Assessing heart failure in clinical practice

Ovidiu Chioncel

History…. …..medical art

Abortive, and Stillborn	445	Grief	11
Affrighted	1	Jaundies	43
Aged	628	Jawfain	8
Ague	43	Impostume	74
Apoplex, and Meagrom	17	Kil'd by several accidents	46
Bit with a mad dog	1	King's Evil	38
Bleeding	3	Lethargie	2
Bloody flux, scowring, and flux	348	Livergrown	87
		Lunatique	5
Brused, Issues, sores, and ulcers,	28	Made away themselves	15
		Measles	80
Burnt, and Scalded	5	Murthered	7
Burst, and Rupture	9	Over-laid, and starved at nurse	7
Cancer, and Wolf	10		
Canker	1	Palsie	25
Childbed	171	Piles	1
Chrisomes, and Infants	2268	Plague	8
Cold, and Cough	55	Planet	13
Colick, Stone, and Strangury	50	Pleurisie, and Spleen	36
Consumption	1797	Purples, and spotted Feaver	38
Convulsion	241	Quinsie	7
Cut of the Stone	5	Rising of the Lights	98
Dead in the street, and starved	6	Sciatica	1
		Scurvey, and Itch	9
Dropsie, and Swelling	267	Suddenly	62
Drowned	34	Surfet	86
Executed, and prest to death	18	Swine Pox	6
Falling Sickness	7	Teeth	470
Fever	1108	Thrush, and Sore mouth	40
Fistula	13	Tympany	13
Flocks, and small Pox	531	Tissick	34
French Pox	12	Vomiting	1
Gangrene	5	Worms	27
Gout	4		

Causes of death London 1632

Dropsis and swelling

Table 1 Clinical features of heart failure and their accuracy for the detection of congestion

	Sensitivity	Specificity
Dyspnoea	50%	73%
Dyspnoea on exertion	66%	52%
Orthopnoea	66%	47%
Third heart sound	73%	42%
Bilateral leg oedema	94%	10%
Weight change	9%	97%
Jugular venous reflux	50%	75%
Resting jugular venous distention	70%	79%
Jugular venous distention >8 cm	48%	78%
Hepatomegaly	51%	62%
Chest X-ray findings		
Cardiomegaly	66%	96%
Redistribution	60%	68%
Interstitial oedema	60%	73%
Pleural effusion	43%	79%

Definition

ESC European Society of Cardiology

European Heart Journal (2021) 42, 3599–3726
doi:10.1093/eurheartj/ehab368

ESC GUIDELINES

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

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC

Authors/Task Force Members: Theresa A. McDonagh* (Chairperson) (United Kingdom), Marco Metra * (Chairperson) (Italy), Marianna Adamo (Task Force Coordinator) (Italy), Roy S. Gardner (Task Force Coordinator) (United Kingdom), Andreas Baumbach (United Kingdom), Michael Böhm (Germany), Haran Burri (Switzerland), Javed Butler (United States of America), Jelena Čelutkienė (Lithuania), Ovidiu Chioncel (Romania), John G.F. Cleland (United Kingdom), Andrew J.S. Coats (United Kingdom), Maria G. Crespo-Leiro (Spain), Dimitrios Farmakis (Greece), Martine Gilard (France), Stephane Heymans

- Heart failure is not a single pathological diagnosis, but a clinical syndrome consisting of cardinal symptoms (e.g. breathlessness, ankle swelling, and fatigue) that are accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles, and peripheral oedema).
- It is due to a structural and/or functional abnormality of the heart that results in elevated intracardiac pressures and/or inadequate cardiac output at rest and/or during exercise.

Under-diagnosis of Heart Failure

- non-specific nature of the symptoms and signs
  - of patients presenting to hospital with heart failure for the first time, it has been reported that approxi-mately 40% had presented to their primary care physician in the preceding 5 years and reported at least one symptom of heart failure[1]
  - one-in-six persons aged >65 years presenting to primary care with breathlessness on exertion will have unrecognized heart failure (mainly heart failure with preserved ejection fraction [HFpEF])[2]
- delays for the additional investigations

1.Bottle A, Kim D, Aylin P, Cowie MR, Majeed A, Hayhoe B. Routes to diagnosis of heart failure: Observational study using linked data in England. Heart. 2018;104:600–605
2.van Riet EES, Hoes AW, Limburg A, Landman MAJ, van der Hoeven H, Rutten FH. Prevalence of unrecognized heart failure in older persons with shortness of breath on exertion. Eur J Heart Fail. 2014;16:772–777
.

Waiting time for echo or cardiology visit

In **Belgium**, one study showed 63% of patients in primary care with suspected HF received an echo.[17]

In **Ireland**, a study of patients with a diagnosis of HF in primary care reveals only 40% received an echo.[20]

In **Finland**, a study showed echo was only available for 32% of patients in regional hospitals, but 78% in university hospitals, and 68% in central hospitals.[16]

In the **Netherlands**, one study found that only 10% of GPs routinely perform an echo to support the diagnosis of HF.[8]

In **Germany**, a study showed only 17.2% of patients received an echo in primary care settings.[18]

In **Scotland**, only 58% of HF patients are diagnosed with an echo.[11]

HFPN Report 2022

ESC European Society of Cardiology

European Journal of Heart Failure (2021)
doi:10.1002/ejhf.2115

POSITION PAPER

Universal definition and classification of heart failure:

A report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure

Endorsed by Canadian Heart Failure Society, Heart Failure Association of India, the Cardiac Society of Australia and New Zealand, and the Chinese Heart Failure Association.

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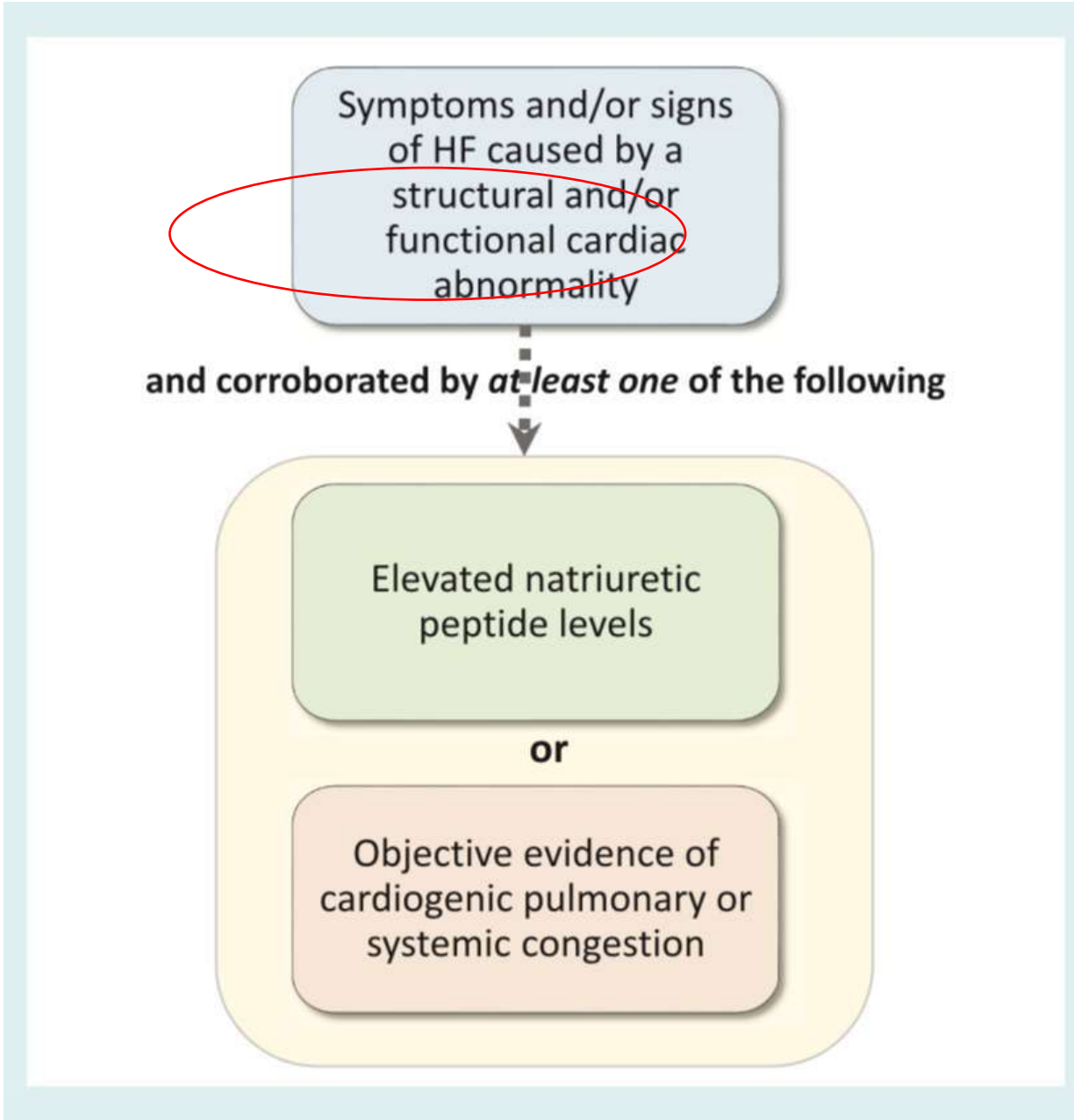
The Comprehensive RWI Data Supplement table is available in the *Appendix*. Affiliations are also listed in the *Appendix*



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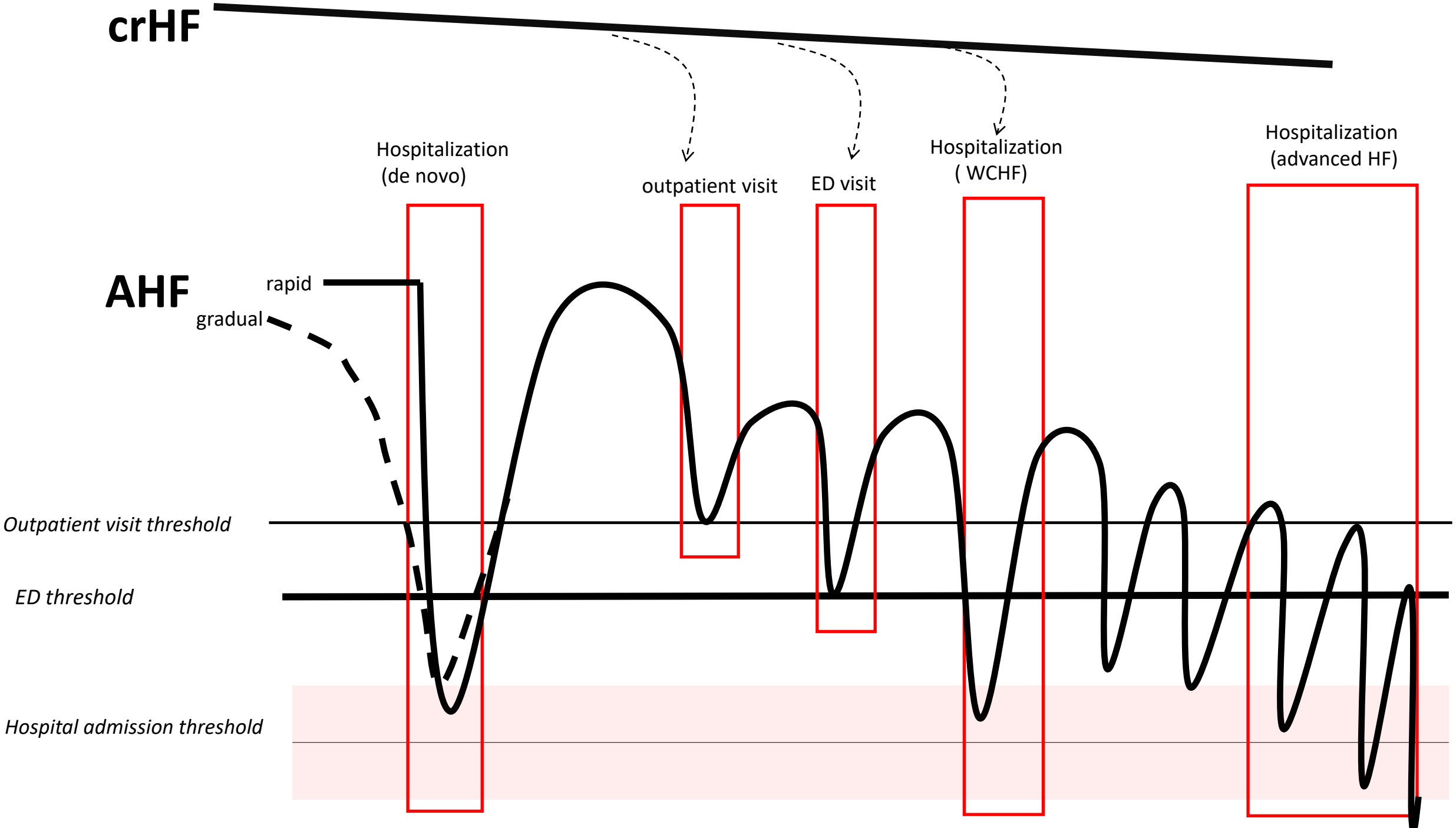
- **UNIVERSAL DEFINITION OF HF**
  HF is a clinical syndrome with current or prior

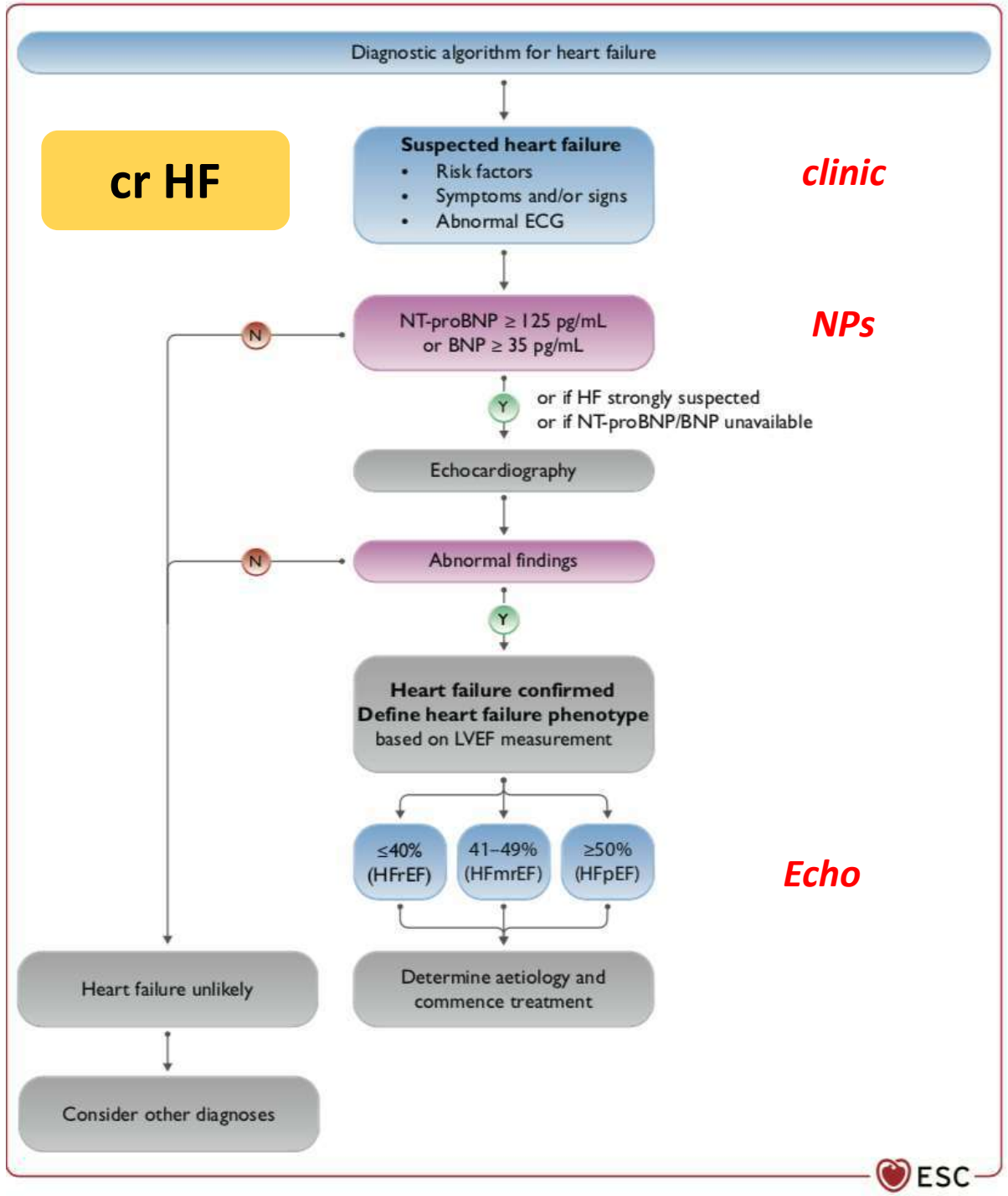
  - **Symptoms and/or signs (*Table 6*) caused by a structural and/or functional cardiac abnormality (as determined by EF <50%, abnormal cardiac chamber enlargement, E/E′ >15, moderate/severe ventricular hypertrophy or moderate/severe valvular obstructive or regurgitant lesion)**
  - **and corroborated by *at least one* of the following:**

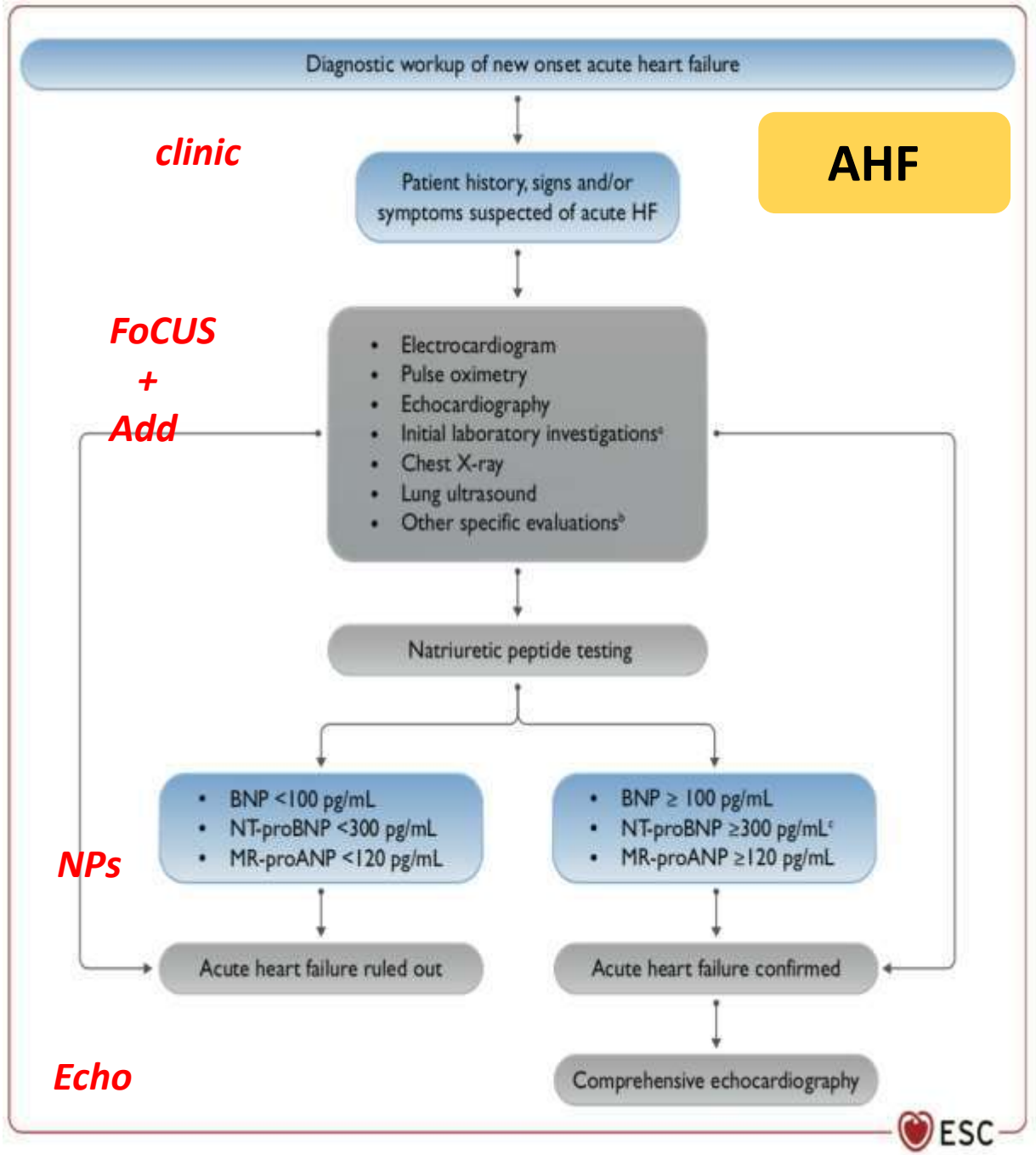
    - Elevated natriuretic peptide levels (for values refer to *Table 7*)
    - Objective evidence of cardiogenic pulmonary or systemic congestion by diagnostic modalities such as imaging (e.g. by chest X-ray or elevated filling pressures by echocardiography) or haemodynamic measurement (e.g. right heart catheterization, pulmonary artery catheter) at rest or with provocation (e.g. exercise).

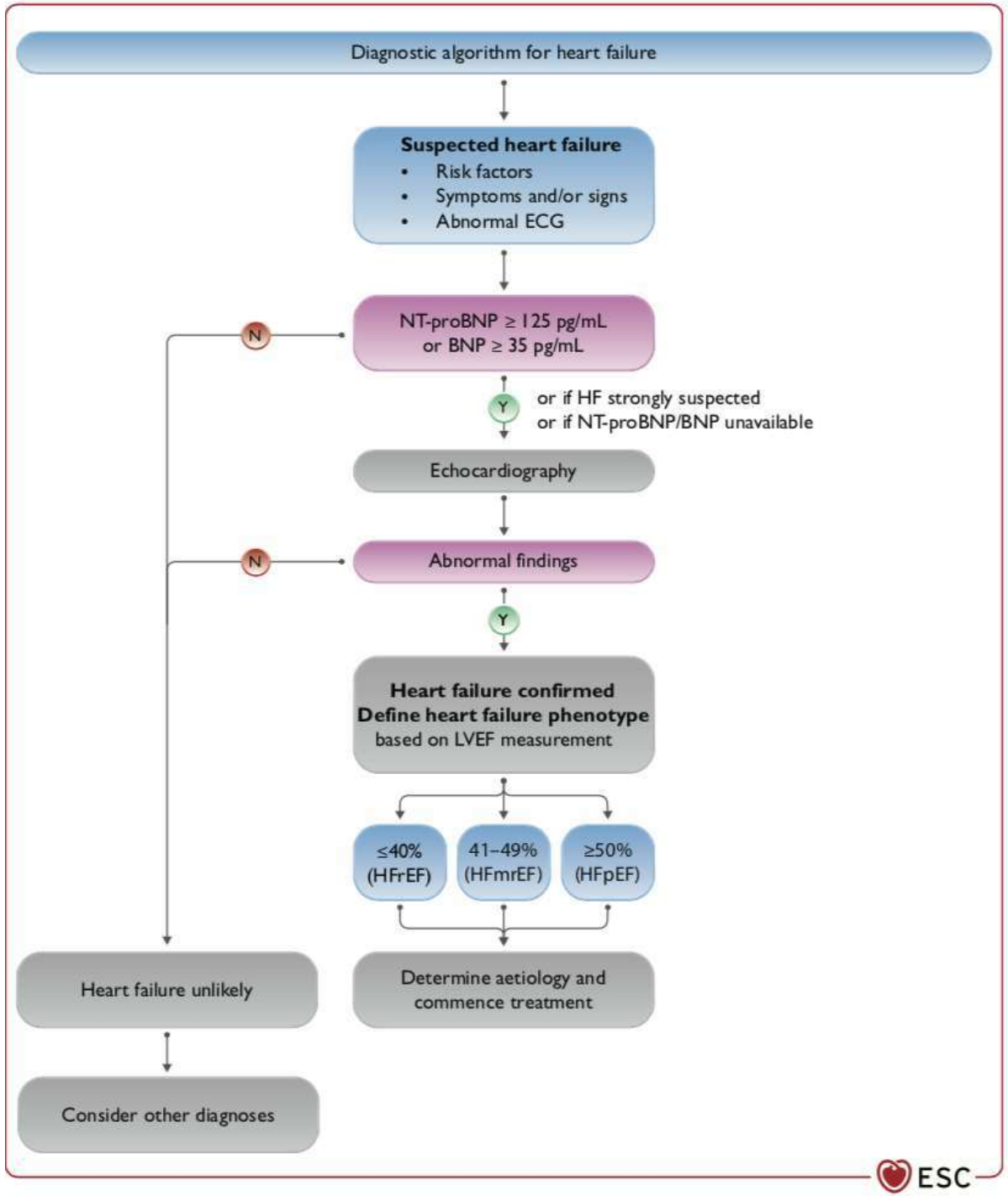
Diagnosis of HF-highly dependent of clinical settings

- Ambulatory HF
- Acute HF
  - In-hospital
  - Worsening in ED
  - Worsening in ambulatory settings
- Community


crHF
Hospitalization
(de novo)
outpatient visit
ED visit
Hospitalization
(WCHF)
Hospitalization
(advanced HF)
AHF
rapid
gradual
Outpatient visit threshold
ED threshold
Hospital admission threshold


cr HF
Diagnostic algorithm for heart failure
Suspected heart failure
• Risk factors
• Symptoms and/or signs
• Abnormal ECG
clinic
NT-proBNP ≥ 125 pg/mL
or BNP ≥ 35 pg/mL
NPs
N
Y
or if HF strongly suspected
or if NT-proBNP/BNP unavailable
Echocardiography
N
Abnormal findings
Y
Heart failure confirmed
Define heart failure phenotype
based on LVEF measurement
≤40%
(HFrEF)
41–49%
(HFmrEF)
≥50%
(HFpEF)
Echo
Heart failure unlikely
Determine aetiology and
commence treatment
Consider other diagnoses
ESC


