The use of ultrasound in the management of large-vessel vasculitis: an evolving concept

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Received on August 22, 2018; accepted in revised form on August 30, 2018.

Clin Exp Rheumatol 2018; 36 (Suppl. 114): S96-S102.

Key words: ultrasonography, diagnostic imaging, vasculitis, giant cell arteritis, Takayasu's arteritis

Competing interests: none declared.

ABSTRACT

Imaging is increasingly recognised as an essential element in the management of several rheumatologic conditions. Ultrasound is in widespread use as a safe, reproducible, and directly interpretable method for diagnosis and evaluation of arthritis and increasingly of large-vessel vasculitis (LVV). Indeed, the diagnosis and management of LVV are being transformed through the use of imaging. Increasing and more standardised evidence is being produced on the role of colour duplex sonography in the management of LVV. Nonetheless, some controversies and unresolved issues remain. This review describes current findings and reviews future perspectives in the use of ultrasound for the diagnosis and management of LVV.

The role of ultrasound in the diagnosis of LVV

What do we know/what is new?

Large-vessel vasculitis (LVV) comprises two main diseases: giant cell arteritis (GCA) and Takayasu's arteritis (TAK) (1). Diagnosis is based primarily on clinical features, with non-specific laboratory markers of systemic inflammation. Therefore, more objective findings to support the diagnosis are desirable. Traditionally, temporal artery biopsy has been the cornerstone to confirm the diagnosis of GCA (2, 3). With recognition that GCA often can include extra-cranial large-vessel involvement, and the characteristic widespread vascular involvement of TAK, imaging has become more prominent in the evaluation of LVV.

Colour duplex sonography (CDS) is gaining an increasing and more standardised role in supporting the diagnosis and management of LVV. Current high-end equipment has improved diagnostic accuracy and the level of anatomical and pathologic details detected by ultrasound, leading to expanding evidence supporting the concept that CDS has higher sensitivity and comparable specificity compared to the current gold standard (temporal artery biopsy) in GCA. Moreover, there is increasing interest in the potential role that individual ultrasound characteristics such as halo distribution or size might have in determining disease severity or response to therapy. A major drive to research in this area is the significant reduction in visual loss arising from more rapid diagnosis of GCA achieved by implementing clinical evaluation with ultrasound-based fast-track clinics (4).

Standardised consensus-based definitions of ultrasound elementary lesions have been formulated by the OMERACT Large Vessel Vasculitis Ultrasound Working Group (5). The expert panel defined the distinctive characteristics between normal or abnormal ultrasound findings of temporal end extracranial large arteries based on a systematic literature review (SLR). The reliability of these definitions was then tested in a web-based exercise, demonstrating excellent intra-rater and inter-rater agreement (91–99%) for "halo sign" and "compression sign".

The halo sign and the compression sign are regarded as the most relevant abnormalities suggestive for GCA and agreement amongst experts was 100% and 83.3%, respectively. Evidence of stenosis or occlusion were excluded from the definition of the primary findings which indicated the presence of vasculitis, because a halo is usually visible in these areas in patients with active vasculitis. These standardised definitions can be used for future research, including randomised controlled trials, and will improve the comparability of different studies and the quality of future evidence.

The Role of Ultrasound Compared to Biopsy of Temporal Arteries in the Di-

agnosis and Treatment of Giant Cell Arteritis (TABUL) study assessed the diagnostic accuracy and the cost-effectiveness of CDS in a multi-centre prospective cohort study of patients suspected of having new onset GCA (6). TABUL demonstrated the feasibility of developing and implementing an ultrasound training programme with good intra-rater reliability. Notably, the reliability in interpreting histologic results was similar to that of ultrasound (interclass correlation coefficient 0.61 and 0.62, respectively). The study demonstrated a greater sensitivity but lower specificity of CDS compared to temporal artery biopsy and proposed the best diagnostic strategy to be a combination of clinical judgment and CDS (leading to the highest sensitivity 93%, with a specificity of 77%). Only in cases of high clinical suspicion, but a negative scan, should biopsy be considered. The proposed pathway, placing ultrasound as the primary investigation in all cases with medium to high clinical suspicion of GCA, was the most cost-effective strategy.

