Cardiovascular risk management in rheumatoid arthritis

Michele Senni

Chief

Cardiologia 1 - Scompenso e Trapianti di Cuore

ASST Papa Giovanni XXIII

Bergamo

Agenda

1. Epidemiology of CV risk in RA

2. Atherosclerosis, Inflammation and CV risk in RA

1. Targeting traditional CV risk factors in RA and treatment

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1. Epidemiology of CV risk in RA

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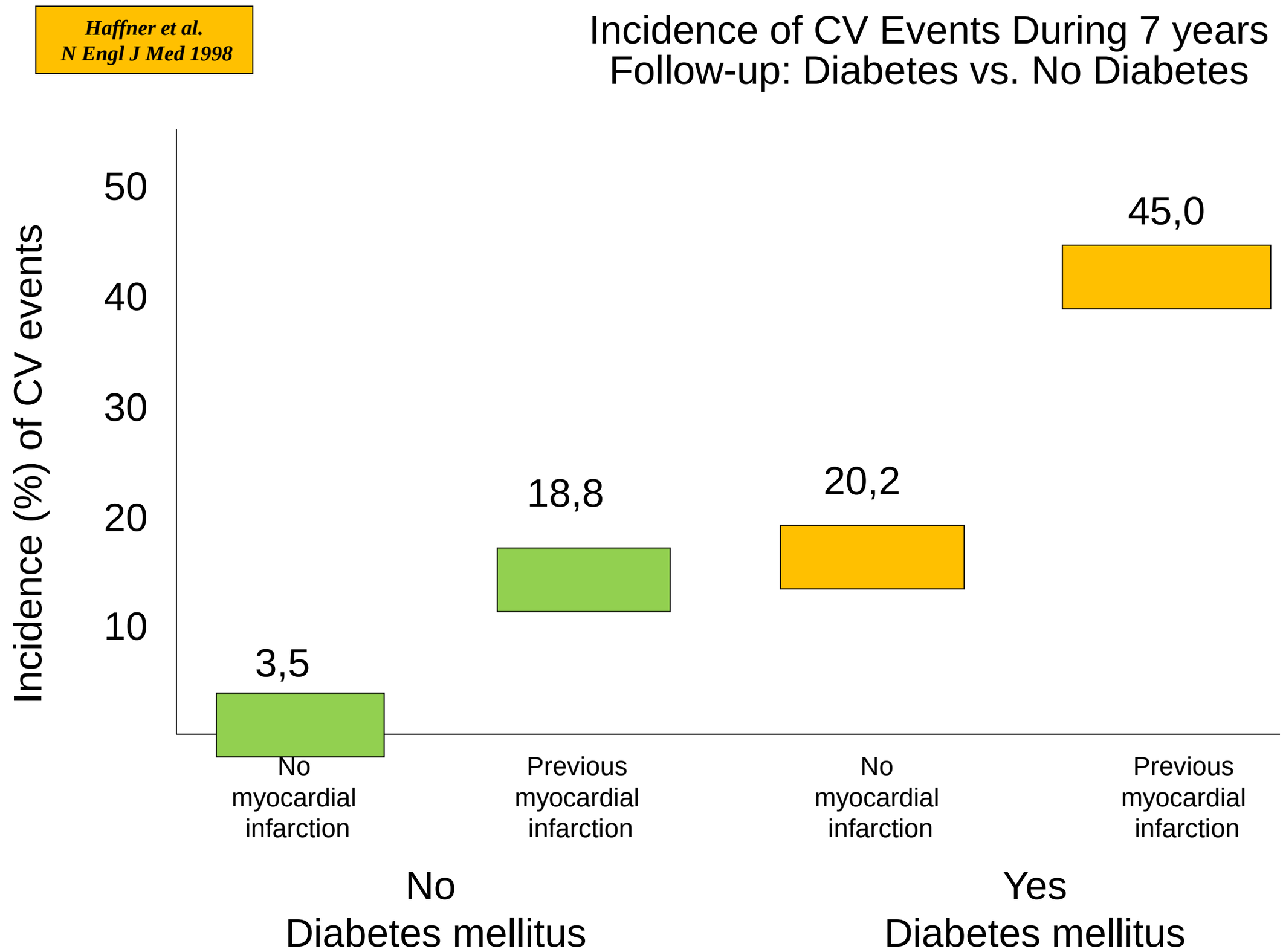
What cardiologist are aware



Arthritis & Rheumatism (Arthritis Care & Research)
Vol. 59, No. 12, December 15, 2008, pp 1690–1697
DOI 10.1002/art.24092
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ORIGINAL ARTICLE

Risk of Cardiovascular Mortality in Patients With Rheumatoid Arthritis: A Meta-Analysis of Observational Studies

J. ANTONIO AVIÑA-ZUBIETA,[1] HYON K. CHOI,[1] MOHSEN SADATSAFAVI,[2] MAHYAR ETMINAN,[2] JOHN M. ESDAILE,[1] AND DIANE LACAILLE[1]

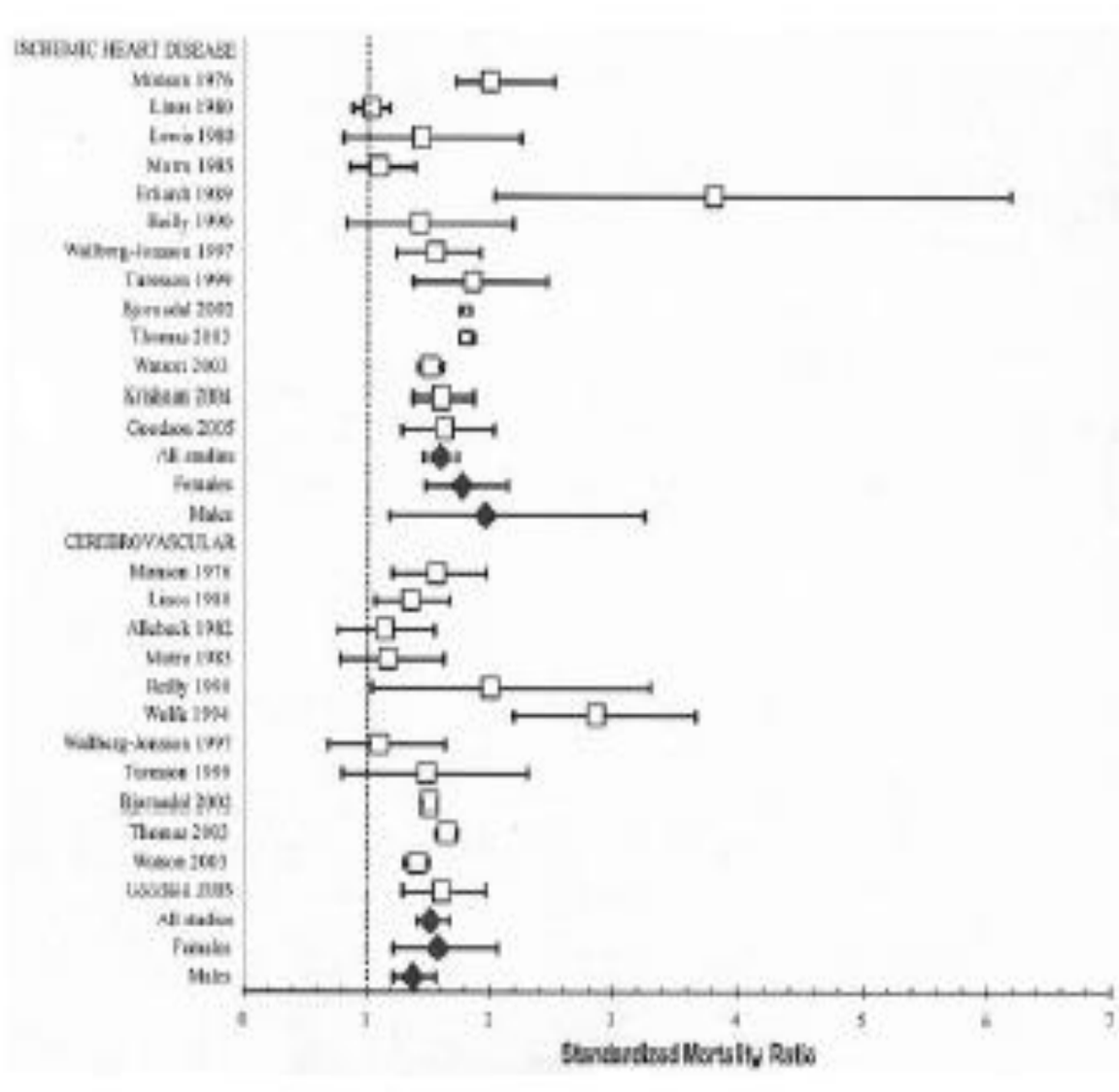


Figure 3. Meta-analysis of studies with cause-specific cardiovascular disease mortality in patients with rheumatoid arthritis.

EXTENDED REPORT

Patterns of cardiovascular risk in rheumatoid arthritis

D H Solomon, N J Goodson, J N Katz, M E Weinblatt, J Avorn, S Setoguchi, C Canning, S Schneeweiss

Ann Rheum Dis 2006;**65**:1608–1612. doi: 10.1136/ard.2005.050377

Results: 25 385 adults who had at least three diagnoses for rheumatoid arthritis during the study period were identified. During the 5-year study period, 375 patients with rheumatoid arthritis had a hospital admission for myocardial infarction, 363 had a hospitalisation for stroke, 437 died from cardiovascular causes and 1042 had one of these outcomes. The rate ratio for a CVD event in patients with rheumatoid arthritis was 1.6 (95% confidence interval (CI) 1.5 to 1.7), and the rate difference was 5.7 (95% CI 4.9 to 6.4) per 1000 person-years. The rate ratio decreased with age, from 3.3 in patients aged 18–39 years to 1.6 in those aged ≥75 years. However, the rate difference was 1.2 per 1000 person-years in the youngest age group and increased to 19.7 per 1000 person-years in those aged ≥75 years. Among patients with a prior CVD event, the rate ratios and rate differences were not increased in rheumatoid arthritis.

