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Temporal Artery Biopsy Debate: Positive TAB Result Prolongs Steroid Use in Giant Cell Arteritis

Brett Ponich, MD*†
Ann-Sophie Lafreniere, MD*†
Rebecca Hartley, MD, MSc, FRCSC†
Claire F. Temple-Oberle, BA, MD, MSc, FRCSC*†

Background: Temporal artery biopsy (TAB) in diagnosing giant cell arteritis has been criticized due to surgical risks, a high false negative rate, and redundant information when patients already met American College of Rheumatology criteria. The objective of this study was to investigate TAB's impact on steroid treatment duration.
Methods: A retrospective chart review garnered patient demographics, symptoms, comorbidities, and steroid treatment duration in patients undergoing TAB at a single center. Steroid treatment was compared between TAB+ and TAB - patients.
Results: One hundred seven patients undergoing TAB were included. Patients were predominantly women (70.1%) with a median age of 74 years (46 -91). Of 107 TAB results, 74 (69.2%) were negative, 23 (21.5%) were positive, and 10 (9.3%) were found to be indeterminate. In TAB+ patients, the mean erythrocyte sedimentation rate was not significantly different than TAB - patients (60.2 versus 43.7, $P = 0.45$), nor was the median C-reactive protein (38.8 versus 18.1, $P = 0.17$). Regarding steroid use, both TAB+ and TAB - patients had a similarly high rate of prebiopsy steroid initiation (82.6% versus 70.3%, $P = 0.32$). More TAB+ patients remained on steroids at 6 weeks (95.0% versus 57.4%, $P = 0.004$), 6 months (95% versus 37.7%, $P < 0.001$), 1 year (65.0% versus 31.1%, $P = 0.024$), and 18 months (50.0% versus 19.7%, $P = 0.045$). By 2 years, the difference no longer met significance (35.0% versus 14.8%, $P = 0.12$). $P = 0.12$).
Conclusion: TAB positivity does seem to influence maintenance of steroids up to 18 months after biopsy. *(Plast Reconstr Surg Glob Open 2022;10:e4652; doi: 10.1097/GOX.0000000000004652; Published online 22 November 2022.)*

INTRODUCTION

Temporal artery biopsy (TAB) is currently the standard test to diagnose giant cell arteritis (GCA) due to its near 100% specificity; however, this procedure has a sensitivity of 15%–40%[1,2] and has important, and likely underreported, surgical complications.[3] A recent survey of Canadian plastic surgeons found that nearly half (42%) of respondents reported having had a complication when performing TAB.[4] Complications reported were bleeding, dehiscence, infection, alopecia, and facial nerve injury.[4]

To diagnose GCA clinically, the American College of Rheumatology (ACR) has criteria that have a reported sensitivity of 93% and specificity of 91%.[5] To meet cutoff for GCA, three of the five following criteria must be met: an increased erythrocyte sedimentation rate (ESR) (≥50 mm/h by Westergren method), age greater than 50 years, temporal artery tenderness, new-onset localized headache, and a positive TAB result.[5] TAB is still a commonly performed procedure, even when three of the ACR criteria have already been met, that is, even when the diagnosis of GCA has been met by the ACR criteria. In this scenario, the utility of TAB is unclear, especially in light of newer noninvasive ways to analyze the temporal artery, such as high-resolution ultrasound.[6,7]

GCA is an immune-mediated vasculitis that can result in blindness if left untreated.[3,8,9] Corticosteroids remain first-line treatment and 40–60 milligrams (mg) daily is recommended.[10] Stopping steroids within 6 months is associated with a high rate of recurrence, up to 90%.[9,11] Often, length of treatment can last 1–2 years. A recent systematic review has called into question whether the TAB result influences long-term steroid treatment.[12] For instance,

*From the *Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada; and †Section of Plastic and Reconstructive Surgery, University of Calgary, Calgary, Alberta, Canada.*

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63% of patients were maintained on long-term steroids despite a negative TAB result.

The objective of our study was to determine whether at our center, steroid treatment duration differed between TAB positive (TAB+) and TAB negative (TAB–) patients.

