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Step forward towards treat-to-target management of giant cell arteritis: patients stratification aiming to targeted remission – updated guidelines

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Abstract

Background The aim of this work is to develop guidelines for health care professionals in the giant cell arteritis diagnosis and management, based on patients' stratification and targeted outcome measures.

Results Fourteen expert panel had completed the two rounds surveys. After the end of round two, twenty three recommendations were released distributed on 8 domains. The percentage of the agreement on the recommendations was 76.9% to 100%. All 23 key questions were answered at the end of the second round with agreement upon.

Conclusion Patient stratification facilitate the initiation of an appropriate management approach for patients with giant cell arteritis aiming at achieving targeted disease remission state and prevention of visual loss and/or development of ischaemic events. Treat to Target approach is a new concept in giant cell arteritis management which aims to provide tight control to achieve and maintain disease remission. This work defined the treatment targets in relation to the disease stage.

Keywords Giant cell arteritis, GCA, Guidelines, Treat to target, Patient reported outcomes

Background

Giant cell arteritis (GCA) is a primary vasculitis affecting both cranial and extra-cranial manily large-sized vessels [1]. Characteristic symptoms include recent onset temporal headache, acute visual affection, jaw claudication and polymyalgia rheumatica (PMR). The annual incidence of GCA is approximately 15–25 cases per 100,000 persons and nearly exclusively occurs in people over 50 years old [2]. Whilst the incidence of GCA increases with age, it is twice as common in women as men [3]. The lifetime risk of GCA in women is 1% compared to 0.5% in men [3, 4].

GCA is a medical emergency as it poses a risk of sudden irreversible loss of vision, stroke, tongue or scalp necrosis or other peripheral limb ischaemic events. However, there has been a misconception by the medical

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healthcare professionals that GCA is a headache disease of older adults which shows swift and good response to glucocorticoid therapy [5]. Such imposing impression of the disease made it less appealing to the medical community particularly the rheumatologists [4]. In clinical practice GCA can be multifaceted. This has been attributed to the acute onset and seriousness of the disease, diagnostic obscurity, particularly as the patients tend to seek advice from variable medical specialities, as well as the morbidity associated with GCA treatment [5]. Emerging evidence suggests that this naive concept of GCA should be dumped. This has been supported by the advances in the investigation and management of the disease. The definition of a specific ultrasonography (US) pattern in GCA has transformed the management approach of this disease in day-to-day standard practice [6–8].

Over the past decade there has been an increased awareness of GCA. Recent studies have broadened both the GCA diagnostic and treatment spectrum [9, 10]. However, despite these fundamental developments, many critical clinical questions remain unanswered for GCA which has affected the key areas of management. Furthermore, there is large heterogeneity in treatment strategies of GCA in clinical practice. These critical gaps in knowledge and medical care highlighted the imperative need to update the current management recommendation and develop improved diagnostic pathways, aiming to set up individualized and targeted management approach for GCA patients. The objective of this guideline is to provide up-to-date, evidence-based recommendations for the targeted assessment and management of GCA.

Methods

Design

Using a multi-step process strategy, the GCA consensus treatment guidelines were produced based on study. The Clinical, Evidence-based, Guidelines (CEG) guideline development methodology, which entails reaching a consensus based on the majority of available scientific data and clinical experience, served as the basis for the study design. With the ultimate aim of offering an expert opinion, the objective is to ascertain the degree of agreement among experts regarding a specific topic. The work complied with the meta-analyses and recommended publishing items for systematic reviews reporting requirements [11].

Study teams

Core team

To supervise, plan, and support the development of the project's scope and preliminary clinical questions, as well as the appointment of the expert panel and article drafting. The project's original PICOT clinical questions and project scope were developed with support from the core team. Using the PICOT process helps develop a careful and thoughtful question that makes the search for evidence easier, Formulate the PICOT question in general terms: Based on the EBSCO Health example, while P = GCA patients, I = making consensus via online survey rounds, C = the well-known evidence based previous studies, and O = development of GCA Treat-to-Target management guidelines.

Key questions used to develop the guidelines

A set of structured key questions (supplement 1) that identify the target population, the approach taken in the investigation, the comparison(s) employed, the outcomes used to quantify efficacy, effectiveness, or risk, as well as time (PICOT), served as the focal point of these guidelines [12]. The following procedures were followed in order to gather the evidence needed to respond to the clinical questions: developing the clinical questions, organising the questions, looking for evidence, critically assessing and selecting the evidence, presenting the findings, and formulating recommendations. The questions served as the foundation for the methodical literature search, which led to the development of the clinical treatment guidelines.

Literature review team

The extraction of data and the quality of evidence assessment must be completed in order to perform the literature search. The team was guided by an experienced consultant for literature reviews, and an expert in methodology assisted in conducting the study of the literature based on the particular research questions that were selected to centre on GCA management.

Data sources

Using the PubMed/MEDLINE, EMBASE, and Cochrane databases, a systematic literature search was conducted to obtain appropriate evidence-based background knowledge for deliberations. The experts in charge of the literature review revised the data abstraction, published recommendations, and quality of evidence rating [13, 14]. They performed this review by providing a comprehensive list of recommendations for the management of GCA, which was based on both their own clinical expertise and the available research evidence. The Oxford Centre for Evidence-based Medicine (CEBM) approach was used to determine the level of evidence for each component (supplement 2) [14].

Study selection

Relevant studies were selected by applying inclusion and exclusion criteria to the literature retrieved with the search strategies.

Inclusion criteria

Systematic reviews, uncontrolled trials, randomised controlled trials (RCTs), observational studies (cohort, case control, and cross-sectional), and articles with economic evaluations were among the articles that were included. Trials were considered eligible if participants with GCA from any type of healthcare setting and therapy were included, independent of gender. The classification evidence and recommendations utilised in the included research should be clearly specified. Additionally, the formal procedure (Delphi exercise, panel conference) for formulating recommendations was described.

Exclusion criteria

Editorials, commentary, conference abstracts, narrative/personal reviews that do not rely on evidence, and submissions without an English translation were excluded.

Expert panel

Those are going to be chosen by the core team. In addition to actively participating in GCA-related scientific research, participants should possess professional expertise, training, and experience..

Target audience

The purpose of these guidelines is to support medical professionals who monitor and treat patients with GCA. Additionally, patients and those in charge of commissioning care for patients with GCA in the National Health Service should find the guidelines to be a useful resource.

Delphi

The Delphi procedure is a tried-and-true method designed to find consensus views among experts in the field in order to address research question(s). Its system is built around a sequence of expert-addressed questionnaires, or "rounds" [15].

