Ρευματική νόσος:

Πρέπει να φοβόμαστε

τη νόσο ή τη θεραπεία

στο καρδιαγγειακό σύστημα;

Λιβανός Μιχάλης
Καρδιολόγος
Βουλευτης Β' Πειραιά

ΒΟΥΛΗ ΤΩΝ ΕΛΛΗΝΩΝ

Σύγκρουση συμφερόντων

Καμία σύγκρουση συμφερόντων

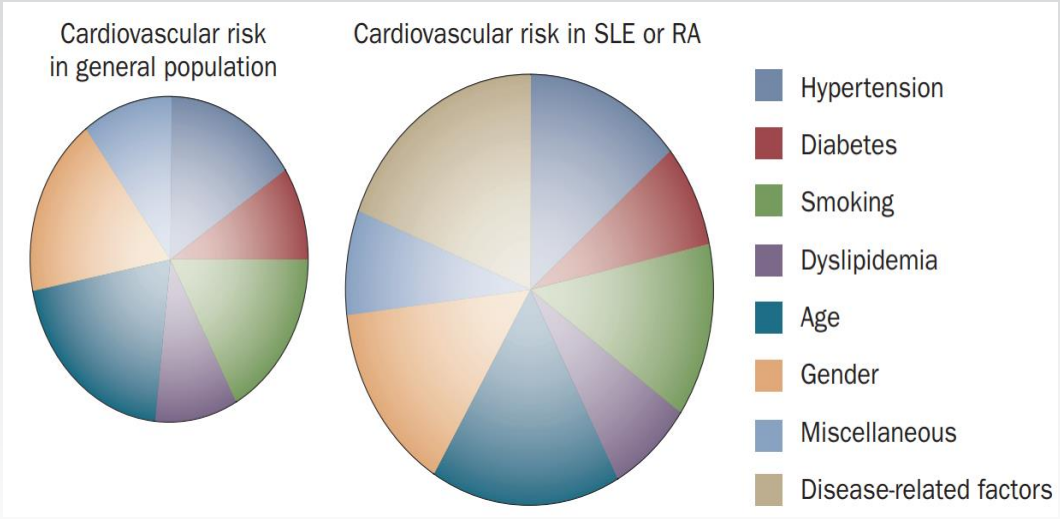
Ροή της παρουσίασης

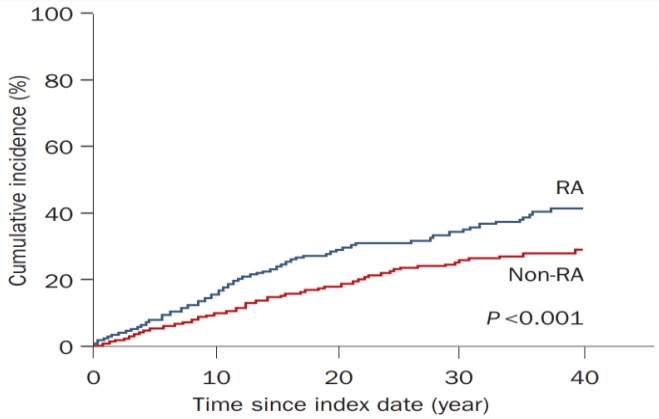
Εισαγωγή	Γιατί αυτή η παρουσίαση;
Παρουσίαση περιστατικού	Ασθενής με Ψωριασική Αρθρίτιδα και Στεφανιαία νόσο
Ανοσολογία της Καρδιολογίας	Μηχανισμοί αθηροσκλήρωσης
Ρευματολόγος ως Καρδιολογος	Αρχές θεραπείας του καρδιαγγειακού
Νόσος και καρδιαγγειακό σ.	Αυξημένος καρδιαγγειακός κίνδυνος ή όχι;
Ανοσοτροποποίηση και ΚΑ	Αυξημένα καρδιαγγειακά συμβάματα ή όχι;
Θεραπευτική απόφαση	…με οδηγό την παθοφυσιολογία και την κλινική

Εισαγωγή

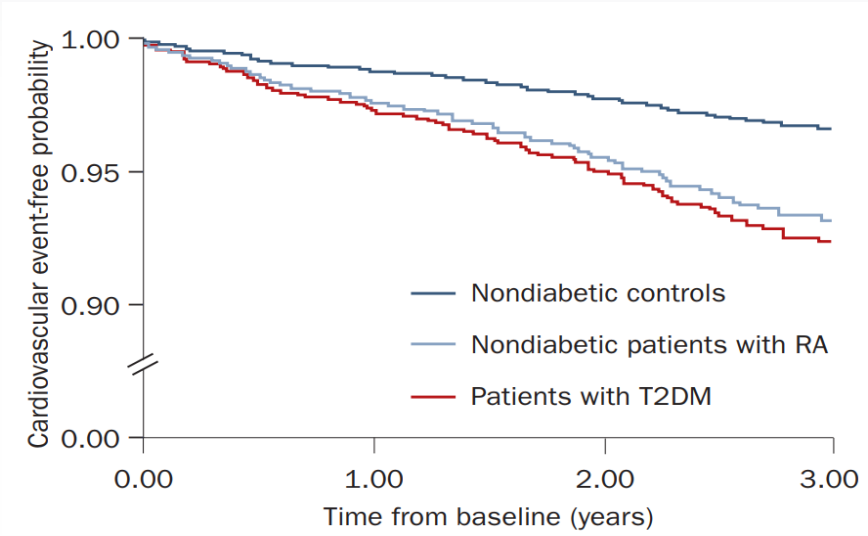
Γιατί αυτή η παρουσίαση…;

Disease	RA	SLE	APS	SSc	AS	PsA
MI	✓	✓	✓	✓	✓	✓
CHF	✓	✓		✓	✓	
PAD	✓	✓	✓			✓
PH				✓		
Myocardial diseases	✓	✓		✓	✓	✓
Endocardial diseases	✓	✓	✓		✓	
Valvular disease	±	✓	✓		✓	
Pericarditis	✓	✓		✓	✓	
Arteritis (coronary, aorta)						
Conduction defects	±			✓	✓	✓





Number at risk					
RA	575	336	133	51	7
Non-RA	583	386	189	75	15



Symmons, D. P. M. & Gabriel, S. E. Nat. Rev. Rheumatol. 7, 399–408 (2011)

Nicola, P. J. et al. Arthritis Rheum. 52, 412–420 (2005)

Peters,M. J. et al.Arthritis Rheum. 61, 1571–1579 (2009)

Όμως ταυτόχρονα…

FDA

Search Menu

IN THIS SECTION

← Drug Safety and Availability

FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions

Approved uses also being limited to certain patients

Share Tweet Email

12/2021 Update: The issues described below have been addressed in product labeling. Health care professionals and patients can access the approval letters and latest prescribing information in Drugs@FDA:

ELSEVIER

The European Journal of Heart Failure 4 (2002) 559–561

The European Journal of Heart Failure

www.elsevier.com/locate/heafai

Clinical trials update: RENEWAL (RENAISSANCE and RECOVER) and ATTACH

A.P. Coletta*, A.L. Clark, P. Banarjee, J.G.F. Cleland

Department of Academic Cardiology, University of Hull, Castle Hill Hospital, Cottingham, Kingston upon Hull, HU15 5JQ, UK

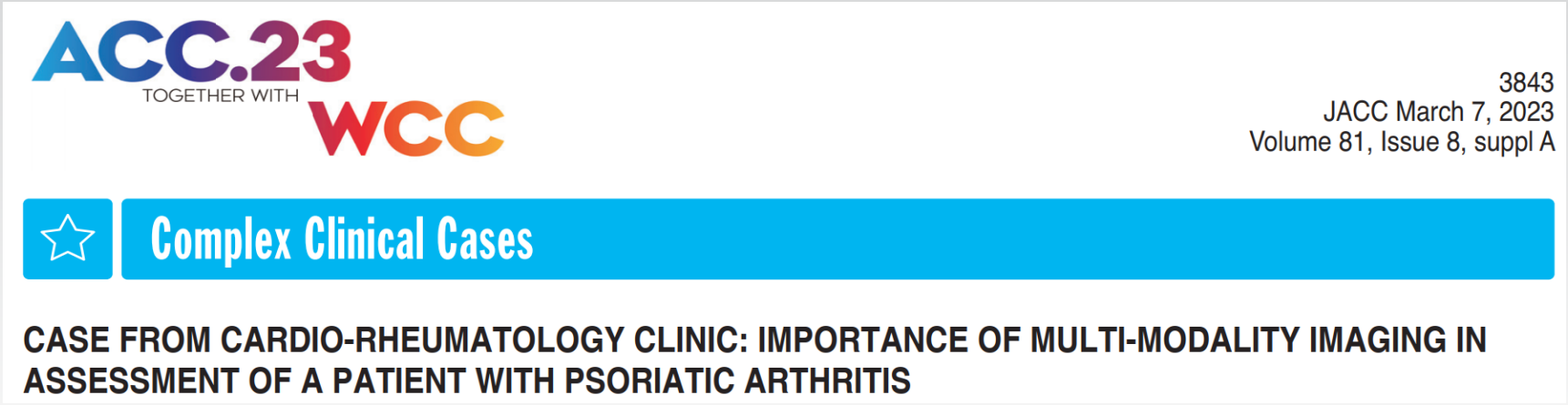
Received 17 June 2002; accepted 1 July 2002

NYHA III & IV:

Avoid use of Tumor Necrosis Factor alpha inhibitors

Παρουσίαση Περιστατικού

Ασθενής με αυξημένο καρδιαγγειακό κίνδυνο



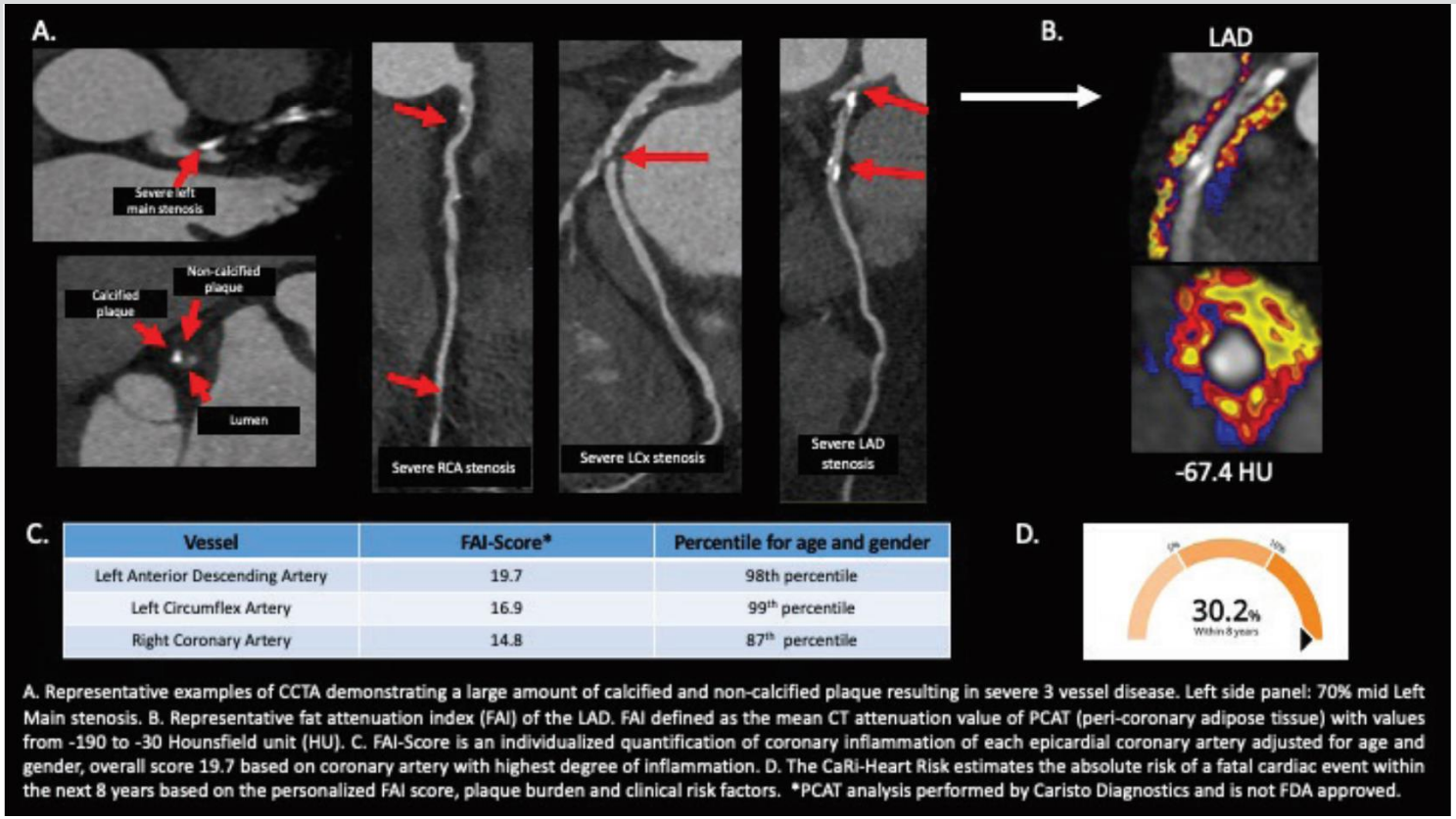
61-χρονος ασθενής με ***ενεργό*** ΨΑ υπό αντι-TNFa αναστολέα (etanercept) προσέρχεται στο ρευματολογικό εξωτερικό ιατρείο με δύσπνοια προσπαθείας