AHF
Diagnostic workup of new onset acute heart failure
clinic
Patient history, signs and/or
symptoms suspected of acute HF
FoCUS
+
Add
• Electrocardiogram
• Pulse oximetry
• Echocardiography
• Initial laboratory investigations[a]
• Chest X-ray
• Lung ultrasound
• Other specific evaluations[b]
Natriuretic peptide testing
NPs
• BNP <100 pg/mL
• NT-proBNP <300 pg/mL
• MR-proANP <120 pg/mL
• BNP ≥ 100 pg/mL
• NT-proBNP ≥300 pg/mL[c]
• MR-proANP ≥120 pg/mL
Acute heart failure ruled out
Acute heart failure confirmed
Echo
Comprehensive echocardiography
ESC



Suspected heart failure

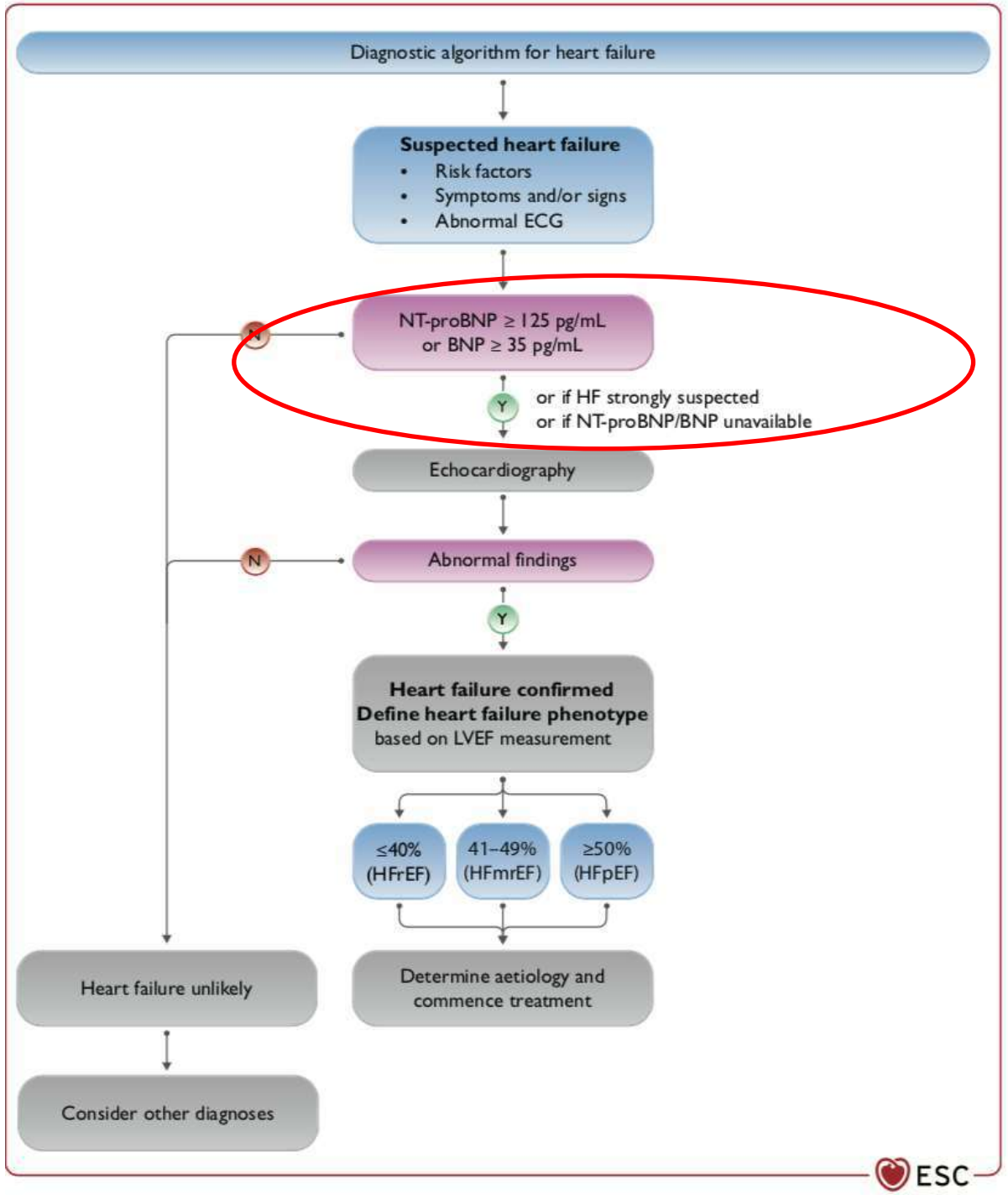
- Risk factors

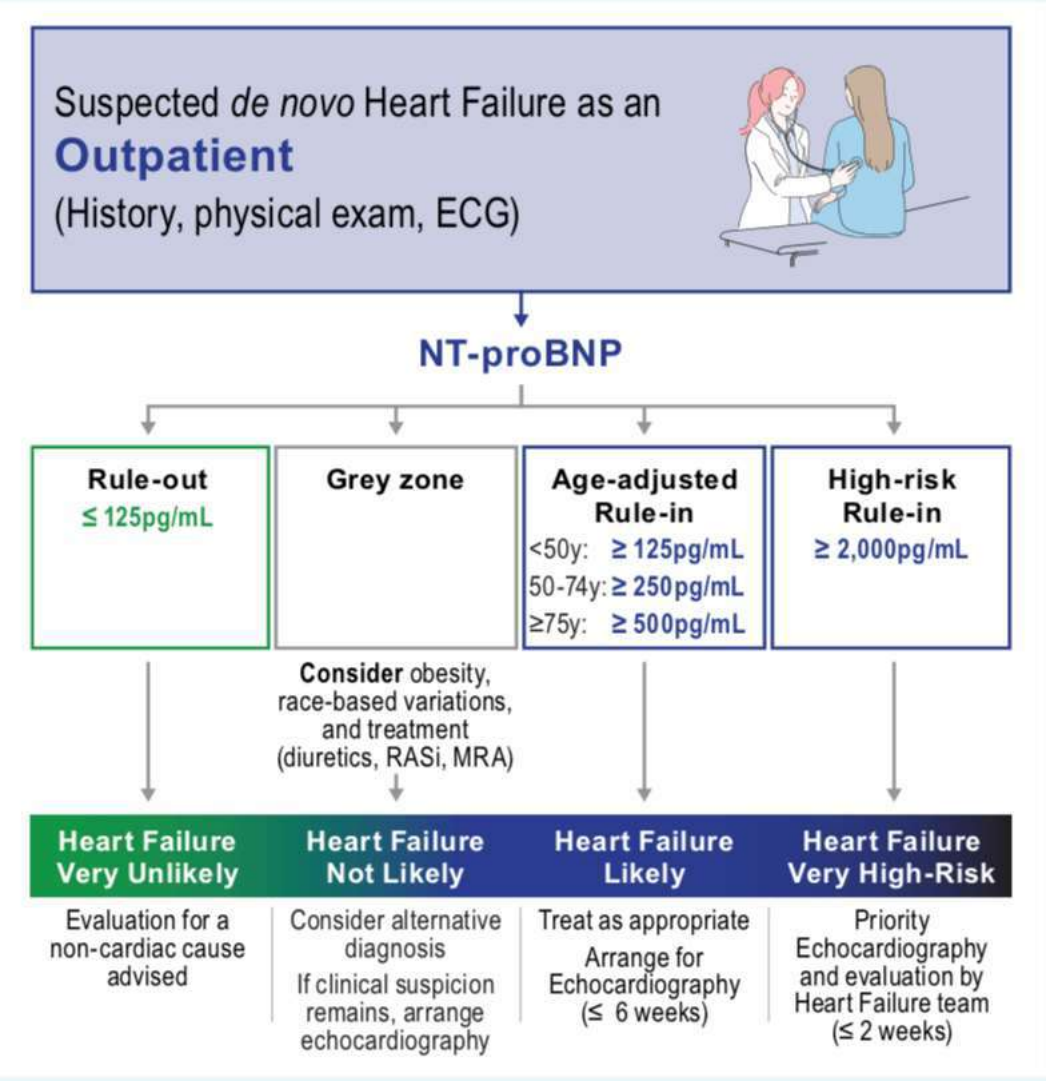
ESC European Society of Cardiology
European Journal of Preventive Cardiology
doi:10.1093/eurjpc/zwab147

Preventing heart failure: a position paper of the Heart Failure Association in collaboration with the European Association of Preventive Cardiology

Table 7 Populations attributable risks for developing heart failure in Europe

PAR	Schrage et al.[172] (2020)	Magnussen et al.[173] (2019)		Uijl et al.[174] (2019)						Pujades-Rodriguez et al.[175] (2015)		Baena-Diez et al.[176] (2010)
	All	Men	Women	Men			Women			Men	Women	All
				55–65 years	65–75 years	>75 years	55–65 years	65–75 years	>75 years			
Hypertension	15.9	13	9	9.2	—	7.5	—	—	—	—	—	50
Diabetes	13	11	8	4.5	3.7	1.6	10.3	4.3	2.3	—	—	—
Obesity	28	22	30	9.1	5.7	2	14.3	7.5	2.3	—	—	43
Smoking	15.1	12.5	8	8	2.9	—	8	3.4	—	7.9	8.3	—
Cholesterol	3.6	0.5	3	—	—	—	—	—	—	—	—	—
Low physical activity	—	—	—	—	5	5.3	6	5.7	6.4	—	—	—
History of MI	—	8	2	—	—	—	—	—	—	—	—	—
History of stroke	—	1	1	—	—	—	—	—	—	—	—	—
History of COPD	—	—	—	17.2	17.1	16.1	23.9	19.6	13.8	—	—	—
History of AF	—	—	—	16.5	11.9	11.4	23.8	16.1	15.6	—	—	—
History of ischemic heart disease	—	—	—	—	—	—	—	—	—	—	—	18.6
Combined PAR %	75.6	63	59	64.5	46.3	43.9	86.3	56.6	40.4	—	—	—





Practical algorithms for early diagnosis of heart failure and heart stress using NT-proBNP: A clinical consensus statement from the Heart Failure Association of the ESC . European Journal of Heart Failure (2023)

NT-proBNP in asymptomatic patients with risk factors: heart stress

Various risk factors, such as HTN, atherosclerotic CV disease, diabetes, obesity, and others, contribute to an increased susceptibility to the development of HF.

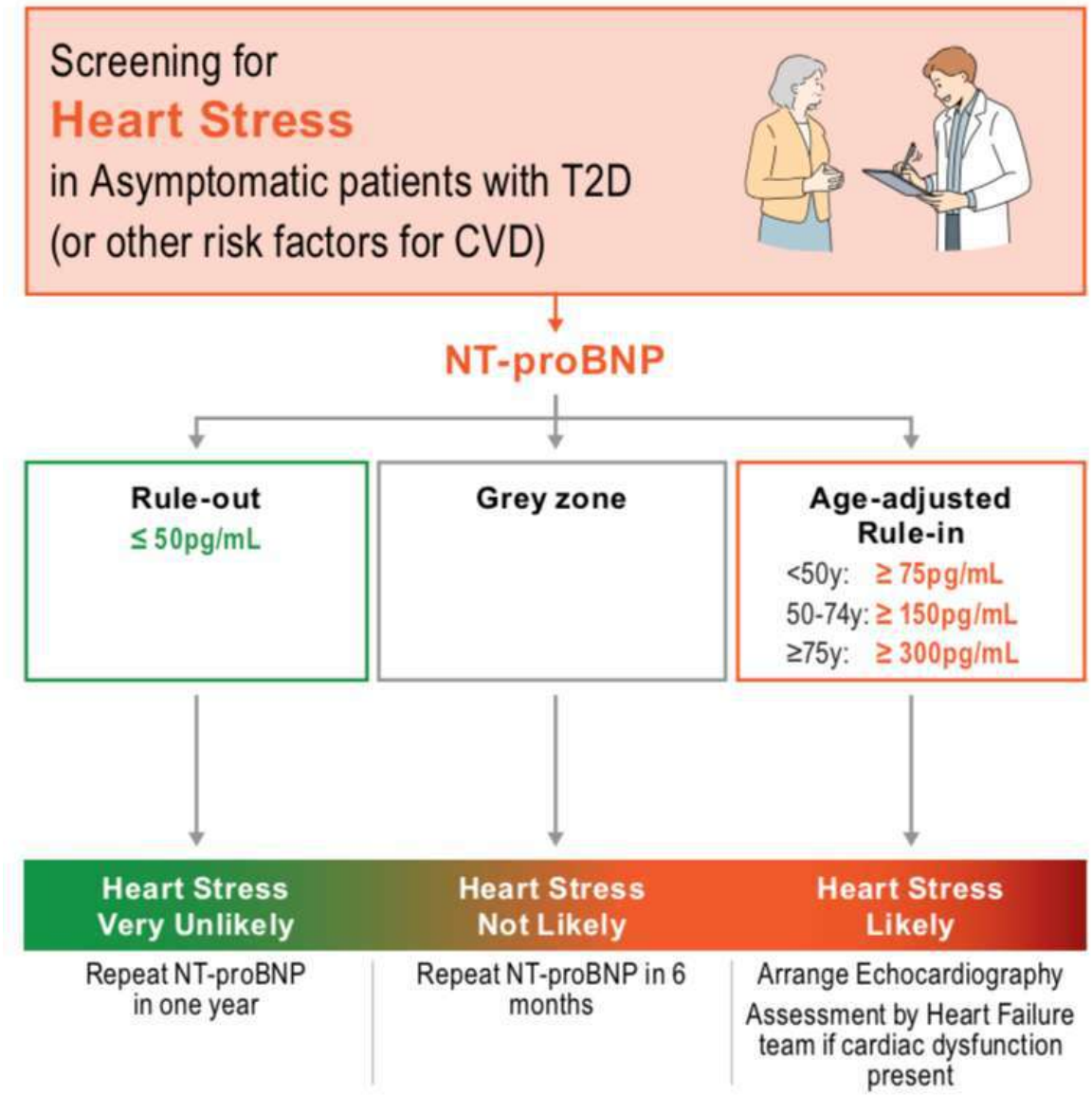
ESC European Society of Cardiology

European Journal of Heart Failure (2023)
doi:10.1002/ejhf.3036

POSITION PAPER

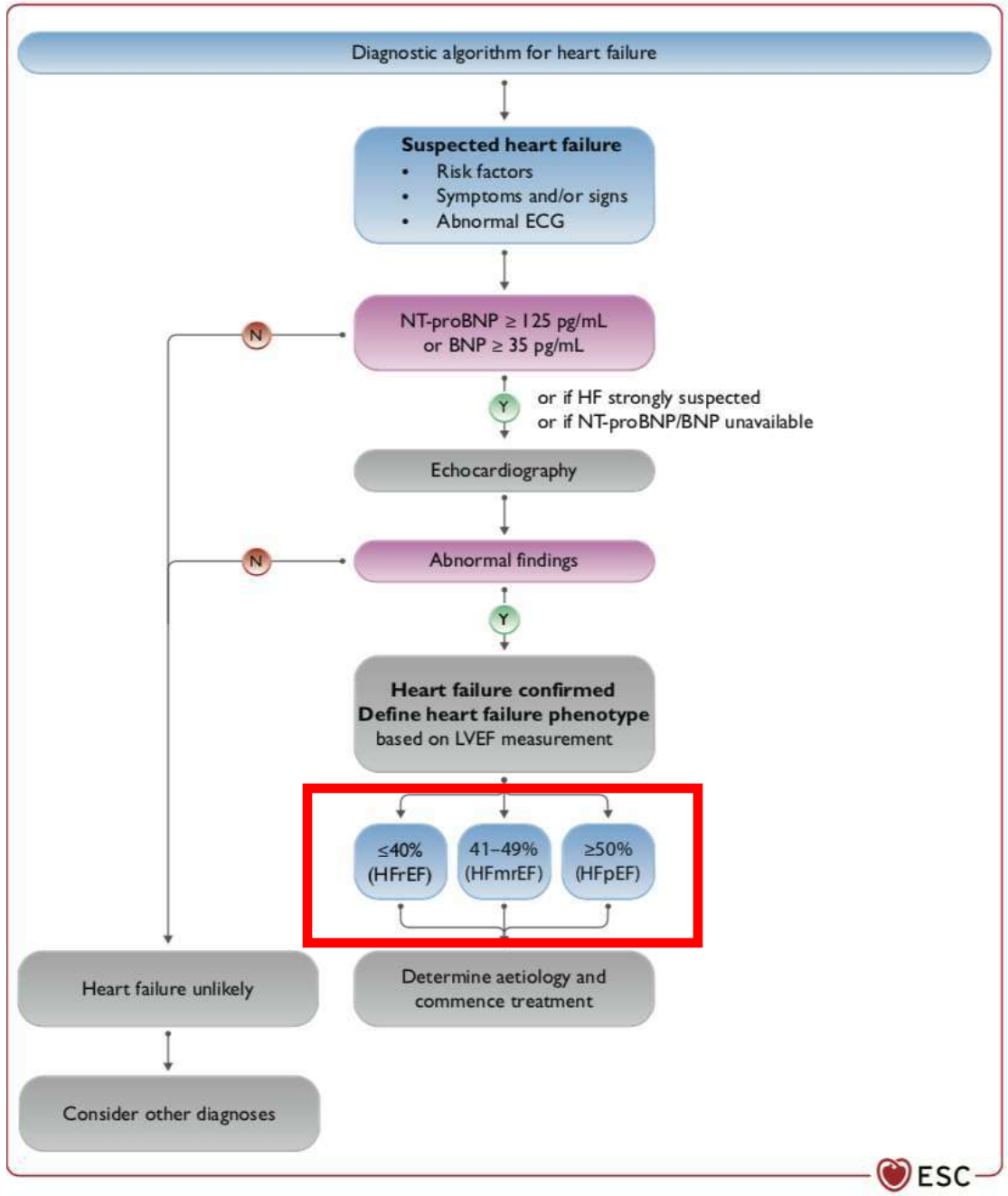
Practical algorithms for early diagnosis of heart failure and heart stress using NT-proBNP: A clinical consensus statement from the Heart Failure Association of the ESC

Antoni Bayes-Genis[1]*, Kieran F. Docherty[2], Mark C. Petrie[2], James L. Januzzi[3], Christian Mueller[4], Lisa Andreson[5], Biykem Bozkurt[6], Javed Butler[7], Ovidiu Chioncel[8], John G.F. Cleland[9], Ruxandra Christodorescu[10], Stefano Del Prato[11], Finn Gustafsson[12], Carolyn S.P. Lam[13], Brenda Moura[14,15], Rodica Pop-Busui[16], Petar Seferovic[17,18], Maurizio Volterrani[19,20], Muthiah Vaduganathan[21], Marco Metra[22], and Giuseppe Rosano[23]



Recommended diagnostic tests in all patients with suspected chronic heart failure

Recommendations	Class[a]	Level[b]
BNP/NT-proBNP[c]	I	B
12-lead ECG	I	C
Transthoracic echocardiography	I	C
Chest radiography (X-ray)	I	C
Routine blood tests for comorbidities, including full blood count, urea and electrolytes, thyroid function, fasting glucose and HbA1c, lipids, iron status (TSAT and ferritin)	I	C



- Echocardiography is recommended as the key investigation for the . assessment of cardiac function. As well as the determination of the .LVEF, echocardiography also provides information on other parameters such as chamber size, eccentric or concentric LVH, regional . wall motion abnormalities (that may suggest underlying CAD, . Takotsubo syndrome, or myocarditis), RV function, pulmonary . hypertension, valvular function, and markers of diastolic . function

HF with reduced EF (HFrEF):

- HF with LVEF ≤40%

HF with mildly reduced EF (HFmrEF):

- HF with LVEF 41–49%

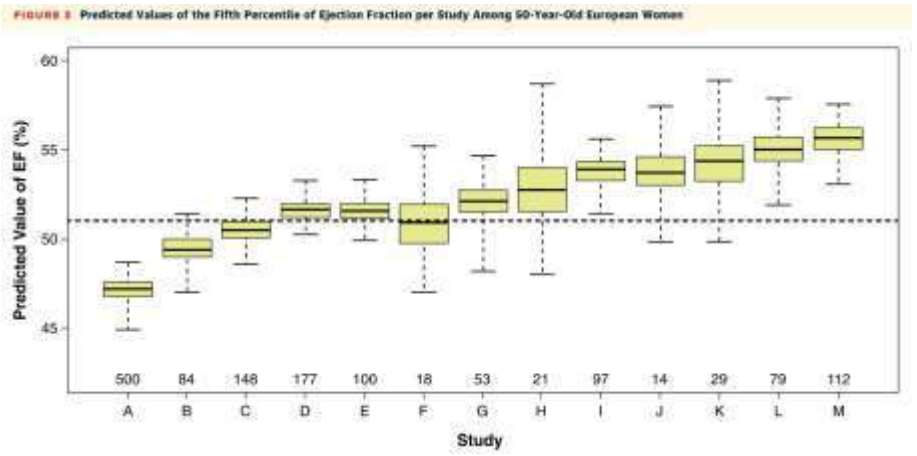
HF with preserved EF (HFpEF):

- HF with LVEF ≥50%

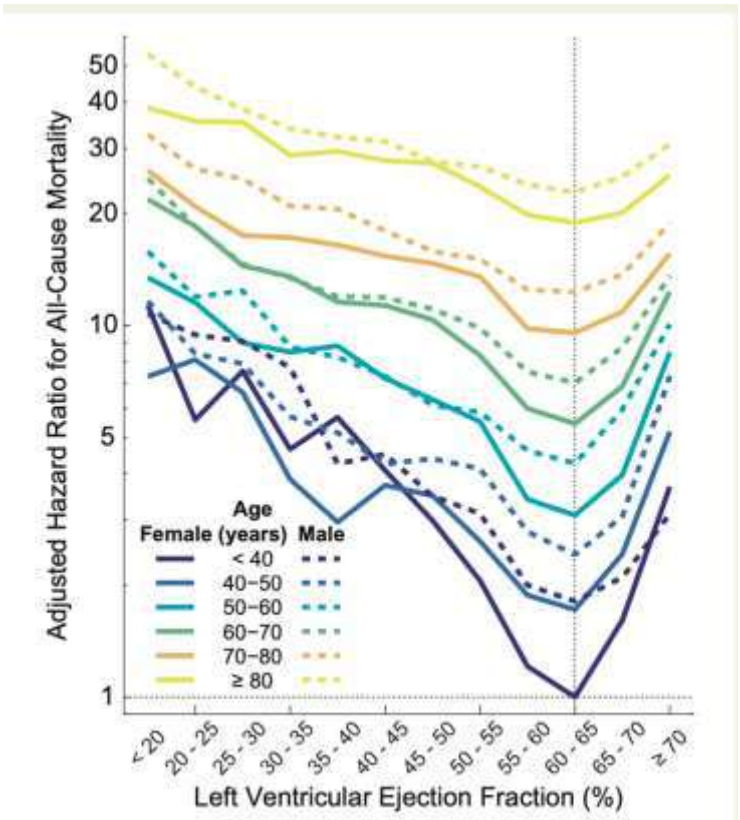
HF with improved EF (HFimpEF):

- HF with a baseline LVEF ≤40%, a ≥10 point increase from baseline LVEF, and a second measurement of LVEF >40%

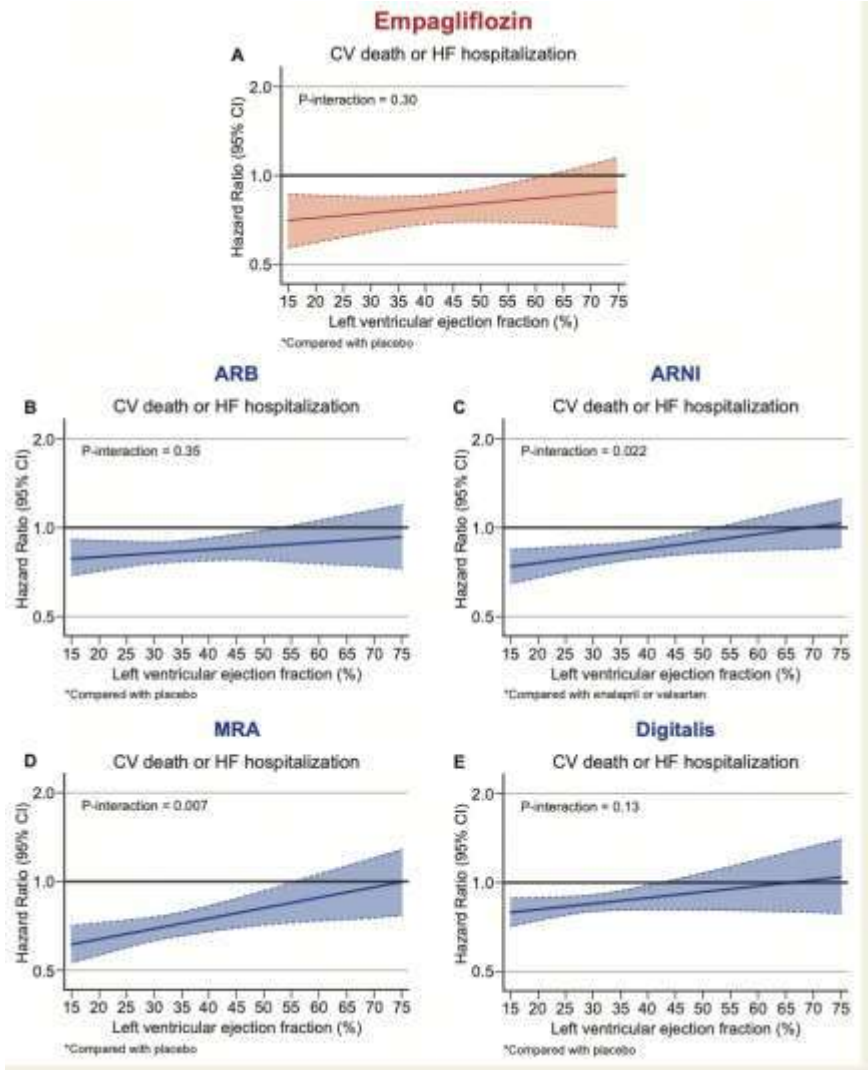
Where is the best LVEF cut off for HFpEF?



