Diagnostic and Management Trends of Giant Cell Arteritis: A Physician Survey

TIMOTHY J. DREHMER, DINESH KHANNA, RONALD J. MARKERT, and ROBERT A. HAWKINS

ABSTRACT. ***Objective.*** Opinions regarding diagnostic and treatment issues in giant cell arteritis (GCA) vary widely, yet few controlled trials exist to address these issues. Our objective was to compare espoused clinical policies regarding diagnosis and treatment of GCA among physicians involved in GCA care.

Methods. Utilizing professional society directories, US physicians were randomly selected to receive an 11-question survey. One hundred surveys were mailed to each of the following: family medicine, general internal medicine, general/vascular surgery, neurology, ophthalmology, otolaryngology, and rheumatology. Data were analyzed according to specialty and specialty group: rheumatology, medical specialties (family medicine, general internal medicine, neurology), and surgical specialties (general/vascular, ophthalmology, and otolaryngology).

Results. The percentage of surveys returned was 34.7%. Analysis was limited to the 79% participating in at least one aspect of GCA care. Greater than 90% of respondents believe that temporal arteritis biopsy (TA Bx) should be performed in all suspected cases of GCA. Eighty-five percent of rheumatology believe TA Bx is indicated even when pretest probability of GCA is high, compared to 65% of medical specialties ($p = 0.03$). Eighty percent of rheumatology believe steroid usage decreases the yield of TA Bx, compared to 62% of surgical specialties ($p = 0.04$). When initial TA Bx is negative, medical specialties (26%) and surgical specialties (31%) were more likely than rheumatology (5%) to decline contralateral biopsy, even if the contralateral side is symptomatic ($p = 0.04$ and 0.01, respectively).

Conclusion. Considerable variation exists regarding key elements of diagnosis and treatment in the evaluation of suspected GCA. The morbidity of GCA and the potential toxicity of therapy highlights the need for controlled trials to address these issues. (J Rheumatol 2005;32:1283–9)

Key Indexing Terms:
GIANT CELL ARTERITIS TEMPORAL ARTERY BIOPSY
PHYSICIANS' PRACTICE PATTERNS CORTICOSTEROIDS

Giant cell arteritis (GCA), is a well-recognized form of systemic vasculitis[1]. It usually affects persons older than 50 years of age, and may be associated with headache, jaw claudication, loss of vision and polymyalgia rheumatica[1,2]. The diagnosis is usually suspected on the basis of clinical presentation and the characteristic elevation of acute phase reactants. It is customarily confirmed by biopsy demonstrating the presence of characteristic granulomatous inflammation of the temporal arteries. Ideal management would establish or exclude the diagnosis with a high degree of certainty, minimize visual loss or other serious complication, and limit treatment toxicity.

Patients with suspected GCA may present to any of a number of medical specialists, including primary care physicians, surgeons, and rheumatologists. It is possible that the care of such a patient may vary, depending on the specialist to whom the patient presents. Despite much discussion in the medical literature regarding appropriate timing of temporal artery biopsy (TA Bx) in suspected cases and timing of corticosteroid use in relation to the biopsy, these issues remain controversial. The possibility of blindness or other serious complication relating to delays in diagnosis and treatment further raise the stakes. Unfortunately, there are few large controlled trials to address these important issues, and opinions regarding the appropriate approach to diagnosis and management of GCA vary widely.

The objective of our survey was to compare espoused clinical policies in the diagnosis and management of GCA held among physicians involved at some level in the care of GCA.

MATERIALS AND METHODS

Study subjects. Seven hundred physicians throughout the United States, representing 7 specialties (100 each), were randomly selected utilizing professional society directories. Specialties included family medicine, internal medicine, rheumatology, neurology, general and vascular surgery, ophthalmology, and otolaryngology. Respective society directories utilized included: American College of Rheumatology (1999), American Academy of Neurology (1998-99), American Academy of Ophthalmology (1999), and Official ABMS (American Board of Medical Specialties) Board Certified

From the Department of Internal Medicine, Division of Rheumatology, Wright State University School of Medicine, Dayton, Ohio, USA.

T.J. Drehmer, MD, Associate Professor of Medicine; D. Khanna, MD, MS, Clinical Instructor of Medicine; R.J. Markert, PhD, Professor of Medicine; R.A. Hawkins, MD, Associate Clinical Professor of Medicine.

Address reprint requests to Dr. T.J. Drehmer, Division of Rheumatology, Department of Internal Medicine, Wright State University School of Medicine, 128 East Apple Street/CHE second floor, Dayton, OH 45409. E-mail: timothy.drehmer@wright.edu

Accepted for publication December 20, 2004.

