

2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Giant Cell Arteritis and Takayasu Arteritis.

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Dr. Archer was employed by Northwestern University while she was involved in this project but resigned from the project in March 2020, when she took a position at Janssen, her current employer. Janssen had no financial or other interest in this project and had no input in the design, content, data collection, or analysis, and had no role in the writing or approval of this article, with all opinions and conclusions expressed herein those of the authors.

8 2021 08 7 2021 73 8 494881 1071 1087 05 08 2025 13 08 2025 13 08 2025 14 08 2025 This file is available for text mining. It may also be used consistent with the principles of fair use under the copyright law. Objective To provide evidence-based recommendations and expert guidance for the management of giant cell arteritis (GCA) and Takayasu arteritis (TAK) as exemplars of large vessel

vasculitis.

Clinical questions regarding diagnostic testing, treatment, and management were developed in the Patient population, Intervention, Comparator, and Outcome (PICO) format for GCA and TAK (27 for GCA, 27 for TAK). Systematic literature reviews were conducted for each PICO question. Grading of Recommendations Assessment Development and Evaluation (GRADE) methodology was used to rate the quality of the evidence. Recommendations were developed by the voting panel, comprised of adult and pediatric rheumatologists and patients. Each recommendation required at least 70% consensus.

We present 22 recommendations and 2 ungraded position statements for GCA, and 20 recommendations and 1 ungraded position statement for TAK. These recommendations and statements address clinical questions relating to the use of diagnostic testing, including imaging, treatments and surgical interventions in GCA and TAK. Recommendations for GCA include support for the use of glucocorticoid-sparing immunosuppressive agents and use of imaging to identify large vessel involvement. Recommendations for TAK include use of non-glucocorticoid immunosuppressive agents with glucocorticoids as initial therapy. There were only 2 strong recommendations; the remaining recommendations were conditional due to the low quality of evidence available for most PICO questions.

These recommendations provide guidance regarding the evaluation and management of patients with GCA and TAK, including diagnostic strategies, use of pharmacologic agents, and surgical interventions.

Giant cell arteritis (GCA) and Takayasu arteritis (TAK) are systemic vasculitides that primarily affect large and medium-sized vessels. 1 GCA can present with both cranial and extracranial manifestations. Cranial manifestations include headaches, scalp tenderness, vision loss, and jaw claudication. Large vessel ("extracranial") involvement results in arterial stenosis and aneurysms, causing absent pulses, and limb claudication. 2 GCA is more common in individuals of Northern European descent who are older than 50 years of age. The diagnosis is based on the clinical presentation, pathological abnormalities on temporal artery biopsy, and/or evidence of large vessel involvement on vascular imaging. 1 – 6 Glucocorticoids are the mainstay treatment for GCA, but tocilizumab has been approved by the FDA for the treatment of GCA. 7 , 8

Takayasu arteritis (TAK) causes granulomatous inflammation of the aorta and its branches. It is more common in younger women. 9 , 10 Clinical manifestations include constitutional symptoms, elevated inflammatory markers, and arterial stenosis and/or aneurysms resulting in limb claudication and absent pulses. 11 Treatment options include glucocorticoids, non-glucocorticoid immunosuppressive agents, and surgical management of vascular abnormalities. 12

As GCA and TAK share clinical manifestations, similar questions arise regarding their treatment and management. Recent studies have broadened treatment options for GCA, and vascular imaging is increasingly used for diagnosis and management. This guideline was developed to provide evidence-based recommendations for the evaluation and management of GCA and TAK.

This guideline follows the ACR guideline development process (<https://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice-Guidelines>) using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology to rate the quality of evidence and develop recommendations 13 – 15 . ACR policy guided management of conflicts of interest and disclosures (<https://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice-Guidelines/Vasculitis>). Supplementary Appendix 1 presents a detailed description of the methods. Briefly, a Literature Review team undertook systematic literature reviews for pre-determined questions specifying the clinical population, intervention, comparator, and outcomes (PICO). An in-person Patient Panel of 11 individuals with different types of vasculitis, including 3 patients with GCA or TAK, moderated by a member of the

Literature Review team, reviewed the evidence report (along with a summary and interpretation by the moderator) and provided patient perspectives and preferences about their personal experiences regarding clinical and treatment aspects of their disease. The Voting Panel comprised of nine adult rheumatologists, five pediatric rheumatologists, and 2 patients, reviewed the Literature Review team's evidence summaries and, bearing in mind the Patient Panel's deliberations, formulated and voted on recommendations. A recommendation required 70% consensus of the Voting Panel.

A strong recommendation is typically supported by moderate or high-quality evidence (e.g., multiple randomized controlled trials). For a strong recommendation, the recommended course of action would apply to all or almost all patients. Only a small proportion of clinicians/patients would not want to follow the recommendation. In rare instances, a strong recommendation may be based on low or very low certainty evidence. For example, an intervention may be strongly recommended if it is considered low-cost, without harms, and the consequence of not performing the intervention may be catastrophic. An intervention may be strongly recommended against if there is high certainty that the intervention leads to more harm than the comparison with low or very low certainty about its benefit 16 .

A conditional recommendation is generally supported by lower quality evidence or a close balance between desirable and undesirable outcomes. For a conditional recommendation, the recommended course of action would apply to the majority of the patients, but the alternative is a reasonable consideration. Conditional recommendations added always warrant a shared decision-making approach. We specify conditions under which the alternative may be considered.

In some instances, the committee found that the evidence for a particular PICO question did not support a graded recommendation or did not favor one intervention over the other. However, the voting panel believed the PICO question addressed a commonly encountered clinical question which has not been fully clarified and requires further investigation and thus felt that providing guidance for this question was warranted. For these situations, we present "ungraded position statements" which reflects general views of the voting panel.

In this evidence-based guideline, we explicitly use the best evidence available and present that in a transparent manner for the clinician reader/user 10 . In some instances, this includes randomized trials directly comparing the interventions under consideration. The GRADE system rates evidence that comes exclusively from the collective experience of the Voting Panel and patient panel members as "very-low-quality" evidence 15 .

For each recommendation, Supplementary Appendix 2 provides details regarding the PICO questions and the GRADE evidence tables.

For the GCA evidence report, 399 articles were reviewed to address 27 PICO questions. For the TAK evidence report, 347 articles were reviewed to address 27 PICO questions.

Table 1 presents definitions of selected terms used in the recommendations, including disease states such as severe disease, dosing ranges for glucocorticoids, categorization of medications, and disease assessments. Tables 2 and 3 present the recommendations with their supporting PICO questions and level of evidence. We present 22 recommendations and 2 ungraded position statements for GCA. All but one of the recommendations are conditional due to low or very low-quality evidence. Figure 1 presents key recommendations for the treatment of Giant Cell Arteritis (GCA).

In patients with suspected GCA, we conditionally recommend an initial unilateral temporal artery biopsy over bilateral biopsies.

Initially, a unilateral biopsy is recommended. However, bilateral temporal artery biopsies may be appropriate if the symptoms are not clearly localized to one temporal artery. Proceeding with the

contralateral biopsy is also appropriate if the unilateral biopsy is negative and additional evidence for cranial GCA is sought. 17

In patients with suspected GCA we conditionally recommend a long-segment temporal artery biopsy (>1 cm) over a short-segment temporal artery biopsy (<1 cm).

A longer segment of the temporal artery is preferred since GCA is a focal and segmental disease, and the added morbidity of obtaining a larger segment is very low. A shorter segment obtained on biopsy can result in reduced diagnostic yield and a missed diagnosis. This recommendation is conditional due to a lack of high-quality evidence, but the Voting Panel emphasized obtaining longer biopsies when possible. 18 , 19

In patients with suspected GCA, we conditionally recommend obtaining a temporal artery biopsy within two weeks of starting oral glucocorticoids over waiting longer than two weeks for a biopsy.

Overall, biopsies should be obtained as soon as possible to maximize the likelihood of detecting histopathologic changes. Studies suggest that histopathologic changes indicating GCA are more likely to be detected in a temporal artery biopsy if obtained within 2 weeks of starting glucocorticoids; however, histopathologic changes have been detected in biopsies obtained much later than 2 weeks. 20 – 28 A biopsy obtained 2 weeks after starting glucocorticoids could be informative and may be considered at the discretion of the physician and patient.

