Quality standards for the care of people with giant cell arteritis in secondary care

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Key Words:

Giant Cell Arteritis, Large vessel vasculitis, Quality Standards, Pathways

Key Messages:

- These are the first quality standards developed for the care of people with suspected GCA.
- Access to care is a theme that runs through all nine quality standards
- Each quality standard is accompanied by auditable metrics

Introduction

Giant cell arteritis (GCA) is the commonest primary systemic vasculitis in adults. It has significant health economic costs and societal burden (1, 2), which is likely to get worse with an aging population. British and European recommendations endorse early specialist review (3, 4). In England, 49% of centres provide a diagnostic ultrasonography service but there is wide variation in access and speed of delivery (5). 34% of hospitals in England did not have any formal clinical pathway for assessing GCA (5). Primary care physicians require pathways (6), and the experience of secondary care physicians suggests that establishing a robust one is difficult (5).

Treatment recommendations provide an impetus for improvement in standards of care. Those with auditable metrics provide an even greater driver for change. For example, adoption of national standards for the treatment of early inflammatory arthritis in the United Kingdom has proven to be a significant catalyst for improvement in care (7). We have formed a multidisciplinary group aiming to create standards to bring about similar nationwide improvement in the care of GCA.

Methods

Steering committee

A steering committee consisting of nine rheumatologists, five ophthalmologists, three vasculitis nurse specialists, and patient support group representation was formed. FLC was appointed as the clinical fellow in charge of the project.

Identification of themes

The steering committee were asked to anonymously put forward up to five aspects of service essential for best practice. The full-length responses were qualitatively analysed by FLC and CBM to identify common themes. Responses were also used to create a word cloud as a pictorial representation of common themes (Figure 1).

Creation of recommendations, quality metrics and voting

These common themes were condensed into domain headings, which were ranked in order of importance by each committee member using the SurveyMonkey platform. The top ten domains were explored in the consultation phase. FLC and CBM created draft statements using the qualitative analysis of the initial responses. These were then discussed with all members via two virtual meetings, with immediate edits of the recommendations. Quality metrics for each domain were created using the text of the statement. These were then circulated for agreement. Recommendations that did not meet 75% agreement were redrafted following further consultation and voting as per OMERACT standards (8). This process was repeated till there was agreement on all the statements.

Results

The unifying domains are as in Table 1. After the ranking, the 3 lowest ranked domains dropped were, Tocilizumab access, Audit and Governance, and Research.

The only quality standard requiring revision before 75% consensus was achieved related to 'Patient access', which passed on the second round. Rheumatology and Ophthalmology provision were amalgamated because the standards and metrics were similar. The final standards, metrics and the level of agreement are as in Table 2.

Quality Standards

1. There should be an established pathway for the investigation and care of individuals with suspected GCA, which is agreed across primary and secondary care, with clear entry and exit points, and clear time frames for initiation of investigations and glucocorticoid treatment.
   Agreed metrics
   a. Agreed across primary and secondary care
   b. Clear entry and exit points
   c. Clear time frames for initiating investigations and glucocorticoid treatment

(Level of agreement 83.3%)

A primary care survey highlighted the need for standardised pathways to access secondary care for individuals with suspected GCA (6). Rapid access pathways with diagnostic ultrasonography at their core have been shown to reduce inpatient admissions, incidence of visual loss and healthcare costs (9,10,11). Even where ultrasonography is not yet available, the formation of a referral pathway still improves referral and diagnostic rate (11). In Norwich, UK, when an agreed pathway was developed the referral rate and number of patients diagnosed with GCA started rising immediately, before the introduction of ultrasonography. In 2012, only 19 individuals diagnosed with GCA had been referred. In the subsequent two years the number of referrals rose to 35 and 52, and from those GCA diagnoses rose to 22 and 25 respectively (11). Agreement with primary care groups is essential for an effective pathway. Most primary care physicians may not see more than two newly diagnosed GCA cases per year (12). Any pathway should therefore be clearly signposted and acknowledged by all stakeholders to mitigate barriers to prompt care (6).

