THU0297 A NOVEL ULTRASOUND SCORING SYSTEM FOR GIANT CELL ARTERITIS

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Background: Colour duplex sonography (CDS) can be used for giant cell arteritis (GCA) to detect inflammatory oedema of the vascular wall, known as "halo". A standardized, quantitative score to grade the severity and extension of vascular involvement detected by CDS has not yet been developed.
Objectives: To develop and test different scoring models of CDS findings in patients with new onset GCA, and to correlate the models with final diagnosis, histologic findings, and outcome.
Methods: We selected patients with a positive CDS and a confirmed diagnosis of GCA from the Temporal Artery Biopsy vs Ultrasound in Diagnosis of GCA (TABUL) study (1). We designed CDS models combining different ultrasonographic information based on available evidence, or hypothesized clinical relevance of size, anatomical distribution, and extent of halos, summing up to a final numeric score.
Results: We included 135 GCA patients (male/female: 43/92), age 73.3±8. Fourty four patients (24%) had a positive CDS, but not a final diagnosis of GCA. We designed 8 different CDS models (Figure 1). Models 1, 4, 6, and 7 were significantly associated with a confirmed diagnosis of GCA (Table 2). Model 7 better discriminated patients with GCA from non-GCA: area under the curve (AUC): 0.844 (0.766–0.923). All, except models 5 and 8, correlated with a temporal artery biopsy (TAB) result diagnostic for GCA. Most models correlated with histologic findings involving the media or transmural infiltrate, but not with small vessel or adventitial involvement. None of the models correlated with permanent ischaemic sequelae, however, the low number of events might have affected the results.

Figure 1. Ultrasound scoring models

Model	Scoring formula
Model 1	Sum of sites with halos in TA and AX
Model 2	Defined as either bilateral halo on any TA branches OR bilateral halo on AX
Model 3	(Number of sites with halo on TA * average halo thickness among TA branches) + (number of sites with halo on AX * average halo thickness on AX)
Model 4	(Number of sites with halo on TA * maximum halo thickness among TA branches) + (number of sites with halo on AX * maximum halo thickness among AX)
Model 5	(Average halo thickness among TA + add "1" if bilateral halo on TA) + (average halo thickness among TA + add "1" if bilateral halo on AX)
Model 6	(Maximum halo thickness among TA + add "1" if bilateral halo on TA) + (maximum halo thickness among AX + add "1" if bilateral halo on AX)
Model 7	(Maximum thickness among TA * 2 if bilateral) + (maximum halo thickness among AX * 2 if bilateral)
Model 8	(Average thickness among TA * 2 if bilateral) + (average halo thickness among AX * 2 if bilateral)

TA: temporal artery; AX: axillary artery; * multiply by.

Conclusions: The CDS findings that better correlate with a diagnosis of GCA, and TAB findings are: the number of positive sites, the size of the halo (maximum, rather than average thickness), and the presence of bilateral halos, variably combined into a unique score. We plan to test these models in a new cohort of patients with suspected GCA, to determine their validity.
References:
[1] 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 2016;20:1–238.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4069