Duftner *et al*. (7) performed a systematic literature review and meta-analysis to inform EULAR recommendations for the use of imaging in LVV. The detection of a halo sign at the level of the temporal artery (sensitivity 77%, specificity 96%) and MRI of cranial arteries (sensitivity 73%, specificity 88%) provided a high diagnostic value for GCA. The role of imaging in the assessment of large-vessel GCA (LV-GCA) or TAK was less well defined. Barra *et al*. (8) recently published the results of a SLR and meta-analysis focusing on imaging modalities for the diagnosis and disease activity assessment in TAK. Despite the small sample size of several studies and cross-sectional design, ultrasound was reported to have lower pooled sensitivity (81%) compared to magnetic resonance angiography (92%) or computed tomography angiography (>90%) for the diagnosis of TAK. ^{18}F-fluorodeoxyglucose-positron emission tomography (FDG-PET) had a sensitivity of 81% to detect disease activity. A lower sensitivity of CDS compared to more comprehensive imaging modalities is expected, because it is not possible to use CDS to inspect relevant anatomic areas such as the thoracic aorta. Moreover, magnetic resonance angiography or computed tomography angiography offer the advantage over CDS of providing a complete overview of vascular damage (stenosis or aneurysms) (9-12).

The first EULAR recommendations for the use of imaging in large-vessel vasculitis in clinical practice have been recently published (13). Early diagnostic imaging tests are recommended to complement the clinical assessment of disease, ensuring that there is an adequate level of expertise and availability. Further diagnostic tests should not delay the initiation of treatment. The authors emphasised that imaging should be the initial investigation of choice, given the low invasiveness, completeness of assessment with evaluation of multiple vessels, and ready availability. However, temporal artery biopsy should still be used in centres without expertise in imaging modalities. In cases with a high clinical suspicion for GCA and a positive imaging test – primarily ultrasound of temporal artery and/or axillary arteries or alternatively high-resolution MRI of superficial cranial arteries – no additional tests are needed to confirm the diagnosis. Similarly, in low clinical probability settings and negative imaging, a diagnosis can be excluded. In all other scenarios, further imaging modalities or temporal artery biopsy should be pursued to reach greater diagnostic certainty. In patients with suspected TAK, the preferred imaging modality is MRI, performed by experts in the field, to search for mural inflammation and/or luminal changes.

Despite the fact that imaging represents the preferred test according to availability, training, equipment and settings, the EULAR task force did not discard the role of temporal artery biopsy in doubtful cases not clarified by imaging modalities or when imaging is not available or not performed routinely with adequate expertise (14). Moreover, ultrasound results should always be contextualised and interpreted together with clinical judgment since false positive CDS findings have occasionally been reported in other vasculitides, infectious diseases, local neoplastic processes or severe arteriosclerosis (9, 13, 15, 16).

An area of growing interest is the potential value of additional ultrasound information detected by CDS in the diagnosis and outcome prediction of LVV (17). A number of previous publications had proposed different cut-off values for pathologically large intima-media thickness (IMT) (18-20), but recently Schäfer *et al*. (21) defined cut-off values to distinguish IMT size in the temporal, facial and axillary arteries in patients with GCA compared to control cases with different rheumatologic conditions. The IMT in vasculitic segments of arteries from patients with GCA were 0.65mm (standard deviation 0.18), 0.54mm (SD 0.18), 0.50mm (SD 0.17), 0.53mm (SD 0.16) and 1.7mm (SD 0.41) for the common superficial temporal arteries, the frontal and parietal branches, the facial arteries and the axillary arteries, respectively. The proposed cut-off values were 0.42, 0.34, 0.29, 0.37 and 1.0 mm, respectively

Czihal *et al*. (22) assessed the diagnostic accuracy of B-mode compression sonography of the temporal artery and B-mode CDS measurement of axillary arteries IMT for the diagnosis of GCA against clinical and/or histological diagnosis. The compression sign (23) with measurement of maximum thickness of temporal artery wall remaining visible upon transducer compression had an excellent area under the curve (AUC) of 0.95 for the diagnosis of GCA, with a cut-off ≥0.7 mm yielding a sensitivity and specificity of 85% and 95%. The cut-off value for axillary arteries IMT in the diagnosis of LV-GCA was ≥1.2 mm, with a sensitivity and specificity of 81.3% and 96.1%, respectively. The AUC was equally high (0.91). Using the combination of temporal artery compression and the threshold size of axillary arteries IMT (cut-off ≥0.7/1.2 mm) improved the overall sensitivity and specificity for a clinical diagnosis of GCA to 85.3% and 91.4%, respectively.

A better definition of the IMT value to be considered compatible with GCA could be helpful in the differential diagnosis with other conditions or age-

related changes and severe atherosclerosis. De Miguel and colleagues (24) explored whether or not the increase in IMT associated with arteriosclerotic disease correlated with an increase in temporal artery IMT that could affect the interpretation of CDS in elderly patients referred for suspected GCA. De Miguel *et al*. recruited consecutive patients ≥50 years old with high vascular risk but no signs or symptoms of LVV. The carotid IMT (particularly if >0.9 mm) correlated with temporal artery IMT (>0.3 mm). The authors suggested that an IMT of the temporal artery branches >0.34 mm with at least two branches involved should be used as more restrictive diagnostic criteria for defining the presence of GCA, in patients with pre-existing arteriosclerotic diseases. Relying only on the echogenicity of the halo could be misleading in these patients because sometimes arteriosclerosis might result in hypoechoic increase in IMT, at least in the carotid arteries (24).