Pathways needs clear entry and exit points. Entry points should consider that GCA is a medical emergency and include clear timeframes for initial assessment. Exit pathways should lead to further investigations where necessary for individuals where GCA has been ruled out. Alternative rheumatic diseases (13) and cancer (14) have been seen. The pathway may assist in the pickup of these other diseases but is not intended to be a rapid diagnostic service for all headaches. Investigations for suspected GCA have been proposed by British and European guidelines, allowing for the possibility of picking up GCA mimics, but the initiation of glucocorticoid therapy should not wait till the results are available (3, 4).

2. Patients with suspected new or relapsing disease should always be able to access a clinician with appropriate expertise or an adviceline, leading to a preliminary management plan within 24 hours of patient access and a definitive review within 2 working days.
   Agreed metrics
   a. Defined nominated clinician at point of new presentation
   b. Patients with suspected relapse should be able to access GCA service during working hours
   c. Point of access must lead to a preliminary treatment plan at presentation, with review and verification of this plan by a specialist team within 2 working days

(Level of agreement 100%)

GCA is a medical emergency and timely patient access is imperative to avoid harm, which might be catastrophic and irreversible. The appropriate nature of access depends on whether this is new or relapsing disease. New disease has a risk of permanent visual loss, which is about 12.5-15% (15, 16). It is unrealistic to be able to provide 24-hour expert care for a rare disease, so there must be a 'nominated clinician' for initial contact. Out of hours this may be the emergency department or the acute medicine clinician but may be any clinician who is recognised in the agreed pathway. In a clinical trial where there was a 92% relapse rate due to rapid glucocorticoid taper, none of the participants experienced visual loss (17). While rare, visual loss in the context of relapsing GCA has been known to happen (18). For individuals with suspected relapse, access to an adviceline may be more appropriate (11). Calls could be triaged by a clinician with appropriate skills to make definitive decisions. In all cases, the initial contact must lead to preliminary investigations and treatment with glucocorticoids if new or relapsing GCA is suspected.

A definitive review by a clinician with specialist expertise within 2 working days of the referral is needed in all cases to verify the plan and avoid long-term diagnostic uncertainty. Time is of the essence because diagnostic modalities have diminishing returns after the onset of glucocorticoid therapy. Ultrasonography appearances may normalise 2-4 weeks after commencing glucocorticoids (19). The diagnostic yield from 18-FDG-PET-CT drops significantly between 3-10 days (20). A biopsy may remain positive for a long time, the yield probably dropping after 4 weeks (21).

3. There should be nominated leads in rheumatology and ophthalmology with an interest in GCA who coordinate care, collaborate with the other specialities in the hospital, and run dedicated connective tissue disease/vasculitis clinics for follow-up of patients with GCA.
   Agreed metrics
   a. Clinical leads for GCA in rheumatology and ophthalmology
   b. Collaboration with other specialities that care for patients with GCA in the hospital
   c. Dedicated follow-up in CTD/vasculitis clinics or medical ophthalmology clinics

(Level of agreement 88.9%)

In England, 80% of centres report rheumatologists as the primary point of referral for GCA (5). In a Maltese study, rheumatologists were more efficient users of diagnostics and more likely to adhere to treatment recommendations as compared to non-rheumatologists (22). With the risk of permanent visual loss, especially when there may not be any manifestations outside of the eye (23) it is imperative to have ophthalmology input, which includes medical ophthalmology where available. Interdisciplinary care from these specialities has been shown to improve quality of care (11). However, GCA can present to several specialities in a hospital setting and lead clinicians collaborating with these other doctors will improve pathways and patient access. Follow-up of these patients should be in dedicated clinics within rheumatology and/or ophthalmology, utilising the complementary skills of both specialities.

4. Diagnostic ultrasonography for GCA should be adequately resourced with high-quality equipment and cross-cover to ensure that it is not dependent on a single machine or operator. Diagnostic ultrasonography for GCA should be performed within 7 days of starting glucocorticoids and the images should be reported using validated definitions and stored in the medical records.

