Stadtspital Zürich

Bei Rheuma leidet häufig auch das Herz

Die rheumatologische Perspektive

Zürich, 03.10.2024

Dr. med. Django Russo

Oberarzt m.e.V.
Abteilung für Rheumatologie Stadtspital Zürich

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Chefarzt
Abteilung für Rheumatologie Stadtspital Zürich

ESC European Society of Cardiology

European Heart Journal (2017) **38**, 2649–2662
doi:10.1093/eurheartj/ehx321

CURRENT OPINION
Heart failure/cardiomyopathy

Diagnosis and management of myocardial involvement in systemic immune-mediated diseases: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Disease

Alida L.P. Caforio[1]*, Yehuda Adler[2], Carlo Agostini[3], Yannick Allanore[4], Aris Anastasakis[5], Michael Arad[6], Michael Böhm[7], Philippe Charron[8,9], Perry M. Elliott[10], Urs Eriksson[11], Stephan B. Felix[12], Pablo Garcia-Pavia[13], Eric Hachulla[14], Stephane Heymans[15,16], Massimo Imazio[17], Karin Klingel[18], Renzo Marcolongo[3], Marco Matucci Cerinic[19], Antonis Pantazis[20], Sven Plein[21], Valeria Poli[22], Angelos Rigopoulos[23], Petar Seferovic[24], Yehuda Shoenfeld[25], Josè L Zamorano[26], and Ales Linhart[27]

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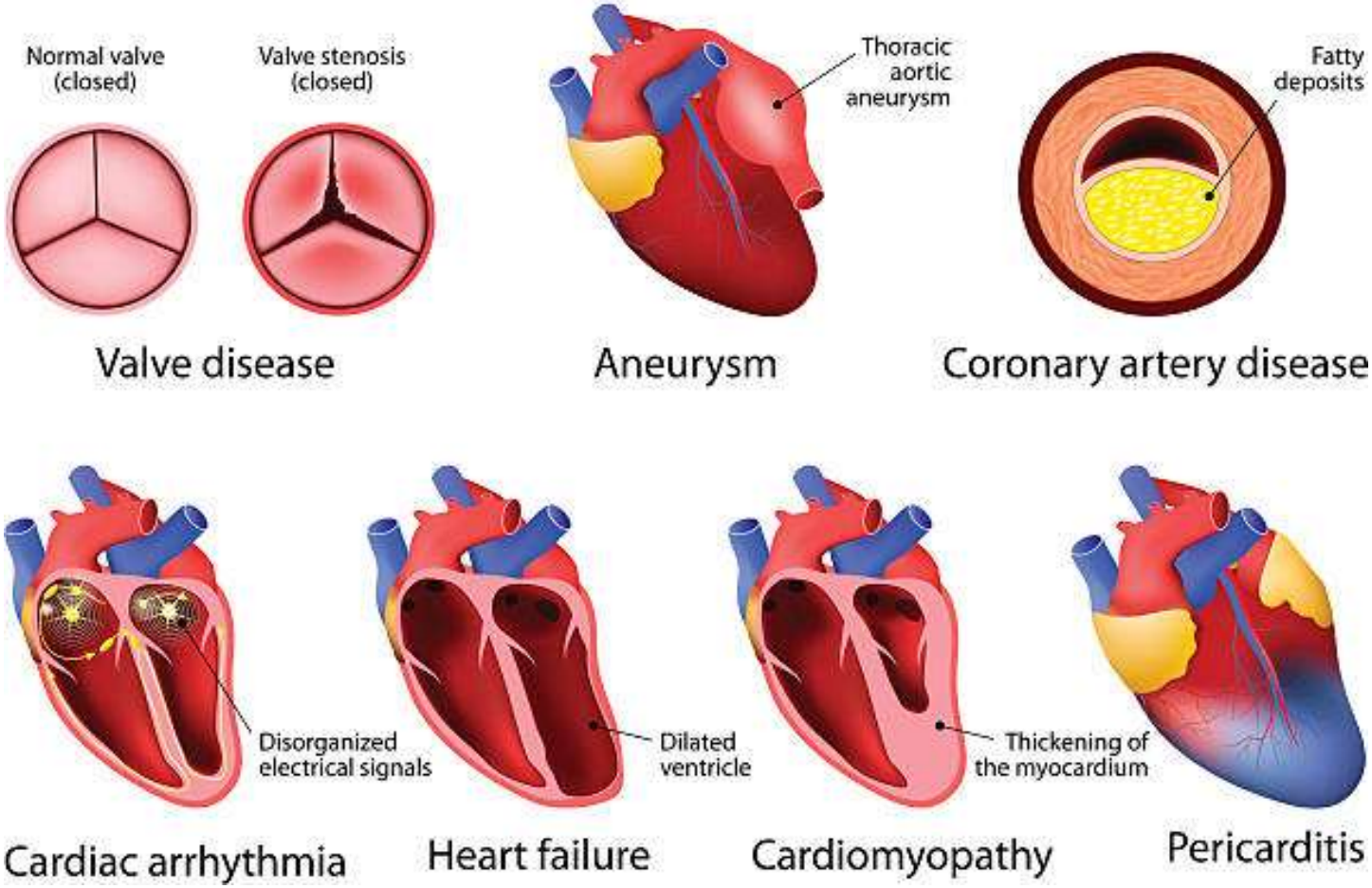
Types of heart disease



Internist 2007 · 48:284–289
DOI 10.1007/s00108-006-1778-5
Online publiziert: 16. Januar 2007

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Klinik für Rheumatologie & Klinische Immunologie, Katholisches Krankenhaus St. Josef, Zentrum für Innere Medizin der Kliniken Essen Süd

Schwerpunktherausgeber
B. E. Strauer, Düsseldorf

Das Herz bei rheumatologischen Erkrankungen

Tab. 1 Kardiale Manifestationen bei verschiedenen rheumatischen Erkrankungen

Diagnose	Perikarditis	Myokarditis	Myokard-infarkt	DCM	Aorten-vitium	Mitral-vitium	PAH	Reiz-leitungs-störung
Rheumatoide Arthritis	+	+	(+)[a]	–	–	–	–	(–)
Spondylitis ankylosans	–	–	–	–	+	–	–	(+)
SLE	+++	++	+ (APS) (+)	(+)	–	++ (APS)	(+)	+[b]
Systemische Sklerose	+	(+)	(+)	+	–	–	++	(+)
Primär systemische Vaskulitiden	(+)	++	+	(+)	+	–	–	(+)

SLE: Systemischer Lupus erythematodes; APS: Antiphospholipidsyndrom; DCM: dilatative Kardiomyopathie; PAH: pulmonal-arterielle Hypertonie. [a] *Durch Atherosklerose als chronischer Krankheitsschaden;* [b] *Kongenitaler AV-Block. (+): seltene; +: mögliche; ++: typische; +++: häufige Manifestation; –: untypisch*

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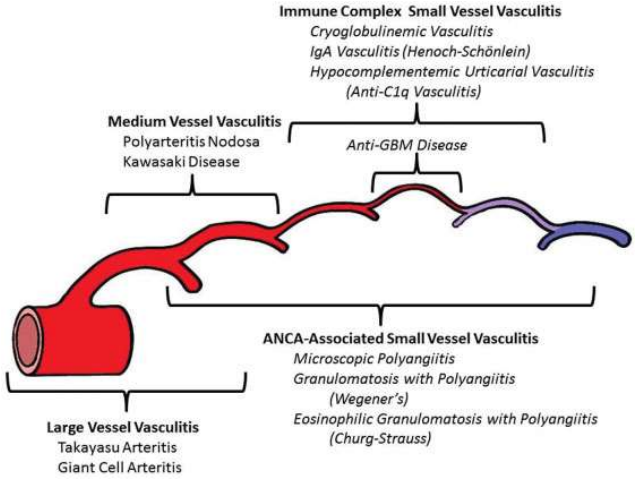
Geschichte des Churg-Strauss-Syndroms „EGPA“

2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides



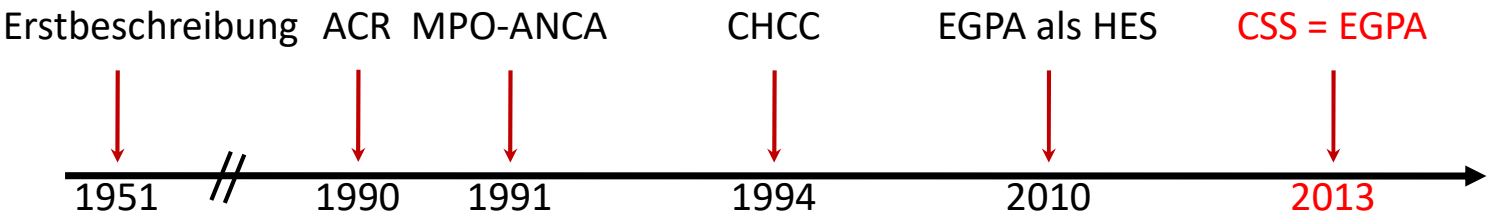
Small vessel vasculitis (SVV)

Antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis (AAV)

Microscopic polyangiitis (MPA)

Granulomatosis with polyangiitis (Wegener's) (GPA)

Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)



Arthritis Rheum. 2013 Jan;65(1):1-11

Cardiac manifestations of rheumatological disease: a synopsis for the cardiologist

Gautam Sen,[1] Patrick Gordon,[2] Daniel M Sado [1]

Vaskulitis	Kardiale Mitbeteiligung
Klein-Gefäss-Vaskulitis (SVV) - GPA/ MPA/ EGPA	➢ Ca. 10% Perikarditis ➢ Ca. 2% Myokarditis / Fibrose (MPA) ➢ Arteriosklerose Risiko erhöht !!
Mittel-Gefäss-Vaskulitis - PAN, Kawasaki	➢ Gesamt ca. 5% Prävalenz ➢ Coronare Aneurysmata, Stenosen, Thrombosen ➢ Arteriosklerose Risiko erhöht !!
Grossgefäss-Vaskulitis (LVV) - GCA und TAK	➢ Coronardissektion (bis 5%) ➢ Aortitis ➢ teils mit Aortenklappeninsuffiziens ➢ Arteriosklerose Risiko erhöht !!