Ethnic-Specific Normative Reference Values for Echocardiographic LA and LV Size, LV Mass, and Systolic Function The EchoNoRMAL Study



Routinely reported ejection fraction and mortality in clinical practice: where does the nadir of risk lie?



Re-emergence of heart failure with a normal ejection fraction?

HFpEF Diagnosis ….

8 Heart failure with preserved ejection fraction

8.1 The background to heart failure with preserved ejection fraction

This guideline acknowledges the historical changes in nomenclature and the lack of consensus on the optimal LVEF cut-off to define the group of patients with HF without overtly reduced EF. The term 'preserved' was originally proposed in the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM) Programme to refer to patients with an EF (>40%) that was not clearly 'reduced' or completely 'normal'.[252] While the current guidelines have designated patients with an LVEF 41–49% as HFmrEF, we recognize that there will be debate about what constitutes 'mildly reduced' EF, what these EF cut-offs should be, and whether they should be different for men and women.[14,253] The EACVI defines sys-

8.3 The diagnosis of heart failure with preserved ejection fraction

The diagnosis of HFpEF remains challenging. Several diagnostic criteria have been proposed by societies and in clinical trials.[260] These criteria vary widely in their sensitivities and specificities for diagnosing HFpEF. More recently, two score-based algorithms (H_2FPEF and HFA-PEFF) have been proposed to aid the diagnosis.[259,261] While the generalizability of the scores has been tested in various trial and observational cohorts, their diagnostic performance has varied.[262–269]

Both scores assign a substantial proportion of suspected HFpEF patients as intermediate likelihood, wherein additional diagnostics are proposed. Thus, depending on which score is used, different patients will be referred for additional testing or allocated as having HFpEF. Furthermore, physicians may not have access to all the specialized tests recommended by the specific diagnostic algorithms. This limits the broad clinical applicability of the scores and demonstrates the ongoing diagnostic uncertainty in HFpEF.[267]

Who are these patients?

European Journal of Heart Failure (2017)
doi:10.1002/ejhf.813

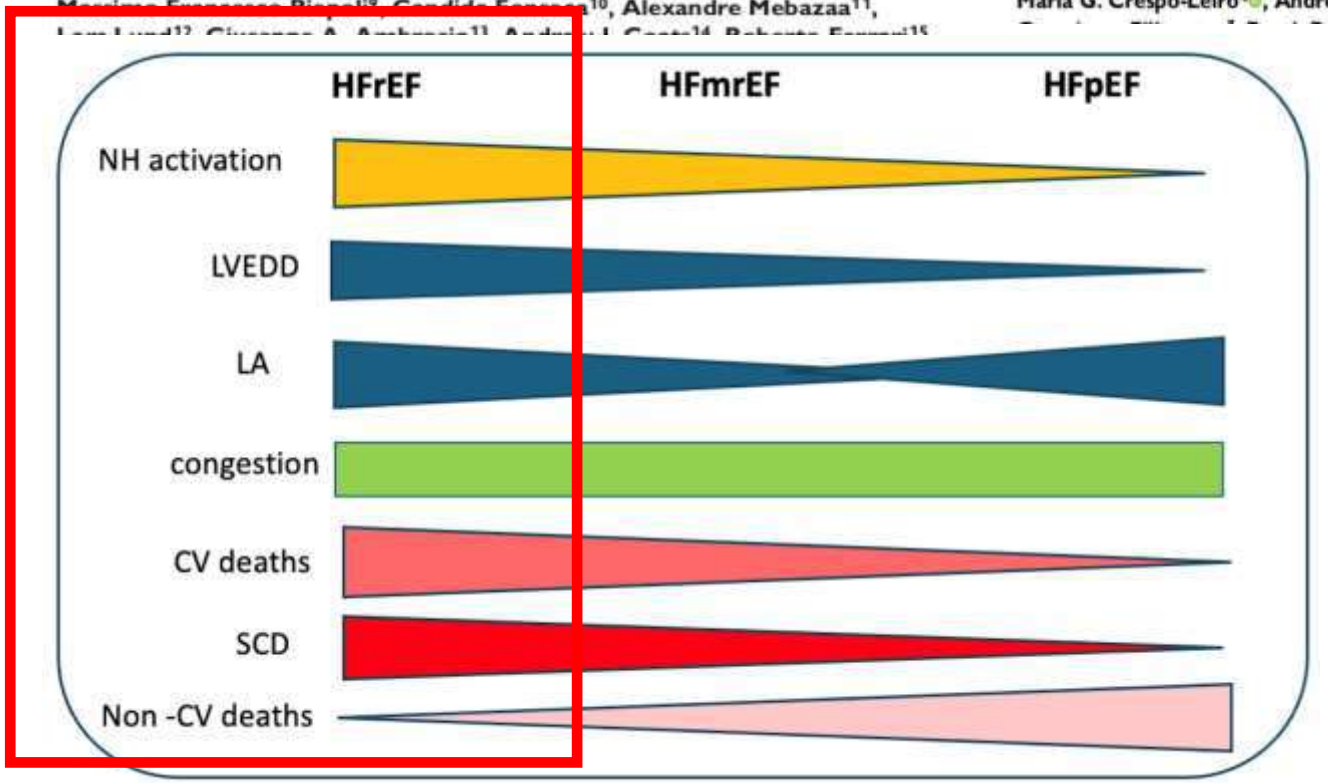
Epidemiology and one-year outcomes in patients with chronic heart failure and preserved, mid-range and reduced ejection fraction: an analysis of the ESC Heart Failure Long-Term Registry

Ovidiu Chioncel[1]*, Mitja Lainscak[2], Petar M. Seferovic[3], Stefan D. Anker[4], Maria G. Crespo-Leiro[5], Veli-Pekka Harjola[6], John Parissis[7], Cecile Laroche[8], ... Alexandre Mebazaa[11], ...

ESC European Society of Cardiology
European Journal of Heart Failure (2022) 24, 335–350
doi:10.1002/ejhf.2408
RESEARCH ARTICLE

A comprehensive characterization of acute heart failure with preserved versus mildly reduced versus reduced ejection fraction – insights from the ESC-HFA EORP Heart Failure Long-Term Registry

Agnieszka Kapłon-Cieślicka[1], Lina Benson[2], Ovidiu Chioncel[3], Maria G. Crespo-Leiro[4], Andrew J.S. Coats[5], Stefan D. Anker[6], ...



HFpEF compared to HFrEF

- 6-8 years older
- More W
- Less IHD more HTN
- More AF, LVH, CKD, Sleep Apnoea, Cancers
- Similar clinical congestion

HFpEF definitions in EU/US/JAP Guidelines

Table 5 Current heart failure classifications according to left ventricular ejection fraction in contemporary clinical practice guidelines

Society	HF classification according to LVEF	LVEF	Additional requirements
ACCF/AHA[3]	• Heart failure with reduced ejection fraction (HFrEF)	≤40%	Symptoms and signs
	• Heart failure with preserved ejection fraction (HFpEF)	≥50%	Symptoms and signs
	a) HFpEF, borderline	41–49%	Symptoms and signs
	b) HFpEF, improved	>40%	Symptoms and signs
ESC[4]	• Heart failure with reduced ejection fraction (HFrEF)	<40%	Symptoms and signs
	• Heart failure with mid-range ejection fraction (HFmrEF)	40–49%	Symptoms and signs, elevated levels of natriuretic peptides and at least one additional criterion of relevant structural heart disease (LVH or LAE) or diastolic dysfunction
	• Heart failure with preserved ejection fraction (HFpEF)	≥50%	Symptoms and signs, elevated levels of natriuretic peptides and at least one additional criterion of relevant structural heart disease (LVH or LAE) or diastolic dysfunction
JCS/JHFS[5]	• Heart failure with reduced ejection fraction (HFrEF)	<40%	
	• Heart failure with mid-range ejection fraction (HFmrEF)	40% to <50%	
	• Heart failure with preserved ejection fraction (HFpEF)	≥50%	
	• Heart failure with preserved ejection fraction, improved (HFpEF improved) or heart failure with recovered ejection fraction (HFrecEF)	≥40%	

HFpEF definitions in RCTs

Table 3 Summary of heart failure inclusion criteria for recent clinical trials – heart failure with preserved ejection fraction

Trial	Age, NYHA class	LVEF	Natriuretic peptides	HF hospitalization
TOPCAT[30]	Age ≥50 years NYHA II–IV	LVEF ≥45%	BNP ≥100 pg/mL or NT-proBNP ≥360 pg/mL	Within previous 12 months, with management of HF as a major component
PARAGON-HF[31]	Age ≥50 years NYHA II–IV	LVEF ≥45% and LAE LVH	If NSR, NT-proBNP >200 pg/mL If AF: >600 pg/mL or If no previous hospitalization and If NSR: NT-proBNP >300 pg/mL If AF: NT-proBNP >900 pg/mL	Within previous 9 months
EMPEROR-Preserved[32]	Age ≥18 years NYHA II–IV (at least 3 months)	LVEF >40% (no prior history of LVEF ≤40%)	NT-proBNP >300 pg/mL in NSR or >900 pg/mL in AF	Within 12 months OR evidence of structural changes (LAE or increased LVM) on echo
DELIVER[33]	Age ≥40 years NYHA II–IV	(LVEF >40% and evidence of structural heart disease (i.e. LAE or LVH)	Elevated natriuretic peptides	Medical history HF ≥6 weeks before enrolment with at least intermittent need for diuretic treatment

Lower NPs levels in HFpEF

Lower wall stress
Constrictive pericarditis
Obesity/Insulin resistance (high rate of NP clearence in obese)
Stage of disease

HFpEF Diagnosis

- Clinical diagnosis of HF and LVEF >50% not attributable to an underlying cause such as an infiltrative cardiomyopathy, hypertrophic cardiomyopathy, valvular disease, pericardial disease, or high-output HF.

HFpEF mimics

TABLE 1 Diagnostic Clues and Recommended Testing for HFpEF Mimics

HFpEF Mimic	Clinical Clues	Diagnostic Testing
Cardiac amyloidosis	Increased LV wall thickness Musculoskeletal issues (carpal tunnel syndrome, lumbar spinal stenosis) Neuropathy (sensory or autonomic)	Monoclonal protein screen (serum/urine immunofixation electrophoresis and serum free light chains) Technetium pyrophosphate scan (interpreted in the context of a negative monoclonal protein screen) Endomyocardial biopsy if monoclonal protein screen is positive
Hypertrophic cardiomyopathy	Unexplained LV hypertrophy LV outflow tract obstruction Family history	CMR if diagnosis is uncertain based on echocardiogram
Cardiac sarcoidosis	Extracardiac disease (pulmonary, ocular, dermatologic) High-degree atrioventricular block (especially if age <60 y) Ventricular arrhythmias	CMR FDG-PET scan Tissue biopsy (cardiac or extracardiac)
Hemochromatosis	Family history or history of frequent blood transfusions Diabetes Erectile dysfunction	Ferritin and transferrin *HFE* genetic testing CMR with T2* imaging
Fabry disease	Angiokeratomas Sensory neuropathy Proteinuria X-linked inheritance	Serum alpha-galactosidase level (in men) *GLA* genetic testing Biopsy of affected tissue
High-output HF	Echocardiogram with 4-chamber enlargement and/or increased LV outflow tract VTI	Investigate and treat underlying cause: anemia, arteriovenous malformations, cirrhosis, fistulas, thiamine deficiency
Myocarditis	Antecedent viral infection Elevated troponin in the absence of coronary artery disease Heart block and/or ventricular arrhythmias	CMR Endomyocardial biopsy
Pericardial disease	Prior cardiac surgery, chest radiation, or pericarditis Right-sided HF symptoms	CMR Right and left heart catheterization to demonstrate discordance in LV/RV pressure tracings during inspiration

Objective evidence of ***cardiac structural, functional*** and serological abnormalities consistent with the presence of left ventricular diastolic dysfunction

Parameter[a]	Threshold	Comments
LV mass index **Relative wall thickness**	≥**95** g/m^2 (Female), ≥**115** g/m^2 (Male) >**0.42**	Although the presence of concentric LV remodelling or hypertrophy is supportive, the absence of LV hypertrophy does not exclude the diagnosis of HFpEF
LA volume index[a]	>**34** mL/m^2 (SR)	In the absence of AF or valve disease, LA enlargement reflects chronically elevated LV filling pressure (in the presence of AF, the threshold is >40 mL/m^2)
E/e' ratio at rest[a]	>**9**	Sensitivity 78%, specificity 59% for the presence of HFpEF by invasive exercise testing, although reported accuracy has varied. A higher cut-off of 13 had lower sensitivity (46%) but higher specificity (86%).[71,259,274]
NT-proBNP **BNP**	>**125** (SR) or >**365** (AF) pg/mL >**35** (SR) or >**105** (AF) pg/mL	Up to 20% of patients with invasively proven HFpEF have NPs below diagnostic thresholds, particularly in the presence of obesity
PA systolic pressure **TR velocity at rest**[a]	>**35** mmHg >**2.8** m/s	Sensitivity 54%, specificity 85% for the presence of HFpEF by invasive exercise testing[259,261]

ESC European Society of Cardiology

European Heart Journal - Cardiovascular Imaging (2021) **22**, 505–515
doi:10.1093/ehjci/jeaa253

Diastolic dysfunction and mortality in 436 360 men and women: the National Echo Database Australia (NEDA)

David Playford [1]*, Geoff Strange [1], David S. Celermajer [2], Geoffrey Evans [3], Gregory M. Scalia [4], Simon Stewart [5,6], and David Prior [7,8]; On behalf of the NEDA Investigators

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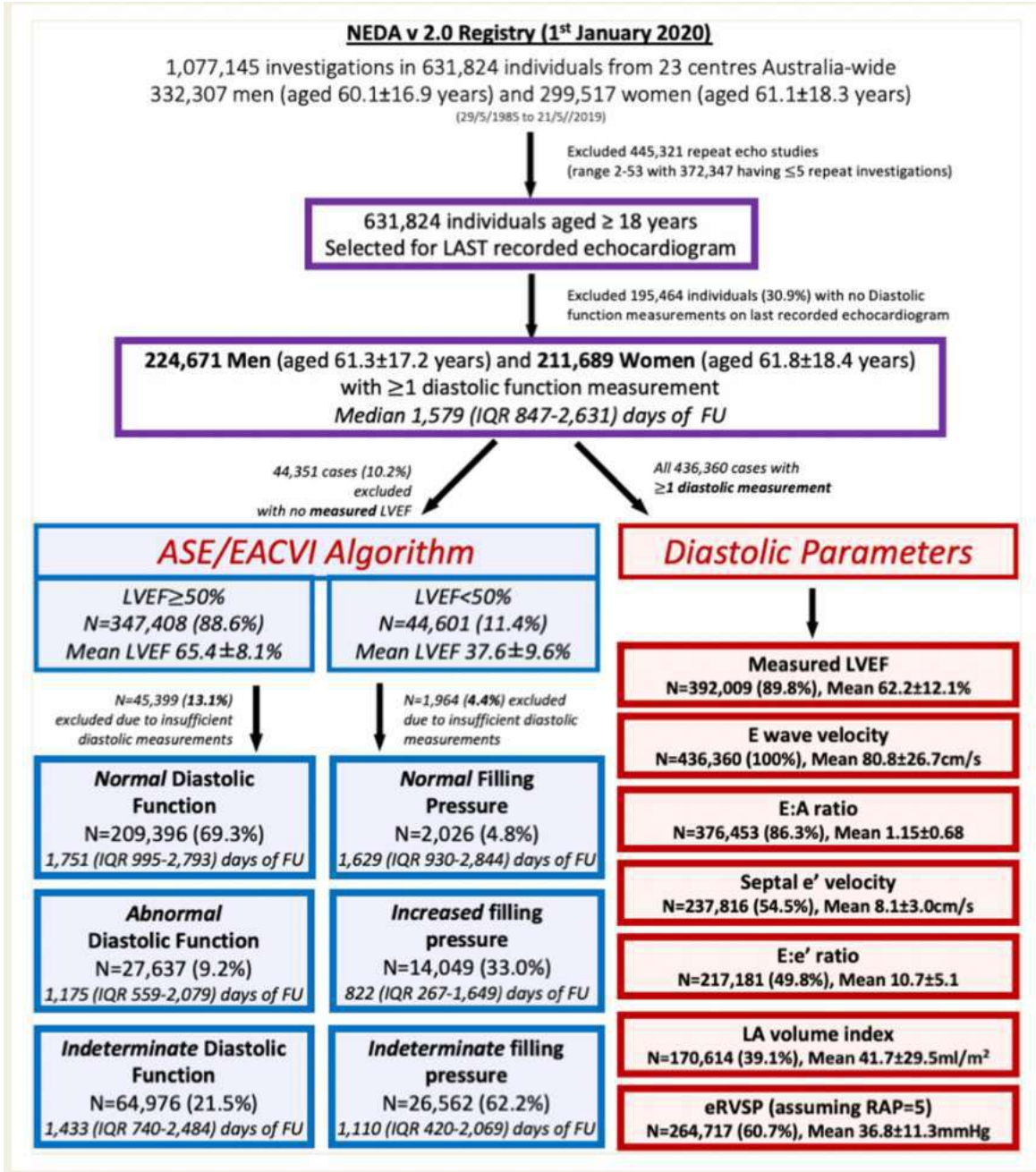
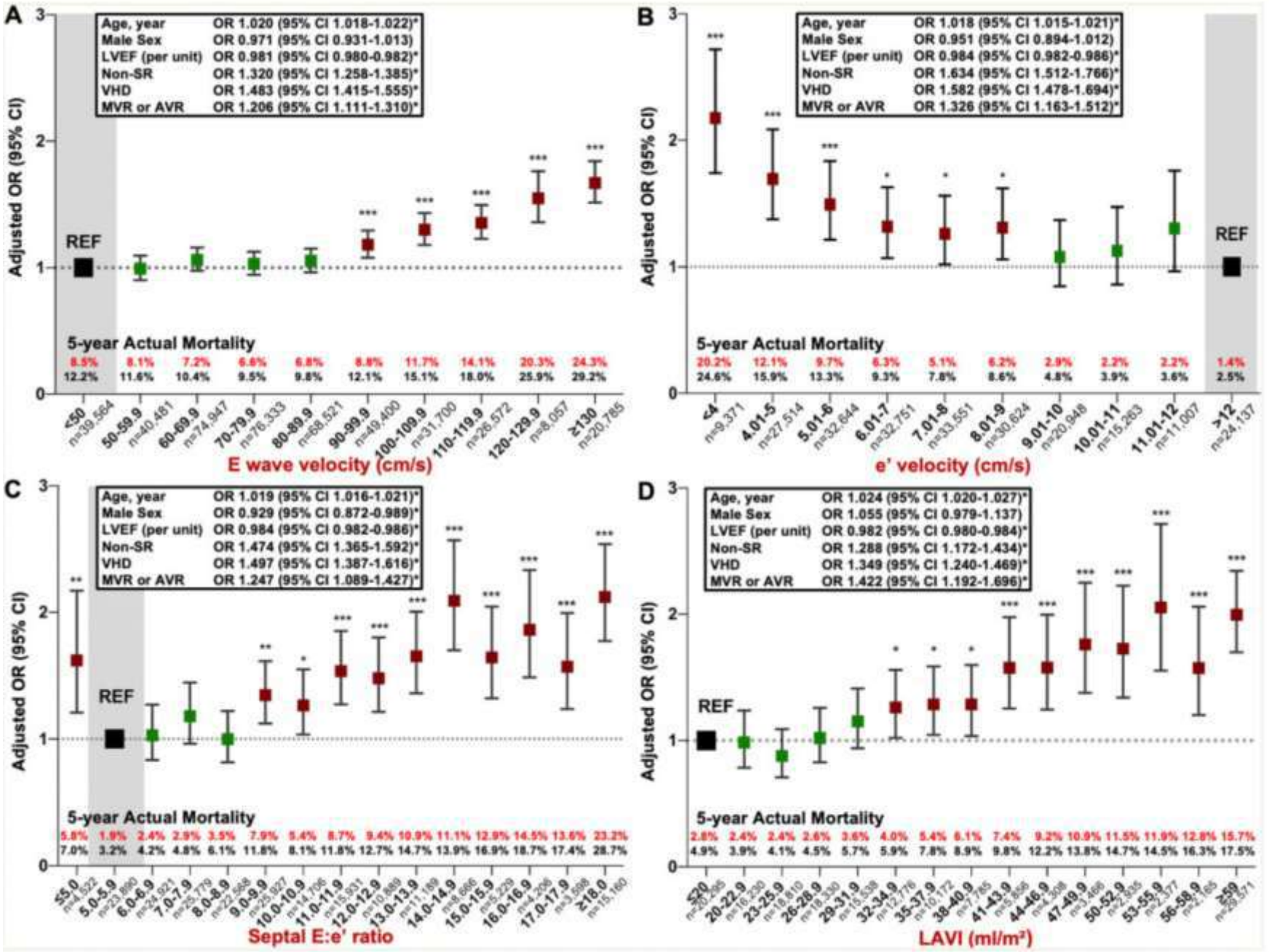
Aims To examine the characteristics/prognostic impact of diastolic dysfunction (DD) according to 2016 American Society of Echocardiography (ASE) and European Society of Cardiovascular Imaging (ESCVI) guidelines, and individual parameters of DD.

Methods and results Data were derived from a large multicentre mortality-linked echocardiographic registry comprising 436 360 adults with ≥1 diastolic function measurement linked to 100 597 deaths during 2.2 million person-years follow-up. ASE/European Association of Cardiovascular Imaging (EACVI) algorithms could be applied in 392 009 (89.8%) cases; comprising 11.4% of cases with 'reduced' left ventricular ejection fraction (LVEF < 50%) and 88.6% with 'preserved' LVEF (≥50%). Diastolic function was indeterminate in 21.5% and 62.2% of 'preserved' and 'reduced' LVEF cases, respectively. Among preserved LVEF cases, the risk of adjusted 5-year cardiovascular-related mortality was elevated in both DD [odds ratio (OR) 1.31, 95% confidence interval (CI) 1.22–1.42; $P < 0.001$] and indeterminate status cases (OR 1.11, 95% CI 1.04–1.18; $P < 0.001$) vs. no DD. Among impaired LVEF cases, the equivalent risk of cardiovascular-related mortality was 1.51 (95% CI 1.15–1.98, $P < 0.001$) for increased filling pressure vs. 1.25 (95% CI 0.96–1.64, $P = 0.06$) for indeterminate status. Mitral E velocity, septal e' velocity, *E*:e' ratio, and LAVi all correlated with mortality. On adjusted basis, pivot-points of increased risk for cardiovascular-related mortality occurred at 90 cm/s for E wave velocity, 9 cm/s for septal e' velocity, an *E*:e' ratio of 9, and an LAVi of 32 mL/m^2.

Conclusion ASE/EACVI-classified DD is correlated with increased mortality. However, many cases remain 'indeterminate'. Importantly, when analysed individually, mitral E velocity, septal e' velocity, *E*:e' ratio, and LAVi revealed clear pivot-points of increased risk of cardiovascular-related mortality.





Specific thresholds of increased mortality were identified at

- 90 cm/s for E-wave velocity,
- 9 cm/s for septal e' velocity,
- E:e' ratio of 9,
- LAVi of 32mL/m2.

