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Polymyalgia Rheumatica – Giant Cell Arteritis

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Polymyalgia Rheumatica (PMR)

PMR- Epidemiology

- Inflammatory condition causing pain and stiffness **in the neck, shoulder** and hip regions
- First described by **Bruce in 1888**
- The term PMR was introduced by **Barber in 1957**
- ≥ 50 years old, peak incidence 70-79 year age group[3]
- Female predominance (2/3)
- North European/Scandinavian ancestry

Hunder GG. Mayo Clin Proc. Aug;81(8):1071-83

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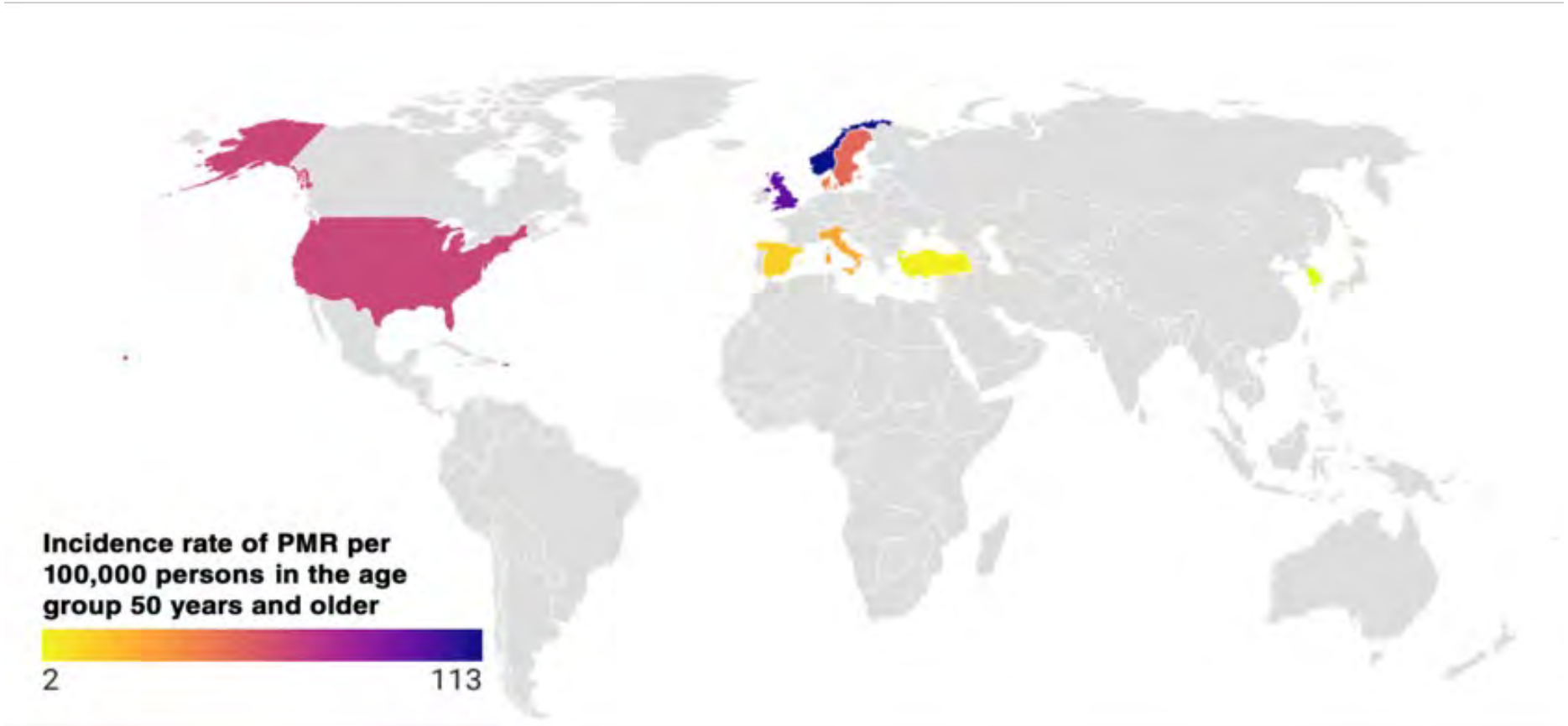
Epidemiology PMR



Lundberg IE et al. J Intern Med. 2022 Nov;292(5):717-732.

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Pathogenesis

- Largely unknown
- Arthroscopic biopsies demonstrate **synovitis and vascular proliferation**
- Infiltrating cells were mainly **macrophages and memory T-cells** (a few B-cells)
- Mild synovitis does not fully explain the musculoskeletal manifestations and extra-articular features
- Some authors suggest that PMR is a disorder of predominantly extra-articular synovial structures

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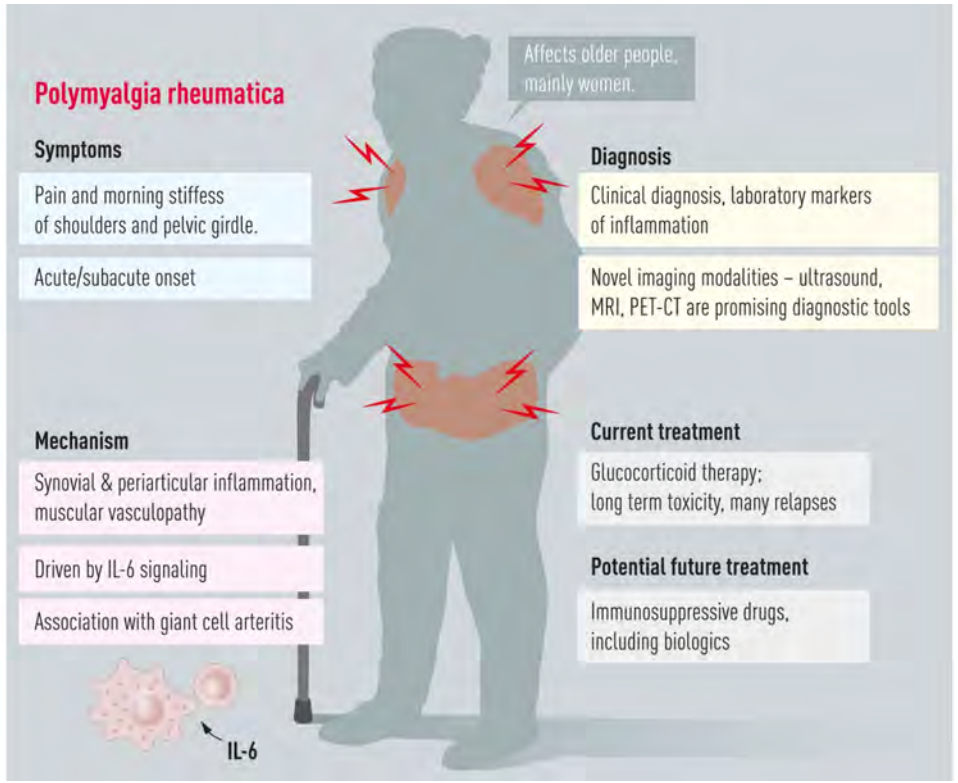
Clinical Presentation

- Relatively acute onset proximal muscle pain and stiffness
- Pronounced morning stiffness
- Symptoms fully developed within days or weeks
- Occasionally, more insidious onset with non-specific symptoms
- Many patients undergo investigations for malignant diseases



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Laboratory findings

- **No specific lab findings**
- Most common & important is the **elevation of ESR and CRP**
- Other lab findings include:
    1. Normochromic normocytic anemia
    2. Thrombocytosis
    3. Leukocytosis
    4. Increase of other acute phase reactants on plasma protein electrophoresis

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Imaging in PMR

- Ultrasound
- MR
- CT
- FGD PET scan

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Imaging - Ultrasound

The most common findings include

1. **Subacromial/subdeltoid bursitis**
2. **Biceps tenosynovitis**
3. Glenohumeral joint inflammation
4. **Peri-trochanteric bursitis**
5. Hip synovitis