BMJ

Sen G, *et al*. *Heart* 2021;**107**:1173–1181. doi:10.1136/heartjnl-2019-316460

British Cardiovascular Society

Cardiac manifestations of rheumatological disease: a synopsis for the cardiologist

Gautam Sen,[1] Patrick Gordon,[2] Daniel M Sado [1]

Vaskulitis	Kardiale Mitbeteiligung
Systemischer Lupus erythematodes (SLE)	➢ Ca. 25% Perikarditis ➢ Ca. 10% Myokarditis ➢ Bios 10% Klappen Veränderungen (Libman-Sacks) ➢ Arteriosklerose Risiko 6fach erhöht !!
Sjögren Syndrom	➢ Reiz-Leitungsstörungen ➢ Perikarditis ➢ Arteriosklerose Risiko bis 3fach erhöht !!
Systemische Sklerose / Myositis	➢ Perikarditis bis 15% ➢ Myokarditis mit Fibrose ➢ PAH bis ca. 15% ➢ Arteriosklerose und Mikrovaskuläre Veränderungen

BMJ

Sen G, *et al*. *Heart* 2021;**107**:1173–1181. doi:10.1136/heartjnl-2019-316460

British Cardiovascular Society

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Nephrotisches Syndrom und Rheuma

VASAS VASCULITIS Association Switzerland

Renale Histopathologie	Ätiologie	
«Minimal Change»-Erkrankung (MCD)	Idiopathisch	
	Medikamente	• Nichtsteroidale Antirheumatika, Lithium, Bisphosphonate, Interferon, Rifampicin, Ampicillin, Impfungen
	Neoplasien	• Lymphom, Thymom
Membranöse Nephropathie (MN)	Primär	• 70 % Anti-PLA2R-Antikörper • Anti-THSD7A-Antikörper (10% der Anti-PLA2R-negativen Formen)
	Neoplasien	• Solide Tumoren (Lunge, Kolon, Mamma), Lymphome
	Infekte	• Hepatitis B (selten auch Hepatitis C) • Bakteriell (Lues) • Wurmerkrankungen (Filariasis, Schistosomiasis, Bandwurm) • Malaria
	Medikamente	• NSAR, Penicillamin, Gold, Captopril
	Autoimmunerkrankungen/ andere	• Systemischer Lupus erythematodes (Lupus-Nephritis ISN/RPS-Klasse V), IgG4-Erkrankung, Sarkoidose, Sjögren-Syndrom • Allogene Stammzelltransplantation/«graft-versus host disease»
Fokal-segmentale Glomerulosklerose (FSGS)	Idiopathisch	
	Genetisch	• Bislang mehr als 50 betroffene Gene beschrieben • Bei Kindern meist Mutation im Nephrin- oder Podocin-Gen • Bei Adoleszenten/Erwachsenen meist im Apha-actinin-4-, TRPC6-, INF2- oder MYOE1-Gen
	Glomeruläre Hyperfiltration	• Verminderte Nephronmasse (Frühgeburt, renale Dysplasie, Einnierigkeit) • Adipositas • Diabetes mellitus • Zyanotische Herzvitien
	Virale Infekte	• HIV, Cytomegalovirus, Parvovirus B19
	Drogen/Medikamente	• Heroin, Lithium, Bisphosphonate (Pamidronat), Calcineurininhibitoren, Interferon, anabole Steroide
	Andere Schädigung	• Arterielle Hypertonie, Alport-Syndrom, Refluxnephropathie
Glomerulosklerose Kimmelstiel-Wilson	Diabetische Nephropathie	• Diabetes mellitus
Glomeruläre Amyloiddeposition	Systemische Amyloidose	• AA-Amyloidose - Rheumatoide Arthritis, M. Crohn, Bronchiektasen, familiäres Mittelmeerfieber • AL-Amyloidose - Myelom, monoklonale Gammopathie • Hereditäre Formen - Transthyretin-Mutation

Tab. 2: Die häufigsten Ursachen des nephrotischen Syndroms und deren Ätiologie

Quelle: www.universimed.com

Serum-Amyloid A (SAA)
146 mg/L (Norm <6.4 mg/L)

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AA-Amyloidose

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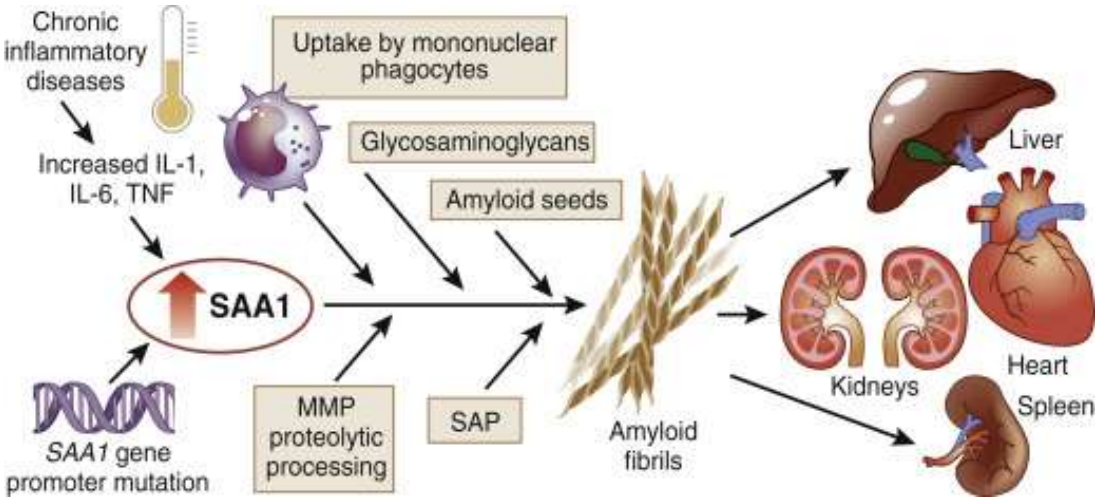
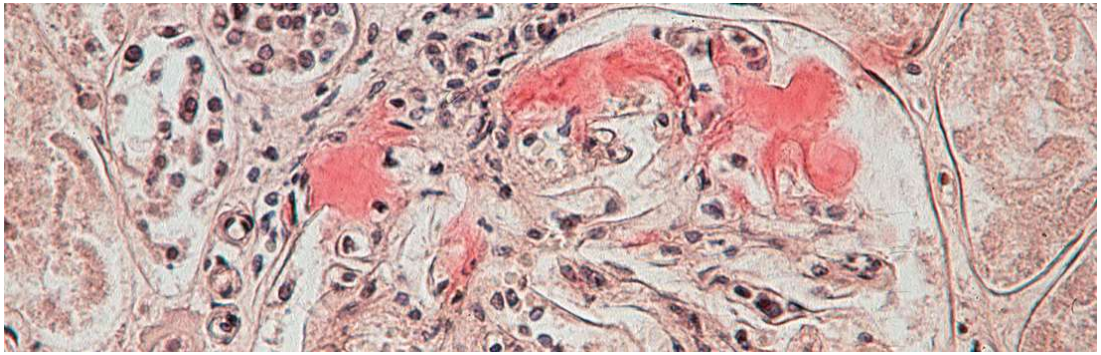


DIAGNOSE



Obici L AA amyloidosis without systemic inflammation: when clinical evidence validates predictions of experimental medicine. *Kidney Int*.
Deutsche Gesellschaft für Amyloid-Krankheiten

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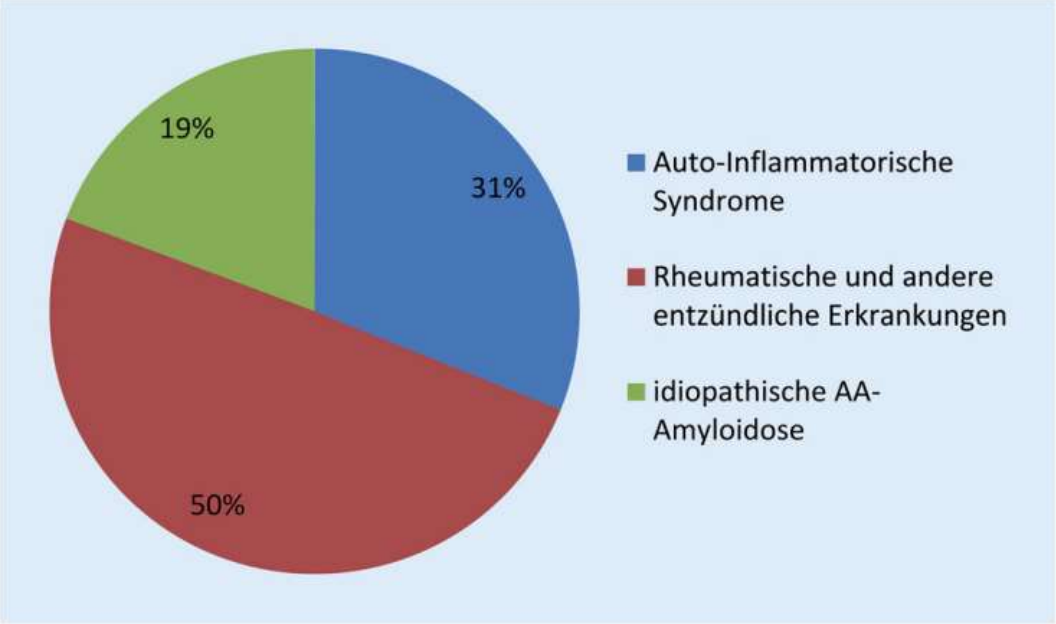
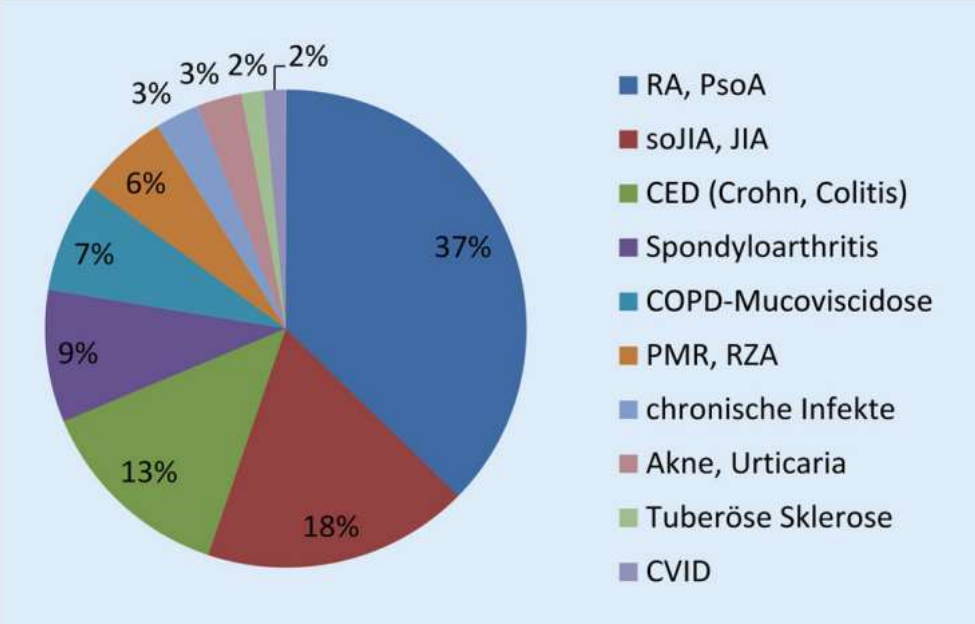
Ätiologie der AA-Amyloidose

