Autoimmunity Reviews 18 (2019) 56–61

Contents lists available at ScienceDirect

Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev

Diagnostic performance of temporal artery ultrasound for the diagnosis of giant cell arteritis: a systematic review and meta-analysis of the literature

Marina Rinagel[a], Emmanuel Chatelus[a], Sandrine Jousse-Joulin[b], Jean Sibilia[a], Jacques-Eric Gottenberg[a], François Chasset[c], Laurent Arnaud[a,*]

[a] Service de rhumatologie, Hôpitaux Universitaires de Strasbourg, Université de Strasbourg, Centre National de Référence des Maladies Systémiques Autoimmunes Rares RESO, F-67000 Strasbourg, France
[b] Department of Rheumatology, Cavale Blanche Hospital and Brest Occidentale University, Brest, France
[c] AP-HP, Service de Dermatologie et d'Allergologie, Hôpital Tenon, F-75020 Paris, Université Paris VI Pierre et Marie Curie, Sorbonnes Universités, France

ARTICLE INFO

Keywords:
Giant cell arteritis
Ultrasound
Temporal artery biopsy
Systematic review
Sensitivity
Specificity
Likelihood ratios

ABSTRACT

Despite major recent advances in the therapeutic management of Giant cell arteritis (GCA), the diagnosis accuracy of temporal artery ultrasound remains controversial in this disease. We performed a systematic review to determine the sensitivity, specificity, and summary positive (LR+) and negative (LR-) likelihood ratios of temporal artery ultrasound for the diagnosis of GCA. For this, we searched EMBASE, MEDLINE and the Cochrane Database of Systematic Reviews without language restriction. Original articles reporting on diagnostic accuracy of temporal artery ultrasound compared to temporal artery biopsy, for the diagnosis of GCA, were selected. Sensitivity and specificity from each study were used to fit a bivariate diagnosis accuracy model. Of 1280 articles identified, 48 underwent full-text review, and 25 were included. Based on a total of 20 studies, the sensitivity and specificity of hypoechoic halo compared to positive temporal artery biopsy were respectively of 68% (95% CI: 57–78) and 81% (95%CI: 75–86). The summary mean positive and negative likelihood ratios were respectively of 3.64 (95%CI: 2.76–4.73) and 0.40 (0.28–0.52). Taking into account 11 studies reporting on the presence of any abnormal sign on temporal artery ultrasound yielded similar results with largely overlapping 95% confidence interval regions. This study provides the summary estimates of the diagnostic properties of temporal artery ultrasound compared to temporal artery biopsy, for the diagnosis of GCA. Those parameters allow the calculation of the post-test probability of GCA in a given patient, based on the results of temporal artery ultrasound and will help improving the diagnosis strategy for this common disease.

1. Introduction

Giant cell arteritis (GCA) is the most common form of systemic vasculitis in adults [1]. The disease is characterized by a panarteritis of medium to large-sized arteries [2], especially in the extracranial branches of the carotid artery [3,4]. Despite recent advances, the pathogenesis of the disease remains largely unknown [5,6]. Only half of patients have enlarged, nodular, or nonpulsatile temporal arteries [7]; therefore normal temporal arteries on physical examination do not exclude the diagnosis of GCA. Almost all patients have a markedly elevated Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP) levels [8]. The 1990 Criteria of the American College of Rheumatology (ACR) requires at least 3 of the following to classify a patient as having GCA: age of ≥50 years, new onset of localized headache, temporal artery tenderness on palpation or decreased pulsation, erythrocyte sedimentation rate (ESR) ≥ 50 mm/h, and abnormal temporal artery biopsy [9]. Up to now, the diagnosis of GCA is usually confirmed by a biopsy of the temporal artery (TAB, temporal artery biopsy), showing typical findings including infiltration of the vessel wall with mononuclear inflammatory cells and occasional giant cells, intimal proliferation, and thrombosis. While other imaging methods, such as 18FDG-PET have emerged [10,11], temporal artery biopsy remains the gold standard for the diagnosis of GCA, but the segmental nature of the disease can be responsible for false-negative results [7]. Color duplex sonography (CDS) of the superficial temporal artery and large vessels is an emerging diagnostic tool for GCA [12]. CDS has greatly improved the non-invasive full length visualization of arterial wall abnormalities in medium sized arteries, and may visualize a halo sign (hypoechoic ring around the lumen of the temporal artery), as well as stenosis and/or occlusion. Nevertheless, CDS use remains

* Corresponding author at: Department of rheumatology Hôpital de Hautepierre, 1 Avenue Molière BP 83049, 67098 Strasbourg, Cedex, France.
E-mail address: Laurent.arnaud@chru-strasbourg.fr (L. Arnaud).

https://doi.org/10.1016/j.autrev.2018.07.012
Received 26 July 2018; Accepted 30 July 2018
Available online 05 November 2018
1568-9972/

Table 1
Characteristics of included studies.

