SALUTE E MEDICINA DI GENERE CLINICA

ORGANIZZAZIONE DEI SERVIZI E BILANCIO DI GENERE

CRSMG
Centro di Coordinamento Regionale per la Salute e la Medicina di Genere Toscana

Azienda USL Toscana centro
Servizio Sanitario della Toscana

Lo scompenso cardiaco e il genere

Gabriele Grippo

7 novembre 2023 ore 8.30-17.00 Aula Marino Marini – Uniser Pistoia,
Via Sandro Pertini 358

Epidemiologia

Ministero della Salute

*«Lo scompenso cardiaco rappresenta la **prima causa di ricovero in ospedale negli ultrasessantacinquenni,** anche per questo è considerato un problema di salute pubblica di enorme rilievo»*

«A soffrire di scompenso cardiaco in Italia sono circa 600.000 persone e si stima che la sua prevalenza raddoppi a ogni decade di età (dopo i 65 anni arriva al 10% circa)»

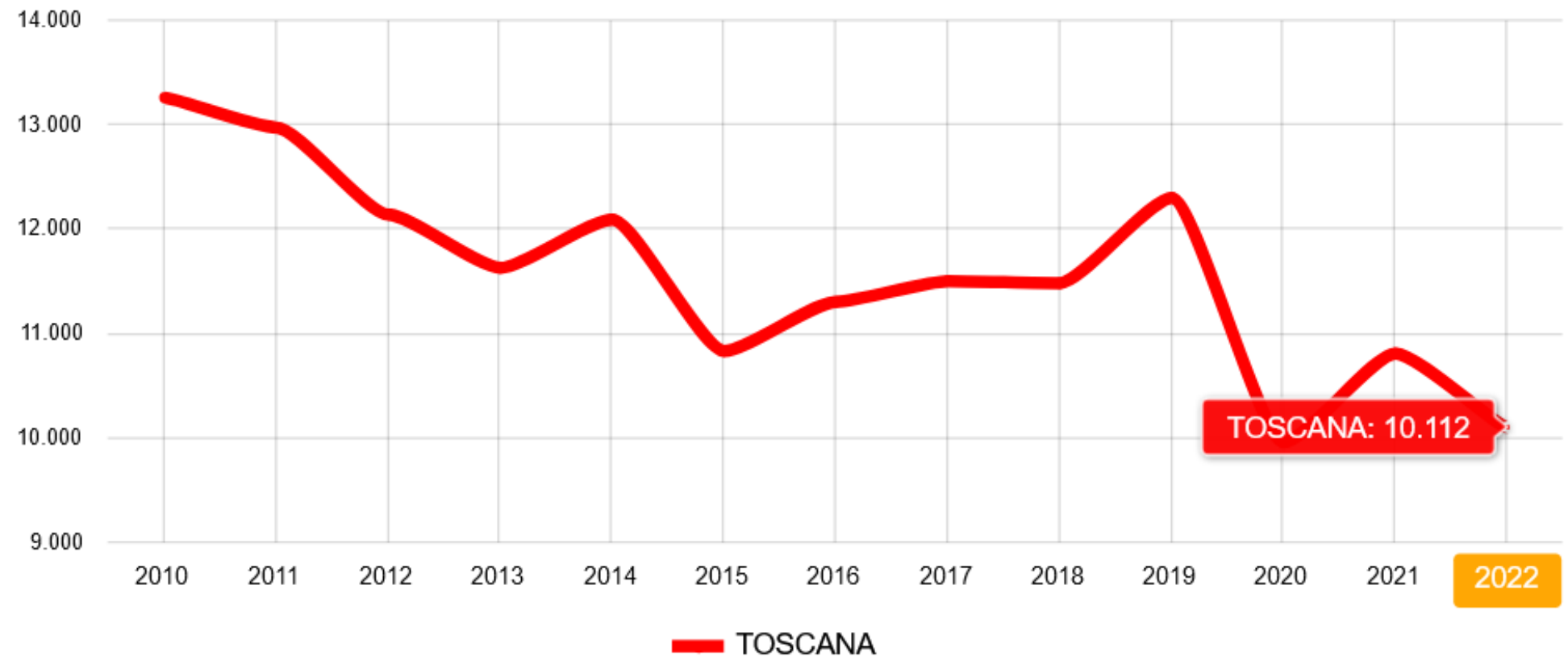
Epidemiologia

ARS TOSCANA
agenzia regionale di sanità

Scompenso cardiaco: volume di ricoveri - erogazione

Numero - Totale

Fonte: RT Scheda dimissione ospedaliera (SDO)



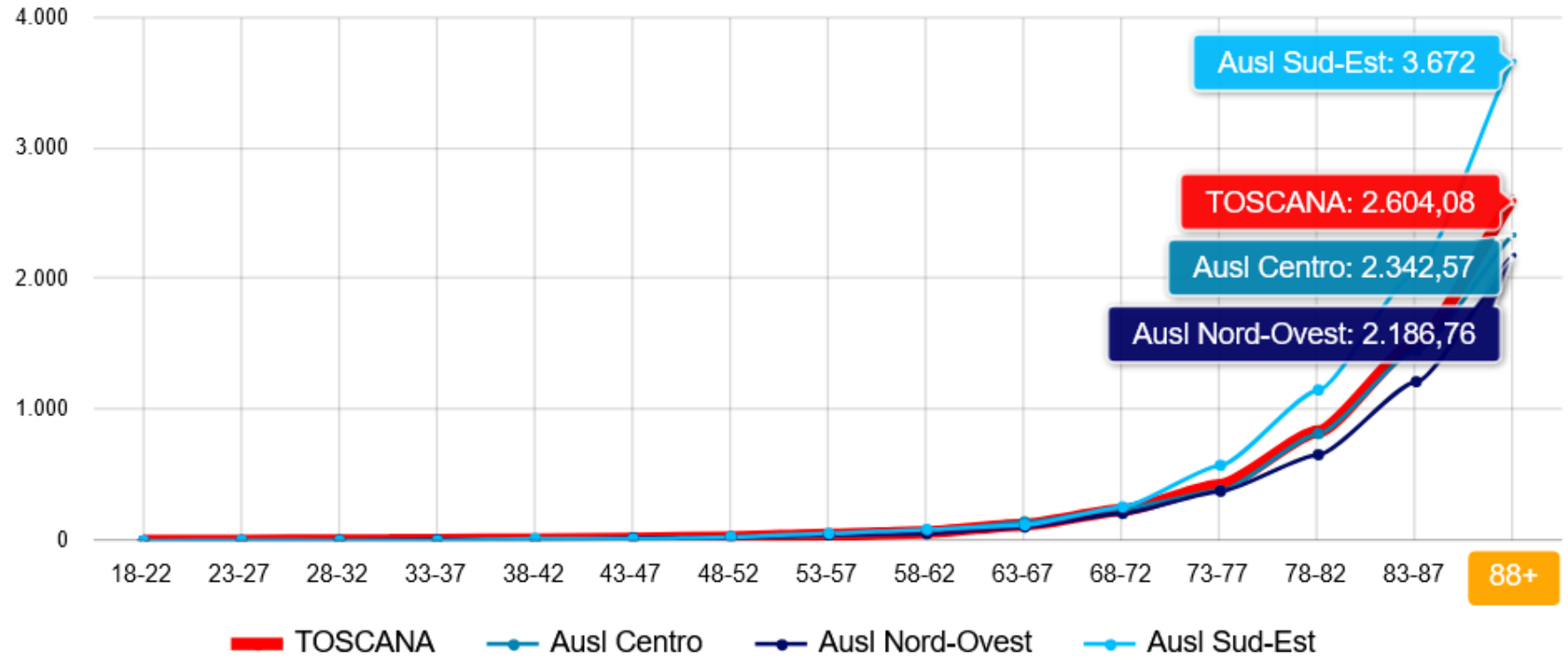
Epidemiologia

ARS TOSCANA
agenzia regionale di sanità

D03Cc - Ospedalizzazione in età adulta per scompenso cardiaco

Tasso standardizzato per sesso ed età (x 100000) - Anno 2022 - Totale

Fonte: RT Scheda dimissione ospedaliera (SDO), ISTAT Popolazione residente in Toscana al 1° gennaio



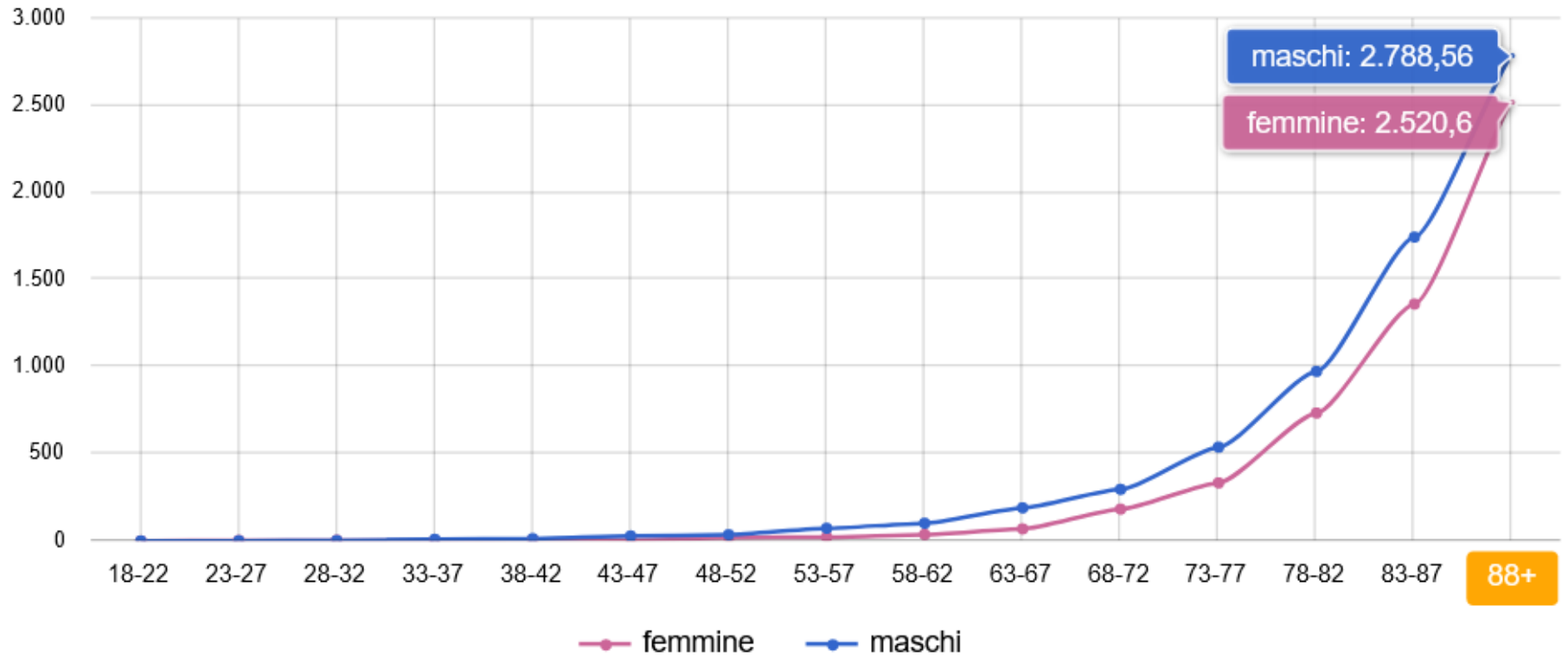
Epidemiologia

ARS TOSCANA
agenzia regionale di sanità

D03Cc - Ospedalizzazione in età adulta per scompenso cardiaco

Tasso standardizzato per sesso ed età (x 100000) - Anno 2022 - Maschi

Fonte: RT Scheda dimissione ospedaliera (SDO), ISTAT Popolazione residente in Toscana al 1° gennaio



