NEWS, VIEWS AND THE STEROID BLUES: VASCULITIS 2021

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OBJECTIVE

Review new data regarding disease pathogenesis, clinical manifestations, treatment and outcomes in systemic vasculitis

DISCLOSURES

Advisory board, Genentech

Advisory board, Chemocentryx

UNMET NEEDS IN SYSTEMIC VASCULITIS

- Accurate assessment of subclinical disease activity
- Reliable predictors of disease flare
- Data-driven guidelines for surveillance
- Dependence on glucocorticoid therapy for both induction and maintenance
- Identification of at-risk population for infection, cancer, CVD and appropriate screening and interventions
- Personalized medicine

IMPACT OF UNMET NEEDS

- Patients are overtreated, and at increased risk of complications
- Patients are undertreated, with increased flares and disease damage
- Infection and cardiovascular disease remain major source of morbidity and mortality
- Patient and physician stress from insecurity about disease status


LOW
MODERATE
FRUSTRATION
HIGH

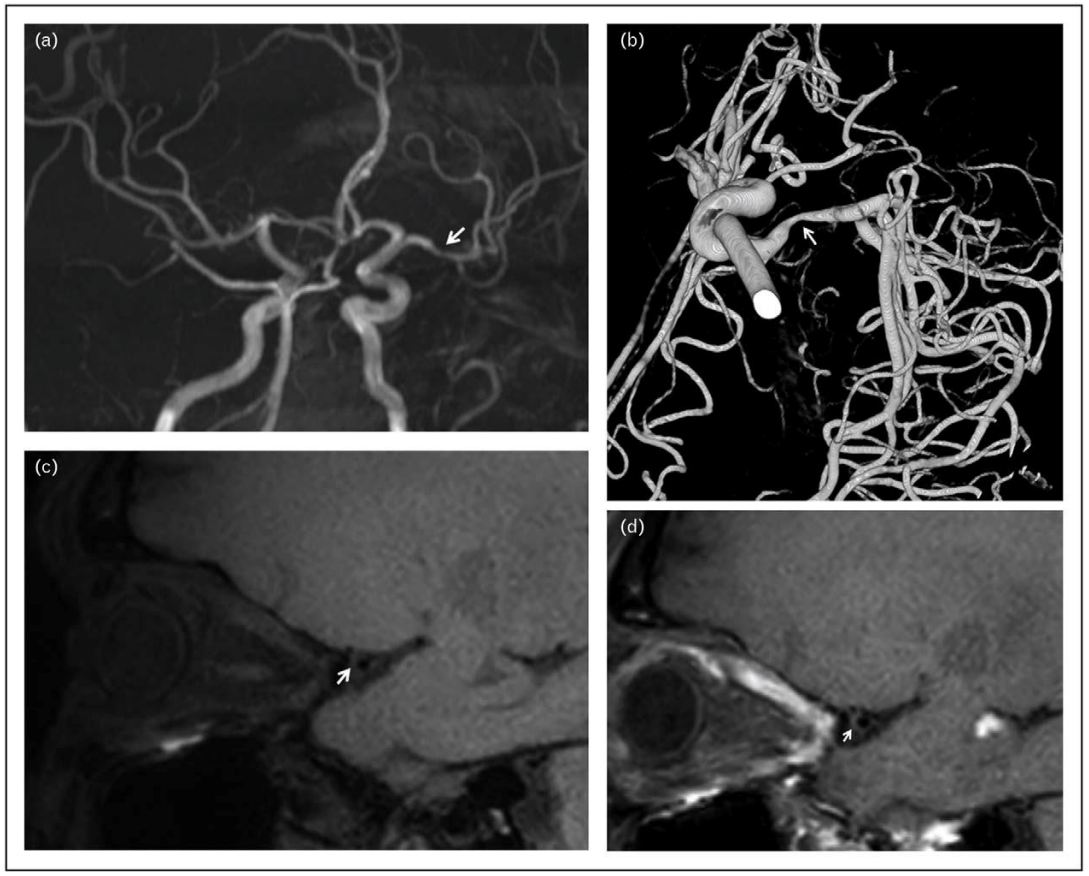
NEWS

INTRACRANIAL VESSEL WALL IMAGING

- Diagnosis of vasculitis involving CNS remains difficult
- Brain biopsy reveals alternative diagnosis in ~1/3 of patients with angiographic diagnosis
- Better way to fine tune less invasive diagnostic tool?
- Vessel wall imaging MRI based tool
- Specific MRI magnet strength and channels required
- 3 dimensional sequences used
- VISTA (Philips), CUBE (GE), SPACE (Siemens)

Arslan S *et al.*, Curr Opin Rheum, 2021

DIAGNOSTIC FEATURES



- Wall enhancement
- Eccentric vs. concentric wall changes
- Lesion pattern
- Location

Arslan S *et al.*, Curr Opin Rheum, 2021

Table 1. Vessel wall imaging features of intracranial diseases

Disease	Lesion pattern	Location	Vessel wall thickening pattern	Wall enhancement
CNS vasculitis	Asymmetric narrowings and dilatations	Multifocal areas, distal ICA and vertebral arteries	Concentric wall thickening	Almost always present
Giant cell arteritis	Asymmetric narrowings and dilatations	Multifocal areas, extracranial and intracranial arteries	Concentric wall thickening	Often present
Intracranial atherosclerosis	Multiple eccentric, focal wall thickening and remodeling	Multifocal areas, distal ICA and vertebral arteries	Eccentric wall thickening	Present or not present
After thrombectomy	Wall thickening	Thrombectomised segment	Eccentric or concentric wall thickening	Often present
Arterial dissection	Aneurysmal dilatation, intimal flap, intramural hematoma	Distal ICA and vertebral arteries	Eccentric wall thickening	Often present
Reversible cerebral vasoconstriction syndrome	Smooth wall thickening and segmental narrowing	Widespread	Concentric wall thickening	Often not present
Moyamoya disease	Marked narrowing, puff of smoke appearance	Distal ICA and proximal MCA	Concentric wall thickening	Present or not present
Intracranial aneurysm	Depends on the type of aneurysm	–	–	Presence of enhancement is associated with risk of rupture

CNS, central nervous system; ICA, internal carotid artery; MCA, middle cerebral artery.

Arslan S *et al*, Curr Opin Rheum, 2021

INTRACRANIAL VESSEL WALL IMAGING

- Increases accuracy of diagnosis of cerebral vasculitis from 8.3% to 95%
- Can be used to identify area for biopsy
- Identification of enhancing atherosclerotic plaque identifies patient at risk for recurrent stroke
- Can be used to evaluate treatment response in CNS vasculitis

Arslan S *et al.*, Curr Opin Rheum, 2021

AORTIC EVENTS IN GCA

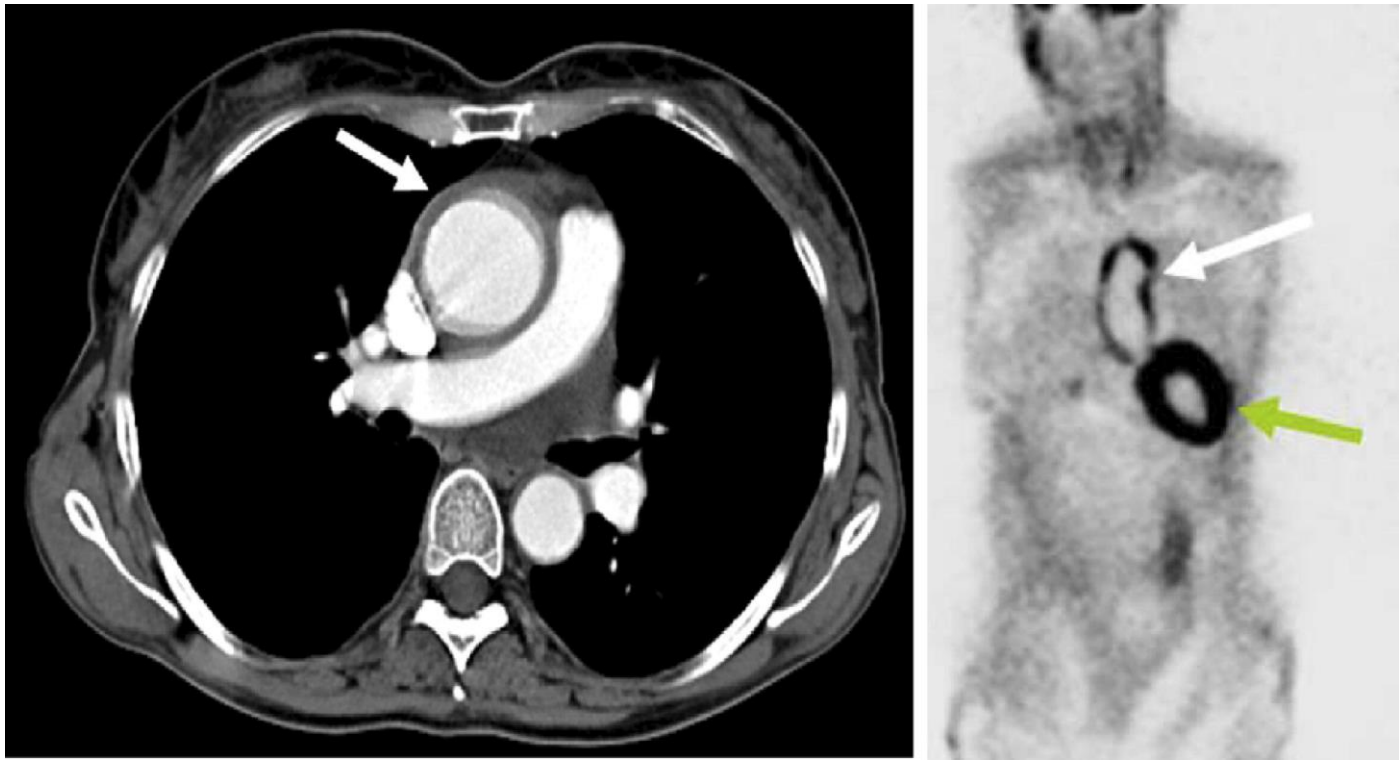
- Present at diagnosis in GCA patients in 40-60% of cases
- Aortic involvement often not part of routine surveillance
- Complications can occur early on or later in disease course
- Study objective was to evaluate clinical presentation of GCA and aortitis outcomes
- 171 patients with GCA and aortitis from 5 medical centers in France
- 55 patients with symptomatic aortitis: chest, back or abdominal pain, or previously unknown aortic insufficiency associated with dyspnea

