7th Advances in Heart Failure 2024

10 e 11 de Outubro

FACULDADE DE MEDICINA DA UNIVERSIDADE DO PORTO

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GET DONE EVENTS

7th Advances in Heart Failure 2024
10 e 11 de Outubro
FACULDADE DE MEDICINA DA UNIVERSIDADE DO PORTO

O Advento do Fim da Fração de Ejeção

É possível definir qual a fração de ejeção normal?

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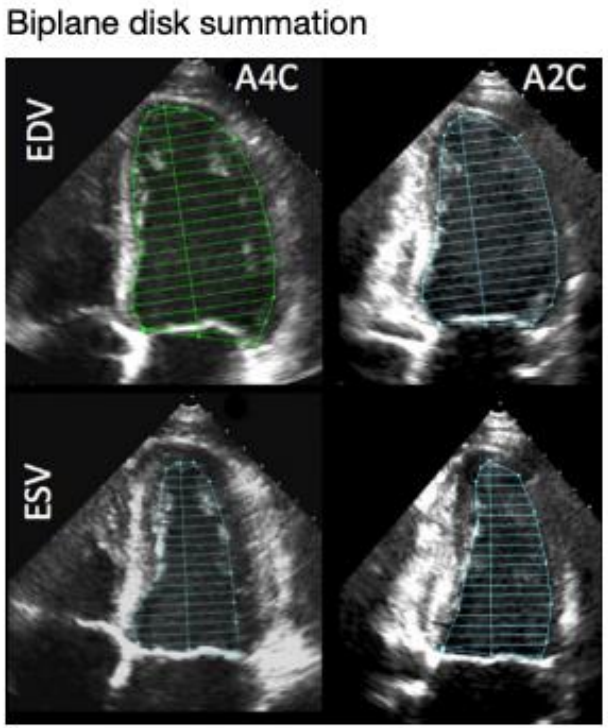
Why do we use ejection fraction?

Ejection Fraction

$$EF = \frac{(EDV - ESV)}{EDV}$$



Extensively used for quantifying LV systolic function, mostly because of the **simplicity of its measurement**

Predict prognostic

- every 1% decrease of baseline LVEF value points to 4% increase in incident heart failure risk

Guide management

- pharmacological and non pharmacological measures (ICD, referral for valvular interventions)

Assess response to therapy

- serial evaluations

May be calculated using several cardiac imaging techniques including 2D and 3D echo, CMR, CT and SPECT

Echocardiography is the most commonly used modality due to its simplicity, low cost, and widespread accessibility

Ejection Fraction

GUIDELINES AND STANDARDS

Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging

J Am Soc Echocardiogr 2015;28:1-39.

LV volume estimates may be derived from 2DE or 3DE, as described above (section 1.2). The biplane method of disks (modified Simpson's rule) is the currently recommended 2D method to assess LV EF by consensus of this committee. Table 4 lists 2DE-derived biplane LV EF, including normal ranges and consensus-based severity partition cutoffs according to gender. In patients with good image quality, 3DE-based EF measurements are accurate and reproducible and should be used when available and feasible.[6,10,15,16,19,20]

Table 4 Normal ranges and severity partition cutoff values for 2DE-derived LV EF and LA volume

	Male				Female			
	Normal range	Mildly abnormal	Moderately abnormal	Severely abnormal	Normal range	Mildly abnormal	Moderately abnormal	Severely abnormal
LV EF (%)	52–72	41–51	30–40	<30	54–74	41–53	30–40	<30
Maximum LA volume/BSA (mL/m^2)	16–34	35–41	42–48	>48	16–34	35–41	42–48	>48

Ejection Fraction

Current guidelines recognize distinct HF patient phenotypes on the basis of LVEF:

- reduced LV systolic function (LVEF ≤ 40%, HFrEF)
- mildly reduced LV systolic function (HFmrEF)
- preserved systolic function (LVEF ≥ 50%, HFpEF)

Classification based mainly on patient selection in clinical trials of drug therapy for HF

TABLE 1 HF classifications according to LVEF and LVEF grading in international cardiac societies guidelines.

Society name	HF classification/LVEF grading	LVEF
ESC (2)	HF with reduced LVEF (HFrEF)	≤40%
	HF with preserved LVEF (HFpEF)	≥50%
	HF with mildly reduced LVEF (HFmrEF)	41%–49%
ACCF/AHA (15)	HF with reduced LVEF (HFrEF)	≤40%
	HF with improved LVEF (HFimpEF)	previous ≤40% and >40% at a follow-up
	HF with mildly reduced LVEF (HFpmrEF)	41%–49%
	HF with preserved LVEF (HFpEF)	≥50%
JCS/JHFS (16)	HF with reduced LVEF (HFrEF)	<40%
	HF with preserved LVEF (HFpEF)	≥ 50%
	HF with midrange LVEF (HFmrEF)	40%–<50%
	HF with recovered LVEF (HFrecEF)	LVEF improved during the treatment
	HF with worsened LVEF (HFworEF)	LVEF decreased with the treatment
	HF with unchanged LVEF (HFuncEF)	no major change in LVEF
NHFA/CSANZ (17)	HF with reduced LVEF (HFrEF)	<50%[a]
	HF with preserved LVEF (HFpEF)	≥50%
BSE (18)	Severly impaired LVEF	≤35%
	Impaired LVEF	36%–49%
	Borderline low LVEF	50%–54%
	Normal LVEF	≥55%

Front. Cardiovasc. Med. 11:1340708.

Is ejection fraction an accurate measurement?