ΗΚΓ: κφ / **Triplex διαθωρακικό**: Φυσιολογική κινητικότητα τοιχώματος ΑΡ/ΔΕ κοιλοτήτων
Σπινθηρογράφημα: χωρίς στοιχεία ισχαιμικής καρδιοπάθειας

LDL **137 mg/dL**, Hs-CRP **12.7 mg**/L. BMI **31**

Θεραπευτική απόφαση: Παρά τον αρχικό φυσιολογικό έλεγχο, ο ασθενής είχε ***σημαντικούς παράγοντες καρδιαγγειακού κινδύνου*** με ***συνεχιζόμενη συστηματική φλεγμονή*** και ήταν παραπέμφθηκε στην καρδιο-ρευματολογική κλινική

Δεν ήταν αυτό που περιμέναμε… ή μήπως ήταν…



Vessel	FAI-Score*	Percentile for age and gender
Left Anterior Descending Artery	19.7	98th percentile
Left Circumflex Artery	16.9	99th percentile
Right Coronary Artery	14.8	87th percentile

A. Representative examples of CCTA demonstrating a large amount of calcified and non-calcified plaque resulting in severe 3 vessel disease. Left side panel: 70% mid Left Main stenosis. B. Representative fat attenuation index (FAI) of the LAD. FAI defined as the mean CT attenuation value of PCAT (peri-coronary adipose tissue) with values from -190 to -30 Hounsfield unit (HU). C. FAI-Score is an individualized quantification of coronary inflammation of each epicardial coronary artery adjusted for age and gender, overall score 19.7 based on coronary artery with highest degree of inflammation. D. The CaRi-Heart Risk estimates the absolute risk of a fatal cardiac event within the next 8 years based on the personalized FAI score, plaque burden and clinical risk factors. *PCAT analysis performed by Caristo Diagnostics and is not FDA approved.

CT στεφανιογραφία: Σοβαρού βαθμού στένωση 3 αγγείων - CAD with 70% αριστερή κύρια στένωση και αθηρωματικές πλάκες υψηλού κινδύνου

Θεραπευτική παρέμβαση: ***CABG 3 αγγείων + στατίνη + ασπιρίνη***
+ ***πιο επιθετική θεραπεία για την ΨΑ***
!!!

Ανοσολογία της καρδιολογίας

Τα πράγματα αλλάζουν στην καθημερινότητα μας…

MEDPAGETODAY®

Cardiology > Prevention

Colchicine's Rebirth as Cardiovascular Drug Approved by FDA

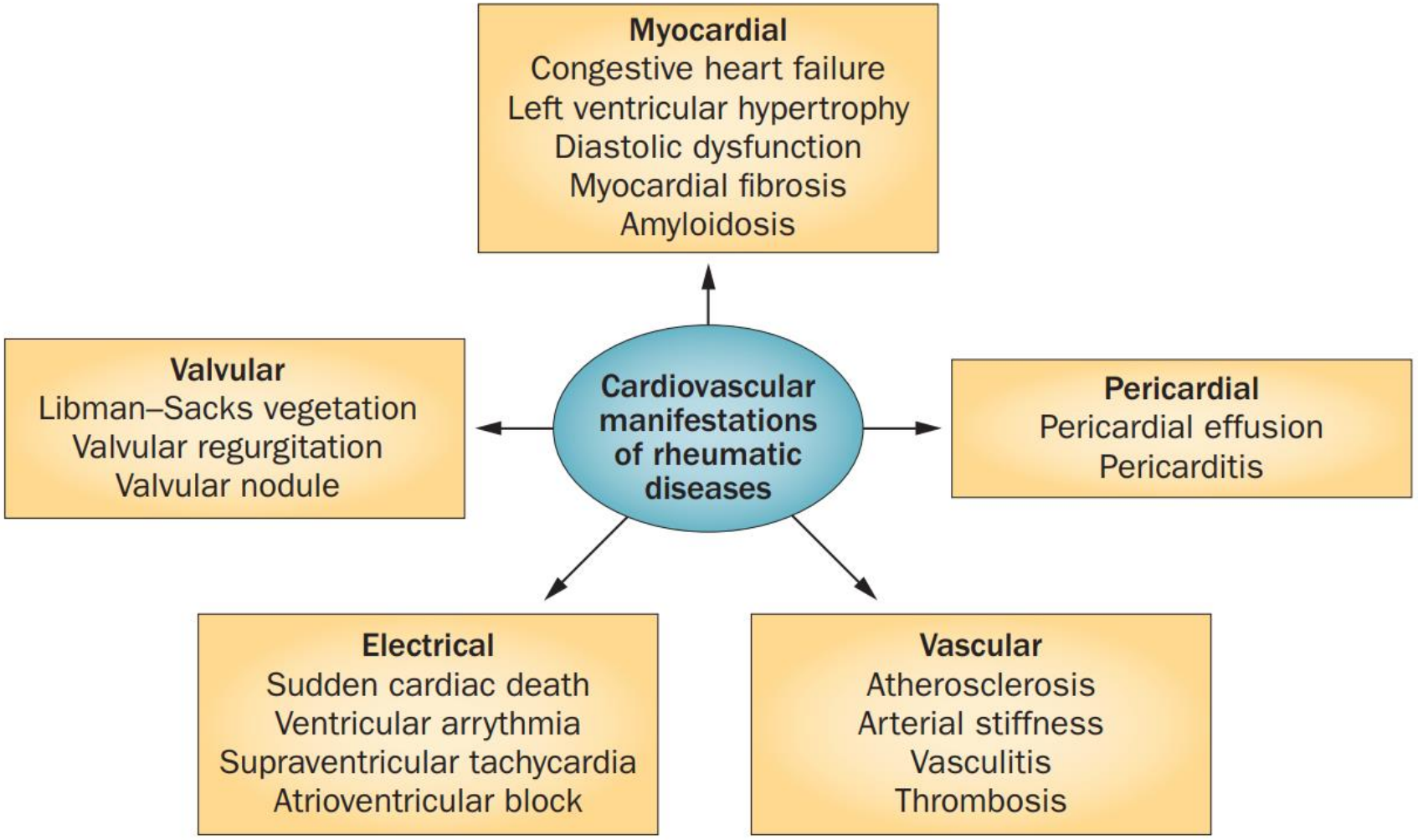
— Repurposed anti-inflammatory drug may be used alone or in combination with standard meds

by Nicole Lou , Senior Staff Writer, MedPage Today
June 20, 2023

The FDA approved colchicine (Lodoco) for cardiovascular prevention in adults with established atherosclerotic disease or multiple risk factors, making it the first anti-inflammatory medicine with such an indication.

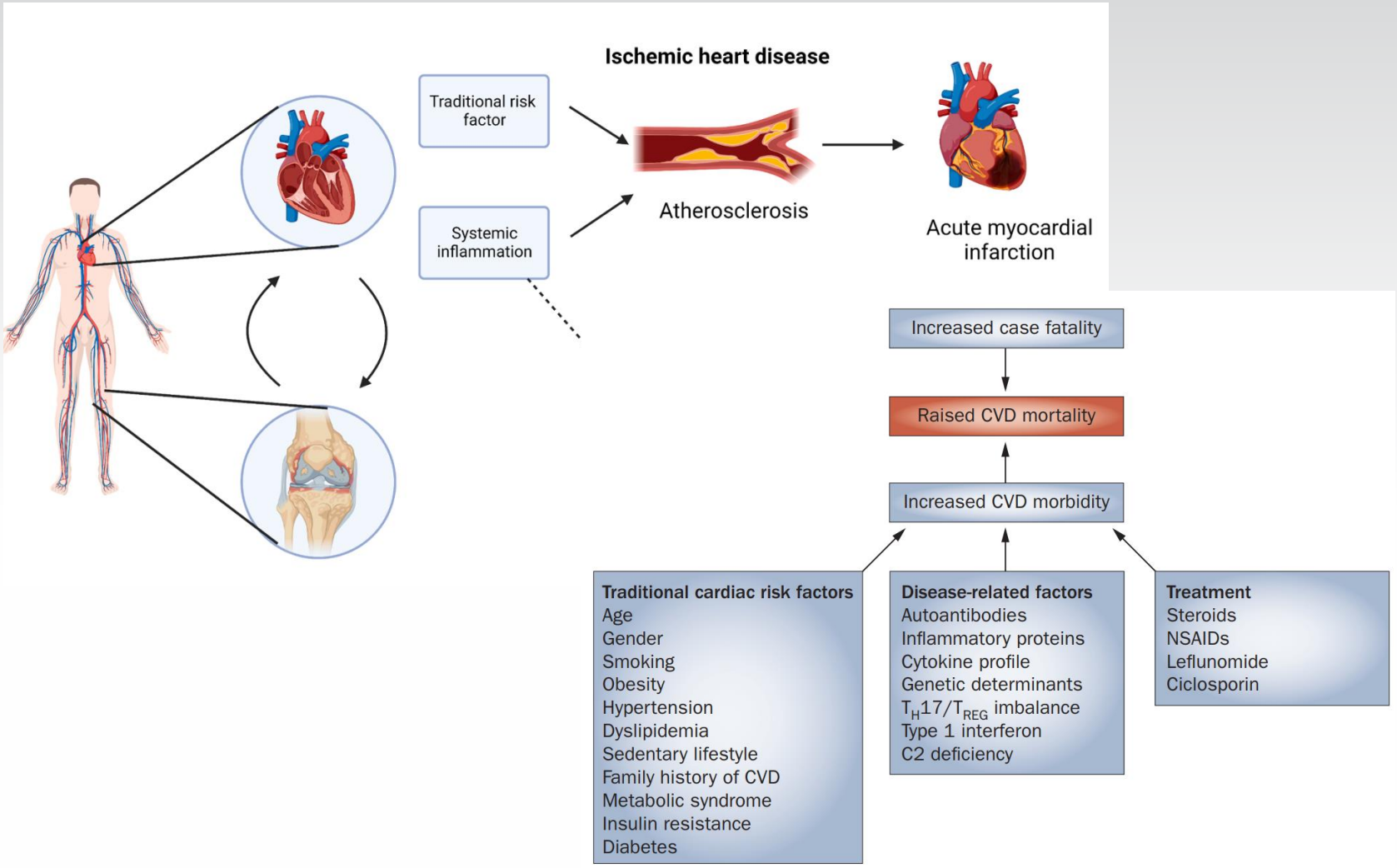
The **U.S. Food and Drug Administration (FDA)** has approved LODOCO as the ***first anti-inflammatory atheroprotective cardiovascular treatment*** demonstrated to reduce the risk of myocardial infarction (MI), stroke, coronary revascularization, and cardiovascular death in adult patients with established atherosclerotic disease or with multiple risk factors for cardiovascular disease.

Οι Ρευματικές / Φλεγμονώδεις παθήσεις ως αίτιο αυξημένης νοσηρότητας στο καρδιαγγειακό σύστημα



Prasad, M. et al. Nat. Rev. Cardiol. 12, 168–176 (20

Δεν είναι μόνο η επιταχυνόμενη αθηροσκλήρωση…



Johri Nis et al. Health Sci Rev 8 (2023)
Symmons, D. P. M. & Gabriel, S. E. Nat. Rev. Rheumatol. 7, 399–408 (2011)

Κοινή παθολογία και κοινοί μηχανισμοί ιστικής βλάβης!