Espitia *et al.*, Arthritis Res Therapy, 2021

AORTIC EVENTS IN GCA

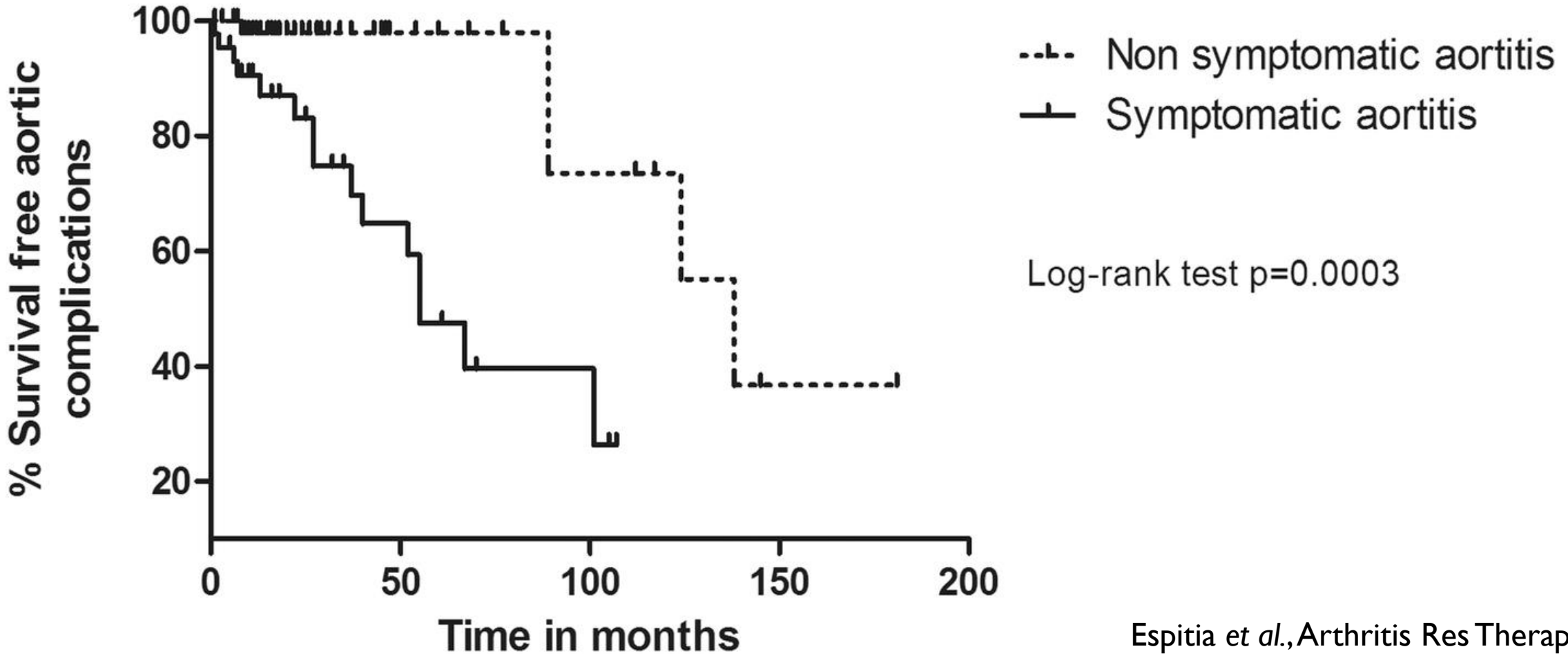
Symptomatic aortitis patients more likely to have:

- Jaw pain or claudication
- Fatigue/malaise
- Aneurysm/dissection/thickening
- Hypertension
- Active or recent tobacco use
- IV steroids at diagnosis



Espitia *et al.*, Arthritis Res Therapy, 2021
Janssen *et al.*, J Vasc Surg, 2008

SURVIVAL WITHOUT AORTIC COMPLICATIONS



Espitia *et al.*, Arthritis Res Therapy, 2021

PREDICTORS OF AORTIC EVENTS

- Symptomatic aortitis (HR 6.64)
- GCA relapse (HR 3.62)
- Events:
  - 15 new aneurysms
  - 4 known aneurysms requiring surgery due to increase
  - 4 dissections

Espitia *et al.*, Arthritis Res Therapy, 2021

VZV AND GCA

- GCA long suspected to be infectious associated inflammatory disease of medium and large arteries
- Recent studies have implicated VZV infection, with conflicting data
- Challenges have included VZV antigen choice, number of sections, skip lesion nature of this disorder
- Comprehensive evaluation of temporal arteries on 38 AION patients (14 with GCA)
- Biopsies completely sectioned, with avg of 146 serial sections reviewed and stained for VZV glycoprotein E
- Confirmatory staining for VZV IE63 protein + PCR if staining positive

Verdijik *et al.*, JID, 2021

FINDINGS

- 4 cases, 2 with GCA had positive VZV-glycoprotein E
- None confirmed by VZV IE63 or PCR
- Other findings frequently associated with false positive findings identified in these biopsies
- Does not support acute infection as cause

- Post-infectious phenomenon?

Verdijik *et al.*, JID, 2021

STROKE IN ANCA-ASSOCIATED VASCULITIS

- Purpose: incidence rate, predictors, and outcomes of stroke
- 325 patients with controls matched by age, gender, and years of stroke diagnosis
- 1997-2016
- 6% of patients suffered stroke during follow up period
- Incidence of stroke highest in the first year after vasculitis diagnosis
- Patients diagnosed under the age of 65 had a 3.2 fold increase in stroke risk compared to background population

Tabakovic *et al.*, Arthritis Rheum, 2020

Table 2 Predictors of stroke in patients with ANCA associated vasculitis using Cox-regression analysis

	Univariate analysis		*Multivariate analysis*	
Predictors	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**
Age at AAV diagnosis*	1.31 (0.94-1.81)	0.10	1.42 (0.97-2.08)	0.06
Sex, male	1.18 (0.49-2.86)	0.70	0.80 (0.31-2.06)	0.64
MPO-ANCA	1.35 (0.56-3.24)	0.50	0.52 (0.06-4.26)	0.54
PR3-ANCA	0.76 (0.31-1.89)	0.56	1.08 (0.12-9.26)	0.94
Platelet count**	1.05 (1.00-1.11)	0.04	1.06 (1.01-1.12)	0.01
MucMembeyes	2.84 (0.95-8.54)	0.06	3.14 (0.95-10.30)	0.06

*: age increased by 10 years, **: platelets increased by 20, PR3: Proteinase-3, MPO: Myeloperoxidase, ANCA: Antineutrophil cytoplasmic antibody, HR: Hazard ratio, Mucmembeyes: Mucocutaneous/eyes involvement. Hazard-ratios were calculated by using Cox-regression analysis. P-value of <0.05 was regarded as statistically significant.

Tabakovic *et al.*, Arthritis Rheum, 2020

LEFLUNOMIDE FOR VASCULITIS

- Retrospective analysis of treated patients in the VCRC and CanVasc
- 93 total patients
  - 45 GPA, 8 MPA, 12 eGPA
  - 14 GCA
  - 9 TAK
  - 5 PAN
- Main reason for use: active disease
- Mean duration of treatment: 2.3 ± 2.3 years

Mustapha *et al.*, Clin Exp Rheum, 2021

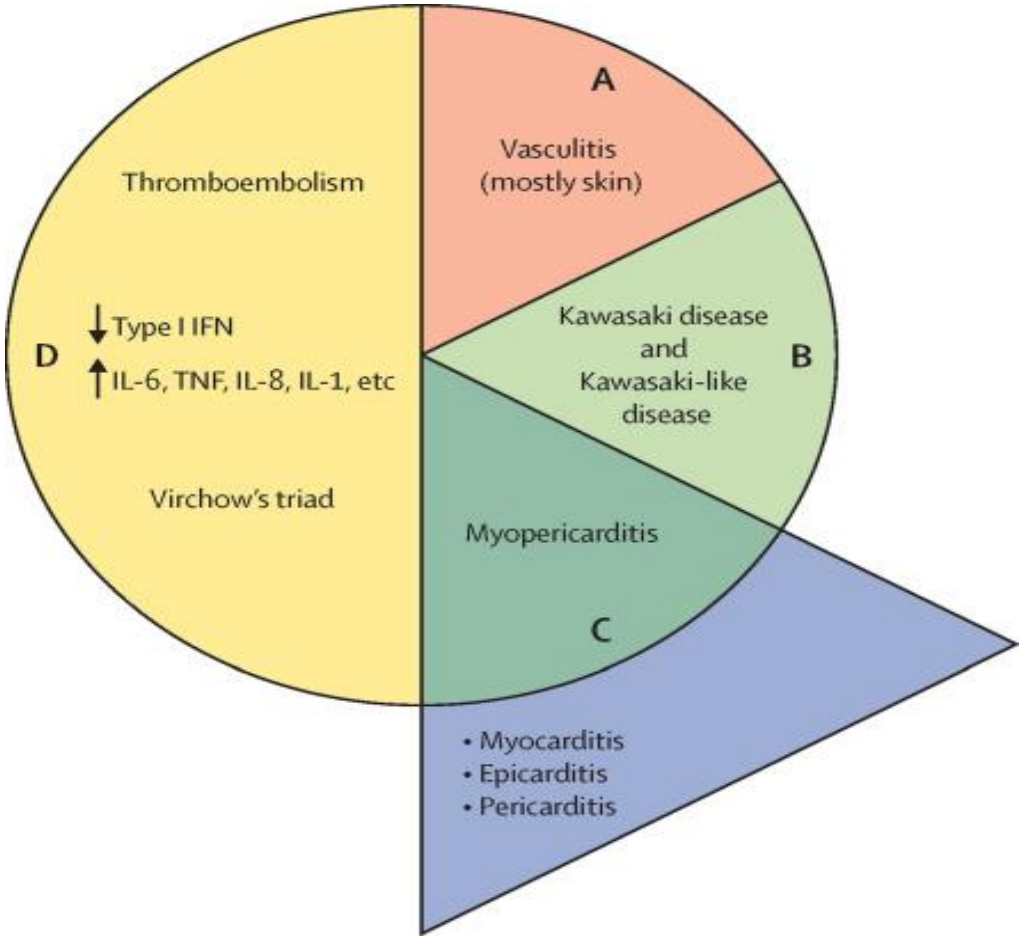
LEFLUNOMIDE FOR VASCULITIS: SUMMARY

- About 2/3 of vasculitis patients had treatment response (BVAS 0)
- Remission maintained at 24 months in 50% of cohort
- 9 GPA patients were able to maintain remission following severe relapse
- Poorest response in eGPA (asthma)
- 50% of GCA patients had no relapse at 12 months of therapy
- No unanticipated adverse effects
- 19% discontinued due to side effects

