

# Questioning the Utility of Temporal Artery Biopsy in Giant Cell Arteritis: A Negative Biopsy May Facilitate Decision-making

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

**Background:** Plastic surgeons are frequently consulted to perform temporal artery biopsy (TAB), even though patients meet the American College of Rheumatology diagnostic criteria for giant cell arteritis (GCA) and are already treated. This study aimed to analyze the impact of TAB on steroid duration in patients undergoing TAB.

**Methods:** We undertook a prospective study of adult patients undergoing TAB for GCA in Calgary. Consecutive, multicenter recruitment was performed over 2 years. Primary outcomes included initiation or discontinuation and duration of corticosteroids.

**Results:** Twenty-one TABs were performed in 20 patients. Nineteen percent of TABs were positive, and 71.4% negative. In 9.5% of patients, accidental sampling of a vessel other than the superficial temporal artery occurred. Fifty-two percent of patients received steroids before TAB, of which the mean duration was 8.0 days for TAB+ (positive temporal artery biopsy result) patients and 8.4 days for TAB- (negative temporal artery biopsy result;  $P = 0.22$ ) patients. Before TAB, the American College of Rheumatology score was 2.5 for TAB+ patients and 2.4 for TAB- ( $P = 0.74$ ). Postbiopsy, the American College of Rheumatology score was 3.5 for TAB+ patients (therefore reaching diagnostic threshold of 3) but remained 2.4 for TAB- ( $P = 0.02$ ). TAB+ patients were treated for 352.3 days, whereas TAB- patients for 16.7 days ( $P = 0.29$ ). Complications were more likely with long-term (>6 weeks) steroids ( $P = 0.17$ ).

**Conclusion:** In patients with a low suspicion of GCA, a negative TAB helps bolster physician confidence and leads to a shorter steroid duration. (*Plast Reconstr Surg Glob Open* 2023; 11:e5035; doi: 10.1097/GOX.0000000000005035; Published online 9 June 2023.)

## INTRODUCTION

Temporal artery biopsy (TAB) remains the gold standard to diagnose giant cell arteritis (GCA) due to its near absolute specificity.<sup>1</sup> The American College of Rheumatology has outlined a set of five criteria to help clinicians diagnose GCA: (1) age at onset 50 years or older; (2) a new headache; (3) temporal artery abnormality such as tenderness to palpation or decreased pulsation; (4) erythrocyte sedimentation rate 50 mm/h or more; (5) abnormal artery biopsy showing vasculitis with

mononuclear cell or granulomatous inflammation. The presence of any three criteria out of five yields a sensitivity of 93.5% and a specificity of 91.2%.<sup>2</sup> Notably, one of the criteria is a positive TAB result, although this is not required to make the diagnostic cutoff.<sup>2</sup> Treatment is routinely initiated prior to performing a TAB because if left untreated, this autoimmune vasculitis can result in vision loss.<sup>3</sup> A TAB is not without consequences: its sensitivity is only 15%–40%,<sup>4</sup> and 42% of Canadian surgeons have had postoperative complications in their practice.<sup>5</sup> In the light of this information, we questioned the utility of performing TAB. We surveyed Canadian plastic surgeons on their perceived contribution of TAB and its influence on the management of patients with

From the Division of Plastic and Reconstructive Surgery, University of Calgary, Calgary, Alberta, Canada.

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suspected GCA, and 40% questioned whether the TAB result contributed to changes in corticosteroid duration and dose.<sup>5</sup> After this survey, our team performed a systematic review showing that 63% of patients remained on steroids despite a negative TAB result.<sup>6</sup> We then retrospectively reviewed 107 patients who underwent TAB within our center and found signal of utility in that patients with a positive TAB result (TAB+) remain on steroids for a longer duration than patients with a negative TAB result (TAB-) (65% TAB+ at 1 year, versus 31% TAB-,  $P = 0.02$ ).<sup>7</sup>

The objective of this study was to triangulate these intersecting and conflicting findings in a prospective analysis of the impact of TAB on the duration of steroid treatment between TAB+ and TAB- patients within our institution.