Conclusions: This study confirms that rheumatoid arthritis is a risk factor for CVD events and shows that the rate ratio for CVD events among subjects with rheumatoid arthritis is highest in young adults and those without known prior CVD events. However, in absolute terms, the difference in event rates is highest in older adults.

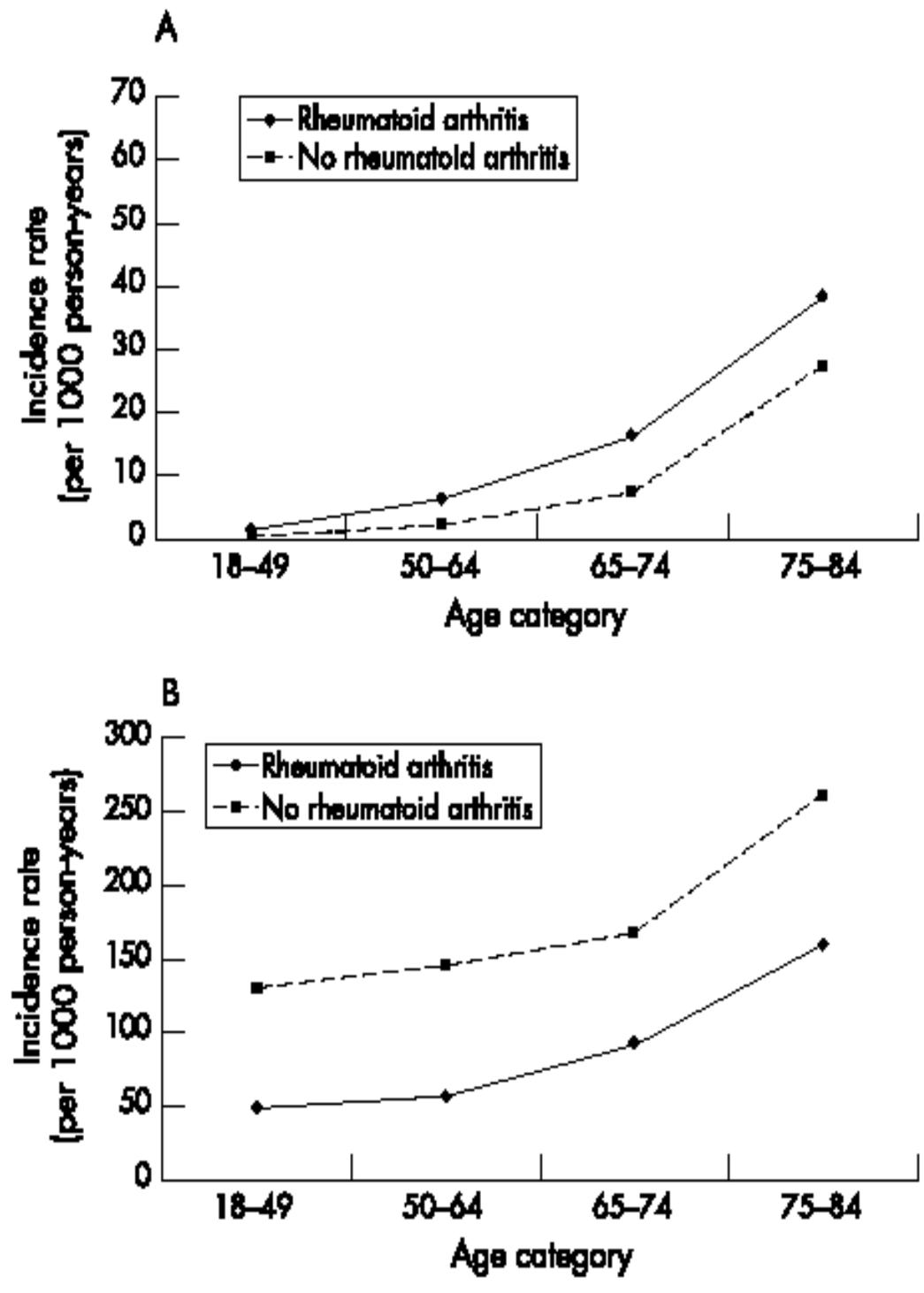
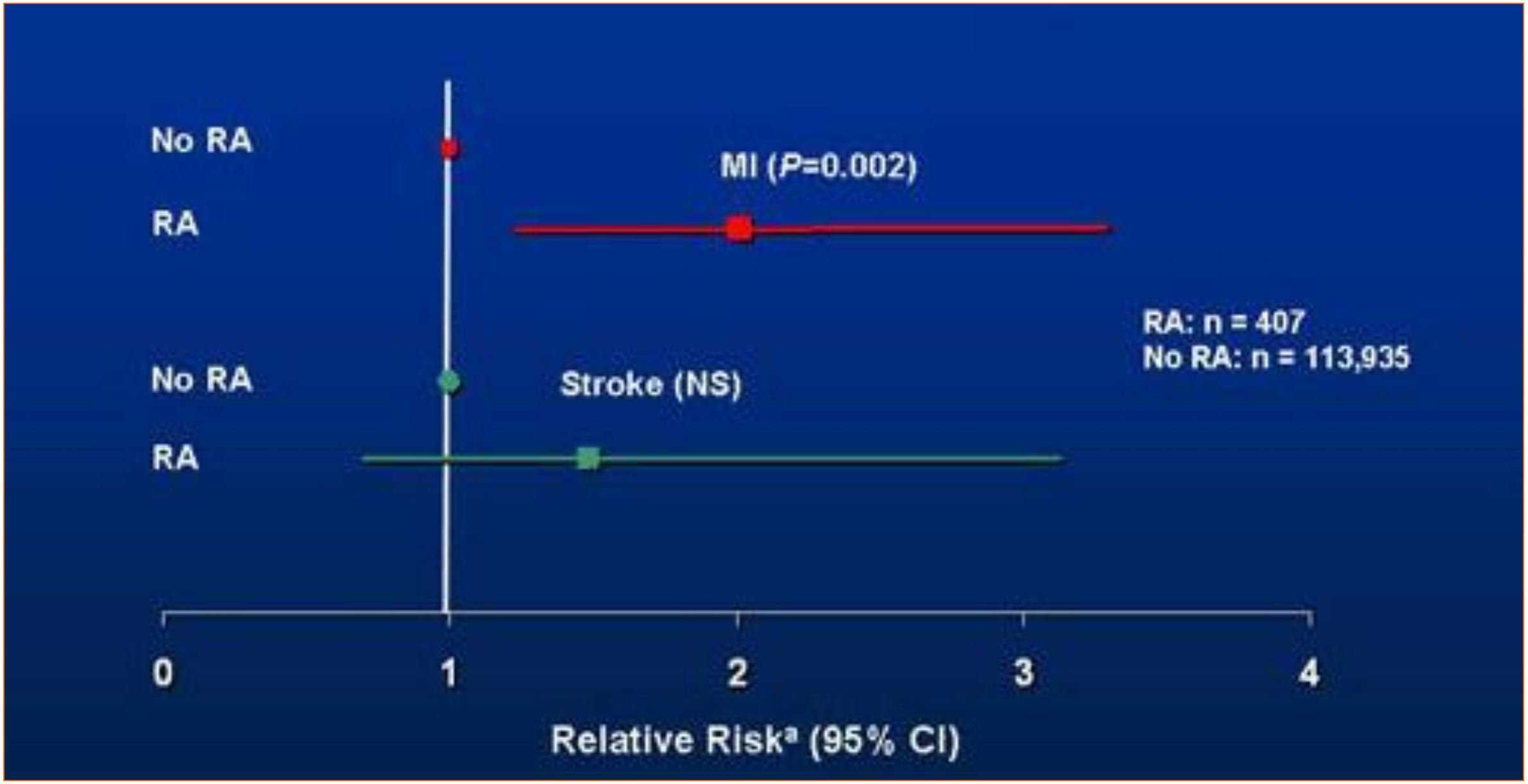


Figure 2 Incidence rates of cardiovascular events among subjects (A) with no prior event; (B) with prior event.

Relative Risk of MI and Stroke in Women with RA

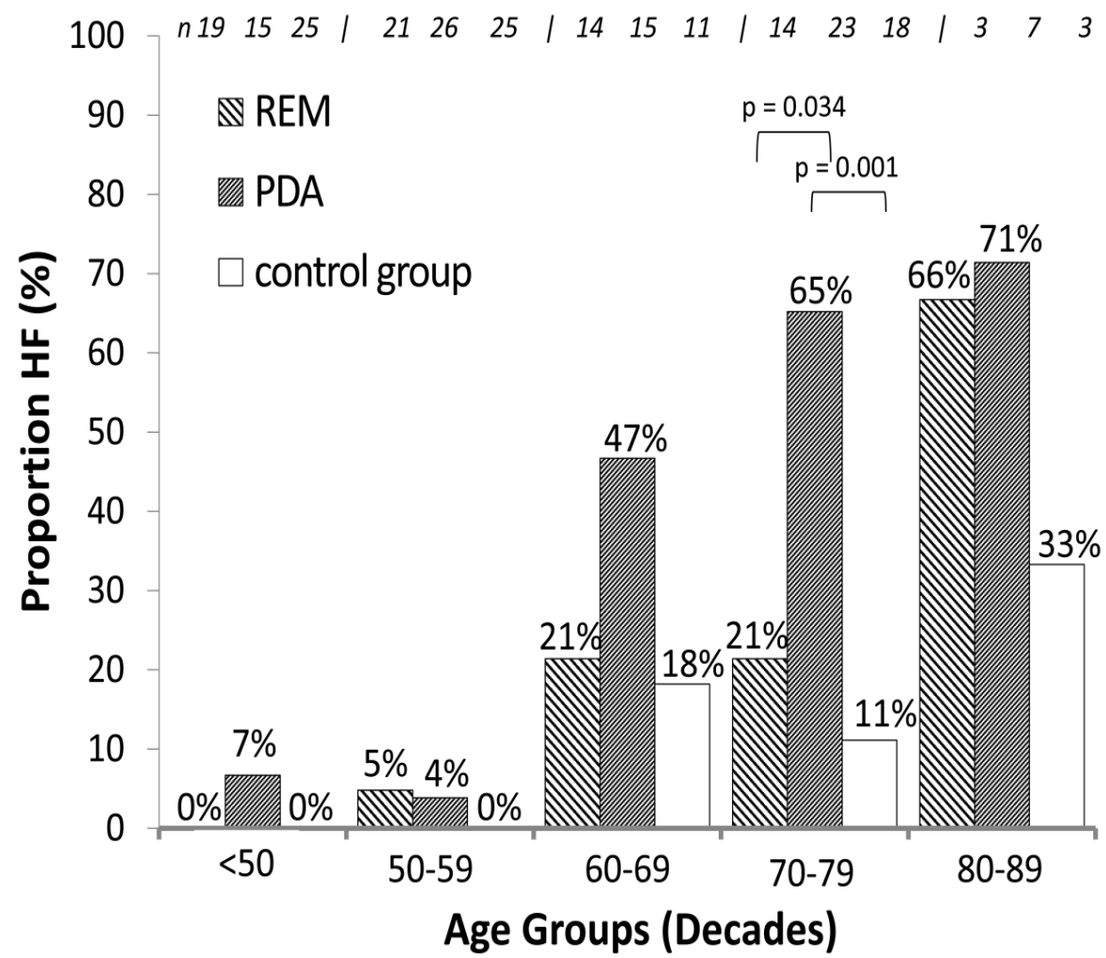


Circulation 2003; 107: 1303-1307

Increased Prevalence of Diastolic Heart Failure in Patients with Rheumatoid Arthritis Correlates with Active Disease, but Not with Treatment Type