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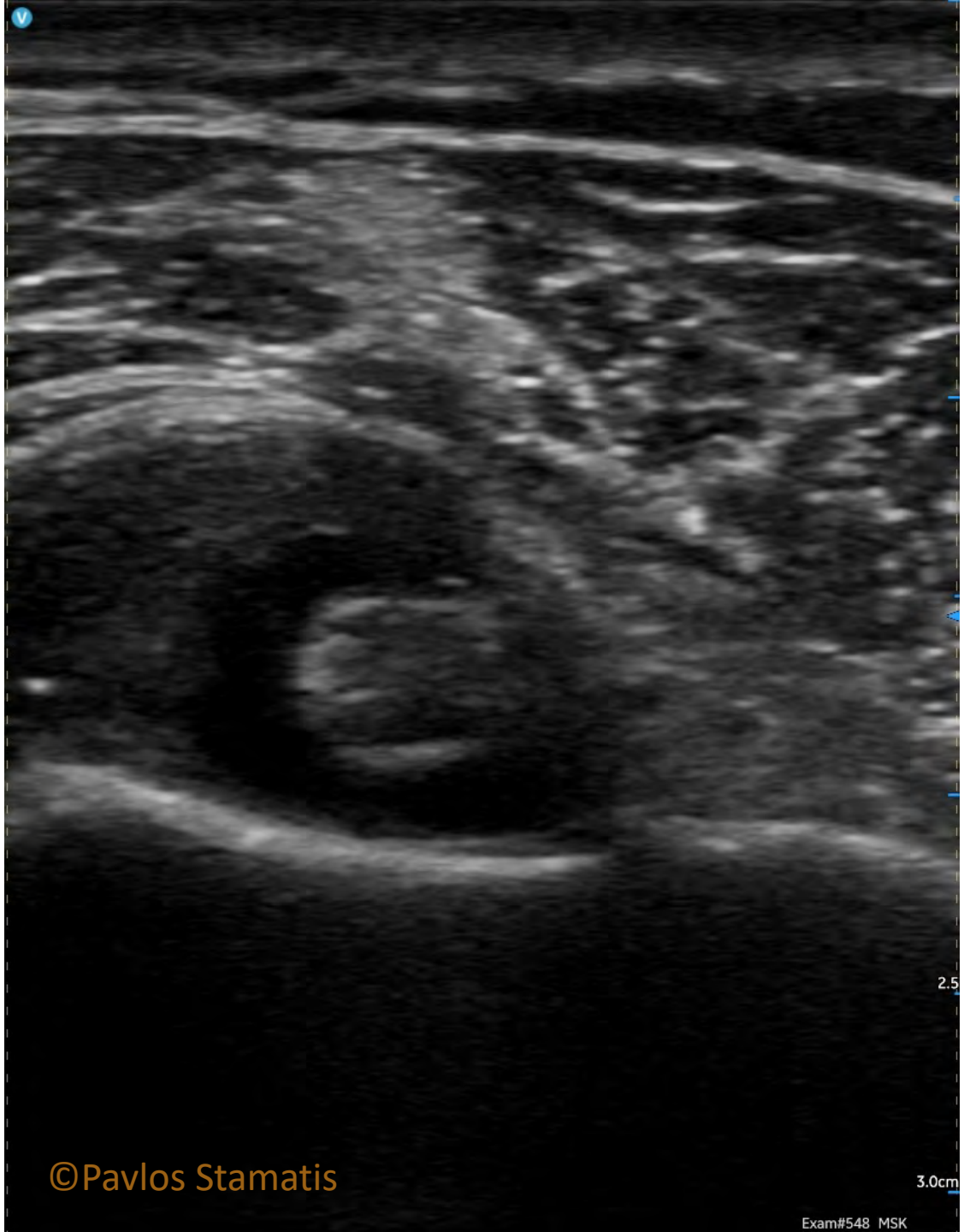
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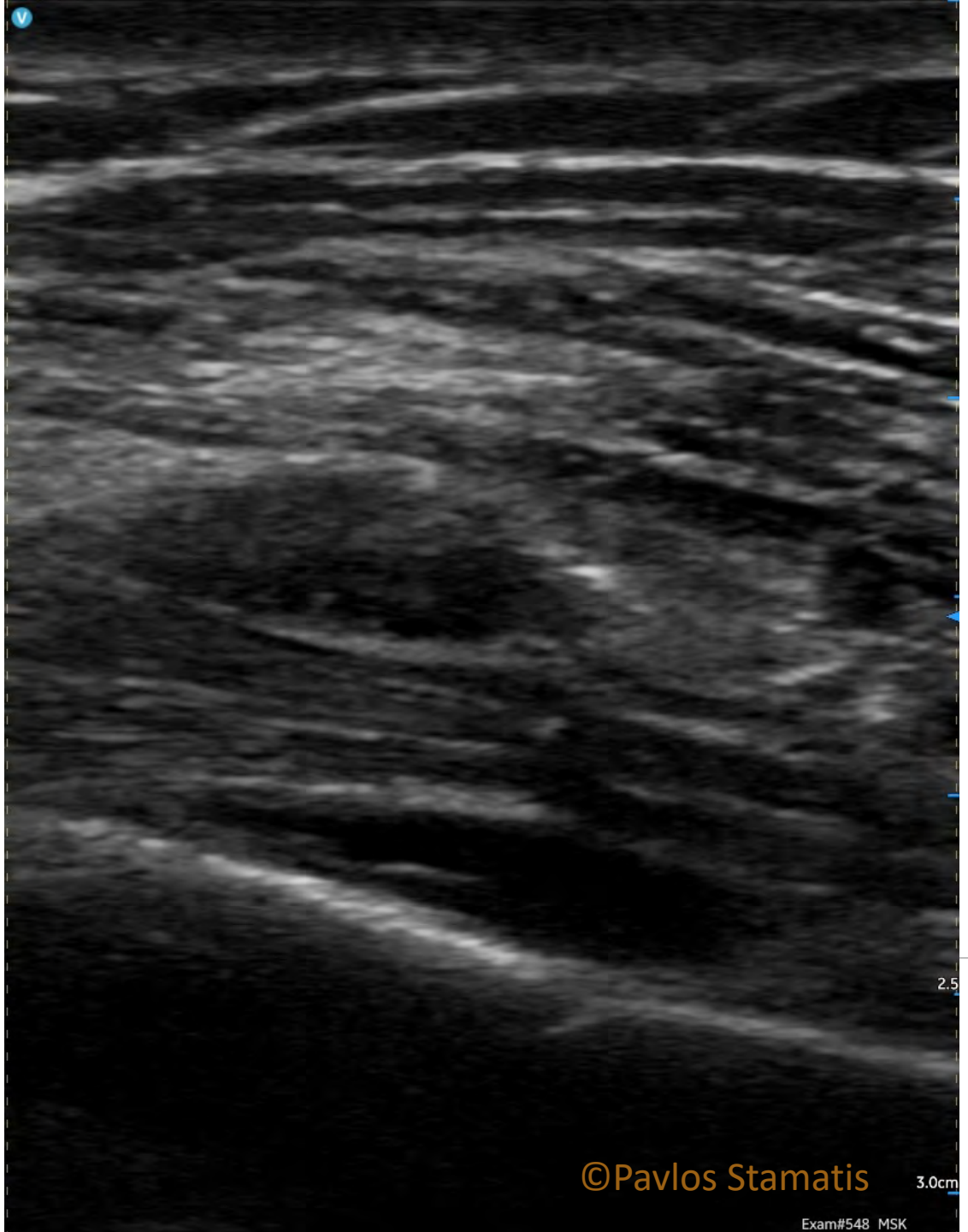
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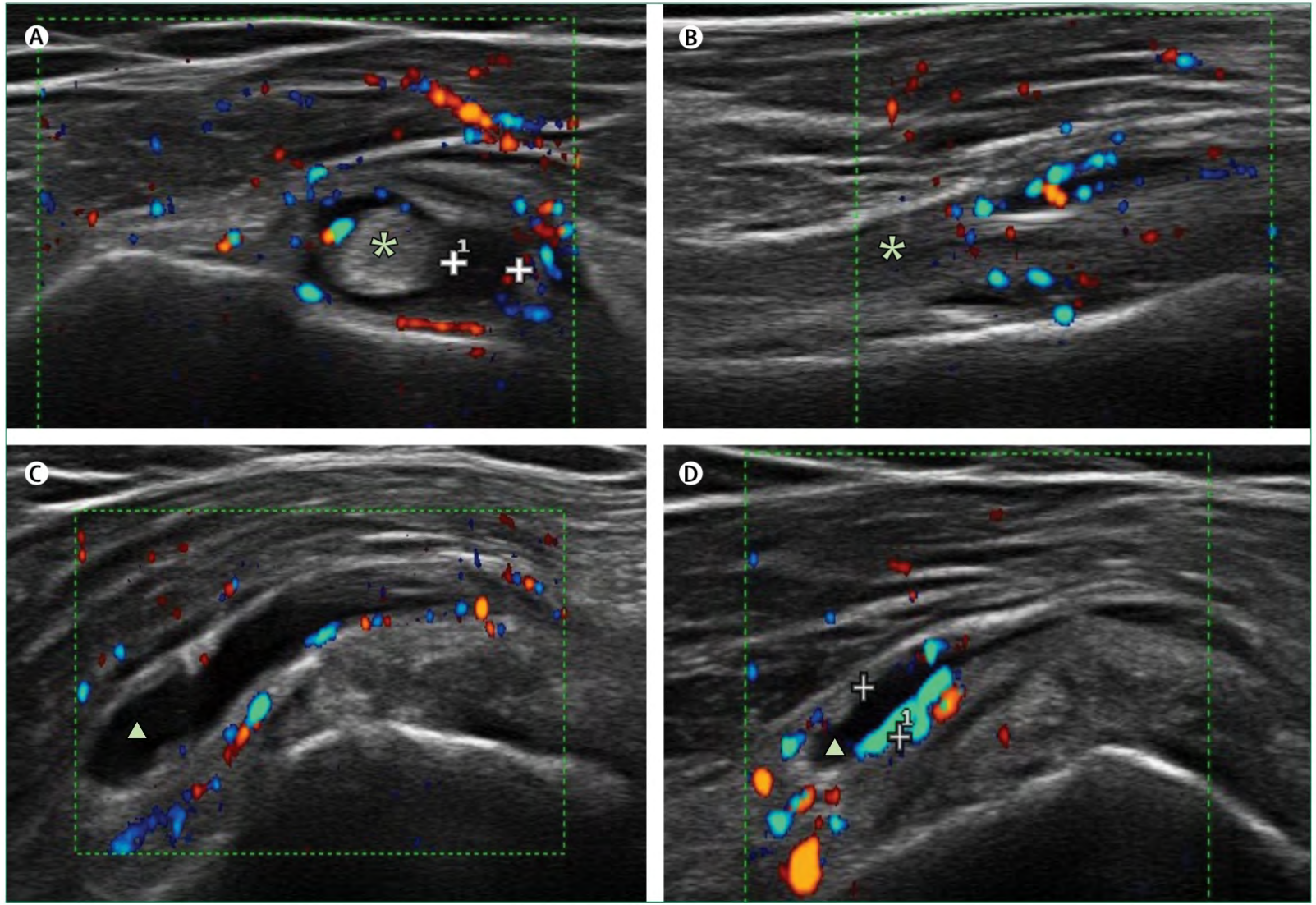

***Figure 3*: Ultrasonography of the shoulders in a patient with polymyalgia rheumatica**
Ultrasonography images show typical findings at periarticular soft tissues. (A) Transverse view of bilateral biceps tenosynovitis. (B) Longitudinal view of bilateral biceps tenosynovitis. (C) Longitudinal view of the subacromial bursa. (D) Longitudinal view of the subacromial bursa with increased vascularisation. In all locations, an increase of power Doppler signal can be seen around the tendon (*) and at the synovial tissue of the tendon sheath and the subacromial bursa. + indicates the margins of the synovial fluid. Δ indicates the interior of the subacromial bursa.

González-Gay MA et al. Lancet. 2017 Oct 7;390(10103):1700-1712

Imaging - MRI

- Typical findings in MRI include a characteristic pattern of symmetrical inflammation in:

1. Rotator cuff
2. Biceps tendon
3. Glenohumeral joint (enhancement of joint capsule, synovial hypertrophy, joint effusion)
4. Greater trochanter
5. Acetabulum
6. Ischial tuberosity

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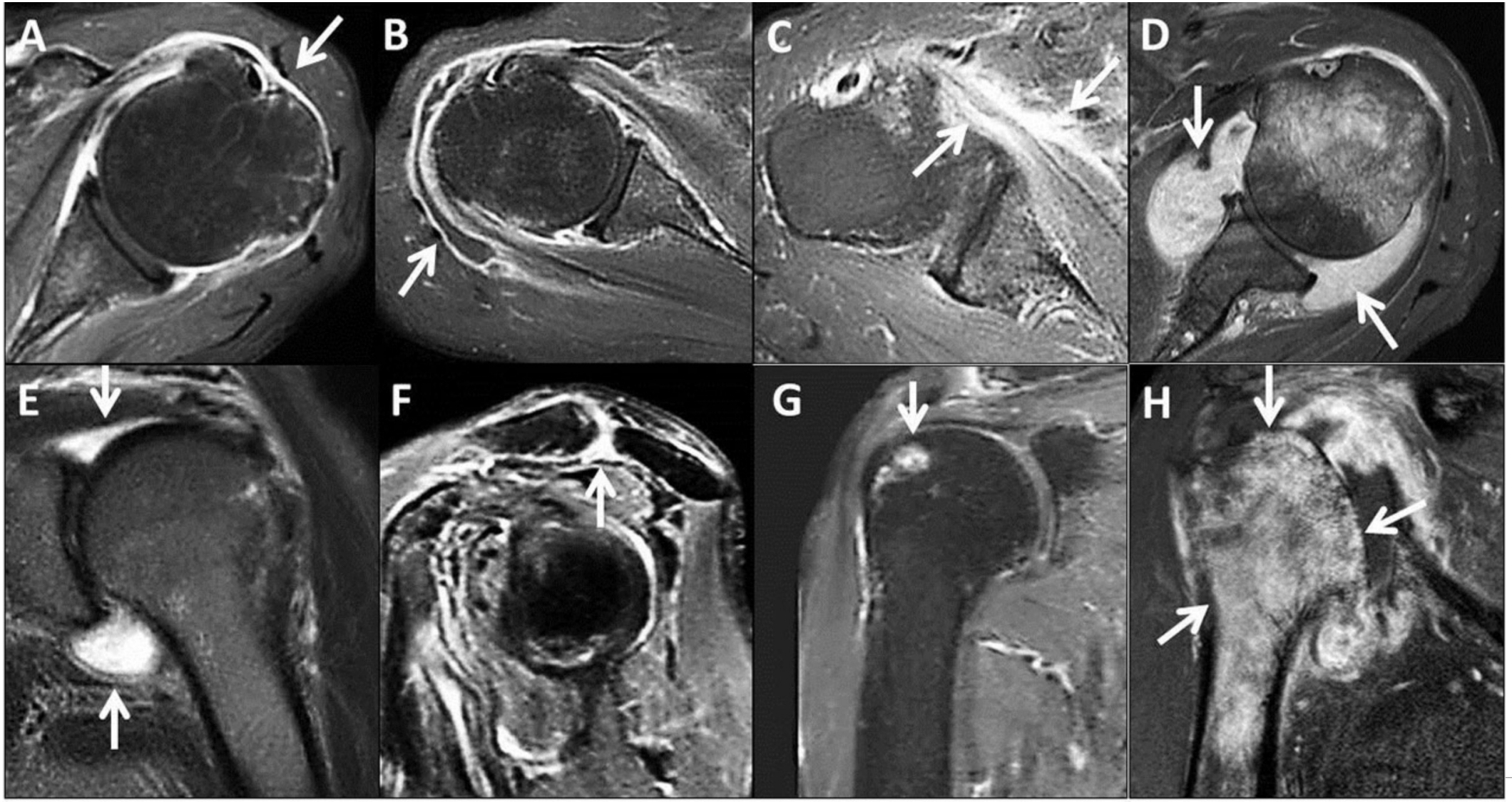


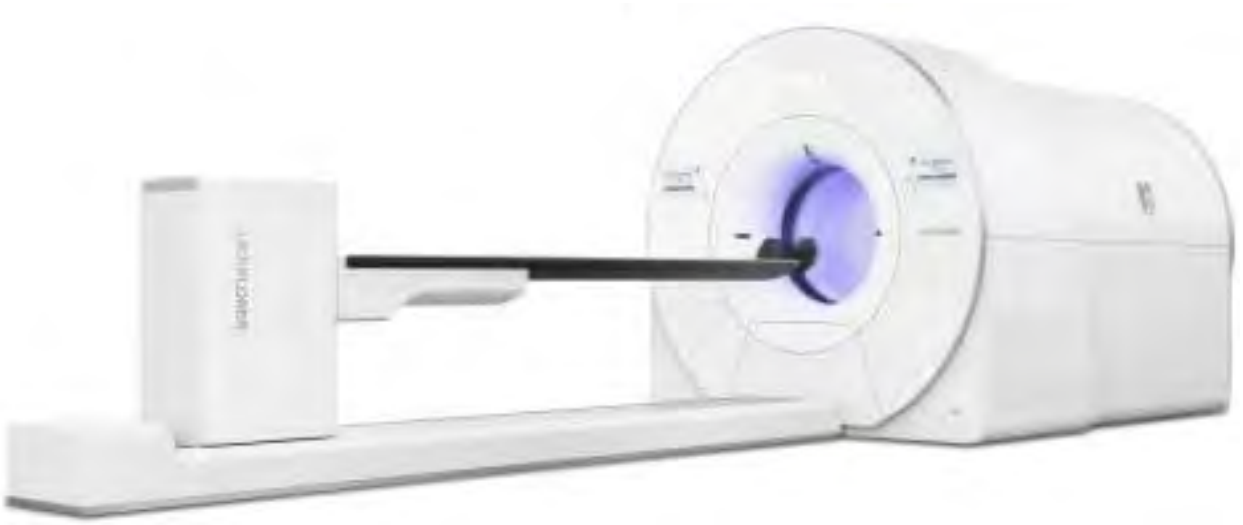
Fig. 2. Representative images of gadolinium-enhanced magnetic resonance imaging in shoulders.
A: Enhancement of shoulder joint capsule, **B**: enhancement of rotator cuff tendon, **C**: enhancement of biceps tendon, **D**: synovial hypertrophy, **E**: shoulder joint effusion, **F**: enhancement of glenohumeral joint, **G**: focal bone oedema in humerus heads and **H**: diffuse bone oedema in humerus heads.

