, 23.1) N=4041	1.23 (1.09, 1.40)	P<.001
Platelets Mean (95% CI)	280 (277, 283) N=6414	306 (299, 313) N=1553	272 (269, 275) N=1861	2.01 (1.72, 2.35)	P<.001

Table 2. Mean platelet count was higher in patients with positive TAB (306, 95% CI [299, 313]) compared to those with negative TAB (272, 95% CI [269, 275]). Similarly, both ESR (63, 95% CI [61, 64]) and CRP (28.1, 95% CI [25.4, 30.9]) were elevated in patients with positive biopsies, compared with those who tested negative (52, 95% CI [51, 53] and 21.7, 95% CI [20.3, 23.1], respectively). ESR, CRP, and platelets were considered categorical variables when determining the odds ratios.

Discussion *(≥500 words)*

Although the diagnostic gold standard of GCA is a TAB, they can be time-consuming and mildly invasive with risk of damage to the facial nerve, inadequate tissue sampling, and repeat biopsy, often in patients on multiple anti-coagulants. Despite these uncertainties, taking into account a positive TAB along with common presenting signs in the diagnosis of GCA has been shown to have a 93% sensitivity in the general population when performed at an adequate length (>1.5 cm). Therefore, much attention has been paid to maximizing the yield on diagnostic studies by identifying the most specific and sensitive clinical criteria. Although well characterized in the general population, the clinical indications and accuracy of TABs in the diagnosis of GCA in a veteran population remain poorly understood. We performed retrospective analysis on all patients with a diagnosis of GCA or history of TAB seen within the national VA health care system, in order to identify differences in demographics, risk factors, associated systemic conditions, and biopsy yield in the veteran GCA population. We identified several clinical factors associated with positive TAB results including: age at procedure, male gender, aortic aneurysm dissection, polymyalgia rheumatica, and elevated platelets, ESR, and CRP. Our study limitations include the retrospective nature of the study, significantly higher male to female distribution (which was expected in our veteran population), and incongruent diagnostic coding of GCA within the VINCI database. Despite the benefits of the large amount of patient data within the VINCI database, more subjective data such as patient's reported symptoms and text-based pathology reports were difficult to query and assess without individual chart review. For example, an early difficulty we found was in defining a true diagnosis of GCA. Diagnosis codes for GCA were unreliable as patients would often have preemptive diagnoses in their chart despite a negative or incomplete TAB. We attempted to eliminate these patients from analysis by requiring a new diagnosis of GCA within 2-8 after the procedure was complete. Future directions include looking further at other factors that may be associated with TAB findings as well as seeing if having multiple of these factors may affect overall likelihood of having a positive biopsy. This work comprises the largest database in existence of patients with GCA in the American health care system, and serves as a model for future epidemiologic studies of rare diseases in neuro-ophthalmology.

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Conclusions *(2-3 summary sentences)*

GCA is the most common primary systemic vasculitis in adults, however, the indications and accuracy of TABs in the veteran population remain poorly understood. Our work comprises the largest database of veteran patients with GCA and found several clinical factors associated with positive temporal artery biopsy, including: age, male gender, aortic aneurysm dissection, polymyalgia rheumatica, and elevated platelets, ESR, and CRP.

References *(JAMA style format)*

1. Ing EB, Wang DN, et al. Systematic Review of the Yield of Temporal Artery Biopsy for Suspected Giant Cell Arteritis. Neuroophthalmology. 2018 Jun 19;43(1):18-25.

2. United States Census Bureau. "Veteran Status – Census Bureau Table."Explore Census Data.

3. Selby LD, Park-Egan BAM, Winges KM. Temporal Artery Biopsy in the Workup of Giant Cell Arteritis: Diagnostic Considerations in a Veterans Administration Cohort. J Neuroophthalmol. 2020; 40(4):450-456.