The minimum accepted standard for CDS assessment of a patient with suspected LVV includes the evaluation of temporal and axillary arteries, known to increase the diagnostic yield of ultrasound (9, 13, 18). The adjunctive benefit of including other cranial vessels such as facial or occipital arteries was assessed in a prospective study of 93 patients with GCA. The facial artery was involved in 40% of cases and the occipital artery in 31.2% of patients. These two arterial sites exclusively showed a halo (without co-existing temporal artery involvement) in 18.2% of patients (25). Vertebral arteries can also have an adjunctive diagnostic role (26). Therefore, maintaining a high level of suspicion and extending CDS examination to more anatomical sites might be of value in clinically suggestive cases (25, 27).

Controversies and future perspectives

As outlined above, there have recently been significant advances in the diagnostic role of ultrasound for GCA. On the other hand, there is insufficient data on diagnostic accuracy of CDS in other forms of LVV, although definitions of individual lesions and IMT values have been reported for TAK and idiopathic aortitis (5). Despite our improved knowledge on the use of CDS for the diagnosis of GCA, there remain unresolved issues.

The assessment of IMT and its pathological cut-off values have not been included in the definitions of halo because of the lack of consensus and the need for further validation in GCA.

Schäfer *et al*. (21) performed IMT measurements at pre-specified arterial segments (1 cm distal to the emergence from deeper structures for the common superficial temporal artery, 1 cm distal to the bifurcation for frontal and parietal branches and at the mid-point of the mandibular bone for the facial artery) with a good interclass correlation coefficient between the two expert sonographers. However, further investigation of the reproducibility of such cut-offs in longitudinal cohorts of patients with variable localisation of halos along the involved arterial segments is needed. Moreover, the proposed cut-off values were compared to patients with other rheumatologic conditions potentially associated with high cardiovascular risk and atherosclerosis and not with healthy individuals. Nevertheless, the control group selected by Schäfer *et al*. (21) might indeed be more representative of the average elderly patient with increased cardiovascular comorbidities referred for suspected, but then non-confirmed vasculitis. Therefore, further studies are needed to characterise the role of measuring IMT for the diagnosis and monitoring of GCA and LVV.

The role of CDS to assess the extent and severity of disease at baseline and as an outcome measure requires further clarification. Czihal *et al*. reported a poorer response to treatment in patients with GCA who had ultrasound evidence of more extensive vessel involvement (28) (cranial and extracranial) compared to those with either isolated abnormalities in cranial or extracranial areas; this needs to be confirmed in larger studies. Large prospective studies are needed to confirm the prognostic role of ultrasound so that in future we can potentially tailor treatment based on baseline imaging and biomarker information.

The availability of high quality CDS is increasing, but in order to apply it effectively in LVV, it requires a high level of expertise to perform and interpret the findings correctly; this can be achieved with continuing training programmes. Moreover, the interpretation of imaging findings for the differential diagnosis between vasculitis and comorbid conditions should be improved and standardised. Recent reports have suggested a promising role for different applications of CDS or new diagnostic tools that could improve the management of LVV in the future. Contrast-enhanced ultrasound (CEUS) of carotid arteries has been reported to optimise the visualisation of the lumen border and vessel wall vascularisation as a sign of disease activity in patients with LVV (29, 30). Apart from ultrasonographic assessment, new imaging modalities are being investigated, especially in ophthalmology, to improve the detection of GCA and further reduce the rate of permanent visual loss. Changes specific to GCA have been reported with tests such as dynamic contour tonometry (31) and optical coherence tomographic angiography (32). Nevertheless, until a confirmatory test with the optimal sensitivity to detect the disease is found with the reliable characteristics of a true gold standard, the role of clinical evaluation still remains crucial in reaching a final diagnosis of LVV.

The role of ultrasound in the management and monitoring of LVV

What do we know/what is new?

As a tool with limited cost, relatively short time requirements and a lack of radiation, ultrasound has become increasingly used in the follow-up and monitoring of patients with LVV.

Despite being an investigator-dependent test in which the skill and the experience of the operator influence the diagnostic accuracy of the method, CDS has proven to be a very useful tool for diagnosis of LVV. However, after the diagnosis, physicians must decide on the most appropriate follow-up method. Currently, whilst use of CDS is an appealing modality, the evidence for its role in monitoring disease remains uncertain.