Nakamura H et al. Clin Exp Rheumatol. 2021 Jan-Feb;39(1):84-90.

Imaging - FDG PET

- The typical PET CT findings include increased uptake in the:

1. Sternoclavicular joints
2. Shoulders
3. Ischial tuberosities
4. Greater trochanters
5. Spinous processes



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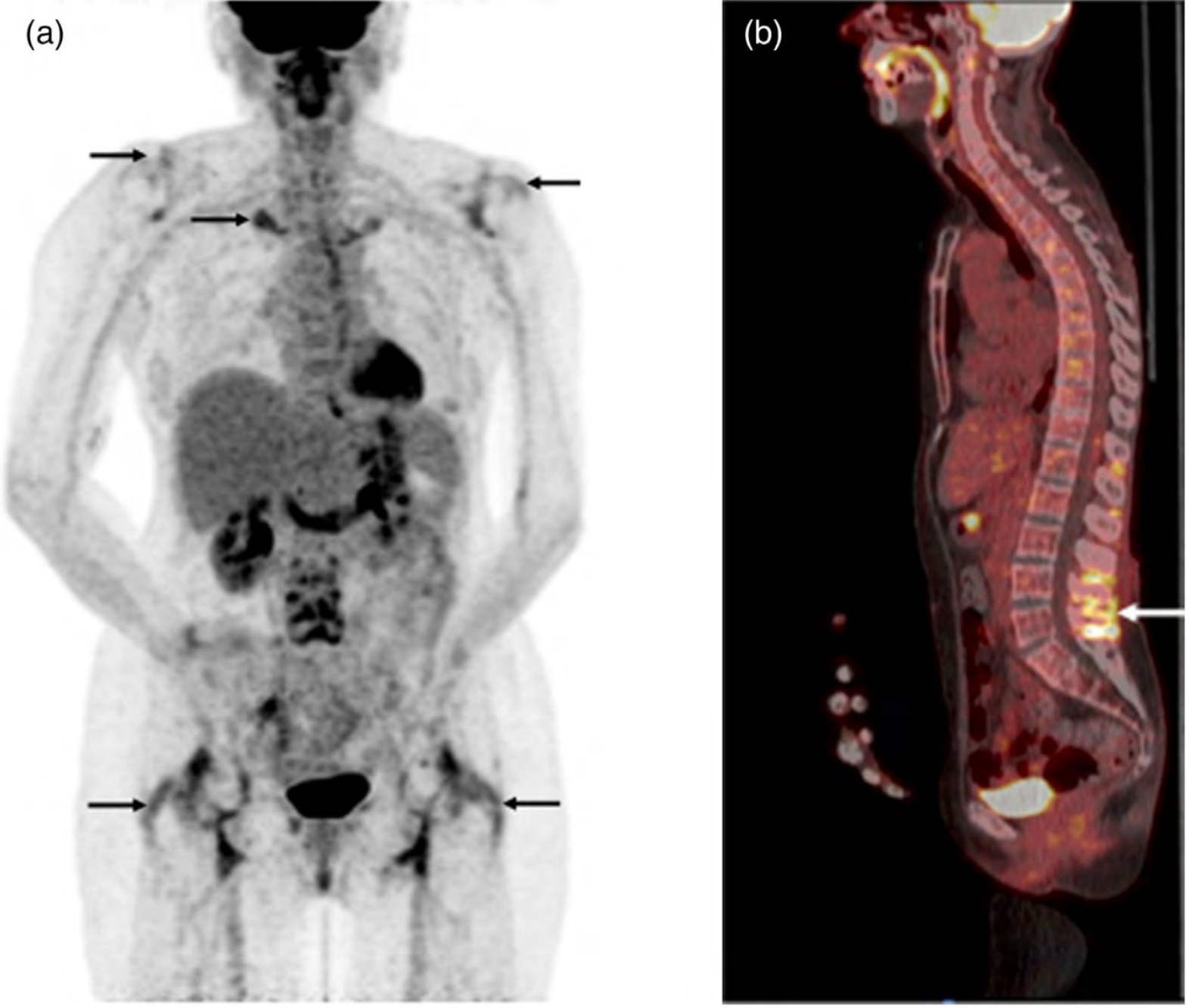

Courtesy of **Associate Professor Fredrik Hedeer** Lund University by **Lundberg et al**, Journal of Internal Medicine, 2022, 292;717-732

Diagnosis

No gold standard (no specific clinical manifestations, serology or lab findings)

In daily practice diagnosis relies on the following combination of principles:

1. New-onset symptoms of both morning stiffness and pain in shoulder and pelvic girdle in a person aged ≥50 years
2. Evidence of systemic inflammation (elevated ESR and CRP)
3. Positive imaging findings, mainly ultrasound
4. Negative RF and CCP
5. No other disease that would explain better the findings
6. Abrupt response to glucocorticoids

EULAR/ACR 2012 Classification Criteria PMR

Table 6 PMR classification criteria scoring algorithm—required criteria: age 50 years or older, bilateral shoulder aching and abnormal CRP and/or ESR*

	Points without US (0–6)	Points with US† (0–8)
Morning stiffness duration >45 min	2	2
Hip pain or limited range of motion	1	1
Absence of RF or ACPA	2	2
Absence of other joint involvement	1	1
At least one shoulder with subdeltoid bursitis and/or biceps tenosynovitis and/or glenohumeral synovitis (either posterior or axillary) and at least one hip with synovitis and/or trochanteric bursitis	Not applicable	1
Both shoulders with subdeltoid bursitis, biceps tenosynovitis or glenohumeral synovitis	Not applicable	1

*A score of 4 or more is categorised as PMR in the algorithm without US and a score of 5 or more is categorised as PMR in the algorithm with US.
†Optional ultrasound criteria.
ACPA, anticitrullinated protein antibody; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PMR, polymyalgia rheumatica; RF, rheumatoid factor; US, ultrasound.

Of note, the classification criteria are not used for diagnostic purposes

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Dasgupta B et al. *Annals of the Rheumatic Diseases* 2012;**71**:484-492.

Differential Diagnosis

1. Rheumatoid Arthritis
2. Myositis
3. Malignancy
4. Remitting Seronegative Symmetric Synovitis with Pitting Oedema (RS3PE)
5. Cervical spondylosis
6. Hip osteoarthritis
7. Hypothyroidism (diffuse pain, fatigue and fibromyalgia-like syndrome)

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Medical Management GCA

Treatment

- **Oral GCs** remain the cornerstone
- **NSAIDs** have no place in the treatment of PMR
- **Methotrexate (per os or sc) 7.5-15mg/week** can be used as Prednisolone-sparing agent
- Limited data for Azathioprine
- Negative RCTs regarding **TNF-a inhibitors**
- **Kevzara (Sarilumab) IL-6 receptor blocker** is first biologic to gain FDA approval based on SAPHYR phase 3 study

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Glucocorticoid reduction schemes

- Based on expert opinion
- Initial dose 12.5– 25 mg Prednisolone daily
- Gradually taper with 2.5mg/month down to 10mg per day
- After that slower tapering with 1.25mg every 4-6 weeks until discontinuation

Due to the prolonged use of GCs in this group of older patients consider to start anti-osteoporotic treatment

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Mortality

- The diagnosis of PMR does not have a significant impact on life expectancy
- However, it is important to treat early comorbid diseases such as GC-induced diabetes, hypertension and osteoporosis

Partington R et al. Arthritis Care Res (Hoboken). 2021 Dec;73(12):1853-1857
Myklebust G, et al. Scand J Rheumatol. 2003;32(1):38-41

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The association of PMR and GCA

The epidemiology of the connection

- First connection 1960, when Paulley and Hughes, suggested that PMR and GCA are clinical phenotypes of the same disease[1]
- 16-21% of PMR patients may later develop GCA [2,3]
- 40-60% of GCA patients may have as presenting symptom PMR [4,5,6]
- PMR is also the most common symptom during GCA relapses

[1]**Paulley JW, Hughes JP.** Br Med J. 1960 Nov 26;2(5212):1562-7
[2]**Dejaco C et al.** Rheumatology (Oxford). 2017 Apr 1;56(4):506-515
[3]**Salvarani C et al.** Arthritis Rheum. 1995 Mar;38(3):369-73
[4]**Tuckwell K et al.** Semin Arthritis Rheum. 2017 Apr;46(5):657-664
[5]**Pucelj NP et al.** Clin Rheumatol. 2019 Feb;38(2):285-290
[6]**Naderi N et al.** Scand J Rheumatol. 2017 May;46(3):215-221

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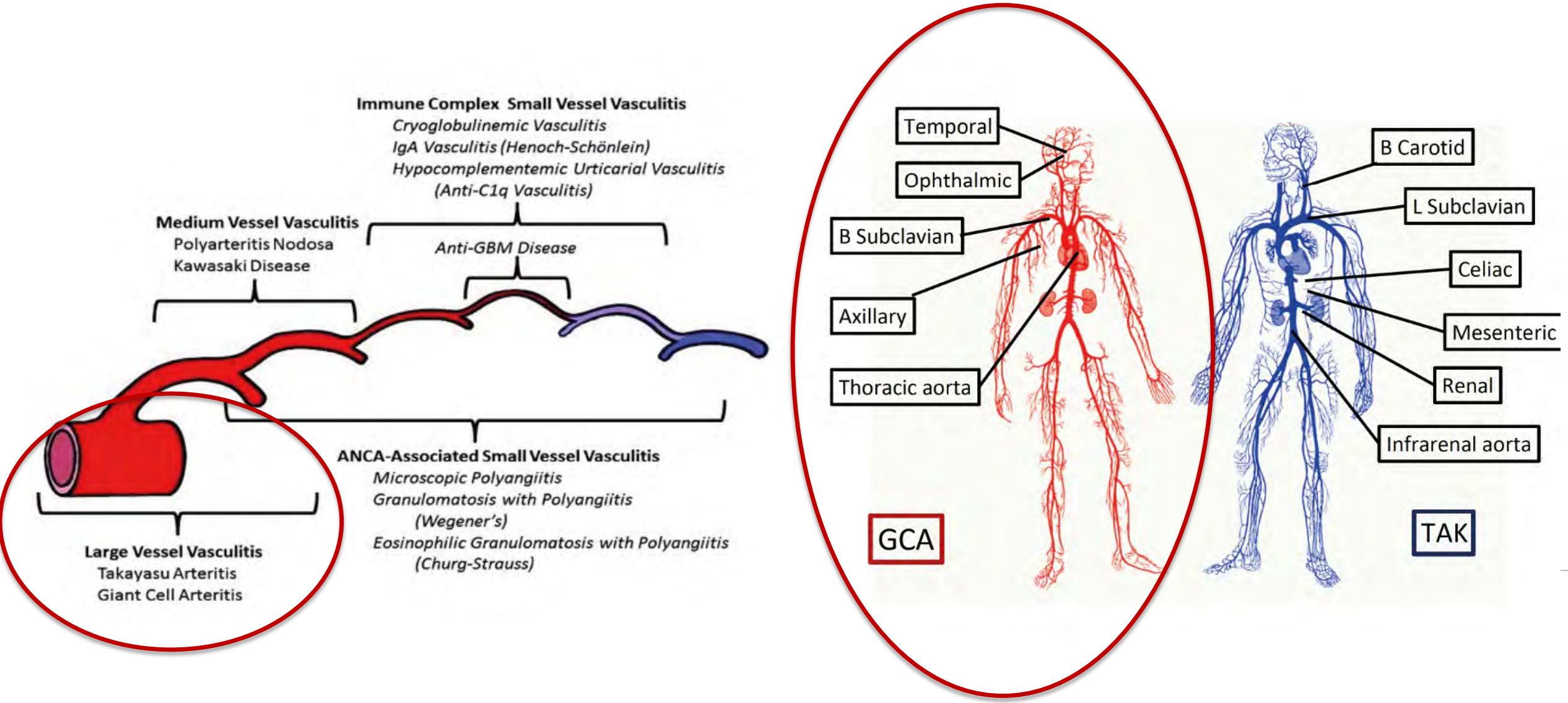
Giant Cell Arteritis (GCA)


