



ACCADEMIA di  
ALTA FORMAZIONE CLINICA  
per MEDICI del TERRITORIO

# Accademia di Alta Formazione Clinica per Medici del Territorio

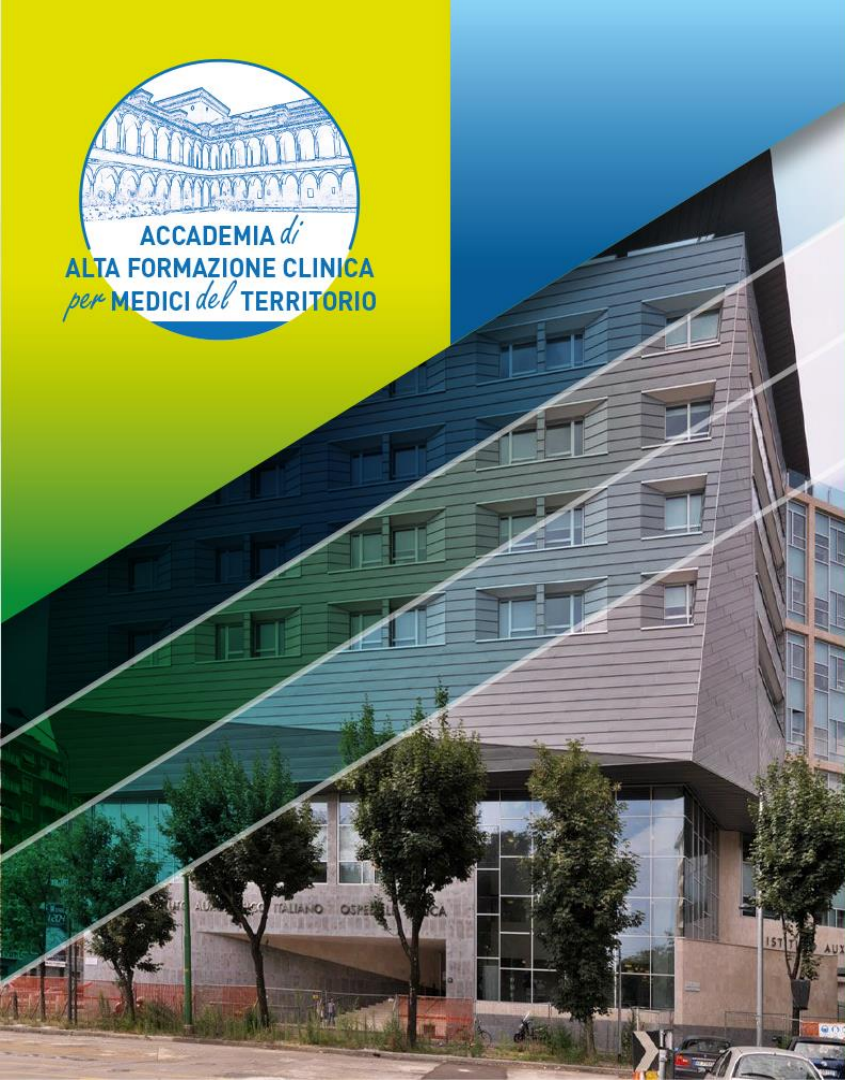
*In memoria del Maestro Alberto Zanchetti*

**TERZO PERCORSO FORMATIVO - ANNO 2024**

Responsabile Scientifico  
**Fabio Lucio Albini**

**Auxologico**  
IRCCS

Milano, Istituto Auxologico Italiano IRCCS Ospedale San Luca



# Lo Scompenso diastolico nelle varie classi NYHA.

L'importanza di offrire con gli SGLT2i  
una protezione cardio-  
nefro-metabolica ai pazienti con  
Insufficienza Cardiaca

Dott. Sergio Caravita

Cosa c'è in un nome?

Ciò che chiamiamo rosa anche con  
un altro nome conserva sempre il  
suo profumo

*W Shakespeare*

# SCOMPENSO DIASTOLICO: COSA C'E' IN UN NOME

Scompenso diastolico

Insufficienza cardiaca diastolica

Insufficienza cardiaca a normale frazione di eiezione

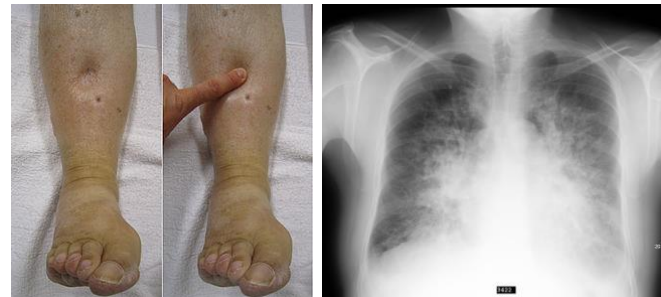
Insufficienza cardiaca a frazione di eiezione preservata

= Heart Failure with preserved Ejection Fraction (HFpEF)



Sindrome clinica caratterizzata da

- sintomi (dispnea da sforzo, faticabilità...) e/o
  - segni (edemi declivi, congestione polmonare...)
- secondari a disfunzione diastolica del ventricolo sinistro

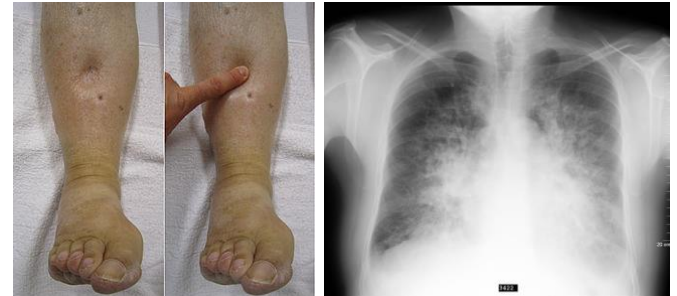


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Sindrome clinica caratterizzata da

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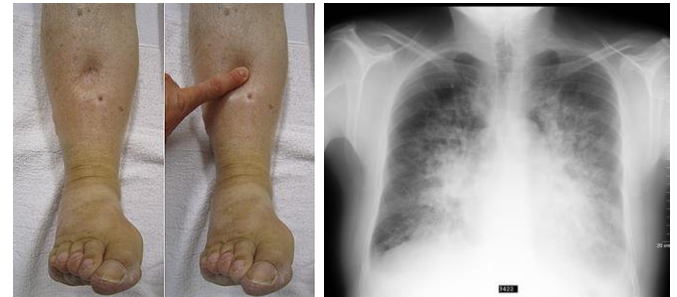


# SCOMPENSO DIASTOLICO: COSA C'E' IN UN NOME



Sindrome clinica caratterizzata da

- sintomi (dispnea da sforzo, faticabilità...) e/o
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- secondari a **disfunzione diastolica del ventricolo sinistro**



# SCOMPENSO DIASTOLICO: PATOGENESI

## Forme «primitive»

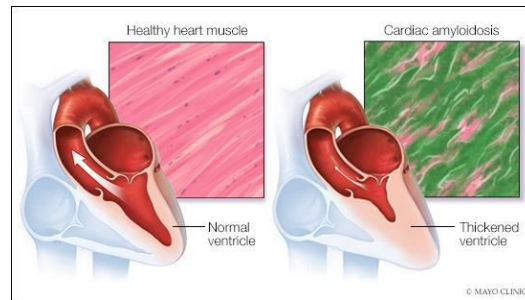
Meccanismi biomolecolari complessi, caratterizzati da

- Infiammazione sistemica
- alterazioni funzionali e strutturali (fibrosi interstiziale)

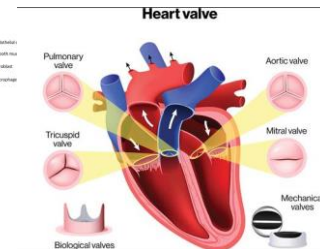
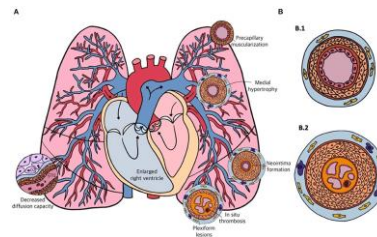
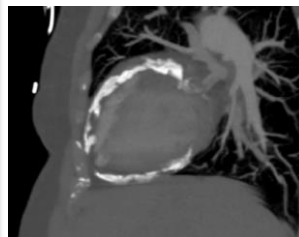
del ventricolo sinistro

Associati a **invecchiamento cardiovascolare!** E comorbilità / stile di vita (fumo, sedentarietà, obesità, diabete, ipertensione, sindrome metabolica, steatosi epatica, insufficienza renale cronica...)

## Forme secondarie di scompenso diastolico (es amiloidosi cardiaca)

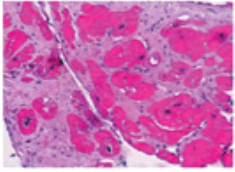


## Mimickers (costrizione pericardica, malattie vascolari polmonari, valvulopatie)



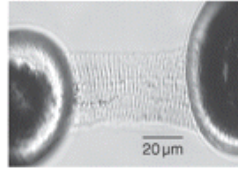
# SCOMPENSO DIASTOLICO: FISIOPATOLOGIA

## Alterazioni strutturali (fibrosi)



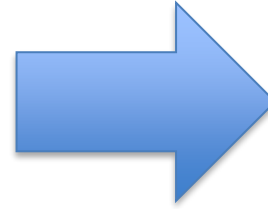
- Extracellular matrix
- Amount of collagen
- Abundance of collagen type 1
- Collagen cross-linking

## Alterazioni funzionali (cardiomiociti)

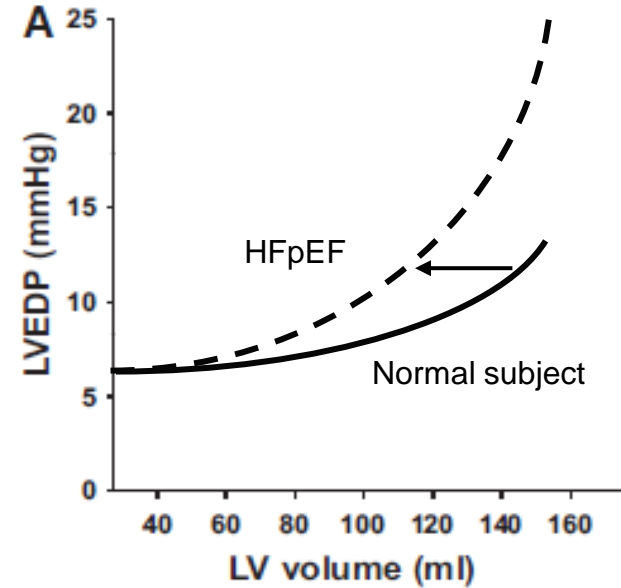


- Cardiomyocytes
- Ca<sup>2+</sup> removal
- Cross-bridge detachment
  - High-energy phosphates
- Cytoskeletal protein titin
  - Isoform shifts
  - Phosphorylation
  - Oxidation

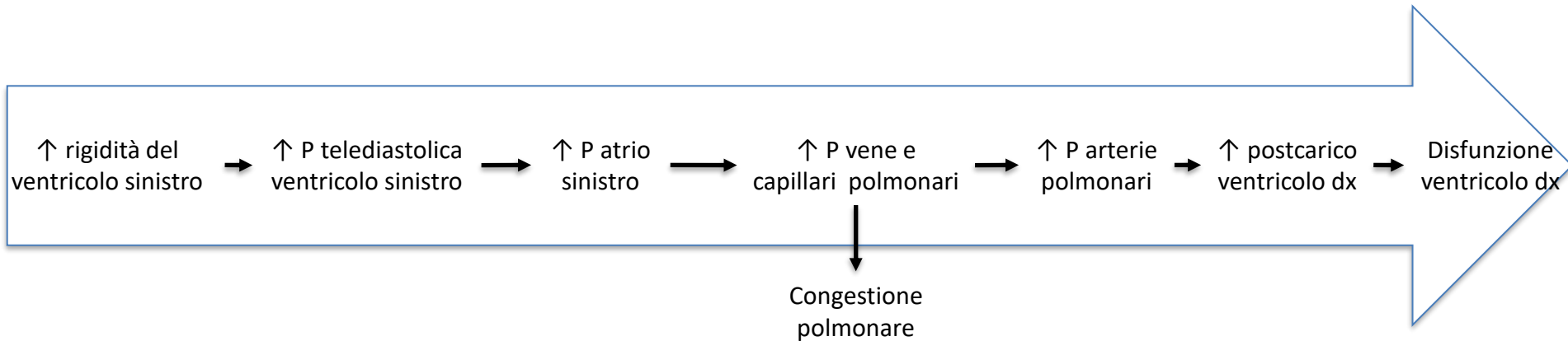
Matricellular proteins



## Diastolic pressure-volume relationship

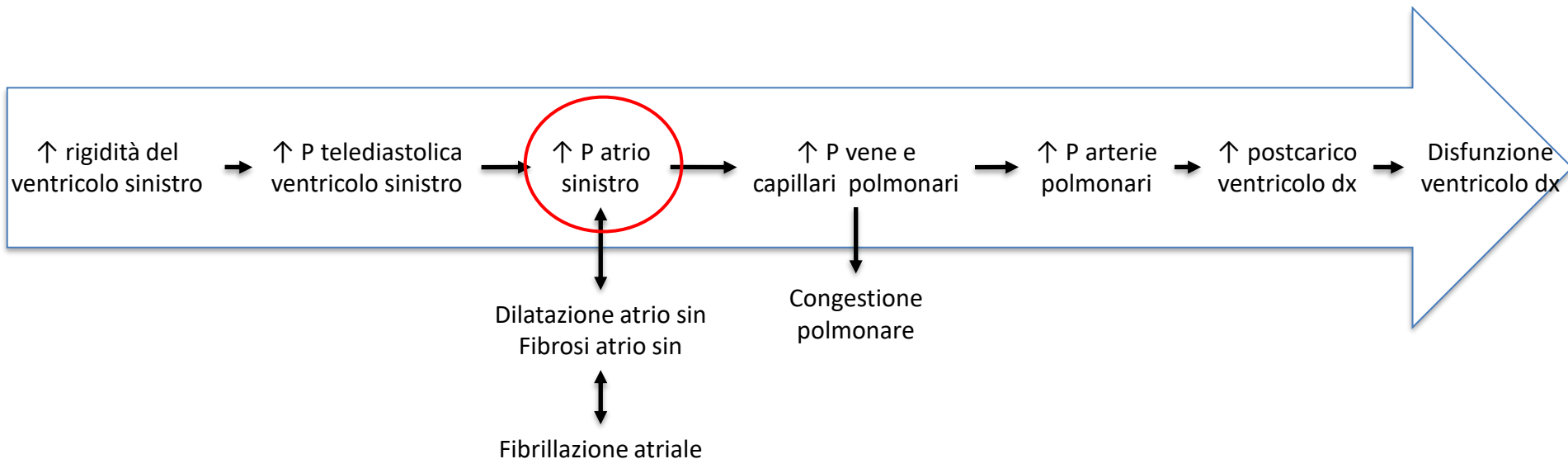


# DALLA DISFUNZIONE DIASTOLICA VS, ALLA DISFUNZIONE VD

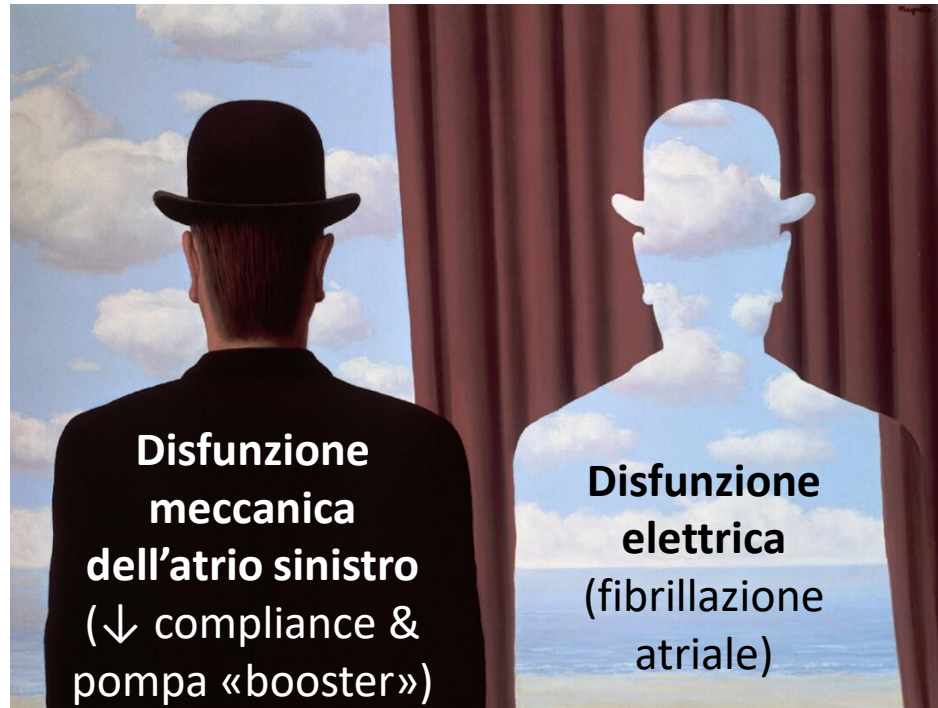


# IL PUNTO DI VISTA DELL'ATRIO SINISTRO

Camera cardiaca dalle pareti sottili, che ci prova a mantenere il sistema «compensato»