Consensus process

To reach a consensus on the GCA's T2T (Treat to Target) strategy, two Delphi rounds were conducted. The structured Delphi method guarantees that each participant's opinion is given equal weight. Online surveys were used to carry out the Delphi process. Ten items related to the GCA treatment plan were included in the first round of the electronic questionnaire.

Voting process

Voting was conducted in two time-limited rounds via live online delivering. Every task force member received an invitation to participate and advance notice of the start and end times of each voting session. Votes were collected and processed anonymously, and special access links were distributed. During the voting process, feedback on possible ambiguity, unidentified overlaps, and rephrasing of each statement was received. Voting on the statements was restricted to task force members alone.

Chronogram of Delphi rounds

The first round took place between 3rd Feb -8th Feb 2023 (6 days). The aspects about which respondents did not reach consensus in this first round were revised in view of the comments and included in the second round. The second round took place on 19th of Feb 2023 (11 days after the first round) and lasted for 6 days (till 24th of Feb 2023).

Rating

Every statement received a score ranging from 1 to 9, where 1 denoted "complete disagreement" and 9 represented "complete agreement." In general, the numbers 1–3, 4–6, and 7–9 stand for disagreement, uncertainty, and agreement, in that order. No statement required voting, and participants were urged not to vote if they thought a statement was outside their purview. "Uncertainty" in one's vote indicates "discomfort regarding the accuracy of the recommendation." Following each voting session, the scientific committee evaluated the comments that were added to all of the statements. Throughout each vote round, members were encouraged to voice their opinions, especially when there was a disagreement. Because of this, the panel was able to determine when the statement was misunderstood and to remove the vote on it.

Definition of consensus

Prior to the data analysis, a consensus definition was established. In order to reach consensus and become a recommendation in this guideline, at least 80% of participants required to indicate agreement (scoring 7–9) or disagreement (score 1–3) [15–17]. A statement was retired if it obtained a mean vote of less than three or a "low" degree of agreement. Statements that scored in the (4–6) range of the uncertainty score were modified in accordance with the feedback. A recommendation was considered to have "high" levels of agreement following the second voting round if all votes cast on it fell inside the range of agreement (7–9) [18, 19].

Developing the clinical care standards framework

In assisting in the standardised identification of guideline components, a structured template was created based on the responses to the structured key questions and the literature research. The information extraction and provision formats for each guideline component have been specified.

Ethical aspects

This study was performed in accordance with the Helsinki Declaration. This was a multistep process which followed the "Clinical, Evidence-based, Guidelines" (CEG) initiative protocol (ethical approval code: 34842/8/21, ethical board Tanta University).

Results

Literature research and evidence selection:

After removing the duplicates, 607 of the 788 records that the search produced were examined (171). We obtained the whole texts of 145 possible documents after filtering. The literature review contained thirty-three documents. The findings were compiled, summarised, and developed into recommendations for the treatment of GCA patients. After that, they were debated, changed, and submitted to a vote**.**

Expert panel characteristics

The Delphi form was sent to expert panel ($n=14$), of whom 13 (92.8%) completed the two rounds. The participants were 2 from the USA, 6 from Europe, and 5 from Africa (Egypt). 11 of the experts' panel were rheumatologists in addition to 2 patients.

Delphi round 1

The 23 items in this round, which addressed the major clinical questions, included: all of the clinical questions that were addressed in the rounds that followed. Every domain and question was accepted (all respondents strongly agreed or agreed), and no questions were removed from the list.

Delphi round 2

Based on the literature search, a list of 23 sectioned recommendations were generated using the input from round 1. The response rate for round 2 was 92.8% from the experts' panel (13/14). Wording modifications were suggested for 14 statements. The statements were modified and amended. For all statements the consensus was reached (as $\geq 80\%$ of respondents strongly agreed or agreed). There were no significant differences between the grading of the patients and healthcare professionals. The main differences were regarding the priority of ultrasound scanning (favoured by the European and Egyptian teams) Vs temporal artery biopsy (favoured by the American team).

Statements and grade of recommendations (GOR) for the management of GCA

These are a list of the recommendations made in order to address the main clinical questions. Under each part, there is information on the mean degree of agreement among the expert panel members, the percentage of agreement, the level of evidence (LOE), and the grades of recommendations. A suggestion of an algorithm for the stratification of patients with GCA and the recommended management approach is demonstrated in Table 1. Table 2 shows the Treat to Target proposal for GCA.

Overarching principles

- Former term "temporal arteritis" might be misleading or confounding, as virtually any large or medium-sized artery may be affected.
- There is a misunderstanding that giant cell arteritis is just a cranial disease affecting temporal arteries. In fact, it is a systemic inflammatory disorder presenting with critically ischaemic manifestations with several patients showing involvement of the aorta and its branches.
- GCA may present with isolated extra-cranial involvement.
- Every GCA patient should be assessed for PMR clinical manifestations. PMR may appear as a symptom of relapse in GCA. Also, PMR patients who sustain recurrent relapses or unable to withdraw glucocorticoid therapy, should be assessed for GCA [20]
- The classic approach to giant cell arteritis diagnosis based on clinical assessment with occasional histological confirmation should be replaced by a fast-track imaging-based comprehensive diagnostic pathway.
- Management of GCA is multidisciplinary and led by a rheumatologist with experience in the management of GCA. Subject to the patient's specific presentation, the multidisciplinary team include ophthalmologists, neurologists and plastic and vascular surgeons.
- A suspected diagnosis of GCA should be confirmed by imaging or temporal artery biopsy.
- Comprehensive clinical assessment should include assessment of the temporal arteries as well as extracranial vascular territories, including axillary and subclavian arteries, in order to look for any one-sided vascular stenosis. Arterial pressures should also be measured in all four limbs.