Mustapha *et al.*, Clin Exp Rheum, 2021

COVID-19 AND VASCULITIS

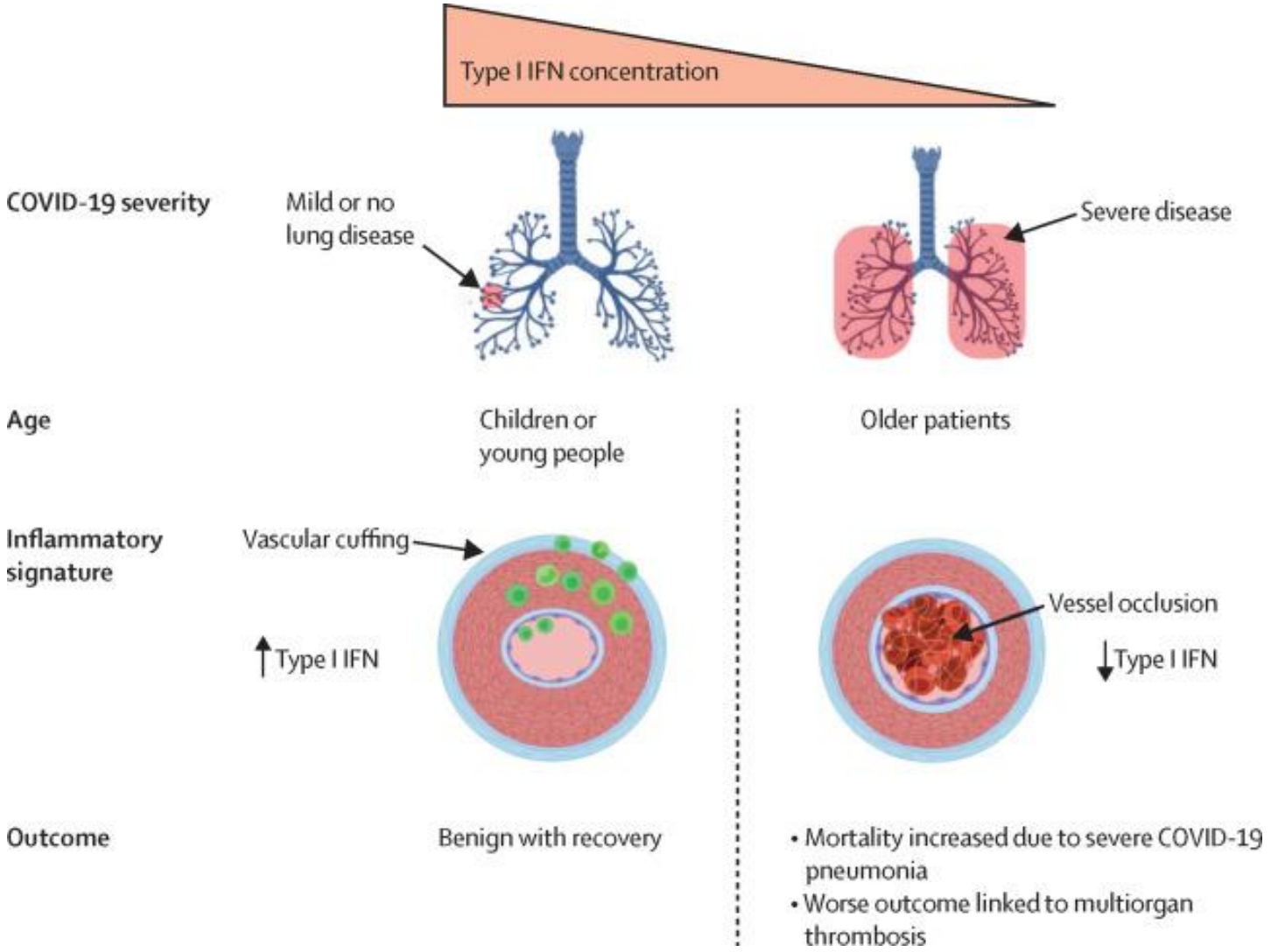
- Vascular disease in COVID-19 infection clearly linked to morbidity and mortality
- Both vascular thrombosis and vasculitis pathologically demonstrated
- Infectious, immune mediated, or vasculitis mimic?



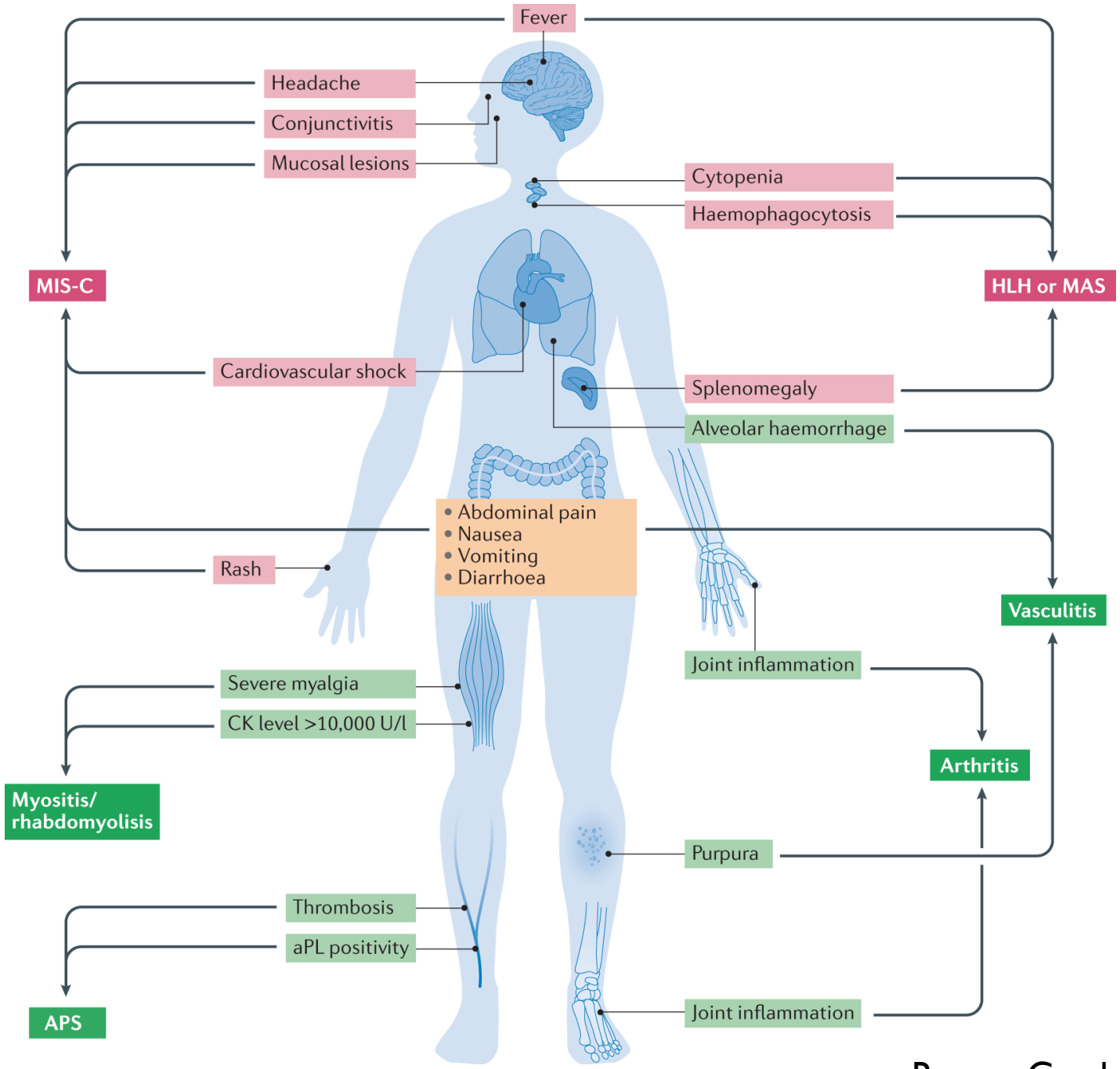
McGonagle *et al.*, Lancet Rheum, 2021

COVID-19 AND VASCULITIS

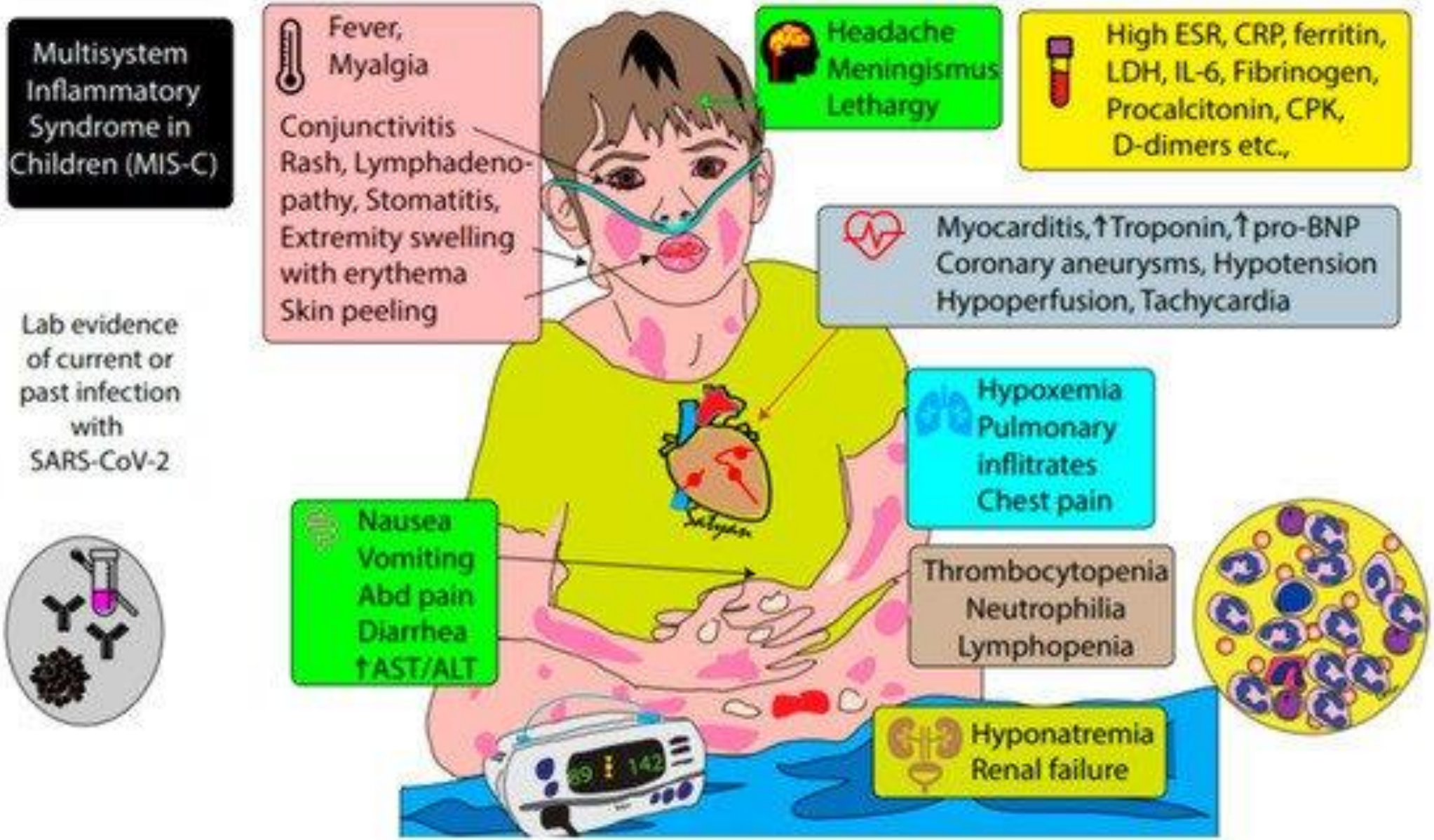
- Subsets based on age/severity
- Reversible inflammatory disease with better prognosis
- Severe disease with inflammation, tissue destruction, thrombosis
- Poor initial IFN response followed by overproduction of cytokines (storm)