VASAS VASCULITIS Association Switzerland



Grunderkrankungen bei 135 Patienten mit AA-Amyloidose (Amyloidosezentrum Heidelberg)



Rheumatologische/ entzündliche Erkrankungen bei 67 Patienten mit AA-Amyloidose

In 30 % der Fälle kann keine zugrunde liegende entzündliche Erkrankung eruiert werden

Blank N, Hegenbart U, Schönland S. Ursachen und Therapie der systemischen AA-Amyloidose *Z Rheumatol*. 2016

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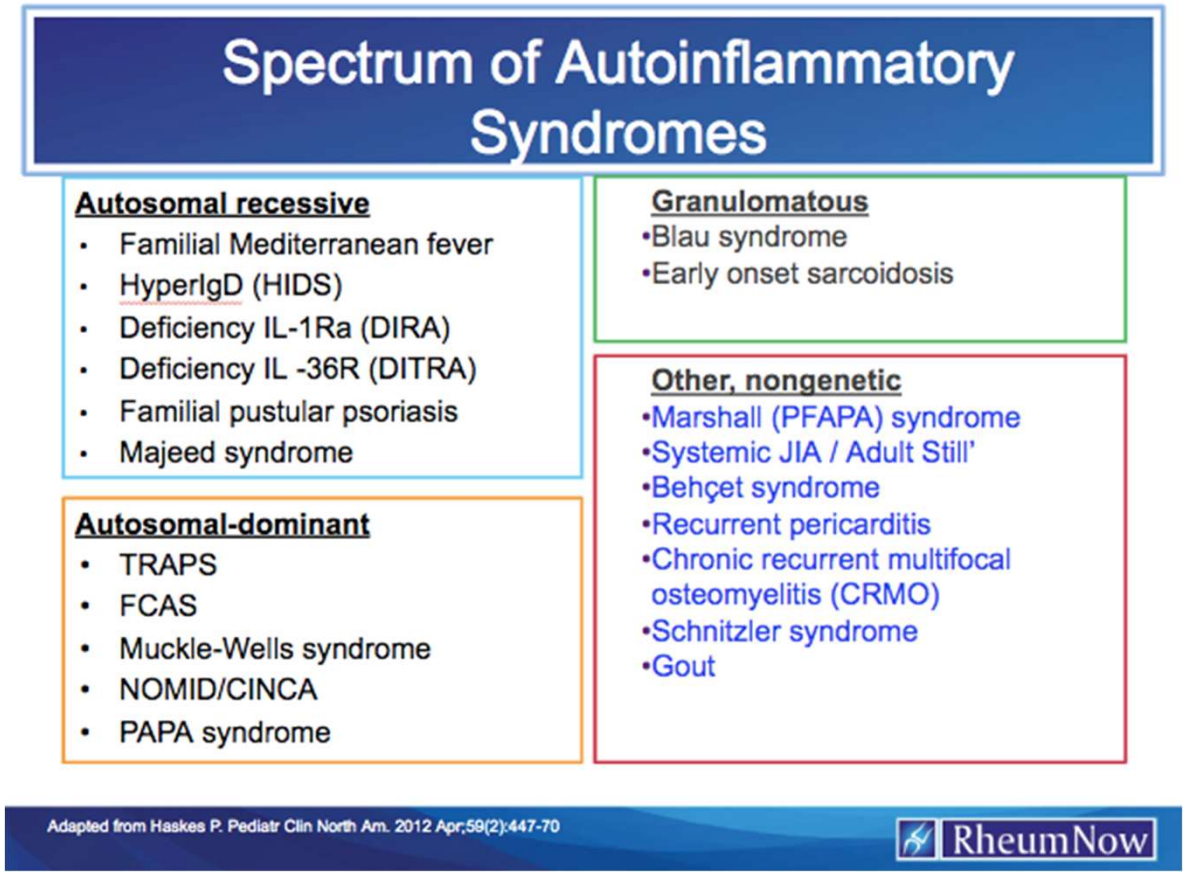
Autoinflammatorische Syndrome

VASAS VASCULITIS Association Switzerland



Quelle: www.rhuemanow.com und www.ling-app.com und www.officeguycartoons.com

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Familiäres Mittelmeerfieber

VASAS VASCULITIS Association Switzerland

BACKGROUND

* HEREDITARY AUTOINFLAMMATORY DISORDER AFFECTING THOSE of MEDITERRANEAN & MIDDLE EASTERN ORIGIN

SIGNS & SYMPTOMS

* RECURRENT FEVERS
* INFLAMMATION
  ~ CHEST, ABDOMEN, or JOINTS
* HEADACHES
* RASHES
* ONSET BEFORE 20 YO
* EPISODES LAST 2-4 HRS & UP to 4 DAYS

DIAGNOSIS

* TEL-HASHOMER DIAGNOSTIC CRITERIA
* BLOOD TESTS
* GENETIC TESTING

CAUSES

* AUTOSOMAL RECESSIVE MUTATION
  ~ MEFV GENE on CHROMOSOME 16, ENCODING PYRIN
  ~ ABOUT 10% HAVE NO IDENTIFIABLE MUTATIONS in MEFV GENE
* SOME AUTOSOMAL DOMINANT TRANSMISSIONS DOCUMENTED
  ~ MOST SEVERE PHENOTYPIC MANIFESTATION of FMF LINKED to M694V & M680I MUTATIONS

TREATMENT

* PREVENT KIDNEY FAILURE:
  ~ COLCHICINE
  ~ IL-1 INHIBITORS

Quelle: www.osmosis.org

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Familiäres Mittelmeer-"fieber"

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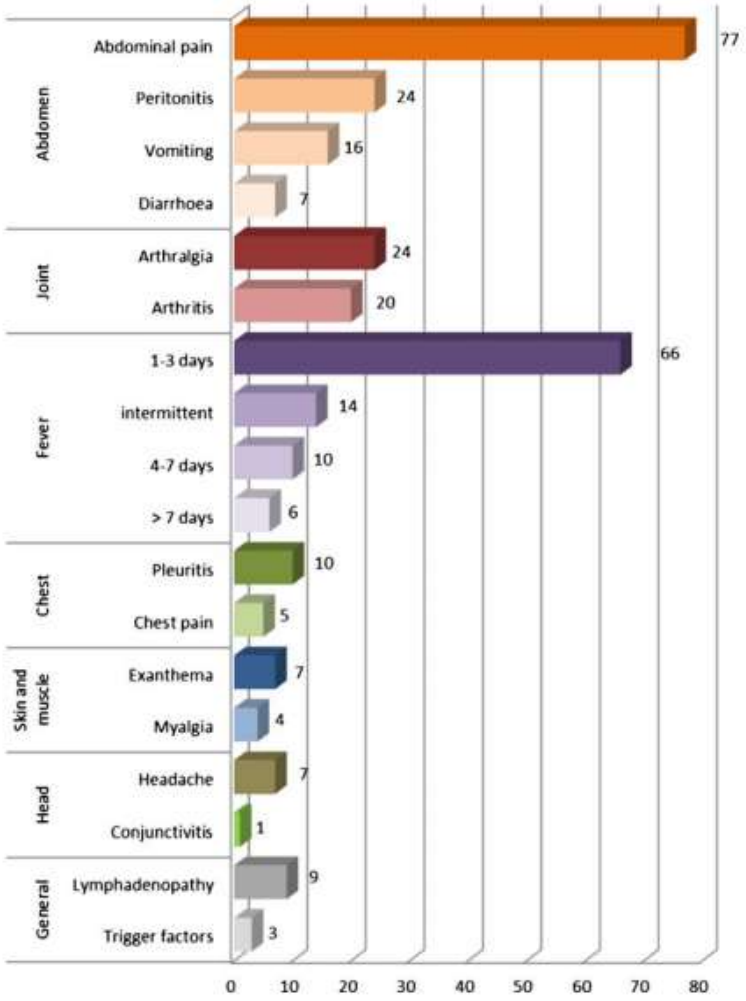
Fig. 2 Clinical features of children with FMF in the Clinic-ESPED survey (n1=100; homozygous *n*=44, compound heterozygous *n*=50, complex heterozygous *n*=6; the heterozygous group *n*=22 is not included in this figure)



Fieber muss nicht immer vorhanden sein !

Lainka E et al. Familial Mediterranean fever in Germany: epidemiological, clinical, and genetic characteristics of a pediatric population. *Eur J Pediatr*.