Immune Complex Small Vessel Vasculitis
Cryoglobulinemic Vasculitis
IgA Vasculitis (Henoch-Schönlein)
Hypocomplementemic Urticarial Vasculitis
(Anti-C1q Vasculitis)
Medium Vessel Vasculitis
Polyarteritis Nodosa
Kawasaki Disease
Anti-GBM Disease
ANCA-Associated Small Vessel Vasculitis
Microscopic Polyangiitis
Granulomatosis with Polyangiitis
(Wegener's)
Eosinophilic Granulomatosis with Polyangiitis
(Churg-Strauss)
Large Vessel Vasculitis
Takayasu Arteritis
Giant Cell Arteritis
Temporal
Ophthalmic
B Subclavian
Axillary
Thoracic aorta
GCA
B Carotid
L Subclavian
Celiac
Mesenteric
Renal
Infrarenal aorta
TAK

Giant Cell Arteritis - Introduction

- The most common non-infectious vasculitis
- Affects predominantly the elderly
- Very uncommon before the age of 50, incidence peaks in the 70-79 year old group
- Female predisposition with 3:1 ratio
- North to south gradient
- Incidence 1.1-27 per 100 000 individuals ≥50 years

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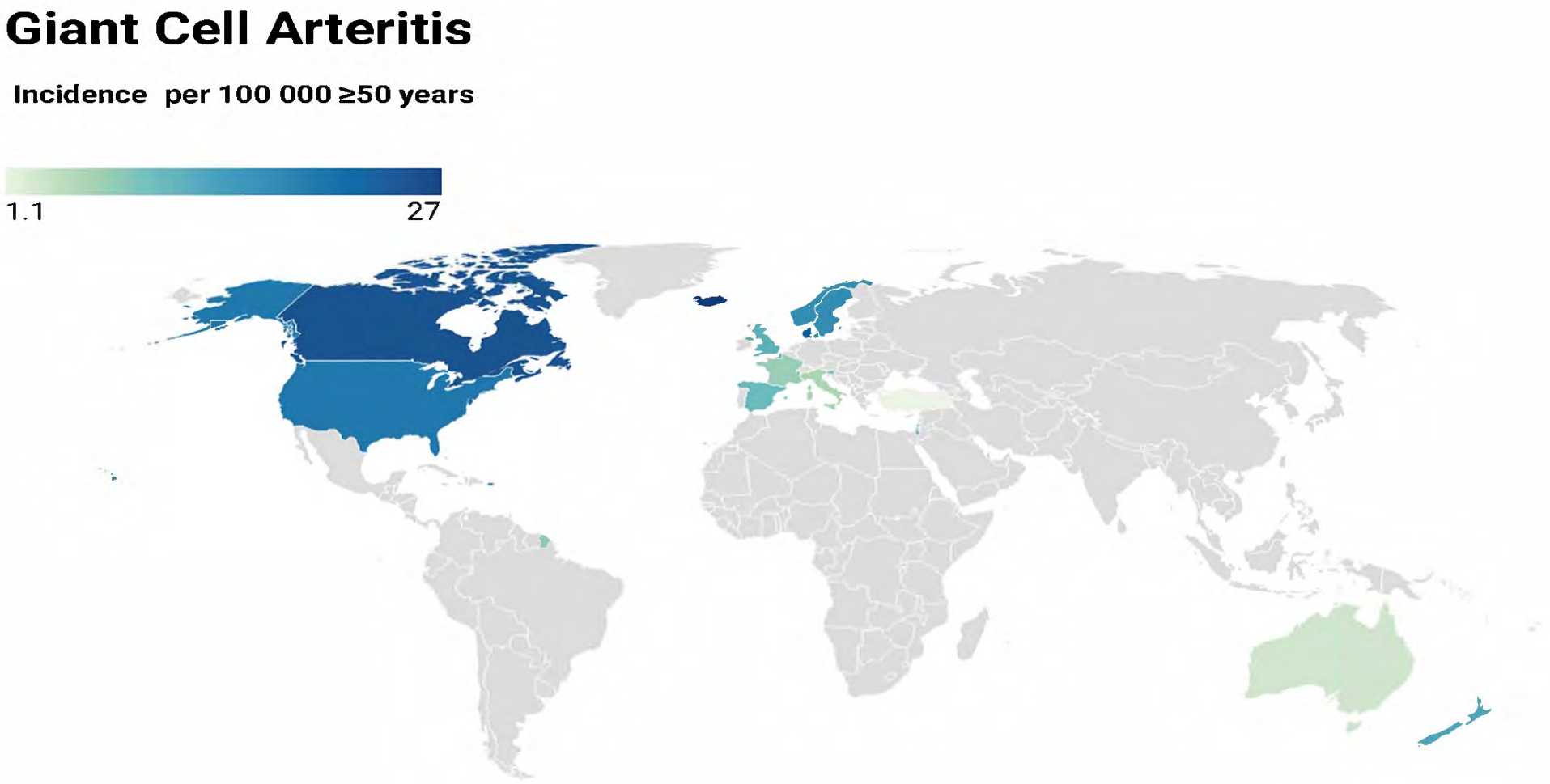
Epidemiology GCA



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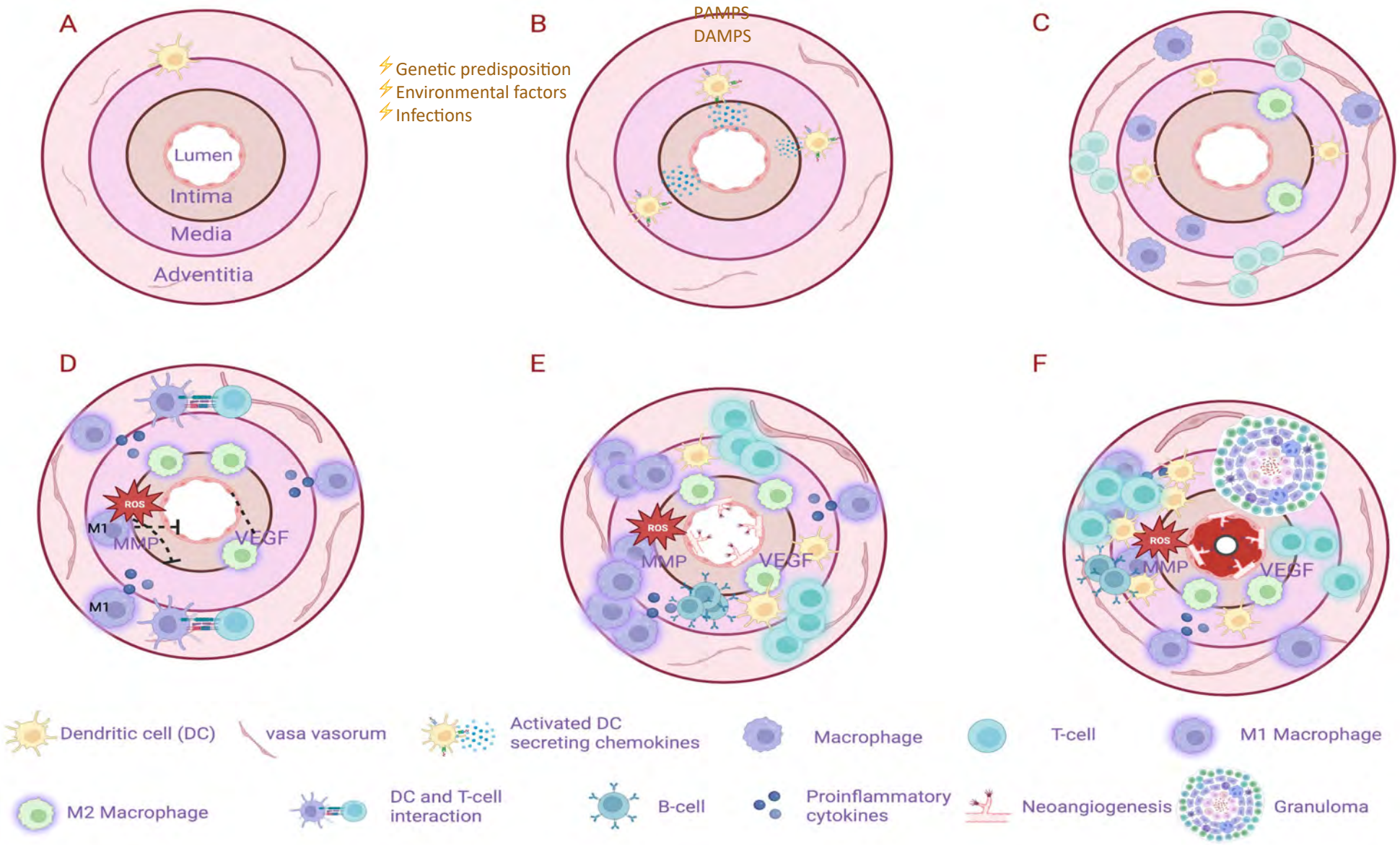
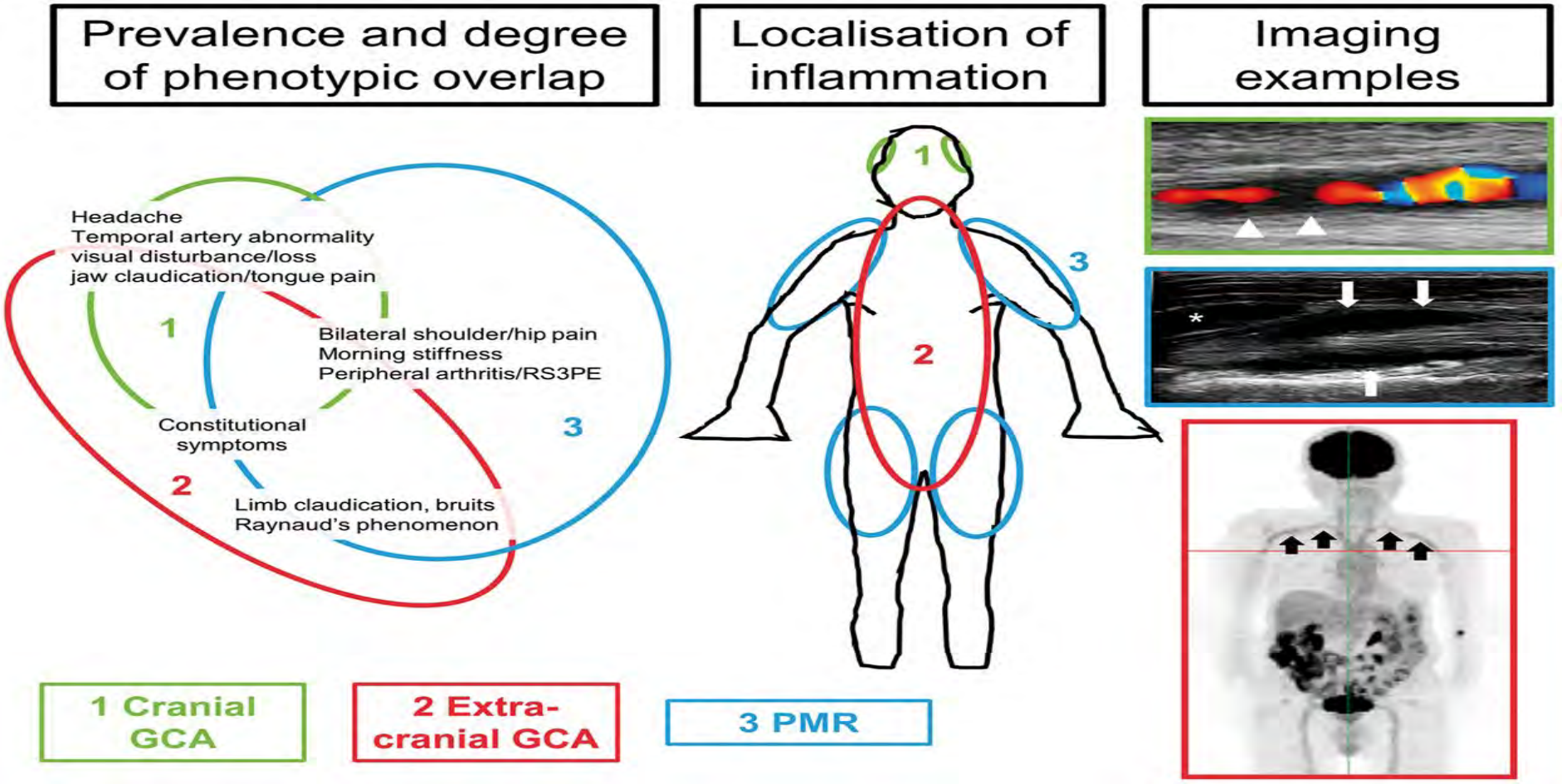
@Pavlos Stamatis