Table I. Time to halo disappearance evaluated by ultrasound and sensitivity/specificity at diagnosis and after glucocorticoid treatment.

Study	N of GCA/ N positive CDS	Territories scanned	CDS timing	Sensitivity/specificity at diagnosis (%)	Time to halo disappearance	GC dose
Schmidt *et al*. 1997 (33)	30/22	CSTA, FB, PB	Before biopsy and every 3-4 days until halo disappearance	73/100	16 [7-56] days	NS
Karahaliou *et al*. 2006 (35)	22/18	CSTA, FB, PB	Prior to treatment and 14±1 days after	82/91 100% specificity if bilateral halo	22 days 14 days in 50% of patients	NS
Pérez Lòpez *et al*. 2009 (34)	30/22	CSTA, FB, PB, OphA	Baseline and 6 weeks and 6 months after starting treatment	73/80	50% of patients had a halo detectable 6 weeks and 6 months after GC	1mg/kg/day and, if visual symptoms 3 pulses of 1g/ day methylprednisolone
De Miguel *et al*. 2012 (38)	30/38*	CSTA, FB, PB	Baseline, every 2 weeks for the first month and every 4 weeks thereafter until halo disappearance	NS	8 [2-30] weeks	NS
Habib *et al*. 2012 (39)	16/13	CSTA, FB, PB	Before treatment and at 2,4,8 and 12 weeks after treatment	81/88 100% specificity if bilateral halo	3 [2-4] weeks	40 to 60 mg daily for 1-3 months with gradual tapering thereafter
Hauenstein *et al*. 2012 (40)	36/28	CSTA, FB, PB	After 0-1 days; 2-4 days and more than 4 days of GC	After 0-1 days: 87.5/91.7 After 2-4 days: 50/100 After >4 days: 50/80	NS	NS
Monti *et al*. 2018 (36)	118/52	CSTA, FB, PB, AX	At each visit and when suspected flare	If <7 days of GC 63.3/100 If ≥7 days of GC 43.6/98.3 If <7 days of GC and highly suspicious clinical picture 81.8/100	NS	≥30 mg/day

AX: axillary artery; CSTA: common superficial temporal artery; FB: frontal branch; NS: not specified; OphA: ophthalmic artery; PB: parietal branch; SA: subclavian artery.

While CDS offers a good window to visualise cranial and axillary arteries, it has limited value on the assessment of other vascular territories, such as the thoracic aorta, where other imaging modalities, such as MRI and/or CT and FDG-PET, have greater advantage. This poses a problem when considering CDS for the monitoring of LVV patients, especially in the case of LV-GCA or TAK.

Besides the vascular beds affected, another point to consider in the use of CDS to monitor disease activity and damage in LVV is when to re-evaluate patients. Imaging signs of inflammation, particularly the 'halo' sign at the temporal artery, usually disappear between 2 to 4 weeks after initiating glucocorticoid therapy (Table I). Moreover, the role of imaging in the assessment of a suspected flare or relapse is still to be elucidated, since the literature on this topic is limited and mainly descriptive, not adding further insight to the value of imaging compared with a clinical definition of flare only. This issue was recently reviewed in the EULAR imaging recommendations for LVV; it is suggested that during follow-up, when flare is suspected, imaging might be helpful to confirm or exclude it. However, imaging is not routinely recommended for patients in clinical and biochemical remission or with a clear-cut clinical flare. When clinical and laboratory parameters are inconclusive, imaging might assist in the decision of whether or not to change treatment (13).

Time to halo disappearance is influenced by various factors and, in the studies outlined in Table I, different methodologies and length of treatment before the first ultrasound evaluation was performed are key factors to consider. In the 1997 study by Schmidt *et al*. glucocorticoid usage before the first scan varied considerably: 5 patients had not received glucocorticoid, 10 had received treatment for less than 24 hours, 11 for 1 to 10 days beforehand, and 4 had been treated with doses of glucocorticoid that were too low to suppress disease activity (33). Pérez López (34), studied patients with GCA who had received a mean of 5 days (range 1–10) of glucocorticoids prior to ultrasound, whilst Karahaliou *et al*. recruited patients who underwent their first CDS before receiving any glucocorticoid therapy (35).

The length of glucocorticoid treatment before the first ultrasound evaluation is indeed crucial, because sensitivity and specificity of ultrasound rapidly decreases after treatment, as demonstrated by several authors (Table I). Luqmani *et al*., in the TABUL study, showed that the sensitivity of CDS decreased from 64% with ≤1 day of glucocorticoids to 47% if ≥ than 2 days of glucocorticoids, while maintaining relatively similar specificity (81 and 82%) (6).