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Genetische Abklärung FMF

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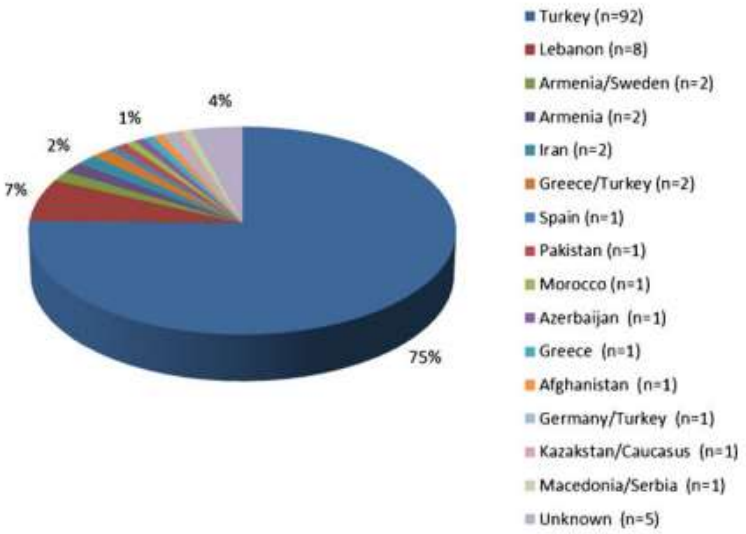
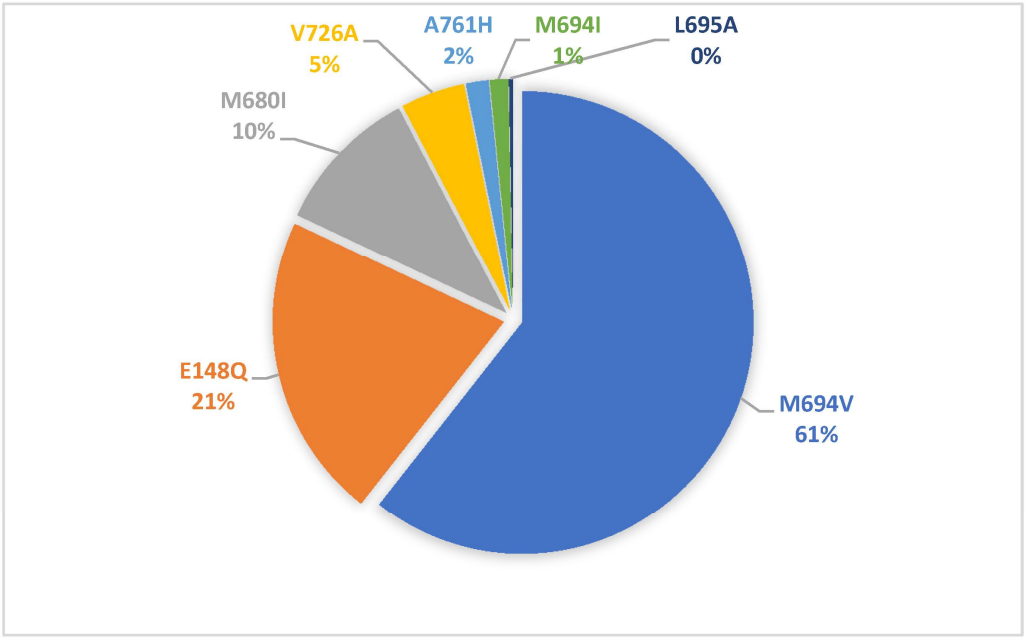
Fig. 1 Origin of children with FMF in the Clinic-ESPED survey (n1=122)





Arici ZS, et al. Evaluation of E148Q and Concomitant AA Amyloidosis in Patients with Familial Mediterranean Fever. *J Clin Med*. 2021
Lainka E et al. Familial Mediterranean fever in Germany: epidemiological, clinical, and genetic characteristics of a pediatric population. *Eur J Pediatr*.

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Colchizin und FMF

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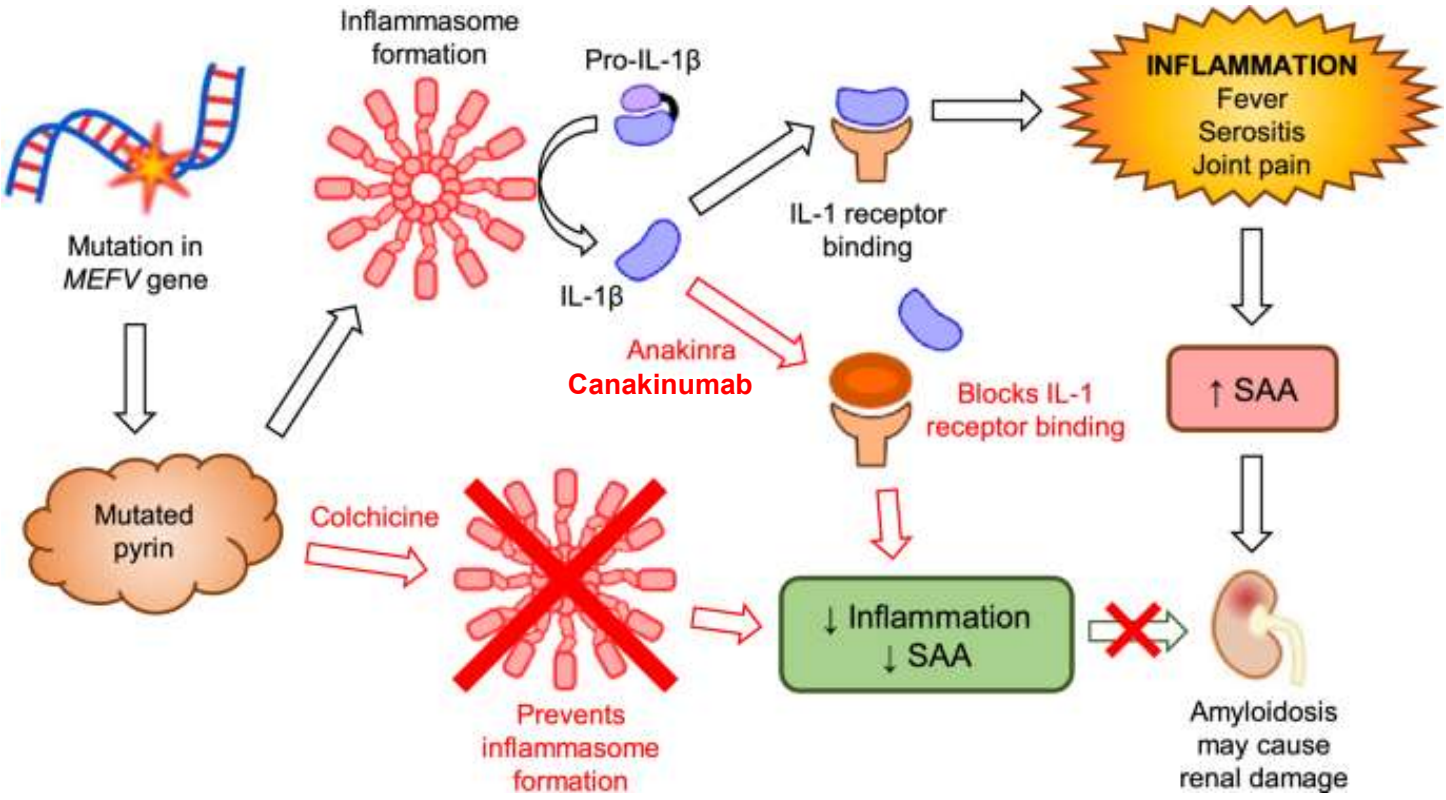

Arnold Lee et al. Anakinra in familial Mediterranean fever: a profile of its use Drugs&Therapy Perspectives 2021

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Colchizin und CVD

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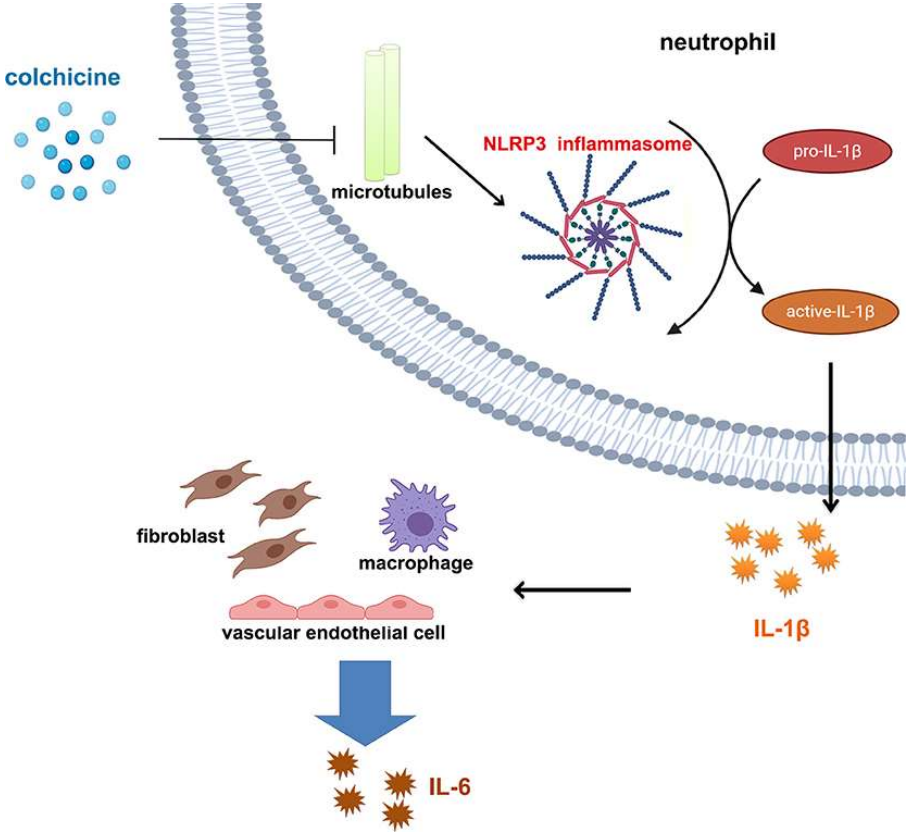

