XII Meeting. State of the Art in

HEART FAILURE

CLINICAL PRACTICE AND ORGANIZATIONAL MODELS

Venue: Hotel Meliá María Pita, A Coruña

A Coruña 26-27 September 2025

A Coruña Heart Failure Academy

#ACORUÑAHF2025

Obesity and HF.
What have we learned in pathophysiology and management?

Obesidad e IC.
¿Qué hemos aprendido en fisiopatología y manejo?

Almudena Castro
CARDIÓLOGA
Hospital Universitario La Paz

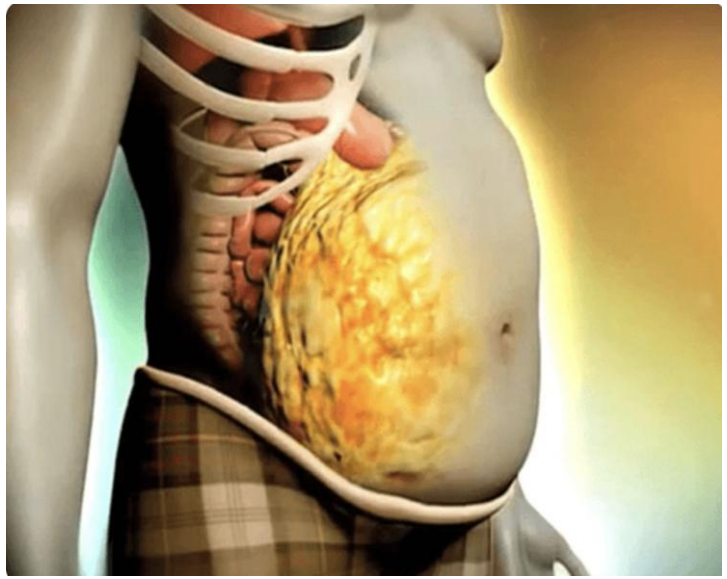
SERVIZO GALEGO DE SAÚDE · ÁREA SANITARIA DA CORUÑA E CEE · inibic · SOCIEDADE GALEGA DE CARDIOLOXÍA · UNIVERSIDADE DA CORUÑA · ciber | CV · UNIÓN EUROPEA Fondo Europeo de Desarrollo Regional · XUNTA DE GALICIA · galicia

Disclosure of Conflict of Interest

Consultant, Speaker and Researcher for:

BI, MSD, Astra Zeneca, Esteve, Novartis, Novo Nordisk, Amgen, Menarini

Towards a Redefinition of Obesity

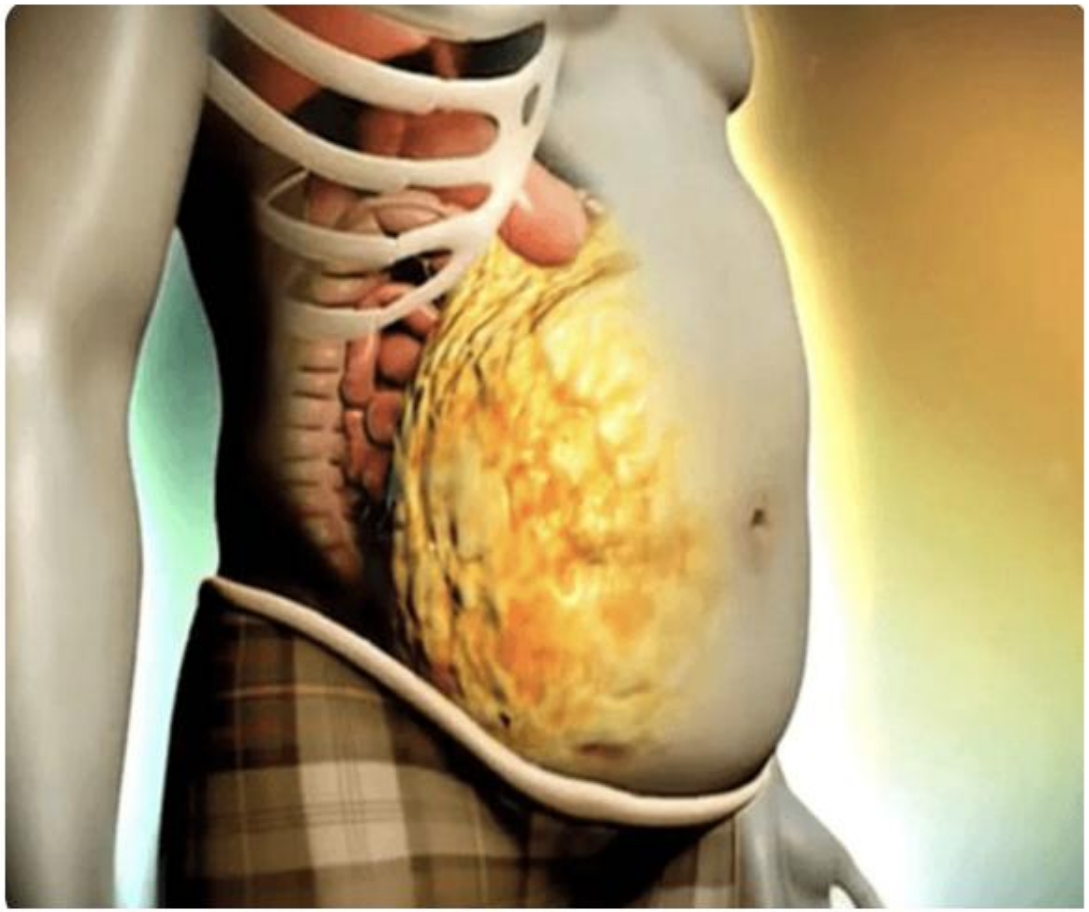


Chronic Metabolic Adipose Disease (CMAD)

Myth-Busting:

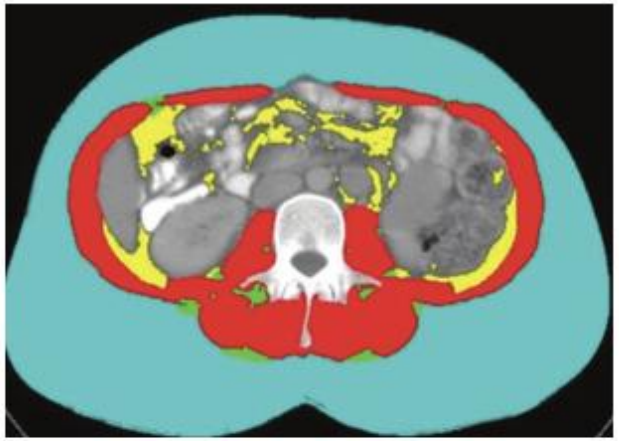
1.

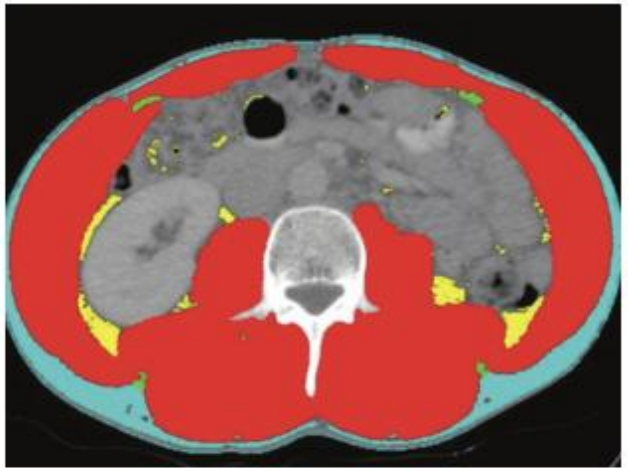
Low BMI does NOT exclude ectopic fat accumulation.



Myth-Busting:

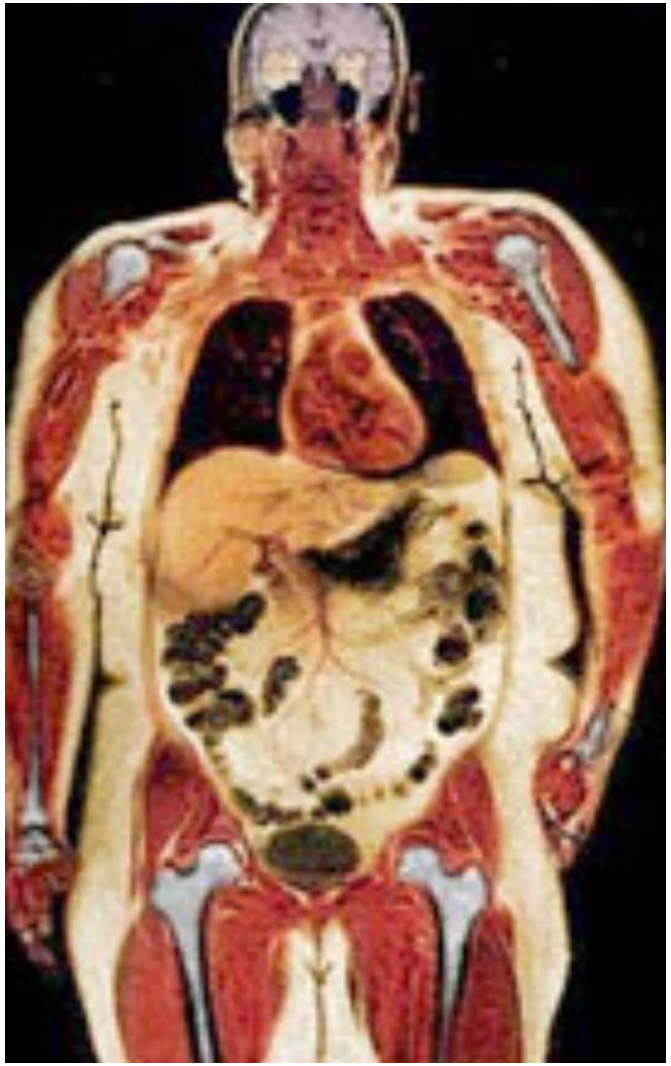
2.

