A SZÍV IMMUNPATHOMECHANIZMUSÚ BETEGSÉGEI

Dr Végh Judit PhD

SE Reumatológiai és Immunológiai Klinika
Intenzív Terápiás osztály

Klinikai Immunológia és allergológia szakvizsga előkészítő tanfolyam

2025.09.29-10.10.

SEMMELWEIS
EGYETEM 1769

A SZÍV IMMUNMECHANIZMUSÚ BETEGSÉGEI

- PERICARDITIS
  - SICCA
  - EXUDATÍV
  - CONSTRITÍV
- MYOCARDITIS
  - INFECTIV
  - NONINFECTIV
- ENDOCARDITIS
  - INFECTIV
  - THROMBOTICUS
  - AUTOIMMUN
- CORONARITIS
- ATHEROSCLEROSIS
- INGERK. ÉS VEZ. RENDSZER ZAVARAI

INFLAMMATÓRIKUS MYOPERICARDITIS
INFLAMMATÓRIKUS PERIMYOCARDITIS
INFLAMMATÓRIKUS MYOPERICARDIALIS SZINDROMA

Elsődlegesen a szív alkotórészei ellen irányul az autoimmun folyamat (szervspecifikus)

iCMP, Reumás láz

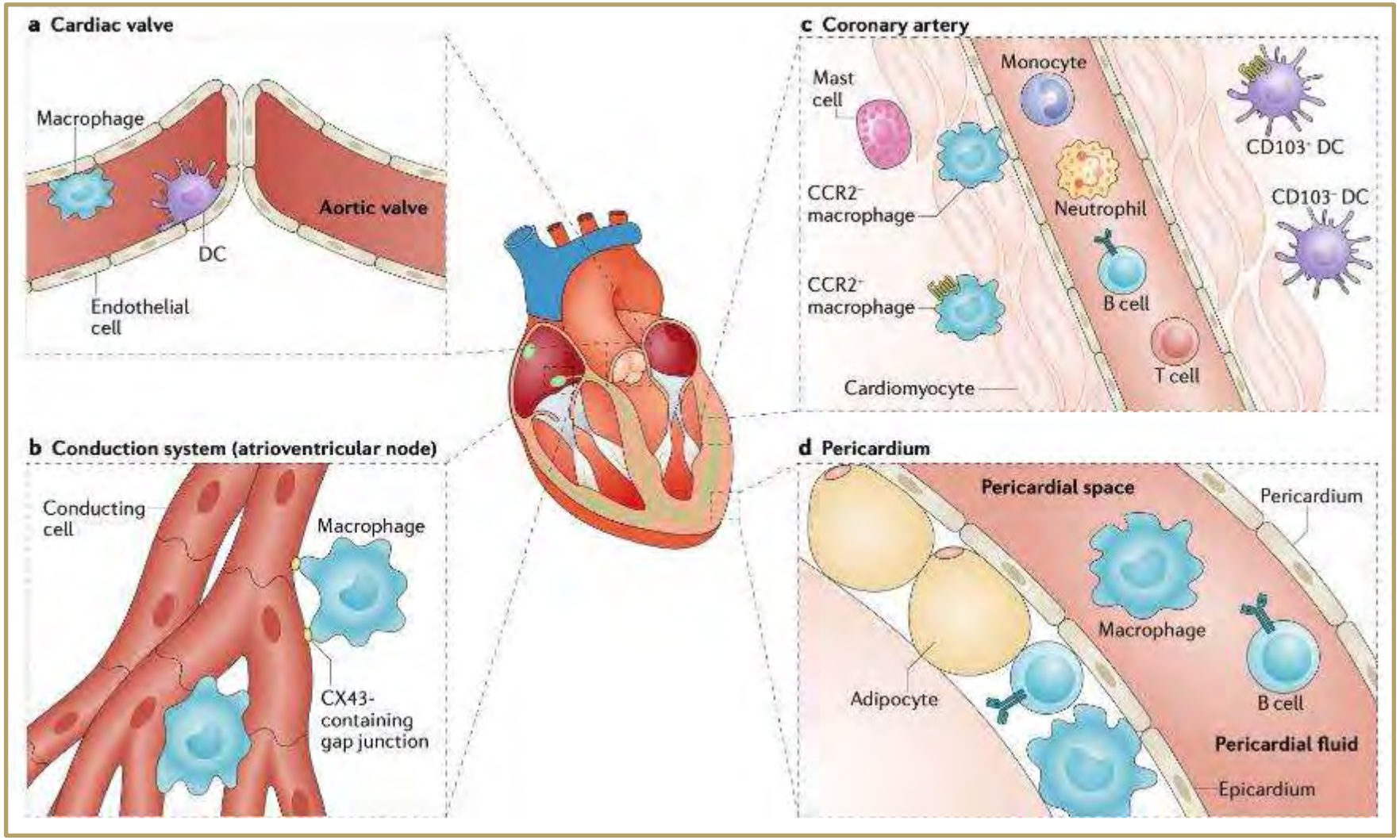
- PRIMAER

Egyéb autoimmun betegség részjelensége

PSS, RA, SLE, Sjögren sy, SPA, Vasculitis, PsA

- SECUNDAER

IMMUNHOMEOSZTÁZIS A SZÍVBEN



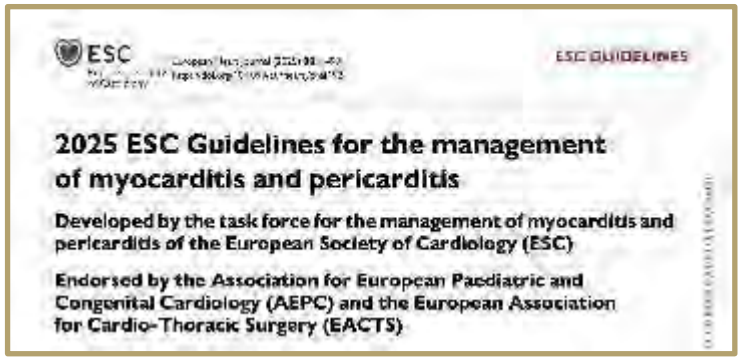
Cardioimmunology: the immune system in cardiac homeostasis and disease.Swirski FK, Nahrendorf M.Nat Rev Immunol. 2018 Dec;18(12):733-744. doi: 10.1038/s41577-018-0065-8.

PERICARDITIS

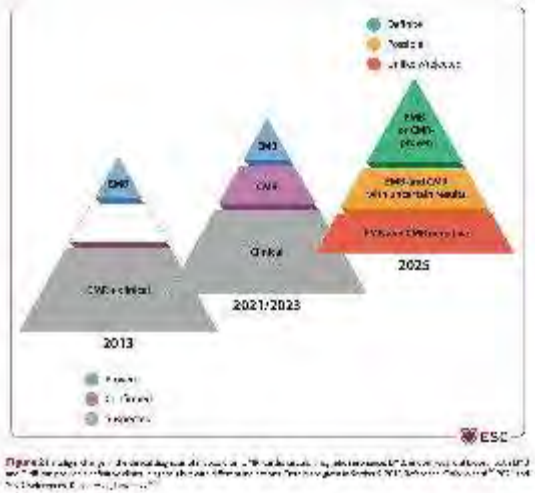
MYOCARDITIS

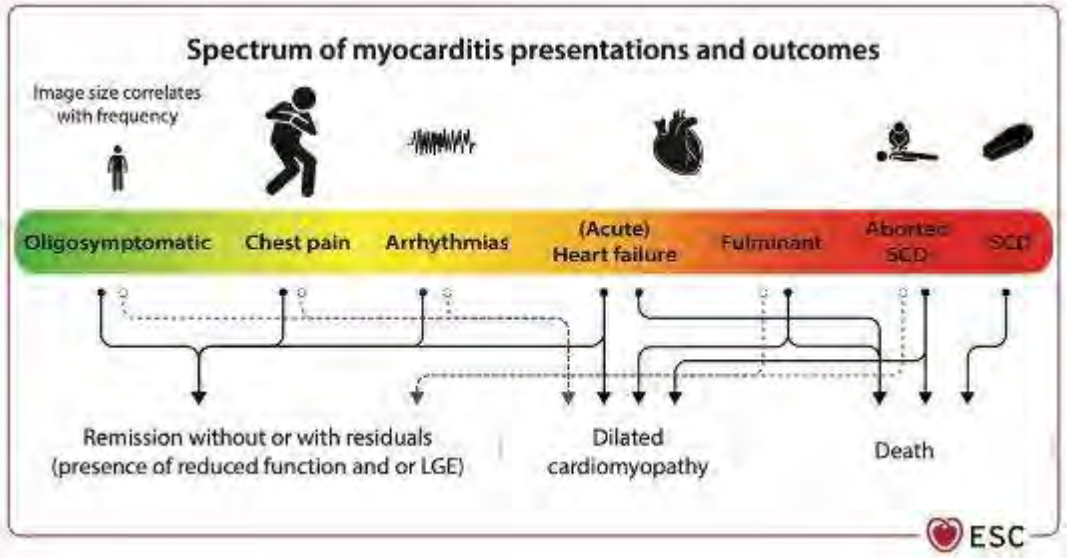
CARDIOMYOPATHIÁK IMMUNOLÓGIAI VONATKOZÁSAI

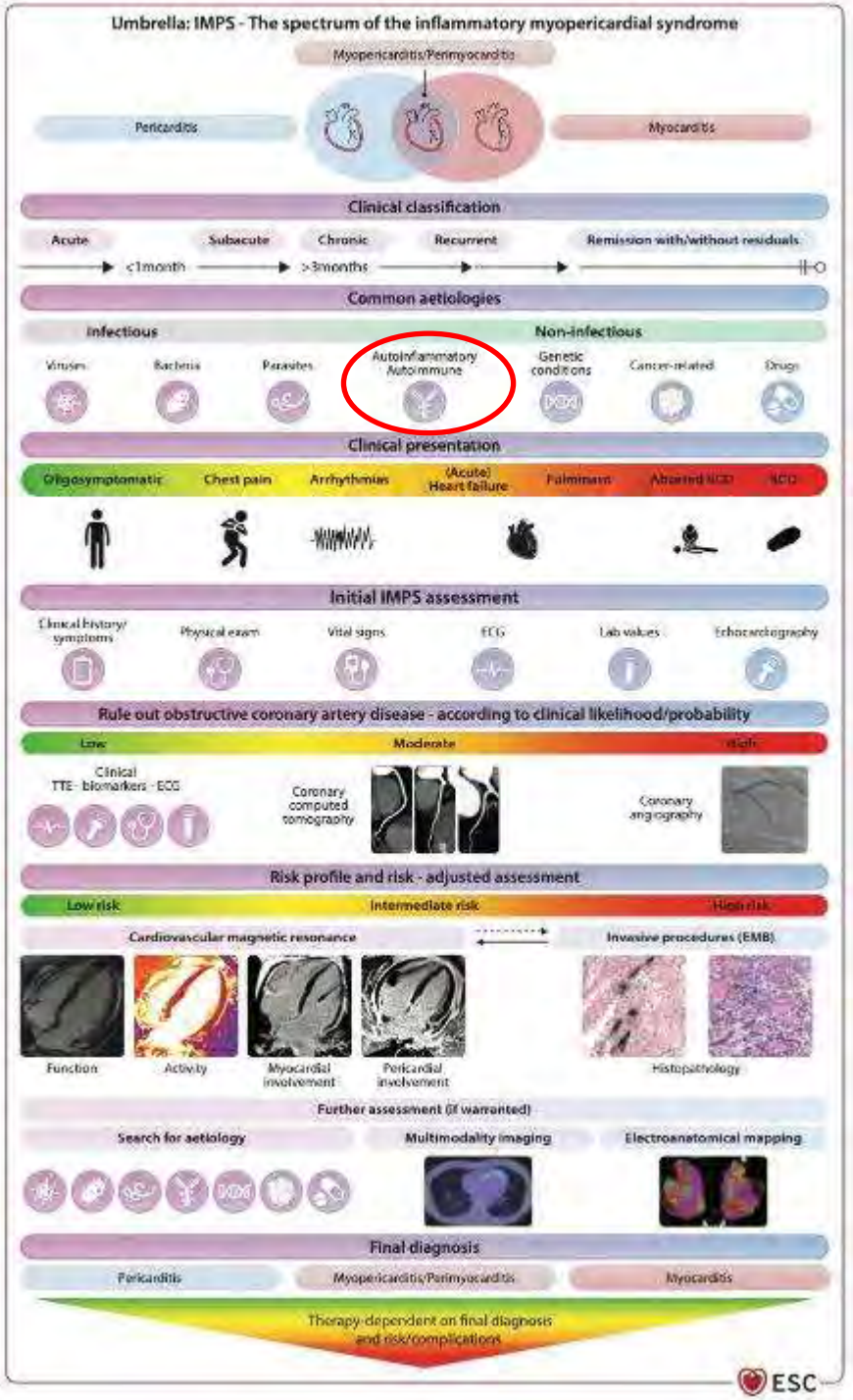
IMPS – INFLAMMATÓRIKUS MYOPERICARDIALIS SZINDROMA



- Általában együtt fordul elő
  perimyocarditis – myopericarditis
- Spektrumbetegség
- PARADIGMAVÁLTÁS





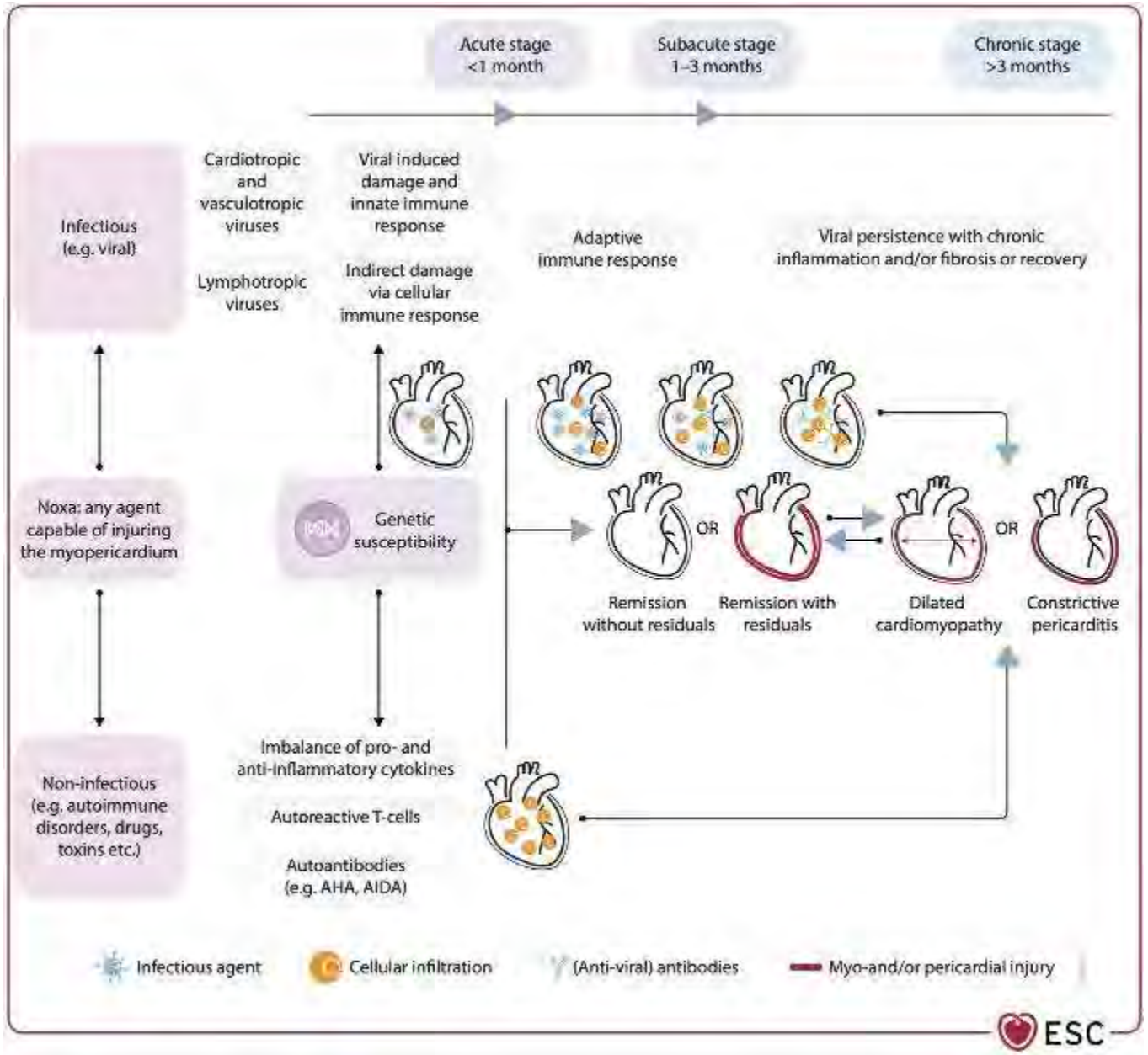


IMPS – terminológia - stádiumok

Terminology	Definition
IMPS	Umbrella term for inflammatory myocardial and pericardial syndromes
Myopericarditis	Predominant pericarditis[a]
Perimyocarditis	Predominant myocarditis[b]
Acute myocarditis	Duration of symptoms ≤4 weeks Fulminant if: • Acute onset[28] and haemodynamically unstable patients requiring inotropes or mechanical circulatory support
Complicated myocarditis	AM and ≥1 of the following:[28] • LVEF <50% on echocardiogram • Sustained ventricular arrhythmias • Advanced heart block • Heart failure • Cardiogenic shock
Acute pericarditis	Duration of symptoms ≤4 weeks
Subacute/ongoing myocarditis	Duration of symptoms >4 weeks to ≤3 months
Subacute/incessant pericarditis[c]	Duration of symptoms >4 weeks to ≤3 months
Chronic myocarditis/ pericarditis	Duration of symptoms >3 months
Inflammatory cardiomyopathy	Chronic myocarditis in association with cardiac dysfunction and ventricular remodelling with clinical phenotype of hypokinetic, either dilated or non-dilated cardiomyopathy with/without arrhythmogenic substrate
Recurrent myocarditis/ pericarditis	New symptoms or disease activity after clinical remission
Remission without residuals	Regression/absence of symptoms, normalization of ECG, biomarkers, imaging abnormalities (echocardiography and CMR)
Remission with residuals	Regression/absence of symptoms, persistence of abnormalities on ECG, biomarkers and/or imaging (functional and/or structural abnormalities in echocardiography or CMR)

2025 ESC Guidelines for the management of myocarditis and pericarditis.
Schulz-Menger J, et al. Eur Heart J. 2025. Aug 29:ehaf192. doi: 10.1093/eurheartj/ehaf192.

IMPS – stádiumok

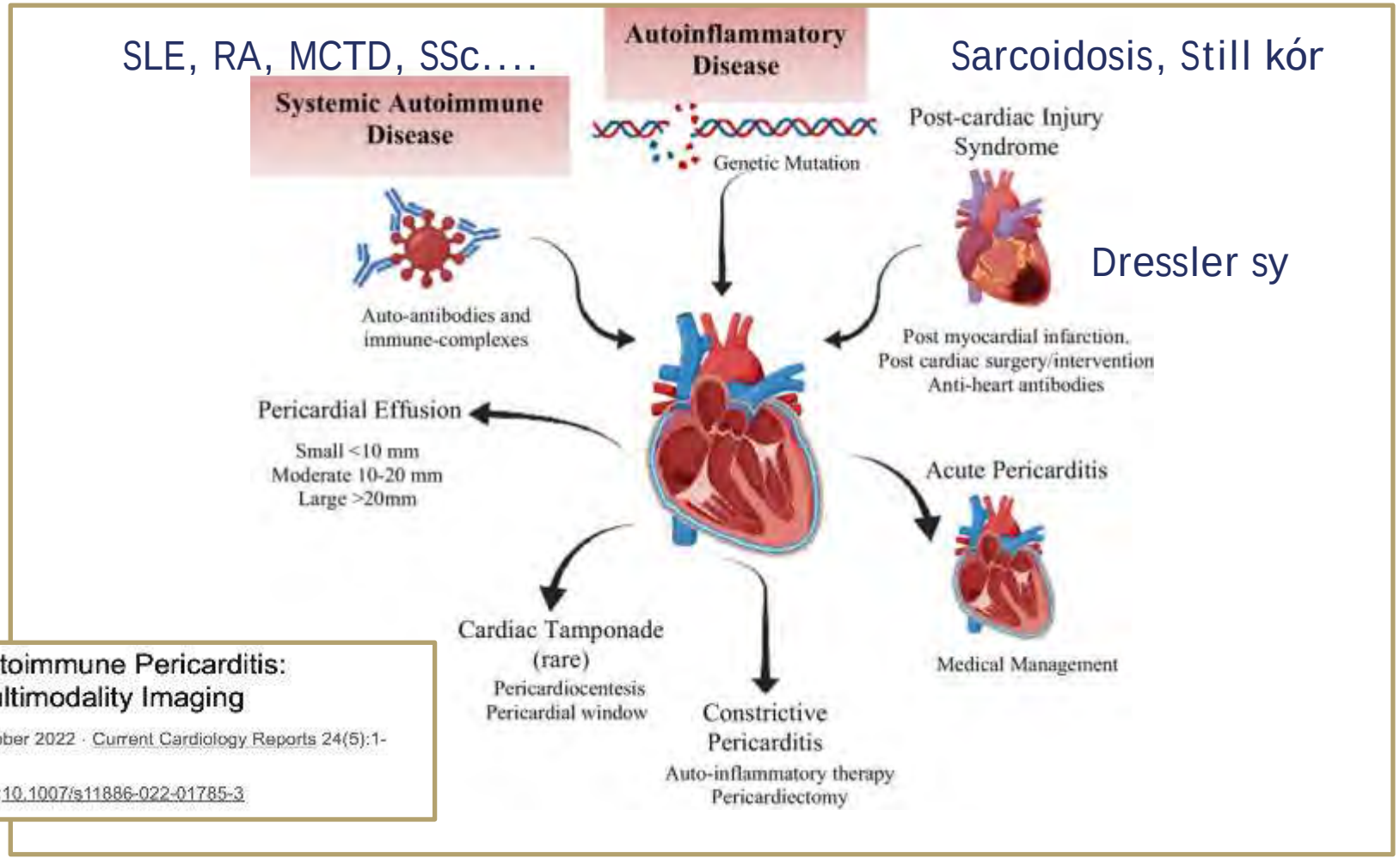


2025 ESC Guidelines for the management of myocarditis and pericarditis.
Schulz-Menger J, et al. Eur Heart J. 2025. Aug 29:ehaf192. doi: 10.1093/eurheartj/ehaf192.

PERICARDITIS

Dr Végh Judit PhD
főorvos

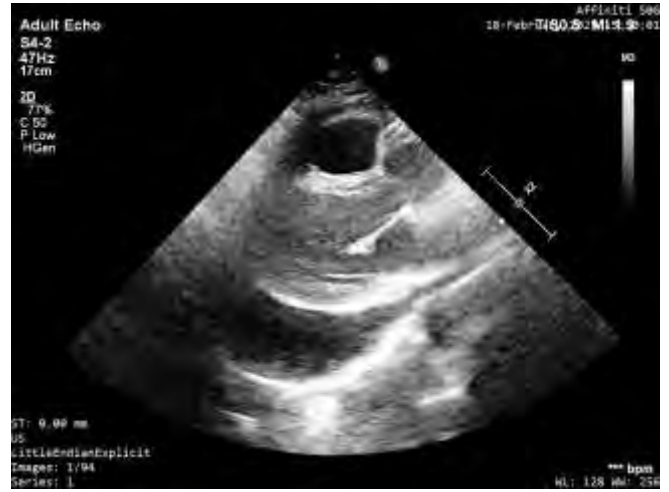
Autoimmun PERICARDITIS okai és kimenetele

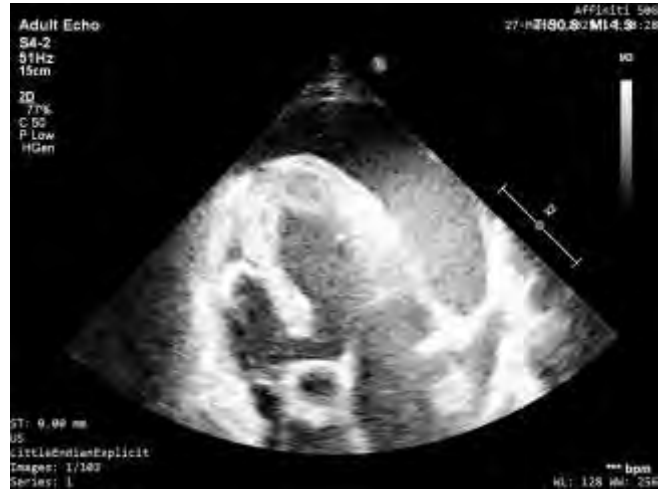


Autoimmune Pericarditis: Multimodality Imaging

October 2022 · Current Cardiology Reports 24(5):1-13

DOI:10.1007/s11886-022-01785-3

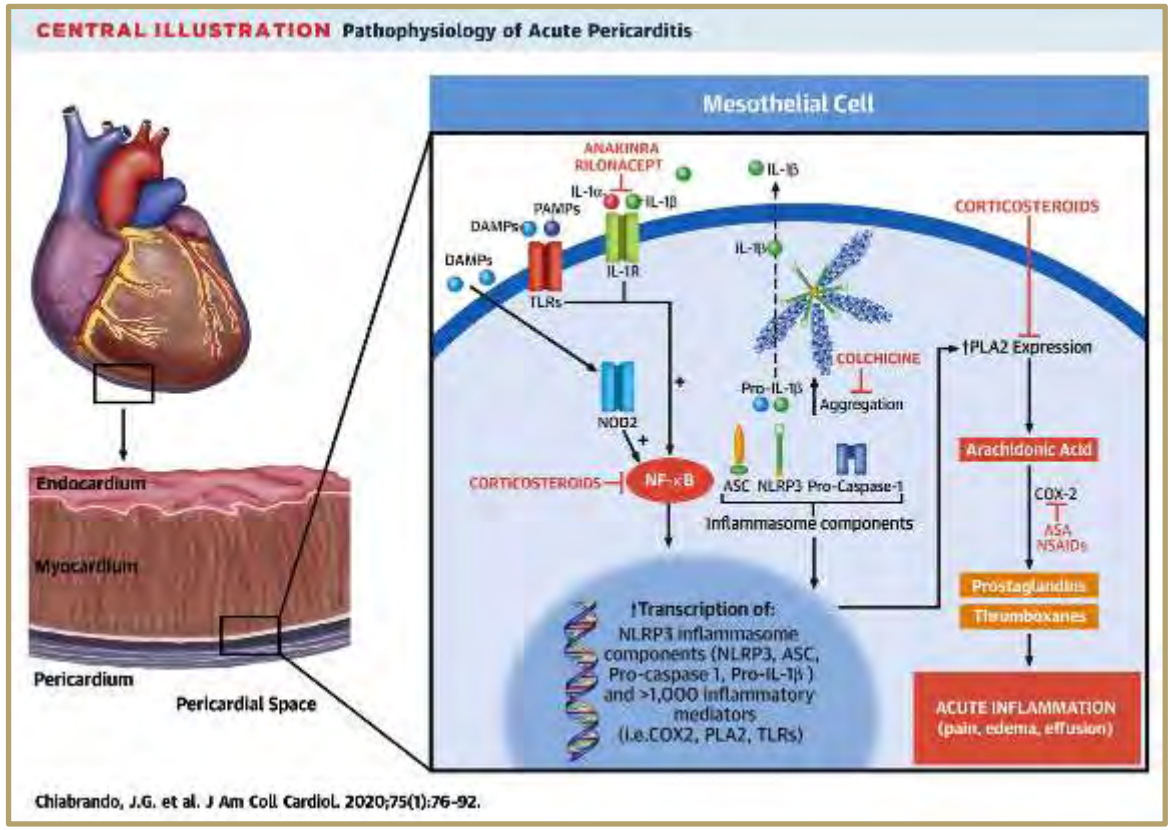




PERICARDITIS

MECHANIZMUS

- hypersensitiv reakció
- hapten mechanizmus
- autoantitestek
- Danger elmélet : toxicus ártalom - sejthalál danger szignál (DAMP)



Diagnosztikus kritériumok

Pericarditis
Clinical presentation[b] with >1 additional criterion
Clinical presentation[b] with 1 additional criterion
Only clinical presentation[b] without additional criteria

Pericarditis	Additional criteria
Pericardial rubs	
PR depression, widespread ST-segment elevation	
C-reactive protein elevation	
New or worsening pericardial effusion	
Pericardial oedema and/or LGE (CMR findings)	

2025 ESC Guidelines for the management of myocarditis and pericarditis.
Schulz-Menger J, et al. Eur Heart J. 2025. Aug 29:ehaf192. doi: 10.1093/eurheartj/ehaf192.