Table 1 Suggested algorithm for the GCA patients' stratification

Disease state	Risk	Impact on management recommendation
Disease activity: -Elevated acute phase reactant / biomarkers -Presence of constitutional symptoms -Presence of PMR symptoms	-Risk of relapse -presence of extracranial large vessel affection	Likely to require longer treatment with glucocorticoids
Disease severity: -predominant cranial manifestations	-Risk of ischemic vascular complications	-IV methylprednisolone Induction therapy -Less likely to require long-term GG therapy
Possibility of accrual damage: -Large vessel involvement on imaging -Aortic inflammation at baseline - Ischaemic complications -Halo score grade	-Risk of relapse -Risk of aortic dilation or aneurysm	Adjuvant therapy Long-term GC therapy
Presence of Comorbidities: -DM, CVS, glaucoma	-Poor GC benefit: Risk ratio - developing disease- and therapy-related complications	Adjuvant therapy at baseline -Preventive measures to minimize disease associated complications
Relapsing disease	Long-term vascular damage	Higher steroid dose + adjuvant therapy

GCA Giant cell arthritis, *PMR* Polymyalgia rheumatic, *GC* Glucocorticoids, *CVS* Cardiovascular system, *DM* Diabetes mellitus

Table 2 Treat to target of giant cell arteritis

		Early stage	Established stage
Targets	Clinical	Avoid visual loss or other vascular damage/tissue ischemia,	-maintain remission with the minimal effective dose of therapy, -maintain GCA disease related tissue and vascular integrity (whenever appropriate),
	Therapy	Rapid achievement of remission	-Drug-free remission may be targeted, -minimization of glucocorticoid use and relapse prevention, along with avoidance of damage accrual
	Disease Activity score[a]	In remission	In remission
	PROMs:		
	-Patient reported disease activity	In remission	In remission
	-Benefit-risk ratio of therapy	Optimum	Optimum
	-Functional disability	Improved	Improved
	-Quality of life	Improved	Improved
	-Comorbidities	Controlled	Controlled
	-Patient motivation	Improved	Improved

[a] There is no approved disease activity score published yet. Currently, there is a study to develop a GCA disease activity score that has been submitted for publication

GCA Giant cell arthritis

- GCA differential diagnosis include migraine, trigeminal neuralgia, tension headache or visual disturbances attributed to other causes. These conditions should be checked and distinguished from GCA-related symptoms.
- Once the diagnosis of GCA is confirmed, treatment should be started promptly.
- GCA management should target control of the disease symptoms, avert any damage attributed to GCA, consider any relevant comorbidities and minimize treatment associated side effects. In the meantime, GCA management should aim to maximise the individual patient's health-related quality of life.
- Although glucocorticoids play a pivotal role in controlling the initial inflammation, they are unable to fully extinguish disease activity and halt long-term vascular remodelling and damage.
- The presence of associated comorbidities and current medications should be considered in the decision-making process.
- The current one-size-fits-all treatment approach leads to absolute dependence on glucocorticoids and paves the way for developing glucocorticoid-related and disease-related complications.
- GCA treatment strategy should be guided by disease stratification. This can be achieved through using clinical, biomarkers, histology, and imaging parameters as well as the presence of associated comorbidities and possible medical therapy associated complications.

- Regular follow-up and monitoring of disease activity should be tailored to the individual patient's symptoms, clinical findings and disease activity laboratory measures. The follow-up visits' frequency is decided in view of the disease activity status and current medications.
- PMR may be present before, during or after the diagnosis of GCA has been established, and vice versa.
- Glucocorticoid therapy should be started immediately in patients with a high clinical suspicion of GCA, even before histologic confirmation or imaging tests are available.
- Patients' education plays a vital role in the management of GCA particularly for its key warning symptoms, possible complications and its treatment (including treatment-related complications). As GCA and PMR are interlinked, patients should receive information on both conditions. The patients should be aware of the risk of relapse and possible ischaemic complications should they stop glucocorticoids therapy abruptly on their own.
- Management of GCA should be based on a shared decision between the patient and the rheumatologist, and should consider the outcome of management, targets, efficacy, safety and costs.

Diagnosis: Q. what is the recommended approach to GCA diagnosis?

Level of evidence: 4C, level of agreement: Mean ± SD: 8.15 ± 1.2, percentage of agreement: 92.3%, Level of agreement: High.

Clinical symptoms (Red Flags)

Key symptoms

- New-onset of persistent localised headache, often in the temporal area.
- Constitutional symptoms (e.g. weight loss > 2 kg, low-grade fever, fatigue, night sweats).
- Jaw pain and/or tongue claudication.
- Acute visual symptoms such as amaurosis fugax, acute visual loss, diplopia.
- Symptoms of polymyalgia rheumatica.
- Limb claudication.

Signs: clinical examination

Cranial disease

- Tenderness and / or thickening of the superficial temporal arteries with or without reduced pulsation.
- Scalp tenderness.

Extra-cranial disease

- Bruits (particularly in the axilla).
- Arterial blood pressure asymmetry, reduced pulses/ blood pressure of the upper limbs.
- Pathological findings during ophthalmologic examination including anterior ischaemic optic neuropathy, oculomotor cranial nerve palsy/palsies, central retinal artery occlusion, branch retinal artery occlusion and/or choroidal ischaemia.
- Distal ischaemic events, necrosis or gangrene.
- Detection of aneurysm or dissection of aorta and main branches associated with elevated inflammatory makers.

Non-specific manifestations: without evidence of infection or neoplastic disease:

– Fever
– Fatigue/ malaise
– Unexplained anaemia
– Risk Factors for visual loss:

Older age, history of transient visual loss and jaw claudication were independent predictors of visual loss, while fever and rheumatic symptoms were protective [21].

– Hypertension and ischaemic heart disease were also identified as potential risk factors for cranial ischaemic complications [22, 23].
– Risk factors for aortic aneurysms:

Smoking, male sex, hypertension and pre-existing cardiovascular disease as well as inflammation of the aorta or its proximal branches [24–28].

Diagnostic work-up

Fast Track GCA pathway: Q. is there a role for GCA fast track approach?

Level of evidence: 5D, level of agreement: Mean±SD: 8.07±2.2, percentage of agreement: 92.3%, Level of agreement: High

– Immediate treatment of GCA implies that the diagnosis is also confirmed rapidly.
– The fast track GCA pathway offers timely evaluation of cranial GCA and has become the gold standard method of assessment and treatment of patients referred with suspected GCA.
– Fast track US clinics for GCA offer the suspected GCA patients prompt chance for clinical and sonographic assessment, facilitating immediate initiation

of high-dose glucocorticoids (GC), consequently reducing the symptom-to-therapy lag. Therefore, it aims to lessen numbers of negative outcomes as sight loss and subsequently loss of independence and mobility which is associated with increase health care use and cost.

The role of imaging: Q. what is the role of imaging in the diagnosis of GCA?