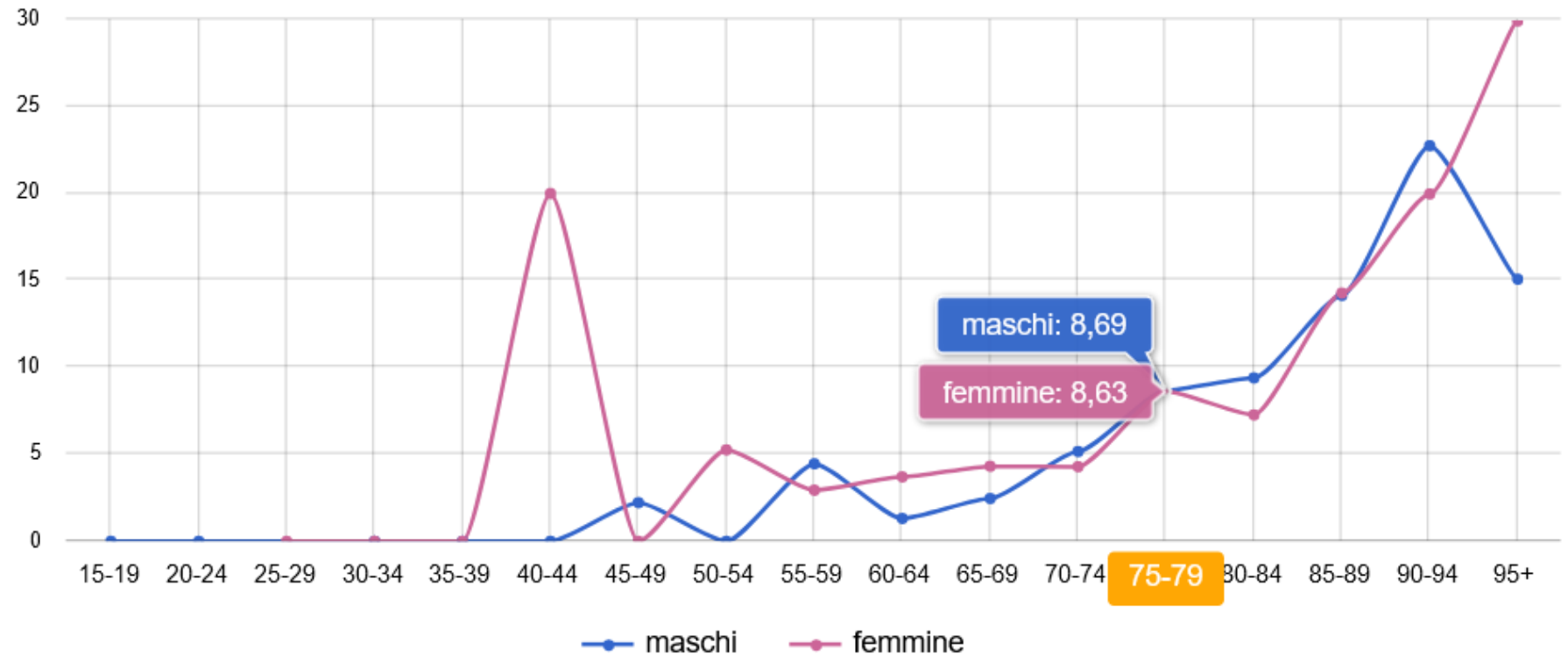
Epidemiologia

ARS TOSCANA
agenzia regionale di sanità

Scompenso Cardiaco Congestizio, rischio di morte a 30g - erogazione

Tasso grezzo - Anno 2022 - Toscana

Fonte: RT Scheda dimissione ospedaliera (SDO), RT Anagrafe Assistibili Toscana



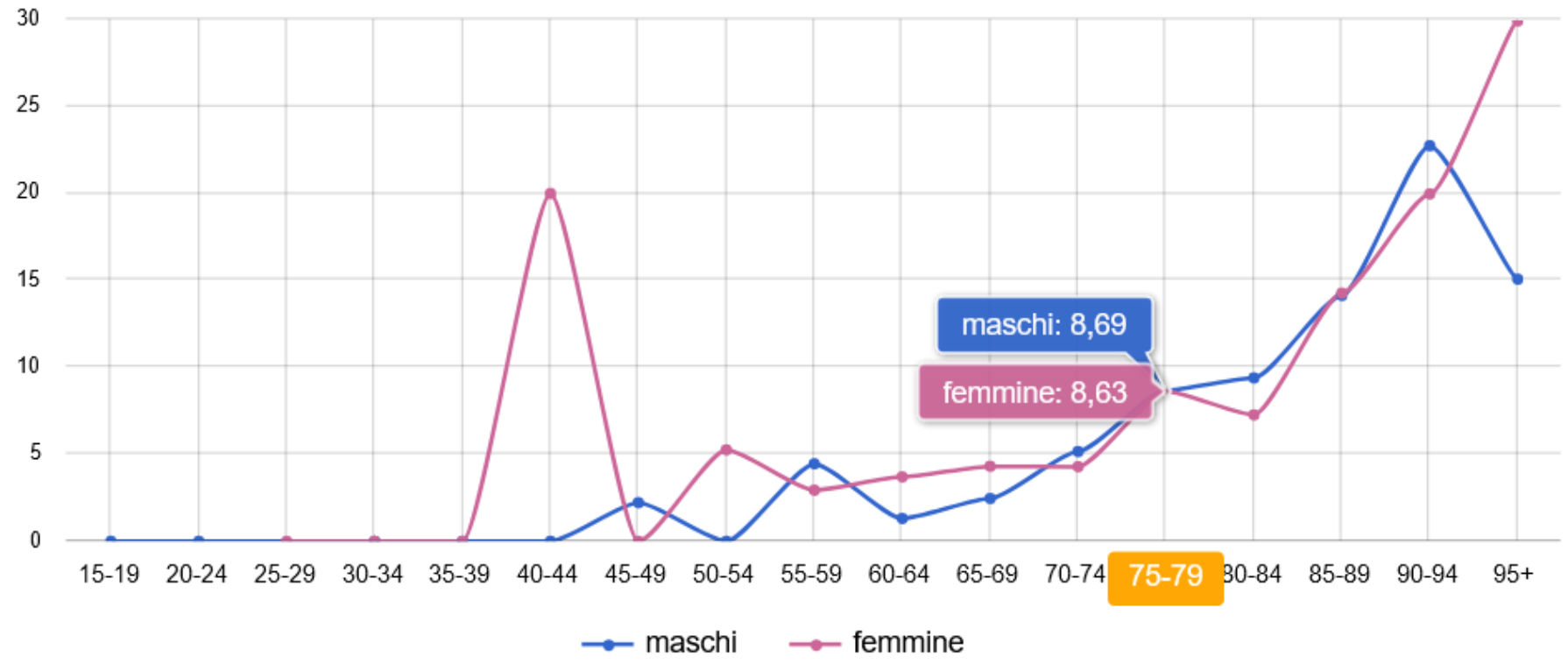
Epidemiologia

ARS TOSCANA
agenzia regionale di sanità

Scompenso Cardiaco Congestizio, rischio di morte a 30g - erogazione

Tasso grezzo - Anno 2022 - Toscana

Fonte: RT Scheda dimissione ospedaliera (SDO), RT Anagrafe Assistibili Toscana



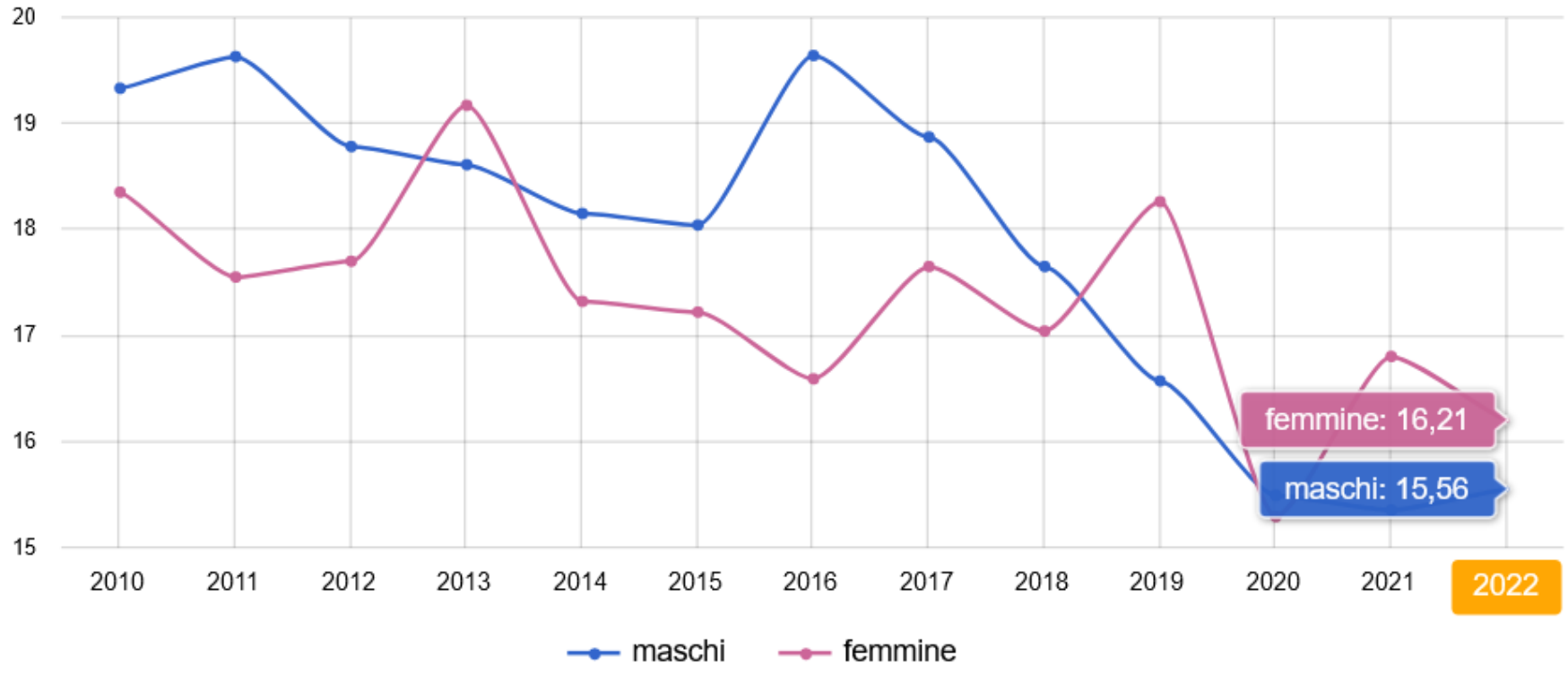
Epidemiologia

ARS TOSCANA
agenzia regionale di sanità

Scompenso Cardiaco Congestizio, rischio di riammissione a 30g - erogazione

Tasso aggiustato (x 100) - Totale - REGIONE TOSCANA

Fonte: RT Scheda dimissione ospedaliera (SDO)



Definizione di insufficienza cardiaca

E' una sindrome clinica composta da:

- sintomi cardinali (ad es. dispnea, gonfiore e affaticamento)
- segni (ad es pressione venosa giugulare, crepitii polmonari e periferica edema).

Anomalia strutturale e/o funzionale del cuore che determina pressioni intracardiache elevate e/o gittata cardiaca inadeguata a riposo e/o durante esercizio.

Dovuto a ***disfunzione miocardica: sistolica, diastolica o entrambe.***

La patologia delle valvole, del pericardio e dell'endocardio e le anomalie del ritmo e della conduzione cardiaca possono causare o contribuire all'insufficienza cardiaca

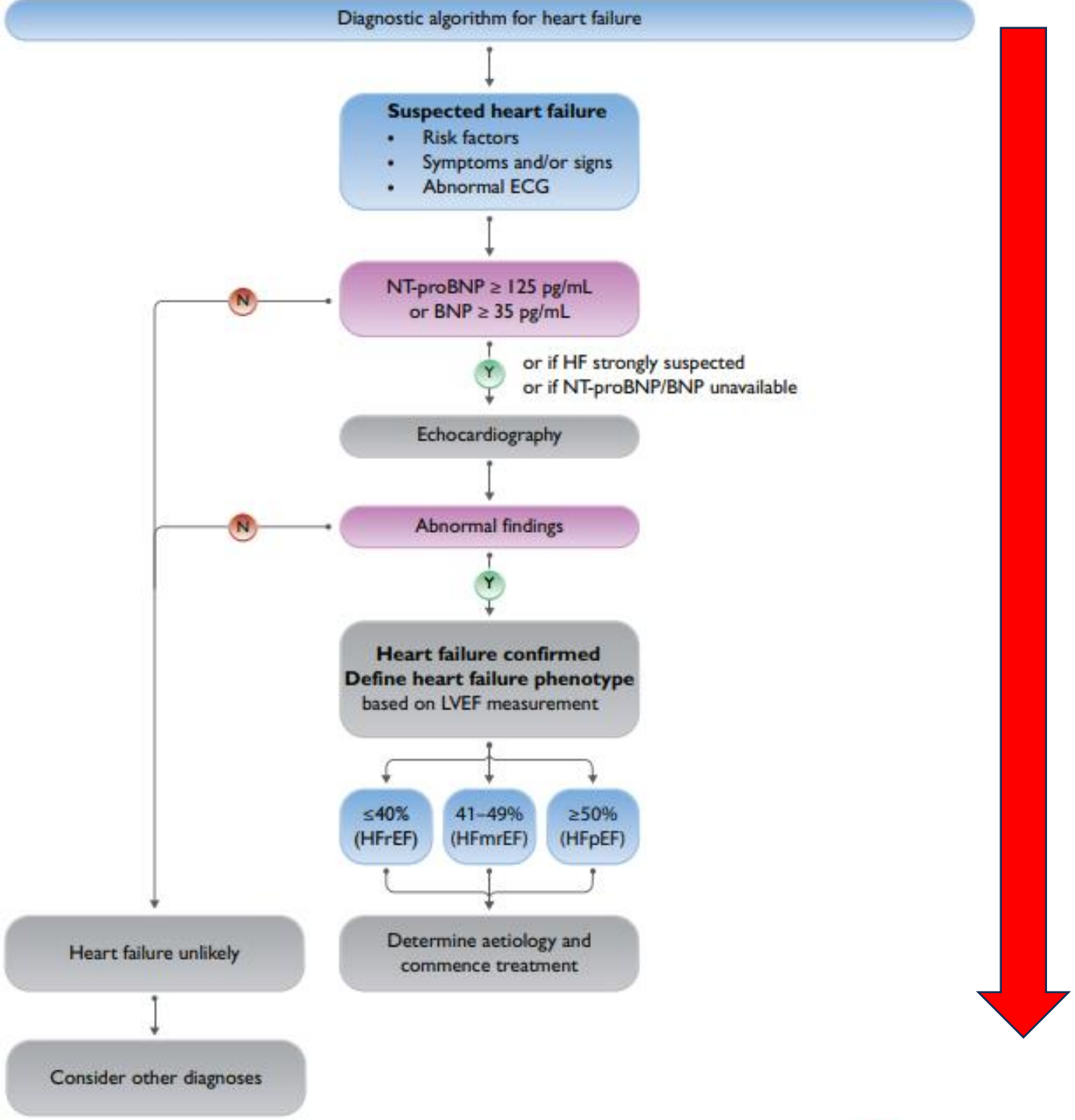
Cause di insufficienza cardiaca

Table 5 Causes of heart failure, common modes of presentation and specific investigations

Cause	Examples of presentations	Specific investigations
CAD	Myocardial infarction	Invasive coronary angiography
	Angina or "angina-equivalent"	CT coronary angiography
	Arrhythmias	Imaging stress tests (echo, nuclear, CMR)
Hypertension	Heart failure with preserved systolic function	24 h ambulatory BP
	Malignant hypertension/acute pulmonary oedema	Plasma metanephrines, renal artery imaging
		Renin and aldosterone
Valve disease	Primary valve disease e.g., aortic stenosis	Echo – transoesophageal/stress
	Secondary valve disease, e.g. functional regurgitation	
	Congenital valve disease	
Arrhythmias	Atrial tachyarrhythmias	Ambulatory ECG recording
	Ventricular arrhythmias	Electrophysiology study, if indicated
CMPs	All	CMR, genetic testing
	Dilated	
	Hypertrophic	
	Restrictive	Right and left heart catheterization
	ARVC	
	Peripartum	
	Takotsubo syndrome	CMR, angiography
	Toxins: alcohol, cocaine, iron, copper	Trace elements, toxicology, LFTs, GGT
Congenital heart disease	Congenitally corrected/repaired transposition of great arteries	CMR
	Shunt lesions	
	Repaired tetralogy of Fallot	
	Ebstein's anomaly	
Infective	Viral myocarditis	CMR, EMB
	Chagas disease	
	HIV	Serology
	Lyme disease	
Drug-induced	Anthracyclines	
	Trastuzumab	
	VEGF inhibitors	
	Immune checkpoint inhibitors	
	Proteasome inhibitors	
	RAF+MEK inhibitors	
Infiltrative	Amyloid	Serum electrophoresis and serum free light chains, Bence Jones protein, bone scintigraphy, CMR, CT-PET, EMB
	Sarcoidosis	Serum ACE, CMR, FDG-PET, chest CT, EMB
	Neoplastic	CMR, EMB
Storage disorders	Haemochromatosis	Iron studies, genetics, CMR (T2* imaging), EMB
	Fabry disease	α-galactosidase A, genetics, CMR (T1 mapping)
	Glycogen storage diseases	
Endomyocardial disease	Radiotherapy	CMR
	Endomyocardial fibrosis/eosinophilia	EMB
	Carcinoid	24 h urine 5-HIAA
Pericardial disease	Calcification	Chest CT, CMR, right and left heart catheterization
	Infiltrative	
Metabolic	Endocrine disease	TFTs, plasma metanephrines, renin and aldosterone, cortisol
	Nutritional disease (thiamine, vitamin B1 and selenium deficiencies)	Specific plasma nutrients
	Autoimmune disease	ANA, ANCA, rheumatology review
Neuromuscular disease	Friedreich's ataxia	Nerve conduction studies, electromyogram, genetics
	Muscular dystrophy	CK, electromyogram, genetics

5-HIAA = 5-hydroxyindoleacetic acid; ACE = angiotensin-converting enzyme; ANA = anti-nuclear antibody; ANCA = anti-nuclear cytoplasmic antibody; ARVC = arrhythmogenic right ventricular cardiomyopathy; BP = blood pressure; CAD = coronary artery disease; CMP = cardiomyopathy; CMR = cardiac magnetic resonance; CK = creatinine kinase; CT = computed tomography; ECG = electrocardiogram; Echo = echocardiography; EMB = endomyocardial biopsy; FDG = fluorodeoxyglucose; GGT = gamma-glutamyl transferase; HIV = human immunodeficiency virus; h = hour; LFT = liver function test; LGE = late gadolinium enhancement; MEK = mitogen-activated protein kinase; PET = positron emission tomography; TFT = thyroid function test; VEGF = vascular endothelial growth factor.