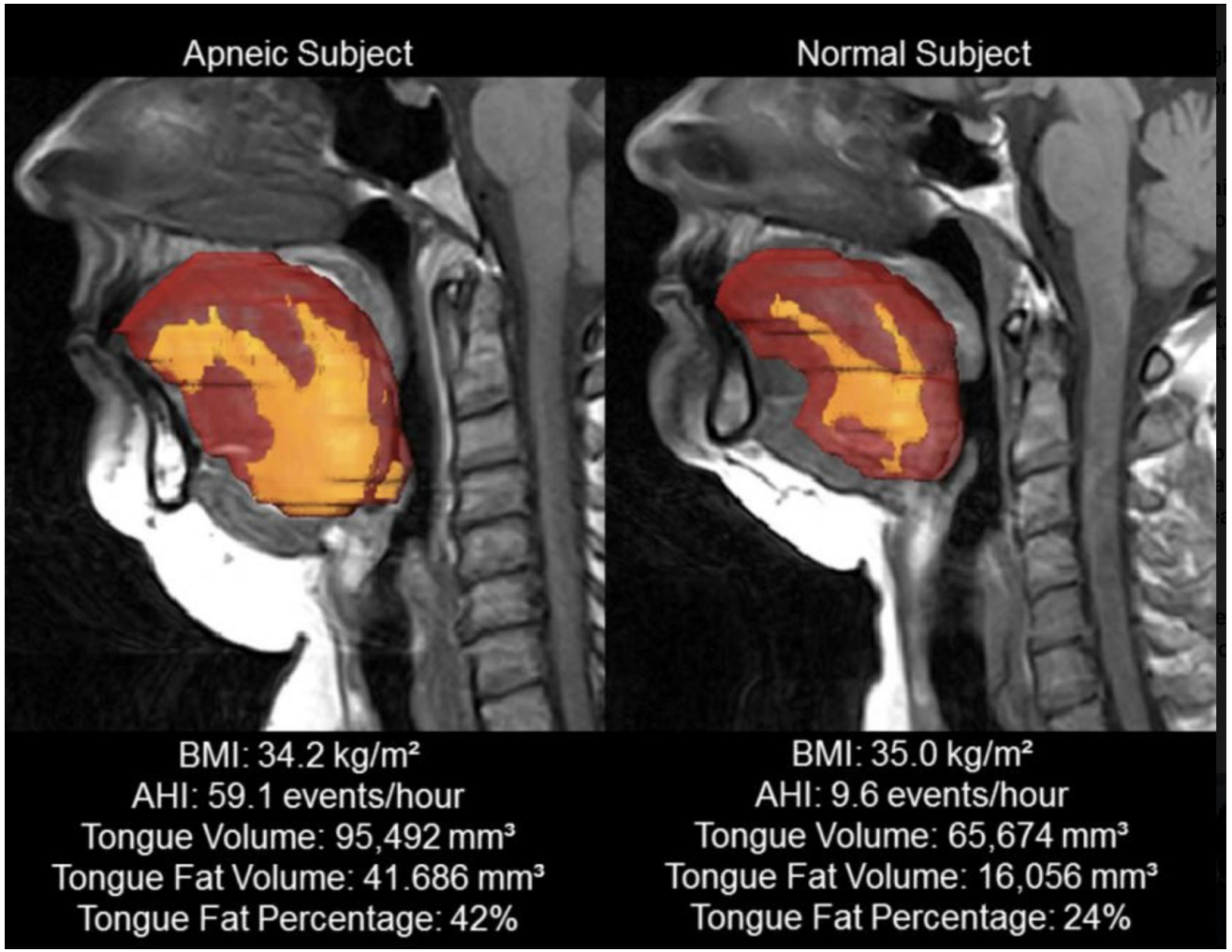




A high BMI does NOT necessarily imply ectopic fat

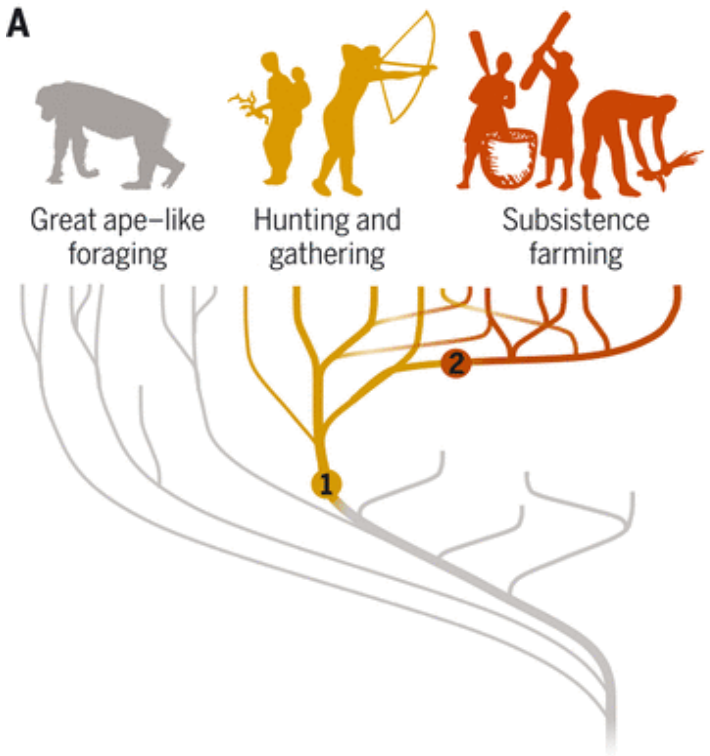
The place really matters

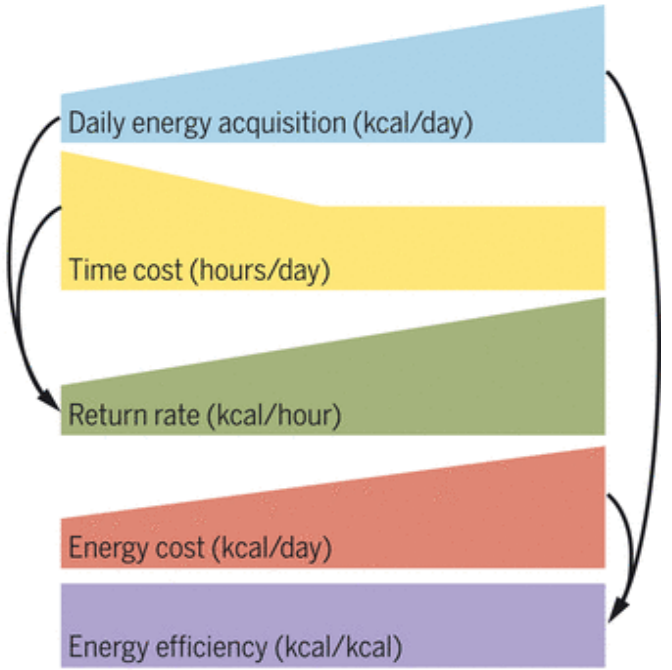




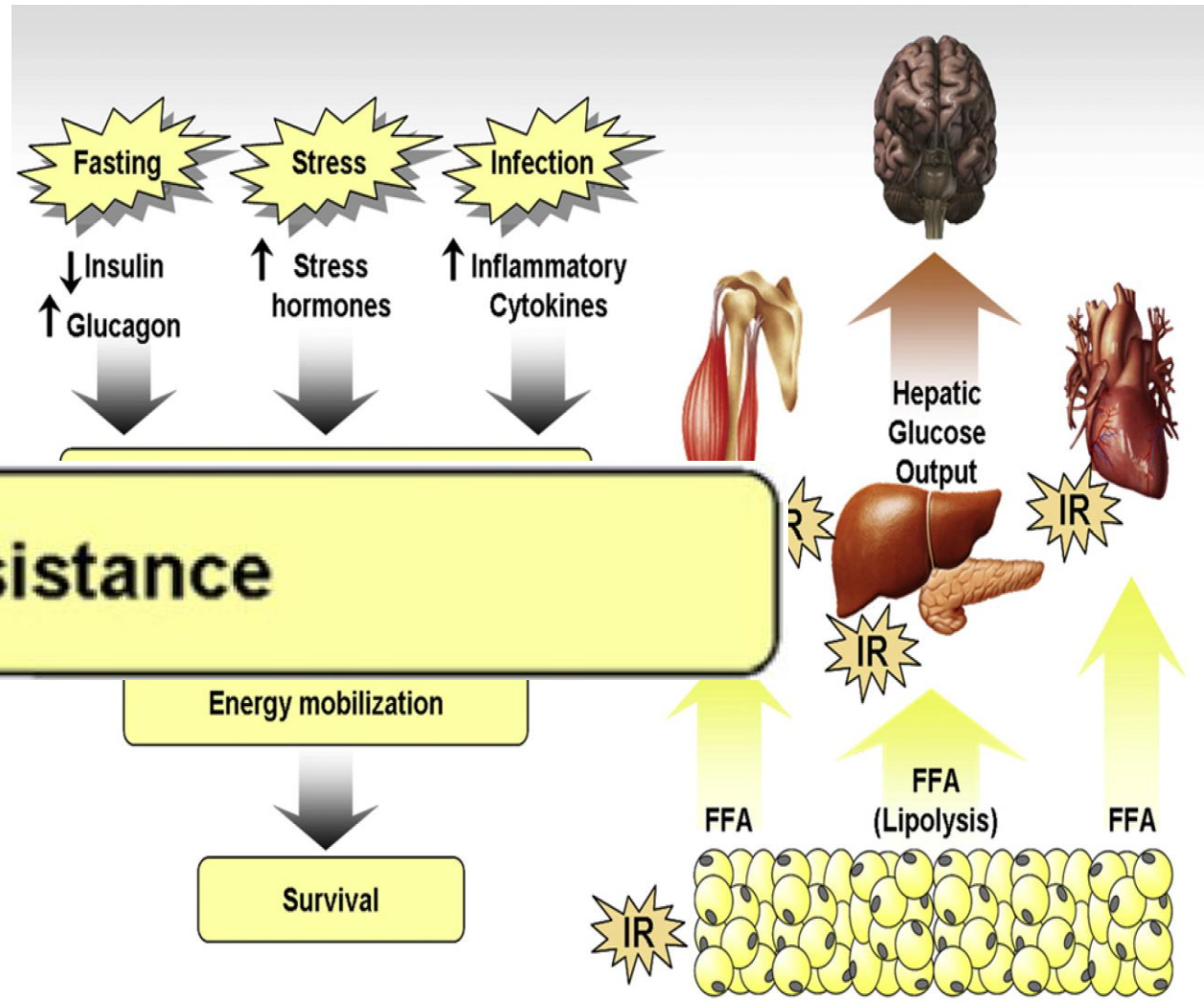
SLEEP, Vol. 37, No. 10, 2014 , Tongue Fat in Patients with Obstructive Sleep Apnea—Kim et a

Evolution based on energy efficiency





The energetics of uniquely human subsistence strategies, Volume: 374, Issue: 6575, DOI: (10.1126/science.abf0130)



Insulin resistance

Energy mobilization

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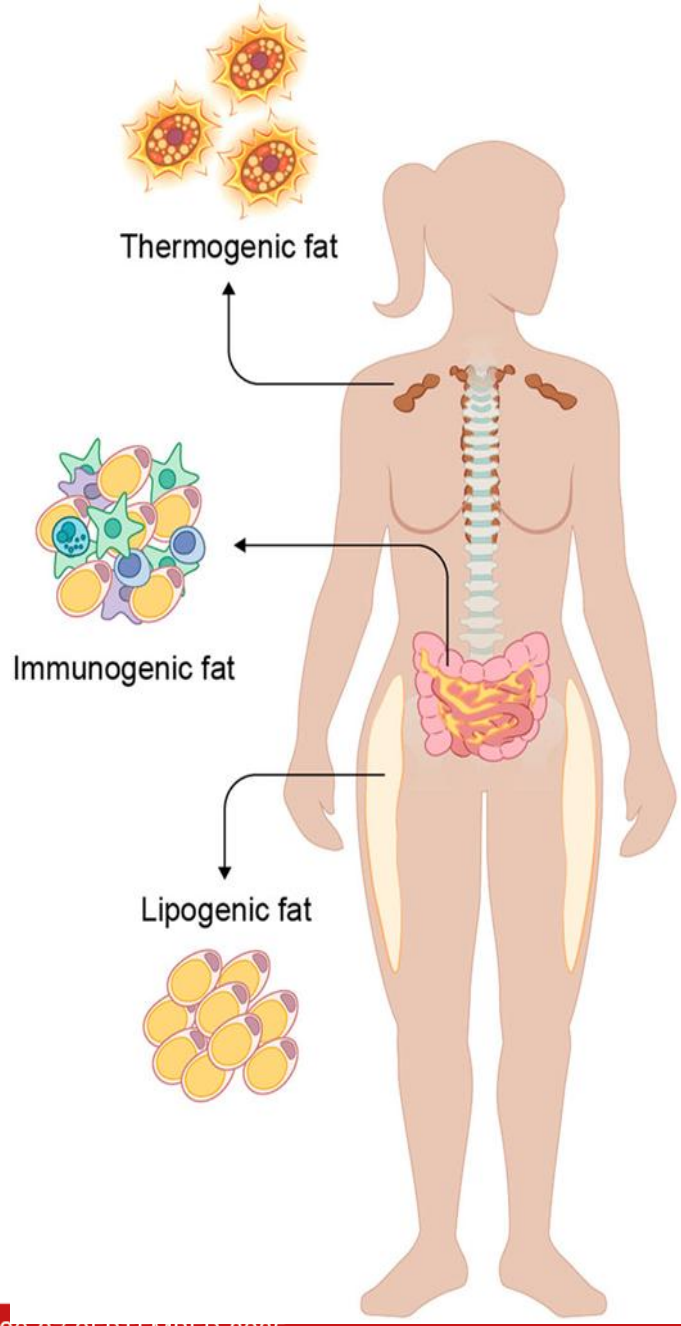
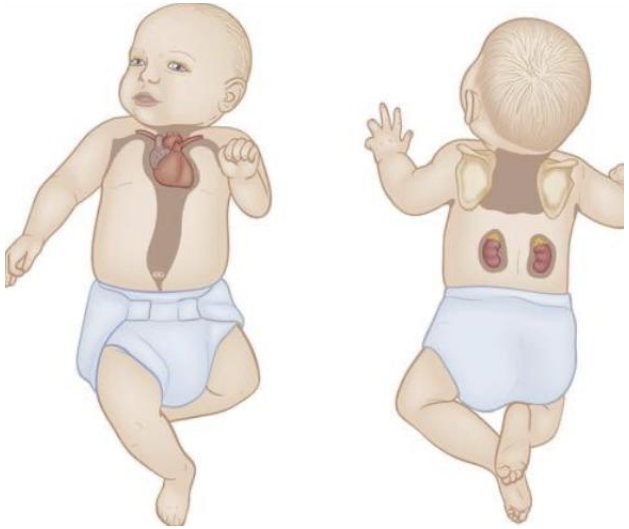
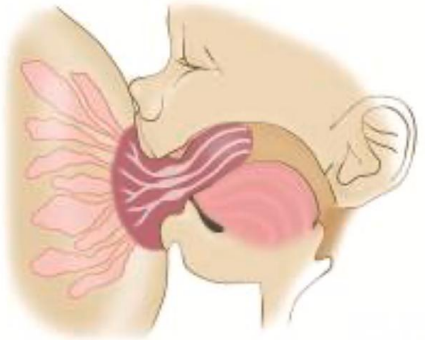
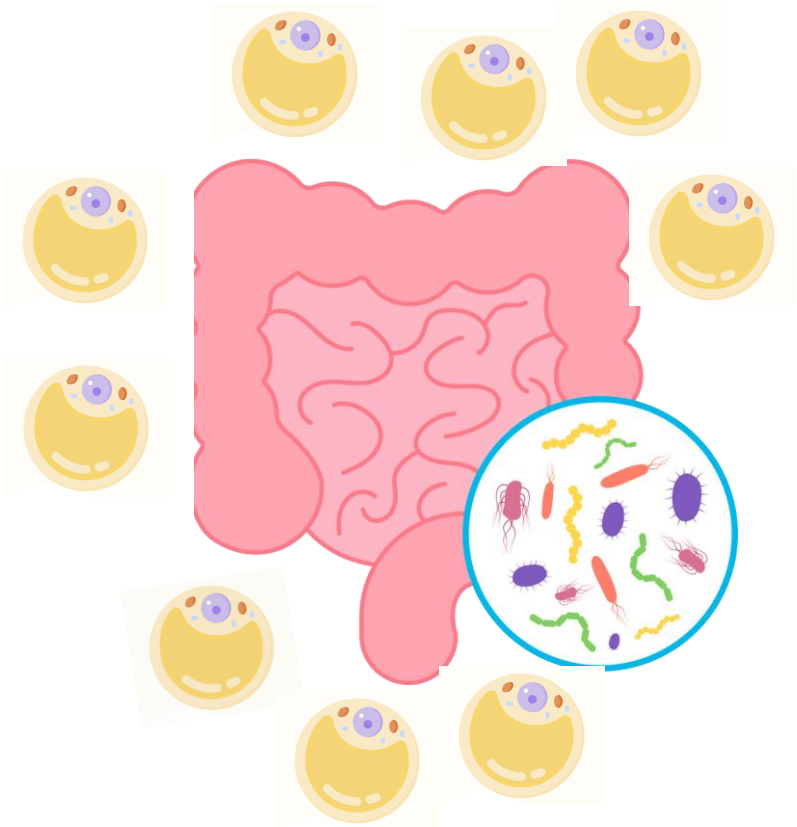


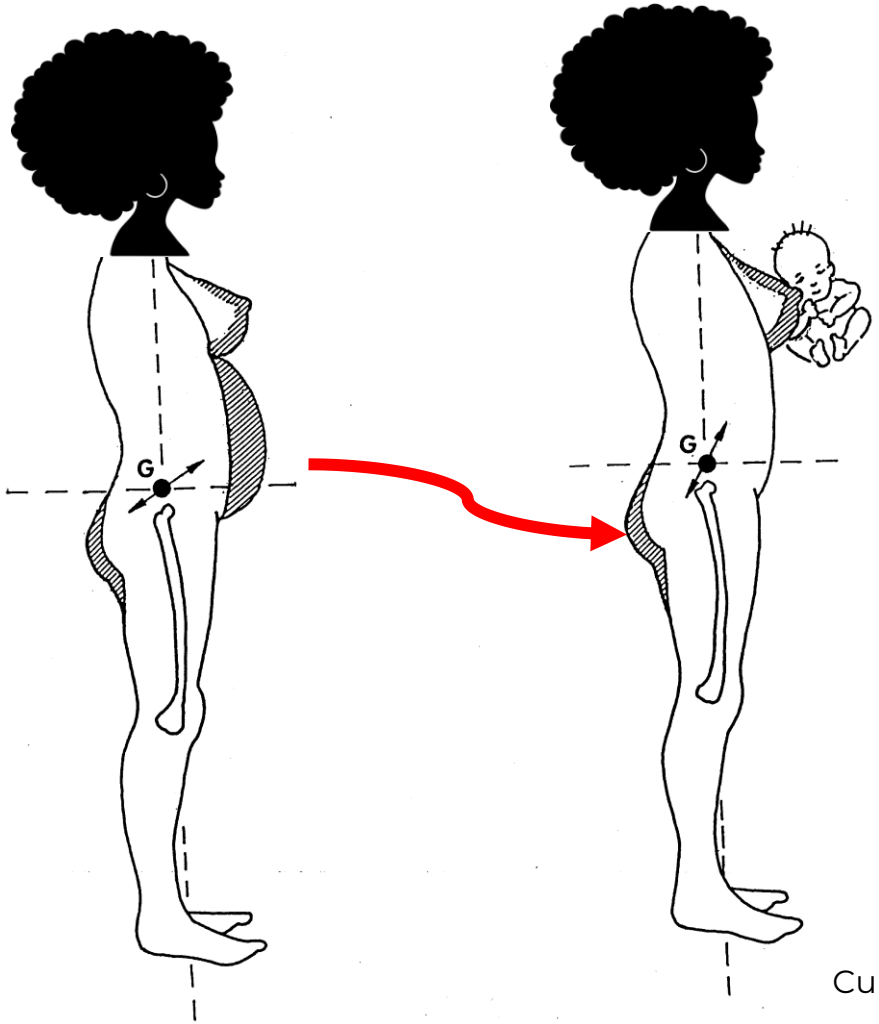






Andreas Kraag Ziegler & Camilla Scheele. npj Metabolic Health and Disease | (2024)2 :34

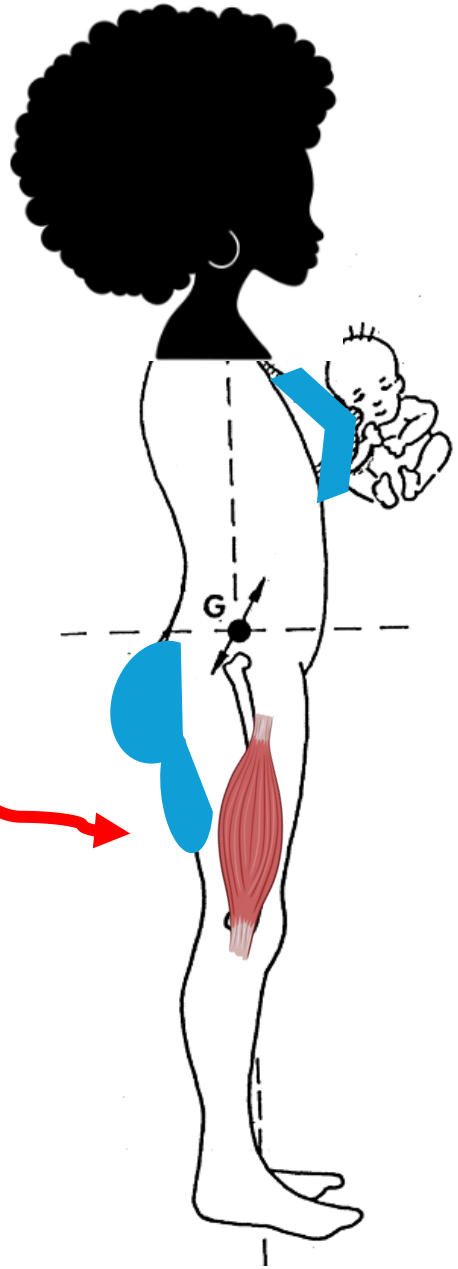
The Evolution of Gluteal/Femoral Fat Deposits and Balance during Pregnancy in Bipedal Homo