In patients with suspected GCA, we conditionally recommend temporal artery biopsy over temporal artery ultrasound for diagnosis of GCA.

In general, rheumatologists and radiologists in the United States are less experienced in using ultrasound to diagnose temporal artery involvement in GCA compared to their counterparts in Europe. Therefore, temporal artery biopsy remains the optimal approach to diagnosing GCA in the United States because ultrasound is operator-dependent, and results are influenced by treatment (i.e., inflammatory signs quickly disappear with glucocorticoid treatment). In centers with appropriate training and expertise using temporal artery ultrasound, ultrasound may be a useful and complementary tool for diagnosing GCA. 29 – 33

In patients with suspected GCA, we conditionally recommend temporal artery biopsy over magnetic resonance imaging of cranial arteries for establishing a diagnosis of GCA.

Protocols to image the cranial vessels using different modalities including magnetic resonance imaging (MRI) have been developed which can be helpful to establish a diagnosis of giant cell arteritis. 30 , 31 , 34 – 37 However, lack of technical expertise with this modality in the United States as well as lack of widespread validation of this approach limits the applicability of MRI with contrast of the cranial vessels as a replacement for temporal artery biopsy at the current time.

In patients with suspected GCA and a negative temporal artery biopsy (or biopsies), we conditionally recommend non-invasive vascular imaging of the large vessels with clinical assessment to aid in diagnosis over clinical assessment alone.

Imaging the large vessels may provide additional evidence of disease (“extracranial” GCA) when the diagnosis is uncertain following negative temporal artery biopsies. 28 , 34 , 38 – 44 Potential diagnostic imaging modalities include magnetic resonance (MR) or computed tomography (CT) angiography of neck/chest/abdomen/pelvis, ultrasonography, and 18F-fluorodeoxyglucose positron emission tomography (PET). 43 , 45

In patients with newly diagnosed GCA, we conditionally recommend obtaining non-invasive vascular imaging to evaluate for large vessel involvement.

Baseline non-invasive imaging with MR or CT angiography of neck/chest/abdomen/pelvis in patients with newly diagnosed GCA can detect large vessel involvement and can be compared with subsequent routine monitoring if indicated. 46 In a patient with large vessel involvement, routine non-invasive vascular imaging can identify early and long-term complications such as aneurysms and stenoses, and assess stability of existing lesions. In patients without large vessel involvement, routine and repeated monitoring with vascular imaging may or may not be necessary.

In patients with newly diagnosed GCA without manifestations of cranial ischemia, we conditionally recommend initiating treatment with high dose oral glucocorticoids over pulse intravenous glucocorticoids.

Cranial ischemic manifestations include visual and neurological involvement such as amaurosis fugax, vision loss and stroke. Some studies have suggested that the use of pulse intravenous glucocorticoids in this group of patients could decrease relapses and increase remission rates. However, routine use of pulse intravenous glucocorticoids can also be associated with increased risks including infections that may outweigh the benefits, especially in the elderly. 47 , 48

In patients with newly diagnosed GCA with threatened vision loss, we conditionally recommend initiating treatment with pulse intravenous glucocorticoids over high dose oral glucocorticoids.

Studies investigating the effect of pulse intravenous glucocorticoids in patients with GCA and cranial ischemia have reported conflicting results. However, this population is at high risk for vision loss as well as toxicity from glucocorticoid use. Pulse intravenous glucocorticoids can be used in patients with the highest risk of vision loss, but this decision should be guided by the patient's clinical condition, values, and preferences. 49 , 50

In patients with newly diagnosed GCA, we conditionally recommend dosing oral glucocorticoids daily over an alternate day schedule.

This recommendation is conditional solely due to the low level of evidence, which indicates higher remission rates in patients receiving daily dosing. The panel did not identify any situations in which alternate day dosing of prednisone would be preferred. 51

In patients with newly diagnosed GCA, we conditionally recommend initiating treatment with high dose oral glucocorticoids over moderate dose oral glucocorticoids.

We recommend starting high dose oral glucocorticoids to achieve rapid disease control followed by tapering the glucocorticoid dose to avoid prolonged high dose treatment (weeks-months) and reduce toxicity. The dosing and duration of oral glucocorticoid therapy can be variable depending on a patient's manifestations and comorbidities and whether use of a glucocorticoid sparing agent was also initiated. Studies supporting the efficacy and lower toxicity of moderate dose glucocorticoids are of low quality, which prevents the voting panel from recommending moderate dose glucocorticoids as initial therapy. Moderate dose glucocorticoids may be used in patients with significant risk for severe glucocorticoid toxicity and patients with low risk for vision loss or other life/organ-threatening complications. 48 – 53

In patients with newly diagnosed GCA, we conditionally recommend using oral glucocorticoids with tocilizumab over oral glucocorticoids alone.

The GiACTA trial demonstrated that tocilizumab has a significant glucocorticoid sparing effect in GCA and thus tocilizumab should be considered for initial treatment. However, methotrexate with glucocorticoids as well as glucocorticoids alone can also be considered as initial treatment for newly diagnosed GCA. The decision between tocilizumab with glucocorticoids, methotrexate with glucocorticoids, or glucocorticoid monotherapy for initial therapy should be made based on the physician's experience, the patient's clinical condition, values, and preferences. Lack of long-term

follow up for tocilizumab and cost may limit tocilizumab use. 8 , 54 Abatacept with glucocorticoids can also be considered if these other agents are not effective. 55

In patients with GCA with active extracranial large vessel involvement, we conditionally recommend treatment with oral glucocorticoids combined with a non-glucocorticoid immunosuppressive agent over oral glucocorticoids alone.

Management of GCA patients with new, persistent, or worsening extracranial symptoms (e.g., limb claudication) or signs (e.g., imaging findings) attributed to GCA can include the addition of non-glucocorticoid immunosuppressive agents. These agents include biologic agents (e.g., tocilizumab) as well as oral therapies (e.g., methotrexate). 56 , 57 However, the Voting Panel recognizes that there are few high-quality studies evaluating the efficacy of these agents for this patient group. While there is stronger clinical evidence supporting the use of tocilizumab compared to methotrexate for the treatment of GCA, methotrexate can be considered for patients unable to use tocilizumab due to factors such as recurrent infections, history of gastrointestinal perforations or diverticulitis, or cost.

The optimal duration of therapy with glucocorticoids for GCA is not well-established and should be guided by the patient's values and preferences.

Factors that may influence the duration of therapy include the patient's clinical manifestations, toxicity related to glucocorticoid use, number of flares, physician's experience, and the patient's preferences. 8 Overall, the patient panel emphasized minimizing the use of glucocorticoids as much as possible, but recognized that longer-term use may be needed in some patients to avoid flares.

In patients with newly diagnosed GCA, we conditionally recommend against using an HMG-CoA reductase inhibitor ("statin") specifically for the treatment of GCA.

Use of statins are not known to provide a clinically significant immunosuppressive effect for GCA. Whether statins are warranted to decrease the patient's risk of cardiovascular events is a separate clinical question, and depends on the patient's risk factors for cardiovascular disease. 58 – 60

In patients with GCA who have critical or flow-limiting involvement of the vertebral or carotid arteries, we conditionally recommend adding aspirin.

There are few data regarding this clinical question, but the antiplatelet activity of aspirin may be beneficial in preventing ischemic events in patients with vascular narrowing causing decreased cerebral blood flow. 61 – 64 The efficacy of aspirin to prevent ischemic events in patients without vertebral or carotid narrowing remains unclear at this time.

In patients with GCA who relapse while on moderate or high dose glucocorticoids, we conditionally recommend adding a non-glucocorticoid immunosuppressive drug.

Relapses of any type while on moderate to high dose glucocorticoids indicate that it is unlikely that the patient will be able to taper glucocorticoids to a low dose. Thus, glucocorticoid-sparing therapy should be considered.

In patients with GCA who relapse with symptoms of cranial ischemia, we conditionally recommend adding a non-glucocorticoid immunosuppressive agent and increasing the dose of glucocorticoids over increasing the dose of glucocorticoids alone.

Non-glucocorticoid immunosuppressive agents considered in this situation include tocilizumab and methotrexate. 8 , 65 , 66 Relapses with symptoms of polymyalgia rheumatica may be controlled with increasing the dose of glucocorticoids alone.