Medical Specialists (1999). Surveys were mailed to each selected physician. If there was no response after one month, a second survey was sent. Returned surveys were analyzed by specialty, with further analysis according to the following groups: rheumatology (Rheum), medical specialties [(MS) family medicine, internal medicine, and neurology]; and surgical specialties [(SS) general and vascular surgery, ophthalmology, and otolaryngology].

The survey. In our 11-question survey (Figure 1) the first 3 questions established the clinician's specialty, as well as their degree of involvement or lack of involvement in the care of patients with suspected GCA, including whether or not they performed TA Bx. Question 4 established variations in clinical policies regarding the utility of TA Bx, as a function of varying levels of disease probability. We asked participants to respond with Strongly Agree (SA), Agree (A), Disagree (D), or Strongly Disagree (SD). We combined those who responded SA with those who responded A, for statistical analysis. Similarly, D and SD responses were combined. In Question 5 clinicians were asked if they believed steroids lessen the yield (sensitivity) of TA Bx. Question 6 established the timing of a biopsy following initiation of corticosteroids, to avoid a diminishing effect upon the yield of the biopsy. Only respondents who answered affirmatively to Question 5 were asked to answer Question 6. Questions 7 and 8 established variations in clinical policies regarding the need for simultaneous, bilateral TA biopsy, versus unilateral or sequential biopsies. Respondents not favoring bilateral simultaneous TA Bx were asked to choose from among 3 additional options in the event TA Bx of the most symptomatic side was negative. These options were to: (1) perform contralateral TA Bx in all cases, (2) perform contralateral TA Bx only if this contralateral side is symptomatic, and (3) not perform a contralateral biopsy. Finally, questions 9 to 11 addressed timing, total daily dose, and dosage regimen of corticosteroids, in the treatment of GCA in a hypothetical 70 kg patient with GCA and visual symptoms.

The following simplifying assumptions were made:

1. Clinicians treat GCA with corticosteroids initially;
2. Physicians agreeing or strongly agreeing that TA Bx need not be obtained when GCA is very likely (defined as "at least 80% likely") would treat patients empirically for GCA;
3. Physicians agreeing or strongly agreeing that TA Bx need not be obtained when GCA is unlikely (defined as "not greater than 20% likely") would not treat patients empirically for GCA.
4. Regarding physicians who prefer unilateral or bilateral sequential TA Bx over bilateral simultaneous biopsies, we assumed that no physician would proceed with an additional biopsy when initial biopsy was positive for GCA.

Statistical analysis. Specialty group categorical variables were compared using Fisher's exact test. Specialty group continuous variables were compared by one-way analysis of variance with Tukey's multiple range test. Inferences were made at the 0.05 level of significance, with no adjustment for multiple tests.

RESULTS

Of the 700 surveys mailed, 243 were returned, for an overall response rate of 34.7%. Eight respondents indicated a specialty other than the 7 mentioned above, or failed to designate a specialty. These surveys were excluded from further analysis. The remaining 235 surveys were analyzed. Of the 235 respondents, 186 (79%) participated in the diagnosis and management of GCA. As shown in Table 1, 89% of Rheum, 71% of MS, and 82% of SS reported participation in at least one aspect of GCA care. We next evaluated the level of participation in managing GCA provided by each specialty group. Physicians who reported participating in at least one aspect of GCA care were further characterized

The Survey

1. Which of the following best describes your specialty? (check one)
   - ___ Family Medicine
   - ___ General Internal Medicine
   - ___ General Surgery
   - ___ Rheumatology
   - ___ Internal Medicine subspecialty other than Rheumatology
   - ___ Neurology
   - ___ Ophthalmology
   - ___ Otolaryngology
   - ___ Vascular Surgery
   - ___ Other (please specify)

2. How are you involved in the care of patients with giant cell arteritis (GCA), also known as temporal arteritis? (circle one)
   - A. I do not participate in the diagnosis or management.
   - B. I both diagnose and provide long term management of the patient. (*You may circle this whether or not you perform biopsies)*
   - C. I perform temporal artery biopsies but usually do not otherwise participate in diagnosis or management.
   - D. I provide long term management of the patient after the diagnosis is confirmed.
   - E. I refer patients with newly diagnosed GCA to other physicians for long term management.

3. Do you perform TA biopsies? (circle one)

   Yes No

4. Please circle your response to each of the following statements.

   SA – Strongly agree; A – Agree; D – Disagree; SD – Strongly disagree

   A. TA biopsy should be obtained in all suspected cases of GCA.
   SA A D SD

   B. TA biopsy need not be obtained when GCA is very likely (at least 80%).
   SA A D SD

   C. TA biopsy need not be obtained when GCA is unlikely (not greater than 20%).
   SA A D SD

5. Do you believe that steroids lessen the yield (sensitivity) of a TA biopsy?

   Yes No

   If yes, answer number "6". If no, skip number "6".