Pathogenesis



Stamatis P et al. Front Med (Lausanne). 2022 Nov 17;9:1058600

Clinical Presentation and Disease Spectra



Dejaco C et al. Rheumatology (Oxford). 2017 Apr 1;56(4):506-515

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Most common symptoms at disease onset

Study	Cases	Headache	Jaw claudication	Scalp tenderness	Visual symptoms	Constitutional symptoms	PMR
Zenone, 2013	98	76%	35%	N/A	15%**	46%	31%
Alba, 2014	106	78%	47%	46%	N/A	51%	51%
Grossman, 2016	82	76%	24%	N/A	27%	61%	32%
Tuckwell, 2017	119	71.4%	32.8%	36.1%	5.1%**	N/A	43%
Pucelj, 2019	169	71.6%	45%	N/A	33.1%	69.2%	14.2%

Stamatis P. Clinical and Epidemiological studies in GCA. Lund University Dissertation Series 2021

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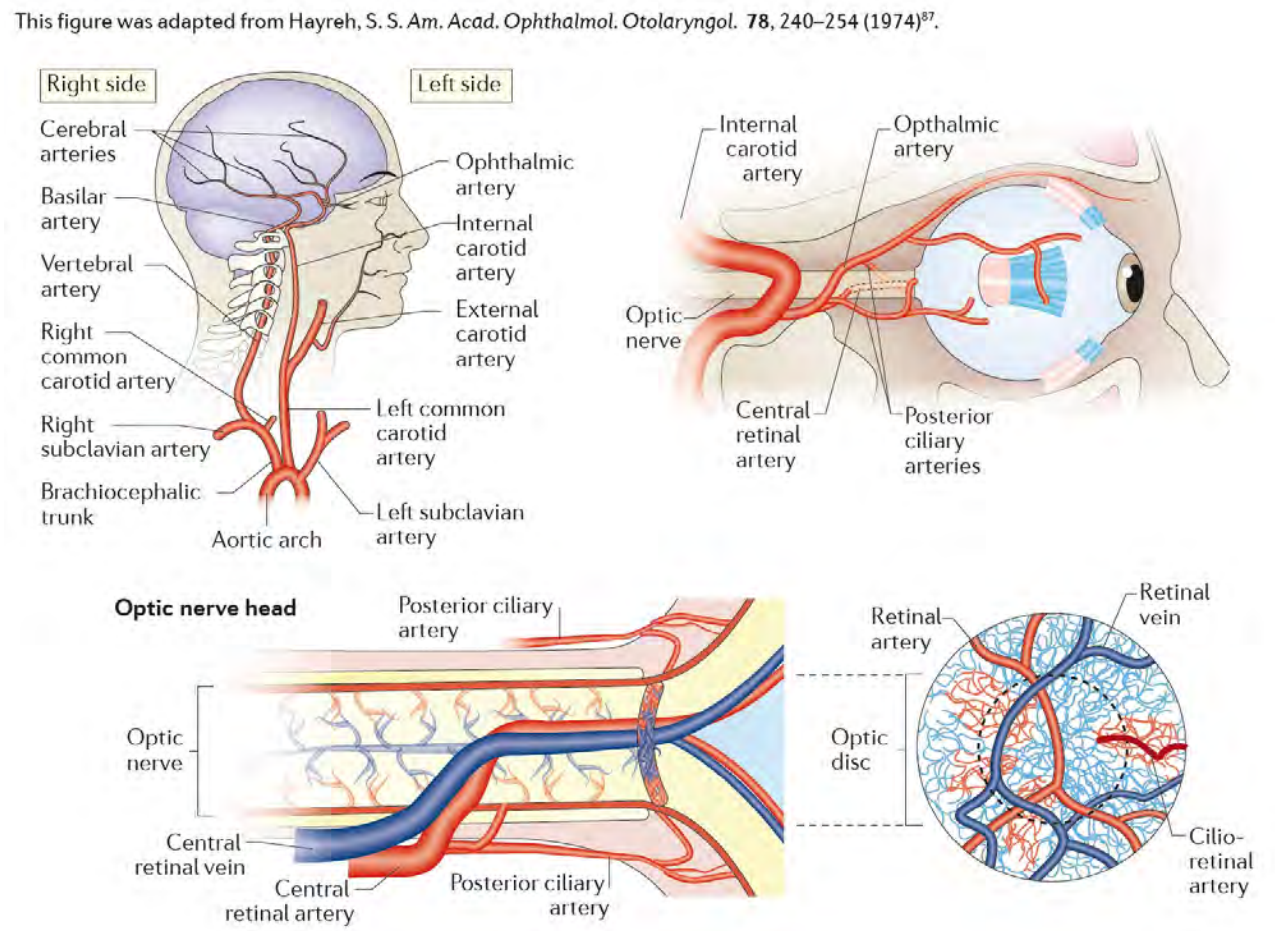
Visual manifestations

- Historical cohorts **20-30%**
- Recent studies lower prevalence
- Blurred vision, diplopia, amaurosis fugax, **partial visual field loss and permanent painless complete loss of vision**
- **Mechanism:** AION due to arteritis in the posterior ciliary arteries



Soriano, A. *Nat Rev Rheumatol* **13**, 476–484 (2017)

Cerebrovascular events

- **Stroke or TIA**
- First 4 weeks after the diagnosis
- Mainly vasculitis affecting the **posterior circulation** (vertebral and/or basilar arteries)
- 1.5-7%

Gonzalez-Gay MA et al. Medicine. 2009;88(4):227-35
Zenone T et al. Rheumatology international. 2013;33(12):3017-23
Samson M et al. J Neurol Neurosurg Psychiatry. 2015;86(2):216-21
de Boysson H et al. J Rheumatol. 2017;44(3):297-303.

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Large artery involvement

- **Younger disease onset** compared to cranial-GCA phenotype
- **Subclavian and axillary a**. most common arterial sites
- PMR frequent
- Large artery stenosis, aortitis (presented as mural thickness), **aortic aneurysm and aortic dissection**
- Incidence rate of any manifestation 30.5 per 1000 person-years
- Incidence of aortic aneurysm and dissection 18.7 per 1000-person years

Nuenninghoff DM et al. Arthritis Rheum. 2003;48(12):3522-31
Gonzalez-Gay MA et al. Medicine. 2004;83(6):335-41
Kermani TA et al. Semin Arthritis Rheum. 2019;48(4):707-13.
Gribbons KB et al. Arthritis Care Res (Hoboken). 2020 Nov;72(11):1615-1624

Laboratory Findings

- No specific laboratory tests for the diagnosis
- **CRP** more sensitive than **ESR**
- Combo of elevated **CRP and thrombocytosis** yields better sensitivity and specificity
- **Anemia of chronic disease** and **elevated ALP** may be present at disease onset
- **Haptoglobin** has emerged as a possible biomarker, especially in patients receiving Tocilizumab
- **Up to 5%** of GCA patients with biopsy-confirmed GCA may have normal ESR and CRP

Temporal Artery Biopsy

- **Unilateral** from the most symptomatic side
- Bilateral TAB only in selected cases, as it increases diagnostic accuracy by only 3-14%
- **Skip lesions** are reported to occur in 8.5-28% of TAB+ GCA cases
- A post-fixation length of 5-10mm which corresponds to a **prefixation surgical length of at least 10-15mm** was considered sufficient for diagnosis
- **The treatment should not delay** while waiting to perform a TAB

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A typical positive TAB

- Granulomatous infiltrate comprised mainly **of CD4+ lymphocytes and macrophages**
- **Transmural inflammation**: inflammatory infiltrate appears as concentric rings with relatively spared media layer
- In severe cases, all 3 layers are affected causing **panarteritis**
- **Giant cells** are absent in 25-50% positive TABs

Cavazza A et al. Am J Surg Pathol. 2014 Oct;38(10):1360-70

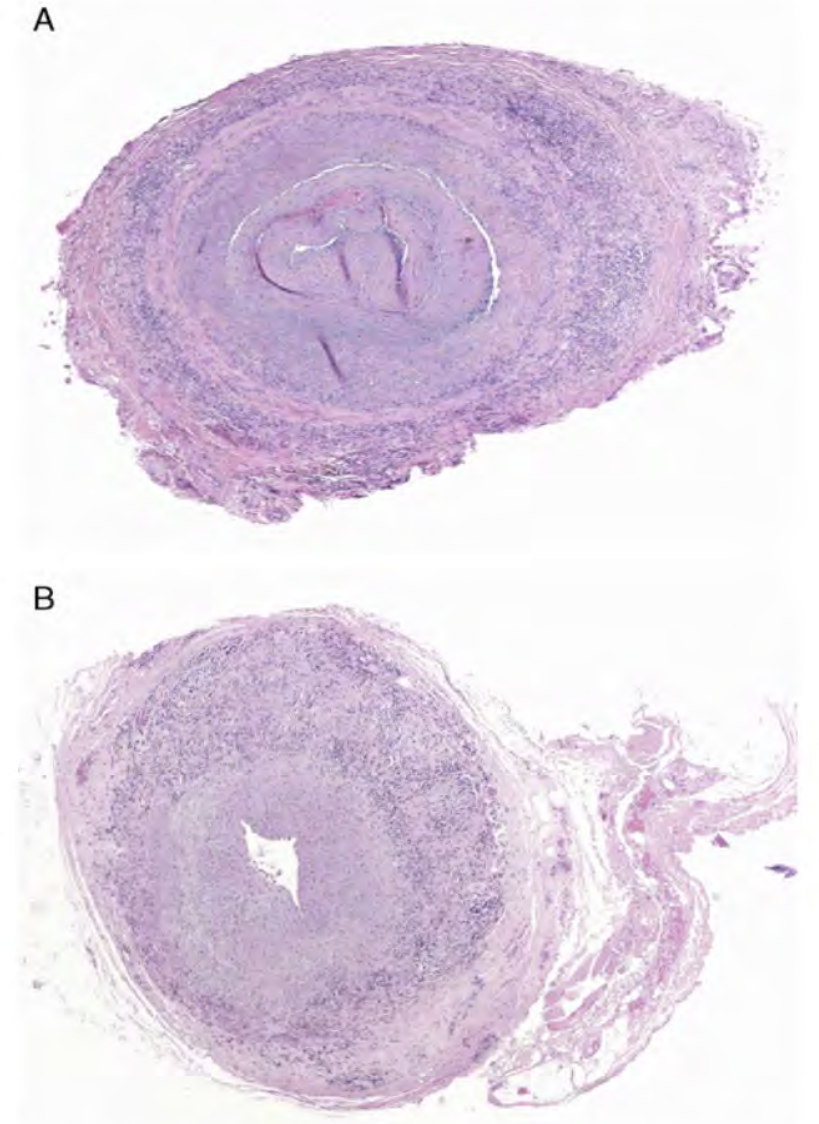
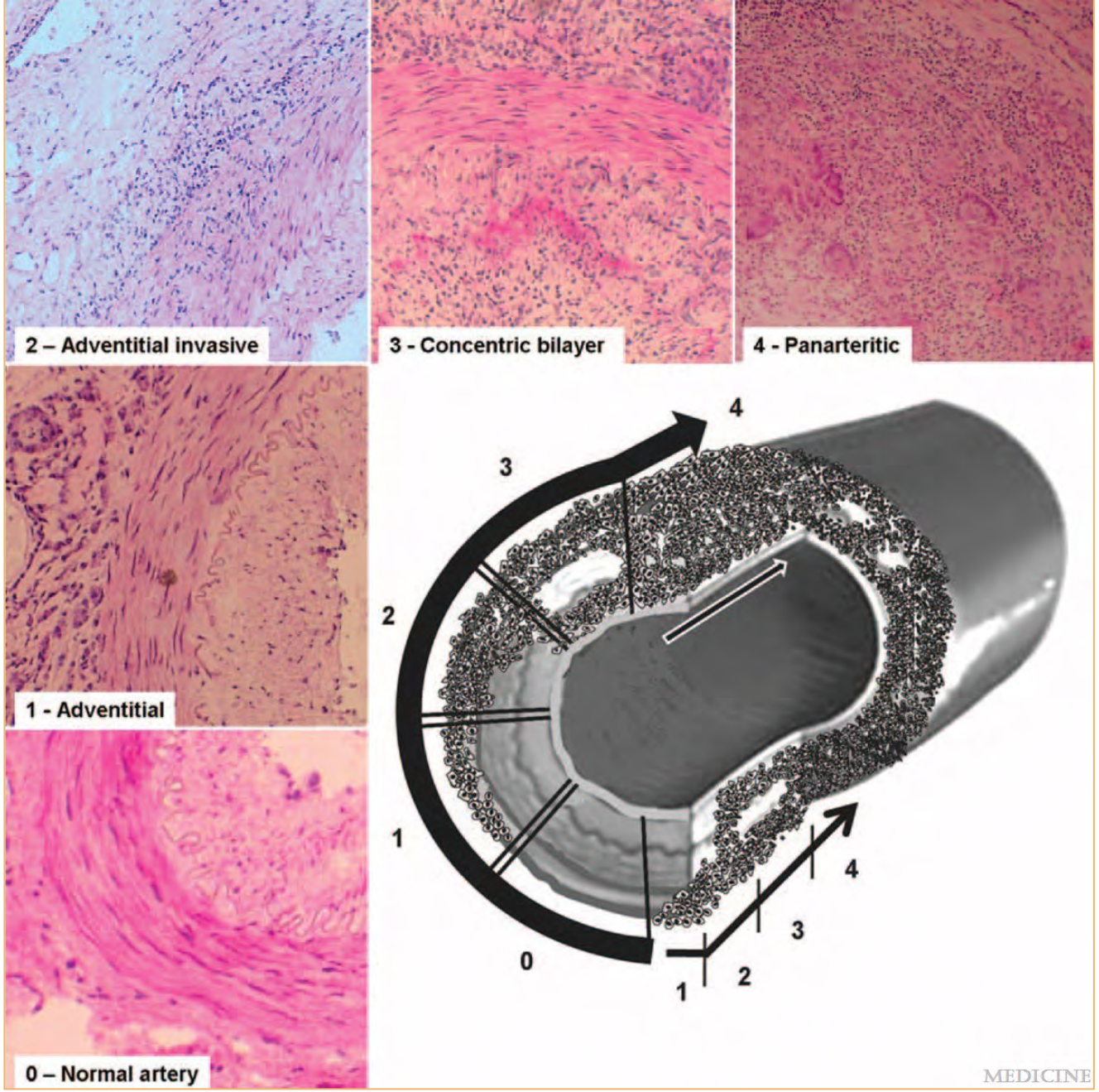