In patients with GCA who relapse with cranial symptoms while on glucocorticoids, we conditionally recommend adding tocilizumab and increasing the dose of glucocorticoids over adding methotrexate and increasing the dose of glucocorticoids.

Tocilizumab is an effective glucocorticoid sparing agent for GCA 8 , 54 . While there are no comparative studies, the glucocorticoid sparing effect seen with methotrexate is smaller than the effect seen with tocilizumab. 8 , 55 , 65 – 67 While the glucocorticoid sparing effect of tocilizumab is best quantified using the subcutaneous formulation 8 , intravenous tocilizumab has also been shown to be glucocorticoid sparing. 54 Again, methotrexate can be considered for patients who are unable to tolerate or have limited access to tocilizumab.

For any patient requiring surgical vascular intervention for GCA, the type and timing of intervention should be a collaborative decision between the vascular surgeon and rheumatologist.

In patients with severe GCA and worsening signs of limb/organ ischemia on immunosuppression, we conditionally recommend escalating immunosuppression over surgical intervention with escalation of immunosuppression.

Because patients can develop collateral blood vessels to improve distal blood flow, immunosuppression is recommended as initial therapy in patients with GCA and worsening limb/organ ischemia. However, clinical situations that would warrant consideration of immediate surgical intervention include aortic aneurysms at high risk of rupture and impending/progressive tissue or organ infarction or damage. 68 – 70

In patients with GCA undergoing vascular surgical intervention, we conditionally recommend using high dose glucocorticoids during the peri-procedural period if the patient has active disease.

This recommendation pertains to patients with GCA undergoing a vascular surgical intervention due to a complication of GCA (e.g., aneurysm or stenosis). There are limited data regarding the use of high dose glucocorticoids during the peri-procedural period in GCA, and thus support for this recommendation is based in part on the experience in TAK (TAK Recommendation #20). As in TAK, high doses of oral glucocorticoids in the perioperative setting are recommended if the disease is active or if the clinician is concerned that the patient may have active disease.

In patients with GCA in remission, we strongly recommend long-term clinical monitoring over no clinical monitoring.

The optimal frequency and length of monitoring are not well established, and depends on factors including the duration of remission, site of involvement, risks of disease progression, whether the patient is on immunosuppressive therapy, and reliability of the patient to report new signs or symptoms. 48 , 69 Clinical monitoring may include history taking, exam, laboratory and imaging studies. This is a strong recommendation given minimal risks and potential catastrophic outcomes if monitoring is not performed.

In patients with GCA who have rising inflammatory markers alone, we conditionally recommend clinical observation and monitoring without escalation of immunosuppression.

Increases in inflammatory markers such as erythrocyte sedimentation rate and C-reactive protein can be nonspecific. 69 Therefore, increasing immunosuppression is not warranted in the setting of increased inflammatory markers in the absence of other signs of disease activity. However, increased inflammatory markers may warrant more frequent clinical and/or radiographic assessments for active disease.

Table 1 presents definitions of selected terms used in the recommendations, and Tables 4 and 5 present the recommendations with their supporting PICO questions and level of evidence. - We

present 20 recommendations and 1 ungraded position statement for TAK. All recommendations except for one are conditional due to the availability of only low or very low-quality evidence. Figure 2 presents key recommendations for the treatment of Takayasu Arteritis (TAK).

In patients with severe active TAK not on immunosuppression, we conditionally recommend initiating treatment with high dose oral glucocorticoids over pulse intravenous glucocorticoids followed by high dose oral glucocorticoids.

There is no evidence that pulse intravenous glucocorticoids are more effective than high-dose oral glucocorticoids in this setting. Pulse intravenous glucocorticoids may be considered for patients with life- or organ-threatening disease. In children, alternate steroid dosing regimens (e.g., pulse intravenous glucocorticoids with low daily oral dosing) may be preferred to improve compliance and potentially reduce adverse consequences such as impacting growth. 71

In patients with newly active severe TAK, we conditionally recommend initiating treatment with high-dose glucocorticoids over low-dose glucocorticoids.

A higher dose of glucocorticoid is recommended due to the potential for organ damage or life-threatening events. However, lower doses of glucocorticoids may be considered for patients with newly active non-severe disease, (e.g., patients with constitutional symptoms and without limb ischemia). 72

In patients with TAK who achieved remission on glucocorticoids for at least 6–12 months, we conditionally recommend tapering off glucocorticoids over long-term treatment with low dose glucocorticoids for remission maintenance.

The optimal duration of glucocorticoid use in TAK is unknown. Glucocorticoid exposure should be limited if possible, to minimize toxicity. Glucocorticoids may be continued for a longer duration if disease is not adequately controlled or the patient experiences frequent relapses.

In patients with active TAK, we conditionally recommend using a non-glucocorticoid immunosuppressive agent plus glucocorticoids over glucocorticoids alone.

Non-glucocorticoid immunosuppressive agents are recommended over monotherapy with glucocorticoids to minimize glucocorticoid-related toxicity. Methotrexate is often used as the initial non-glucocorticoid immunosuppressive agent but other therapies such as TNF- α inhibitors and azathioprine can be considered as well. 70 – 73 Methotrexate is often preferred in children since it is usually well tolerated. Glucocorticoid monotherapy can be considered for mild disease or if the diagnosis is uncertain. Patient-specific factors such as alcohol use, plans for childbearing, medication compliance, and medical comorbidities may influence the immunosuppressant chosen. 73 , 74

In patients with active TAK, we conditionally recommend using other non-glucocorticoid immunosuppressive therapy over tocilizumab as initial therapy.

As discussed in Recommendation 4 above, non-glucocorticoid immunosuppressive agents such as methotrexate, TNF- α inhibitors, and azathioprine can be used as initial therapy for TAK. We recommend these agents over tocilizumab for initial therapy since the efficacy of tocilizumab in TAK is not established at this time. While tocilizumab has been shown to be efficacious for giant cell arteritis, tocilizumab did not achieve its primary efficacy endpoint in the only randomized trial for this therapy in TAK conducted thus far. 74 , 75 Tocilizumab may be considered for patients with inadequate response to other immunosuppressive therapies. Abatacept is not recommended since it was shown in a small randomized controlled trial to be not efficacious for TAK. 74 , 76

In patients with TAK refractory to treatment with glucocorticoids alone, we conditionally recommend adding a TNF- α inhibitor over adding tocilizumab.

We recognize that among the biologic therapies, some practitioners favor TNF- α inhibition while others favor IL-6 inhibition (tocilizumab) in this situation. Overall, the Voting Panel favored TNF- α inhibitors over tocilizumab since there is more clinical experience and data with TNF- α inhibitors than with tocilizumab for TAK. TNF- α inhibitors have been shown to induce remission and decrease relapses in observational studies. 77 – 79 Clinical experience for tocilizumab in TAK is provided by a randomized controlled trial and small case series. In the randomized trial, a trend towards a longer time to relapse was seen in the tocilizumab arm but the difference was not statistically significant. However, this study was felt to be underpowered (36 participants). Of note, tocilizumab use also affects acute phase markers which may impact ability to gauge disease activity. Thus, while the panel favors TNF- α inhibitor use, we recognize that tocilizumab may also be considered, especially when TNF- α inhibitors are contraindicated. 75

In patients with TAK and asymptomatic progression of a previously identified vascular lesion seen on imaging without evidence of inflammation, we conditionally recommend continuing current therapy over escalating/changing immunosuppression.

Vascular lesions can progress due to a number of factors that may not be related to active disease, such as “healing fibrosis” in response to effective treatment. Intervention is not always needed since collateral circulation frequently develops over time. However, the location and the extent of the lesion of the affected vessel should be considered. Escalating immunosuppression may be warranted if significant progression has developed rapidly (e.g., weeks to months) after a period of stable disease. 80 , 81

In patients with active TAK and critical cranial or vertebrobasilar involvement, we conditionally recommend adding aspirin or another anti-platelet therapy.

Small observational studies suggest a decreased risk of ischemic events with anti-platelet therapy but an increased risk of bleeding. 82 Therefore, anti-platelet therapy is usually used for patients at a higher risk for ischemic events (e.g., patients with flow limiting vertebrobasilar disease or stents). Anti-platelet therapy should be used with caution after surgical procedures or if there is an increased risk of bleeding. 81

In patients with TAK, we conditionally recommend adding inflammatory markers to clinical monitoring as a disease activity assessment tool.