Limitations of Ejection Fraction

Dependent on image quality and endocardial border definition

Geometrical assumptions of ellipsoid ventricular cavity

- inaccurate in IHD, severely remodelled LV

Need to identify true apex

Difficulties in high HR, AF, LBBB

Highly intra, interobserver and temporal variability

- up to 7% intrapatient
- 28% ← 35% → 42%

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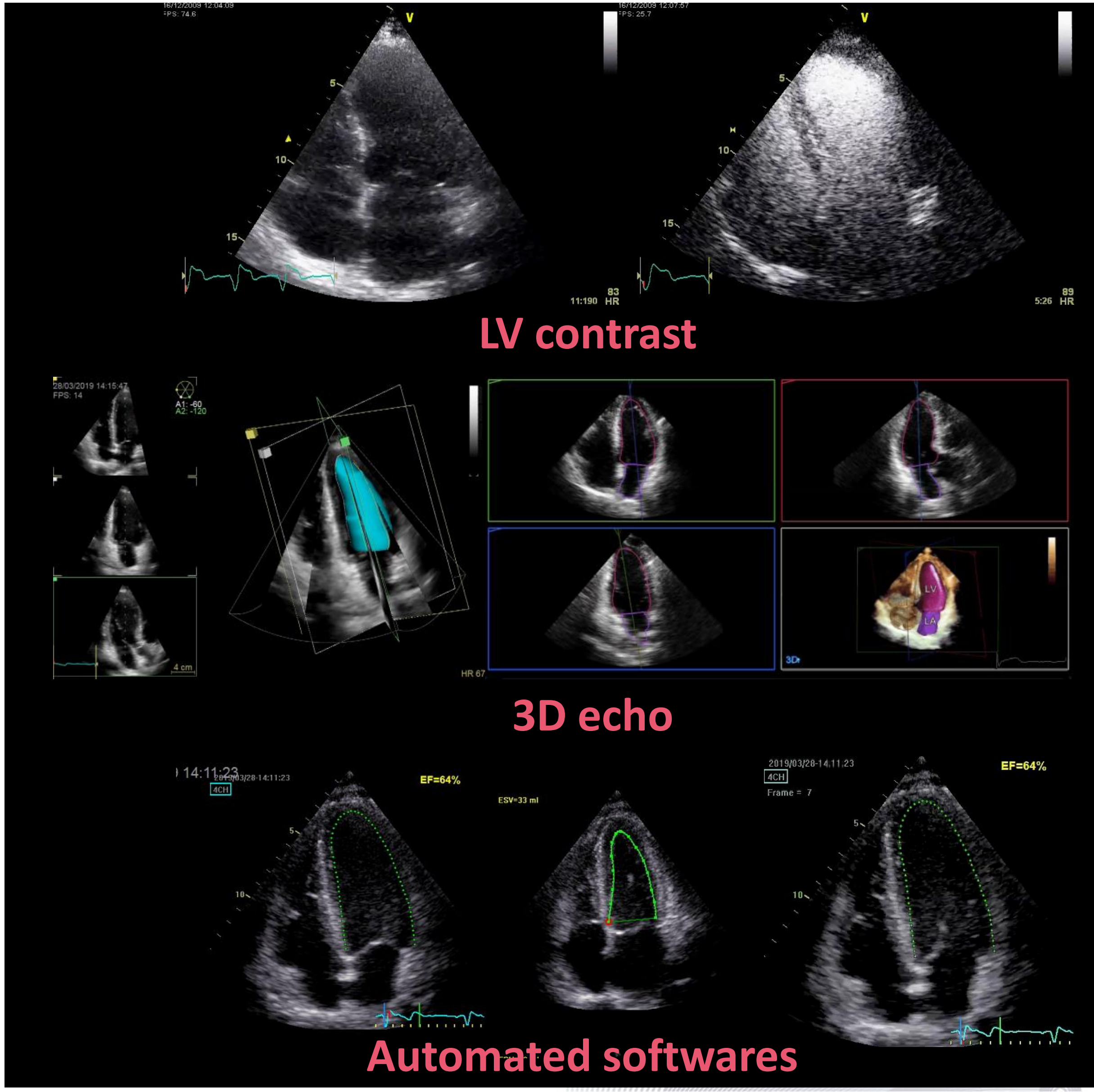
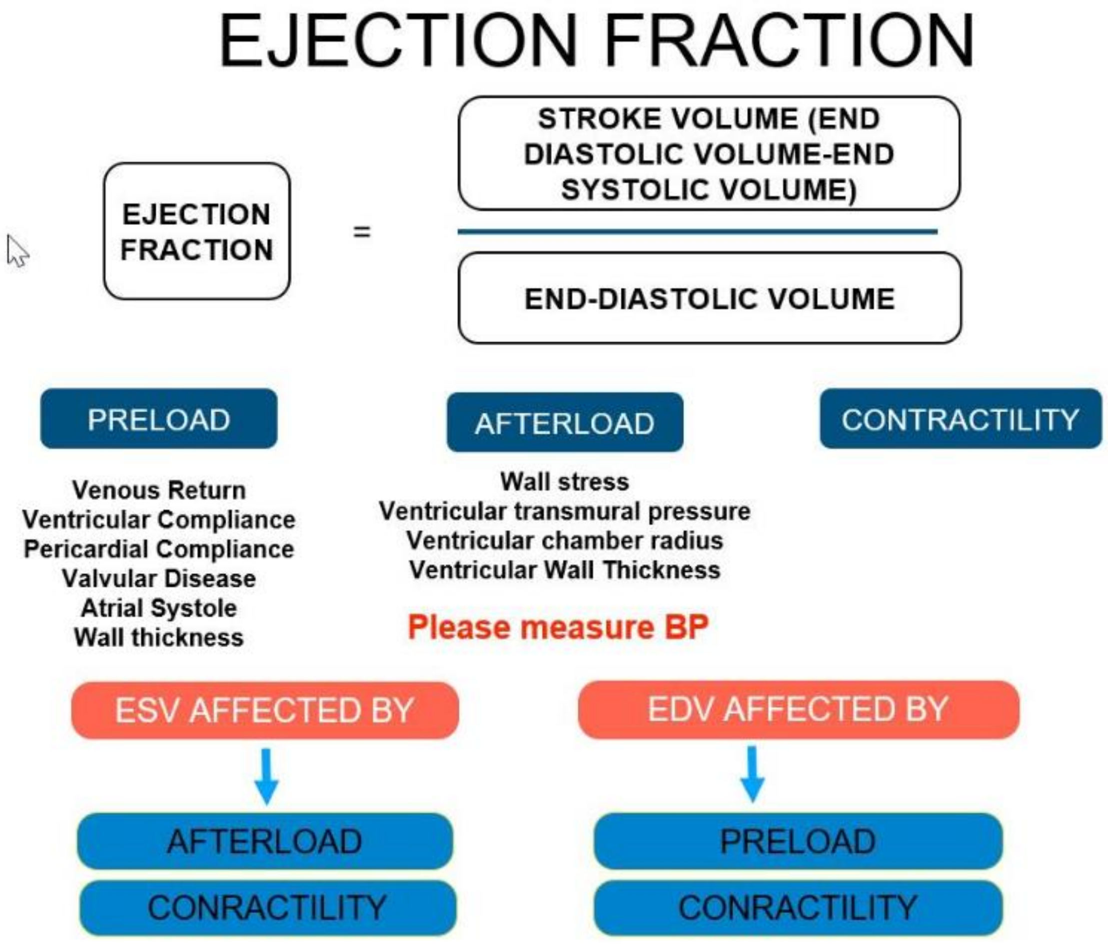
Relevance of experienced hands / eyes
> 10 % change = meaningful LVEF difference



Limitations of Ejection Fraction



Heart, Vessels and Transplantation 2019; 3.

SV and EDV dependency

- a dilated LV with increased EDV and ESV as in heart failure or athlete’s heart generates normal SV with lower LVEF values
- a small ventricle with decreased volumes may show normal LVEF value albeit with low SV

Load dependency

- blood pressure
- volemic status
- concomitant valvular disease

Limitations of Ejection Fraction

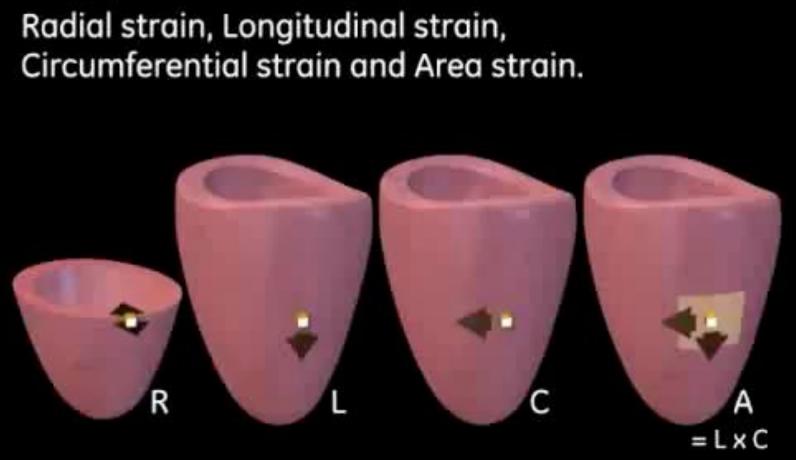
LVEF does not represent myocardial contractility