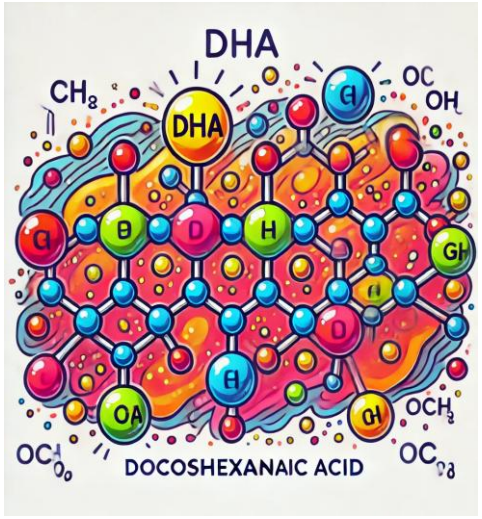


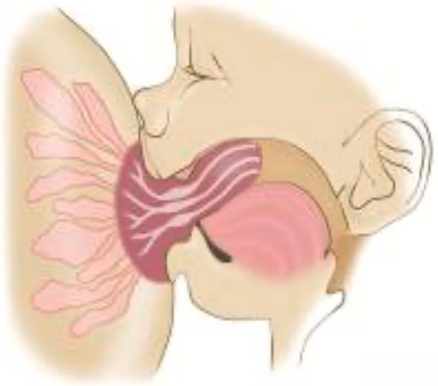
Current Anthropology, 2001. (42)issue 4, pages 572-574

gluteofemoral fat

estrogens



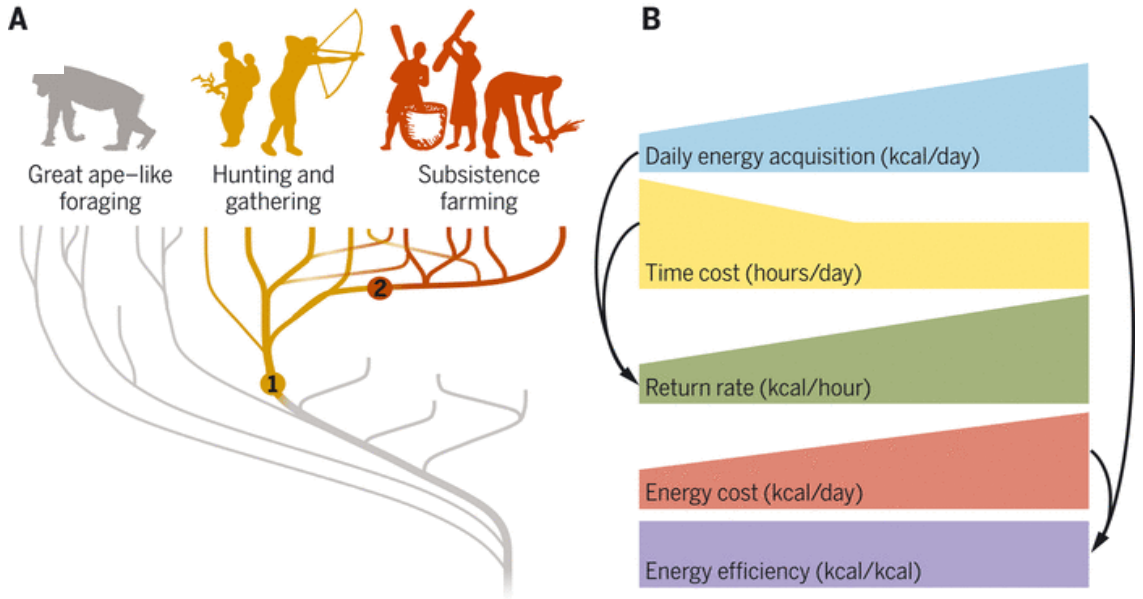




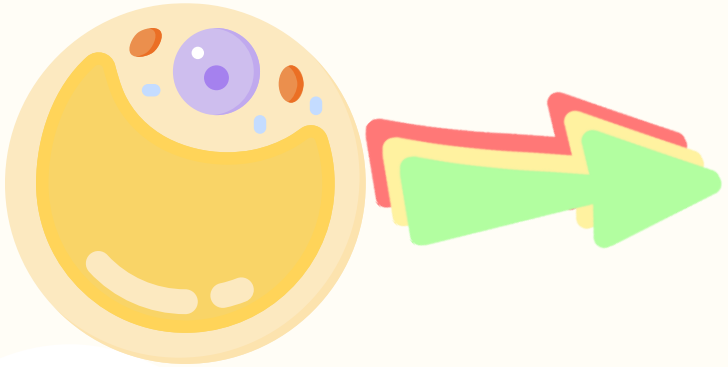
1. Posture and biomechanics
2. Metabolic health
3. Reproductive and developmental health
4. Skeletal and muscular health
5. Hormonal regulation
6. Cerebral development

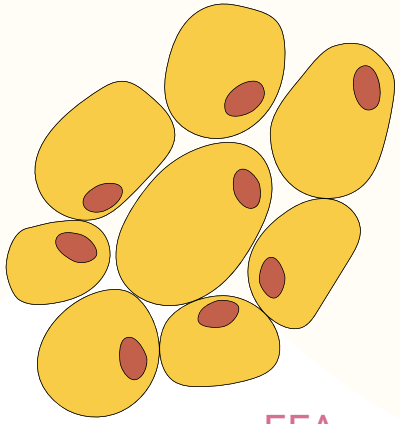
Front Nutr. 2024;11:1368966. doi:10.3389/fnut.2024.1368966

Evolution based on energy efficiency



Adaptado de
Michael Lehrke et al. *JACC* 2019; 73:1945-1947.



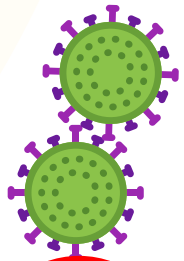


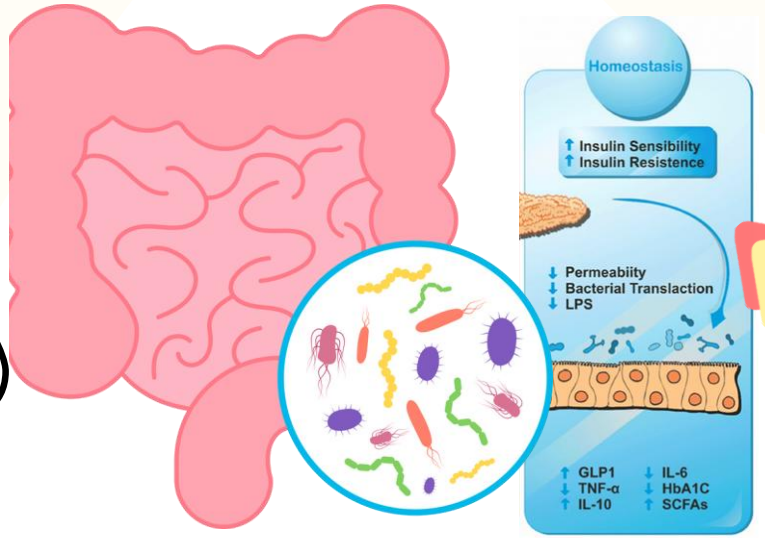
Adipokin

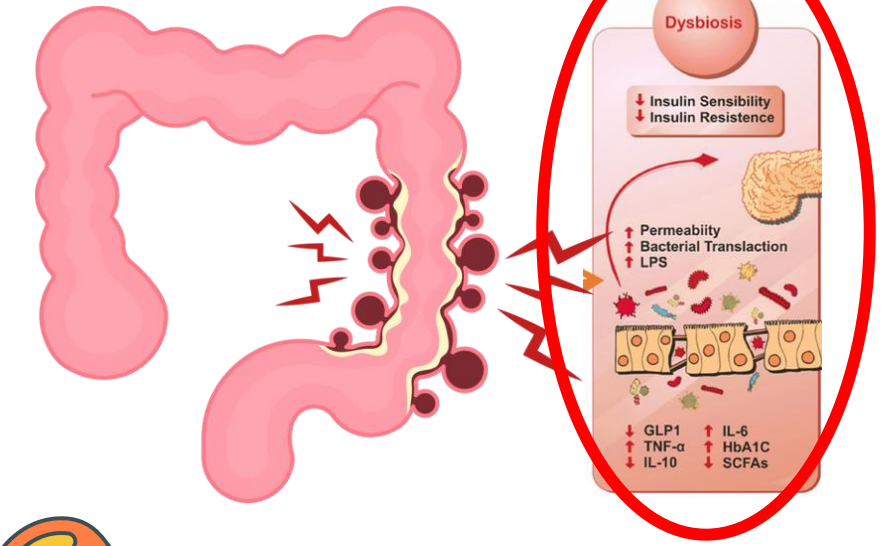
Leptin

M2 a M1

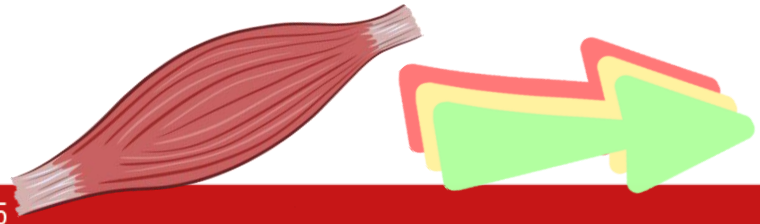
FFA

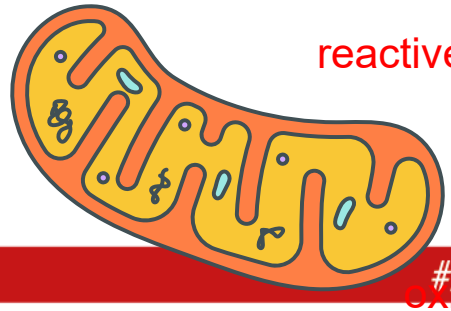






reactive oxygen species



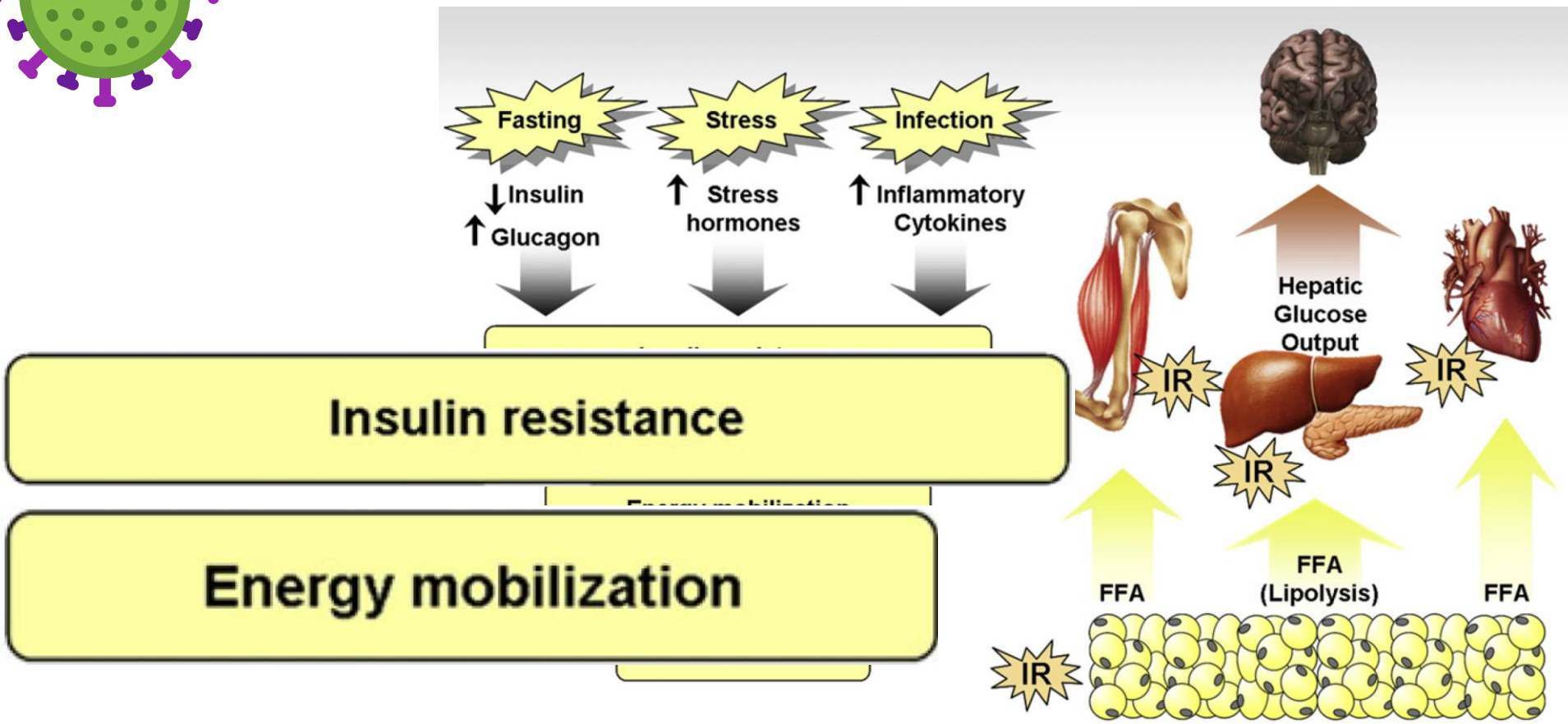


lactate

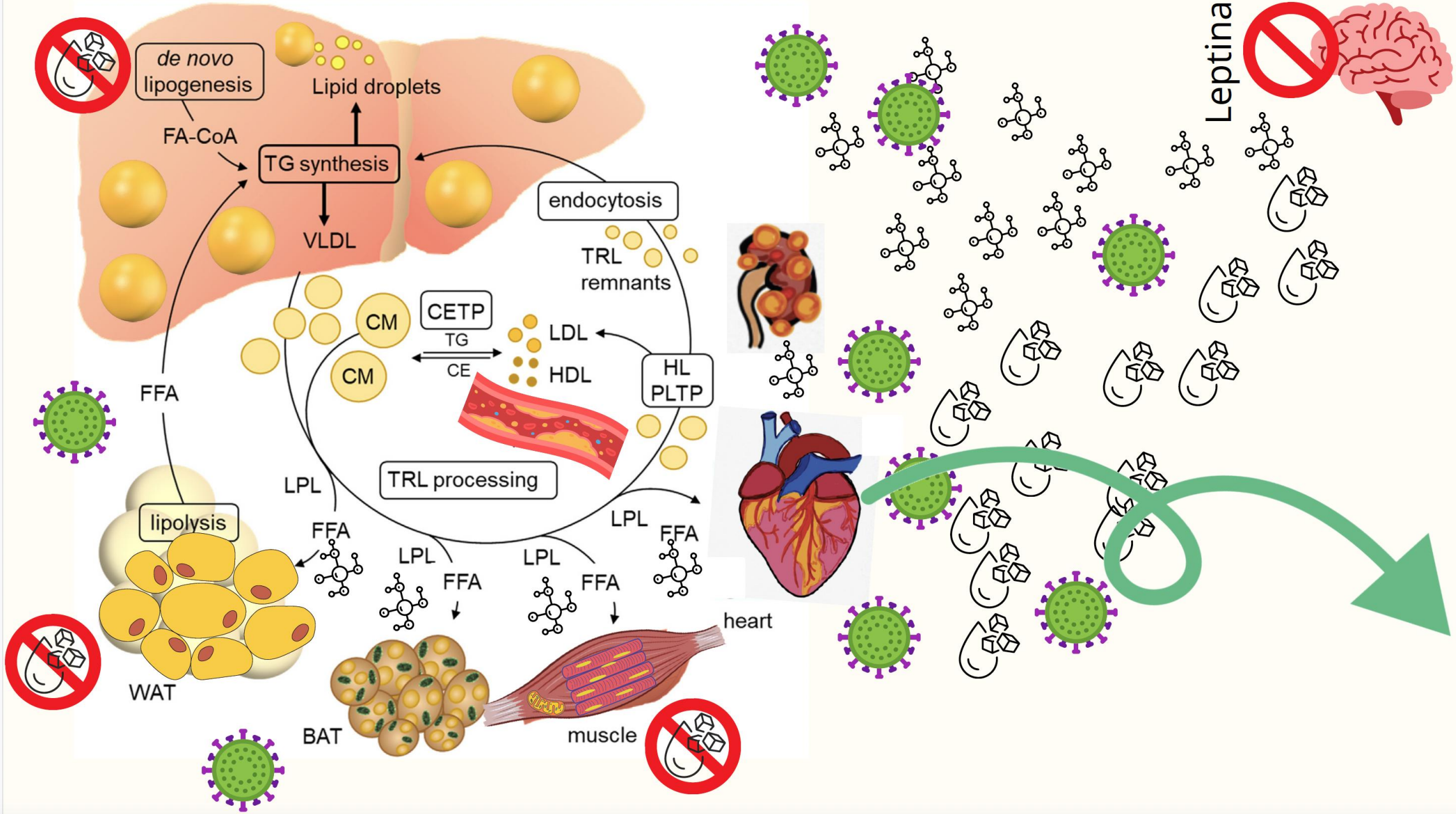
oxidative stress

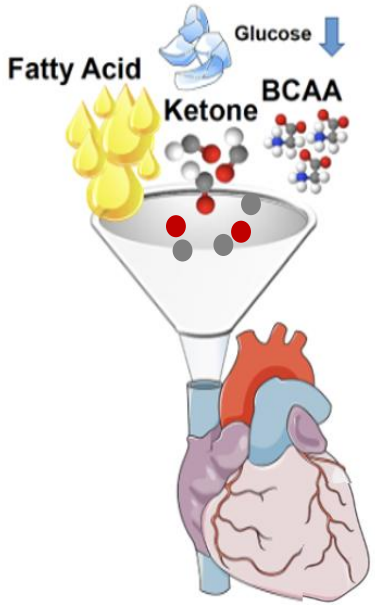
chronic metainflammation

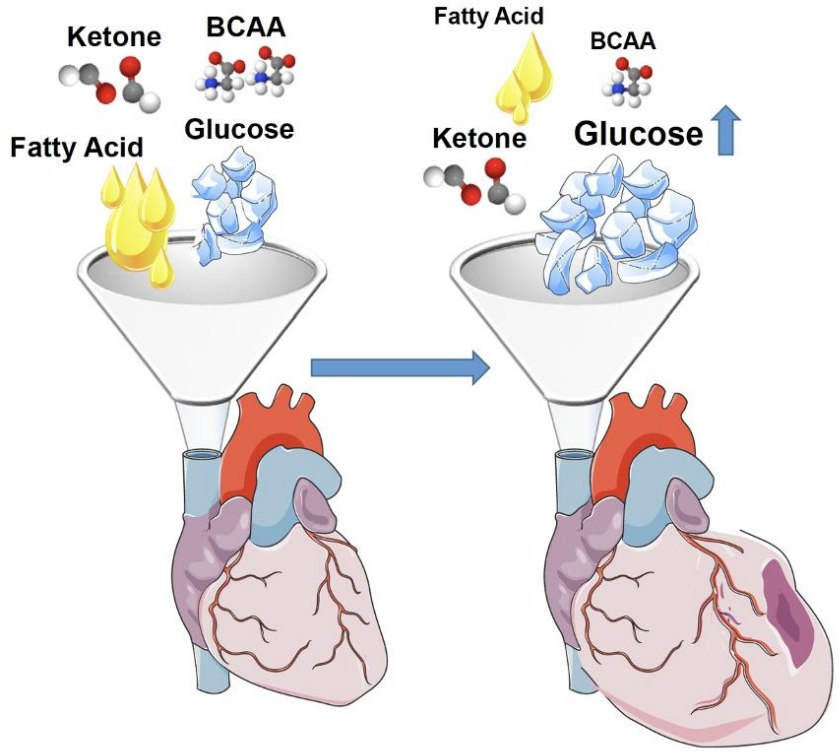
chronic metainflammation



Tsatsoulis A et al. *Metabolism*. 2013;62(5):622-633


de novo lipogenesis
Lipid droplets
FA-CoA
TG synthesis
VLDL
endocytosis
TRL remnants
CM
CM
CETP
TG
CE
LDL
HDL
HL PLTP
FFA
TRL processing
LPL
lipolysis
FFA
LPL
FFA
LPL
FFA
LPL
FFA
WAT
BAT
muscle
heart
Leptina