Level of evidence: 3C, level of agreement: Mean±SD: 8.0±1.2, percentage of agreement: 84.6%, Level of agreement: High

- Imaging should not delay initiation of treatment.
- If GCA is suspected in a patient, an early imaging test is recommended to complement the clinical criteria for diagnosing GCA, assuming high expertise and prompt availability of the imaging technique.
- Neither imaging nor TAB are 100% sensitive. However, in rare cases, both imaging and biopsy are negative.
- In patients in whom there is a high clinical suspicion of GCA and a positive imaging test, the diagnosis of GCA may be made without an additional test (biopsy or further imaging). In patients with a low clinical probability and a negative imaging result, the diagnosis of GCA can be considered unlikely. In all other situations, additional efforts towards a diagnosis are necessary.
- Ultrasound guidance appears not to improve the diagnostic yield of TAB.

Imaging in clinically suspected cases

Level of evidence: 3C, level of agreement: Mean±SD: 8.15±0.89, percentage of agreement: 92.3%, Level of agreement: High

- Imaging examination should be done by a trained specialist using appropriate equipment, operational procedures and settings. The reliability of imaging, which has often been a concern, can be improved by specific training.
- The diagnosis of GCA should be confirmed in every patient referred for suspected diagnosis of GCA.
- If the clinical probability in suspected GCA cases is high, a provisional diagnosis of GCA may be made, which needs to be confirmed or revised during follow-up.
- Imaging of the temporal arteries by ultrasound or MRI identifies only 77% and 73% of cases, respectively, with clinical diagnosis as reference standard for GCA.
- If the clinical suspicion of GCA persists, performing a second test can be considered if the first was negative.

Imaging modalities

Ultrasound: Q. Should a suspected diagnosis of GCA be confirmed by US imaging?

Level of evidence: 2B, level of agreement: Mean±SD: 7.69±1.6, percentage of agreement: 76.9%, Level of agreement: high

- Ultrasound of temporal ± axillary arteries is recommended as the first imaging modality in patients with suspected predominantly cranial GCA. A non-compressible 'halo' sign is the ultrasound finding most suggestive of GCA.
- Measuring the flow in the vertebral or carotid arteries is advised.
- The value of ultrasonography for monitoring the inflammation at temporal arteries is limited. US imaging can be used in cases of suspected relapse or when labs are not useful (e.g. patient treated with tocilizumab)
- Ultrasonography of large arteries such as the carotids or the axillary artery might be more useful for monitoring disease because wall swelling in these larger arteries persists longer than in superficial cranial arteries despite therapy.
- US may reach a specificity above 90% (specificity may be decreased in patients with atherosclerotic disease)

Other imaging modalities: Q. Is there a room for other imaging modalities in the diagnosis of GCA?

Level of evidence: 4C, level of agreement Mean±SD: 7.85±1.63, percentage of agreement: 84.6%, Level of agreement: High

- To investigate mural inflammation, high resolution MRI of cranial arteries may be used as an alternative for GCA diagnosis if ultrasound is not available or inconclusive.
- CT and PET are not recommended for the assessment of inflammation of cranial arteries.
- Ultrasound, PET, MRI and/or CT may be used for detection of mural inflammation and/or luminal changes in extracranial arteries to support the diagnosis of Large Vessel-GCA. Ultrasound is of limited value for assessment of aortitis.

- Conventional angiography is not recommended for the diagnosis of GCA as it has been superseded by the previously mentioned imaging modalities.
- Whilst imaging is not routinely recommended for patients in clinical and biochemical remission, if a relapse is suspected in a GCA patient, imaging might be helpful to confirm or exclude it.
- In patients with GCA, MR angiography (MRA), CTA and/or ultrasound may be used for long-term monitoring of structural damage, particularly to detect stenosis, occlusion, dilatation and/or aneurysms.
- The screening frequency and the most appropriate imaging method should be decided on an individual basis.

Temporal Artery Biopsy (TAB): Q. Shall Temporal Artery biopsy be considered in every patient with suspected GCA?

Level of evidence: 5, level of agreement Mean±SD: 7.69±1.93, percentage of agreement: 76.9%, Level of agreement: high

- In case no facility to imaging is available, TAB would be the alternative approach to diagnosing GCA.
- Initially unilateral TAB is recommended over bilateral biopsies.
- Bilateral temporal artery biopsies may be appropriate if the symptoms are not clearly localized to one temporal artery.
- A long-segment temporal artery biopsy specimen (> 1 cm) is recommended over a short-segment temporal artery biopsy specimen (< 1 cm).
- Obtaining a temporal artery biopsy specimen within two weeks of starting oral glucocorticoids is recommended over waiting longer than 2 weeks for a biopsy.

Patients' stratification: Q. Can the GCA patients be stratified according to their disease status or the presence of comorbidities?

Level of evidence: 4C, level of agreement: Mean±SD: 8.23±1.1, percentage of agreement: 84.6%, Level of agreement: High

- There is not "one size fit all" glucocorticoids regimen for all newly diagnosed GCA patients, with empirical disease-modifying agents added only to patients with an increased risk of steroid-related adverse effects or when a flare occurs.
- GCA varies in extent and severity, therefore management should be guided by disease stratification and target the prevention of poor treatment outcomes.
- Patients' stratification facilitates the achievement of treatment targets, tailoring the medical management approach and prediction of the disease outcomes.
- Patient can be stratified according to: Disease activity, disease severity, chances of accrual damage and the presence of comorbidities (Table 1).

Treat to Target: Q. Can GCA be treated to a target? What are the treatment targets?

Level of evidence: 5D, level of agreement: Mean ± SD: 8.15 ± 1.2, percentage of agreement: 84.6%, Level of agreement: High

- Recently definite targeted outcome measures have been identified [29], yet, there is no definite tool to calibrate disease activity. Broadly, the ultimate goal of T2T in rheumatology is to achieve remission in these outcome measures and improve patients' quality of life through:
- Better disease control
- Optimization of immunosuppressive therapy
- Minimization of disease-related vascular damage
- Minimization of treatment side effects.
- The GCA treatment target is a multifaceted concept in GCA, having different domains and declinations depending on the disease phase.
- Therefore, targets can be stratified according to the disease stage (Table 2):
- early stages: the targets are: avoid visual loss or other vascular damage/tissue ischemia, rapid initiation of treatment and achievement of remission
- in established stage: the targets are: maintain remission with the minimal effective dose of therapy, maintain GCA disease related tissue and vascular integrity (whenever appropriate), drug-free remission may be targeted, minimization of glucocorticoid use and relapse prevention, along with avoidance of damage accrual.
- Definition of remission and relapse are key-concept in a T2T strategy.
- Disease outcome measures should be included in identifying disease remission.
- GCA-response can be used to quantify response to therapy, remission and relapse
- Patient perspective: Patient-reported outcomes are an important approach to ensure that patients' per-

spectives have been included both in trials and in clinical practice.