ESC
European Society
of Cardiology



Signs of Heart Failure and Congestive Heart Failure

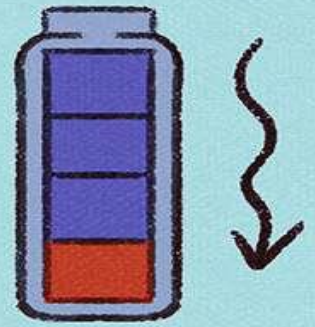
Chest pain (especially during exertion)

Swelling of legs, hands, and feet

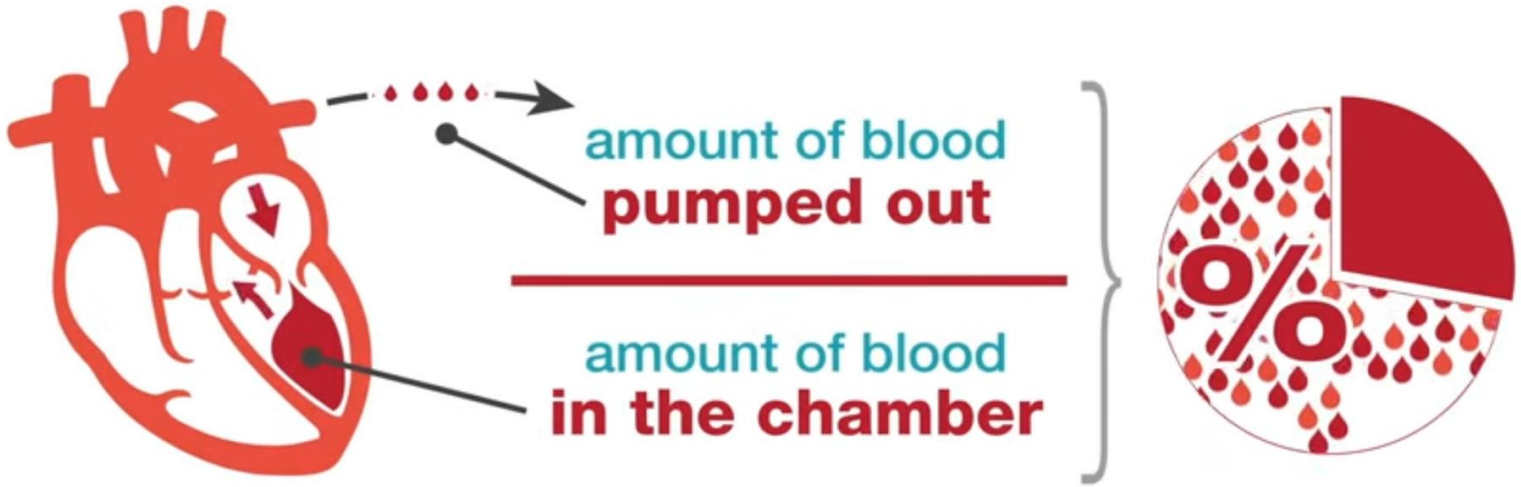
Table 6 Symptoms and signs typical of heart failure

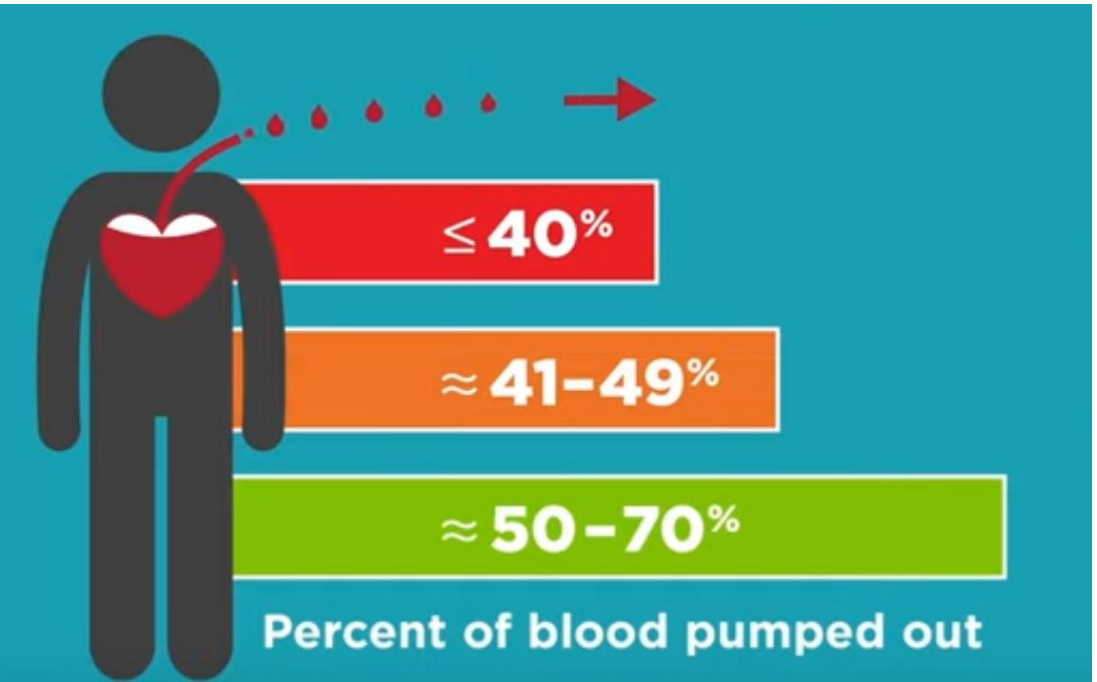
Symptoms	Signs
Typical	**More specific**
Breathlessness	Elevated jugular venous pressure
Orthopnoea	Hepatojugular reflux
Paroxysmal nocturnal dyspnoea	Third heart sound (gallop rhythm)
Reduced exercise tolerance	Laterally displaced apical impulse
Fatigue, tiredness, increased time to recover after exercise	
Ankle swelling	
Less typical	**Less specific**
Nocturnal cough	Weight gain (>2 kg/week)
Wheezing	Weight loss (in advanced HF)
Bloated feeling	Tissue wasting (cachexia)
Loss of appetite	Cardiac murmur
Confusion (especially in the elderly)	Peripheral oedema (ankle, sacral, scrotal)
Depression	Pulmonary crepitations
Palpitation	Pleural effusion
Dizziness	Tachycardia
Syncope	Irregular pulse
Bendopnea[a]	Tachypnoea
	Cheyne-Stokes respiration
	Hepatomegaly
	Ascites
	Cold extremities
	Oliguria
	Narrow pulse pressure

Dizziness/ lightheadedness



Sudden fatigue or weakness

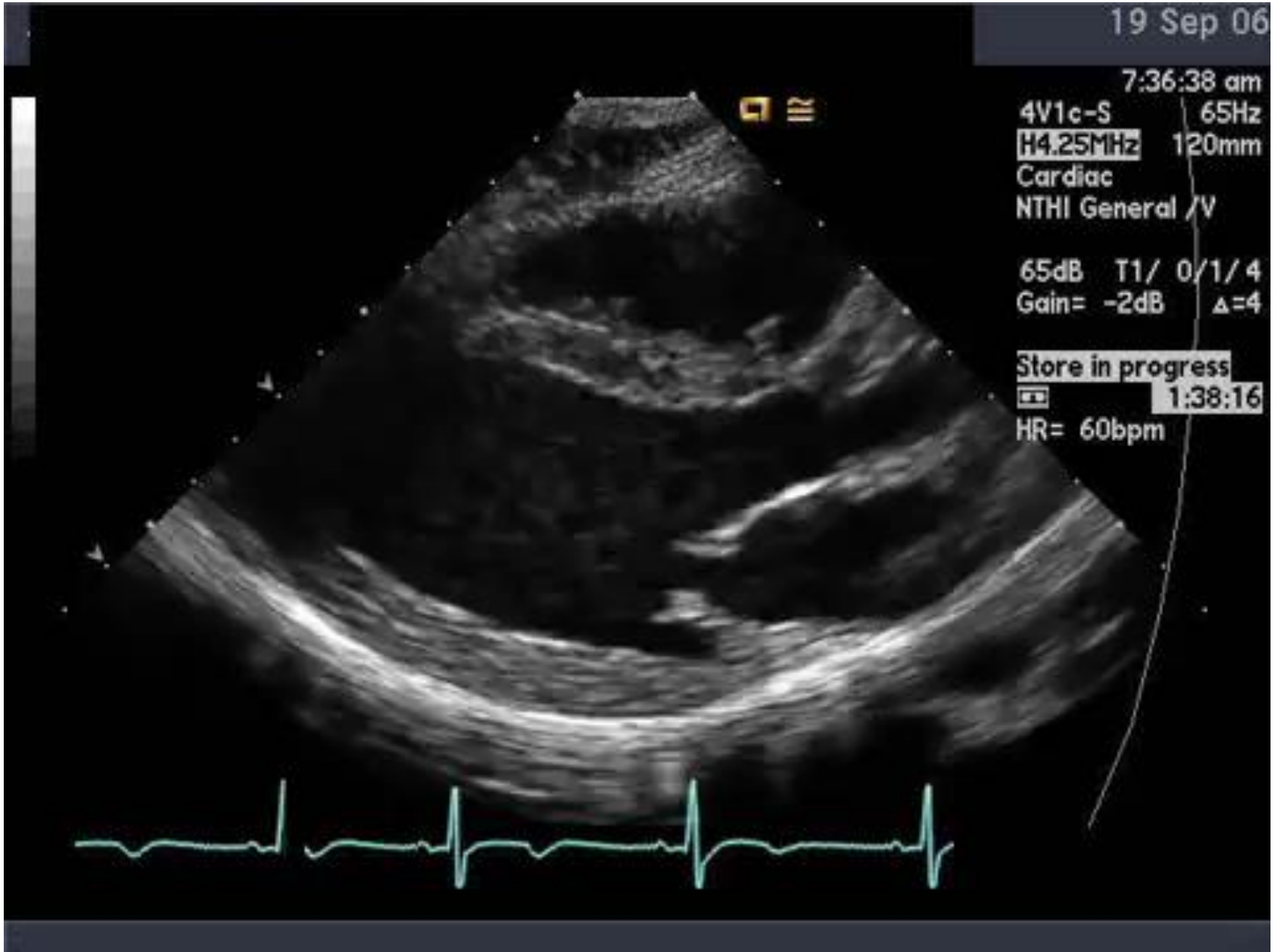




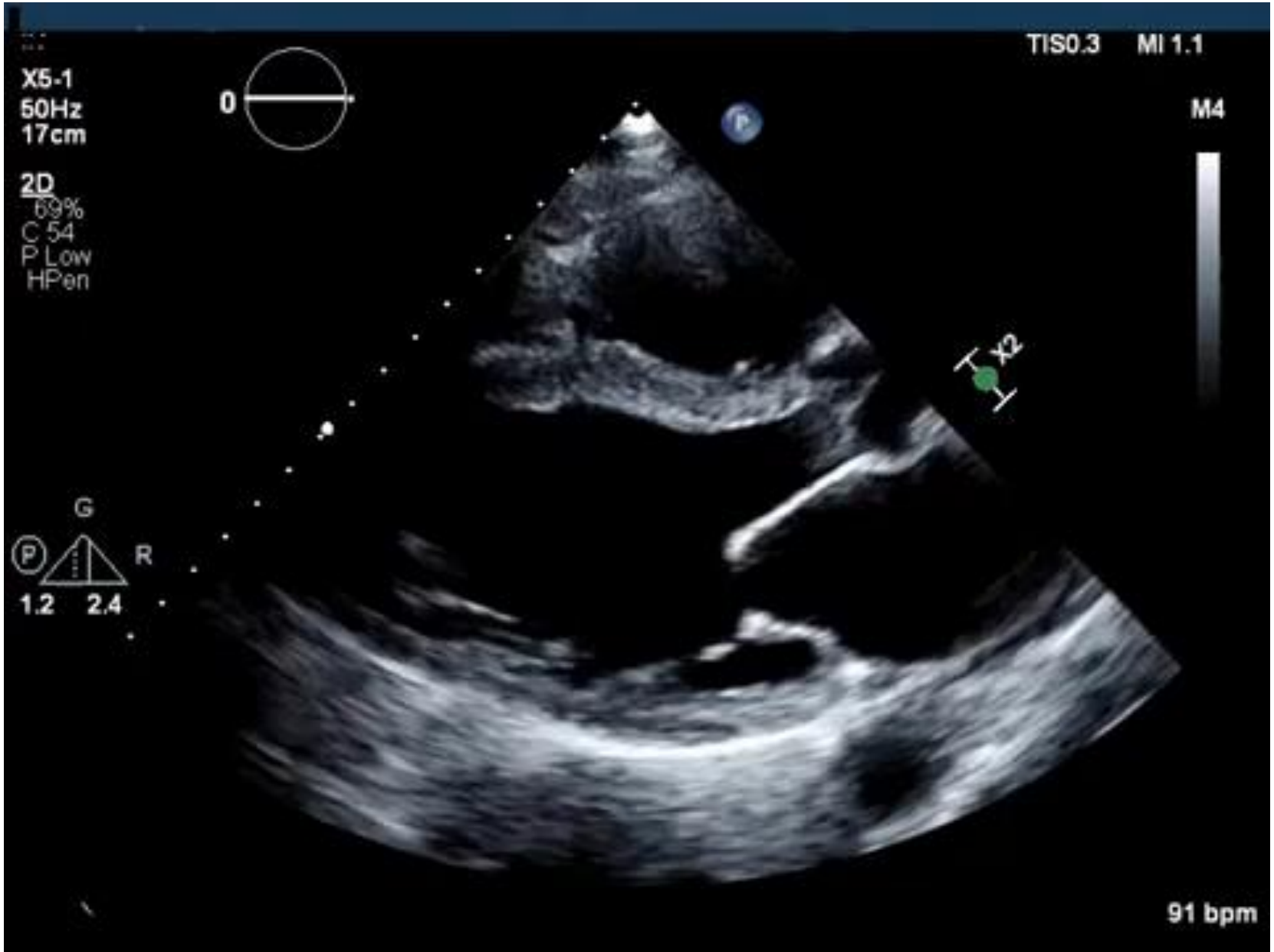
$$EF(\%) = \frac{SV}{EDV} \times 100$$

$$EF(\%) = \frac{70}{120} \times 100 = 58\%$$

Ecocardiogramma normale



Ecocardiogramma disfunzione sistolica



ESC
European Society of Cardiology
European Heart Journal (2021) **42**, 3599–3726
doi:10.1093/eurheartj/ehab368