6. Within what time frame should a TA biopsy be performed following the initiation of steroids in order to avoid compromising the yield (sensitivity) of the biopsy? (circle the appropriate response)

   Days 1 2 3 4 5 6 7

   Weeks 1 2 3 4

   Months 1-3 4-6 7-9 10-12

7. Should simultaneous bilateral TA biopsies be performed when GCA is suspected?

   Yes No

   If yes, skip number '8'. If no, answer number '8'.

8. If TA biopsy of the most symptomatic side is negative, then (circle one)
   - A. Perform contralateral TA biopsies in all cases.
   - B. Perform contralateral TA biopsy, only if the contralateral side is symptomatic.
   - C. There is no need for contralateral TA biopsy.

9. Concerning the timing of corticosteroid therapy in the treatment of suspected GCA, treatment should be initiated. (circle one)
   - A. As soon as the diagnosis of GCA is considered, even if TA biopsy results are not available.
   - B. Treatment should be initiated after confirmation of GCA by TA biopsy.

10. In a 70 kg. patient with GCA and visual symptoms, your initial dosage of oral prednisone would be_____ mg/day.

11. For the patient in number 10, the initial dose of prednisone should be given as: (circle one)
    - A. single dose.
    - B. divided BID dose.
    - C. divided TID dose.
    - D. divided QID dose.

Figure 1. Giant cell arteritis survey.

regarding their level of participation. As shown in Table 2, all Rheum, 76% of MS, and only 40% of SS participated in both the initial diagnosis and longterm management of GCA. Responses by these physicians were used for statistical analysis. Of surgeons surveyed, 37% performed TA Bx, while no Rheum or MS reported performing this procedure. The number of SS who reported performing TA Bx was not evenly distributed across all subgroups. Ninety-three percent of the general and vascular surgeons, 44% of the otolaryngologists, and only 9% of the ophthalmologists performed TA Bx.

Table 1. Survey responses regarding degree of participation in the care of patients with giant cell arteritis, reported by different specialties. Values are (%).

	Rheumatologists	Medical Specialists	Surgical Specialists
Surveys sent	100	300	300
Surveys returned	56 (56)	87 (29)	92 (31)
Physicians involved in at least one aspect of GCA care	50 (89)	62 (71)	75 (82)

Table 2. Aspect of participation in giant cell arteritis reported by different specialists. Values are percentages within each group.

	Rheumatologists, n = 50	Medical Specialists, n = 62	Surgical Specialists, n = 75
Initial and longterm management	100	76	40
Longterm management only	0	3	3
Perform TA biopsy	0	0	37
Refer for longterm management	0	21	20

Diagnostic Issues in GCA (Table 3)

Temporal artery biopsy as a function of pretest probability. Ninety-two percent of Rheum, 83% of MS, and 89% of SS believed that TA Bx should be obtained in all suspected cases of GCA. Eighty-five percent of Rheum, but only 65% of MS ($p = 0.03$ vs Rheum), and 76% of SS (not significant) believed that TA Bx was indicated in patients with a high probability of GCA (at least 80% likely). Fifty-four percent of Rheum, 49% of MS, and 51% of SS believed that TA Bx was indicated in patients with a low probability of GCA (not greater than 20% likely; not significant). Note that 92% of rheumatologists agreed that TA Bx should be performed in all suspected cases, yet only 85% agreed that biopsy should be done in the setting of high probability. This phenomenon resulted from combining Strongly Agree with Agree, and Strongly Disagree with Disagree. In other words, among respondents who agreed that biopsy should be performed in all patients, many marked A, rather than SA. If a respondent generally agreed with the principle of biopsy in all patients with suspected GCA, but believed that some patients may not absolutely require it, the pattern of responses may reflect A and D, rather than SA and SD.

Table 3. Preference of temporal artery biopsy and its timing in the diagnosis of giant cell arteritis reported by different specialists. Values are No. (%) within each group.