Thomas Schau, Michael Gottwald, Olga Arbach, Martin Seifert, Maren Schöpp, Michael Neuß, Christian Butter, and Michael Zänker

Variables	Control Group, n = 77	RA Group, n = 157	p
HF	5 (6)	38 (24)	0.001
HFNEF	5 (6)	36 (23)	0.002
HFREF	0	2 (1)	
Age, yrs, mean ± SD	59 ± 12	61 ± 13	0.307
Female	53 (69)	107 (68)	0.882
BMI > 30 kg/m²	10 (13)	59 (38)	< 0.001
Hypertension	31 (40)	88 (56)	0.026
Present smoker	20 (26)	55 (36)	0.182
Pack-yrs, median (IQR)	10 (2–16)	15 (6–26)	0.023
Diabetes mellitus	6 (8)	21 (13)	0.280
Hypercholesterolemia	27(35)	38 (24)	0.089
CKD/eGFR < 60 ml/min	5 (6)	24 (15)	0.060
CAD	2 (3)	12 (8)	0.237
Stroke/TIA	2 (3)	3 (2)	0.665
PAD	2 (3)	15 (10)	0.062



J Reumathol 2015

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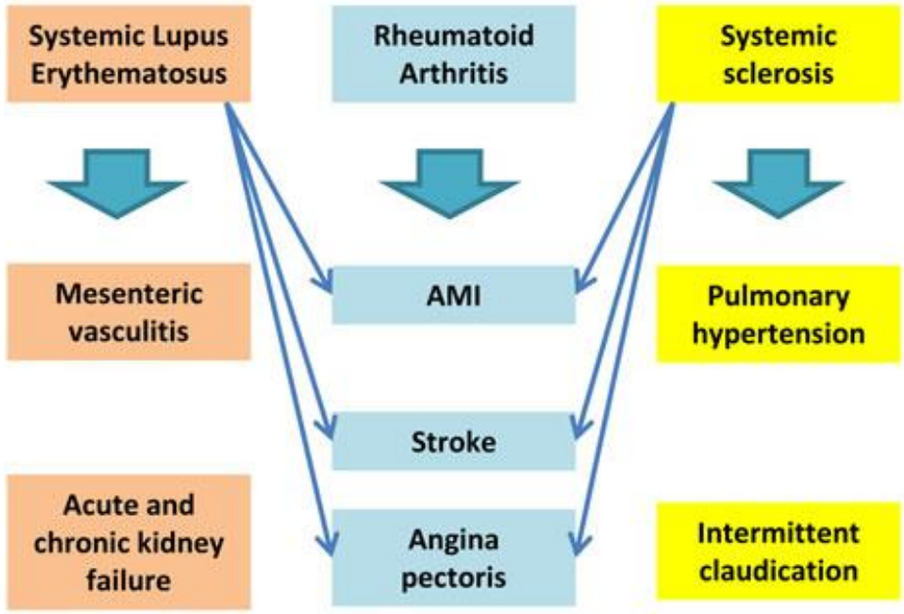
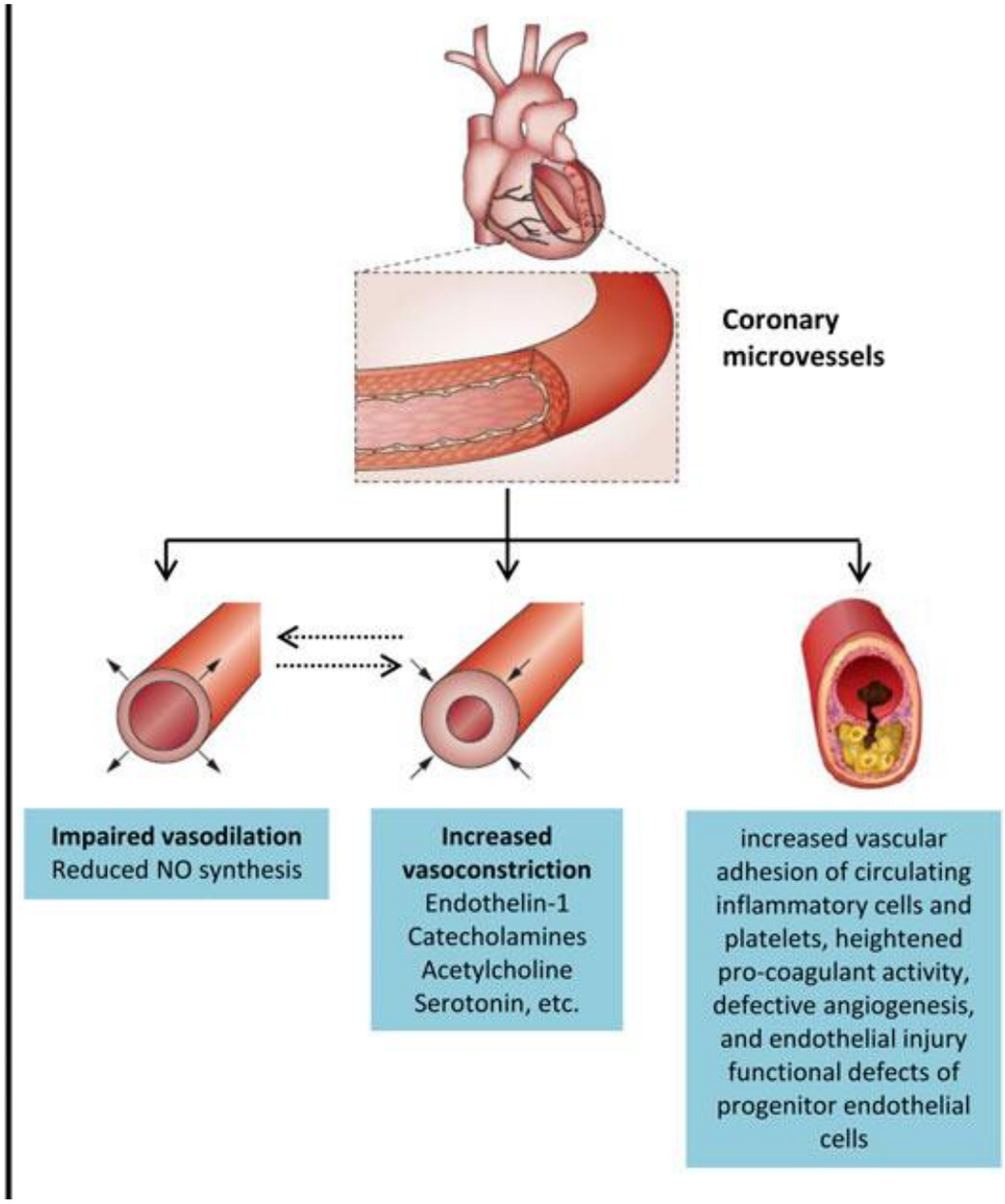
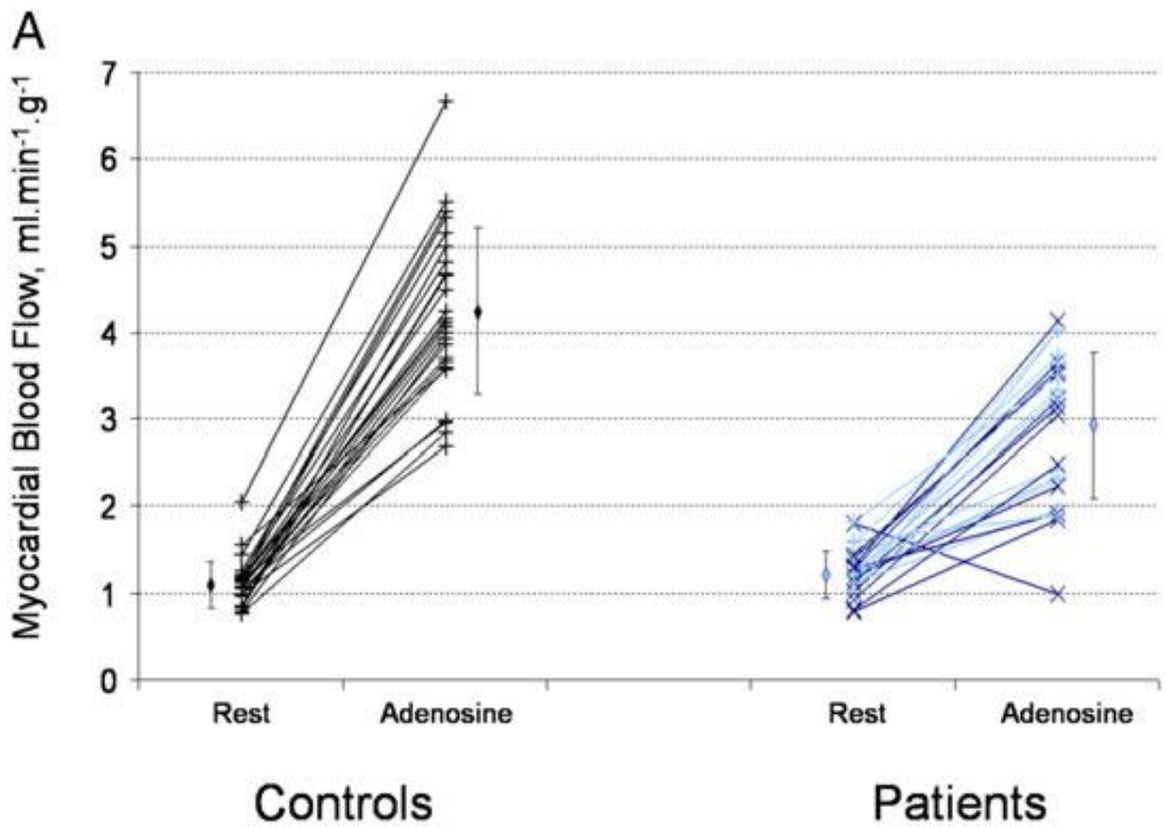
Vascular manifestations in RA



