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RESEARCH ARTICLE

Trans-Thoracic Echocardiographic Parameters for Prognostic Assessment Across the Spectrum of Heart Failure

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ABSTRACT

Heart failure with increasing life expectancy has become the leading cause of morbidity and mortality in modern day world, begetting great economic burden. Usually diagnosed by specific criteria, Framingham's being the most commonly employed, heart failure has been classified on the basis of left ventricular ejection fraction measured by transthoracic echocardiography as heart failure with preserved ejection fraction (HFpEF, LVEF ≥ 50%), heart failure with mid-range EF (HFmrEF, LVEF 41-49%) and heart failure with reduced EF (HFrEF, LVEF ≤ 40%), constituting the "**spectrum**". For the diagnosis of HFpEF, elevated biochemical markers and presence of cardiac structural abnormalities or diastolic dysfunction are also required whereas for the other types only ejection fraction, with appropriate symptoms/signs are needed. It is quite clear that echocardiography plays a central role in diagnosis and classification of heart failure. Mostly, of the prognostic markers mortality and hospitalization have been assessed in clinical trials. Here also echocardiography plays a prominent role and every modality of it (with numerous parameters) including M-mode, 2D, color, spectral and tissue Doppler along with recent addition of strain imaging provide important clues. These clues not only work for heart failure as a whole but also for the individual classes. Many studies have provided insights into the comparative efficacy of these markers across the spectrum. The prognostic power of these echo parameters has been assessed either individually or in combination. Various scoring systems have also been formulated. An individual patient can transit through the classes of heart failure over time and certain echo parameters provide an indication in this regard as well. Structural parameters of both sides of the heart along with functional and hemodynamic assessment provide prognostic insights with strain measures showing superiority. No large-scale clinical trial has yet been done in which all the parameters across the spectrum of heart failure have been studied. An appraisal of clinically important echo markers for prognostic assessment across the spectrum is the subject of this descriptive review.

Keywords: Heart failure, echocardiography, prognosis, phenotypes of heart failure, and ejection fraction.

Introduction

Heart failure (HF) is a leading cause of morbidity and mortality in the present-day world since its declaration as an emerging epidemic in 1997[1]. Initially thought to result from systolic or diastolic ventricular dysfunction, many other clinical scenarios have been noted for this clinical entity. The economic burden of HF is colossal, and mortality is high in the first five years after diagnosis (in various forms)[2]. Left ventricular ejection fraction remains the central pillar for 'classification of HF' in cases with pertinent symptoms and signs. Additionally, elevation of biochemical marker (NT-proBNP) and cardiac structural abnormalities in the form of left ventricular hypertrophy (LVH) or left atrial enlargement (LAE) are also part of it. Three classes have been defined based on these parameters i.e., heart failure with preserved (HFpEF), mildly reduced (HFmrEF) and reduced (HFrEF) ejection fraction constituting the "**spectrum of heart failure**".[3]

Echocardiography has immense importance in the diagnoses and classification of HF. Trans-thoracic echocardiography (TTE) estimates LVEF, structural abnormalities (LVH and LAE) and diastolic function comprehensively. Thus, it can be said that 'diagnosis and classification of HF' revolves around echocardiography.

Echocardiography has great prognostic potential also, demonstrated by clinical studies with mortality and HF hospitalization being studied mostly. Other less studied features include atrial fibrillation, trajectory of LVEF and cardiac transplant etc. In cases of HFpEF three risk scores are used for prognostic assessment. Only clinical parameters are utilized in MAGGIC score, H2FPEFF utilizes clinical parameters and two echo parameters, and HFA-PEFF is a three-step algorithm with clinical parameters in step 1, multiple echo parameters in step 2 and exercise-induced parameters in step 3. Kosmala MP, in 201 patients of HFpEF, demonstrated the prognostic ability of the three risk scores for the composite endpoint of death and HF re-hospitalization. The best AUC was noted for HFA-PEFF step 3 score 0.766 ± 0.034, outperforming AUC of HFA-PEFF step 2 algorithm, H2FPEF score, and MAGGIC risk score.[4] Thus, addition of echo parameters to baseline clinical parameters provides more prognostic information, especially if exercise echo parameters are included.

Parameters of TTE differ across the three types of HF. In 547 patients of HF, (HFpEF = 137, HFmrEF = 61, and HFrEF = 349), Linde C et al found HFpEF patients showed smaller left ventricular (LV) diameters and volumes ($p < 0.001$) and higher septal and relative wall thickness ($p < 0.001$). Patients with HFrEF showed a higher E/e' ($p = 0.017$) and left atrial volume index (LAVI), ($p = 0.040$) whereas, HFmrEF subjects showed intermediate values for LV mass, volumes, and right ventricle (RV) volumes but had the highest proportion of LVH and the lowest proportion of elevated E/é. Thus, these phenotypes differ in baseline echo parameters, resulting in different prognoses.[5]

A single TTE parameter may not provide much prognostic information and a combination of them shows better results. Built on these combinations, various scoring systems have been devised. To date, no single combination or scoring system has been evaluated across the spectrum of heart failure for all the endpoints. In the present narrative review, the prognostic importance of various echocardiographic parameters has been described with clinical evidence to delineate their utility across the spectrum of heart failure.