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Table 3 Definition of heart failure with reduced ejection fraction, mildly reduced ejection fraction, and preserved ejection fraction

Type of HF		HFrEF	HFmrEF	HFpEF
Criteria	1	Symptoms ± signs[a]	Symptoms ± signs[a]	Symptoms ± signs[a]
	2	LVEF ≤40%	LVEF 41–49%[b]	LVEF ≥50%
	3	–	–	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides[c]

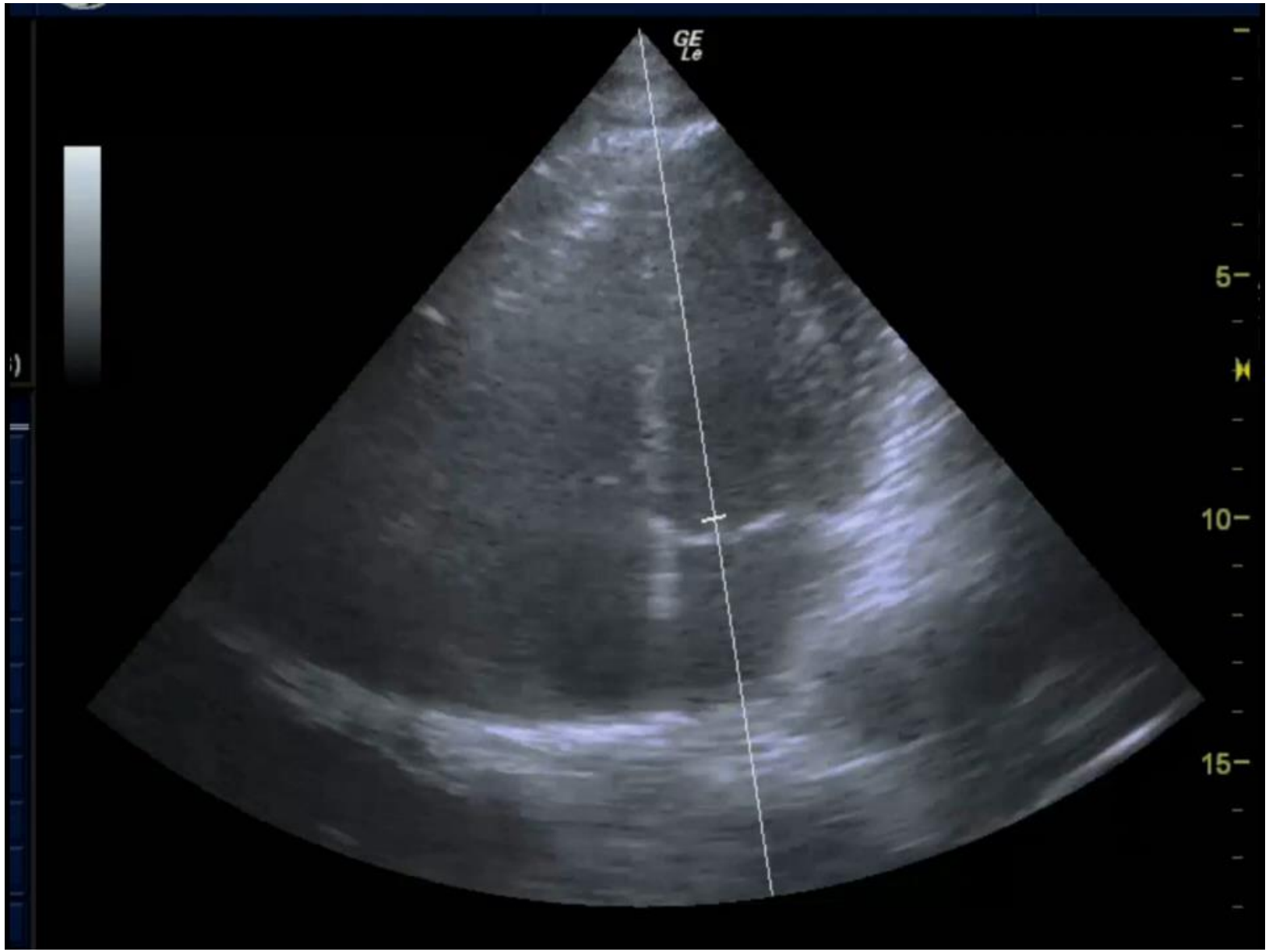
HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LV, left ventricle; LVEF, left ventricular ejection fraction.

[a]Signs may not be present in the early stages of HF (especially in HFpEF) and in optimally treated patients.

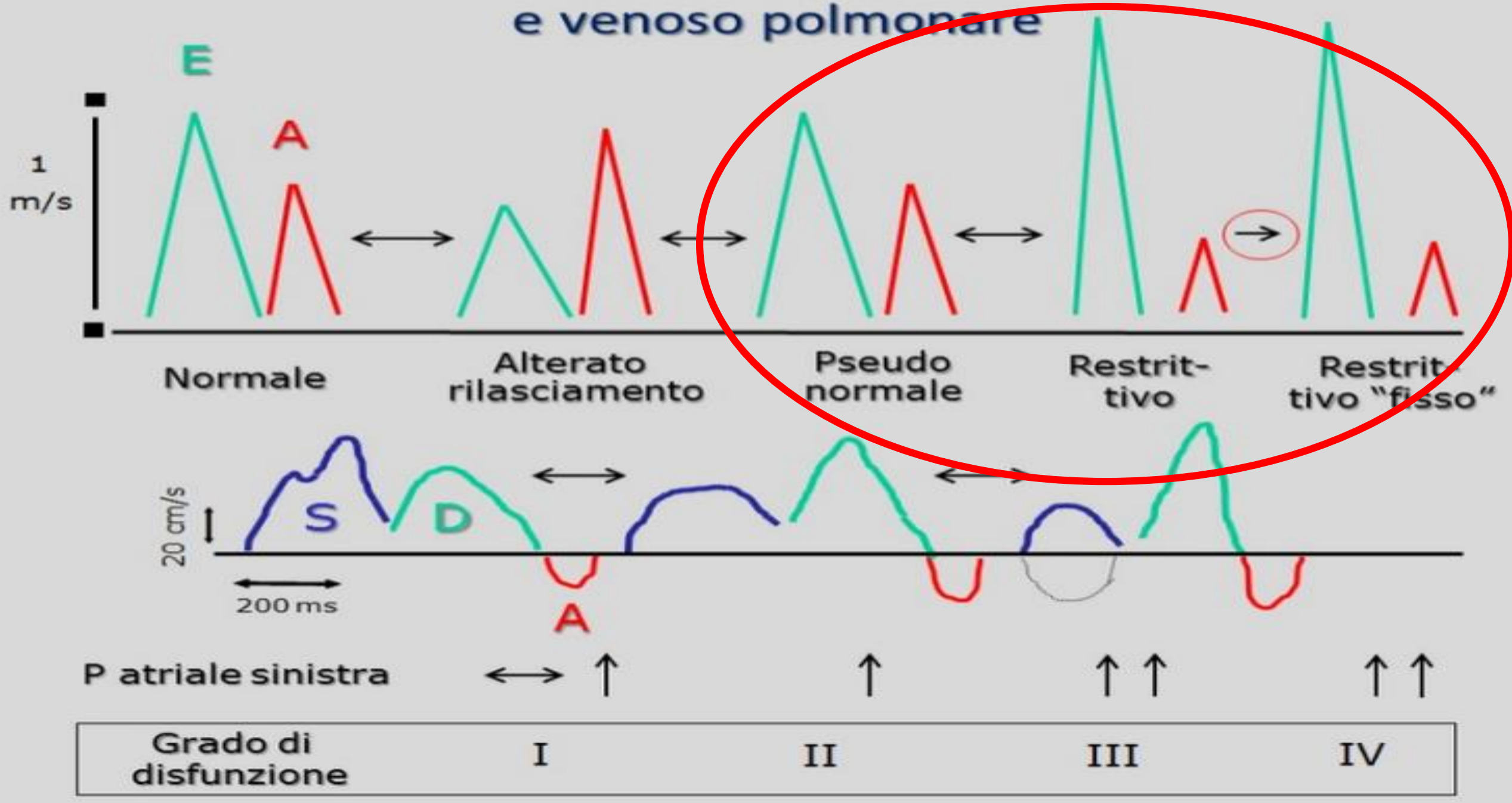
[b]For the diagnosis of HFmrEF, the presence of other evidence of structural heart disease (e.g. increased left atrial size, LV hypertrophy, or echocardiographic measures of impaired LV filling) makes the diagnosis more likely.

[c]For the diagnosis of HFpEF, the greater the number of abnormalities present, the higher the likelihood of HFpEF.

