### Role of echocardiography in HF

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 Although heart failure (HF) is often defined clinically, it has a large pre-clinical spectrum and its diagnosis, staging, response to therapy, and etiology are often determined by echocardiography



### HF classification

Only echocardiography can truly categorize individuals into

"no HF," preclinical stage A or stage B. Stage B HF may be

an incidental finding on echocardiography in the absence of

not only history, symptoms and clinical signs, but also without

any risk factors for HF (no prior stage A). In stages C and D, echocardiography serves as a prognostic tool to stage

### HF classification

 Echocardiographically, HF is often classified based on LV ejection fraction (LVEF) as that with reduced (HFrEF, LVEF ≤40%), mid-range (HFmrEF, LVEF 41%–49%) or preserved (HFpEF, LVEF ≥50%) ejection fraction (EF).

### EF

• The use of LV-EF to characterize patients with HF has certainly advantages. LV-EF is a universally known index, is immediately understandable being a percentage, can be calculated using all cardiac imaging techniques and, most importantly, it can be estimated visually even if it cannot be measured. All these aspects make LV-EF very easy to obtain and helpful to rapidly communicate among physicians about the patient.

### overcome the limitations of LV-EF

• To overcome the limitations of LV-EF, a hemodynamic categorization of HF patients, taking into account both LV forward flow and filling pressure, has been proposed

• . The aims of this article, therefore, are to verify whether Doppler echocardiographic evaluation of LV hemodynamics: 1) has acceptable feasibility, accuracy and reproducibility to be suggested for practical application, and, 2) can improve diagnosis, prognostic assessment and guide to treatment in patients with HF.

# Pathophysiological basis for a hemodynamic approach to heart failure

Ventricular function is based on a complex muscle-pump system that achieves adequate ejection of blood without an increase in filling pressure both at rest and during exercise. HF can be defined as a clinical syndrome that results from impairment of ventricular filling and/or ejection of blood [2]. On the basis of this definition, a reduced ventricular blood ejection and an increased ventricular filling pressure are the two main features of HF, which determine signs and symptoms of this syndrome

## similar approach in cardiogenicshock

• Interestingly, a similar approach has been recently adopted in phenotyping hemodynamic presentation of cardiogenic shock, as reported in a recent scientific statement [11]. In this statement, 5 hemodynamic subgroups of cardiogenic shock have been described, based on the assessment of cardiac index (CI), pulmonary capillary wedge pressure (PCWP), systemic vascular resistance index, central venous pressure and systolic blood pressure, advocating a hemodynamic approach to help in defining not just ejection volume (which is expected to be low in cardiogenic shock), but rather ventricular preload (PCWP or central venous pressure), volume status, and systemic vascular resistance, with the recognition of inherent consequences in prognosis and therapeutic management

### Echocardiographic evaluation of blood ejection

 Parameters and cut-off values Cardiac output (CO, 1/min) is a measure of the anterograde pump function. It is generally expressed as CI (1/min/m2), that is, normalized by the body surface area. If only the amount of blood ejected by the LV per beat is considered, then the anterograde pump function can be expressed as stroke volume index (SVI, ml/m2). Normal accepted values of CI and SVI are >2.5 l/min/m2 and > 35 ml/ m2

# parameters of anterograde pump function can be divided in two groups: per-beat (SD, SV, SVI) and per-minute (MD, CO, CI)

• Overall, parameters of anterograde pump function can be divided in two groups: per-beat (SD, SV, SVI) and per-minute (MD, CO, CI) parameters. In HF patients, per-minute parameters include the compensatory effect of tachycardia and evaluate the ability of the heart to pump enough blood into the circulation to meet the body's demands, while per-beat parameters focus more on ventricular contraction. A comparison between per-beat and perminute parameters is needed to establish which is the best LV output index to predict prognosis in HF patients.

#### ECHOCARDIOGRAPHIC EVALUATION OF LV BLOOD EJECTION



# Echocardiographic evaluation of left ventricular filling pressure Parameters and cut-off values

 The term LV filling pressure refers to different intracardiac pressures: the mean PCWP, the mean left atrial (LA) pressure, the LV pre-A pressure, and the LV end-diastolic pressure (LV-EDP) [35]. Mean PCWP and LA pressure correlate better with LV pre-A pressure, while LV-EDP is the highest LV filling pressure after the atrial contraction.  Different pressures have also different correlates with Doppler variables: in fact, some Doppler variables correlate with an increase in LV-EDP only and others reflect an increase in both LA pressure and LV-EDP [35]. In summary, different LV filling pressures are not always interchangeable, thus use of Doppler variables to evaluate LV filling pressure should take this aspect into account. In general, assessment of mean PCWP or LA pressure should be preferred. LV filling pressures are considered elevated when

the PCWP is >12 mmHg or when the LV-EDP is>16 mmHg

 The algorithm for LV filling pressure estimation combines LA volume index as an indicator of long-term elevation of LV filling pressure with Doppler velocities, which reflect LV filling pressure at the time of the echocardiographic examination (Fig. 2) a low SD was an independent predictor of all cause mortality regardless of whether LV-EF was

above or below 50% [49]. In contrast, CI was not associated with mortality at the multivariate analysis. The authors suggested it could be related to higher HRs in patients with low SD which normalizes CI