Agreed metrics

a. Provision of high-quality equipment (≥18Mhz linear probe for temporal artery; linear ≥10 MHz probe for axillary artery)
b. Experienced, certified, or validated lead operator and a resilient service (not dependent on just one person)
c. Timely provision (within 7 days of starting glucocorticoids)
d. Use of validated definitions to report the images
e. Recording of images in medical records

(Level of agreement 77.8%)

Ultrasonography for the diagnosis of GCA has been validated to international standards (24). It is the recommended primary diagnostic test where the skill is available (3, 4, 25). The superficial temporal artery is about 1.5 mm in diameter (26) and requires a high-resolution probe to view the intima-media complex. Higher resolution probes provide greater diagnostic confidence, but as a minimum we recommend the use of 18 MHz probe (27). Imaging of the axillary artery increases diagnostic yield significantly (28). The axillary artery has an average diameter of 6.5 mm (29) and therefore a probe of at least 10 MHz would suffice for diagnostic views (30).

The under-diagnosis of GCA is associated with ischaemic complications, and over-diagnosis with glucocorticoid toxicity. It is a diagnosis associated with high litigation costs (5). The service provision for ultrasonography should be resilient i.e., not reliant on a single individual or machine. In the absence of formal ultrasonography certification, it is important to establish some form of service validation against another diagnostic modality (31), or operator (32, 33). Currently there is no minimum number of scans recommended prior to launching a service and this will inevitably vary depending on prior experience with ultrasonography.

Ultrasonography is sensitive to change, with an optimum window in which the scan should be performed. There is evidence that the size of the diagnostic abnormality, the 'halo' sign, diminishes with duration of glucocorticoid therapy in the first week (34). Acute changes have been seen for up to 4 weeks (19). Experienced operators and better machinery improve the diagnostic yield. As a consensus we set the metric at 7 days, even though there were good arguments to support a lowering to within 3 days, especially as we were setting the benchmark for definitive assessment at 2 days. We accept this is a pragmatic approach, balancing the need for an early diagnosis against the practicalities of running a service for a rare disease.

Specific sonographic lesions associated with GCA are the 'halo' and 'compression' sign. We recommend the use of validated definitions to describe these lesions when reporting (35). Progress has been made to define cut-offs for intima-media complex thickness, but no consensus has yet been reached to enable inclusion in recommendations. Under the auspices of OMERACT, response criteria are being developed for use in clinical trials. Currently we would not advocate the use in routine clinical practice (36). Ultrasonography is a dynamic interpretation of the anatomy, but it is recommended representative still images are labelled using internationally accepted nomenclature and stored within the patient's permanent record.

5. Temporal artery biopsy provision should be adequately resourced and should not be dependent on a single surgeon. The biopsy should be of an adequate size, harvested within 4 weeks of starting glucocorticoids and reported in a standardised manner.
   Agreed metrics
   a. Identified resource provision – theatre list, surgeon, pathologist
   b. Experienced surgeon with cross-cover (across different specialities if necessary)
   c. Timely provision (within 4 weeks of starting glucocorticoids)
   d. Standardisation of technique, length of sample and reporting of specimen

(Level of agreement 83.3%)

Where ultrasonography is not available or equivocal in its conclusion, international recommendations advocate the need for temporal artery biopsy (3, 4, 25). If required, it should be done as soon as possible. The need for urgent biopsies by physicians who do not perform them produces challenges for prioritising and accessing theatre resources (37). The procedure does not fall within the remit of any specific surgical speciality, thus creating the challenge of identifying appropriate personnel for the procedure (6, 11, 37). With the investment ophthalmologists have in the clinical aspects of GCA, they are the most likely candidates to develop expertise to optimise the yield of the harvested specimen (38). General and vascular surgeons may have the necessary skills and form part of cross-cover. Identification of surgical personnel who perform this procedure regularly, with subsequent standardisation of techniques, improves the diagnostic yield and minimises the risk of complications (11, 37, 38). International recommendations advocate post-fixation biopsy length should be at least 1 cm (3, 4).