THU0298 LONG TERM OUTCOME OF PATIENTS WITH TAKAYASU ARTERITIS- A SINGLE CENTRE STUDY

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Background: Takayasu Arteritis (TA), a large vessel vasculitis is characterised by a variable clinical course and outcome that differs across populations. Most studies are limited by small sample size.
Objectives: (i) To study treatment outcome in our TA patients with a follow up of ≥12 months (ii) Construct a prediction model for subset of patients with sustained inactive disease.
Methods: Consecutive patients with TA attending our clinics between 1998 and April 2016 were recruited. Details of baseline demography, clinical profile, angiography, disease extent using DEI.Tak, laboratory parameters and TADS (Takayasu arteritis damage score) were recorded. At each follow up visit, disease activity was assessed by Indian Takayasu Activity score (ITAS-2010 (CRP) and imaging, while damage was assessed by TADS for patients who followed up for ≥12 months (retrospectively for 179 and prospectively for 72 patients). Treatment response was classified as complete response (CR), partial response and no-response. Sustained inactive disease was defined as maintenance of CR throughout the follow up with steroid dose reduced to ≤5mg/day. Relapse was defined as return of active disease after CR. Statistical analysis was performed using SPSS-16. Intergroup comparisons were performed by nonparametric test. Logistic regression was used for determining independent associations. Optimal cut off values were determined using receiver operating curve and prediction model was constructed. Efficacy of medications was compared by Cox proportional hazards model.
Results: Baseline details were noted for 503 patients: mean age at onset of 25.6±11.1 years, disease duration 12 (6–48) months, diagnostic delay 6 (3–24) months) and 77.9% were females.
Among 251 patients with follow up of at least 12 months, 95.2% received steroids along with II line immunosuppressant in 93.6% (mycophenolate in 63.7%). Tocilizumab was given induction or rescue therapy to 44 patients. Revascularisation procedures were performed in 71.7%. Complete (ITAS 2010 = 0, CRP <6mg/L, angiowise non-progression) and partial response was achieved in 176 patients (70.1%) and 42 (16.7%) respectively within 6 months.
During a median follow up of 42 (IQR: 24–81) months, 116 (46.2%) maintained complete response till their last follow up with cumulative relapse free survival of 83%, 70% and 55% at 1, 2 and 3 years respectively. A model including baseline CRP≤6.1mg/L, type 4 disease and DEI.Tak <9 predicted sustained inactive disease with an AUC of 70.2 (63.3–77.2, p=0.000). Initial steroid dosage of 0.5mg/kgday was similar to 1mg/kg/day in terms of response or relapse. Overall, there were only 15 (5.9%) patients who never responded to treatment. There were 2 fatalities. At the last visit, 176 (70.5%) had stable disease. Damage progression (delta TADS) was lower in patients with sustained inactive disease than the rest, p=0.000.
Conclusions: Medical management arrested disease activity, damage progression and mortality in our cohort. Low baseline CRP and DEI.Tak scores and type 4 disease independently predicted sustained inactive disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4258

THU0299 UNDERSTANDING THE HETEROGENEITY OF LARGE-VESSEL VASCULITIDES

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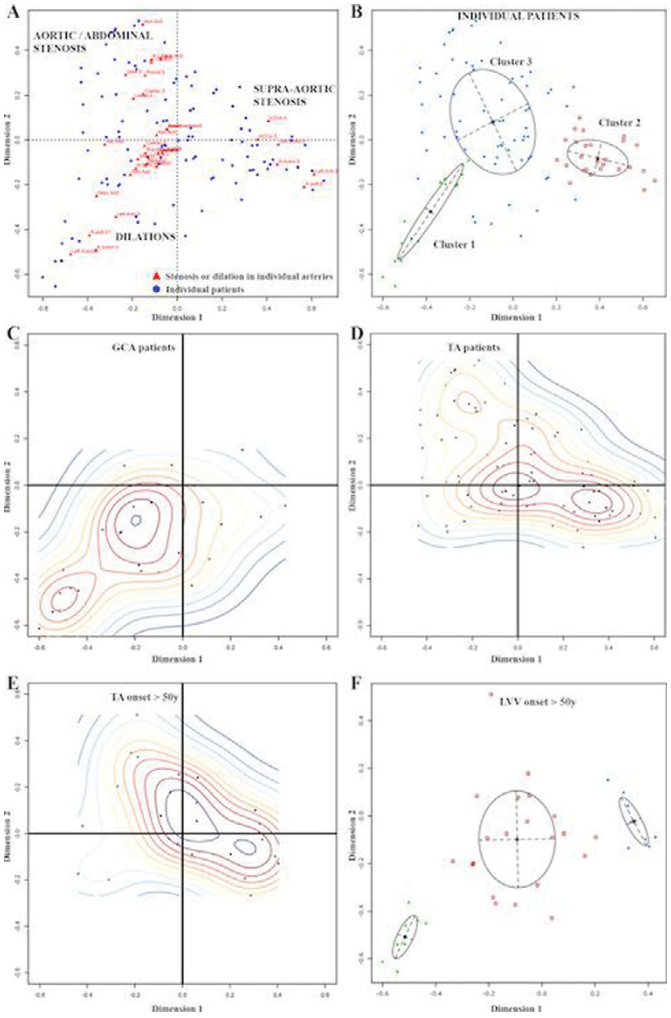
Background: Adult large-vessel vasculitides (LVV) are rare conditions, currently classified as two different diseases, Takayasu arteritis (TA) and giant cell arteritis (GCA), on an empirical basis. Insight into phenotypic and pathogenic differences between the two is scarce at best. Arterial involvement, despite being the central disease feature, has been poorly addressed by research. We have developed two novel, imaging-based scores (the arteritis stenosis score [ASS] and arteritis dilation score [ADS]). ASS and ADS define stenotic and aneurysmal disease in a