## METHODS

A prospective cohort study following the STROBE guidelines for cohort studies<sup>8</sup> was conducted in Calgary, Alberta, Canada, from March 2020 to April 2022 inclusively. (See appendix, Supplemental Digital Content 1, which shows a checklist of items that should be included in reports of cohort studies. <http://links.lww.com/PRSGO/C603>.) Ethics approval was obtained from our institution (REB20-0122). Consecutive adult patients over 18 years of age undergoing a TAB to rule in or out a diagnosis of GCA performed by the plastic surgery team were eligible. Patients meeting inclusion criteria who consented to participate were included in the study.

The primary outcomes were initiation or discontinuation, and duration of corticosteroid therapy. We considered a difference in treatment duration clinically significant if the TAB+ and TAB- groups differed by 4 weeks or more (response to treatment allows for steroid tapering after 2–4 weeks<sup>9</sup>). Data collection included age, sex, comorbidities, length of biopsy (in millimeters), time to biopsy (in days), presenting symptoms (ie, jaw claudication, headache, scalp tenderness), presence and duration of steroid treatment before TAB, dose of prebiopsy steroids, mean time to biopsy after symptom onset, mean follow-up period, and prebiopsy American College of Rheumatology (ACR) classification criteria for GCA. The timeline of events, namely when corticosteroid therapy was started and/or stopped, and the biopsy date were recorded. Data were collected prospectively using a form completed at the time of biopsy, and ended in July 2022. TAB results and details of GCA management were obtained via patient electronic medical records. Of note, physicians managing the corticosteroid treatment were not blinded to our investigation.

An independent  $t$  test with a  $P$  value less than 0.05 was used to determine if there was a significant difference in the duration of steroid treatment between TAB+ and TAB- patients.

In Calgary, TABs are performed in a minor surgery setting under local anesthesia. The superficial temporal artery (STA) is identified with a Doppler and marked. An incision is made over the STA through skin and

## Takeaways

**Question:** Does temporal artery biopsy impact the management of patients with suspected giant cell arteritis?

**Findings:** A negative temporal artery biopsy helps bolster physician confidence and leads to a shorter steroid duration.

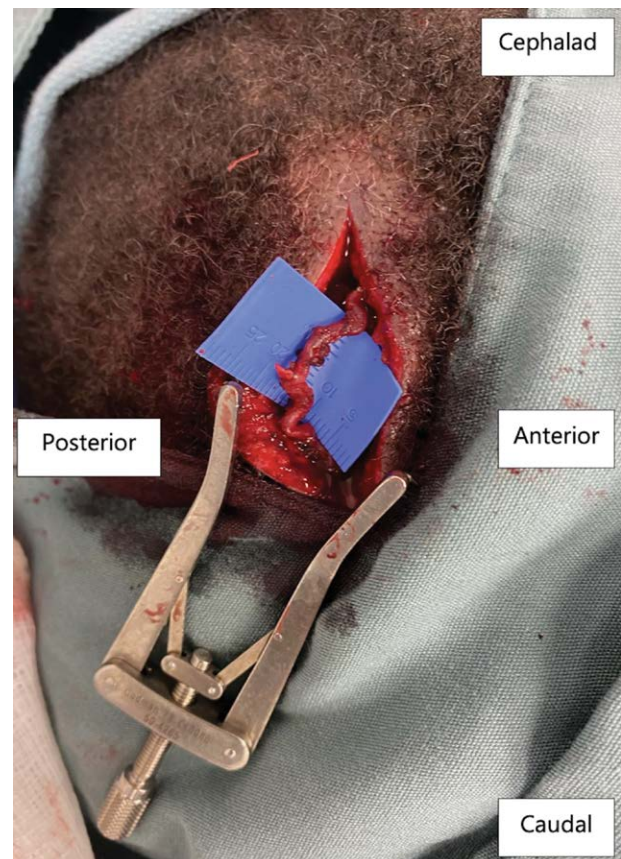
**Meaning:** To better balance risks related to surgical complications and diagnostic benefits, we suggest performing temporal artery biopsy only in patients with a prebiopsy American College of Rheumatology score less than 3.