ORIGINAL RESEARCH

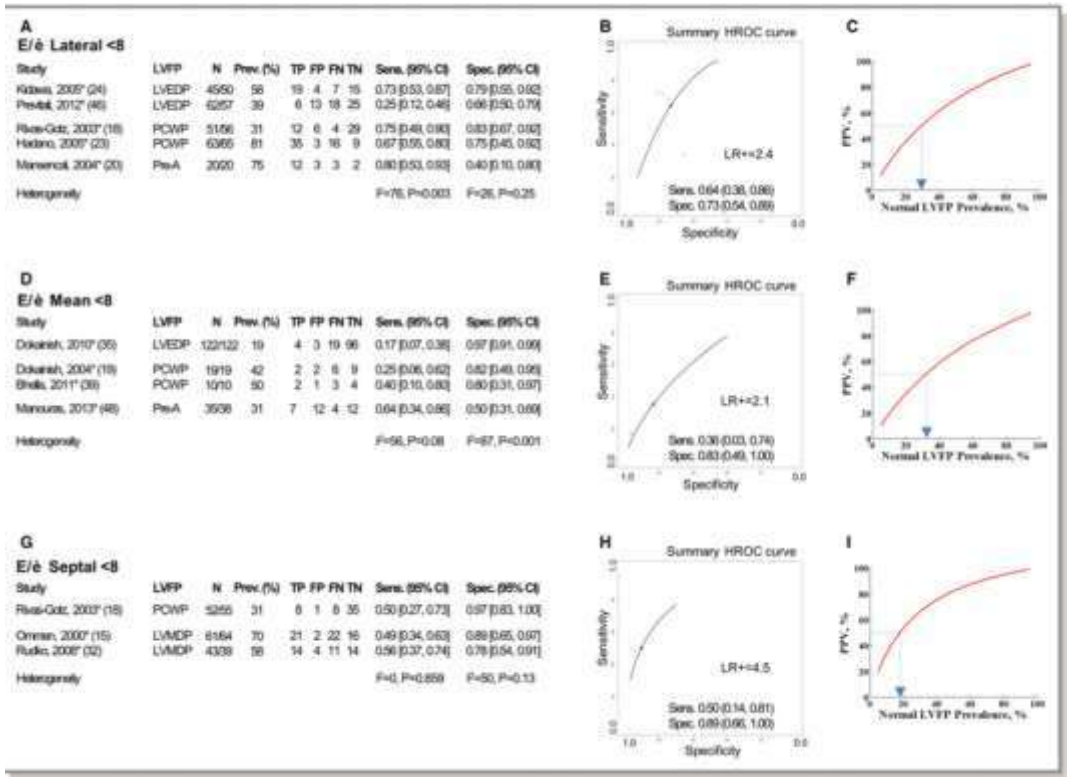
Diagnostic Accuracy of Tissue Doppler Index E/è for Evaluating Left Ventricular Filling Pressure and Diastolic Dysfunction/Heart Failure With Preserved Ejection Fraction: A Systematic Review and Meta-Analysis

Oleg F. Sharifov, MD, PhD; Chun G. Schiros, PhD; Immaculada Aban, PhD; Thomas S. Denney, Jr, PhD; Himanshu Gupta, MD, FACC

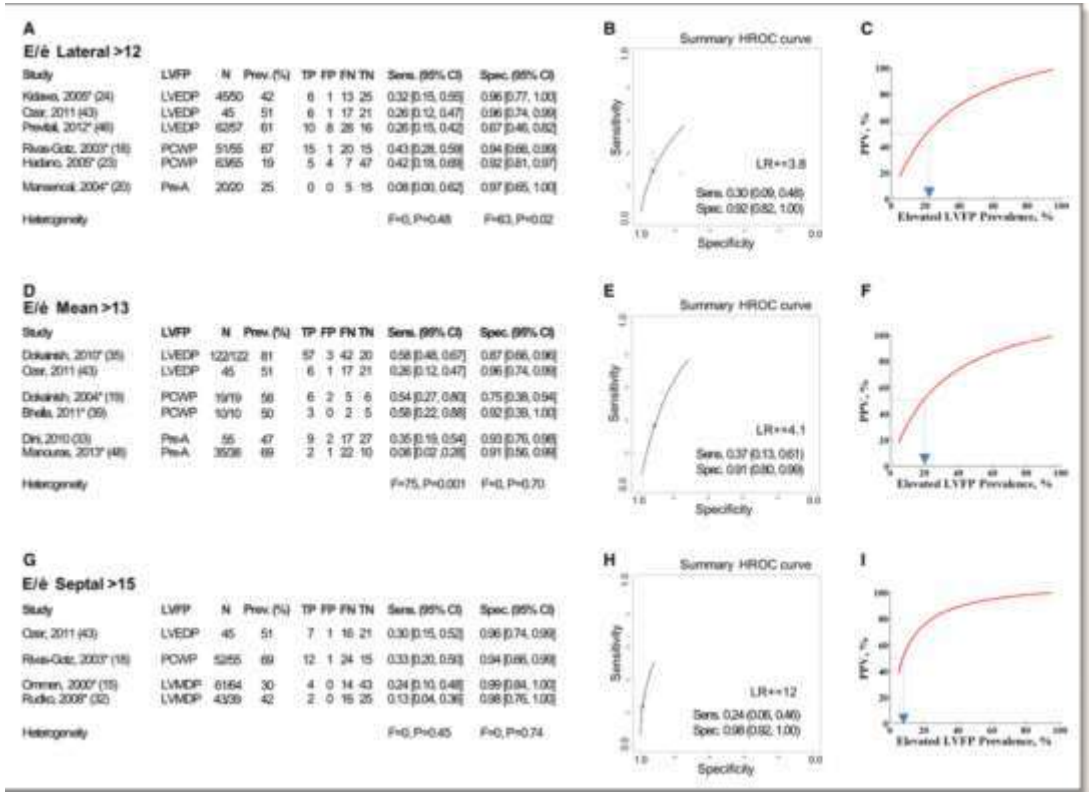
24 studies reporting E/e' and invasive LVFP in preserved EF

The poor-to-mediocre correlation of E/e' to LVFP

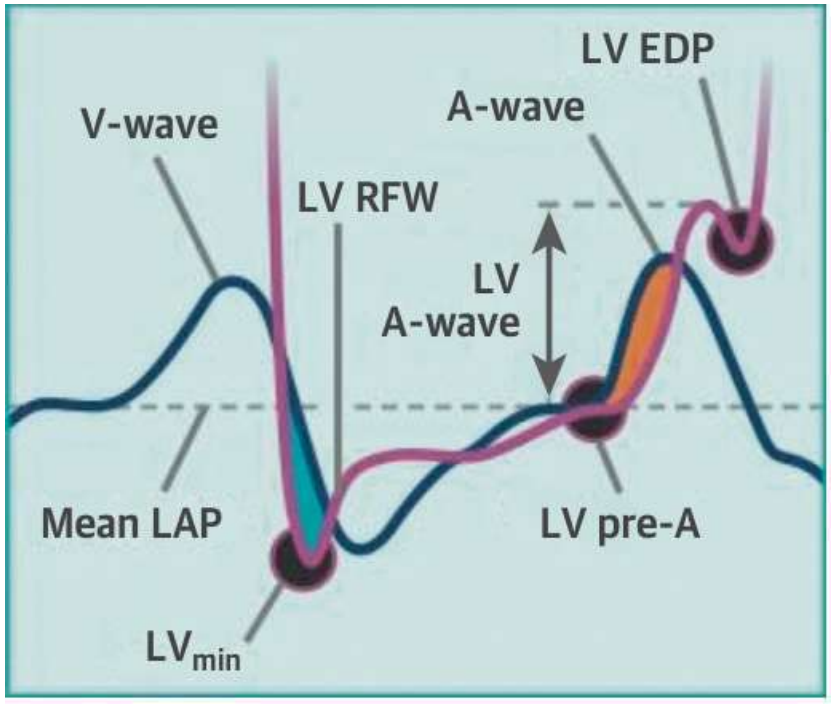
Diagnostic accuracy of E/e recommended by the American Society of Echocardiography to identify ***normal left ventricular filling pressure*** (LVFP).

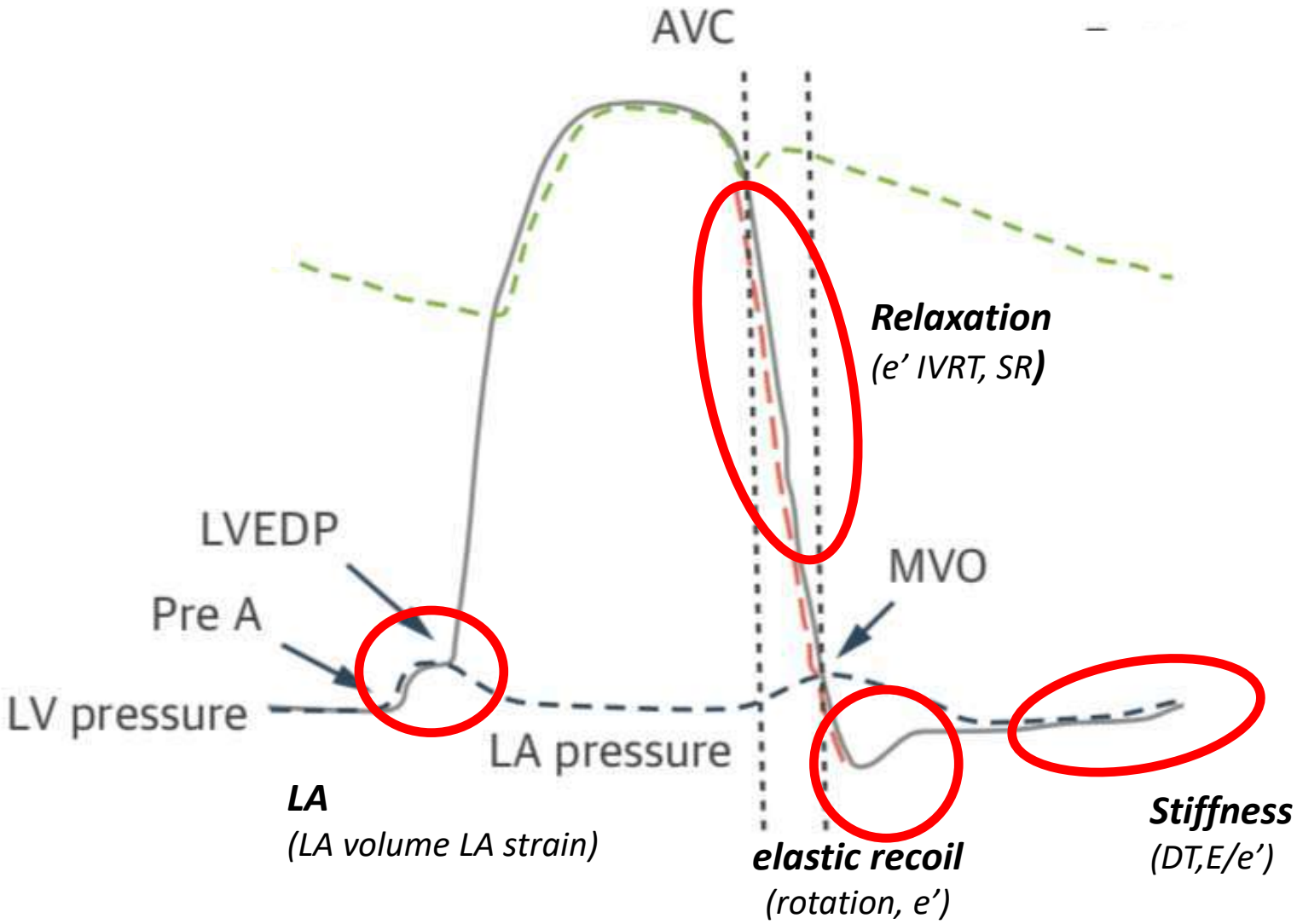


Diagnostic accuracy of E/e recommended by the American Society of Echocardiography to identify ***elevated left ventricular filling pressure*** (LVFP).

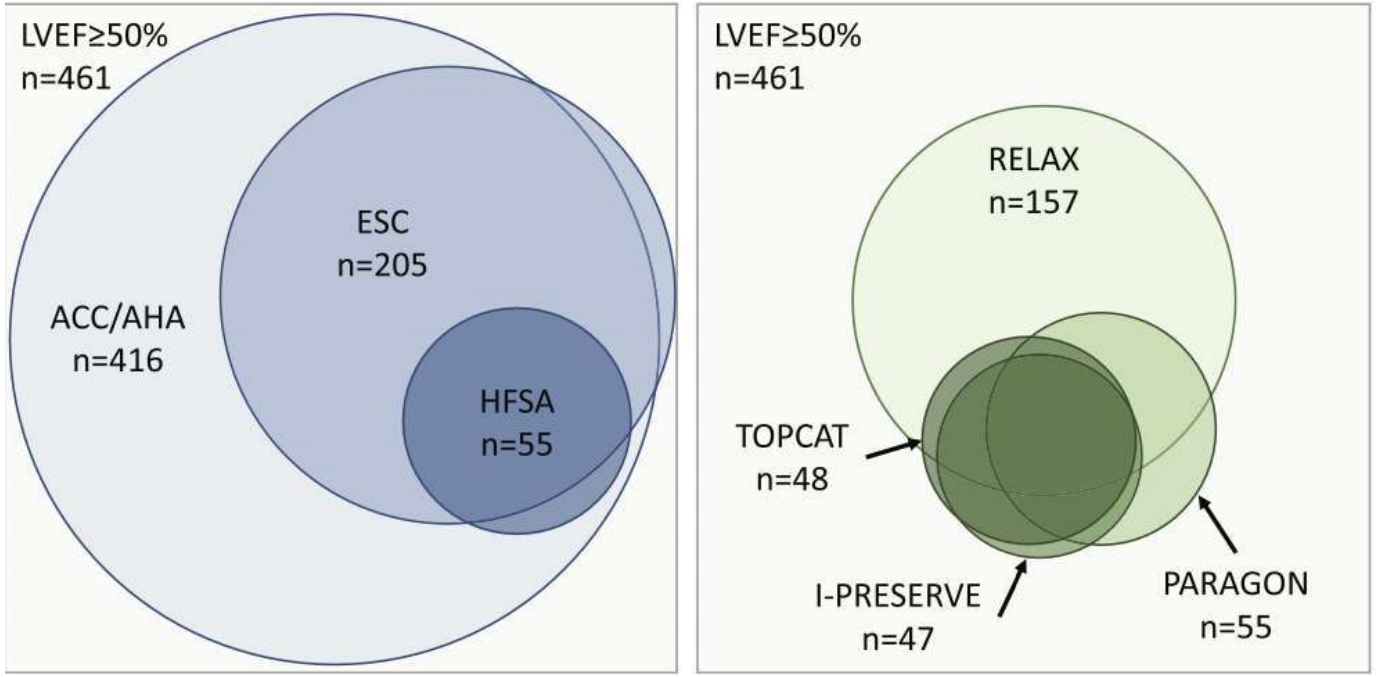


What we measure?





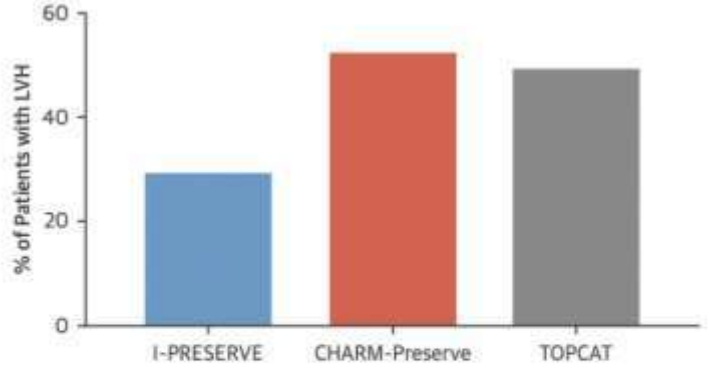
The application of different HFpEF definitions captures distinct groups



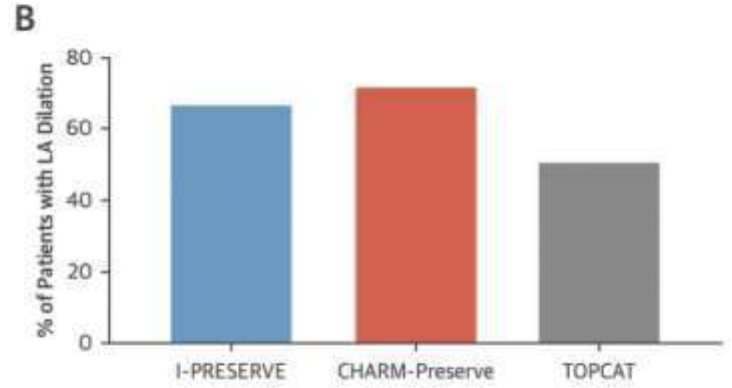
Circulation. 2019;140:353–365. DOI: 10.1161/CIRCULATIONAHA.118.039136

Functional and Morphologic Heterogeneity in HFpEF RCTs

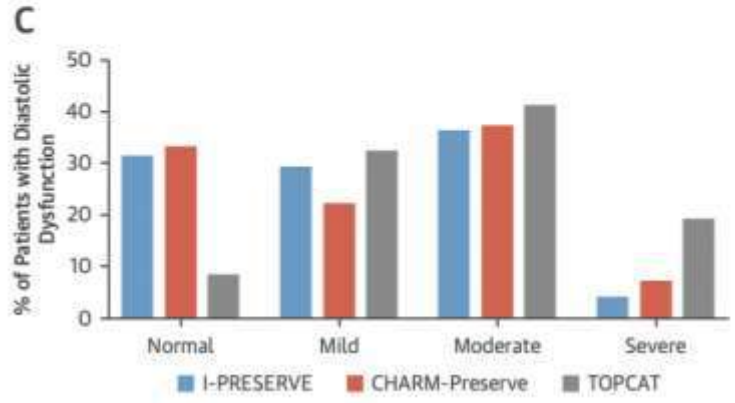
LVH



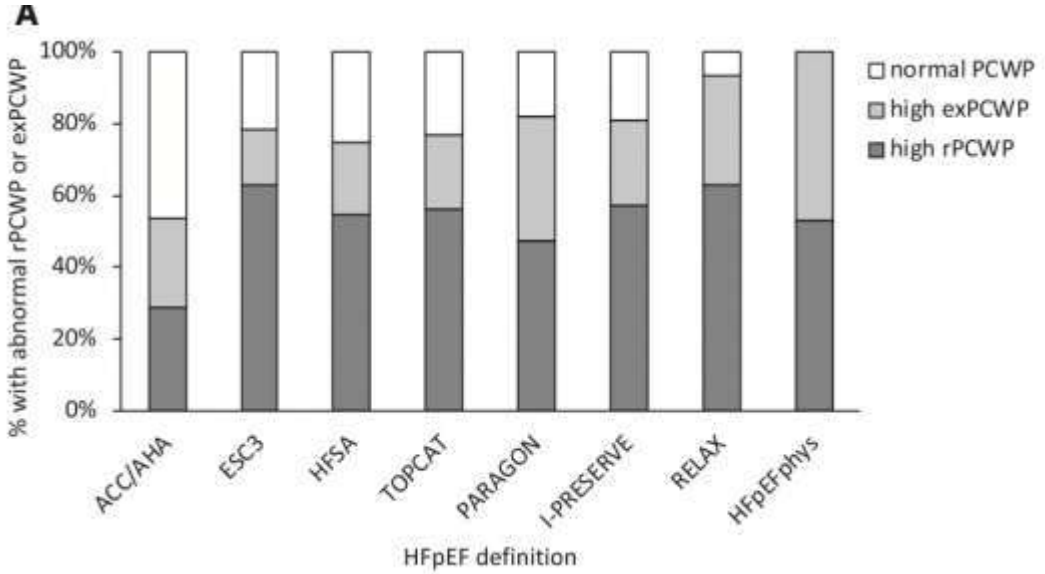
LA



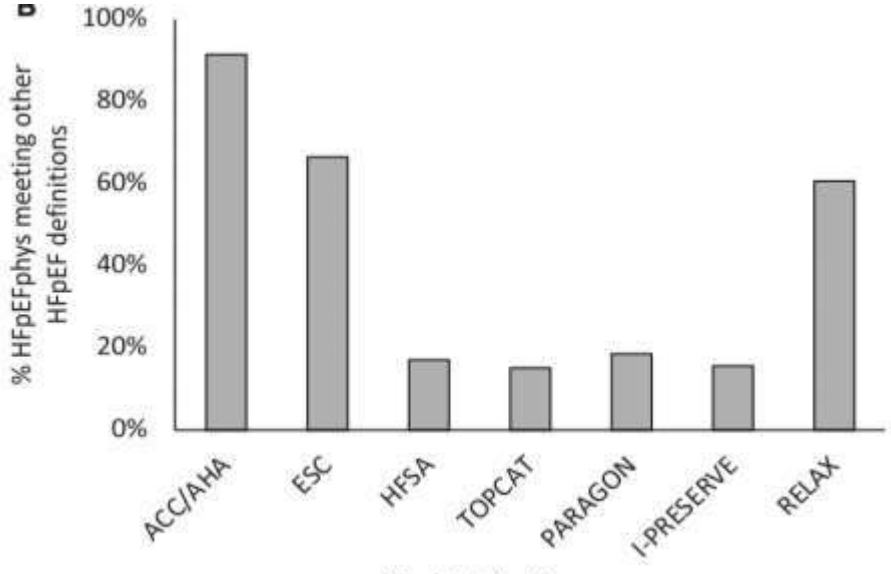
E/E’

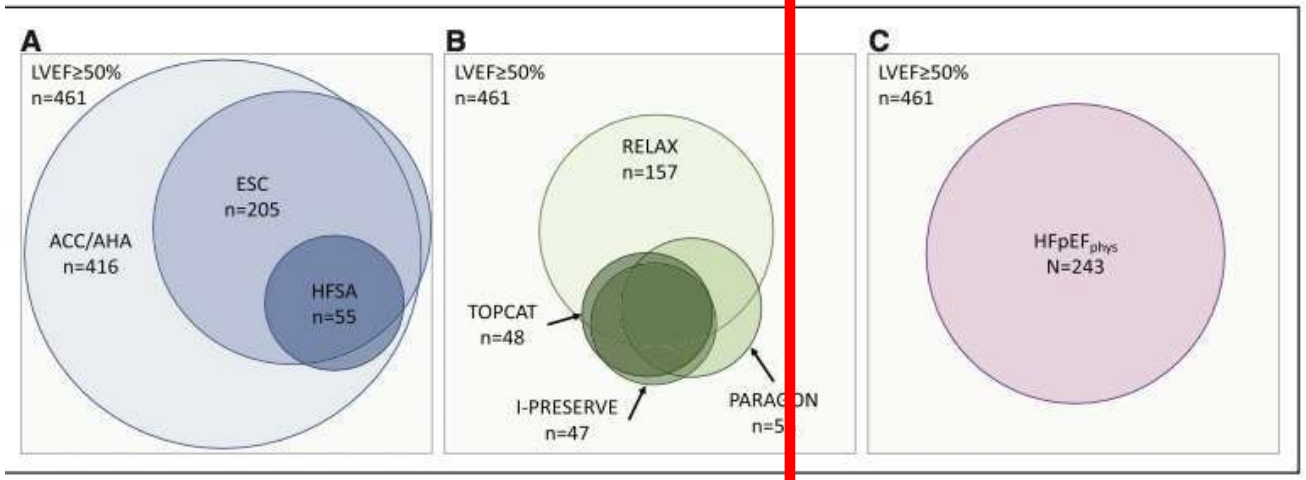


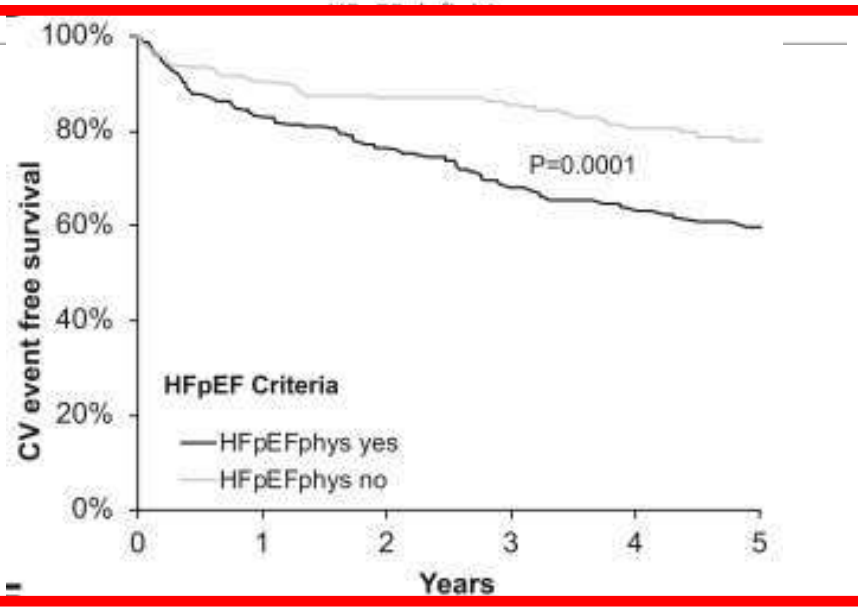
5%-45% of patients with any classification had normal PCWP



10%-80% of patients with high PCWP are not included in a classification







Circulation: Heart Failure

ORIGINAL ARTICLE

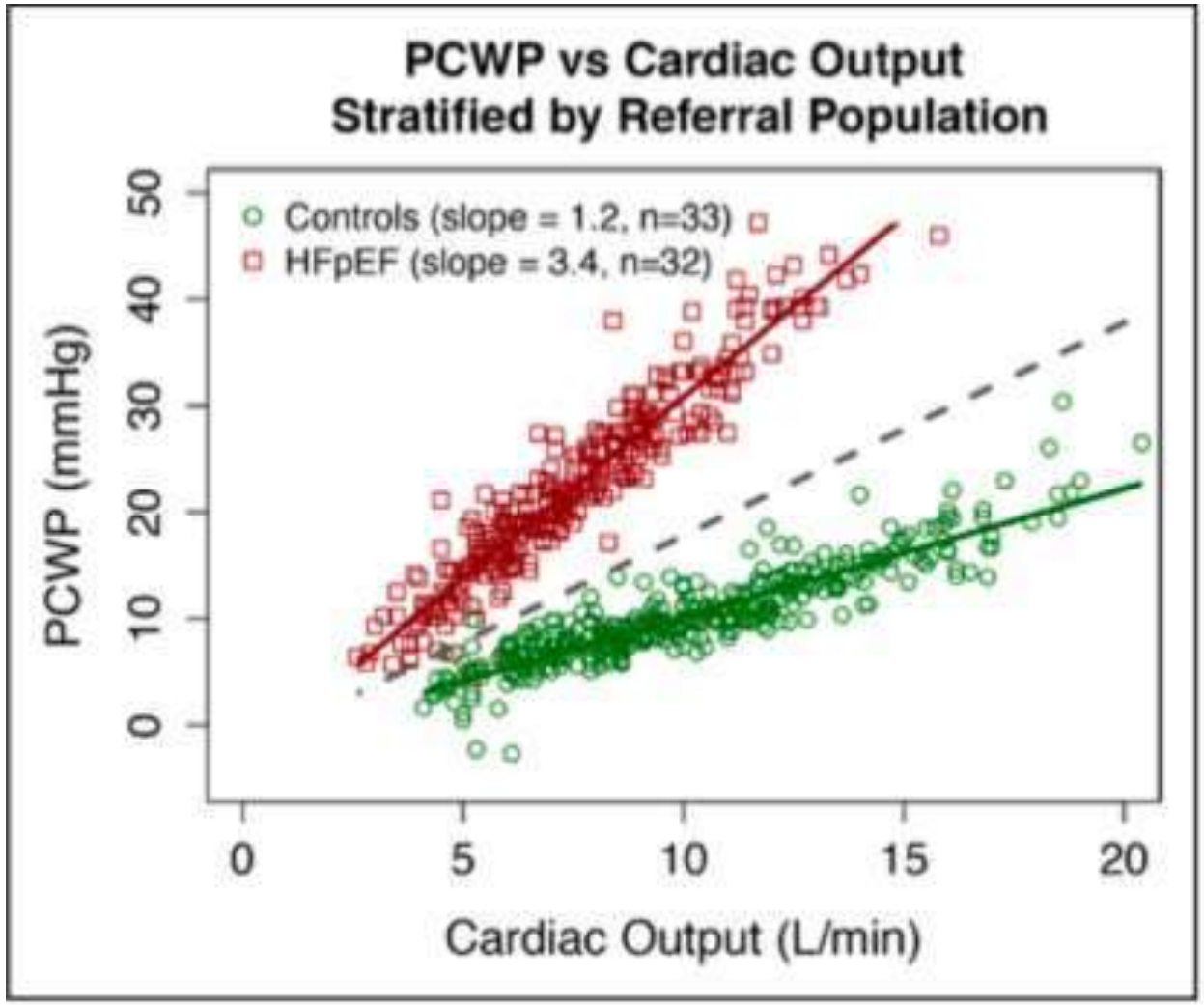
Pulmonary Capillary Wedge Pressure Patterns During Exercise Predict Exercise Capacity and Incident Heart Failure