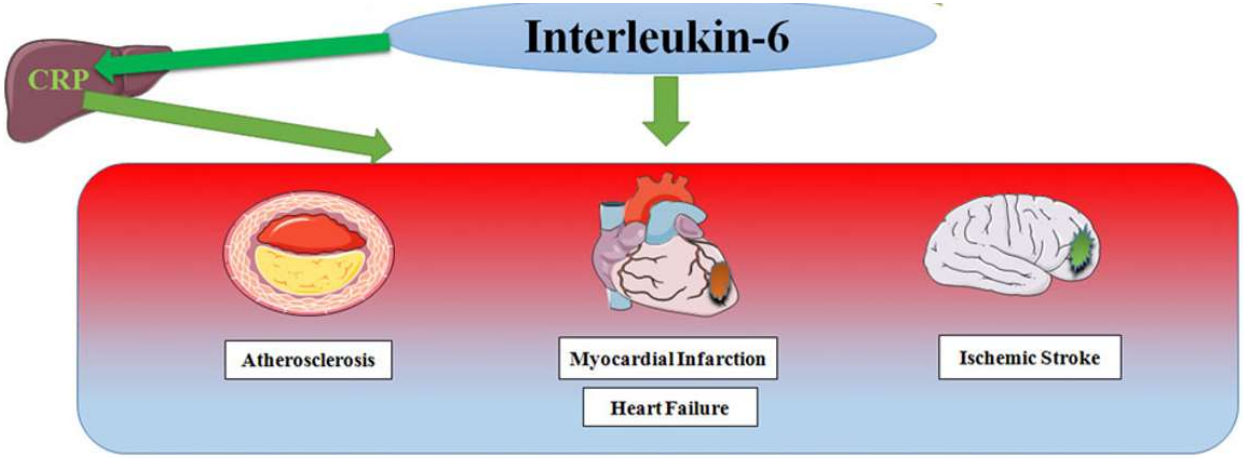

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Colchizin und ASCVD

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Review

Colchicine in atherosclerotic cardiovascular disease

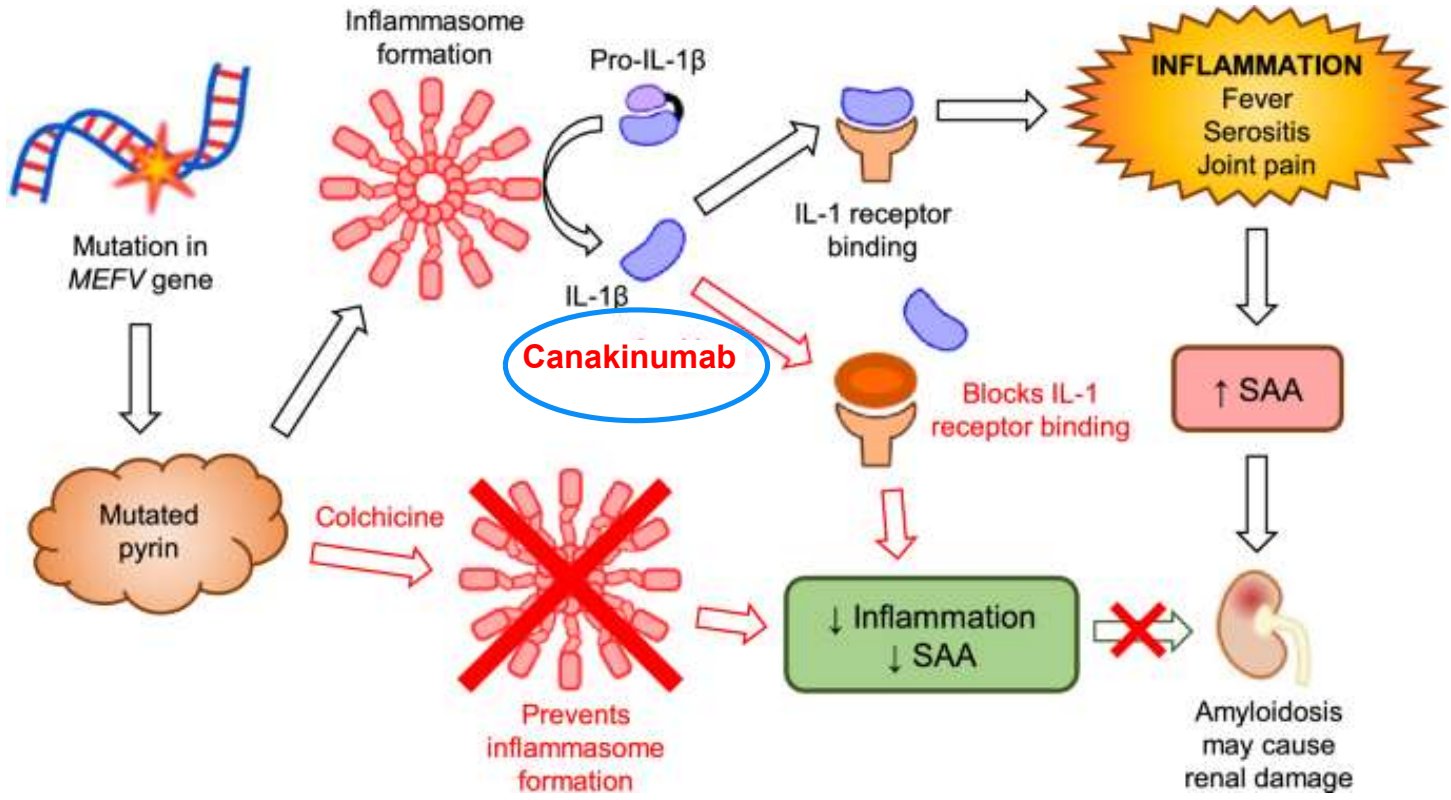
Bradley Tucker [1,2], Neil Goonetilleke,[3] Sanjay Patel [1,4], Anthony Keech [1,4]

Heart

Table 2 Efficacy of colchicine in the completed cardiovascular outcome trials

	MACE		CV death		Non-CV death		All-cause death	
Trial	Colchicine Events/total (%)	Placebo Events/total (%)	Colchicine Events/total (%)	Placebo Events/total (%)	Colchicine events/total (%)	Placebo Events/total (%)	Colchicine Events/total (%)	Placebo Events/total (%)
LoDoCo2[23]	115/2762 (4.2%)	157/2760 (5.7%)	20/2762 (0.7%)	25/2760 (0.9%)	53/2762 (1.9%)	35/2760 (1.3%)	73/2762 (2.6%)	60/2760 (2.2%)
COPS[25]	12/396 (3.0%)	16/399 (4.0%)	3/396 (0.8%)	1/399 (0.3%)	5/396 (1.3%)	0/399 (0.0%)	8/396 (2.0%)	1/399 (0.3%)
COLCOT[24]	111/2366 (4.7%)	130/2379 (5.5%)	20/2366 (0.8%)	24/2379 (1.0%)	23/2366 (1.0%)	20/2379 (0.8%)	43/2366 (1.8%)	44/2379 (1.8%)
LoDoCo[22]	12/282 (4.3%)	25/250 (10.0%)	0/282 (0.0%)	4/250 (1.6%)	5/282 (1.8%)	5/250 (2.0%)	5/282 (1.8%)	9/250 (3.6%)
Deftereos[19]	–	–	1/112 (0.9%)	1/110 (0.9%)	0/112 (0.0%)	0/110 (0.0%)	1/112 (0.9%)	1/110 (0.9%)
Total	250/5806 (4.3%)	328/5788 (5.7%)	44/5918 (0.7%)	55/5898 (0.9%)	86/5918 (1.5%)	60/5898 (1.0%)	130/5918 (2.2%)	115/5898 (1.9%)
P value	2p=0.005		2p=0.339		2p=0.060		2p=0.726	

Back to the case



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Fall 3

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Das **Heerfordt-Syndrom** (*Febris uveoparotidea*) wurde nach dem dänischen Ophthalmologen Christian Frederick Heerfordt (* 1871, † 1953) benannt und ist eine chronische Entzündung der Ohrspeicheldrüse (*Parotis*) und der Tränendrüse.

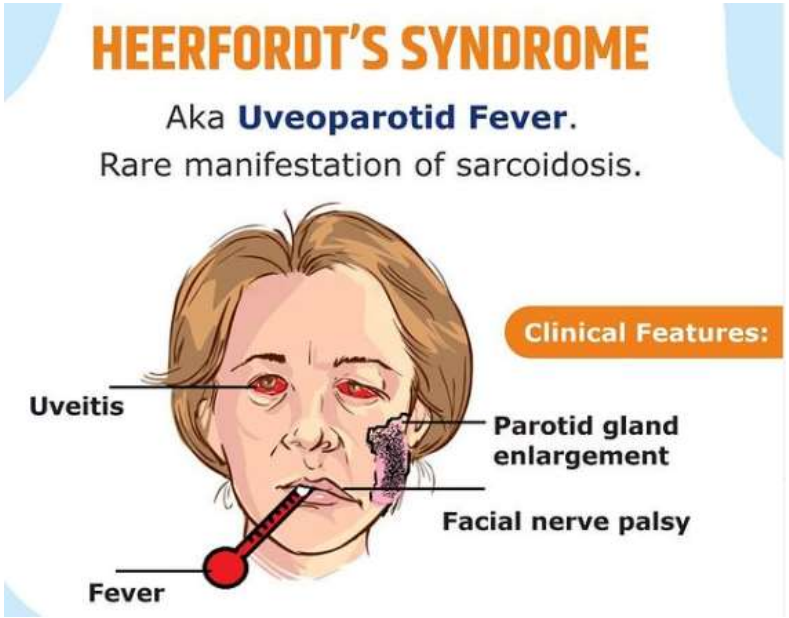
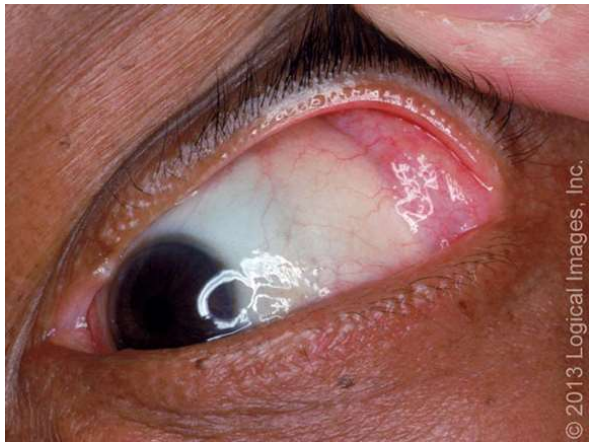
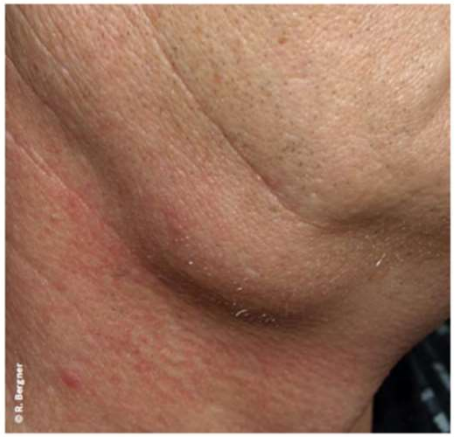
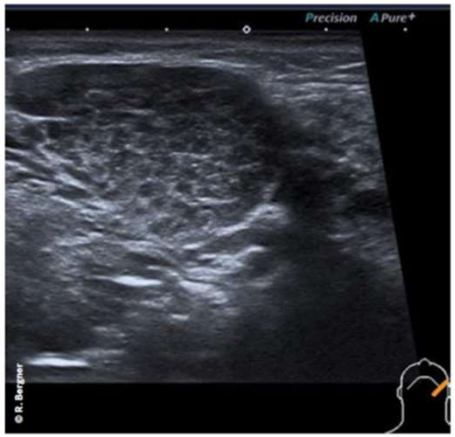