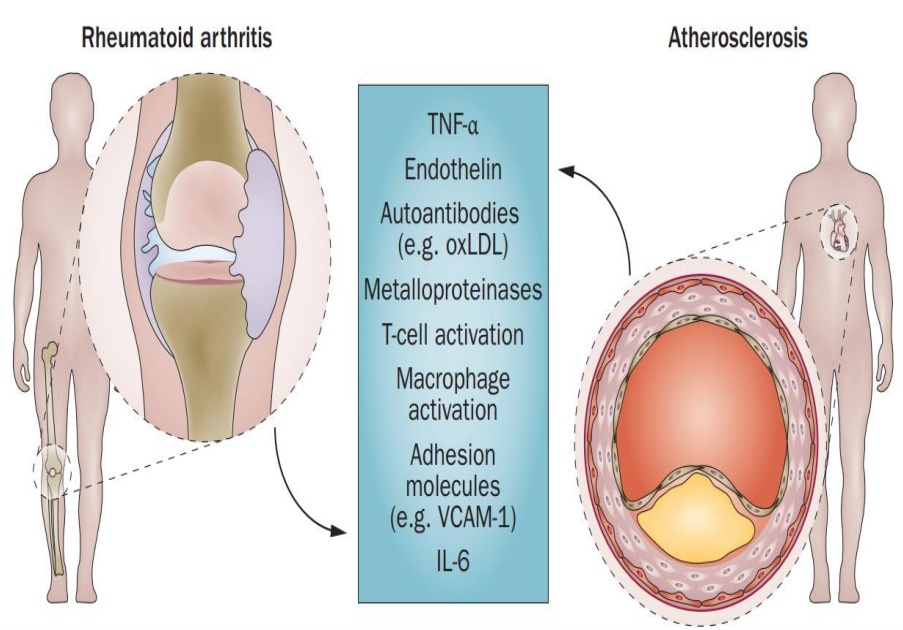


Table 1 Shared disease mechanisms in rheumatic diseases and CVD

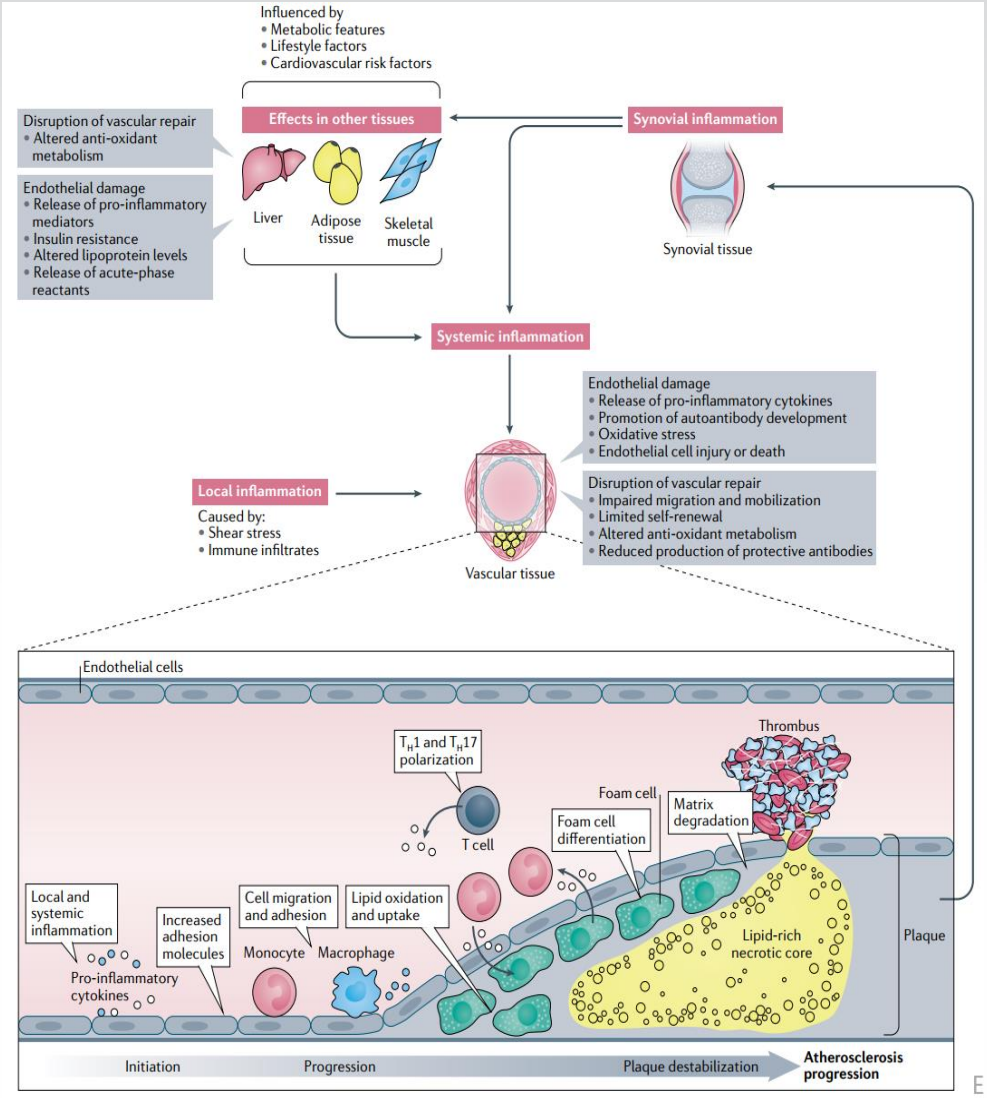
Mechanism	Pathway in vascular disease	References
Cytokine-induced macrophage migration and activation	Ox-LDL scavenging and formation of vulnerable atherosclerotic plaque	Ross 1999 Hansson 2005 Dixon and Symmons 2007
Cytokine-induced upregulation of procoagulant factors	Increased systemic thrombodiatesis	McEntegart et al 2001; Sattar et al 2003
Systemic endothelial activation with upregulation of MHC class II molecules	Endothelial dysfunction Increased T-cell migration and activation	Vallbracht et al 2002; Turesson 2004
Clonal expansion and activation of abnormal T-cells	Cytotoxicity leading to plaque damage Local cytokine upregulation	Park et al 1997 Liuzzo et al 1999 Michel et al 2007
Anti-phospholipid antibodies	Increased arterial and venous thrombodiatesis	Toloza et al 2004

Table 16.3 Prevalence of traditional risk factors

Prevalence	Smoking	Hypertension	DM	Dyslipidemia	Obesity
RA	↑↑	↑	↑↑	↑↑	↑
SLE	↑	↑↑	↑	↑	↑
General population	↑	↑	↑	–	↑

Prasad, M. et al. Nat. Rev. Cardiol. 12, 168–176 (2015)
Turesson, C.. et al. Vasc Health Risk Manag 4(8); 608-814 (2008)

Η φλεγμονή της ρευματικής νόσου ως παράγοντας κινδύνου



IL-2-mediated
- ↑ Angiogenesis
- Pro-inflammatory macrophages
- ↑ Inflammation
- ↓ Tissue healing

IL-15-mediated
- ↓ Systolic and diastolic heart function
- ↑ Atherosclerosis progression
- ↑ Infarct size

IL-6-mediated
- ↑ Lipid levels
- Lipid composition pro-atherogenic
- ↑ Heart failure?
- ↑ Myocardium fibrosis versus
- ↑ Heart survival pathways (stabilization in ischaemia-reperfusion injury)

IL-12-mediated
- ↑ Atherosclerosis
- ↑ Ischaemic cardiomyopathy
- ↑ Cardiomyocyte apoptosis
- ↑ Myocardium fibrosis

EPO-mediated
- ↑ Erythropoiesis (↓ heart function in anaemia)

TPO-mediated
- ↑ Thromboembolism?

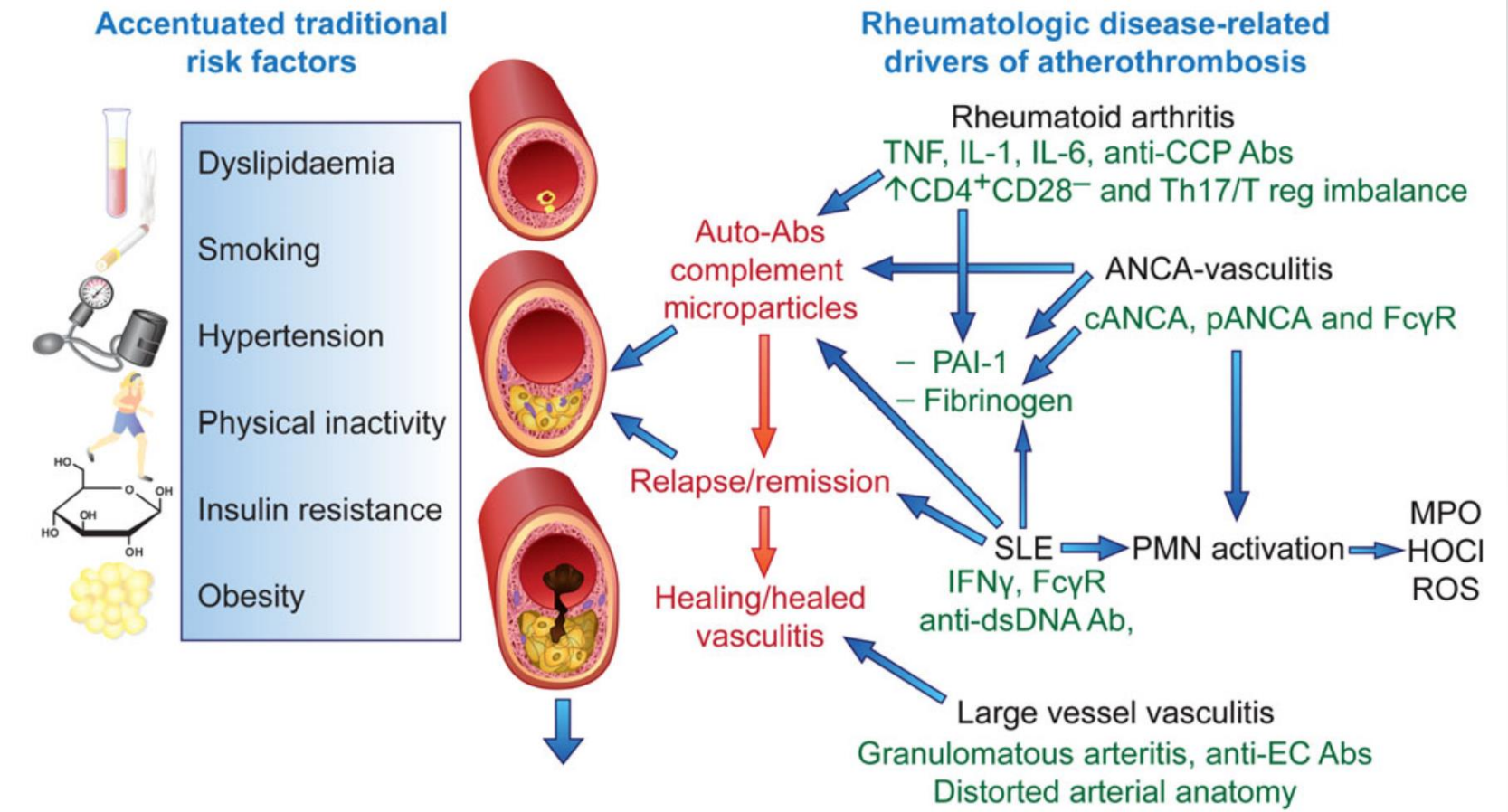
IFNγ-mediated
- ↑ Atherosclerosis
- ↑ Foam cell formation

IFNα/β-mediated
- ↑ EBV and/or CMV viral infection-mediated vascular pathologies

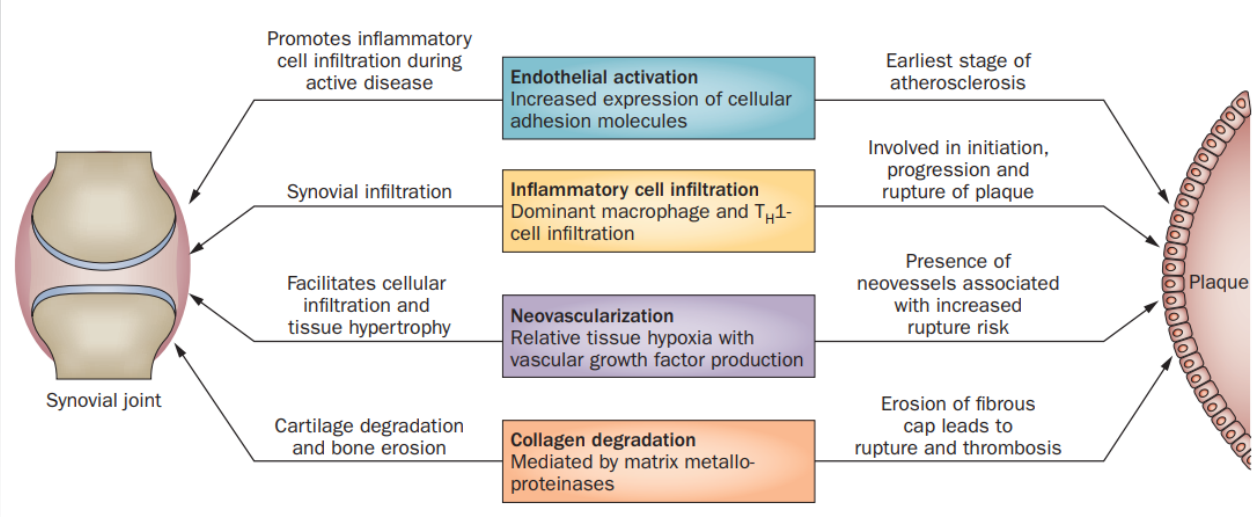
Szekanecz, Z., Buch, M.H., Charles-Schoeman, C. et al. Nat Rev Rheumatol 20, 101–1 (2024).