PERICARDITIS kezelés

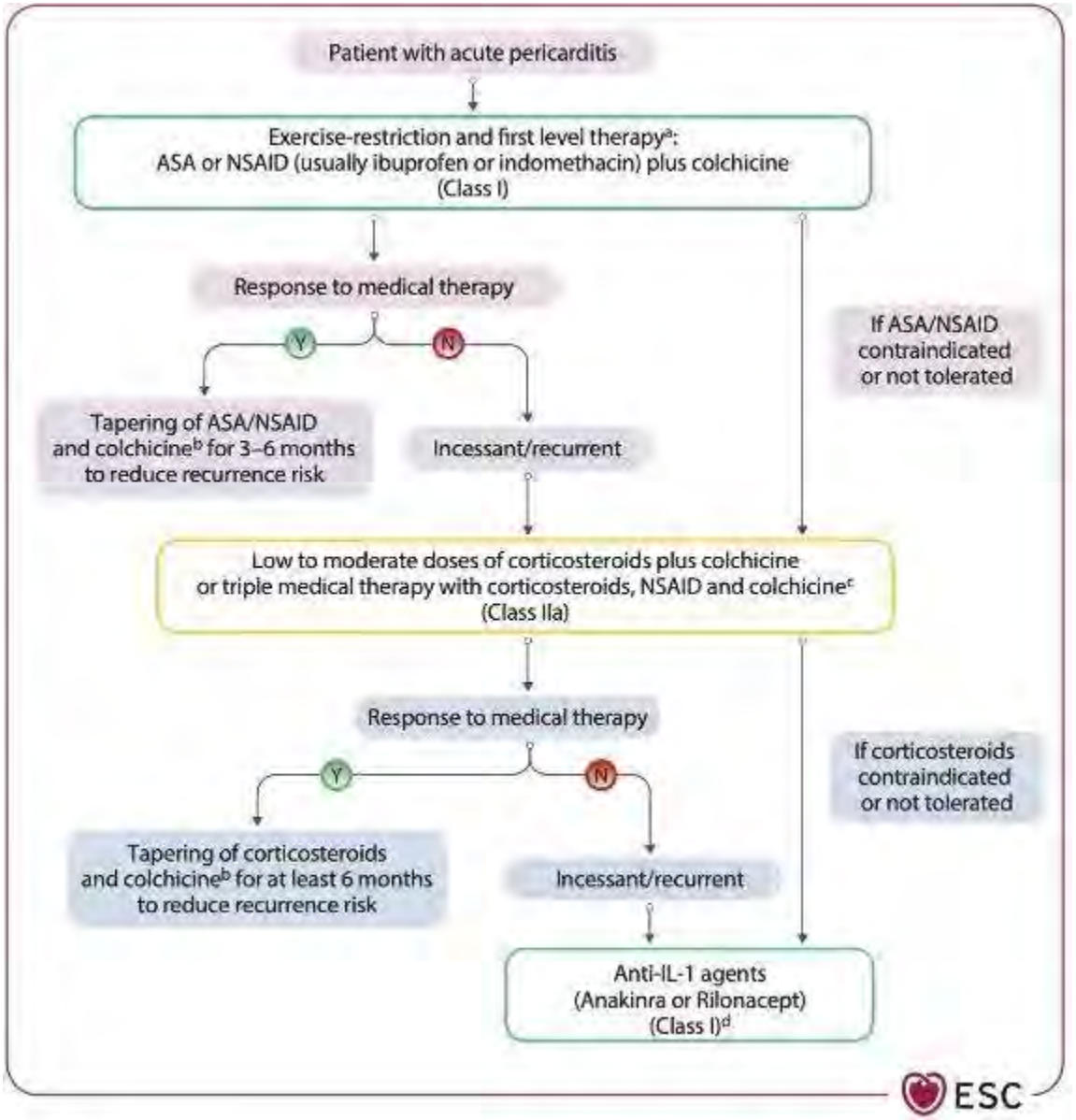
Therapy	Dosing	Duration[a]	Tapering[a]
Aspirin[a]	750–1000 mg 3 times daily	1–2 weeks	Decrease by 250 mg every 1–2 weeks
Ibuprofen[a]	600–800 mg 3 times daily	1–2 weeks	Decrease by 200 mg every 1–2 weeks
Indomethacin	25–50 mg 3 times daily	1–2 weeks	Decrease by 25 mg every 1–2 weeks
Colchicine[b]	0.5 mg once daily (<70 kg or severe renal impairment) or 0.5 mg twice daily	3–6 months	Not required
Prednisone	0.2–0.5 mg/kg/day	2–4 weeks	Several months
Treatment for recurrences only:			
Azathioprine	Starting with 1 mg/kg/day then gradually increased to 2–3 mg/kg/day	Several months	Several months
IVIG	400–500 mg/kg i.v. daily for 5 days	5 days	Not required
Anakinra	1–2 mg/kg/day up to 100 mg/day in adults	At least 6 months/ >12 months	Needed (at least 3–6 months)/ unknown
Rilonacept	320 mg once daily followed by 160 mg weekly		

© ESC 2025

Prednisone dose[a]	Starting dose 0.20–0.50 mg/kg/day[a]	Tapering[b]
Prednisone daily dose	>50 mg	10 mg/day every 1–2 weeks
	50–25 mg	5–10 mg/day every 1–2 weeks
	25–15 mg	2.5 mg/day every 2–4 weeks
	<15 mg	1.25–2.5 mg/day every 2–6 weeks

© ESC 2025

Autoimmun **betegségek** - lehet **aktivitási** jel
First line : steroid
Scleroderma - steroid **ritkán**, ekkor igen !



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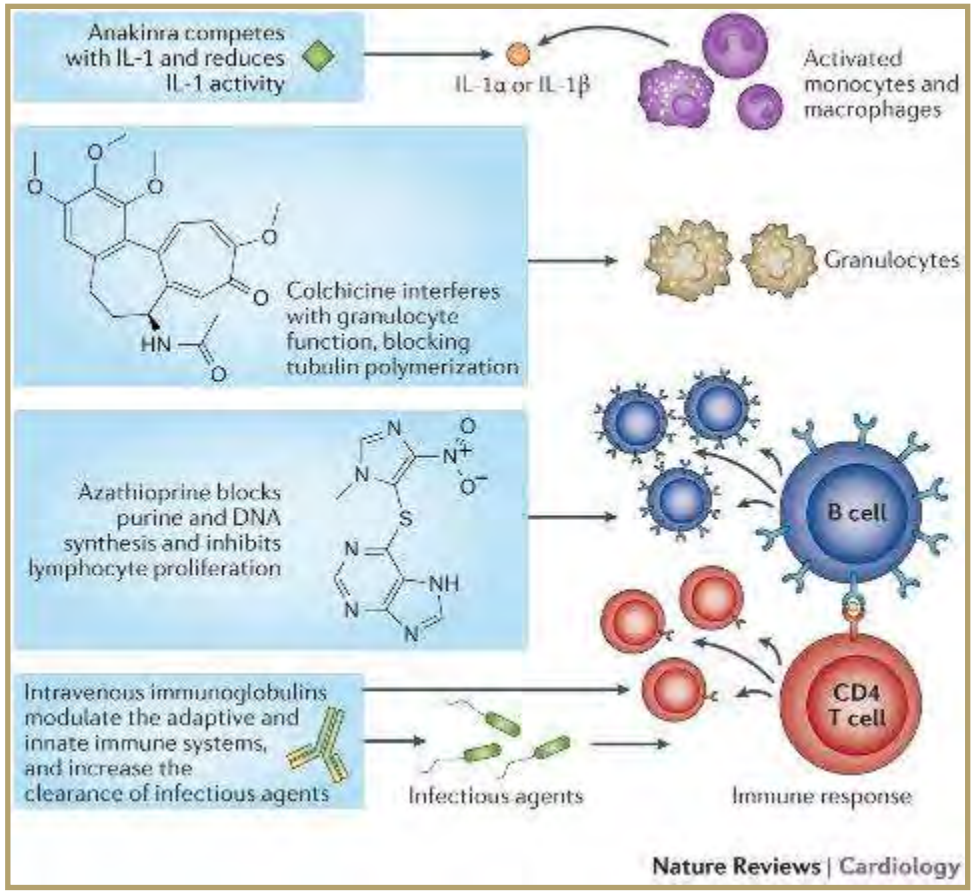
© ESC 2025



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First line : steroid
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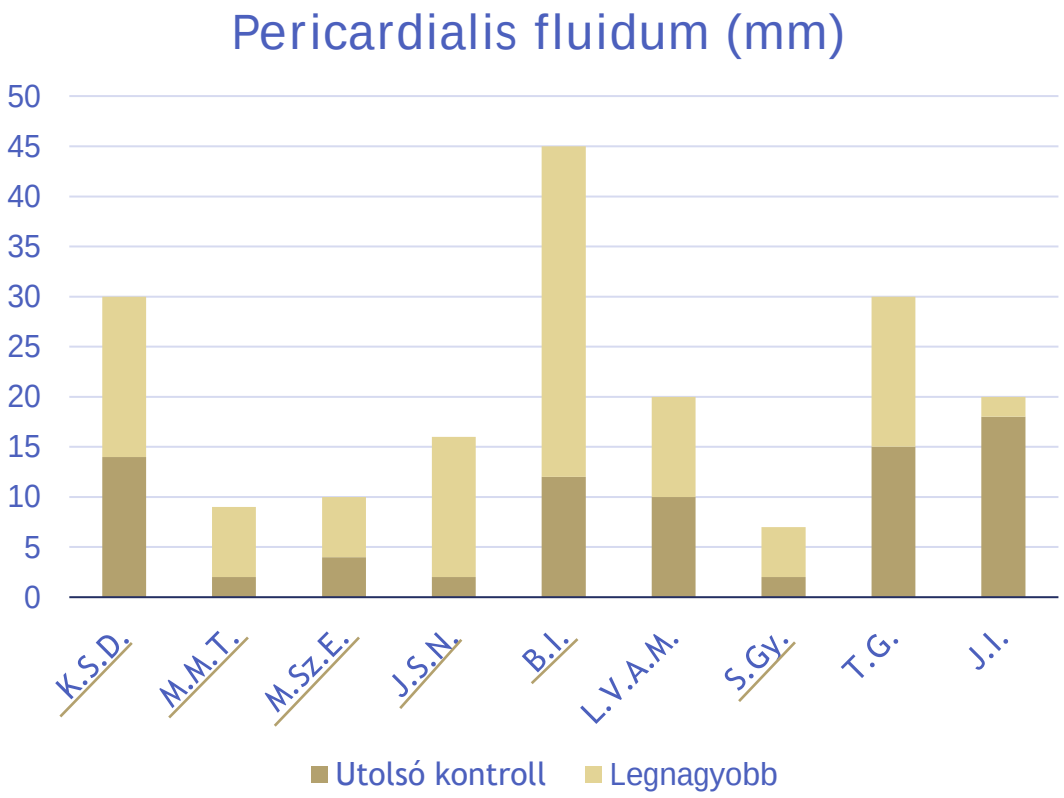
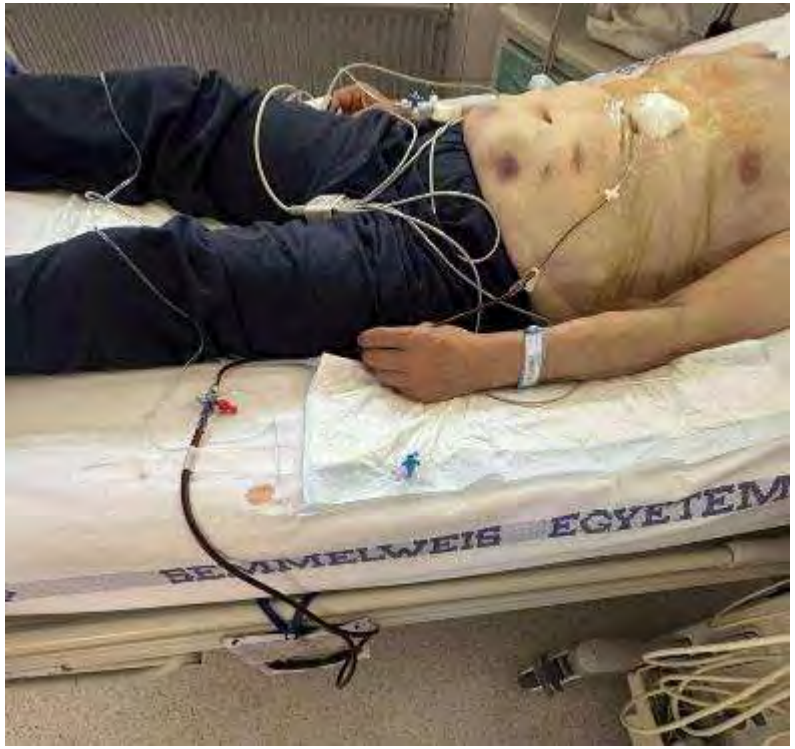
IL-1 gátlóval szerzett tapasztalatok

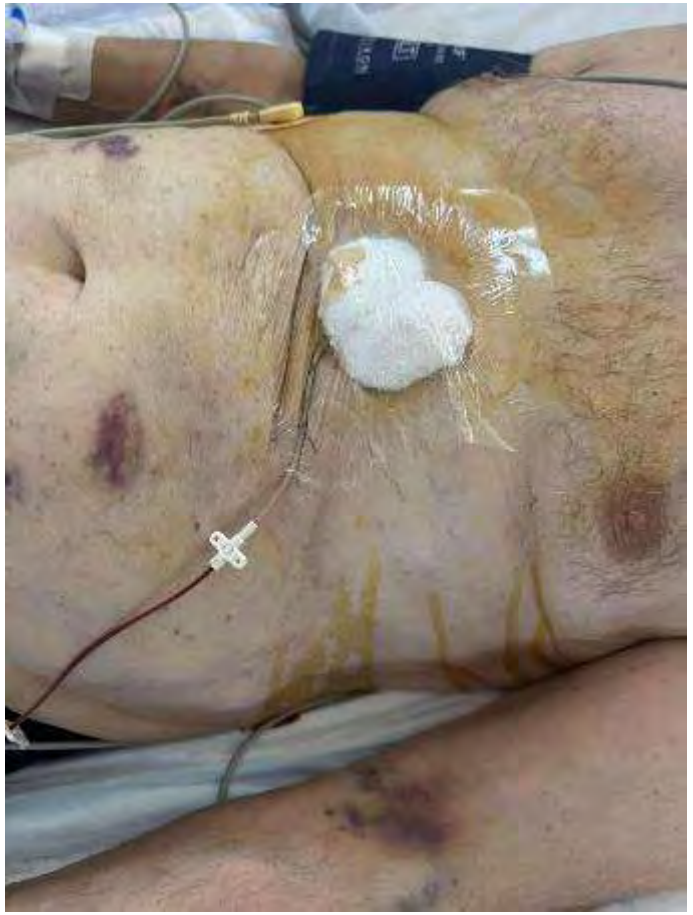
2024. szeptember és 2025. augusztus közötti időszak

Név	AI betegség	Immunszerológia	CRP	We	PCT	Gyógyszeres terápia
K.S.D.	RP	**negatív**	6,1	34	<0,5	Kineret sc. inj + Colchicin, sz.e Ibuprofen
M.M.T.	RP	RF neg. ACCP 30	48	82	<0,5	Kineret sc. inj
M.Sz.E	RA	RF 112 ACCP > 1600 Nuklearis AT poz.	45,7	40	<0,5	Medrol + Kineret sc. inj.
J.S.N.	SLE+Sj	ANA poz 1:160 SSA 141, SSB 210 dsDNS 20, C1q 54	112	86	<0,5	Plaquenil + Imuran + Kineret sc. inj
B.I.	RA	RF 48 ACCP 620	76	55	<0,5	MTX + Medrol + Kineret sc. inj + Colchicin + Plaquenil
L.V.A.M	SSc+Sj	ANA 1:160 Centromer AT poz. SSA 119	8	48	<0,5	**Nem kap terápiát** **Malignus folyamat kizárása**
S.Gy.	RA	RF 195 ACCP >1600	111	69	<0,5	MTX + Kineret sc. inj
T.G.	**Kivizsgálás**	ANA poz 1:80 C4 ↓	24	36	<0,5	Colchicin
J.I	**Kivizsgálás**	**Negatív** QF poz.	12	20	<0,5	Medrol**, látens TBC miatt** Rifampicin

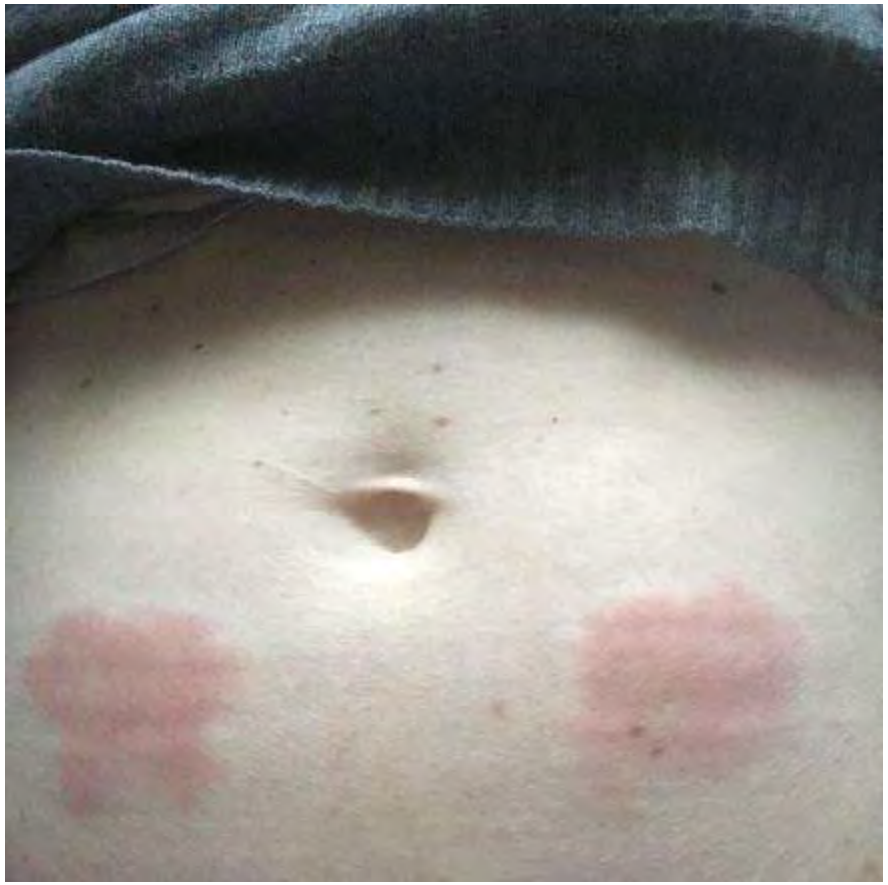


PERICARDIOCENTEZIS





Egy betegnél pericardiocentesis, majd fenestráció történt
Saját felvétel, a beteg beleegyezésével



Injekció beadás helyén létrejött reakció
Saját felvétel, a beteg beleegyezésével

MYOCARDITIS

CARDIOMYOPATHIÁK IMMUNOLÓGIAI VONATKOZÁSAI

Dr Végh Judit PhD
főorvos

INFLAMMATÓRIKUS CARDIOMYPATHIA

WHO 1995

Trachtenberg BH, Hare JM: Inflammatory Cardiomyopathic syndromes. Circ Res 2017 Sep 15;121(7):803-818. doi: 10.1161/CIRCRESAHA.117.310221.