	Rheumatologists	Medical Specialists	Surgical Specialists
Indication for TA Bx	(n = 49)	(n = 57)	(n = 70)
All suspected cases	45 (92)	47 (83)	62 (89)
≥ 80% probability	40 (85)†	37 (65)	51 (76)
≤ 20% probability	26 (54)	28 (49)	33 (51)
Steroids lessen TA Bx yield	(n = 46) 37 (80)††	(n = 57) 40 (70)	(n = 65) 40 (62)
Timing of TA Bx	(n = 43)	(n = 46)	(n = 53)
1–3 days	7 (16)	10 (22)	12 (23)
4–7 days	24 (56)	27 (59)	26 (49)
8–14 days	10 (23)	7 (15)	12 (23)
> 14 days	2 (5)	2 (4)	3 (6)
Bilateral simultaneous TA Bx initially	(N = 48) 11 (23)	(n = 57) 10 (18)	(N = 65) 7 (11)
If negative unilateral TA Bx perform contralateral Bx	(n = 40)	(n = 43)	(n = 49)
All cases	19 (48)	16 (37)	15 (31)
Only if contralateral Sxs	19 (48)	16 (37)	19 (39)
No Contralateral Bx	2 (5)	11 (26)§	15 (31)¶

† Rheumatologists more likely than medical specialists to believe TA biopsy indicated when pretest probability ≥ 80% ($p = 0.03$ with Fisher's exact test). †† Rheumatologists more likely than surgical specialists to believe that steroids lessen the yield of TA biopsy ($p = 0.04$ with Fisher's exact test). § Medical specialists more likely than rheumatologists to indicate no need for contralateral TA biopsy ($p = 0.04$ with Fisher's exact test). ¶ Surgical specialists more likely than rheumatologists to indicate no need for contralateral TA biopsy ($p = 0.01$ with Fisher's exact test).

Corticosteroid effects on biopsy yield. Eighty percent of Rheum believed that corticosteroids lessen the yield of TA Bx compared to 70% of MS (not significant). On the other hand, among SS, only 62% believed that corticosteroids lessened the yield of TA Bx ($p = 0.04$ vs Rheum). Among survey participants that felt corticosteroids would lessen the yield of TA Bx, there were no differences or trends between any of the groups regarding the appropriate timing of TA Bx in relation to initiation of corticosteroids to avoid compromising the yield. Overall, 20% of respondents felt that TA Bx should be performed within 3 days of starting corticosteroids, and 95% of respondents felt it should be done within 14 days.

Simultaneous vs sequential temporal artery biopsies. Twenty-three percent of Rheum felt that bilateral simultaneous TA Bx should be performed at the time GCA is suspected, compared to 11% of SS and 18% of MS (not significant). Regarding respondents not favoring bilateral simultaneous TA Bx, MS (26%) and SS (31%) were more likely than Rheum (5%) to indicate no need for a contralateral TA Bx ($p = 0.04$ and 0.01, respectively), when faced with a negative unilateral biopsy.

Treatment Issues in GCA (Table 4)

Timing of corticosteroids. The vast majority of all survey respondents (94% overall) felt that corticosteroids should be initiated as soon as GCA is suspected, even prior to obtaining TA Bx results. There was no statistical difference among groups.

Initial dosage of corticosteroids. In a hypothetical 70 kg patient with GCA and visual symptoms, the SS recommended a higher initial daily dosage of prednisone (80.5 mg ± 20.5) than both Rheum (66.3 mg ± 13.1) and MS (69.6 mg ± 19.7) ($p < 0.05$ for both comparisons). The high mean initial dose in the SS group is explained on the basis of high recommended doses on the part of ophthalmology (85.66 mg ± 16.5) and otolaryngology (83.34 mg ± 17.1). Note that there was also some variation within MS, with family medicine specialists using 67.25 mg ± 21.9 mg and neurologists using 73.6 mg ± 21 mg of initial daily dosage of prednisone.

Dosage regimen. MS and SS were more likely than Rheum to recommend a once-daily dosing regimen ($p = 0.02$ and 0.003, respectively). The regimen most frequently recommended by Rheum was twice a day dosing (43%). Only 16% of all respondents recommended 3 or 4 times per day dosing regimen.

DISCUSSION

Issues regarding diagnosis and treatment are frequently debated among specialists involved in the care of patients with suspected GCA. The purpose of our survey was to compare self-reported clinical policies in the diagnosis and management of GCA among different specialties involved in the care of GCA. The survey cohort was selected based upon the presumed involvement with GCA. As expected, most of Rheum participated in both diagnoses and longterm management of patients with GCA when compared to other subspecialties, and most SS were involved in performing the TA Bx.

Temporal Artery Biopsy as a Function of Pretest Probability

We found that the majority of physicians surveyed would recommend TA Bx for patients with high probability of GCA, although proportions differed among specialties. However, a substantial minority of physicians in each specialty would not recommend TA Bx in this setting (15% of Rheum to 35% of MS). Since we did not ask for justification, we can only speculate why none was recommended. Perhaps physicians who chose not to pursue TA Bx for patients with high likelihood of GCA made this choice with the notion that the biopsy result, positive or negative, would have little or no effect upon the initial treatment of these

Table 4. Treatment preference of giant cell arteritis reported by different specialists. Values are No. (%) within each group.