METHODS

A retrospective chart review was performed on patients undergoing TAB by plastic surgeons in Calgary, Alberta, from 2008 to 2020 after ethics approval was obtained (REB20-0122). Data collected included patient demographics, symptoms, and comorbidities; time to biopsy; TAB result and length; as well as steroid dose and treatment duration. Data were collected from paper charts in medical records at Foothills Medical Centre as well as electronic charts. In patients where ESR results were missing, C-reactive protein (CRP), if present, was used as a surrogate. A CRP score of greater than 26.9 mg/L was used as a substitute to satisfy the ACR criteria.[13] ACR scores were calculated for each patient based on the collected data. Duration of steroid treatment was categorized into groups using 6 weeks, 6 months, 1 year, 18 months, and 2 years as cutoffs. Steroid treatment was considered long term if treatment was received for longer than 6 weeks.

Of note, the main outcome, TAB result, was categorized as positive, negative, or indeterminate. Statistical analyses were performed using chi-squared test or Fisher exact test for dependent categorical variables; Kruskal-Wallis for continuous, nonparametric-dependent variables (ie, ESR and CRP); and one-way ANOVA for continuous, parametric-dependent variables. Statistical significance was set with a P value of less than 0.05.

RESULTS

Patient Demographics

One hundred seven TAB pathology reports with sufficient detail on indication, pathology, and duration of steroid treatment comprised the study population.

Takeaways

Question: Does temporal artery biopsy (TAB) impact steroid treatment duration in patients with suspected giant cell arteritis (GCA)?

Findings: A retrospective chart review of 107 patients undergoing TAB was performed. Patients with negative TAB had a shorter duration of steroids for the first 18 months of treatment; however, foregoing TAB could be considered if the ACR criteria for GCA have already been met.

Meaning: TAB result appears to affect short-term treatment; however, its utility remains in question.

Seventy-five TABs (70.1%) were performed on female patients, and median age was 74 years. Seventy-four TAB results were negative for GCA (69.2%), while 23 were positive (21.5%). Ten (9.3%) pathology reports resulted in an indeterminant result. The mean length of biopsy specimen was 1.70 cm. Fifty-four biopsies were taken from the right side, while 53 were taken from the left. In terms of comorbidities, 18 patients had previously been diagnosed with polymyalgia rheumatica, and 25 had hypothyroidism (Table 1).

GCA Symptoms

The most common GCA symptom was headache, followed by temporal tenderness, vision abnormality, and jaw claudication (Table 2). The mean ESR (mm/h) was 60.2 for the TAB+ group, 43.7 for the TAB– group, and 58.6 for the indeterminate group, while the median CRP (mg/L) was 38.8 versus 18.1 versus 20.9, respectively (Table 3). There was no significant difference between TAB+ and TAB– ESR or CRP ($P = 0.45$ and $P = 0.17$).

ACR

Eighty-nine TABs reported an ESR prior to TAB and were used to calculate mean ACR scores. The TAB+ patients had a similar mean prebiopsy ACR score compared with

Table 1. Temporal Artery Biopsy Patient Demographics and Comorbidities

Demographics and Comorbidities	TAB Positive %	Indeterminate (%)	TAB Negative (%)	Total
Number of patients	23 (21.5)	10 (9.3)	74 (69.2)	107
Mean age (y)	75	72	73	73
Female	13 (17.3)	9 (12.0)	53 (70.7)	75
PMR	6 (33.3)	3 (16.7)	9 (50.0)	18
Osteoporosis	4 (22.2)	0 (0.0)	14 (77.8)	18
Hypothyroid	5 (20.0)	1 (4.0)	19 (76.0)	25
Diabetes	2 (20.0)	2 (20.0)	6 (60.0)	10
Thromboembolic event	0 (0.0)	1 (1.0)	10 (90.9)	11

PMR, polymyalgia rheumatica.