FIGURE 3. A, A classical example of TMI, with 2 concentric bands of inflammation, the thickest along the external elastic lamina and the thinner along the internal elastic lamina, with a relative sparing of the interposed media ("concentric rings" appearance). B, A more severely inflamed temporal artery, with inflammation extending to efface the media.



Description and Validation of Histological Patterns and Proposal of a Dynamic Model of Inflammatory Infiltration in Giant-cell Arteritis

Hernández-Rodríguez, José; Murgia, Giuseppe; Villar, Irama; Campo, Elías; Mackie, Sarah L.; Chakrabarty, Aruna; Hensor, Elizabeth M.A.; Morgan, Ann W.; Font, Carme; Prieto-González, Sergio; Espígol-Frigolé, Georgina; Grau, Josep M.; Cid, Maria C.

Medicine95(8):e2368, February 2016.
doi: 10.1097/MD.0000000000002368

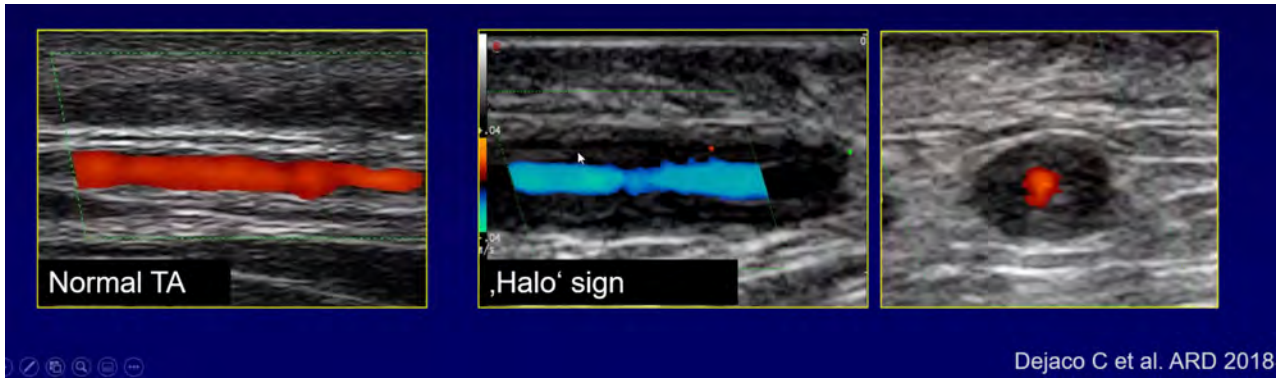
Hypothetical model of the sequential invasion of the artery by Inflammatory cells according to our histological findings.

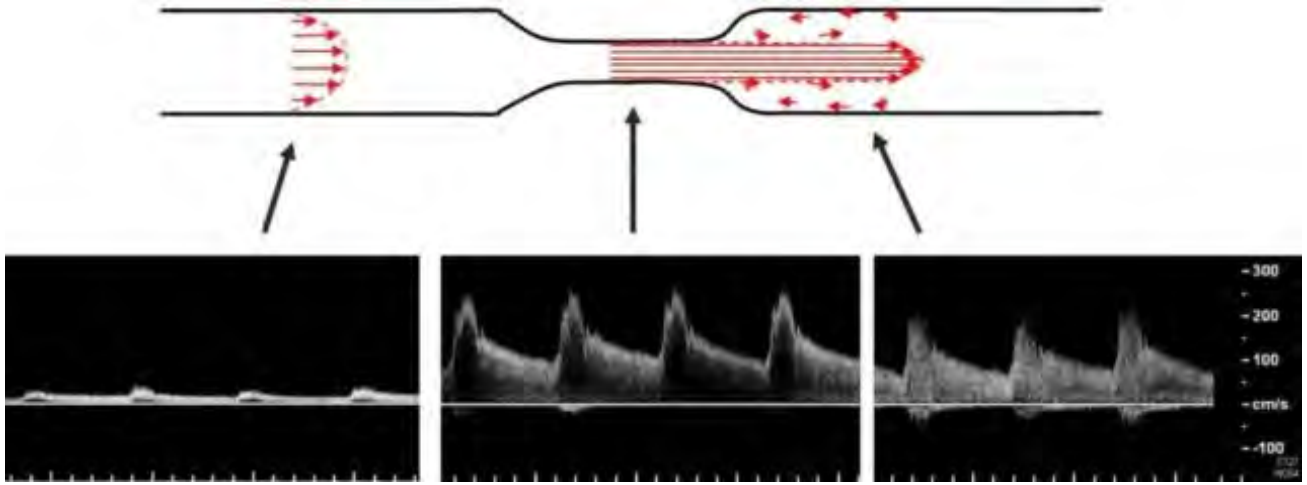
Imaging in GCA

	Ultrasound	MRI/MRA	CT	PET-CT
Clinical phenotypes				
cGCA	++	+	-	-
LV-GCA	+	++	++	++
PMR+ cGCA	++	+	-	+
PMR+LV-GCA	+	++	++	++

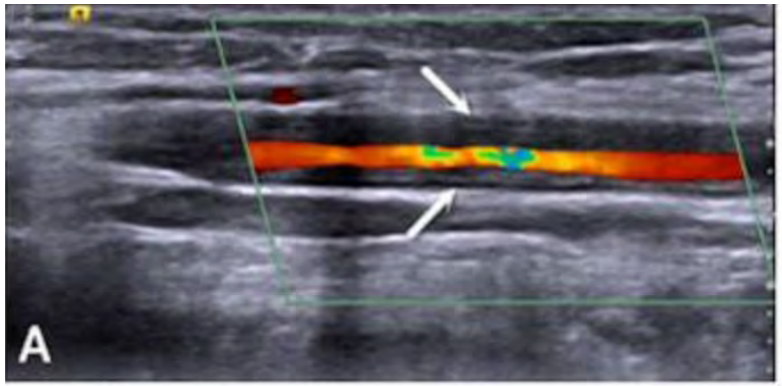
Stamatis P. Clinical and Epidemiological Studies on GCA. Lund University Dissertation Series 2021