INFLAMMATÓRIKUS MYOPERICARDIALIS SZINDROMA

ESC 2025

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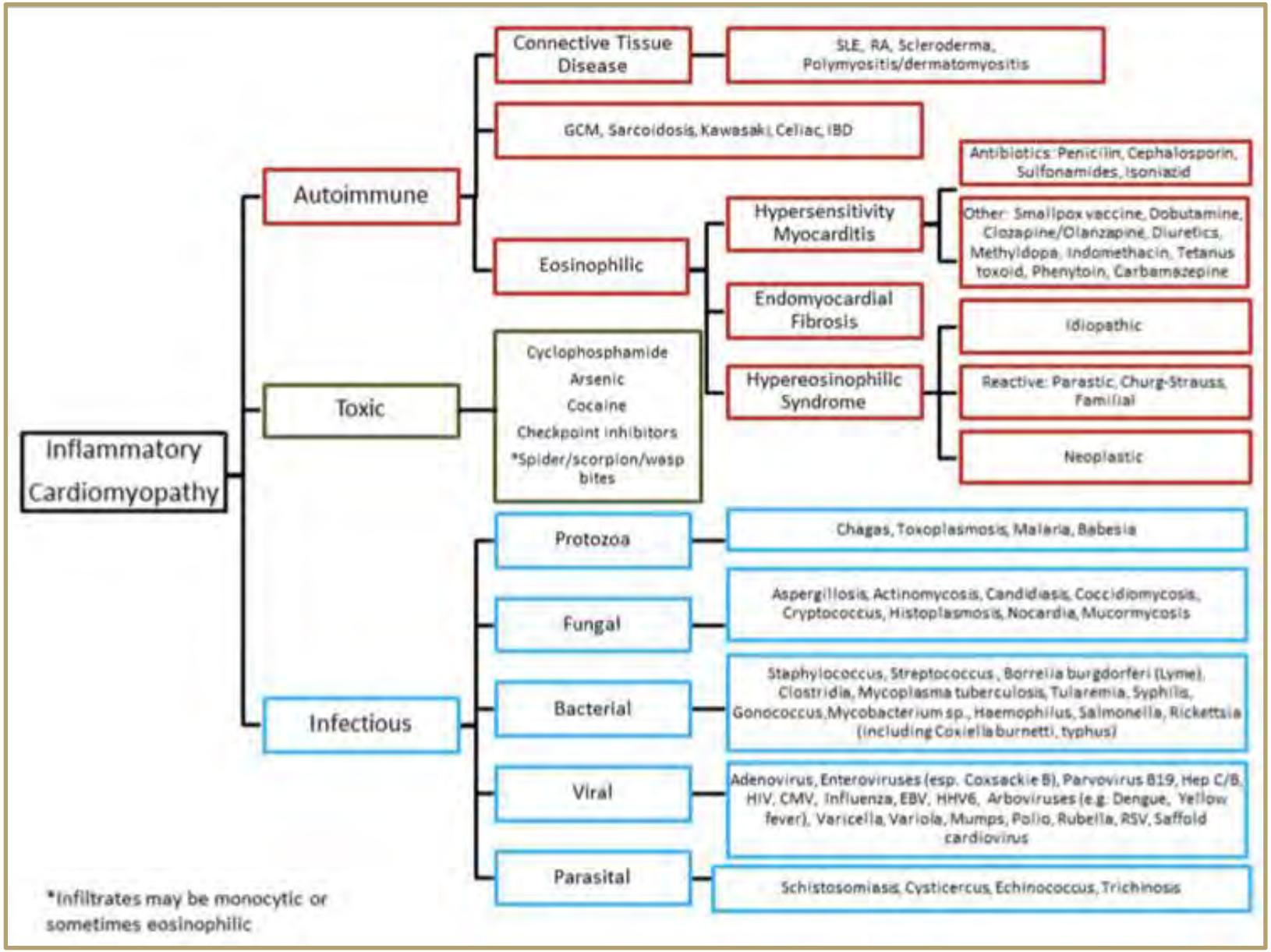
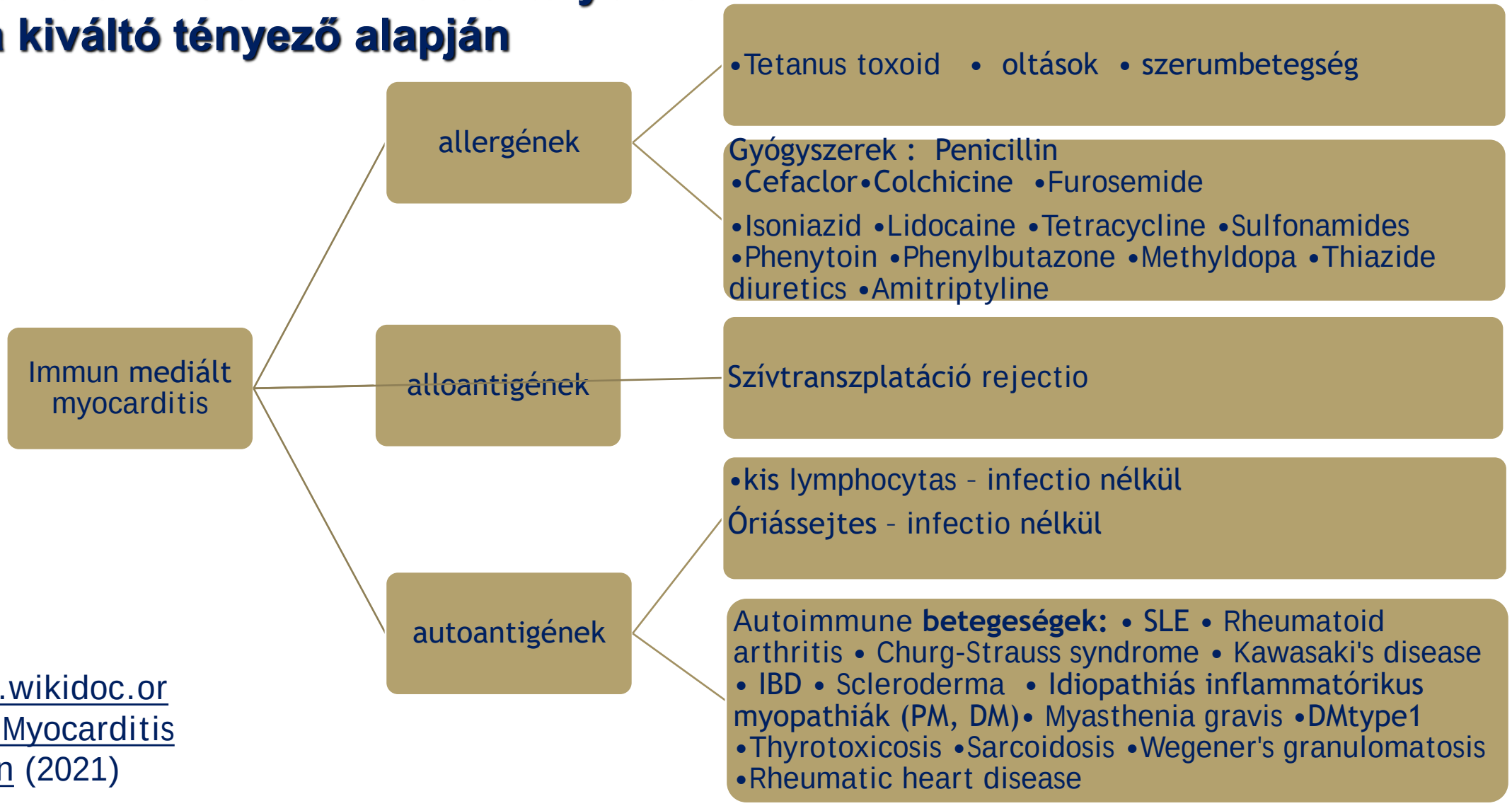


Immun mediált MYOCARDITIS osztályozás a kiváltó tényező alapján

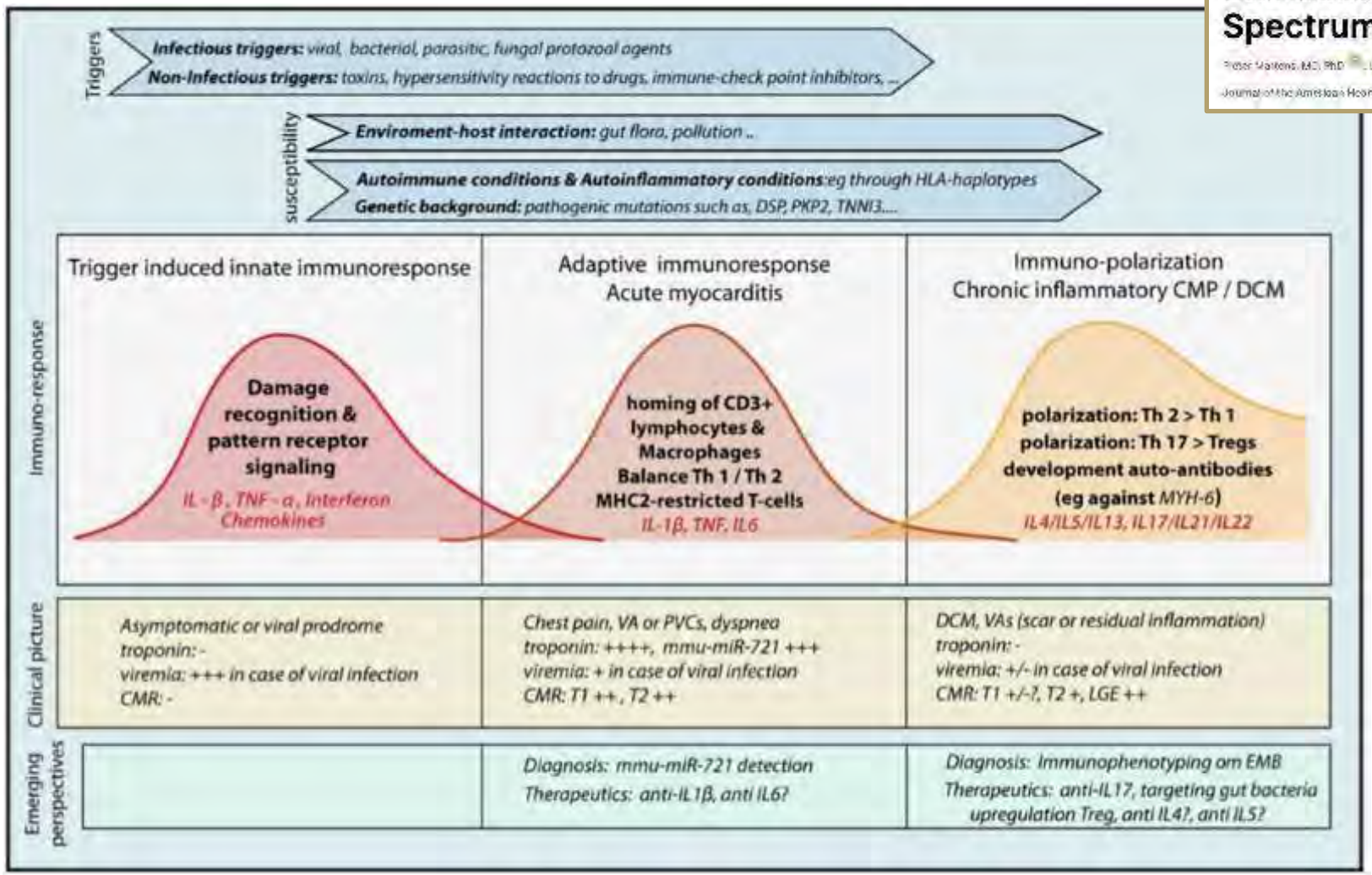


https://www.wikidoc.org/index.php/Myocarditis_classification (2021)

MYOCARDITIS LEFOLYÁSA


REVIEW ARTICLE

Diagnostic Approach for Suspected Acute Myocarditis: Considerations for Standardization and Broadening Clinical Spectrum



MYOCARDITIS - T HELPER SEJTEK

Journal of Clinical Medicine

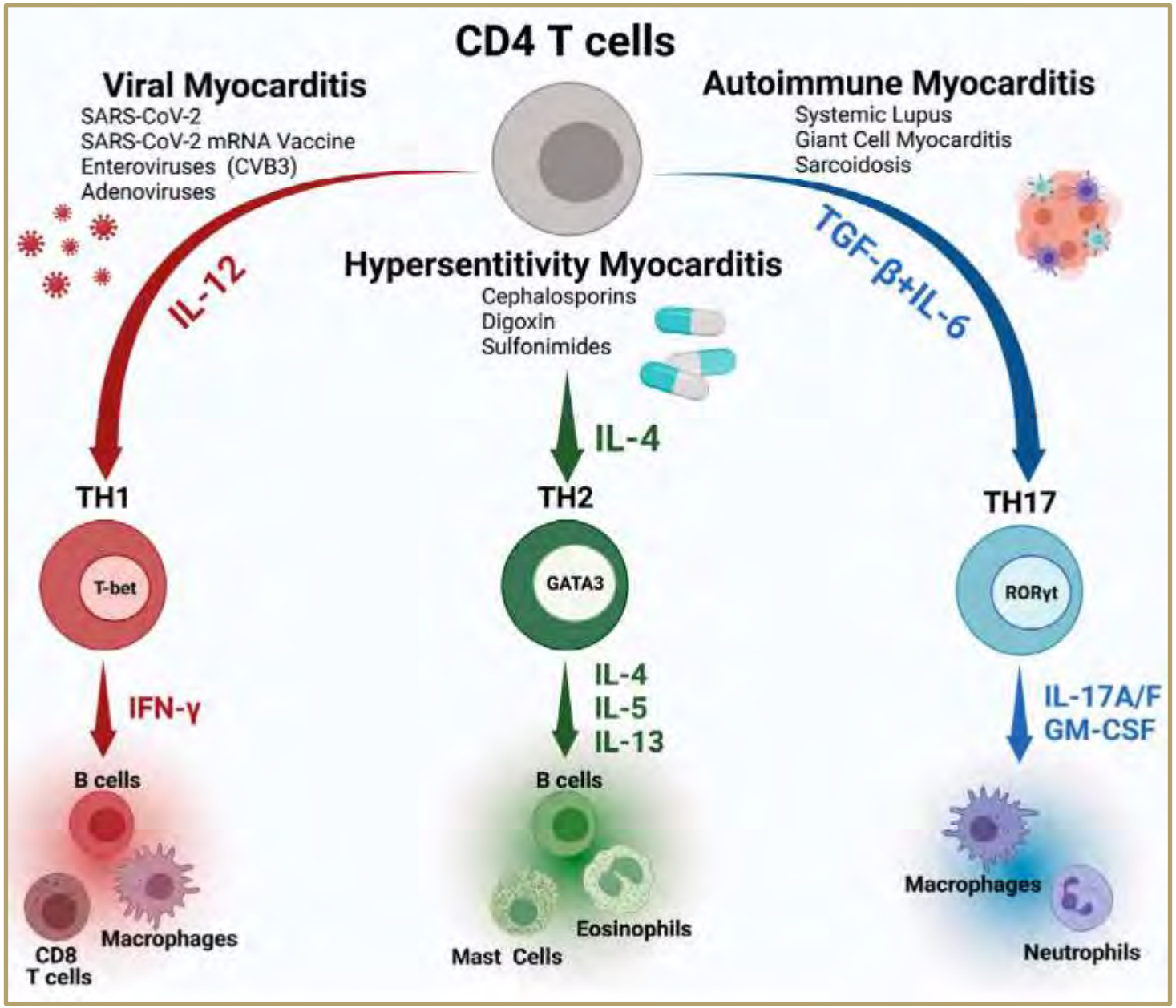
MDPI

Conference Report

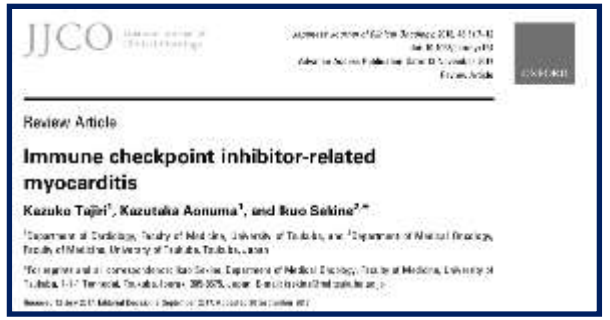
Meeting the Challenges of Myocarditis: New Opportunities for Prevention, Detection, and Intervention—A Report from the 2021 National Heart, Lung, and Blood Institute Workshop

Daniela Čihákova [1,2], Yang Shi [3], Bishow Adhikari [3], W. Patricia Bandettini [3], Madeleine W. Cunningham [4], Narasimhan Danthi [3], Matthias G. Friedrich [5], Peter Liu [6], Lisa Schwartz Longacre [3], Douglas L. Mann [7], Filip K. Swirski [8], W. H. Wilson Tang [9], Guofei Zhou [10] and Leslie T. Cooper, Jr. [11,*] on behalf of the Workshop Speakers

J. Clin. Med. **2022**, *11*, 5721. https://doi.org/10.3390/jcm11195721



Immun CHECK POINT INHIBITOR related MYOCARDITIS


JJCO

Review Article

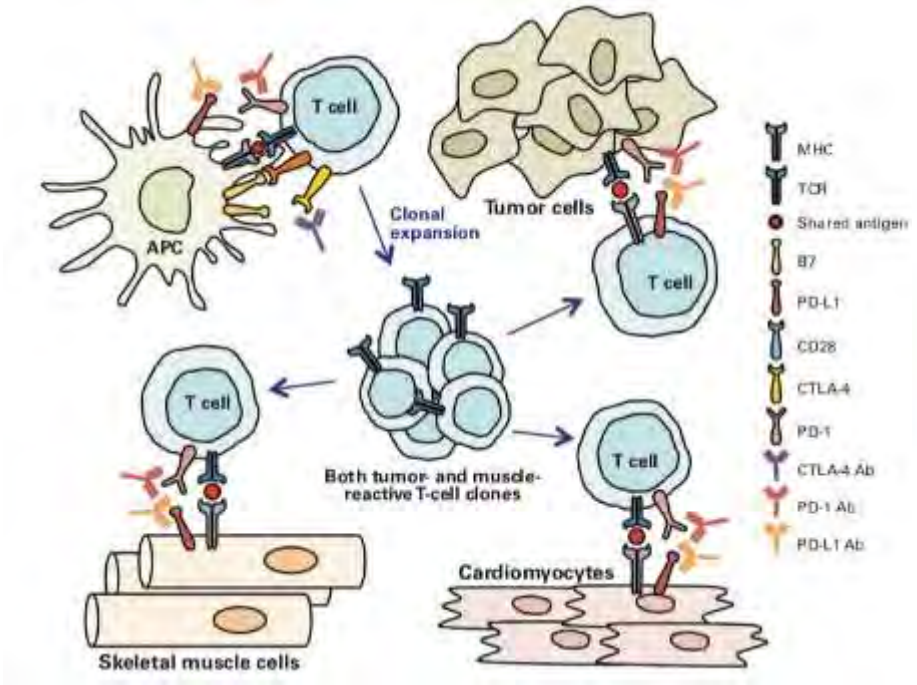
Immune checkpoint inhibitor-related myocarditis

Kazuko Tajiri[1], Kazutaka Aonuma[1], and Ikuo Sekine[2,*]

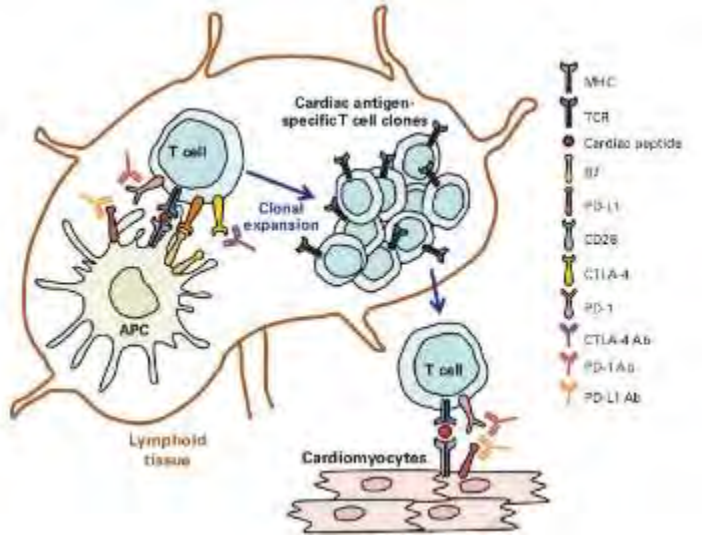
Fulmináns myocarditis
•kezelés 2-4 hetében
•Troponin, CK
•EKG, ehocardiographia
•(nincs DCM, de akineticus)

Kombinációban különösen (nivolumab + ipilimumab) – mortalitás 60 %

Pemprolizumab – PD-1 ell AT
Nivolumab - PD-1 ell AT
Atezolimumab – PD-L1 ell AT
Ipilimumab – CTLA-4 ell AT



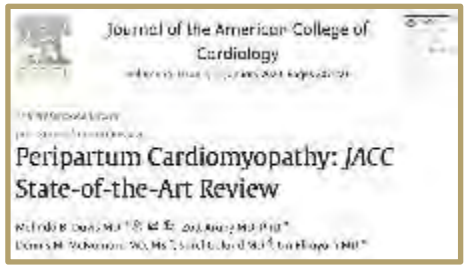
A szívizomzaton és a simaizomzaton ugyanaz az ag presentálódik, mint a tumorsejteken



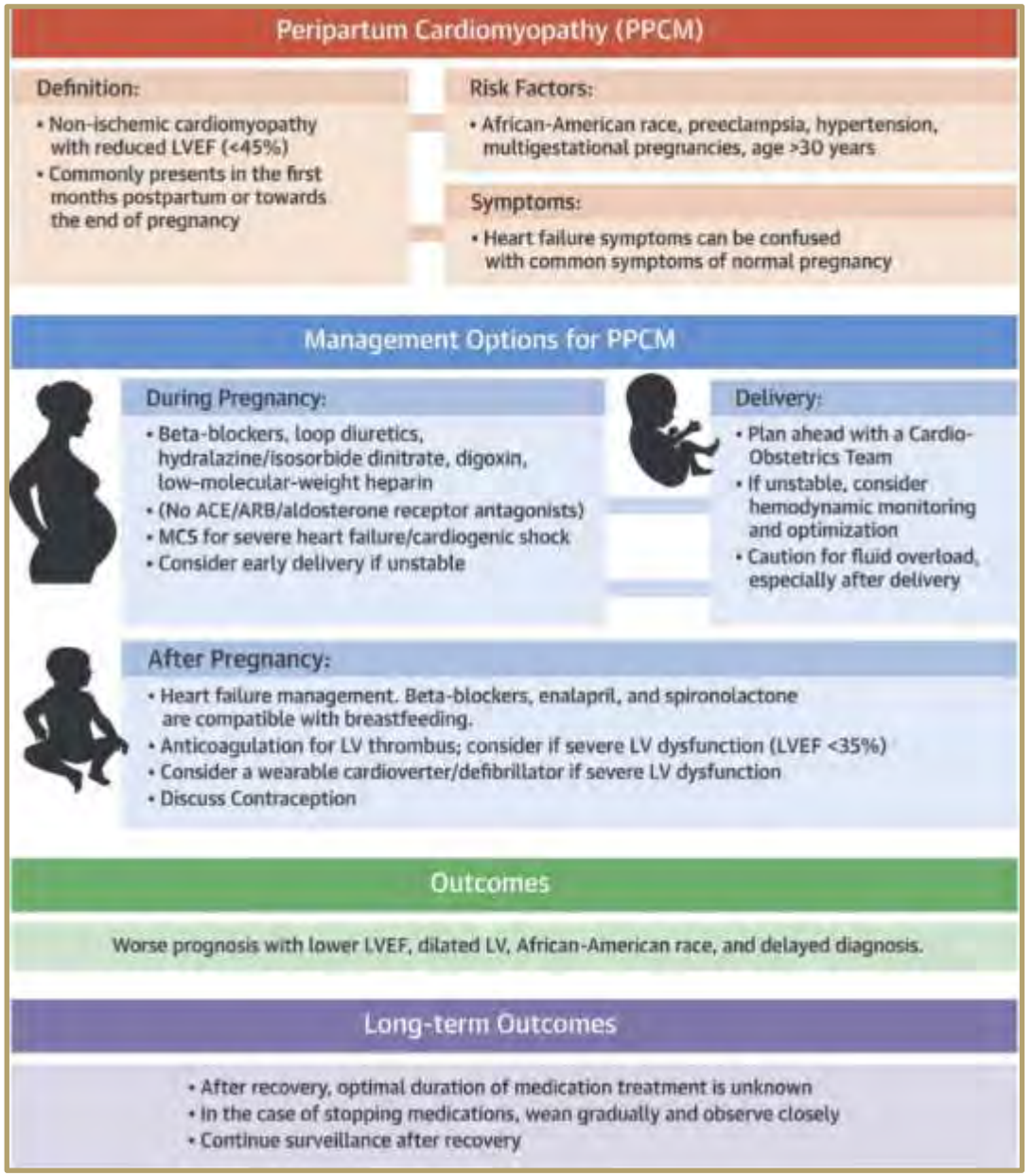
PD-1-PD-L1 és a CTLA-4-B7 kapcsolódás elmaradásával az autoreaktív T sejt klónok aktiválódhatnak

PERIPARTUM CARDIOMYOPATHIA

A terhesség utolsó hónapja
v szülés utáni első 5 hónap alatt



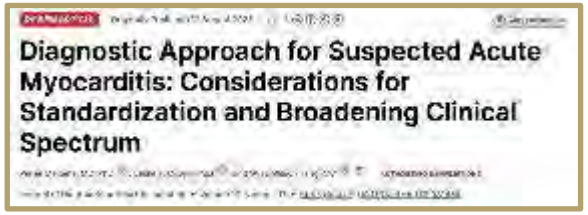
- Etiológiai teóriák:
  - PROLAKTIN **-kóros** neurohormonalis **válasz**
  - MYOCARDITIS (vírusinfectio) – biopsziás minta/MR
    - gyulladásos sejtek jelenléte, necrosis, fibroticus átalakulás
  - Autoimmun folyamat – ***KIMÉRIZMUS***
    abnormalis immunválasz a foetalis antigénekre
  - *TNFa, Il-6, CRP,*
  - Genetikai meghatározottság : családi előfordulás, esetleírások
  - Selénhiány (egyéb táplálkozási hiányállapot)
  - Abnormalis HAEMODINAMIKAI VÁLASZ
    a terhesség alatti fiziológiás változásokra



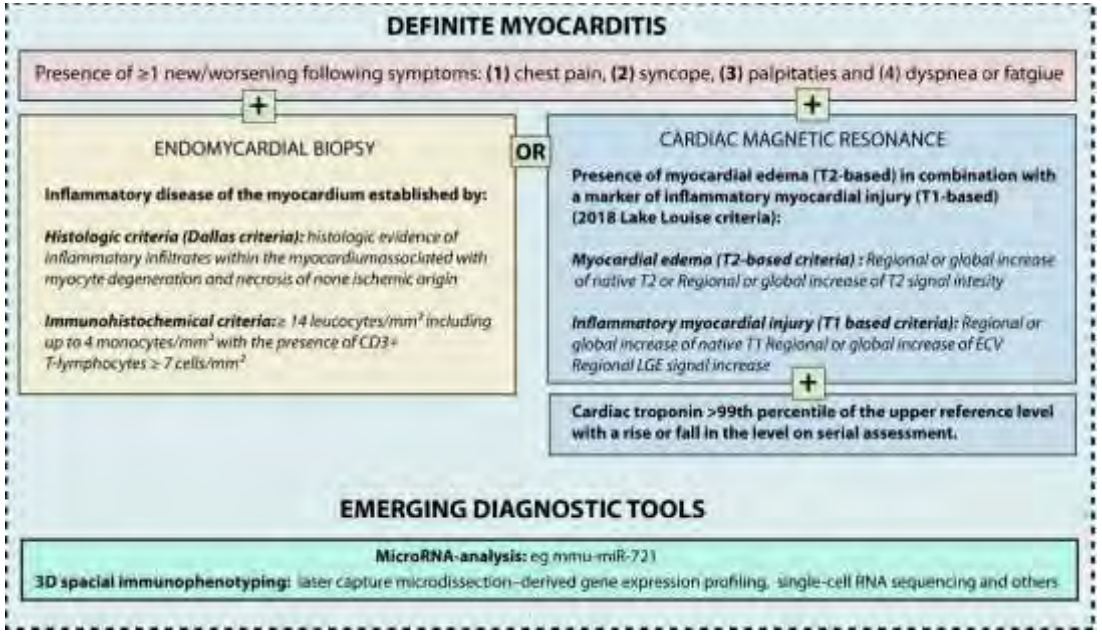
MYOCARDITIS

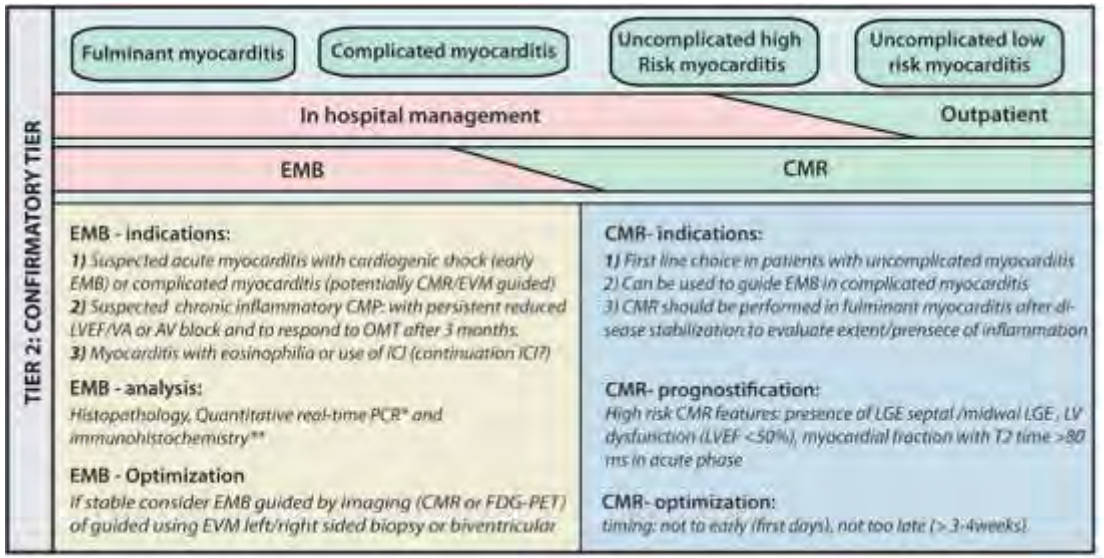
Klinikai jellemzők, diagnozis

Klinikum: nagyon széles skála
DCM esetén : szívelégtelenség tünetei
3:1 ffi dominancia