The sensitivity to change of CDS has been demonstrated by Monti *et al*. (36), further emphasising the potential importance of this imaging technique. In this recent study, the percentage of

patients with just one site showing halo was lower in new onset compared with follow-up (9% *vs*. 47% p=0.001) or flaring patients (9% *vs*. 31%, p=0.02) with GCA. Moreover, the thickness of halo of the axillary arteries was significantly reduced from initial referral to follow up and flare (1.6±0.4 to 1.4±0.2 in follow up, p=0.01, and 1.4±0.2 in flare, p=0.02). By contrast, differences in the halo size of temporal arteries were non-significant.

Clinically, halo disappearance often correlates with improvement in clinical and laboratory findings and even though its precise role in follow-up still needs clarification and robust reproducible data, CDS is emerging as an important tool, especially in clinically flaring patients on treatment, whose inflammatory markers are not always elevated.

When managing LVV, apart from evaluating the persistence or disappearance of signs of inflammation, it is important to monitor for potential structural damage. The frequency of screening as well as the imaging method applied should be decided on an individual basis (13).

García-Martínez *et al*. (37) systematically screened patients with GCA for evidence of aortic structural damage every 4 years and found that aortic diameters increased over time, significantly in the case of the ascending (39±11 *vs*. 42±15, p=0.018) and descending aorta (28±5 *vs*. 29±4, p=0.03), in patients with aortic structural damage at the baseline CT scan, indicating progressive dilatation over time in the damaged aortic segments.

The careful monitoring for structural damage following diagnosis is of crucial importance in LVV, because survival is worse in patients with aortic dissection/aneurysm, when compared to the general population, as demonstrated by Kermani *et al*. In this 2013 study, the incidence of artery stenosis remained relatively constant beyond 5 years from diagnosis of GCA (p=0.77) but the incidence of aortic aneurysm/dissection increased after 5 years (p=0.009), with worse survival rates for these patients (41).

A more recent prospective study, enrolling 187 patients with GCA followed over a mean of 4.39±2.22 years, demonstrated LV involvement in 123 patients (subclavian 42%, axillary 32%, thoracic aorta 20%) and, in 106 with serial imaging, new arterial lesions were noted in 39%, all of whom already had baseline abnormalities, often in the absence of symptoms of active disease (42).

Compared to GCA, there is only limited data on the value of ultrasound in TAK. Fan *et al*. prospectively included 51 patients with TAK (with follow up information in 20 cases), to evaluate wall thickness and outer vessel wall diameter of their carotid arteries. Between 2 and 5 follow-up examinations were performed for each patient. After treatment was started, the wall thickness and outer diameter of the carotid arteries increased in patients who subsequently relapsed but decreased in patients who remained in remission, however, these differences were non-significant (43).

Monitoring of structural damage was a topic of consideration in the EULAR imaging recommendations. According to these, in patients with LVV (GCA or TAK), regular imaging with magnetic resonance angiography, computed tomography angiography and/or ultrasound may be used for long-term monitoring of structural damage, namely in patients showing signs or symptoms of stenosis/occlusion or aneurysms and in patients with recurrent or persistent inflammation of large arteries and/or the aorta.

As for the ideal imaging method, the choice should consider the affected vessel(s), local settings and expertise. For aortic inflammation and dilatation, MRI or CT are mentioned as preferable. MRI in specific, has advantage over ultrasound, given that this is a procedure easier to standardise, less operator dependable and that allows the exploration of multiple vascular beds at the same time, reducing the possibility of missing inflamed sites. However, ultrasound also presents advantages and, for monitoring stenosis of the axillary/subclavian arteries ultrasound is easily performed. The EULAR task force stressed the lack of solid evidence regarding the most appropriate imaging tools for follow-up and monitoring of LVV and mainly based their recommendations on expert opinion.

Controversies and future perspectives

The best imaging method for follow-up and monitoring of patients with LVV as well as the timings to perform such evaluation are still a matter of debate, in the absence of robust evidence. A chest radiograph performed every 2 years to monitor for aortic aneurysm and abdominal ultrasound is current practice in some countries (44), however there is no evidence for the benefit of this practice (13).

Outcome prediction is another topic in need of further investigation. Of note, a study by Blockmans *et al*., enrolling 54 patients with GCA with a mean follow-up period of 47±30 months, compared PET positive *vs*. PET negative patients, having aortic dilatation as the main outcome. In this study there was a significant increase in ascending and descending aorta diameter in PET positive patients (40 *vs*. 37 mm, p=0.025 and 34 *vs*. 31 mm, p=0.044, respectively), prompting the authors to infer a possible predictive role for PET for aortic dilatation (45).