## Le due facce della fibrosi dell'atrio sinistro



# Le due facce della fibrosi dell'atrio sinistro

↑ rigidità del  
ventricolo sinistro



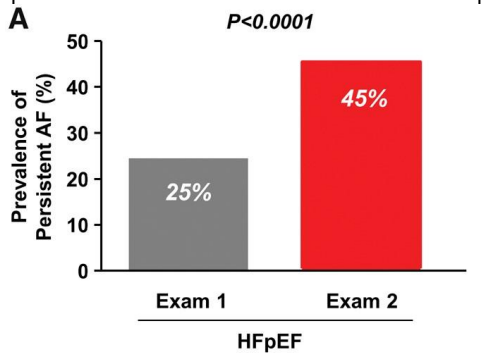
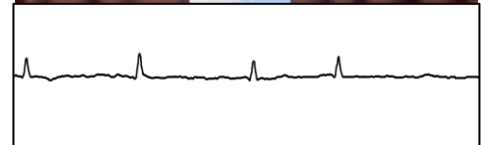
**Disfunzione  
meccanica  
dell'atrio sinistro  
(↓ compliance &  
pompa «booster»)**

**Disfunzione  
elettrica  
(allargazione  
del QTc)**

Disfunzione  
ventricolo dx

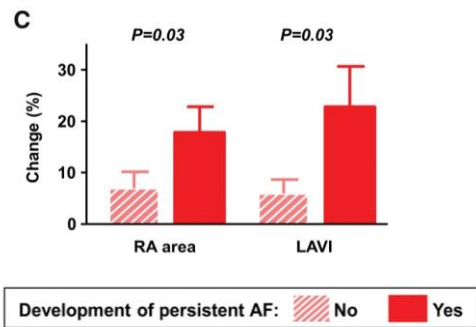
# La fibrillazione atriale e l'HFpEF

## Fibrillazione atriale

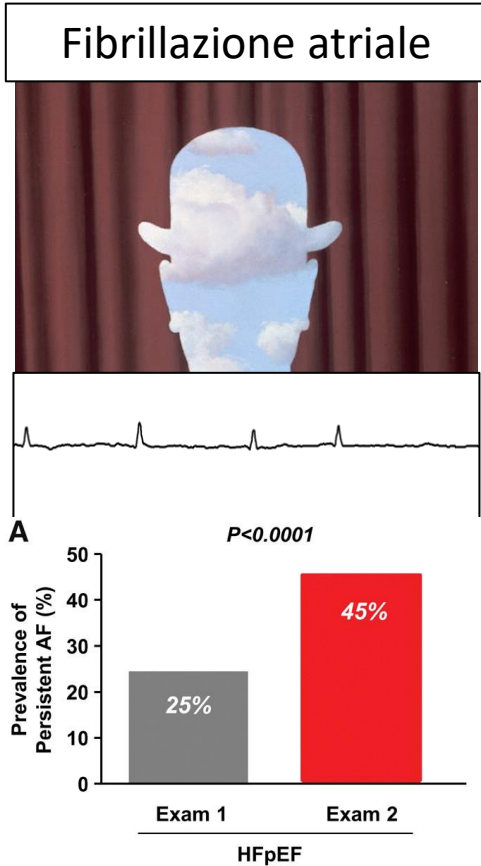


Sovraccarico  
volemico

Dilatazione bi-atriale

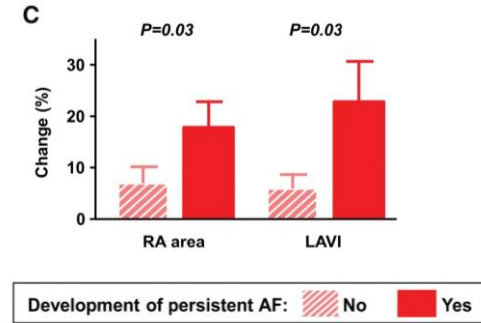


# La fibrillazione atriale e l'HFpEF

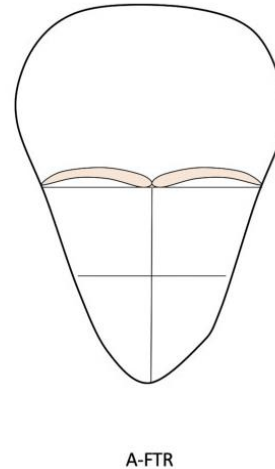


Sovraccarico  
volemico

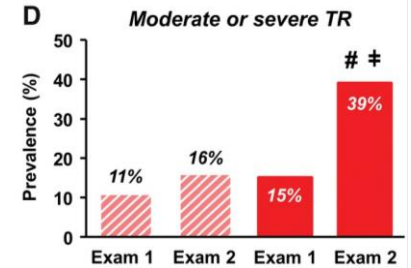
Dilatazione bi-atriale!



Rimodellamento  
dell'anello  
tricuspidale

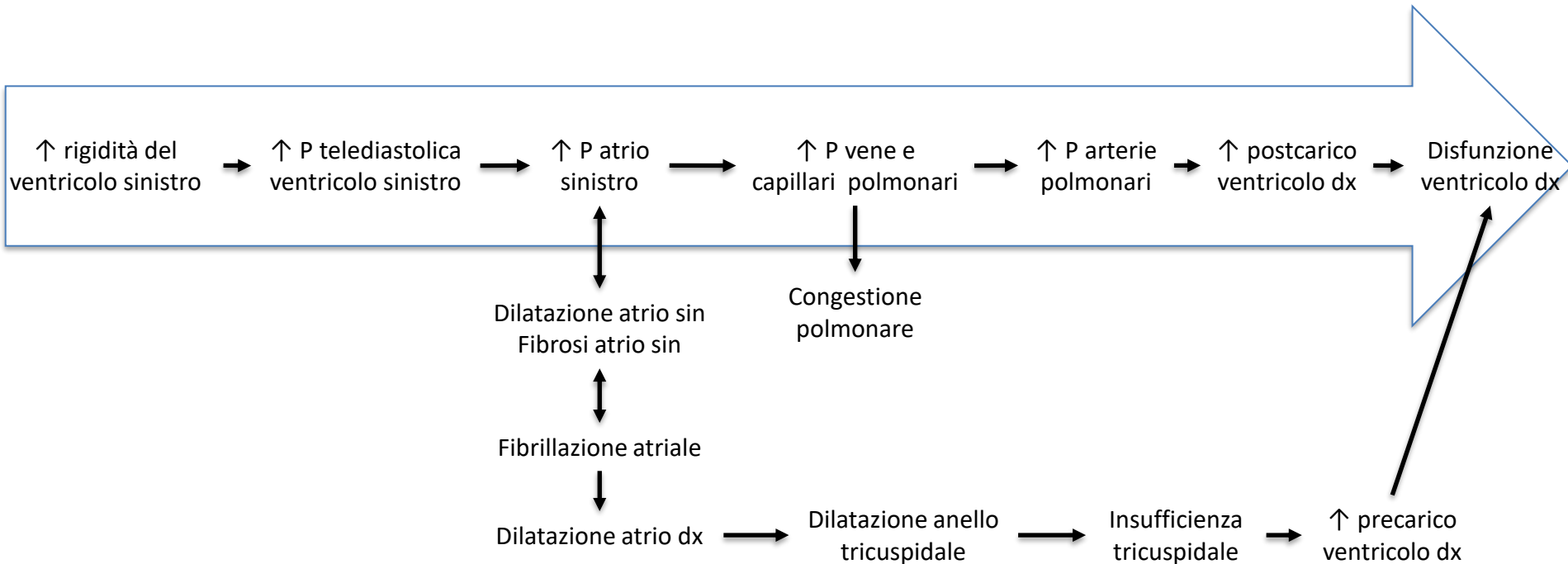


Insufficienza  
tricuspidale

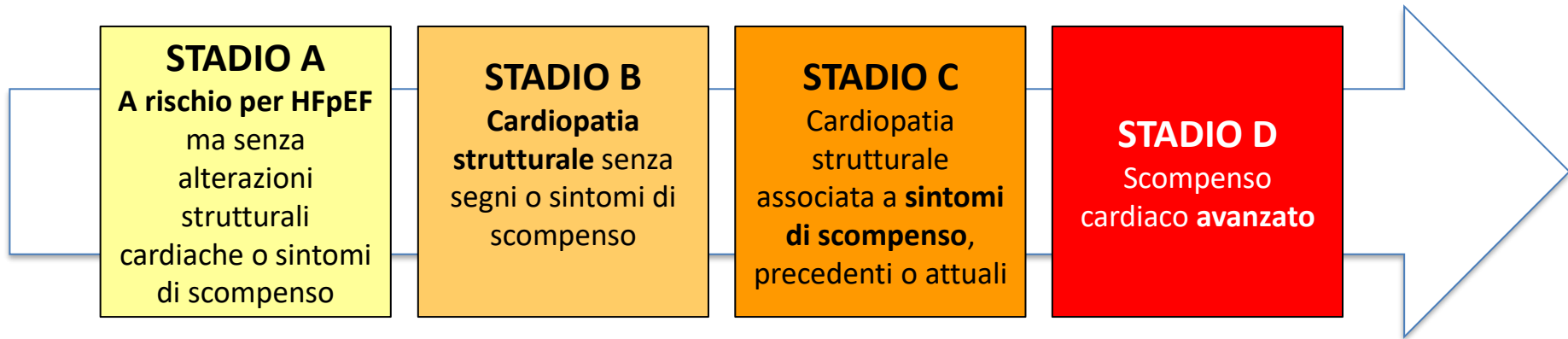


**Disfunzione  
ventricolare destra  
indipendente  
dall'ipertensione  
polmonare**

# DALLA DISFUNZIONE DIASTOLICA VS, ALLA DISFUNZIONE VD



# SCOMPENSO DIASTOLICO: STADIAZIONE



# SCOMPENSO DIASTOLICO: STADIAZIONE E SINTOMI

## STADIO A

A rischio per HFpEF  
ma senza  
alterazioni  
strutturali  
cardiache o sintomi  
di scompenso

## STADIO B

Cardiopatia  
strutturale senza  
segni o sintomi di  
scompenso

## STADIO C

Cardiopatia  
strutturale  
associata a sintomi  
di scompenso,  
precedenti o attuali

## STADIO D

Scompenso  
cardiaco avanzato

## NYHA I

Non sintomi o  
limitazione  
dell'attività di vita  
ordinaria

## NYHA II

Lieve limitazione /  
sintomi nell'attività  
di vita ordinaria

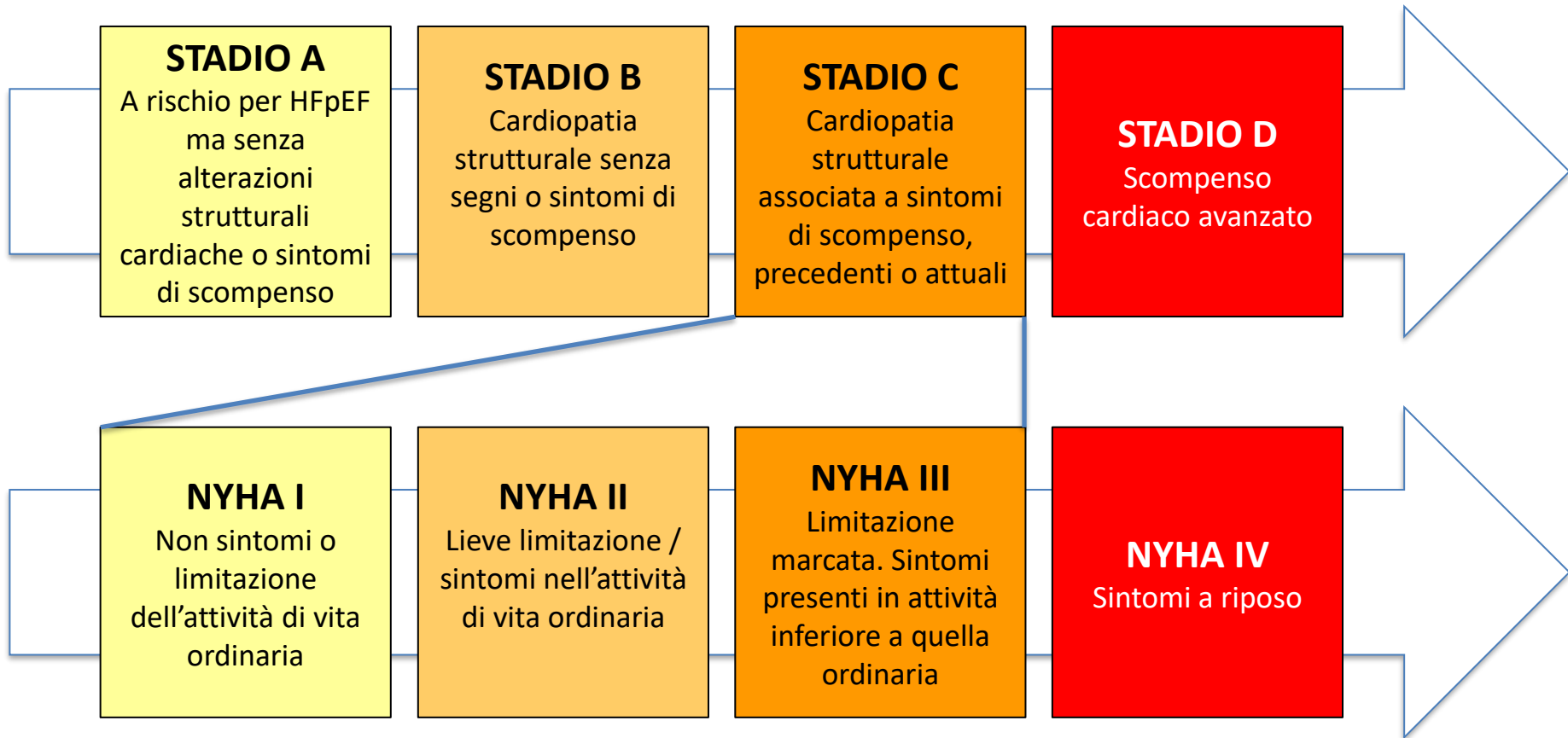
## NYHA III

Limitazione  
marcata. Sintomi  
presenti in attività  
inferiore a quella  
ordinaria