Diagnostic Approach for Suspected Acute Myocarditis: Considerations for Standardization and Broadening Clinical Spectrum

Vizsgálatok :
Általános labor - AST/ASO
Troponin (CK)
Immunserológia- szívizom ellenes AT
Infect serologia
Mellkas Rtg,
Echocardiographia
Cardiális MR
Izotópdiagnosztika
(Ga 67, In111-el jelölt antimyozinAT)
Endomyocardialis biopszia





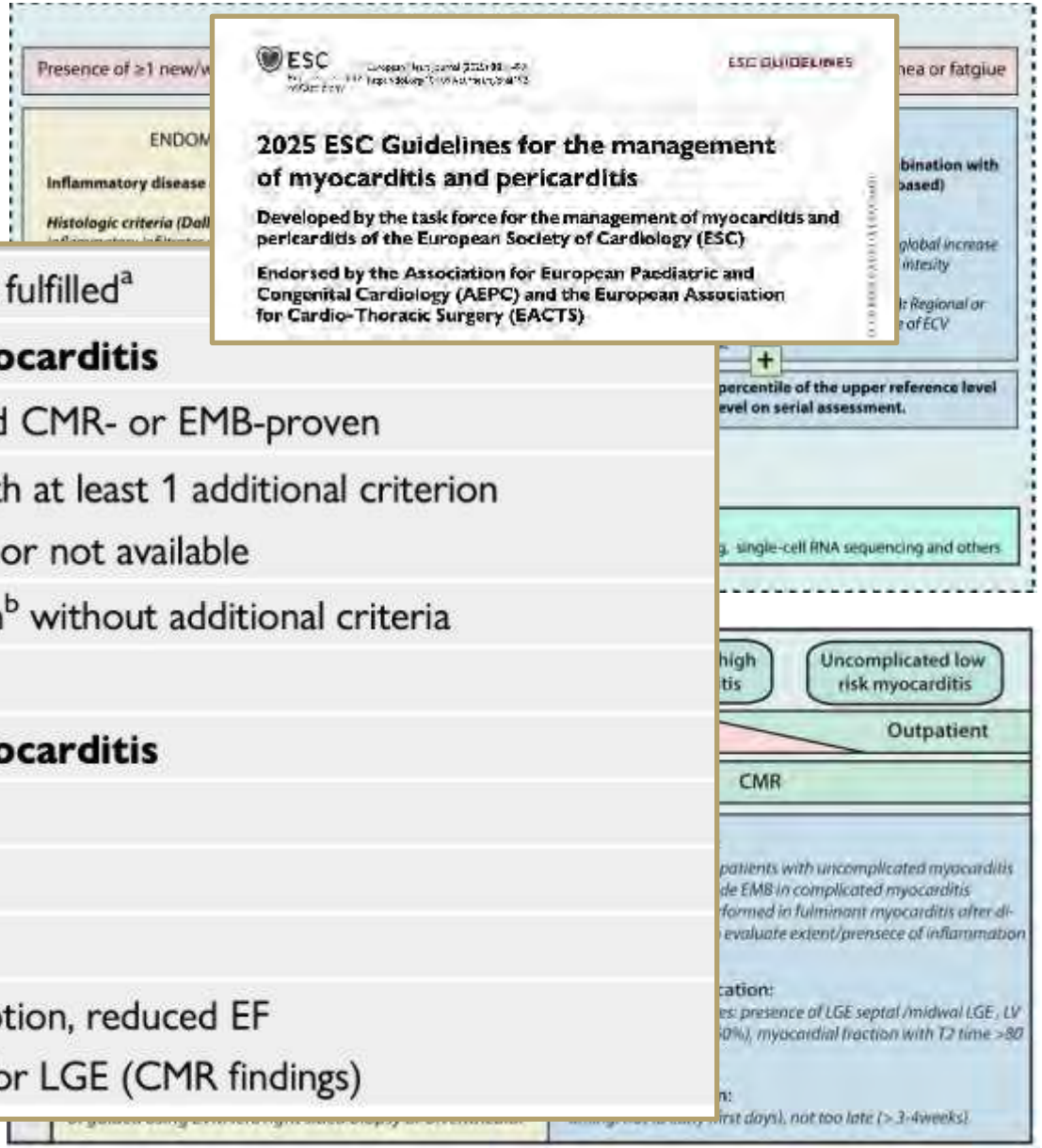
MYOCARDITIS

Klinikai jellemzők, diagnozis

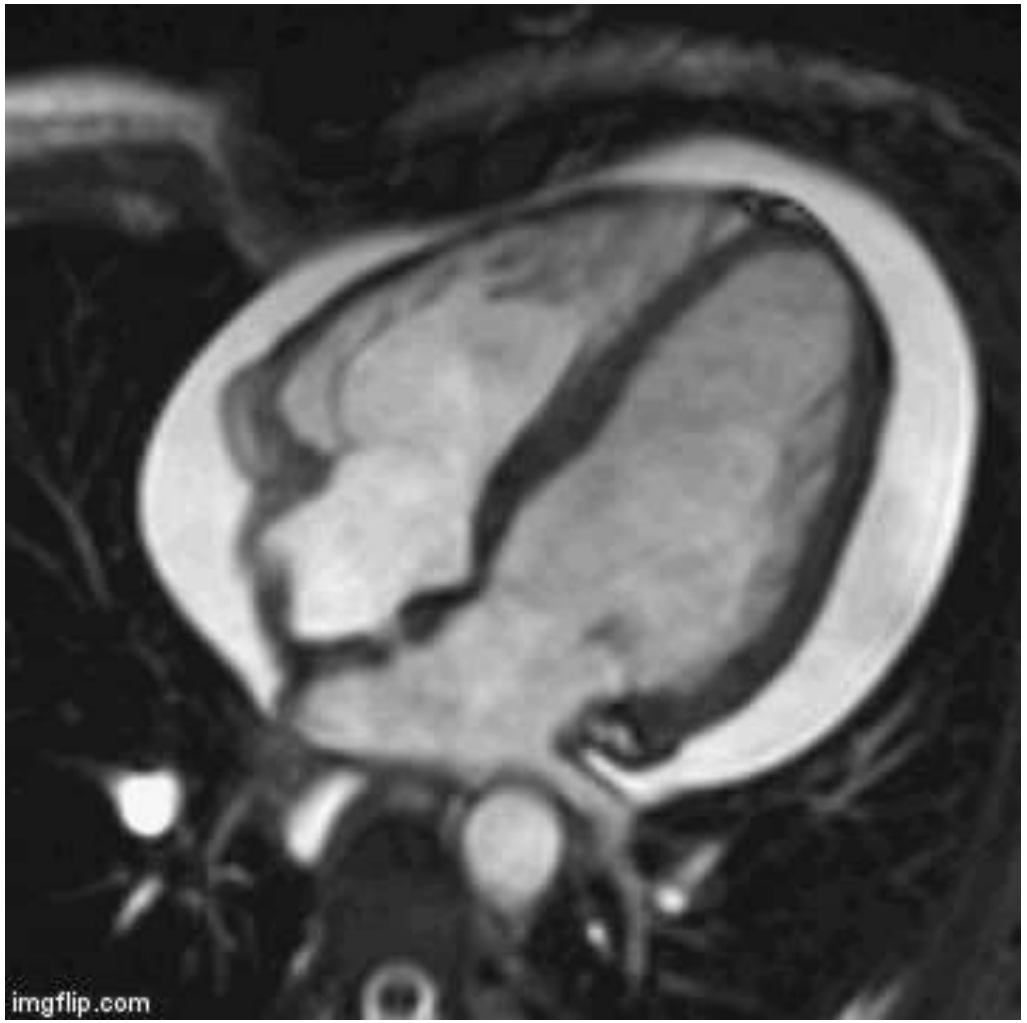
Klinikum: r
DCM esetér
3:1 ffi dom

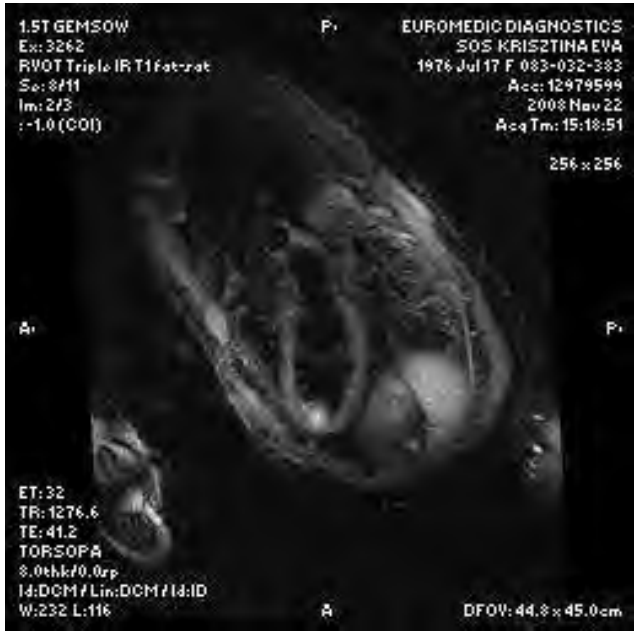
Vizsgálatok
Általános la
Troponin (
Immunsero
Infect sero
Mellkas Rtg
Echocardio
Cardiális M
Izotópdiagr
(Ga 67, In1
Endomyoca

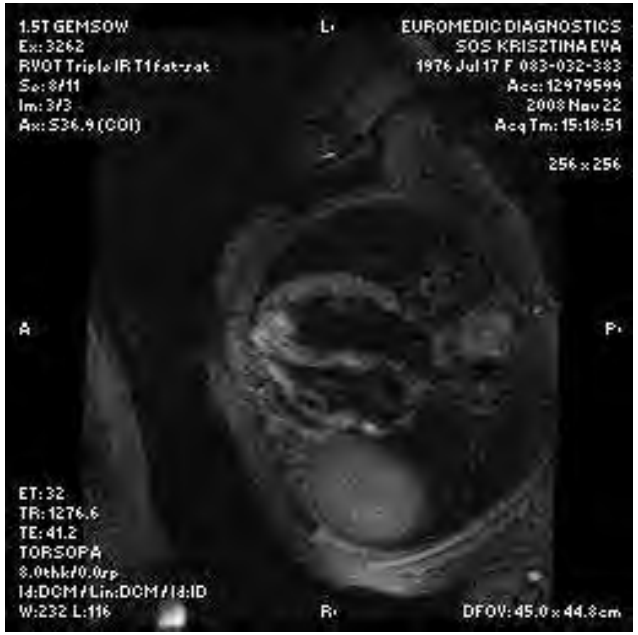
If diagnostic criteria for myocarditis and/or pericarditis are fulfilled[a]	
	Myocarditis
Definite	Clinical presentation[b] and CMR- or EMB-proven
Possible	Clinical presentation[b] with at least 1 additional criterion CMR- or EMB-uncertain or not available
Unlikely/rejected	Only clinical presentation[b] without additional criteria
Additional criteria beyond clinical presentations[b]	
	Myocarditis
Clinical[b]	Non-specific findings
ECG[c]	ST-T changes
Biomarkers	Troponin elevation
Imaging[d]	Abnormal strain, wall motion, reduced EF Myocardial oedema and/or LGE (CMR findings)



CARDIALIS MR







Meeting the Challenges of Myocarditis: New Opportunities for Prevention, Detection, and Intervention—A Report from the 2021 National Heart, Lung, and Blood Institute Workshop

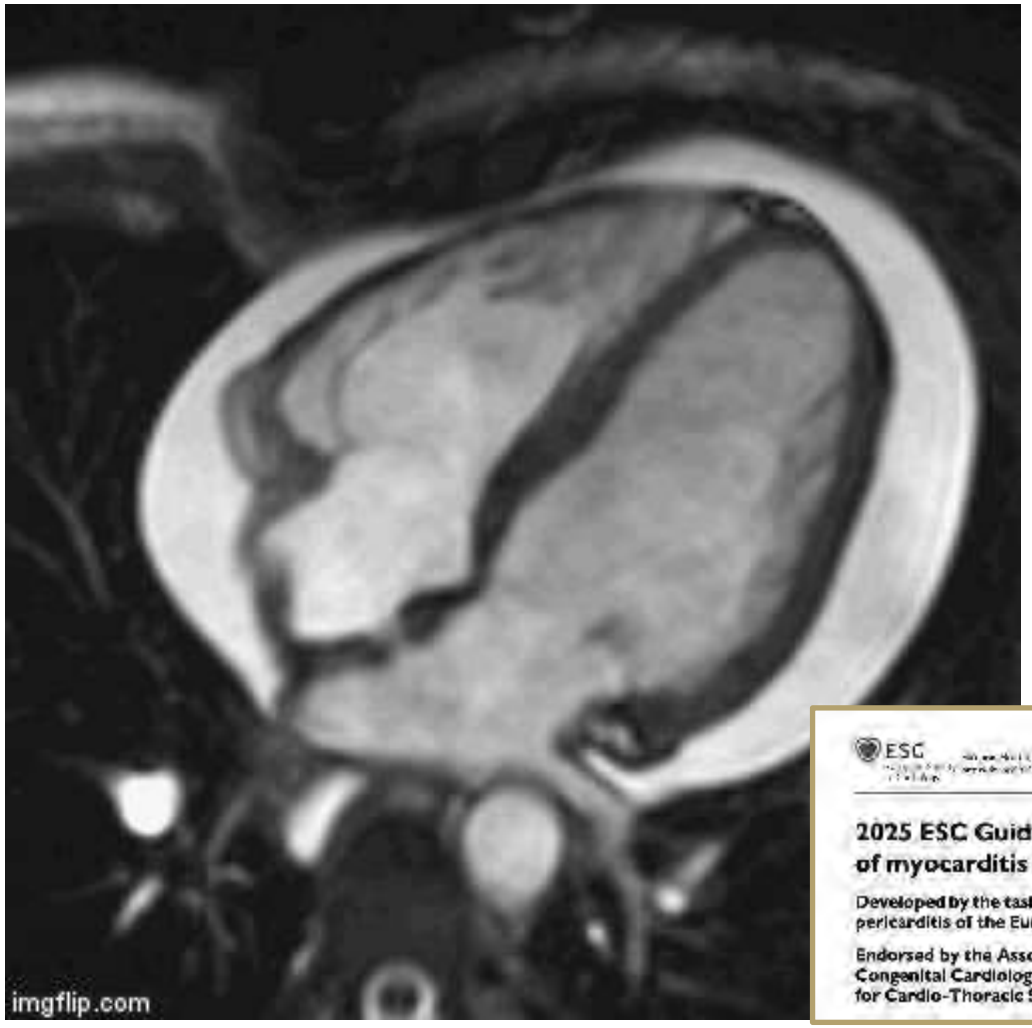
J. Clin. Med. 2022, 11, 5721. https://doi.org/10.3390/jcm11195721

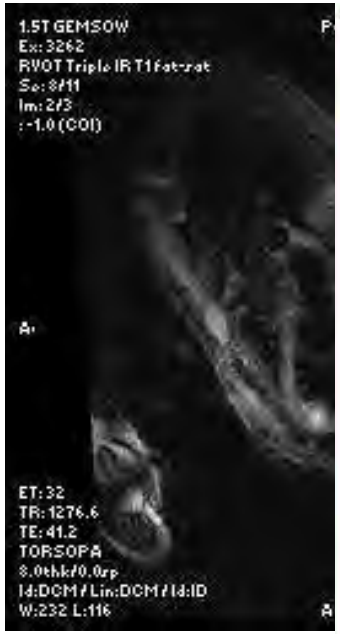
Table 1. An Overview of Imaging Modalities Used in the Evaluation of Patients Presenting with Myocarditis.

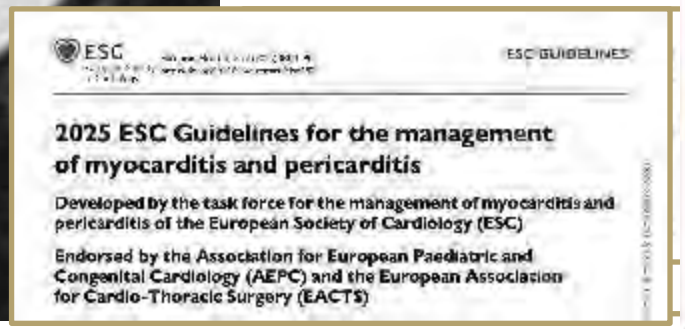
	Transthoracic Echocardiography	Positron Emission Tomography	Cardiovascular Magnetic Resonance
Ventricular volumes, myocardial mass, systolic function	+++	—	++—
Ventricular strain, myocardial mechanics	+++	—	++
Inflammation	++	+——	++—
Fibrosis/Infiltration	++	——	++—
Pericardium/Pericardial disease	+++	+	++—
Alternate diagnoses of chest pain syndromes	++	——	++—
Cost	Inexpensive	Most expensive	Increasingly affordable; cost-effective
Strengths	Portable, widely accessible in most medical institutions, rapid assessment of systolic function and wall motion abnormalities	Highly validated in inflammatory state; molecular and metabolic characterization	High spatial resolution, highly reproducible, volumetric coverage, tissue-specific tissue characterization
Limitations	Dependence on optimal acoustic window, nonspecific findings	Exposure to ionizing radiation with use of nuclear tracers, special preparation required	Specific Hardware/software requirements with fewer centers of excellence available; claustrophobia, use of gadolinium contrast

A higher number of "+" symbols indicates a higher strength or utility in the category.

CARDIALIS MR



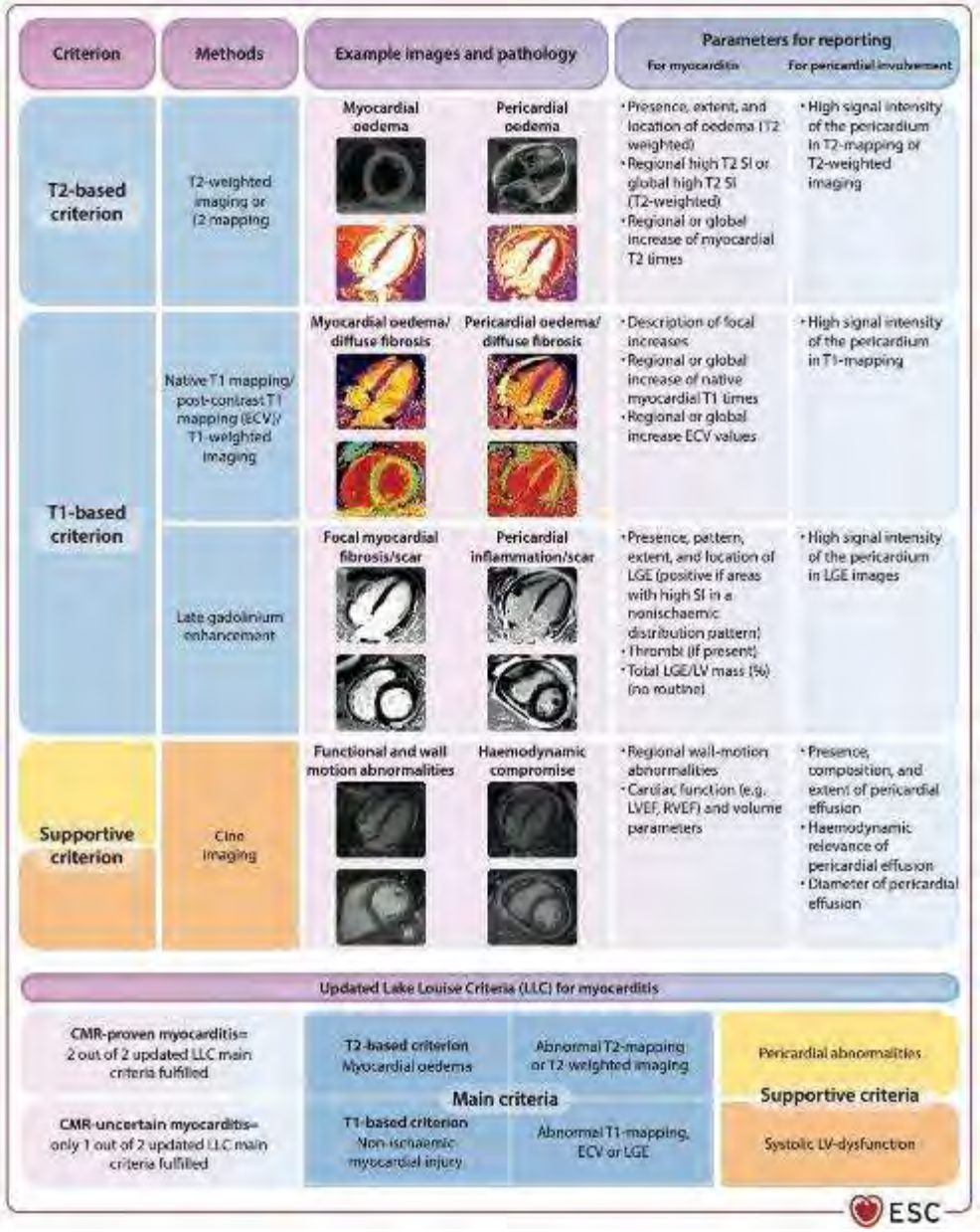



ESC GUIDELINES

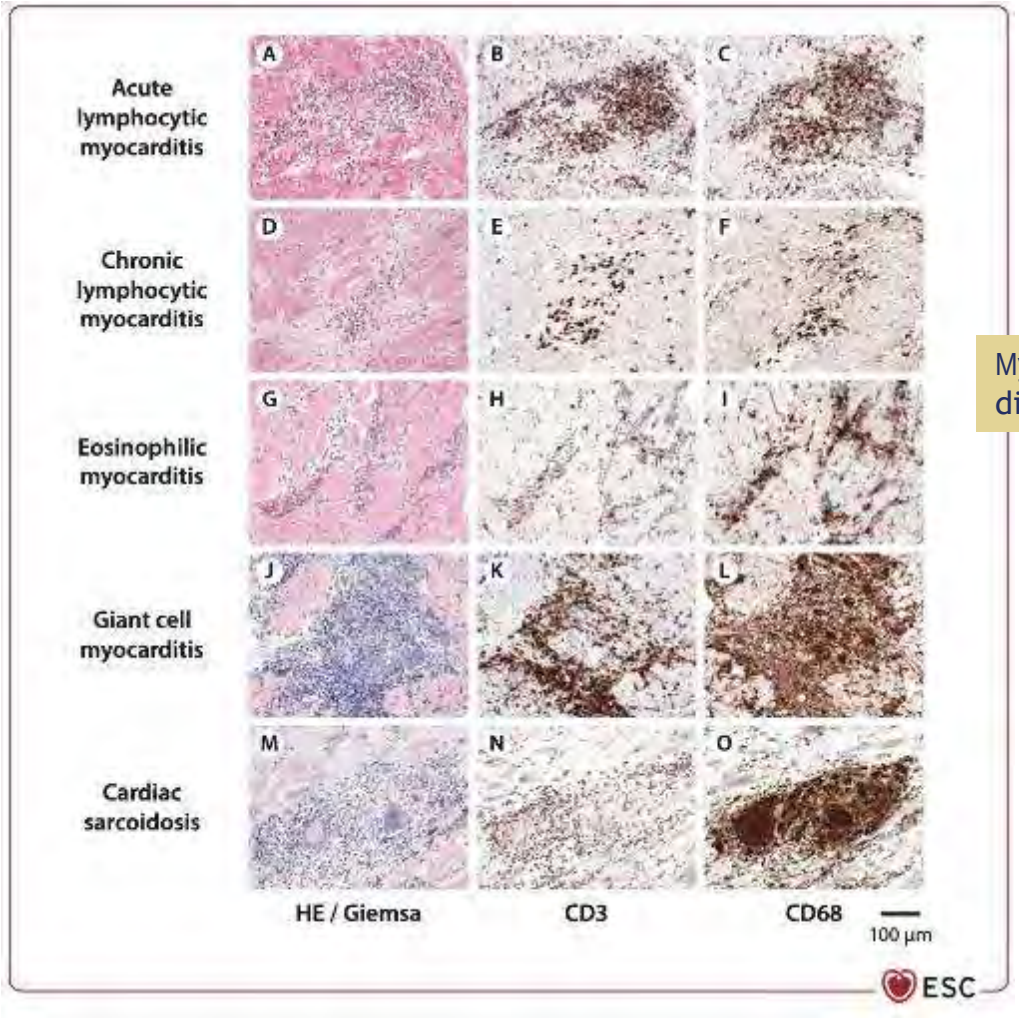
2025 ESC Guidelines for the management of myocarditis and pericarditis

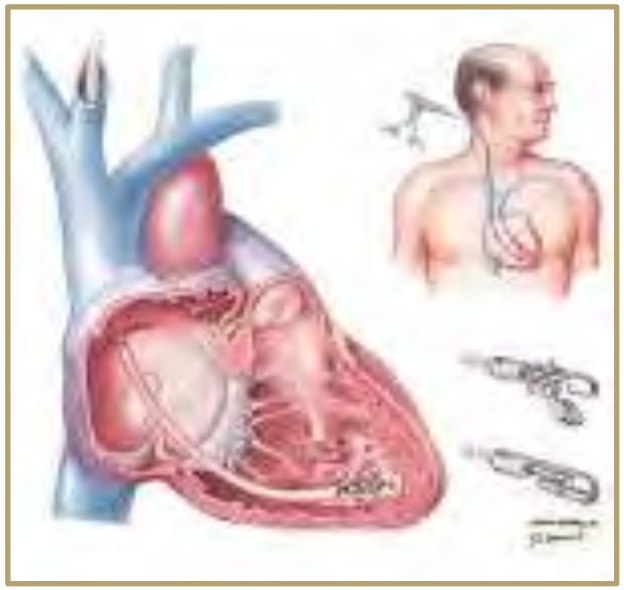
Developed by the task force for the management of myocarditis and pericarditis of the European Society of Cardiology (ESC)

Endorsed by the Association for European Paediatric and Congenital Cardiology (AEPC) and the European Association for Cardio-Thoracic Surgery (EACTS)



ENDOMYOCARDIALIS BIOPSZIA





Indikáció :

- High risk betegek
- Haemodinamikai instabilitás
- Intermediate risk, de nem reagál a th-ra
- Spec forma felmerül
- Vírus (kórokozó) genom kimutatás

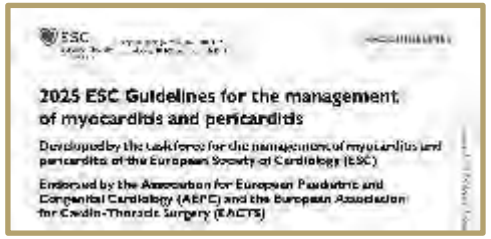
Myocarditis szövettani diagnosztikus kritériumok

	Predominant inflammatory cells	Myocyte necrosis	Infections PCR positive (viruses, etc.)
Active lymphocytic myocarditis	$CD3^+$ T lymphocytes >7/mm², $CD68^+$ macrophages	yes	yes/no
Persistent lymphocytic myocarditis	$CD3^+$ T lymphocytes >7/mm², $CD68^+$ macrophages	yes	yes/no
Resolved lymphocytic myocarditis	–	no	yes/no
Eosinophilic myocarditis (acute stage)	Eosinophils, $CD3^+$ T lymphocytes, $CD68^+$ macrophages	yes	yes/no
Giant-cell myocarditis (acute stage)	Eosinophils, $CD68^+$ giant cells, $CD3^+$ T lymphocytes, $CD68^+$ macrophages	yes	no
Sarcoidosis	$CD68^+$ giant cells, granuloma, $CD3^+$ T lymphocytes, $CD68^+$ macrophages	yes/no	no

© ESC 2025

2025 ESC Guidelines for the management of myocarditis and pericarditis.
Schulz-Menger J, et al. Eur Heart J. 2025. Aug 29:ehaf192. doi: 10.1093/eurheartj/ehaf192.