Methodology

Electronic data search was done by keywords on Pub-med and Google Scholar. Articles were accessed for prognostic assessment of echocardiographic parameters in HF. Concordant references were scrutinized and articles consonant with the theme of this review were included.

Definition and Classification

"Clinical syndrome of heart failure (HF) presents with typical symptoms and signs, due to deranged cardiac structure and function".[6]

Three parameters are needed for the diagnosis of 'HF class' viz, presence of symptoms/signs, LVEF and presence of structural abnormalities (LVH/LAE) or diastolic dysfunction. For the diagnosis of HFpEF all components are needed, whereas for HFmrEF and HFrEF only LVEF is considered although presence of other criteria consolidates the diagnosis.[3] The cut-offs of LVEF for the three classes of HF are as shown in figure 1.

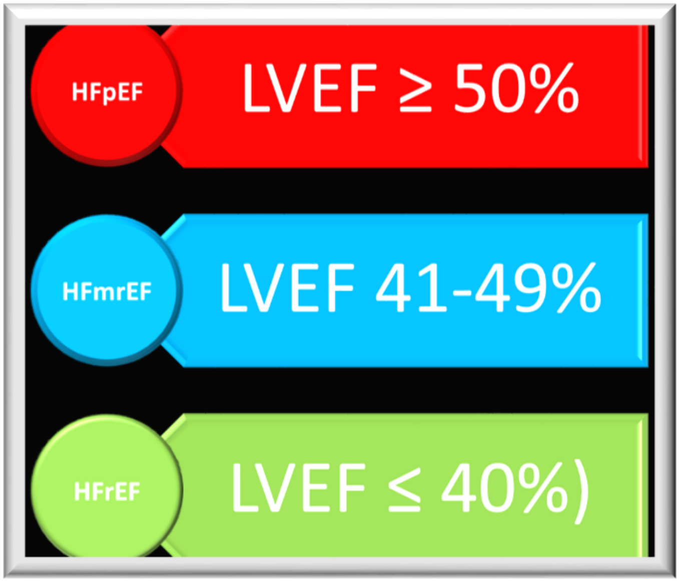

Figure 1. Classification of heart failure according to ejection fraction (EF).

The interobserver (8-21%) and intra-observer (6 to 13%) variation in the measurement of EF makes such stricter classification difficult to apply in clinical practice[7]. Hence, some guideline-forwarding agencies do not include HFmrEF class in their recommendations[8]. Furthermore, the correlation of LVEF measurement by echo with other modalities like SPECT and CMR is moderate at best. Another group has also been described as 'HF with improved or recovered EF' (HFimpEF/HFrecEF), which comprises of subjects with initial EF < 40% showing ≥ 10% improvement overtime, with follow-up EF > 40%.[9] About 10-40% of HF patients show this favorable change.

Epidemiology

The prevalence of HF varies from 1-2% in the general population, estimated to be 1.5 to 1.9% in US and Canada and 1-2% in Europe[10,11]. In East Asian countries, prevalence has been reported to be 1-3% whereas in South Asia it is 1.5-4.6% (robust data is lacking).[12,13] In China, reported prevalence is 1.36%.[14]

Echo-guided studies have shown a prevalence of 4.2% as registries include only established cases.[15] The European long-term registry of HF mentions the phenotypic prevalence as: HFpEF-60%, HFmrEF-24%, and HFrEF-16%. HFpEF is more commonly seen in females and elderly.[16] Prevalence increases with age being <1% below 55 years and > 10 % above 70 years of age.[17]

Prevalence of different types of HF varies across practice disciplines as well. Boer AR et al, in their observational study (age 65-79 years) of three disciplines, viz high-risk communities (n = 1407), general practitioners' clinics (n=30) and cardiology clinics (n=34), noted a shift across the three types of practices from HFpEF to HFrEF with women getting less and different risk profiles for the three classes.[18]

Debate is ongoing about the status of mid-range HF (described for the first time in 2014) due to many reasons. Left ventricular EF is not a static parameter, measurement is subject to inter- and intra-observer variability and depends on many physiological parameters like loading conditions, heart rate, rhythm, associated cardiac and medical conditions.[19] However, HFmrEF is a distinct class of HF as demonstrated by clinical studies for clinical endpoints (mortality and hospitalization). It accounts for 7-25% of cases of HF in various clinical studies. With time, slightly more than one-third patients of HFmrEF remain in the same group whereas 25-30% transit to HFpEF and 25-37% to HFrEF.[20]

In the general population, incidence varies from 100 to 500 per 100,000 persons. With an expected 50% deaths five years after the diagnosis, this catastrophe takes a great toll.[21]

Prognostic Endpoints of Hf:

Clinical trials have studied many prognostic endpoints of HF, figure 2. Mortality and HF hospitalization, either individually or as a composite, have been studied mostly. Components of HF spectrum differ with regard to these endpoints.