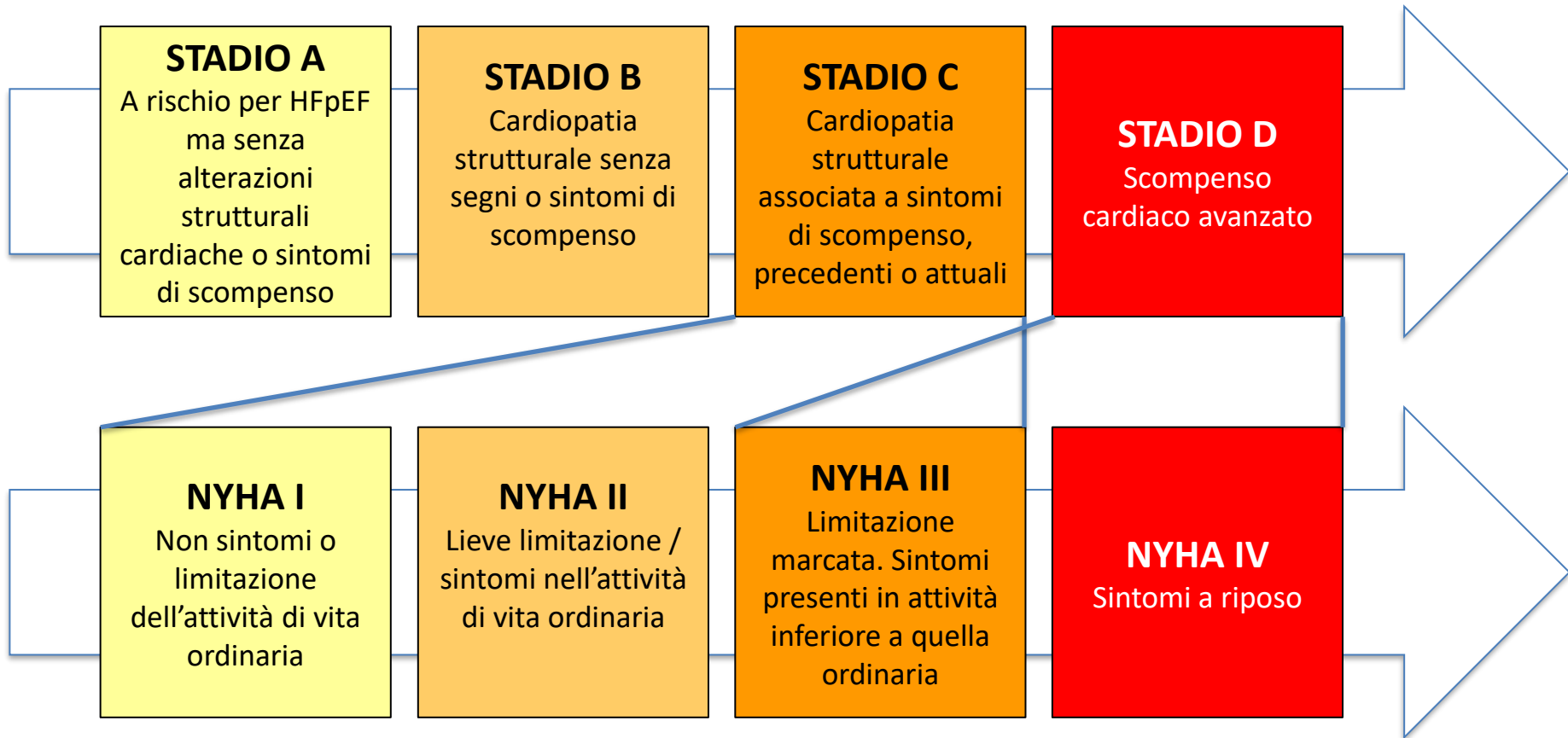
## NYHA IV

Sintomi a riposo

# SCOMPENSO DIASTOLICO: STADIAZIONE E SINTOMI



# SCOMPENSO DIASTOLICO: STADIAZIONE E SINTOMI



# SCOMPENSO DIASTOLICO: COSA C'E' IN UN NOME

Scompenso diastolico

Insufficienza cardiaca diastolica

Insufficienza cardiaca a normale frazione di eiezione

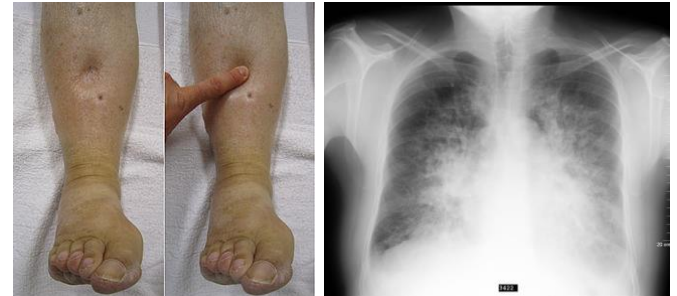
Insufficienza cardiaca a frazione di eiezione preservata

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Sindrome clinica caratterizzata da

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# SCOMPENSO DIASTOLICO: COSA C'E' IN UN NOME

Scompenso diastolico

Insufficienza cardiaca diastolica

Insufficienza cardiaca a normale frazione di eiezione

Insufficienza cardiaca a frazione di eiezione preservata

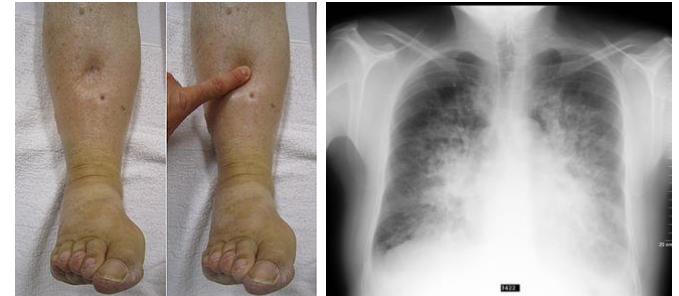
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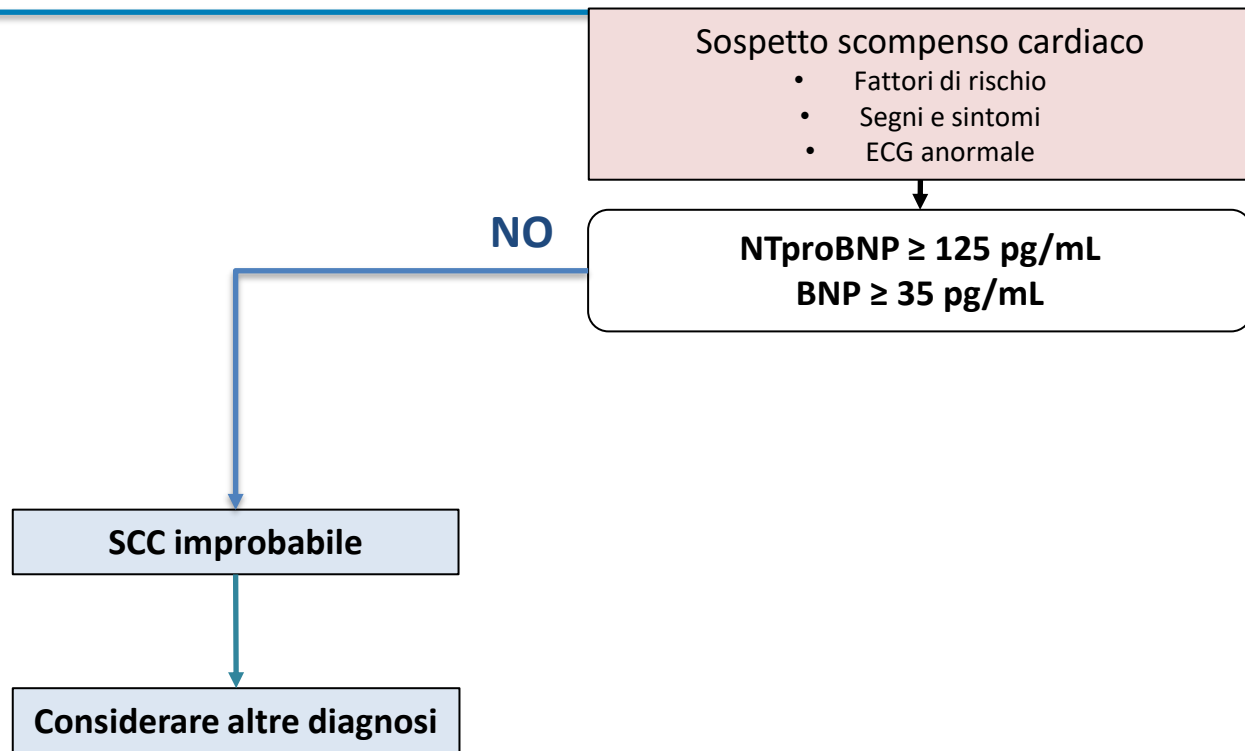
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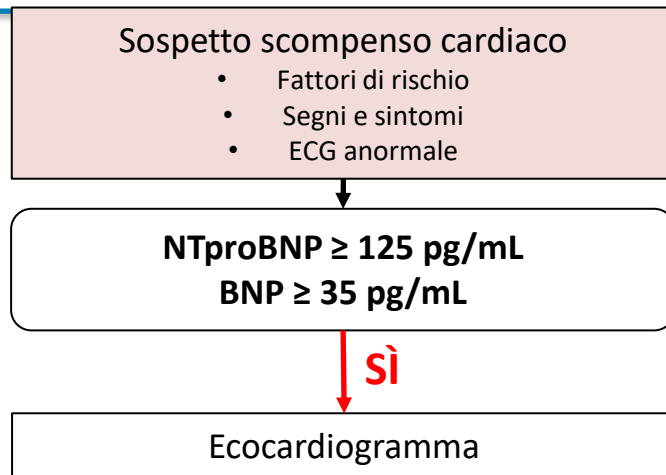
**secondari a disfunzione diastolica del ventricolo sinistro**



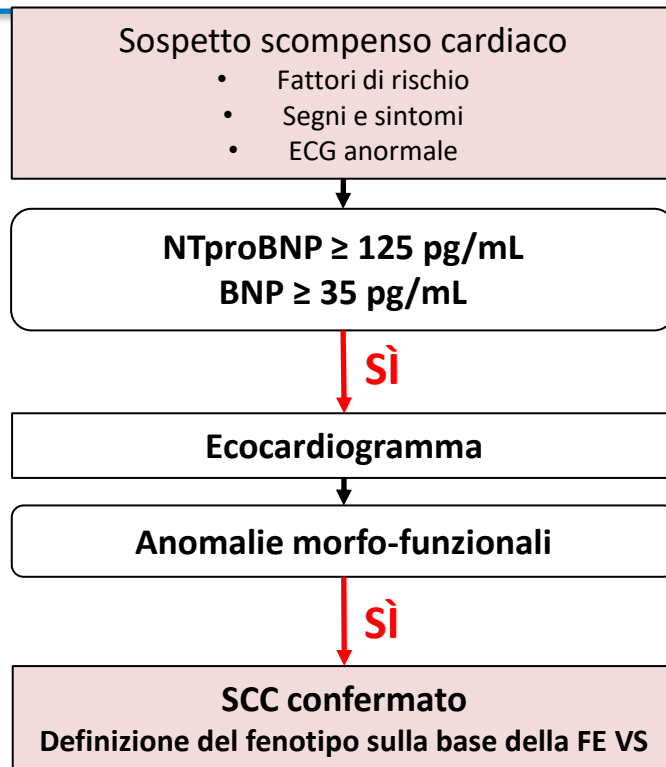
# La diagnosi di HFpEF: il punto di vista delle linee guida sullo SCC



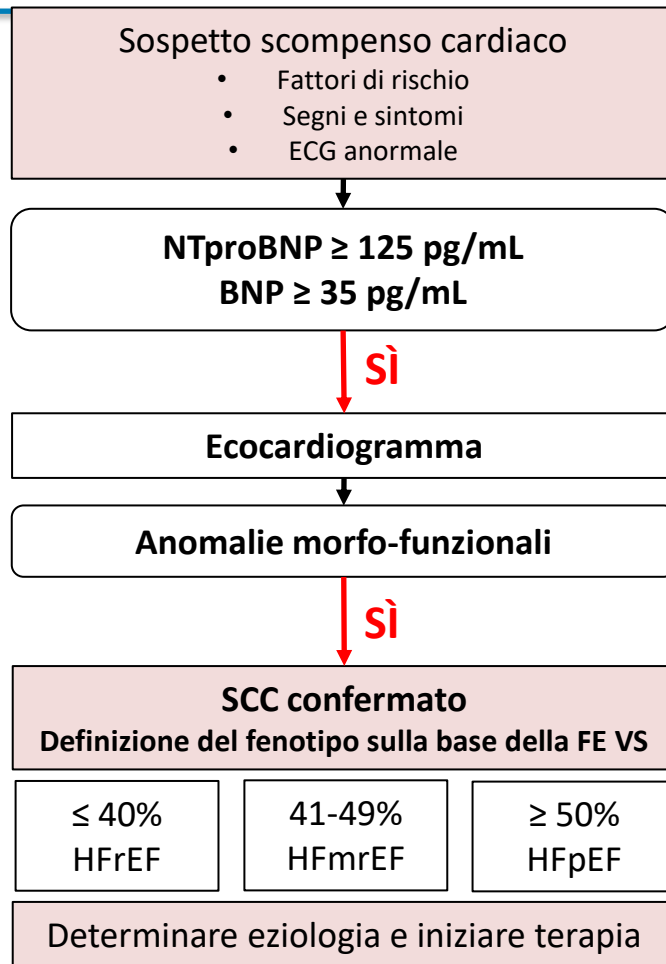
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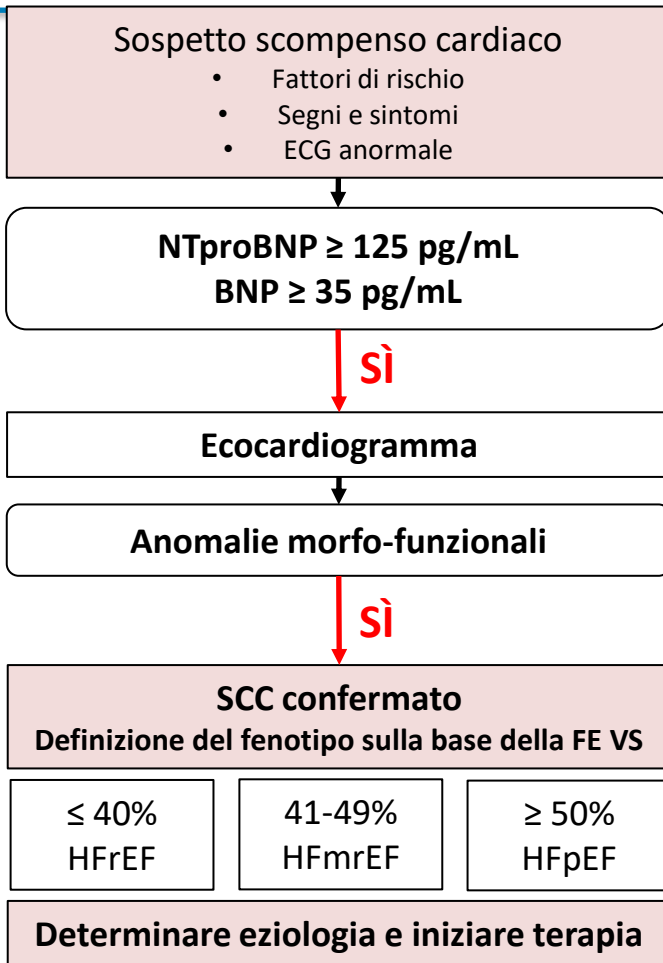
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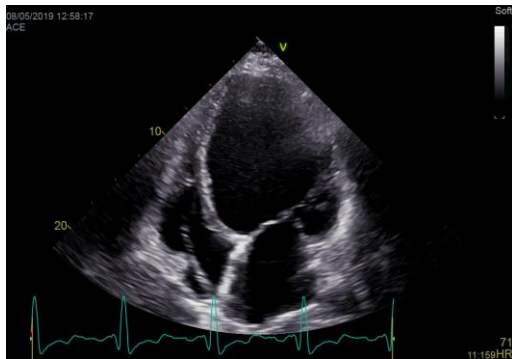
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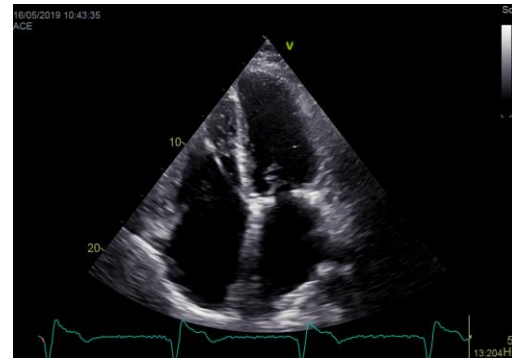
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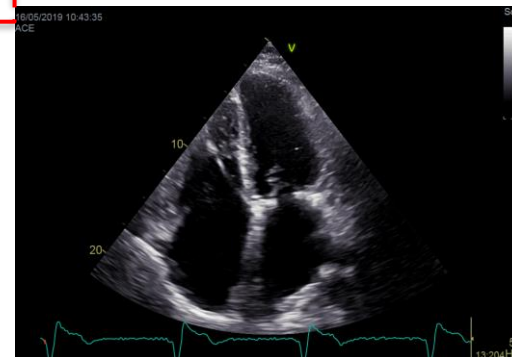
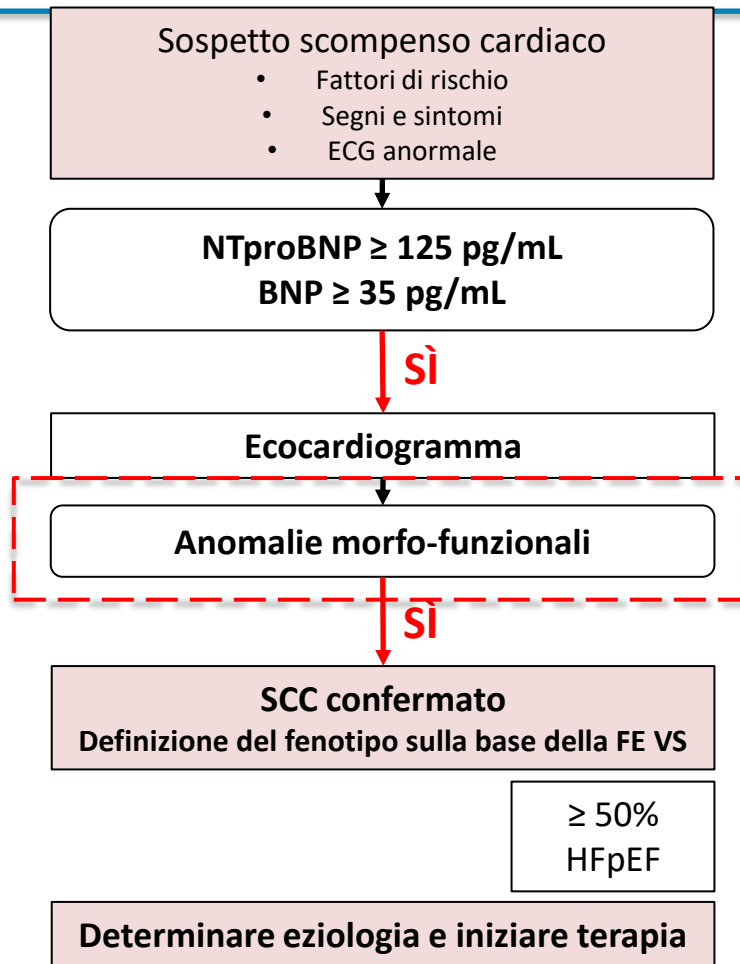
«Disfunzione sistolica (+ alte pressioni di riempimento)»