Table 2. Common GCA Symptoms and Prebiopsy Management of TAB Patients

Symptoms and Biopsy Management	TAB Positive (%)	Indeterminate (%)	TAB Negative (%)	Total
Headache	16 (21.6)	6 (8.1)	52 (70.3)	74
Jaw claudication	11 (36.7)	5 (16.7)	14 (46.7)	30
Temporal tenderness	10 (22.2)	4 (8.9)	31 (68.9)	45
Vision abnormalities	12 (27.9)	4 (9.3)	27 (62.8)	43
Received prebiopsy steroids (% of n)	19 (82.6)	7 (70.0)	52 (70.3)	78

Table 3. Management and ACR Scores of TAB Patients

Management and Scores	TAB Positive (%)	Indeterminate (%)	TAB Negative (%)	Total Group
N	23	10	74	107
Mean prebiopsy steroid dose (mg)	57.2	45.6	40.4	33.4
Mean postbiopsy steroid dose (mg)	60	50	63	61.2
Median duration of prebiopsy steroids (d)	2	2	2	2
Median onset of symptoms to biopsy (d)	21.5	20	14	18.5
Mean ESR (mm/h)	60.2	58.6	43.7	48.3
Median CRP (mg/L)	38.8	20.9	18.1	45.2
Prebiopsy mean ACR score (using ESR)	2.71	2.56	2.38	2.48
Prebiopsy mean ACR score (using CRP)*	2.61	2.33	2.35	2.38

*CRP of 26.9 mg/L is equivalent to ESR 50.

TAB– patients (2.71 versus 2.38). The indeterminate group mean prebiopsy ACR score was 2.56. In lieu or in addition to ESR, 84 TABs reported CRP. Using CRP as a substitute for ESR, the prebiopsy mean ACR score was higher in the TAB+ group (2.61 versus 2.35). The indeterminate score was 2.33. Ten TAB+ patients (43.5%), 30 TAB– patients (40.5%), and five TAB indeterminate patients (50.0%) had an ACR score greater than or equal to 3 when calculating with ESR, while 10 (43.5%) TAB+, 27 (36.5%) TAB–, and four (40.0%) TAB indeterminate patients had an ACR score greater than or equal to 3 when calculating with CRP.

Of the 30 TAB– patients who met ACR criteria prebiopsy, 18 (60.0%) went on to have long-term steroid treatment. All TAB+ patients went on to long-term steroid treatment, regardless of ACR score.

Steroid Use

Seventy-eight patients received corticosteroids prior to biopsy (Table 2). The mean daily prebiopsy steroid dose was 57.2 mg in patients who later received a TAB+ result, 40.4 mg in the TAB– patients, and 45.6 mg in the TAB indeterminate patients. There was no difference in prebiopsy steroid initiation in the patients who were ultimately found TAB+ than TAB– (95.0% versus 83.9%, $P = 0.32$). Seven (70%) indeterminate results were treated with prebiopsy steroids.

The postbiopsy steroid dose was similar whether the patient was TAB+ or TAB– (60.0 versus 61.6 mg, respectively); however, TAB indeterminate was lower (50.0 mg).

Steroid Duration

More TAB+ patients than TAB– patients were treated with steroids at 6 weeks (95% versus 57.4, $P = 0.004$), 6 months (95% versus 37.7%, $P < 0.001$), 1 year (65.0% versus 31.1%, $P = 0.02$), and 18 months (50.0% versus 19.7%, $P = 0.04$). Thirty-five percent of TAB+ patients were still being treated at 2 years; however, this was not significantly different than TAB– patients (35.0% versus 14.8%, $P = 0.12$) (Fig. 1). (**See appendix, Supplemental Digital Content 1**, which displays steroid treatment duration, **http://links.lww.com/PRSGO/C259**.)