- 3 layers of myocardial fibers - longitudinal contraction, circumferential shortening and radial thickening
- EF predominantly evaluates radial function
- EF misses to detect intial suble changes in LV function

Deformation Imaging

- Myocardial deformation (++ STE) provides accurate information in early phases of disease
- **Higher sensitivity in detecting subtle systolic LV variation**
- **Less load dependent**
- **May have higher prognostic value**

- **GLS is the most commonly studied parameter**
- Highly reproducible (inter- and intraobserver variability < 4%)
- Normal ranges are still somewhat vendor- and software-dependent



Limitations of Ejection Fraction in HF

LVEF arbitrarily divides HF patients
HFrEF - evidence-based therapy has proved effective
HFpEF - uncertain results of therapy, limited to certain subgroups
HFmrEF - transition phenotype; up to 20% of all patients, heterogeneous population mostly with HFrEF whose LVEF partially improved with therapies and a smaller proportion with HFpEF whose LVEF declined

However HF is a dynamic syndrome that may progress or improve over time according to the changes in the underlying pathophysiological processes

LVEF cannot distinguish between resolution of the underlying myocardial pathology or improvement with persistence of subclinical myocardial dysfunction

What to do with patients with HFrEF (LV EF <40%) that show improvement or even normalization of LV EF, with an absolute increase of EF ≥10%, spontaneously or as a result of a good response to therapy?
Would this mean full recovery of systolic LV function?
Would we discontinue optimal therapies?

Limitations of Ejection Fraction in HF

HFpEF

- ✓ Approximately 70% of patients with symptomatic HFpEF have recovered from low LVEF → these patients still have high rate of HF hospitalization
- ✓ Several studies have shown significant impairment of myocardial function, assessed by myocardial strain despite preserved EF (LVEF may be normal in patients with LV hypertrophy and small LV cavities)
- ✓ LVEF does not provide pathophysiological distinctions between systolic and diastolic dysfunction

Limitations of Ejection Fraction in HF

LVEF as a powerful predictor of fatal and non-fatal cardiovascular outcomes

→ true only when the systolic function is below 45%

→ prognostic capability reduces significantly in patients with LVEF> 45% (limited sensibility to predict SCD)

Large studies of patients hospitalized with EF have shown similar mortality rates across the LVEF spectrum

LVEF has no significant relationship with other prognostic markers

→ symptoms

→ NT-proBNP

→ biomarkers associated with inflammation, cellular proliferation, and metabolism

→ amount of fibrosis (induces electrophysiological heterogeneity which promotes the development of ventricular arrhythmias)

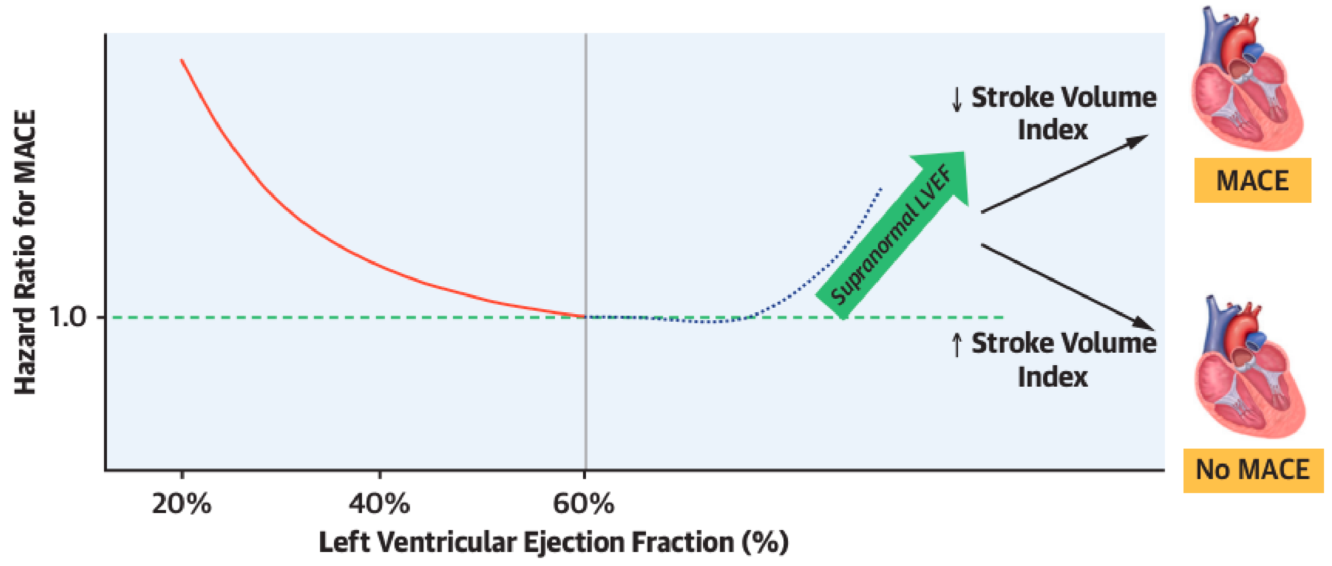
Currently, some of the most effective therapeutics in HF are beneficial in low normal EF (tx agnostic to EF)

Supra normal Ejection Fraction

Epidemiological data:

- ✓ **U-shaped relationship between mortality and LVEF in patients with LVEF ≥ 65%** (supra-normal LV function)
- ✓ mortality rates similar to HFrEF
- ✓ ++ snLVEF with low SV

CENTRAL ILLUSTRATION Supranormal Ejection Fraction, Stroke Volume, and Cardiovascular Outcomes Among Community-Dwelling Individuals



Shah S, et al. J Am Coll Cardiol HF. 2022;10(8):583-594.