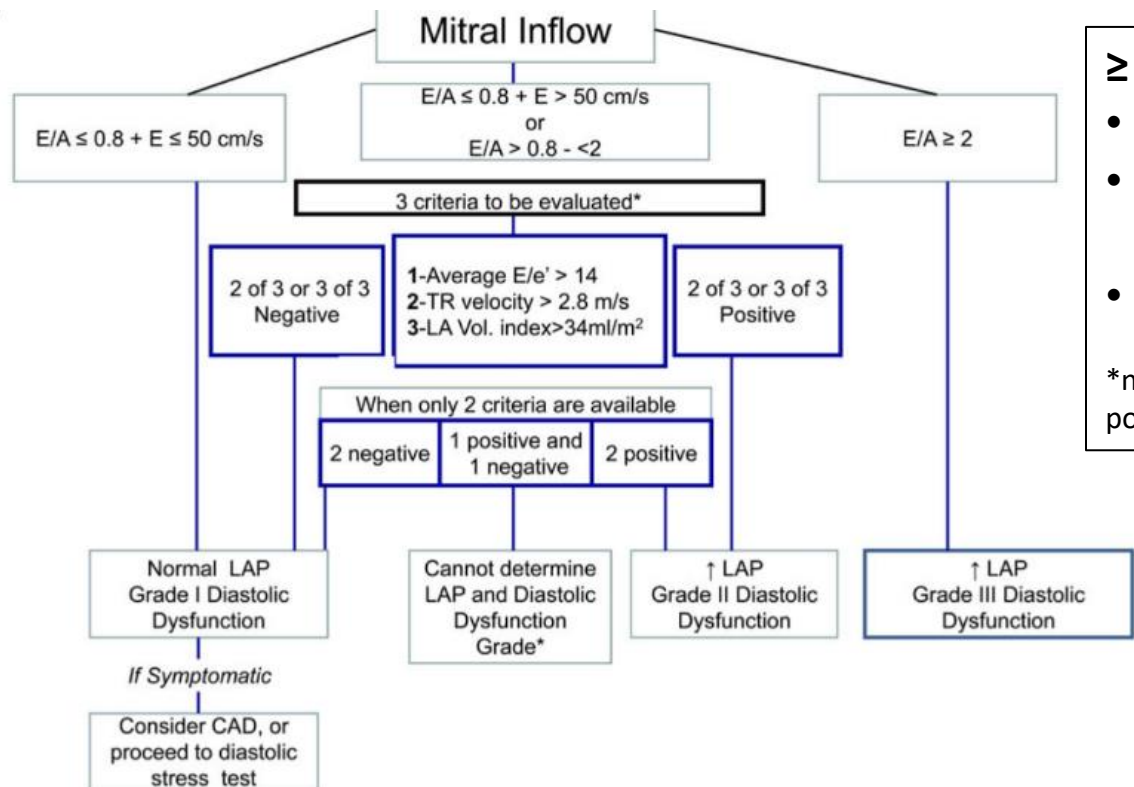
«Alte pressioni di riempimento (disfunzione diastolica)»



# La diagnosi di HFpEF: il punto di vista delle linee guida sullo SCC



# Anomalie morfo-funzionali cardiache all'ecocardiogramma

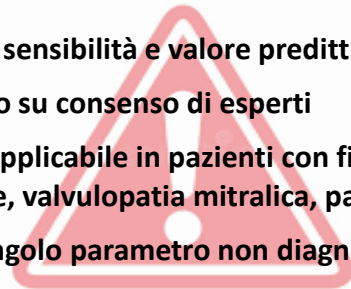


**≥ 2 parametri tra:**

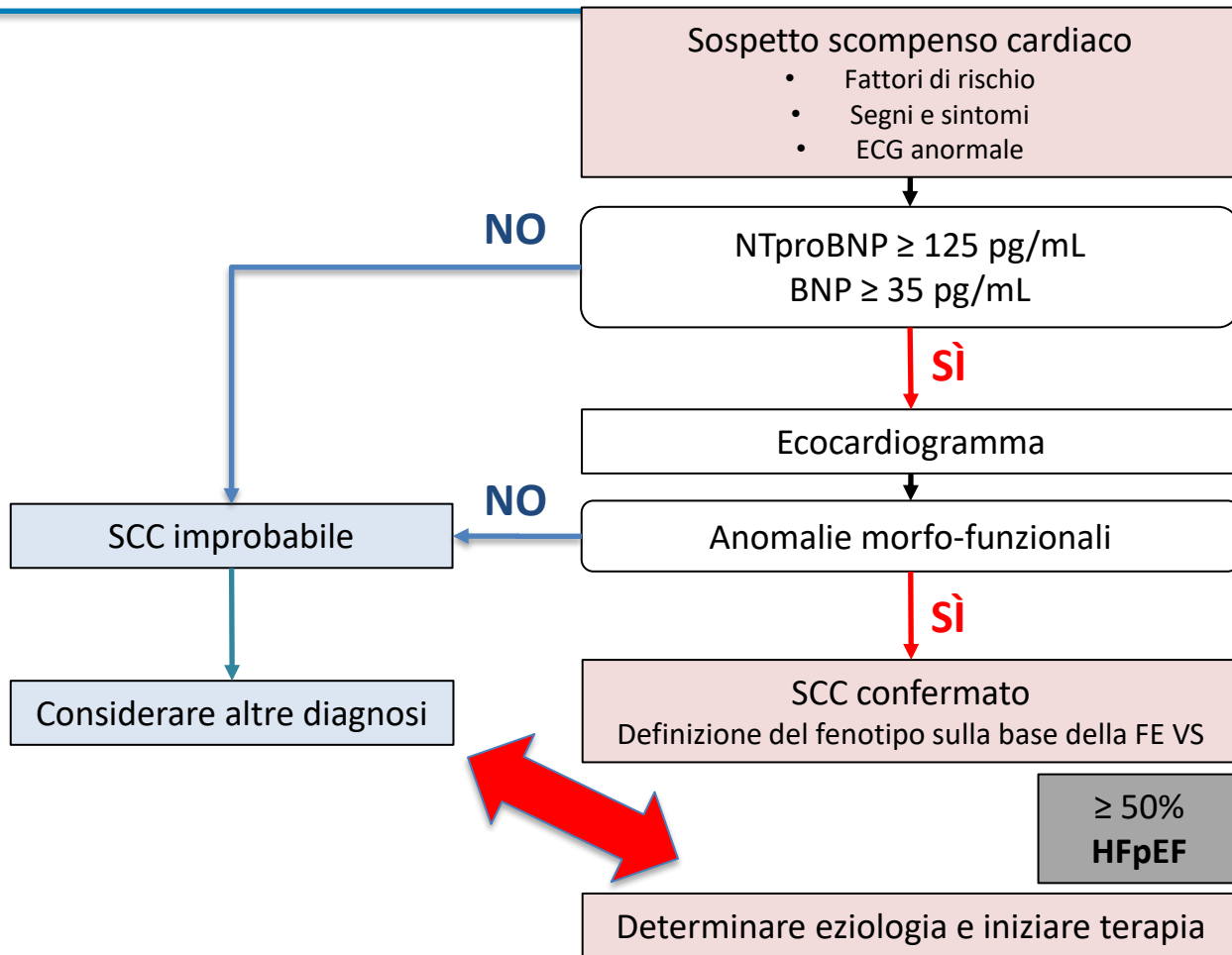
- $E/e' > 14$
- Velocità di rigurgito tricuspide  $> 2.8 \text{ m/s}$  (=PAPs  $> 35 \text{ mmHg}$ )\*
- Volume AS  $> 34 \text{ mL/m}^2$

\*non vale se c'è il sospetto di una malattia vascolare polmonare

- **Bassa sensibilità e valore predittivo negativo**
- **Basato su consenso di esperti**
- **Non applicabile in pazienti con fibrillazione atriale, valvulopatia mitralica, pacemaker**
- **Un singolo parametro non diagnostico**

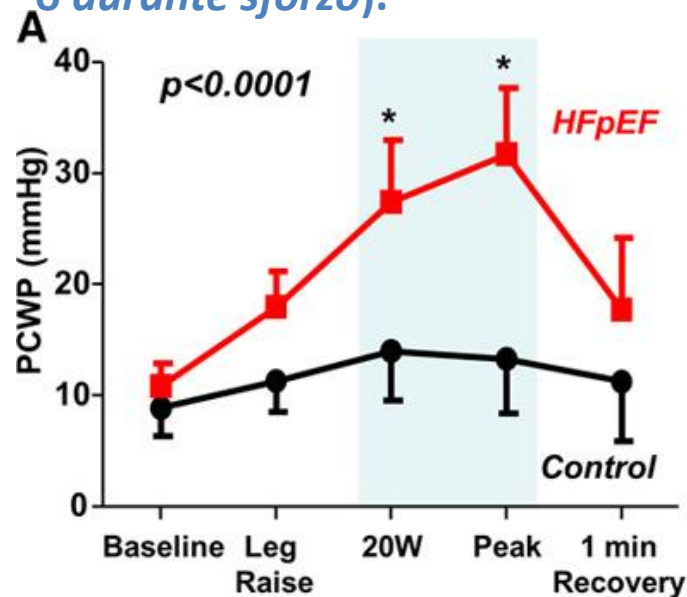


## Le zone d'ombra...

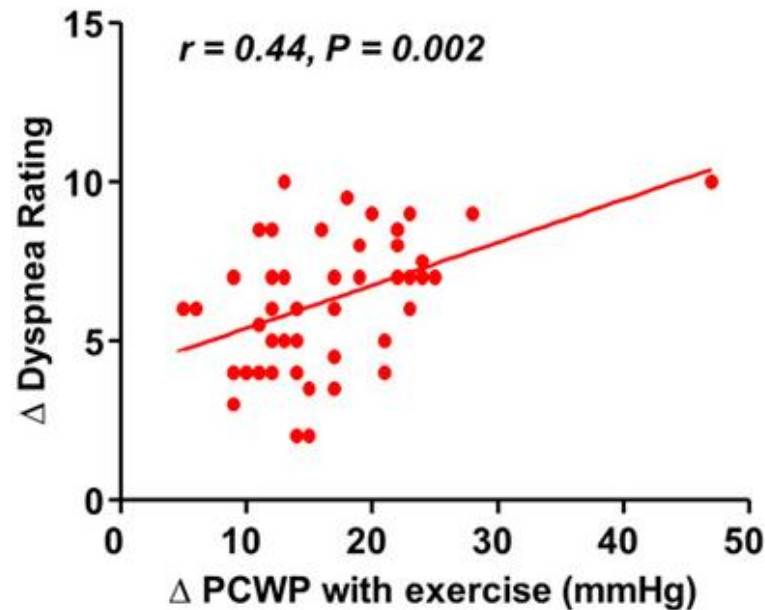


## Lo scompenso cardiaco secondo la fisiopatologia

**Definizione «fisiopatologica» di scompenso cardiaco sec Braunwald:** incapacità del cuore a pompare sangue in maniera confacente ai fabbisogni metabolici dell'organismo, o **la possibilità di mantenere una gittata cardiaca adeguata scapito di alte pressioni di riempimento (a riposo o durante sforzo).**



BNP/ NTproBNP ed ecocardio spesso non patologici!!!!