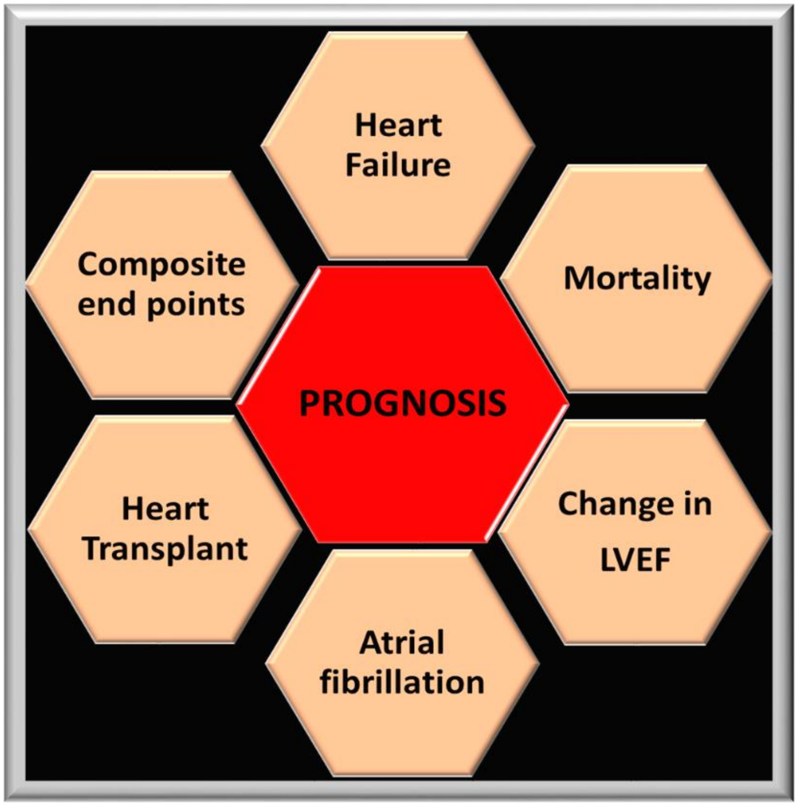

Figure 2. Prognostic endpoints of heart failure.

Mortality risk across the spectrum of HF varies across the world. An American meta-analysis and a Korean study have shown similar mortality across the three categories.[22,23] Although previous studies showed lesser mortality rates in HFpEF patients as compared to HFrEF group (MAGGIC trial and a large meta-analysis), recent European and Chinese studies documented more deaths in HFpEF, a nearly two-fold higher incidence than HFrEF.[24-28]

In a meta-analysis of 12 studies (mean FU = 31 ± 5 months), Lauritsen J et al found that all-cause mortality was significantly lower in HFmrEF than in HFrEF and HFpEF (26.8% vs. 29.5% and 31%. $p < 0.001$, and $p = 0.014$ respectively). Cardiovascular mortality was also lowest in HFmrEF (9.7% vs. 13% and 12.8%, $p < 0.001$).[29]

Three prognostic markers viz., drop in EF with shift in HF class, recurrent hospitalization, and mortality were evaluated in a large study (8632 patients FU, 10 years) by Huusko et al across the spectrum of HF (HFpEF = 4042, HFmrEF = 1468 and HFrEF = 3122). From HFmrEF and HFpEF patients, 26 and 10 % deteriorated to an HFrEF phenotype respectively. Although HFrEF patients showed significantly higher rate of first hospitalization, subsequent hospitalizations were nearly equal across the spectrum with each hospitalization increasing mortality risk by 2.2 – 2.3-fold. All-cause mortality was higher in HFpEF group whereas cardiovascular mortality was higher in HFrEF group.[30]

For mortality, HFpEF shows the highest risk whereas, for hospitalization, the three groups differ little. Trajectory change in LVEF will be elaborated subsequently.

A single echo parameter will not be able to discern the prognosis. This has been remarkably shown by Sharifov OF et al in their meta-analysis of 24 studies evaluating E/e' for assessment of left ventricular filling pressure (LVFP). None of the studies provided a good correlation (< 50% for estimation of normal or elevated LVFP) with invasively measured filling pressures (LVEDP, PCWP, LVMDP or pre-A).[31]

Echo Parameters of Prognostic Importance In Heart Failure Spectrum

In HF, from M-mode to strain analysis, numerous echo parameters have been studied for prognosis across the spectrum. Prognostic ability of these parameters would be detailed overall and in sub-types. Wherever possible, comparison of the parameters across the spectrum would be done. As the present classification of HF came into vogue in 2016, heart failure studies done previously had been using different EF cut-offs. To avoid any ambiguity, the mean EF (SD) would be mentioned.

I. CHAMBER AND VESSEL PARAMETERS

All cardiac chambers are routinely measured by M-mode and 2D-echo with structural and functional parameters derived. Many of these measured and derived parameters have prognostic importance.

A. Left atrium

Of the left atrial (LA) parameters, diameter, area, and volume (both maximum and minimum), figure 3, and functional parameters like LA expansion index and LA emptying fraction have been studied.