Ecocardiogramma: diastole

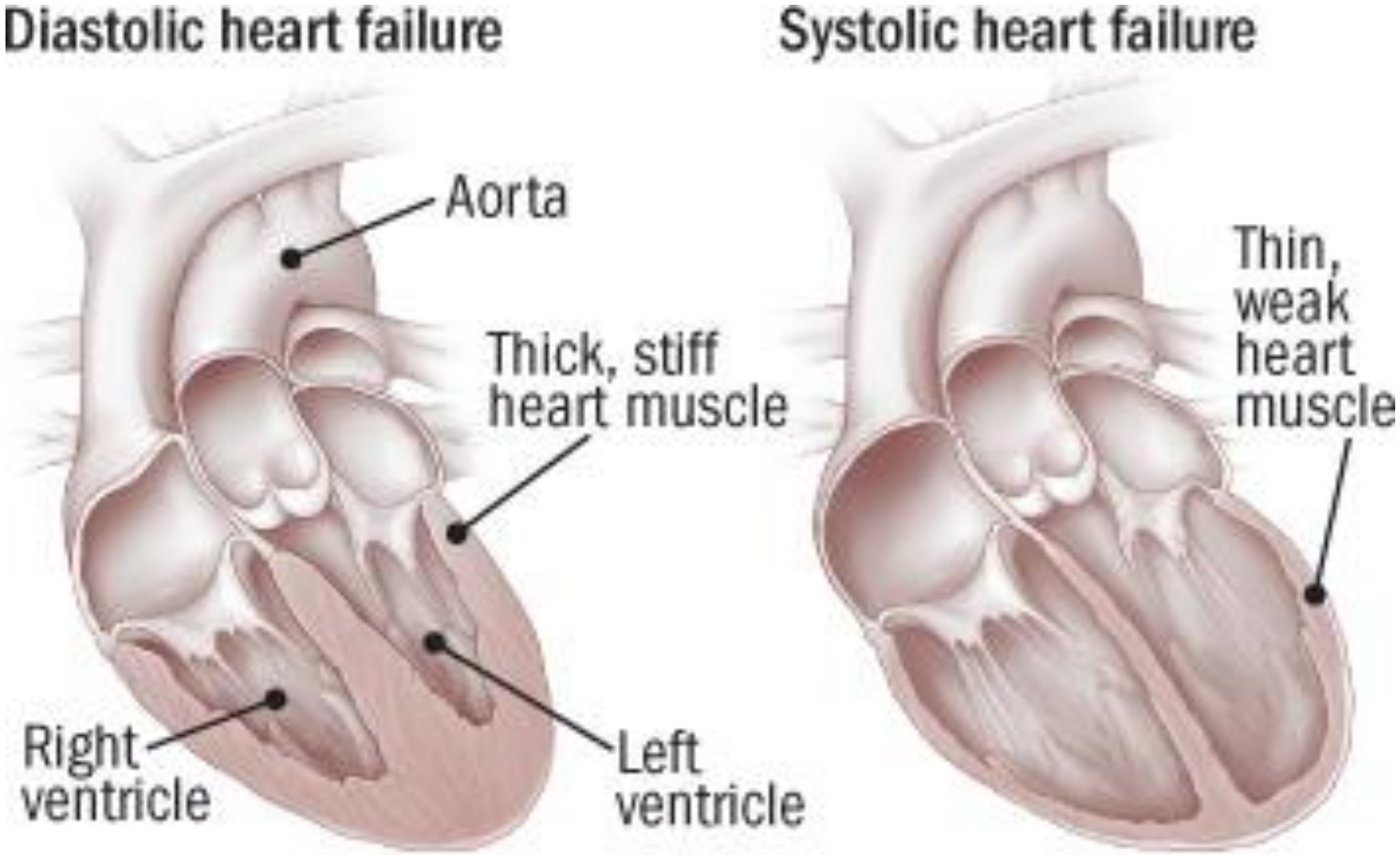


Utilizzo dei profili di flusso transmitralico e venoso polmonare

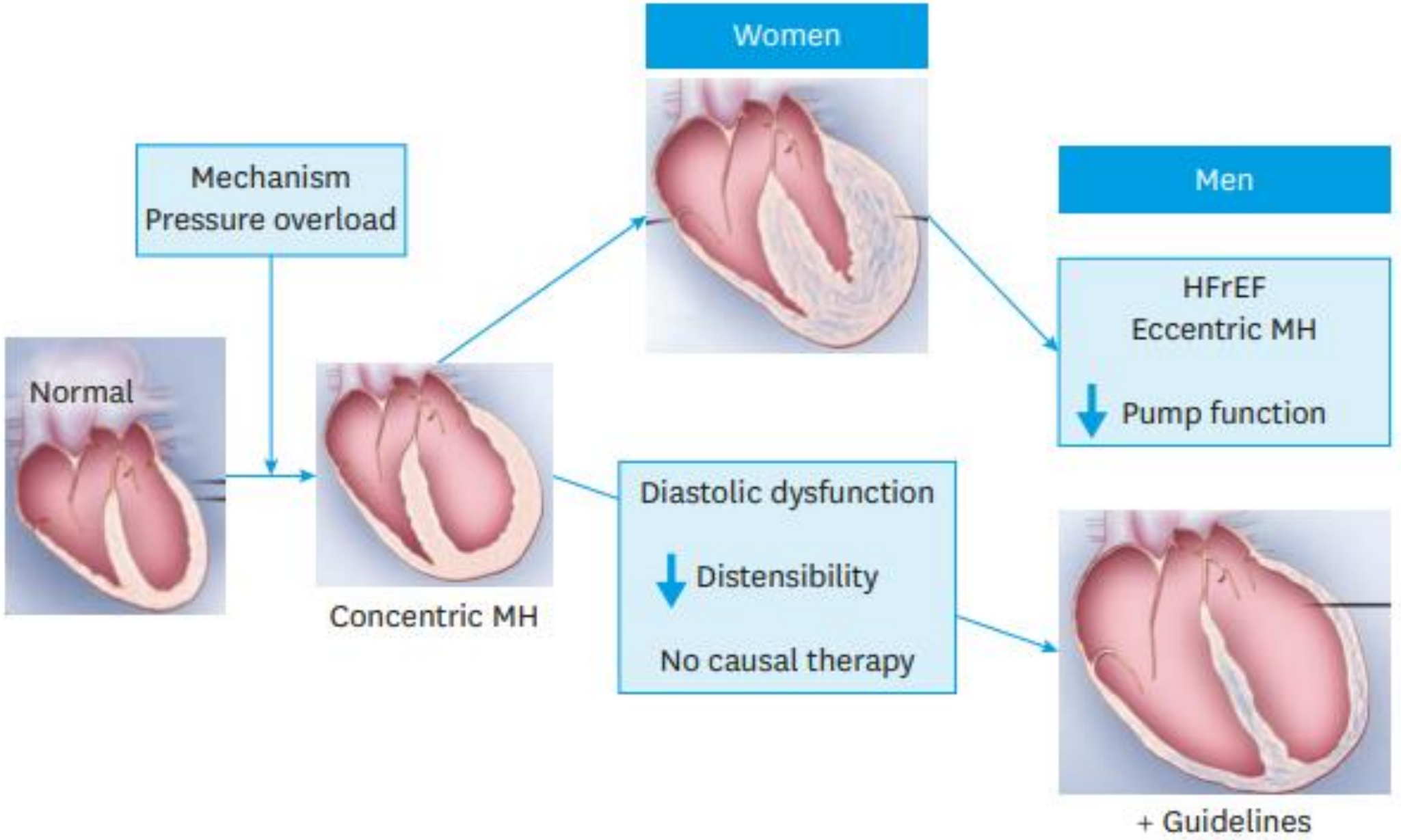


Grado di disfunzione	I	II	III	IV

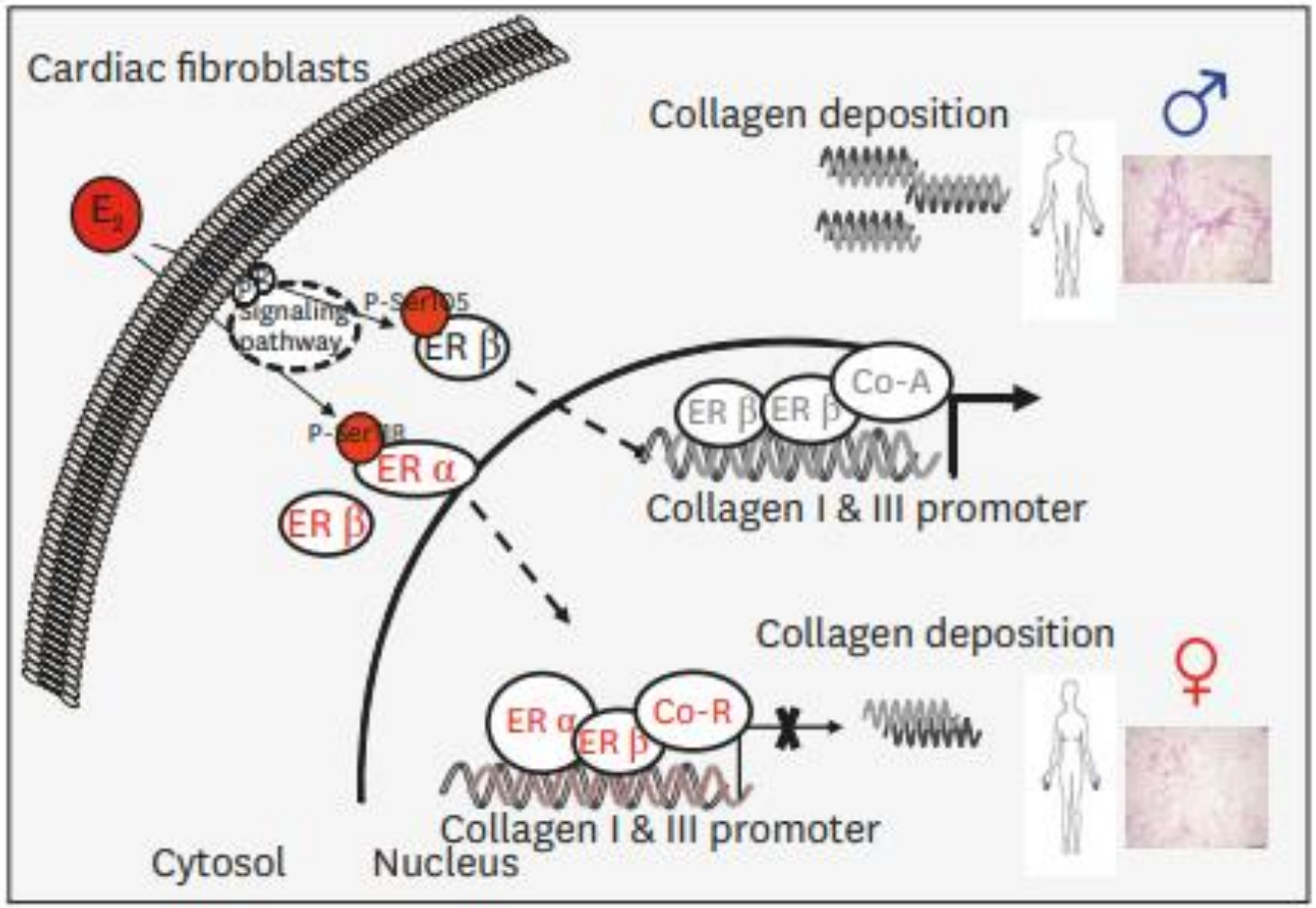
Types of heart failure: Diastolic and systolic



Types of heart failure: Diastolic and systolic



Pathophysiology



Clinical implications

- Aortic stenosis
- Hypertension
- Arteriosclerosis

Figure 3. Sex-specific E2/ER mediated collagen regulation underlies sex differences in cardiac fibrosis. Interaction of E2, ER α and ER ß with pro- and anti-fibrotic pathways in women and men. E2 activates ER α and ER ß in a sex specific manner, leading to a stronger transcriptional activation of pro-fibrotic pathways in men than in women. Adapted from Regitz-Zagrosek and Kararigas G.[23]
ER = estrogen receptor.

Pathophysiology

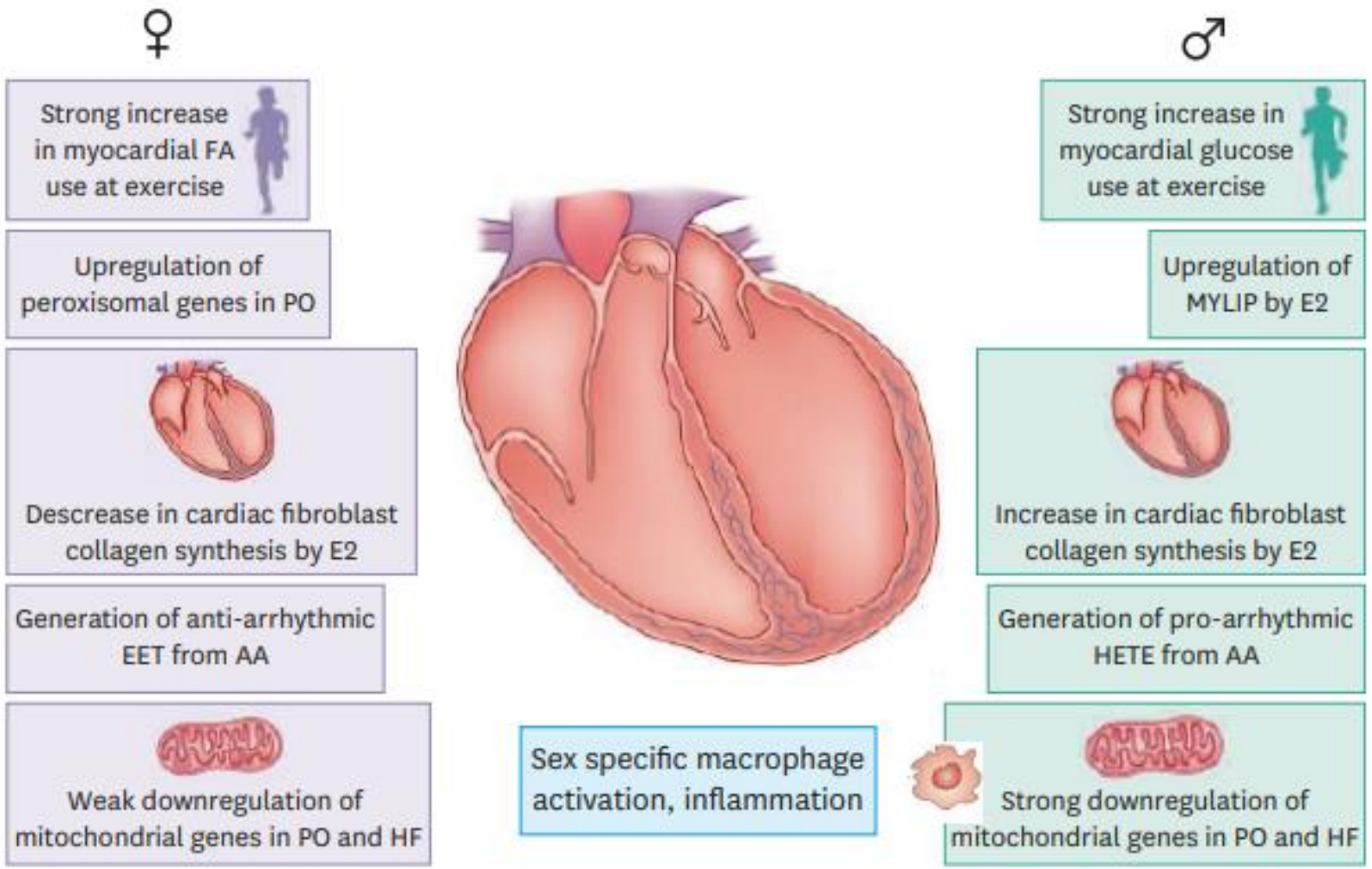


Figure 4. Summary of sex differences in myocardial pathophysiology. Adapted from Gerdts and Regitz-Zagrosek.[29]
AA = arachidonic acid; EET = epoxyeicosanoids; FA = fatty acid; HETE = hydroxyeicosatetraenoic; HF = heart failure; MYLIP = myosin regulatory light chain interacting protein; PO = pressure overload.

Pathophysiology

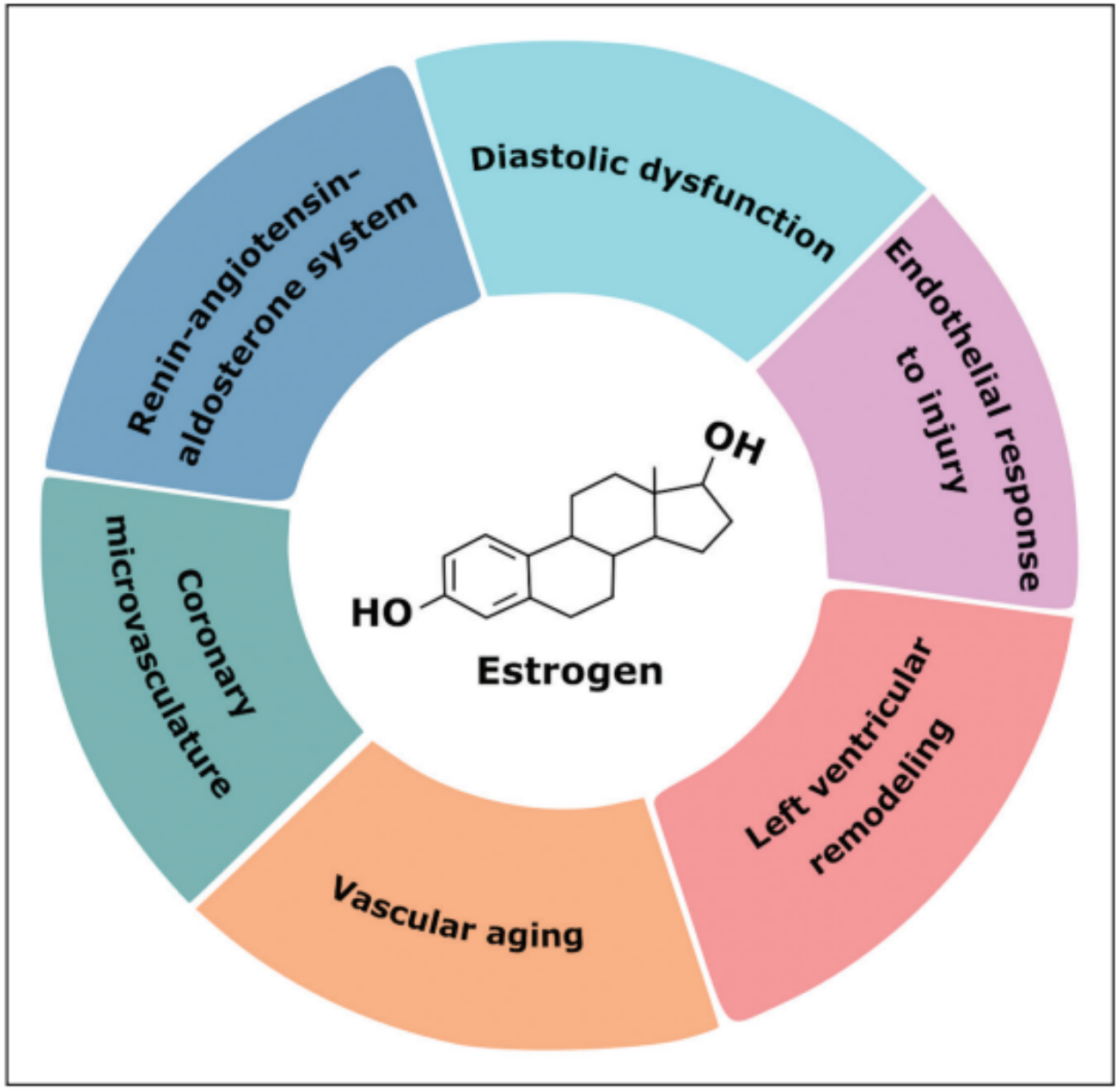


Figure 2. Postulated estrogen-mediated mechanisms in heart failure.
Estrogen modulates a variety of pathophysiologic processes including endothelial response to injury, the renin-angiotensin-aldosterone system, and left ventricular remodeling. Additionally, estrogen has roles in maintaining diastolic function and in the coronary microvasculature. These may explain sex differences in heart failure pathophysiology at a mechanistic level.