In a study involving 40 subjects who had a biopsy at baseline and a second between 3 to 12 months later, the second biopsy continued to demonstrate inflammation in 60% of samples. The amount of granulomatous inflammation dropped over 12 months (39). In a study of 181 subjects with GCA, 78% had arteritis on biopsy. Of 161 biopsies done in the first week of starting glucocorticoid therapy 76% were positive, and 80% of 20 biopsies done in the 2-4th weeks were positive (21). We accept biopsies may remain diagnostic for longer, but consensus set our benchmark at 4 weeks.

Inadequate processing may produce false negative results (40). The finding of 'healed arteritis' has low reliability and cannot be adequately differentiated from age-related changes (41). A pathologist with an interest in GCA should report the sample and contribute to the standardisation of this, including the turn-around time, which has been reported to be widely variable (5).

6. PET scan for large vessel vasculitis should be done within 7 days of the request and reported by an experienced radiologist.
   Agreed metrics
   a. Access to PET scan within 7 days of starting glucocorticoids
   b. Reported by an experienced radiologist

(Level of agreement 88.9%)

Where ultrasonography is not available or equivocal in its conclusion, international recommendations advocate for a second confirmatory test, which may be an 18-FDG-PET-CT scan (3, 4, 25). Since all individuals would have commenced glucocorticoid therapy at first suspicion of GCA, time is of the

essence. After three days of glucocorticoid therapy, there is minimal effect on the diagnostic reliability of 18-FDG PET-CT scanning, but at 10 days there is significant drop in FDG uptake (20). We felt that imaging within 7-days should be practically achievable without affecting the diagnostic efficacy. This is also the agreed NHS England time standard for PET-CT service provision.

PET-CT has not been validated to the standard of ultrasonography in GCA. Various scoring methods for image interpretation have been suggested and is an evolving field (42). The aorta and its immediate branches are prone to atherosclerotic disease in the demographic group susceptible to GCA. For these reasons, it is important images are reported by a radiologist with experience of nuclear medicine in general, and specifically large vessel vasculitis. Having a standardised image assessment improves interobserver agreement (43).

7. There should be a provision and protocol for intravenous glucocorticoid. The shared care of oral glucocorticoid (prednisolone) should include a written tapering plan and monitoring of complications of long-term glucocorticoid therapy.
   Agreed metrics
   a. Clear written protocol for oral glucocorticoids (prednisolone) shared with primary care and the patient
   b. Provision for and a written protocol for intravenous glucocorticoids (methylprednisolone)
   c. Follow-up monitoring for complications of glucocorticoid therapy

(Level of agreement 100%)

The role of intravenous glucocorticoid therapy in GCA is contentious and international recommendations acknowledge the poor quality of the evidence, conditionally recommending its use be considered (3, 4). There should be a clear written protocol advising on indications and contraindications for intravenous glucocorticoids, including dosing and duration.

Several different prednisolone initiation and tapering plans exist (summarised in (44)), none of which have been formally tested against another regimen. The thrust of these recommendations was not to dictate which should be used, but to recommend clear written instructions for the patient and their primary care physician on the proposed reduction plan in the absence of relapsing disease or tolerance issues. Glucocorticoid complications are numerous, occurring in over 80% of individuals (45). They probably contribute to impaired quality of life in patients with GCA (44) and may be responsible for raising their mortality (47). For unknown reasons prednisolone is being used for longer and in higher doses now as compared to pre-1980 (48). To mitigate the effect of inadvertent continuation, we recommend there should be dedicated monitoring of glucocorticoid taper, including preventing self-treatment for suspected relapse, as well as development of silent complications like hypertension, diabetes mellitus and osteoporosis.

8. Individuals diagnosed with GCA should be provided with written educational material about aspects of their care and have the opportunity to be educated by a health professional within 1 month of diagnosis and receive updates as required.
   Agreed metrics
   a. Specialist nurse or equivalent led education about, but not limited to, disease and high-dose glucocorticoids within 1 month of starting treatment

b. Provision of written information about disease, glucocorticoids (including taper) and other immunosuppressive drugs used in the treatment
c. Provision of refresher education as led by patient identified need

(Level of agreement 94.4%)

GCA is almost unknown to the general population. In a survey of patients attending an internal medicine clinic, only 11 of 216 (2 of whom were being treated for it) knew what GCA was (49). Consequently, the need for education is of high priority for patients (50). Information about a new diagnosis and long-term treatment plan is a lot to receive in one clinic appointment, especially whilst being unwell. Having the opportunity to revisit key information may help to reduce patient anxiety and improve concordance (51). This is probably best delivered in a specialist nurse education (or equivalent) clinic to provide holistic care (11). Patients should be able to receive written information (information leaflets), or online resources from validated sources. Contact details for patient charities and support groups should be made available. Patients should have access to refresher education as per their need.