Study / Years	Nb of patients	Nb of female n (%)	Age	Nb of patient with positive TAB	Nb of patient with a halo sign	Nb of patient with any CDS abnormality
Muratore et al. (2013)	160	47 (74.6)	75 ± 8*	63	65	NA
Aschwanden et al. (2013)	80	55 (69)	72 ± 10*	20	30	NA
Del Blanco Alonso et al. (2013)	32	20 (62.5)	78 (61–88)§	3	6	NA
Black et al (2013)	50	36 (72)	69.2 (33–90)§	5	5	NA
Pfenninger et al (2012)	85	52 (61)	F: 71.5 (55–91)§ M: 71.6 (44–91)§	27	4	15
Maldini et al (2010)	77	49 (64)	72.2 ± 9.1*	6	1	NA
Ciancio et al (2009)	13	NA	NA	10	10	NA
Pérez Lopéz et al (2009)	60	GCA: 18 (60)	GCA: 78(64–93)§	29	26	28
Bley et al (2008)	59	32 (54)	71 ± 8.7*	24	26	NA
Zaragoza garcia et al (2007)	23	14 (60)	74 (57–85)§	5	5	8
Karahaliou et al (2006)	55	GCA: 13 (59) Non-GCA: 17 (52)	GCA: 70 (52–90)§ Non-GCA: 74(50–91)§	22	21	NA
Reinhard et al (2004)	83	49 (59)	68 ± 11*	33	23	25
Schmidt et al (2003)	36	22 (61)	71(50–90)§	32	24	NA
Murgatroyd et al (2003)	26	NA	NA (55–95)§	7	12	NA
LeSar et al (2002)	32	21 (65.6)	73.1 ± 9.2*	7	8	12
Salvarani et al (2002)	86	55 (64)	73 ± 8*	15	21	NA
Nesher et al (2002)	69	NA	NA	9	16	NA
Schmid et al (2002)	20	11 (55)	74 ± 7* 75 (59–84)§	12	6	NA
Venz et al (1998)	20	12 (60)	76.3 ± 8.75*	6	8	NA
Schmidt et al (1997)	30	21 (70)	73 (52–86)§	21	18	24
Croft et al (2015)	87	GCA: 26 (72) Non-GCA: 34 (67)	GCA: 75 ± 9* Non-GCA: 71 ± 8*	8	NA	13
Romera-Villegas et al (2004)	68	48 (70.6)	77 (64–88)§	22	NA	25
Pfadenhauer et al (2003)	67	51 (76)	69 (NA)§	33	NA	36
Brunzholzl et al (1998)	145	84 (58)	69.6 ± 8.7* 69.6 (45–88)§	20	NA	13
Luqmani et al (2016)	381	274 (72)	71 (64–78)§	101	NA	162

TAB: temporal artery biopsy; CDS: Color duplex sonography; NA: not available; *mean age +/− SD; §median age (range); GCA: giant cell arteritis.

controversial in routine clinical practice and more importantly requires skilled sonographers.

In this study, we performed a systematic review and meta-analysis to assess the summary sensibility and specificity of temporal artery ultrasound compared to temporal artery biopsy for the diagnosis of GCA. Our main interest was to determine the positive (LR+) and negative (LR-) likelihood ratios across these studies. Those alternative statistics have several particularly powerful properties that make them more useful clinically at the bed-side to estimate the post-test probability of GCA, based on CDS findings.

Other meta-analysis have been performed but there are not recent and without likelihood ratios measurement [13–15].

2. Material and methods

This meta-analysis of diagnostic accuracy studies was performed according to the PRISMA methodology.

3. Literature search and information sources

We searched EMBASE, MEDLINE and the Cochrane Database of Systematic Reviews (until the 1st of March 2017) for original articles without language restrictions. The search strategy combined free text search, exploded MESH/EMTREE terms and all synonyms of the following Medical Subject Headings terms: giant cell arteritis, temporal artery biopsy and temporal artery ultrasound (see eMethod1).