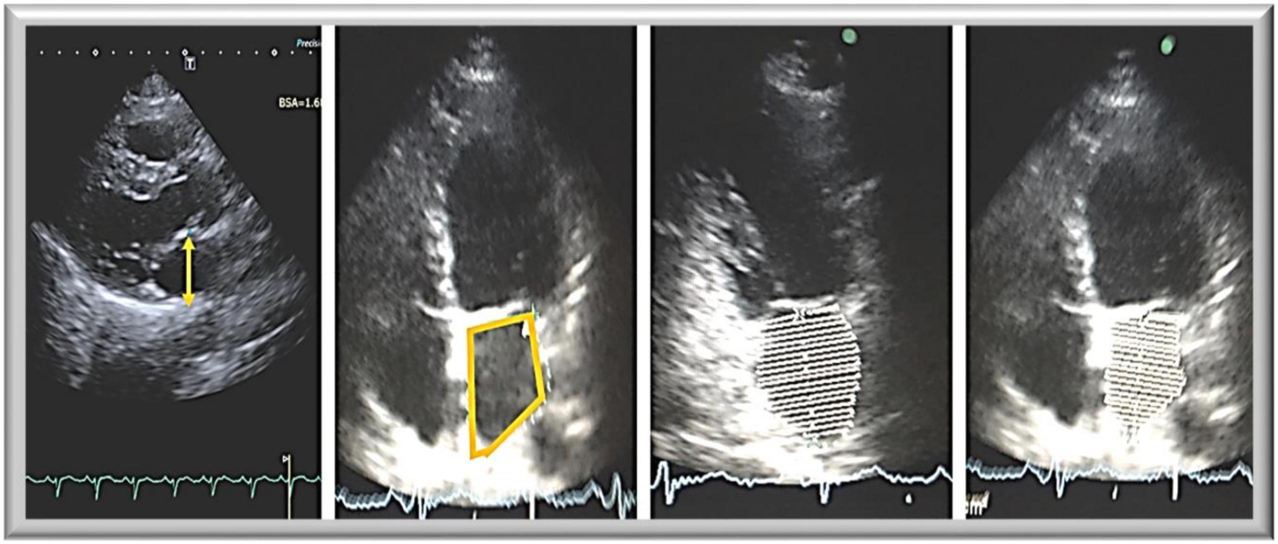

Figure 3. Echo derived left atrial parameters of prognostic importance: A-diameter, B-area, C and D-volume in apical 4 chamber view.

Left atrial diameter (LAD), a simple echo measurement studied in 368 patients of HF, (EF= 32.3±13.1%, FU 2 years) showed significant prognosis as compared to other echo measures (LVEDD, LVESD, mitral regurgitation, and diastolic dysfunction). A cut point of $25mm/m^2$ showed significantly higher mortality (10.9% vs 30.1%, p=0.001).[32] Reduction in LAD during treatment of HF also showed prognostic importance in a study of 673 patients (FU = 180 days) with EF= 46 ± 15.7 %. Endpoints reached in reduction group were significantly better than in non-reduction group (13.3% vs 22.2%, p=0.002) and this remained significant even after adjusting fifteen confounders. No significant difference was noted across the spectrum of HF.[33]

Rossi A et al, in 1157 patients (a meta-analysis of 18 trials- MeRGE trial) of HFrEF, found LA area to have prognostic importance for HF hospitalization and mortality (HR 1.03 per cm^2, p <0.0001). This association was independent of NYHA functional class, LVEF or filling pattern and became more significant when LA area was indexed.[34]

The left atrial volume index (LAVI) has prognostic value regarding endpoints as demonstrated by Tamura H in 166 HF patients (all three groups). Risk increased with increasing LAVI (HR 1.427; p < .05) and the group with LAVI >53.3 mL/m^2 showed the highest event rates. Interestingly, EF didn't show significant risk and LAVI also outperformed E/e' as a prognostic marker.[35]

Parameters of LA differ in groups of HF as shown by Kanagala P et al in 234 HF patients (HFpEF = 140; HFrEF =46; control = 48) with a median FU of 1446 days. Although differences were not noted in primary and secondary endpoints, LAVI was non-significantly higher in HFrEF group, and LA emptying fraction was lower in the same group. E/E' was significantly higher in HFrEF group.[36]

Left atrial volume is usually measured at its maximum (LAVImax) extent, but LA minimum volume (LAVImin) has shown higher prognostic value than LAVImax. Shin SH et al, in 347 patients of HFpEF (derived from a cohort of TOPCAT trial), measured LAVImin by strain analysis. For a primary composite endpoint (mortality plus heart failure and non-fatal cardiac arrest), LAVImin was associated with greater risk (HR, 1.35; 95% CI, 1.12–1.61) and also for secondary endpoint (HF hospitalization) (HR, 1.42; 95% CI, 1.17–1.71), being superior to LAVImax (p = 0.032).[37] Comparative prognostic significance of LAVImin as compared to LAVImax has also been demonstrated for the onset of first atrial fibrillation/flutter in a cohort of 547 patients on multivariate analysis. In this analysis, LAVImin remained significant (p = 0.02) as compared to LAVImax (p=0.79).[38]