9. There should be defined local and regional MDT that formally discusses complex cases.
   Agreed metrics
   a. Representation from rheumatology, ophthalmology, allied health professional and other specialities as appropriate for the hospital
   b. Formal local and regional MDT which discusses complex cases
   c. Discussion of cases with diagnostic dilemma, missed diagnosis, serious harm to patient, planned surgical intervention

(Level of agreement 94.4%)

GCA can present to many specialities and have multi-organ involvement (sight impairment, hearing impairment, neurological involvement, tongue involvement, limb claudication, iatrogenic complications needing endocrine, bone health and cardiology support). We propose there should be a multi-disciplinary team to discuss complex cases for those reasons. The proposed core membership includes rheumatology, ophthalmology, and a specialist nurse or equivalent. Depending on the other issues it may need input from allied specialities like physiotherapy, occupational therapy, dietetics, psychology etc. Formal local and regional MDTs discussing complex cases, including the need for specialist imaging and access to high-cost drugs, increase accountability and safety. All cases posing a diagnostic dilemma, involving diagnostic delay, where harm has been caused or where surgical intervention is planned must be discussed to ensure all aspects of the care have been covered.

Discussion

Progress in the understanding and management of GCA has been slow (Figure 2). There is a need for quality standards to catalyse improvements in care (52). We present the first consensus quality standards developed by rheumatologists, ophthalmologists, specialist nurses with input from a patient charity. We represent general and teaching hospitals; centres with fast-track pathways and those aspiring towards it. The authorship also represents views from individuals with expertise in rare

diseases and commissioning of specialist services. We represent every geographical region from England. This broad representation is a strength of these proposed quality standards.

We follow in the footsteps of international recommendations for the management of GCA – first made in 2009 and updated in 2020 (3, 4). We echo some of the GCA specific recommendations made by the 'Get IT Right First Time' initiative in England, which is based upon the actual state of services across all hospitals in the country (5). We present the first set of auditable quality standards with defined metrics, which although based upon international recommendations and scientific literature, is more explicit and will help form blueprints upon which secondary care service development may proceed. We have considered a wide amount of literature but accept that the standards are based on consensus and not a systematic literature review. The recommendations were developed at a time of national lockdown when face to face meetings were not possible. The virtual meetings may not have allowed for as robust a discussion as may have happened otherwise.

Over- and underdiagnosis of GCA are problems in equal measure. We have tried to address both challenges with our proposed quality standards. Timely assessment of individuals with suspected GCA, with appropriate availability of diagnostics, will optimise this balance. We have included clear time frames for initiating investigations and glucocorticoid treatment, as well as recommending clear exit points to prevent continued inadvertent use of glucocorticoids.

As a next step we hope to survey every hospital in England providing GCA services to form a map of the skill sets available (Supplementary Data S1 – Self-assessment Tool, available at *Rheumatology* online). We hope national commissioning bodies will take note of these recommendations, and that they provide clinicians and centres with leverage to push for the adequate resources needed to achieve them.

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Ethics Statement

The views expressed are those of the authors. Ethics approval was not required for this project as per UK Health Research Authority guidance.

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Conflict of Interest

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Data Availability

The authors confirm that the data supporting the findings of this study are available within the article and supplementary materials.