As for ultrasound, few studies presented relevant results regarding possible prediction of outcome; of note, involvement of multiple *vs*. only one temporal artery branch was associated with a longer time until halo disappearance in one study (12.6 *vs*. 6.5 weeks, p<0.01) (38).

To emphasise the need for further studies of the role of imaging in the long term management of LVV, the EULAR task force responsible for the EULAR imaging recommendations–delineated important topics for the future research agenda, including: investigate the additional value of the different imaging modalities in the assessment of disease activity during follow-up over clinical and laboratory assessment alone and investigate the value of imaging (*e.g*. assessment of the extent of vascular involvement) as well as individual vasculitis signs (*e.g*. 'halo' sign, contrast enhancement as compared with wall thickening) as a prognostic factor for LVV outcomes (13).

Conclusions

CDS of cranial, axillary and other accessible arteries can significantly improve the diagnosis and management of LVV. The role of ultrasound in the diagnosis of GCA is supported by robust evidence and recently published recommendations. Importantly, however, a high level of expertise, correct machine settings, and clinical judgment are essential elements when interpreting ultrasonographic findings.

The additional contribution of CDS in monitoring and follow-up of LVV is still uncertain, but with promising evidence. We still do not know which, if any, of the currently available imaging modalities are effective in screening patients for structural damage and aneurysm development; or how often patients should be screened for these complications.

Take home messages

- CDS of temporal and axillary arteries is recommended as the primary diagnostic tool for investigation of suspected GCA in centres with availability and expertise in this technique.
- Sensitivity of CDS for GCA decreases rapidly following glucocorticoid treatment, which means that timely evaluation is crucial.
- In LVV, CDS offers a good visualisation window for temporal, axillary arteries and abdominal aorta, but is limited for the evaluation of thoracic aorta, for which CTA and MRA are preferred imaging options.
- Arterial imaging in GCA should be performed at diagnosis and subsequent imaging should be considered, especially if baseline abnormalities are noted.
- Timing for imaging re-evaluation should be decided on an individual basis.