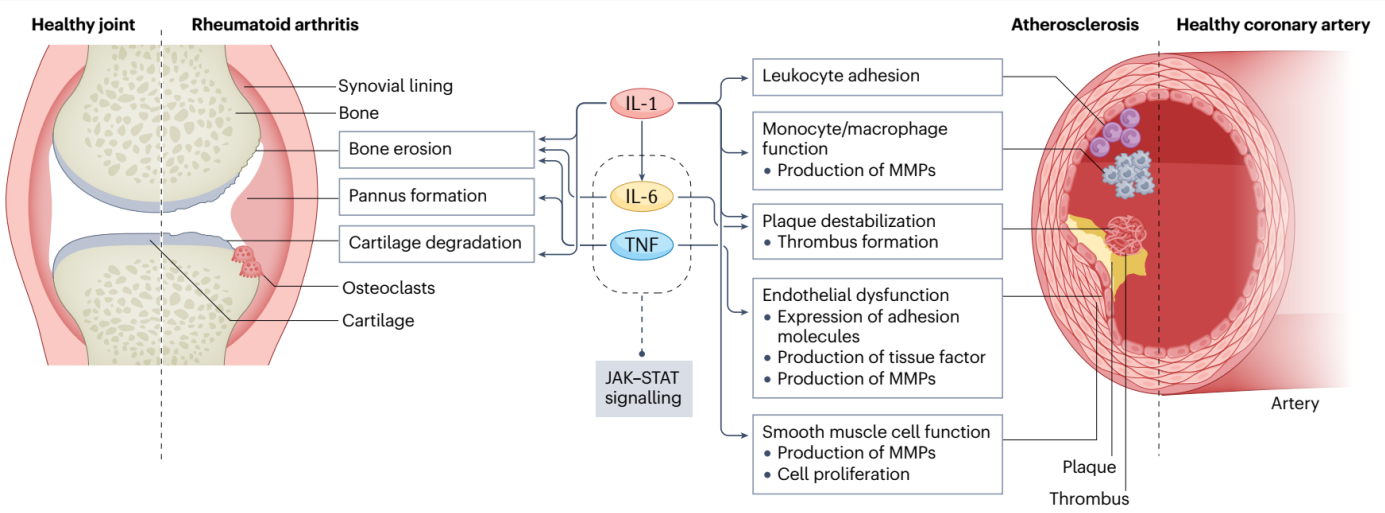
Αρχες θεραπείας

Με οδηγό το ιστορικό και την παθοφυσιολογία



Σκέψου σαν ρευματολόγος…





Weber, B.N., Giles, J.T. & Liao, K.P. Nat Rev Rheumatol 19, 417–428 (2023)

Αποκρούοντας τη φλεγμονή θα σταματήσουμε την ΚΑ νόσο στον γενικό πληθυσμό;

THE PRESENT AND FUTURE

JACC STATE-OF-THE-ART REVIEW

Targeting the Immune System in Atherosclerosis

JACC State-of-the-Art Review

Tian X. Zhao, MD, MPHIL, Ziad Mallat, MD, PHD

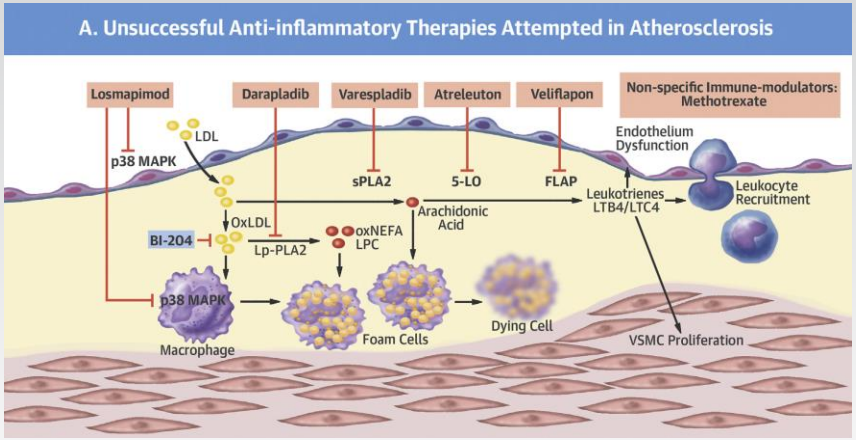


TABLE 1 Attempted Anti-Inflammatory Therapies, Their Pathways, and Possible Reasons for Failure

Drug Name	Pathway	Clinical Trial (Ref. #)	Number, Primary Endpoint	Possible Reasons
BI-204 (MLDL1278A)	oxLDL antibody	1. GLACIER (25)	1. n = 177, arterial inflammation on FDG-PET	• Low levels of inflammation in patient population • Fcγ receptor stimulation
Darapladib	Lp-PLA2 inhibitor	1. Mohler et al. (30) 2. IBIS-2 (31) 3. STABILITY (32) 4. SOLID-TIMI 52 (33)	1. n = 959, plasma Lp-PLA(2) activity 2. n = 330, atheroma deformability on IVUS and CRP 3. n = 15,828, cardiovascular death, MI, or stroke 4. n = 13,206, composite of major cardiovascular events	• Lp-PLA2 activity predicted cardiovascular events only in participants with a history of stable vascular disease • Widespread statin use in trials • Lp-PLA2 did not decrease markers of system inflammation • Inconsistent results from genetic studies
Varespladib	sPLA2s inhibitor	1. FRANCIS (35) 2. VISTA-16 (36)	1. n = 625, change in LDL-C 2. n = 5,145, composite of major cardiovascular events	• Marginal reduction of CRP • Some sPLA2s are atheroprotective—varespladib too nonspecific • Negative Mendelian randomization studies—may be a biomarker
Atreleuton	5-LO inhibitor	1. Tardif et al. (45) 2. Gaztanaga et al. (46)	1. n = 191, blood stimulated leukotriene LTB4 2. n = 52, arterial inflammation on FDG-PET	• Total deletion of 5-LO did not affect atherosclerosis in mice • May affect specialized pro-resolvin mediators
Veliflapon	FLAP inhibitor	1. Hakonarson et al. (44)	1. n = 191, changes in levels of biomarkers	• Genetic data for FLAP associates with CAD only in certain population
Losmapimod	p38 MAPK inhibitor	1. Elkhawad et al. (54) 2. SOLSTICE (55) 3. LATITUDE-TIMI (56)	1. n = 99, arterial inflammation on FDG-PET 2. n = 526, safety outcomes, efficacy—CRP, BNP, troponin 3. n = 3,503, composite of major cardiovascular events	• Insufficient reduction of systemic and vascular inflammation • Can promote endoplasmic reticulum stress-induced apoptosis in macrophages and enhances plaque necrosis
Methotrexate	Dihydrofolate reductase inhibitor	1. CIRT (3)	1. n = 4,786, composite of major cardiovascular events	• Low level of inflammation in patient population • Irrelevant mechanistic pathway

HIGHLIGHTS

- Atherosclerosis is an inflammatory disease. However, this hypothesis remained unproved in the clinic due to the failure of previously attempted anti-inflammatory therapies in reducing cardiovascular events.
- Reasons for the previous failures include redundant inflammatory pathways, overlap with pathways targeted by existing therapies, and little support for a causal role of the targeted pathways in genetic studies.
- CANTOS showed that selective targeting of inflammation through inhibition of IL-1β improves cardiovascular outcomes. Several therapies targeting the innate and the adaptive arms of the immune system are currently in clinical trials.

Zhao and Mallat JACC 73; 13 (2019)

Αποκρούοντας τη φλεγμονή θα σταματήσουμε την ΚΑ νόσο στους ασθενείς με ρευματικές παθήσεις;

THE PRESENT AND FUTURE

JACC STATE-OF-THE-ART REVIEW

Targeting the Immune System in Atherosclerosis

JACC State-of-the-Art Review

Tian X. Zhao, MD, MPHIL, Ziad Mallat, MD, PHD

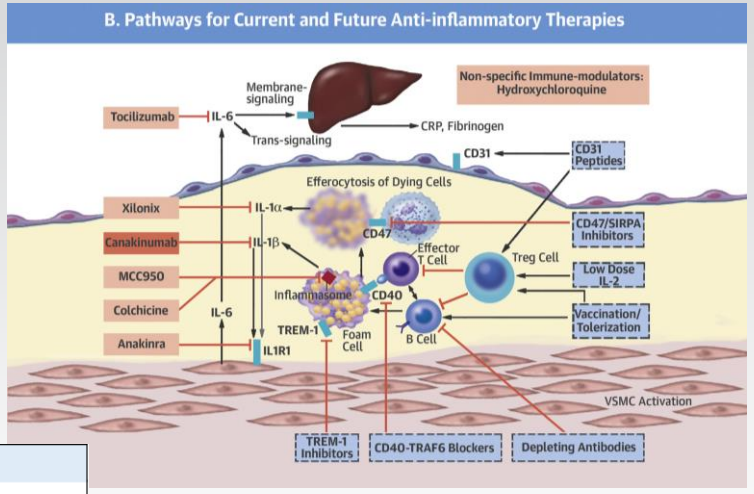
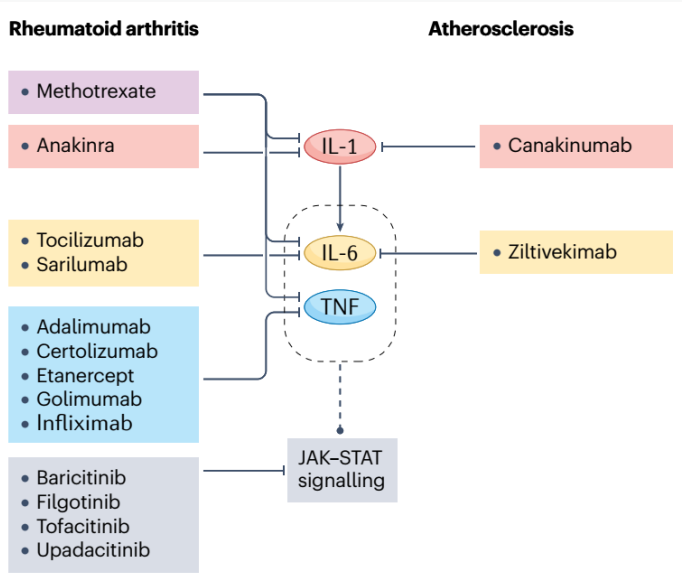


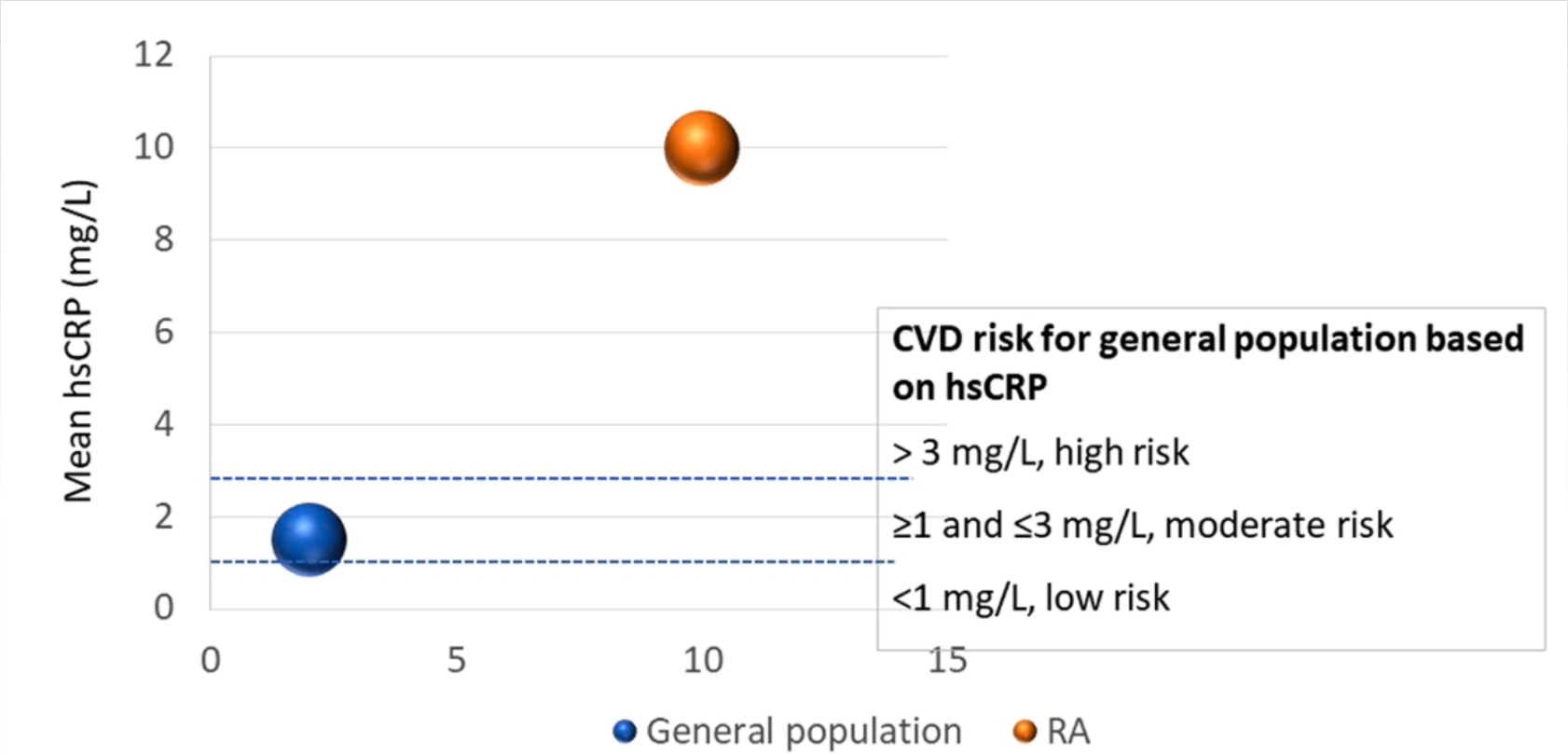
TABLE 2 Therapies Currently in Clinical Trials, Their Pathways and Potential Pros and Cons for Their Future Development and Progress