 All the evidence reported above support the addition of the LV output evaluation to that of LV-EF for prognosis assessment in HF patients (Table 2). Further investigations are needed to compare accuracy of per-beat (SD, SV, SVi) and perminute analysis (MD, CO, CI) in predicting outcomes. The hemodynamic assessment of HF patients should be seen as complimentary to the etiology and pathological substrate of HF, which constitute, in many cases, the major prognostic determinants. In this regard Felker et al. [50] showed that, even after adjustments for hemodynamic variables, patients with cardiomyopathy due to ischemic heart disease have a worse survival than patients with non-ischemic causes of cardiomyopathy.

#### Resting echocardiographic characterization of heart failure patients

(for outcome prediction and guide to therapy)



Specific subgroups of patients with heart

failure

 There are subgroups of HF patients with specific hemodynamic features to be taken into account separately: those with high CO, isolated right HF and with resting normal flow and pressure. Echocardiography can also
play a role in these subgroups.



# Conclusions

A pathophysiological approach to HF patients based on assessment of cardiac hemodynamics (ventricular forward flow

and filling pressure) would be desirable to overcome the significant limitations of the HF categorization based on LV-EF

only. Such an approach could be reliably applied in clinical

practice using echocardiography, which has been shown to be feasible and accurate to evaluate both LV forward flow and

filling pressure in the setting of HF. Dedicated investigations

are needed to set-up a echocardiography-based hemodynamic categorization for both ambulatory and hospitalized HF patients, with the aim to establish new non-invasive modalities

for prognosis assessment and guide to therapy.

# Conventional echocardiographic parameters ('old') in heart failure

• Basically, the conventional ECHO parameters are aimed at evaluating the pump function, the filling profile of the left ventricle (LV), and the haemodynamics of the right ventricle (RV).

### STE

- To overcome the limitations of EF, LV analysis can be obtained by speckle tracking echocardiography (STE);
- GLS is useful as an early diagnostic and prognostic marker in HF [15]. In patients with HFrEF, GLS was an index of myocardial fibrosis
  [16] and an independent predictor of all-cause mortality, superior to other echocardiographic parameters, particularly in male subjects and in sinus rhythm

• Numerous factors (arrhythmias, mitral insufficiency, and loading conditions), however, can affect the accuracy of the filling indices especially in terms of specificity. In particular, atrial fibrillation represents the most common condition that can invalidate the applicability and predictive power of the functional and cardiac filling indices.

### after-load mismatch

- Echocardiography is the first-line diagnostic modality for the recognition of structural heart disease characterized by increased wall thickness secondary to pressure overload or myocardial diseases (primary or due to the involvement in systemic diseases). Due to the increased filling pressure, patients with HFpEF may develop a reduced pre-load reserve which makes the LV intolerant to increased or previously tolerated post-load values, with the development of pump dysfunction and reduction of the EF (condition of 'after-load mismatch').
- It follows that HFpEF can veer towards stable forms of HFrEF due to progression of the underlying disease or present fluctuations of HFrEF due to the onset of trigger factors capable of reducing the pre-load reserve LV (e.g. Tachycardia, high blood pressure).

# LA

- The size of the left atrium (LA) represents an important morphological index for the diagnostic recognition and the clinical-therapeutic management of patients with HFpEF.
- The LA enlargement constitutes an independent prognostic parameter in the heart diseases with HFpEF and is associated with a high risk of atrial fibrillation. The evaluation by stress-ECHO of the onset of pulmonary hypertension represents a modality of high clinical efficacy to evaluate the LA reserve in heart diseases potentially responsible for HFpEF.

### New parameters in heart failure

• The EF, although it represents an index of high clinical impact, is influenced, for the same level of myocardial contractility, by the loading conditions (pre- and afterloading) and is not synonymous with LV systolic function. Cardiac function presupposes a complex structural organization of the myocardial fibres which, by virtue of their distribution and the respective contraction sequence, are responsible for the physiological alternation of contraction-relaxation aimed at maintaining an adequate cardiac output without increasing the filling pressure. The distribution of myocardial fibres determines an articulated three-dimensional (3D) contraction function characterized by a longitudinal-circumferential shortening component and a radial thickening component.