MYOCARDITIS KEZELÉS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Carsten Tschöpe et al. Myocarditis and inflammatory cardiomyopathy: current evidence and future directions. Nat Rev Cardiol . 2021 Mar;18(3):169-193. doi: 10.1038/s41569-020-00435-x.Epub 2020 Oct 12.


Immune checkpoint inhibitor-related myocarditis

Spontán vírus clearance (?)

EMB findings	Inflammation-negative Virus-negative	Inflammation-positive Virus-negative	Inflammation-negative Virus-positive	Inflammation-positive Virus-positive
Differential diagnosis	• Post-myocarditis • Dilated cardiomyopathy (genetically tested, if appropriate)	• Lymphocytic myocarditis • Eosinophilic myocarditis • Giant-cell myocarditis • Cardiac sarcoidosis	Viral latency	• Virus-active myocarditis • Virus-associated myocarditis
Standard therapy	Optimal medical therapy for heart failure and risk-adjusted therapy			
	Clinically unstable disease, non-resolving disease or no response to standard therapy			
Aetiology-directed therapeutic options	No aetiology-specific therapy available Autoantibody targeting (?)	Tailored immunosuppressive therapy in experienced health-care centres Autoantibody targeting (?)	No aetiology-specific therapy available Autoantibody targeting (?)	• Antiviral therapy (?): enteroviruses, herpesviruses, HCV • Immunomodulation (?): adenoviruses, enteroviruses • IVIG (?): enteroviruses, B19V infection with high viral DNA copies in cardiac tissue and viraemia • Antiviral plus immunosuppressive therapy (?): herpesvirus infection without viraemia • Immunosuppressive therapy (?): B19V infection with low viral DNA copies in cardiac tissue and no viraemia • Autoantibody targeting (?)

MYOCARDITIS KEZELÉS

Carsten Tschöpe et al. Myocarditis and inflammatory cardiomyopathy: current evidence and future directions. Nat Rev Cardiol . 2021 Mar;18(3):169-193. doi: 10.1038/s41569-020-00435-x.Epub 2020 Oct 12.

2025 ESC Guidelines for the management of myocarditis and pericarditis. Schulz-Menger J, et al. Eur Heart J. 2025. Aug 29:ehaf192. doi: 10.1093/eurheartj/ehaf192.

		1 vonal	2 vonal	3 vonal
Vírus - GYULLADÁS +	lymphocytas	Steroid : enyhe : 1 mg/ttkg /nap Súlyos : 4-14 mg/ttkg/nap, majd 1 mg/ttkg /nap	Steroid +AZA, Cy, MMF, MTX	IVIg , PEX
	Eosinophyl	Steroid : enyhe : 1 mg/ttkg /nap Súlyos : 4-14 mg/ttkg/nap, majd 1 mg/ttkg /nap	Steroid +AZA, Cy, MMF, MTX	IVIg , PEX
	Óriássejtes	Steroid : enyhe : 1 mg/ttkg /nap Súlyos : 4-14 mg/ttkg/nap, majd 1 mg/ttkg /nap + AZA, Cy, MMF,	ATG, CYC, RTX,	
	Sarcoidosis	Steroid : enyhe : 1 mg/ttkg /nap Súlyos : 4-14 mg/ttkg/nap, majd 1 mg/ttkg /nap	MTX, AZA, MMF, CYC	Infliximab/adalimumab, RTX
	Lyme	A:p.o AB – 21 nap - Doxyxcyclin, Amoxicillin, Cefuroxim - B: Iv-Cetriaxone	Iv Cefotaxim / penicillin G	
	ImmunCP inhibitor	Nagy dózisú steroid 500-1000 mg/nap 3 napig, majd leépítés Súlyos : 7-14 mg/ttkg/nap) – (24-48 óra)	MMF, ATG, abatacept, alemtuzumab	Infliximab/adalimumab, RTX
VÍRUS + gyulladás		Antiviralis, IVIg		
VÍRUS + GYULLADÁS +		BetaINF, Immunadszopcio+ IVIg pocapavir, pleconaril, telbivudine stb, HCQ,	IL-6 Rantag., IL-1beta inhib	Anti-IL-17, IL-1 R antibody,

Szívtranszplantáció (HTX) – DCM, szívelégtelenség esetén

MYOCARDITIS KEZELÉS

Carsten Tschöpe et al. Myocarditis and inflammatory cardiomyopathy: current evidence and future directions. Nat Rev Cardiol . 2021 Mar;18(3):169-193. doi: 10.1038/s41569-020-00435-x.Epub 2020 Oct 12.

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	Eosinophyl	Steroid : enyhe : 1 mg/ttkg /nap Súlyos : 4-14 mg/ttkg/nap, majd 1 mg/ttkg /nap	Steroid +AZA, Cy, MMF, MTX	IVIg , PEX
	Óriássejte		CYC, RTX,	
	Sarcoidosi		AZA, MMF,	Infliximab/adalimumab, RTX
	Lyme		fotaxim / cillin G	
	ImmunCP inhibitor	majd leépítés Súlyos : 7-14 mg/ttkg/nap) – (24-48 óra)	ATG, abatacept, alemtuzumab	Infliximab/adalimumab, RTX
VÍRUS + gyulladás		Antiviralis, IVIg		
VÍRUS + GYULLADÁS +		BetaINF, Immunadszopcio+ IVIg pocapavir, pleconaril, telbivudine stb, HCQ,	IL-6 Rantag., IL-1beta inhib	Anti-IL-17, IL-1 R antibody,

DCM, szívelégtelenség, cardiogen shock esetén
- Szívelégtelenség ajánlás szerinti kezelése
- Keringéstámogatás, lélegeztetés stb
- Mechanikus keringéstámogatás – ECMO, VAD

Szívtranszplantáció (HTX)

ENDOCARDITIS

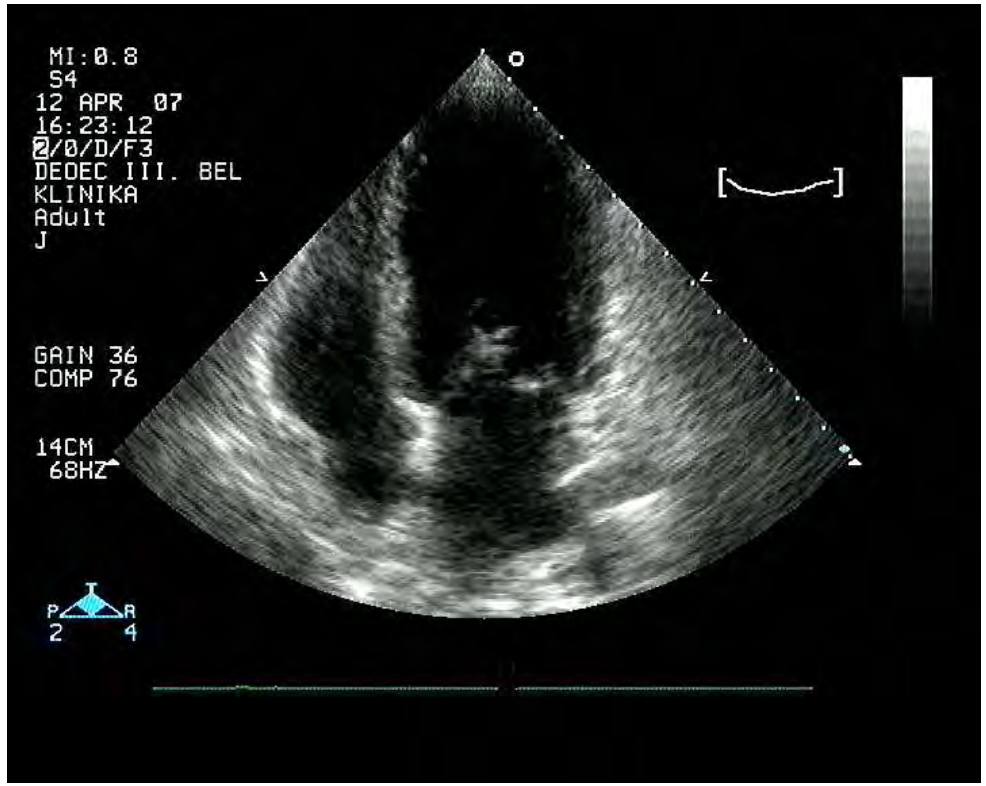
Dr Végh Judit PhD
főorvos

ENDOCARDITIS / VALVULOPATHIA

- Infectiv
- Non-infectiv

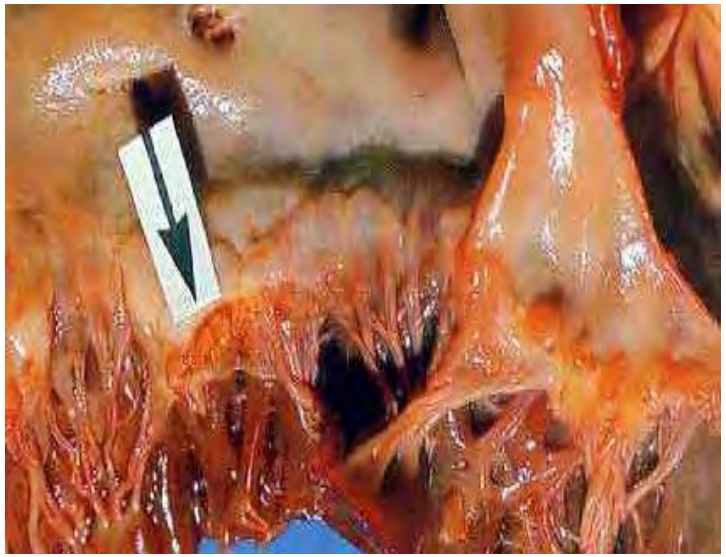
-NBTE - non-bacterial-thromboticus endocarditis
=Asepticus
=Libman-Sacks (SLE, APS)
=Verrucosus
=Marantic

- Loeffler **féle** (eosinophylia)



Harriet Hurrell, Ross Roberts-Thomson , Bernard D Prendergast : **Non-infective endocarditis**
Heart. 2020 Mar;106(6):423-429. doi: 10.1136/heartjnl-2019-315204. Epub 2020 Jan 6.

ENDOCARDITIS



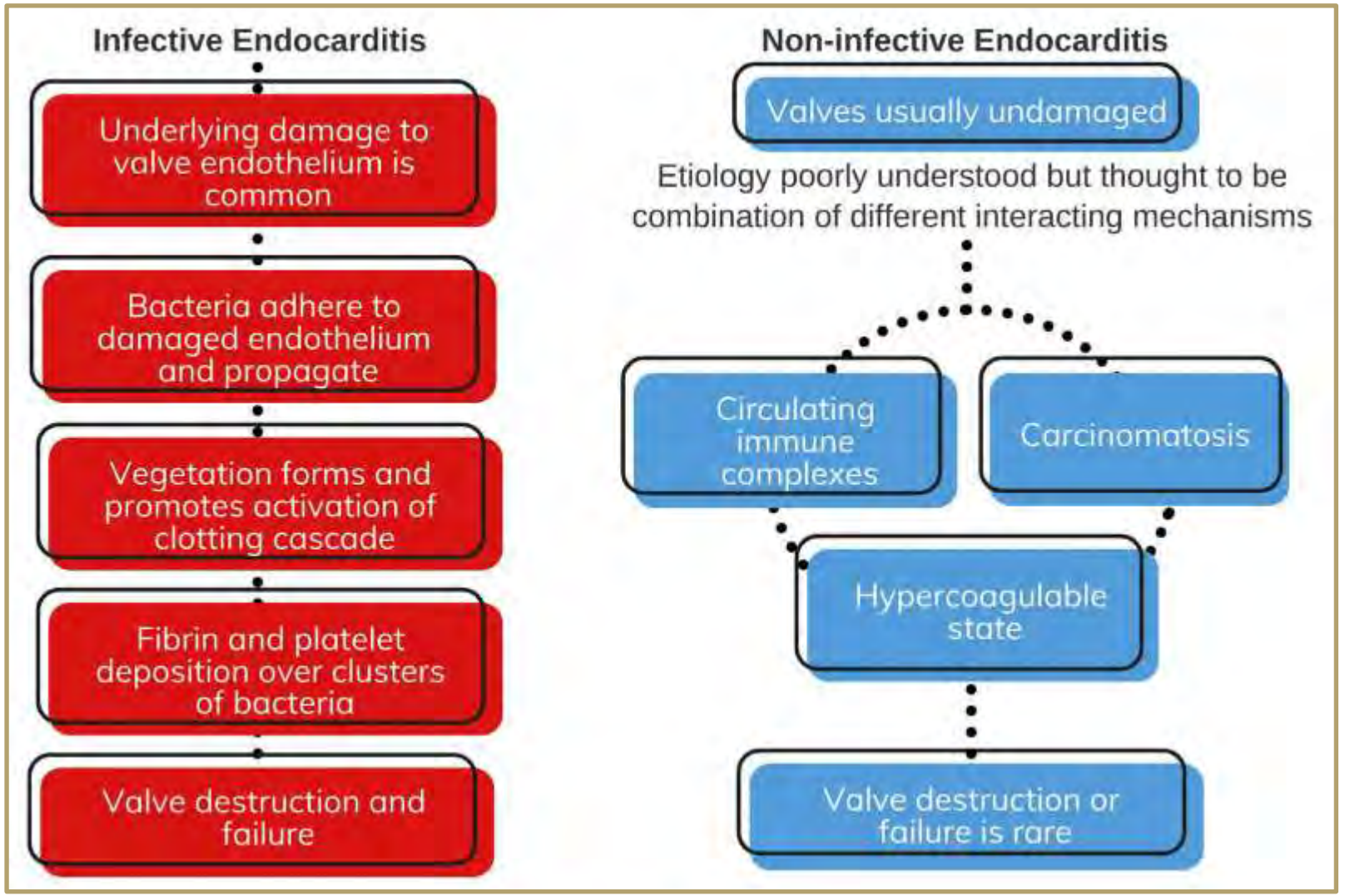
NBTE
Libman-sacks

Harriet Hurrell , Ross Roberts-Thomson , Bernard D Prendergast : **Non-infective endocarditis**
Heart. 2020 Jul;106(13):1023-1029. doi: 10.1136/heartjnl-2019-315204.Epub 2020 May 6.

alapbetegség	NBTE előfordulása
Autoimmun betegségek	
• SLE	4-43 %
• APS	41 %
• RA	esetismertetések
• GPA (granulomatosis poliangitissel)	esetismertetések
• Behcet	esetismertetések
HIV	esetismertetések
Neoplasma	19 %
• adenocc	(neoplasma + NBTE esetek) 62 %-a
• Pancreas neoplasma	(neoplasma + NBTE esetek) 25-50 %-a
• Tüdő neoplasma	(neoplasma + NBTE esetek) 25-30 %-a
Hypercoagulabilitással járó állapotok	50 % fölött
• DIC	
• Sepsis	
• Égés	
• APS	
• Neoplasma	

NBTE : non-bacterial-thromboticus endocarditis

ENDOCARDITIS PATHOPHYSIOLOGIA



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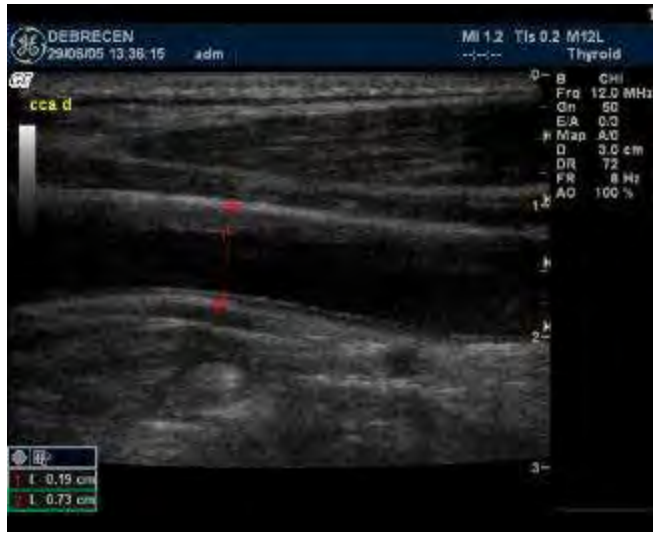
CORONARITIS

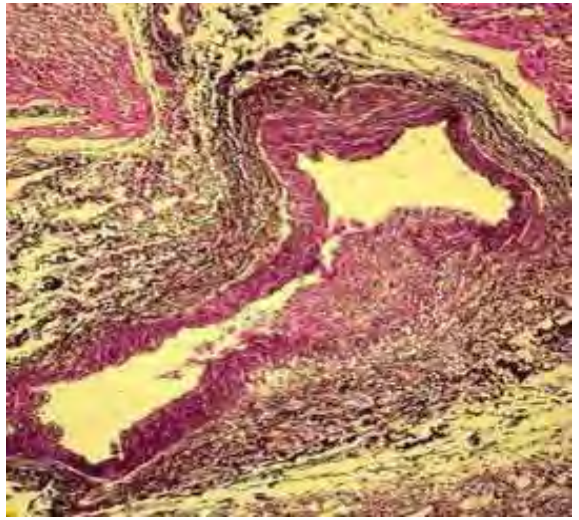
ACCELERÁLT ATHEROSCLEROSIS

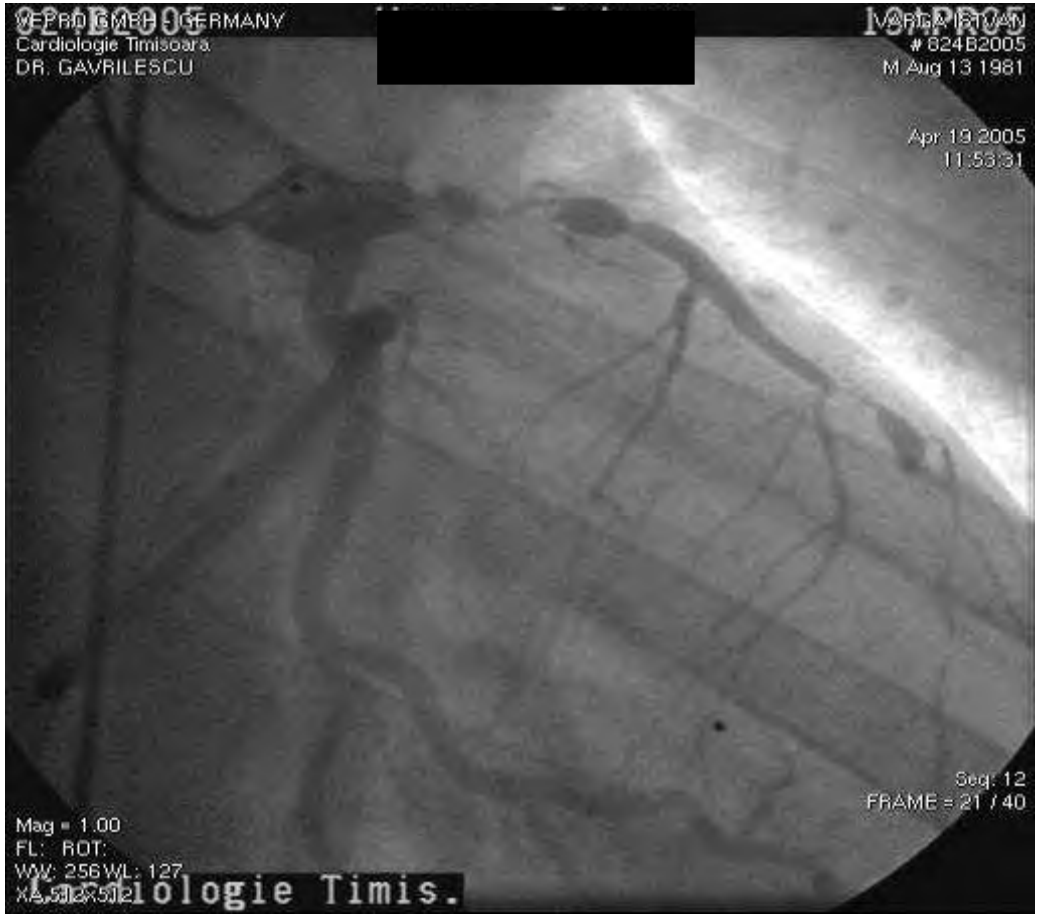
CORONARITIS

- VASCULITIS részjelensége
- Takayasu, Kawasaki, PAN, SLE, RA

- Klinikum:
- Acut coronaria syndroma képe
- Labor, EKG, echocardiographia, coronarographia



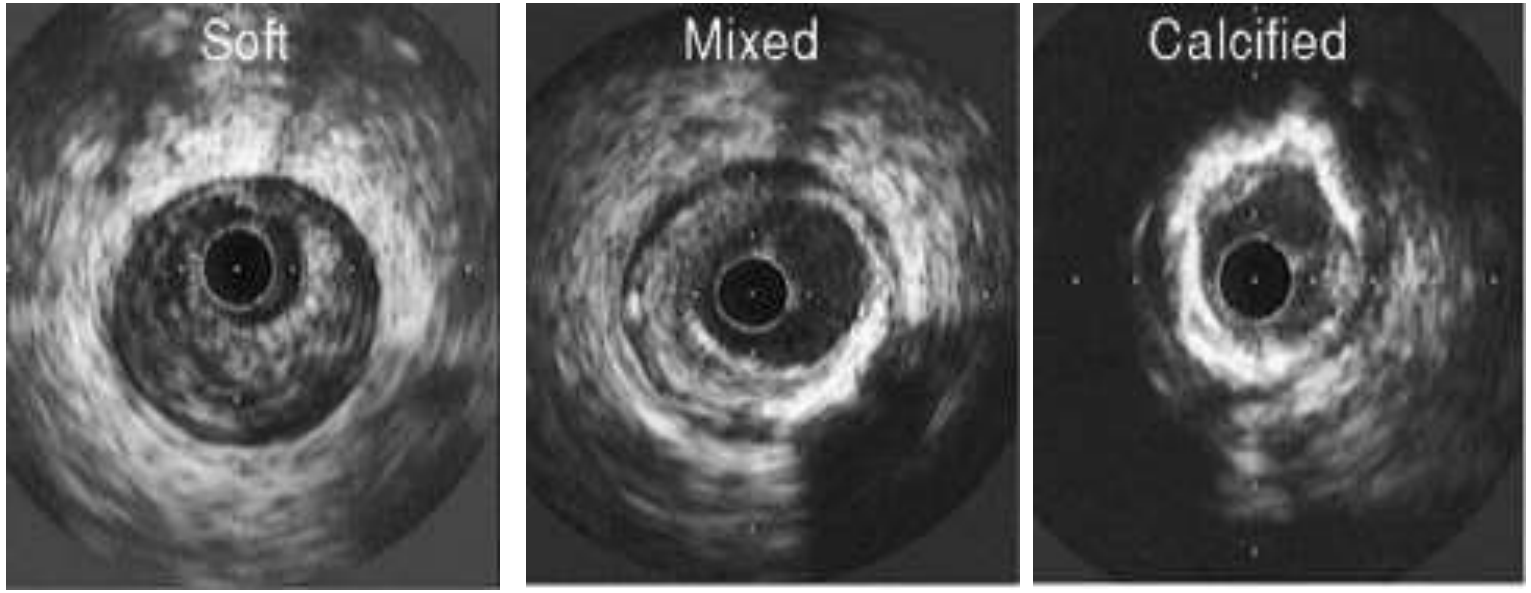




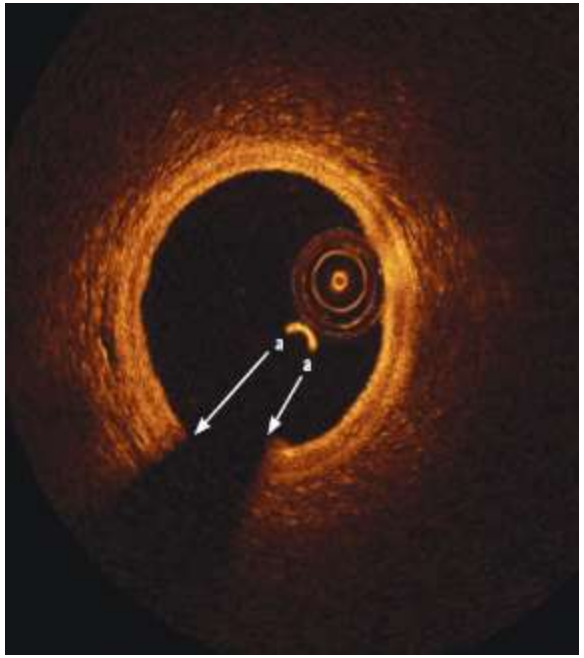
Arteriogramm- a.coronaria aneurysma és occlusio