Australopithecus afarensis

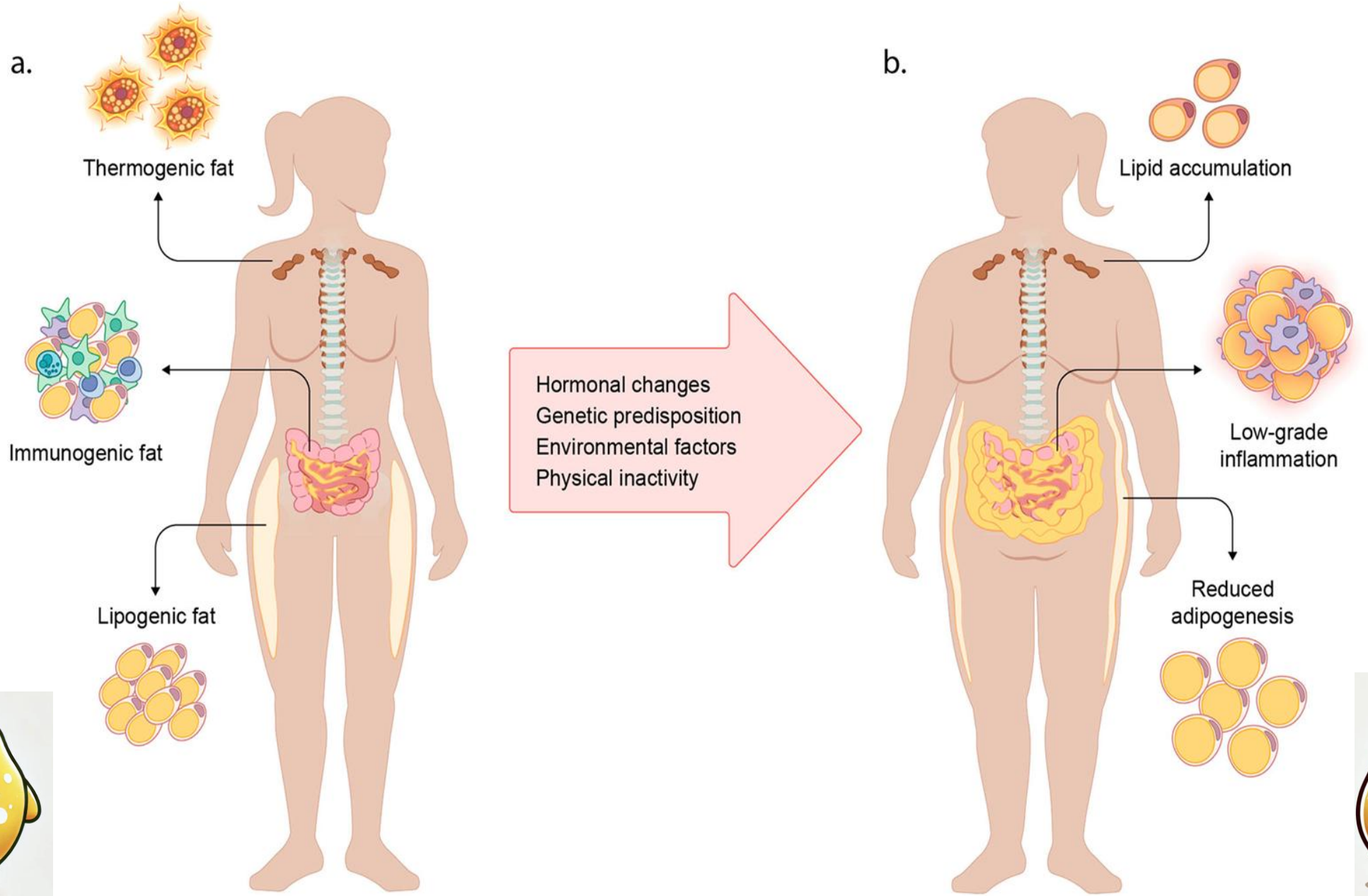
Homo sapiens

99.9%

0.1%

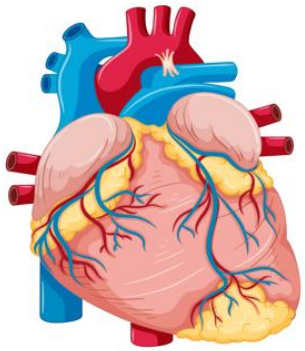
Adaptado de

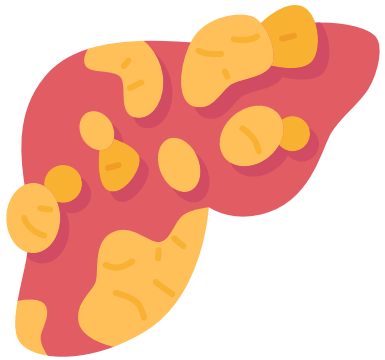
Michael Lehrke et al. *JACC* 2019; 73:1945-1947.

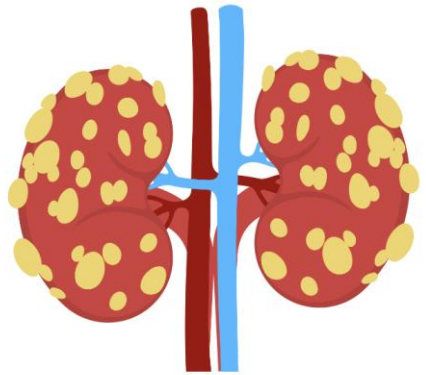


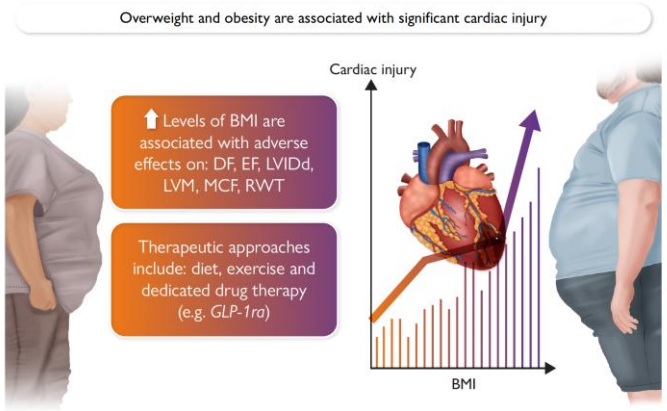
Andreas Kraag Ziegler & Camilla Scheele. npj Metabolic Health and Disease | (2024)2 :34

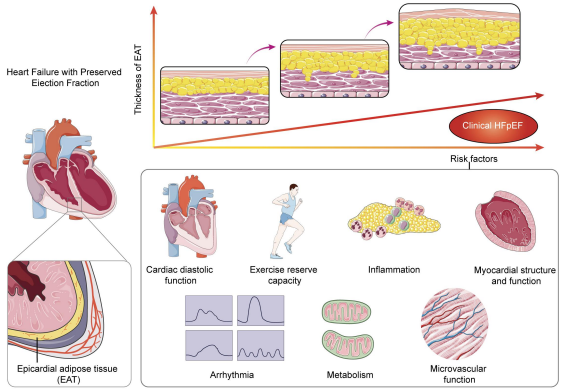
Grasa visceral, epicárdica. Estestosis sistémica

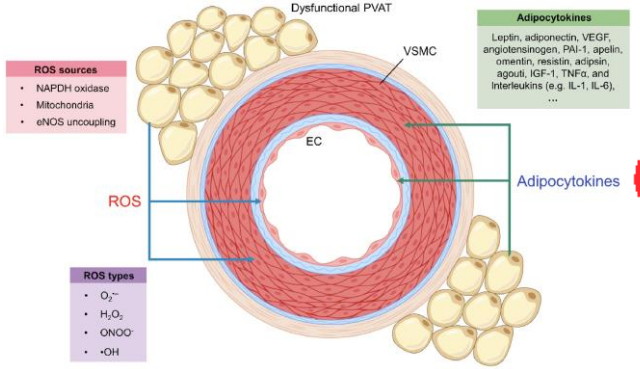




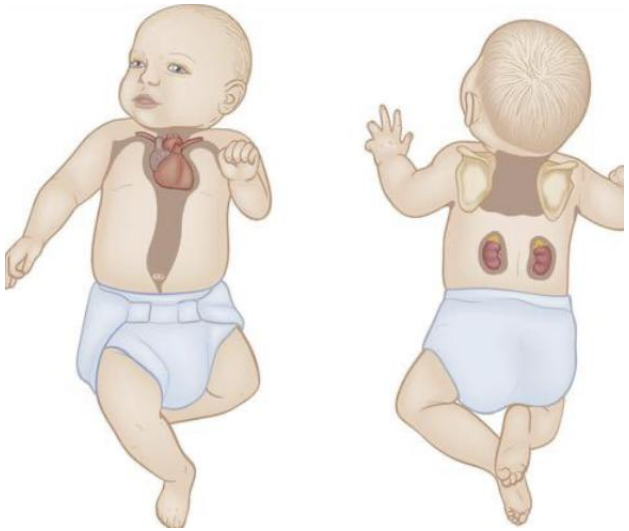








Angry adipocyte



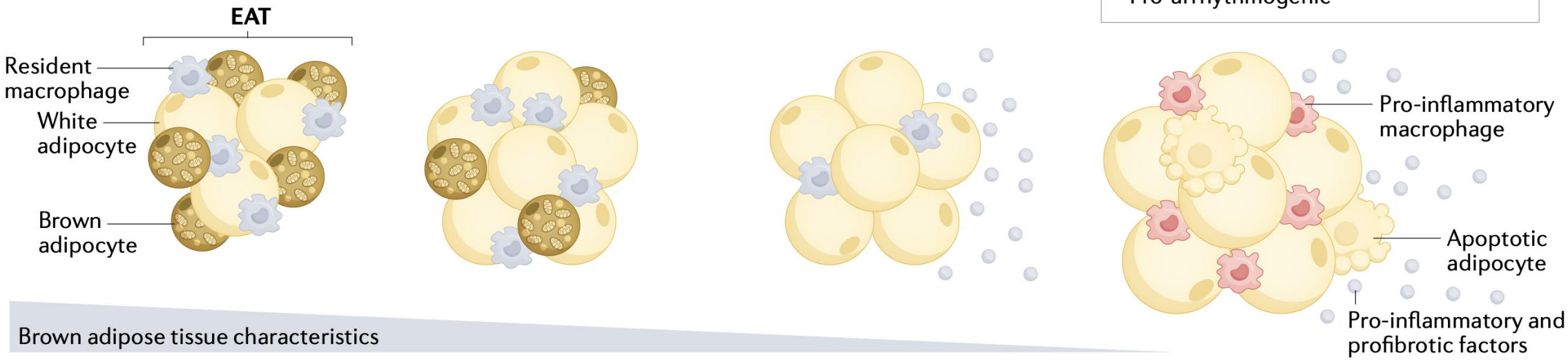
Has been proposed that EAT growing could be an adaptive process in states of atrial myocardium disease such as AF.
However, this adaptive mechanism could also turn deleterious, given
the harmful effects associated
to EAT hypertrophy

Neonate and early years of life
- Cardioprotective
- Thermogenic

Childhood to adulthood
- Cardioprotective
- Fuel for the myocardium

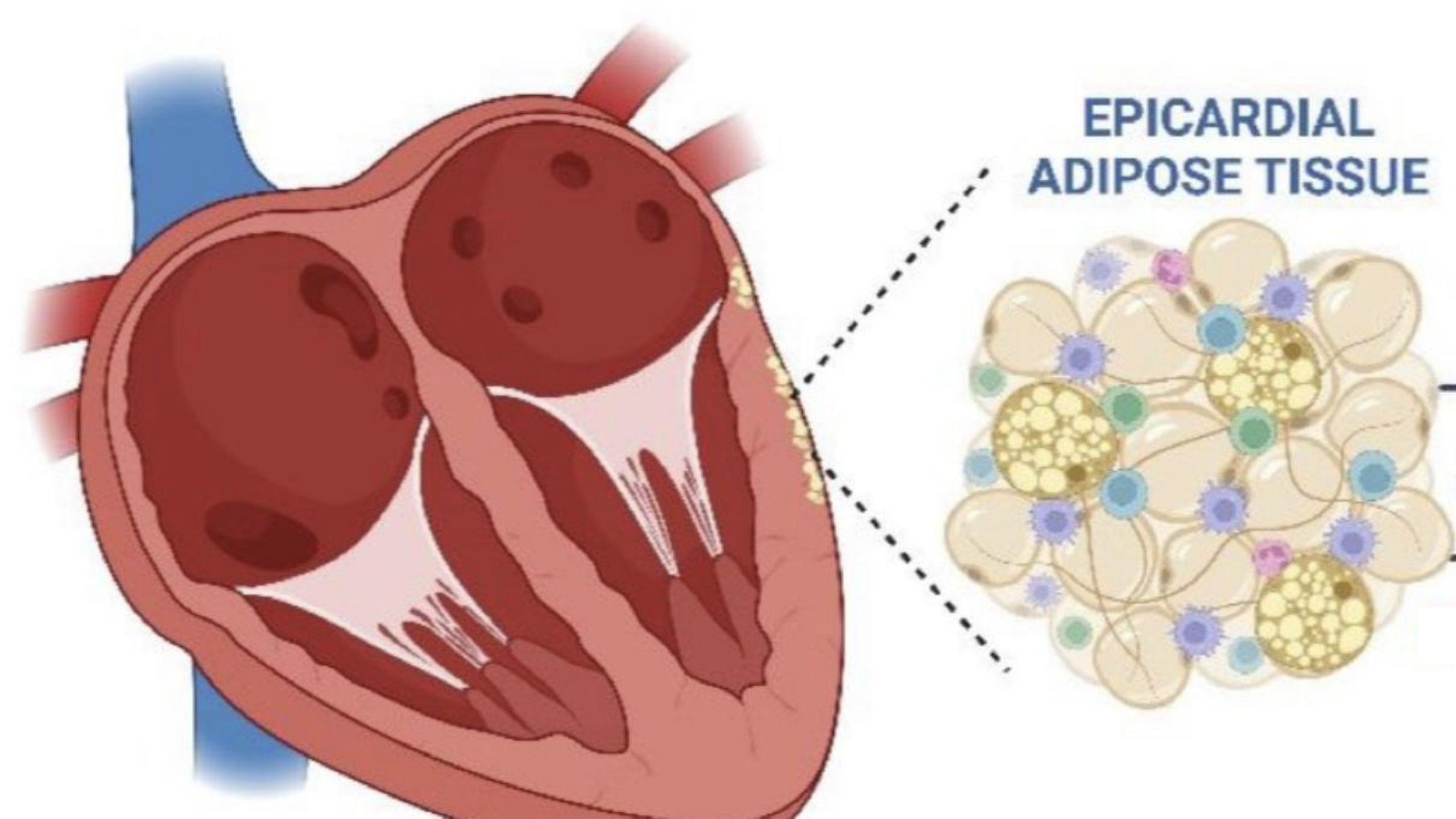
Old age
↓Thermogenic function
↑ Profibrotic and pro-apoptotic factors