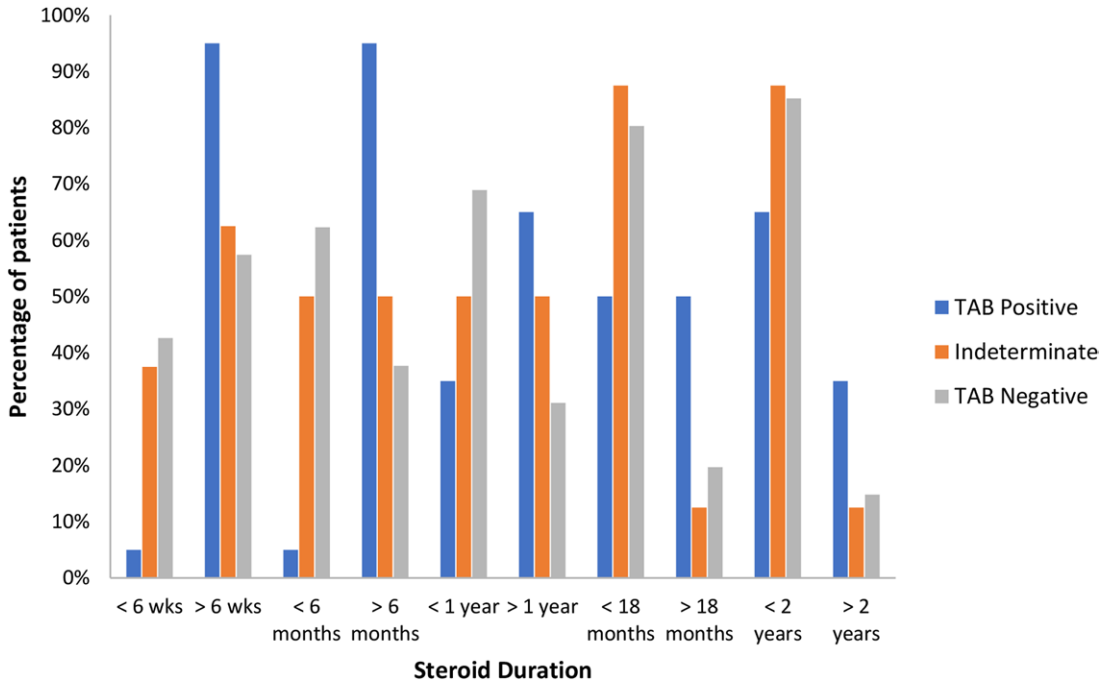

Fig. 1. Steroid treatment duration.

Referring Specialty

Rheumatology was the most common specialty referring patients to plastic surgeons (5 TAB+/41 referrals) for TAB, followed by neurology (6/23), emergency medicine (5/13), ophthalmology (2/5), internal medicine (1/4), and family medicine (2/4). Specialties were grouped into primary care (emergency + family), internal medicine (internal medicine + rheumatology), and specialty (neurology + ophthalmology), and compared using a Fisher exact test. There was no significant difference between referring specialty and TAB result ($P = 0.17$).

Biopsy Length

There was no difference in the mean biopsy specimen length among the TAB +, TAB–, and indeterminant groups (1.79, 1.67, 1.74 cm, $P = 0.23$). This suggests that biopsy length did not impact TAB results in this study.

DISCUSSION

We performed a retrospective review of TABs performed in Calgary by plastic surgeons and found that TAB+ patients were more likely to be continued on steroids for the first 2 years. However, the positivity rate remained low, and a notable portion of results were indeterminant. Physicians must weigh the costs and benefits of putting a patient through a surgical procedure, with a good chance the result will be negative or indeterminant. Furthermore, if the biopsy returns as negative, it is likely to be counted as a false negative.[1]

TAB Positivity Rate Was Low

The rate of TAB positivity was 21.5%, which is similar to previous studies[15–18] and highlights that even in patients presenting with symptoms of GCA, less than one-quarter have a positive TAB. This starts to raise the question about the utility of TAB, especially considering the strong sensitivity and specificity of the ACR criteria. Due to the low sensitivity of TAB (15%–40%[1,2]), using TAB to rule out GCA in patients with low pretest probability is inappropriate. Instead, clinical assessment may be more reliable to diagnose GCA. The presence of skip lesions might explain the reported low TAB positivity rate[18]; however, the average biopsy specimen length in our study was within the recommended range of 1.5–2.0 cm.[19]

Indeterminate Result Was Common

Nearly one in ten pathology reports resulted in an indeterminate result. Pathology reported changes to the internal elastic lamina of the temporal artery but could not comment on diagnosis of GCA. This offers a unique challenge for physicians interpreting these results as there is no definitive diagnosis. Prebiopsy steroid initiation and dose for TAB indeterminate patients, as well as postbiopsy treatment duration, was similar to TAB– patients. Half of TAB indeterminate patients remained on steroids past 1 year, suggesting that physicians would rather treat than risk missing the diagnosis.