Therapy HFpEF

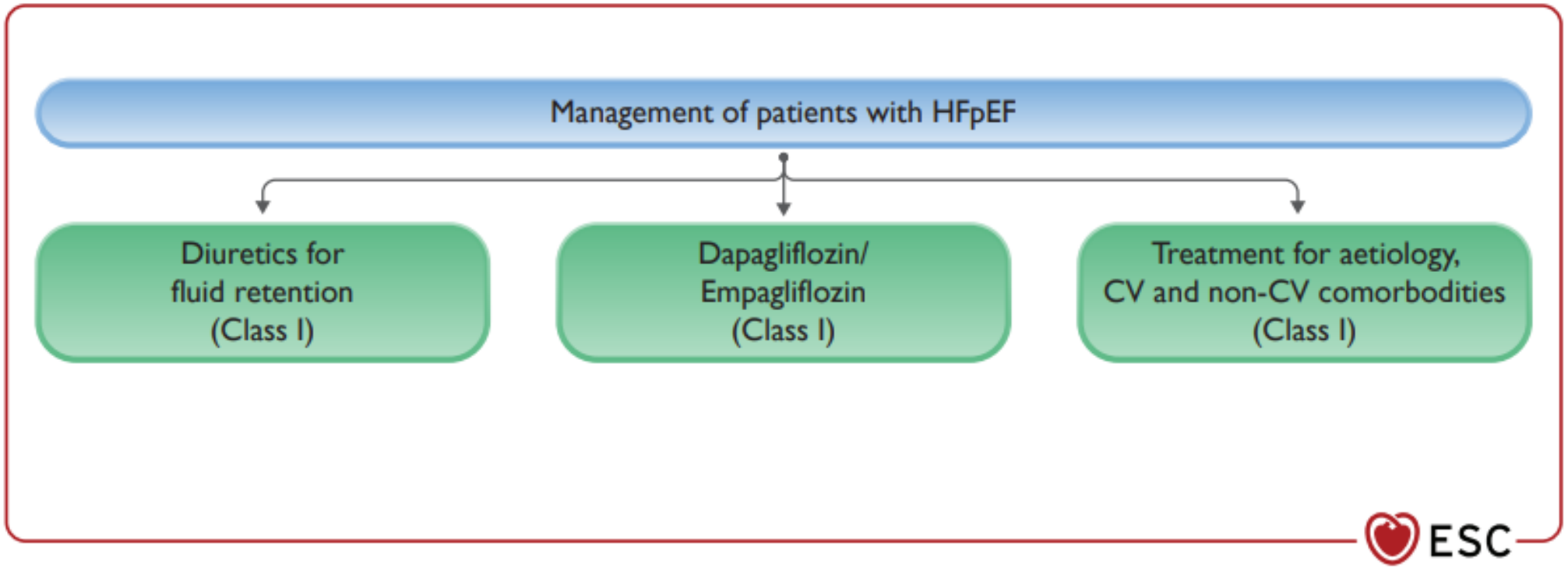


Figure 2 Management of patients with heart failure with preserved ejection fraction. CV, cardiovascular; HFpEF, heart failure with preserved ejection fraction.

Therapy HFmrEF

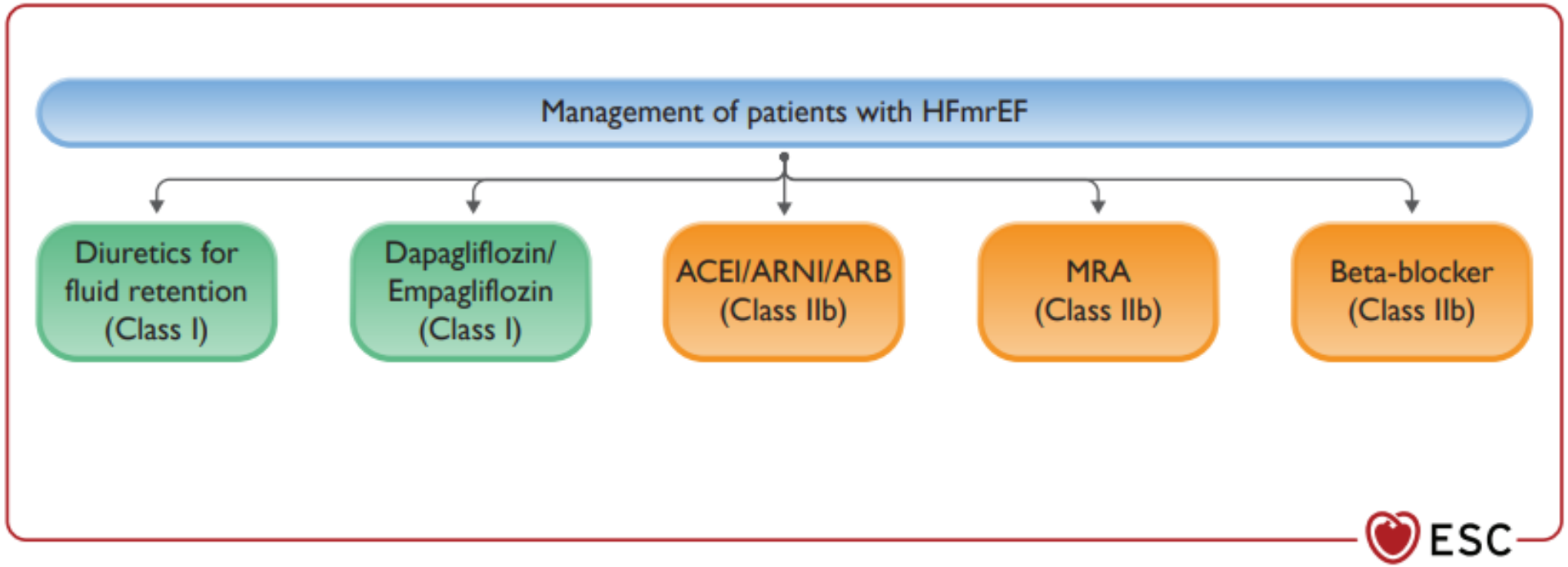
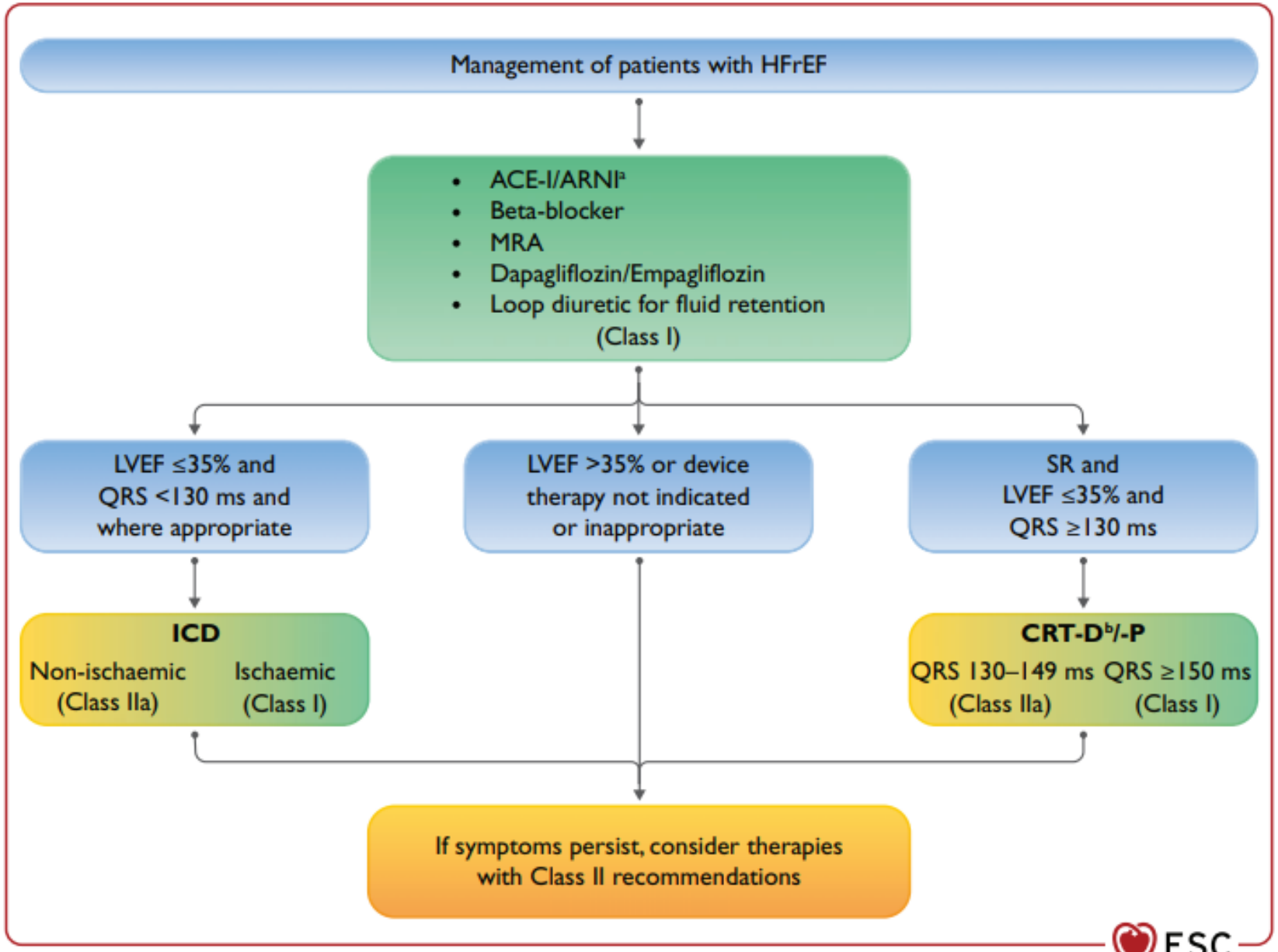


Figure 1 Management of patients with heart failure with mildly reduced ejection fraction. ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; HFmrEF, heart failure with mildly reduced ejection fraction; MRA, mineralocorticoid receptor antagonist.

Therapy HFeEF



Medical therapy

Table 1. Sex Differences in Risk of Mortality and/or Hospitalization in Heart Failure with Reduced Ejection Fraction

Study	End point	Risk (95% CI)	
		Women	Men
ACEI			
ACEI meta-analysis[12]	Mortality	OR, 0.79 (0.59–1.06)	OR, 0.76 (0.65–0.88)
ACEI meta-analysis[12]	Mortality and HF hospitalizations	OR, 0.78 (0.59–1.04)	OR, 0.63 (0.55–0.73)
ACEI meta-analysis[13]	Mortality	RR, 0.92 (0.81–1.04)	RR, 0.82 (0.74–0.90)
ARB			
Val-HeFT*	Mortality	HR, 0.93 (0.68–1.27)	HR, 1.04 (0.90–1.19)
Val-HeFT*	HF hospitalizations	HR, 0.74 (0.55–0.98)	HR, 0.73 (0.62–0.86)
CHARM trials*	CV mortality or HF hospitalization	HR, 0.81 (0.67–0.98)	HR, 0.82 (0.73–0.91)
ELITE II[18]	Mortality	HR, 1.14 (0.8–1.8)	HR, 1.12 (0.9–1.4)
ARNI			
PARADIGM-HF[10]	CV mortality or HF hospitalization	Not reported but *P* value for interaction=0.63	Not reported but *P* value for interaction=0.63
Aldosterone blockers			
Meta-analysis[19]	CV mortality or HF hospitalization	aHR, 0.73 (0.62–0.86)	aHR, 0.69 (0.62–0.77)
Nitrate+hydralazine			
A-HEFT[20]	Mortality	HR, 0.33 (0.16–0.71)	HR, 0.79 (0.46–1.35)
A-HEFT[20]	Mortality or HF hospitalization	HR, 0.58(0.39–0.86)	HR, 0.67 (0.49–0.92)
B-blocker therapy			
US Carvedilol HF[21]	Mortality	HR, 0.23 (0.07–0.69)	HR, 0.41 (0.22–0.80)
COPERNICUS[22]	Mortality	RR, 0.63 (0.39–1.04)	RR, 0.68 (0.54–0.86)
CIBIS II[23]	Mortality	RH, 0.53 (0.42–0.67)	RH, 0.37 (0.19–0.69)
MERIT-HF[24]	Mortality	RR, 0.93 (0.58–1.49)	RR, 0.63 (0.50–0.78)
Ivabradine			
Ivabradine[25]	CV mortality or HF hospitalization	HR, 0.74 (0.60–0.91)	HR, 0.84 (0.76–0.94)
Digitalis			
Digitalis[26]	Mortality	aHR, 1.23 (1.02–1.47)	aHR, 0.93 (0.85–1.02)
Digitalis[26]	HF hospitalizations	HR, 0.87 (0.72–1.04)	HR, 0.66 (0.60–0.73)
SGLT2 inhibitors			
DAPA-HF[11]	HF hospitalization, IV therapy, or CV mortality	HR, 0.79 (0.59–1.06)	HR, 0.73 (0.63–0.85)
EMPEROR-Reduced[17]	CV mortality or HF hospitalization	HR, 0.59 (0.44–0.80)	HR, 0.80 (0.68–0.93)

Digossina

Nel 1997, il Digitalis Investigation Group ha confermato l'efficacia della terapia con digossina per pazienti con HF. Successivamente, le linee guida hanno fortemente sostenuto l'uso della digossina nell'HFrEF, senza considerare il sesso.