Functional parameters of LA, like LA emptying fraction (LAEF), have shown prognostic value, especially in HFrEF patients. This has been demonstrated by Modin D et al in 818 HFrEF patients on a median FU of 3.3 years for the endpoint of mortality. Only LAEF (HR: 1.11, p< 0.033 per 5% decrease) remained significant for the endpoint on uni- and multivariate analysis.[39]

Left atrial expansion index (LAEI), another parameter of LA function, has shown significantly greater prognostic importance as compared to LAVI. Hsiao SH, in 1735 patients of HFrEF (median FU 2.7 years), found that as compared to the highest quartile of LAEI, the lowest quartile had a 3.1-fold and 17.8-fold higher hazard of HF events and all-cause mortality respectively. This finding was more significant than conventional parameters.[40]

In patients of HFrEF and HFmrEF, improvement in LV function shows good prognosis. In this regard, reverse remodeling of left atrium is also of prognostic importance. Shiba M et al, in a registry study of HF patients, assessed echo parameters at index hospitalization and 6 months after discharge with subsequent FU of 210 days for the composite endpoint of death or HF re-hospitalization. In the two groups of HF, 227 patients showed a recovered EF whereas 170 did not. The endpoint was significantly lower in HFrecEF group (8.9% versus 23.4%, log-rank p= 0.0002). Left atrial reverse remodeling (> 5% diameter change) showed lesser primary endpoint in HFrecEF group (4.7% versus 18.0%; p= 0.01), but not in non-HFrecEF group (24.4% versus 22.6%, p= 0.28).[41]

Left atrial size has prognostic importance regarding success of cardiac resynchronization therapy. Smaller LA size foretells greater response.[42,43]

B. <u>Left ventricle (LV)</u>

Of the LV measurement dimensions, mass and EF estimation are prognostically relevant, figures 4 A and B. Left ventricular end diastolic dimension (LVEDD) in HF patients is associated with prognosis. Pereira J et al, in a study of 308 HF patients (with EF < 50%), assessed for EF recovery (full > 50% EF attained, and partial EF improved but remained <50%). LVEDD < 60 mm was found to be an independent predictor of recovery (OR: 3.12, 95% CI 1.56 -6.25).[44] Left ventricular mass in HF patients has prognostic significance as demonstrated by Markus MRP et al in 587 patients. Each 50 g/m increment in LV mass has a relative risk of 1.22 for death.[45] Higher LV mass index and low relative wall thickness are significantly associated with mortality (log-rank 23.92; P < .0001) as demonstrated by Dini FL in 536 patients of HF with EF < 50%.[46]

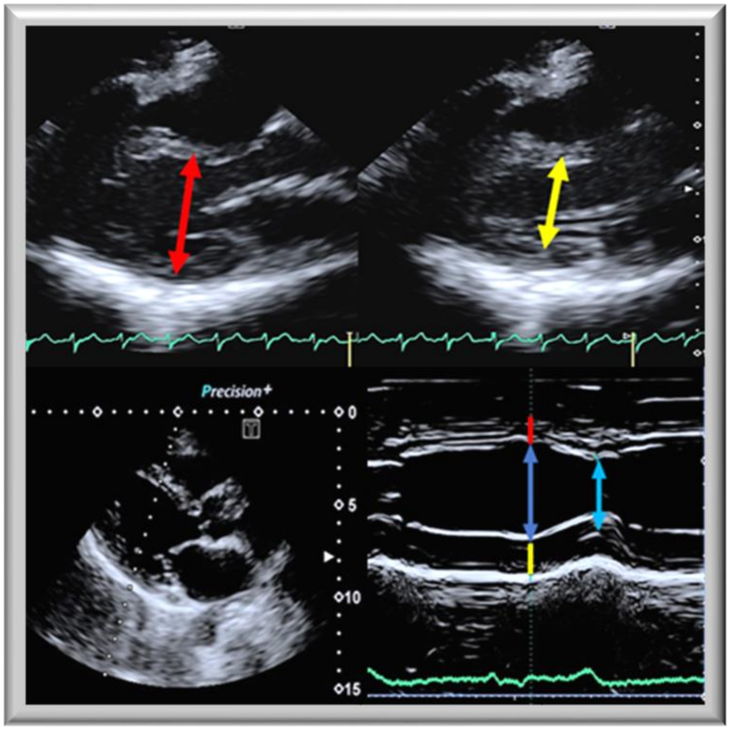

Figure 4A. Left ventricular parameters of prognostic significance in HF, upper panel 2D measurement of LV diastolic (red arrow) and systolic dimension (yellow arrow), lower panel 2D directed measurement of LV for mass estimation

