JAMA Insights | CLINICAL UPDATE

# Polymyalgia Rheumatica and Giant Cell Arteritis

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**Polymyalgia rheumatica (PMR)** should be included in the differential diagnosis of patients with acute onset of bilateral upper extremity pain, which is often worse with or following rest.[1] Giant cell arteritis (GCA) is characterized by headache and sometimes acute vision loss. PMR and GCA almost exclusively affect persons aged at least 50 years and frequently have overlapping symptoms, such as fever, fatigue, weight loss, depression, and night sweats, and elevations of inflammatory markers, such as erythrocyte sedimentation rate and C-reactive protein. Based on data from 2015, the overall age- and sex-adjusted prevalence rate in the US of PMR was estimated at 701 per 100 000 population aged at least 50 years and of GCA was estimated at 204 per 100 000 population aged at least 50 years.[2] This JAMA Insights article provides an update for a previous review and a suggested algorithm for the diagnosis and management of PMR and CGA.[1]

Supplemental content

## Novel Diagnostic Studies of Positron Emission Tomography/Computed Tomography

Both PMR and GCA are diagnosed by clinical features, the presence of elevated inflammatory markers, and imaging. Bilateral subdeltoid bursitis is present on ultrasonography in 69% of patients with PMR.[1] In GCA, ultrasonography, 18F-fluorodeoxyglucose positron emission tomography (PET)/computed tomography (CT), magnetic resonance imaging, and CT can demonstrate vascular inflammation by vessel wall thickening and, when used, tracer or contrast agent uptake. Temporal artery biopsy (TAB) is an alternative to imaging to confirm CGA.[1] The **Table** summarizes select studies on the use of PET/CT for diagnosis of PMR and GCA.

In a study[3] involving 99 patients, PET/CT had a sensitivity of 85.1% and specificity of 87.5% for the diagnosis of PMR; in another study[4] involving 64 patients, PET/CT had a sensitivity of 71% and a specificity of 91% for the diagnosis of GCA. An important aspect of the latter study is that cranial arteries could also be reliably assessed by modern PET/CT protocols, previously thought to be either impossible or unreliable.

PET/CT is most useful in patients with GCA with suspected involvement of the aorta and its major branches or when other diagnoses that mimic PMR or GCA should be ruled out. Some disadvantages of PET/CT are the high cost of the test (average Medicare reimbursement was about $1377 in 2018), radiation exposure, and the intrinsic limitation of resolution to approximately 2.4 mm. Another limitation is the difficulty of obtaining scans before or within the first days of glucocorticoid therapy. This is an important shortcoming because delaying the initiation of glucocorticoid therapy due to the unavailability of a diagnostic test is not acceptable given the imminent risk of visual loss in GCA, and because the sensitivity of PET/CT rapidly declines after initiation of glucocorticoid therapy. Hence, ultrasonography remains the primary imaging method for initial diagnosis of PMR and GCA.

## No Treatment Advances in PMR and Tocilizumab Approved for GCA

Glucocorticoid therapy is the currently recommended first-line treatment for both PMR and GCA, and is associated with well-known adverse effects (most commonly osteoporosis, cardiovascular complications, infections, cataracts, diabetes, weight gain, and cushingoid habitus).[1] In a study of 359 patients with PMR, the risks of developing glucocorticoid-related adverse events, such as diabetes, arterial hypertension, hyperlipidemia, or osteoporotic fractures, were not higher than in age- and sex-matched individuals derived from the general population. Only cataracts were more common in patients with PMR than in the control group.[5]

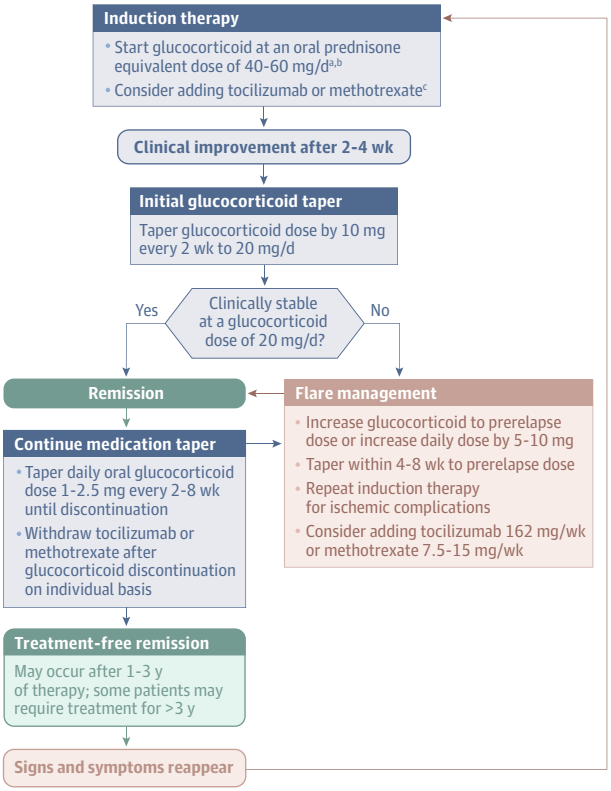
Methotrexate can be used as a glucocorticoid-sparing strategy in both PMR and GCA, but this approach is not supported by strong evidence.[1] The efficacy and glucocorticoid-sparing effects of tocilizumab, an interleukin-6 receptor α inhibitor, in GCA were recently