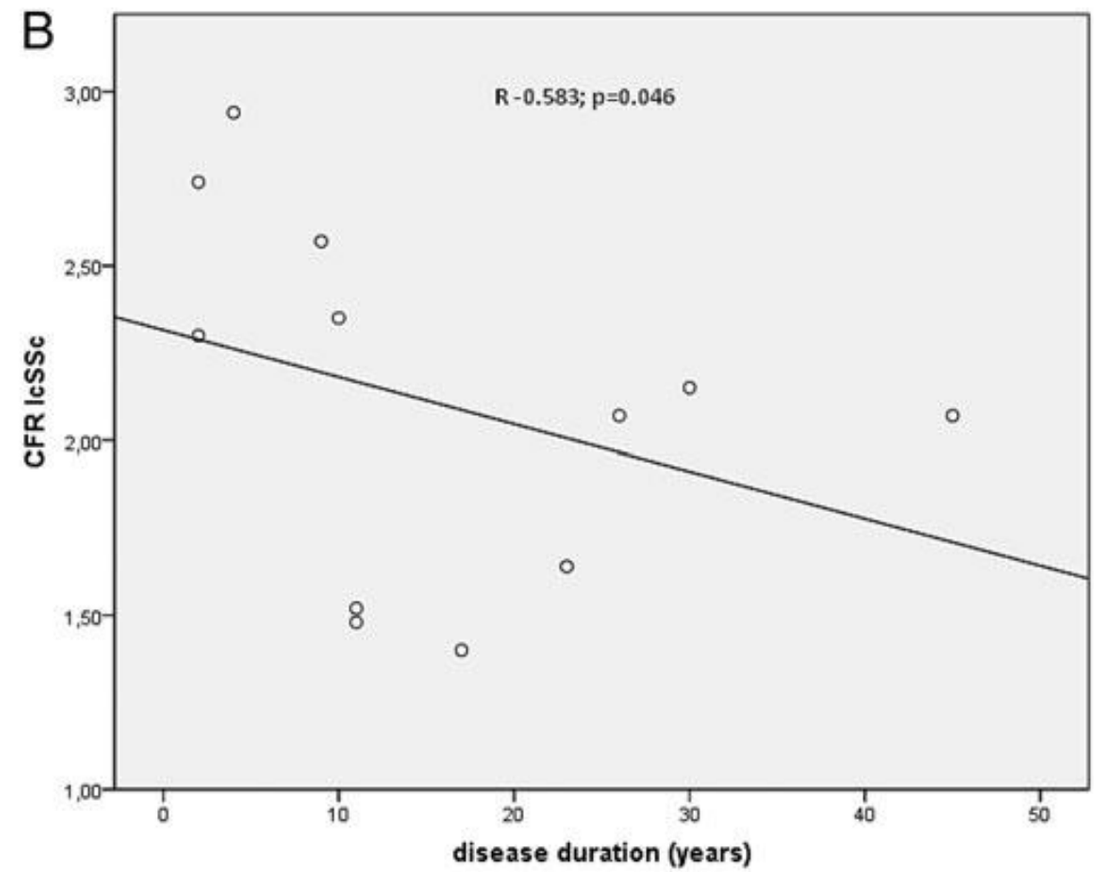


Camici et al. Nat Rev Cardiol 2015

Coronary flow reserve in RA



Recio-Mayoral et al. Eur Heart J 2009



Faccini et al. Circ J 2015

What are the predictors of the increased risk of atherosclerosis?

	HR	95% CI
Age (per decade)	2.9	(2.1-4.1)
Female Sex	0.9	(0.5-1.8)
Presence of RF	3.0	(1.3-5.8)
CRP > 5 mg/l	3.3	(1.4-7.6)
Smoking	2.0	(0.8-2.0)
HAQ (disability score)	0.9	(0.6-1.5)

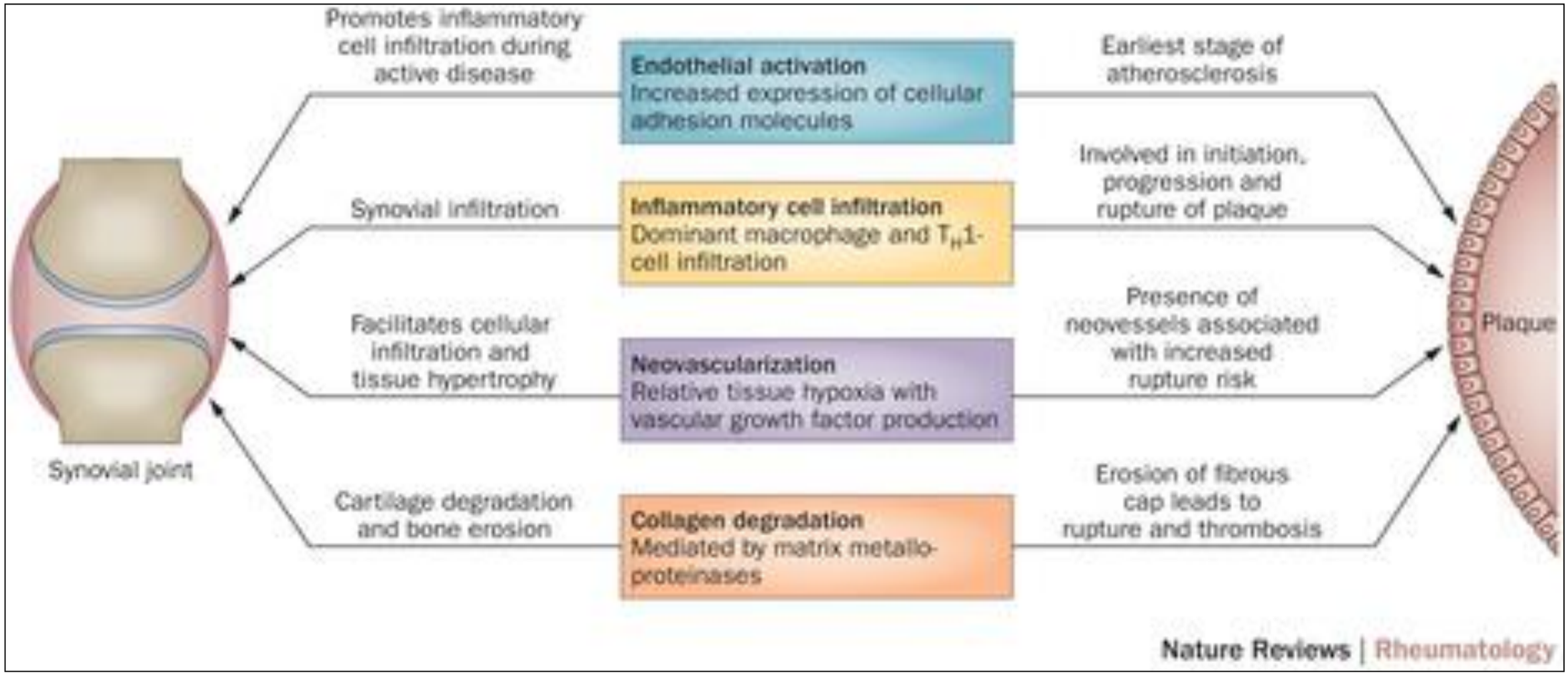
Goodstone NJ, Arth Rheumatod 2005; 52: 2293-2299

Atherosclerosis in rheumatoid arthritis: is it all about inflammation?