PCWP=pressione di incuneamento capillare polmonare (equivalente alla pressione atriale sinistra)

# Probabilità di HFpEF secondo il H2FPEF score

## A Simple, Evidence-Based Approach to Help Guide Diagnosis of Heart Failure With Preserved Ejection Fraction

*Circulation.* 2018;138:861–870. DOI: 10.1161/CIRCULATIONAHA.118.034646

	Clinical Variable	Values	Points
<b>H<sub>2</sub></b>	<b>H</b> heavy	Body mass index > 30 kg/m <sup>2</sup>	2
	<b>H</b> ypertensive	2 or more antihypertensive medicines	1
<b>F</b>	Atrial <b>F</b> ibrillation	Paroxysmal or Persistent	3
<b>P</b>	<b>P</b> ulmonary Hypertension	Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg	1
<b>E</b>	<b>E</b> lder	Age > 60 years	1
<b>F</b>	<b>F</b> illing Pressure	Doppler Echocardiographic E/e' > 9	1
<b>H<sub>2</sub>FPEF score</b>			<b>Sum (0-9)</b>

Total Points	0	1	2	3	4	5	6	7	8	9
Probability of HFpEF	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	0.95	

**Alto valore predittivo positivo (score > 5)...**

## SCOMPENSO DIASTOLICO: PERCHE' NE PARLIAMO. L'EPIDEMIOLOGIA

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Epidemia cardiovascolare del nuovo millennio

Circa 32 milioni di persone affette in tutto il mondo

Incidenza: 1-4 casi/1000 persone/anno

Prevalenza: 1-2% della popolazione generale

Un individuo su quattro di età > 45 anni svilupperà uno scompenso diastolico

Le ospedalizzazioni per scompenso cardiaco rappresentano l'1-2% di tutti i ricoveri ospedalieri

Tasso ospedalizzazione  $\approx$  1.4 annuo

La mortalità a 30 giorni dal ricovero varia dal 5% al 20% e dipende fortemente dall'età al momento del ricovero

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**FREQUENTE**

Un individuo su quattro di età > 45 anni svilupperà uno scompenso diastolico

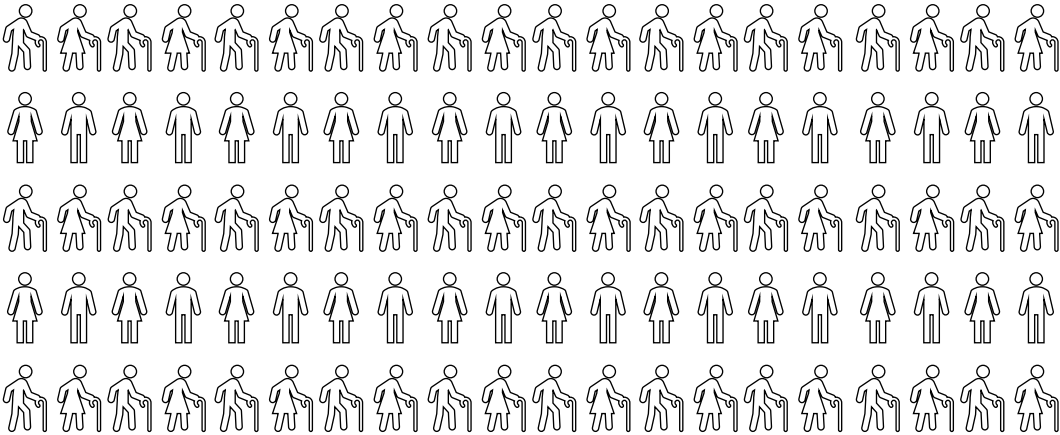
Le ospedalizzazioni per scompenso cardiaco rappresentano l'1-2% di tutti i ricoveri ospedalieri

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**GRAVE**

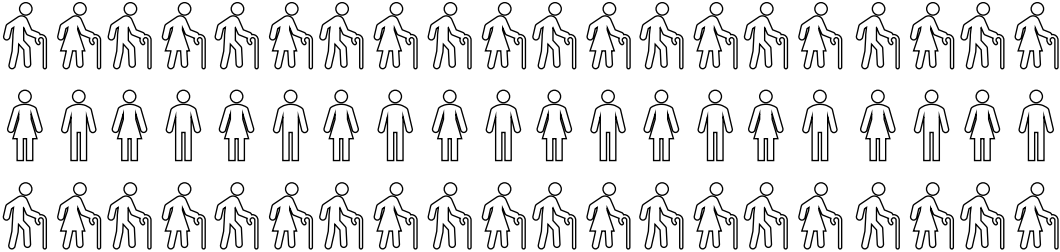
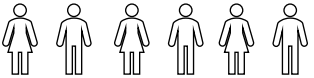
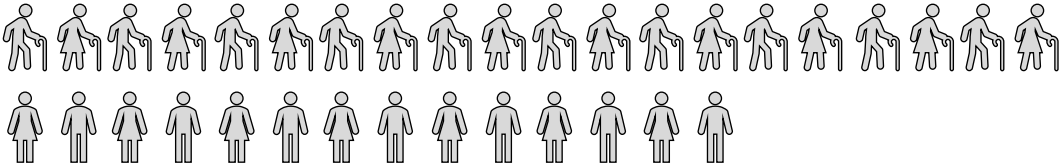
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# PRESI 100 INDIVIDUI DI ETA' > 70 ANNI



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35% ha dispnea

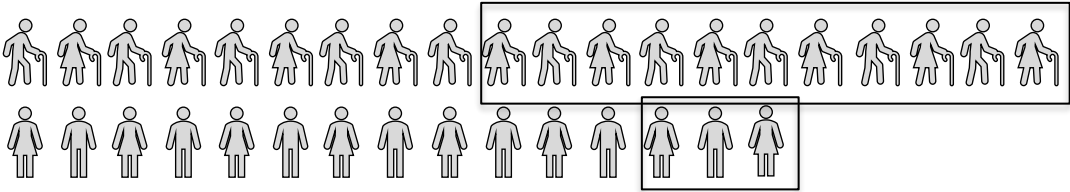


65% non «lamenta» dispnea

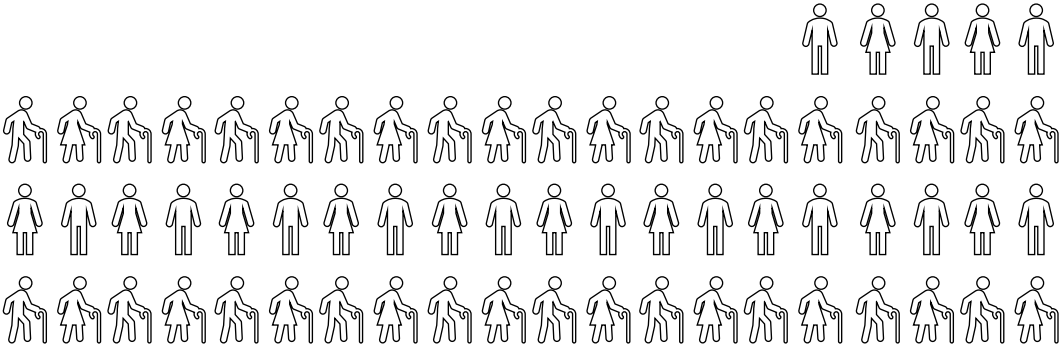
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35% ha dispnea

Dispnea pneumogena nota

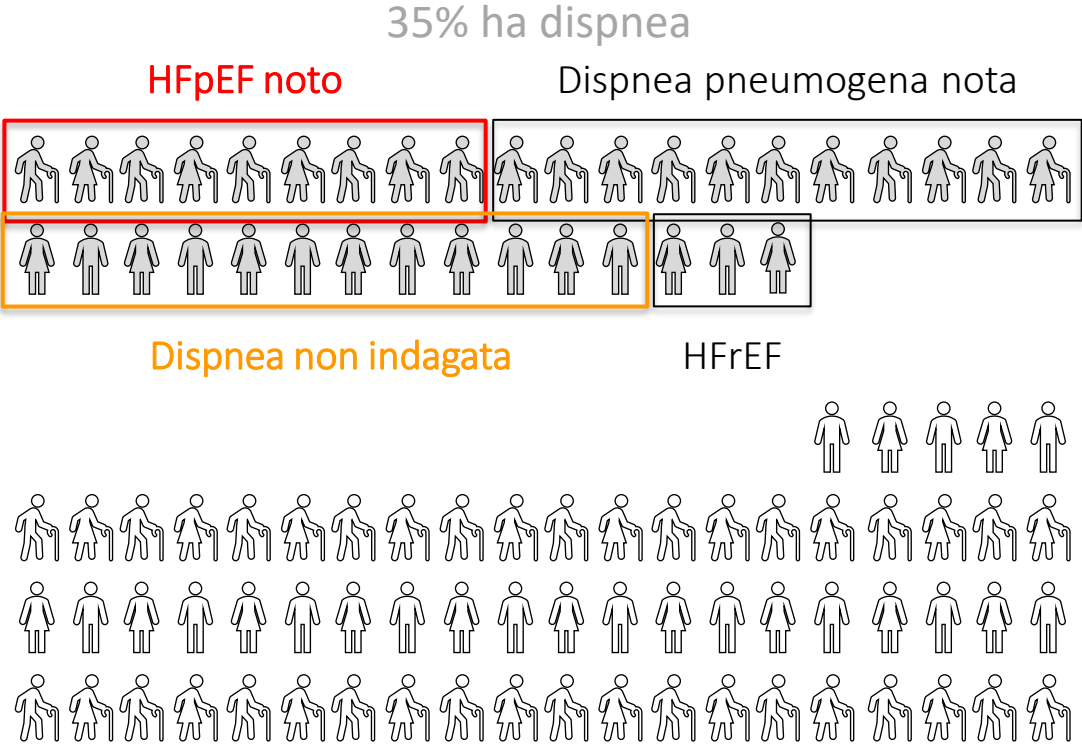


HFrEF



65% non «lamenta» dispnea

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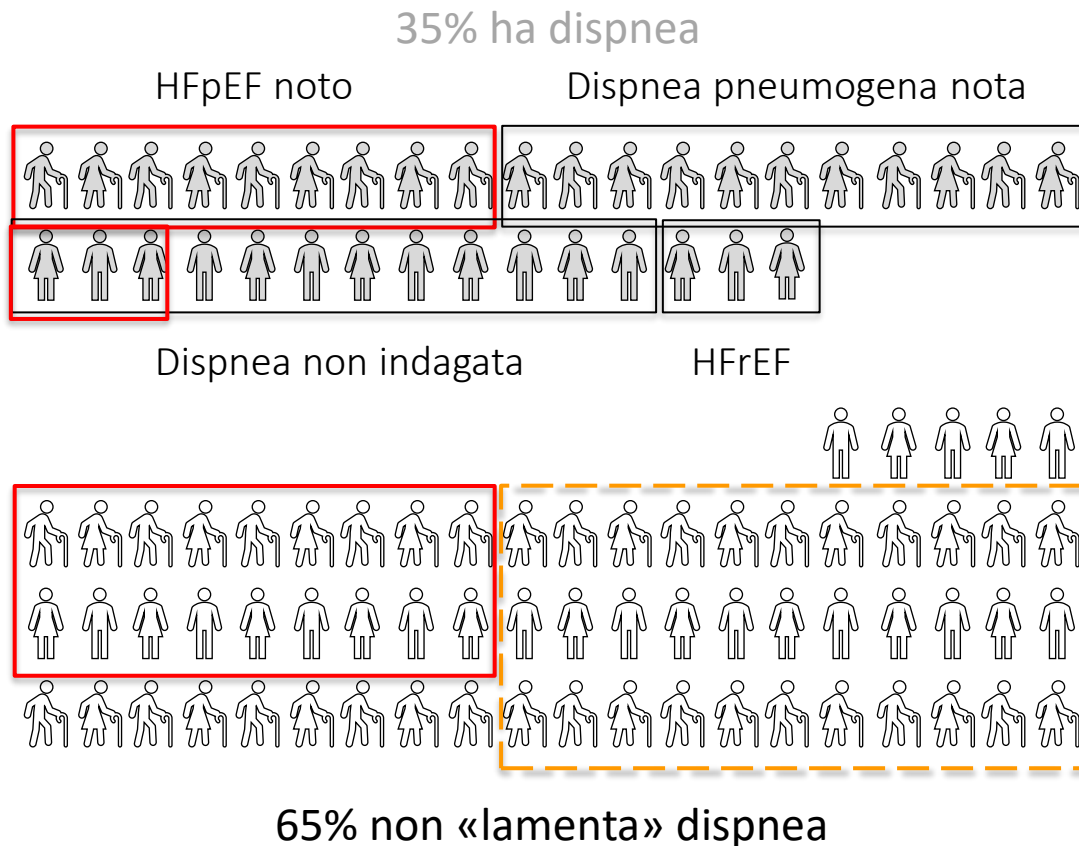


65% non «lamenta» dispnea

# PRESI 100 INDIVIDUI DI ETA' > 70 ANNI

> 1/3 DEGLI  
INDIVIDUI  
DISPNOICI  
HANNO  
HFPEF

1/3 DEGLI  
INDIVIDUI  
ASINTOMATICI  
HA UN'ALTA  
PROBABILITA'  
DI HFPEF



LA META' DEGLI  
INDIVIDUI  
ASINTOMATICI  
HA UNA  
PROBABILITA'  
INTERMEDIA DI  
HFPEF

# DEFINIZIONE DI SCOMPENSO DIASTOLICO vs CANCRO

## CANCRO

### SCOMPENSO DIASTOLICO

Sindrome clinica caratterizzata da

- sintomi (dispnea da sforzo, faticabilità...)  
e/o
- segni (edemi declivi, congestione polmonare...)

secondari a disfunzione diastolica del ventricolo sinistro

Table 1. Select definitions of cancer.

Definition of cancer	Source	Date
In medicine, a roundish, hard, unequal, scirrhous tumor of the glands, which usually ulcerates, is very painful, and generally fatal.	An American Dictionary of the English Language. (Webster) (35)	1828
A tumor is a new growth of tissue which apparently originates and grows spontaneously, possesses an atypical architecture, does not subserve the uses of the organism, and reaches no definite termination of growth.	Textbook of General Pathological Anatomy and Pathogenesis (Ziegler) (36)	1898
A malignant tumour eating the part it is in, spreading indefinitely, & recurring when removed.	Oxford Dictionary (37)	1919
A tumor is an autonomous new growth of tissue.	Neoplastic Disease - a treatise on tumors (Ewing) (38)	1919
Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body.	National Cancer Institute (1)	2023
Cancer isn't a single disease. Cancer is a group of diseases characterized by the uncontrolled proliferation of cells. Ignoring the body's signal to stop, malignant cells multiply to form tumors in organs and tissues or, in the case of blood cancers, crowd out normal cells in the blood stream and bone marrow.	American Association for Cancer Research (7)	2023
Cancer is when abnormal cells divide in an uncontrolled way. Some cancers may eventually spread into other tissues.	Cancer Research UK (39)	2023
A group of diseases in which cells in the body change and grow out of control. Most types of cancer cells form a lump, or mass called a tumor.	American Cancer Society (8)	2023
Cancer is a generic term for a large group of diseases that can affect any part of the body. Other terms used are malignant tumours and neoplasms. One defining feature of cancer is the rapid creation of abnormal cells that grow beyond their usual boundaries, and which can then invade adjoining parts of the body and spread to other organs; the latter process is referred to as metastasis. Widespread metastases are the primary cause of death from cancer.	World Health Organization (20)	2023
Cancer refers to diseases in which abnormal cells divide out of control and are able to invade other tissues. Cancer cells can spread to other parts of the body through the blood and lymph systems, which help the body get rid of toxins.	Centers for Disease Control and Prevention (40)	2023
A malignant tumor of potentially unlimited growth that expands locally by invasion and systemically by metastasis	Merriam-Webster Medical Dictionary - online (41)	2023
A malignant neoplasm (including both carcinoma and sarcoma) which arises from the abnormal and uncontrolled division of cells and which invades and destroys the surrounding tissues.	Oxford Reference - online (42)	2023
A group of diseases in which abnormal cells grow in an uncontrolled way, sometimes forming tumors.	Harvard Medical Dictionary of Health Terms - online (43)	2023
A cancer is an abnormal growth of cells (usually derived from a single abnormal cell). The cells have lost normal control mechanisms and thus are able to multiply continuously, invade nearby tissues, migrate to distant parts of the body, and promote the growth of new blood vessels from which the cells derive nutrients.	Merck Manuals - online (44)	2023
Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body.	Wikipedia - online (45)	2023

# DEFINIZIONE DI SCOMPENSO DIASTOLICO vs CANCRO

## CANCRO

### SCOMPENSO DIASTOLICO

Sindrome clinica caratterizzata da

- sintomi (dispnea da sforzo, faticabilità...) e/o
- segni (edemi declivi, congestione polmonare...)

secondari a disfunzione diastolica del ventricolo sinistro

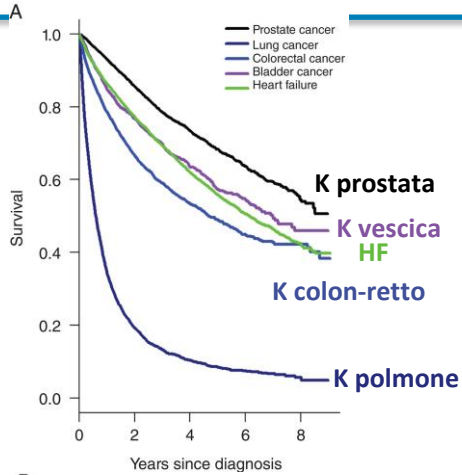
Table 1. Select definitions of cancer.