McGonagle *et al.*, Lancet Rheum, 2021

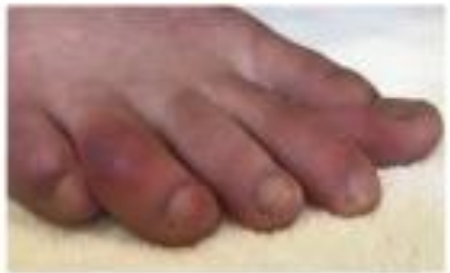


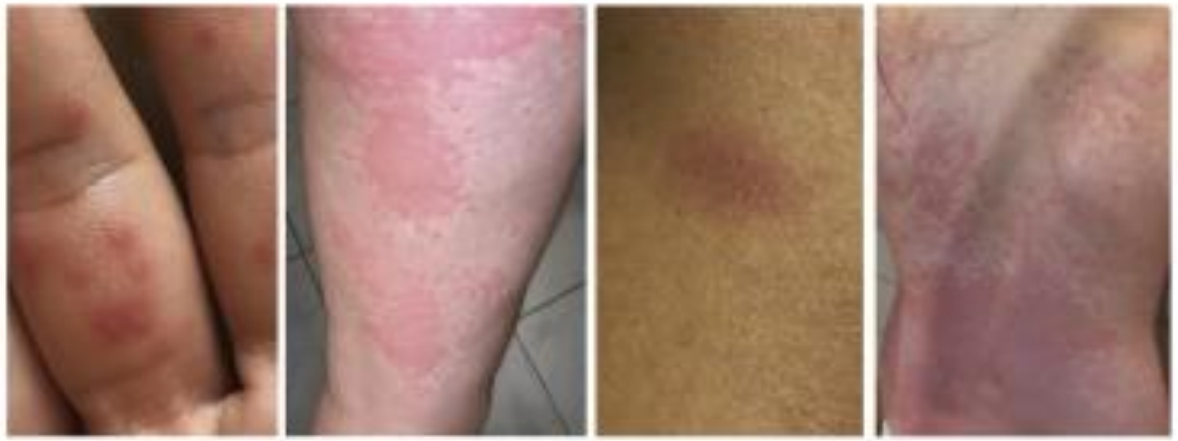
Ramos-Casalos *et al.*, Nat Rev Rheum, 2021

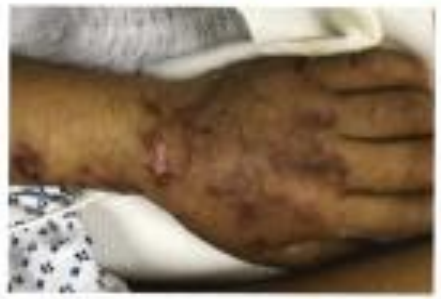


Nakra *et al.*, Children, 2020

Severity of COVID-19*







Pernio

- Feet (84%) and hands (32%)
- Pain/burning (71%) and pruritus (36%)
- After other COVID-19 symptoms (49%)
- Fever (35%), cough (35%);19% asymptomatic
- 16% hospitalized

Vesicular/ Urticarial/ Macular Erythema/ Morbilliform

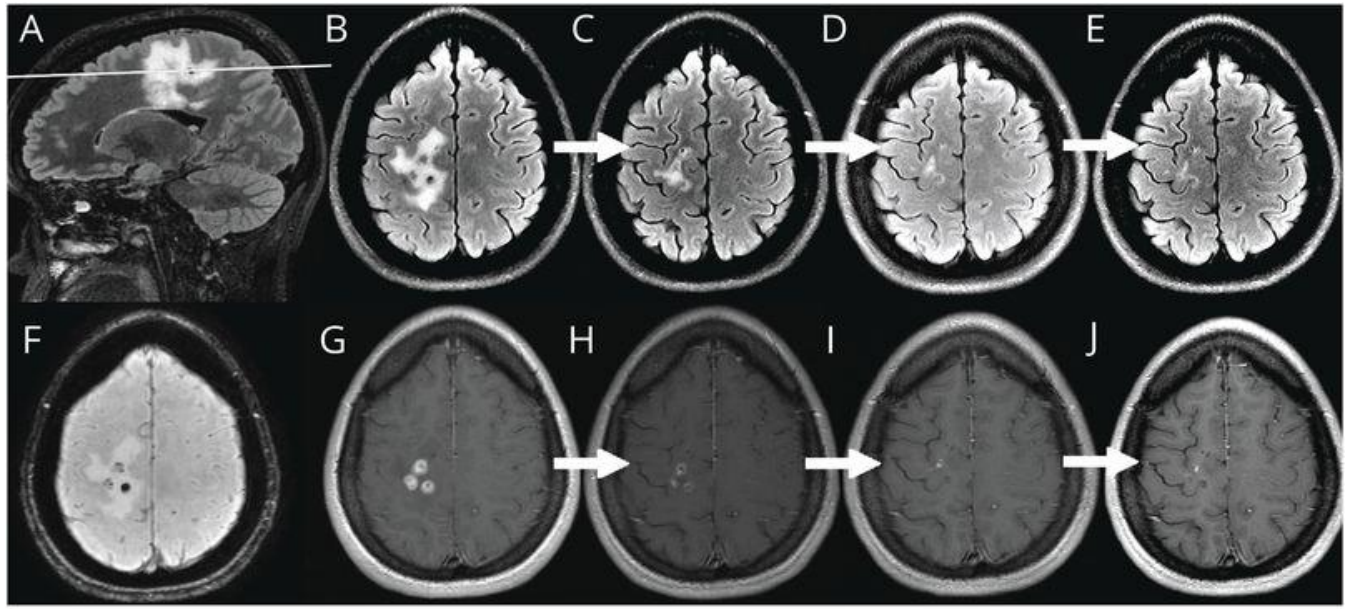
- Trunk and extremities
- Pruritus in 61-74%
- Typically after other COVID-19 symptoms (19%)
- Fever (65-74%), cough (52-66%), sore throat (39-50%), shortness of breath (28-45%)
- 22-45% hospitalized across groups