4. Study selection and eligibility criteria

Observational studies were considered if: 1) they assessed the sensitivity and/or specificity of temporal artery ultrasound compared to that of temporal artery biopsy; 2) for the diagnosis of CGA according to the 1990 ACR criteria. Editorials, case reports and reviews were excluded from the study.

The quality of studies was assessed using the QUADAS Scale for diagnostic accuracy studies [16].

5. Data extraction

The recorded information for each selected study included the study design, patient characteristics, ultrasound characteristics, number and type of patients with ultrasound lesions (hypoechoic halo, occlusion or stenosis), and the positive number of temporal artery biopsy. We have included all studies assessing the sensibility and specificity of temporal artery ultrasound comparatively to temporal artery biopsy. Data were extracted independently by 2 investigators (M.R & E.C.). Discrepancies were solved in consensus after additional review of the studies, or after consultation of a third reviewer (L.A.) in case of persistant disagreement.

6. Ultrasound lesions

Ultrasound lesions compatible with GCA were hypoechoic halo, occlusion or stenosis of temporal artery. We also assessed the number of positive temporal artery biopsy and number of CDS showing hypoechoic halo, occlusion, stenosis or any for the diagnostic of giant cell arteritis.

7. Statistical analyses

For each study, the number of true positive, false negative, true negative and false positive were independently extracted by 2

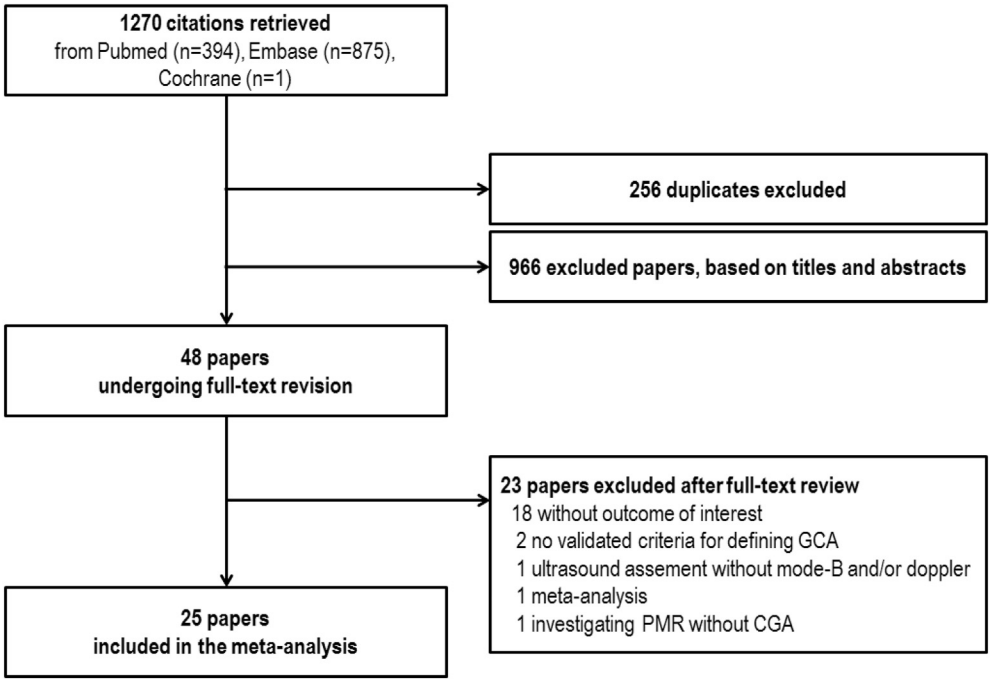

Fig. 1. Study flow chart.