While inflammatory markers are an imperfect indicator of disease activity, they may be helpful for clinical monitoring. 80 , 83

In patients with TAK in apparent remission, we strongly recommend long-term clinical monitoring over no clinical monitoring.

The frequency of monitoring depends on factors including the duration of remission, sites of involvement, risks of disease progression, the patient’s immunosuppressive regimen, and ability and likelihood of the patient reliably reporting new signs or symptoms of TAK. This is a strong recommendation given minimal risks and potential catastrophic outcomes without monitoring. 80 , 83

In patients with TAK in apparent clinical remission but with rising inflammatory markers, we conditionally recommend clinical observation without escalation of immunosuppression.

As discussed in GCA Recommendation 22, increases in inflammatory markers can be nonspecific, and intensifying immunosuppression in the setting of increased inflammatory markers alone may

not be warranted. More frequent clinical and/or radiographic assessments for active disease can be considered. 77 , 80 , 83

In patients with TAK, we conditionally recommend using non-invasive imaging over catheter-based dye angiography as a disease activity assessment tool.

Non-invasive imaging such as CT angiography, MR angiography, or PET are recommended because these imaging modalities provide information regarding vascular wall inflammation, while catheter-based angiography primarily provides information regarding the vascular lumen. Catheter-based angiography can be used to accurately determine central blood pressures, as part of surgical planning, or if non-invasive modalities do not provide adequate information. Identifying active disease based on non-invasive imaging at this time can be challenging since the hallmarks of active disease have not been definitely established. 43 , 45 , 84

In patients with known TAK, we conditionally recommend regularly scheduled non-invasive imaging in addition to routine clinical assessment.

Routine imaging is recommended since vascular changes in TAK can occur when the disease is considered clinically quiescent. The optimal interval between imaging studies is not well-established, and ranges vary (e.g., every 3–6 months or longer). The interval may be shorter early in the disease course, and longer with established, quiescent disease. Since sedation may be required for imaging studies in children and can be associated with potential risks and complications, routine imaging of inactive disease in children is at the discretion of the treating clinician, while considering risks and benefits. 85 , 86

In patients with TAK in apparent clinical remission but with signs of inflammation in new vascular territories (e.g., new stenosis or vessel wall thickening) on vascular imaging, we conditionally recommend treatment with immunosuppressive therapy.

A new arterial stenosis is concerning for evidence of recent active disease, and thus usually warrants immunosuppressive therapy. Other findings suggestive of active disease on MR or CT angiography include vascular edema, contrast enhancement, and increased wall thickness, and may result in luminal damage over time. Findings of active disease by PET are defined by supra-physiologic FDG uptake in the arterial wall. However, abnormal findings in the vascular wall identified by imaging are not necessarily specific for vascular inflammation. The implication of finding vessel wall edema or enhancement on imaging remains an area of investigation and the clinical importance of such findings on CT angiography, MR angiography, and PET is not certain. 43 , 45 , 80 , 83 – 86 Thus, all therapeutic decision making in this context should occur after review of the imaging with a radiologist to help determine whether the observed imaging changes represent active disease.

For any patient requiring surgical vascular intervention, the type and timing of intervention should be a collaborative decision between the vascular surgeon and rheumatologist.

In patients with known TAK and persistent limb claudication without evidence of ongoing active disease, we conditionally recommend against surgical intervention.

Patients with TAK can develop collateral circulation bypassing the stenosis that is causing the limb claudication, and thus surgical intervention may not be needed. 87 However, surgical intervention can be considered for patients whose activities are significantly impacted by limb claudication.

In patients with known TAK with worsening signs of limb/organ ischemia on immunosuppression, we conditionally recommend escalating immunosuppression over surgical intervention with escalation of immunosuppression.

Immunosuppression is recommended to control vascular inflammation to improve or prevent worsening blood flow. However, clinical situations that could warrant immediate surgical intervention include coronary artery involvement and impending/progressive tissue or organ infarction. 88 – 90

In patients with TAK with renovascular hypertension and renal artery stenosis, we conditionally recommend medical management over surgical intervention.

Medical management includes anti-hypertensive drugs and immunosuppression if TAK is active. Surgical intervention (including catheter-based interventions) may be warranted for hypertension refractory to medical management in spite of optimized immunosuppression or in the setting of worsening renal function. 12 , 91 – 94

In patients with TAK and stenosis of a cranial/cervical vessel without clinical symptoms, we conditionally recommend medical management over surgical intervention.

Medical therapy is recommended if only a single vessel is involved due to the substantial risks of surgery. Surgical interventions can be considered if multiple vessels are involved. This recommendation is based on indirect evidence obtained from neurological experience and studies, since there is no direct evidence for TAK. 90 , 95 – 98

In patients with TAK with worsening signs of limb/organ ischemia, we conditionally recommend delaying surgical intervention until the disease is quiescent over performing surgical intervention while the patient has active disease.

Observational studies have suggested improved outcomes if surgical intervention is performed when disease is not active. However, surgical intervention during active disease may be necessary if the patient has life- or organ-threatening manifestations such as stroke, loss of viability of a limb, or myocardial ischemia. 99 – 101 We recognize determining the level of disease activity in TAK can be challenging.

In patients with TAK undergoing surgical intervention, we conditionally recommend using high dose glucocorticoids in the peri-procedure period if the patient has active disease.

This recommendation pertains to patients with TAK undergoing a vascular surgical intervention due to a complication of TAK. High doses of oral glucocorticoids in the perioperative setting are recommended if the disease is active or if the clinician is concerned that the patient may have active disease. 90 , 96 , 102

This guideline presents the ACR/VF recommendations for use of diagnostic testing, treatment, clinical and laboratory monitoring, and surgical intervention for patients with GCA or TAK. Overarching themes of the recommendations include the preference of temporal artery biopsy over cranial imaging studies for diagnosis of GCA within the United States, the use of large-vessel imaging for GCA and TAK for diagnosis and disease monitoring, and limiting glucocorticoid exposure to minimize toxicity. Almost all recommendations are conditional due to the low-quality evidence, reflecting the paucity of randomized clinical trials in these diseases.

Our recommendations regarding the use of temporal artery imaging differs from the recommendations presented by the European League Against Rheumatism (EULAR). In their recommendations regarding the use of imaging in large vessel vasculitis, 103 EULAR indicates that the diagnosis of GCA may be made with a positive imaging test (e.g., temporal artery ultrasound or MRI of the cranial vessels) without additional testing such as temporal artery biopsy. However, the imaging recommendations presented by EULAR assume adequate expertise with these modalities. There is limited experience with temporal artery ultrasound and MRI of the cranial vessels as a diagnostic replacement for temporal artery biopsy in the United States, and thus we continue to

recommend temporal artery biopsy as the diagnostic test of choice at this time. However, we hope and anticipate that as experience with imaging of the temporal arteries to detect giant cell arteritis (e.g., temporal artery ultrasound, MRI, and/or FDG-PET) increases in the US, patients in the US will be able to benefit from these diagnostic tests. Also, in contrast to EULAR, we favor initial treatment of GCA with glucocorticoids and a glucocorticoid sparing agent, 104 , 105 given the well-recognized toxicity of glucocorticoids.

When reviewing the data abstracted for the PICO questions, it is clear that many critical clinical questions remain unanswered for GCA and TAK, and the lack of sufficient clinical evidence for these questions is reflected in the ungraded position statements presented in this guideline. For example, the optimal duration of therapy for any treatment and how best to monitor disease status is unknown. Few “glucocorticoid-sparing” agents have been identified through high-quality data. Accurate and validated indicators of disease activity have not been established or widely used for GCA or TAK. Interpretation of imaging studies in GCA and TAK can be challenging, and the clinical significance of persistent vascular wall inflammation during clinically quiescent disease is unclear.

Given these critical gaps in knowledge, we encourage additional research into the management of GCA and TAK. Studies that may greatly benefit patient care include:

Translational studies contributing to the understanding of disease pathogenesis to facilitate development of more targeted therapies

Randomized clinical trials identifying new therapeutic options for the management of GCA and TAK

Randomized clinical trials comparing the effectiveness of currently used immunosuppressive therapies

Longitudinal studies with biospecimen collection and routine vascular imaging to identify biomarkers of disease activity, indicators of disease prognosis, and the clinical sequelae of abnormalities identified on vascular imaging

We are hopeful that additional investigations into GCA and TAK will enable a more tailored approach to patient management to improve disease outcomes and minimize treatment toxicities.