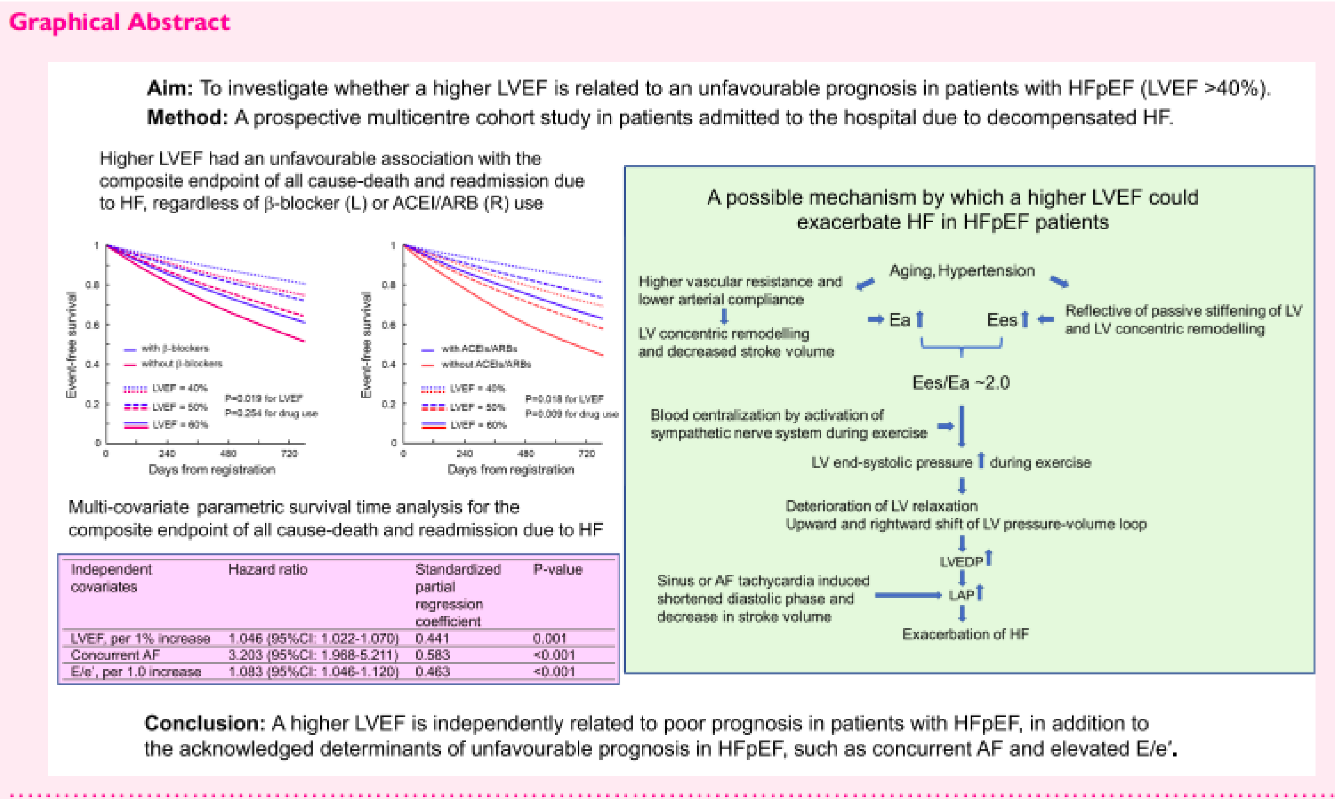
Supranormal ejection fraction, assessed by CMR, is associated with increased risk of MACE among middle-aged community-dwelling adults. CMR = cardiac magnetic resonance; LVEF = left ventricular ejection fraction; MACE = major adverse cardiovascular events.

Supra normal Ejection Fraction

Also in HfpEF:

- ✓ A higher LVEF, concurrent AF and elevated E/e' ratio was independently related to poor prognosis
- ✓ Discrimination threshold value LVEF≥57.2%
- ✓ snLVEF is a distinct phenotype within HFpEF

Maybe because these patients have no access to OMT?



European Heart Journal - Cardiovascular Imaging (2023) 24, 293–300

Ejection Fraction in HF

”It's an artificial metric”

“It doesn't have any physiological significance”

“We would encourage you to forget about ejection fraction”

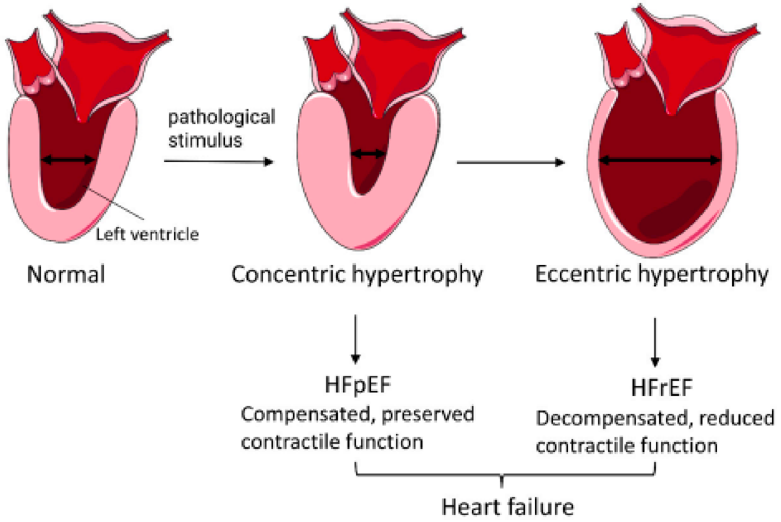
What should we evaluate beyond EF?

Other echo parameters

LV mass and RWT

Associated with heightened cardiovascular mortality

- Normal geometry (normal LVMI and RWT <0.42)
- Concentric remodeling (normal LVMI with increased RWT >0.42)
- **Eccentric hypertrophy (increased LVMI and RWT <0.42)**
- **Concentric hypertrophy (increased LVMI and RWT >0.42)**



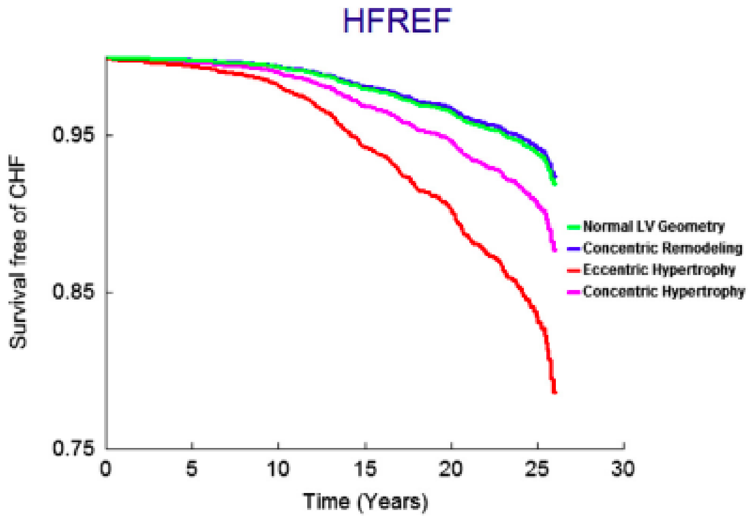
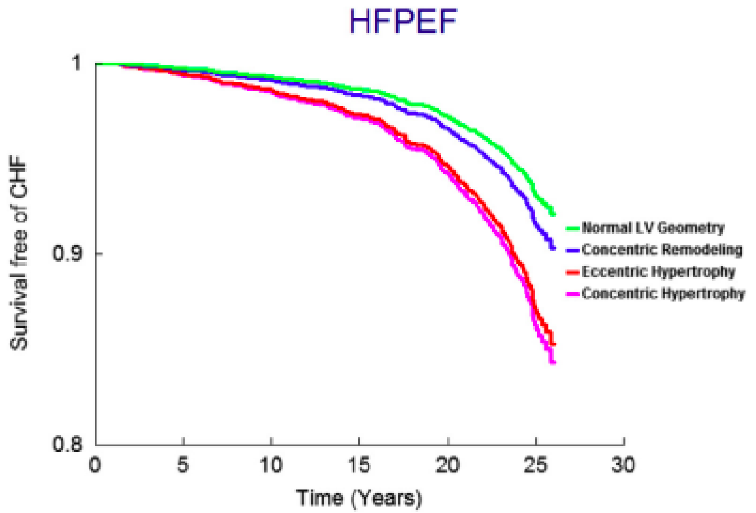


Figure 2. Age- and gender-adjusted survival free of HFREF according to LV hypertrophy pattern. CHF = congestive HF.