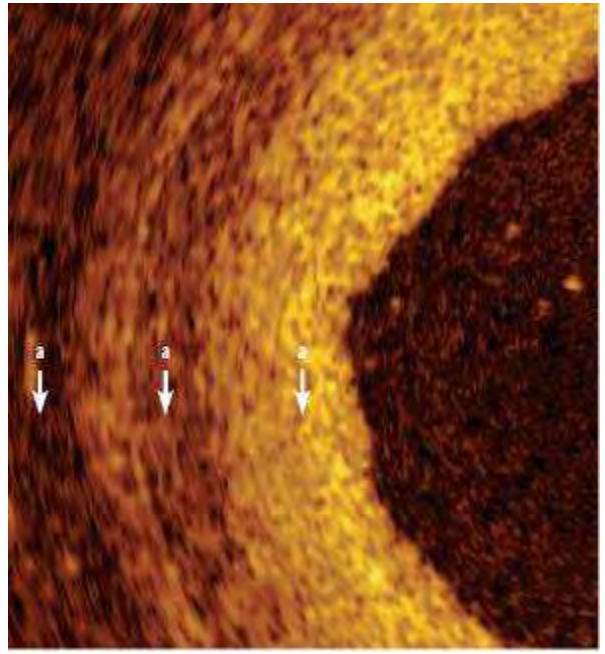
CORONARITIS

IVUS
Intravascularis ultrasonographia
Plaque morfológia

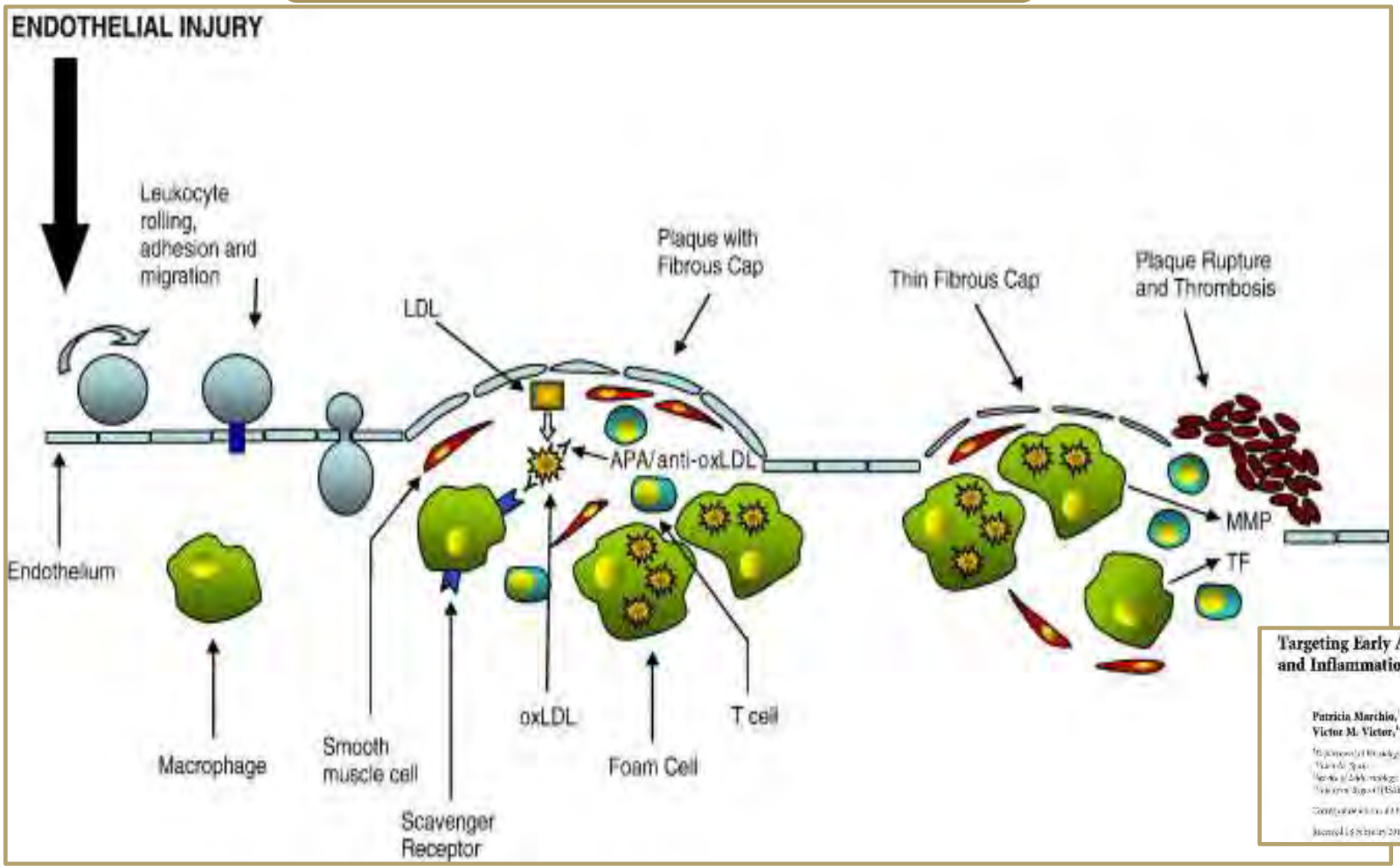


OCT
Optikai koherencia tomographia
Normál coronaria anatómia





ATHEROSCLEROSIS



1871-lipid-elmélet

1986 krónikus gyulladás (nem spec)

2012 erek falában Tsejt-APC interakció (Ag specifikus)

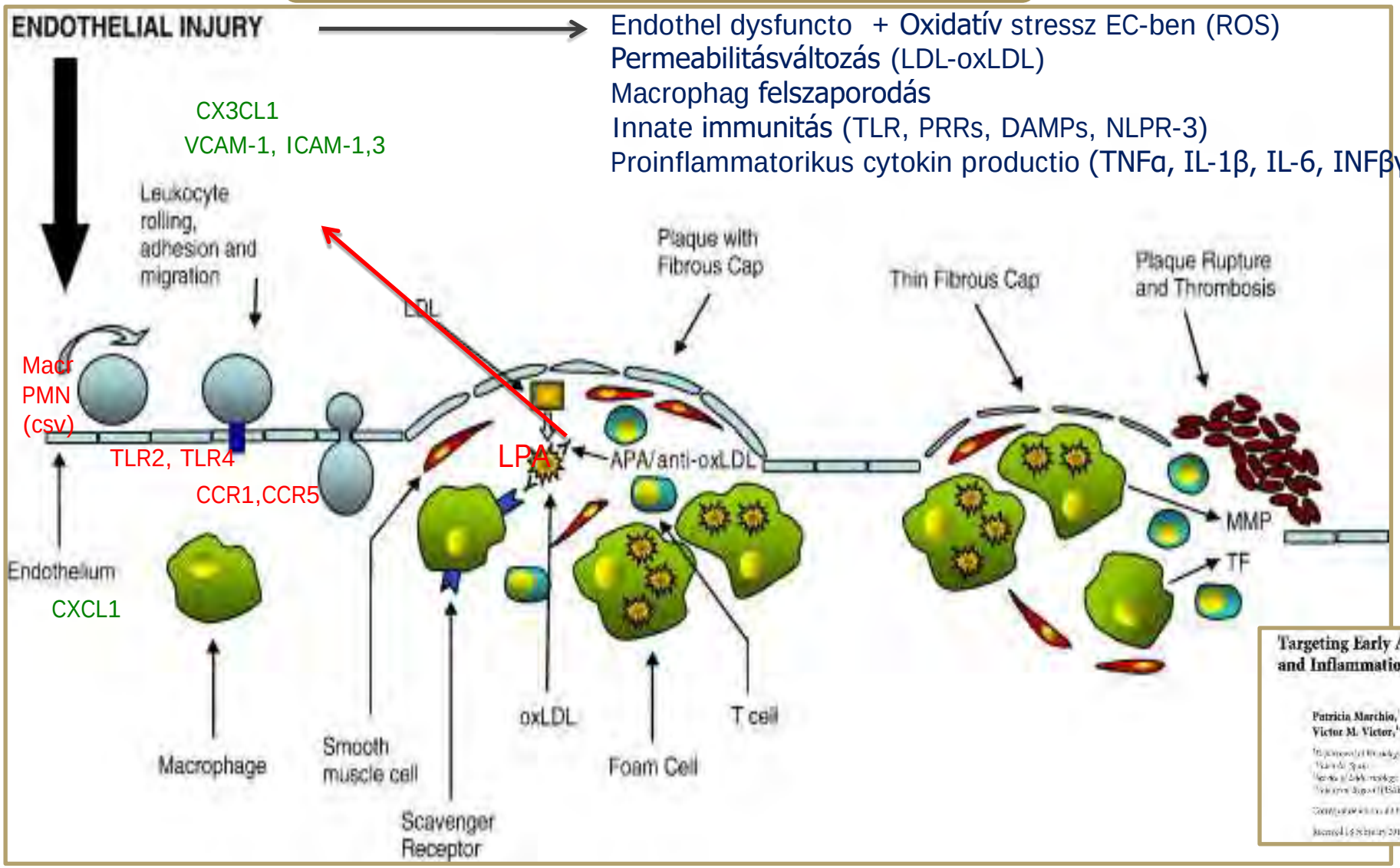
Elsődleges antigének : oxLDL, HSP, béta 2GPI


Targeting Early Atherosclerosis: A Focus on Oxidative Stress and Inflammation

Patricia Marchio, Sol Guerra-Ojeda, José M. Vila, Martin Aldasoro, Victor M. Victor, and María D. Mauricio

Endothelial Dysfunction, Autoimmunity Reviews 2006,5, 101-105,
Ruisanchez Éva: A tizofoszfatidsav szerepe az értónus szabályozásában, 2017 PhD

ATHEROSCLEROSIS



Endothel dysfuncto + Oxidatív stressz EC-ben (ROS)
Permeabilitásváltozás (LDL-oxLDL)
Macrophag felszaporodás
Innate immunitás (TLR, PRRs, DAMPs, NLPR-3)
Proinflammatorikus cytokin productio (TNFα, IL-1β, IL-6, INFβγ…)

Targeting Early Atherosclerosis: A Focus on Oxidative Stress and Inflammation

Patricia Marchio, Sol Guerra-Ojeda, José M. Vila, Martin Aldasoro, Victor M. Victor, and María D. Mauricio

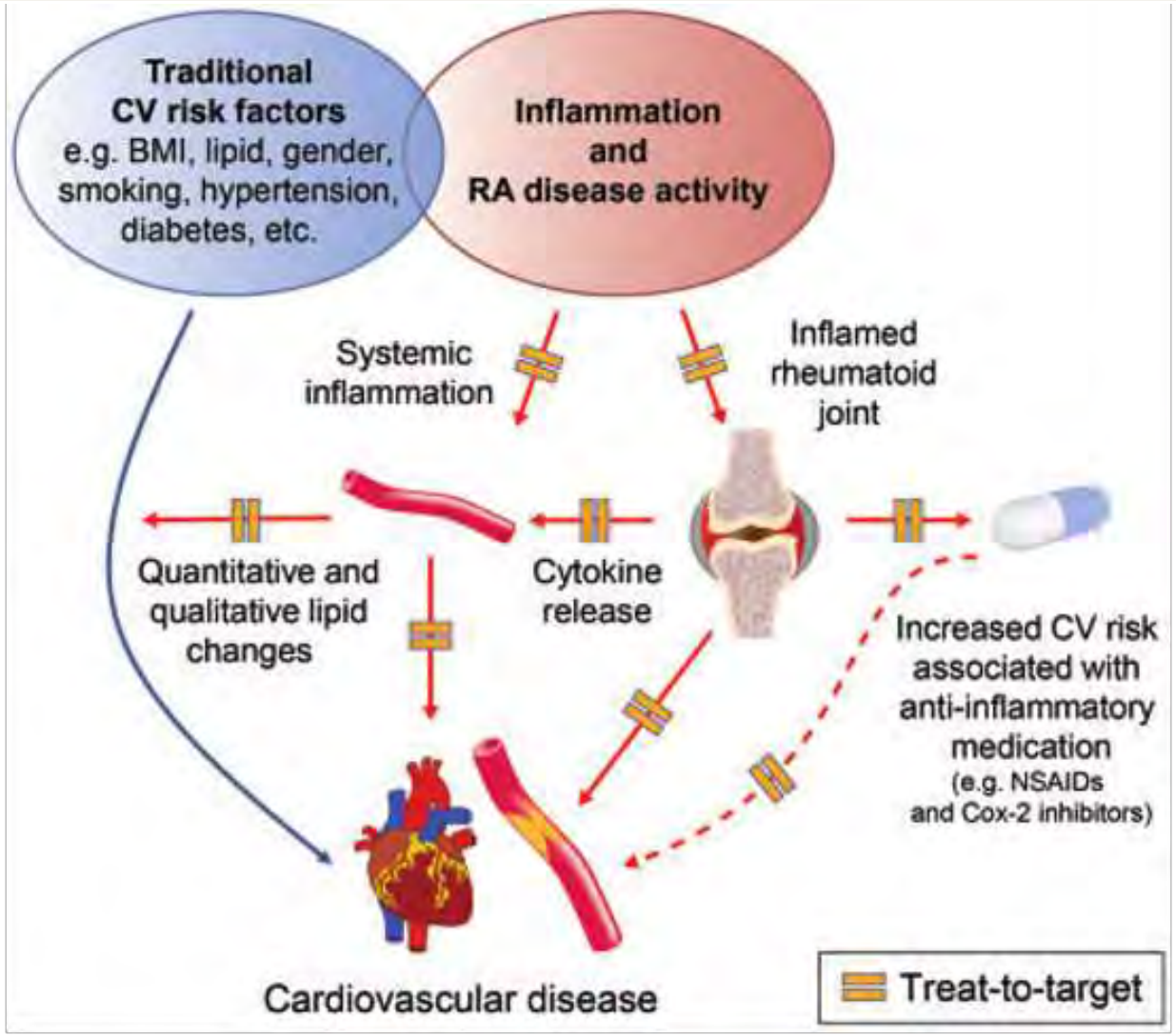
Endothelial Dysfunction and Inflammation, Arteriosclerosis, Thrombosis, and Vascular Biology. 2005;25:932-943
Ruisanchez Éva: A lizofoszfatidsav szerepe az értónus szabályozásában, 2017 PhD

EMELKEDETT CARDIOVASCULARIS RIZIKÓ OKAI

TRADICIONALIS CV RIZIKÓ

általános CV rizikófelmérés

DM, hypertonia, doh, mobilitás



doi:10.1093/rheumatology/keu224

ALAPBETEGSÉG FÜGGŐ RIZIKÓ

SPA: Aortitis, Aorta billentyű elégtelenség, AV block
SLE : Liebmann Sacks, Loeffler endocarditis
SSC: myocardialis fibrosis

KEZELÉS DEPENDENS RIZIKÓ

NSAID
corticosteroidok
antiTNFα
JAK gátlók

MACROPHAGOK SZEREPE

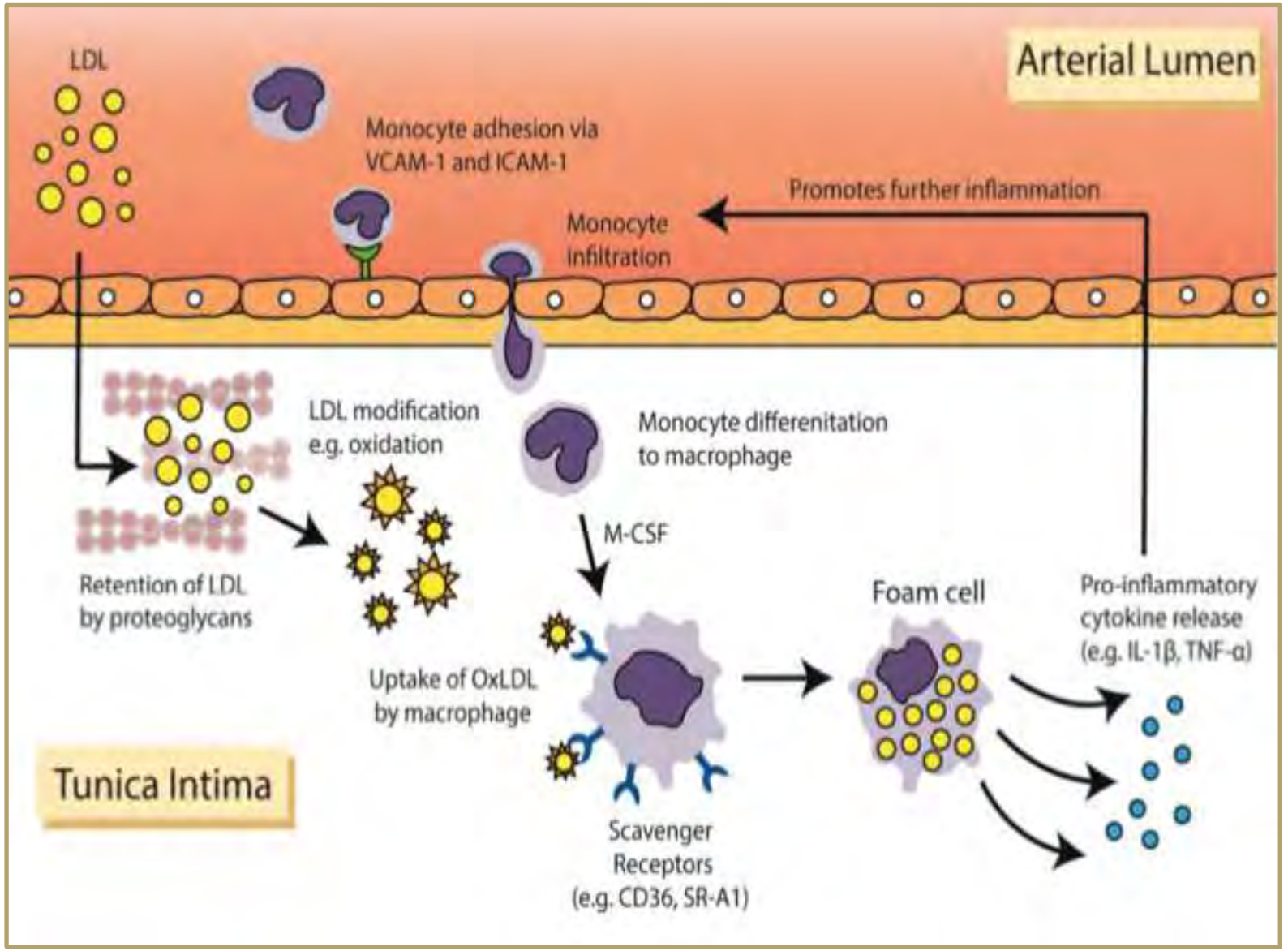
Journal of Clinical Medicine

MDPI

Review

Inflammation as a Therapeutic Target in Atherosclerosis

Mau T Nguyen [1], Samja Fernando [1,2], Nisha Schwarz [1], Joanne TM Tan [1], Christina A Bursill [1,2] and Peter J Psaltis [1,2,3,*]



ACS / PLAQUE RUPTÚRA KIALAKULÁSÁNAK MECHANIZMUSA

Instabil plaque
- vékony fibrin sapka + kollagén

- M1 macroph - MMPs termelésével a fibrinsapka kiszakadását elősegítik
- Innate immunrendszer sejtjei:
- Th1 – IFN-γ
- Th: CD28+null (IFN-γ, TNF-α termelés, apoptozis rezistens)

Plaque **ruptúra**

Plaque erosio
- nem kíséri kimutatható gyulladás
- lokalis endothelsejt károsodás

(oxidativ stress, haemodinamikai zavar, hypoxia stb)
- TLR aktiváció – neutrofil NETózis -
- thrombusképződés

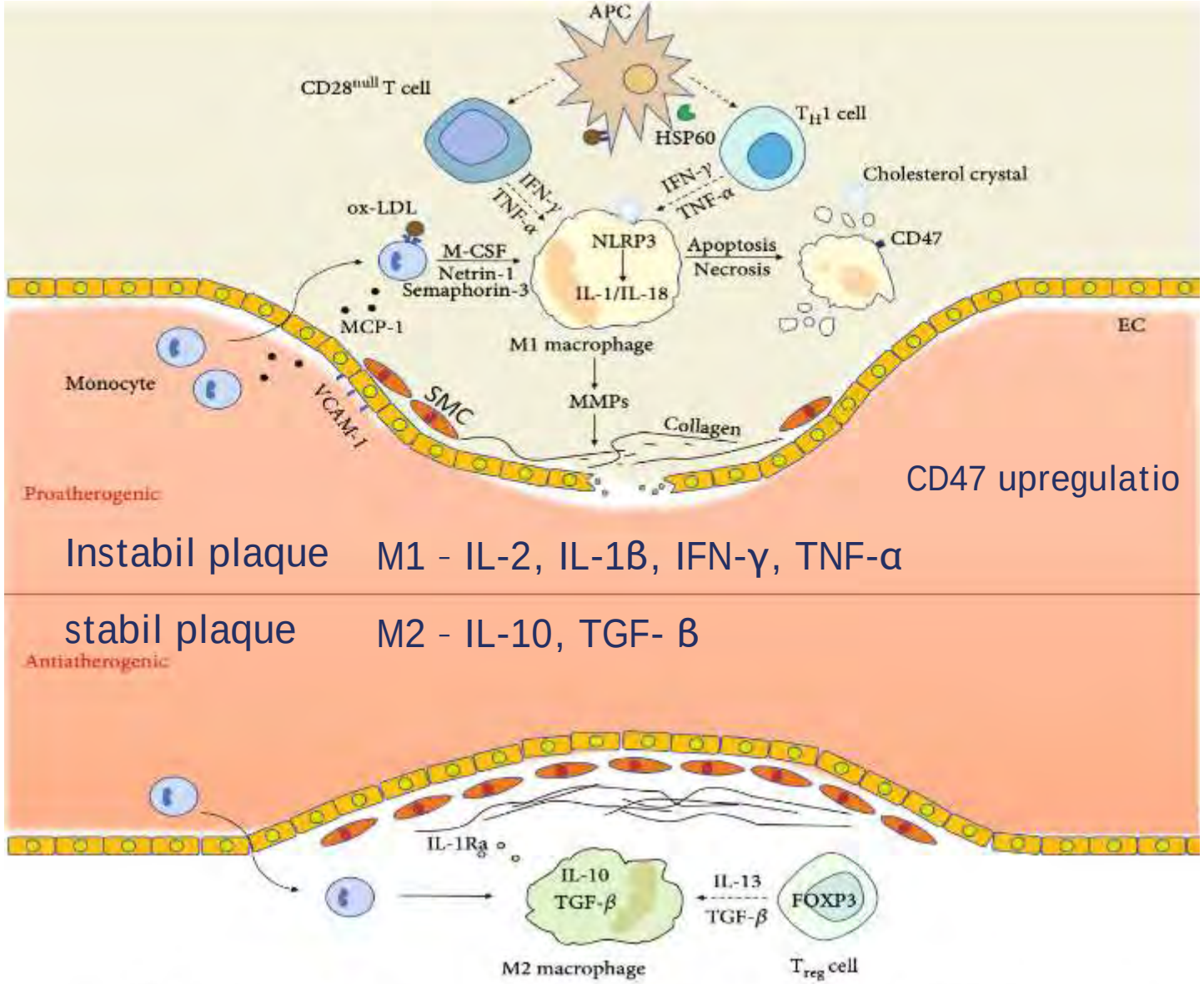


FIGURE 1: Immune and inflammation pathways in the pathogenesis of acute coronary syndrome.

Immune and Inflammation in Acute Coronary Syndrome: Molecular Mechanisms and Therapeutic Implications.
Wang H et al:.J Immunol Res. 2020 Aug 18;2020:4904217. doi: 10.1155/2020/4904217. eCollection 2020.

ACCELERÁLT ATHEROSCLEROSIS GYULLADÁSOS RHEUMATOLÓGIAI KÓRKÉPEKBEN

- Chronicus autoimmun gyulladással járó megbetegedésekben észlelhető (RA, SLE, AP sy, Vasculitis, Myositis, SP A)
- Szisztémás sclerosisban diffúz vasculopathia, a microvascularis eltértések dominálnak

↓

- A tradícionális rizikófaktorokkal nem magyarázható fokozott cardiovascularis érintettség észlelhető
- nem kontrollált krónikus gyulladás

↳ accelerált atherosclerosis

- Az autoimmun megbetegedésekhez társuló korai atherosclerosis nagyon gyakran tünetmentes

!