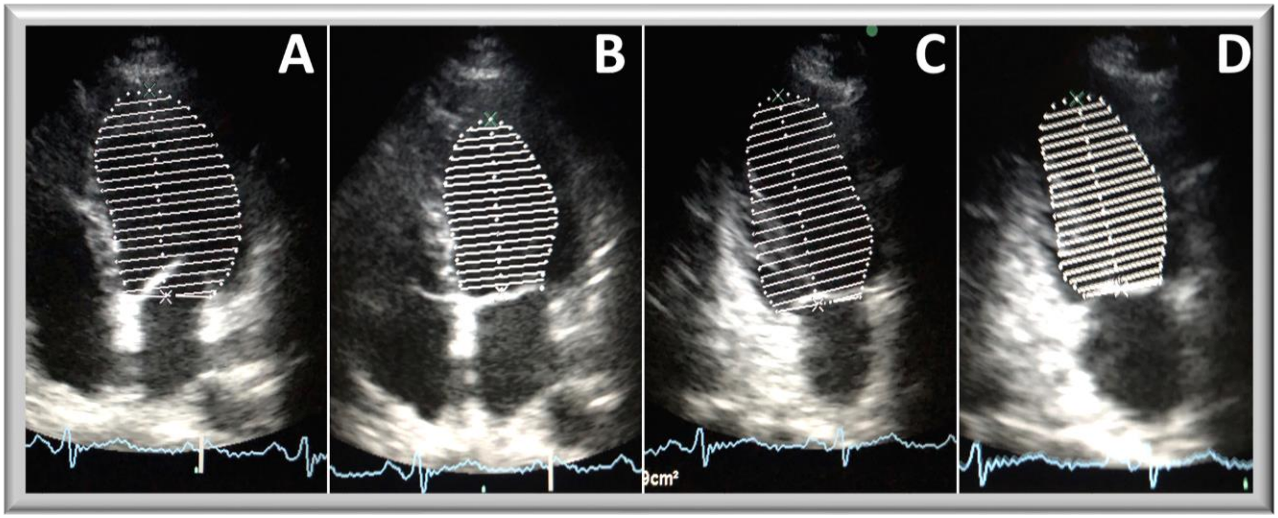

Figure 4B. LVEF estimation by Bi-plane Simpson's method. A and B apical 4 chamber views, C and D apical 2 chamber views.

Trajectory of LVEF as a prognostic marker

Change in LVEF with therapy has been noted on FU and the trajectory or direction of change has shown prognostic importance across the spectrum of HF. From a large registry of 4942 patients (Swedish heart failure registry), the change in class of HF with time was evaluated by analyzing echo at two-point times at least 6 months apart across the spectrum. The percentage of patient movement (trajectory of LVEF change) is as shown in figure 5.[47]

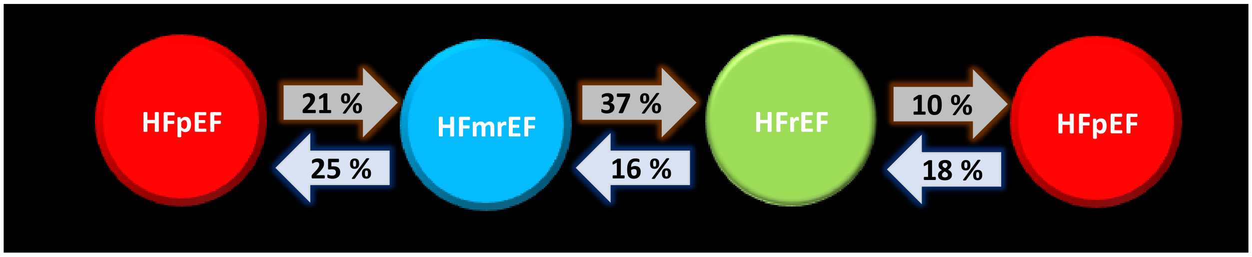

Figure 5. Trajectory change of HF class.

Prognostic improvement is noted only in cases who normalize their EF. Albert J et al, in a study of 633 patients of acute HF (categorized into three groups as per classification of HF), found that 61.2% patients with EF 30-40% improved to mid-range or normal EF at 6 months of FU whereas those with EF <30%, nearly 41.6% patients improved their class of EF. Further FU till 18 months did not show much change in those with normalized EF but patients with midrange and reduced EF categories continue to improve significantly ($p = 0.002$ and $p < .001$ for HFmrEF and HFrEF respectively). This improvement in EF is mirrored in endpoints (mortality risk and composites of death or HF hospitalizations and death plus HF hospitalizations), significant only in patients who normalized their EF at 6 or 18-month FU and not in those who remained in mid-range EF at these points in time. Due to these different trajectories pursued by patients presenting with acute HF they recommended a 6 monthly echo-based FU and continuation of GDMT till the end of life in such patients.[48]

Rastogi A et al studied 168 patients with HFmrEF (at the time of entry into study). From electronic data records, the status of these patients was searched, and trajectory determined. Seventy-three percent of patients moved to HF improved EF group whereas 17% moved to the deteriorated group and 10% remained in the same group. Left ventricular end systolic dimension (LVESD) was lower ($p = 0.022$) in deteriorated group with greater diastolic dysfunction as compared to the improved group. The improved EF group showed better composite endpoint ($p < 0.001$).[49]