subcutaneous tissue. Dissection is carried to the superficial temporoparietal fascia to identify the STA (Fig. 1). At minimum, a 2-cm-long segment is resected and sent to the laboratory for further pathological analysis. Hemostasis is achieved, and after thorough irrigation, the skin is closed with dissolvable sutures.

## RESULTS

### Patients Were Older Women

A total of 20 patients were recruited, for a total of 21 TABs, between October 2020 and March 2022 from



**Fig. 1.** Identification and dissection of the STA.

**Table 1. Patient Characteristics**

Patient	Age	Gender	Presenting Symptom	TAB Result
1	73	Man	Visual loss	Positive
2	58	Woman	Visual loss	Negative
3	55	Man	N/A	Negative
4	42	Man	N/A	Negative
5	87	Woman	N/A	Negative
6	70	Woman	Headache	Positive
7	81	Woman	Jaw claudication	Negative
8	57	Woman	Headache	Negative
9	94	Woman	Visual loss	Negative
10	58	Man	Headache	Negative
11	74	Man	Visual loss	Positive
12	61	Woman	Headache	Negative
13	79	Woman	Headache	Failed
14	56	Woman	Headache	Negative
15	87	Man	Jaw claudication	Negative
16	81	Man	Headache	Negative
17	79	Woman	Headache	Failed
18	73	Woman	Headache	Negative
19	73	Woman	Headache	Negative
20	73	Man	Visual loss	Negative
21	87	Man	Visual loss	Positive

N/A, not available.

multiple centers in Calgary. Patient characteristics are presented in Table 1. The mean age was 71.3 years old. TAB+ patients were slightly older than TAB- (76 years old versus 69,  $P = 0.39$ ). The mean age of patients with a failed biopsy (f-TAB) was 79. Fifty-two percent of patients were women.

#### Breakdown of TAB Results Showed a Low Positivity Rate

Nineteen percent ( $n = 4$ ) of TABs performed were positive (TAB+), 71.4% ( $n = 15$ ) were negative (TAB-), and 9.5% ( $n = 2$ ) failed (f-TAB). This last group represents patients in whom accidental sampling of a vessel other than the STA led to inconclusive pathological analysis. Variables of interest according to TAB result are presented in Table 2. Given the small sample size, f-TAB patients were excluded from further data analysis.

#### Visual Changes Were More Common in Patients with Positive Biopsy

The time between the onset of symptoms and biopsy was 35.5 days in TAB+ and 19.3 days in TAB- patients ( $P = 0.96$ ). In TAB+ patients, the chief complaint at the time of initial presentation was visual changes in 75.0% of patients and headache in 25.0%. None of the TAB+ patients had jaw claudication as onset symptom. In TAB- patients, the chief complaint at the time of initial presentation was visual changes in 20%, headaches in 87.5%, and jaw claudication in 15.4%.

#### Most Patients Received Corticosteroid Therapy before TAB

Fifty-two percent of patients received corticosteroids before the biopsy. The mean duration of steroid therapy received before the biopsy was 8.0 days for TAB+ patients and 8.4 for TAB- ( $P = 0.22$ ).

**Table 2. Variables of Interest according to TAB Positivity, with Statistical Analysis**

Variables	TAB+, Mean (SD)	TAB-, Mean (SD)	<i>P</i>
N	4	15	0.012
Age	76 (7.5)	69.1 (15)	0.390
Female/male sex	1/3	9/6	0.303
Duration of prebiopsy corticosteroids (d)	8 (7.1)	8.4 (19.4)	0.216
Surgical length of TAB specimen (mm)	22.8 (8.7)	13.8 (3.7)	0.005
Time from onset of symptoms to TAB (d)	35.5 (49)	19.3 (19.8)	0.955
Treatment duration (d)	352.3 (202.5)	16.7 (30.9)	0.001
Prebiopsy ACR score	2.5 (0.6)	2.4 (0.7)	0.738
Postbiopsy ACR score	3.5 (0.6)	2.4 (0.7)	0.019
Follow-up duration (d)	285 (226)	155 (161)	0.365

ACR, American College of Rheumatology; mm, millimeters; SD, standard deviation.