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A tumor is a new growth of tissue which apparently originates and grows spontaneously, possesses an atypical architecture, does not subserve the uses of the organism, and reaches no definite termination of growth.	Textbook of General Pathological Anatomy and Pathogenesis (Ziegler) (36)	1898
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Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body.	Textbook of Pathology (39)	2023
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Cancer is when abnormal cells divide in an uncontrolled way and eventually spread into other tissues.	Journal of Cancer Research UK (39)	2023
A group of diseases in which cells in the body divide in an uncontrolled way. The types of cancer cells form a lump, or mass, in the body.	American Cancer Society (8)	2023
Cancer is a generic term for a large number of diseases. Other terms used are carcinoma, sarcoma, and leukemia. A defining feature of cancer is the rapid, uncontrolled growth of cells beyond their usual boundaries, and which can metastasize to other parts of the body and spread to other organs; the latter process is called metastasis. Widespread metastases are the primary cause of death in many cancer patients.	World Health Organization (20)	2023
Cancer refers to diseases in which abnormal cells divide out of control and are able to invade other tissues. Cancer cells can invade other parts of the body through the blood and lymph systems, which help the body get rid of toxins.	Centers for Disease Control and Prevention (40)	2023
A malignant tumor of potentially unlimited growth that expands locally by invasion and systemically by metastasis	Merriam-Webster Medical Dictionary - online (41)	2023
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Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body.	Wikipedia - online (45)	2023

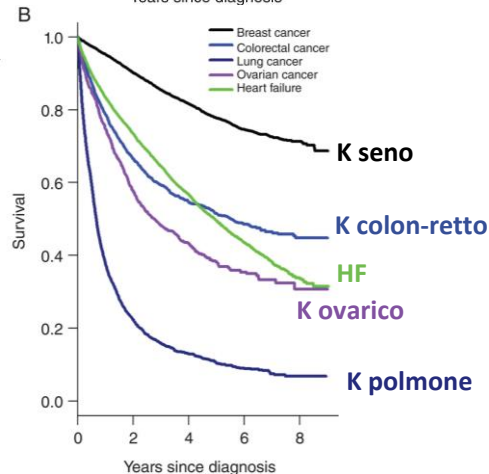
NESSUNA MENZIONE A SINTOMI

# Prognosi: HF vs cancro

UOMINI



DONNE



56 658 individui in Scozia

**MEN :**

	<b>Prostate</b>	<b>Lung</b>	<b>Colorectal</b>	<b>Bladder</b>	<b>HF</b>
Prob[alive after 30d]	99.6% [99.5,99.8]	91.3% [90.5,92.1]	97.6% [97.1,98.0]	98.9% [98.5,99.4]	98.5% [98.2,98.7]
Prob[alive after 1y]	93.1%* [92.1,93.7]	34.7% [33.3,36.2]	78.6% [77.3,79.9]	84.8% [83.2,86.4]	86.4% [85.7,87.0]
Prob[alive after 5y]	68.3%* [66.8,69.8]	8.4% [7.4,9.6]	48.9% [47.0,50.9]	57.3% [54.5,60.2]	55.8% [54.6,57.1]

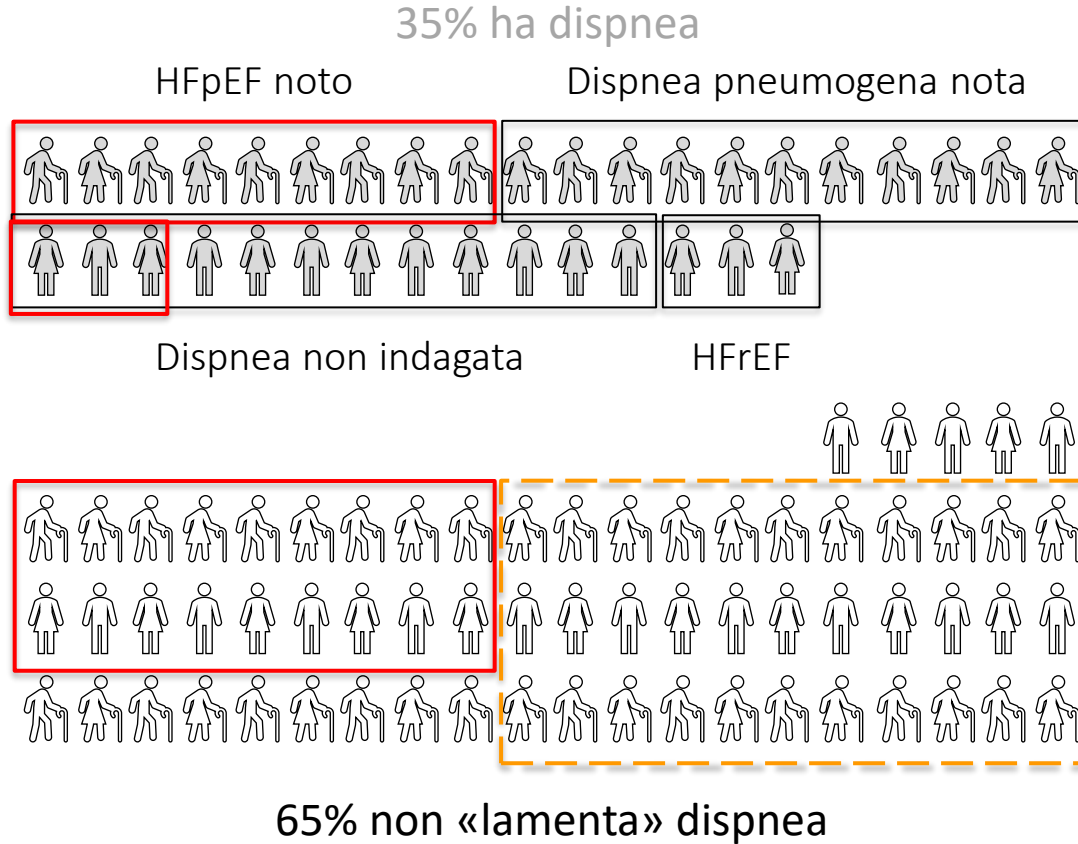
**WOMEN :**

	<b>Breast</b>	<b>Colorectal</b>	<b>Lung</b>	<b>Ovarian</b>	<b>HF</b>
Prob[alive after 30d]	99.5% [99.3,99.6]	97.8% [97.3,98.3]	90.8% [89.9,91.7]	96.8% [95.9,97.8]	97.8% [97.5,98.1]
Prob[alive after 1y]	95.2%* [94.8,95.6]	78.7% [77.3,80.1]	37.7% [36.2,39.4]	74.8% [72.3,77.3]	83.4% [82.6,84.2]
Prob[alive after 5y]	77.7%* [76.7,78.8]	51.5% [49.4,53.6]	10.4% [9.1,11.8]	38.2% [34.9,41.9]	49.5% [48.2,50.8]

# PRESI 100 INDIVIDUI DI ETA' > 70 ANNI

> 1/3 DEGLI  
INDIVIDUI  
DISPNOICI  
HANNO  
HFPEF

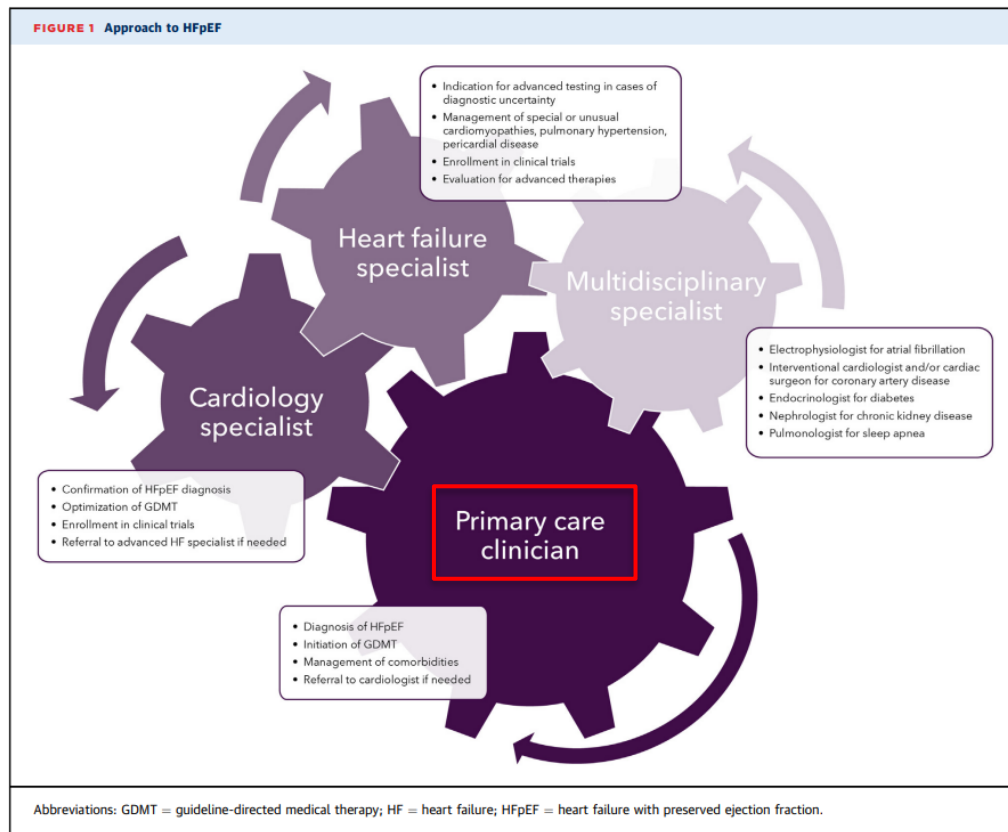
1/3 DEGLI  
INDIVIDUI  
ASINTOMATICI  
HA UN'ALTA  
PROBABILITA'  
DI HFPEF



LA META' DEGLI  
INDIVIDUI  
ASINTOMATICI  
HA UNA  
PROBABILITA'  
INTERMEDIA DI  
HFPEF

# SCOMPENSO DIASTOLICO: IL RUOLO CENTRALE DEL MMG

## Epidemia cardiovascolare del nuovo millennio





# Pensiamo all'HFpEF e alla disfunzione diastolica ventricolare sinistra !

Valutiamo la probabilità in maniera semplice

	Clinical Variable	Values	Points
<b>H<sub>2</sub></b>	<b>H</b> heavy	Body mass index > 30 kg/m <sup>2</sup>	2
	<b>H</b> ypertensive	2 or more antihypertensive medicines	1
<b>F</b>	Atrial <b>F</b> ibrillation	Paroxysmal or Persistent	3
<b>P</b>	<b>P</b> ulmonary Hypertension	Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg	1
<b>E</b>	<b>E</b> lder	Age > 60 years	1
<b>F</b>	<b>F</b> illing Pressure	Doppler Echocardiographic E/e' > 9	1
<b>H<sub>2</sub>FPEF score</b>			<b>Sum (0-9)</b>

Total Points      0      1      2      3      4      5      6      7      8      9

Probability of HFpEF      0.2      0.3      0.4      0.5      0.6      0.7      0.8      0.9      0.95

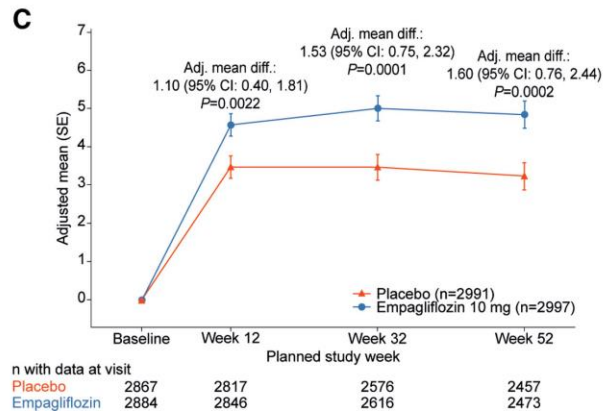
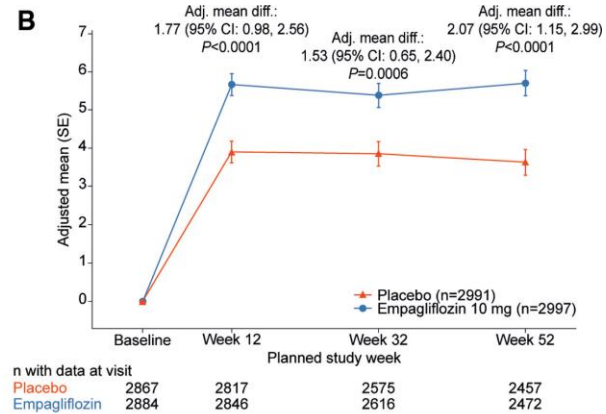
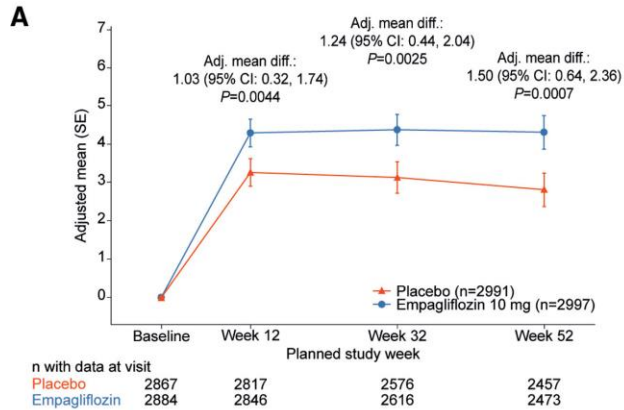
# Trattare i casi ovvi

FIGURE 9 Treatment Algorithm for Guideline-Directed Medical Therapy in HFpEF\*

HFpEF Treatment

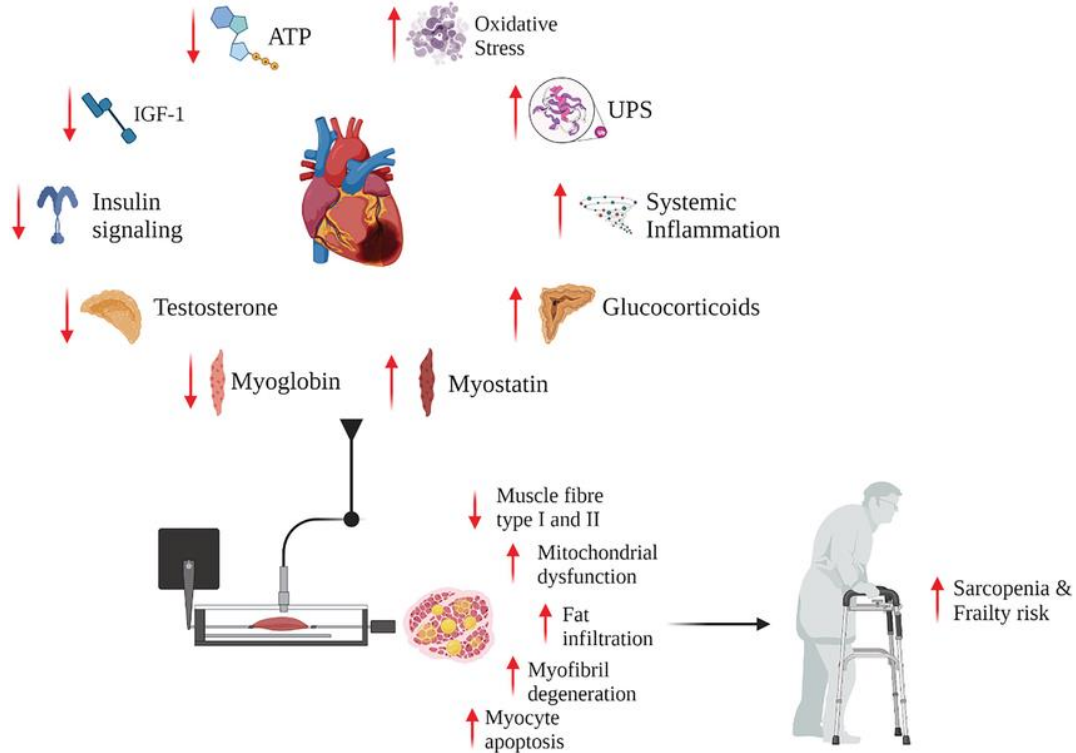
SGLT2i

# Non aspettiamoci miracoli dai farmaci sui sintomi e sulla qualità di vita!



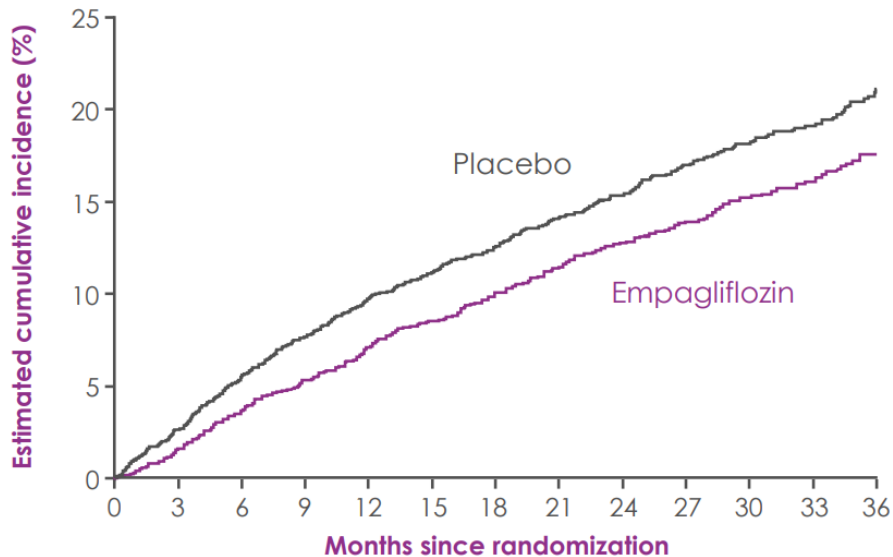
# Non aspettiamoci miracoli dai farmaci: il concetto della fragilità

I sintomi: dipendono dallo scompenso cardiaco o «dalla vecchiaia» ?