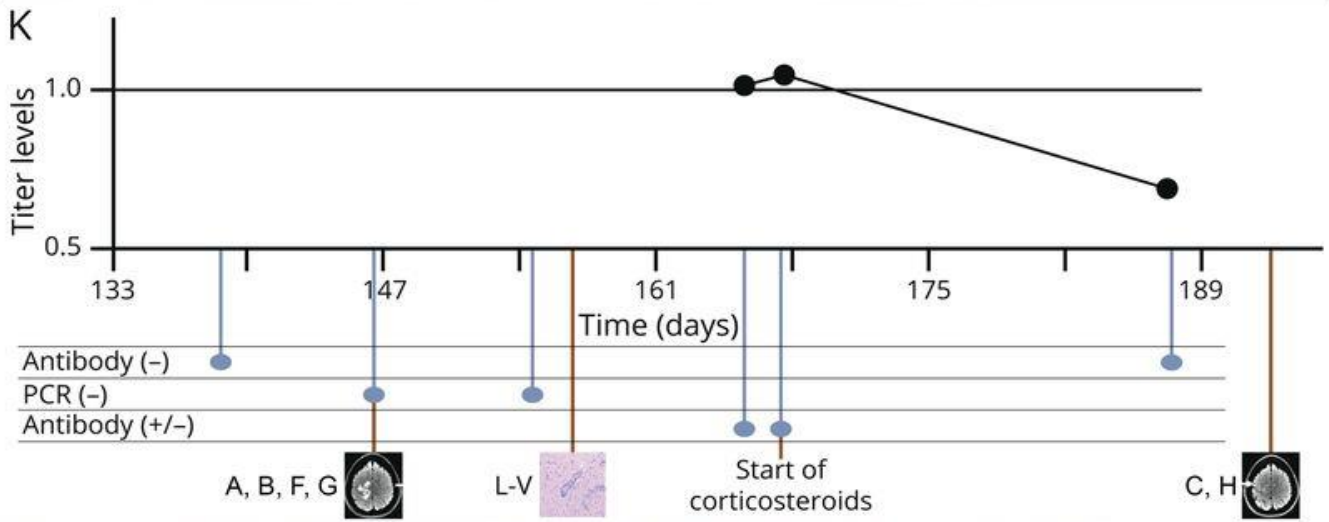
Retiform purpura

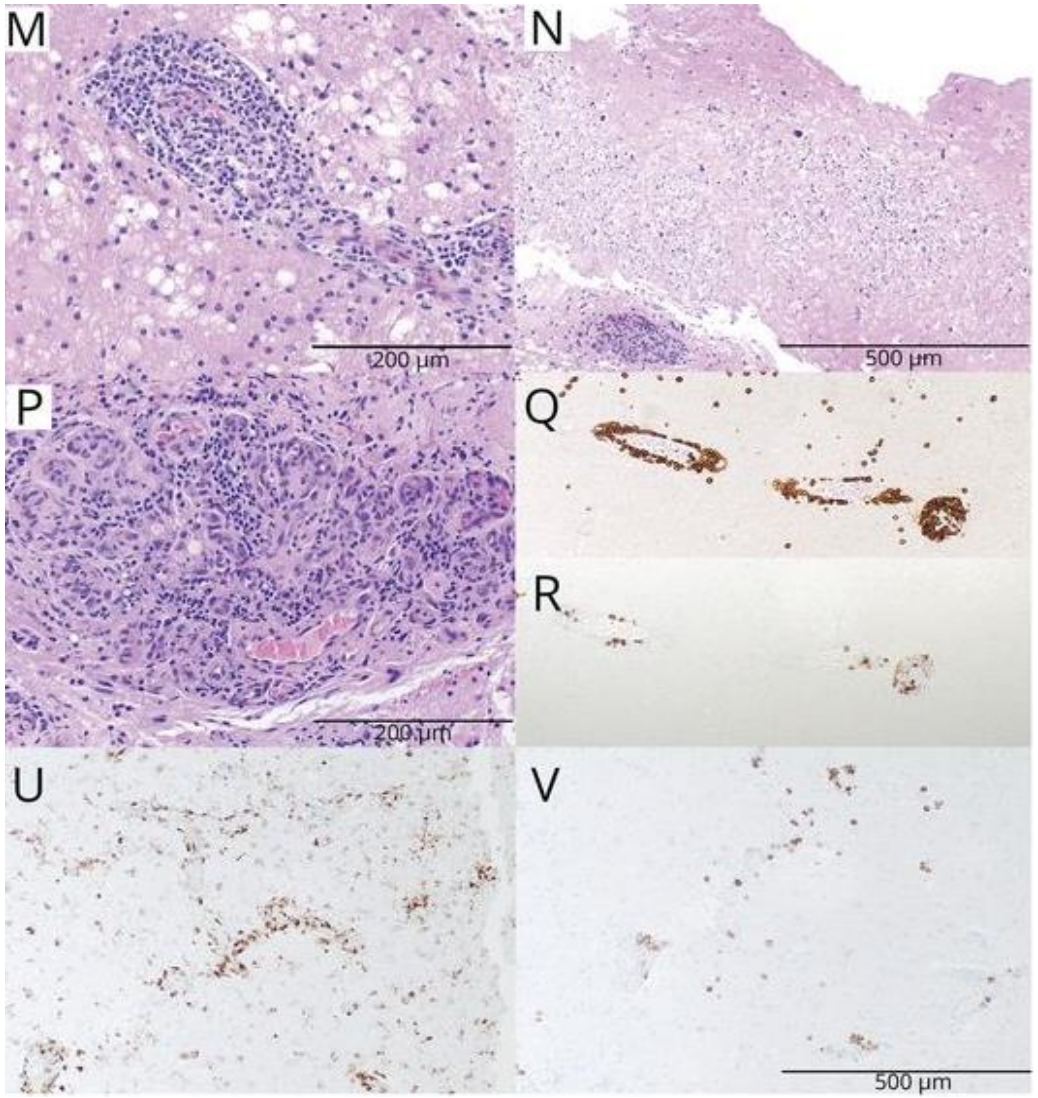
- Extremities and buttocks
- Often asymptomatic (73%)
- After other COVID -19 symptoms (91%)
- Fever (64%), cough (73%), and shortness of breath (73%)
- 100% hospitalized
- 82% with ARDS