Abbildung: www.dbmc.com







Skriptum Rheumatologie

Mit Genehmigung von Prof. R. Bergner / LU

BILDIMPULSE SKRIPTUM RHEUMATOLOGIE

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Extrapulmonale Sarkoidose

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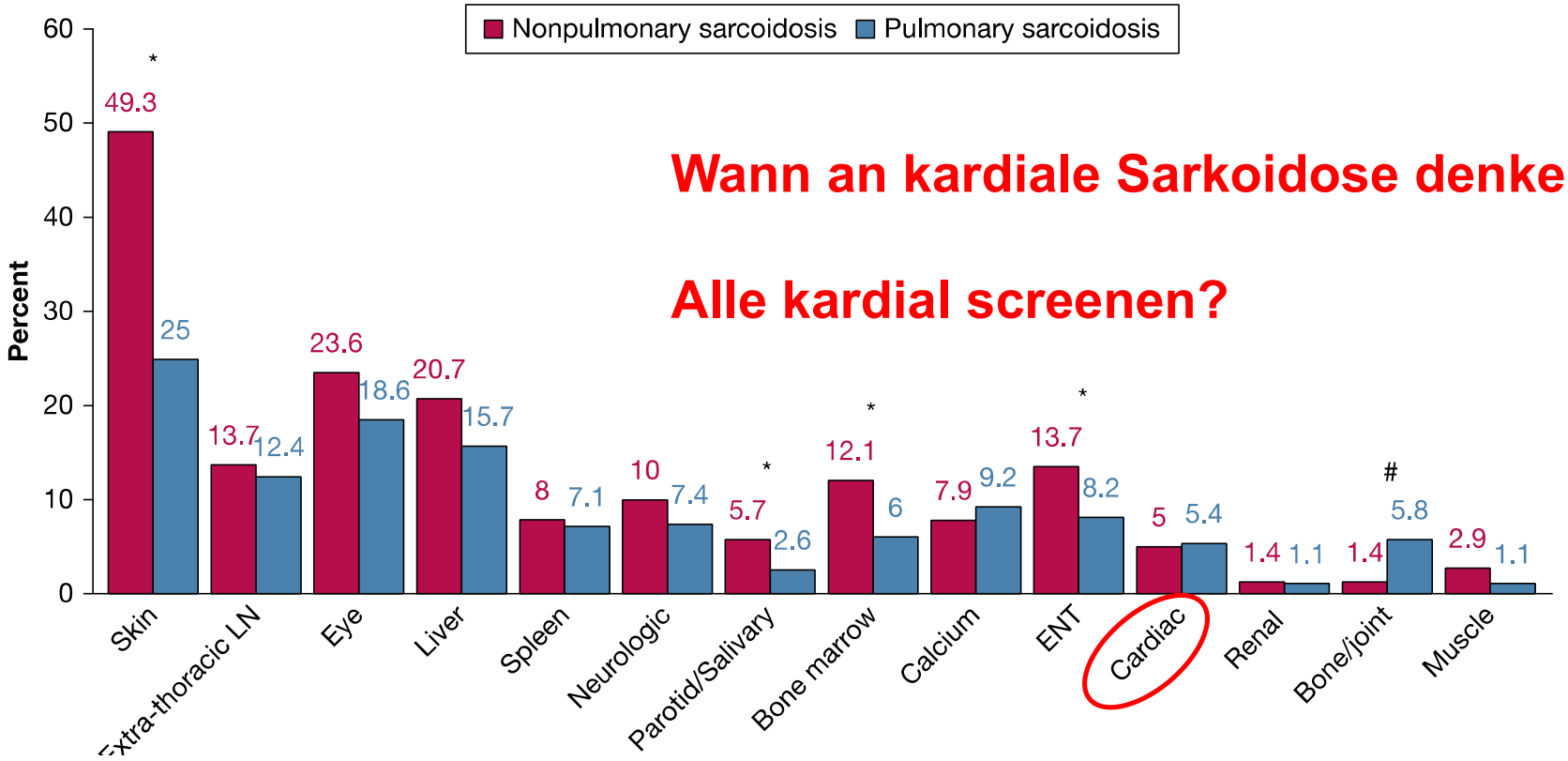

Wann an kardiale Sarkoidose denken?

Alle kardial screenen?

CHEST 2018; 154(2):349-356

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Phänotypen der Sarkoidose

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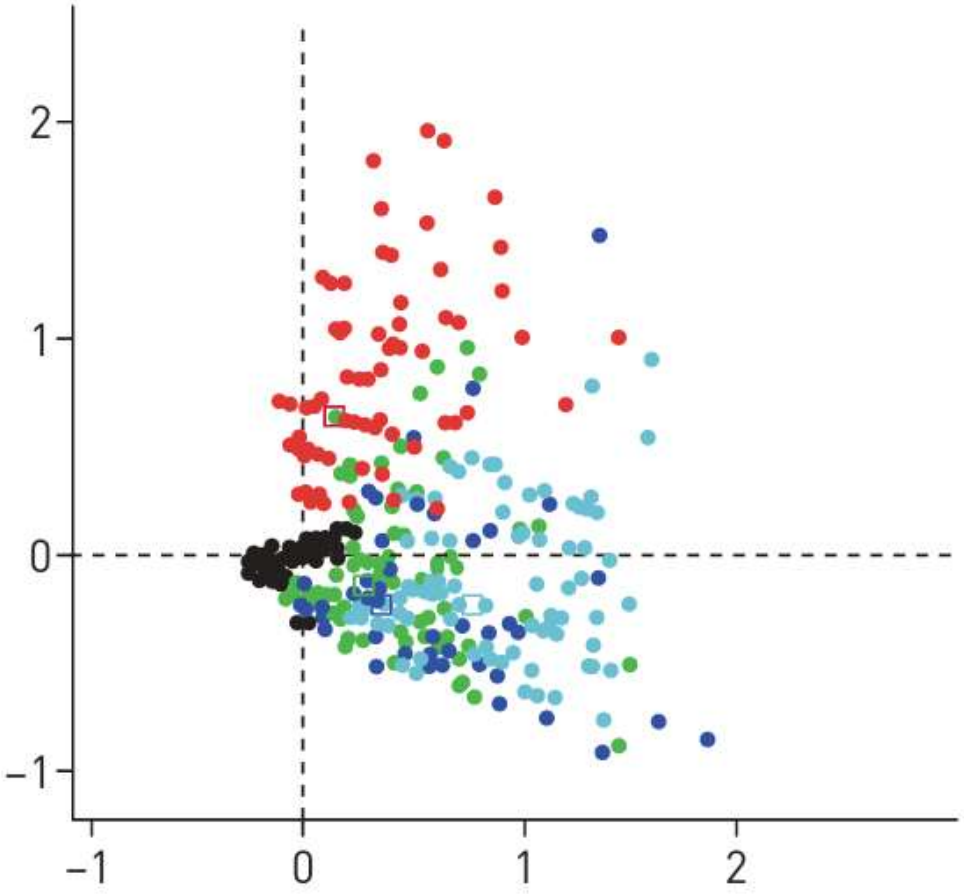

Cluster 1: Abdominal (Niere/Milz/Leber)

Cluster 2: Auge-Herz-Haut-ZNS

Cluster 3: Muskuloskelettal-Haut

Cluster 4: Pulmonal-Lymphknoten

Cluster 5: Extrapulmonal

Schupp JC et al. Phenotypes of organ involvement in sarcoidosis. *Eur Respir J*. 2018

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Kardiale Sarkoidose

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Tab. 1 Klinische Manifestationen bei kardialer Sarkoidose und ihre Prävalenz [10, 13–20]

Klinische Manifestation	Prävalenz in Studien (in %)
AV-Block	26–62
Schenkelblock	12–61
Supraventrikuläre Tachykardie	0–15
Ventrikuläre Tachykardie	2–42
Herzinsuffizienz	10–30
Plötzlicher Herztod	12–65

Skowasch, D., Gaertner, F., Marx, N. *et al.* Diagnostik und Therapie der kardialen Sarkoidose. *Kardiologe* 2020

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Kardiale Sarkoidose - Screening

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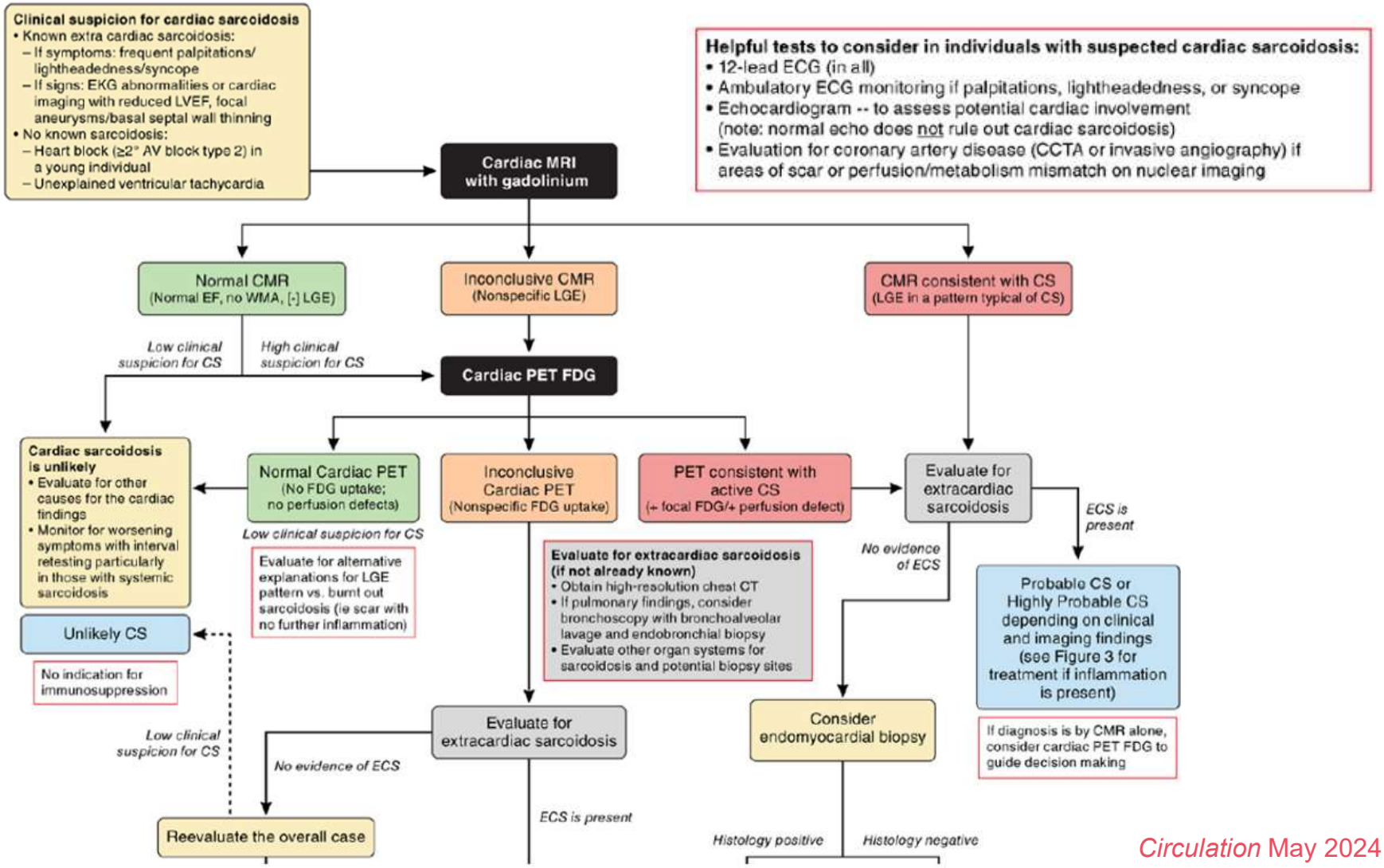