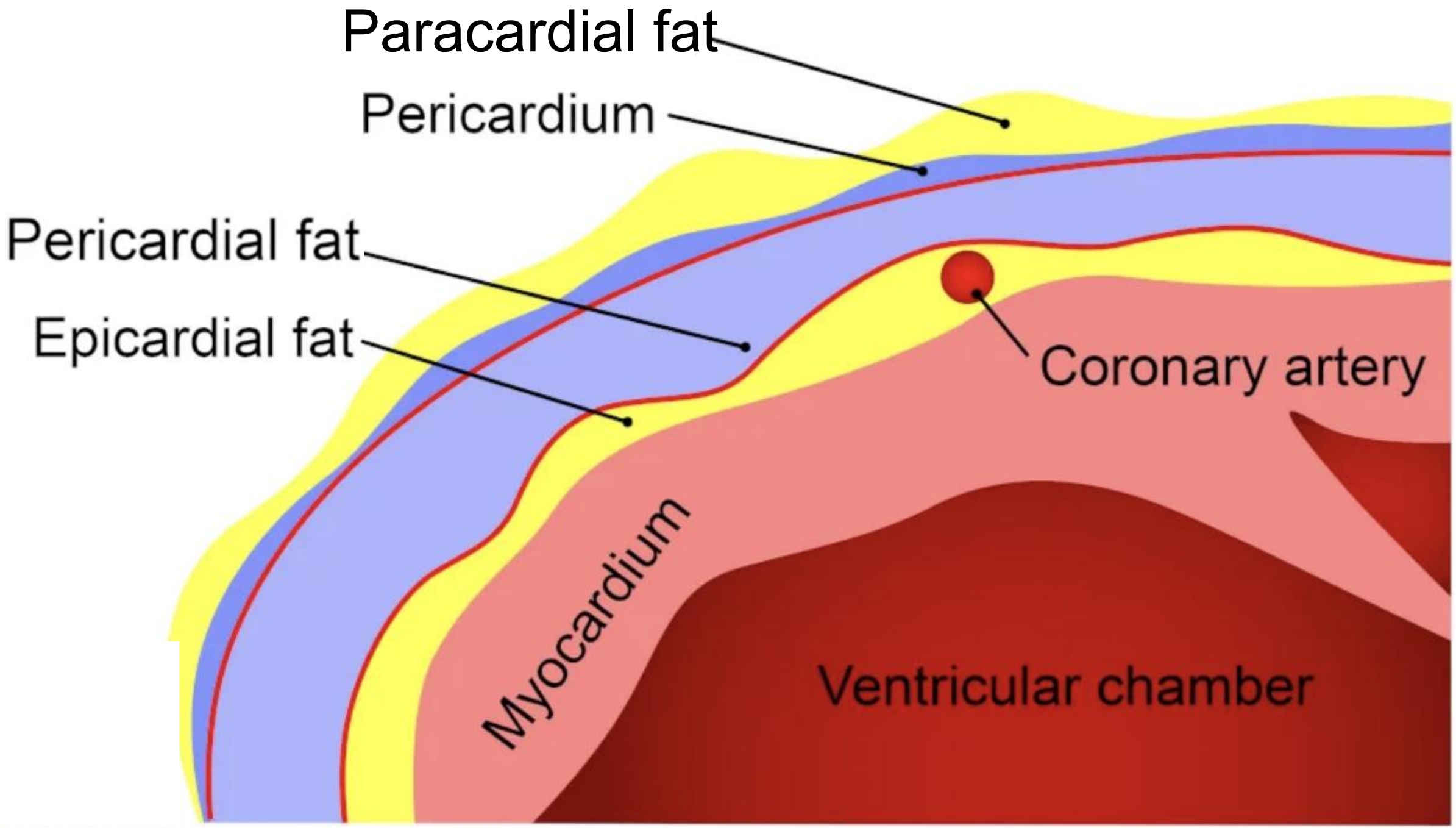
Pathological conditions
Atrial fibrillation, coronary artery disease, diabetes mellitus, heart failure, obesity
- Pro-atherogenic
- Pro-arrhythmogenic



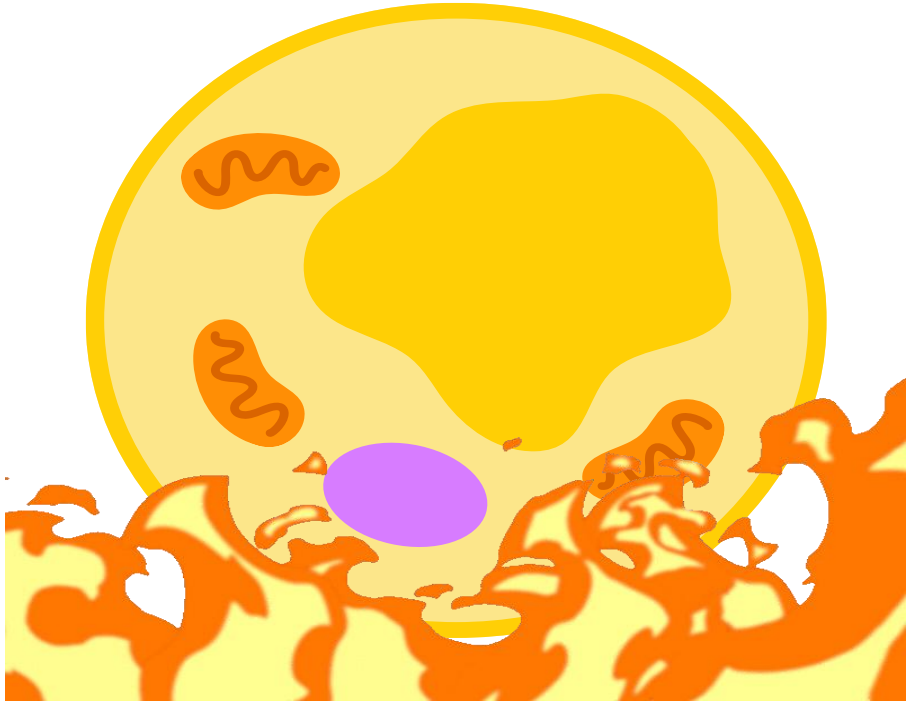
Brown adipose tissue characteristics

Christensen RH et al. Therapeutic Advances in Endocrinology and Metabolism, 2020;1

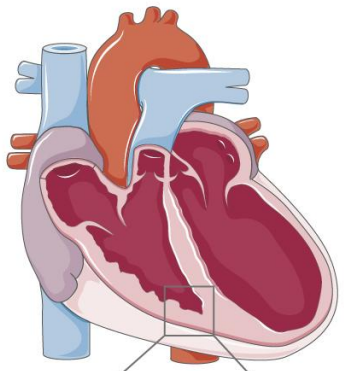

EPICARDIAL
ADIPOSE TISSUE

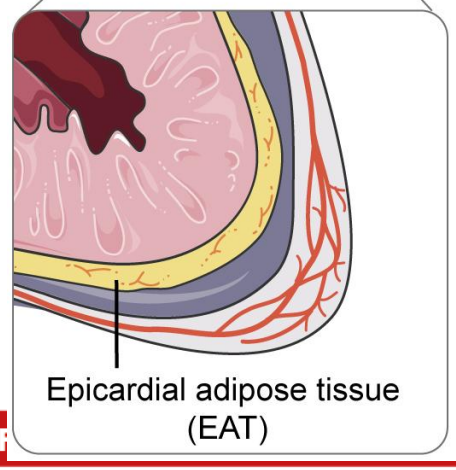

Paracardial fat
Pericardium
Pericardial fat
Epicardial fat
Coronary artery
Myocardium
Ventricular chamber

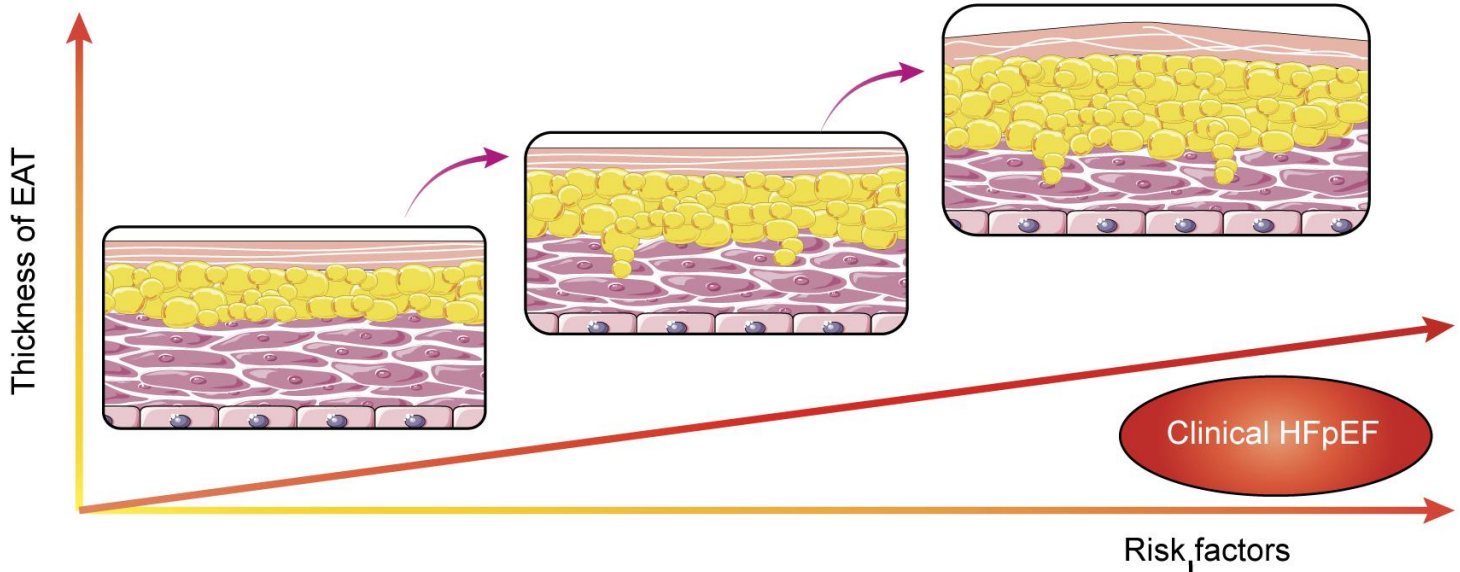
Obesity and HFpEF

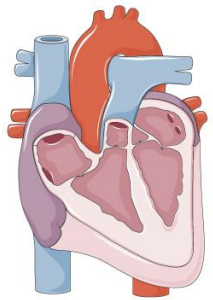


Heart Failure with Preserved Eiection Fraction

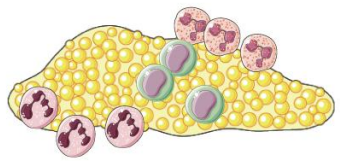


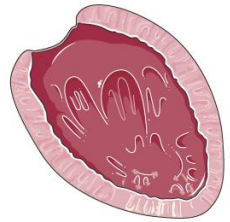


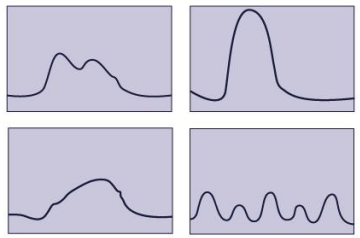


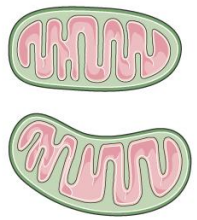

Cardiac diastolic function

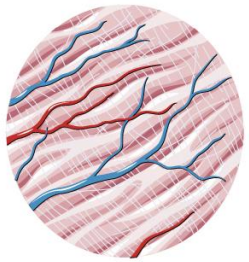

Exercise reserve capacity


Inflammation


Myocardial structure and function


Arrhythmia


Metabolism


Microvascular function

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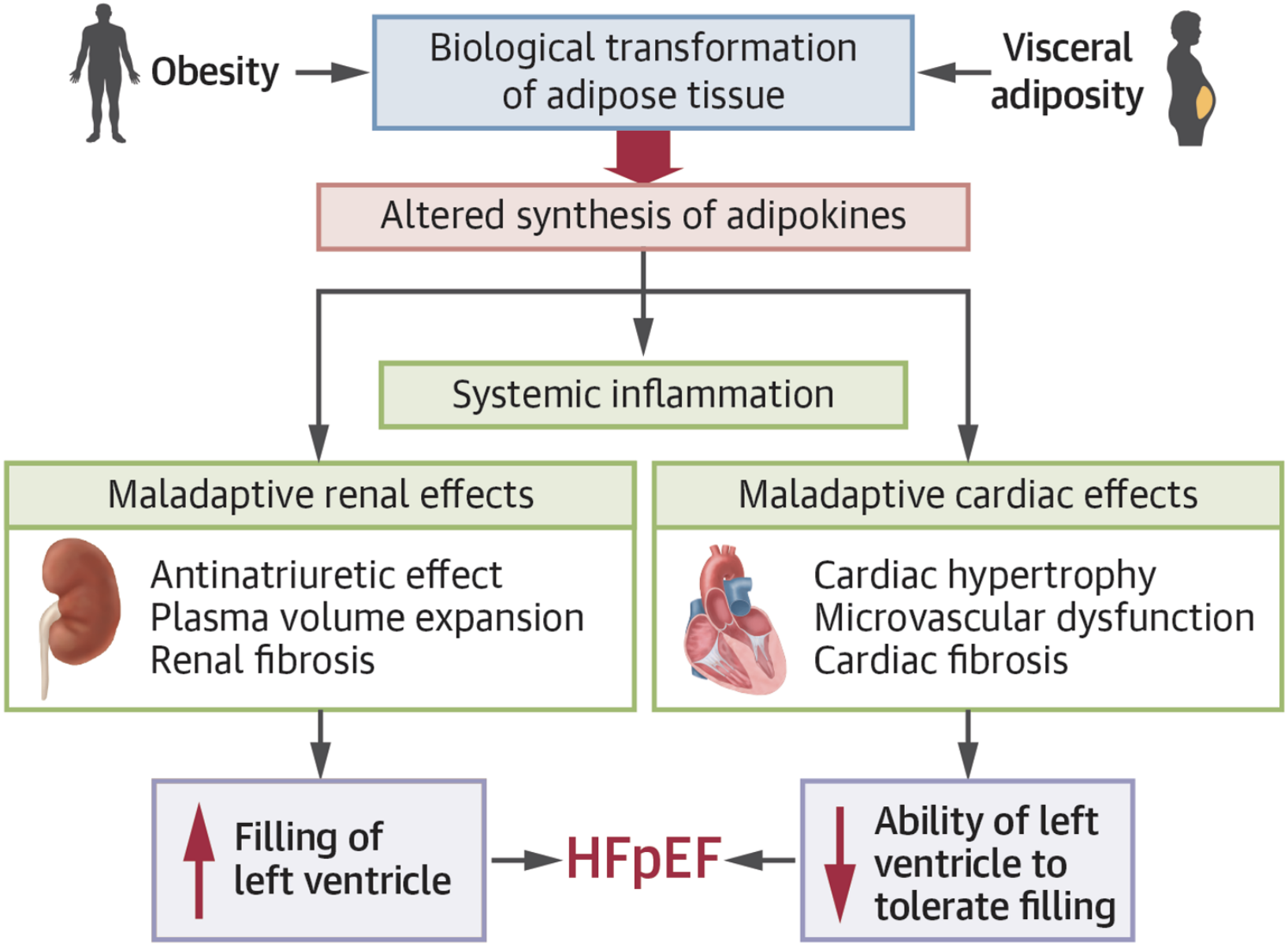
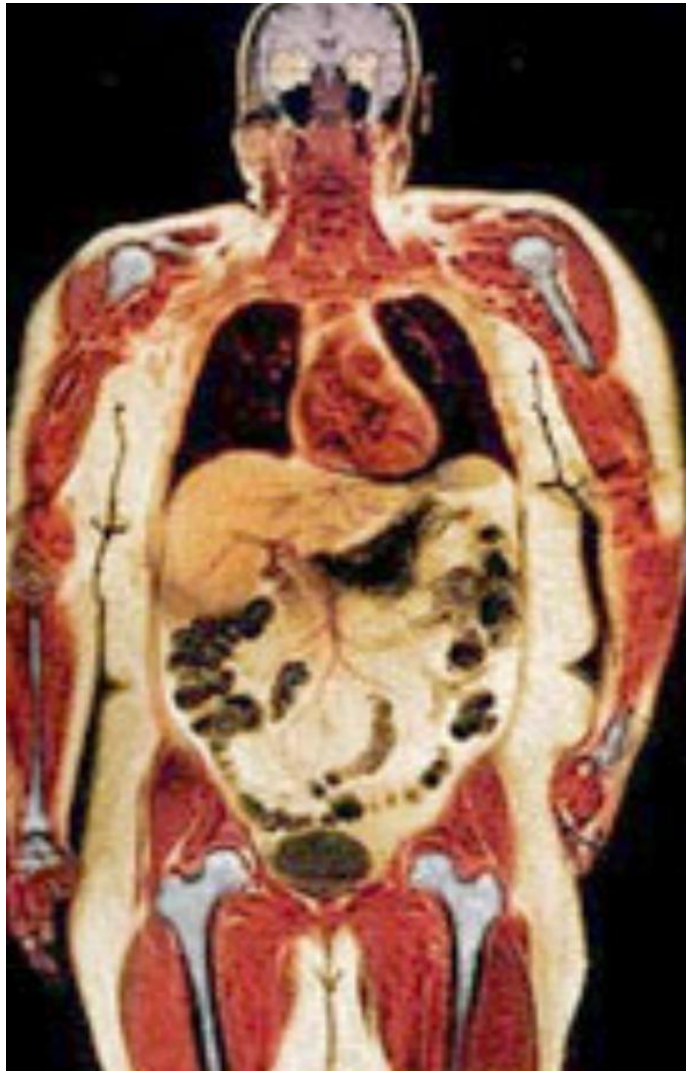
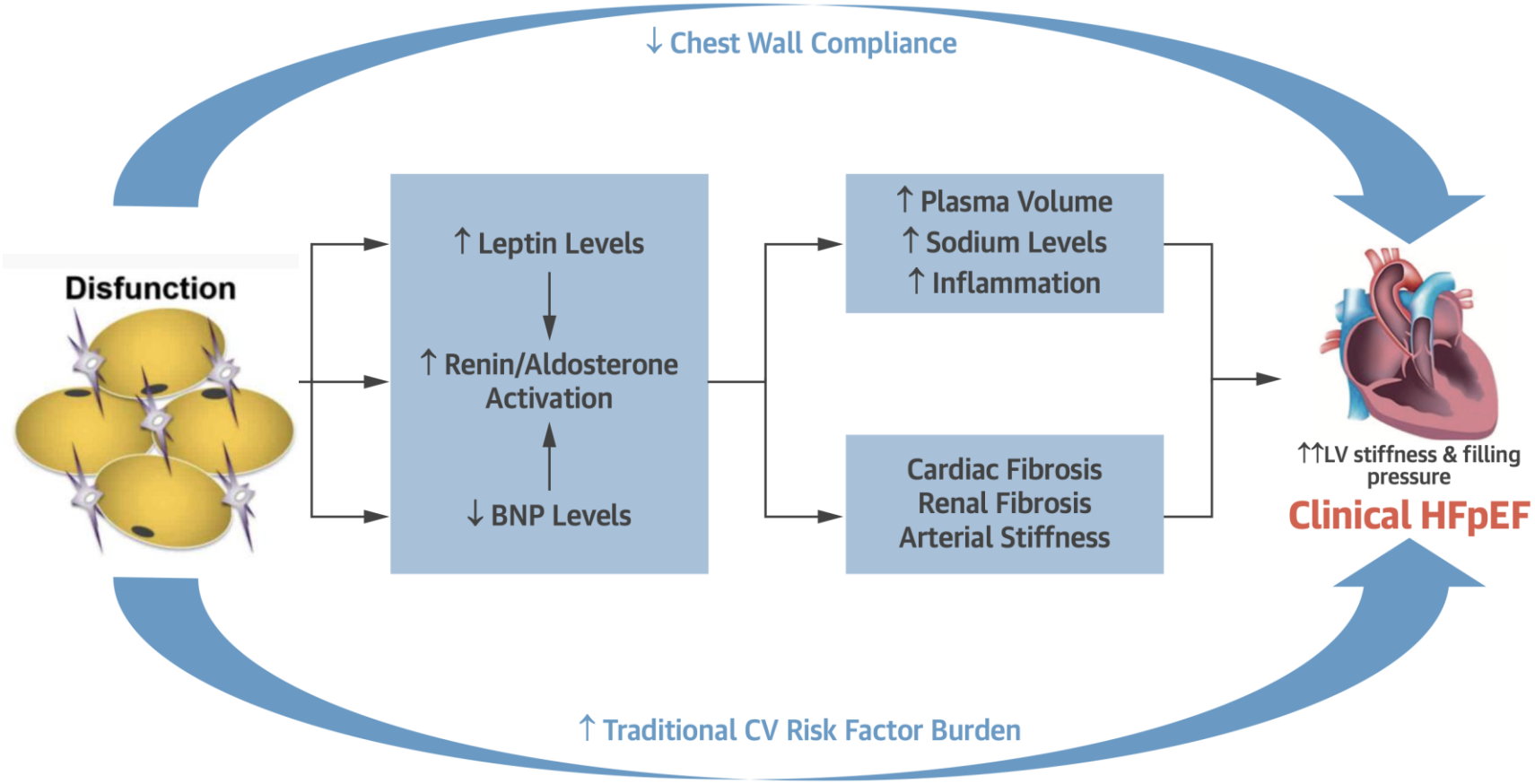
Li Q, Muhib et al. Rev Cardiovasc Med. 2024 Sep 3;25(9):311