**TAB Specimens Were Longer with Positive Biopsy**

Surgical length of the biopsy specimen was 22.8mm in TAB+ and 13.8mm in TAB- patients ( $P = 0.01$ ).

**A Positive Biopsy Helped Meet Diagnostic Threshold of ACR Criteria**

Before TAB, the ACR score was 2.5 for TAB+ patients and 2.4 for TAB- ( $P = 0.738$ ). Postbiopsy, the ACR score was 3.5 for TAB+ patients, but remained 2.4 for TAB- ( $P = 0.02$ ). TAB+ patients were followed up for 285 days, whereas TAB- patients, for 155 days ( $P = 0.37$ ).

**TAB+ Patients Remained on Corticosteroids Longer than TAB-**

TAB+ patients were treated for up to 352 days and TAB- patients for 17 days ( $P = 0.29$ ) (Fig. 2).

**Complications Arose from Long-term Steroids**

Complications related to steroid therapy amongst TAB+ patients were the following: adrenal insufficiency ( $n = 1$ ), palpitations ( $n = 2$ ), dyspepsia ( $n = 1$ ), difficulty sleeping and irritability ( $n = 1$ ), and Pneumocystis jiroveci pneumonia ( $n = 1$ ). A long-term course ( $>6$  weeks) of steroids was associated with a higher incidence of complications, compared with a short-term course ( $P = 0.17$ ).

Procedural issues included sampling of the wrong blood vessel ( $n = 2$ ). There was no documented surgical complication related to TAB.