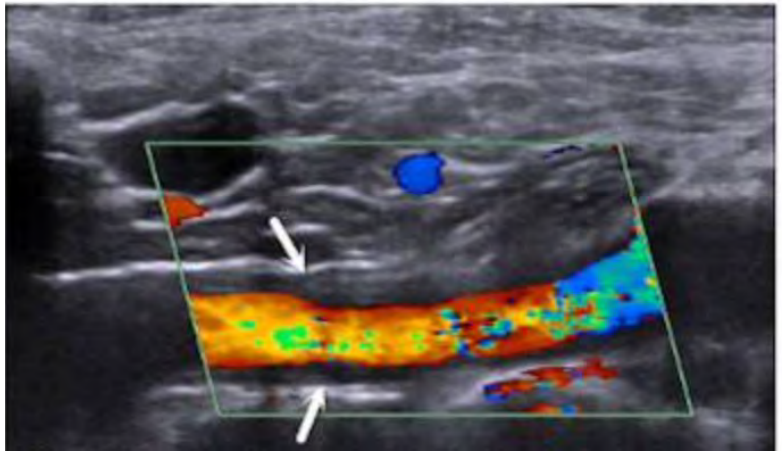
Imaging - Ultrasound

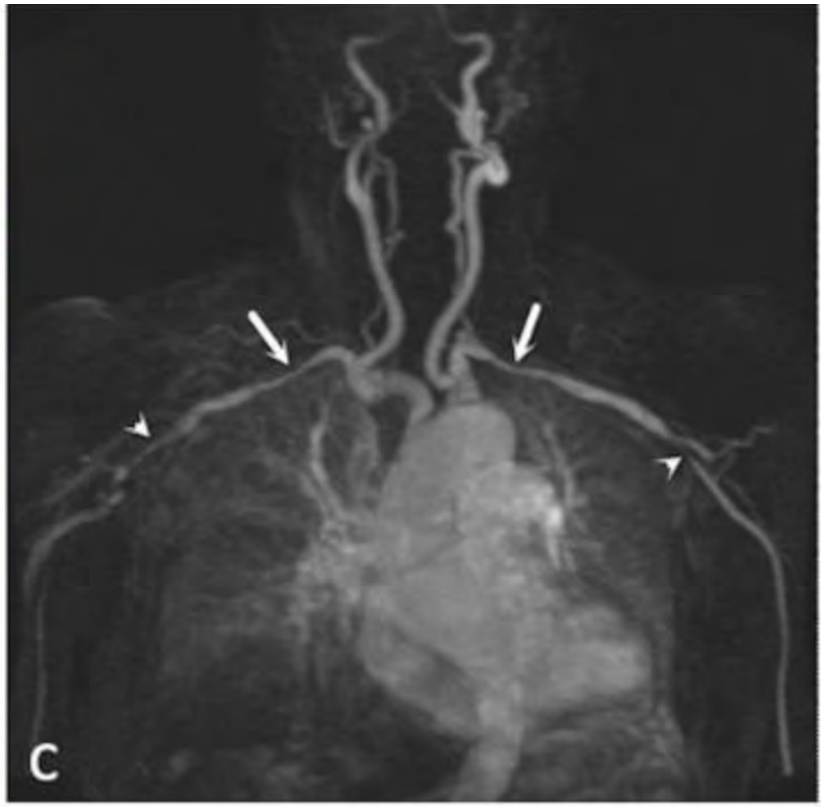




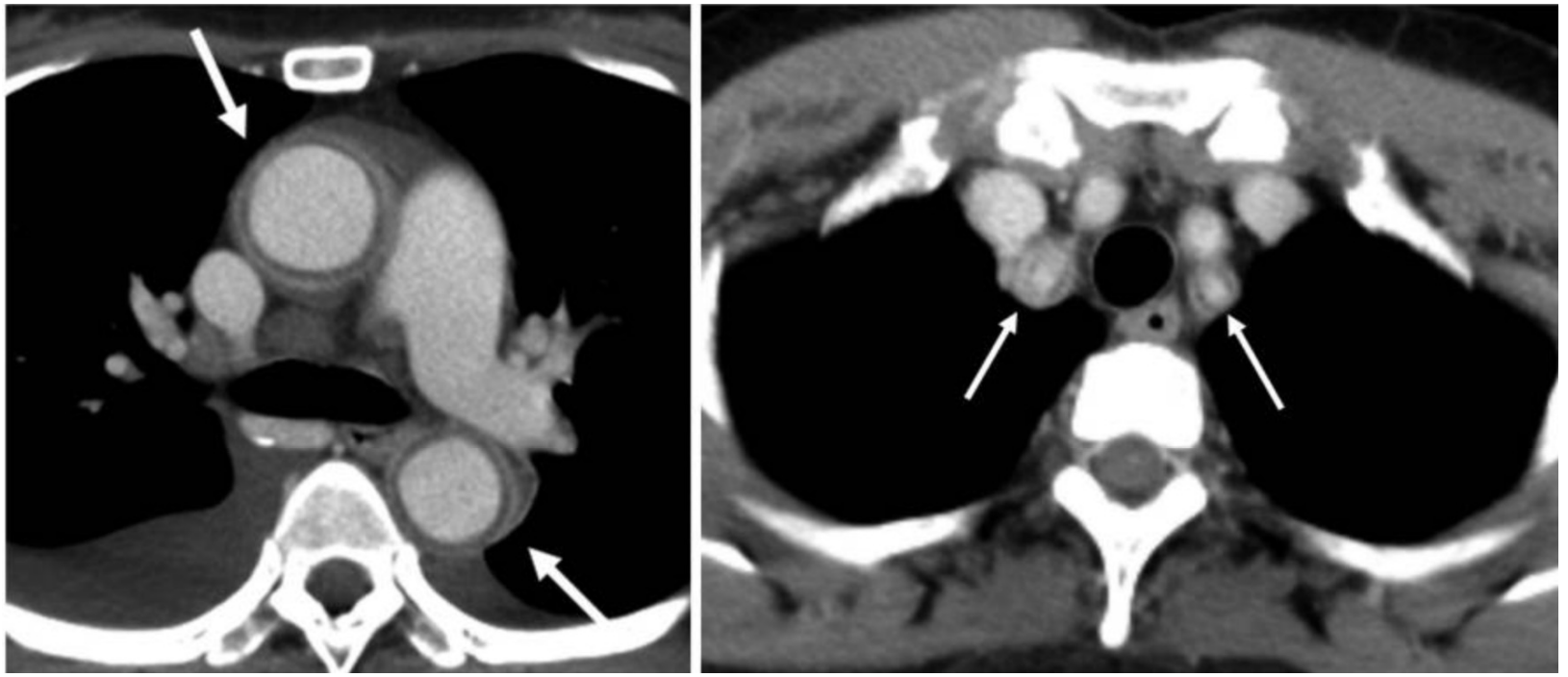
Imaging – Ultrasound/MRA

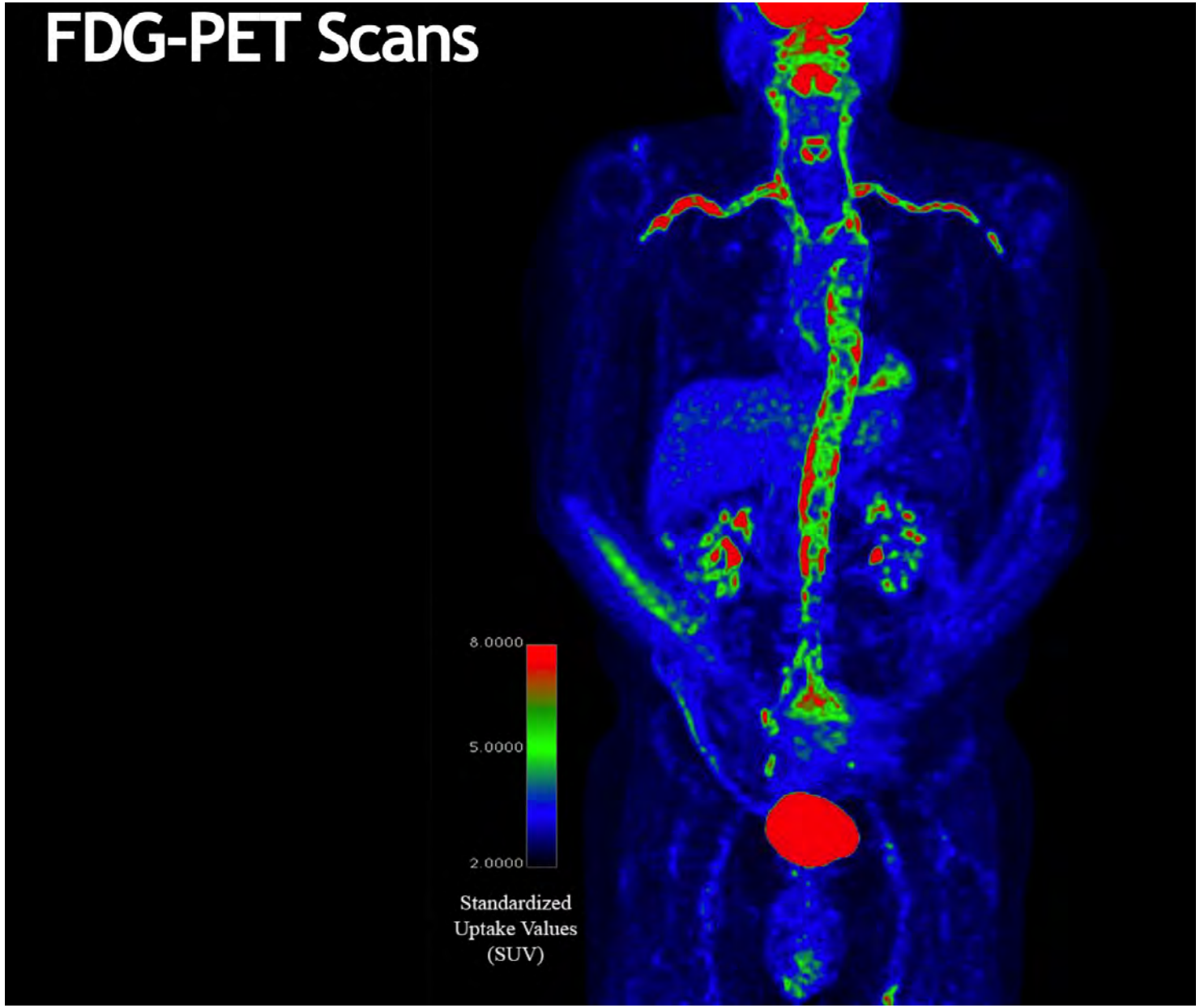






Imaging - CTA




FDG-PET Scans
8.0000
5.0000
2.0000
Standardized
Uptake Values
(SUV)

Diagnosis

- **TAB and imaging are complementary**
- Diagnostic approach center-dependent (access to high quality US? Expertise on CTA or MRA?)
- Modify your treatment approach based on the clinical phenotype
- If vasculitis is present on imaging and clinical symptoms suggest GCA a TAB is no longer required for the diagnosis

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2022 AMERICAN COLLEGE OF RHEUMATOLOGY / EULAR

CLASSIFICATION CRITERIA FOR **GIANT CELL ARTERITIS**

CONSIDERATIONS WHEN APPLYING THESE CRITERIA

- These classification criteria should be applied to classify the patient as having giant cell arteritis when a diagnosis of medium-vessel or large-vessel vasculitis has been made
- Alternate diagnoses mimicking vasculitis should be excluded prior to applying the criteria

ABSOLUTE REQUIREMENT

Age ≥ 50 years at time of diagnosis	

ADDITIONAL CLINICAL CRITERIA

Morning stiffness in shoulders/neck	+2
Sudden visual loss	+3
Jaw or tongue claudication	+2
New temporal headache	+2
Scalp tenderness	+2
Abnormal examination of the temporal artery[1]	+2

LABORATORY, IMAGING, AND BIOPSY CRITERIA

Maximum ESR ≥ 50 mm/hour or maximum CRP ≥ 10 mg/liter[2]	+3
Positive temporal artery biopsy or halo sign on temporal artery ultrasound[3]	+5
Bilateral axillary involvement[4]	+2
FDG-PET activity throughout aorta[5]	+2

Sum the scores for 10 items, if present. A score of ≥ 6 points is needed for the classification of GIANT CELL ARTERITIS.

1. Examination of the temporal artery showing absent or diminished pulse, tenderness, or hard 'cord-like' appearance.
2. Maximum erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) values prior to initiation of treatment for vasculitis.
3. Presence of either definitive vasculitis on temporal artery biopsy or halo sign on temporal artery ultrasound. There are no specific histopathologic criteria to define definitive vasculitis on temporal artery biopsy. Presence of giant cells, mononuclear leukocyte infiltration, and fragmentation of the internal elastic lamina were independently associated with histopathologic interpretation of definite vasculitis in the DCVAS cohort[24]. Halo sign is defined by the presence of an homogenous, hypoechoic wall thickening on ultrasound [25].
4. Bilateral axillary involvement is defined as luminal damage (stenosis, occlusion, or aneurysm) on angiography (computed tomography, magnetic resonance, or catheter-based) or ultrasound, halo sign on ultrasound, or fluorodeoxyglucose uptake on positron emission tomography.
5. Abnormal fluorodeoxyglucose (FDG) uptake in the arterial wall (e.g., greater than liver uptake by visual inspection) throughout the descending thoracic and abdominal aorta on positron emission tomography (PET).

BMJ Publishing Group Ltd and European League Against Rheumatism Ann Rheum Dis 2023;82:e52

ARD

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Medical Management GCA

Glucocorticoids

- **Without cranial ischemia:** high doses of steroids (40-60 mg) *
- **With visual symptoms:** IV pulse followed by high doses of steroids
- **Once disease is controlled:** tapering of GCs with target dose ≤5mg after 1 year

* ACR recommends doses up to 80mg

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GIACTA trial reduction schemes

Prednisone 26-Week Taper (n=200)							Prednisone 52-Week Taper (n=50)						
Taper week	**Dose, mg/day**	**5 mg**	**2.5 mg**	**1 mg**	**Placebo**		**Taper week**	**Dose, mg/day**	**5 mg**	**2.5 mg**	**1 mg**	**Placebo**
1	60	Open-label supplied by sponsor Patient starts at any of these incremental doses				Open-label	1	60	Open-label supplied by sponsor Patient starts at any of these incremental doses			
2	50						2	50				
3	40						3	40				
4	35						4	35				
5	30						5	30				
6	25						6	25				
7	20						7	20				
8	15	3			1	Blinded	8	17.5	3	1		
9	12.5	2	1		1		9	17.5	3	1		
10	12.5	2	1				10	15	3			
11	10	2			1		11	15	3			
12	9	1		4			12	12.5	2	1		2
13	8	1		3			13	10	2			2
14	7	1		2			14	10	2			1
15	6	1		1			15	10	2			
16	6	1		1			16	10	2			
17	5	1			4		17	9	1		4	
18	5	1			4		18	9	1		4	
19	4			4	1		19	9	1		4	
20	4			4	1		20	9	1		4	
21	3			3	1		21	8	1		3	
22	3			3	1		22	8	1		3	
23	2			2	2		23	8	1		3	
24	2			2	2		24	8	1		3	
25	1			1	2		25	7	1		2	
26	1			1	2		26	7	1		2	
27	0				3		27	7	1		2	
28	0				3		28	7	1		2	
29	0				2		29	6	1		1	
30	0				2		30	6	1		1	
31	0				2		31	6	1		1	
32	0				2		32	6	1		1	
33	0				1		33	5	1			
34	0				1		34	5	1			
35	0				1		35	5	1			
36	0				1		36	5	1			
37	0				4		37	4			4	
38	0				4		38	4			4	
39	0				4		39	4			4	
40	0				4		40	4			4	
41	0				3		41	3			3	
42	0				3		42	3			3	
43	0				3		43	3			3	
44	0				3		44	3			3	
45	0				2		45	2			2	
46	0				2		46	2			2	
47	0				2		47	2			2	
48	0				2		48	2			2	
49	0				1		49	1			1	
50	0				1		50	1			1	
51	0				1		51	1			1	
52	0				1		52	1			1	
53	0				1		53	0				1
54	0				1		54	0				1
55	0				1		55	0				1
56	0				1		56	0				1
57	0				1		57	0				1
58	0				1		58	0				1

Adjunctive therapy at the time of diagnosis

- **EULAR 2018:** *in high-risk patients for GC-related adverse events*
- **ACR 2021:** in almost all patients (conditional recommendation)

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Tocilizumab

- Based on GIACTA trial
- Open label 2-year extension phase
- Different recommendations in EULAR18 and ACR21 guidelines regarding the timing of initiation of treatment

Stone JH et al. N Engl J Med. 2017 Jul 27;377(4):317-328.
Stone JH et al. The Lancet Rheumatology. 2021;3(5):e328-e36.