*Severity calculated based on percentage of patients hospitalized for COVID-19

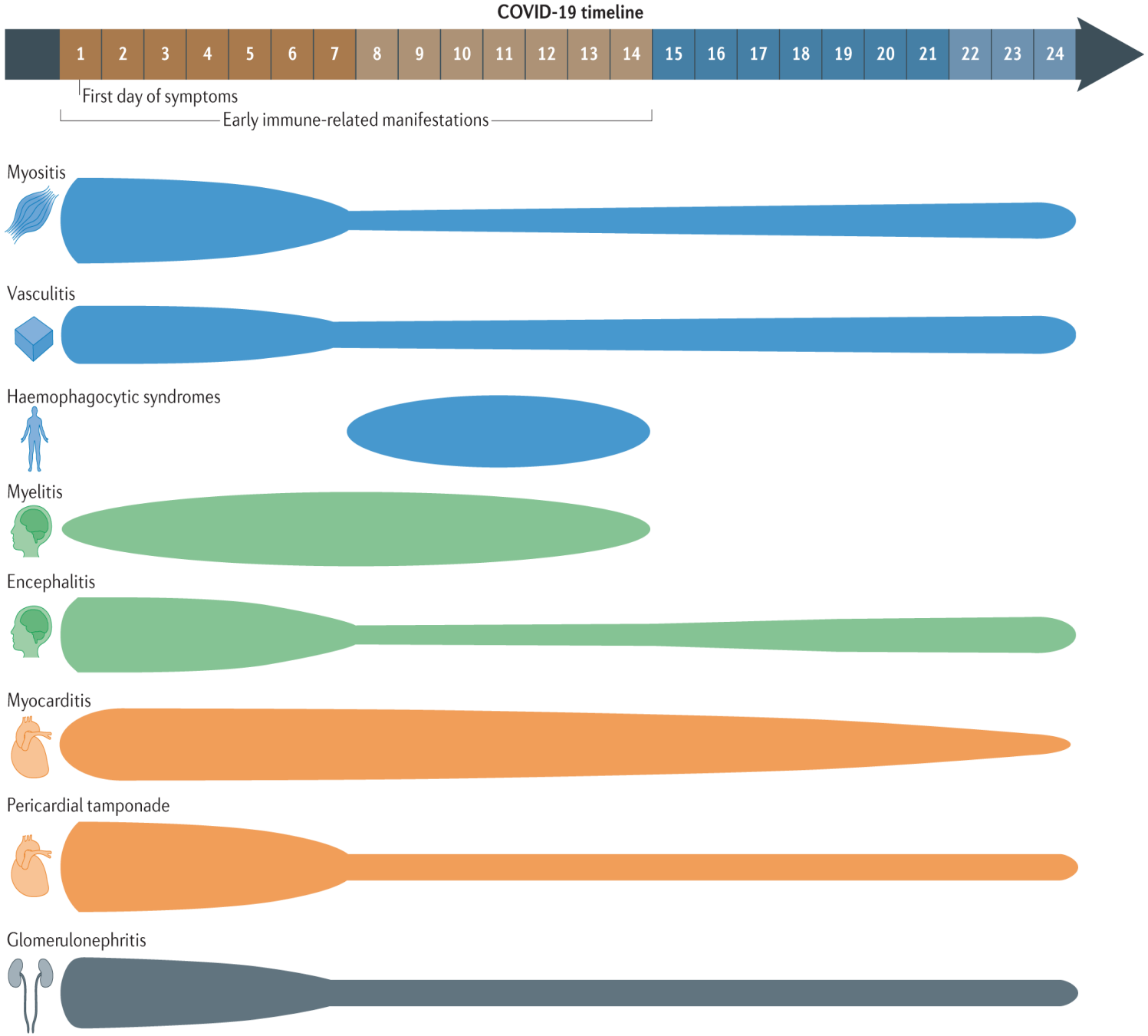
Freeman *et al.*, JAAD, 2020



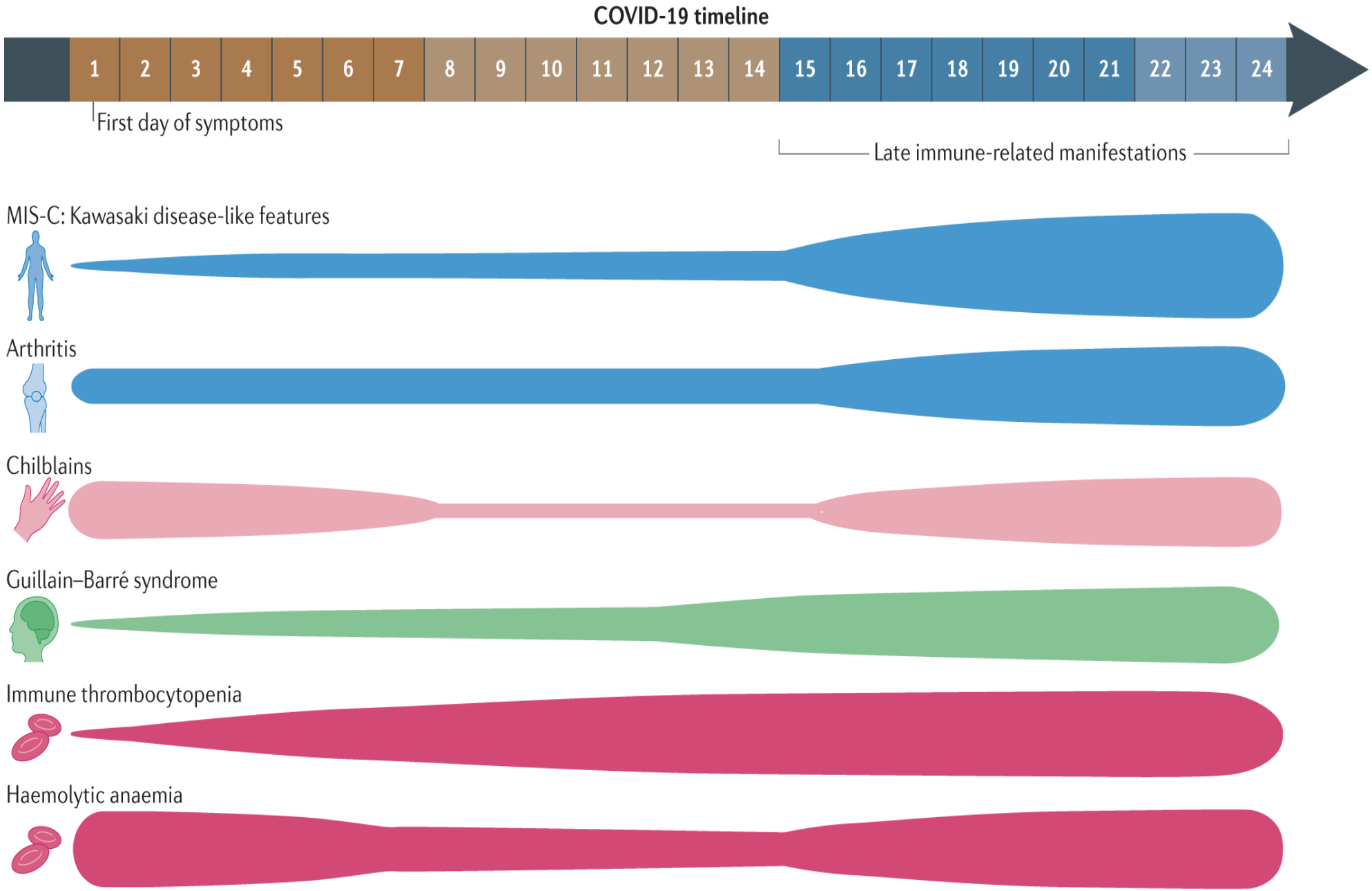




Garrett *et al.*, Neurol Neuroimmunol Neuroinflamm, 2021



Ramos-Casalos *et al.*, Nat Rev Rheum, 2021

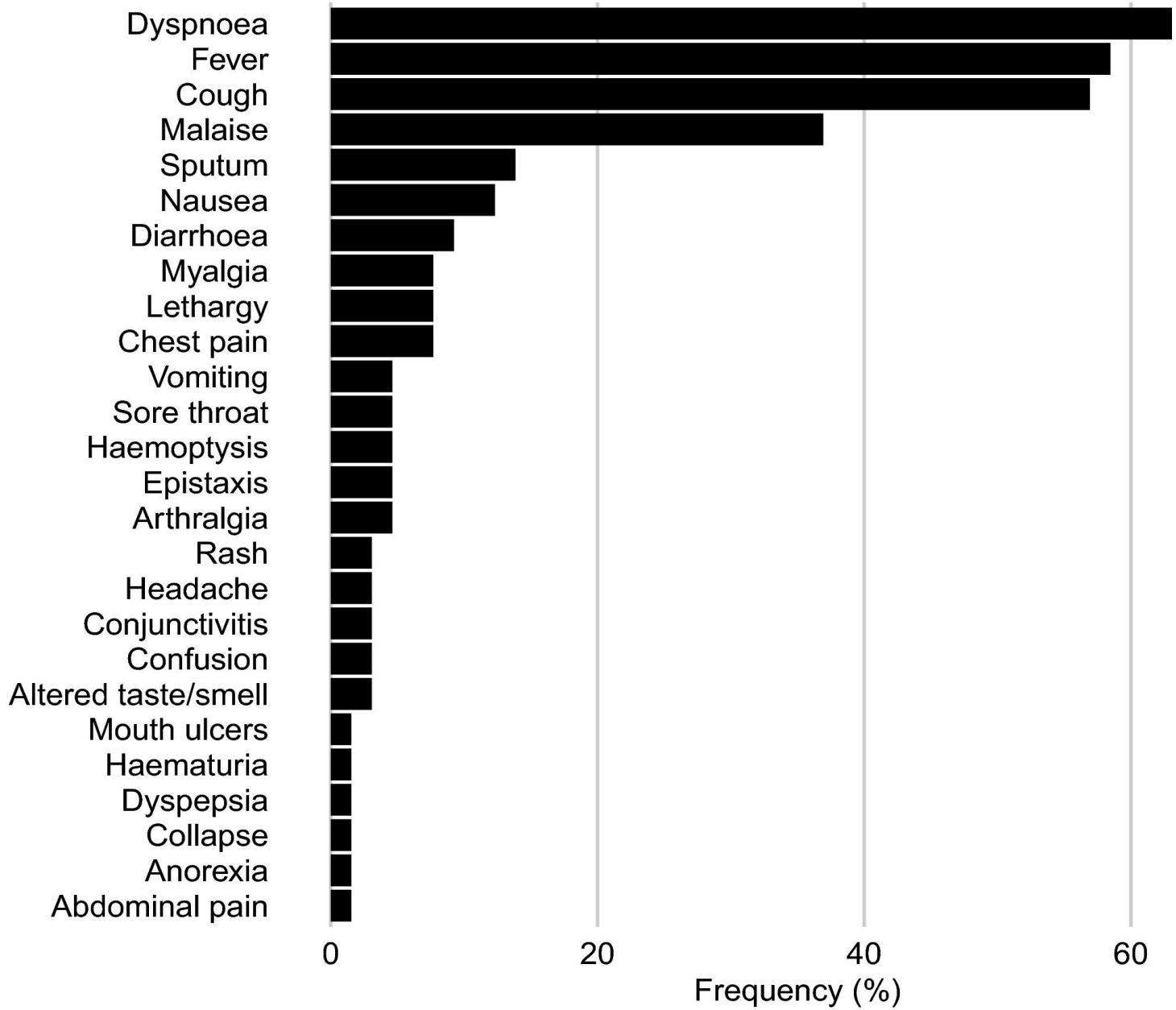


Ramos-Casalos *et al.*, Nat Rev Rheum, 2021

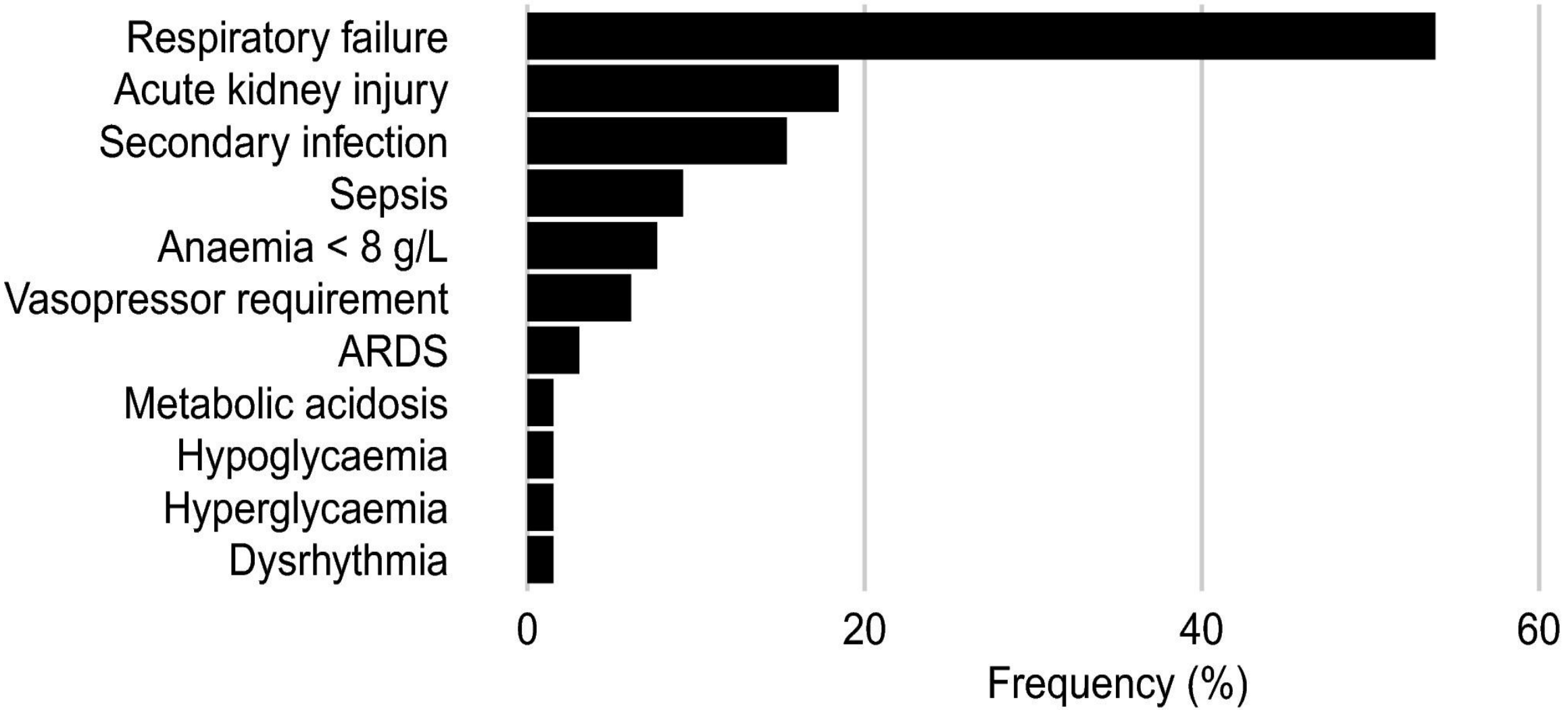
RISK FACTORS FOR SEVERE COVID-19 IN VASCULITIS

- Multicenter cohort (Ireland, UK)
- 65 patients, 85% ANCA vasculitis
- Median age 70; 49% women
- 91% required hospitalization
- 11% ICU
- 28% deaths

Rutherford *et al.*, Arthritis Rheum, 2021



Rutherford *et al.*, Arthritis Rheum, 2021



Rutherford *et al.,* Arthritis Rheum, 2021

Table 3. Unadjusted and adjusted ORs for potential risk factors and association with severe outcomes*

	No. of severe outcomes/ no. of cases (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Female	13/26 (50)	1.04 (0.51–2.10)	1.05 (0.52–2.13)
Age	–	1.01 (0.98–1.05)	1.01 (0.98–1.05)
Vasculitis diagnosis			
GPA (referent: not GPA)	12/24 (50)	1.71 (0.62–4.81)	2.19 (0.68–7.63)
MPA (referent: not MPA)	7/25 (28)	0.53 (0.17–1.52)	0.43 (0.13–1.36)
Comorbidities (referent: individual comorbidity not present)			
Hypertension	12/25 (48)	1.46 (0.71–3.04)	1.39 (0.64–3.04)
CVD	8/17 (47)	1.32 (0.59–2.93)	1.08 (0.52–2.23)
Respiratory disease	10/13 (77)	7.50 (1.99–36.94)	7.53 (1.93–38.22)†
Diabetes	6/13 (46)	1.25 (0.51–2.99)	1.20 (0.48–2.92)
Renal disease	12/30 (40)	1.00 (0.49–2.03)	1.05 (0.52–2.14)
End-stage kidney disease	6/17 (35)	0.85 (0.25–2.65)	0.77 (0.22–2.48)
Smoking status			
Ever smoker (referent: never)	9/18 (50)	2.25 (0.65–8.05)	2.33 (0.62–9.28)
Immunosuppressive therapy			
Any immunosuppressive therapy (referent: not receiving immunosuppressive therapy)	24/55 (44)	3.10 (0.70–21.79)	3.66 (0.77–27.29)
GCs (referent: no prednisone)			
Prednisone (any dose)	22/45 (49)	3.35 (1.02–13.2)	3.66 (1.09–14.9)‡
Prednisone 1.0–5.0 mg/day	10/19 (53)	3.89 (0.98–17.93)	3.76 (0.91–18.02)
Prednisone ≥5.1 mg/day	12/26 (46)	3.00 (0.82–12.86)	3.32 (0.86–15.35)
Other immunosuppressive therapy			
Azathioprine (referent: not receiving azathioprine)	6/12 (50)	1.65 (0.46–5.97)	1.57 (0.42–5.85)
CYC (referent: not receiving CYC)	5/10 (50)	1.62 (0.41–6.48)	1.83 (0.44–7.76)
Rituximab (referent: not receiving rituximab)	9/22 (41)	1.06 (0.36–3.01)	1.25 (0.40–3.90)

Rutherford *et al.*, Arthritis Rheum, 2021

SUMMARY

- Underlying respiratory disease and baseline steroid use associated with severe outcomes of COVID-19
- Other risk factors noted in general population not correlated
- Disease duration, disease activity, other immunosuppressive agents did not show significant associations
- Small, sick cohort may not be generalizable to all