Treatment

Can the treatment of GCA be splitted into phases?

Level of evidence: 5D, level of agreement: Mean+SD: 8.31±1.1, percentage of agreement: 84.6%, Level of agreement: High

Treatment can be splitted into: Induction and maintenance phases

Induction phase

- Immediate glucocorticoid prescription is recommended when GCA is confirmed or strongly suspected.
- The initial oral GC dose is oral prednisolone 40–60 mg once daily.
- If there are cranial ischaemic symptoms, e.g. visual disturbance, amaurosis fugax, vision loss, and stroke, 250-500mg IV methylprednisolone is recommended as induction dose for three days followed by oral GC course starting at a dose of 60mg/day
- Referral for intravenous GC therapy should not delay treatment with oral GC.
- There is no clear evidence that starting doses of above 60 mg per day are more effective than 60 mg per day in the prevention of ischaemic events or other relevant endpoints.
- Weight-adapted glucocorticoids therapy is not recommended.
- Daily oral glucocorticoids therapy is recommended. Alternative approaches e.g. alternate-day schedule is not recommended.
- Moderate-glucocorticoids dose is not advised, but may be used in patients with significant risk of severe glucocorticoid toxicity and in patients with low risk of vision loss or other life-or organ-threatening complications.
- Adding aspirin is recommended for GCA patients who have critical or flow-limiting involvement of the vertebral or carotid arteries.
- For GCA patients with active extracranial large vessel involvement e.g. limb claudication or signs (e.g. imaging findings) attributed to GCA, it is recommended to give a combination of oral glucocorticoids with a nonglucocorticoid immunosuppressive: either oral therapies such as methotrexate or biologic agents (e.g., tocilizumab). Methotrexate can be considered for patients unable to use tocilizumab due to factors such as recurrent infections, history of gastrointestinal perforations or diverticulitis, and cost.
- The use of statins is not known to provide a clinically significant immunosuppressive effect for GCA, hence it is not recommended. Prescribing statins as a measure 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, consequently, should be considered on individual basis.
- Initial assessment for response should be in 2–4 weeks' time after starting the steroid therapy.
- Induction course duration is four weeks.
- *Risk factors for prolonged treatment course:*

A 'strong inflammatory response' (defined as three or four of the following features: ESR ≥85 mm/h and haemoglobin <11 g/dl, weight loss, fever) has been associated with a higher rate of relapse and prolonged course of treatment [30–32]. Imaging evidence of large vessel-GCA (LV-GCA) may be associated with prolonged glucocorticoid treatment compared with patients with cranial GCA who did not have imaging evidence of LV-GCA [33, 34].

Maintenance phase

- A regimen for glucocorticoids tapering should start once the disease is controlled.
- The glucocorticoids tapering regimen must weigh the risk of relapse against the risk of glucocorticoids-related adverse events.
- There are several plans for tapering of the glucocorticoids dose. General plan is cut the steroids dose down to a target dose of 15–20 mg/day within 2–3 months and after one year to ≤5 mg/day (Table 1).
- There is no data available regarding the optimal length of glucocorticoids therapy, it usually takes about two years or more before GCs can be stopped.
- In patients receiving GC-sparing therapy, faster glucocorticoids tapering and earlier withdrawal of GCs should be considered on an individual basis.

GCA "patients at risk": Q. Is it important to identify GCA patients who are at risk?

Level of evidence: 5D, level of agreement: Mean±SD: 8.31±0.95, percentage of agreement: 92.3%, Level of agreement: High

These are the GCA who would be candidates for biologic therapy, these include:

Patients at high risk of glucocorticoid toxicity or who have relapsing or refractory disease. These are the:

> Patients with a persisting high burden of inflammatory disease, multiple relapses with an inability to wean glucocorticoids, non-response to methotrexate, co-morbidities or the presence of other factors that increase glucocorticoid-related adverse events, as well as resistance to glucocorticoid therapy.
> "Patients at risk" of disease complications and/or treatment-related adverse events.

Management of Relapse: Q. How to manage relapses in GCA?

Level of evidence: 5D, level of agreement: Mean±SD: 8.38±0.77, percentage of agreement: 100%, Level of agreement: High

- Relapse rates in the range of 34%–75% may occur in GCA patients treated with glucocorticoids therapy [35].
- Relapse risk is high particularly after early taper and/or reduction of the glucocorticoids dose below 5 mg/day.
- Relapse can be either:
- Major Relapse: Recurrence of active disease with either of the following:
- Clinical features of ischaemia (including jaw claudication, visual symptoms, visual loss attributable to GCA, scalp necrosis, stroke, limb claudication).
- Evidence of active aortic inflammation resulting in progressive aortic or large vessel dilatation, stenosis or dissection.
- Minor Relapse:

Recurrence of active disease, not fulfilling the criteria for a major relapse

-Initial treatment is reinstitution or a dose-increase of glucocorticoids which may differ according to whether it is minor (increase GC to last effective dose) or major (increase GC to 40-60mg/day) relapse.

- Relapses should warrant the assessment of glucocorticoids benefit: risk ratio as high cumulative GC exposure may lead to an increased risk of glucocorticoids-related adverse events.
- Adjunctive therapy, combined with increasing the glucocorticoids dose, should be considered in selected GCA patients (refractory* or relapsing disease, the presence comorbidities or an increased risk of glucocorticoids associated adverse effects or complications). Adding tocilizumab and increasing the dose of glucocorticoids is preferable over methotrexate combined with increasing the glucocorticoids dose for GCA patients who experience disease relapse with cranial or new extra-cranial symptoms while receiving glucocorticoids. Methotrexate can be considered for patients who are unable to tolerate or have limited access to tocilizumab.
- Patients who are treated with methotrexate adjunctive therapy: 'treatment failure', is defined as having two or more relapses or having a relapse that was not controlled by an increment of prednisone dose [36–39].
- Relapses with symptoms of polymyalgia rheumatica may be controlled by increasing the dose of glucocorticoids alone. If no response, PMR can be considered as a relapse of the GCA.
- Refractory GCA: Inability to induce remission (with evidence of reactivation of disease) despite the use of standard care therapy

Glucocorticoids tapering: Q. How to plan for glucocorticoids tapering?

- Glucocorticoids overtreatment should be avoided.
- Fast tapering-off glucocorticoids is often associated with relapse.
- Tapering glucocorticoids is a high priority, then stopping the adjunctive therapy, if both medications have been prescribed in combination.