Circulation May 2024

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Kardiale Sarkoidose - Screening

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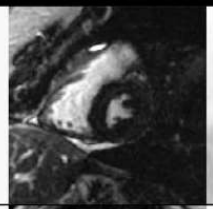
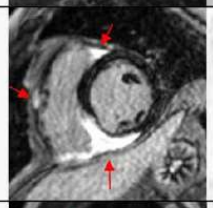
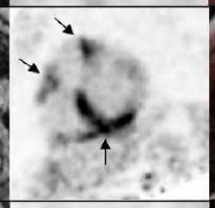
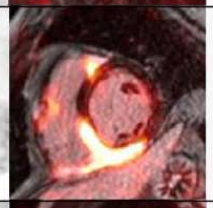
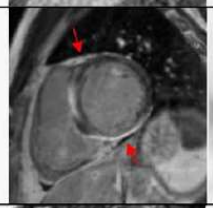
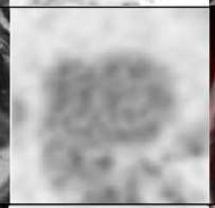
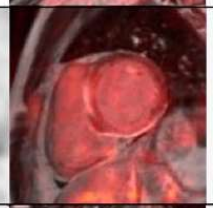
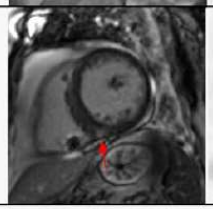
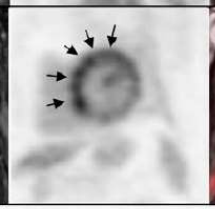
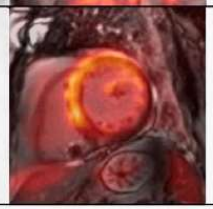
Phenotypes	CMR	FDG PET	PET-MR	Typical Presentation
A Focal septal FDG uptake with or without corresponding LGE				Heart block
B Multifocal LGE and FDG uptake in a pattern consistent with cardiac sarcoidosis				Heart block Ventricular arrhythmias LV systolic dysfunction
C Multifocal LGE in a pattern consistent with cardiac sarcoidosis without FDG uptake				Ventricular arrhythmias LV systolic dysfunction
D LGE or FDG uptake in a pattern NOT consistent with cardiac sarcoidosis				Miscellaneous, including other presentations, such as palpitations, dyspnea, dizziness, ventricular ectopy

Figure 1. CMR and corresponding PET findings by progression of disease.

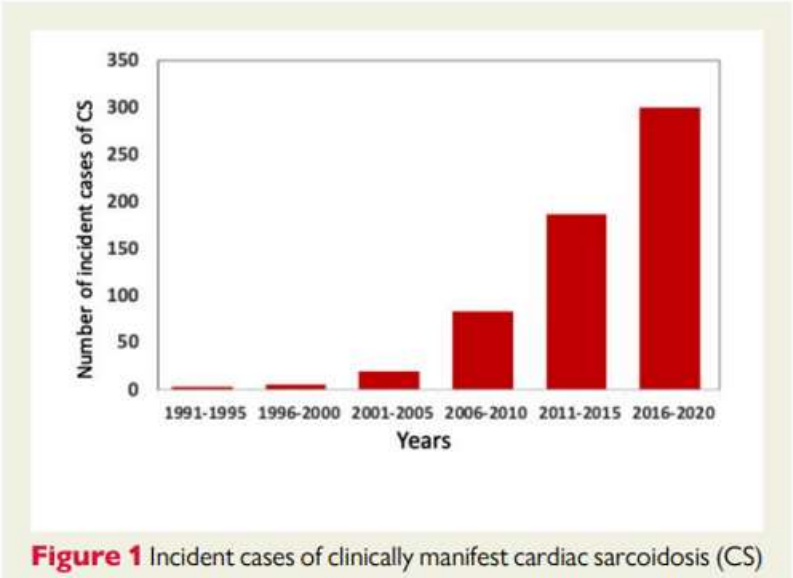


Figure 1 Incident cases of clinically manifest cardiac sarcoidosis (CS)

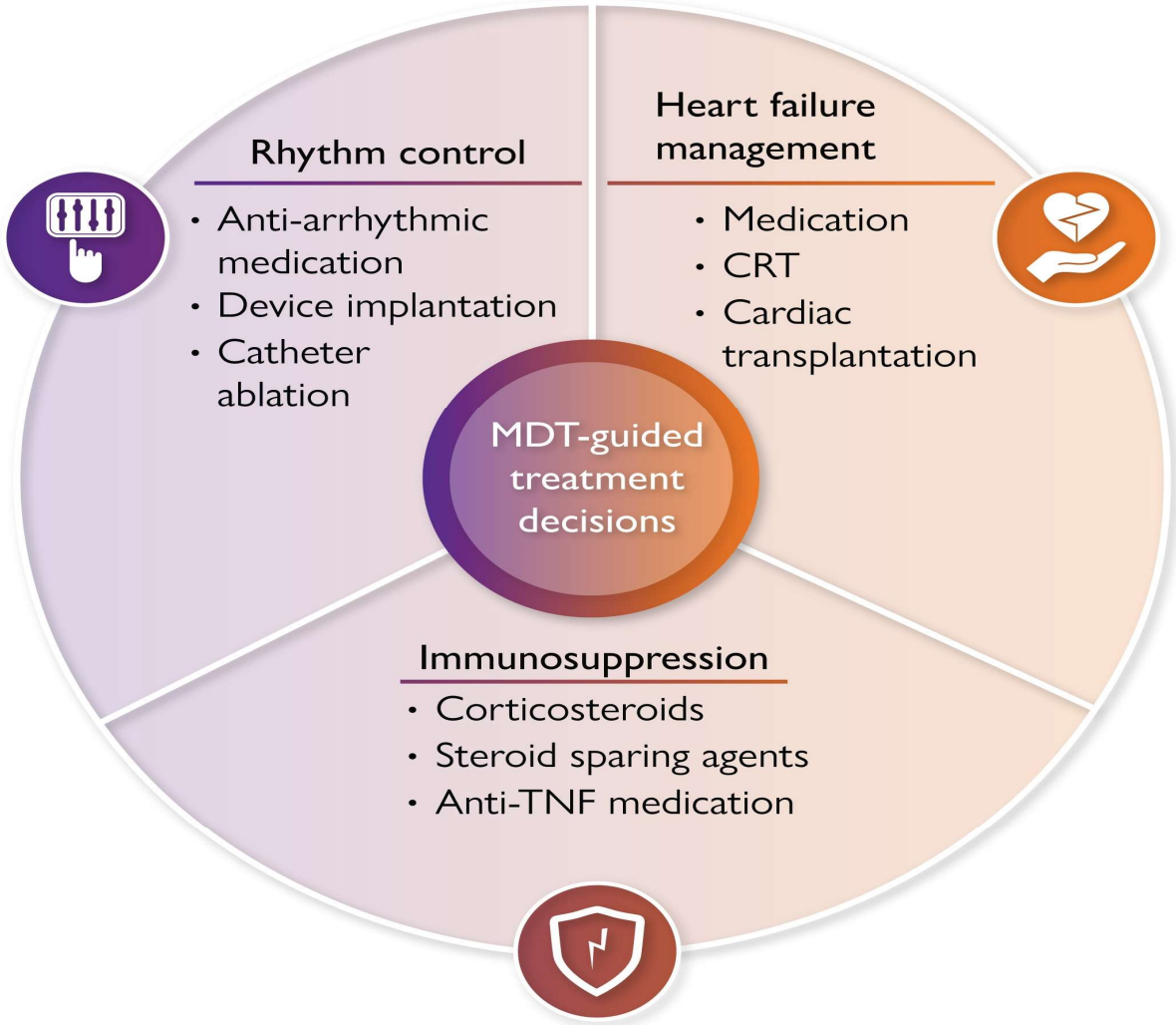
Cheng RK et al. Diagnosis and Management of Cardiac Sarcoidosis: A Scientific Statement From the American Heart Association *Circulation*. 2024

Lehtonen J et al Cardiac sarcoidosis: phenotypes, diagnosis, treatment, and prognosis. *Eur Heart J*.