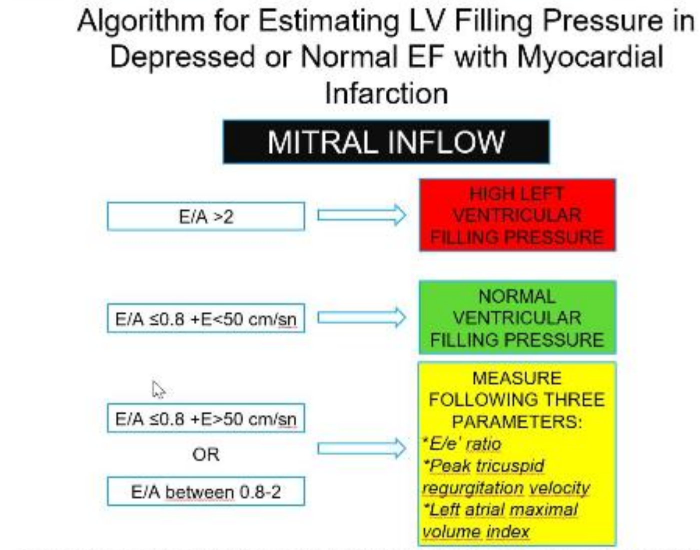
Am J Cardiol 2014;113:117e122)

Other echo parameters

High Left Ventricular Pressure: E/E’ ratio

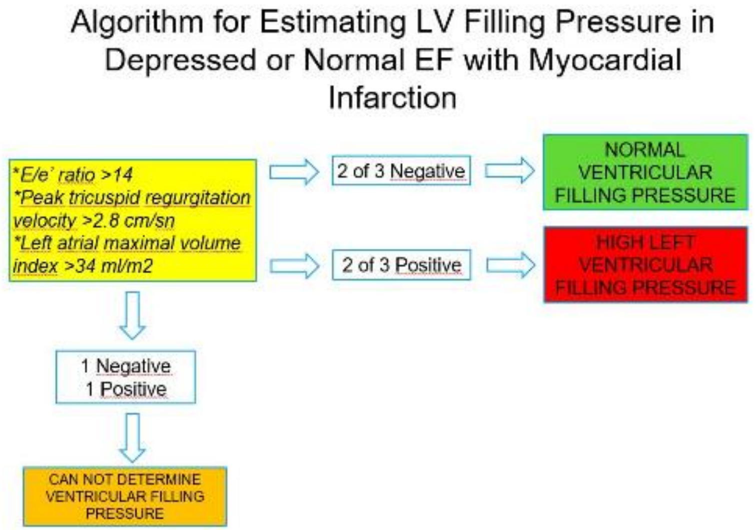
Many echocardiographic parameters have been used for estimating LVFPs:
- mitral inflow E/A ratio
- mitral A wave duration-pulmonary vein A duration
- E/e’ ratio
- …

E/E’ is the most robust parameter
- ✓ Very high specificity (77-100%)
- ✓ Poor sensitivity (0- 73%)
- ✓ Modest correlation with invasively determined LVFP
- ✓ **Strong surrogate marker for cardiovascular death, heart failure hospitalization, or aborted cardiac arrest**
- ✓ E/E’ ratio ≥15 as a major criterion for HFpEF diagnosis (values 10-14 are less sensitive but accepted as minor criterion)



Modified from Andersen OS, Smiseth OA, Dokainish H, et al. Estimating Left Ventricular Filling Pressure by Echocardiography. J Am Coll Cardiol 2017;69:1937–1948

A)



Other echo parameters

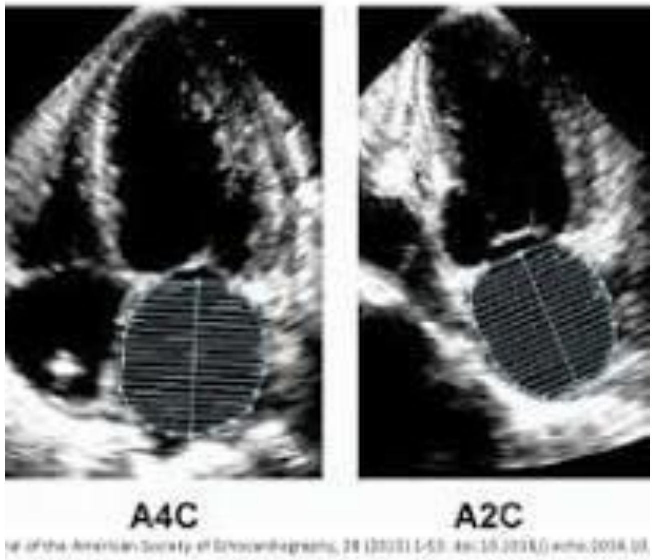
LA Volume

Left atrial volume index (LAVi) is a powerful surrogate marker for long- standing high LVFPs

LAVi>34mL/m2 **independently predicts death, heart failure, AF and ischemic stroke** in patients without AF or valvular heart disease

Permanent AF causes larger LAV, which usually 35% more dilated than LAV in sinus rhythm (18)

LAVi > 34 ml/m2 + E/e' ratio >14 + peak TR velocity > 2.8 m/sec is used as a marker for high LVFP



Left Atrial Volume Index

Sinus Rhytm	Atrial Fibrillation
Major Criterion: >34 ml/m2	Major Criterion: >40 ml/m2
Minor Criterion: 29-34 ml/m2	Minor Criterion: 34-40 ml/m2

Modified from Pieske B, Tschöpe C et al . 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). *Eur Heart J* 2019.