Abstract THU0297 – Table 2. Correlation of the different models with clinical and histologic variables

Median (IQR)		Model 1	Model 2		Model 3	Model 4	Model 5	Model 6	Model 7	Model 8
			0	1						
Predicting a diagnosis of GCA	0	2 (1–3)	25 (57%)	19 (43%)	3 (2–4.2)	1 (0.4–2.3)	2.7 (1.9–3.4)	1 (0.4–1.8)	0 (0–1.4)	1.3 (0.6–2.7)
	1	3 (1–5)	60 (44%)	75 (56%)	3.3 (1.8–6.2)	2.1 (0.8–4.4)	3.2 (2.1–3.7)	1.6 (0.7–2.3)	2 (1.2–2.8)	1 (0–1.8)
	p	**0.028**	0.21		0.52	**<0.001**	0.47	**0.003**	**<0.001**	0.35
TAB diagnostic for GCA	0	2 (1–3.5)	31 (61%)	20 (39%)	2.5 (1.2–3.4)	1 (0.6–2.4)	2.1 (1.2–3.5)	1.2 (0.4–1.7)	1.4 (1–2)	0.3 (0–2.2)
	1	3 (2–5)	24 (32%)	52 (68%)	5 (2.9–7.5)	2.8 (1.8–6)	3.5 (2.7–4)	1.9 (1.4–2.5)	2.2 (1.4–3)	1.1 (0.2–1.6)
	p	**<0.001**	**0.002**		**0.007**	**<0.001**	0.064	**<0.001**	**0.008**	0.90
Transmural infiltrate	0	2 (1–3.3)	34 (61%)	22 (39%)	2 (1.3–3.4)	1.1 (0.6–2.4)	1.9 (1.1–3.3)	1.1 (0.4–1.7)	1.4 (1.1–2)	0.2 (0–2.2)
	1	3 (2–4)	6 (23%)	20 (77%)	2.8 (1.6–3.2)	2.6 (1.5–3.6)	2.8 (2.2–3.1)	1.9 (1.5–2.3)	1.7 (1.2–2.5)	0.8 (0.2–1.2)
	p	**0.011**	**0.003**		0.96	**0.003**	0.51	**0.002**	0.29	0.96

Comparison between satisfying (1) or not satisfying (0) the considered variable.

core-set of 17 arteries and respectively represent the sum of stenosis and dilation scores in individual arteries[1].
Objectives: To use ASS, ADS and the stenosis and dilation scores of individual arteries to describe a cohort of LVV patients and identify heterogeneity between patients.
Methods: The ASS, ADS and individual artery scores have been derived from 110 LVV (81 TA, 29 GCA) patients. Model-based clustering optimising the Bayesian Information Criterion and principal component analysis were performed.
Results: Arterial involvement was shown to be differed in GCA and TA: TA has higher ASS than GCA (median, IQR: 20, 11–29 Vs 5, 0–11; $p<0.001$) and lower ADS (0, 0–5 Vs 6, 0–13; $p=0.019$). The scatterplot of ASS and ADS revealed incomplete overlap of arterial involvement in GCA and TA. No differences were seen in TA with disease onset before or after 40 yrs. Age at onset, ASS and ADS did not correlate in TA, suggesting stenotic and aneurysmal arterial remodelling are independent. In GCA, ASS and ADS were negatively correlated ($\rho=-0.401$; $p=0.031$) and ADS correlated with age at onset ($\rho=0.383$; $p=0.040$), suggesting the existence of a biologic "switch" between arterial stenosis and dilation, regulated by age at onset.
We accounted for geographical distribution of lesions by evaluating the scores of individual arteries with correspondence analysis. Arterial involvement was symmetric with tripolar segregation: stenosis in the supra-aortic branches, stenosis in the aorto-abdominal district and arterial dilation (Fig 1A). When patients exhibited the first two components, three different clusters were recognised (Fig 1B), with different ASS, ADS and damage as assessed by the TA damage score ($p<0.001$ for all tests). 27/29 (93%) of GCA patients were included in cluster 1 and 3, while 77/81 (95%) of TA clustered in 2 and 3. Of interest, density graphs showed (i) a different distribution of arterial involvement in GCA and TA (Fig 1C-D), and (ii) potential for identification of novel disease subsets (2 in GCA and 3 in TA). A comparable distribution was seen in TA with onset before or after 40 yrs (Fig 1E). Lastly, when patients with disease onset after 50 yrs (11 TA, 28 GCA) were studied, a trimodal distribution was observed, suggesting discrete phenotypes of arterial involvement exist, rather than a continuum (Fig 1F).