# Role of strain indices in the phenotype of heart failure

• HF with prevalent longitudinal myocardial dysfunction: many cardiopathies induce, in the early stages, a dysfunction of the sub-endocardial layer which can cause an alteration of the longitudinal function with normal EF values due to the compensatory effect of parietal hypertrophy and the contractile reserve of the epicardial layer. Although the finding of alterations in the filling indices indicative of the increase in intracavitary pressure would lead, for the preserved pump function (EF > 50%), towards the diagnosis of 'diastolic decompensation', the HFpEF frameworks actually underlie a reduction in the longitudinal deformation and a related reduction of the relaxation function as an epiphenomenon of a primary alteration of the 'systolic function'

### HF with transmural dysfunction:

• the involvement of the whole myocardial thickness can be consequent to the progressive extension of the anomalies of the subendocardial layer towards the epicardial one with a proportional reduction of the pump function due to the lack of compensation of the circumferential fibres and evolution towards forms of HFrEF. Conversely, pathological processes with transmural involvement, as in the case of myocardial infarction, can lead to an LV pump dysfunction typical of HFrEF in relation to the extent of the damage.

### HF with prevalent circumferential dysfunction:

• some cardiac diseases, such as those involving the pericardium, tend to involve the subepicardial layer. The involvement of the subepicardial layer determine the alteration of the circumferential function and of the twist mechanism of the left ventricle, while maintaining the systolic pump function as a compensation for the preserved longitudinal function derived from the subendocardial fibres. The alteration of the circumferential function also occurs in cases of myocarditis, as demonstrated by the altered enhancement observed with MRI. In these cases, both described forms of heart failure can occur with preserved and reduced EF

### HF with prevalent or isolated atrial dysfunction:

• LA impairment may represent the phenotype of concomitant or even early cardiomyopathies compared to LV impairment and is an important target for specific therapeutic strategies. The analysis of LA deformation indices can identify HFpEF frameworks without evidence of impairment of cardiac filling indices that can underlie an autonomous or early LA impairment ('atrial myopathy') regardless of LV dysfunction.



### GLS

 Impaired contraction of one layer (say, subendocardial) may be compensated by another layer thereby maintaining an apparent "normal LVEF" during early stages of HF. Subendocardial fibers are more susceptible to injury/ ischemia, and hence, their impairment leads to reduced longitudinal function and right-handed helix shortening with unbalanced subepicardial left-handed helix shortening and increased circumferential shortening. Reduced longitudinal strain (with exaggerated or normal circumferential function) with preserved LVEF is often seen in patients with increasing age, hypertension, diabetes mellitus, and obesity who have HFpEF  In the Treatment of Preserved Cardiac Function Heart Failure

With an Aldosterone Antagonist (TOPCAT) trial, among HFpEF patients, reduced GLS was the most important echocardiographic predictor of cardiovascular death or worsening HF.



# E/A >2

- E/A >2 may also be seen in athletes and individuals under 40 years of age (due to supranormal suction force generated during early diastole), and immediately after direct current cardioversion (diminutive A wave due to atrial stunning).
- Occasionally, a mitral "L wave" may be seen in LV diastolic dysfunction but may also be seen rarely in normal individuals with bradycardia. It represents ongoing LV filling in mid diastole.
- Septal E/e' >15 generally reflects PCWP >20 mmHg, and if the ratio is <8, it usually means that the PCWP is normal.</li>



# LA

- LA structure and function are meaningful markers of LV filling pressure (in the absence of mitral valve abnormalities).
  HFpEF
  - makes the less compliant LV overtly dependent on the atrial pump function. LA dilation is found in about half of all patients with HFpEF, while atrial fibrillation is seen in nearly 40% of HFpEF.
- Of late, "LA peak reservoir strain" has emerged as a newer parameter showing promise in recognizing earlier stages of HFpEF.

## **High-Output Cardiac Failure**

- High-output cardiac failure is a less common form of heart failure, and although it may sound contradictory at first, in the simplest form, it is still the heart's inability to provide sufficient blood for the body's demand.
- Most patients with heart failure are either classified as a systolic or diastolic dysfunction with increased systemic vascular resistance, however, patients with high output cardiac failure have normal cardiac function and decreased systemic vascular resistance, either secondary to diffuse arteriolar dilation or possible bypass of the arterioles and capillary beds, leading to activation of neurohormones.
- This activity reviews the cause, pathophysiology, and presentation of high output heart failure and stresses the role of the interprofessional team in its management.