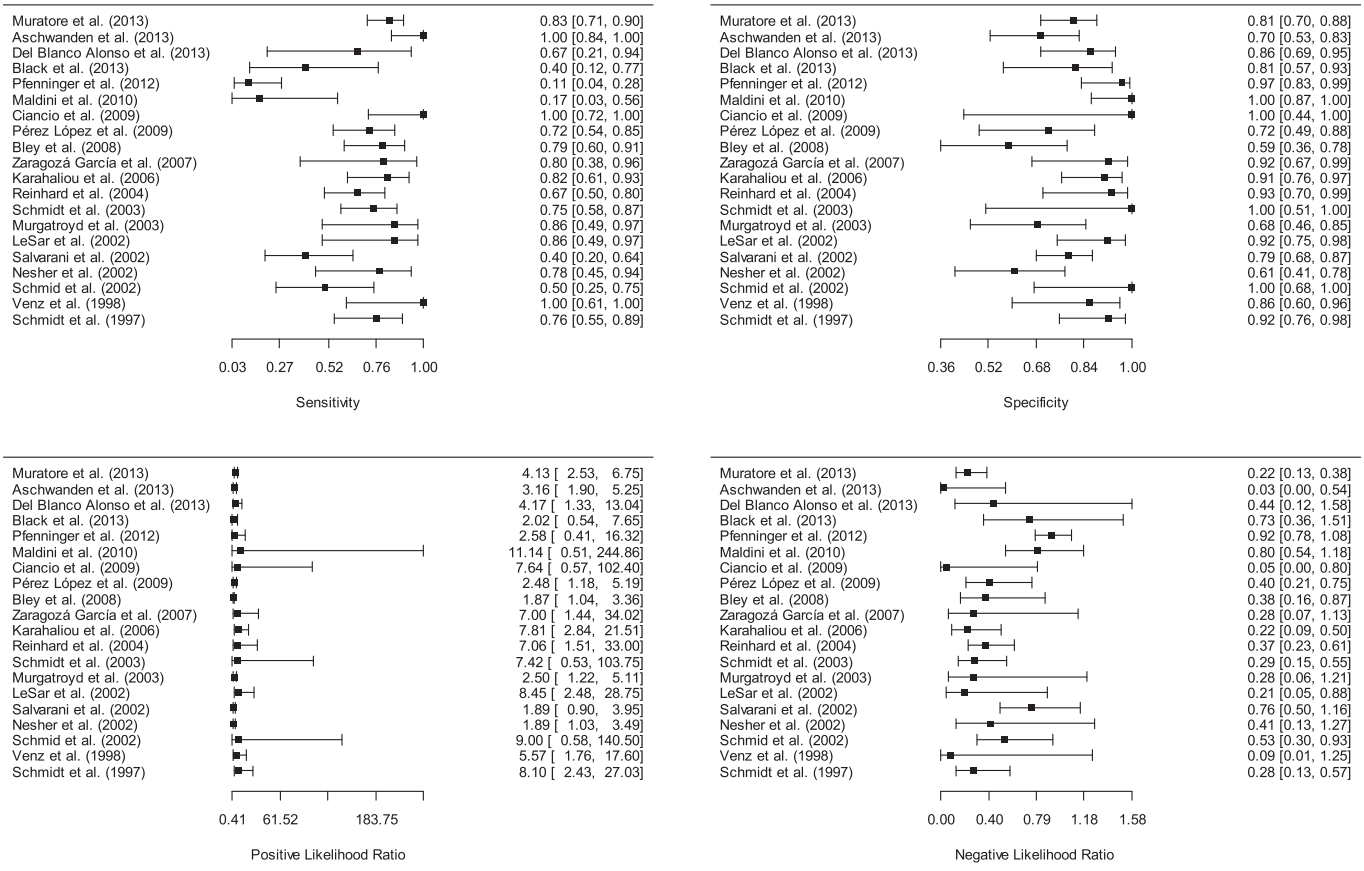

Fig. 2. Sensitivity, specificity, LR+ and LR- for individual studies reporting on the halo sign.

investigators (M.R & E.C.). We used The R software (version 3.3.2) with the "mada" package (https://cran.r-project.org/web/packages/mada/index.html) to fit a bivariate diagnostic accuracy model, as described by Reitsma et al. [17] Summary receiver operating characteristic (SROC) curves were fit based on the model parameters, and used to compute summary sensitivity and specificity and their 95% confidence interval across all included studies. The Markov Chain Monte Carlo procedure (with 100,000 iterations) was used to generate summary positive and negative likelihood ratios, according to the method proposed by Zwindermann & Bossuyt [18].