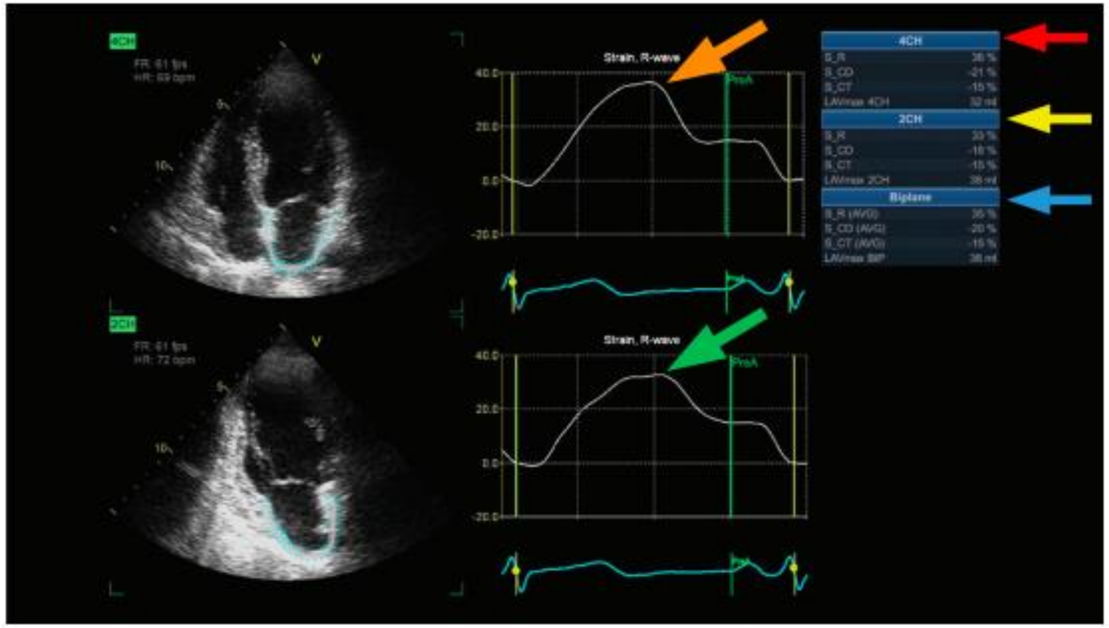
Other echo parameters

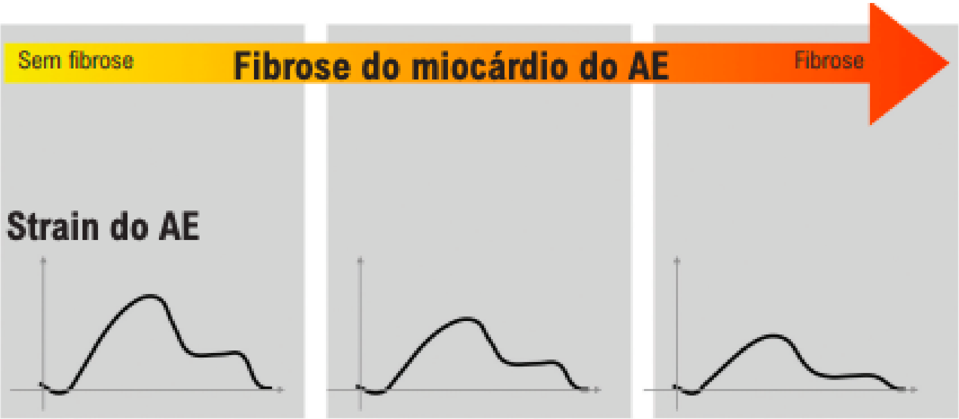
Left Atrial Global Strain During Reservoir Phase

LA function
- ✓ reservoir during ventricular systole
- ✓ conduit during early diastolic phase
- ✓ atrial contraction during late phase of diastole

LA strain has a reverse correlation with decreasing left ventricular diastolic function
Higher sensitivity for detecting diastolic dysfunction

Normal LA global reservoir strain value is > 35%
LA global strain value < 20-23% points to very severely reduced LA function

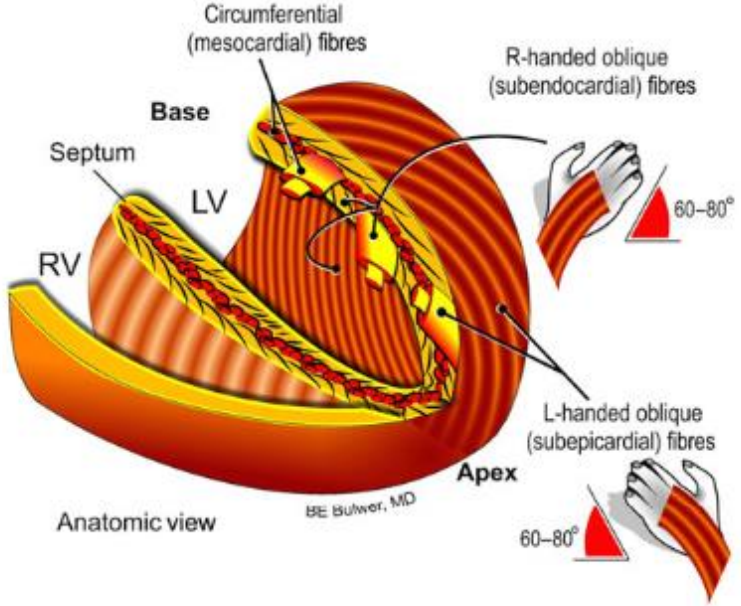




Other echo parameters

European Heart Journal (2016) 37, 1642–1650

Left Ventricular Global Longitudinal Strain (LV-GLS)



Detection of early myocardial dysfunction

- ✓ Tissue Doppler (but angle dependency)
- ✓ speckle-tracking based strain imaging (preferred route)

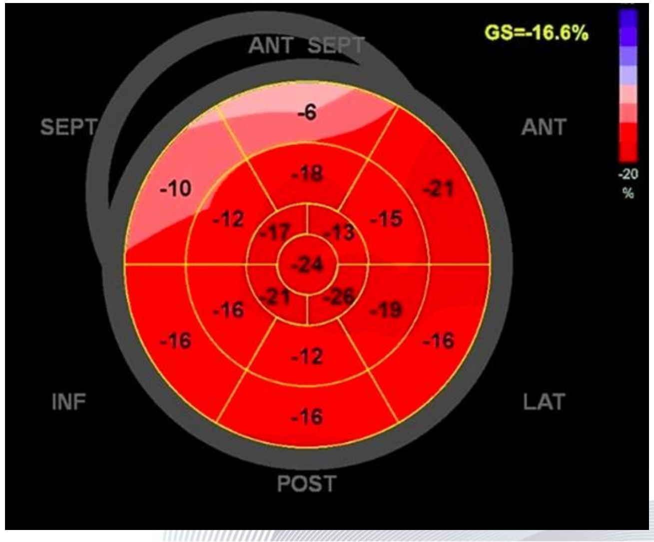
Normal value for LV-GLS is around -20%

Better inter-observer and intra-observer variability (5% to 8% relative difference)

May show variation according to a particular software or vendor used

Prognostic information in patients with normal or near normal LVEF values

- ✓ low LV-GLS associates with higher cardiovascular event risk
- ✓ prognostic value incremental to risk factors and LVEF
- ✓ the change in LV-GLS is also a stronger predictor of all-cause mortality than change in LVEF value



LV-GLS decreased in patients with HfpEF and has an added useful prognostic information

GLS <16% minor functional abnormality in the diagnostic algorithm HfpEF

Heart Fail Rev (2020) 25:9–17

Other echo parameters

Circulation: Heart Failure
Volume 16, Issue 5, May 2023; Page e010252
https://doi.org/10.1161/CIRCHEARTFAILURE.122.010252

American Heart Association.

EMERGING INVESTIGATORS

Echocardiographic Features Beyond Ejection Fraction and Associated Outcomes in Patients With Heart Failure With Mildly Reduced or Preserved Ejection Fraction

† BNP available in 617/2237 patients, NT-proBNP available in 1711/2337 patients.

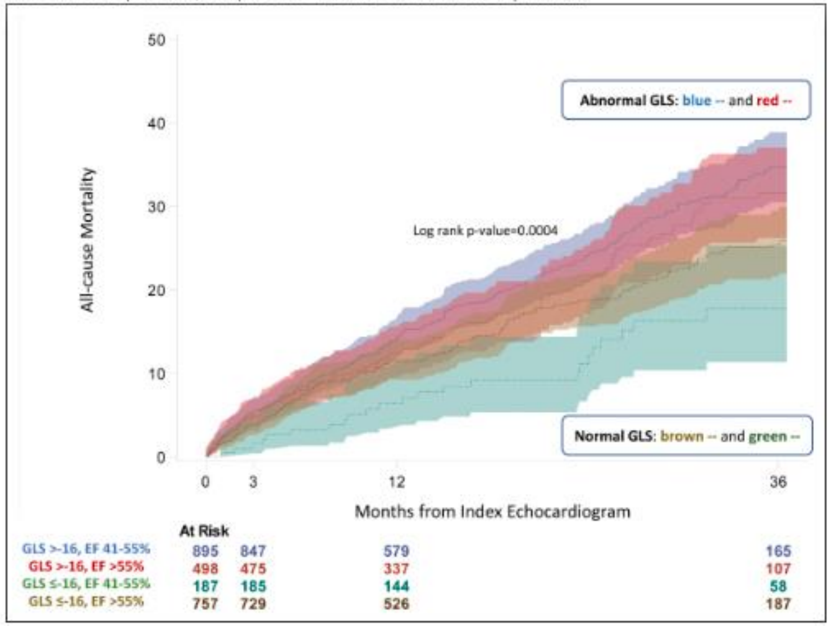


Figure 2. Kaplan-Meier curves for all-cause mortality by left ventricular ejection fraction (LVEF) and left ventricular global longitudinal strain (LV GLS status).