Drug Name	Pathway	Trial Reference– Patient Population– Primary Trial Endpoint	Pro	Con
Colchicine	NLRP3 inflammasome inhibitor	NCT01709981–undergoing coronary angiography– IL6 level NCT02594111–undergoing coronary angioplasty–Peri-procedural MI (troponin) NCT02551094–acute MI- composite of major cardiovascular events NCT01906749–ACS–composite of	Licensed small-molecule drug. Has reduced a composite endpoint of CV events in a small randomized, observer-blinded trial	Significant side effects, especially gastrointestinal
MCC950	NLRP3 inflammasome inhibitor	N/A	Small molecule and specific inhibitor of NLRP3. Positive results in preclinical models	More specific inhibitors being developed
Anakinra	IL-1 receptor antagonist	NCT01950299–STEMI patients–CRP levels	Early phase studies show decrease in inflammation in the short-term	Rebound effect of CRP and IL-6 on stopping of unknown significance. Genetic studies of *IL1RN* (encoding IL-1Ra) are not supportive
Xilonix	Anti-IL-1α antibody	Sayed El et al. (88)–patients needing percutaneous revascularization–composite of major cardiovascular events	May target senescence and necrosis-dependent inflammation. Well tolerated	Did not decrease CRP and limited clinical data available
Tocilizumab	Anti-IL-6R antibody	NCT03004703–STEMI–myocardial salvage on MRI	Licensed drug Supportive genetic studies	Non-specific blocker of both membrane and trans IL-6 signaling. Alteration of lipid parameters
Hydroxychloroquine	Multiple	NCT02874287-CAD–change in CRP NCT02648464–NSTEMI–composite of major cardiovascular events	Licensed small-molecule drug. Supportive retrospective epidemiological data	Long-term inhibition of TLR7 and TLR9 may be detrimental
IL-2 (low-dose)	Treg cells expansion	Zhao et al. (114)-ACS–patient safety and vascular inflammation on ^{18}F-FDG/PET	Licensed drug, effective in other human inflammatory disease models. Supportive preclinical data	More selective Treg promoters being developed



Zhao, T.X. and Mallat, Z., J Am Coll Cardiol. 2019;73(13):1691–706)

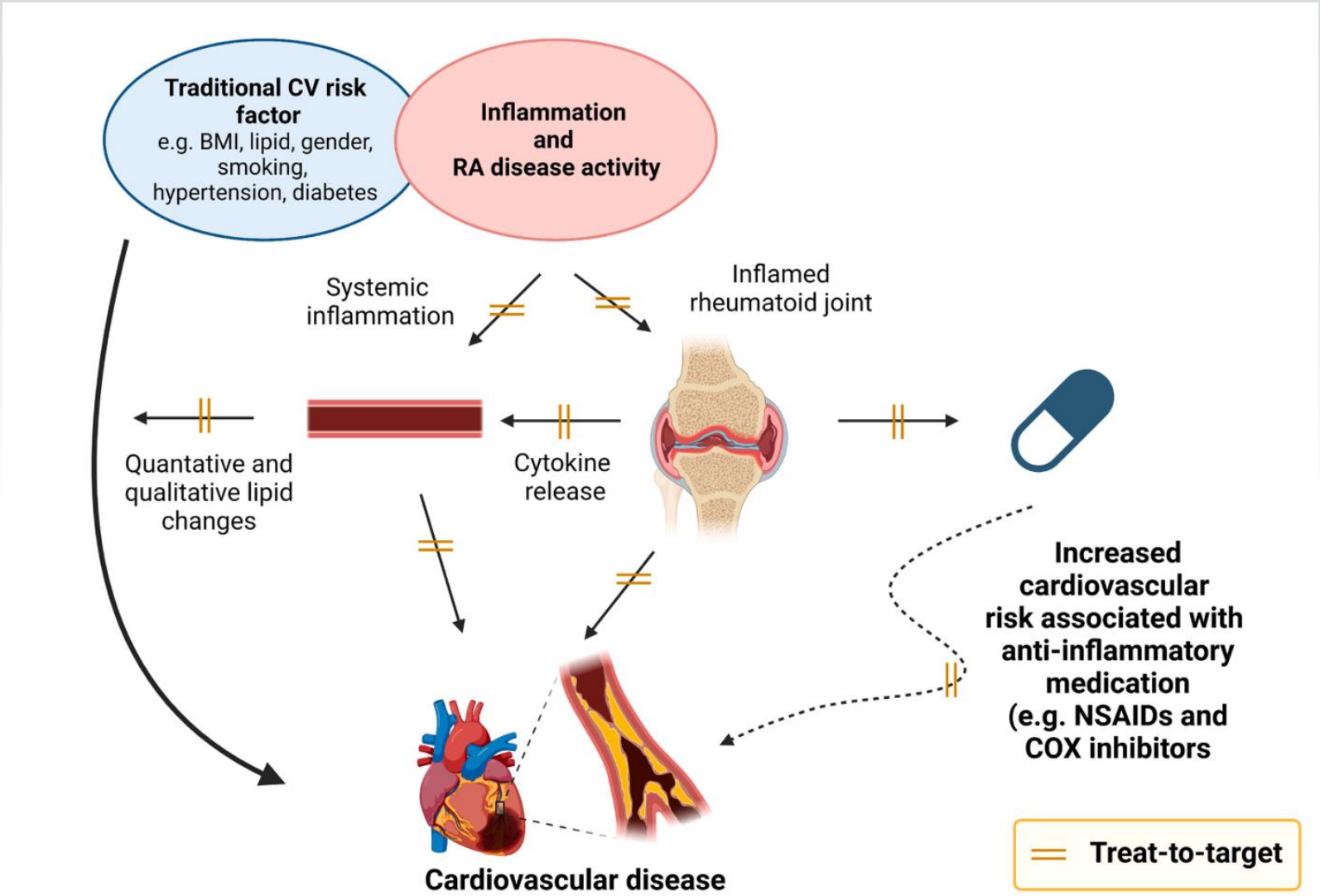
Η φλεγμονή είναι ο νο1 εχθρός που πρέπει να ελεγχθεί



Values of hsCRP in RA patients compared to general population with CV risk estimation
[*General population, Brigham Rheumatoid Arthritis Sequence Study (BRASS);
**RA, National Health and Nutrition Examination Survey (NHANES)]

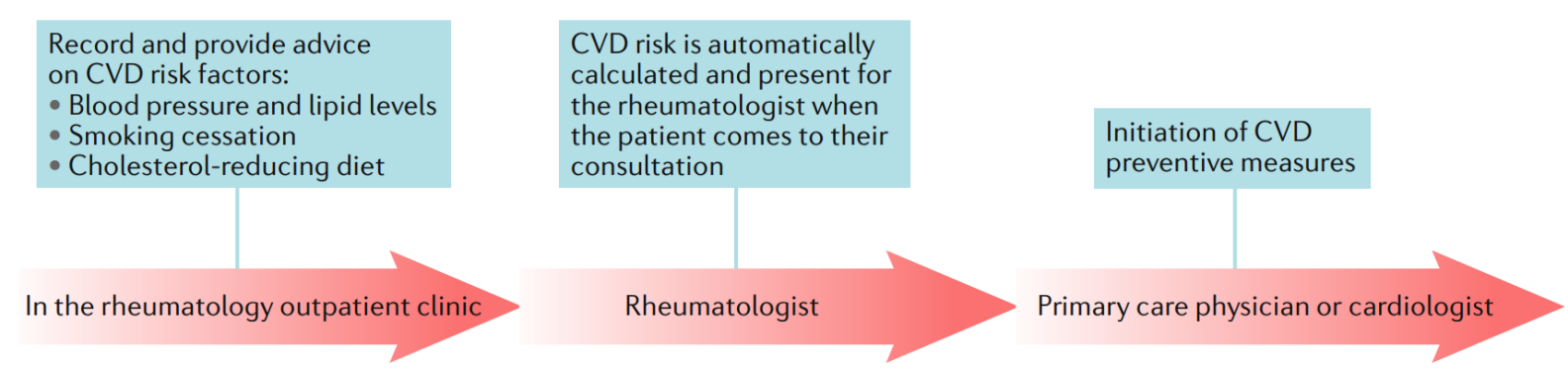
Johri Nis et al. Health Sci Rev 8 (2023)

…ούτε μόνο καλός ρευματολόγος !!



Johri Nis et al. Health Sci Rev 8 (2023)

…πρέπει να γίνεις και καλός καρδιολόγος !!



Risk calculator	Target population	CVD outcome	Applicable age range (years)	Treatment threshold (%)
Framingham risk score (Adult Treatment Panel III)	USA	Coronary heart disease including myocardial infarction	30–74	10
Framingham risk score for general CVD	USA	CVD events (fatal and non-fatal) including acute coronary syndrome (myocardial infarction and unstable angina pectoris), chronic ischaemic heart disease (stable angina pectoris), coronary revascularization (percutaneous coronary intervention and coronary artery bypass graft surgery), coronary death, other cardiovascular death, cerebrovascular events (ischaemic cerebrovascular accident and transient ischaemic attack), peripheral vascular events (non-coronary revascularization procedures and peripheral artery disease) and heart failure	30–74	20
ACC/AHA pooled cohort equation	USA	Atherosclerotic CVD events (defined as first occurrence of non-fatal myocardial infarction, coronary heart disease death, or fatal or non-fatal stroke)	40–79	7.5
Reynolds Risk Score	USA	Myocardial infarction, ischaemic stroke, coronary revascularization and cardiovascular death	50+	10
QRISK2	UK	Coronary heart disease, stroke and transient ischaemic attack	35–74	10
SCORE	EU	Fatal CVD events	40–79	5

- Patients with rheumatoid arthritis (RA) have an **increased risk of cardiovascular disease (CVD)** compared with the general population.
- The improvement of CVD risk prevention in patients with RA is an **unmet need**.
- CVD risk calculators developed for use in the general population **inaccurately predict CVD in patients with RA**, but the addition of RA-specific risk factors does not improve CVD risk prediction
- The **use of ultrasonography of the carotid arteries** improves CVD risk classification in patients with RA by identifying atherosclerotic plaques.

Johri Nis et al. Health Sci Rev 8 (2023)

Semb, A.G., Ikdahl, E., Wibetoe, G. et al. Nat Rev Rheumatol 16, 361–379 (2020).

…πρέπει να γίνεις και καλός καρδιολόγος !!

EULAR recommendations for cardiovascular risk management in rheumatic and musculoskeletal diseases, including systemic lupus erythematosus and antiphospholipid syndrome

George C Drosos ,[1] Daisy Vedder ,[2] Eline Houben,[3] Laura Boekel ,[2] Fabiola Atzeni,[4] Sara Badreh,[5] Dimitrios T Boumpas ,[6,7] Nina Brodin,[8,9] Ian N Bruce,[10,11] Miguel Ángel González-Gay ,[12] Søren Jacobsen ,[13,14] György Kerekes,[15] Francesca Marchiori,[16] Chetan Mukhtyar ,[17] Manuel Ramos-Casals,[18] Naveed Sattar,[19] Karen Schreiber,[20] Savino Sciascia ,[21] Elisabet Svenungsson ,[22] Zoltan Szekanecz ,[23] Anne-Kathrin Tausche,[24] Alan Tyndall,[25] Vokko van Halm,[26] Alexandre Voskuyl,[27] Gary J Macfarlane ,[28] Michael M Ward ,[29] Michael T Nurmohamed,[2,30] Maria G Tektonidou [1,7]

Box 1 Research agenda and future perspectives

1. Validation of existing generic and modified CVR prediction tools in large prospective studies, and development of new disease-specific equations.
2. Additive value of vascular imaging and/or circulating biomarkers in CVR assessment in RMDs.
3. Identification of patient subgroups with higher CVR.
4. Long-term effects of current and new drugs for RMDs on CVR factors and cardiovascular events.
5. Role of antithrombotic agents used in some RMDs (eg, aspirin, LMWH in SLE/APS) to reduce the overall CVR in these patients.
6. Need for large educational campaigns within the rheumatological and other medical specialties and patient associations to increase CVR awareness.
7. Best implementation methods for the CVR recommendations.

APS, antiphospholipid syndrome; CVR, cardiovascular risk; LMWH, low-molecular weight heparin; RMDs, rheumatic and musculoskeletal diseases; SLE, systemic lupus erythematosus.