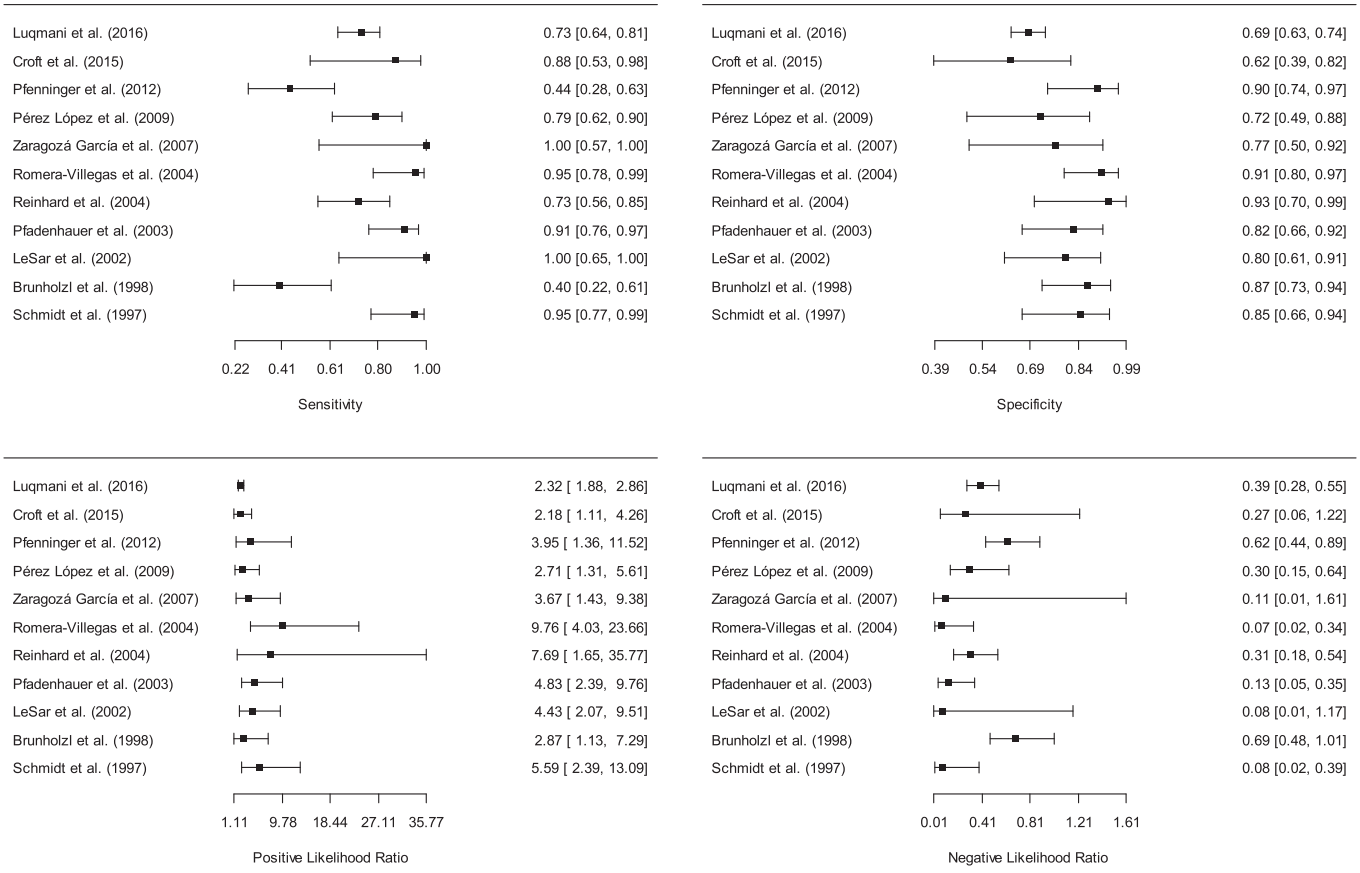

Fig. 3. Sensitivity, specificity, LR+ and LR- for individual studies reporting on any CDS abnormality.