	Rheumatologists	Medical Specialists	Surgical Specialists
Cortisone started when	(n = 48)	(n = 58)	(n = 62)
GCA suspected	47 (98)	53 (91)	58 (94)
Dose of prednisone in 70 kg patient, mg, ± SD	66.3 ± 13.1	69.6 ± 19.7	80.5 ± 20.5†
Dosing schedule of cortisone	(n = 49)	(n = 56)	(n = 58)
Once daily	14 (29)	34 (61)††	34 (59)§
BID	21 (43)	16 (29)	14 (24)
TID	11 (22)	3 (6)	3 (5)
QID	3 (6)	3 (5)	7 (12)

† Surgical specialists recommend higher dose than rheumatologists or medical specialists ($p < 0.05$, Tukey's multiple range test following ANOVA). †† Medical specialists more likely to give once a day dosing than rheumatologists ($p = 0.02$, Fisher's exact test). § Surgical specialists more likely to give once a day dosing than rheumatologists ($p = 0.003$, Fisher's exact test).

patients, or that an "unnecessary" procedure would expose the patient to needless risk. Additionally, some respondents may have little experience with longterm management issues in GCA patients, and therefore have little appreciation for the value of obtaining a TA Bx at the time of presentation.

There are several compelling arguments in favor of obtaining an early TA Bx.

1. When done properly, by an experienced surgeon, TA Bx is a very safe procedure[3].
2. While it is true that issues regarding initial management may not be affected by the results of the biopsy, in patients deemed to have a high likelihood of GCA, results of a biopsy may have a significant effect upon clinical decisions made at a future time. In the patient whose headache persists, who develops a toxicity from treatment, or in whom a new symptom develops that changes the clinical paradigm, it is quite possible that a negative baseline TA Bx may be the one important piece of data persuading a clinician to abandon corticosteroid therapy, or to consider other diagnoses.

In a clinical decision analysis on this topic, Buchbinder, *et al*[4] compared 4 different management strategies for suspected GCA, as a function of disease probability: (1) Treat no patients; (2) treat all patients; (3) perform TA Bx and treat only those with a positive Bx; and (4) perform TA Bx and treat all cases irrespective of the result. They concluded that option 1 was only appropriate for disease probabilities less than 2%, and option 3 was most appropriate for intermediate disease probabilities. Option 4 was felt to be preferred when the likelihood of disease was 81%, whereas option 2, empiric therapy without benefit of TA Bx, was preferred only when disease probability exceeds 90%. However, they maintained that TA Bx may be of value even when it does not directly affect initial management. Their final conclusion was that "...temporal artery biopsy should...be performed [even at] high probabilities of disease, although it may not specifically determine management strategy." Similarly, Asch, *et al*[5] argued that the results of a test have value independent of its direct effect upon management. This concept of "knowing for the sake of knowing" is felt to be of particular value when the disease treatment carries the potential for serious side effects (e.g., high dose corticosteroids).

3. A positive biopsy confirms the diagnosis sufficiently to allow the clinician to stop further testing in pursuit of an alternative diagnosis, whereas a negative biopsy may appropriately lead to discontinuation of corticosteroid therapy, or in the case of patients with high disease probability, closer vigilance for the development of an alternative diagnosis during corticosteroid therapy.
4. Finally, there is evidence that the results of a TA Bx may have prognostic significance. Gonzalez-Gay, *et al* demonstrated that patients with a positive TA Bx have a higher risk of severe ischemic complications compared to those with a negative biopsy[6]. While it is possible that a scenario could be created to compel even the most aggressive clinician to defer TA Bx, we agree with Stone, *et al*, that deferral should probably be a rare exception[7].

We also found that a substantial proportion of physicians would recommend not obtaining a TA Bx for patients with low probability of GCA. Apparently a "test threshold" for these physicians was higher than 20%. We did not set out to determine the most appropriate test threshold. Presumably, these physicians would not treat such patients with steroids, but again this is only an inference. While a 20% likelihood of disease may justify no further evaluation, and no "empiric" therapy for some diseases, this threshold would certainly not be appropriate for all diseases.

What should the optimal test threshold be? A 20% likelihood of GCA may not be sufficiently low to "rule out" GCA on clinical grounds, given the potential morbidity of the disease. While there is no empiric data, 2 published decision analyses suggest that the threshold should be substantially lower than 20%. Buchbinder, *et al*[4] concluded that ruling out GCA on clinical grounds alone was only appropriate when the probability of disease was less than 2%. In a decision analysis by Elliot, *et al*[8], a policy to decline biopsy and empiric therapy was considered appropriate only for a likelihood threshold below 1.4%. Had we provided an additional option for "very low probability of GCA" (such as < 2% probability), perhaps survey responses would have differed.