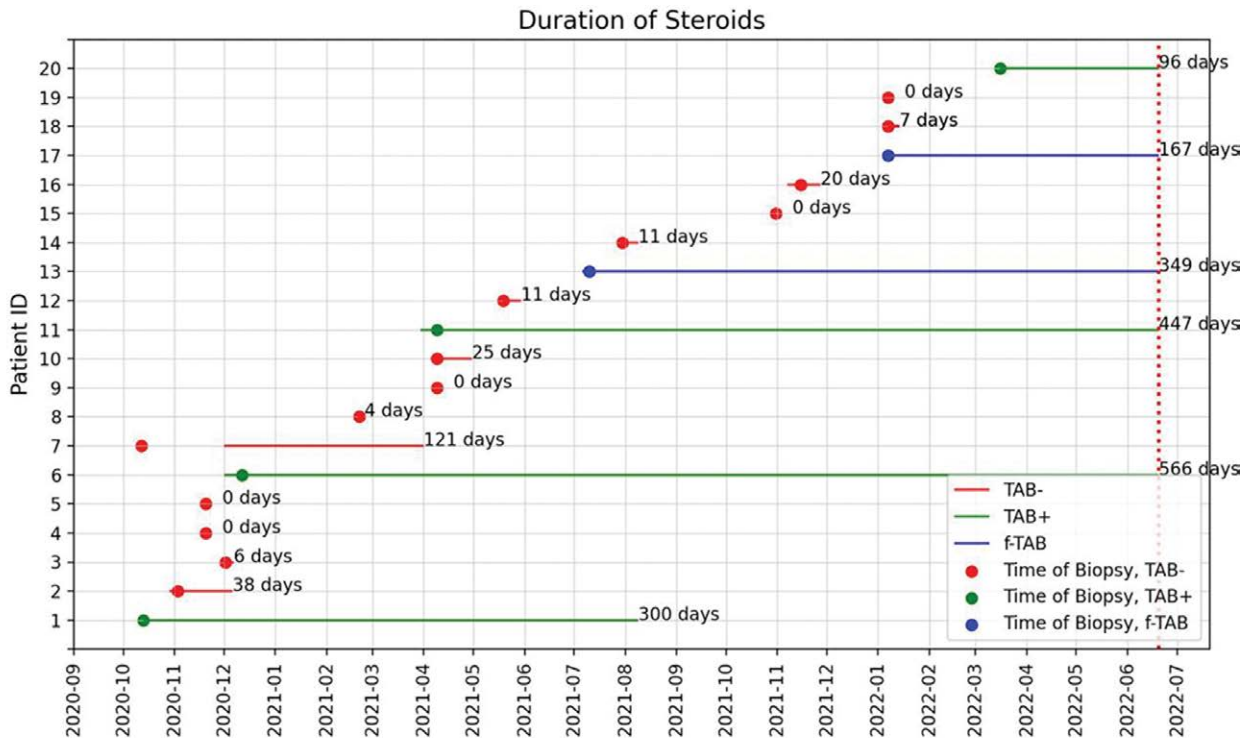
**Failed Biopsies**

Patient characteristics who had a failed biopsy (f-TAB) are reported in Table 3. The time between the onset of symptoms and biopsy was 22 days in f-TAB. Fifty percent of f-TAB patients presented with headache, and 50% with visual changes. The mean duration of steroid therapy received

**Table 3. Variables of Interest for f-TAB**

Variables	f-TAB
N	2
Age	79
Female sex	2
Male sex	0
Duration of prebiopsy corticosteroids (d)	3.5
Surgical length of TAB specimen (mm)	9
Time from onset of symptoms to TAB (d)	22
Treatment duration (d)	258
Prebiopsy ACR score	2.5
Postbiopsy ACR score	2.5
Follow-up duration (d)	106

mm, millimeters; f-TAB, failed temporal artery biopsy.



TAB: temporal artery biopsy; TAB-: negative temporal artery biopsy; TAB+: positive temporal artery biopsy; f-TAB: failed temporal artery biopsy; ID: identification

**Fig. 2.** Duration of therapy based on TAB result.

before the biopsy was 3.5 days. Surgical length of the biopsy specimen was 9mm. The pre- and postbiopsy ACR scores were 2.5. Patients were treated for up to 106 days. Given the uncertainty of the diagnosis, these two patients were treated clinically and were still receiving ongoing steroids when this article was submitted. Interestingly, they both developed steroid-related complications, and were placed on methotrexate as an alternate treatment.

## DISCUSSION

We performed a multi-centered, prospective review of TABs performed in Calgary by plastic surgeons and found that TAB- patients were more likely to have their corticosteroids discontinued shortly following a negative biopsy result. We also found that the overall TAB positivity rate remained low (19.1%), and close to 10% of the TAB results were inconclusive, which is comparable to the reported literature.<sup>6,10-13</sup> Additionally, the average prebiopsy ACR scores were nondiagnostic; in other words, they did not reach the predictive threshold of 3.

### A Negative TAB Result Was Associated with a Shorter Duration of Corticosteroid Therapy

Our results demonstrated a significant difference in the total steroid therapy duration between TAB+ and TAB- patients, which is illustrated in [Figure 2](#). In this study, steroids were promptly discontinued after a negative biopsy result, whereas TAB+ patients were maintained on steroids for longer. As demonstrated by the steroid-related complications reported in this study, steroid therapy is not without consequences and prompt discontinuation of treatment in patients in whom they are not indicated is important. This contradicts our previous findings. We had previously postulated in a retrospective review of 107 patients in Calgary that physicians seemed less inclined to trust a negative TAB result, with 31% of patients remaining on steroids at 1 year despite a negative biopsy result.<sup>7</sup> TAB- patients included in this study had a similar prebiopsy ACR score (2.4) to those in the retrospective study (2.38), indicating similar severity in presentation. It is possible that rheumatologists within the Calgary area have changed their practice and moved toward a faster tapering of steroids in the light of new clinical evidence. Anecdotally, we have noticed that our previously published work on the topic has sparked discussions between the surgical team and the physicians requesting TABs about their utility and ultimate impact on management, which in some cases has resulted in choosing other diagnostic tests. This change in practice could have introduced a selection bias into the results.