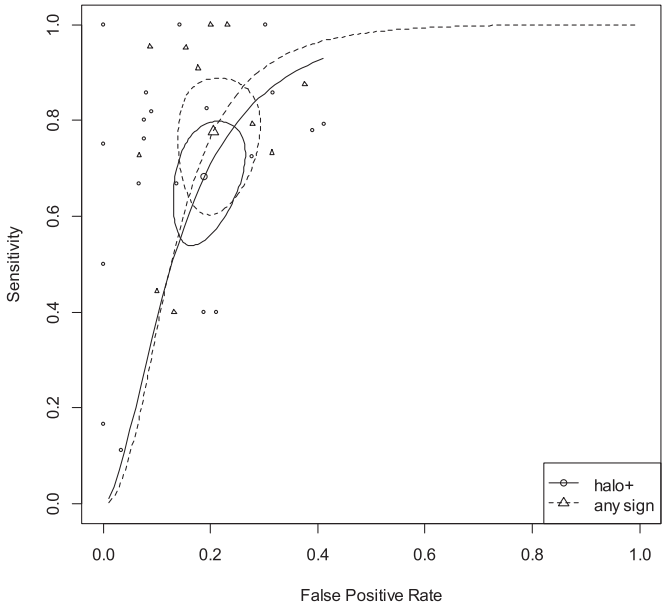

Fig. 4. Comparison of the Summary receiver operating characteristic curves for presence of the halo sign (full line) or any abnormal CDS(dotted line) with temporal artery biopsy for the diagnosis of GCA. Small-sized circles (presence of the halo sign) and triangles (any abnormal CDS) show the sensitivity and false positive rate for individual studies. The larger circle (halo sign) and triangle (any abnormal CDS) show the summary sensitivity and false positive rate, with their 95% confidence area.

8. Results

8.1. Literature search and assessment of publication bias

Our literature search identified 1270 citations of potential interest, from which 25 studies (for a total of 1062 patients) met the inclusion criteria and were included in this meta-analysis [12,19–42]. The average age at inclusion ranged from 55 to 95 years. The detailed characteristics of these 25 studies are reported in Table 1. The quality of the studies according to the QUADAS-2 Scale for diagnostic accuracy studies is reported in the eTable1 [17]. (See Fig. 1.)

8.2. Sensitivity and specificity of hypoechoic halo

Based on a total of 20 included studies reporting on the halo sign [19–28,32–36,38–42], the sensitivity and specificity of hypoechoic halo compared to positive temporal artery biopsy were respectively of 68% (95% CI: 57–78) and 81% (95%CI: 75–86). The summary mean positive and negative likelihood ratios were respectively of 3.64 (95%CI: 2.76–4.73) and 0.40 (0.28–0.52) (Fig. 2).

8.3. Sensitivity and specificity of any abnormalities (hypoechoic halo and/or stenosis and/or occlusion)

Based on 11 studies with available data [12,19,21,24,28–31,37,40,42], the diagnostic value of any abnormalities in CDS comparatively to temporal artery biopsy was similar, with a sensitivity of 78% (95CI%: 64–87), a specificity of 79% (95% CI: 73–85). The summary LR+ was 3.80 (95CI%: 2.73–5.19), and the summary LR- was 0.29 (95CI%: 0.16–0.45), with largely overlapping 95% confidence interval regions between the use of the halo sign only, or the use of any abnormalities in CDS (Figs. 2 and 3).

9. Discussion

This systematic review and meta-analysis of 25 diagnosis accuracy studies assessed the sensibility and specificity of temporal artery ultrasound compared to temporal artery biopsy for the diagnosis of GCA and enabled us to determine the summary diagnosis properties of CDS, including the very clinically useful LR+ and LR- across all published studies.

The determination of the summary mean positive and negative likelihood ratios (respectively of 3.64 [95%CI: 2.76–4.73] and 0.40 [0.28–0.52]) for the presence of the halo sign may prove very useful in routine clinical practice, as a given individual with a pre-test probability of GCA of 50% would have a post-test probability of 78% if the halo sign is present, and of only 29% in the absence of this sign.

An important finding it that taking into account any CDS abnormalities increased only slightly the sensitivity compared to using the halo sign (78% versus 68%, respectively), with a very similar specificity (79% versus 81%, respectively), while the 95% confidence interval area largely overlapped (Fig. 4).

Among the limitations of this meta-analysis is the observational design of included studies. Also, it is likely that at least in some cases, the CDS may have been performed by very skilled sono-rheumatologists while this may not fully reflect current practices across all centers. Among the strengths of this work are that we performed a systematic review of the literature without any language restriction, and pooled the results of individual studies to obtain summary estimates more likely to reflect the global diagnosis properties of CDS in GCA (Figs. 3 and 4).

10. Conclusion

This systematic review and meta-analysis provides valuable estimates of positive and negative likelihood ratios for abnormal temporal artery ultrasound compared to temporal artery biopsy for the diagnosis of GCA. These summary parameters may prove very useful to assess the risk of GCA routinely at the bed-side. Another important finding it that taking into account any CDS abnormalities increased only slightly the sensitivity compared to using the halo sign, with a very similar specificity are largely overlapping 95% confidence interval area, which may have some very practical implications.

Conflicts of interest

All authors have declared no conflicts of interest.

References

[1] Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum 2008 Jan;58(1):26–35.