Aaron S. Eisman, BS*
Ravi V. Shah, MD*
Bishnu P. Dhakal, MD
Paul P. Pappagianopoulos, MEd
Luke Wooster, BS
Cole Bailey, BA
Thomas F. Cunningham, BS
Kathryn M. Hardin, BS
Aaron L. Baggish, MD
Jennifer E. Ho, MD
Rajeev Malhotra, MD
Gregory D. Lewis, MD

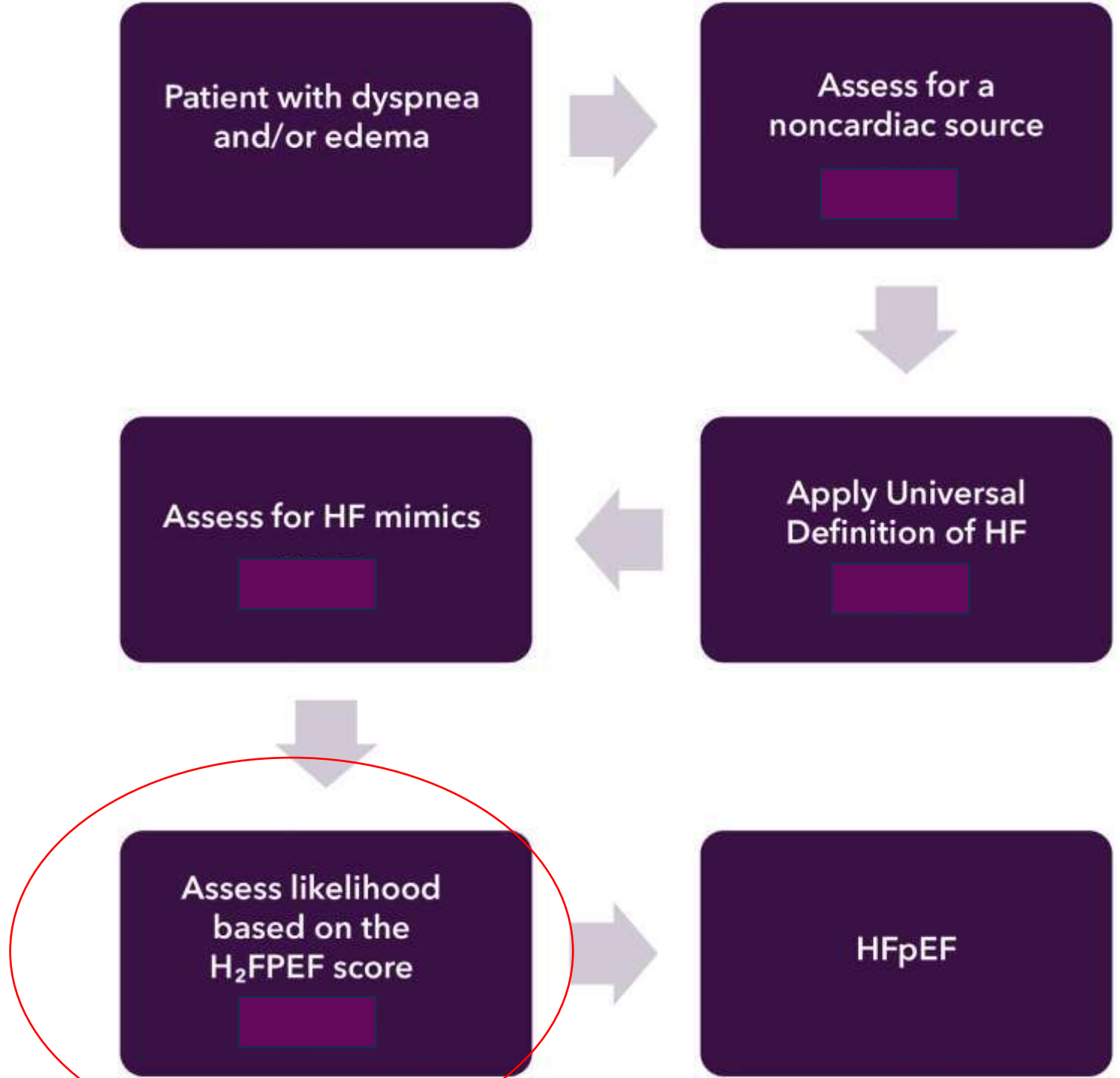
BACKGROUND: Single measurements of left ventricular filling pressure at rest lack sensitivity for identifying heart failure with preserved ejection fraction (HFpEF) in patients with dyspnea on exertion. We hypothesized that exercise hemodynamic measurements (ie, changes in pulmonary capillary wedge pressure [PCWP] indexed to cardiac output [CO]) may more sensitively differentiate HFpEF and non-HFpEF disease states, reflect aerobic capacity, and forecast heart failure outcomes in individuals with normal PCWP at rest.

METHODS AND RESULTS: We studied 175 patients referred for cardiopulmonary exercise testing with hemodynamic monitoring: controls (n=33), HFpEF with resting PCWP≥15 mm Hg (n=32), and patients with dyspnea on exertion with normal resting PCWP and left ventricular ejection fraction (DOE-nlrW; n=110). Across 1835 paired PCWP-CO measurements throughout exercise, we used regression techniques to define normative bounds of "PCWP/CO slope" in controls and tested the association of PCWP/CO slope with exercise capacity and composite cardiac outcomes (defined as cardiac death, incident resting PCWP elevation, or heart failure hospitalization) in the DOE-nlrW group. Relative to controls (PCWP/CO slope, 1.2±0.4 mm Hg/L/min), patients with HFpEF had a PCWP/CO slope of 3.4±1.9 mm Hg/L/min. We used a threshold (2 SD above the mean in controls) of 2 mm Hg/L/min to define abnormal. PCWP/CO slope >2 in DOE-nlrW patients was common (n=45/110) and was associated with reduced peak Vo_2 ($P<0.001$) and adverse cardiac outcomes after adjustment for age, sex, and body mass index (hazard ratio, 3.47; $P=0.03$) at a median 5.3-year follow-up.

CONCLUSIONS: Elevated PCWP/CO slope during exercise (>2 mm Hg/L/min) is common in DOE-nlrW and predicts exercise capacity and heart failure outcomes. These findings suggest that current definitions of HFpEF based on single measures during rest are insufficient and that assessment of exercise PCWP/CO slope may refine early HFpEF diagnosis.



The hashed line represents a PCWP/CO slope of 2.0, which nearly perfectly discriminates the 2 groups.


Patient with dyspnea and/or edema
Assess for a noncardiac source
Apply Universal Definition of HF
Assess for HF mimics
Assess likelihood based on the H_2FPEF score
HFpEF

HFpEF Diagnostic Scores

Circulation

ORIGINAL RESEARCH ARTICLE

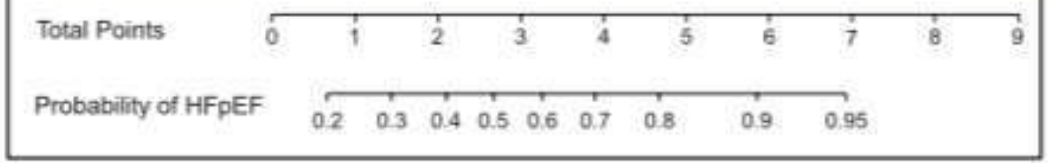
A Simple, Evidence-Based Approach to Help Guide Diagnosis of Heart Failure With Preserved Ejection Fraction

Editorial, see p 871

Yogesh N.V. Reddy, MD
Rickey E. Carter, PhD
Masaru Obokata, MD, PhD
Margaret M. Redfield, MD
Barry A. Borlaug, MD

BACKGROUND: Diagnosis of heart failure with preserved ejection fraction (HFpEF) is challenging in euvolemic patients with dyspnea, and no evidence-based criteria are available. We sought to develop and then validate noninvasive diagnostic criteria that could be used to estimate the

	Clinical Variable	Values	Points
H_2	Heavy	Body mass index > 30 kg/m²	2
	Hypertensive	2 or more antihypertensive medicines	1
F	Atrial Fibrillation	Paroxysmal or Persistent	3
P	Pulmonary Hypertension	Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg	1
E	Elder	Age > 60 years	1
F	Filling Pressure	Doppler Echocardiographic E/e' > 9	1
	H_2FPEF score		Sum (0-9)



ESC European Society of Cardiology
European Journal of Heart Failure (2020) 22, 391–412
doi:10.1002/ejhf.1741

HFA CONSENSUS RECOMMENDATION

How to diagnose heart failure with preserved ejection fraction: the HFA–PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC)

Burkert Pieske[1,2,3,4*], Carsten Tschöpe[1,2,5], Rudolf A. de Boer[6], Alan G. Fraser[7], Stefan D. Anker[1,2,5,8], Erwan Donal[9], Frank Edelmann[1,2], Michael Fu[10], Marco Guazzi[11,12], Carolyn S.P. Lam[13,14], Patrizio Lancellotti[15], Vojtech Melenovsky[16], Daniel A. Morris[1], Eike Nagel[17,18], Elisabeth Pieske-Kraigher[1], Piotr Ponikowski[19], Scott D. Solomon[20], Ramachandran S. Vasan[21], Frans H. Rutten[22], Adriaan A. Voors[6], Frank Ruschitzka[23], Walter J. Paulus[24], Petar Seferovic[25], and Gerasimos Filippatos[26,27]

	Functional	Morphological	Biomarker (SR)	Biomarker (AF)
Major	septal e' < 7 cm/s or lateral e' < 10 cm/s or Average E/e' ≥ 15 or TR velocity > 2.8 m/s (PASP > 35 mmHg)	LAVI > 34 ml/m² or LVMI ≥ 149/122 g/m² (m/w) and RWT > 0,42 #	NT-proBNP > 220 pg/ml or BNP > 80 pg/ml	NT-proBNP > 660 pg/ml or BNP > 240 pg/ml
Minor	Average E/e' 9 -14 or GLS < 16 %	LAVI 29-34 ml/m² or LVMI > 115/95 g/m² (m/w) or RWT > 0,42 or LV wall thickness ≥ 12 mm	NT-proBNP 125-220 pg/ml or BNP 35-80 pg/ml	NT-proBNP 365-660 pg/ml or BNP 105-240 pg/ml

Major Criteria: 2 points	≥ 5 points: HFpEF
Minor Criteria: 1 point	2-4 points: Diastolic Stress Test or Invasive Haemodynamic Measurements

Phenotyping in HFpEF and management consideration

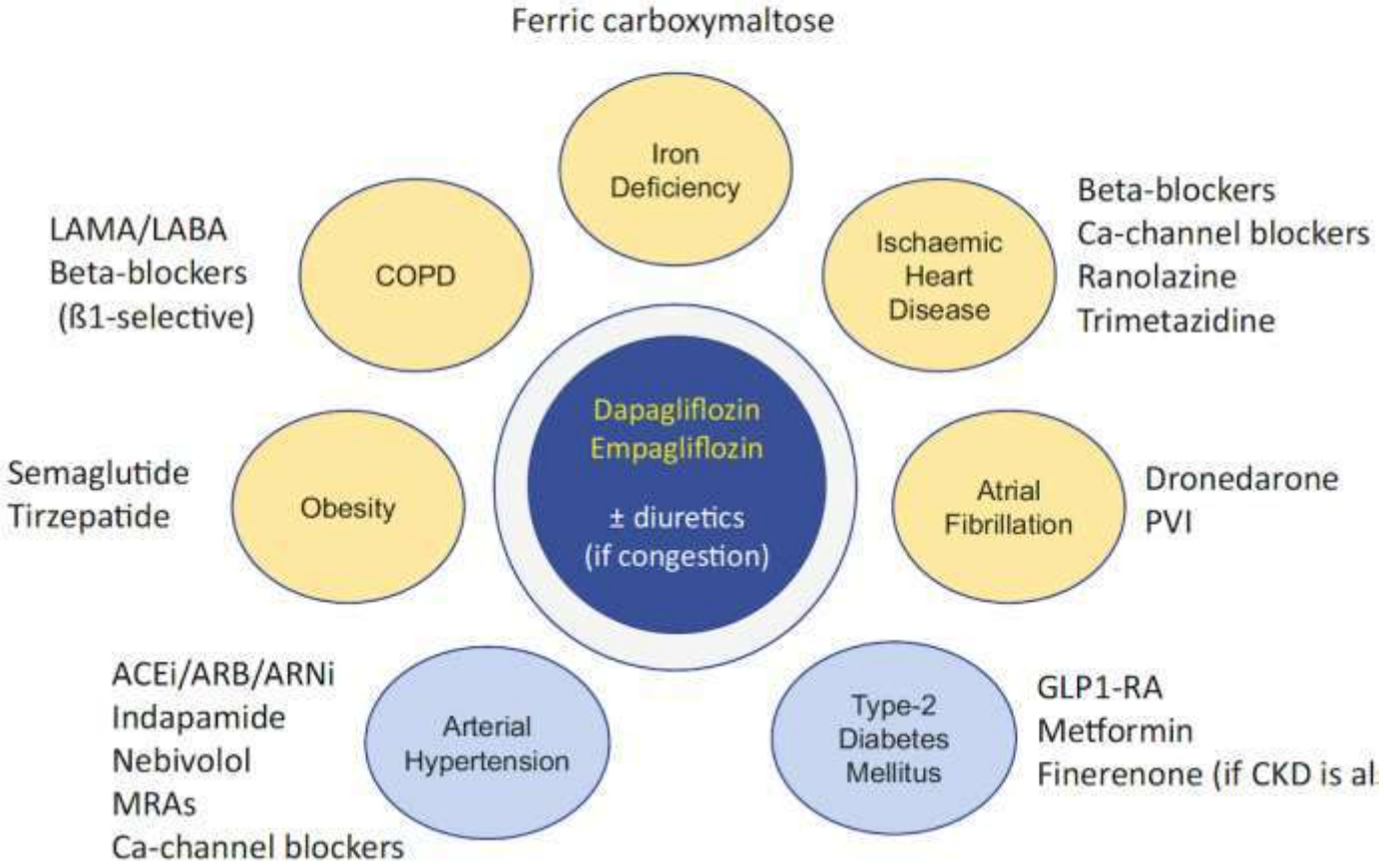
ESC European Society of Cardiology
European Journal of Heart Failure (2023)
doi:10.1002/ejhf.2894

CONSENSUS STATEMENT

Patient phenotype profiling in heart failure with preserved ejection fraction to guide therapeutic decision making. A scientific statement of the Heart Failure Association and the European Heart Rhythm Association of the European Society of Cardiology, and the European Society of Hypertension

Stefan D. Anker[1*], Muhammad Shariq Usman[2], Markus S. Anker[3], Javed Butler[2,4], Michael Böhm[5], William T. Abraham[6], Marianna Adamo[7], Vijay K. Chopra[8], Mariantonietta Cicoira[9], Francesco Cosentino[10], Gerasimos Filippatos[11], Ewa A. Jankowska[12], Lars H. Lund[10], Brenda Moura[13], Wilfried Mullens[14], Burkert Pieske[15], Piotr Ponikowski[12,16], Jose R. Gonzalez-Juanatey[17], Amina Rakisheva[18], Gianluigi Savarese[10], Petar Seferovic[19], John R. Teerlink[20], Carsten Tschöpe[1,21], Maurizio Volterrani[22], Stephan von Haehling[23], Jian Zhang[24], Yuhui Zhang[24], Johann Bauersachs[25], Ulf Landmesser[3,26], Shelley Zieroth[27], Konstantinos Tsioufis[28], Antoni Bayes-Genis[29], Ovidiu Chioncel[30], Felicita Andreotti[31,32], Enrico Agabiti-Rosei[33], Jose L. Merino[34], Marco Metra[7], Andrew J.S. Coats[35], and Giuseppe M.C. Rosano[22]

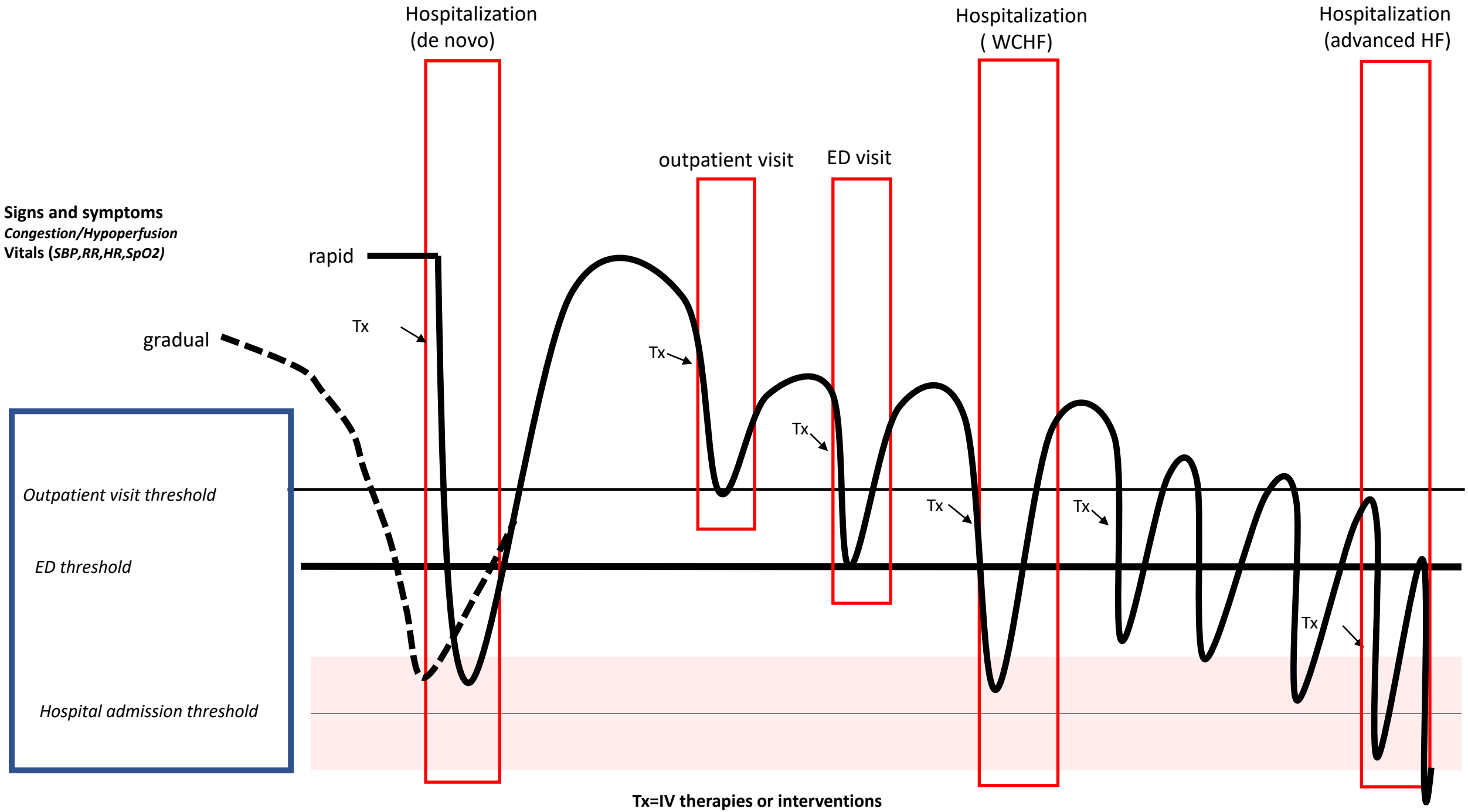
Patient profiling in HFpEF and consequent therapeutic considerations



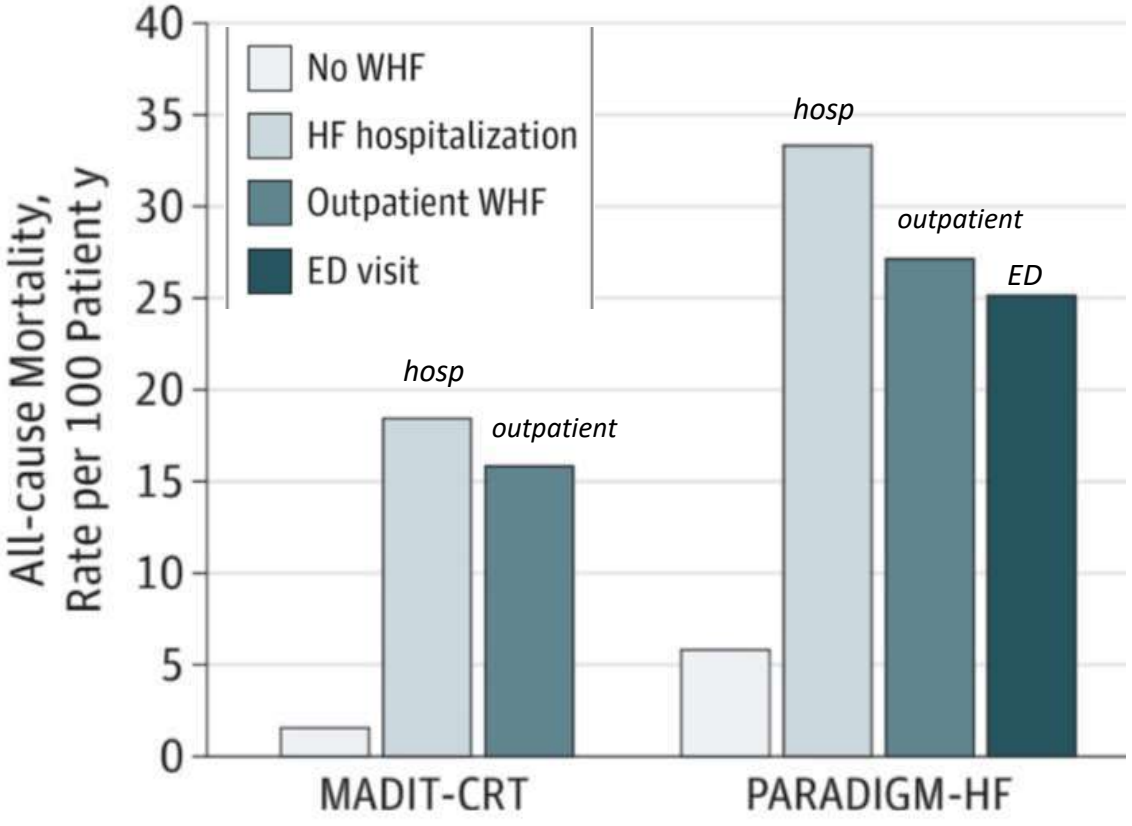
2021 HF Guidelines: AHF Definition

Acute HF (AHF) refers to rapid or gradual onset of symptoms and/or signs of HF, severe enough for the patient to seek urgent medical attention, leading to an unplanned hospital admission or an emergency department visit. Patients with AHF require urgent evaluation with subsequent **initiation or intensification of treatment**, including *IV therapies or procedures*. Clinical severity and in-hospital trajectory are determined by the complex interplay between precipitants, the underlying cardiac substrate, and the patient's comorbidities.

2005	2008	2012	2016
Acute heart failure is defined as the **rapid onset** of symptoms and signs secondary to abnormal cardiac function. It may occur with or without previous cardiac disease. The **cardiac dysfunction** can be related to systolic or diastolic dysfunction, to abnormalities in cardiac rhythm, or to preload and afterload mismatch. It is often life threatening and requires **urgent treatment.** AHF can present itself as acute *de novo* (new onset of acute heart failure in a patient without previously known cardiac	Acute heart failure (AHF) is defined as a **rapid onset or change** in the signs and symptoms of HF, resulting in the need for **urgent therapy**. AHF may be either *new HF or worsening* of pre-existing chronic HF. Patients may present as a medical emergency such as acute pulmonary oedema. The **cardiac dysfunction** may be related to ischaemia, abnormalities in cardiac rhythm, valvular dysfunction, pericardial disease, increased filling pressures or elevated systemic resistance.	Acute heart failure (AHF) is the term used to describe the **rapid onset of, or change** in, symptoms and signs of HF. It is a **life- threatening** condition that requires immediate medical attention and usually leads to **urgent admission to hospital**. In most cases, AHF arises as a result of deterioration in patients with a previous diagnosis of HF (either HF-REF or HF-PEF), and all of the aspects of chronic management described in these guidelines apply fully to these patients. AHF may also be the first presentation of HF *('de novo' AHF)*.	AHF refers to **rapid onset or worsening** of symptoms and/or signs of HF. It is a **life-threatening** medical condition requiring **urgent** evaluation and treatment, typically leading to **urgent hospital admission**. AHF may present as a first occurrence (*de novo*) or, more frequently, as a consequence of acute decompensation of chronic HF, and may be caused by primary **cardiac dysfunctio**n or precipitated by extrinsic factors, often in patients with chronic HF.