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Methotrexate

- Metanalysis of 3 RCTs
- Effective in reducing relapse and cumulative GC-dose
- Low doses of MTX were used
- Pooled estimate of 161 individuals, 84 receiving MTX and 77 placebo

Mahr et al. Arthritis Rheum. 2007;56(8):2789-97

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Leflunomide

Efficacy of leflunomide in the treatment of vasculitis / N. Mustapha et al.

Table II. Response to treatment with leflunomide among patients with vasculitis.

	All patients	Type of vasculitis					
		GPA	MPA	EGPA	GCA	TAK	PAN
Number of patients (%)	93	45	8	12	14	9	5
Efficacy at 6 months	62 (67%)	31 (69%)	6 (75%)	4 (33%)	9 (64%)	8 (89%)	4 (80%)
Reason for treatment inefficacy							
Active disease	19 (20%)	7 (16%)	-	6 (50%)	4 (29%)	1 (1%)	1 (20%)
Adverse events	12 (13%)	7 (16%)	2 (25%)	2 (17%)	1 (7%)	0	0
Sustained remission at 12 months	54 (58%)	27 (63%)	6 (75%)	4 (33%)	7 (54%)	8 (89%)	3 (60%)
Sustained remission at 24 months	46 (50%)	23 (58%)	5 (71%)	4 (33%)	7 (54%)	7 (88%)	2 (40%)

Given percentages are for the proportion of patients in each type of vasculitis with available data, which was incomplete at 12 and/or 24 months for 7 individuals (2 lost to follow-up after 12 months [MPA and TAK]; 4 had not yet reached 12 and/or 24 months with LEF [3 GPA and 1 GCA]; one with GPA died of natural causes before 24 months of LEF).

EGPA: eosinophilic granulomatosis with polyangiitis; GCA: giant cell arteritis; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; PAN: polyarteritis nodosa; TAK: Takayasu's arteritis.

Mustapha N et al. Clin Exp Rheumatol. 2021 Mar-Apr;39 Suppl 129(2):114-118

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TNFα - inhibitors

- No place in the treatment of GCA
- **3 negative trials** (Infliximab, Etanercept and Adalimumab)

Seror et al. Ann Rheum Dis 2014;73:2074–81.
Martinéz-Taboada VM et al. Ann Rheum Dis 2008;67:625–30.
Hoffman GS *et al.* *Ann Int Med* 2007;146:621–30.

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Abatacept

- Can also be considered if MTX and TCZ are not effective or in patients unable to tolerate these agents

Langford CA et al. Arthritis Rheumatol. 2017 Apr;69(4):837-845

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Mavrilimumab

- **Human monoclonal antibody that inhibits the human granulocyte macrophage – colony stimulating factor (GM-CSF) receptor**
- Positive phase two **26 weeks** trial
- No safety issues
- **Superior to prednisolone alone arm** regarding time to relapse and sustained remission
- Longer treatment is needed to determine response durability and quantify GC-sparing effect

Cid MC et al. Ann Rheum Dis. 2022 May;81(5):653-661.

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Summary of ongoing trials in GCA

Trial name	Population	Intervention	Comparator	Primary outcome
METOGIA	Active GCA (new or relapse)	Tocilizumab for 12 months	Methotrexate for 12 months	Relapse or Prednisolone deviation at 3 years
MAGICA	GCA in remission	Gradual taper of Tocilizumab	Abrupt discontinuation Tocilizumab	Relapse free survival at 26 weeks
GigAINt	New GCA with cranial symptoms or PMR	Secukinumab	Placebo	Time to relapse
GCAptAIN	Active GCA (new or relapse)	Secukinumab	Placebo	Sustained remission at week 52
SELECT-GCA	Active GCA (new or relapse)	Upadacitinib (Dose A or B) + 26-week GC taper	Placebo + 52-week GC taper	Sustained remission at week 52
ABAGART	Active GCA (new or relapse)	Abatacept	Placebo	Sustained remission at week 52
THEIA	Active GCA (new or relapse)	Guselkumab	Placebo	Sustained GC-free remission at week 28

Mortality

- In total, no increased risk for mortality compared to the reference population
- Increased mortality found the first 2 years after the diagnosis mainly due to CV events

Hill CL et al. Semin Arthritis Rheum.2017;46(4):513-9
Mohammad AJ et al. Ann Rheum Dis.2015;74(6):993-7

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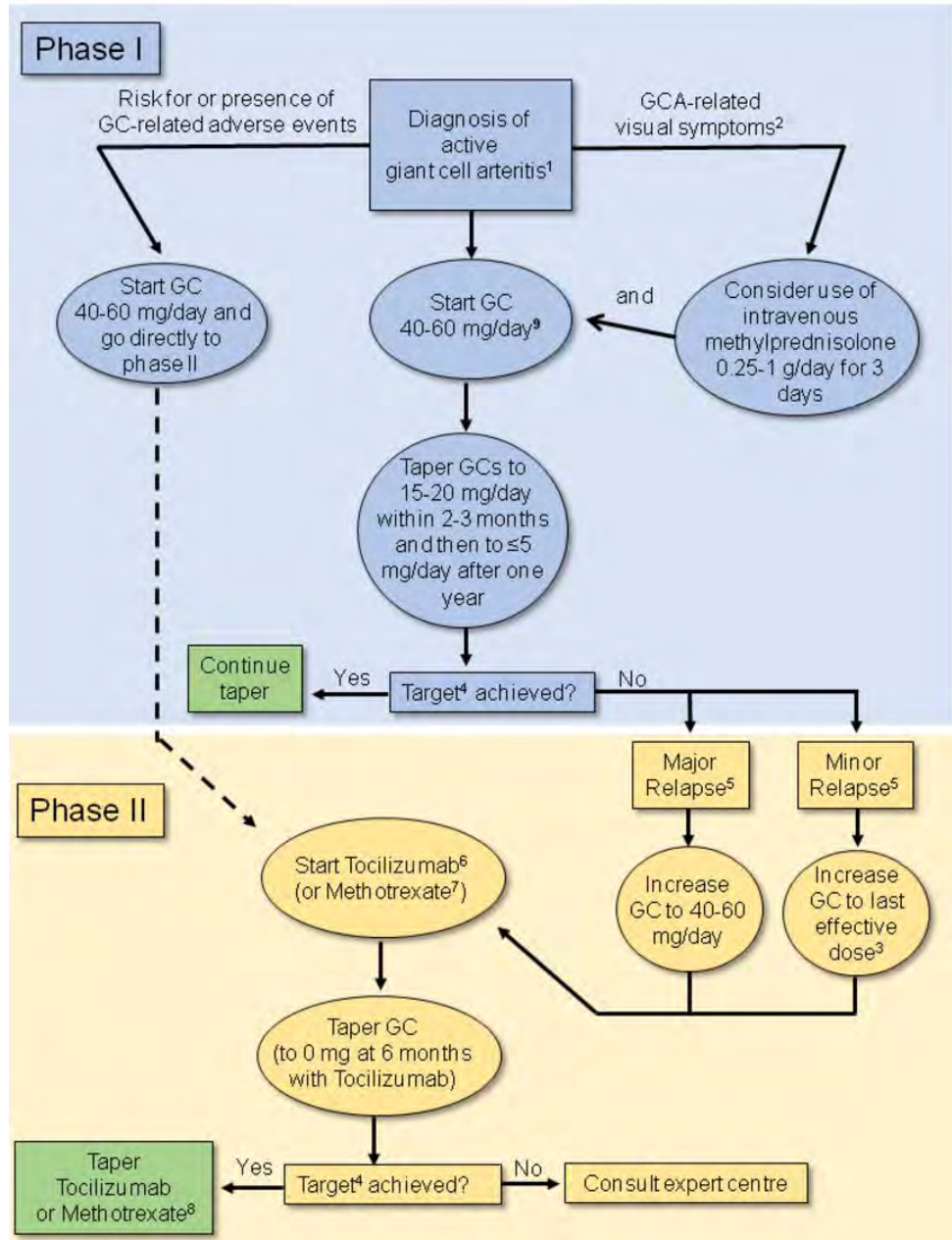
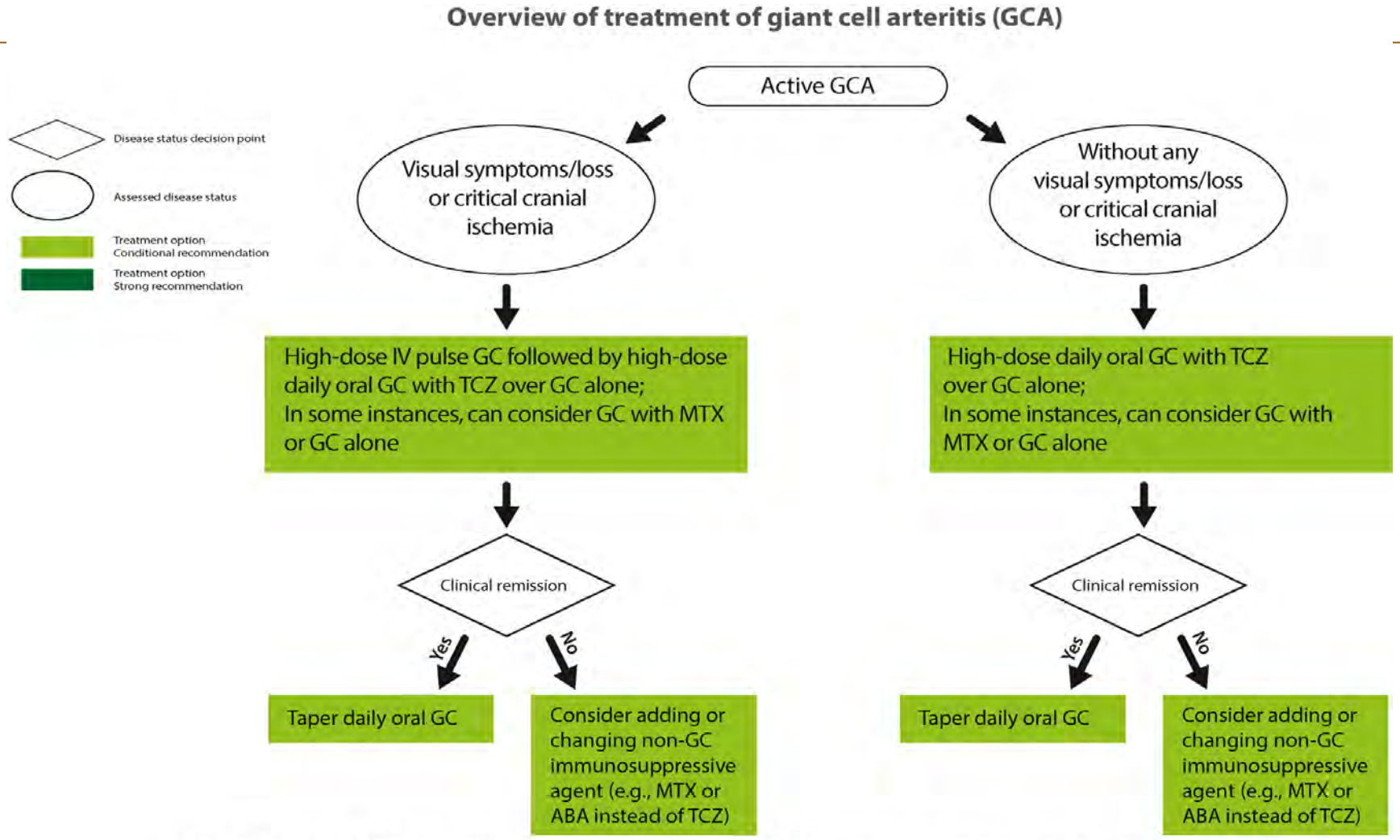
2018 EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF GIANT CELL ARTERITIS



ACR 2021 Guidelines for GCA



ABA = abatacept, AZA = azathioprine, GC = glucocorticoids, IV = intravenous, MTX = methotrexate, TCZ = tocilizumab

Arthritis & Rheumatology, Volume: 73, Issue: 8, Pages: 1349-1365, First published: 08 July 2021, DOI: (10.1002/art.41774)

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