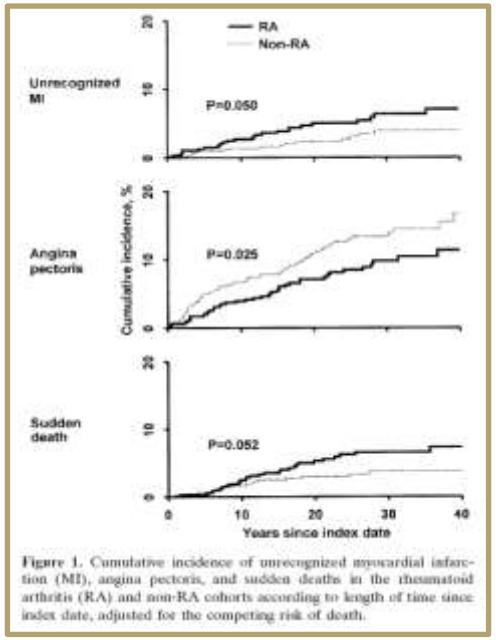
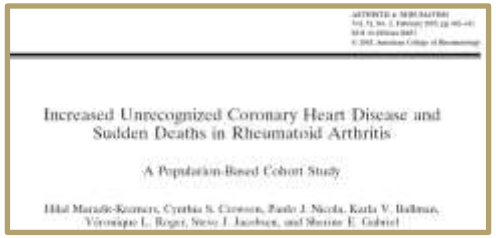


Figure 1. Cumulative incidence of unrecognized myocardial infarction (MI), angina pectoris, and sudden deaths in the rheumatoid arthritis (RA) and non-RA cohorts according to length of time since index date, adjusted for the competing risk of death.



Increased Unrecognized Coronary Heart Disease and Sudden Deaths in Rheumatoid Arthritis

A Population-Based Cohort Study

ACCELERÁLT ATHEROSCLEROSIS THERAPIÁS MEGFONTOLÁSOK

Ann Rheum Dis. 2017 Jan;76(1):17-28. doi: 10.1136/annrheumdis-2016-209775. Epub 2016 Oct 3. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. Agca et.al.

- **Szisztémás gyulladás tartós szuprimálása a cardiovascularis rizikót csökkenti** (MTX, antiTNF alfa, MMF-SLE- Jak gátlók !)

- **A hagyományos rizikófaktorok tekintetében szigorúbb célérték betartása (EULAR 2015) – RA 1,5x**

- **Statin kezelés – PLEIOTROPH HATÁSOK**
  - 30-50%-al csökkentik a morbiditást és mortalitást RA-ban (Packard)
  - Placebo controlált vizsgálat (Mc Garey):40 mg/nap atorvastatin:

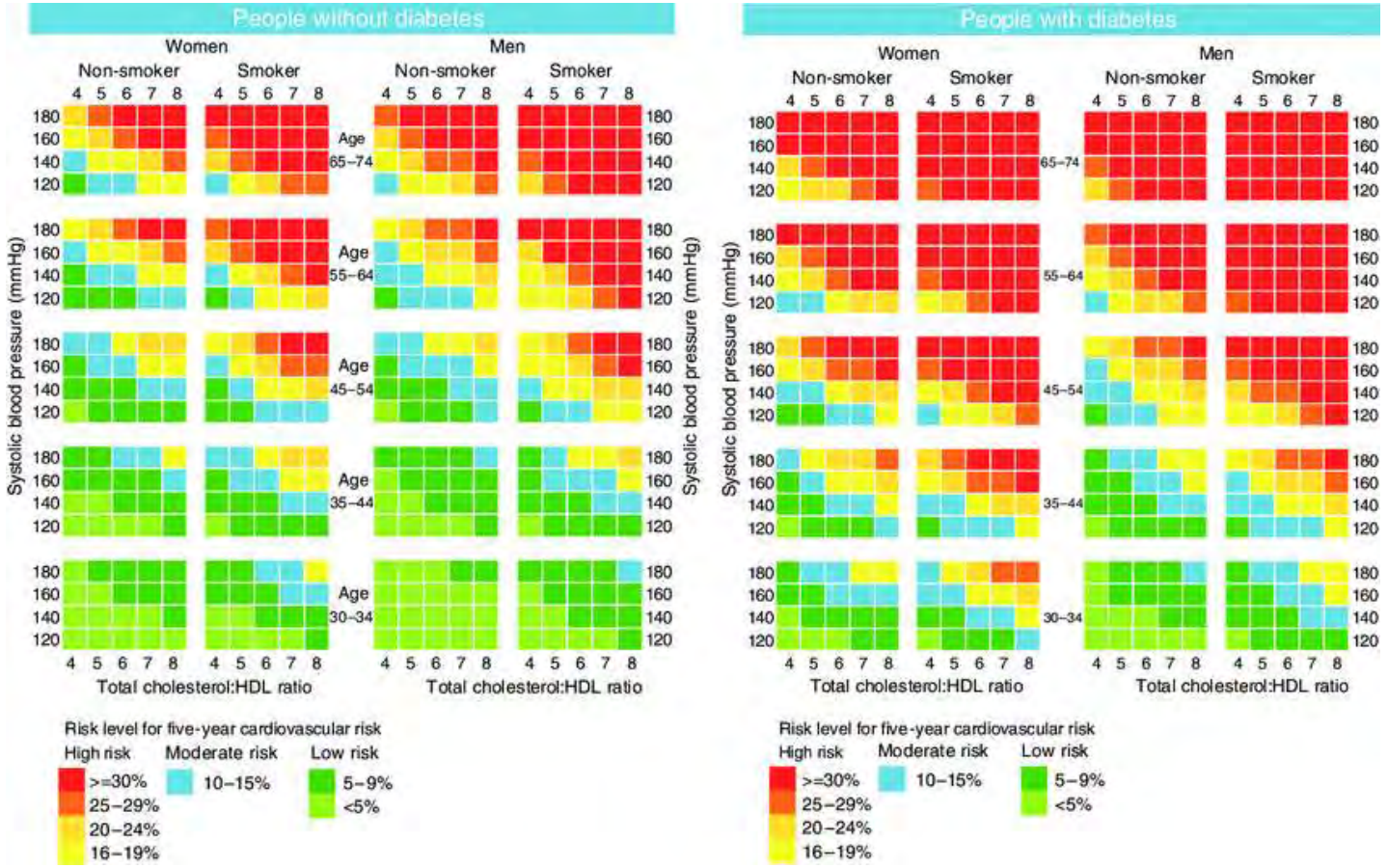
  LDL-C (45%), triglycerid (18%), betegség aktivitás (10%), CRP(50%), We(28%) csökkenés
- **Rendszeres szűrővizsgálatok**
- **Rendszeres CV szűrés**

KLASSZIKUS RIZIKÓMODELLEK

SCORE :
Framingham : www.mdcalc.com
ASCVD calc : www.tools.acc.org

széles körben használatosak

gyulladásos reumatológiai kórképekben alulbecsülik a tényleges rizikót
(nem számolnak a gyulladásos aktivitással és immunmediált tényezőkkel)



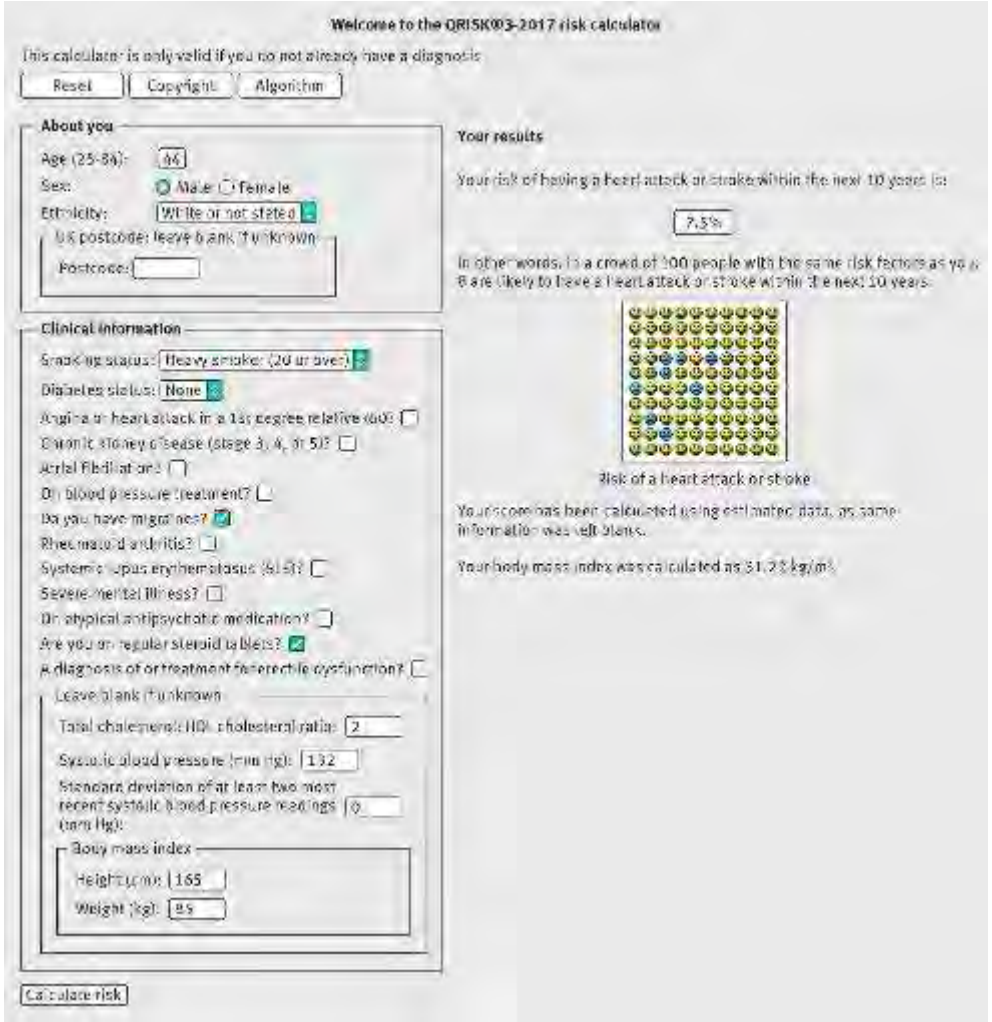
SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. SCORE2 working group and ESC Cardiovascular risk collaboration. European Heart Journal (2021) 42, 2439–2454 .(doi: 10.1093/eurheartj/ehab310)

Peters MJ, et al. (2009). "Cardiovascular risk management in rheumatoid arthritis." *Ann Rheum Dis*, 68(9): 1392-1395.

KARDIOVASCULARIS RIZIKÓ FELMÉRÉS - QRISK3

REUMA SPECIFIKUS MODELL
10 éves rizikófelmérés
Validálás 2017

Figyelembe veszi a krónikus gyulladás okozta emelkedett rizikót
www.qrisk.org

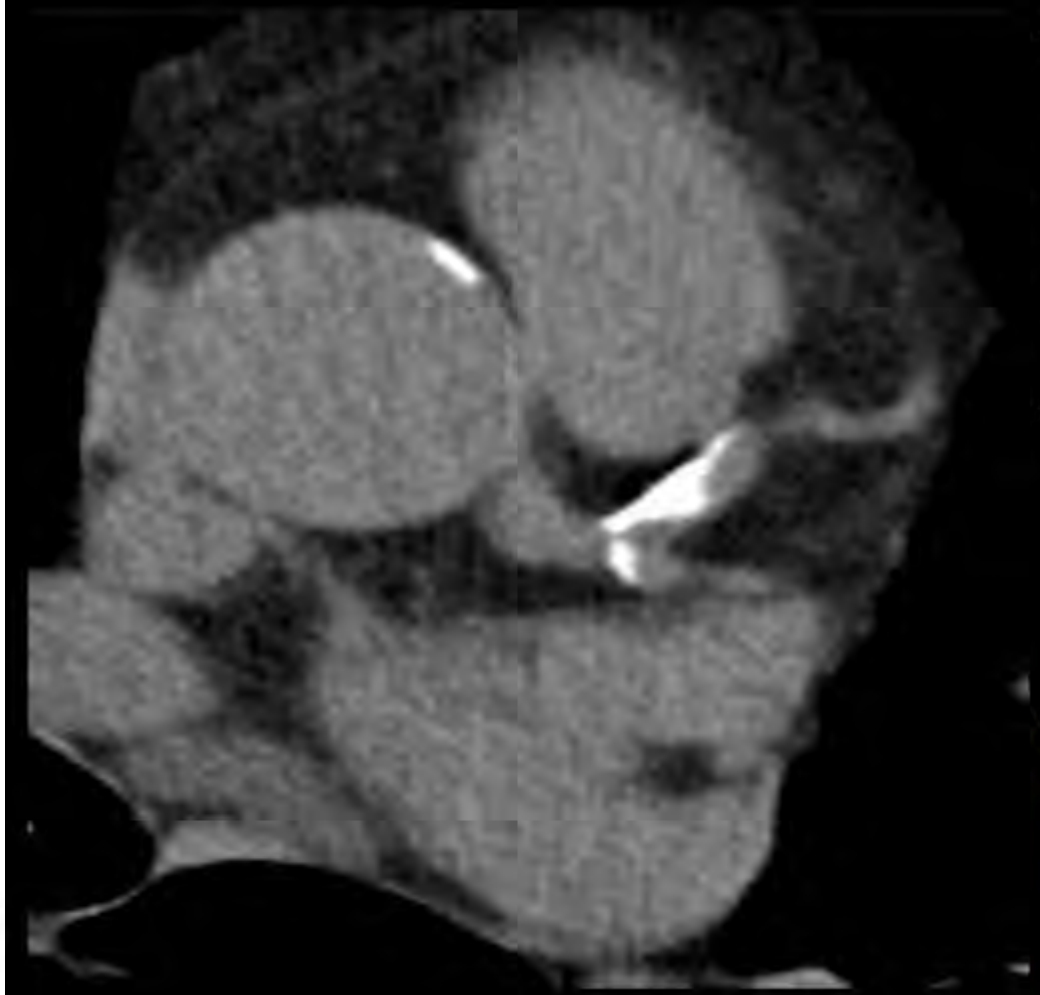


Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: prospective cohort study

BMJ 2017; 357 doi: https://doi.org/10.1136/bmj.j2099 (Published 23 May 2017)Cite this as: *BMJ* 2017;357:j2099

CORONARIA CT-**NATÍV**

Ca-score



- A meszes plakk területének (mm^2) és plakkon belül mért legmagasabb denzitás érték (HU) alapján meghatározott koefficiensnek a szorzata
- Koefficiens 1-4: 1: 130-199 HU
  2: 200-299 HU
  3: 300-399 HU
  4: ≥400 HU
- Meszes lézió detekciós küszöbe:

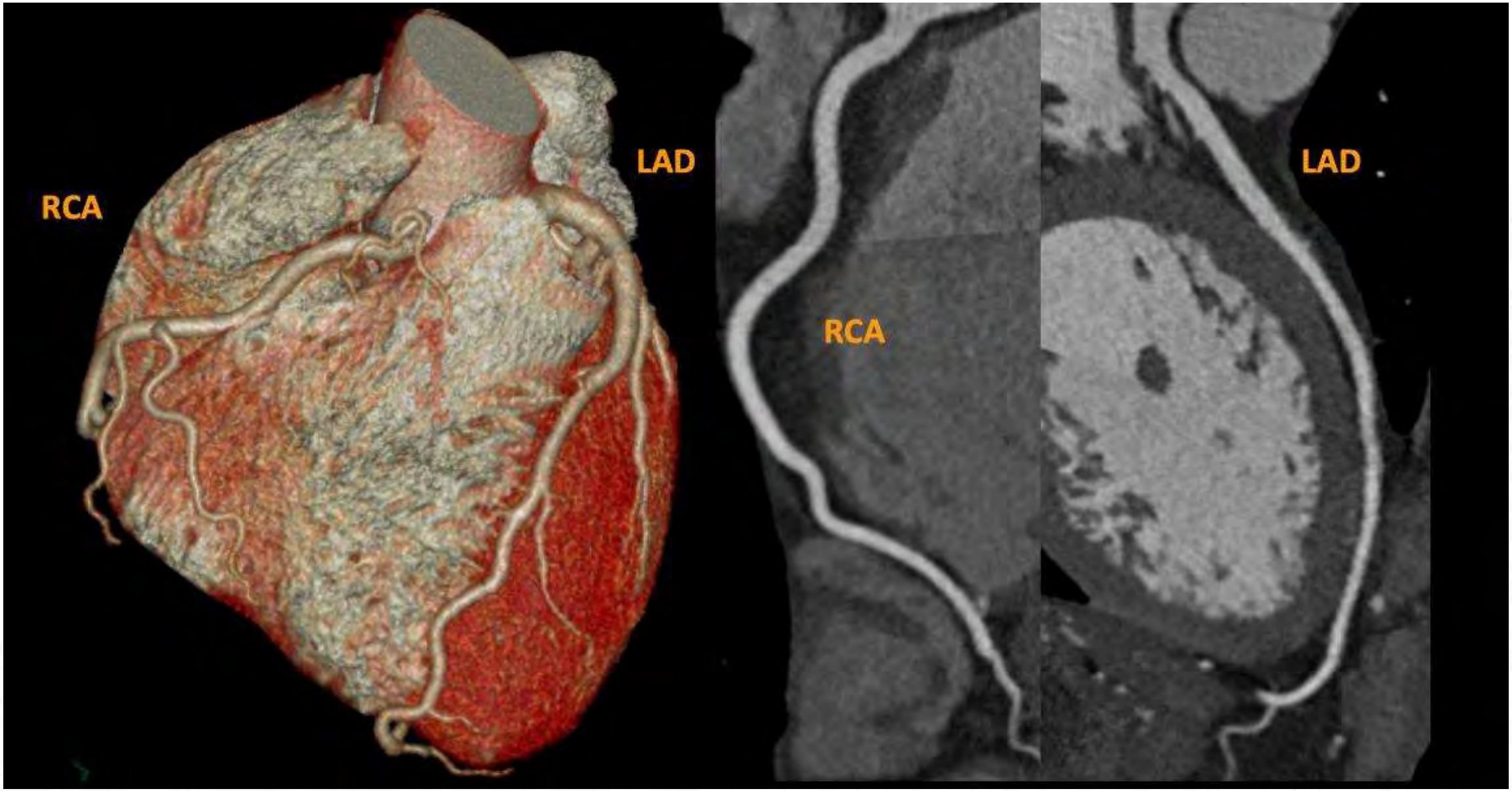
Példa:
Egy meszes lézió maximális denzitása 400 HU, területe 8 mm^2 → A Ca-score: 4x8=32

SCORE	RIZIKÓ
0	Nincs
0-99	Alacsony
100-399	Közepes
400-999	Magas
≥1000	Extrém magas

Detrano et al. NEJM 2008;358:1336-45
Budoff et al., J Am Coll Cardiol. 2007

DE !
Nem kalcifikált plaque-ot nem mutatja

CORONARIA CT-ANGIOGRAPHIA



„LOW GRADE” - „HIGH GRADE” GYULLADÁS ÉS AZ ATHEROSCLEROSIS

- **túlsúly**
- **étkezési szokások**
- genetika
- **alacsony fizikai aktivitás**
- **dohányzás**
- **hiányállapotok**

Low grade **gyulladás**

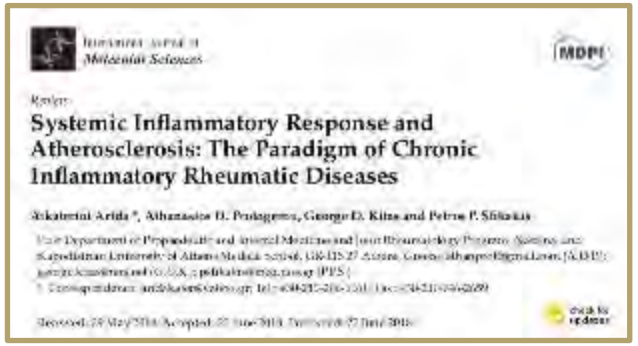
CRP normalis

Hagyományos rizikófaktor útvonal

e.g. Lipid, insulin resistencia,

Haemosztáziseltérések stb.

CV


Systemic Inflammatory Response and Atherosclerosis: The Paradigm of Chronic Inflammatory Rheumatic Diseases

Accelerált atherogenesis

Szisztémás autoimmun **betegség**

High grade systemas **gyulladás**

CRP emelkedett

(~10-50 mg/l)

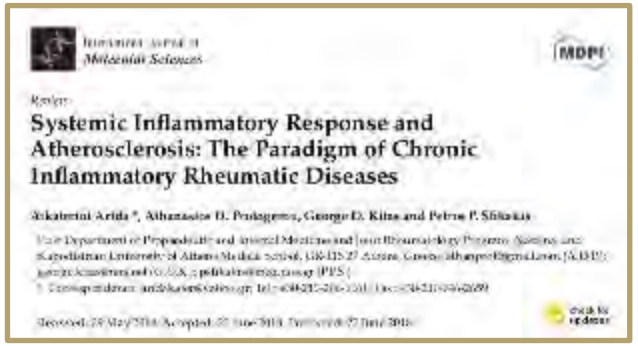
Számos rizikófaktort atherogen **irányba befolyásol**

- ***Atherogén lipid profil***
- Insulin resistencia
- Haemostázis eltérések
- Oxidative stress
- Emelkedett homocystein
- ***Endothel dysfunctio***

CV

Myocardium **microvasculatúra eltérések**
Független a coronária artériák szűkületétől

„LOW GRADE” - „HIGH GRADE” GYULLADÁS ÉS AZ ATHEROSCLEROSIS


Systemic Inflammatory Response and Atherosclerosis: The Paradigm of Chronic Inflammatory Rheumatic Diseases

- **túlsúly**
- **étkezési szokások**
- genetika
- **alacsony fizikai aktivitás**
- **dohányzás**
- **hiányállapotok**

Low grade **gyulladás**

CRP normalis

Hagyományos rizikófaktor útvonal

e.g. Lipid, insulin resistencia,

Haemosztáziseltérések stb.

CV

Accelerált atherogenesis

Statinok

Szisztémás autoimmun **betegség**

High grade systemas **gyulladás**

CRP emelkedett (~10-50 mg/l)

Számos rizikófaktort atherogen **irányba befolyásol**

- ***Atherogén lipid profil***
- Insulin resistencia
- Haemostázis eltérések
- Oxidative stress
- Emelkedett homocystein
- ***Endothel dysfunctio***

CV

Myocardium **microvasculatúra eltérések**
Független a coronária artériák szűkületétől

DMARD- NSAID - MTX -**Biológiai kezelés**

GCs (?)

Table 1. Major published clinical trials involving anti-inflammatory agents in atherosclerotic heart disease.

Trial Name	Study Design	Patient Number	Intervention	Primary Outcomes	Results	Benefit Observed
Broad-spectrum anti-inflammatory approach						
Methotrexate						
Cardiovascular Inflammation Reduction Trial (CIRT) [77]	Phase 3 multicentre, randomised, double-blind, placebo-controlled	4786	Oral low methotrexate (target dose of 15–20 mg weekly) vs. placebo	Non-fatal myocardial infarction, non-fatal stroke and cardiovascular death	HR 1.01; 95% CI 0.82–1.25; $p = 0.91$	✗
Colchicine						
Low-dose colchicine for secondary prevention of cardiovascular disease (LoDoCo) [78]	Phase 3 multicentre, randomised, double-blind, placebo-controlled	532	Colchicine 0.5 mg/day vs. placebo	MI, fatal or non-fatal out-of-hospital cardiac arrest, or non-cardioembolic ischaemic stroke	HR 0.33; 95% CI 0.18–0.59; $p < 0.001$	✓
Narrow-spectrum anti-inflammatory approach						
IL-1β						
Anti-inflammatory Therapy with Canakinumab for Atherosclerosis (CANTOS) [76]	Phase 3 multicentre, randomised, double-blind, placebo-controlled	10,061	Subcutaneous injection of canakinumab (50 mg, 150 mg or 300 mg) every 3 months vs. placebo	Non-fatal MI, non-fatal stroke and cardiovascular death	HR 0.85; 95% CI 0.74–0.98; $p = 0.021$ in the 150 mg-treated group	✓
Lipoprotein-associated phospholipase A2 (Lp-PLA$_2$)						
SOLID-TIMI 52 [79]	Phase 3 multicentre, randomised, double-blind, placebo-controlled	13,026	Daily oral darapladib 160 mg vs. placebo	Coronary heart disease death, non-fatal MI and urgent revascularisation for myocardial ischaemia	HR 1.00; 95% CI 0.91–1.09; $p = 0.93$	✗
P38 mitogen-activated protein kinase (MAPK)						
LATITUDE-TIMI 60 [80]	Phase 3 multicentre, randomised, double-blind, placebo-controlled	3503	Oral losmapimod 7.5 mg twice daily vs. placebo	Non-fatal MI, severe recurrent ischaemia requiring urgent coronary artery revascularisation and cardiovascular death	HR 1.16; 95% CI 0.91–1.47; $p = 0.24$	✗

Abbreviations: CI, confidence interval; HR, hazard ratio; IL, interleukin; mg, milligrams; MI, myocardial infarction. The green tick sign represents that the intervention was associated with a significant benefit whereas a red cross represents that there was no significant benefit observed.