Conclusions: Arterial involvement differs in TA and GCA, although some overlap exists. Elderly TA is similar to juvenile TA, while a potential biologic "switch", yet to be identified, regulating the final outcome of arterial remodelling and influenced by ageing, is present in GCA. Three main patterns of arterial involvement appear to exist. LVVs represent the composition of different discrete subsets rather than a phenotypic continuum.
References:
[1] : Tombetti et al. EULAR 2015 Poster FRI0258.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6386

THU0300 CENTRAL NERVOUS SYSTEM INVOLVEMENT IN GRANULOMATOSIS WITH POLYANGIITIS (WEGENER) IN A LARGE SERIES OF PATIENTS WITH ANCA-ASSOCIATED VASCULITIDES (AAV).REVAS STUDY-GEAS-SEMI

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Background: GPA is a necrotizing systemic vasculitis that usually involves ENT, lung and kidneys. Neurological manifestations appear in 25–50% of patients, usually involving peripheral nervous system. CNS involvement, has been reported in only 7–11% of cases
Objectives: to describe the clinical features and outcome of patients with GPA and CNS involvement in a large series of patients with AAV
Methods: multicenter retrospective-longitudinal study that encompassed patients diagnosed with AAV between Jan 1995 and Nov 2014 in 21 Centres from Spain (REVAS Study). Statistical anlysis was performed using SSPS vs20 package
Results: 455 patients (188 GPA, 167 MPA and 100 EGPA) were included. Mean age at diagnosis was 55.7±17.2y. ANCA were positive in 86.8% of cases (35.8% C-ANCA, 51% P-ANCA). Median time to diagnosis was 4 weeks (IQR 10). Median follow-up time was 80 months (IQR 105). Neurological involvement was documented in 156 (34.5%) patients, but only 33 (7.3%) presented CNS involvement at disease onset. From those patients, 20 (60.6%) had GPA. Mean age at diagnosis of patients with GPA and CNS involvement was 51.1±16.7y. ANCA were positive in all cases (15 C-ANCA-PR3, 5 P-ANCA-MPO). Headache was the main neurological symptom (60%) followed by sensory (45%) and motor impairment (35%). MRI and/or angio-CT scan were performed in all cases. Cerebral ischaemic lesions were observed in 10 patients, and granulomatous lesions in 9, including pachymeningitis (n=6), spinal cord pachymeningitis (n=2) and isolated granulomatous lesions (n=1). Lumbar puncture was performed in 8 (40%) patients and revealed CSF abnormalities in 70. Diagnosis was confirmed by meningeal biopsy (n=2), ENT biopsies (n=5) and renal biopsy (n=2) in patients with CNS granulomatous lesions, and by renal, pulmonary or peripheral nerve biopsy in patients with CNS ischemic lesions. Headache was predominant in patients with granulomatous lesions, while sensory and motor impairment were predominant in patients with ischemic lesions. Mean BVAS at disease onset was 29.2±9.7, significantly higher than in GPA total cohort (18.2±9.2). Renal involvement was more common in patients with ischaemic lesions than in those with granulomatous (80% vs. 40%, $p<0.001$), and ENT involvement in patients with granulomatous forms (70% vs. 50%, $p<0.005$). Most patients (70%) received oral CF for induction therapy. Two patients received rituximab. For maintenance therapy, 25% of patients received AZA, 20% MMF and the remaining CF. 70% of patients received TM-SX. During follow-up, 58.8% and 40% of patients developed bacterial and opportunistic infections, respectively. Infections were related to oral CF therapy ($p=0.029$). Long-term neurological sequelae were noted in patients with ischaemic lesions (40%) and spinal cord pachymeningitis (100%)
Conclusions: Patients with GPA and CNS involvement have more severe disease at presentation and more treatment-related side effects than patients without CNS involvement. Long-term neurological sequelae are more frequent in patients with ischaemic lesions and spinal cord pachymeningitis
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2520