Overarching principles	LoA* (SD)
A. Clinicians should be aware of increased CVR in patients with RMDs including gout, vasculitis, SSc, myositis, MCTD, SS, SLE and APS. For all RMDs, reduction of disease activity is likely to lessen CVR.	9.92 (0.39)
B. Rheumatologists are responsible for CVR assessment and management in collaboration with primary care providers, internists or cardiologists and other healthcare providers.	9.55 (1.12)
C. CVR factor screening should be performed regularly in all individuals with RMDs. Risk management should include screening for and strict control of CVR factors (smoking cessation, management of blood pressure, lipids and diabetes). CVR assessment is recommended within 6 months of diagnosis and repeated based on individual patient characteristics and risk levels.	9.55 (0.84)
D. Patient education and counselling on CVR, treatment adherence and lifestyle modifications, such as healthy diet and regular physical activity, are important in the management of CVR in these patients.	9.88 (0.42)

:Drosos GC, Vedder D, Houben E, et al. Ann Rheum Dis 2022;81:768–779.

…πρέπει να γίνεις και καλός καρδιολόγος !!

EULAR recommendations for cardiovascular risk management in rheumatic and musculoskeletal diseases, including systemic lupus erythematosus and antiphospholipid syndrome

George C Drosos [1], Daisy Vedder [2], Eline Houben,[3] Laura Boekel [2], Fabiola Atzeni,[4] Sara Badreh,[5] Dimitrios T Boumpas [6,7] Nina Brodin,[8,9] Ian N Bruce,[10,11] Miguel Ángel González-Gay [12], Søren Jacobsen [13,14] György Kerekes,[15] Francesca Marchiori,[16] Chetan Mukhtyar [17] Manuel Ramos-Casals,[18] Naveed Sattar,[19] Karen Schreiber,[20] Savino Sciascia [21] Elisabet Svenungsson [22], Zoltan Szekanecz [23], Anne-Kathrin Tausche,[24] Alan Tyndall,[25] Vokko van Halm,[26] Alexandre Voskuyl,[27] Gary J Macfarlane [28] Michael M Ward [29], Michael T Nurmohamed,[2,30] Maria G Tektonidou [1,7]

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 74, NO.

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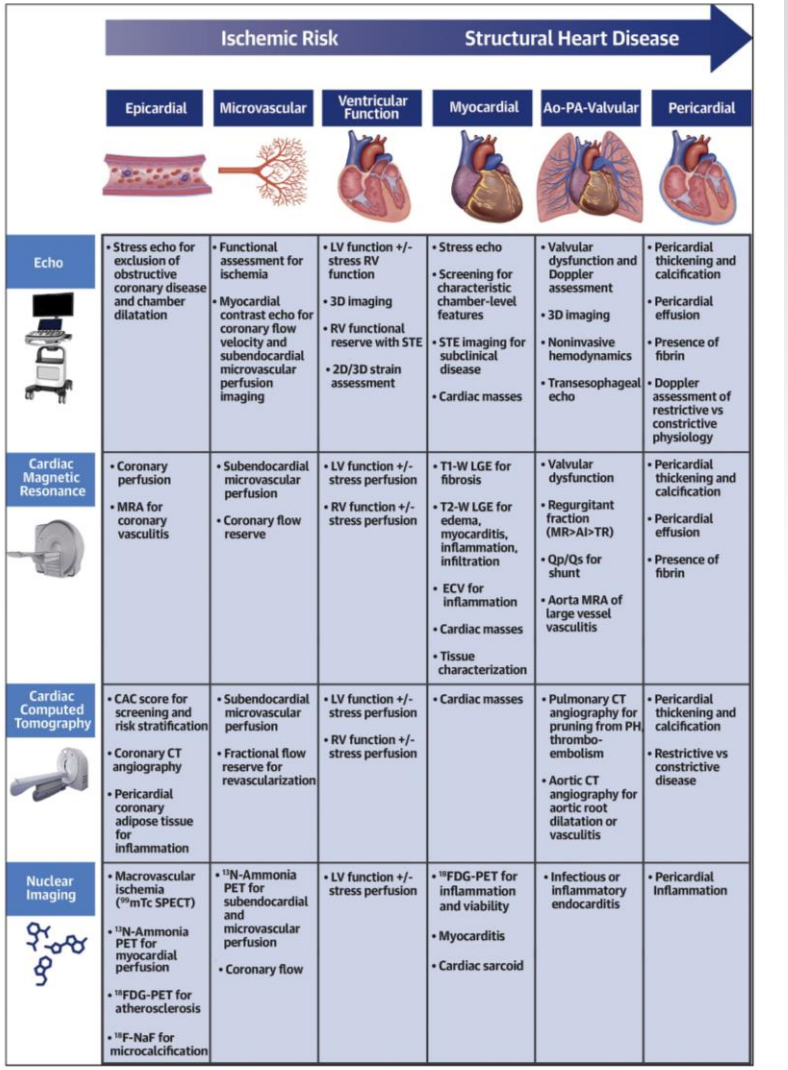
CLINICAL PRACTICE GUIDELINE: EXECUTIVE SUMMARY

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines



Web BN, J Am Coll Cardiol. 2023;82(22):2128-2151.

:Drosos GC, Vedder D, Houben E, et al. Ann Rheum Dis 2022;81:768–779.

…ούτε μόνο καλός παθολόγος

!!

Table 2 | **Blood pressure treatment targets in patients with rheumatoid arthritis**

Age group (years)	Additional comorbidities	SBP targets	DBP targets
18–65	Hypertension	130 mmHg or lower if tolerated; not <120 mmHg	70–79 mmHg
	Diabetes mellitus		
	CAD		
	Stroke or TIA		
	CKD	<140 to 130 mmHg if tolerated	
Over 65	All comorbidities	130–139 mmHg if tolerated	

Table 4 | **Recommended glycaemic and lipid targets in patients with rheumatoid arthritis and diabetes mellitus**

Patient population	Recommendation	Treatment targets
Most patients (adjusted according to duration of diabetes mellitus, age and comorbidities)	Glycaemic control	Glycated haemoglobin <7.0% (<53 mmol/mol)
Very high CVD risk	Lipid-lowering therapy	LDL cholesterol <1.4 mmol/l (<55 mg/dl) and LDL cholesterol lowering >50%
High CVD risk	Lipid-lowering therapy	LDL cholesterol <1.8 mmol/l (<70 mg/dl) and LDL cholesterol lowering >50%
Moderate CVD risk	Lipid-lowering therapy	LDL cholesterol <2.6 mmol/l (<100 mg/dl)

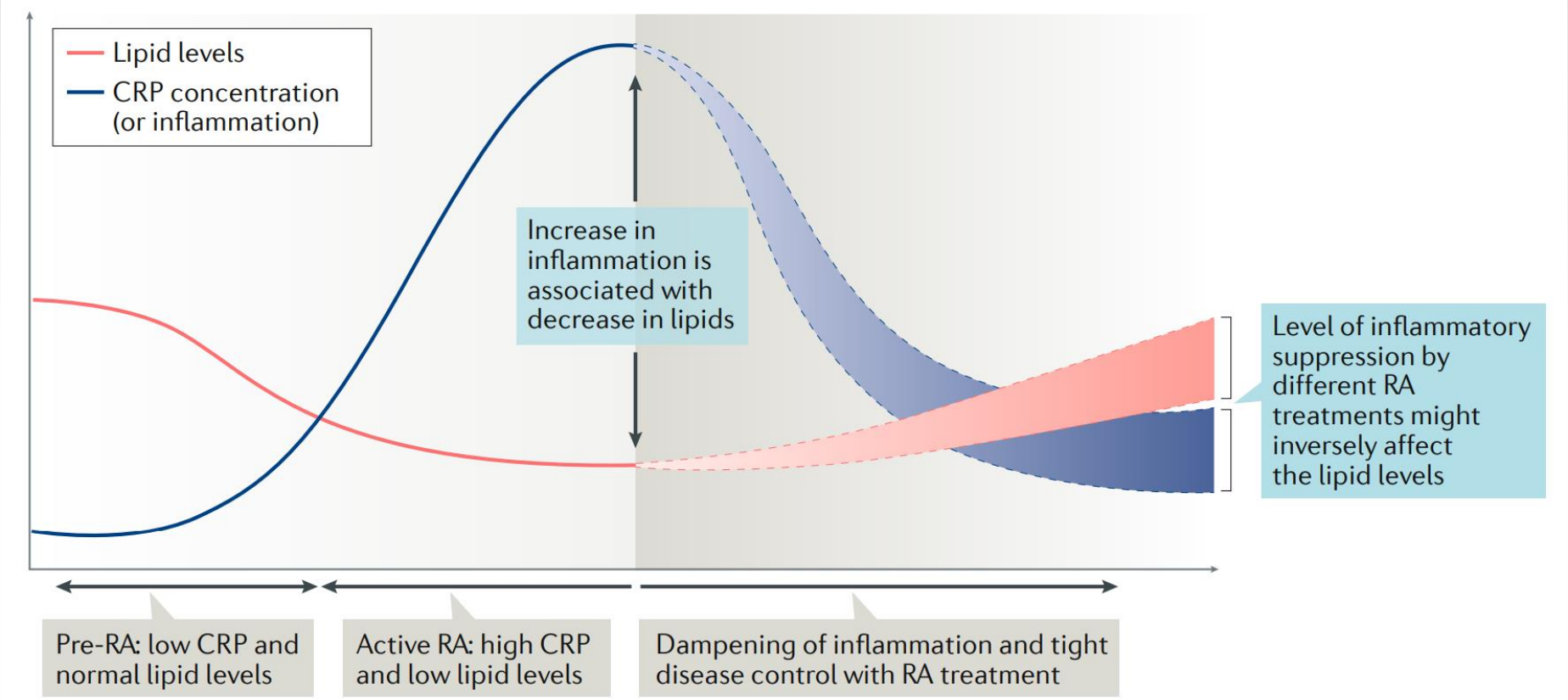
CVD risk class[a]	Description	Target levels	Intervention
LDL cholesterol			
Low	CVD risk <1%	LDL cholesterol <3.0 mmol/l (<116 mg/dl)	Consider adding a lipid-lowering drug (a statin or ezetimibe) if LDL cholesterol is 3.0 to <4.9 mmol/l; add a statin if LDL cholesterol >4.9 mmol/l
Moderate	CVD risk ≥1% to <5% and LDL cholesterol 2.6 to <3 mmol/l (100 to <115 mg/dl)	LDL cholesterol <2.6 mmol/l (<100 mg/dl)	Consider adding a lipid-lowering drug (statins, statins and ezetimibe or ezetimibe monotherapy) if LDL cholesterol 2.6 to <4.9 mmol/l; add a statin if LDL cholesterol ≥4.9 mmol/l
High	CVD risk ≥5% and <10% and LDL cholesterol 1.8 to <2.6 mmol/l (70 to <100 mg/dl) and/or diabetes mellitus and/or a total cholesterol >8.1 mmol/l	LDL cholesterol <1.8 mmol/l (<70 mg/dl) or ≥50% reduction of baseline LDL	Statins; statins and ezetimibe; ezetimibe monotherapy; a statin and a PCSK9 inhibitor; PCSK9 inhibitor monotherapy
Very high	CVD risk >10% and LDL cholesterol >1.8 mmol/l (70 mg/dl) and/or established CVD	LDL cholesterol <1.4 mmol/l (<55 mg/dl) or ≥50% reduction of baseline LDL cholesterol	Statins; statins and ezetimibe; ezetimibe monotherapy; a statin and a PCSK9 inhibitor; PCSK9 inhibitor monotherapy
HDL cholesterol			
Increased risk	HDL cholesterol <1.0 mmol/l (<40 mg/dl) in men and <1.2 mmol/l (<45 mg/dl) in women	No target HDL cholesterol level, but recommended HDL cholesterol >1.0 mmol/l (>40 mg/dl) in men and >1.2 mmol/l (>45 mg/dl) in women	Exercise; diet; weight loss; moderate alcohol intake

- Χειρισμός φαρμάκων για συνοσηρότητες
- Γνώση κατευθυντήριων οδηγιών σε πολλαπλά χρόνια νοσήματα
- Αντιμετώπιση απορρύθμισης συνοσηροτήτων (ΜΣΑΦ, ΚΣ)
- Χορήγηση κατάλληλων DMARDs

Semb, A.G., Ikdahl, E., Wibetoe, G. et al. Nat Rev Rheumatol 16, 361–379 (2020).

The lipid paradox…

To treat or not to treat ??? …and which is the true value to expect?



Semb, A.G., Ikdahl, E., Wibetoe, G. et al. Nat Rev Rheumatol 16, 361–379 (2020).