Sarah Skeoch & Ian N. Bruce

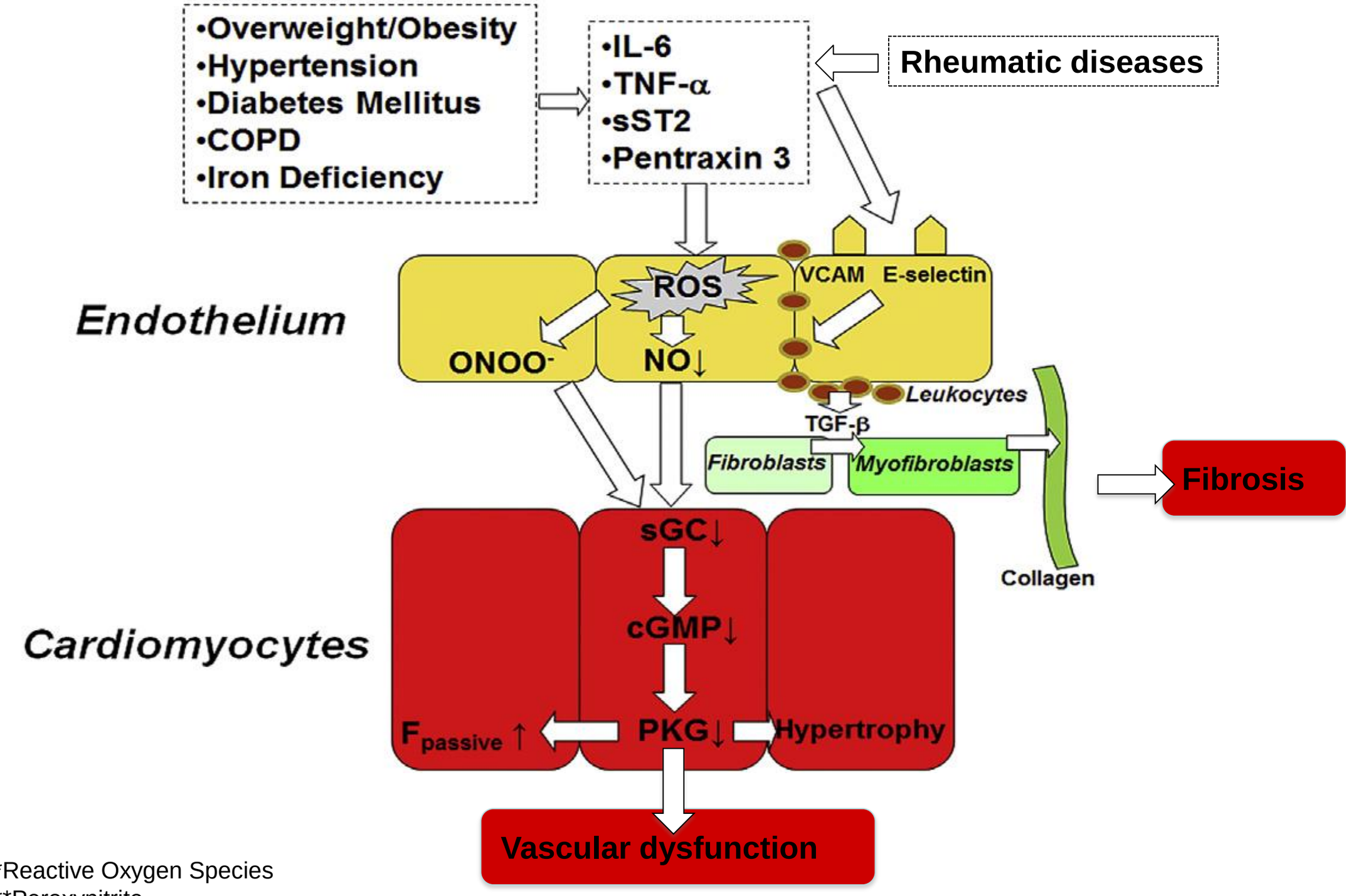
Nature Reviews Rheumatology **11**, 390–400 (2015) doi:10.1038/nrrheum.2015.40

Published online 31 March 2015



Important pathological features common to both atherosclerotic plaque and the inflamed rheumatoid synovium

Comorbidities induce Myocardial-Vascular Dysfunction and Remodeling



*Reactive Oxygen Species
**Peroxynitrite
**Vascular Cell Adhesion Molecule
***Trasforming Growth Factor β

Adapted from Paulus and Tschoepe JACC. 2013

Left ventricular remodeling and diastolic dysfunction in RA

Variables	Control Group, n = 77	RA Group, n = 157	p	Subanalysis RA Group HF, n = 38 (24%)	No HF, n = 119 (76%)	p
LV geometry						
Normal	34 (44)	48 (32)	0.040*	7 (17)	41 (34)	0.175*
Remodeling	23 (30)	55 (34)	0.523*	10 (27)	45 (39)	0.242*
Concentric hypertrophy	12 (16)	38 (24)	0.174*	18 (48)	20 (17)	< 0.001*
Excentric hypertrophy	8 (10)	16 (10)	1.000*	3 (8)	13 (10)	0.763*
Diastolic dysfunction	30 (39)	92 (59)	0.003	33 (87)	59 (50)	< 0.001
Grade 1	28 (36)	34 (22)	0.019*	12 (32)	22 (18)	0.113*
Grade 2	2 (3)	52 (33)	< 0.001*	17 (46)	35 (29)	0.112*
Grade 3	0	6 (4)	0.194*	4 (11)	2 (2)	0.031*

Schau T et al. J Rheumatol 2015

JACC: CARDIOVASCULAR IMAGING
VOL. 8, NO. 5, 2015
ISSN 1936-878X/$36.00
http://dx.doi.org/10.1016/j.jcmg.2014.12.025
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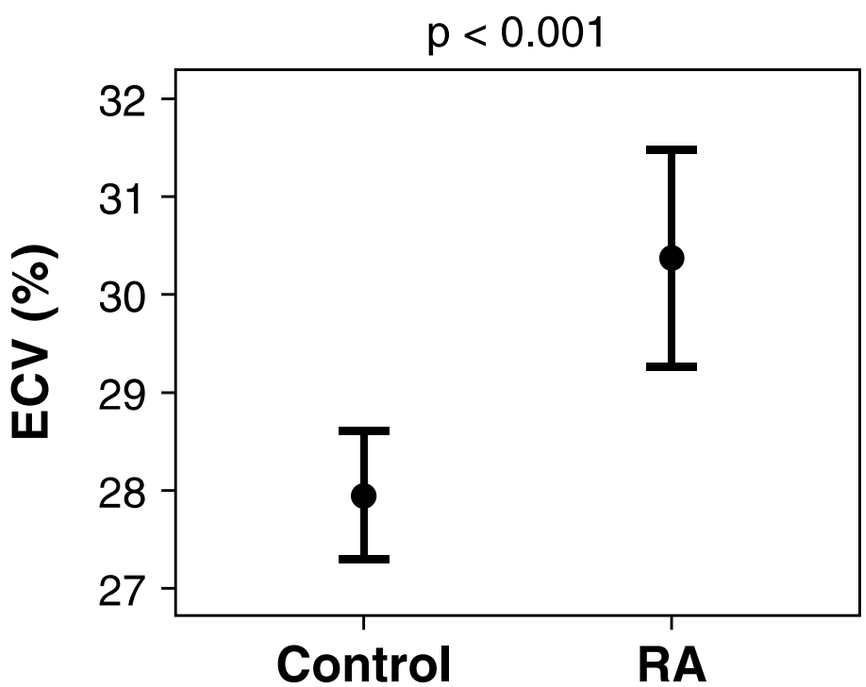
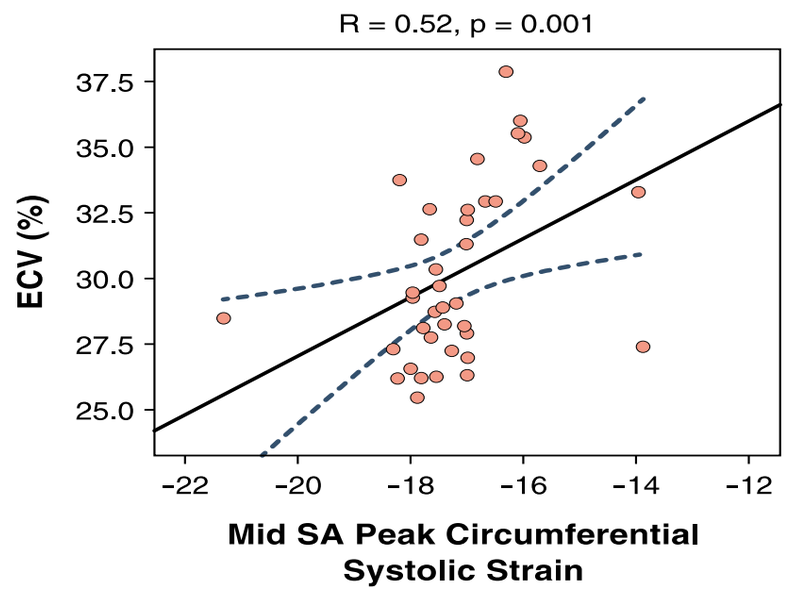
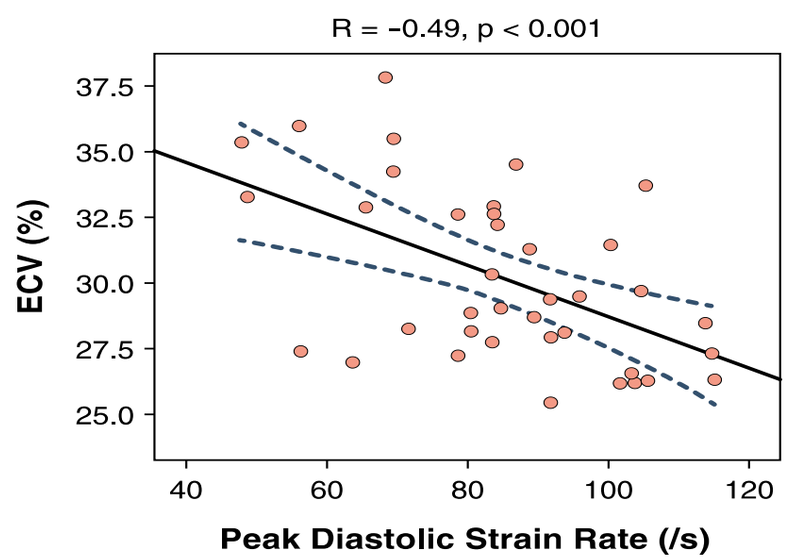
Diffuse Myocardial Fibrosis and Inflammation in Rheumatoid Arthritis

Insights From CMR T1 Mapping

Ntobeko A.B. Ntusi, FCP (SA), DPhil,*† Stefan K. Piechnik, PhD, MScEE,* Jane M. Francis, DCR (R), DNM,* Vanessa M. Ferreira, MD, DPhil,* Paul M. Matthews, MD, DPhil OBE,‡§ Matthew D. Robson, PhD,* Paul B. Wordsworth, MA,‖ Stefan Neubauer, MD,* Theodoros D. Karamitsos, MD, PhD*¶