Tuttavia, in un'analisi post hoc di sottogruppi, la digossina è stata associata con una mortalità significativamente più alta tra le donne

I livelli nell'intervallo normale superiore sono stati ritenuti responsabili degli effetti sfavorevoli sulla sopravvivenza riportato nelle donne.

Medical therapy

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Digitalis[26]	Mortality	aHR, 1.23 (1.02–1.47)	aHR, 0.93 (0.85–1.02)
Digitalis[26]	HF hospitalizations	HR, 0.87 (0.72–1.04)	HR, 0.66 (0.60–0.73)
SGLT2 inhibitors			
DAPA-HF[11]	HF hospitalization, IV therapy, or CV mortality	HR, 0.79 (0.59–1.06)	HR, 0.73 (0.63–0.85)
EMPEROR-Reduced[17]	CV mortality or HF hospitalization	HR, 0.59 (0.44–0.80)	HR, 0.80 (0.68–0.93)

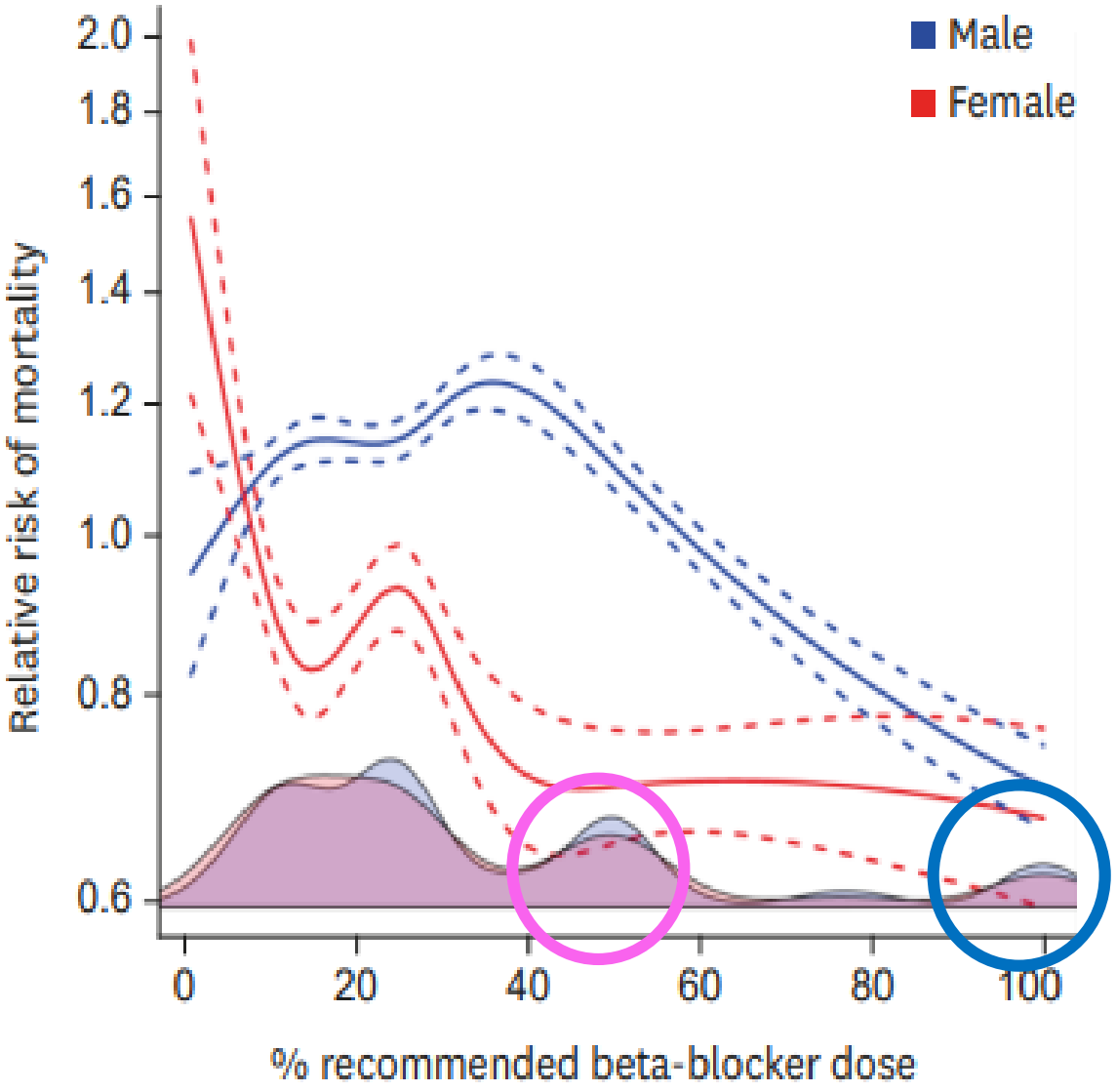
Beta-bloccanti

I beta-bloccanti sono pietre miliari nel trattamento dello scompenso cardiaco.

Raccolta dei risultati di mortalità da MERIT-HF, CIBIS II e COPERNICUS hanno mostrato benefici in termini di sopravvivenza in entrambe le donne e uomini.

La mancanza di prove in alcuni ampi studi sui beta-bloccanti è quindi probabilmente dovuta a la sottorappresentanza delle donne negli studi clinici e i beta-bloccanti rappresentano un trattamento efficace nelle donne.

Medical therapy



Una recente analisi nello studio BIology Study to TAilored Treatment (BIOSTAT) nello studio sullo scompenso cardiaco cronico condotto in 11 paesi europei hanno scoperto che le donne con HFrEF necessitavano di dosi più basse di beta-bloccanti. Metoprololo e propranololo vengono metabolizzati principalmente da citocromo epatico CYP2D6 che ha un'attività inferiore nelle donne rispetto agli uomini. Propranololo raggiunge livelli plasmatici fino all'80% più alti nelle donne rispetto agli uomini.

L'effetto ottimale del beta-bloccante metoprololo può essere raggiunto a dosi inferiori nelle donne rispetto agli uomini: una dose di 50 mg

La dose di metoprololo nelle donne adulte ha fornito un'esposizione al farmaco approssimativamente simile a quella di 100 mg dose negli uomini adulti.

I contraccettivi orali possono interagire con il metabolismo del metoprololo e oltre aumentarne i livelli plasmatici.

Poiché le donne sperimentano più frequentemente effetti avversi con beta-bloccanti rispetto agli uomini, potrebbe essere utile mantenere le dosi basse e condurre più studi sul dosaggio ottimale di beta-bloccanti nelle donne sono necessari.

Medical therapy

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ACEI meta-analysis[12]	Mortality and HF hospitalizations	OR, 0.78 (0.59–1.04)	OR, 0.63 (0.55–0.73)
ACEI meta-analysis[13]	Mortality	RR, 0.92 (0.81–1.04)	RR, 0.82 (0.74–0.90)
ARB			
Val-HeFT*	Mortality	HR, 0.93 (0.68–1.27)	HR, 1.04 (0.90–1.19)
Val-HeFT*	HF hospitalizations	HR, 0.74 (0.55–0.98)	HR, 0.73 (0.62–0.86)
CHARM trials*	CV mortality or HF hospitalization	HR, 0.81 (0.67–0.98)	HR, 0.82 (0.73–0.91)
ELITE II[18]	Mortality	HR, 1.14 (0.8–1.8)	HR, 1.12 (0.9–1.4)
ARNI			
PARADIGM-HF[10]	CV mortality or HF hospitalization	Not reported but *P* value for interaction=0.63	Not reported but *P* value for interaction=0.63
Aldosterone blockers			
Meta-analysis[19]	CV mortality or HF hospitalization	aHR, 0.73 (0.62–0.86)	aHR, 0.69 (0.62–0.77)
Nitrate+hydralazine			
A-HEFT[20]	Mortality	HR, 0.33 (0.16–0.71)	HR, 0.79 (0.46–1.35)
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B-blocker therapy			
US Carvedilol HF[21]	Mortality	HR, 0.23 (0.07–0.69)	HR, 0.41 (0.22–0.80)
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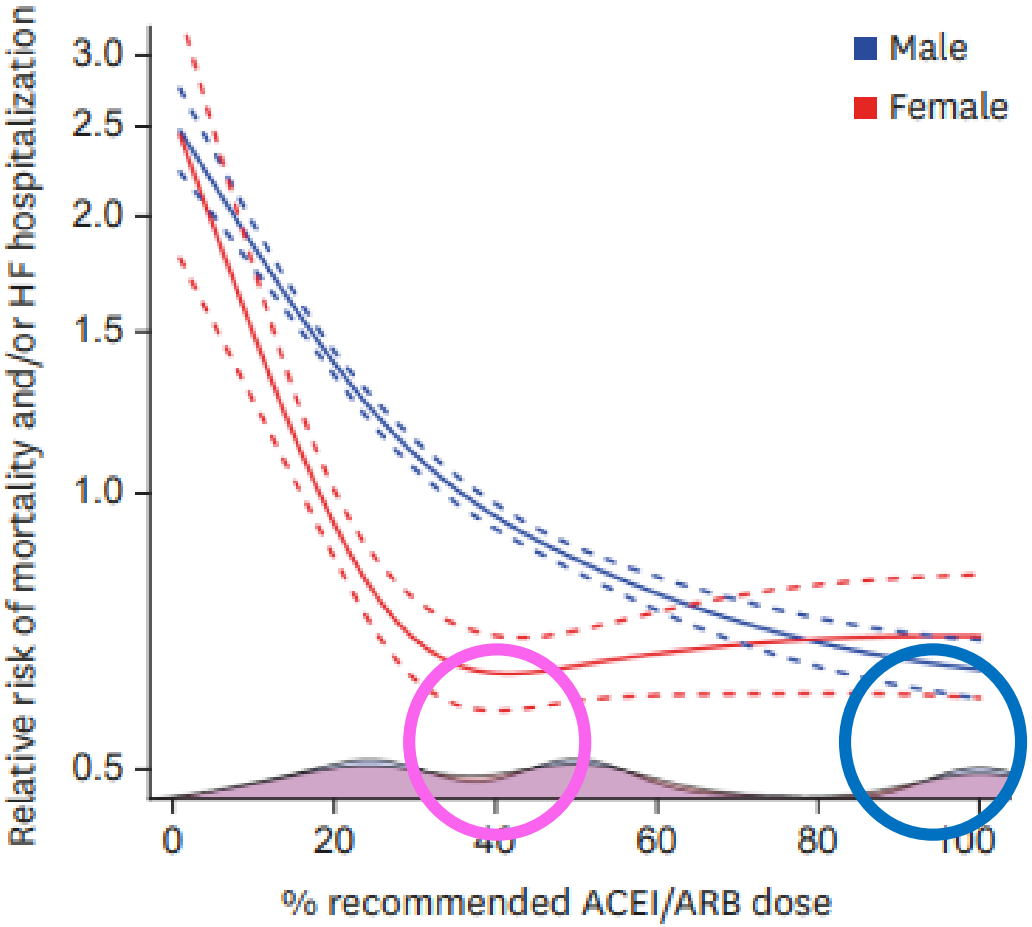
ACEI

Nei primi studi multicentrici, ad es. CONSENSO I, SAVE e SOLVD, ACEI hanno portato a risultati molto più piccoli riduzione della mortalità nelle donne rispetto agli uomini. Anche i successivi studi AIRE e HOPE
come una serie di studi più piccoli, hanno mostrato un beneficio significativo degli ACEI nelle donne, suggerendo che beneficiano del trattamento tanto quanto gli uomini.

2 ampie meta-analisi sugli ACEI (inibitori dell'enzima di conversione dell'angiotensina) non hanno mostrato alcun beneficio definitivo di un ACEI nelle donne

Medical therapy



Più recentemente, lo studio BIOSTAT HF ha suggerito che le donne con HFrEF raggiungevano gli stessi effetti del trattamento, ovvero mortalità e riduzione degli eventi cardiovascolari, con dosi più basse rispetto agli uomini e non traggono beneficio dall'aumento della dose alle dosi raccomandate dalle linee guida

Medical therapy

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ARNI			
PARADIGM-HF[10]	CV mortality or HF hospitalization	Not reported but *P* value for interaction=0.63	Not reported but *P* value for interaction=0.63
Aldosterone blockers			
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SGLT2 inhibitors			
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Angiotensin II receptor blockers (ARB)

Medical therapy

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ARNI			
PARADIGM-HF[10]	CV mortality or HF hospitalization	Not reported but *P* value for interaction=0.63	Not reported but *P* value for interaction=0.63
Aldosterone blockers			
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Sacubitril-valsartan

Recentemente, in un ampio studio randomizzato sono state riscontrate differenze sessuali del tutto insospettate studio controllato (RCT), che confrontava la combinazione inibitore della neprilisina/ARB sacubitril valsartan e ARB valsartan in pazienti con HFpEF.
L'inibizione della neprilisina aumenta peptidi natriuretici endogeni biologicamente attivi e altri composti vasoattivi, con una maggiore generazione di cGMP, una molecola di segnalazione che è ridotta in HFpEF, ed è benefico nell'HFEF.
Sacubitril-valsartan non ha comportato un tasso significativamente più basso di ricoveri totali per scompenso cardiaco e morte per cause cardiovascolari in una coorte mista dei pazienti con HFpEF/HFmEF. ***Tuttavia, ha portato a una riduzione significativa del tasso di eventi rispetto a valsartan nelle donne, che non è stato osservato negli uomini.*** Pertanto, il farmaco è risultato efficace nelle donne, ma non negli uomini.

Medical therapy

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Antagonisti dei recettori dell'aldosterone

Un primo studio non ha riscontrato differenze nell'effetto dello spironolattone sullo scompenso cardiaco sintomatico uomini e donne.
Tuttavia solo il 30% dei pazienti arruolati erano donne e il lo studio non aveva la potenza necessaria per rilevare le differenze di sesso.
EPHESUS, maggiore beneficio per le donne, trattate con eplerenone, a 30 giorni non confermato 16 mesi.