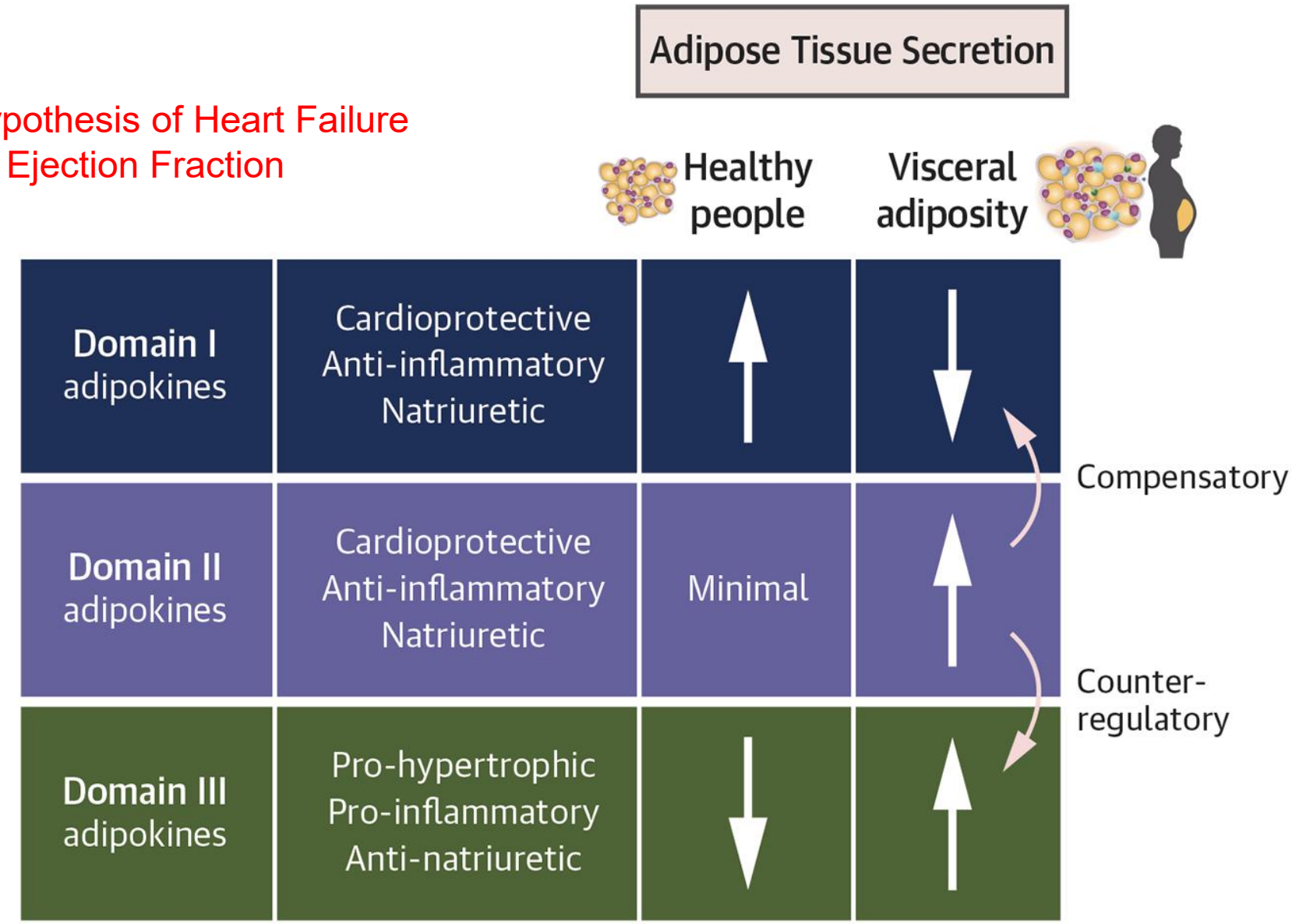
Packer M. J Am Coll Cardiol. 2025;85(2):179-193.



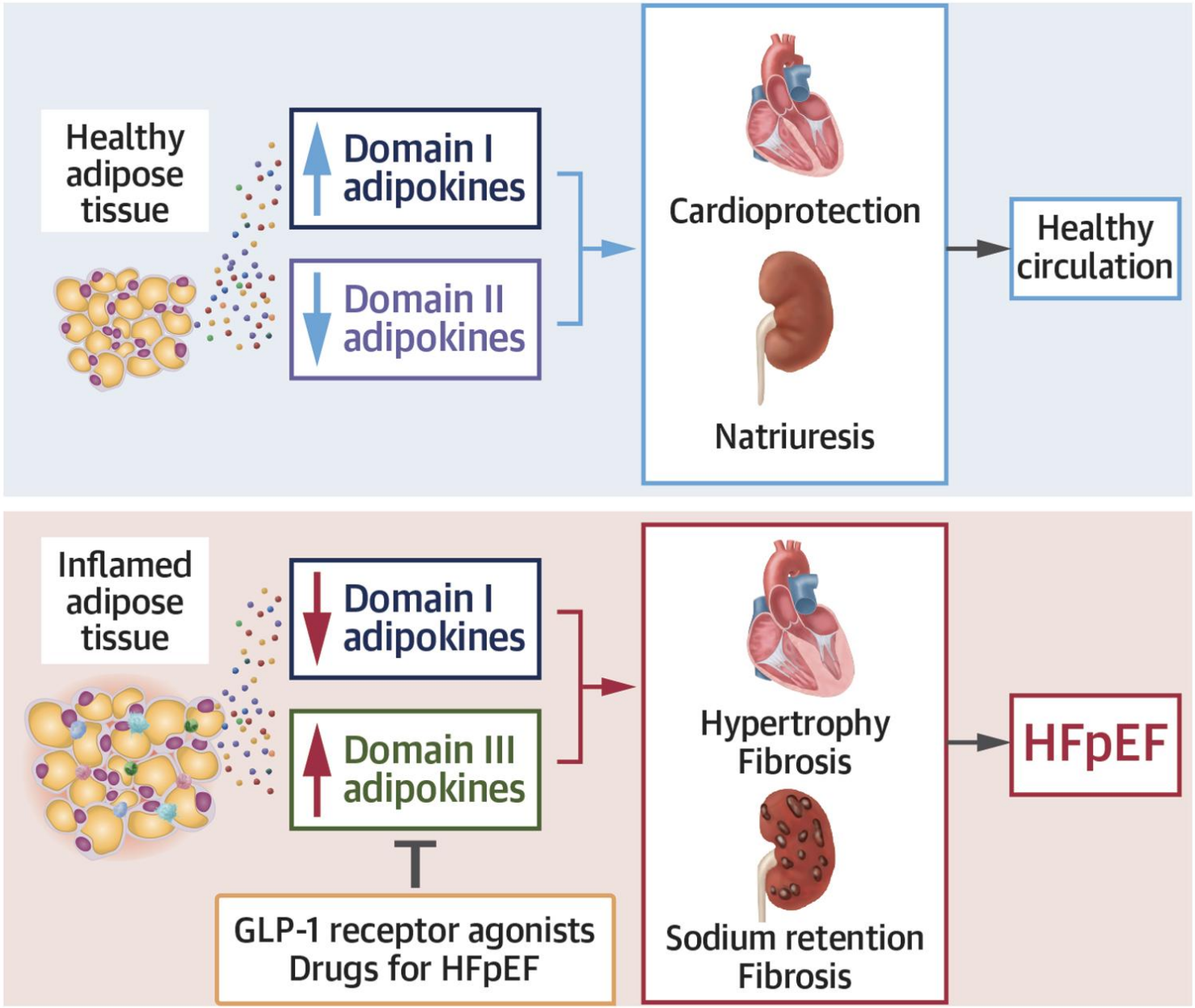


Pandey, A. et al. J Am Coll Cardiol HF. 2018;6(12):975-82.
Modificada

The Adipokine Hypothesis of Heart Failure With a Preserved Ejection Fraction

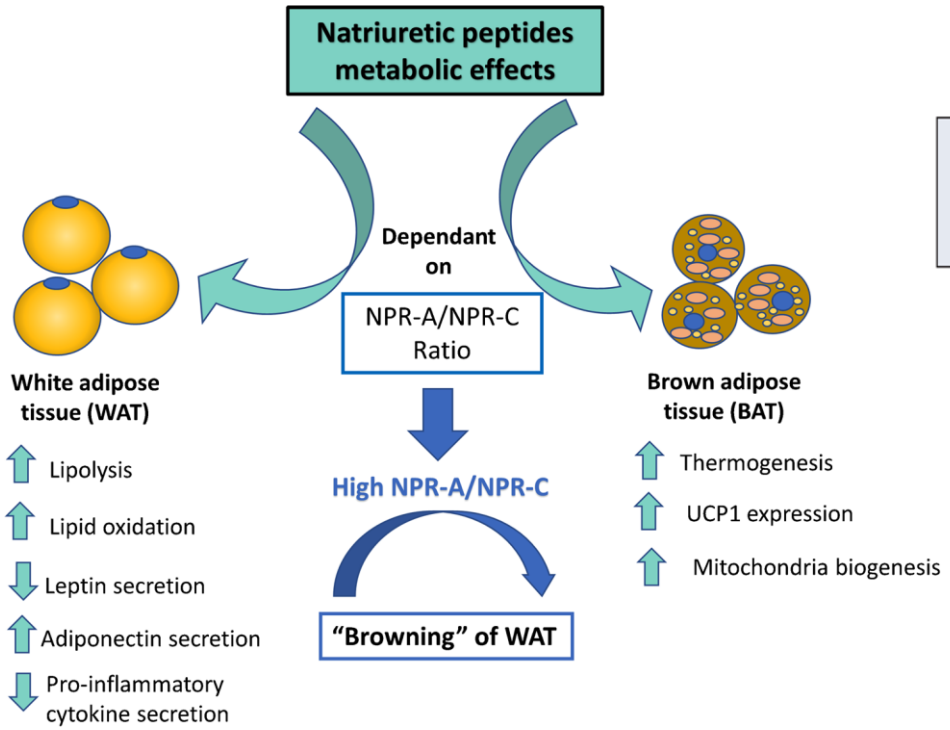


Packer M. J Am Coll Cardiol. 2025;85(2):179-193.

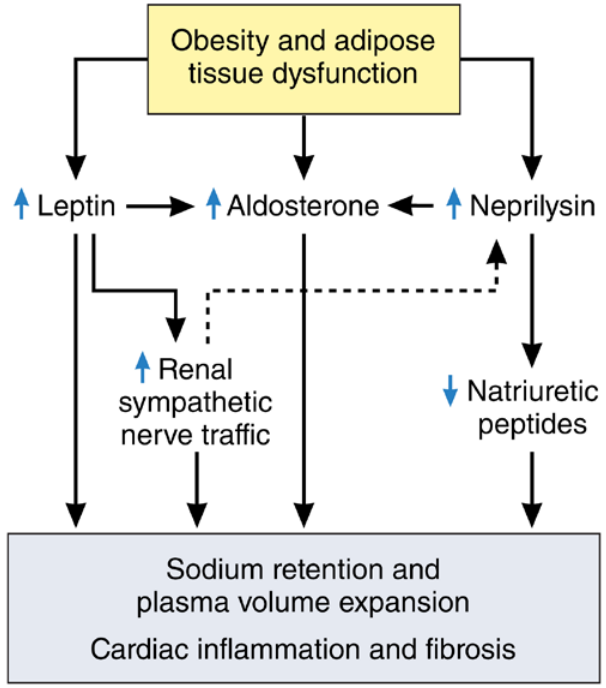


Packer M. J Am Coll Cardiol. 2025;85(2):179-193.

Role of natriuretic peptides in the cardiovascular-adipose communication: a tale of two organs

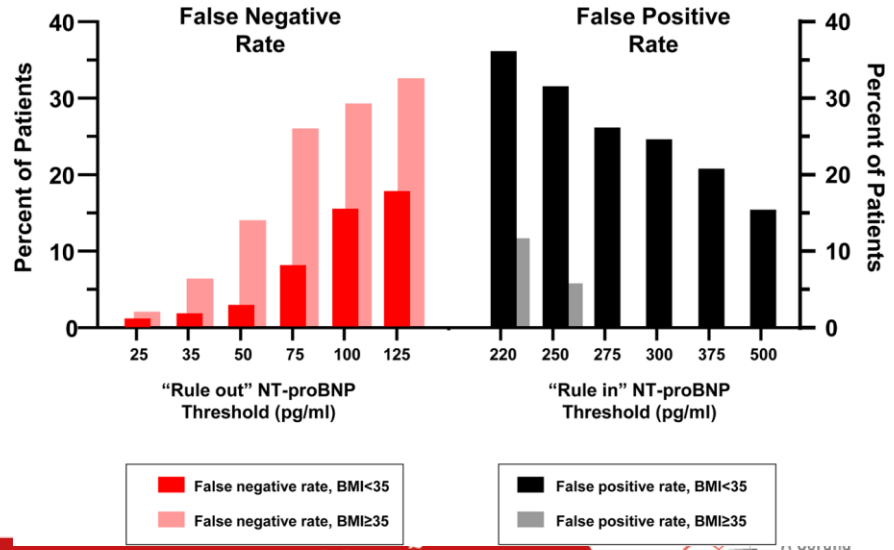


Rukavina Mikusic NL et al, . Pflugers Arch. 2022 Jan;474(1):5-19.