Zhang X, in a retrospective study of 1160 patients of HFrEF, found that subjects showing an improvement in EF > 20% (HF with recovered EF) have better prognosis regarding mortality ($p = 0.0184$) till 2 years (not later than that) and HF re-hospitalization (p = 0.0413) till 4 years. Of the echocardiographic variables, LV end diastolic diameter, IVS thickness, and RV diameter were the only parameters showing significant differences in the two groups. This emphasizes the need of EF re-estimation in HFrEF as this entity comprises of different phenotypes.[50]

Similar findings were noted by Ghimire A et al in 3124 patients (with HFrEF) who improved EF on follow-up (and moved to HF with recovered EF category) and had lower mortality and morbidity.[51] Recovery of EF can be gauged by certain clinical and echo parameters. Shah MA et al studied eight echo parameters in a cohort of 67 patients of HFrEF at the time of admission and after a mean interval of 10.5 months. Left ventricular volumes (systolic and diastolic), LA volume, RV, inferior vena caval enlargement, tricuspid annular plane systolic excursion (TAPSE), and deceleration time were associated with non-improvement in EF in uni-variate analysis, whereas on multi-variate analysis, smaller LV and LA volumes along with better TAPSE were associated with recovered EF.[52]

C. Right ventricle (RV)

Right ventricular diameter, area, and wall thickness have also shown to predict outcome in HFpEF.[53]

D. Right atrium (RA)

Of RA parameters, volume index has been studied by single plane Simpson's method with increasing measurements showing higher mortality rates.

E. Inferior vena cava (IVC)

Size of inferior vena cava and its collapsibility index are employed to estimate mean right atrial pressure (mRAP). In evaluation of left ventricular filling pressure (LVFP) by echo, three parameters are considered viz, LAVI, TRV and E/e'. LVFP status is defined by the normality or otherwise majority of parameters. However, at times (23% of cases), only two parameters are obtainable, and if the results are discrepant, the condition is labelled 'indeterminate'. In such a situation, Mele D et al, in 465 patients (FU = 2.5 years, IQR 1.8-3.2), found that estimation of mRAP can reclassify such subjects to high or normal pressure groups and has prognostic importance. Amongst the subjects showing mRAP higher than 8 mmHg, the endpoints were more frequent (HR, 2.72; 95% CI, 1.25–5.9; p = .012) and interestingly this happened only in the group of indeterminate LVFP and not seen in the other two groups. The association was equal for HFrEF or HFpEF. Thus, estimation of mRAP from IVC provides significant information for re-classification of LVFP group and prognosis.[54]

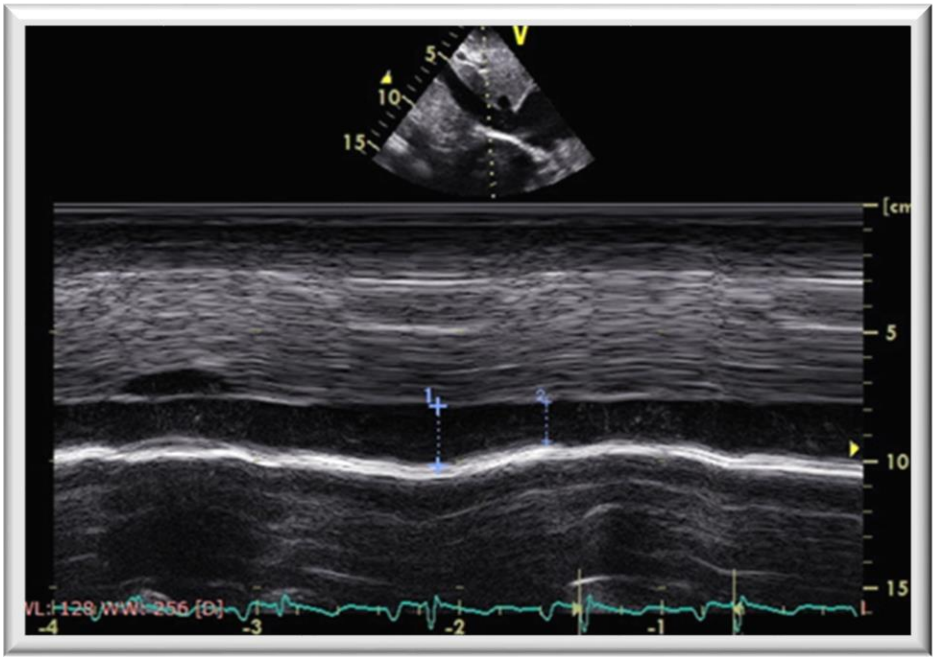

Figure 6: Inferior vena cava size, a prognostic marker in HF.

Enlargement of inferior vena cava (IVC) could be a sign of congestion, and of HF, figure 6, with size correlating with prognosis. In 568 patients of HF (LVEF = 42 ± 13%), Pellicori et al, on a FU of 567 (IQR 413 to 736) days, found the highest tertile of IVC size correlated with the endpoints of rehospitalization and death (40% risk). Inferior vena cava diameter showed the highest AUC (0.76 with a 95% CI 0.71 to 0.81; chi-square 78.44; p < 0.001) as compared to other echo parameters (LAVI, TAPSE, TR gradient, and LV strain) for endpoints, irrespective of LVEF.[55]

II. MITRAL IN-FLOW AND DIASTOLIC FUNCTION PARAMETERS

Mitral valve inflow assessment provides information for diastolic function and also shows certain other features of prognostic importance.