Και με τι να θεραπεύσω την …«φλεγμονή»;

Table 2 **Anti-rheumatic drugs and cardiovascular risk**

Agent	Effect on risk biomarkers	Effect on CV outcome
Glucocorticoids	↑BP, ↑TG, ↑glucose, ↓CRP	Prolonged high dose: worsen[40,41,47] Suppression of active SLE protective[39]
NSAIDs/COXIBs	↑BP, ↑thrombosis risk, ↓renal function	Worsen. May improve in RA[83–85]
MTX	↓CRP, ↑adenosine	↓Risk in observational studies[66]
Mycophenolate	↓CRP and plaque inflammation[98]	Minimal data[47]
Hydroxychloroquine	↓LDL, ↓thrombosis risk	Reduced risk in RA and SLE[64]
Anti-TNFα	↓CRP, ↑LDL, ↑TG[54]	Worsens cardiac failure. ↓May MI risk[67,68,93,94]
Anti-IL-6	↓CRP, ↓FN, ↑LDL, ↑TG[54]	No data[64]
Anti-IL-1	↓CRP, ↓FN, ↓IL-6[64]	No data, study in progress
B-cell depletion	Long-term treatment may ↓LDL[64]	No data
Cyclosporine	↑BP, ↑LDL, ↓renal function	Worsen

BP, blood pressure; TG, triglycerides; LDL, low-density lipoprotein; CRP, C-reactive protein; NSAIDs, traditional non-steroidal anti-inflammatory drugs; COXIBs, COX-2 selective anti-inflammatory drugs; RA, rheumatoid arthritis; MTX, Methotrexate; SLE, systemic lupus erythematosus; FN, fibrinogen; IL-6, interleukin-6.

Mason JC and Libby P. European Heart Journal (2015) 36, 482–489

Νόσος και καρδιαγγειακό σύστημα

Ρευματικές νόσοι και καρδιαγγειακός κίνδυνος

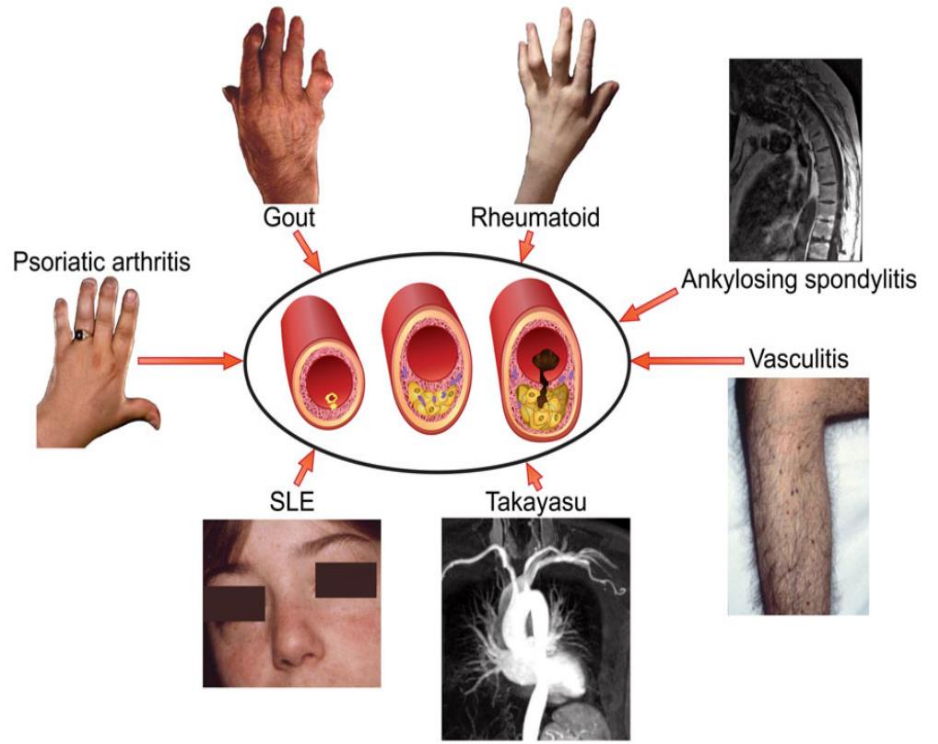
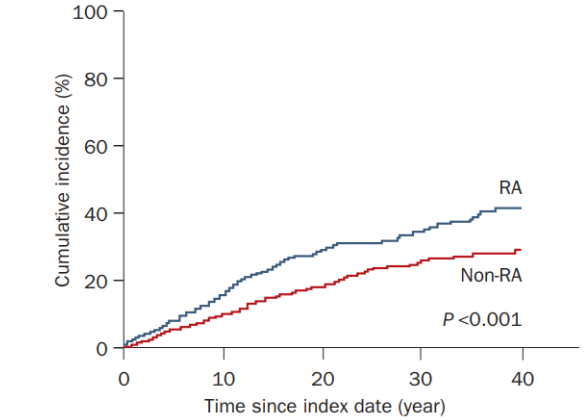


Table I Coronary artery involvement and the rheumatic diseases[4,5,7,8]

Premature atherosclerosis	Coronary arteritis
Systemic lupus erythematosus	Systemic lupus erythematosus
Rheumatoid arthritis	Takayasu arteritis
Ankylosing spondylitis	Kawasaki disease
Psoriatic arthritis	Giant cell arteritis
Gout	Polyarteritis nodosa
ANCA-associated vasculitis	Granulomatous polyangiitis
Takayasu arteritis	Churg–Strauss syndrome
Giant cell arteritis	Rheumatoid arthritis
Inflammatory myopathies	

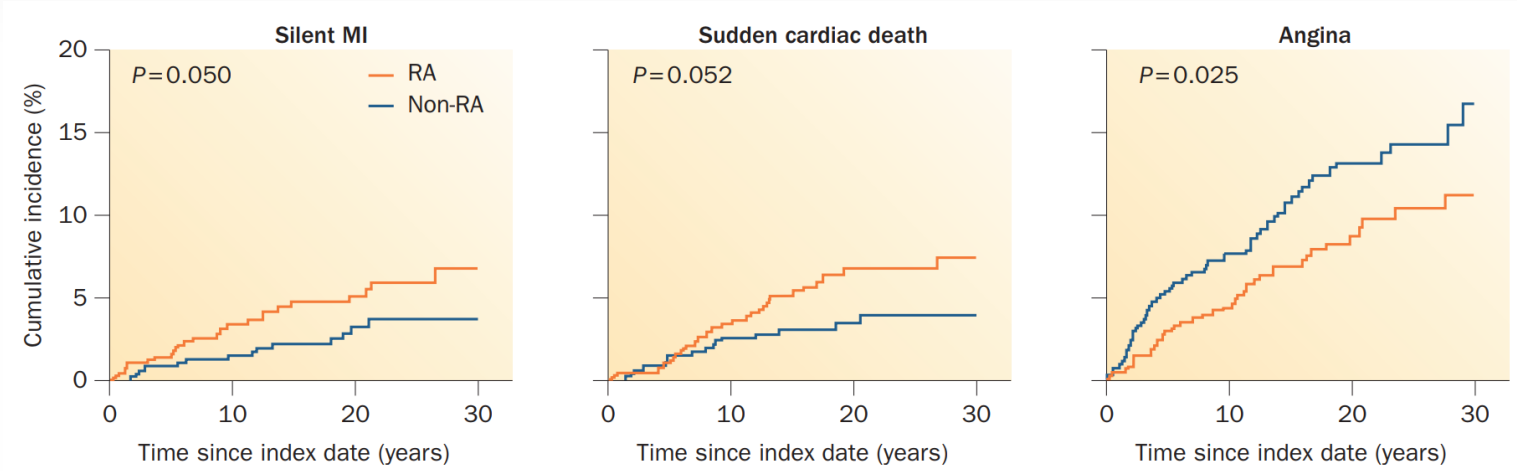
Mason JC and Libby P. European Heart Journal (2015) 36, 482–489

Ρευματοειδής Αρθρίτιδα και καρδιαγγειακός κίνδυνος



Number at risk					
RA	575	336	133	51	7
Non-RA	583	386	189	75	15

RA	Atherosclerotic	• Myocardial infarction. • Congestive heart failure. • Peripheral arterial disease.
	Non-atherosclerotic	• Pericarditis. It is possible to occur as an inflammatory manifestation of RA. • Myocarditis and endocarditis. They are also possible to occur as a complication in RA. • Vasculitis. (e.g., aortitis, coronary arteritis) It can cause neurovascular disease (e.g., mononeuritis multiplex), cutaneous ulceration, or organ infarction based on the affected artery. • Other less common complications. Conduction abnormalities • Amyloidosis. • Pulmonary hypertension.



Mason JC and Libby P. European Heart Journal (2015) 36, 482–489
Prasad, M. et al. Nat. Rev. Cardiol. 12, 168–176 (2015)
Symmons, D. P. M. & Gabriel, S. E. Nat. Rev. Rheumatol. 7, 399–408 (2011);

Συστηματικός ερυθηματώδης λύκος και καρδιαγγειακός κίνδυνος

Table 1 | Standardized mortality ratios in patients from the Toronto SLE cohort*

Cohort (by entry date)‡	Standardized mortality ratios (with 95% CI) by follow-up period			
	1970–1978	1979–1987	1988–1996	1997–2005
1 (1970–1978)	13.84 (9.78–19.56)	4.86 (3.31–7.13)	3.07 (1.93–4.87)	3.23 (1.98–5.28)
2 (1979–1987)	NA	6.45 (4.51–9.22)	3.54 (2.51–5.01)	3.92 (2.53–6.08)
3 (1988–1996)	NA	NA	4.24 (2.28–7.88)	3.93 (2.47–6.23)
4 (1997–2005)	NA	NA	NA	3.81 (1.98–7.32)

*Adapted from Urowitz, M. B. *et al. J. Rheumatol.* **35**, 2152–2158 (2008),[23] with permission from T
Journal of Rheumatology. ‡All patients (n=1,241) were recruited to the Toronto SLE cohort 1970–2
Abbreviations: NA, not applicable; SLE, systemic lupus erythematosus.

SLE	Pericardium	• Pericarditis. • Pericardial effusion.
	Myocardium	• ECG findings: Prolonged PR intervals. • MRI to help in diagnosis.
	Endocardium and valves	• Systolic murmur: Possibly from hyperdynamic state because of anemia. • Libman-sacks endocarditis .

Table 2 | Summary of independent predictive risk factors for vascular outcomes in 5 large SLE cohorts*‡

Study details	Baltimore[43]	Pittsburgh[36]	LUMINA[106]	Toronto inception[44]	SLICC-RAS[45]
Year of publication	1992	1997	2004	2007	2010
Type of cohort	Prevalent	Prevalent	Inception, patients had <5 years disease at study start	Inception, patients had <1 year disease at study start	Inception, patients had <1 year disease at study start
Number of patients in the cohort	229	498 (all women)	546	561	637
Definition of endpoint	CAD	CAD	ACE	ACE	ACE§
Number of patients with ≥1 endpoint	19	33	34	54	22
Independent risk factors for endpoints identified in each study					
Older age at diagnosis	✓	✓	✓	×	✓
Longer duration of SLE	✓	×	✓	×	NS
Male gender	×	NA	×	×	✓
Longer duration of prednisolone use	✓	✓	Not analyzed	×	×
Hypercholesterolemia	✓	✓	×	×	×
Hypertension	✓	×	×	×	×
Smoking	×	×	✓	✓	×
Neuropsychiatric lupus	Not analyzed	Not analyzed	Not analyzed	✓	×
Antiphospholipid antibodies	×	Not analyzed	✓	×	×

- Πολλαπλές συνοσηρότητες
- Αυξημένος καρδιαγγειακός κίνδυνος σε πρώιμη νόσο
- Επιταχυνούμενη, προϊούσα και πρώιμη αθηροσκλήρωση
- Επιβάρυνση μεταβολικού προφίλ με κορτικοστεροειδή

Urowitz, M. B. et al. Arthritis Care Res. 62, 881–887 (2010

Ουρική Αρθρίτιδα και καρδιαγγειακός κίνδυνος

Incident Gout: Risk of Death and Cause-Specific Mortality in Western Sweden: A Prospective, Controlled Inception Cohort Study

Mats Dehlin, Tatiana Zverkova Sandström and Lennart TH Jacobsson*

Department of Rheumatology and Inflammation Research, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Conclusions: An increased risk for CVD, renal disease, and diseases of the digestive system in patients with gout ***highlights the importance of addressing CVD risk factors in gout management***. Gout was associated with reduced mortality from dementia, which may have implications on urate lowering therapy and possible effects on dementia risk