[2] De Boysson H, Daumas A, Vautier M, Parienti J-J, Liozon E, Lambert M, et al. Large-vessel involvement and aortic dilation in giant-cell arteritis. A multicenter study of 549 patients. Autoimmun Rev 2018 Apr 1;17(4):391–8.

[3] Jennette JC, Falk RJ. Bacon PA, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum 2013 Jan;65(1):1–11.

[4] Samson M, Corbera-Bellalta M, Audia S, Planas-Rigol E, Martin L, Cid MC, et al. Recent advances in our understanding of giant cell arteritis pathogenesis. Autoimmun Rev 2017 Aug 1;16(8):833–44.

[5] Ciccia F, Rizzo A, Ferrante A, Guggino G, Croci S, Cavazza A, et al. New insights into the pathogenesis of giant cell arteritis. Autoimmun Rev 2017 Jul 1;16(7):675–83.

[6] Régent A, Ly KH, Groh M, Khifer C, Lofek S, Clary G, et al. Molecular analysis of vascular smooth muscle cells from patients with giant cell arteritis: Targeting endothelin-1 receptor to control proliferation. Autoimmun Rev 2017 Apr 1;16(4):398–406.

[7] Buttgereit F, Dejaco C, Matteson EL, et al. Polymyalgia Rheumatica and Giant Cell Arteritis: A Systematic Review. JAMA 2016;315(22):2442–58.

[8] Burja B, Kuret T, Sodin-Semrl S, Lakota K, Rotar Ž, Ješe R, et al. A concise review of significantly modified serological biomarkers in giant cell arteritis, as detected by different methods. Autoimmun Rev 2018 Feb 1;17(2):188–94.

[9] Hunder GG, Bloch DA, Michel BA, et al. The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. Arthritis Rheum 1990;33(8):1122–8.

[10] Salvarani C, Soriano A, Muratore F, Shoenfeld Y, Blockmans D. Is PET/CT essential in the diagnosis and follow-up of temporal arteritis? Autoimmun Rev 2017 Nov 1;16(11):1125–30.

[11] Hommada M, Mekinian A, Brillet P-Y, Abad S, Larroche C, Dhôte R, et al. Aortitis in giant cell arteritis: diagnosis with FDG PET/CT and agreement with CT angiography. Autoimmun Rev 2017 Nov 1;16(11):1131–7.

[12] 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 Eng) 2016 Nov;20(90):1–238.

[13] Karassa FB, Matsagas MI, Schmidt WA, Ioannidis JPA. Meta-analysis: test performance of ultrasonography for giant-cell arteritis. Ann Intern Med 2005 Mar 1;142(5):359–69.

[14] Arida A, Kyprianou M, Kanakis M, Sfikakis PP. The diagnostic value of ultrasonography-derived edema of the temporal artery wall in giant cell arteritis: a second meta-analysis. BMC Musculoskelet Disord 2010 Mar 8;11:44.

[15] Ball EL, Walsh SR, Tang TY, Gohil R, Clarke JMF. Role of ultrasonography in the diagnosis of temporal arteritis. Br J Surg 2010 Dec;97(12):1765–71.

[16] Whiting P, Rutjes AW, Reitsma JB, et al. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. BMC Med Res Methodol 2003 Nov 10;3:25.

[17] Reitsma JB, Glas AS, Rutjes AW, et al. Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. J Clin Epidemiol 2005;58(10):982–90.

[18] Zwinderman AH, Bossuyt PM. We should not pool diagnostic likelihood ratios in systematic reviews. Stat Med 2008;27(5):687–97.

[19] Reinhard M, Schmidt D, Hetzel A. Color-coded sonography in suspected temporal arteritis-experiences after 83 cases. Rheumatol Int 2004 Nov;24(6):340–6.

[20] Ciancio G, Colina M, Corte RL, et al. Color duplex ultrasonography in the diagnosis and management of giant cell arteritis. Conference: ACR Annual Scientific Meeting 2009:60.

[21] Schmidt WA, Kraft HE, Vorpahl K, et al. Color duplex ultrasonography in the diagnosis of temporal arteritis. N Engl J Med 1997 Nov 6;337(19):1336–42.

[22] Schmid R, Hermann M, Yannar A, et al. Color duplex ultrasound of the temporal artery: replacement for biopsy in temporal arteritis. Ophthalmol J Int 2002 Feb;216(1):16–21.

[23] Karahaliou M, Vaiopoulos G, Papaspyrou S, et al. 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(4):R116.