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23045170 10.1002/art.37715 2. Weyand CM , Goronzy JJ . Giant-cell arteritis and polymyalgia rheumatica . N Engl J Med . 2014 ; 371 (17): 1653 . 10.1056/NEJMc1409206 25337759 3. Gonzalez-Gay MA , Vazquez-Rodriguez TR , Lopez-Diaz MJ , Epidemiology of giant cell arteritis and polymyalgia rheumatica . Arthritis Rheum . 2009 ; 61 (10): 1454 – 1461 . 19790127 10.1002/art.24459 4. Koster MJ , Matteson EL , Warrington KJ . Large-vessel giant cell arteritis: diagnosis, monitoring and management . Rheumatology (Oxford) . 2018 ; 57 (suppl_2): ii32 – ii42 . 29982778 10.1093/rheumatology/kex424 5. Mukhtyar C , Guillevin L , Cid MC , EULAR recommendations for the management of large vessel vasculitis . Ann Rheum Dis . 2009 ; 68 (3): 318 – 323 . 18413441 10.1136/ard.2008.088351 6. Salvarani C , Crowson CS , O'Fallon WM , Hunder GG , Gabriel SE . Reappraisal of the epidemiology of giant cell arteritis in Olmsted County, Minnesota, over a fifty-year period . Arthritis Rheum . 2004 ; 51 (2): 264 – 268 . 15077270 10.1002/art.20227 7. Aiello PD , Trautmann JC , McPhee TJ , Kunselman AR , Hunder GG . Visual prognosis in giant cell arteritis . Ophthalmology . 1993 ; 100 (4): 550 – 555 . 8479714 10.1016/s0161-6420(93)31608-8 8. Stone JH , Tuckwell K , Dimonaco S , Trial of Tocilizumab in Giant-Cell Arteritis . N Engl J Med . 2017 ; 377 (4): 317 – 328 . 28745999 10.1056/NEJMoa1613849 9. Hall S , Barr W , Lie JT , Stanson AW , Kazmier FJ , Hunder GG . Takayasu arteritis. A study of 32 North American patients . Medicine (Baltimore) . 1985 ; 64 (2): 89 – 99 . 2858047 10. Schmidt J , Kermani TA , Bacani AK , Diagnostic features, treatment, and outcomes of Takayasu arteritis in a US cohort of 126 patients . Mayo Clin Proc . 2013 ; 88 (8): 822 – 830 . 23849994 10.1016/j.mayocp.2013.04.025 11. Sanchez-Alvarez C , Mertz LE , Thomas CS , Cochuyt JJ , Abril A . Demographic, Clinical, and Radiologic Characteristics of a Cohort of Patients with Takayasu Arteritis . Am J Med . 2019 ; 132 (5): 647 – 651 . 30615861 10.1016/j.amjmed.2018.12.017 12. Labarca C , Makol A , Crowson CS , Kermani TA , Matteson EL , Warrington KJ . Retrospective Comparison of Open versus Endovascular Procedures for Takayasu Arteritis . J Rheumatol . 2016 ; 43 (2): 427 – 432 . 26669920 10.3899/jrheum.150447 13. Alexander PE , Li SA , Gionfriddo MR , Senior GRADE methodologists encounter challenges as part of WHO guideline development panels: an inductive content analysis . J Clin Epidemiol . 2016 ; 70 : 123 – 128 . 26385188 10.1016/j.jclinepi.2015.09.003 14. Andrews J , Guyatt G , Oxman AD , GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations . J Clin Epidemiol . 2013 ; 66 (7): 719 – 725 . 23312392 10.1016/j.jclinepi.2012.03.013 15. Guyatt GH , Oxman AD , Vist GE , GRADE: an emerging consensus on rating quality of evidence and strength of recommendations . BMJ . 2008 ; 336 (7650): 924 – 926 . 18436948 10.1136/bmj.39489.470347.AD PMC2335261 16. Alexander PE , Gionfriddo MR , Li SA , A number of factors explain why WHO guideline developers make strong recommendations inconsistent with GRADE guidance . J Clin Epidemiol . 2016 ; 70 : 111 – 122 . 26399903 10.1016/j.jclinepi.2015.09.006 17. Durling B , Toren A , Patel V , Gilbert S , Weis E , Jordan D . Incidence of discordant temporal artery biopsy in the diagnosis of giant cell arteritis . Can J Ophthalmol . 2014 ; 49 (2): 157 – 161 . 24767221 10.1016/j.jcjo.2013.12.008 18. Mahr A , Saba M , Kambouchner M , Temporal artery biopsy for diagnosing giant cell arteritis: the longer, the better? Ann Rheum Dis . 2006 ; 65 (6): 826 – 828 . 16699053 10.1136/ard.2005.042770 PMC1798165 19. Roth AM , Milsow L , Keltner JL . The ultimate diagnoses of patients undergoing temporal artery biopsies . Arch Ophthalmol . 1984 ; 102 (6): 901 – 903 . 6732572 10.1001/archophth.1984.01040030721028 20. 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 (12): 987 – 992 . 8185147 10.7326/0003-4819-120-12-199406150-00003 21. Allison MC , Gallagher PJ . Temporal artery biopsy and corticosteroid treatment . Ann Rheum Dis . 1984 ; 43 (3): 416 – 417 . 6742903 10.1136/ard.43.3.416 PMC1001361 22. Breuer GS , Neshet R , Neshet G . Negative temporal artery biopsies: eventual diagnoses and features of patients with biopsy-negative giant cell arteritis compared to patients without arteritis . Clin Exp Rheumatol . 2008 ; 26 (6): 1103 – 1106 . 19210879 23. Bury D , Joseph J , Dawson TP . Does preoperative steroid treatment affect the