Corticosteroid effects on biopsy yield. Our survey supports our suspicion that clinicians' opinions vary widely regarding the effect of corticosteroids on the yield of TA Bx and the appropriate timing of them. In our study, 80% of Rheum believed that corticosteroid therapy decreases the yield of TA Bx, while only 70% of SS (58% of ophthalmologists and 63% of otolaryngologists) felt this way. Certainly the existing literature supports some effect on yield over time. But no controlled trial has been done to address this issue; therefore the timing and magnitude of any effect as a function of corticosteroid exposure is still in question. Allison and Gallagher examined 84 patients with biopsy-proven GCA[9]. They found the highest incidence of a positive result in patients biopsied before corticosteroid therapy, but because the study was not randomized, the "pre-test probability" of GCA may have influenced the timing of TA Bx. In a retrospective case study of patients undergoing TA Bx at Mayo Clinic, Achkar and coworkers demonstrated that a biopsy may show arteritis with atypical results, even after 14 days of corticosteroid therapy, in the presence of clinical indication of active disease[10].

The issue of diagnostic yield as a function of corticosteroid exposure is somewhat elucidated by evidence in SCID mice showing persistent inflammatory indicators one week following exposure to dexamethasone[11], and by case reports describing positive TA Bx in patients with GCA taking therapeutic corticosteroids for months, and even years[12–14]. In this regard, Fauchald, *et al*[15] raised the ques-

tion whether the finding of active TA despite longterm steroids truly indicates insufficient immunosuppression. They suggest that these persistent histological findings may not necessarily correlate with clinical activity, and may be of little significance[15].

The single most important issue here is that steroids should be used as soon as the diagnosis is suspected, and the TA Bx should also be performed as soon as it can be arranged. Any delay in the performance of the biopsy should be because of difficulty arranging the procedure, not as a result of the assumption that steroids have no effect on the yield of the biopsy. The observation that a biopsy of the TA may still be "positive" well after the first initiation of corticosteroids should not be used as a reason to delay TA Bx, but neither should the fear of compromising the "yield" of the biopsy with steroids be used as a rationale to delay appropriate therapy. Concern over the effect on yield is not the most compelling reason to press for an expeditious TA Bx in a patient suspected of GCA. TA Bx should be done as soon as possible to limit the exposure to corticosteroids and to finalize a diagnosis expeditiously. TA Bx done with appropriate expediency can help truncate the investigations, thus resulting in less risk in selected patients, less cost, and less *angst* for patient and physician alike.

Simultaneous vs sequential TA Bx. In our study, 23% of Rheum felt that simultaneous bilateral TA Bx should be obtained at baseline, compared to 11% of SS and 18% of MS (not significant). More interesting, however, are the diagnostic patterns of those clinicians that do not routinely submit patients to simultaneous bilateral TA Bx. Of this group, 52.5% of Rheum and 66.4% of non-Rheum reported they would perform contralateral TA Bx only if the patient was symptomatic on the contralateral side. Only 2% of Rheum would stop their diagnostic search entirely following a negative unilateral biopsy, regardless of whether the contralateral side was symptomatic; this is in contrast to 26% of MS and 31% of SS. Ponge and coworkers performed 200 simultaneous bilateral TA Bx prospectively in patients with suspected GCA[16]. Of the 42 patients with at least one positive TA Bx, 20 were positive bilaterally, and 22 were positive unilaterally. In their analysis, 4 patients with GCA would have been missed if only unilateral TA Bx had been performed. A clinical policy that does not involve some provision for proceeding with a contralateral biopsy would, therefore, result in some cases of GCA being missed. In a prospective clinical trial, Hayreh and associates[17] prospectively studied 363 patients who initially underwent a unilateral TA Bx, 76 (20.9%) of whom subsequently underwent a contralateral TA Bx. When they compared the ultimate clinical diagnoses in these patients with the biopsy results[17], they found that in all of the patients who had negative biopsies and low to moderate clinical suspicion for GCA, none developed GCA during clinical followup. Among the 76 patients who underwent bilateral sequential biopsies because of a high clinical suspicion for GCA or equivocal pathologic findings, 7 (9.2%) had evidence of active arteritis in the second artery biopsied. Boyev and coworkers also did a retrospective analysis to compare the value of unilateral versus bilateral TA Bx for the diagnosis of GCA[18]. Five (2.7%) of 182 patients in this study who underwent bilateral simultaneous or sequential TA Bx for possible GCA had different findings on the 2 sides, even though all specimens were adequate, improving the diagnostic yield by 3% of cases. Although their yield was low, they concluded the consequences of delayed diagnosis and complications of GCA, as well as side effects of systemic corticosteroid, mandated consideration of bilateral TA Bx. Some authors suggest that an intraoperative frozen section of the initial TA Bx be reviewed by a pathologist. A contralateral biopsy can then be performed on those with a negative frozen section[18].