Stadtspital Zürich

Kardiale Sarkoidose - Therapie

VASAS VASCULITIS Association Switzerland



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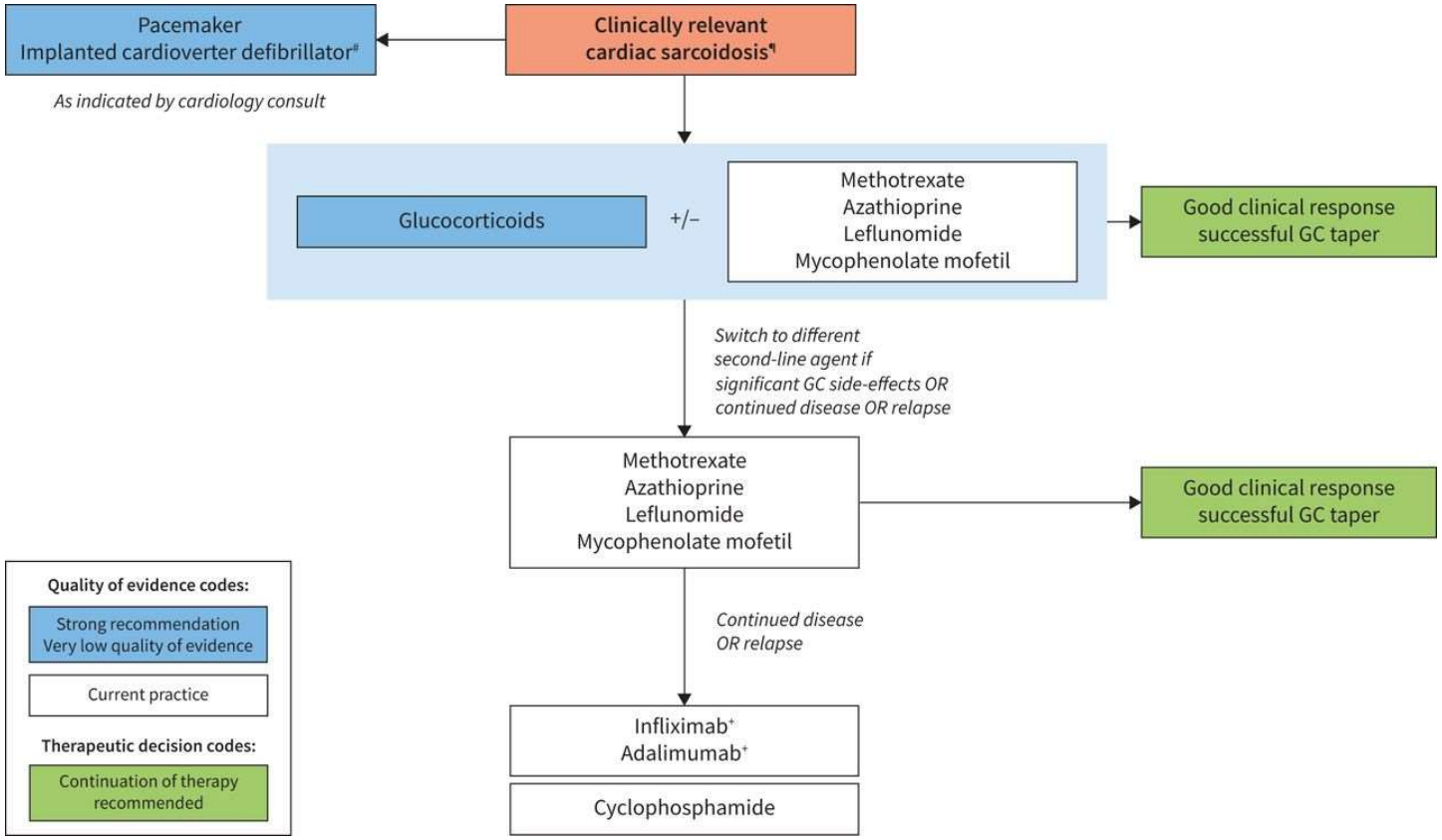
Kardiale Sarkoidose - Immunsuppression

VASAS VASCULITIS Association Switzerland



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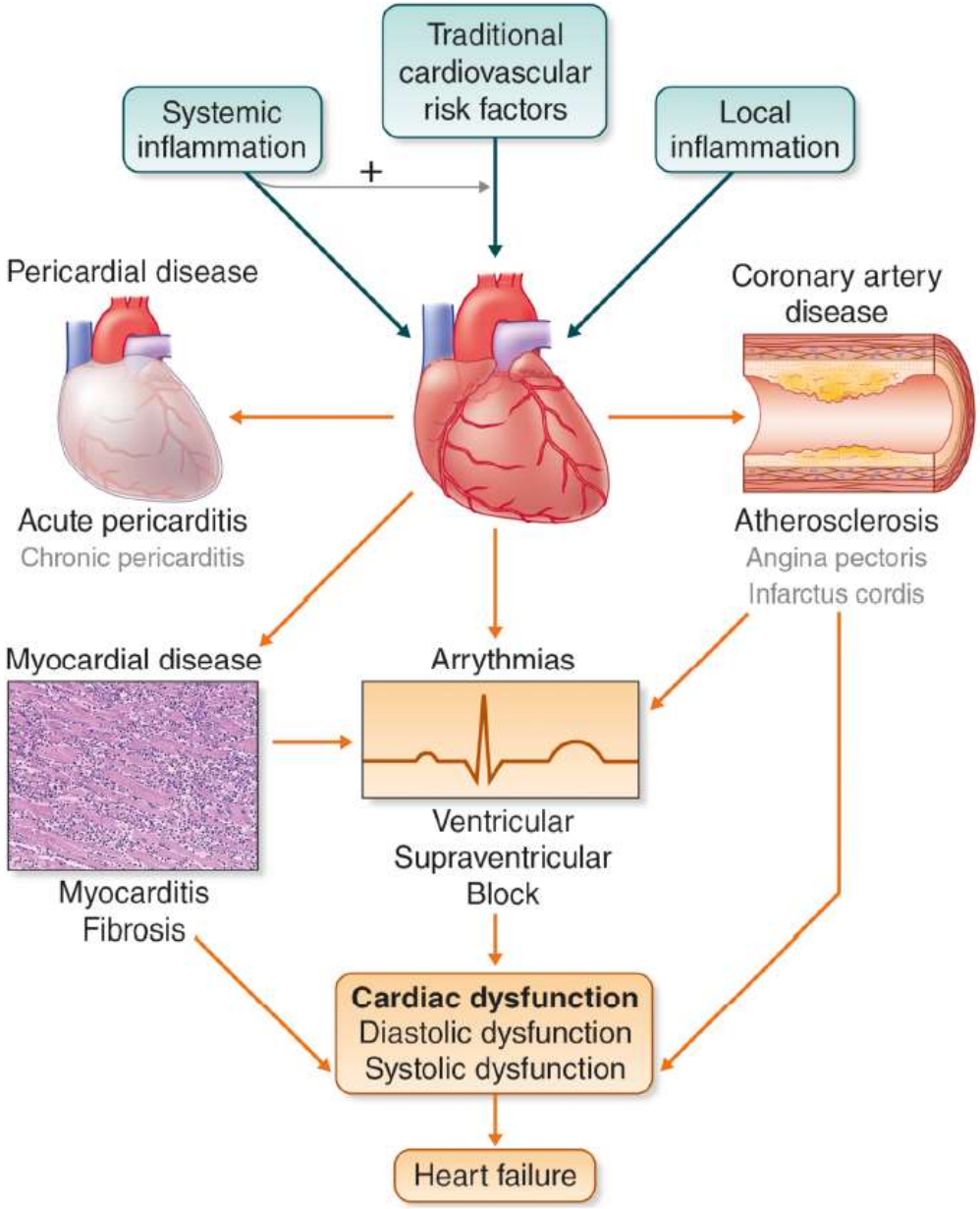
ERS OFFICIAL DOCUMENTS
R.P. BAUGHMAN ET AL.

Eur Respir J 2021; 58: 2004079 **ERS clinical practice guidelines on treatment of sarcoidosis**

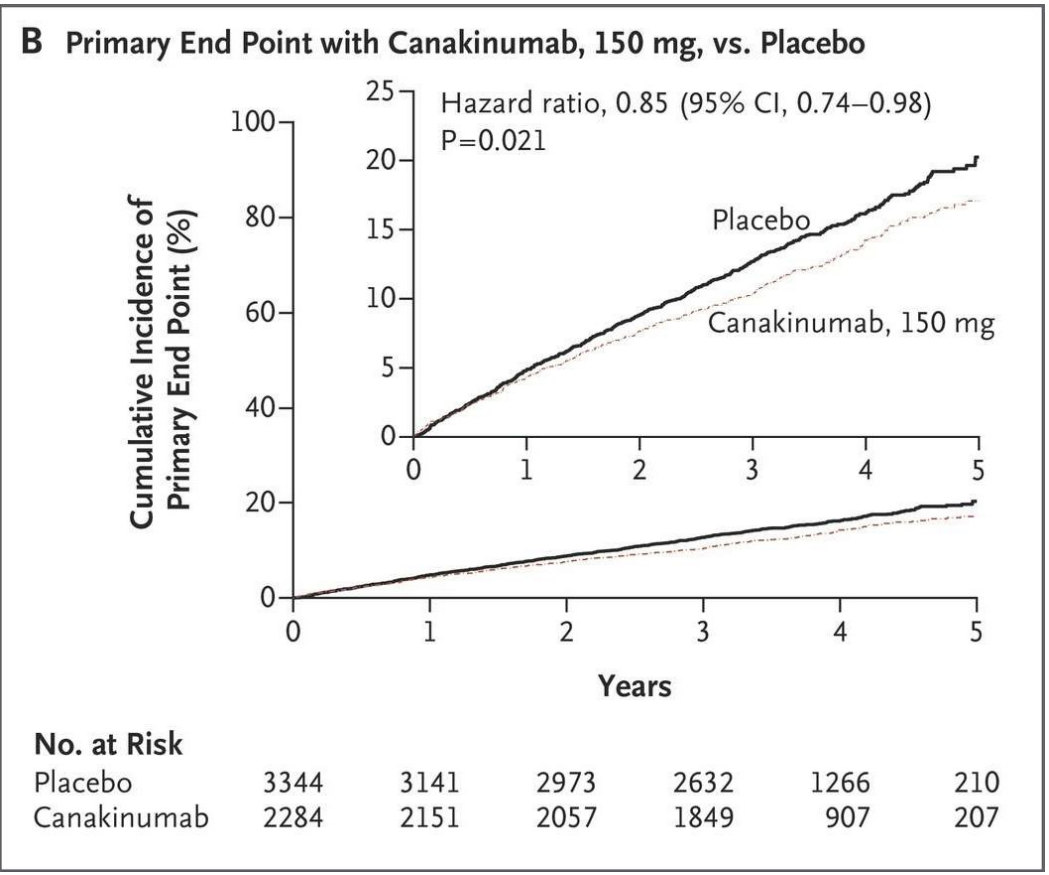


RA –
eine Systemerkrankung

Schwartz T, *et al. RMD Open* 2016;**2**:e000291. doi:10.1136/rmdopen-2016-000291

Stadtspital Zürich

Cumulative Incidence des primären Endpunktes



Signifikante Senkung von CV- Ereignissen durch die IL1 Blockade

Ridker PM et al. N Engl J Med 2017;377:1119-1131

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