histology in giant cell (cranial) arteritis? *J Clin Pathol* . 2012 ; 65 (12): 1138 – 1140 . 22844066 10.1136/jclinpath-2012-200870 24. Gonzalez-Gay MA , Garcia-Porrúa 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 (4): 249 – 256 . 11182025 10.1053/sarh.2001.16650 25. Hall S , Persellin S , Lie JT , O'Brien PC , Kurland LT , Hunder GG . The therapeutic impact of temporal artery biopsy . *Lancet* . 1983 ; 2 (8361): 1217 – 1220 . 6139569 10.1016/s0140-6736(83)91269-2 26. Le K , Boels LM , Lynn AB , Clancy TV , Hooks WB , 3rd, Hope WW . The effect of temporal artery biopsy on the treatment of temporal arteritis . *Am J Surg* . 2015 ; 209 (2): 338 – 341 . 25457237 10.1016/j.amjsurg.2014.07.007 27. Ray-Chaudhuri N , Kine DA , Tijani SO , Effect of prior steroid treatment on temporal artery biopsy findings in giant cell arteritis . *Br J Ophthalmol* . 2002 ; 86 (5): 530 – 532 . 11973248 10.1136/bjo.86.5.530 PMC1771122 28. Maleszewski JJ , Younge BR , Fritzlen JT , Clinical and pathological evolution of giant cell arteritis: a prospective study of follow-up temporal artery biopsies in 40 treated patients . *Mod Pathol* . 2017 ; 30 (6): 788 – 796 . 28256573 10.1038/modpathol.2017.10 PMC5650068 29. Bley TA , Uhl M , Carew J , Diagnostic value of high-resolution MR imaging in giant cell arteritis . *AJNR Am J Neuroradiol* . 2007 ; 28 (9): 1722 – 1727 . 17885247 10.3174/ajnr.A0638 PMC8134183 30. Bowling K , Rait J , Atkinson J , Srinivas G . Temporal artery biopsy in the diagnosis of giant cell arteritis: Does the end justify the means? *Ann Med Surg (Lond)* . 2017 ; 20 : 1 – 5 . 28663795 10.1016/j.amsu.2017.06.020 PMC5479941 31. Hussain O , McKay A , Fairburn K , Doyle P , Orr R . Diagnosis of giant cell arteritis: when should we biopsy the temporal artery? *Br J Oral Maxillofac Surg* . 2016 ; 54 (3): 327 – 330 . 26786198 10.1016/j.bjoms.2015.12.013 32. Luqmani R , Lee E , Singh S , The Role of Ultrasound Compared to Biopsy of Temporal Arteries in the Diagnosis and Treatment of Giant Cell Arteritis (TABUL): a diagnostic accuracy and cost-effectiveness study . *Health Technol Assess* . 2016 ; 20 (90): 1 – 238 . 10.3310/hta20900 PMC5165283 27925577 33. Yuksel V , Guclu O , Tastekin E , Clinical correlation of biopsy results in patients with temporal arteritis . *Rev Assoc Med Bras (1992)* . 2017 ; 63 (11): 953 – 956 . 29451658 10.1590/1806-9282.63.11.953 34. Ghinai A , Zuccoli G , Nicolini A , 1T magnetic resonance imaging in the diagnosis of giant cell arteritis: comparison with ultrasonography and physical examination of temporal arteries . *Clin Exp Rheumatol* . 2008 ; 26 (3 Suppl 49): S76 – 80 . 18799059 35. Hauenstein C , Reinhard M , Geiger J , Effects of early corticosteroid treatment on magnetic resonance imaging and ultrasonography findings in giant cell arteritis . *Rheumatology (Oxford)* . 2012 ; 51 (11): 1999 – 2003 . 22772317 10.1093/rheumatology/kes153 36. Klink T , Geiger J , Both M , Giant cell arteritis: diagnostic accuracy of MR imaging of superficial cranial arteries in initial diagnosis-results from a multicenter trial . *Radiology* . 2014 ; 273 (3): 844 – 852 . 25102371 10.1148/radiol.14140056 37. Rheaume M , Rebello R , Pagnoux C , High-Resolution Magnetic Resonance Imaging of Scalp Arteries for the Diagnosis of Giant Cell Arteritis: Results of a Prospective Cohort Study . *Arthritis Rheumatol* . 2017 ; 69 (1): 161 – 168 . 27483045 10.1002/art.39824 38. Blockmans D , de Ceuninck L , Vanderschueren S , Knockaert D , Mortelmans L , Bobbaers H . Repetitive 18F-fluorodeoxyglucose positron emission tomography in giant cell arteritis: a prospective study of 35 patients . *Arthritis Rheum* . 2006 ; 55 (1): 131 – 137 . 16463425 10.1002/art.21699 39. Hay B , Mariano-Goulart D , Bourdon A , Diagnostic performance of (18)F-FDG PET-CT for large vessel involvement assessment in patients with suspected giant cell arteritis and negative temporal artery biopsy . *Ann Nucl Med* . 2019 ; 33 (7): 512 – 520 . 30976984 10.1007/s12149-019-01358-5 40. Kermani TA , Diab S , Sreih AG , Arterial lesions in giant cell arteritis: A longitudinal study . *Semin Arthritis Rheum* . 2019 ; 48 (4): 707 – 713 . 29880442 10.1016/j.semarthrit.2018.05.002 PMC6226363 41. Nielsen BD , Gormsen LC , Hansen IT , Keller KK , Therkildsen P , Hauge EM . Three days of high-dose glucocorticoid treatment attenuates large-vessel 18F-FDG uptake in large-vessel giant cell arteritis but with a limited impact on diagnostic accuracy . *Eur J Nucl Med Mol Imaging* . 2018 ; 45 (7): 1119 – 1128 . 29671039 10.1007/s00259-018-4021-4 42. Pfadenhauer K , Weinerth J , Hrdina C . Vertebral arteries: a target for FDG-PET imaging in giant cell arteritis? Clinical, ultrasonographic and PET study in 46 patients . *Nuklearmedizin* . 2011 ; 50 (1): 28 – 32 . 21060976 10.3413/nukmed-0335-10-07 43. Quinn KA , Ahlman MA , Malayeri AA , Comparison of magnetic resonance angiography and (18)F-fluorodeoxyglucose positron emission tomography in large-vessel vasculitis . *Ann Rheum Dis* . 2018 ; 77 (8): 1165 – 1171 . 29666047 10.1136/annrheumdis-2018-213102 PMC6045453 44. Schmidt WA , Seifert A , Gromnica-Ihle E , Krause A , Natusch A . Ultrasound of proximal upper extremity arteries to increase the diagnostic

yield in large-vessel giant cell arteritis . *Rheumatology (Oxford)* . 2008 ; 47 (1) : 96 – 101 . 18077499 10.1093/rheumatology/kem322 45. Grayson PC , Alehashemi S , Bagheri AA , (18) F-Fluorodeoxyglucose-Positron Emission Tomography As an Imaging Biomarker in a Prospective, Longitudinal Cohort of Patients With Large Vessel Vasculitis . *Arthritis Rheumatol* . 2018 ; 70 (3) : 439 – 449 . 29145713 10.1002/art.40379 PMC5882488 46. Grayson PC , Tomasson G , Cuthbertson D , Association of vascular physical examination findings and arteriographic lesions in large vessel vasculitis . *J Rheumatol* . 2012 ; 39 (2) : 303 – 309 . 22174204 10.3899/jrheum.110652 PMC3729730 47. Chevalet P , Barrier JH , Pottier P , 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 (6) : 1484 – 1491 . 10852275 48. Mazlumzadeh M , Hunder GG , Easley KA , Treatment of giant cell arteritis using induction therapy with high-dose glucocorticoids: a double-blind, placebo-controlled, randomized prospective clinical trial . *Arthritis Rheum* . 2006 ; 54 (10) : 3310 – 3318 . 17009270 10.1002/art.22163 49. Chan CC , Paine M , O'Day J . Steroid management in giant cell arteritis . *Br J Ophthalmol* . 2001 ; 85 (9) : 1061 – 1064 . 11520757 10.1136/bjo.85.9.1061 PMC1724128 50. 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 (4) : 355 – 367 . 12190776 10.1034/j.1600-0420.2002.800403.x 51. Hunder GG , Sheps SG , Allen GL , Joyce JW . Daily and alternate-day corticosteroid regimens in treatment of giant cell arteritis: comparison in a prospective study . *Ann Intern Med* . 1975 ; 82 (5) : 613 – 618 . 1137255 10.7326/0003-4819-82-5-613 52. Delecoeuillerie G , Joly P , Cohen de Lara A , Paolaggi JB . Polymyalgia rheumatica and temporal arteritis: a retrospective analysis of prognostic features and different corticosteroid regimens (11 year survey of 210 patients) . *Ann Rheum Dis* . 1988 ; 47 (9) : 733 – 739 . 3178314 10.1136/ard.47.9.733 PMC1003589 53. Neshet G , Rubinow A , Sonnenblick M . Efficacy and adverse effects of different corticosteroid dose regimens in temporal arteritis: a retrospective study . *Clin Exp Rheumatol* . 1997 ; 15 (3) : 303 – 306 . 9177927 54. Villiger PM , Adler S , Kuchen S , Tocilizumab for induction and maintenance of remission in giant cell arteritis: a phase 2, randomised, double-blind, placebo-controlled trial . *Lancet* . 2016 ; 387 (10031) : 1921 – 1927 . 26952547 10.1016/S0140-6736(16)00560-2 55. Langford CA , Cuthbertson D , Ytterberg SR , A Randomized, Double-Blind Trial of Abatacept (CTLA-4Ig) for the Treatment of Giant Cell Arteritis . *Arthritis Rheumatol* . 2017 ; 69 (4) : 837 – 845 . 28133925 10.1002/art.40044 PMC5378642 56. Mahr AD , Jover JA , Spiera RF , Adjunctive methotrexate for treatment of giant cell arteritis: an individual patient data meta-analysis . *Arthritis Rheum* . 2007 ; 56 (8) : 2789 – 2797 . 17665429 10.1002/art.22754 57. Seror R , Baron G , Hachulla E , Adalimumab for steroid sparing in patients with giant-cell arteritis: results of a multicentre randomised controlled trial . *Ann Rheum Dis* . 2014 ; 73 (12) : 2074 – 2081 . 23897775 10.1136/annrheumdis-2013-203586 58. Garcia-Martinez A , Hernandez-Rodriguez J , Grau JM , Cid MC . Treatment with statins does not exhibit a clinically relevant corticosteroid-sparing effect in patients with giant cell arteritis . *Arthritis Rheum* . 2004 ; 51 (4) : 674 – 678 . 15334444 10.1002/art.20541 59. Narvaez J , Bernad B , Nolla JM , Valverde J . Statin therapy does not seem to benefit giant cell arteritis . *Semin Arthritis Rheum* . 2007 ; 36 (5) : 322 – 327 . 17204308 10.1016/j.semarthrit.2006.10.001 60. Pugnet G , Sallier L , Fournier JP , Bourrel R , Montastruc JL , Lapeyre-Mestre M . Predictors of Cardiovascular Hospitalization in Giant Cell Arteritis: Effect of Statin Exposure. A French Population-based Study . *J Rheumatol* . 2016 ; 43 (12) : 2162 – 2170 . 27585686 10.3899/jrheum.151500 61. Berger CT , Wolbers M , Meyer P , Daikeler T , Hess C . High incidence of severe ischaemic complications in patients with giant cell arteritis irrespective of platelet count and size, and platelet inhibition . *Rheumatology (Oxford)* . 2009 ; 48 (3) : 258 – 261 . 19129348 10.1093/rheumatology/ken480 62. Narvaez J , Bernad B , Gomez-Vaquero C , Impact of antiplatelet therapy in the development of severe ischemic complications and in the outcome of patients with giant cell arteritis . *Clin Exp Rheumatol* . 2008 ; 26 (3 Suppl 49) : S57 – 62 . 18799055 63. Neshet G , Berkun Y , Mates M , Baras M , Rubinow A , Sonnenblick M . Low-dose aspirin and prevention of cranial ischemic complications in giant cell arteritis . *Arthritis Rheum* . 2004 ; 50 (4) : 1332 – 1337 . 15077317 10.1002/art.20171 64. Salvarani C , Della Bella C , Cimino L , Risk factors for severe cranial ischaemic events in an Italian population-based cohort of patients with giant cell arteritis . *Rheumatology (Oxford)* . 2009 ; 48 (3) : 250 – 253 . 19109317 10.1093/rheumatology/ken465 65. Hoffman GS , Cid MC , Hellmann DB , A multicenter, randomized, double-blind, placebo-controlled trial of adjuvant methotrexate treatment