Rutherford *et al.*, Arthritis Rheum, 2021

VIEWS

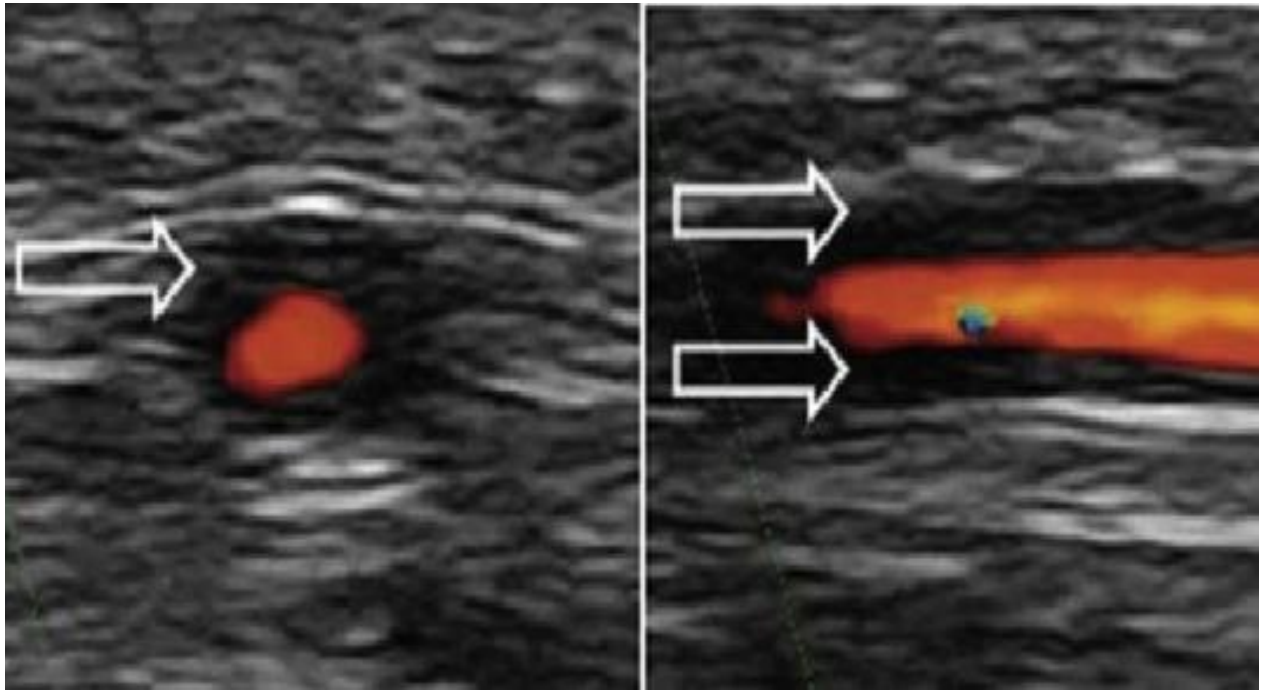
2021 ACR/VF GUIDELINES FOR GCA AND TAK

- Clinical questions developed in population, intervention, comparator, and outcome format
- Systematic literature reviews for each
- Grading of Recommendations Assessment, Development, and Education methodology for evidence rating
- Voting panel of rheumatology required ≥ 70% consensus for each recommendation
- 22 recommendations and 2 ungraded statements for GCA
- 20 recommendations and 1 ungraded statement for TAK

Maz *et al.*, Arthritis Rheum, 2021

GCA: DIAGNOSIS

- Unilateral TA biopsy over bilateral biopsy
- Long segment (>1 cm) TA biopsy still recommended over TA ultrasound or MRI for diagnosis
- In the case of suspected GCA with negative TA biopsy, large vessel imaging recommended
- In newly diagnosed GCA, large vessel imaging recommended



Maz *et al.*, Arthritis Rheum, 2021

GCA: THERAPY

- Initial therapy for GCA should include both glucocorticoids and tocilizumab
- GCA with large vessel involvement should include both glucocorticoids and steroid-sparing immunosuppressive agent
- There is no role for statins in the treatment of GCA
- Aspirin is recommended in GCA patients with vertebral and/or carotid stenosis
- Increase in acute phase reactants alone should not be treated with escalation of immunosuppressive therapy

Maz *et al.*, Arthritis Rheum, 2021

TAKAYASU: THERAPY

- Initial therapy with glucocorticoids should be initiated with oral steroids
- Patients in remission for 6-12 months should be tapered (as opposed to continuing long term low dose therapy)
- Steroid sparing agent + prednisone favored for treatment of active TA in both newly diagnosed disease and relapsing disease
- Tocilizumab is not favored as initial steroid sparing agent (MTX, anti-TNF)
- ASA indicated for stenotic lesions of cranial or vertebrobasilar arteries

Maz *et al.*, Arthritis Rheum, 2021

TAKAYASU: MONITORING

- Immunosuppression should not be escalated on the basis of elevated acute phase reactants alone
- Regularly scheduled noninvasive vascular imaging is recommended in addition to clinical and laboratory monitoring
- Renovascular hypertension should be managed with medical therapy rather than with vascular intervention
- Medical management over surgical intervention in active or quiescent disease unless there is immediate threat to tissue or organ

Maz *et al.*, Arthritis Rheum, 2021

2021 ACR/VF PAN GUIDELINES: DIAGNOSIS

- Use of abdominal vascular imaging-diagnosis and surveillance
- Skin biopsy
- Nerve and muscle biopsy
- Follow up for neurologic involvement

Chung *et al.*, Arthritis Care Res, 2021

PAN: TREATMENT

- Cyclophosphamide still chosen over rituximab as initial therapy
- Combination therapy recommended over steroid monotherapy even for non-severe disease
- Plasmapheresis not indicated as routine therapy
- After sustained remission (18 months) on nonsteroid therapy, attempt should be made to discontinue therapy
- In patients with deficiency of adenosine deaminase 2 (DADA2), treatment with steroids plus anti-TNF agent recommended

Chung *et al.*, Arthritis Care Res, 2021

2021 GUIDELINES ANCA VASCULITIS (GPA/MPA): INDUCTION

- Rituximab recommended over cyclophosphamide for severe disease
- Plasma exchange not routinely recommended for patients with GN, but can be considered for those at higher risk of ESRD
- Plasma exchange is not routinely recommended for DAH
- Reduced-dose glucocorticoid regimen recommended over standard dose for patients with severe disease

Chung *et al.*, Arthritis Care Res, 2021

ANCA GUIDELINES: REMISSION

- Following induction, rituximab favored for remission for severe disease
- Re-dosing at scheduled intervals favored over B cell/ANCA driven treatment
- Methotrexate or azathioprine favored over mycophenolate for maintenance
- Bactrim NOT recommended for remission maintenance
- Replacement IVIG merited not only for secondary hypogammaglobulinemia but may be considered in patients with impaired vaccine response

Chung *et al.*, Arthritis Care Res, 2021

ANCA GUIDELINES: RELAPSE

- Cyclophosphamide for patients who have severe relapse on rituximab
- Switch between therapies favored over combination therapy
- IVIG may be added to either rituximab or cyclophosphamide while waiting for response to induction therapy

Chung *et al.*, Arthritis Care Res, 2021

ANCA GUIDELINES: OTHER

- ANCA titers should not be used in isolation to direct therapy
- PJP prophylaxis should be given with rituximab or cyclophosphamide
- No standard duration of anticoagulation for patients with thrombotic events

Chung *et al.*, Arthritis Care Res, 2021

ANCA GUIDELINES: EGPA

- Rituximab or cyclophosphamide for severe disease induction therapy, but with the following caveats:

  -Cyclophosphamide preferable for cardiac involvement, ANCA negative, or severe neurologic or GI manifestations

  -Rituximab favored if ANCA+, GN, or prior cyclophosphamide

- Mepolizumab + steroids favored over other steroid sparing therapies for non-severe eGPA
- Combination therapy preferred over steroids alone

Chung *et al.*, Arthritis Care Res, 2021

EGPA: CONSIDERATIONS

- Continue leukotriene inhibitors in newly diagnosed patients-and initiation in known patients is acceptable
- Echocardiogram at diagnosis
- Topical/local therapies frequently used in GPA may be useful in eGPA
- PJP prophylaxis with cyclophosphamide use

Chung *et al.*, Arthritis Care Res, 2021

EGPA: FIVE-FACTOR SCORE

- Proteinuria > 1 gm/day
- SCr > 1.58 mg/dL
- GI involvement
- Cardiomyopathy
- CNS involvement
- (ENT, age)

Score associated 5-year mortality:

- 0 (9%)
- 1(21%)
- ≥ 2 (40%)

Guillevin *et al.*, Medicine, 2011

Chung *et al.*, Arthritis Care Res, 2021

RITUXIMAB INDUCTION REGIMENS IN AAV

- Rituximab administration initially driven by RAVE
- RA protocol crept into clinical use
- Head-to-head comparison of the 2 protocols using meta-analysis
- Primary endpoint: proportion of patients in complete remission at 6 months
- Other secondary endpoints: ANCA status, B cell depletion, mean prednisone dose, infections, and death

Benard *et al*,. Arthritis Rheum 72(Suppl); 2020

RITUXIMAB INDUCTION REGIMENS IN AAV

- 27 studies met inclusion criteria
- 506 total patients with GPA or MPA
- 361 with RAVE protocol, 145 with RA protocol
- Majority of patients (83 and 92%) were relapsing
- Overall, complete remission in 88% at 6 months
- No statistically significant difference between groups (RAVE 85%, RA 91%)
- Mean dose of prednisone similar at 6 months
- No significant differences in infections or deaths

Benard *et al.*, Arthritis Rheum 72(Suppl); 2020

STEROID BLUES

USTEKINUMAB IN GCA

- Il-12/23 blocking monoclonal antibody
- Case reports of successful use in LVV
- Prospective, open label trial in active new-onset or relapsing GCA
- 24-week prednisone taper plus 90 mg SC UST at 0, 4, then 8-week intervals to week 44
- Primary endpoint: steroid free remission without relapse through week 52 + normalization of APR
- All patients in remission at 4 weeks
- 13 patients were enrolled, study terminated after 7 of initial 10 patients relapsed
- 3 patients who met definition of steroid free remission did not meet APR criteria

Matza *et al.*, Arthritis Care Res, 2021

RESPONSE OF LVV TO TOCILIZUMAB

- Questions raised from the TCZ trials in GCA about large vessel manifestations and response to therapy
- Single center study from Spain examining FDG-PET/CT serial studies
- 30 patients, primarily women, mean age 65 years, refractory disease
- 83.3% patients with remission clinically
- Less than 1/3 with normalization of FDG-PET at mean time of 10 months

Bilbao *et al.*, Arthritis Rheum 72(suppl 10), 2020

LOW DOSE MEPOLIZUMAB IN EGPA

- Humanized monoclonal antibody binding to IL-5
- Routine use for severe eosinophilia asthma
- Use in eGPA at higher dose (300 mg q 4 weeks)
- Prospective study of lower dose "asthma dose" 100 mg q 4 weeks