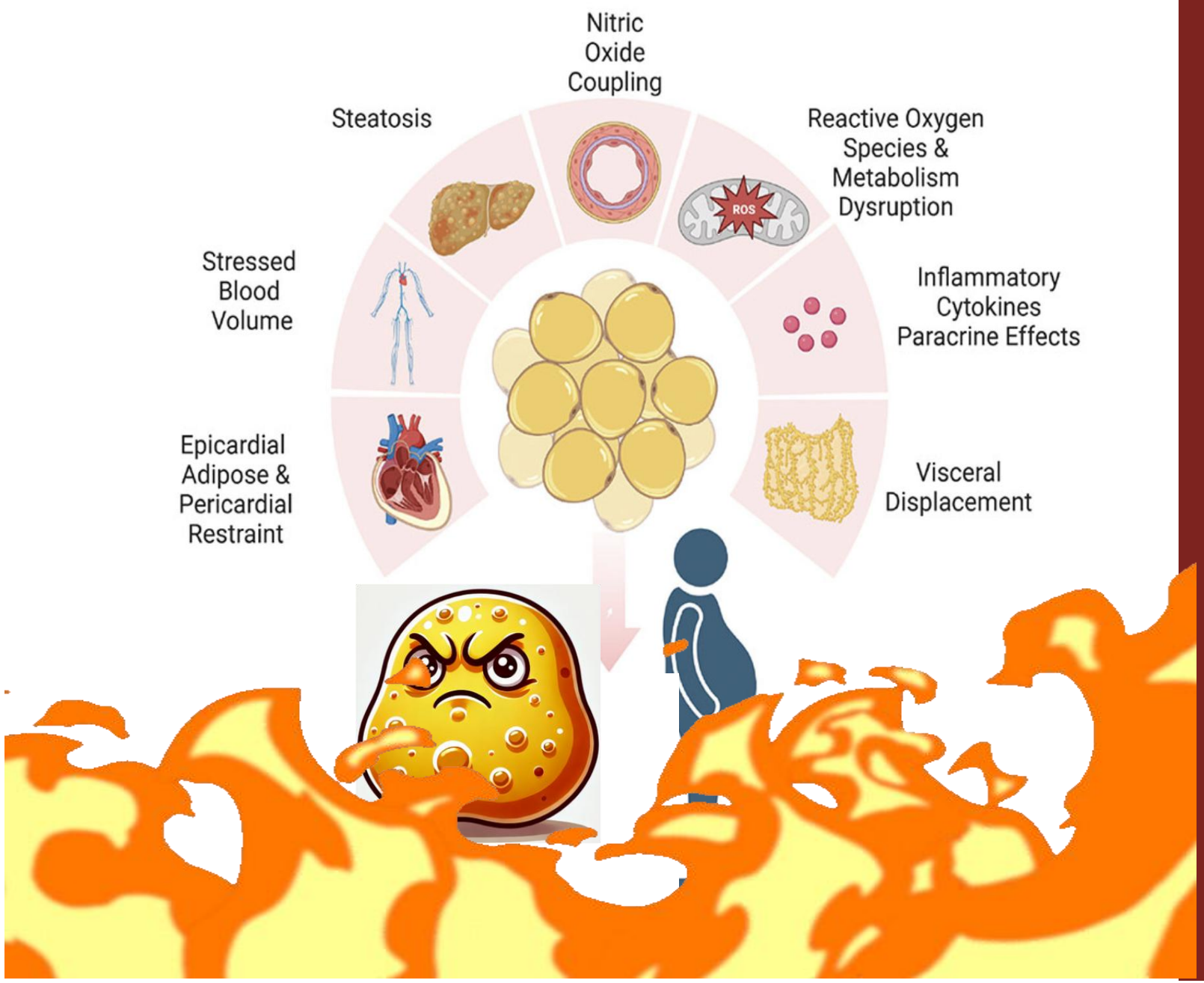
Packer M. Circulation. 2018;137:1614–1631

False-positive and false-negative rates of various rule-out and rule-in NT-proBNP diagnostic thresholds stratified by BMI

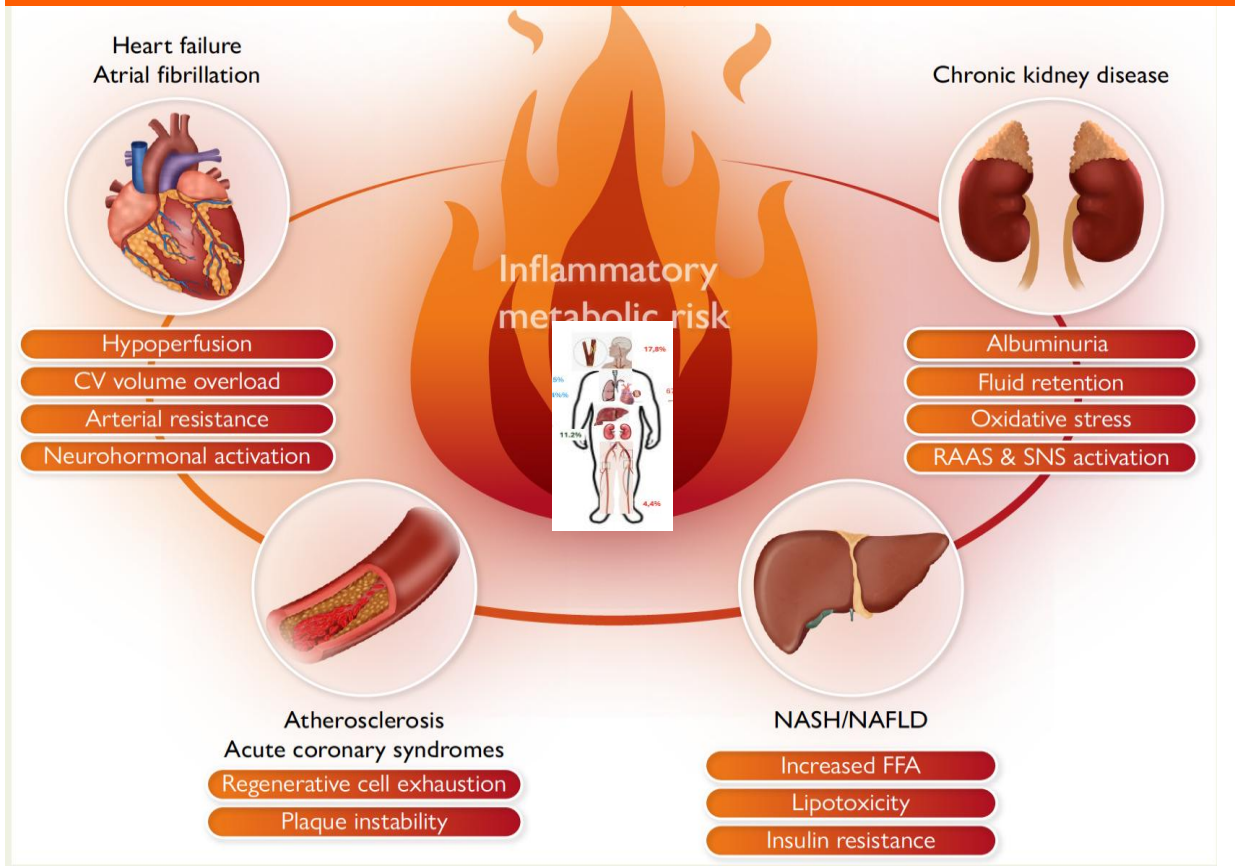


Reddy YNV et al. Circulation. 2025 Apr 8;151(14):976-989

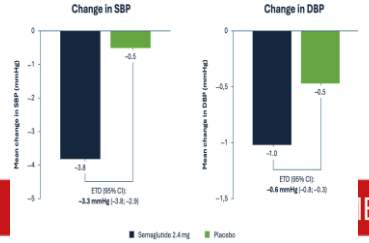
THE BODY ON FIRE

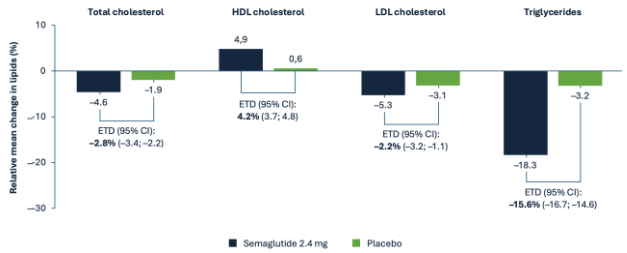


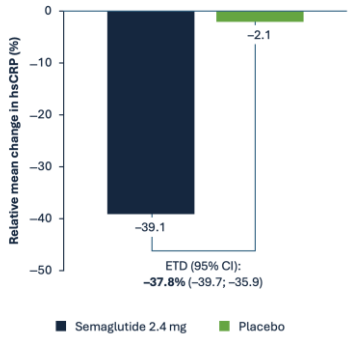
Paciente criterios SELECT

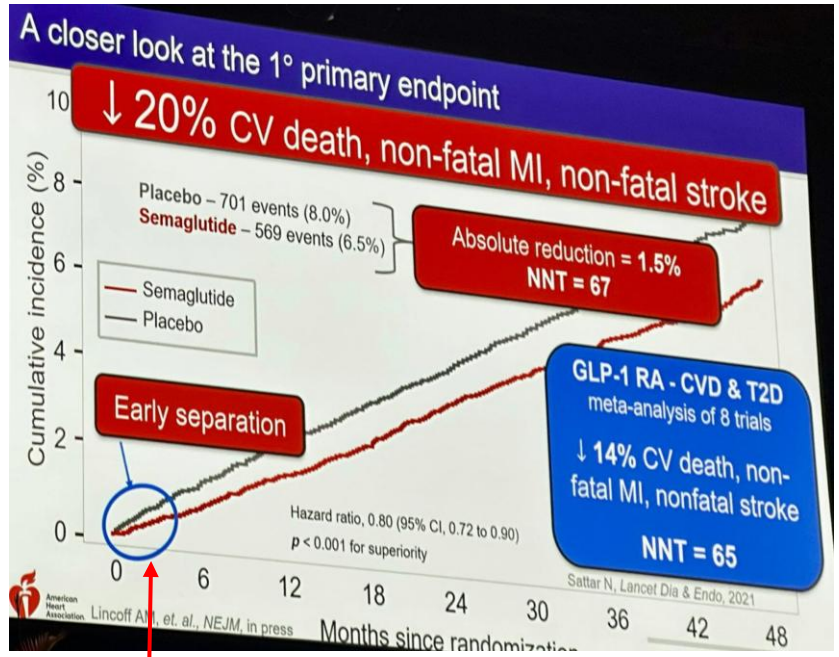


Modificado de Cosentino F et al. European Heart Journal (2023) 44, 4141–4156

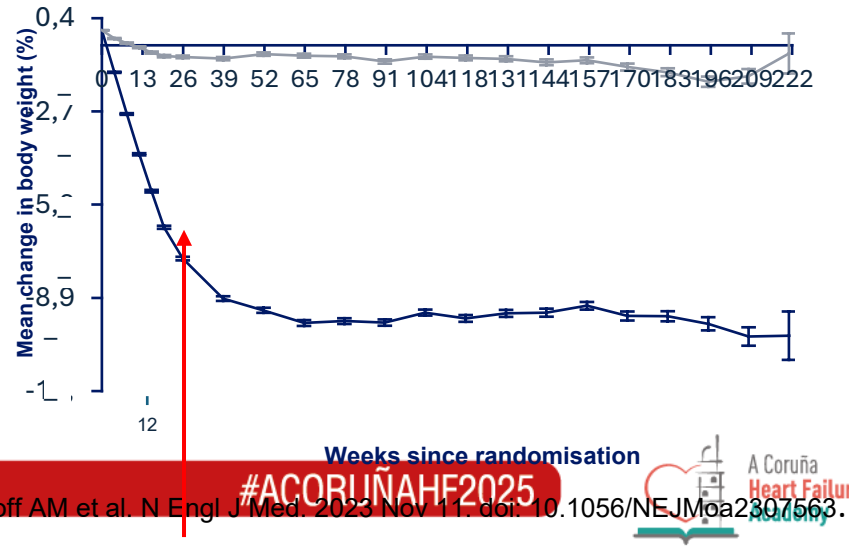








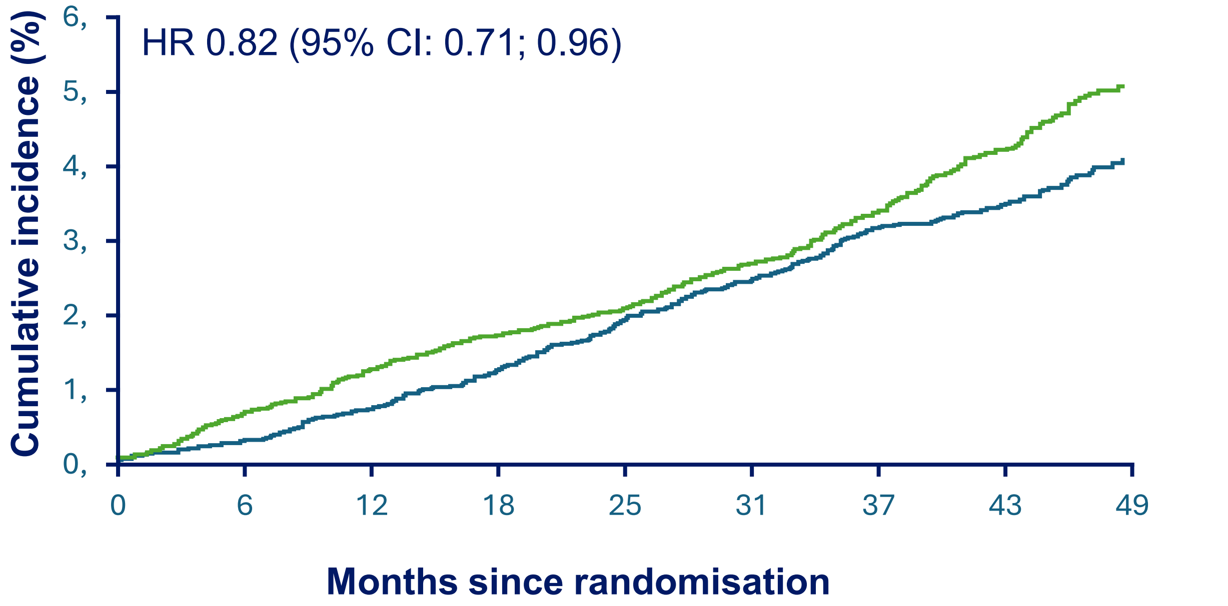
Mean baseline body weight, kg:
Semaglutide 2.4 mg: 96.5 Placebo: 96.8



Lincoff AM et al. N Engl J Med. 2023 Nov 11. doi: 10.1056/NEJMoa2307563.

SELECT trial

Cumulative incidence of composite heart failure events
SELECT: Second confirmatory secondary endpoint

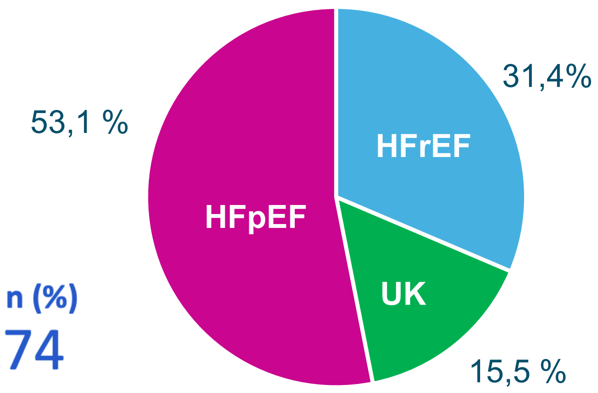


No. at risk									
Semaglutide	8,803	8,740	8,654	8,557	8,425	7,409	5,944	4,277	1,816
Placebo	8,801	8,711	8,601	8,485	8,381	7,341	5,885	4,198	1,766

— Semaglutide 2.4 mg — Placebo

naglutide 2.4 mg reduced the risk of composite HF events by 18%
compared with placebo

Although the 95% CI was <1, superiority testing was not performed per the hierarchical testing procedure*



N=17,605

CHF, n (%)
4,274
(24.3)

Subclass, n (%)	
HFpEF:	2,268 (12.9)
HFrEF:	1,341 (7.6)
Unknown:	662 (3.8)

NYHA class, n (%)	67,8%% II-III
NYHA class I:	1,368 (7.8)
NYHA class II:	2,534 (14.4)
NYHA class III:	362 (2.1)
Unknown:	10 (<0.1)

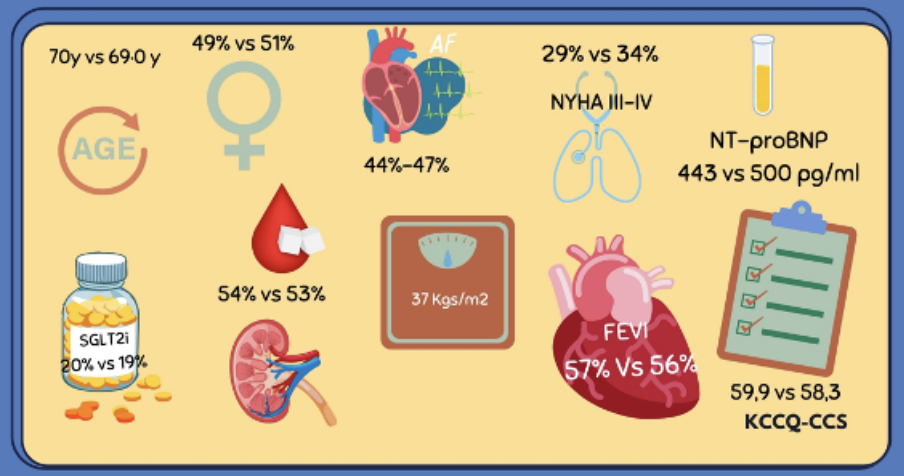
The HR was estimated using a Cox proportional hazards regression model. The proportion of participants with composite heart failure events was 3.4% with semaglutide 2.4 mg and 4.1% with placebo. ... urgent HF visit or CV ... so superiority testing for the remaining confirmatory secondary endpoints was not performed.
Lincoff AM et al. N Engl J Med 2023;DOI:10.1056/NEJMoa2307563.

Semaglutide versus placebo in people with obesity-related heart failure with preserved ejection fraction: a pooled analysis of the STEP-HFpEF and STEP-HFpEF DM randomised trials

Butler J, Lancet. 2024 Apr 27;403(10437):1635–1648..