for giant cell arteritis . *Arthritis Rheum* . 2002 ; 46 (5) : 1309 – 1318 . 12115238 10.1002/art.10262

66. Spiera RF , Mitnick HJ , Kupersmith M , A prospective, double-blind, randomized, placebo controlled trial of methotrexate in the treatment of giant cell arteritis (GCA) . *Clin Exp Rheumatol* . 2001 ; 19 (5) : 495 – 501 . 11579707

67. Hoffman GS , Cid MC , Rendt-Zagar KE , Infliximab for maintenance of glucocorticosteroid-induced remission of giant cell arteritis: a randomized trial . *Ann Intern Med* . 2007 ; 146 (9) : 621 – 630 . 17470830 10.7326/0003-4819-146-9-200705010-00004

68. Both M , Aries PM , Muller-Hulsbeck S , Balloon angioplasty of arteries of the upper extremities in patients with extracranial giant-cell arteritis . *Ann Rheum Dis* . 2006 ; 65 (9) : 1124 – 1130 . 16464985 10.1136/ard.2005.048470 PMC1798271

69. Clifford AH , Arafat A , Idrees JJ , Outcomes Among 196 Patients With Noninfectious Proximal Aortitis . *Arthritis Rheumatol* . 2019 ; 71 (12) : 2112 – 2120 . 30730604 10.1002/art.40855

70. Mennander AA , Miller DV , Liang KP , Surgical management of ascending aortic aneurysm due to non-infectious aortitis . *Scand Cardiovasc J* . 2008 ; 42 (6) : 417 – 424 . 18609056 10.1080/14017430802023086

71. Allen DB . Growth suppression by glucocorticoid therapy . *Endocrinol Metab Clin North Am* . 1996 ; 25 (3) : 699 – 717 . 8879994 10.1016/s0889-8529(05)70348-0

72. Mutoh T , Shirai T , Fujii H , Ishii T , Harigae H . Insufficient Use of Corticosteroids without Immunosuppressants Results in Higher Relapse Rates in Takayasu Arteritis . *J Rheumatol* . 2020 ; 47 (2) : 255 – 263 . 31092708 10.3899/jrheum.181219

73. Molloy ES , Langford CA , Clark TM , Gota CE , Hoffman GS . Anti-tumour necrosis factor therapy in patients with refractory Takayasu arteritis: long-term follow-up . *Ann Rheum Dis* . 2008 ; 67 (11) : 1567 – 1569 . 18677012 10.1136/ard.2008.093260

74. Nakaoka Y , Isobe M , Takei S , Efficacy and safety of tocilizumab in patients with refractory Takayasu arteritis: results from a randomised, double-blind, placebo-controlled, phase 3 trial in Japan (the TAKT study) . *Ann Rheum Dis* . 2018 ; 77 (3) : 348 – 354 . 29191819 10.1136/annrheumdis-2017-211878 PMC5867398

75. Mekinian A , Resche-Rigon M , Comarmond C , Efficacy of tocilizumab in Takayasu arteritis: Multicenter retrospective study of 46 patients . *J Autoimmun* . 2018 ; 91 : 55 – 60 . 29678346 10.1016/j.jaut.2018.04.002

76. Langford CA , Cuthbertson D , Ytterberg SR , A Randomized, Double-Blind Trial of Abatacept (CTLA-4Ig) for the Treatment of Takayasu Arteritis . *Arthritis Rheumatol* . 2017 ; 69 (4) : 846 – 853 . 28133931 10.1002/art.40037 PMC5378643

77. Aeschlimann FA , Eng SWM , Sheikh S , Childhood Takayasu arteritis: disease course and response to therapy . *Arthritis Res Ther* . 2017 ; 19 (1) : 255 . 29166923 10.1186/s13075-017-1452-4 PMC5700506

78. Mekinian A , Comarmond C , Resche-Rigon M , Efficacy of Biological-Targeted Treatments in Takayasu Arteritis: Multicenter, Retrospective Study of 49 Patients . *Circulation* . 2015 ; 132 (18) : 1693 – 1700 . 26354797 10.1161/CIRCULATIONAHA.114.014321

79. Schmidt J , Kermani TA , Bacani AK , Crowson CS , Matteson EL , Warrington KJ . Tumor necrosis factor inhibitors in patients with Takayasu arteritis: experience from a referral center with long-term followup . *Arthritis Care Res (Hoboken)* . 2012 ; 64 (7) : 1079 – 1083 . 22328491 10.1002/acr.21636

80. Comarmond C , Biard L , Lambert M , Long-Term Outcomes and Prognostic Factors of Complications in Takayasu Arteritis: A Multicenter Study of 318 Patients . *Circulation* . 2017 ; 136 (12) : 1114 – 1122 . 28701469 10.1161/CIRCULATIONAHA.116.027094

81. Gulcu A , Gezer NS , Akar S , Akkoc N , Onen F , Goktay AY . Long-Term Follow-Up of Endovascular Repair in the Management of Arterial Stenosis Caused by Takayasu's Arteritis . *Ann Vasc Surg* . 2017 ; 42 : 93 – 100 . 28323230 10.1016/j.avsg.2016.10.066

82. de Souza AW , Machado NP , Pereira VM , Antiplatelet therapy for the prevention of arterial ischemic events in takayasu arteritis . *Circ J* . 2010 ; 74 (6) : 1236 – 1241 . 20467149 10.1253/circj.cj-09-0905

83. Wang X , Dang A , Lv N , Liu Q , Chen B . High-sensitivity C-reactive protein predicts adverse cardiovascular events in patients with Takayasu arteritis with coronary artery involvement . *Clin Rheumatol* . 2016 ; 35 (3) : 679 – 684 . 25665822 10.1007/s10067-015-2873-6

84. Liu YQ , Ling J , Wang ZL . Intravenous digital subtraction angiography in patients with aorto-arteritis (Takayasu's) . *Cardiovasc Intervent Radiol* . 1990 ; 13 (2) : 83 – 87 . 1974827 10.1007/BF02577356

85. Lee KH , Cho A , Choi YJ , The role of (18) F-fluorodeoxyglucose-positron emission tomography in the assessment of disease activity in patients with takayasu arteritis . *Arthritis Rheum* . 2012 ; 64 (3) : 866 – 875 . 21989701 10.1002/art.33413

86. Walter MA , Melzer RA , Schindler C , Muller-Brand J , Tyndall A , Nitzsche EU . The value of [18F]FDG-PET in the diagnosis of large-vessel vasculitis and the assessment of activity and extent of disease . *Eur J Nucl Med Mol Imaging* . 2005 ; 32 (6) : 674 – 681 . 15747154 10.1007/s00259-004-1757-9

87. Vinicki JP , Garcia-Vicuna R , Arredondo M , Sustained remission after long-term biological therapy in patients with large vessel vasculitis: an analysis of ten cases .