In TOPCAT, i soggetti conHF sintomatico e una FE LV ≥45% sono stati randomizzati a spironolattone o placebo. In un'analisi post hoc di sottogruppo, in cui sono stati analizzati solo i soggetti arruolati dalle Americhe la terapia con spironolattone è stata associata a una riduzione della mortalità per tutte le cause nelle donne

Medical therapy

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Nitrati ed idralazina

La sottorappresentazione delle donne negli studi clinici ha stata un'altra preoccupazione con alcuni studi come V-HeFT Non incluso donne quando confrontavano prazosina, isosorbide e idralazina con il placebo in pazienti con scompenso cardiaco.

Isosorbide e l'idralazina sono stati studiati solo nelle donne partecipanti nell'A-HEFT (African American HF Trial) ma non l'hanno fatto è stato studiato tra donne con HFrEF di altre razze.
Nello studio A-HEFT, che ha coinvolto 420 donne con sintomi di scompenso cardiaco moderatamente gravi (New York Heart Association [NYHA] classe III-IV) già in terapia medica secondo le linee guida,la combinazione di terapia con isosorbide e idralazina riduzione della mortalità e dell'ospedalizzazione per scompenso cardiaco. Si è verificata miglioramento della qualità della vita con il trattamento.

Medical therapy

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Ivabradina

è raccomandato per i pazienti sintomatici con HFrEF in ritmo sinusale normale con frequenza cardiaca a riposo ≥ 70 battiti al minuto nonostante la massima terapia con β-bloccanti.

Basato sullo SHIFT che ha coinvolto 1535 donne, ridotto endpoint combinato di morte cardiovascolare e ospedalizzazione per scompenso cardiaco nelle donne e hanno avuto benefici simili negli uomini

Medical therapy

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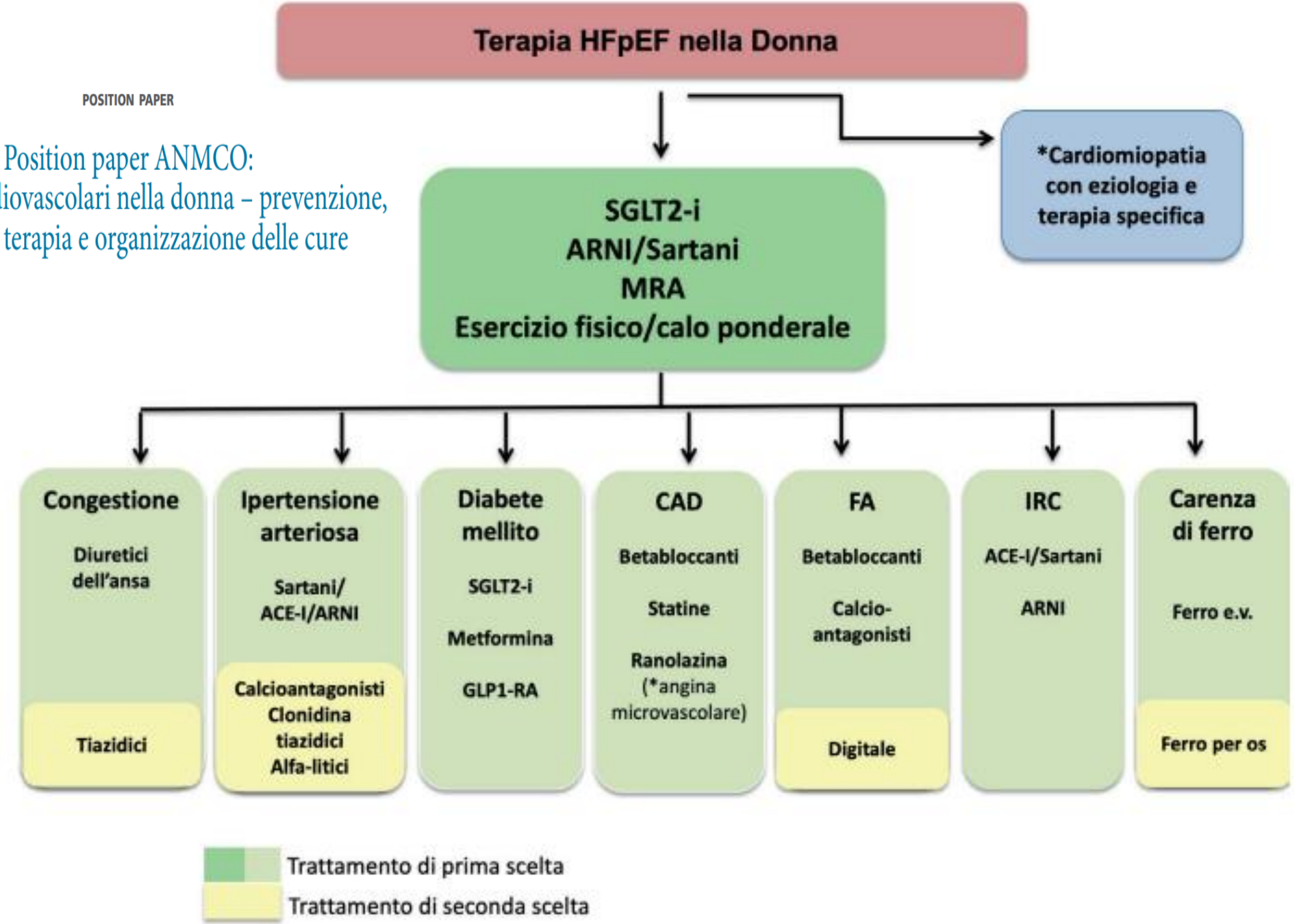
Study	End point	Risk (95% CI)	
		Women	Men
ACEI			
ACEI meta-analysis[12]	Mortality	OR, 0.79 (0.59–1.06)	OR, 0.76 (0.65–0.88)
ACEI meta-analysis[12]	Mortality and HF hospitalizations	OR, 0.78 (0.59–1.04)	OR, 0.63 (0.55–0.73)
ACEI meta-analysis[13]	Mortality	RR, 0.92 (0.81–1.04)	RR, 0.82 (0.74–0.90)
ARB			
Val-HeFT*	Mortality	HR, 0.93 (0.68–1.27)	HR, 1.04 (0.90–1.19)
Val-HeFT*	HF hospitalizations	HR, 0.74 (0.55–0.98)	HR, 0.73 (0.62–0.86)
CHARM trials*	CV mortality or HF hospitalization	HR, 0.81 (0.67–0.98)	HR, 0.82 (0.73–0.91)
ELITE II[18]	Mortality	HR, 1.14 (0.8–1.8)	HR, 1.12 (0.9–1.4)
ARNI			
PARADIGM-HF[10]	CV mortality or HF hospitalization	Not reported but *P* value for interaction=0.63	Not reported but *P* value for interaction=0.63
Aldosterone blockers			
Meta-analysis[19]	CV mortality or HF hospitalization	aHR, 0.73 (0.62–0.86)	aHR, 0.69 (0.62–0.77)
Nitrate+hydralazine			
A-HEFT[20]	Mortality	HR, 0.33 (0.16–0.71)	HR, 0.79 (0.46–1.35)
A-HEFT[20]	Mortality or HF hospitalization	HR, 0.58(0.39–0.86)	HR, 0.67 (0.49–0.92)
B-blocker therapy			
US Carvedilol HF[21]	Mortality	HR, 0.23 (0.07–0.69)	HR, 0.41 (0.22–0.80)
COPERNICUS[22]	Mortality	RR, 0.63 (0.39–1.04)	RR, 0.68 (0.54–0.86)
CIBIS II[23]	Mortality	RH, 0.53 (0.42–0.67)	RH, 0.37 (0.19–0.69)
MERIT-HF[24]	Mortality	RR, 0.93 (0.58–1.49)	RR, 0.63 (0.50–0.78)
Ivabradine			
Ivabradine[25]	CV mortality or HF hospitalization	HR, 0.74 (0.60–0.91)	HR, 0.84 (0.76–0.94)
Digitalis			
Digitalis[26]	Mortality	aHR, 1.23 (1.02–1.47)	aHR, 0.93 (0.85–1.02)
Digitalis[26]	HF hospitalizations	HR, 0.87 (0.72–1.04)	HR, 0.66 (0.60–0.73)
SGLT2 inhibitors			
DAPA-HF[11]	HF hospitalization, IV therapy, or CV mortality	HR, 0.79 (0.59–1.06)	HR, 0.73 (0.63–0.85)
EMPEROR-Reduced[17]	CV mortality or HF hospitalization	HR, 0.59 (0.44–0.80)	HR, 0.80 (0.68–0.93)

Gli SGLT2

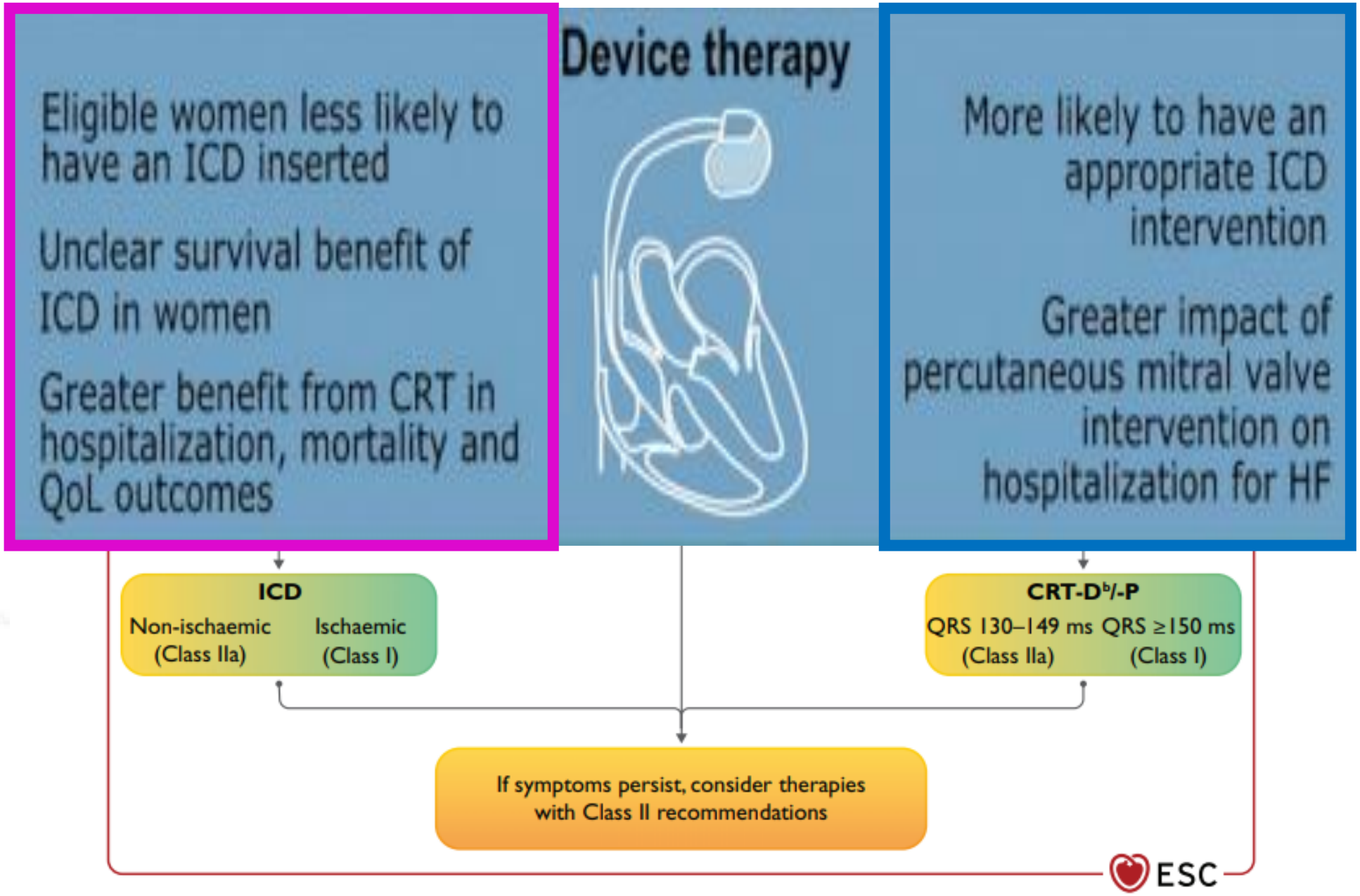
sono indicati nei pazienti con
scompenso sintomatico con o senza diabete di tipo II. In EMPEROR-Ridotto (Empagliflozin Outcome Trial in Pazienti con scompenso cardiaco cronico e frazione di eiezione ridotta), empagliflozin ha ridotto un endpoint combinato di morte cardiovascolare o ospedalizzazione per scompenso cardiaco tra gli 893
donne partecipanti.
Dapagliflozin è un altro SGLT2i con dati limitati specifici per sesso, che hanno mostrato tra i 1109 donne con HFrEF una tendenza alla riduzione l'endpoint combinato di ricoveri per scompenso cardiaco, terapia ambulatoriale endovenosa per scompenso cardiaco o morte cardiovascolare
nello studio DAPA-HF (Dapagliflozin e Prevenzione di Risultati avversi nello scompenso cardiaco).
Questi studi dimostrano alcuni benefici nonostante la sottorappresentanza delle donne HFrEF

POSITION PAPER

Position paper ANMCO:
Malattie cardiovascolari nella donna – prevenzione, diagnosi, terapia e organizzazione delle cure



DEVICE Therapy



Altro…

Cardiac Amyloid

80-90% of patients with ATTR amyloid are men

At presentation, women with higher LVEF and lower wall thickness

Hypertrophic Cardiomyopathy

Women are typically older and more symptomatic at first evaluation

Women are more likely to have obstructive physiology

Greater mortality in women

Cardiac Sarcoid

Lower endomyocardial biopsy utilization for diagnosis in women

Women have lower rates of ventricular arrhythmias and less ICD implantation

Higher in-hospitality mortality in women

Stress Cardiomyopathy

Emotional stress predominant trigger in women, physical stress predominant trigger in men

Male sex is a predictor of adverse events including cardiovascular death, heart failure and ventricular arrhythmias

Concludendo

- *Pattern specifici di scompenso*
- *Variazioni ormonali*
- *Terapia diversificata*
- *Diversa risposta alle terapie con Device*