# Ma aspettiamoci un effetto di SGLT2i su mortalità CV e SCC

## Empagliflozin demonstrated a clinically meaningful 21% RRR in the composite primary endpoint of CV death or HHF



**RRR 21%**  
**ARR 3.3%**  
**NNT\*=31**

**HR: 0.79**  
(95% CI: 0.69, 0.90)  
 $p < 0.001$

Empagliflozin:  
415 (13.8%) patients with event  
Rate: 6.9/100 patient-years  
Placebo:  
511 (17.1%) patients with event  
Rate: 8.7/100 patient-years

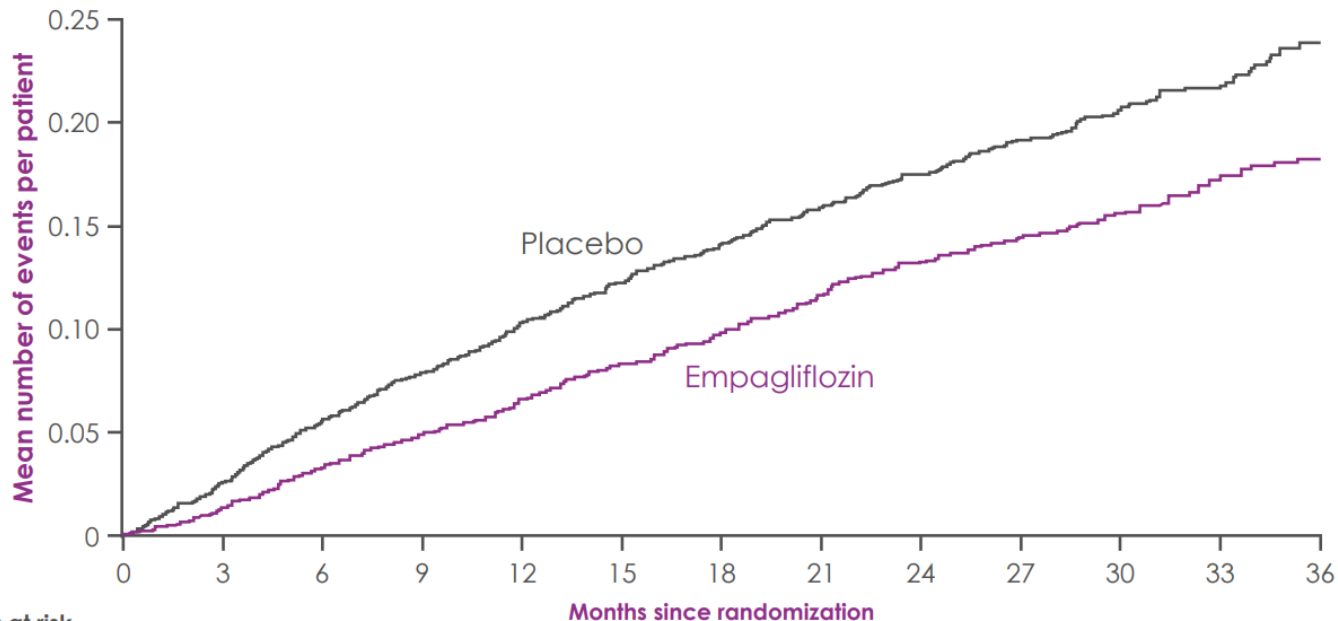
### Patients at risk

Placebo	2991	2888	2786	2706	2627	2424	2066	1821	1534	1278	961	681	400
Empagliflozin	2997	2928	2843	2780	2708	2491	2134	1858	1578	1332	1005	709	402

\*During a median trial period of 26 months. ARR, absolute risk reduction; CI, confidence interval; CV, cardiovascular; HHF, hospitalization for heart failure; HR, hazard ratio; NNT, number needed to treat; RRR, relative risk reduction. Anker S *et al.* *N Engl J Med.* 2021; 10.1056/NEJMoa2107038.

# Ma aspettiamoci un effetto di SGLT2i su mortalità CV e SCC

## EMPEROR-Preserved: Key secondary endpoint – adjudicated total HHF (first and recurrent)



**RRR**  
27%

**HR: 0.73**  
(95% CI: 0.61, 0.88)  
 $p < 0.001$

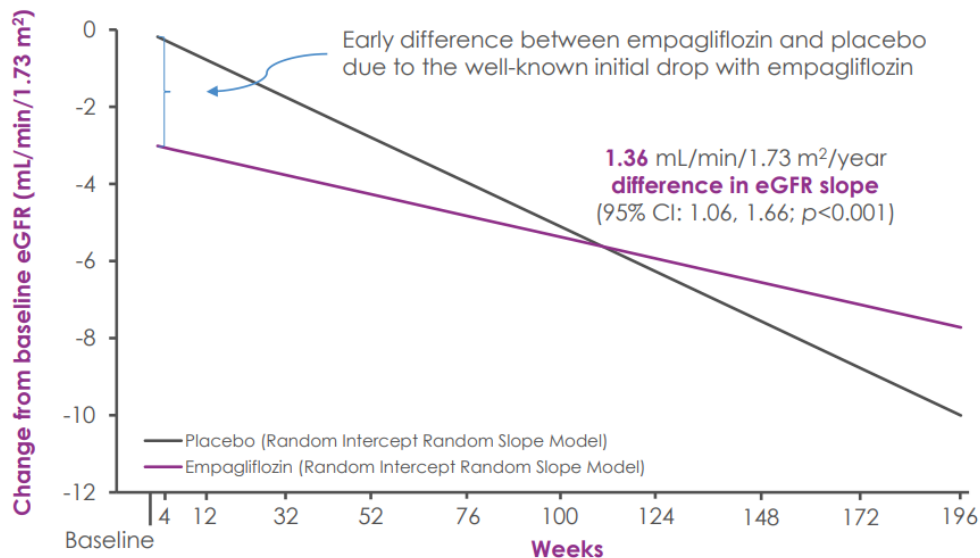
Empagliflozin:  
407 patients  
with event  
Placebo:  
541 patients  
with event

### Patients at risk

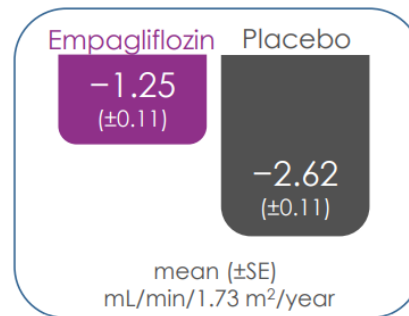
Placebo	2991	2945	2901	2855	2816	2618	2258	1998	1695	1414	1061	747	448
Empagliflozin	2997	2962	2913	2869	2817	2604	2247	1977	1684	1429	1081	765	446

# Ma aspettiamoci un effetto di SGLT2i sul declino della funzione renale

## Empagliflozin protected the kidney by significantly slowing the decline in kidney function



The rate of eGFR decline in patients treated with empagliflozin was half that of patients treated with placebo



eGFR slope = rate of decline (and is a measure for long-term renal function). eGFR slope is analysed based on on-treatment data using a random coefficient model including age, baseline eGFR and baseline LVEF as linear covariates and sex, region, baseline diabetes status, and baseline by time and treatment by time interactions as fixed effects; the model allows for randomly varying slope and intercept between patients.

eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; SE, standard error.

Developed from data reported in Anker S *et al.* *N Engl J Med.* 2021; 10.1056/NEJMoa2107038.

## EMPEROR-Preserved: Changes in vital signs and laboratory findings

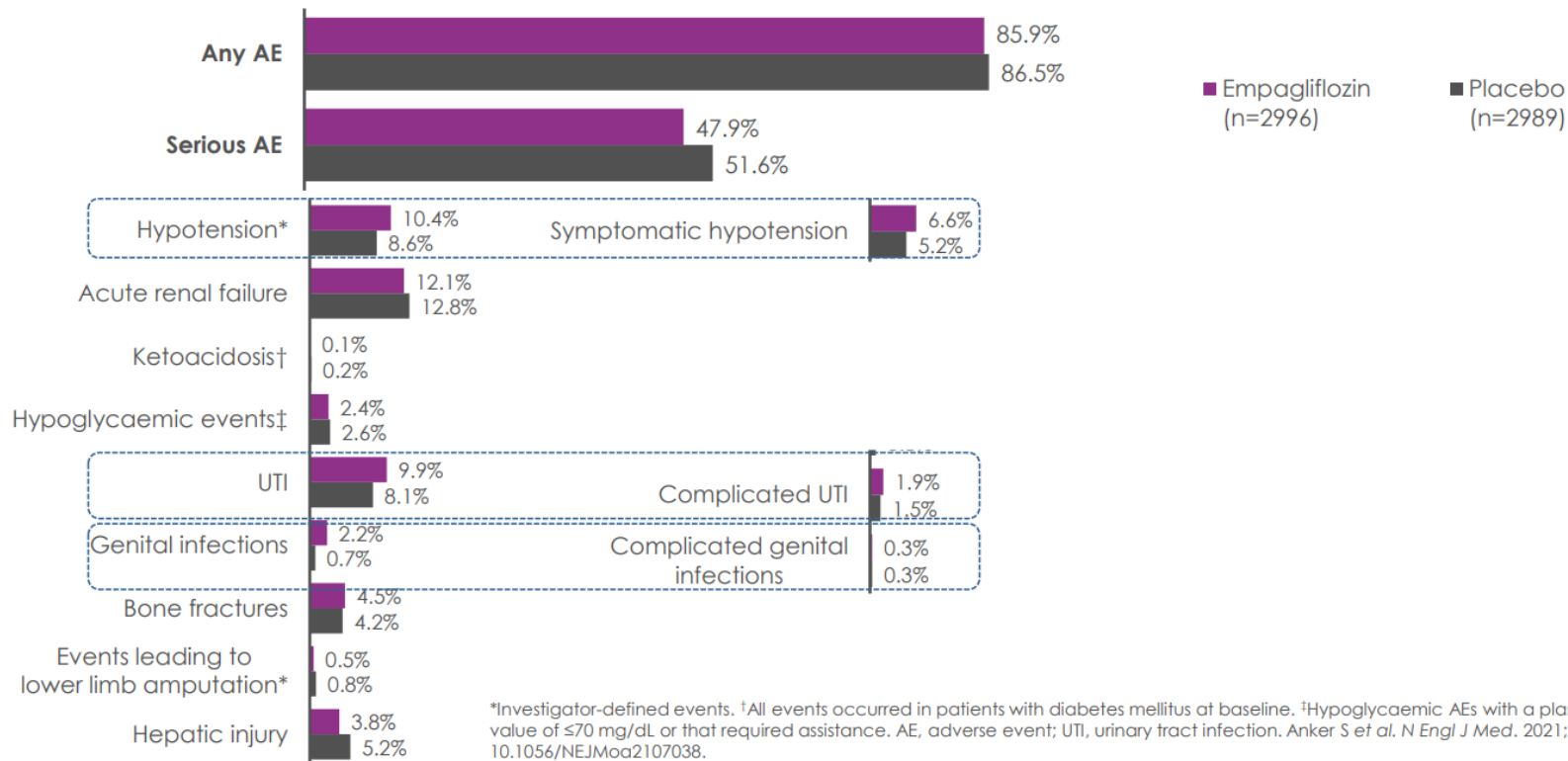
Laboratory and other measurements (change from baseline to 52 weeks)	Empagliflozin (n=2997)	Placebo (n=2991)	Absolute difference (95% CI)
Glycated haemoglobin in patients with diabetes (%), mean $\pm$ SE	-0.16 $\pm$ 0.02	0.03 $\pm$ 0.02	-0.19 (-0.25, -0.14)
Haematocrit (%), mean $\pm$ SE	1.94 $\pm$ 0.07	-0.41 $\pm$ 0.07	2.36 (2.17, 2.54)
Body weight (kg), mean $\pm$ SE	-1.39 $\pm$ 0.09	-0.11 $\pm$ 0.09	-1.28 (-1.54, -1.03)
Systolic blood pressure (mm Hg), mean $\pm$ SE	-1.8 $\pm$ 0.3	-0.6 $\pm$ 0.3	-1.2 (-2.1, -0.3)
Uric acid (mg/dL), mean $\pm$ SE	-0.90 $\pm$ 0.03	-0.10 $\pm$ 0.03	-0.80 (-0.88, -0.72)
NT-proBNP (pg/mL), median (IQR)	-29 (-335, 263)	-9 (-286, 322)	0.95* (0.91, 0.99)

\*Geometric mean ratio

CI, confidence interval; IQR, interquartile range; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; SE, standard error.

Anker S et al. *N Engl J Med.* 2021; 10.1056/NEJMoa2107038.

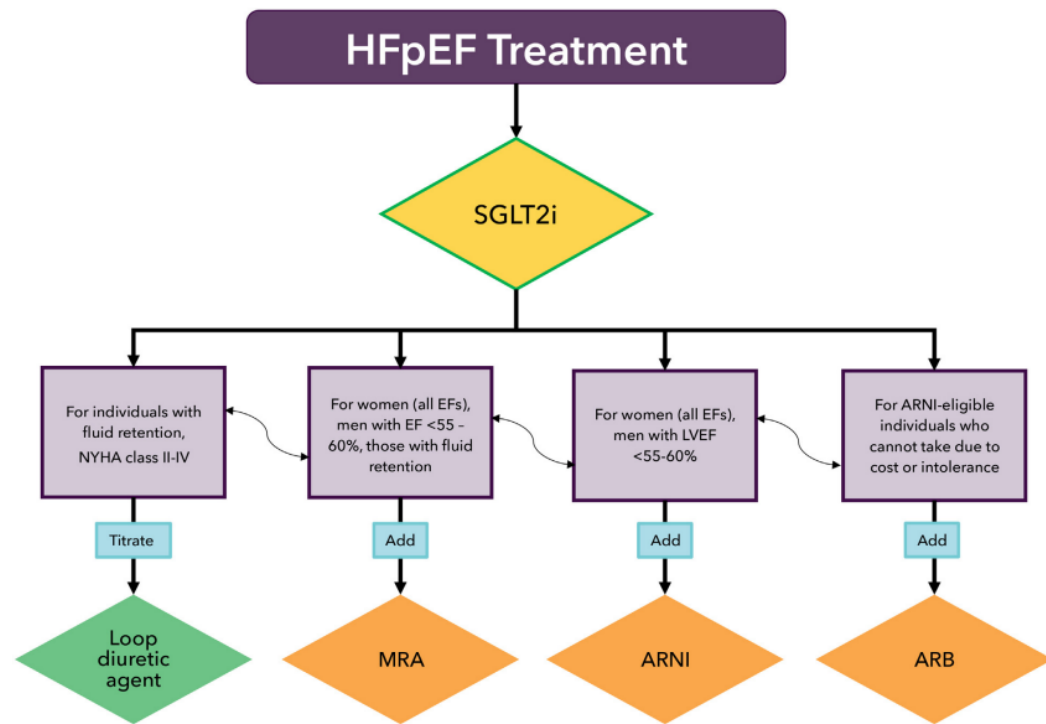
## EMPEROR-Preserved: Selected adverse events of interest



\*Investigator-defined events. †All events occurred in patients with diabetes mellitus at baseline. ‡Hypoglycaemic AEs with a plasma glucose value of  $\leq 70$  mg/dL or that required assistance. AE, adverse event; UTI, urinary tract infection. Anker S *et al.* *N Engl J Med.* 2021; 10.1056/NEJMoa2107038.