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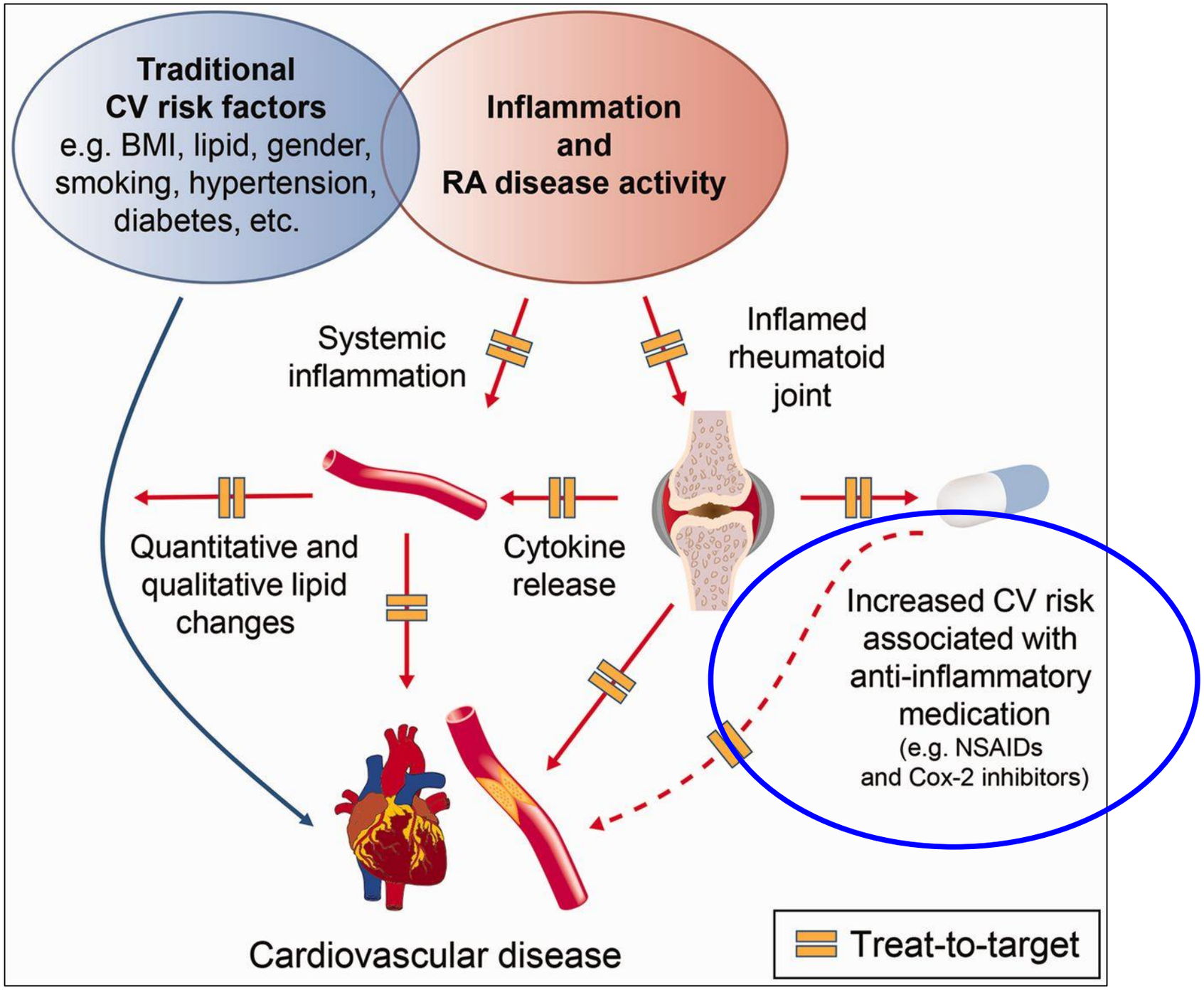
Managing cardiovascular risk factor in RA

Risk factor	Cardiovascular prevention strategies
Smoking	Counseling, nicotine patches or gum, bupropion, varenicicline
Hypertension	Frequent blood pressure monitoring, diet, exercise, stress management, antihypertensives, minimize NSAID and corticosteroid use.
Hyperlipidemia	Diet, exercise, moderate alcohol use*, statins, minimize corticosteroid use, antimalarials*.
Diabetes	Counseling, diet, exercise, oral hypoglycemic agents and/or insulin
Insulin resistance	Counseling, diet, control of inflammation (DMARDS/biologics), PPAR-agonists*
Obesity	Counseling, diet, exercise, minimize corticosteroid use.
High homocysteine	Folic acid supplementation with methotrexate/sulfasalazine use
Family history of CVD	Counseling, monitoring risk factors
Inflammation	DMARDS, biologics, NSAIDS, statins*; PPAR-agonists*
Thrombotic risk	Low dose aspirin/consider anticoagulation when other risk factors for thrombosis are present

* not enough evidence to suggest as standard of care

Impact of tight control of inflammation and disease activity in relation to the reduction of CV risk in RA



Ernest Choy et al. Rheumatology 2014;rheumatology.keu224

Statins May Have A Dual Role In RA

Articles

Trial of Atorvastatin in Rheumatoid Arthritis (TARA): double-blind, randomised placebo-controlled trial

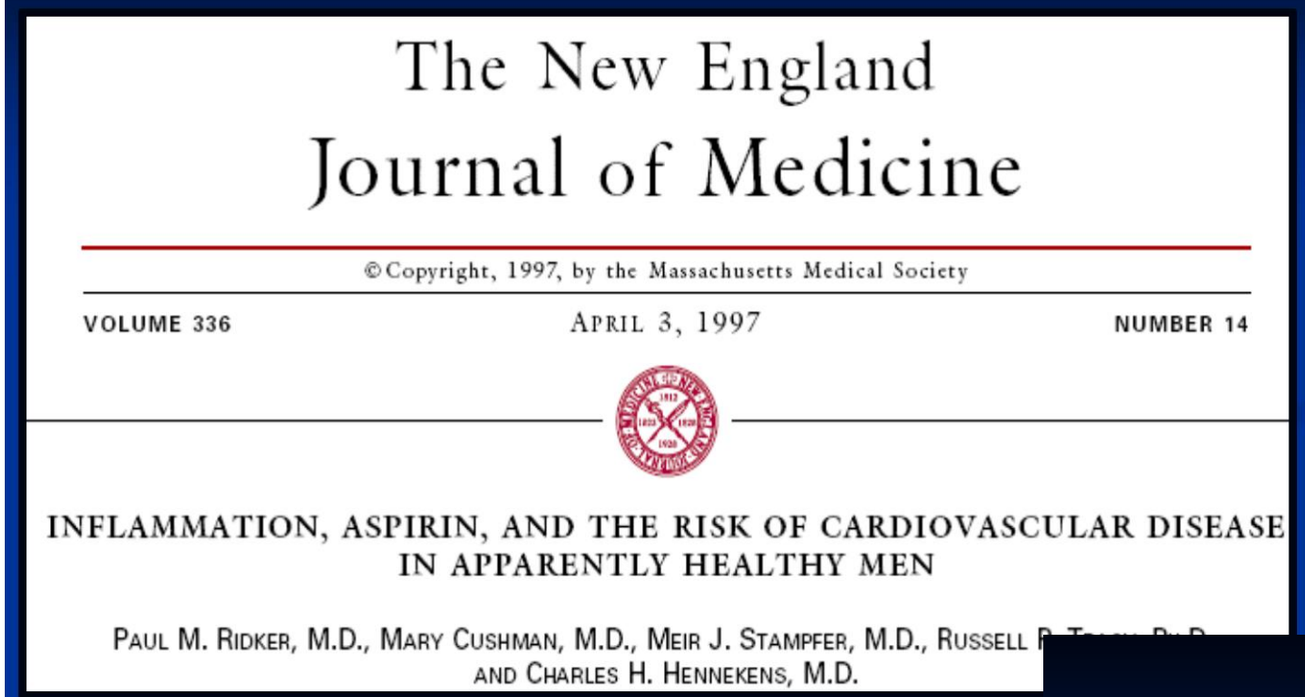
David W McCarey, Iain B McInnes, Rajan Madhok, Rosie Hampson, Olga

Results – After 6 Months Of Treatment

	Atorvastatin (n=58)	Placebo (n=58)	p
Primary outcome measure			
Disease activity score	–0·50 (–0·75 to –0·25)	0·03 (–0·23 to 0·28)	0·004
Secondary outcome measures			
Erythrocyte sedimentation rate (mm/h)	–5·03 (–8·4 to –1·67)	1·91 (–1·61 to 5·44)	0·005
C-reactive protein (log mg/L)	–0·46 (–0·64 to –0·28)	0·12 (–0·09 to 0·34)	<0·0001
Clinical measures			
Tender joint count	–1·21 (–3·28 to 0·86)	0·38 (–1·16 to 1·92)	0·22
Early morning stiffness (log)	–0·47 (–0·82 to –0·12)	–0·13 (–0·47 to 0·22)	0·17
Visual analogue score	–5·07 (–10·5 to 0·36)	1·97 (–3·15 to 7·08)	0·06
Swollen joint count	–2·69 (–3·81 to –1·57)	–0·53 (–1·59 to 0·52)	0·0058
Patient global assessment	–4·14 (–7·80 to –0·48)	0·15 (–4·25 to 4·56)	0·14
Health assessment questionnaire	0·02 (–0·12 to 0·16)	0·04 (–0·04 to 0·13)	0·75
Lipids			
Cholesterol (mmol/L)	–1·48 (–1·73 to –1·23)	–0·01 (–0·14 to 0·12)	<0·0001
Triglyceride (mmol/L)	–0·24 (–0·34 to –0·14)	0·07 (–0·04 to 0·18)	<0·0001
LDL-cholesterol (mmol/L)	–1·40 (–1·63 to –1·17)	–0·07 (–0·23 to 0·10)	<0·0001
HDL-cholesterol (mmol/L)	0·03 (–0·03 to 0·09)	–0·04 (–0·10 to 0·02)	0·097
Other risk markers			
Fibrinogen (g/L)	–0·38 (–0·69 to –0·07)	0·00 (0·19 to –0·20)	0·041
Plasma viscosity (mPa/s)	–0·05 (–0·06 to –0·03)	–0·00 (–0·02 to 0·01)	0·0004
Von Willebrand factor (IU/dL)	–8·5 (–20·6 to 3·58)	–4·53 (–16·7 to 7·6)	0·64
Intercellular adhesion molecule 1 (ng/mL)	–22·6 (–41·6 to –3·7)	2·37 (–18·2 to 22·9)	0·076
Interleukin 6 (pg/mL)	–6·6 (–13·2 to 0·01)	3·84 (–2·85 to 10·5)	0·028