References

1. JENNETTE JC, FALK RJ, BACON PA *et al*.: 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum* 2013; 65: 1-11.
2. GONZÁLEZ-GAY MA, PINA T, BLANCO R: The search for improvement in the sensitivity of temporal artery biopsy in giant cell arteritis. *Rheumatology* (Oxford) 2015; 54: 379-80.
3. GROSSMAN C, BARSHACK I, KOREN-MORAG N, BEN-ZVI I, BORNSTEIN G: Baseline clinical predictors of an ultimate giant cell arteritis diagnosis in patients referred to temporal artery biopsy. *Clin Rheumatol* 2016; 35: 1817-22.
4. DIAMANTOPOULOS AP, HAUGEBERG G, LINDLAND A, MYKLEBUST G: The fast-track ultrasound clinic for early diagnosis of giant cell arteritis significantly reduces permanent visual impairment: towards a more effective strategy to improve clinical outcome in giant cell arteritis? *Rheumatology* (Oxford) 2016; 55: 66-70.
5. CHRYSIDIS S, DUFTNER C, DEJACO C *et al*.: Original article: Definitions and reliability assessment of elementary ultrasound lesions in giant cell arteritis: a study from the OMERACT Large Vessel Vasculitis Ultrasound Working Group. *RMD Open* 2018; 4: e 000598.
6. LUQMANI R, LEE E, SINGH S *et al*.: The Role of Ultrasound Compared to Biopsy of Temporal Arteries in the Diagnosis and Treatment of Giant Cell Arteritis (TABUL): a diagnostic accuracy and cost-effectiveness study. *Health Technol Assess Winch Engl* 2016; 20: 1-238.
7. DUFTNER C, DEJACO C, SEPRIANO A, FALZON L, SCHMIDT WA, RAMIRO S: Imaging in diagnosis, outcome prediction and monitoring of large vessel vasculitis: a systematic literature review and meta-analysis informing the EULAR recommendations. *RMD Open* 2018; 4: e000612.
8. BARRA L, KANJI T, MALETTE J, PAGNOUX C, CANVASC: Imaging modalities for the diagnosis and disease activity assessment of Takayasu's arteritis: A systematic review and meta-analysis. *Autoimmun Rev* 2018; 17: 175-87.
9. MONTI S, FLORIS A, PONTE C *et al*.: The use of ultrasound to assess giant cell arteritis: review of the current evidence and practical guide for the rheumatologist. *Rheumatology* (Oxford) 2018; 57: 227-35.
10. QUINN KA, AHLMAN MA, MALAYERI AA *et al*.: Comparison of magnetic resonance angiography and 18F-fluorodeoxyglucose positron emission tomography in large-vessel vasculitis. *Ann Rheum Dis* 2018; 77: 1165-71.
11. SUN Y, MA L, JI Z *et al*.: Value of whole-body contrast-enhanced magnetic resonance angiography with vessel wall imaging in quantitative assessment of disease activity and follow-up examination in Takayasu's arteritis. *Clin Rheumatol* 2016; 35: 685-93.
12. GERMANÒ G, MONTI S, PONTE C *et al*.: The role of ultrasound in the diagnosis and follow-up of large-vessel vasculitis: an update. *Clin Exp Rheumatol* 2017; 35 (Suppl. 103): S194-8.
13. DEJACO C, RAMIRO S, DUFTNER C *et al*.: EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. *Ann Rheum Dis* 2018; 77: 636-43.
14. DEJACO C, RAMIRO S, DUFTNER C, SCHMIDT WA: Response to: 'The role of temporal artery biopsy in patients with giant cell arteritis is debated' by Moiseev *et al*. *Ann Rheum Dis* 2018; annrheumdis-2018-213284.
15. PLANTÉ-BORDENEUVE T, HENCKAERTS L, LERUT E, VERBEKEN E, BLOCKMANS D: Not every case of temporal arteritis is giant cell arteritis. microscopic polyangiitis involving the temporal artery: a case report and review of the literature. *J Clin Rheumatol* 2017 [Epub ahead of print].
16. JIA L, COUCE M, BARNHOLTZ-SLOAN JS, COHEN ML: Is all inflammation within temporal artery biopsies temporal arteritis? *Hum Pathol* 2016; 57: 17-21.
17. MONTI S, PONTE C, CARRARA G *et al*.: THU0297 A novel ultrasound scoring system for giant cell arteritis. *Ann Rheum Dis* 2017; 76 (Suppl. 2): 316.
18. SCHMIDT WA, SEIFERT A, GROMNICA-IHLE E, KRAUSE A, NATUSCH A: Ultrasound of proximal upper extremity arteries to increase the diagnostic yield in large-vessel giant cell arteritis. *Rheumatology* (Oxford) 2008; 47: 96-101.
19. SCHMIDT WA: Ultrasound in the diagnosis and management of giant cell arteritis. *Rheumatology* 2018; 57 (Suppl. 2): ii22–31.
20. SALVARANI C, SILINGARDI M, GHIRARDUZZI A *et al*.: Is duplex ultrasonography useful for the diagnosis of giant-cell arteritis? *Ann Intern Med* 2002; 137: 232-8.
21. SCHÄFER VS, JUCHE A, RAMIRO S, KRAUSE A, SCHMIDT WA: Ultrasound cut-off values for intima-media thickness of temporal, facial and axillary arteries in giant cell arteritis. *Rheumatology* (Oxford) 2017; 56: 1632.
22. CZIHAL M, SCHRÖTTLE A, BAUSTEL K *et al*.: B-mode sonography wall thickness assessment of the temporal and axillary arteries for the diagnosis of giant cell arteritis: a cohort study. *Clin Exp Rheumatol* 2017; 35 (Suppl. 103): S128-33.
23. ASCHWANDEN M, IMFELD S, STAUB D *et al*.: The ultrasound compression sign to diagnose temporal giant cell arteritis shows an excellent interobserver agreement. *Clin Exp Rheumatol* 2015; 33 (Suppl. 89): S113-5.
24. DE MIGUEL E, BELTRAN LM, MONJO I, DEODATI F, SCHMIDT WA, GARCIA-PUIG J: Atherosclerosis as a potential pitfall in the diagnosis of giant cell arteritis. *Rheumatology* (Oxford) 2018; 57: 318-21.
25. JEŠE R, ROTAR Ž, TOMŠIČ M, HOČEVAR A: The role of colour doppler ultrasonography of facial and occipital arteries in patients with giant cell arteritis: A prospective study. *Eur J Radiol* 2017; 95: 9-12.
26. GEHLEN M, SCHAEFER N, SCHWARZ-EYWILL M, MAIER A: Ultrasound to detect involvement of vertebral artery in giant cell arteritis. *Clin Exp Rheumatol* 2018; 36 (Suppl. 111): S169-70.
27. PINNELL J, TIIVAS C, PERKINS P, BLAKE T, SARAVANA S, DUBEY S: Ultrasonography of occipital arteries to diagnose giant cell arteritis: a case series and literature review. *Clin Rheumatol* 2018; 37: 569-73.
28. CZIHAL M, PILLER A, SCHROETTLE A *et al*.: Impact of cranial and axillary/subclavian artery involvement by color duplex sonography on response to treatment in giant cell arteritis. *J Vasc Surg* 2015; 61: 1285-91.
29. SCHINKEL AFL, VAN DEN OORD SCH, VAN DER STEEN AFW, VAN LAAR JAM, SIJBRANDS EJG: Utility of contrast-enhanced ultrasound for the assessment of the carotid artery wall