Table 3 Suggested glucocorticoids tapering regimen

Phase	Glucocorticoids dose	Tapering regimen
Induction:	40–60 mg	until symptoms and lab results are normal (2–4 weeks)
Tapering Phase 1	60–40 mg	Reduce dose by 10 mg every 2 weeks to 40 mg
Tapering Phase 2	40–20 mg	Reduce dose by 5 mg every 2 weeks to 20 mg
Tapering Phase 3	20–10 mg	Reduce dose by 2.5 mg every 2–4 weeks to 10 mg
Tapering Phase 4	10mg—stop	Reduce dose by 1 mg every 1–2 months if there is no relapse

- Tapering of glucocorticoids therapy should be always balanced against the risk of flare up of disease activity.
- Target: to achieve the minimal effective glucocorticoids dose

Table 3 shows a suggested regimen for tapering glucocorticoids.

Treatment discontinuation: Q. How to plan for treatment discontinuation?

Level of evidence: 5D, level of agreement: Mean+SD: 7.46±1.5, percentage of agreement: 76.9%, Level of agreement: high

Stopping glucocorticoids therapy is one of the main goals of GCA management

Strategies for stopping of glucocorticoid-sparing agents:

Reduce glucocorticoids dose slowly e.g. by 1 mg every 1–2 months if there is no relapse

If the patient is on biologic therapy: increasing the administration interval (i.e. to every 2 weeks or longer), after the first year of weekly tocilizumab, or

To follow-up the first year of tocilizumab therapy with a course of a conventional DMARD (e.g. methotrexate).

Drug-free remission: what is meant by remission?

**Remission* Absence of all clinical signs and symptoms attributable to active LVV and normalisation of ESR and CRP; in addition, for patients with extracranial disease there should be no evidence of progressive vessel narrowing or dilatation (frequency of repeat imaging to be decided on an individual basis)

****Sustained Remission***

1. Remission for at least 6 months.
2. Achievement of the individual target GC dose.

****Glucocorticoids free remission***

1. Sustained remission
2. Discontinued GC therapy (but could still be receiving other immunosuppressive therapy)
3. Drug free remission may be achieved in some patients.
4. Drug free remission was reported in a cohort of patients treated with Tocilizumab [22].

Adjunctive therapy: Q. what is the impact of oral glucocorticoids with non-glucocorticoid immunosuppressive therapy versus oral glucocorticoids alone?

Level of evidence: 4C, level of agreement: Mean±SD: 8.07±1.3, percentage of agreement: 76.9%, Level of agreement: high

- Adjunctive therapy should be used in selected patients with GCA refractory or relapsing disease, the presence or an increased risk of GC related adverse effects or complications: osteoporosis, diabetes, cardiovascular disease or glaucoma.
- While there are no comparative studies, the glucocorticoid-sparing effect seen with methotrexate is smaller than the effect seen with tocilizumab (TCZ).
- While the glucocorticoid-sparing effect of tocilizumab is best quantified using the subcutaneous formulation, IV tocilizumab has also been shown to be glucocorticoid-sparing.
- Methotrexate can be considered for patients who are unable to tolerate or have limited access to tocilizumab.
- Lack of long-term follow-up data on tocilizumab and cost may limit its use.
- Bearing in mind the high prevalence of comorbidities in the elderly population affected by GCA, the decision to use adjunctive immunosuppressive therapy in the individual patient should be balanced against potential risks for treatment-related complications, such as the increased risk of lower intestinal perforations reported in patients with rheumatoid arthritis receiving TCZ.
- Abatacept with glucocorticoids can also be considered if these other agents are not effective.
- There is insufficient evidence to recommend the use of other oral immunosuppressive agents (such as azathioprine, leflunomide or mycophenolate mofetil) in GCA.

Management of patients with comorbidities: Q. What is the impact of identifying the individual patient's comorbidity(ies) at baseline?

Level of evidence: 5D, level of agreement: Mean+SD: 8.15±1.1, percentage of agreement: 84.6%, Level of agreement: High

Diabetes mellitus

Patients with Diabetes Mellitus: use of oral glucocorticoids with methotrexate or tocilizumab can be considered as first line therapy.

Osteoporosis

Consider starting osteoprotective therapy, if the patient has not already started treatment.

Cardiovascular (CVS)

48 who are managing GCA patients should be aware of the increased risk of CVD events, attributable to both disease pathophysiology and glucocorticoid treatment.

- GCA patients, should be monitored not only to maintain clinical remission but also to monitor and attempt to prevent CVD events, including strokes, thoracic aortic aneurysms and dissections, ischemic heart disease, and peripheral vascular disease.
- Consider imaging to evaluate for active disease and/or development of thoracic aortic aneurysm.
- Consider statin and aspirin therapy whenever indicated
- If patient is unable to tolerate steroids, consider switching to tocilizumab weekly SC injection.

Infection

The association between high-dose glucocorticoid therapy and opportunistic infections, particularly pneumocystis jirovecii pneumonia (PJP), is now well established in both non-rheumatological and rheumatological diseases. Trimethoprim/sulfamethoxazole (TMP-SMX) has been proved to be effective as a primary prophylaxis for PJP in patients suffering from rheumatological diseases treated with high dose (⩾30 mg/day prednisone) glucocorticoid therapy, with an overall favourable safety profile.

Improving the Benefit: Risk ratio of glucocorticoids: Q. How important is it to optimize the benefit: risk ratio of glucocorticoids?

Level of evidence: 5, level of agreement: Mean±SD: 8.15±0.9, percentage of agreement: 92.3%, Level of agreement: High

- Optimizing the benefit: risk ratio of glucocorticoids to minimize adverse events while achieving sustained remission is a vital challenge to be considered whilst treating GCA patients.
- Implementation of current treatment recommendations for the optimal use of glucocorticoids could reduce the burden of this treatment
- The risk of glucocorticoid-related harm for the majority of patients taking glucocorticoids for a prolonged period (that is, for 3–6 months or more) is:
- Low if doses of ≤ 5 mg per day prednisone equivalent are prescribed,
- High if doses > 10 mg per day are used.
- At doses between 5 and 10 mg per day, patient-specific risk factors determine the probability of harm.

Monitoring: Q. How to monitor GCA patients in standard practice?

Level of evidence: 5D, level of agreement: Mean+SD: 8.23±1.1, percentage of agreement: 84.6%, Level of agreement: High

Baseline assessment

Assessment of medical status

Determination of pre-existing comorbidities such as hypertension, diabetes mellitus, cataract, cardiovascular disease, peptic ulcer disease, osteoporosis and glaucoma is important as the treatment can initiate or worsen disease status.