Hospitalization
(de novo)
Hospitalization
(WCHF)
Hospitalization
(advanced HF)
outpatient visit
ED visit
Signs and symptoms
Congestion/Hypoperfusion
Vitals (SBP,RR,HR,SpO2)
rapid
gradual
Tx
Tx
Tx
Tx
Tx
Tx
Tx
Outpatient visit threshold
ED threshold
Hospital admission threshold
Tx=IV therapies or interventions

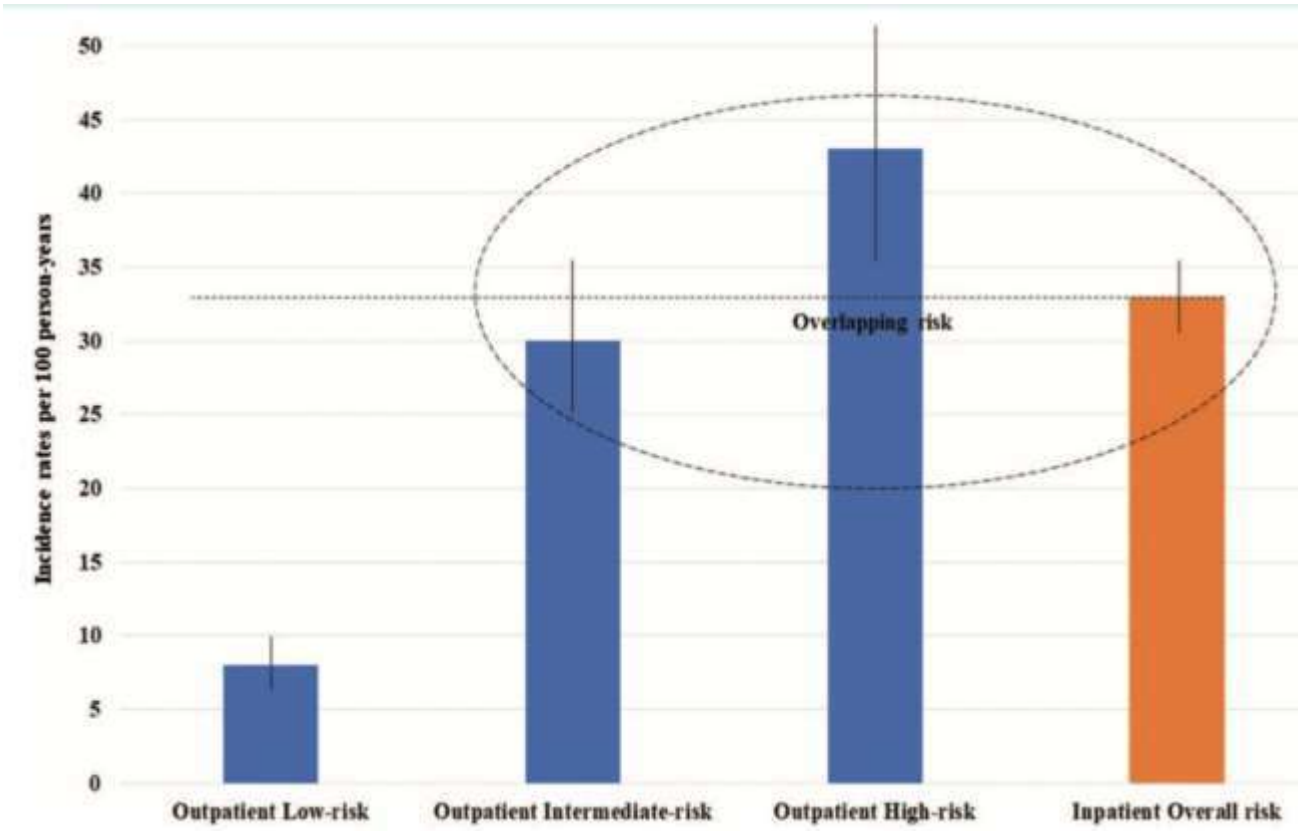
Worsening HF is associated with a high subsequent risk of death, irrespective of treatment as an inpatient, outpatient, or in the emergency department (ED)



ESC European Society of Cardiology
European Journal of Heart Failure (2019) 21, 172–180
doi:10.1002/ejhf.1323
RESEARCH ARTICLE

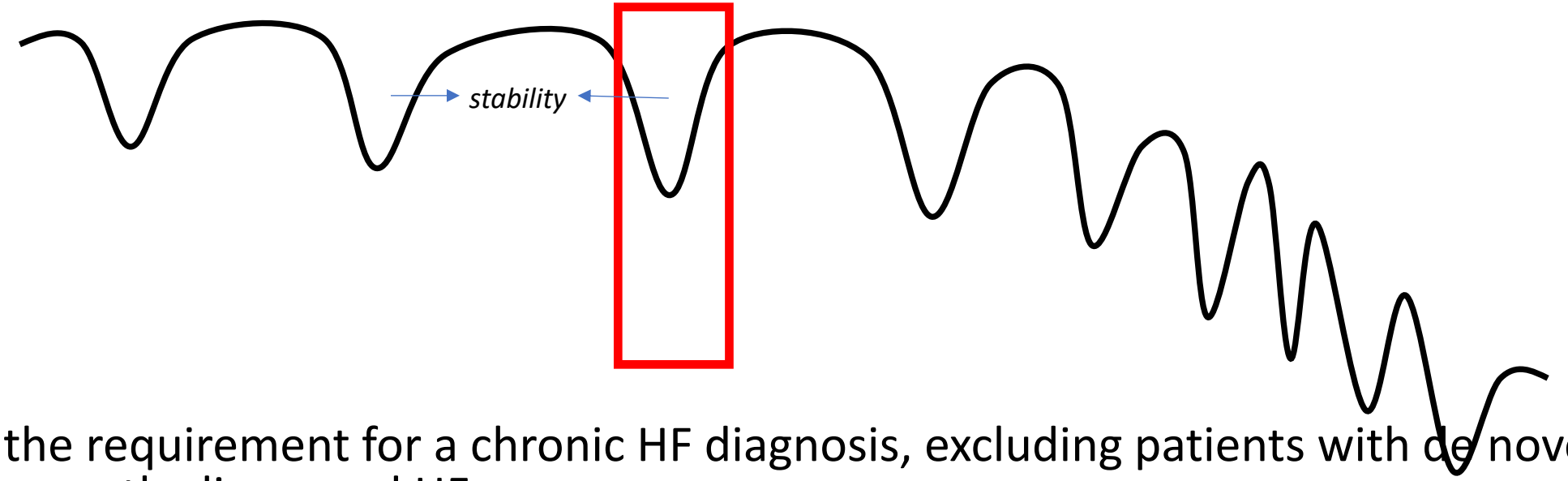
Heart failure in the outpatient versus inpatient setting: findings from the BIOSTAT-CHF study

João Pedro Ferreira[1,2], Marco Metra[3], Ify Mordi[4], John Gregson[5], Jozine M. ter Maaten[6], Jasper Tromp[6], Stefan D. Anker[7,8], Kenneth Dickstein[9,10], Hans L. Hillege[6], Leong L. Ng[11], Dirk J. van Veldhuisen[6], Chim C. Lang[4], Adriaan A. Voors[6], and Faiez Zannad[1]*

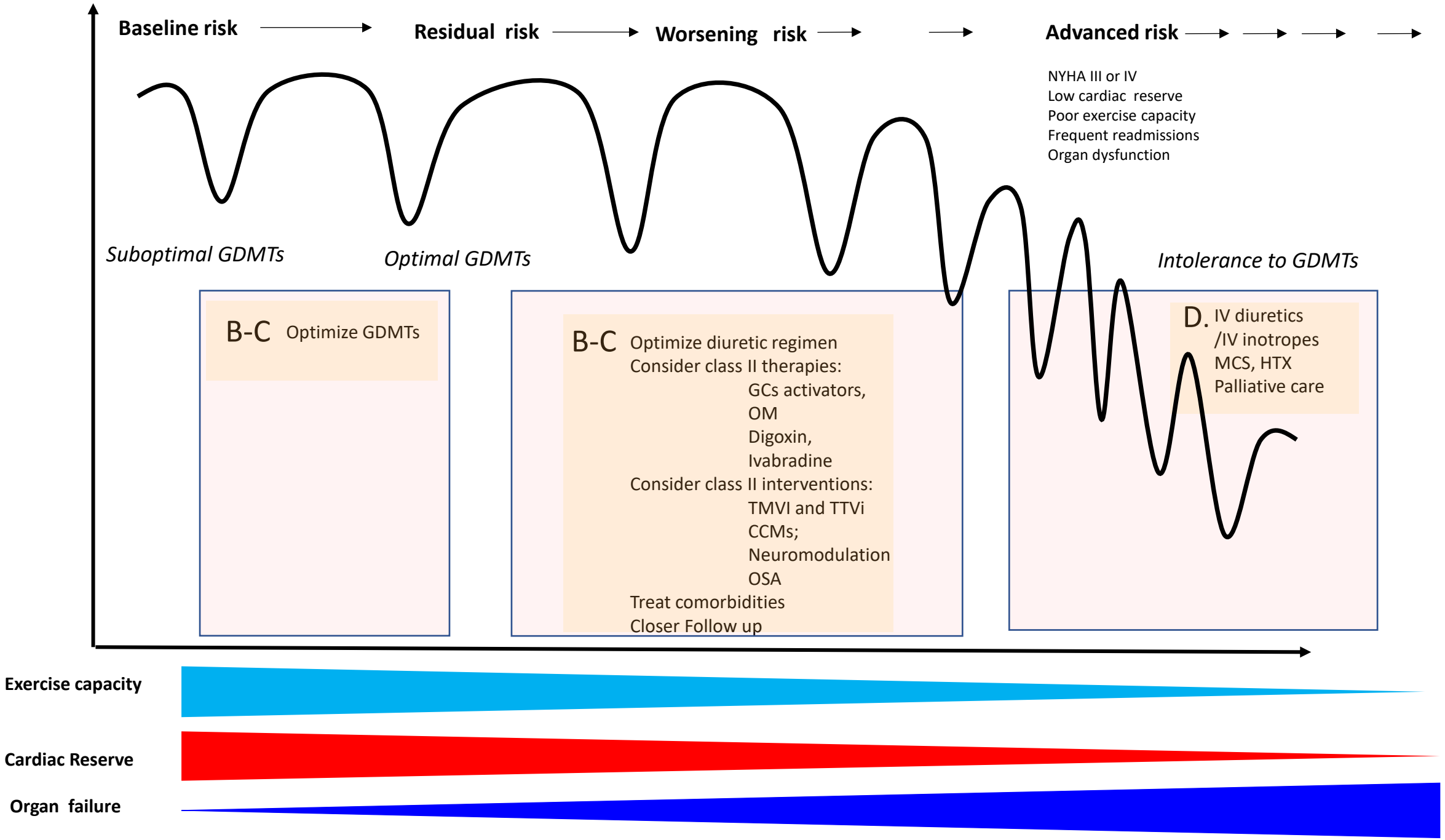


Definition of WHF

- deterioration of HF signs and symptoms after a period of stability that requires escalation of therapy



- the requirement for a chronic HF diagnosis, excluding patients with de novo or recently diagnosed HF.
- Irrespective of venue of care: ED, ambulatory, hospitalization
- **Hospitalization for HF is a sentinel event that signals worse prognosis but also provides key opportunities to redirect the disease trajectory**


Baseline risk
Residual risk
Worsening risk
Advanced risk
NYHA III or IV
Low cardiac reserve
Poor exercise capacity
Frequent readmissions
Organ dysfunction
Suboptimal GDMTs
Optimal GDMTs
Intolerance to GDMTs
B-C Optimize GDMTs
B-C Optimize diuretic regimen
Consider class II therapies:
GCs activators,
OM
Digoxin,
Ivabradine
Consider class II interventions:
TMVI and TTVi
CCMs;
Neuromodulation
OSA
Treat comorbidities
Closer Follow up
D. IV diuretics
/IV inotropes
MCS, HTX
Palliative care
Exercise capacity
Cardiac Reserve
Organ failure

AHF Diagnosis

Physical examination has a sensitivity of only 62% (95% CI 61–64%) and a specificity of 68% (95% CI 67–69%) for a diagnosis of AHF

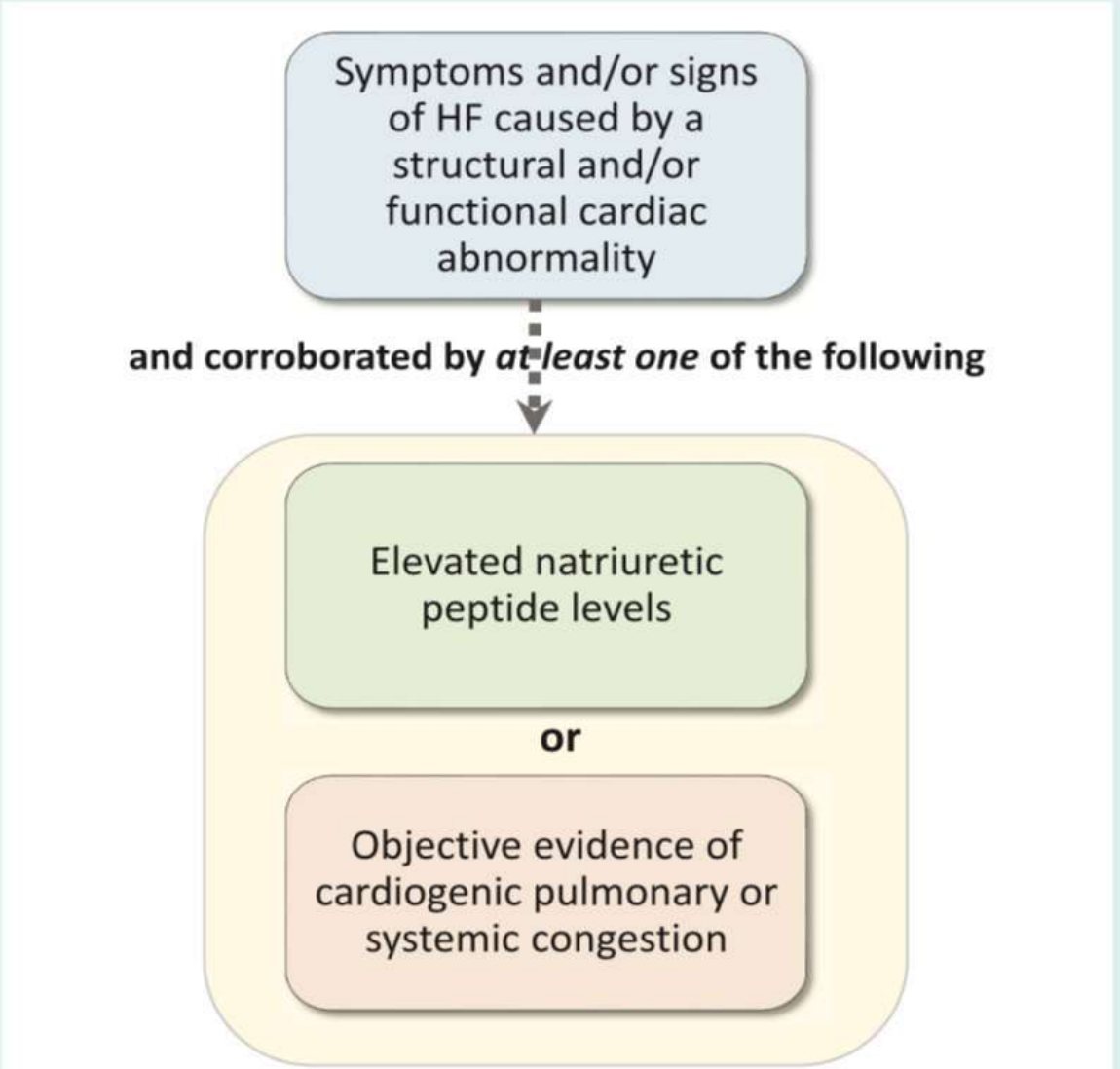


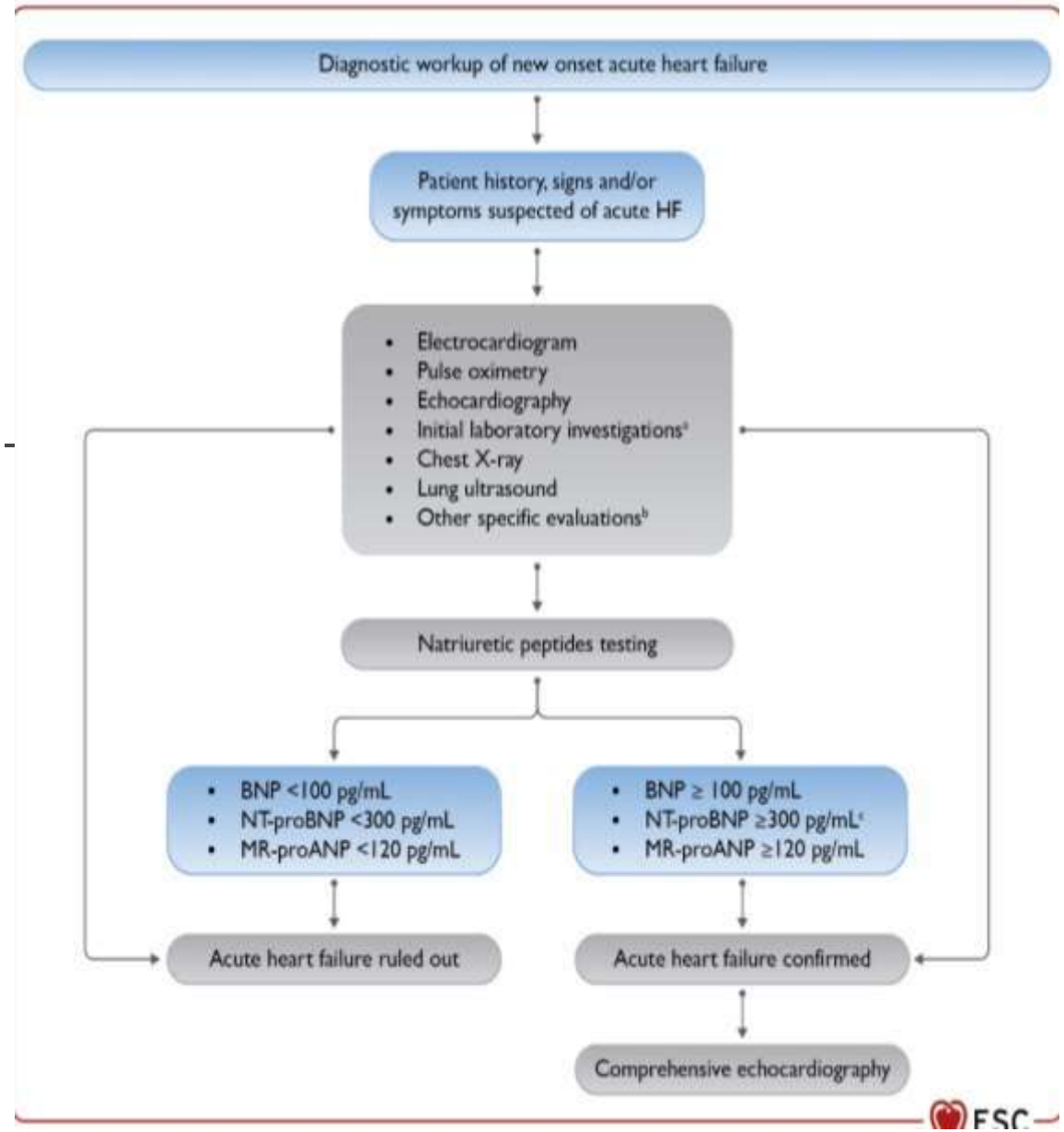
Figure 1 Universal definition of heart failure (HF).

AHF Diagnosis

1.

2.

3.



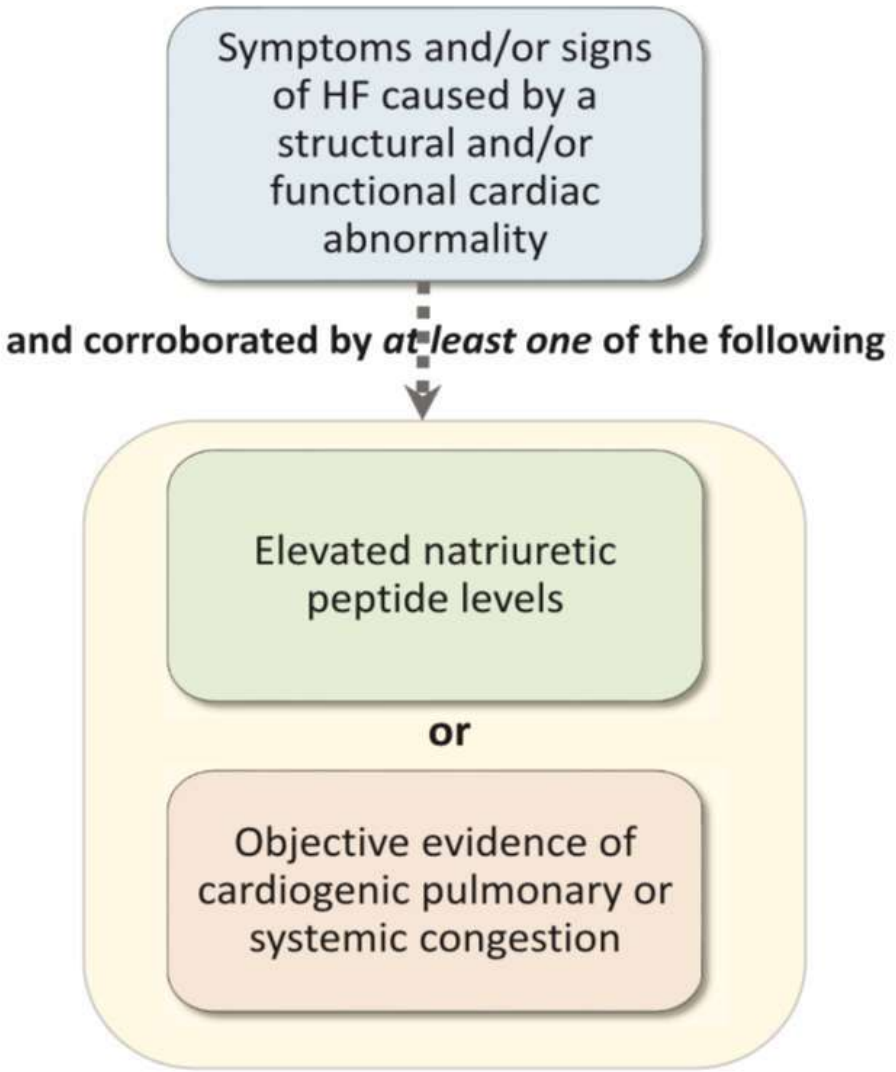
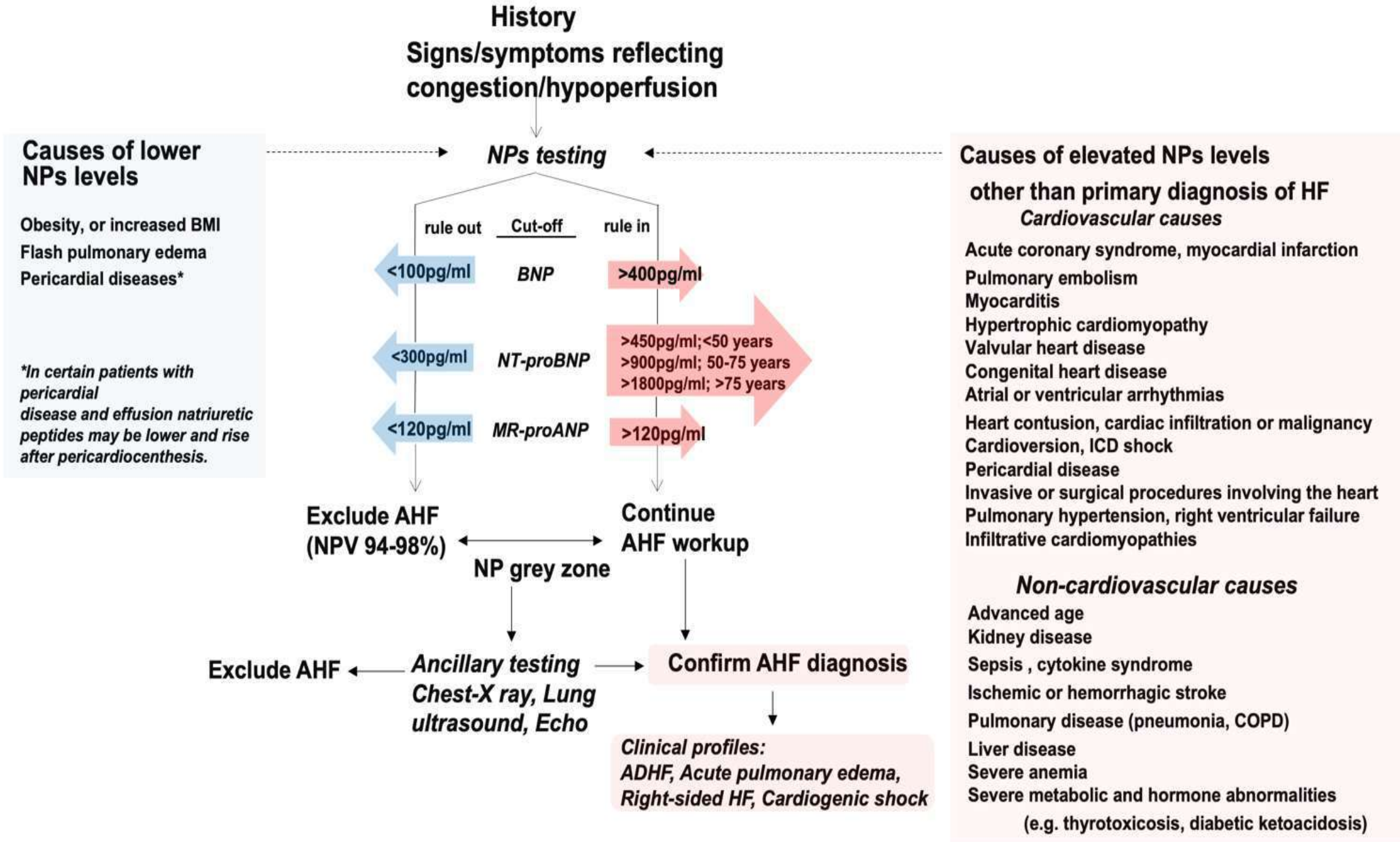


Figure 1 Universal definition of heart failure (HF).