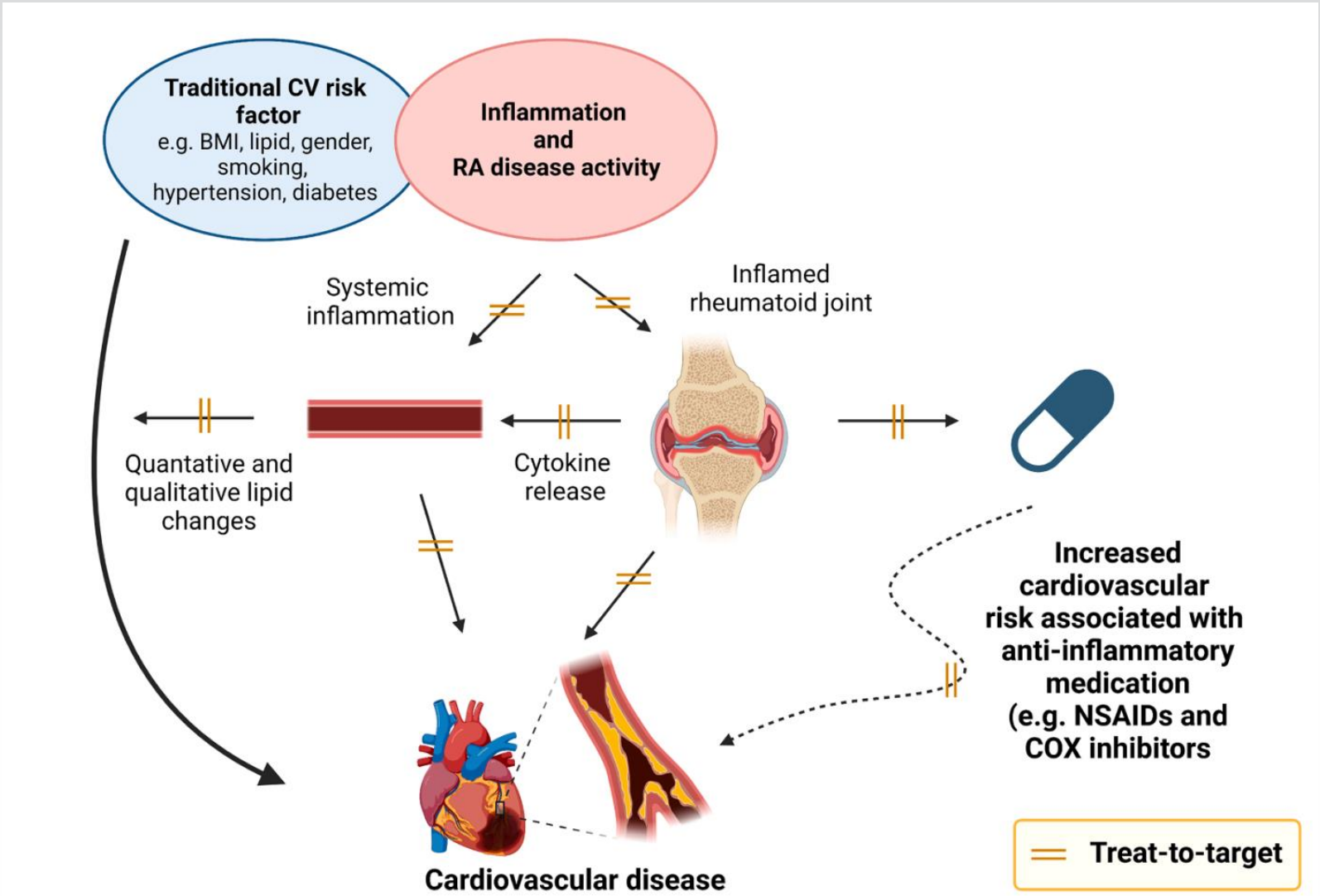
TABLE 3 | Number of deaths and incidence rates, overall and cause-specific, in cases and controls.

Cause of death, n (%)	Gout cases, *n* = 22,055	Incidence rate per 1,000 person-years (95% CI)	Controls, *n* = 98,946	Incidence rate per 1000 person-years (95% CI)	Incidence rate ratio (95% CI)
Total deaths	5,817 (26.4)	47,74 (35.95–63.40)	20,753 (21.0)	37.60 (27.32–51.76)	1.27 (1.23–1.31)
Cardiovascular disease	2,905 (49.9)	23.84 (15.96–35.62)	8,406 (40.5)	15.23 (9.22–25.17)	1.56 (1.50–1.63)

Dehlin M, Sandström TZ and Jacobsson LT (2022) Front. Med. 9:802856.

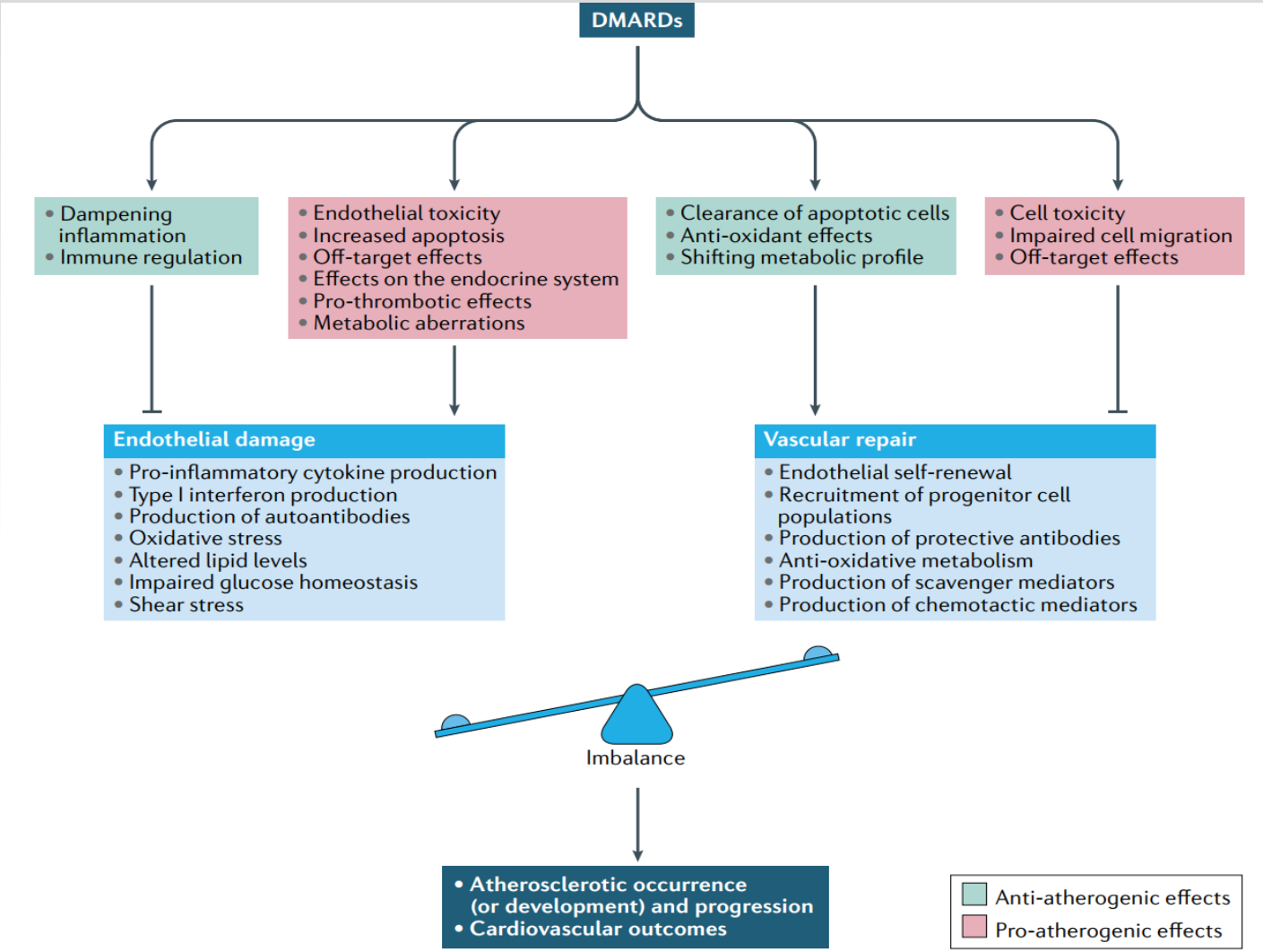
Ανοσοτροποποίηση και καρδιαγγειακός κίνδυνος

Η ανοσοτροποποίηση είναι απαραίτητη (αντι-ΜΣΑΦ/ΚΣ)



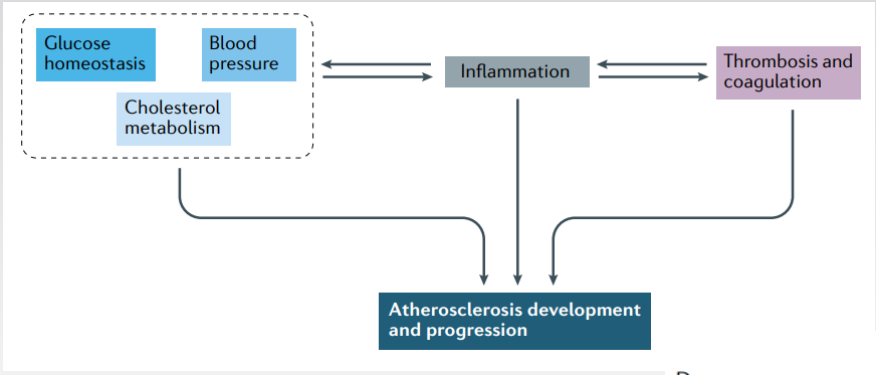
Johri Nis et al. Health Sci Rev 8 (2023)

Είναι η ανοσοτροποποίηση επικίνδυνη στο καρδιαγγειακό;



Atzeni, F., Rodríguez-Carrio, J., Popa, C.D. et al. Nat Rev Rheumatol 17, 270–290 (2021).

Μείωση φλεγμονής και ταυτόχρονα “καρδιο-προστασία”;



Anti-atherogenic effects
Unclear atherogenic effects
Pro-atherogenic effects
No effects

Drugs	Effect on glucose metabolism	Effect on blood pressure	Effect on cholesterol metabolism	Effect on inflammation	Effect on thrombosis and coagulation
Anti-inflammatory drugs					
NSAIDs	○	●	○	●	●
Glucocorticoids	●	●	●	●	○
Conventional synthetic DMARDs					
Hydroxychloroquine	●	●	●	●	●
Sulfasalazine	○	○	○	●	●
Cyclosporine	○	○	○	●	○
Methotrexate	●	○	○	●	○
Lefluomide	○	●	○	●	○
Biologic DMARDs					
TNF inhibitors	●	○	●	●	○
IL-6 inhibitors	○	○	◐	●	○
Rituximab	○	◐	●	●	○
Abatacept	●	○	○	●	○
Targeted synthetic DMARDs					
JAK inhibitors	○	○	◐	●	●

Τι διεγείρει τον αυξημένο ΚΑ κίνδυνο;;

- Απότομη καταστολή της φλεγμονής
- Επίδραση στις συνοσηρότητες
- Επίδραση στο μεταβολισμό
- Προ-θρομβωτικό περιβάλλον

Atzeni, F., Rodríguez-Carrio, J., Popa, C.D. et al. Nat Rev Rheumatol 17, 270–290 (2021).

Θεραπευτική απόφαση και καρδιαγγειακός κίνδυνος

Συμπεράσματα

Ο αποτελεσματικός έλεγχος της νόσου με αντιρευματικά φάρμακα στις ρευματικές νόσους αναμένεται να μειώσει τον καρδιαγγειακό κίνδυνο με τον ίδιο τρόπο που μειώνει τη δραστηριότητα της νόσου, ***μειώνοντας τη φλεγμονή***

- ✓ ***Η θεραπεία με DMARDs*** μπορεί να προάγει δυσμενή αγγειακά αποτελέσματα και να προκαλέσει ***παράδοξες επιδράσεις σε παραδοσιακούς παράγοντες κινδύνου***, δυσκολεύοντας τη διαχείριση του καρδιαγγειακού κινδύνου

- ✓ Συνολικά, η χρήση συμβατικών συνθετικών DMaRD, με εξαίρεση τη ***μεθοτρεξάτη***, σχετίζεται με ορισμένες επιβλαβείς καρδιαγγειακές επιδράσεις, ανάλογα με τις δοσολογίες και τη διάρκεια χρήσης.

- ✓ ***Τα βιολογικά DMARDs*** μπορούν να ***μειώσουν*** το καρδιαγγειακό φορτίο, ***αλλά*** μπορούν επίσης να έχουν παράδοξες επιδράσεις στους παραδοσιακούς παράγοντες καρδιαγγειακού κινδύνου. σε ποιο βαθμό αυτές οι επιδράσεις μεταφράζονται σε καρδιαγγειακό κίνδυνο είναι ασαφές

- ✓ ***Τα στοχευμένα συνθετικά DMARDs*** ενδέχεται να ***συνεπάγονται ελαφρώς υψηλότερο κίνδυνο θρομβωτικών επεισοδίων*** από την τυπική θεραπεία φροντίδας σε ορισμένους ασθενείς, αλλά τα στοιχεία είναι περιορισμένα και απαιτούνται μακροχρόνιες κλινικές μελέτες.

- ✓ Ο ρευματολόγος οφείλει να εκτιμά τον ασθενή του και να ***τροποποιεί τους παράγοντες καρδιαγγειακού κινδύνου***, μειώνοντας της συνοσηρότητες και ***ελαχιστοποιώντας τον κίνδυνο από την χρήση των DMARDs***

Ευχαριστώ πολύ!

Journal of the American Heart Association

EARLY CAREER PERSPECTIVE

Sore, Hot, and at Risk: The Emerging Specialty of Cardio-Rheumatology

Brittany Weber, MD, PhD; Michael Garshick, MD; Katherine P. Liao, MD, MPH; Marcelo Di Carli, MD

‘Ισως μια νέα εξειδίκευση είναι στην πόρτα μας…!