# Trattare i casi ovvi

FIGURE 9 Treatment Algorithm for Guideline-Directed Medical Therapy in HFpEF\*

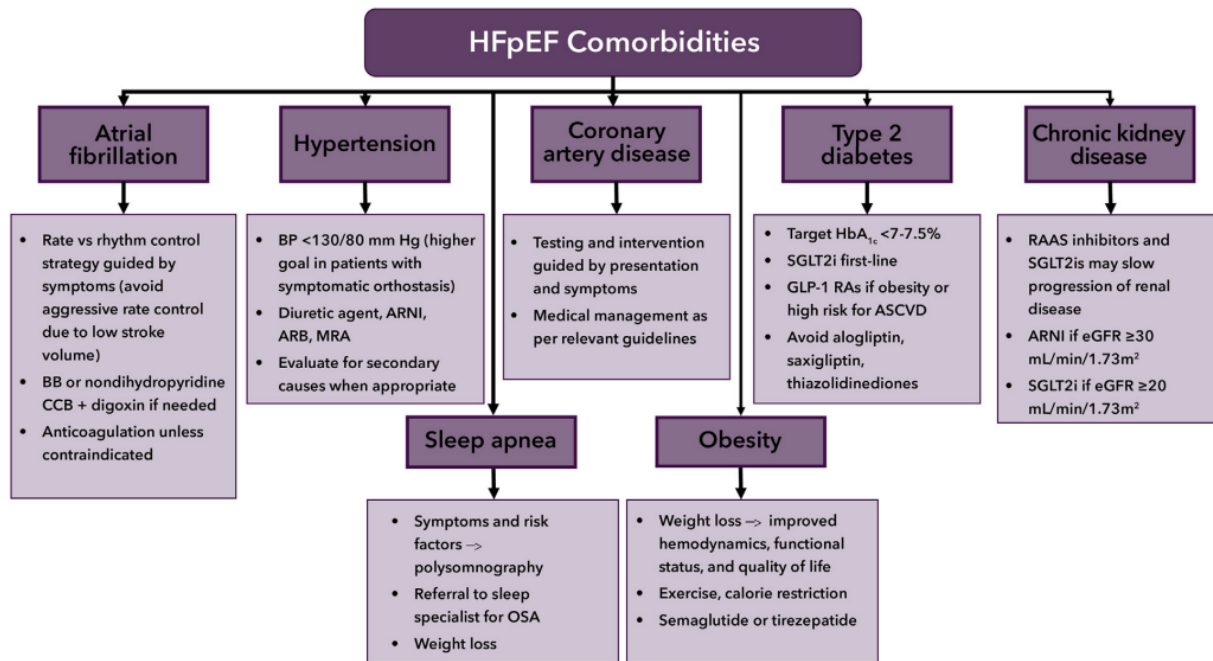


\*Green color identifies a Class 1 therapy from clinical practice guidelines,<sup>14</sup> yellow color indicates a Class 2a therapy, and orange color denotes a Class 2b therapy. SGLT2is receive a Class 2a indication in the 2022 AHA/ACC/HFSA HF Guidelines,<sup>14</sup> but the benefit, now confirmed in 2 randomized trials,<sup>60,61</sup> suggests that SGLT2is may receive a stronger class of recommendation in future guidelines, and thus the box is shaded yellow with a green border. AF = atrial fibrillation; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; EF = ejection fraction; HFpEF = heart failure with preserved ejection fraction; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid antagonist; NYHA = New York Heart Association; SGLT2i = sodium-glucose cotransporter 2 inhibitor.

GLP1a in  
HFpEF obeso!

# Pensare alle comorbidità e al loro trattamento

FIGURE 11 Management of Comorbidities Associated With HFpEF



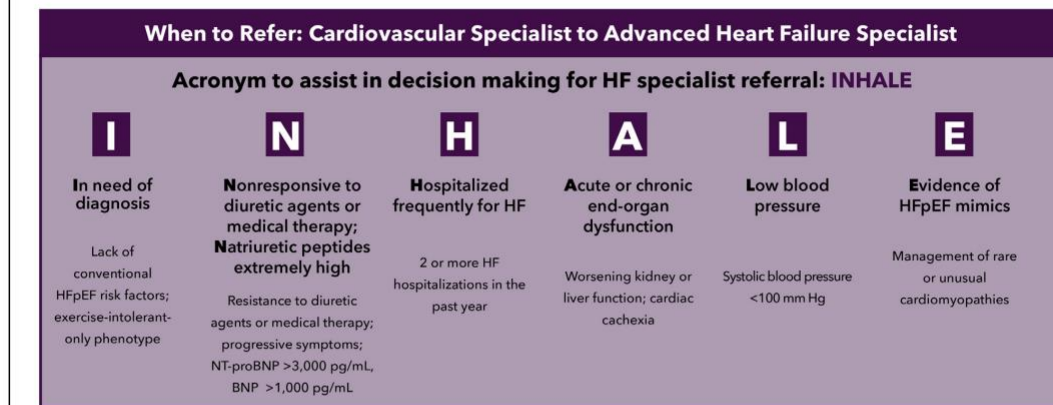
ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; ASCVD = atherosclerotic cardiovascular disease; BB = beta-blocker; BP = blood pressure; CCB = calcium-channel blocker; CPAP = continuous positive airway pressure; eGFR = estimated glomerular filtration rate; GLP1-RA = glucagon-like peptide-1 receptor agonist; HbA<sub>1c</sub> = glycosylated hemoglobin; MRA = mineralocorticoid antagonist; OSA = obstructive sleep apnea; RAS = renin-angiotensin system; SGLT2i = sodium-glucose cotransporter 2 inhibitor.

# Inviare i casi non ovvi !

- Giovani (mimickers)
- Marcata ipertrofia ventricolare sinistra (cardiomiopatie, amiloidosi)
- Insufficienze valvolari atrio-ventricolari
- Ipertensione polmonare +/- disfunzione destra (malattie vascolari polmonari)

➔ Interventi specifici

FIGURE 13 INHALE: Acronym for Advanced HF Specialist Referral\*



\*Most individuals with suspected or proven HFpEF can be managed by a general cardiovascular specialist. However, there are some situations that suggest a special or unusual cardiomyopathy (such as infiltrative or restrictive cardiomyopathy), pulmonary hypertension, or pericardial disease. Features to assist in identification of individuals with advanced HF not classic for HFpEF are summarized in the acronym "INHALE," which includes markers of advanced HF. BNP = B-type natriuretic peptide; BP = blood pressure; HF = heart failure; HFPEF = heart failure with preserved ejection fraction; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association.

## Inviare i casi non ovvi !

---

- Giovani (mimickers)
- Marcata ipertrofia ventricolare sinistra (cardiomiopatie, amiloidosi)
- Insufficienze valvolari atrio-ventricolari
- Ipertensione polmonare +/- disfunzione destra (malattie vascolari polmonari)

➔ Interventi specifici

- Discrepanza tra sintomi e anomalie morfo-funzionali (sia pochi sintomi con grosse anomalie, ma soprattutto sintomi invalidanti con poche anomalie)

# Centro Dispnea e Ipertensione Polmonare

**Prova da sforzo cardiorespiratorio  
combinata con  
ecocardiogramma da sforzo**

- Misura oggettiva della capacità di esercizio
- Diagnosi differenziale tra limitazione cardiogena, pneumogena e muscolare
- Valutazione prognostica
- Valutazione morfo-funzionale cardiaca
- Valutazione emodinamica non invasiva

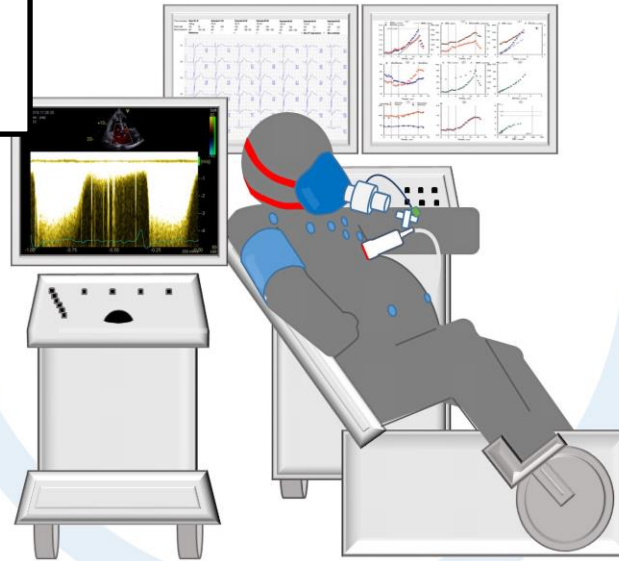
**Valutazione clinica  
cardiologica + ECG**

**Esami di  
laboratorio**

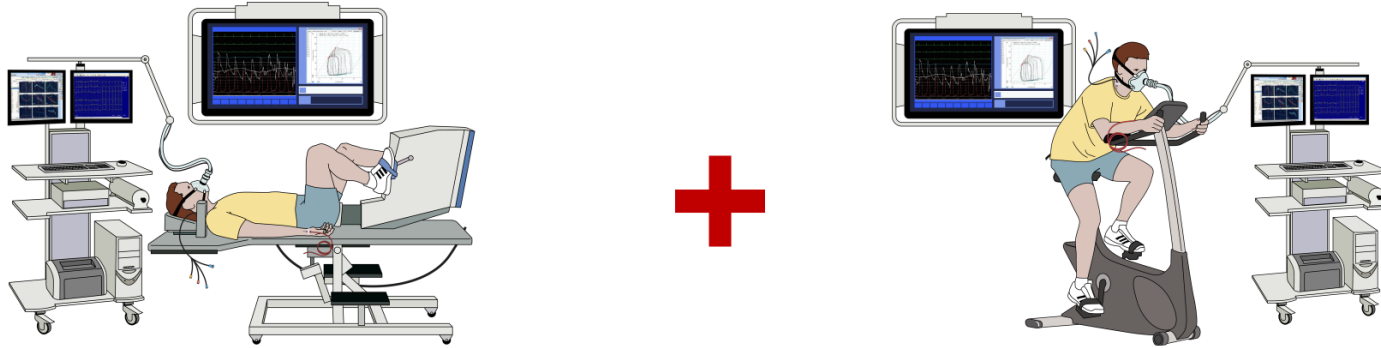
Emocromo, stato marziale,  
HbA1c, creatinina, NTproBNP

**Ecocardiogramma  
a riposo**

**Spirometria**



## Supright Exercise Right Heart Catheterization



### Integrazione informazioni

- emodinamiche
- cardiorespiratorie
- morfo-funzionali cardiache

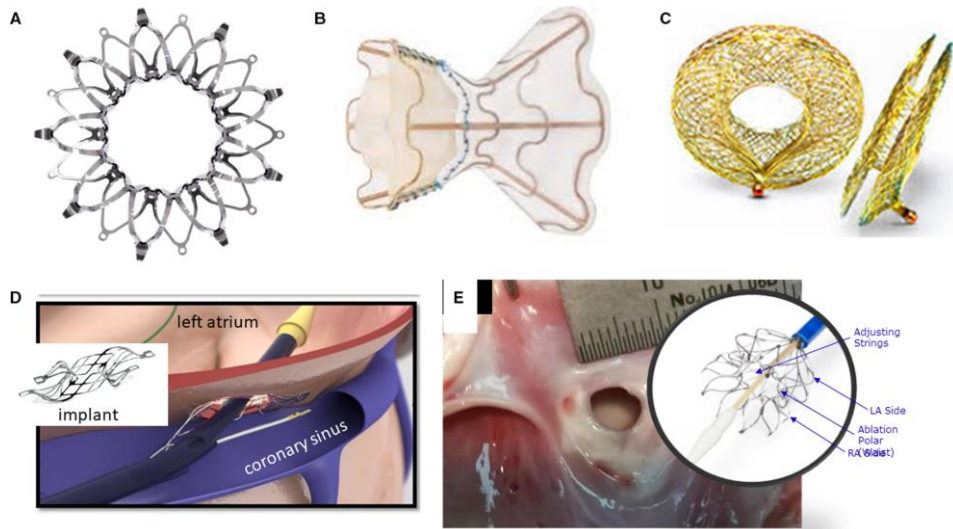
### a riposo e durante stress

Identificazione del meccanismo di limitazione all'esercizio e causale sui sintomi

- ➔ Diagnosi
- ➔ Possibilità di intervento mirato

# TERAPIE INTERVENTISTICHE PER PAZIENTI ANCORA SINTOMATICI

## Terapie interventistiche per «decomprimere» l'atrio sinistro



Unloading of the heart without changing the stressed or unstressed blood volume (venous capacitance is unchanged)

Unloading of the heart via an increase in unstressed blood volume and decrease in stressed blood volume (venous capacitance is increased)

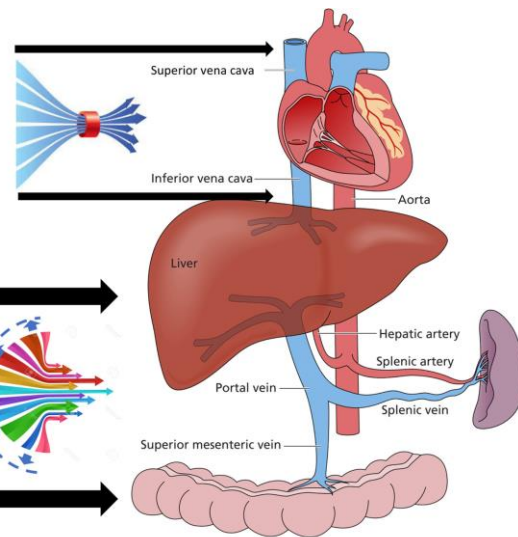
## Terapie interventistiche per ridurre il precarico

Superior Vena Cava Inflow Block - PreCARDIA

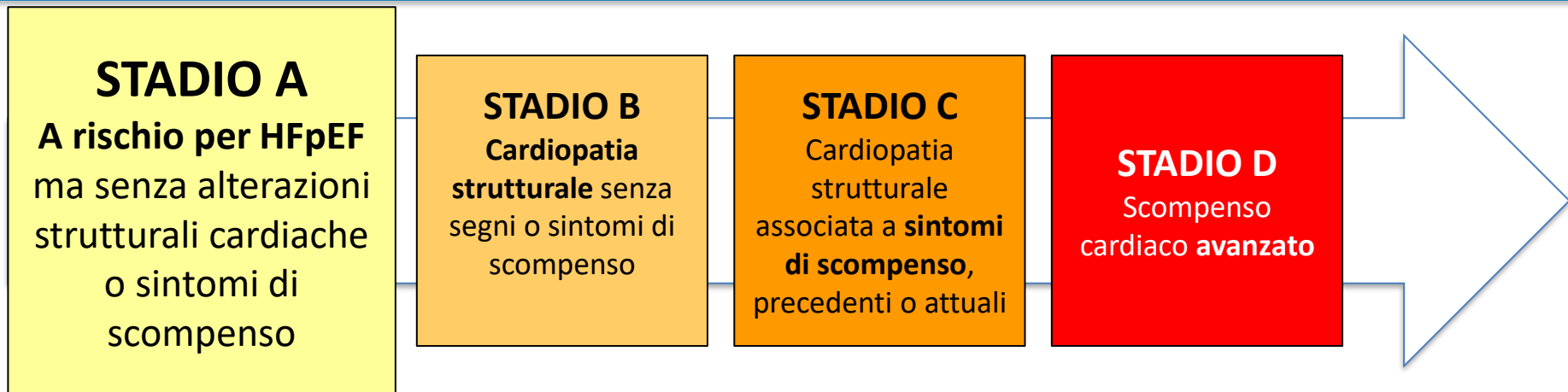
Inferior Vena Cava Inflow Block - Doraya

Pharmacological:  
- ACEI  
- SGLT2  
- Nitroglycerin  
- Milrinone  
- Levosimendan

Splanchnic Nerve Modulation



## La prevenzione dello scompenso diastolico parte a monte



# Grazie per l'attenzione!



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Twitter: @CaravitaSergio



UNIVERSITÀ  
DEGLI STUDI  
DI BERGAMO

Department  
of Management, Information  
and Production Engineering

**Auxologico**  
Ricerca e cura per la tua salute IRCCS