History
Signs/symptoms reflecting congestion/hypoperfusion
NPs testing
Causes of lower NPs levels
Obesity, or increased BMI
Flash pulmonary edema
Pericardial diseases*
*In certain patients with pericardial disease and effusion natriuretic peptides may be lower and rise after pericardiocenthesis.
rule out
Cut-off
rule in
<100pg/ml
BNP
>400pg/ml
<300pg/ml
NT-proBNP
>450pg/ml;<50 years
>900pg/ml; 50-75 years
>1800pg/ml; >75 years
<120pg/ml
MR-proANP
>120pg/ml
Exclude AHF (NPV 94-98%)
NP grey zone
Continue AHF workup
Exclude AHF
Ancillary testing
Chest-X ray, Lung ultrasound, Echo
Confirm AHF diagnosis
Clinical profiles:
ADHF, Acute pulmonary edema,
Right-sided HF, Cardiogenic shock
Causes of elevated NPs levels
other than primary diagnosis of HF
Cardiovascular causes
Acute coronary syndrome, myocardial infarction
Pulmonary embolism
Myocarditis
Hypertrophic cardiomyopathy
Valvular heart disease
Congenital heart disease
Atrial or ventricular arrhythmias
Heart contusion, cardiac infiltration or malignancy
Cardioversion, ICD shock
Pericardial disease
Invasive or surgical procedures involving the heart
Pulmonary hypertension, right ventricular failure
Infiltrative cardiomyopathies
Non-cardiovascular causes
Advanced age
Kidney disease
Sepsis , cytokine syndrome
Ischemic or hemorrhagic stroke
Pulmonary disease (pneumonia, COPD)
Liver disease
Severe anemia
Severe metabolic and hormone abnormalities
(e.g. thyrotoxicosis, diabetic ketoacidosis)

Radiographic pulmonary congestion

International Journal of Cardiology

Mid-term prognostic impact of residual pulmonary congestion assessed by radiographic scoring in patients admitted for worsening heart failure

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ABSTRACT

Aims: Pulmonary congestion is associated with poor prognosis following hospitalization for worsening heart failure (HF), although its quantification and optimal timing during HF hospitalization remains challenging. The aim of this study was to assess the prognostic value of radiographic pulmonary congestion at admission and discharge in patients with worsening HF.

Methods and results: Clinical, echocardiographic, laboratory and chest X-ray data of 252 acute decompensated HF patients were retrospectively studied. Follow-up 1 year). Lung congestion was blindly scored on chest X-ray performed at admission and discharge using a systematic 0–3 score approach. Primary clinical outcome was a composite outcome of re-hospitalization for worsening HF or all-cause death.

Patients were stratified according to the median of congestion score ratio (CSI) at both admission (median CSI (A) = 1.33) and discharge (median CSI (D) = 0.33). BNP levels, LVEF and eGFR did not differ between CSI categories. In multivariable Cox regression analysis, discharge CSI (HR for 1-point increase = 1.81 [1.02 to 3.27], p = 0.04) and discharge BNP were significantly associated with the composite outcome whereas NYHA class, physical signs, admission CSI and echocardiographic data were not. Furthermore, discharge CSI significantly increased reclassification on top of clinical covariates (continuous NRI = 0.45 [0.0 to 0.88], p = 0.05 and IDI = 3.25 [0.0 to 7.6], p = 0.046), while discharge BNP did not significantly improve risk reclassification.

Conclusions: Residual pulmonary congestion assessed by radiographic scoring predicts poor prognosis beyond physical assessment, echocardiographic parameters and BNP. These findings further support the capital prognostic value of radiographic pulmonary congestion in patients hospitalized for worsening HF.

1. Introduction

Signs and symptoms of congestion are the most important contributors of heart failure (HF) hospitalization and readmission [1,2] to a significantly greater degree than low cardiac output [3,4]. Thus, decongestive therapy has been a major goal of acute heart failure management during hospitalization [5]. Discharge congestion variables such as brain natriuretic peptide (BNP) [6,7], physical assessments [8] and lung congestion assessed by lung ultrasound (LUS) [9–11] have been shown to be strongly associated with post-discharge morbidity and mortality [12].

Nevertheless, no standardized evaluation of congestion and subsequent tailored therapeutic management are currently recommended by the latest clinical guidelines [3,13]. In addition, there is evidence that clinical signs and symptoms of congestion on admission are associated with adverse outcome following a hospitalization for worsening HF [14,15]. Consequently, it remains unclear whether the interplay between residual congestion and higher values of admission congestion predicts outcome or whether the change in congestion during hospital stay or achieved discharge decongestion per-se are the best predictors of outcome.

Chest X-ray is a fast, simple and classic method to assess pulmonary congestion, with good specificity and moderate sensitivity in diagnosing HF [16,17]. Representative signs of pulmonary congestion, such as cephalization, peribronchial cuffing and Kerley lines, are widely known in clinical practice [13,16]. Assessment of lung congestion by a composite radiological score is useful to predict the development of overt HF during

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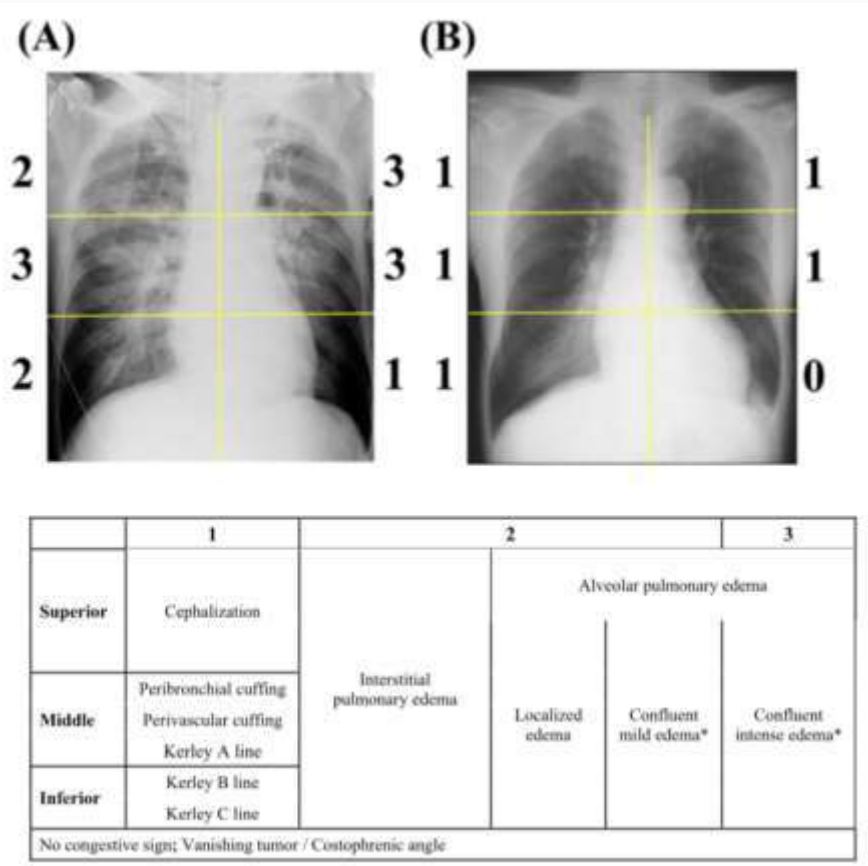
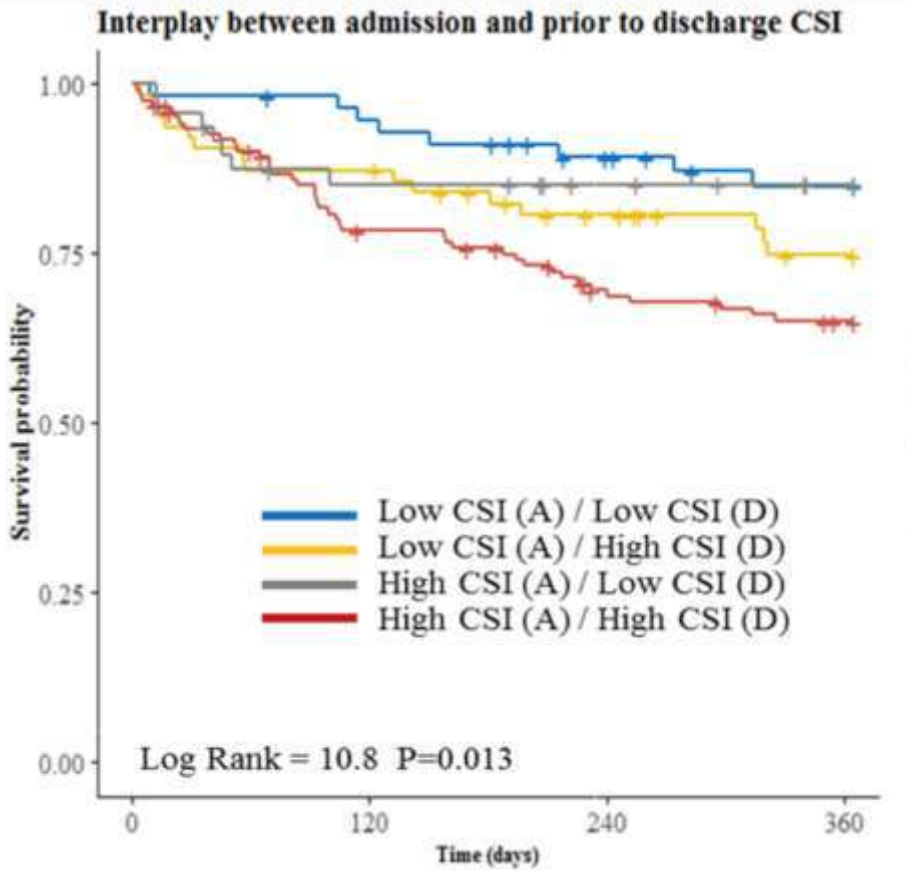


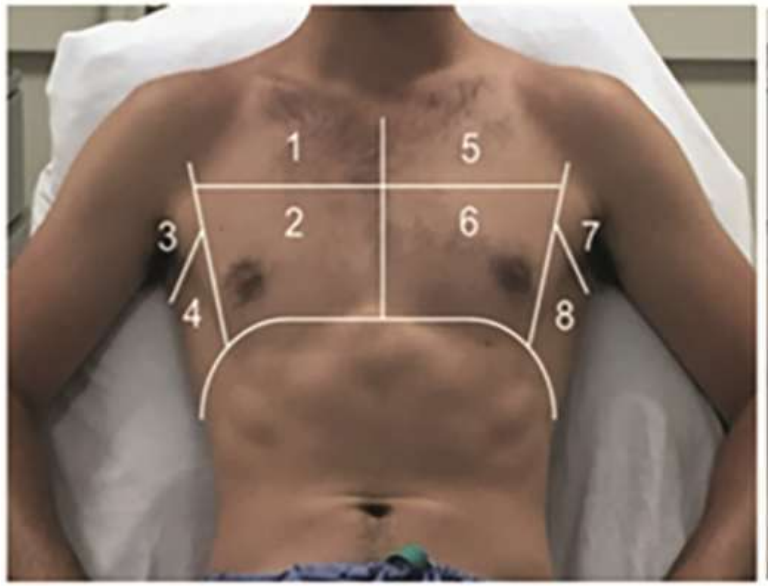
(A) (B)

2 3 1 1
3 3 1 1
2 1 1 0

	1	2			3
			Alveolar pulmonary edema		
Superior	Cephalization	Interstitial pulmonary edema			
Middle	Peribronchial cuffing Perivascular cuffing Kerley A line		Localized edema	Confluent mild edema*	Confluent intense edema*
Inferior	Kerley B line Kerley C line				
No congestive sign; Vanishing tumor / Costophrenic angle					



LUS Admission



8 chest zones

- The visualization of >3 B-lines in two or more intercostal spaces bilaterally should be considered diagnostic for pulmonary oedema;
- sensitivity of 94% (95% CI 81–98%) and specificity of 92% (95% CI 84–96%).

Martindale, J. L. et al. Diagnosing acute heart failure in the emergency department: a systematic review and meta-analysis. Acad. Emerg. Med. 23, 223–242 (2016)

LUS Discharge

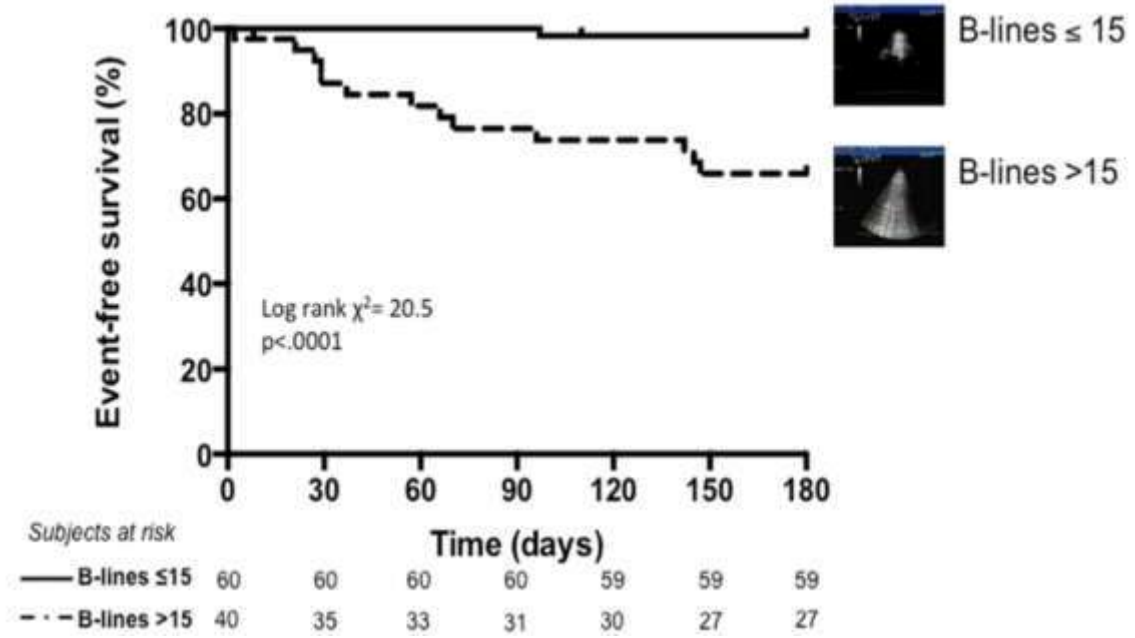
Gargani et al. Cardiovascular Ultrasound (2015) 13:40
DOI 10.1186/s12947-015-0033-4

CARDIOVASCULAR ULTRASOUND

RESEARCH Open Access

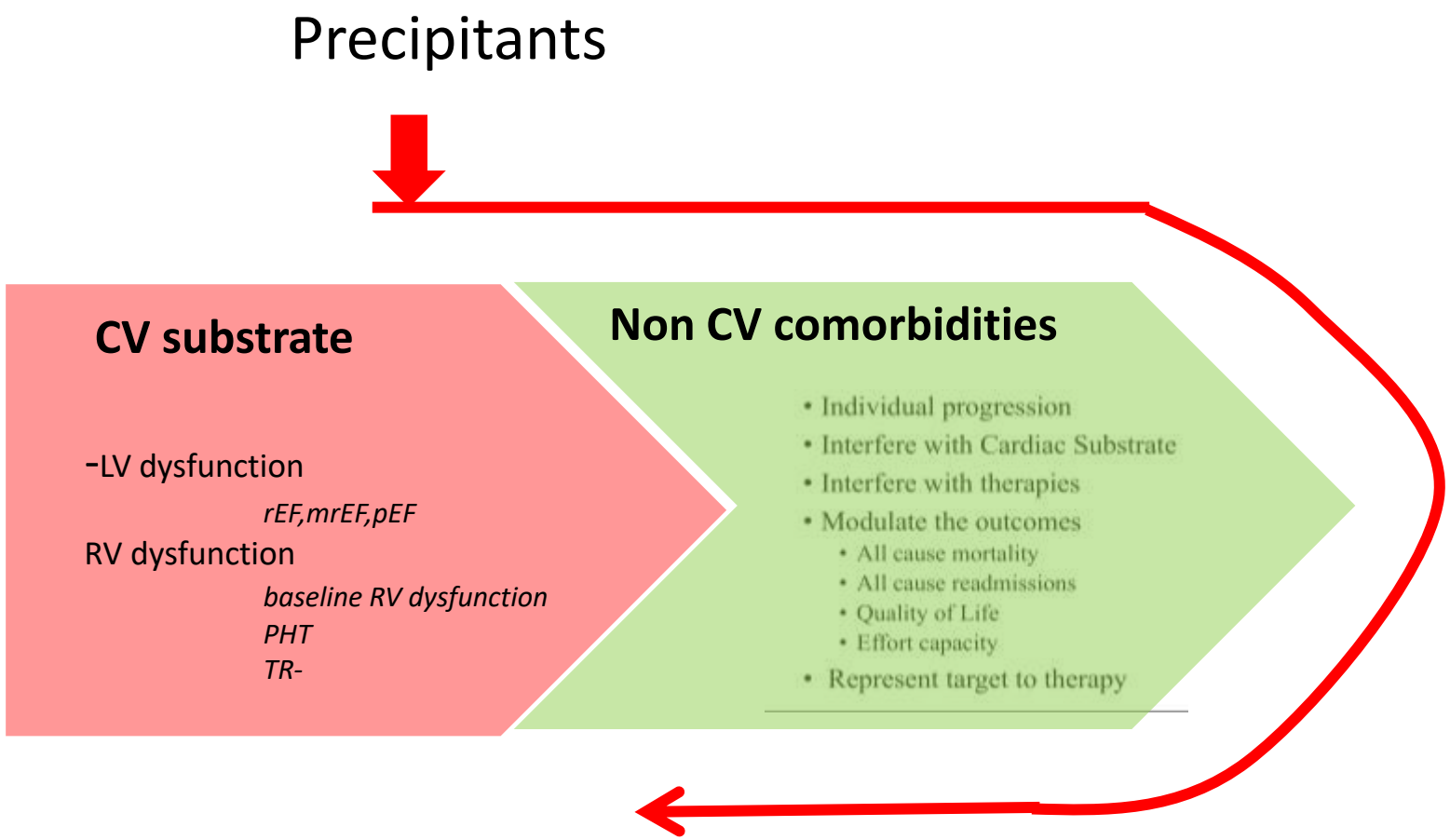
Persistent pulmonary congestion before discharge predicts rehospitalization in heart failure: a lung ultrasound study

Luna Gargani[1*], P. S. Pang[2], F. Frassi[3], M.H. Miglioranza[4], F. L. Dini[5], P. Landi[1] and E. Picano[1]

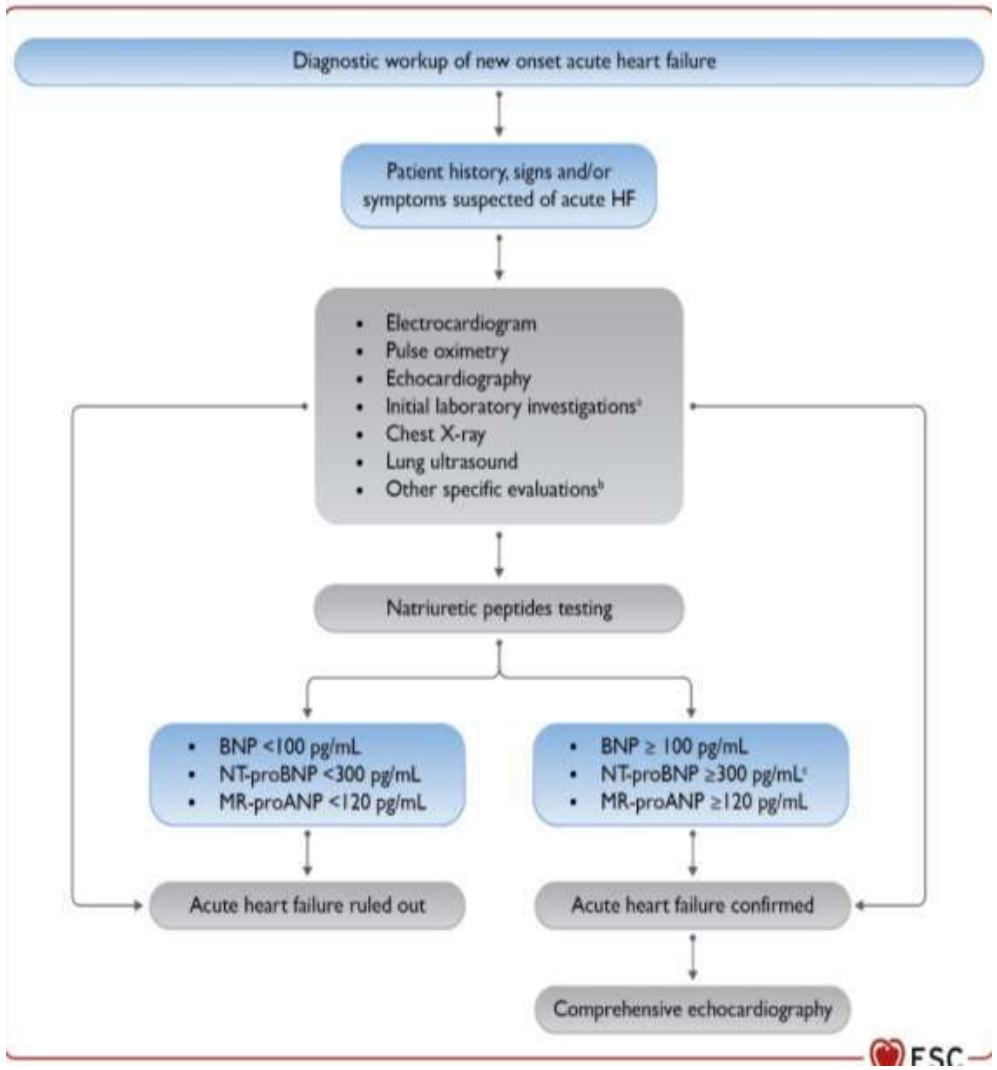


2021 HF Guidelines: AHF Definition

Acute HF (AHF) refers to rapid or gradual onset of symptoms and/or signs of HF, severe enough for the patient to seek urgent medical attention, leading to an unplanned hospital admission or an emergency department visit. Patients with AHF require urgent evaluation with subsequent **initiation or intensification of treatment**, including *IV therapies or procedures*. **Clinical severity and in-hospital trajectory are determined by the complex interplay between precipitants, the underlying cardiac substrate, and the patient's comorbidities.**