~50% patients with preserved LVEF had abnormal GLS

Adverse outcomes similar to patients with impaired LVEF

Significantly worse than patients with normal GLS regardless of LVEF

GLS was the most prognostic echocardiographic feature with regards to mortality and hospitalization outcomes

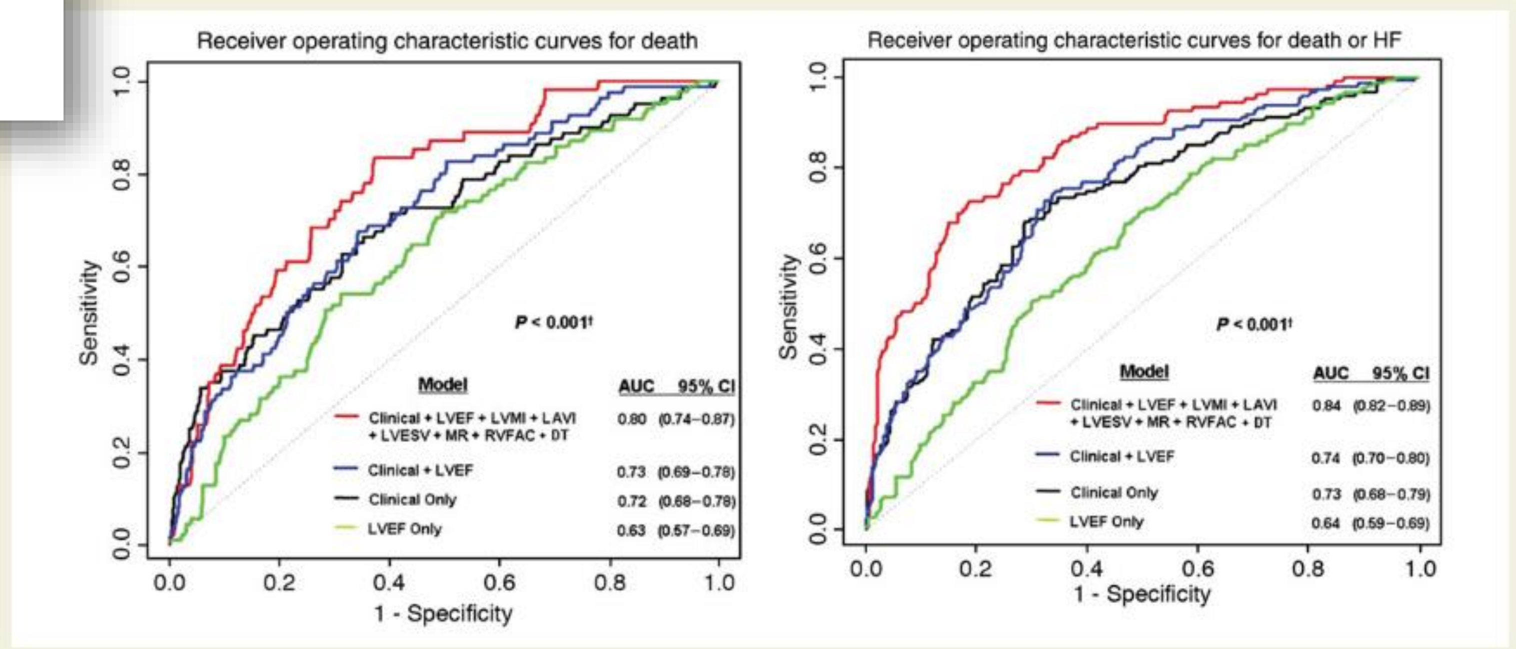
Other echo parameters

European Heart Journal (2016) 37, 1642–1650
doi:10.1093/eurheartj/ehv510

REVIEW

Clinical update

Beyond ejection fraction: an integrative approach for assessment of cardiac structure and function in heart failure



Clinical assessment alone provided good discrimination of 17-month survival

LVEF alone did not substantially improve discrimination – neither for survival, nor survival free of heart failure

Adding multiple echocardiographic markers significantly improved discrimination of survival and survival free of heart failure

ChatGPT

Yes, a normal ejection fraction (EF) is typically considered to be between 55% and 70%. Ejection fraction is a measurement of how much blood the left ventricle pumps out with each contraction, and values outside this range may indicate heart conditions. An EF below 55% may suggest heart failure or other cardiac issues, while a very high EF might indicate other concerns. Always consult a healthcare professional for a proper assessment.

Is it possible to define “normal” ejection fraction?

- ✓ Asymptomatic pts
- ✓ With no relevant cardiac family history
- ✓ With normal diastolic function
- ✓ With normal GLS

Is it possible to define “normal” ejection fraction in HF?

In HF, EF alone may not provide a comprehensive assessment as it oversimplifies the complex pathophysiology of HF and fails to capture the condition’s heterogeneity

EDITORIAL

Left Ventricular Ejection Fraction in Heart Failure: Crazy, Stupid Love—and Maybe, Redemption

Milton Packer, MD

Eur J Prev Cardiol. 2023;30:e032257.

Stockholm-CELOSIA study

- 9176 patients with HF, chronic kidney disease, or diabetes with new-onset HF who had a measurement of LVEF before and after the diagnosis (at least 15 days apart)
- discern the stability of a diagnosis of HFrEF, HFmrEF, or HFpEF over time
- 35% of patients had an interval clinical event between the 2 LVEF measurements, including events that would have decreased LVEF (eg, myocardial infarction), increased LVEF (eg, heart transplantation), or markedly augmented the variability of LVEF (eg, atrial fibrillation)

- **Normal distribution of LVEF**, with a modal value of 40% to 45% (no evidence for 2 or 3 distinct subgroups)
- SD of the within- person **variance was 7.4%**
- **75% to 80% likelihood of HF reclassification on repeated measurement in HFmrEF**
- **25% transition from HFrEF to HFpEF** (improvement in EF following prolonged use of neurohormonal antagonists)
- **< 10% transition from HFpEF to HFrEF** (minimally dilated left ventricle in patients with HFpEF did not subsequently remodel and enlarge)
- less variability in men with an initial diagnosis of HFrEF and in women with an initial diagnosis of HFpEF

EDITORIAL

Left Ventricular Ejection Fraction in Heart Failure: Crazy, Stupid Love—and Maybe, Redemption