Receiving Prebiopsy Steroids Did Not Correlate to TAB Result

There was no relationship between receiving corticosteroid therapy prior to biopsy and a TAB+ result ($P = 0.18$). The majority of patients were started on steroids before TAB regardless of their clinical presentation, which may suggest that physicians have a low threshold to prophylactically start steroids due to the risk of vision loss.[8]

A Positive TAB Was Correlated with a Longer Duration of Corticosteroid Therapy

TAB+ patients were maintained on steroids longer than TAB– patients, which was in contrast to a recent systematic review.[12] Of the TAB+ patients, only one received steroids for less than 6 weeks, suggesting physicians trust a positive TAB. This is consistent with the literature[20] and is in accordance with treatment guidelines[21] as the specificity of TAB nears 100%.[1] It is also possible that TAB+ patients may present more severely and, therefore, are more likely to be continued on steroids. A TAB– result was linked to a shorter steroid treatment duration; however, more than half (57.4%) of TAB– patients remained on steroids long term, reflecting the hesitancy of physicians to rely on a TAB– result. Similarly, other groups found that up to 87%[17,19] of TAB– patients were kept on long-term steroids.

The benefit of a TAB+ result may be in bolstering the physician's comfort to commit a patient to long-term steroid treatment, which carries important associated side effects. However, a TAB– result creates a dilemma for the physician. The significant portion of patients meeting the ACR criteria for diagnosis who still went on to biopsy suggests that a high pretest probability for GCA, and a negative TAB creates a conundrum for clinicians whether or not to continue steroid treatment. While there was a significant difference between TAB result and continuing steroids at 6–18 months, there was not a difference at 2 years. Half of patients with a TAB– result in this study continued on steroid management despite their negative result. Therefore, while physicians appear to trust a TAB+ result, they may be less inclined to trust a negative result for long-term steroid management. There may also be additional factors influencing physicians such as high ACR scores; however, TAB– mean ACR was below the threshold required to meet criteria. It is also plausible that patients with a TAB– biopsy also present less severely and, therefore, are treated for a shorter duration.

ACR Was Similar between Groups But Could Still Prove Valuable

Mean ACR scores between positive and negative groups were similar, which was again in contrast to the previously mentioned systematic review.[12] Nearly half of the TAB+ patients had a prebiopsy ACR score greater than or equal to 3. The utility of TAB in this context would not be diagnostic and may unnecessarily exposed these patients to surgical risks. Additionally, nearly half of TAB– patients also met ACR criteria for GCA diagnosis prior to biopsy, and many of these patients went on to have long-term steroid treatment despite their negative result. In both of these instances, TAB provided no additional management guidance.

Rheumatology Made Most Referrals for TAB

Rheumatologists were the main referral source for TAB, which was likely due to the patient population they are exposed too. However, only 12% of rheumatologist referrals in our study resulted in a positive TAB. While other studies have shown rheumatologists to have a higher positivity rate when requesting TAB compared with nonrheumatologists,[22] this was not the case in our study.

There was no statistical difference in TAB result between specialties when grouped by primary care (emergency medicine and family medicine), internal medicine and rheumatology, and specialists (neurology and ophthalmology) ($P = 0.17$).

Limitations and Strengths

This study was limited by its retrospective nature and small sample size. Some patients who were followed by family physicians and had treatment information recorded on different systems used by private clinics which our team did not have access to. Consequently, these patients were not included, which may have resulted in selection bias.

Strengths of our study include rigorous data collection of secondary outcomes such as patients' symptoms and imaging and inclusion of the indeterminate TAB result.

CONCLUSIONS

The utility of TAB remains in question. In this study, a negative TAB result impacted patient care by decreasing the duration of steroids for the first 18 months of treatment. However, in patients who already met ACR criteria for diagnosis of GCA, TAB could be reconsidered, as there was little impact of the result on patient management.

Claire F. Temple-Oberle, BA, MD, MSc, FRCSC
Foothills Medical Centre
1331 29 st NW
Calgary, AB T2N 2T9
E-mail: claire.temple-oberle@albertahealthservices.ca

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