Table 3: **Differences after 6 months of treatment**

Lancet 2004; 363: 2015-21



The New England
Journal of Medicine

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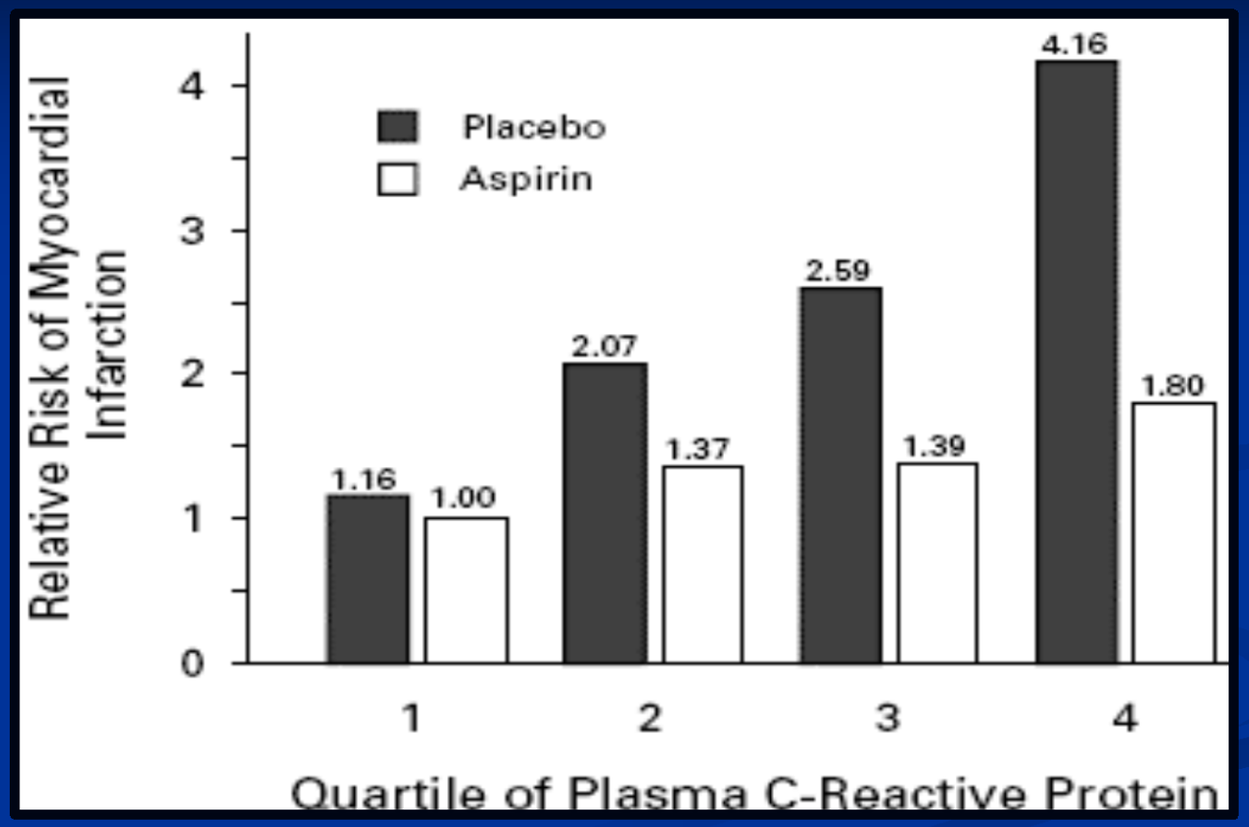
VOLUME 336 APRIL 3, 1997 NUMBER 14

INFLAMMATION, ASPIRIN, AND THE RISK OF CARDIOVASCULAR DISEASE IN APPARENTLY HEALTHY MEN

PAUL M. RIDKER, M.D., MARY CUSHMAN, M.D., MEIR J. STAMPFER, M.D., RUSSELL P. TRACY, PH.D., AND CHARLES H. HENNEKENS, M.D.

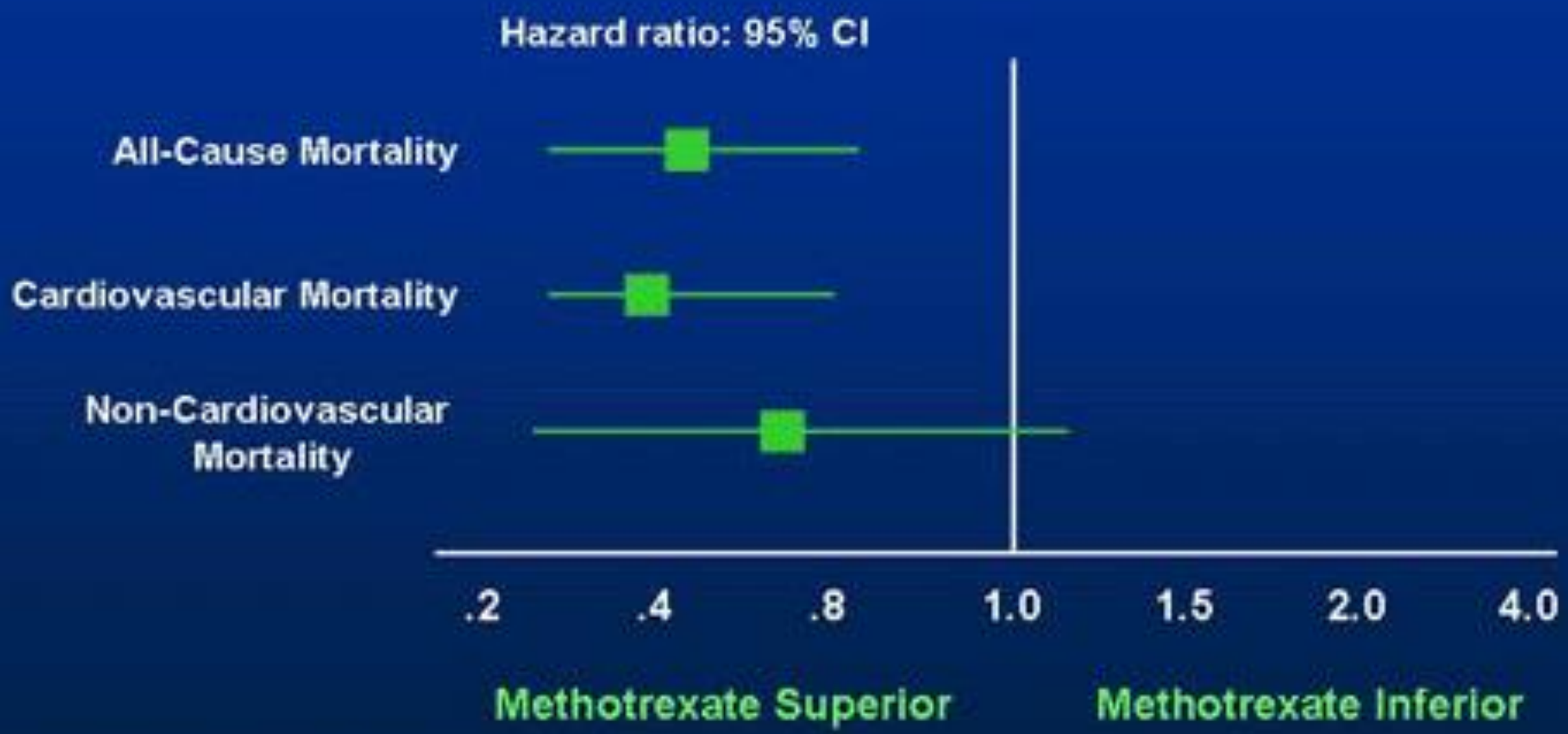
ASA More Effective In Those With High CRP



NEJM 1997; 336: 973-979

Can “Disease-Modifying” Anti-Rhuematic Drugs also modify CV risk?

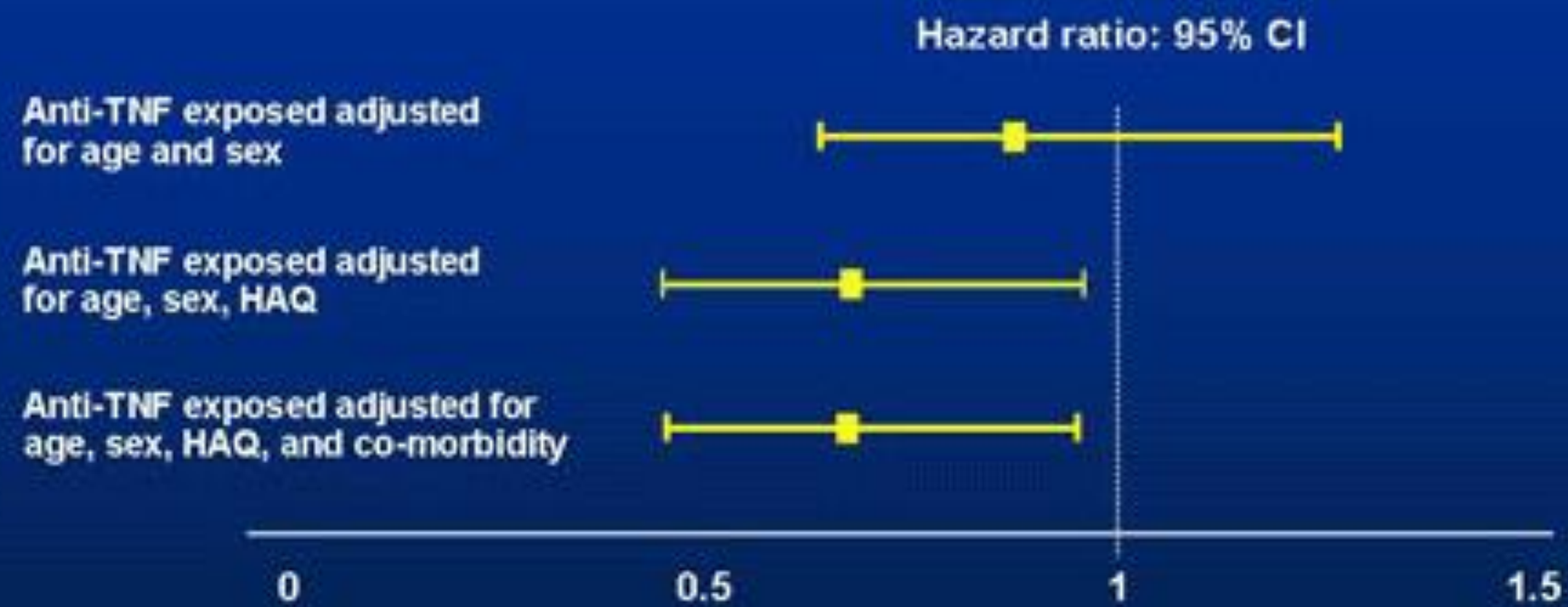
Methotrexate Use Reduces CV Mortality in Patients with RA



HR adjusted for age, sex, RF, calendar year, duration of disease, smoking, education, disease activity measures, and prednisone status.