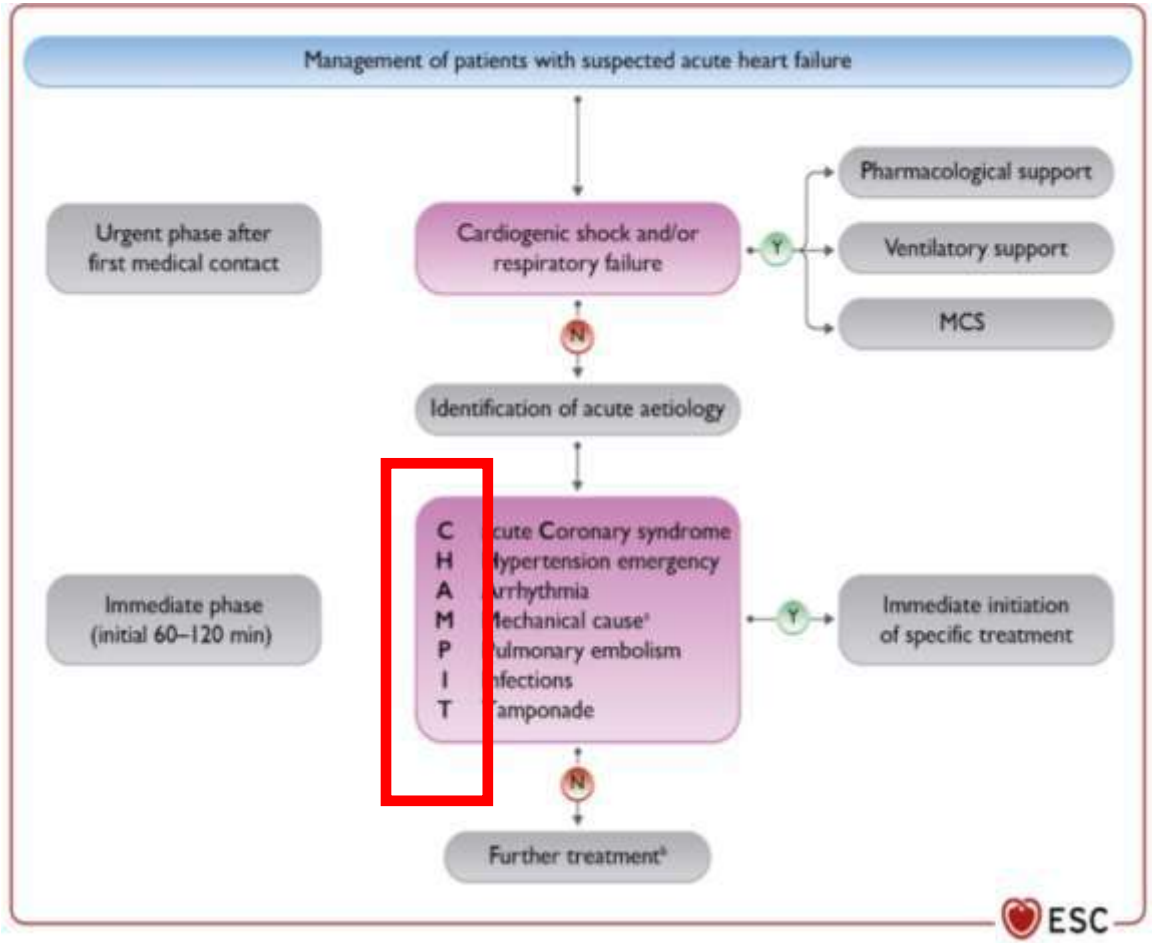
AHF Diagnosis



Diagnostic workup of AHF

Initial management

Initial management of AHF



In-hospital

Clinical presentations:
ADHF,APO, RHF,CS

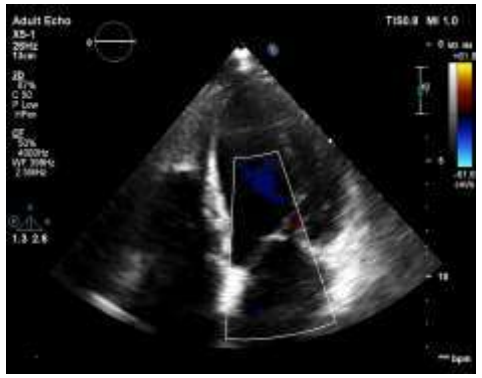
AHF: large diversity of precipitants

These conditions have specific management pathways and triage dispositions should be treated before congestion/hypoperfusion algorithm

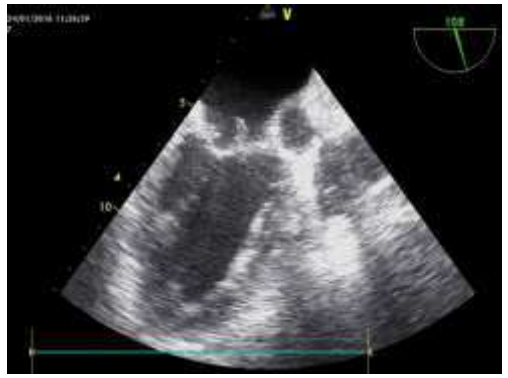
Immediate phase
(initial 60–120 min)

C	acute Coronary syndrome
H	Hypertension emergency
A	Arrhythmia
M	Mechanical cause[a]
P	Pulmonary embolism
I	Infections
T	Tamponade

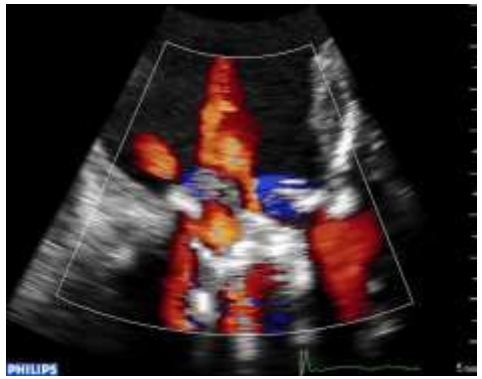
Large anterior MI



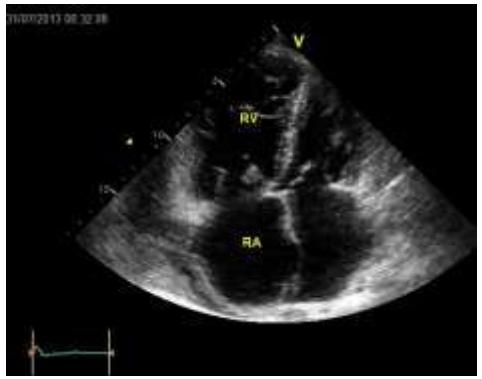
PM rupture



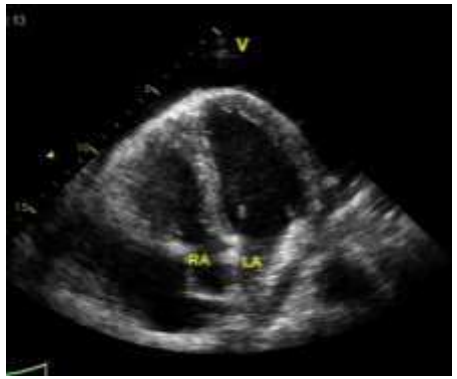
PV thrombosis

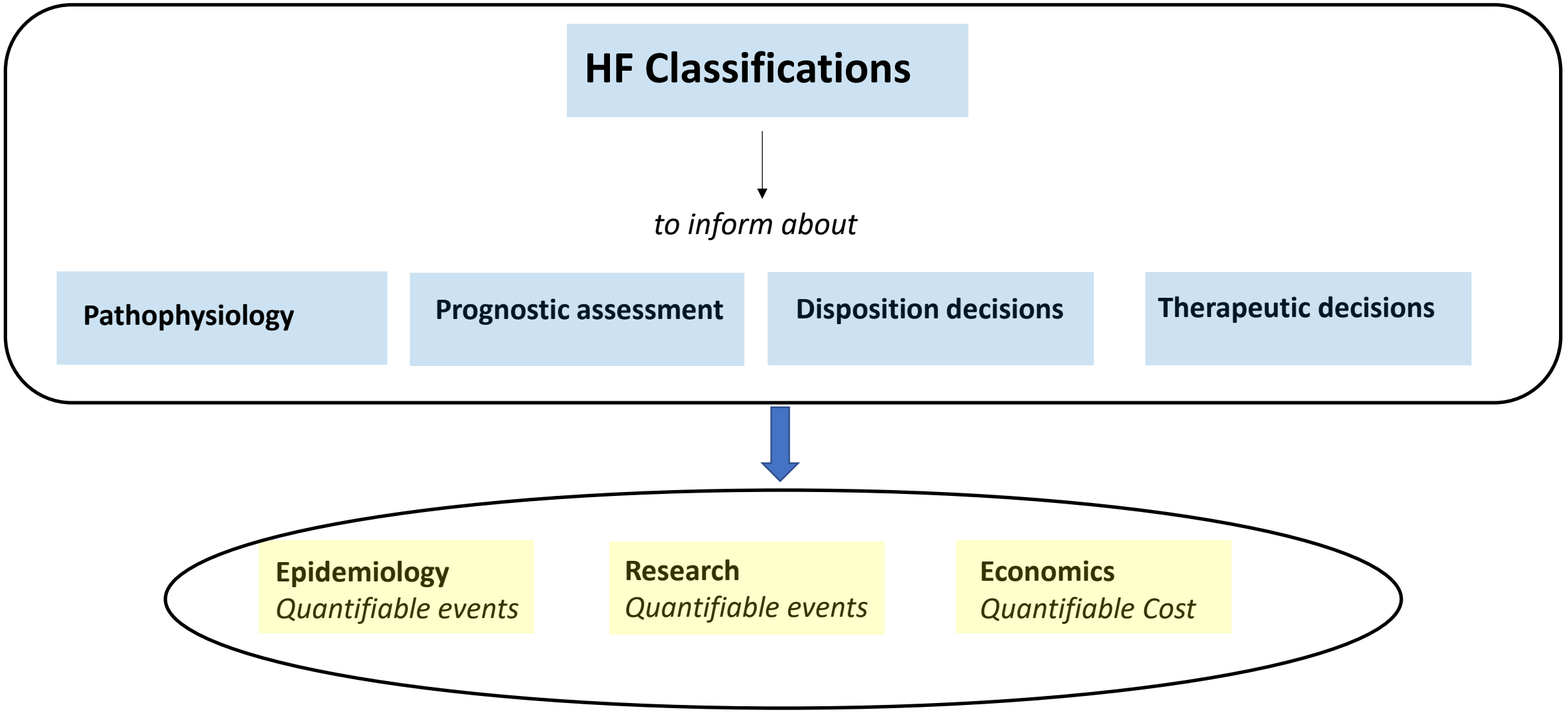


Acute PE



Tamponade




HF Classifications
to inform about
Pathophysiology
Prognostic assessment
Disposition decisions
Therapeutic decisions
Epidemiology
Quantifiable events
Research
Quantifiable events
Economics
Quantifiable Cost

↑↑RAP

↑↑PCWP

Concordant congestion

↑RAP ← ↑PCWP

Right-sided congestion

Left-sided congestion

Acute RVF

ADHF

APO

Peripheral oedema
JVD
Hepatomegaly
HJR

Orthopnoea
Tachypnoea
Rales
S3

APO clinical criteria*

Respiratory distress
- RR>25/min
- Use of accessory muscles

Respiratory failure
- SpO2 <90%,
- ABG: PaO2 < 60 mmHg,
- PaCO2 > 45 mmHg
- PaO2/FiO2 < 300 mmHg

Diagnostic confirmation of APO (at least two criteria)[47]:
- Clear signs of pulmonary congestion on chest X ray or CT scan
- >3 B-Lines in two chest zones on each hemithorax on LUS
- Signs of elevated filling pressures on echo (E/E' > 15)
- BNP > 400pg/ml or N-ProBNP > 900pg/ml
- (or 1800pg/ml in > 75 years)
- Elevated pulmonary capillary pressure on catheterization
- Increased total lung water on pulse contour and thermodilution analysis system

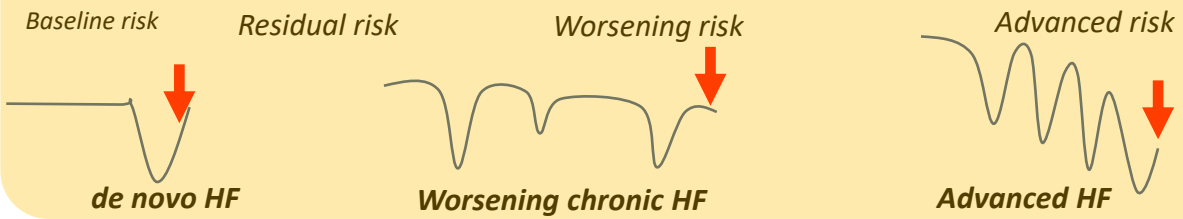
No hypoperfusion

Hypoperfusion

CS

T

Trajectories: HF long term trajectories



A

Acute life threatening aetiologies- CHAMPIT
other potential triggers

C

Clinical profiles

ADHF | APO | RHF | CS

Congestion (right vs left)/Hypoperfusion

I

Individual pump failure phenotype

L vs R vs biV; concordant vs discordant

T

Initial Therapies

Continuous improving

Initial improving then worsening

Refractory symptoms

Downward course with continuous worsening

Escalation of therapies

improving → Optimization of GDMTs

optimal/suboptimal/intolerant

Not improving → Advanced HF therapies

(HTX, LVAD, Palliative care)

T- **T**rajectories

long term **T**rajectories

de novo HF

WCHF

Advanced HF

A-acute **A**etiologies requiring specific treatment (CHAMPIT)

C-**C**linical profiles: ADHF, APO, RHF,CS

congestion

hypoperfusion

congestion and hypoperfusion

I-**I**ndividual pump failure phenotypes

L vs R vs biV

T-**T**herapies

initial **T**herapies

in-hospital **T**rajectories

improving

improving then worsening

refractory symptoms

continuous worsening

escalation **T**herapies

2016

(end stage/refractory/terminal/advanced)

13. Mechanical circulatory support and heart transplantation

13.1 Mechanical circulatory support

For patients with either chronic or acute HF who cannot be stabilized with medical therapy, MCS systems can be used to unload the failing ventricle and maintain sufficient end-organ perfusion. Patients in acute cardiogenic shock are initially treated with short-term assistance using extracorporeal, non-durable life support systems so that more definitive therapy may be planned. Patients with chronic, refractory HF despite medical therapy can be treated with a permanent implantable left ventricular assist device (LVAD). *Table 13.1* lists the current indications for the use of mechanical circulatory assist devices.[393]

13.1.1 Mechanical circulatory support in acute heart failure

To manage patients with AHF or cardiogenic shock (INTERMACS level 1), short-term mechanical support systems, including percutaneous cardiac support devices, extracorporeal life support (ECLS) and extracorporeal membrane oxygenation (ECMO) may be used to support patients with left or biventricular failure until cardiac and other organ function have recovered. Typically the use of these devices is restricted to a few days to weeks. The Survival After Veno-arterial ECMO (SAVE) score can help to predict survival for patients receiving ECMO for refractory cardiogenic shock (online calculator at http://www.save-score.com).[394]

In addition, MCS systems, particularly ECLS and ECMO, can be used as a 'bridge to decision' (BTD) in patients with acute and rapidly deteriorating HF or cardiogenic shock to stabilize haemodynamics, recover end-organ function and allow for a full clinical evaluation for the possibility of either heart transplant or a more durable MCS device.[395]

Evidence regarding the benefits of temporary percutaneous MCS in patients not responding to standard therapy, including inotropes, is limited. In a meta-analysis of three randomized clinical trials comparing a percutaneous MCS vs. IABP in a total of 100 patients in cardiogenic shock, percutaneous MCS appeared safe and demonstrated better haemodynamics, but did not improve 30-day mortality and was associated with more bleeding complications.[396] In a randomized trial on high-risk PCI in patients with impaired LV function (PROTECT II trial), the 30-day incidence of major adverse events was not different for patients with IABP or a haemodynamic support device.[397] Based on these results, temporary percutaneous MCS cannot be recommended as a proven or efficacious treatment for acute cardiogenic shock. In selected patients it may serve as a bridge to definite therapy. A difficult decision to withdraw MCS may need to be made when the patient has no potential for cardiac recovery and is not eligible for longer-term MCS support or heart transplant.

13.1.2 Mechanical circulatory support in end-stage chronic heart failure

Heart transplantation has always been a limited therapeutic option for patients with end-stage chronic HF. The increasing number of patients with refractory, chronic HF and the declining willingness for organ donation have resulted in expanded waiting lists and prolonged waiting times for patients listed for heart transplantation (median 16 months in the region covered by Eurotransplant).[398] More than 60% of patients are transplanted in high-urgency status, leaving little chance for patients listed for less urgent transplantation. Three times more patients are listed for heart transplantation annually than are actually transplanted, and the mortality rate on the Eurotransplant waiting list in 2013 was 21.7%.[398]

More recent data suggest that patients with ongoing LVAD support may have an improved survival on the transplant waiting list.[399] Accordingly, MCS devices, particularly continuous-flow LVADs, are increasingly seen as an alternative to heart transplantation. Initially LVADs were developed for use as a short-term BTT approach (Table 13.1),[400] but they are now being used for months to years in patients who will either face a long-term wait on the transplant list (currently only 10% of patients with an MCS device implanted with a BTT indication will receive an organ within 1 year of listing) or in patients who are not eligible for transplantation as permanent therapy or destination therapy. The number of patients with a permanent LVAD who are considered neither too old nor ineligible for transplantation is constantly growing. For a ma-

Table 13.1 Terms describing various indications for mechanical circulatory support

Bridge to decision (BTD)/ Bridge to bridge (BTB)	Use of short-term MCS (e.g. ECLS or ECMO) in patients with cardiogenic shock until haemodynamics and end-organ perfusion are stabilized, contra-indications for long-term MCS are excluded (brain damage after resuscitation) and additional therapeutic options including long-term VAD therapy or heart transplant can be evaluated.
Bridge to candidacy (BTC)	Use of MCS (usually LVAD) to improve end-organ function in order to make an ineligible patient eligible for heart transplantation.
Bridge to transplantation (BTT)	Use of MCS (LVAD or BiVAD) to keep patient alive who is otherwise at high risk of death before transplantation until a donor organ becomes available.
Bridge to recovery (BTR)	Use of MCS (typically LVAD) to keep patient alive until cardiac function recovers sufficiently to remove MCS.
Destination therapy (DT)	Long-term use of MCS (LVAD) as an alternative to transplantation in patients with end-stage HF ineligible for transplantation or long-term waiting for heart transplantation.

2021

10 Advanced heart failure

10.1 Epidemiology, diagnosis, and prognosis

Many patients with HF progress into a phase of advanced HF, characterized by persistent symptoms despite maximal therapy.[381-383] The prevalence of advanced HF is increasing due to the growing number of patients with HF, ageing of the population, and better treatment and survival of HF. Prognosis remains poor, with a 1-year mortality ranging from 25% -75%.[384-386]

The updated HFA-ESC 2018 criteria for the definition of advanced HF are reported in Table 13.[382] A severely reduced LVEF is common but not required for a diagnosis of advanced HF as it may develop in patients with HFpEF as well. In addition to the reported criteria, extra-cardiac organ dysfunction due to HF (e.g., cardiac cachexia,

2021 criteria for defining Advanced Heart Failure

ESC European Society of Cardiology

European Journal of Heart Failure (2018) 20, 1505–1535
doi:10.1002/ejhf.1236

HFA POSITION STATEMEN

Advanced heart failure: a position statement of the Heart Failure Association of the European Society of Cardiology

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This article updates the Heart Failure Association of the European Society of Cardiology (ESC) 2007 classification of advanced heart failure and describes new diagnostic and treatment options for these patients. Recognizing the patient with advanced heart failure is critical to facilitate timely referral to advanced heart failure centres. Unplanned visits for heart failure decompensation, malignant arrhythmias, co-morbidities, and the 2016 ESC guidelines criteria for the diagnosis of heart failure with preserved ejection fraction are included in this updated definition. Standard treatment is, by definition, insufficient in these patients. Inotropic therapy may be used as a bridge strategy, but it is only a palliative measure when used on its own, because of the lack of outcomes data. Major progress has occurred with short-term mechanical circulatory support devices for immediate management of cardiogenic shock and long-term mechanical circulatory support for either a bridge to transplantation or as destination therapy. Heart transplantation remains the treatment of choice for patients without contraindications. Some patients will not be candidates for advanced heart failure therapies. For these patients, who are often elderly with multiple co-morbidities, management of advanced heart failure to reduce symptoms and improve quality of life should be emphasized. Robust evidence from prospective studies is lacking for most therapies for advanced heart failure. There is an urgent need to develop evidence-based treatment algorithms to prolong life when possible and in accordance with patient preferences, increase life quality, and reduce the burden of hospitalization in this vulnerable patient population.

Keywords Heart failure • Heart transplantation • Heart-assist devices • Extracorporeal membrane oxygenation

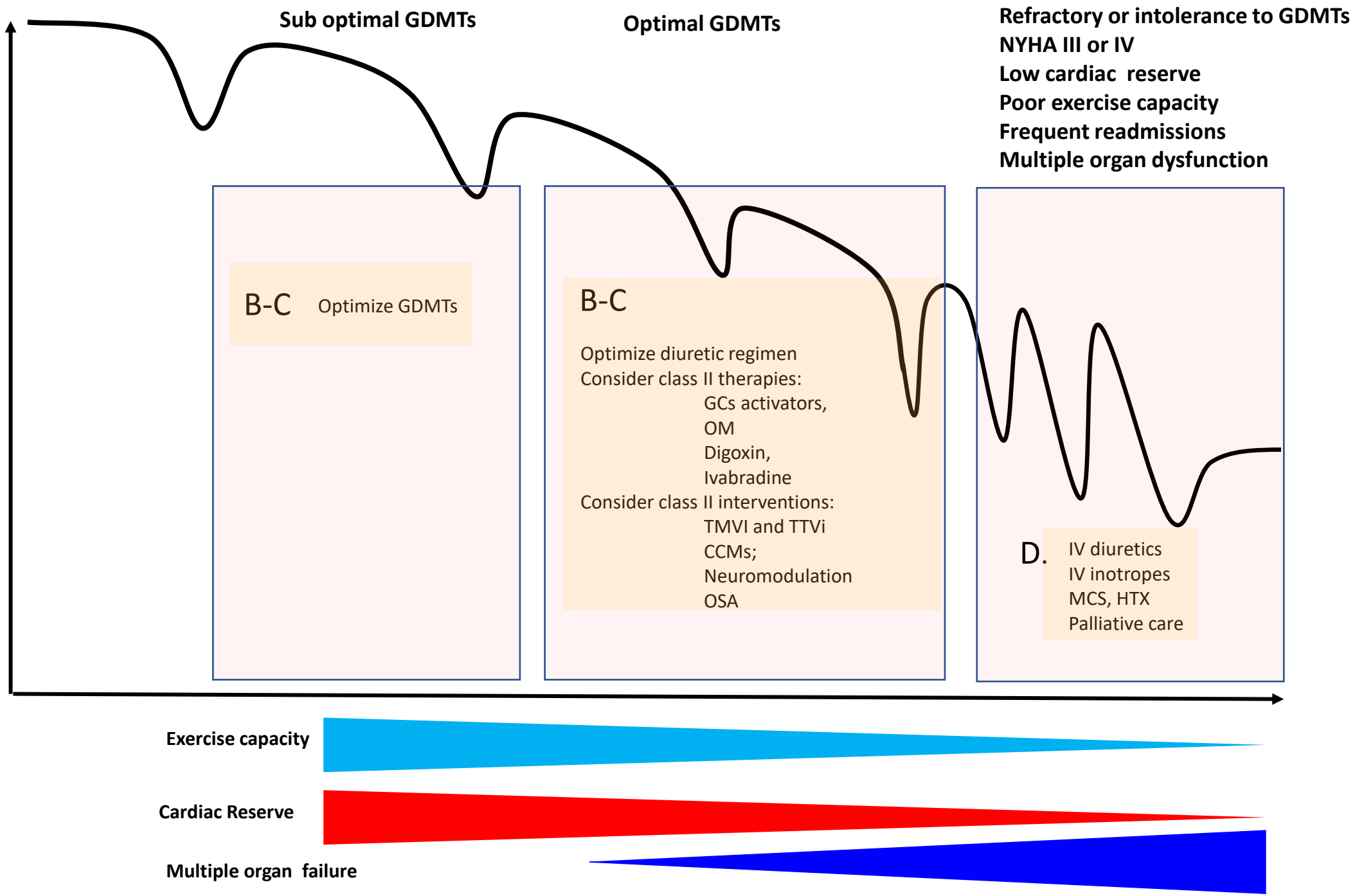
All the following criteria must be present despite OMT:

1. Severe and persistent symptoms of heart failure [NYHA class III (advanced) or IV].

2. Severe cardiac dysfunction defined by (at least one of the following):
   - LVEF (≤30%)
   - Isolated RV failure (e.g., ARVC)
   - Non-operable severe valve abnormalities
   - Congenital abnormalities
   - Persistently high (or increasing) BNP or NT-proBNP values and severe diastolic dysfunction or LV structural abnormalities (according to the definitions of HFpEF)

3. Episodes of pulmonary or systemic congestion requiring high-dose i.v. diuretics (or diuretic combinations) or episodes of low output requiring inotropes or vasoactive drugs or malignant arrhythmias causing >1 unplanned visit or hospitalization in the last 12 months.

4. Severe impairment of exercise capacity with inability to exercise or low 6MWT (<300 m) or pVO_2 <12 mL/kg/min or<50% predicted value, estimated to be of cardiac origin.


Sub optimal GDMTs
Optimal GDMTs
Refractory or intolerance to GDMTs
NYHA III or IV
Low cardiac reserve
Poor exercise capacity
Frequent readmissions
Multiple organ dysfunction
B-C Optimize GDMTs
B-C
Optimize diuretic regimen
Consider class II therapies:
GCs activators,
OM
Digoxin,
Ivabradine
Consider class II interventions:
TMVI and TTVi
CCMs;
Neuromodulation
OSA
D.
IV diuretics
IV inotropes
MCS, HTX
Palliative care
Exercise capacity
Cardiac Reserve
Multiple organ failure

2021 criteria for defining Advanced Heart Failure

ESC GUIDELINES

ESC European Society of Cardiology

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

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC

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ESC Clinical Practice Guidelines Committee (CPG): listed in the Appendix.

All the following criteria must be present despite OMT:

1. Severe and persistent symptoms of heart failure [NYHA class III (advanced) or IV].

2. Severe cardiac dysfunction defined by (at least one of the following):
   - LVEF (≤30%)
   - Isolated RV failure (e.g., ARVC)
   - Non-operable severe valve abnormalities
   - Congenital abnormalities
   - Persistently high (or increasing) BNP or NT-proBNP values and severe diastolic dysfunction or LV structural abnormalities (according to the definitions of HFpEF)

3. Episodes of pulmonary or systemic congestion requiring high-dose i.v. diuretics (or diuretic combinations) or episodes of low output requiring inotropes or vasoactive drugs or malignant arrhythmias causing >1 unplanned visit or hospitalization in the last 12 months.

4. Severe impairment of exercise capacity with inability to exercise or low 6MWT (<300 m) or

Is the patient's prognosis on tolerated medical therapy poor enough that advanced therapies should be considered?

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