Assessment of current medications

Checking the list of current medications the patient is taking. Co-medication with non-steroidal anti-inflammatory drugs (NSAIDs) and anti-coagulants is important both for immediate and long-term care in GCA.

Baseline investigations

Consider performing a screen for infection including dipstick urinalysis and chest X-ray (CXR); and a search for mimicking diseases with protein electrophoresis, thyroid function tests, and anti-cytoplasmic neutrophil antibodies. Baseline CXR, echocardiogram or large-vessel imaging are advocated by some centres to assess for large-vessel complications at baseline, in higher risk groups. Occasionally a contrast-enhanced MRI head and orbits may be indicated examining the anterior visual pathways where the cause of an optic neuropathy is not clear.

Frequency of clinical/laboratory monitoring

- The optimal frequency and length of monitoring depend on factors including the disease activity status, occurrence of relapse, refractory cases, presence of comorbidity(ies), duration of remission, site of involvement, risk of disease progression, whether the patient is receiving immunosuppressive therapy, and reliability of the patient to report new signs or symptoms.
- –Broadly, in the first month, the patient should be reviewed every 2-weeks, routine follow-up visits could be scheduled every 1–3 months during the first year and in 3–6 months intervals afterwards.

- Clinical monitoring include history taking, examinations, and laboratory and imaging studies. GCA mimics should be ruled out.
- GCA might have an increase in levels of inflammation markers alone. Increases in levels of inflammation markers such as ESR or CRP can be nonspecific. Consequently, increasing immunosuppressive therapy is not warranted in the setting of increased levels of inflammation markers in the absence of other signs of disease activity. More frequent clinical observation and monitoring of lab and/or imaging assessment should be adopted.
- In patients with relapse-free remission, annual follow-up under shared care between Rheumatologists and primary care can be considered.
- –Late relapses can occur and the incidence of structural vascular lesions in GCA increases after 5 years from diagnosis.
- Long-term follow-up of patients with GCA that remain asymptomatic can be scheduled on an individual patient basis.
- Routine imaging for activity assessment is not recommended for patients in clinical and biochemical remission, but may be used for long-term monitoring of structural damage, particularly vessel stenosis, dilatation and/or aneurysms.
- Methods and frequency of imaging should be decided on an individual basis.
- GCA-specific patient-reported outcome instruments for use in clinical practice should be included in the standard monitoring protocol.

Imaging monitoring

Level of evidence: 5D, level of agreement: Mean+SD: 8.0±0.8, percentage of agreement: 100%, Level of agreement: High

Quantitative scores, such as ultrasound Halo score or the PET vascular activity score (PETVAS), can be used as imaging outcomes

Surgical management of GCA: Q. what is the role of surgery in the management of GCA?

Level of evidence: 5D, level of agreement: Mean ± SD: 8.53 ± 0.8, percentage of agreement: 92.3%, Level of agreement: High

- 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.
- Patients with severe GCA and worsening signs of limb/organ ischemia who are receiving immunosuppressive therapy, it is advisable to escalate immunosuppressive therapy over surgical intervention.
- For GCA patients undergoing vascular surgical intervention (for a GCA associated complication e.g., aneurysm or stenosis), high-dose glucocorticoids should be administered during the periprocedural period, if the patient has active disease.
- Elective endovascular interventions or reconstructive surgery should be performed during stable remission. However, arterial vessel dissection or critical vascular ischaemia requires urgent referral to a vascular team.

Disease activity: how to define the disease activity status of GCA?

Level of evidence: 5D, level of agreement: Mean ± SD: 8.07 ± 1.1, percentage of agreement: 84.6%, Level of agreement: High

Definitions for GCA disease activity states:

Defining the specific disease activity states is important for framing this guideline. These are listed in Table 4.

PROMs: Q. What are the patient reported outcomes important for the assessment and monitoring of GCA patients?

- Functional disability
- Quality of life
- Severity of disease activity parameters (VAS)
- Disease activity parameters (monitoring)
- Medication associated side effects
- Comorbidities
- Patient motivation

Outcomes: Q. what are the outcome measures for assessment of treatment outcomes in GCA?

- Temporal pain
- Temporal headache
- Sensitivity to touch over the temporal region
- Acute visual changes
- Pain in the jaw
- Pain in the tongue or difficulty to chew
- Cramps in the upper or lower limbs
- Chest or abdominal discomfort
- Pain and stiffness in the neck, lower back, arms/hips
- US scanning
- Lab results (ESR or CRP)

Table 4 Important definitions for GCA disease[a]

Disease activity state	Definition
Suspected GCA	Clinical manifestations suggestive of GCA and not explained by other conditions
Active Disease	1. The presence of typical signs or symptoms of active GCA, *plus*: 2. At least one of the following: - Current activity confirmed by imaging or temporal artery biopsy - GCA associated ischaemic complications - Persistently elevated inflammatory markers (after exclusion of other causes)
Severe Disease	Vasculitis with life-or organ-threatening manifestations (e.g., vision loss, cerebrovascular ischemia, cardiac ischemia, limb ischemia, tongue ischemia)
Non-severe disease	Vasculitis without life-or organ-threatening manifestations (e.g., constitutional symptoms, headache, jaw claudication, symptoms of polymyalgia rheumatica)
Relapse	Recurrence of active disease following a period of remission
Major Relapse	Recurrence of active disease with either of the following: a. Clinical features of ischaemia[a] (including jaw claudication, visual symptoms, visual loss attributable to GCA, scalp necrosis, stroke, limb claudication) b. Evidence of active aortic inflammation resulting in progressive aortic or large vessel dilatation, stenosis or dissection [a]Cranial Ischemia: Visual and neurologic involvement including amaurosis fugax, vision loss, and stroke
Minor Relapse	Recurrence of active disease, not fulfilling the criteria for a major relapse
Refractory	Persistent active disease (inability to induce remission) despite the use of an appropriate course of immunosuppressive therapy
Remission	-Absence of clinical signs or symptoms attributed to active GCA, on or off immunosuppressive therapy -Normal ESR and CRP -No evidence of progressive narrowing or dilatation of blood vessels
Sustained remission	1. Remission for at least 6 months 2. Achievement of the individual target GC dose
Glucocorticoid-free remission	Sustained remission Discontinued GC therapy (but could still be receiving other immunosuppressive therapy)
Clinical monitoring	Assessing for clinical signs and symptoms of active disease, obtaining 4 extremity blood pressures, and obtaining clinical laboratory results, including inflammation marker levels

[a] Quoted with amendments from EULAR consensus definition [35]

GCA Giant cell arthritis, *ESR* Erythrocyte sedimentation rate, *CRP* C-reactive protein, *GC* Glucocorticoids

– Temporal artery biopsy

Discussion

GCA remains a disease that represents a challenge to both healthcare professionals as well as patients for its ambiguous presentation, approach to diagnosis, or its remarkable risk of flares and chronic damage in the long term. Over the past decade several RCTs and a good number of high-quality diagnostic studies have changed the view of GCA as a short-term steroid responsive illness [40–43]. Such expansion in methodology, understanding of the disease pathogenesis as well as extent and severity of its outcomes highlighted the need for up-to-date recommendations for GCA management. This work was carried out to provide evidence-based recommendations for the evaluation and management of GCA.