[24] Pérez López J, Solans Laqué R, Bosch Gil JA, et al. Colour-duplex ultrasonography of the temporal and ophthalmic arteries in the diagnosis and follow-up of giant cell arteritis. Clin Exp Rheumatol 2009 Feb;27(1):S77–82. Suppl 52.

[25] Schmidt D, Hetzel A, Reinhard M, et al. Comparison between color duplex ultrasonography and histology of the temporal artery in cranial arteritis (giant cell arteritis). Eur J Med Res 2003 Jan 28;8(1):1–7.

[26] Muratore F, Boiardi L, Restuccia G, et al. Comparison between colour duplex sonography findings and different histological patterns of temporal artery. Rheumatology (Oxford) 2013 Dec;52(12):2268–74.

[27] Bley TA, Reinhard M, Hauenstein C, et al. Comparison of duplex sonography and high-resolution magnetic resonance imaging in the diagnosis of giant cell (temporal) arteritis. Arthritis Rheum 2008 Aug;58(8):2574–8.

[28] Pfenninger L, Horst A, Stuckmann G, et al. Comparison of histopathological findings with duplex sonography of the temporal arteries in suspected giant cell arteritis. Klin Monbl Augenheilkd 2012 Apr;229(4):369–73.

[29] Croft AP, Thompson N, Duddy MJ, et al. Cranial ultrasound for the diagnosis of giant cell arteritis. A retrospective cohort study. J R Coll Physicians Edinb 2015;45(4):268–72.

[30] Brunhölzl C. Müller HR. Doppler sonography findings in arteriitis temporalis. *Ultraschall Med Stuttg Ger* 1980. 1988 Oct;9(5):232–6.

[31] Pfadenhauer K, Weber H. Duplex sonography of the temporal and occipital artery in the diagnosis of temporal arteritis. A prospective study. J Rheumatol 2003 Oct;30(10):2177–81.

[32] Del Blanco Alonso MI, Alonso Argüeso G, Menéndez Sánchez E, et al. Es necesaria la biopsia de la arteria temporal para el diagnóstico de arteritis de la temporal? *Angiología*. :87–90.

[33] Salvarani C, Silingardi M, Ghirarduzzi A, et al. Is duplex ultrasonography useful for the diagnosis of giant-cell arteritis? Ann Intern Med 2002 Aug 20;137(4):232–8.

[34] Maldini C, Dépinay-Dhellemmes C, Tra TTS, et al. Limited value of temporal artery ultrasonography examinations for diagnosis of giant cell arteritis: analysis of 77 subjects. J Rheumatol 2010 Nov;37(11):2326–30.

[35] Aschwanden M, Daikeler T, Kesten F, et al. Temporal artery compression sign–a novel ultrasound finding for the diagnosis of giant cell arteritis *Ultraschall Med Stuttg Ger* 1980. 2013 Feb;34(1):47–50.

[36] Nesher G, Shemesh D, Mates M, et al. The predictive value of the halo sign in color Doppler ultrasonography of the temporal arteries for diagnosing giant cell arteritis. J Rheumatol 2002 Jun;29(6):1224–6.

[37] Romera-Villegas A, Vila-Coll R, Poca-Dias V, et al. The role of color duplex sonography in the diagnosis of giant cell arteritis. J Ultrasound Med Off J Am Inst Ultrasound Med 2004 Nov;23(11):1493–8.

[38] Black R, Roach D, Rischmueller M, et al. The use of temporal artery ultrasound in the diagnosis of giant cell arteritis in routine practice. Int J Rheum Dis 2013 Jun;16(3):352–7.

[39] Murgatroyd H, Nimmo M, Evans A, et al. The use of ultrasound as an aid in the diagnosis of giant cell arteritis: a pilot study comparing histological features with

ultrasound findings. Eye (Lond) 2003 Apr;17(3):415–9.
[40] Lesar CJ, Meier GH, Demasi RJ, et al. The utility of color duplex ultrasonography in the diagnosis of temporal arteritis. J Vasc Surg 2002 Dec;36(6):1154–60.
[41] Venz S, Hosten N, Nordwald K, et al. Use of high resolution color Doppler sonography in diagnosis of temporal arteritis. ROFO Fortschr Geb Rontgenstr Nuklearmed 1998 Dec;169(6):605–8.
[42] Zaragozá García JM, Plaza Martínez A, Briones Estébanez JL, et al. Value of the Doppler-ultrasonography for the diagnosis of temporal arteritis. Med Clin (Barc) 2007 Oct 6;129(12):451–3.