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Figure 1 Word Cloud formed from the initial suggestions of the committee members

Table 1 Domains identified from word cloud

1. Overarching theme for each of the domains – 'Patient access'
2. Glucocorticoids (standards for timing and dosing)
3. Pathways (referral, diagnostics, management)
4. Ultrasonography (access and timing)
5. Temporal artery biopsy (access and timing)
6. Rheumatology/Rheumatologist (urgent access, specialist expertise, follow-up)
7. Ophthalmology (urgent access, specialist expertise, follow-up)
8. Education (role of nurse, patient empowerment, self-management plan)
9. Multidisciplinary team (at diagnosis, follow-up, regional)
10. Audit and governance
11. PET scan (access and timing)
12. Tocilizumab (access, timing, specialist centre role)
13. Research

Table 2 Recommendation statements, quality metrics and level of agreement

Quality standards	Quality Metrics	Level of agreement
There should be an established pathway for the investigation and care of individuals with suspected GCA, which is agreed across primary and secondary care, with clear entry and exit points, and clear time frames for initiation of investigations and glucocorticoid treatment.	Agreed across primary and secondary care Clear entry and exit points Clear time frames for initiating investigations and steroid treatment	83.3%
Patients with suspected new or relapsing disease should always be able to access a clinician with appropriate expertise or an adviceline, leading to a preliminary management plan within 24 hours of patient access and a definitive review within 2 working days.	Defined nominated clinician at point of new presentation Patients with suspected relapse should be able to access GCA service during working hours Point of access must lead to a preliminary treatment plan at presentation, with review and verification of this plan by a specialist team within 2 working days	100%
There should be nominated leads in rheumatology and ophthalmology with an interest in GCA who coordinate care, collaborate with the other specialities in the hospital, and run dedicated Connective Tissue Disease/Vasculitis clinics for follow-up of patients with GCA.	Clinical leads for GCA in rheumatology and ophthalmology Collaboration with other specialities that care for patients with GCA in the hospital Dedicated follow-up in CTD/Vasculitis clinics/medical Ophthalmology clinics	88.9%

Diagnostic ultrasonography for GCA should be adequately resourced with high-quality equipment and cross-cover to ensure that it is not dependent on a single machine or operator. Diagnostic ultrasonography for GCA should be performed within 7 days of starting glucocorticoids and the images should be reported using validated definitions and stored in the medical records.	Provision of high-quality equipment (≥18Mhz linear probe for temporal artery; linear ≥10 Mhz probe for axillary artery) Experienced, certified, or validated lead operator and a resilient service (not dependent on just one person) Timely provision (within 7 days of starting glucocorticoids) Use of validated definitions to report the images Recording of images in medical records	77.8%
Temporal artery biopsy provision should be adequately resourced and should not be dependent on a single surgeon. The biopsy should be of an adequate size, harvested within 4 weeks of starting glucocorticoids and reported in a standardised manner.	Identified resource provision – theatre list, surgeon, pathologist Experienced surgeon with cross-cover (across different specialities if necessary) Timely provision (within 4 weeks of starting glucocorticoids) Standardisation of technique, length of sample and reporting of specimen	83.3%
PET scan for large vessel vasculitis should be done within 7 days of the request and reported by an experienced radiologist.	Access to PET scan within 7 days of the request Reported by an experienced radiologist	88.9%

There should be a provision and protocol for intravenous glucocorticoid. The shared care of oral glucocorticoid (prednisolone) should include a written tapering plan and monitoring of complications of long-term glucocorticoid therapy.	Clear written protocol for oral glucocorticoids (prednisolone) shared with primary care and the patient Provision for and a written protocol for intravenous glucocorticoids (methylprednisolone) Follow-up monitoring for complications of glucocorticoid therapy	100%
Individuals diagnosed with GCA should be provided with written educational material about aspects of their care and have the opportunity to be educated by a health professional within 1 month of diagnosis and receive updates as required.	Specialist nurse or equivalent led education about, but not limited to, disease and high-dose glucocorticoids within 1 month of starting treatment Provision of written information about disease, glucocorticoids (including taper) and other immunosuppressive drugs used in the treatment Provision of refresher education as led by patient identified need	94.4%
There should be defined local and regional MDT that formally discusses complex cases.	Representation from rheumatology, ophthalmology, allied health professional and other specialities as appropriate for the hospital Formal local and regional MDT which discusses complex cases	94.4%

	Discussion of cases with diagnostic dilemma, missed diagnosis, serious harm to patient, planned surgical intervention	

Figure 2. Timeline of landmark events in GCA