**Table. Diagnostic Studies of Polymyalgia Rheumatica (PMR) and Giant Cell Arteritis (GCA)**

| Source | Patient population | Inclusion criteria | PET/CT | Structures investigated | Pathologies | Sensitivity | Specificity | Reference standard |
|---|---|---|---|---|---|---|---|---|
| Henckaerts et al[3] | 99 patients with suspected PMR (67 confirmed); 58 (59%) women; 2 (2%) underwent TAB | Clinical presentation comprising PMR as differential diagnosis (not further specified) prior to glucocorticoid therapy | Hirez Biograph 16 or Truepoint Biograph 40 | 12 skeletal regions: cervical spinous processes; lumbar spinous processes; and bilateral sternoclavicular joint, ischial tuberosity, greater trochanter, hip, and shoulder; 4 vascular regions: thoracic aorta, abdominal aorta, subclavian arteries, and carotid arteries | Enhancement (score, 0-2 per skeletal region); total skeletal score (0-24) | For a score of 16: 85.1% | For a score of 16: 87.5% | Final diagnosis after 6 mo (considering clinical data and evolution, radiological, biochemical, and PET results) |
| Sammel et al[4] | 64 patients with newly suspected GCA (21 confirmed); 45 (70%) women; 58 (91%) underwent TAB | Age >50 y, ≥2 of 5 ACR criteria for GCA, scheduled for TAB, glucocorticoid therapy within 72 h | Siemens Biograph mCT time-of-flight scanner | 18 artery segments: bilateral temporal, occipital, maxillary, vertebral, carotid, subclavian, and axillary arteries, brachiocephalic artery, ascending aorta, aortic arch, and descending aorta | Primary: global assessment (positive or negative for GCA); secondary: enhancement (score, 0-3 per vascular bed) | For global assessment: 71% (final diagnosis) and 92% (TAB) | For global assessment: 91% (final diagnosis); and 85% (TAB) | Final diagnosis (considering TAB, glucocorticoid dose at 3 mo, and diagnosis of treating clinician) or TAB |

Abbreviations: ACR, American College of Rheumatology; CT, computed tomography; PET, positron emission tomography; TAB, temporal artery biopsy.

Figure. Suggested Treatment Algorithm for Management of GCA




This algorithm is based on assessment of the available literature. It has not been formally tested in a randomized clinical trial.
[a]Administer intravenous methylprednisolone (0.5-1 g/d) for 3 days (in complicated giant cell arteritis [GCA] and patients with GCA without ischemic complications).
[b]If there is established visual loss, start glucocorticoid at an oral prednisone equivalent dose of 60 mg/d to protect the contralateral eye.
[c]For GCA, consider adding tocilizumab, 162 mg/wk, (or methotrexate, 7.5-15 mg/wk) to glucocorticoids in patients at high risk for glucocorticoid adverse effects, relapse, and/or prolonged therapy; consider osteoporosis prevention or therapy according to current recommendations.

demonstrated in the GiACTA trial (eTable in the Supplement).[6] Based on results of this study, which included 251 patients with GCA, the US Food and Drug Administration and, subsequently, the European Medicines Agency granted breakthrough therapy designation for tocilizumab.

Reflecting these novel data, the previously published treatment algorithm has been updated to include recommendations for possible use of tocilizumab as a first-line glucocorticoid-sparing agent for patients with new-onset GCA who are at increased risk of developing glucocorticoid-related adverse effects or complications, relapse, or prolonged therapy and in patients who experience relapse (**Figure**).[1] It remains to be demonstrated whether these subgroups of patients will indeed benefit from tocilizumab treatment in terms of reduced glucocorticoid toxicity, cost-effectiveness, and effect on treatment duration (eTable in the Supplement).[7,8]

Methotrexate may be used as an alternative, particularly when tocilizumab is not accessible (Figure).[1] Depending on dose, route of administration, country-specific prices, and other influencing factors, tocilizumab is 10- to 80-fold more expensive than methotrexate. For example, in the US, the annual cost of treatment with tocilizumab is approximately $18 500.

A clinical trial involving 41 patients with GCA showed that more patients treated with abatacept had relapse-free survival at 12 months compared with placebo (eTable in the Supplement).[9] There was no difference in the frequency or severity of adverse effects between the treatment groups. Potential adverse effects of abatacept include increased risk of infections, allergic reactions, nausea, and headache. The annual cost of treatment with abatacept is approximately $18 700.

## Conclusions

Novel studies of PET/CT have not changed the approach to diagnosis of GCA and PMR. Glucocorticoids are still the first choice to manage both diseases. Tocilizumab is now approved for treatment of patients with GCA as a first-line glucocorticoid-sparing agent. No new strategies have been identified for the management of PMR.


## ARTICLE INFORMATION

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**Published Online:** August 19, 2020. doi:10.1001/jama.2020.10155

**Conflict of Interest Disclosures:** Dr Buttgereit reported receiving grants and personal fees from Horizon Therapeutics and Sanofi; grants from Mundipharma; grants, personal fees, and nonfinancial support from Roche; and personal fees from Galapagos outside the submitted work. Dr Matteson reported receiving grants from Genentech outside the submitted work. Dr Dejaco reported receiving personal fees from Roche, Sanofi, AbbVie, Pfizer, Merck Sharp & Dohme, Union Chimique Belge, Bristol Myers Squibb, Eli Lilly, and Novartis and grants and personal fees from Celgene outside the submitted work.


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