INGERKÉPZÉSI ÉS VEZETÉSI ZAVAROK

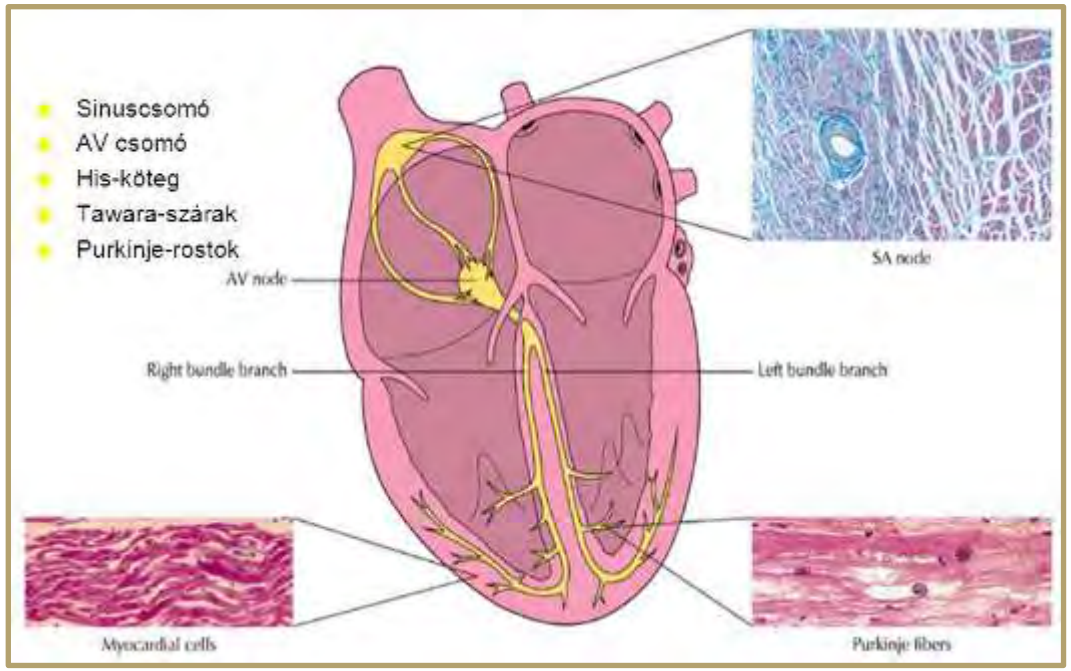
IMMUNOLÓGIAI VONATKOZÁSAI

Dr Végh Judit PhD
főorvos

AZ INGERKÉPZŐ ÉS VEZETŐ RENDSZER AUTOIMMUN JELENSÉGEI

Sinus csomó ellenes AT jelenléte
AV csomó ellenes AT jelenléte
HIS köteg ellenes AT
Purkinje sejt ellenes AT

10x gyakoribb a SSS
3x gyakoribb az AV block
alacsony mindenkiben



Herz. 2000 May;25(3):181-8.
Cardiac rhythm and conduction disturbances: what is the role of autoimmune mechanisms?
Ristic AD1, Maisch B.

CONGENITALIS SZÍVBLOCK

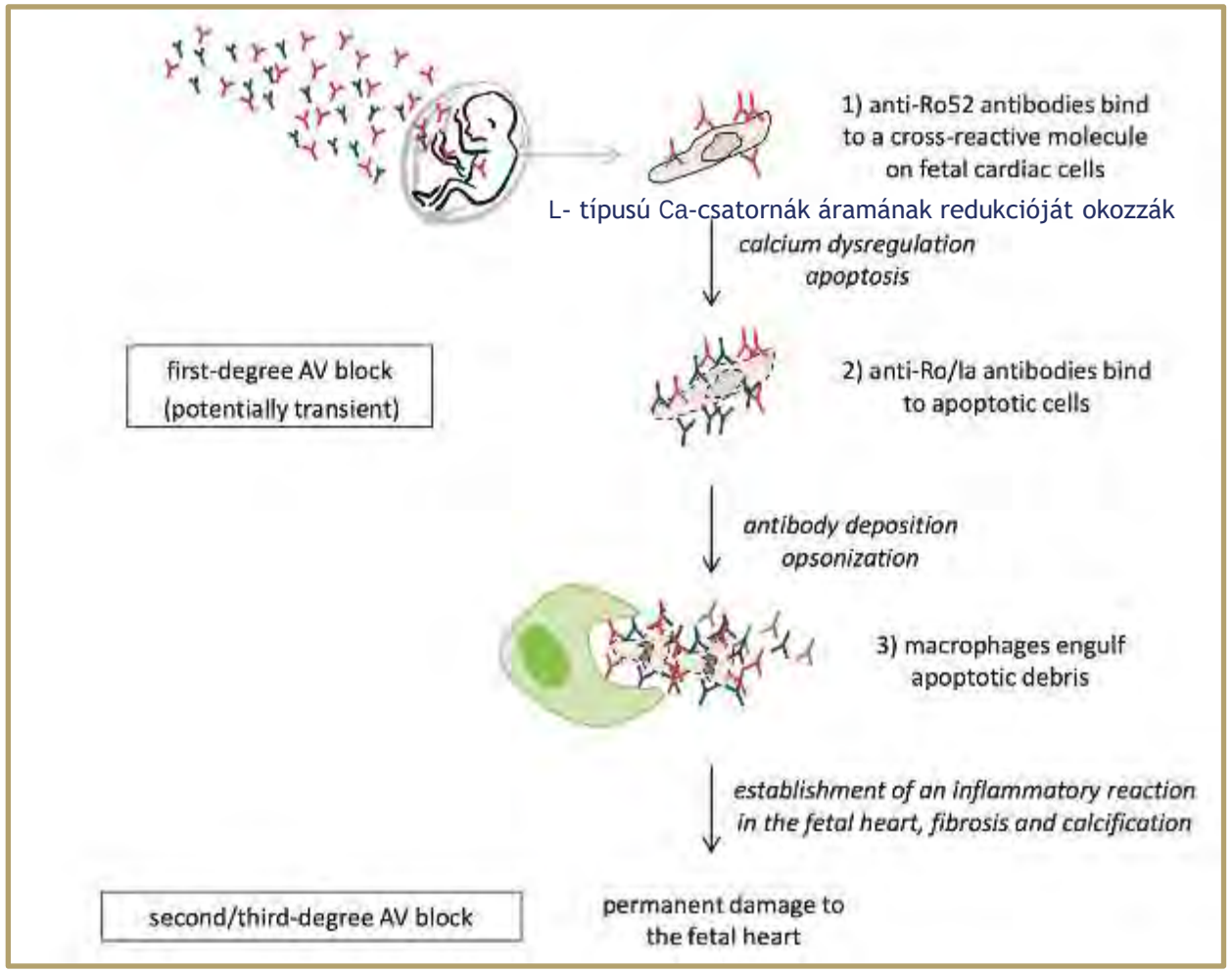
aSSA, aSSB anyák magzataiban alakulhat ki

IgG AB + FcRn + alb
Transplacentaris transzport : 16-22 hét – 10% IgG

SZŰRÉS - MAGZATI ECHOCARDIOGRAPHIA !!

Prevencio :
400 mg/nap hydroxichloroquin
Szeroid-azatioprin- IVIg- autoimmun betegek

Kezelés :
400 mg/nap hydroxichloroquin
Steroid-azathioprin- IVIg (1 gr/ttkg / 2 hét)
PEX (2-3000 ml/alkalom)



AUTOANTITESTEK A RITMUSZAVAROK HÁTTERÉBEN

Sinus bradycardia- AV block :
aSSA –Ca csatorna,
NA csatorna ell at – Na csatorna

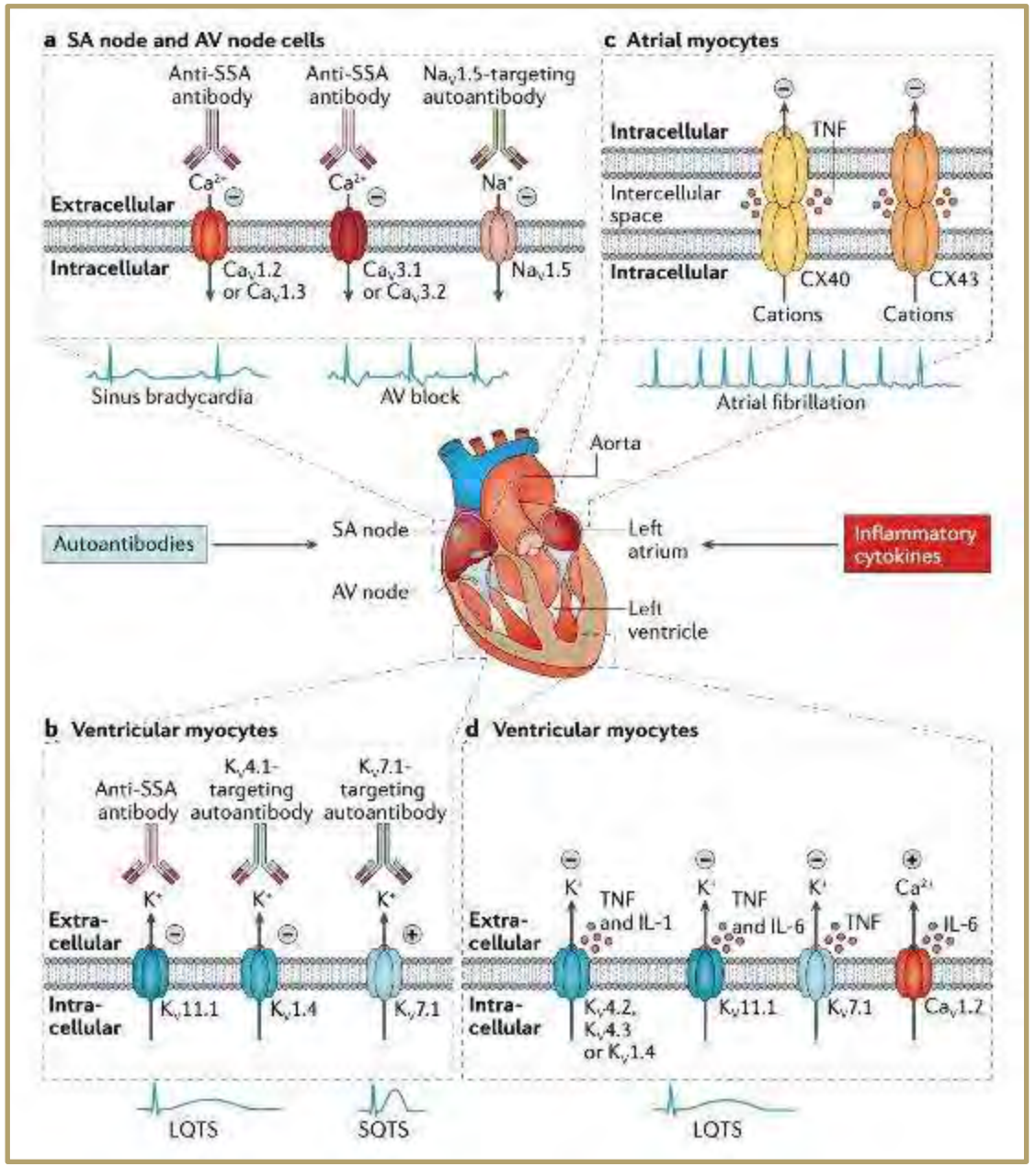
Pitvarfibrillatio :
TNF alfa – CX40, CX43-en keresztül a gap junction funkciót gátolja

longQT
aSSA – K csatorna
TNF alfa – K csatorna
IL-6- cs csatorna gátlás

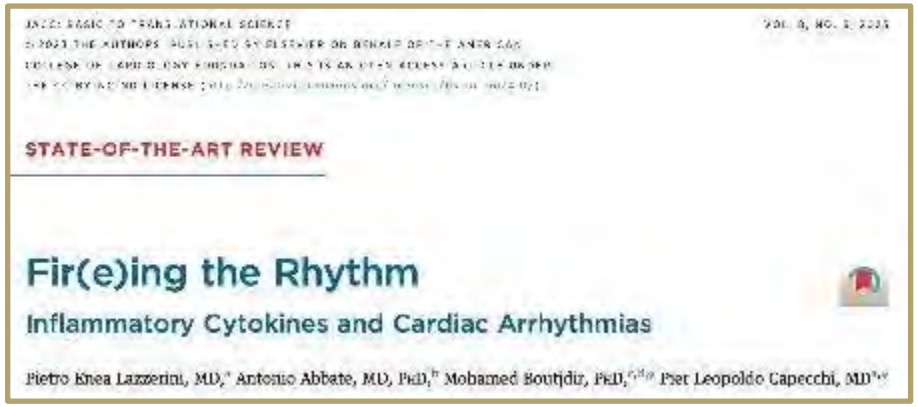
Cardioimmunology of arrhythmias: the role of autoimmune and inflammatory cardiac channelopathies

Pietro Enea Lazzerini ✉, Franco Laghi-Pasini, Mohamed Boutjdir & Pier Leopoldo Capecchi

Nature Reviews Immunology **19**, 63–64 (2019) | Cite this article



INFLAMMATORIKUS CYTOKINEK ARRYTHMOGEN HATÁSA

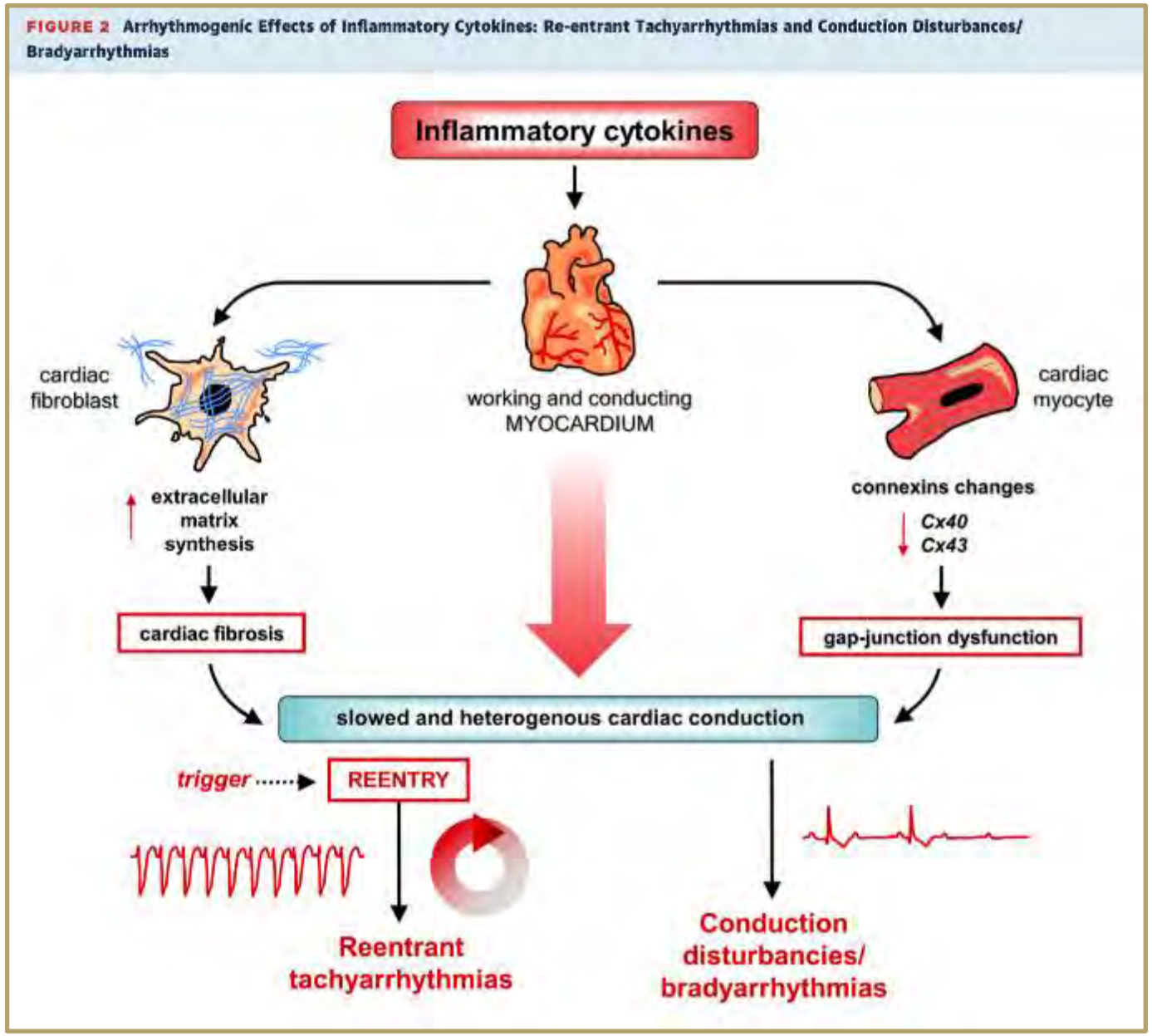


STATE-OF-THE-ART REVIEW

Fir(e)ing the Rhythm

Inflammatory Cytokines and Cardiac Arrhythmias

Pietro Enea Lazzerini, MD,* Antonio Abbate, MD, PhD,† Mohamed Boutjdir, PhD,‡§¶ Pier Leopoldo Capecchi, MD*



INFLAMMATORIKUS CYTOKINEK HATÁSMECANIZMUSA

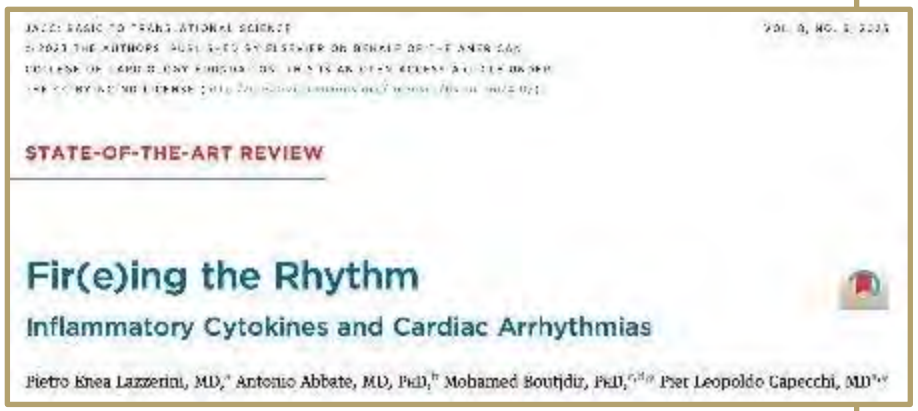
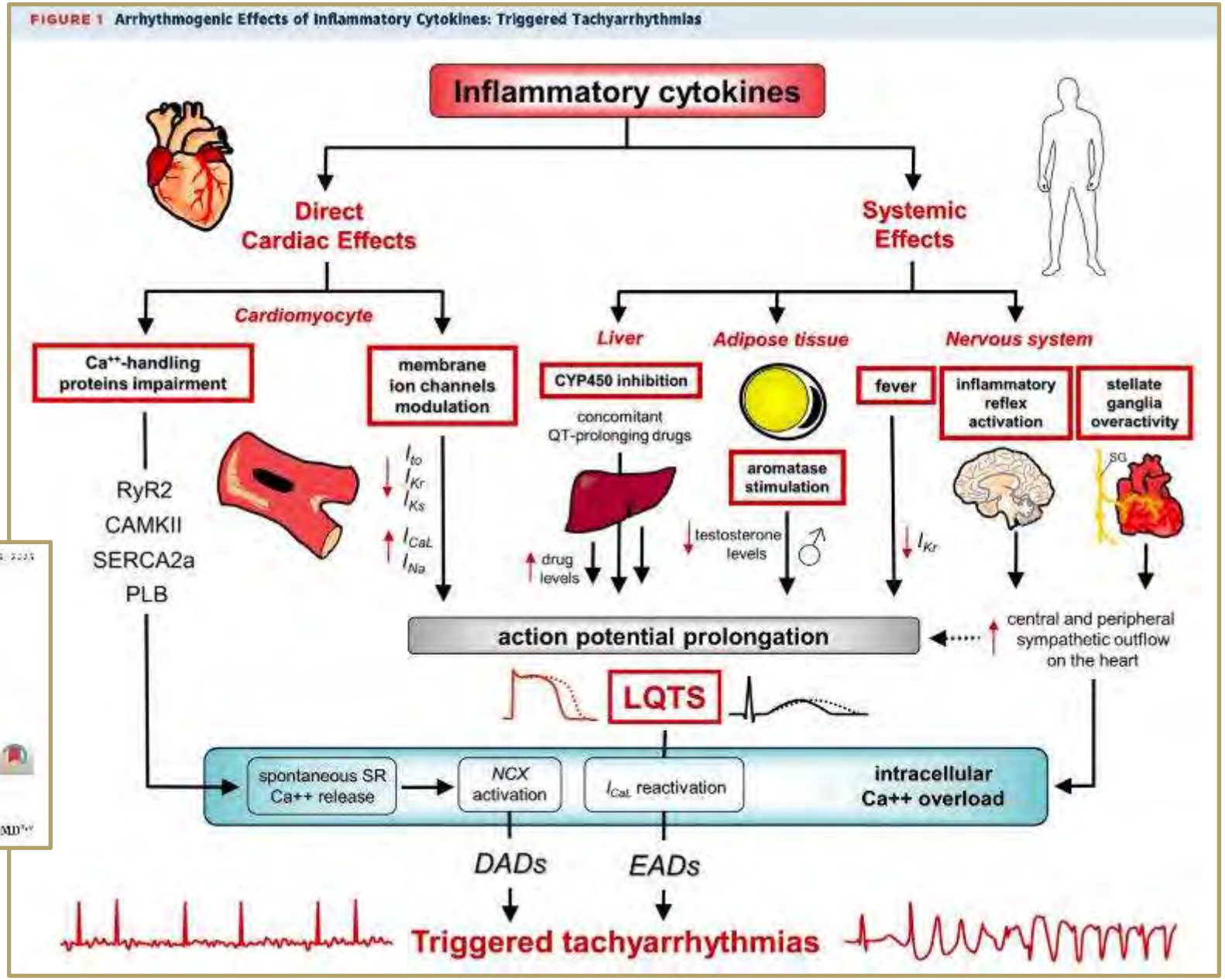
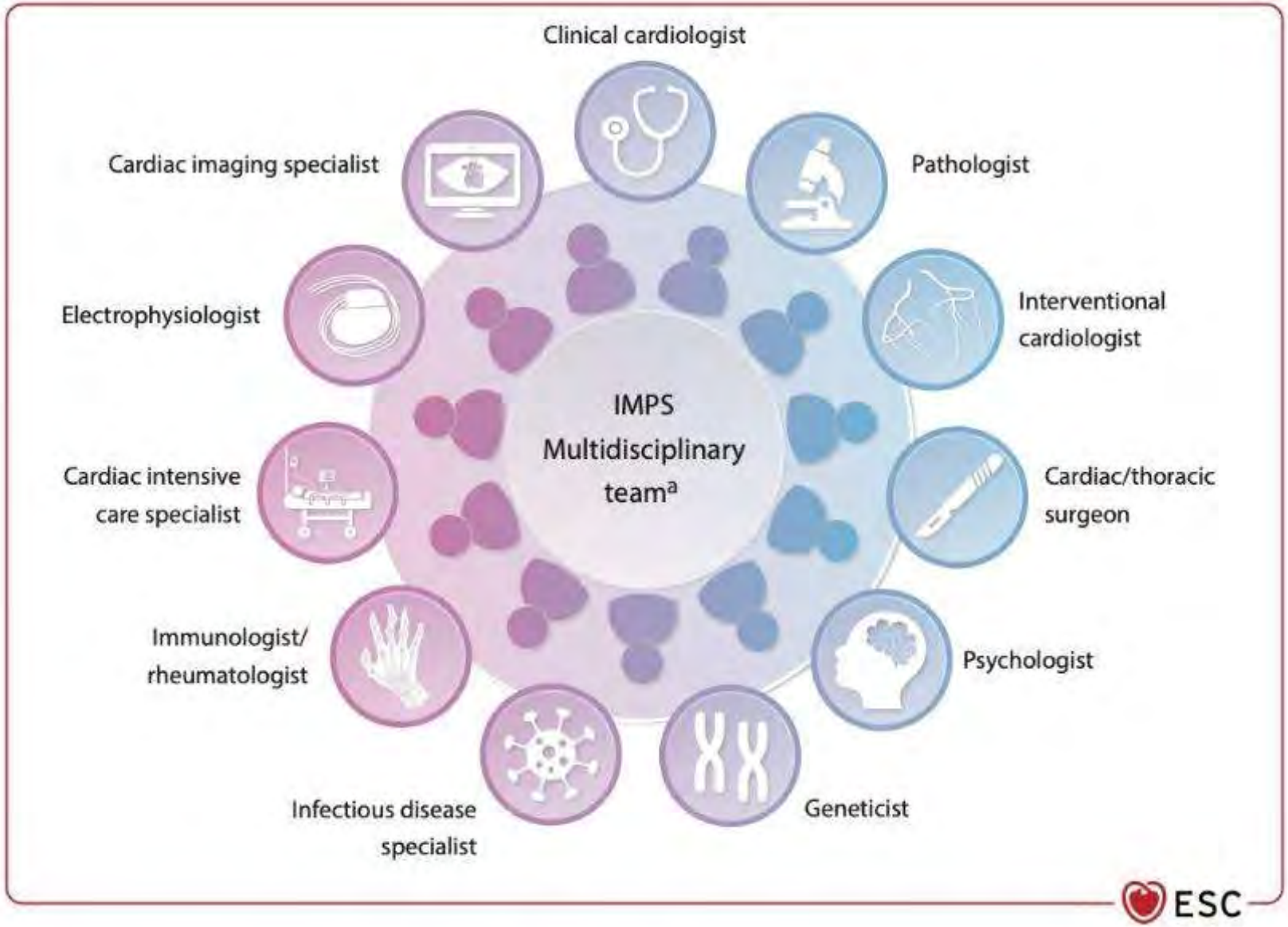


FIGURE 1 Arrhythmogenic Effects of Inflammatory Cytokines: Triggered Tachyarrhythmias




Clinical cardiologist
Cardiac imaging specialist
Pathologist
Electrophysiologist
Interventional cardiologist
IMPS Multidisciplinary team[a]
Cardiac intensive care specialist
Cardiac/thoracic surgeon
Immunologist/ rheumatologist
Psychologist
Infectious disease specialist
Geneticist
ESC

SEMMELWEIS
EGYETEM 1769