Treatment issues in GCA. Corticosteroid therapy is traditionally initiated when GCA is suspected to avoid significant visual loss in one or both eyes[19,20]. Once GCA-related visual loss has occurred, the chance of recovery of vision is slim, even with high doses of oral or intravenous corticosteroids[21,22]. Our study supports that a significant majority of survey participants, from all specialties surveyed, favor the prompt initiation of corticosteroids at the time diagnosis is first considered. A study by Younge, *et al*[23], published after the acquisition of our survey data, established clinical findings that identify patients with increased or decreased chance of having a positive TA Bx result. They propose that these data be used to establish the appropriate timing of glucocorticoid therapy. In our study, there was disagreement regarding the most appropriate initial dose of oral prednisone in patients with suspected GCA. In the literature there is some variation, with most authors starting oral prednisone dose of 1.0 to 1.5 mg/kg/day[16]. Patients with visual symptoms are generally given doses at the higher end of this range. In patients with vision loss secondary to GCA, there are anecdotal reports of visual improvement following intravenous corticosteroids at a dose of 1000 mg of methylprednisolone[17]. In our survey, no provision was made to assess clinical policies in corticosteroid dosing in the setting of suspected GCA and no visual symptoms. A "visual symptom" modifier might have resulted in a higher dosage selection than otherwise suggested if no mention had been made of visual symptoms. Chevalet, *et al* conducted a large randomized trial comparing intravenous, pulse methylprednisone at 240 mg, followed by oral prednisone, to an oral-only prednisone group of GCA patients[24]. One hundred sixty-four patients were studied and no significant differences were observed in the cumulative doses of steroids over 1 year, the time required for normalization of C-reactive protein, and for corticosteroid related side effects. However, outcomes in this study were not reported on the basis of which patients presented with visual signs and symptoms. Perhaps a major reason why our survey uncov-

ered differences between ophthalmology and Rheum, regarding the initial dosage recommendations is that they have a significantly different perspective on the disease. Ophthalmologists are more likely to see GCA patients with visual disturbances, including vision loss, and occult GCA, whereas Rheum evaluate a greater spectrum of presentations[25,26]. Additionally, patients who have had visual loss may be willing to accept a greater degree of risk, i.e. a higher dose of corticosteroids, than those who have no visual symptoms.

Oral corticosteroids can be given as a single dose or divided dosage. In several disease models, there are data to support increased likelihood of adrenal insufficiency when oral corticosteroids are given in divided dose[27]. However, in a prospective study, Hunder and coworkers gave patients with GCA oral prednisone as a single dose and divided dosage 3 times a day[28]. Each of the 20 patients in both groups was analyzed as to arteritis control and corticosteroid side effect profiles. Whereas there was a nonstatistical trend toward better disease control in the divided-dosage group, the side effect profile, including evidence of adrenal insufficiency, was similar in both groups. Perhaps this potential for improved disease control on split dosing explains the difference between Rheum and other survey participants in this parameter.

Treatment of GCA should be tailored to each patient, taking into account many important variables. There is, however, a need for evidenced-based treatment guidelines.

Summary

The diagnosis of GCA is plagued by difficulties in obtaining a biopsy in a timely manner. Once GCA is suspected, prompt initiation of corticosteroid treatment is felt to be needed to protect vision, but may eventually affect TA Bx results. Considerable variation exists regarding key elements of diagnosis and treatment in the evaluation of suspected GCA. The morbidity of GCA and the potential toxicity of therapy highlight the need for controlled trials to address these issues.

ACKNOWLEDGMENT

Special thanks to W. Scott Richardson, MD, for his assistance with aspects of this report relating to clinical decision making.