Choi HK, et al. *Lancet*. 2002;359:1173-1177.

TNF Inhibitor Use is associated with Reduced Mortality in RA



- Registry of Swedish RA patients <80 years
- Mortality in 1430 pts, 921 on TNF blockers

Jacobsson L, et al. *Ann Rheum Dis* 2007; 66:670-675.

International Journal of Cardiology 171 (2014) e125–e126

Contents lists available at ScienceDirect

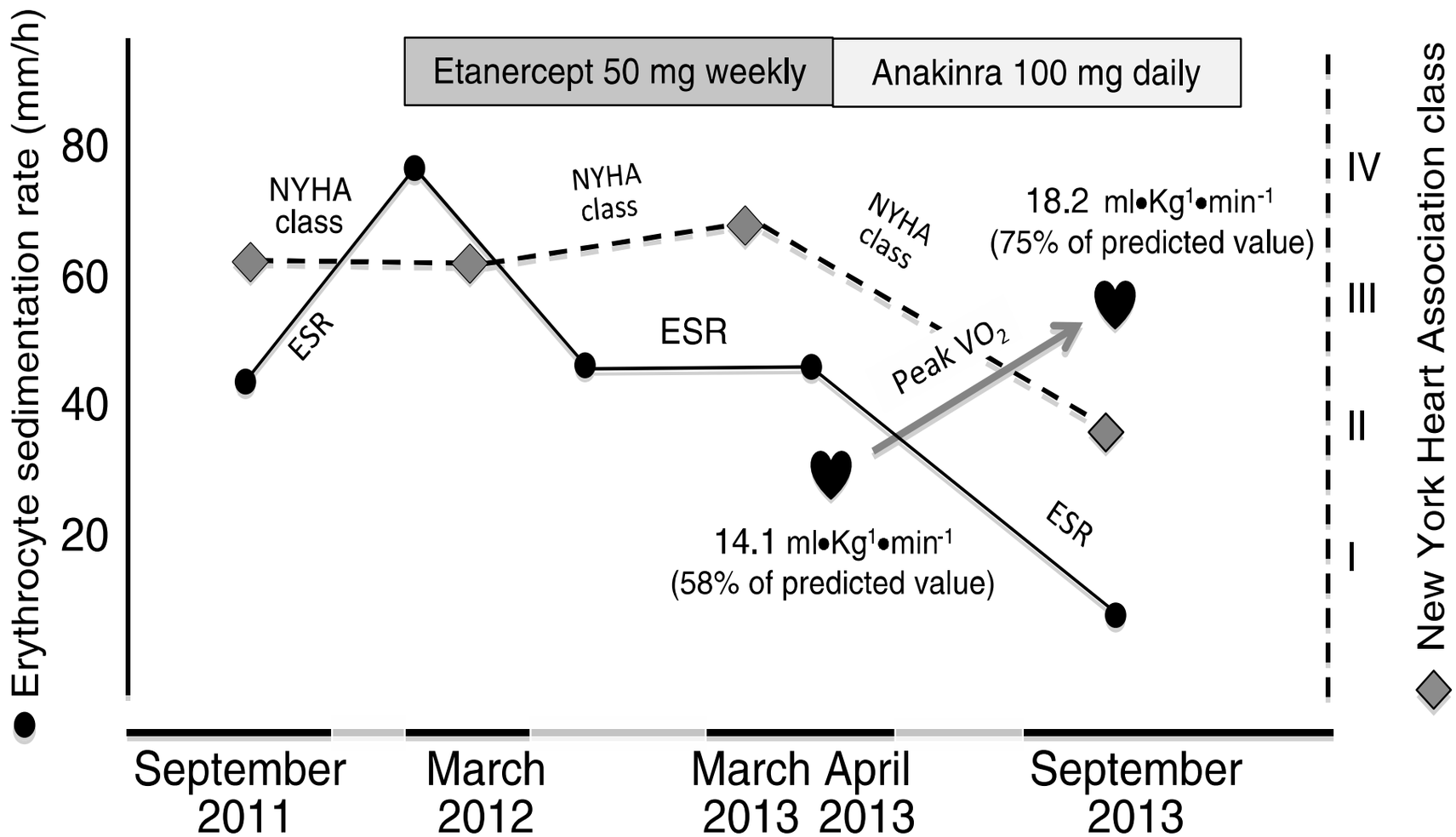
International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Letter to the Editor

Interleukin-1 blockade in rheumatoid arthritis and heart failure: A missed opportunity?

Antonio Abbate [a,*], Justin M. Canada [b], Benjamin W. Van Tassell [c], Christopher M. Wise [d], Charles A. Dinarello [e]



Summary (1)

The **CV risk in RA is increased** and is related to the systemic inflammatory burden as well as an increased prevalence of traditional risk factors.

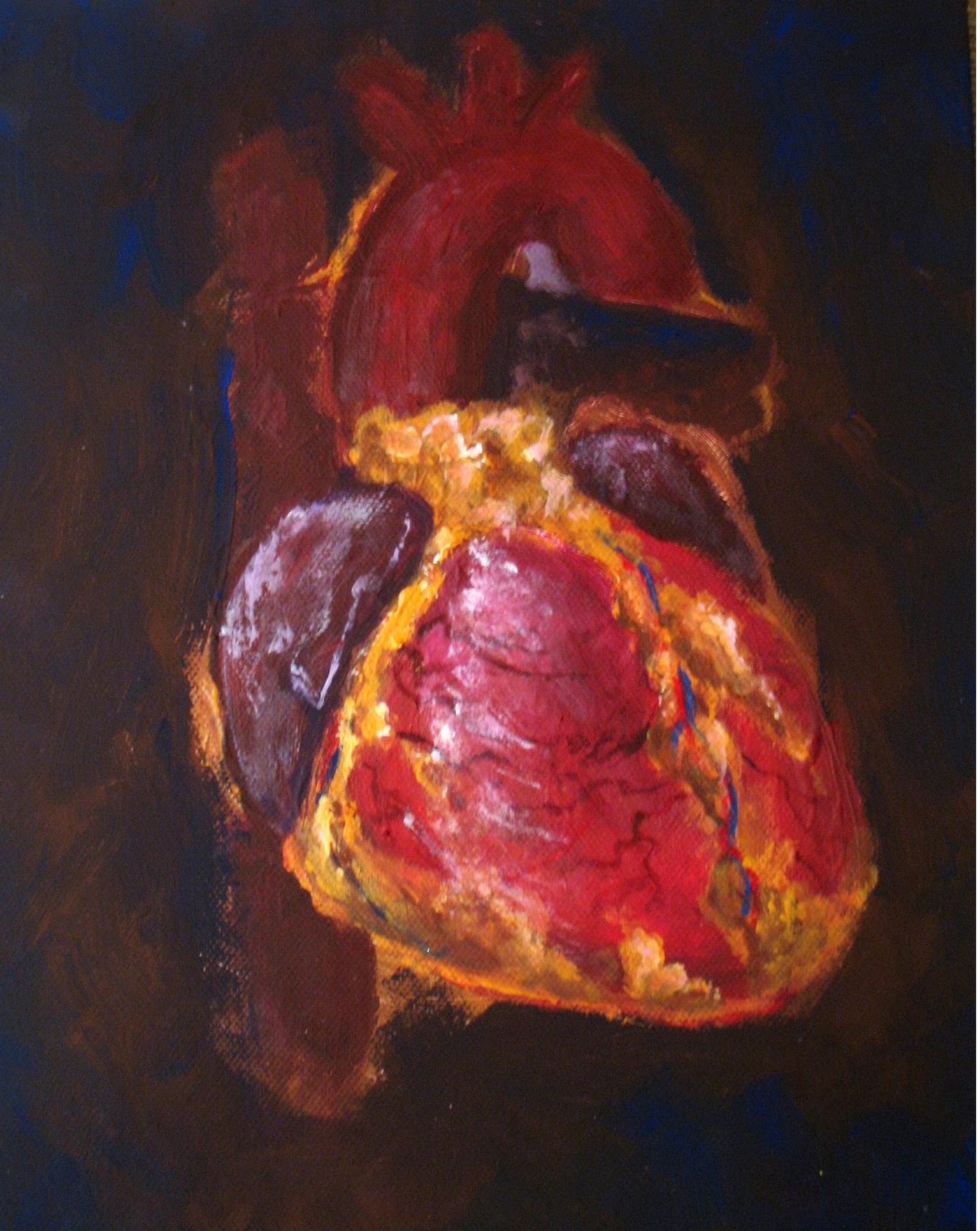
Biomarkers of inflammation play a pivotal role in prevention, screening and follow up.

The suppression of inflammation through tight and sustained disease control is important for lowering CV risk, but also to permit accurate **screening of patients at high CV risk.**

Summary (2)

The **adequate suppression** of the disease activity is necessary to counteract the effects of systemic inflammation on the CV risk in RA and it is considered the cornerstone of managing CV disease complications.

Future research could help the understanding of use of **“Disease-Modifying” Anti-Rheumatic Drugs** in **HFpEF**.



Thank you!