Reumatol Clin . 2017 ; 13 (4): 210 – 213 . 27499427 10.1016/j.reuma.2016.06.003 88. Ando M , Sasako Y , Okita Y , Tagusari O , Kitamura S , Matsuo H . Surgical considerations of occlusive lesions associated with Takayasu's arteritis . Jpn J Thorac Cardiovasc Surg . 2000 ; 48 (3): 173 – 179 . 10793496 10.1007/BF03218116 89. Lee GY , Jeon P , Do YS , Comparison of outcomes between endovascular treatment and bypass surgery in Takayasu arteritis . Scand J Rheumatol . 2014 ; 43 (2): 153 – 161 . 24134435 10.3109/03009742.2013.822096 90. Zheng T , Zhu S , Ou JF , Treatment with Corticosteroid and/or Immunosuppressive Agents before Surgery can Effectively Improve the Surgical Outcome in Patients with Takayasu's Arteritis . J Invest Surg . 2019 ; 32 (3): 220 – 227 . 29313449 10.1080/08941939.2017.1408718 91. Ham SW , Weaver FA . Ex vivo renal artery reconstruction for complex renal artery disease . J Vasc Surg . 2014 ; 60 (1): 143 – 150 . 24594447 10.1016/j.jvs.2014.01.061 92. Khalilullah M , Tyagi S . Percutaneous transluminal angioplasty in Takayasu arteritis . Heart Vessels Suppl . 1992 ; 7 : 146 – 153 . 1360961 10.1007/BF01744561 93. Sharma S , Gupta H , Saxena A , Results of renal angioplasty in nonspecific aortoarteritis (Takayasu disease) . J Vasc Interv Radiol . 1998 ; 9 (3): 429 – 435 . 9618101 10.1016/s1051-0443(98)70294-5 94. Sun Y , Ma L , Ma L , Cyclophosphamide could be a better choice than methotrexate as induction treatment for patients with more severe Takayasu's arteritis . Rheumatol Int . 2017 ; 37 (12): 2019 – 2026 . 29030659 10.1007/s00296-017-3847-6 95. Chen B , Yu HX , Zhang J , Endovascular revascularization for carotid artery occlusion in patients with Takayasu arteritis . Eur J Vasc Endovasc Surg . 2015 ; 49 (5): 498 – 505 . 25784506 10.1016/j.ejvs.2015.01.018 96. Fields CE , Bower TC , Cooper LT , Takayasu's arteritis: operative results and influence of disease activity . J Vasc Surg . 2006 ; 43 (1): 64 – 71 . 16414389 10.1016/j.jvs.2005.10.010 97. Kim HJ , Lee CS , Kim JS , Outcomes after endovascular treatment of symptomatic patients with Takayasu's arteritis . Interv Neuroradiol . 2011 ; 17 (2): 252 – 260 . 21696668 10.1177/159101991101700219 PMC3287280 98. Kim YW , Kim DI , Park YJ , Surgical bypass vs endovascular treatment for patients with supra-aortic arterial occlusive disease due to Takayasu arteritis . J Vasc Surg . 2012 ; 55 (3): 693 – 700 . 22119246 10.1016/j.jvs.2011.09.051 99. Kinjo H , Kafa A . The results of treatment in renal artery stenosis due to Takayasu disease: comparison between surgery, angioplasty, and stenting. A monocentric retrospective study . G Chir . 2015 ; 36 (4): 161 – 167 . 26712071 10.11138/gchir/2015.36.4.161 PMC4732586 100. Park MC , Lee SW , Park YB , Lee SK , Choi D , Shim WH . Post-interventional immunosuppressive treatment and vascular restenosis in Takayasu's arteritis . Rheumatology (Oxford) . 2006 ; 45 (5): 600 – 605 . 16352637 10.1093/rheumatology/kei245 101. Wang X , Dang A , Lv N , Long-term outcomes of coronary artery bypass grafting versus percutaneous coronary intervention for Takayasu arteritis patients with coronary artery involvement . Semin Arthritis Rheum . 2017 ; 47 (2): 247 – 252 . 28457530 10.1016/j.semarthrit.2017.03.009 102. Ham SW , Kumar SR , Wang BR , Rowe VL , Weaver FA . Late outcomes of endovascular and open revascularization for nonatherosclerotic renal artery disease . Arch Surg . 2010 ; 145 (9): 832 – 839 . 20855752 10.1001/archsurg.2010.183 103. Dejaco C , Ramiro S , Duftner C , EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice . Ann Rheum Dis . 2018 ; 77 (5): 636 – 643 . 29358285 10.1136/annrheumdis-2017-212649 104. Best JH , Kong AM , Unizony S , Tran O , Michalska M . Risk of Potential Glucocorticoid-Related Adverse Events in Patients with Giant Cell Arteritis: Results from a USA-Based Electronic Health Records Database . Rheumatol Ther . 2019 ; 6 (4): 599 – 610 . 31656021 10.1007/s40744-019-00180-9 PMC6858477 105. Hellmich B , Agueda A , Monti S , 2018 Update of the EULAR recommendations for the management of large vessel vasculitis . Ann Rheum Dis . 2020 ; 79 (1): 19 – 30 . 31270110 10.1136/annrheumdis-2019-215672 Figure 1. Overview of treatment of giant cell arteritis.

Overview of treatment of Takayasu arteritis based on clinical and radiographic assessments.

Definitions for the disease states, treatments, and disease assessments for giant cell arteritis (GCA) and Takayasu's arteritis (TAK) specified in the Recommendations and Ungraded Position Statements.

Recommendations for diagnostic testing in giant cell arteritis (GCA).

PICO= Population Intervention Comparator Outcome question used in GRADE methodology.

Please refer to Supplementary Appendix 2 for the PICO questions developed for GCA.

Recommendations/Statements for treatment (medical and surgical management) and clinical/laboratory monitoring in giant cell arteritis (GCA).

PICO= Population Intervention Comparator Outcome question used in GRADE methodology.

Please refer to Supplementary Appendix 2 for the PICO questions developed for GCA.

PICO question developed after completion of literature review and evidence reports.

Data from studies already included in evidence reports reviewed, but no dedicated literature review performed for these questions. Recommendation formed from available evidence and expert opinion.

N/A: Ungraded position statement not based on a specific PICO question.

Recommendations/Statement for medical and surgical management in Takayasu arteritis (TAK).

PICO= Population Intervention Comparator Outcome question used in GRADE methodology.

Please refer to Supplementary Appendix 2 for the PICO questions developed for TAK.

N/A: Ungraded position statement not based on a specific PICO question.

Recommendations for clinical/laboratory monitoring and vascular imaging in Takayasu arteritis (TAK).

PICO= Population Intervention Comparator Outcome question used in GRADE methodology.

Please refer to Supplementary Appendix 2 for the PICO questions developed for TAK.

Guidelines and recommendations developed and/or endorsed by the American College of Rheumatology (ACR) are intended to provide guidance for particular patterns of practice and not to dictate the care of a particular patient. The ACR considers adherence to the recommendations within this guideline to be voluntary, with the ultimate determination regarding their application to be made by the physician in light of each patient's individual circumstances. Guidelines and recommendations are intended to promote beneficial or desirable outcomes but cannot guarantee any specific outcome. Guidelines and recommendations developed and endorsed by the ACR are subject to periodic revision as warranted by the evolution of medical knowledge, technology, and practice. ACR recommendations are not intended to dictate payment or insurance decisions, and drug formularies or other third-party analyses that cite ACR guidelines should state this. These recommendations cannot adequately convey all uncertainties and nuances of patient care.

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