The set of recommendations concluded in this work were for the use of diagnostic testing, treatment, clinical and laboratory monitoring, as well as surgical intervention for GCA patients. The overarching principles of the recommendations include the preference, for cranial imaging studies (temporal artery US) for the diagnosis of GCA over temporal artery biopsy. Whilst this disagrees with the American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Giant Cell Arteritis and Takayasu Arteritis [42], it agrees with those presented by the European Alliance of Associations for Rheumatology (EULAR) [43]. Temporal artery biopsy has been recognized as the traditional diagnostic gold standard, but its cons include being an invasive and expensive procedure, has a false-negative rate as high as 60% and has little impact on clinical decision-making. In contrast, the sonographic hallmark of GCA has been defined as a non-compressible halo with a thickened intima-media complex (IMC) [with wide discrepancy in sensitivity (9–100%), specificity (66–100%), positive predictive value (36–100%) and negative predictive value (33–100%) [44]. 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 [45]. There were differences between the USA based rheumatologists who shared in this work versus those are based in Europe or Egypt regarding the reliance on temporal artery biopsy.

This has been attributed to the lack of technical expertise with the US scanning in the United States [42].

The real challenge of giant cell arteritis is not to control the acute inflammatory process, but to ensure long-term, safe prevention of disease relapses and incipient damage. Both the EULAR recommendations [35] and the 2021 ACR recommendations for large vessel vasculitis [42] suggest treating all newly diagnosed GCA patients in the same strategy, i.e. with the same glucocorticoid regimen, and the option of empirically adding disease-modifying agents to patients with an increased risk of steroid-related adverse effects or when a flare occurs. Such management approach which is based simply on one-size-fits-all strategy leads to overreliance on glucocorticoids and high chance of development of glucocorticoid-associated complications. This recommendation suggests patients' stratification as a new approach to identify and manage the patients tailored to their potential risks. Several patients may have pre-existing, or develop, comorbidities during the course of glucocorticoids therapy, which warrant individualized approach of management. Furthermore, the high likelihood of symptomatic relapse in GCA (34–62%) make these patients prone to longer periods and higher doses of glucocorticoid therapy [37]. Furthermore, adding adjunctive therapy such as tocilizumab or methotrexate was reported to achieve superior remission rates in GCA patients and enables faster withdrawal of glucocorticoids therapy [42–45]. Therefore, stratification of GCA would be an ideal strategy particularly for this cohort of patients. A recent article [46] highlighted the need to implement disease stratification in standard practice and suggested using clinical, laboratory, histology, and imaging as parameters for stratification. In medicine, stratification is not a new policy. In fact, it is a common approach which has been implement in oncology, haematology [45, 46] as well as rheumatology (e.g. SLE and ANCA associated vasculitis) [46, 47]. The stratification system is supported by high-quality evidence as a facilitator for the prediction of disease outcome and the tailoring of therapy accordingly [47–49].

This guideline endorsed the Treat to Target concept of GCA. In agreement with the recently published Treat-to-target recommendations in giant cell arteritis and polymyalgia rheumatica [52], the level of agreement was high among the experts who shared in this study. However, in contrast to Dejaco et al. study [50] which considered the GCA treatment target of GCA to be remission, defined as the absence of clinical symptoms and systemic inflammation, this guideline stratified the target according to the disease stage whether early or established. The definition of the Target has also expanded beyond remission state to include also, in addition to clinical remission, avoidance of visual loss or other vascular damage/tissue ischemia, rapid initiation of treatment and achievement of remission, maintenance of remission with the minimal effective dose of therapy, maintain GCA disease related tissue and vascular integrity (whenever appropriate), minimization of glucocorticoid use and relapse prevention, along with avoidance of damage accrual. Patient reported outcomes and Disease activity score (study submitted for publication) have also been added as targets of treatment. T2T recommendations have been endorsed in rheumatology [51–53], and frequently serve as an outcome in clinical trials and observational studies of GCA [52].

Limitations of the study

Despite the low level of evidence in the literature, the level of agreement for each of the statements included in this recommendation was consistently high among the expert panel members.

In conclusion, we are embarking now on the era of targeted GCA management approach with several avenues to stratify, diagnose and manage this cohort of patients. Close partnership with other teams that care for those with GCA including rheumatology, medicine, neurology and primary care, will facilitate early diagnosis and improve long-term management. Therefore, to improve the patients' quality of care and effectively manage their disease, we propose that healthcare professionals dealing with GCA will implement these recommendations into their standard clinical practice. Fast-track GCA pathway, patient stratification, US assessment of the temporal artery, patient reported outcomes as well as quantification of the GCA-response to therapy represent the main pillars of GCA management in the coming decade.

Abbreviations

ACR	American College of Rheumatology
CVS	Cardiovascular
CXR	Chest X-ray
GCA	Giant cell arteritis
GC	Glucocorticoids
GOR	Grade of recommendations
LV-GCA	Large vessel-GCA
MRA	MR angiography
NSAIDs	Non-steroidal anti-inflammatory drugs
CEBM	Oxford Centre for Evidence-based Medicine
PJP	Pneumocystis jirovecii pneumonia
PMR	Polymyalgia rheumatica
RCTs	Randomized controlled trials
TAB	Temporal Artery Biopsy
CEG	The Clinical, Evidence-based, Guidelines"
EULAR	The European Alliance of Associations for Rheumatology
LOE	The level of evidence
TCZ	Tocilizumab
T2T	Treat to Target
TMP-SMX	Trimethoprim/sulfamethoxazole
US	Ultrasonography

Supplementary Information

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Additional file 1.

Additional file 2.

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