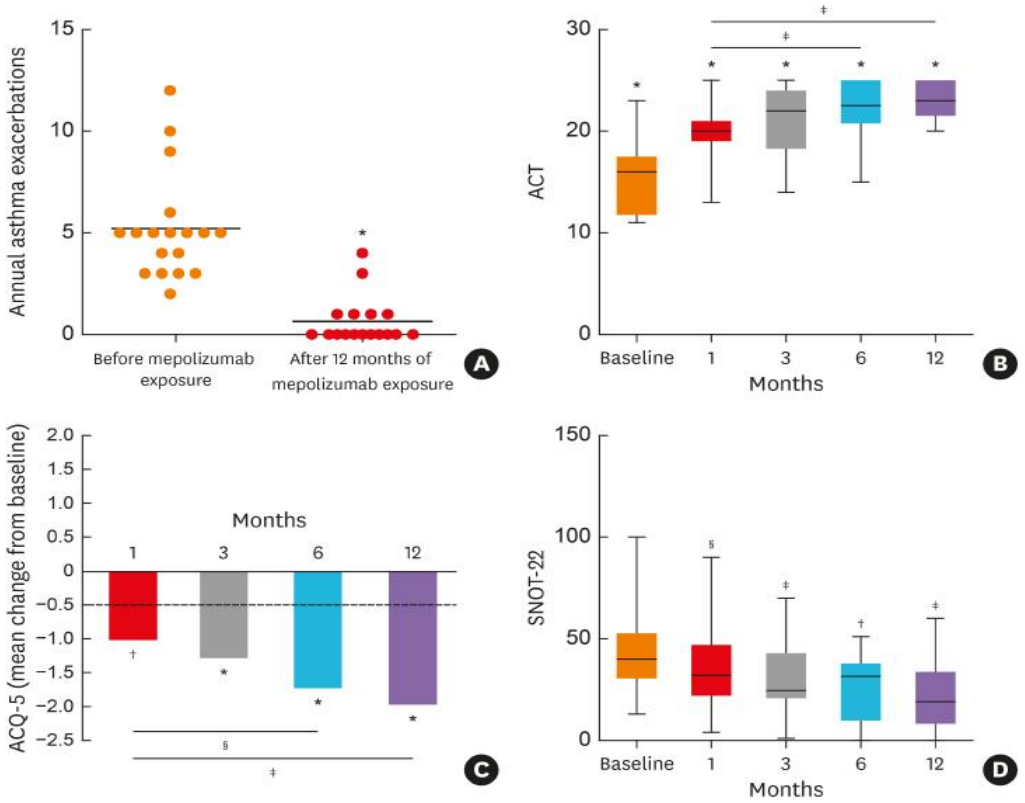
2 case series:

- 8 patients, 12 patients (1990 ACR criteria)
- Asthma exacerbations, steroid sparing effects, clinical remission/relapse
- 12 month follow up

Detoraki *et al.*, Respir Res, 2021
Vultaggio *et al.*, Allergy Asthma Immunol Res, 2020

RESULTS

- Reduction in BVAS/SNOT scores
- Reduction in steroid dose
- Clinical improvement in sinus disease and asthma control
- Drop in blood eosinophil count
- No discontinuation due to drug side effects
- One study with >90% remission at 12 months



Detoraki *et al.*, Respir Res, 2021
Vultaggio *et al.*, Allergy Asthma Immunol Res, 2020

AVACOPAN IN AAV

- Oral selective C5aR antagonist
- Alternate complement pathway and neutrophil activation
- Randomized, double blind, double dummy trial
- Primary question: can avacopan replace steroid tapering regimen in induction therapy for AAV?
- 331 newly diagnosed or relapsing GPA or MPA receiving rituximab or cyclophosphamide induction randomized to either steroid tapering group or avacopan group
- Non-inferiority trial

Jayne *et al.*, NEJM, 2021

THERAPY

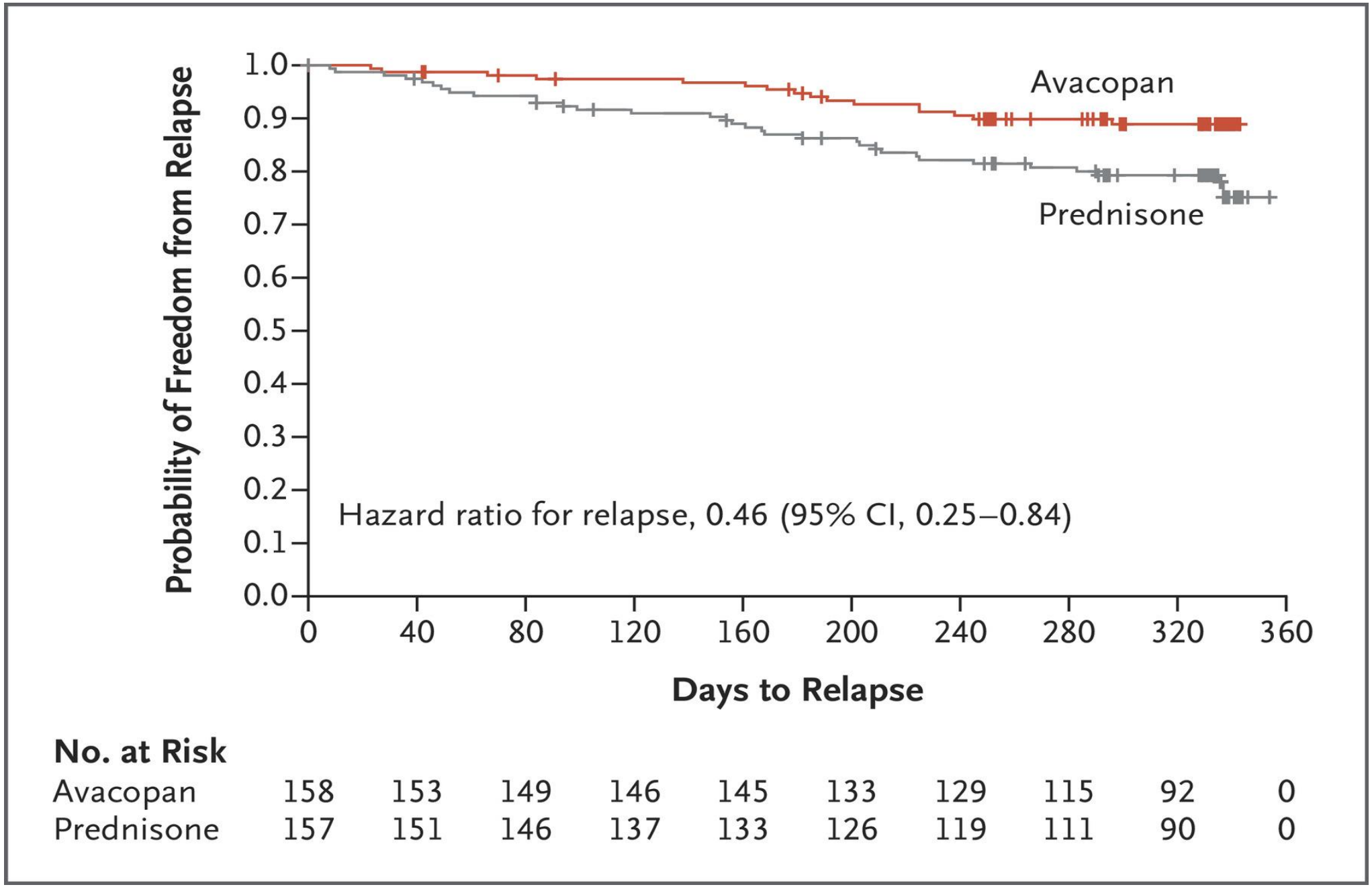
- Patients in both groups allowed to receive steroids up to study entry
- Excluded if more than 3 g IV within 4 weeks or ≥10 mg/day for 6 weeks prior to entry
- Steroids had to be tapered to 20 mg/day or less prior to entry, and off of steroids completely within 4 weeks (open label)
- Induction with rituximab (induction course only) or cyclophosphamide (followed by azathioprine week 15)
- Steroid rescue allowed

Jayne *et al.*, NEJM, 2021

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Avacopan (N=166)	Prednisone (N=164)
Age — yr	61.2±14.6	60.5±14.5
Sex — no. (%)		
Male	98 (59.0)	88 (53.7)
Female	68 (41.0)	76 (46.3)
Race — no. (%)†		
White	138 (83.1)	140 (85.4)
Asian	17 (10.2)	15 (9.1)
Black	3 (1.8)	2 (1.2)
Other	8 (4.8)	7 (4.3)
Body-mass index‡	26.7±6.0	26.8±5.2
Median duration of ANCA-associated vasculitis (range) — mo	0.23 (0–362.3)	0.25 (0–212.5)
Vasculitis disease status — no. (%)		
Newly diagnosed	115 (69.3)	114 (69.5)
Relapsed	51 (30.7)	50 (30.5)
ANCA status — no. (%)		
Antiproteinase 3 positive	72 (43.4)	70 (42.7)
Antimyeloperoxidase positive	94 (56.6)	94 (57.3)
Type of vasculitis — no. (%)		
Granulomatosis with polyangiitis	91 (54.8)	90 (54.9)
Microscopic polyangiitis	75 (45.2)	74 (45.1)
Birmingham Vasculitis Activity Score§	16.3±5.9	16.2±5.7
Vasculitis Damage Index¶	0.7±1.5	0.7±1.4
Immunosuppressant induction treatment — no. (%)		
Intravenous rituximab	107 (64.5)	107 (65.2)
Intravenous cyclophosphamide	51 (30.7)	51 (31.1)
Oral cyclophosphamide	8 (4.8)	6 (3.7)

Jayne *et al.*, NEJM, 2021



Jayne *et al.*, NEJM, 2021

OTHER STUDY POINTS

- Total mean steroid dose:

  Prednisone : 3654 $\pm$ 1710 Avacopan: 1349 $\pm$ 2040

- Total daily steroid dose:

  Prednisone: 11.9 $\pm$ 8.96 Avacopan: 4.4 $\pm$ 6.65

- HRQL, glucocorticoid toxicity index significantly better in avacopan
- Improvement in EGFR significantly higher in avacopan
- No significant differences in adverse effects between groups

Jayne *et al.*, NEJM, 2021

COMMENTS

- Parallel use of steroids up front and additional courses as needed during study
- Analysis of MPO/PR3 + patients combined
- Single treatment course of rituximab
- Nearly 1/3 of patients each group induced with IV cyclophosphamide
- More newly diagnosed patients in cohort (with lower VDI)

Jayne *et al.*, NEJM, 2021

RITUXIMAB AND PMR

- Double-blind, randomized placebo controlled trial
- PMR patients meeting 2012 ACR criteria unable to taper below 7.5 mg/day
- 1:1 rituximab vs. Placebo
- 17 week tapering course of steroids
- Primary outcome: steroid free remission at 21 weeks
- 49 patients enrolled (38 new, 9 relapsing)
- 48% of rituximab and 21% placebo achieved primary outcome
- Infusion reactions, 1 PE

Marsma *et al.*, Lancet Rheum, 2021

SUMMARY

- Steroid sparing agents for vasculitis
- Imaging that may help uncloud CNS vasculitis diagnosis and management
- Clinical features that may help identify increased risk in vasculitis-associated comorbidities and complications of infection
- ACR/VF guidelines addressing some grey areas of diagnosis and management
- COVID-19 and inflammatory vascular disease remains evolving area of interest and concern