in patients with Takayasu or giant cell arteritis. *Eur Heart J Cardiovasc Imaging* 2014; 15: 541-6.
30. GERMANÒ G, MACCHIONI P, POSSEMATO N *et al*.: Contrast-enhanced ultrasound of the carotid artery in patients with large vessel vasculitis: Correlation with positron emission tomography findings. *Arthritis Care Res* 2017; 69: 143-9.
31. ING E, PAGNOUX C, TYNDEL F *et al*.: Lower ocular pulse amplitude with dynamic contour tonometry is associated with biopsy-proven giant cell arteritis. *Can J Ophthalmol* 2018; 53: 215-21.
32. GAIER ED, GILBERT AL, CESTARI DM, MILLER JB: Optical coherence tomographic angiography identifies peripapillary microvascular dilation and focal non-perfusion in giant cell arteritis. *Br J Ophthalmol* 2018; 102: 1141-6.
33. SCHMIDT WA, KRAFT HE, VORPAHL K, VÖLKER L, GROMNICA-IHLE EJ: Color duplex ultrasonography in the diagnosis of temporal arteritis. *N Engl J Med* 1997; 337: 1336-42.
34. PÉREZ LÓPEZ J, SOLANS LAQUÉ R, BOSCH GIL JA, MOLINA CATERIANO C, HUGUET REDECILLA P, VILARDELL TARRÉS M: Colour-duplex ultrasonography of the temporal and ophthalmic arteries in the diagnosis and follow-up of giant cell arteritis. *Clin Exp Rheumatol* 2009; 27 (Suppl. 52): S77-82.
35. KARAHALIOU M, VAIOPOULOS G, PAPASPYROU S, KANAKIS MA, REVENAS K, SFIKAKIS PP: Colour duplex sonography of temporal arteries before decision for biopsy: a prospective study in 55 patients with suspected giant cell arteritis. *Arthritis Res Ther* 2006; 8: R116.
36. MONTI S, FLORIS A, PONTE CB *et al*.: The proposed role of ultrasound in the management of giant cell arteritis in routine clinical practice. *Rheumatology* (Oxford) 2018; 57: 112-9.
37. GARCÍA-MARTÍNEZ A, ARGUIS P, PRIETO-GONZÁLEZ S *et al*.: Prospective long term follow-up of a cohort of patients with giant cell arteritis screened for aortic structural damage (aneurysm or dilatation). *Ann Rheum Dis* 2014; 73: 1826-32.
38. DE MIGUEL E, ROXO A, CASTILLO C, PEITEADO D, VILLALBA A, MARTÍN-MOLA E: The utility and sensitivity of colour Doppler ultrasound in monitoring changes in giant cell arteritis. *Clin Exp Rheumatol* 2012; 30 (Suppl. 70): S34-8.
39. HABIB HM, ESSA AA, HASSAN AA: Color duplex ultrasonography of temporal arteries: role in diagnosis and follow-up of suspected cases of temporal arteritis. *Clin Rheumatol* 2012; 31: 231-7.
40. HAUENSTEIN C, REINHARD M, GEIGER J *et al*.: Effects of early corticosteroid treatment on magnetic resonance imaging and ultrasonography findings in giant cell arteritis. *Rheumatology* (Oxford) 2012; 51: 1999-2003.
41. KERMANI TA, WARRINGTON KJ, CROWSON CS *et al*.: Large-vessel involvement in giant cell arteritis: a population-based cohort study of the incidence-trends and prognosis. *Ann Rheum Dis* 2013; 72: 1989-94.
42. KERMANI TA, DIAB S, SREIH AG *et al*.: Arterial lesions in giant cell arteritis: A longitudinal study. *Semin Arthritis Rheum* 2018.
43. FAN W, ZHU J, LI J, ZHANG W, LI C: Ultrasound morphological changes in the carotid wall of Takayasu's arteritis: monitor of disease progression. *Int Angiol* 2016; 35: 586-92.
44. DASGUPTA B, BORG FA, HASSAN N *et al*.: BSR and BHPR guidelines for the management of giant cell arteritis. *Rheumatology* (Oxford) 2010; 49: 1594-7.
45. BLOCKMANS D, COUDYZER W, VANDERSCHUEREN S *et al*.: Relationship between fluorodeoxyglucose uptake in the large vessels and late aortic diameter in giant cell arteritis. *Rheumatology* (Oxford) 2008; 47: 1179-84.