REFERENCES

1. Hunder GG. Giant cell arteritis and polymyalgia rheumatica. Med Clin North Am 1997;81:195-219.
2. Baldursson O, Steinsson K, Bjornsson J, Lie JT. Giant cell arteritis in Iceland: An epidemiologic and histologic analysis. Arthritis Rheum 1994;37:1007-12.
3. Scott KR. Temporal artery biopsy technique: a clinico-anatomical approach. Ophthalmol Surg 1991;22:519-25.
4. Buchbinder R, Detsky AS. Management of suspected giant cell arteritis: a decision analysis. J Rheumatol 1992;19:1220-8.
5. Asch DA, Patton JP, Hershey JC. Knowing for the sake of knowing: the value of prognostic information. Med Decis Making 1990;10:47-57.
6. Gonzalez-Gay MA, Garcia-Porrua C, Llorca J, Gonzalez-Louzao C, Rodriguez-Ledo P. Biopsy-negative giant cell arteritis: clinical spectrum and predictive factors for positive temporal artery biopsy. Semin Arthritis Rheum 2001;30:249-56.
7. Stone JH, Calabrese L, Hoffman GS, Pusey CD, Hunder GG, Hellmann DB. Vasculitis — a collection of pearls and myths. Rheum Dis Clin North Am 2001;27:677-728.
8. Elliot DL, Watts WJ, Reuler JB. Management of suspected temporal arteritis. A decision analysis. Med Decis Making 1983;3:63-8.
9. Allison MC, Gallagher PJ. Temporal artery biopsy and corticosteroid treatment. Ann Rheum Dis 1984;43:416-7.
10. Achkar AA, Lie JT, Hunder GG, O'Fallon WM, Gabriel SE. How does previous corticosteroid treatment affect the biopsy findings in giant cell (temporal) arteritis? Ann Intern Med 1994;120:987-92.
11. Brack A, Rittner HL, Younge BR, Kaltschmidt C, Weyand CM, Goronzy JJ. Glucocorticoid-mediated repression of cytokine gene transcription in human arteritis-SCID chimeras. J Clin Invest 1997;99:2842-50.
12. Murgatroyd H, Milne A. Positive temporal artery biopsy in a patient on therapeutic doses of steroids for six years. Eye 2001;15:250-1.
13. Guevara RA, Newman NJ, Grossniklaus HE. Positive temporal artery biopsy six months after prednisone treatment. Arch Ophthalmol 1998;116:1252-3.
14. Evans JM, Batts KP, Hunder GG, et al. Persistent giant cell arteritis despite corticosteroid treatment. Mayo Clin Proc 1994;69:1060-1.
15. Fauchald P, Rygvold O, Oystese B. Temporal arteritis and polymyalgia rheumatica. Clinical and biopsy findings. Ann Intern Med 1972;77:845-52.
16. Ponge T, Barrier JH, Grolleau JY, Ponge A, Vlasak AM, Cottin S. The efficacy of selective unilateral temporal artery biopsy versus bilateral biopsies for diagnosis of giant cell arteritis. J Rheumatol 1988;15:997-1000.
17. Hayreh SS, Podhajsky PA, Raman R, Zimmerman B. Giant cell arteritis: validity and reliability of various diagnostic criteria. Am J Ophthalmol 1997;123:285-96.
18. Boyev LR, Miller NR, Green WR. Efficacy of unilateral versus bilateral temporal artery biopsies for the diagnosis of giant cell arteritis. Am J Ophthalmol 1999;128:211-5.
19. Keltner JL. Giant cell arteritis: Signs and symptoms. Ophthalmology 1982;89:1101-10.
20. Rosenfeld SI, Kosmorsky GS, Klingele TG, Burde RM, Cohn EM. Treatment of temporal arteritis with ocular involvement. Am J Med 1986;80:143-5.
21. Hayreh SS, Zimmerman B, Kardon RH, Visual improvement with corticosteroid therapy in giant cell arteritis. Report of a large study and review of literature. Acta Ophthalmol Scand 2002;80:355-67.
22. Cornblath WT, Eggenberger E. Progressive visual loss from giant cell arteritis despite high-dose intravenous methylprednisolone. Ophthalmology 1997;104:854-8.
23. Younge BR, Cook BE Jr, Bartley GB, Hodge DO, Hunder GG. Initiation of glucocorticoid therapy: before or after temporal artery biopsy? Mayo Clin Proc 2004;79:483-91. Erratum in: Mayo Clin Proc 2004;79:709. Mayo Clin Proc 1004;79:1341.
24. Chevalet P, Barrier JH, Pottier P, et al. A randomized, multicenter, controlled trial using intravenous pulses of methylprednisolone in the initial treatment of simple forms of giant cell arteritis: a one year followup study of 164 patients. J Rheumatol 2000;27:1484-91.
25. Hayreh SS, Podhajsky PA, Zimmerman B. Occult giant cell arteritis: ocular manifestations. Am J Ophthalmol 1998;125:521-6.
26. Hayreh SS. Steroid therapy for visual loss in patients with giant-cell arteritis. Lancet 2000;355:1572-3.
27. Myles AB, Bacon PA, Daly JR. Single daily dose corticosteroid treatment. Effect on adrenal function and therapeutic efficacy in various diseases. Ann Rheum Dis 1971;30:149-53.
28. Hunder GG, Sheps SG, Allen GL, Joyce JW. Daily and alternate-day corticosteroid treatment of giant cell arteritis. Ann Intern Med 1975;82:613-8.