Milton Packer, MD

The imperative for a reclassification of heart failure

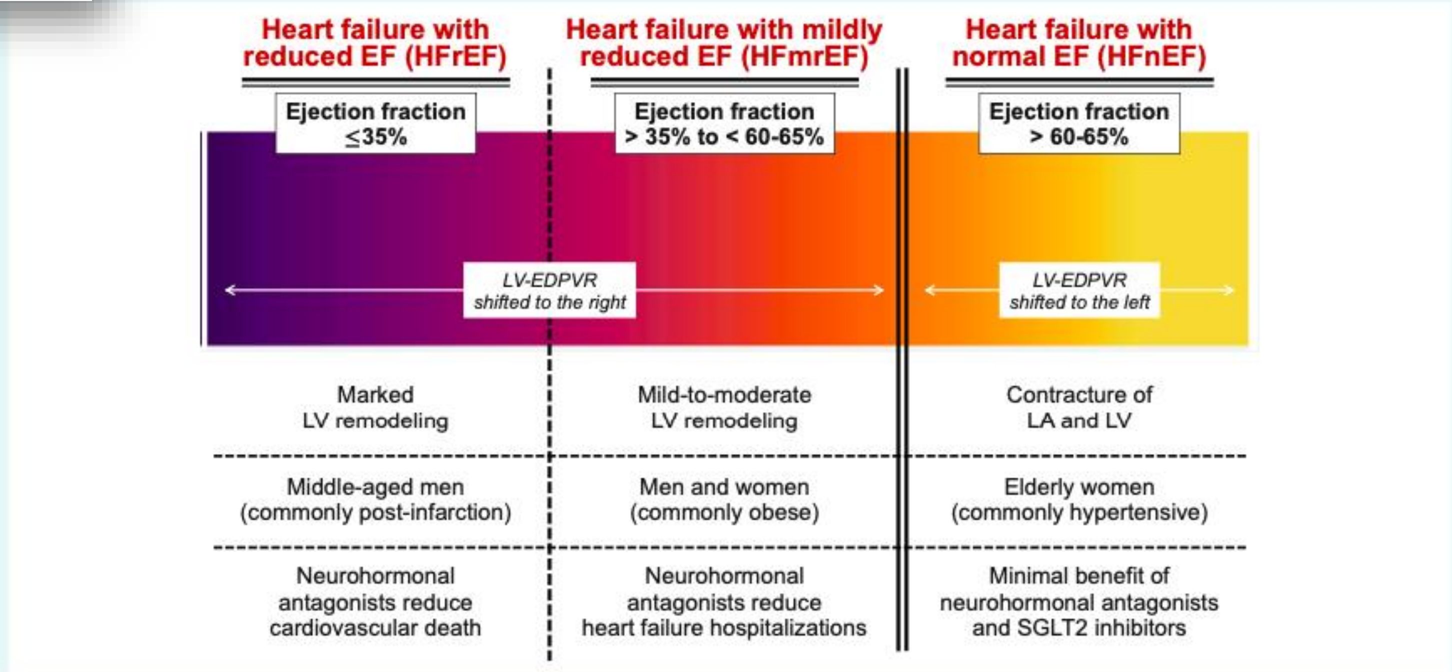
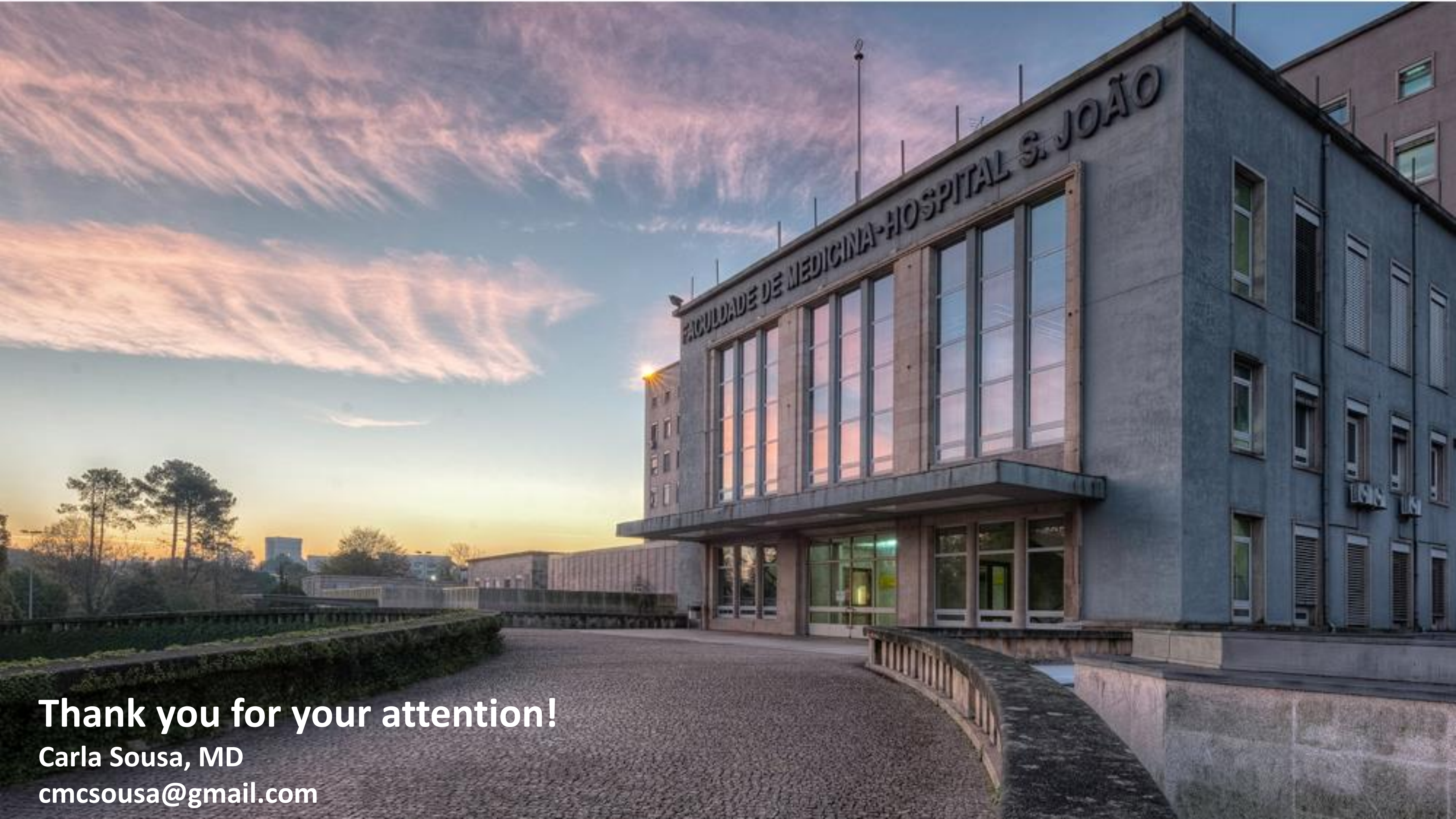


Figure 1 Reclassification of heart failure based on left ventricular (LV) remodelling and contracture phenotypes. The figure shows (1) the principal pathophysiological mechanism; (2) the affected patient population; and (3) the efficacy of neurohormonal antagonists in three groups of patients with heart failure based on ejection fraction (EF). The term 'heart failure with a preserved ejection fraction' is not used. LA, left atrium; LV-EDPVR, left ventricular end-diastolic pressure–volume relationship; SGLT2, sodium–glucose cotransporter 2.

European Journal of Heart Failure (2023) 25, 669–672
J Am Heart Assoc. 2024;13:e034642.



Thank you for your attention!

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