Our results differ from previous literature: a retrospective study run by surgeons and comprising 44 patients with a TAB positivity rate of 15% concluded that the decision-making process with respect to corticosteroid therapy was not influenced by TAB results.<sup>14</sup> This discrepancy in management might be related to local practices. The authors highlighted that the most important factor in decision-making related to management was the patient history.

### A Positive TAB Allowed Patients to Meet the ACR Score Diagnostic Cutoff for GCA Diagnosis

In this study, the mean prebiopsy ACR scores were similar and all below the diagnostic cutoff of 3. A positive biopsy result contributed to making the score higher than the diagnostic cutoff in that patient group. TAB in this context was diagnostic and made the procedure worthwhile, which contrasts with our previous findings.<sup>6</sup> Additionally, TAB- patients did not meet the ACR criteria for GCA diagnosis prior to the biopsy, and most of these patients went on to have their steroid therapy discontinued following a negative TAB result. In this instance, a negative TAB seemed to provide physicians with additional evidence to discontinue therapy.

### Indeterminate Biopsies Are Not Benign

Technical issues, such as incorrect sampling of the STA in this case, do occur with any kind of surgery. A similar percentage of biopsies were indeterminate in our retrospective study.<sup>7</sup> This can lead to repeating the biopsy. In this case, the two f-TAB patients who received steroids for a substantial duration, comparable to TAB+ patients (167 and 349 days), developed steroid-related complications and required switching to a different immunosuppressing agent.

### TAB May Be Useful After All

Through our four-part research program, we have built a longitudinal conversation around the utility of TAB in establishing a GCA diagnosis. We have questioned whether it is appropriate that plastic surgeons should be noncritically thinking technicians who perform procedures of limited clinical utility. Our survey concluded that plastic surgeons were uncertain of TAB's contribution to the treatment and suggested that surgical complications may be more common than thought.<sup>5</sup> Our systematic review concluded that TAB had minimal impact on treatment.<sup>6</sup> Our retrospective review demonstrated that physicians committed to long term steroid treatment following a positive TAB, while a negative result created a conundrum around the decision to continue steroid treatment.<sup>7</sup> In our local context, steroids are usually discontinued with resolution of symptoms. This prospective study demonstrated a clinical benefit following a TAB result, prompting physicians to discontinue steroids rapidly. Before undertaking this program of research, our hypothesis was that TAB was of limited utility. Our use of various research methodologies demonstrated seemingly conflicting results as we are attempting to triangulate the appropriate role and utility for TAB. We propose a refined indication for TAB in patients with suspected GCA, where a TAB would only be performed in patients with a prebiopsy ACR score less than 3.

### Limitations and Strengths

This study was limited by its small sample size and single discipline referral inclusion. Strengths of our study included its prospective nature, rigorous data collection, and inclusion of the indeterminate TAB results.

## CONCLUSIONS

In this study, a negative TAB result shortens the duration of steroids for patients with suspected GCA. Despite potential overuse, physicians in our local context are more likely to discontinue steroid therapy after a negative TAB. To better balance risks related to surgical complications and diagnostic benefits, we suggest performing TAB only in patients with a prebiopsy ACR score less than 3.

**Claire F. Temple-Oberle, MD, MSc, FRCSC**

Foothills Medical Centre

1403 29 Street NW

Calgary, AB, T2N 2T9

Canada

E-mail: [claire.temple-oberle@albertahealthservices.ca](mailto:claire.temple-oberle@albertahealthservices.ca)

## DISCLOSURE

*Authors have no financial interest to declare in relation to the content of this article.*

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