Basal Characteristics

Semaglutide vs placebo

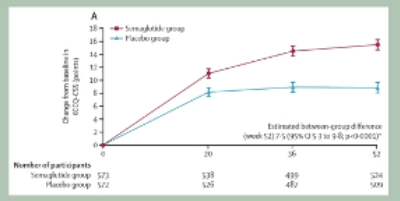


Results from baseline to week 52

1145 patients

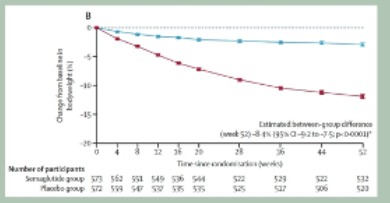
Dual primary endpoints

Change in KCCQ-CSS



15 vs 7,5 points
[95% CI 5·3 to 9·8]; p<0·0001)

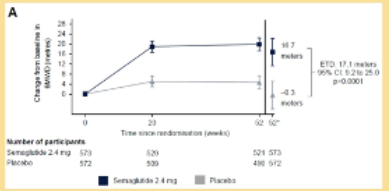
Bodyweight



(−8·4% [−9·2 to −7·5]; p<0·0001)

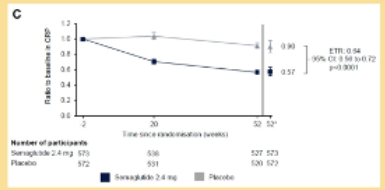
Confirmatory secondary endpoints

mean changes in the 6MWD



17·1 (9·2 to 25·0)
<0·0001

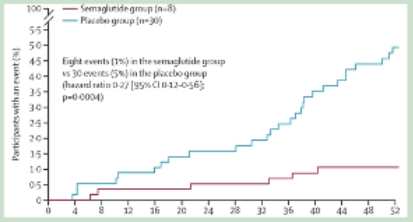
mean changes in the CRP



0·64 (0·56 to 0·72)†
<0·0001

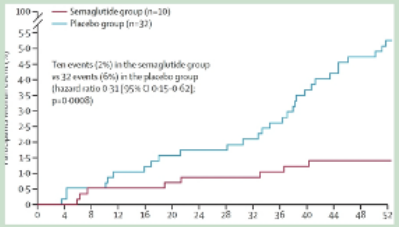
Exploratory endpoints

Time to first heart failure event



8 (1%) semaglutide vs 30 (5%) placebo
HR=0·27 [95% CI 0·12–0·56] p= 0.0004

Time to first HF event or CV death



10 (2%) semaglutide vs 32 (6%) placebo
HR= 0.31 [95% CI 0.15-0.62]; p=0.0008

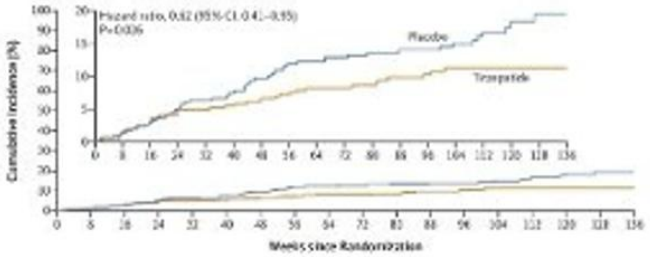
A Coruña Heart Failure Academy

Tirzepatide for Heart Failure with Preserved Ejection Fraction and Obesity SUMMIT Trial Study

Primary Endpoints

DEATH FROM CARDIOVASCULAR CAUSES + WORSENING HEART-FAILURE EVENT

36 patients (9.9%) itirzepatide
56 patients (15.3%) iplacebo
(5.5 and 8.8 events per 100 patient-years of follow-up,)
HR= 0.62; 95% [CI], 0.41 to0.95;
P = 0.026)



Worsening heart-failure events occurred in
29 patients (8.0%) in the tirzepatide and in 52 patients (14.2%) in the placebo
HR= 0.54; (95% CI, 0.34 to 0.85)

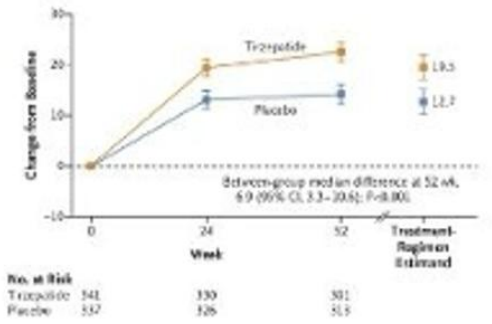
When events managed **only with intensification of oral diuretic therapy were removed** from the primary end-point analysis,
HR= 0.57 (95% CI, 0.34 to 0.95)

Worsening HF event resulting in hospitalization
HR= 0.44 (95% CI, 0.22 to 0.87)

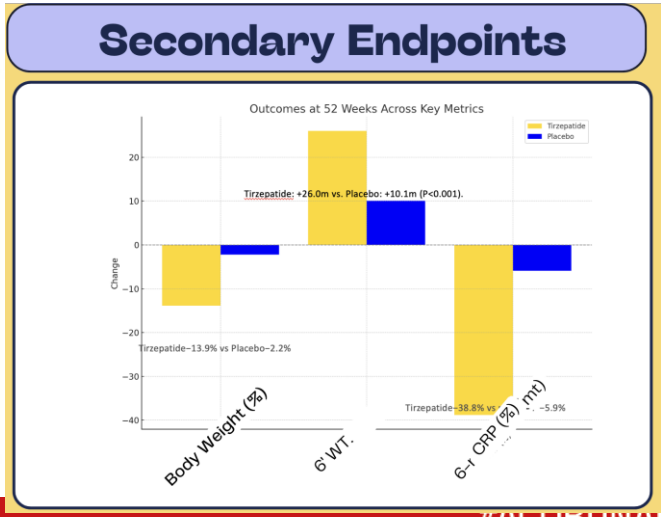
Death from cardiovascular causes
occurred in 8 patients (2.2%) tirzepatide and 5 patients (1.4%) placebo
(HR=1.58; 95% CI, 0.52 to 4.83).

CHANGE IN KANSAS CITY CARDIOMYOPATHY QUESTIONNAIRE CLINICAL SUMMARY SCORE

The mean **increase in the KCCQ-CSS** was 19.5 points in the tirzepatide and 12.7 points in the placebo (between-group. median difference, 6.9 points **95% CI, 3.3 to 10.6;**
P<0.001)



Secondary Endpoints



Safety

Packer M, et al . N Engl J Med. 2024 Nov 16. doi: 10.1056/NEJMoa2410027.

Effect of Semaglutide on Cardiac Structure and Function in Obesity-Related Heart Failure: The STEP-HFpEF Program Echocardiography Substudy

Design of the STEP-HFpEF Program Echocardiography Substudy

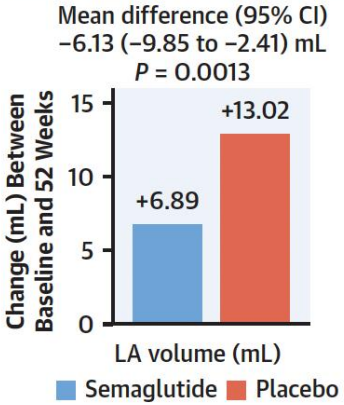
491 participants with symptomatic HF, LVEF ≥45%, and BMI ≥30 kg/m²

Randomized to once-weekly semaglutide (2.4 mg) or matching placebo

Prespecified primary endpoint: Δ in LA volume

Resting echocardiography performed at randomization and 52 weeks

Treatment Effects of Semaglutide on LA Volume and Other Parameters



Benefits of semaglutide on LA remodeling were consistent irrespective of age, sex, BMI, NT-proBNP, hsCRP, diabetes status, AF status, LVEF, and background pharmacotherapy

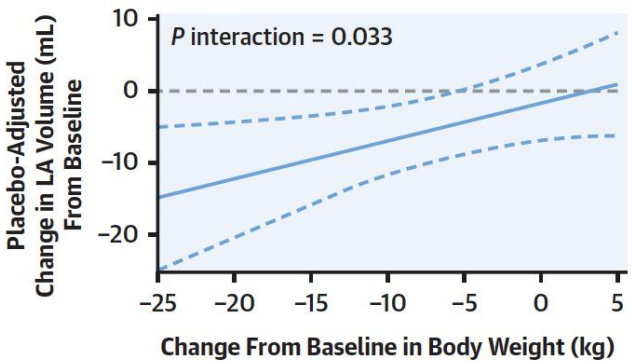
Semaglutide also improved E wave velocity, E/A ratio, E/e' average, and RV remodeling compared with placebo, but did not impact LV mass, LV mechanics, or LA strain

Cardiac Structure and Function in the STEP-HFpEF Program

	LV structure and mechanics		LA size	Left and right heart pressures	
Trial	LV mass, g	LV GLS, %	LA area (cm²)	E/e'	RVSP (mm Hg)
STEP-HFpEF Program	208 ± 69	−14 ± 4	22 ± 5	12 ± 5	26 ± 9
PARAGON-HF	169 ± 57	−16 ± 4	23 ± 6	13 ± 6	34 ± 10
TOPCAT	223 ± 71	−16 ± 4	20 ± 6	12 ± 6	38 ± 11
I-PRESERVE	164 ± 48	---	23 ± 6	10 ± 5	37 ± 13

Higher or worse value | Lower or better value

Benefits of Semaglutide on LA Volume Related to Magnitude of Weight Loss



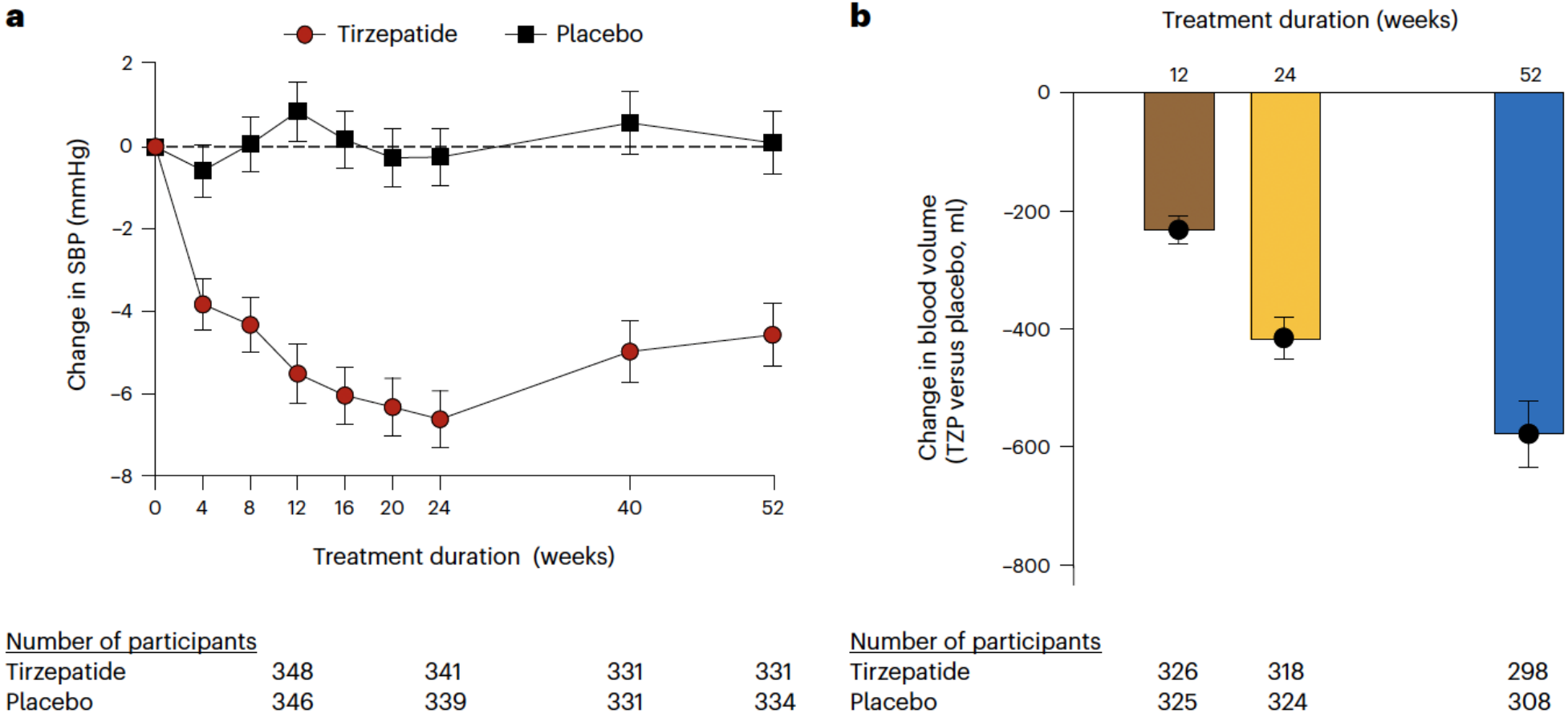
However, benefits of semaglutide on E wave velocity, E/e' average, and RV end-diastolic area were not associated with weight change between baseline and 52 weeks

In the STEP-HFpEF Program echocardiography substudy, semaglutide appeared to improve adverse cardiac remodeling compared with placebo, further suggesting that treatment with semaglutide may be disease modifying among patients with obesity-related HFpEF.

J. Am Coll Cardiol. 2024 Oct 22;84(17):1587-1602. PMID: 39217567.

*Effects of **tirzepatide** on **circulatory overload and end-organ damage** in heart failure with preserved ejection fraction and obesity: a secondary analysis of the SUMMIT trial*

Effects of tirzepatide on pressure overload and volume expansion.

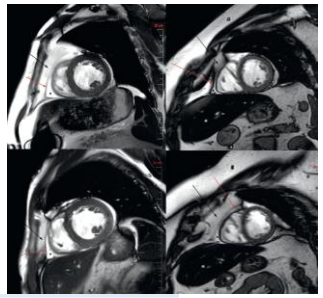


Number of participants				
Tirzepatide	348	341	331	331
Placebo	346	339	331	334

Number of participants			
Tirzepatide	326	318	298
Placebo	325	324	308

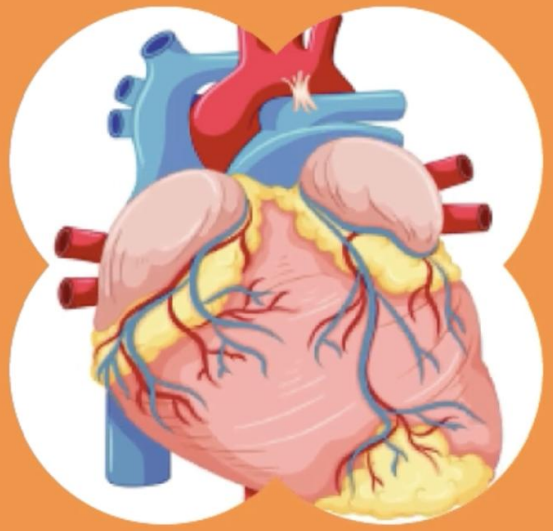
Borlaug BA et al. Nat Med. 2024 Nov 17. PMID: 39551891

Tirzepatide Reduces LV Mass and Paracardiac Adipose Tissue in Obesity-Related Heart Failure
SUMMIT CMR Substudy



	Tirzepatide		Placebo		Placebo-Corrected Difference Over Time	*P* Value
	Baseline	52 Weeks	Baseline	52 Weeks		
LV mass, g	120 ± 33	110 ± 33	122 ± 44	123 ± 47	−11 (−19 to −4)	0.004
LVEDV, mL	139 ± 37	132 ± 42	152 ± 43	151 ± 50	−7 (−16 to 2)	0.10
LVESV, mL	56 ± 25	55 ± 24	63 ± 32	63 ± 34	−2 (−8 to 4)	0.56
LV SV, mL	83 ± 25	77 ± 23	88 ± 21	89 ± 23	−8 (−14 to −2)	0.011
LV CO, L/min	5.5 ± 1.5	5.4 ± 1.4	5.7 ± 1.3	5.7 ± 1.6	0 (−1 to 0)	0.43
LVEF, %	60 ± 11	59 ± 8	60 ± 12	61 ± 11	−1 (−4 to 1)	0.27
LV GCS, %	−21 ± 8	−21 ± 5	−22 ± 5	−21 ± 5	1 (−1 to 3)	0.23
LV GLS, %	−19 ± 7	−18 ± 5	−19 ± 5	−19 ± 5	0 (−1 to 2)	0.66
LV concentricity index (mass/EDV)	0.89 ± 0.20	0.87 ± 0.22	0.82 ± 0.27	0.83 ± 0.27	−0.02 (−0.07 to 0.04)	0.59
Epicardial adipose tissue, mL	47 ± 31	35 ± 20	45 ± 27	36 ± 18	−2 (−9 to 5)	0.57
Pericardial adipose tissue, mL	174 ± 81	147 ± 54	186 ± 73	197 ± 85	−43 (−65 to −21)	<0.001
Paracardiac adipose tissue, mL	221 ± 101	182 ± 65	233 ± 85	232 ± 93	−45 (−69 to −22)	<0.001
LAESV, mL	85 ± 33	78 ± 40	80 ± 31	75 ± 34	−2 (−10 to 6)	0.60
LAEDV, mL	48 ± 32	49 ± 41	48 ± 34	46 ± 32	2 (−5 to 9)	0.56
LAEF, %	42 ± 18	40 ± 18	41 ± 30	45 ± 17	−5 (−11 to 1)	0.10
LA GCS, %	−35 ± 14	−36 ± 11	−35 ± 11	−37 ± 10	1 (−2 to 4)	0.41
LA GLS, %	−25 ± 8	−24 ± 7	−24 ± 7	−25 ± 7	1 (−2 to 3)	0.56

Kramer CM et al. J Am Coll Cardiol. 2024 Nov 5:S0735-1097(24)10414-7.. PMID: 39566869



Cardio-adiposidad

Descifrando la relación entre grasa y patología cardiovascular

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