Tei index is a measure of systolic and diastolic function of ventricle. It is the sum of iso-volumic contraction and relaxation time expressed as a ratio of ejection time. Harjai KJ et al, in 60 patients of HFrEF, showed that Tei index > 1.14 has strong association (more than fivefold) with outcomes (mortality or heart transplant) over a FU of 2 years. This was matched only by the severity of mitral regurgitation and independent of many variables. Mortality curves separated early in their course in the lower and higher quartiles (OR 5.3 95% CI 1.9-14.9 p = .0018).[56] In a similar study, Acil T et al demonstrated in 132 HF patients with mean EF= 31 ± 10% followed up for 224 ± 123 days tissue doppler parameters of E/e' (> 12.5) and Tei index (> 0.9) stood out as the best prognostic indicators.[57]

L wave recorded by PW doppler study during diastasis, figure 7, has shown prognostic importance in patients with LVH and preserved EF. In 177 patients of LVH, L wave was associated with incident HF (HR 4.7, p = .011), and remained significant (HR 4.2, P = .026) after adjustment for CV risk factors.[58]

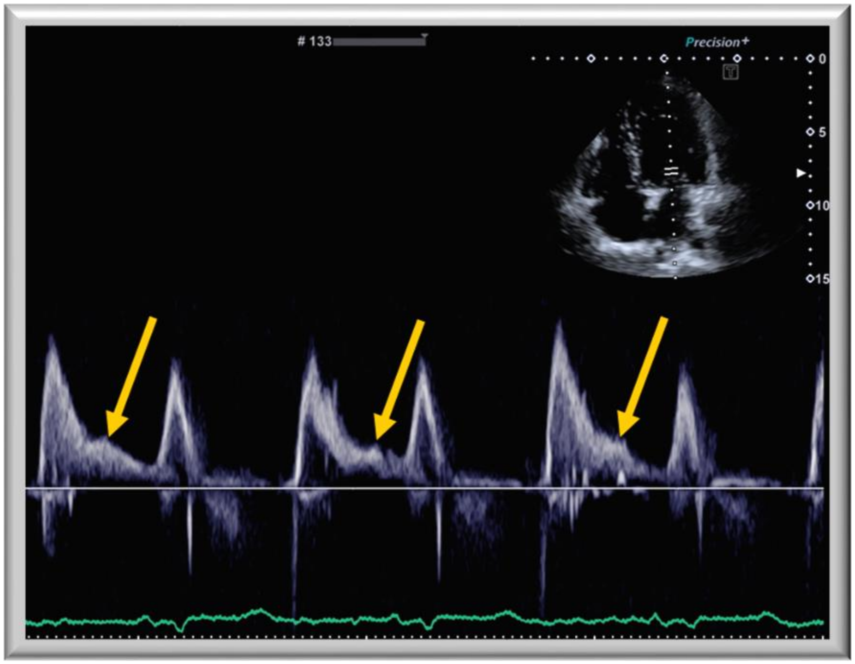

Figure 7. L wave (marked by yellow arrows)

For diagnosis of diastolic dysfunction (DD), numerous parameters are utilized, figure 8. Decisions are made by using a combination of these parameters. These include LAVI, mitral in-flow parameters (E-wave, A-wave, E/A ratio, deceleration time), tissue doppler parameters (e'-wave, E/e' ratio), pulmonary vein flow parameters (S/D ratio, A-wave duration minus Ar-wave duration), TR velocity and recently left atrial strain parameters. The prognostic abilities of these parameters differ.

Xie GY et al divided 100 HF patients with EF < 40% (HFrEF) on the basis of E/A ratio and deceleration time (DT) into two groups: non-restrictive (E/A <2 and DT >140 msec) and restrictive (E/A >2 and DT < 140 msec). Restrictive group showed significantly higher mortality at 1 year (19% vs. 5%, p < 0.05) and at 2 years (51% vs. 5%, p < 0.01). This association of restrictive pattern with mortality outscored other clinical parameters and all echo variables.[59]

Liu D et al assessed a combination of 3 parameters viz, LAVI, E/e', and pulmonary artery systolic pressure (PASP) to define the 3 grades of DD (mild, moderate, and severe) and compare the prognostic importance of this model in HFmrEF and HFrEF (in sinus rhythm and AF patients). They studied 2018 patients (HFmrEF = 951, and HFrEF = 1067) for a median FU of 24 months for primary and secondary endpoints of all-cause and cardio-vascular mortality. Both endpoints were significantly higher in HFrEF with severe DD (all-cause mortality HR = 1.347, p = 0.015 and CV mortality HR = 1.508, p = 0.007), whereas severe DD showed significant prognosis only for all-cause mortality (HR = 1.358, p = 0.046) and not for CV mortality (HR = 1.155, p = 0.469) in HFmrEF.[60]

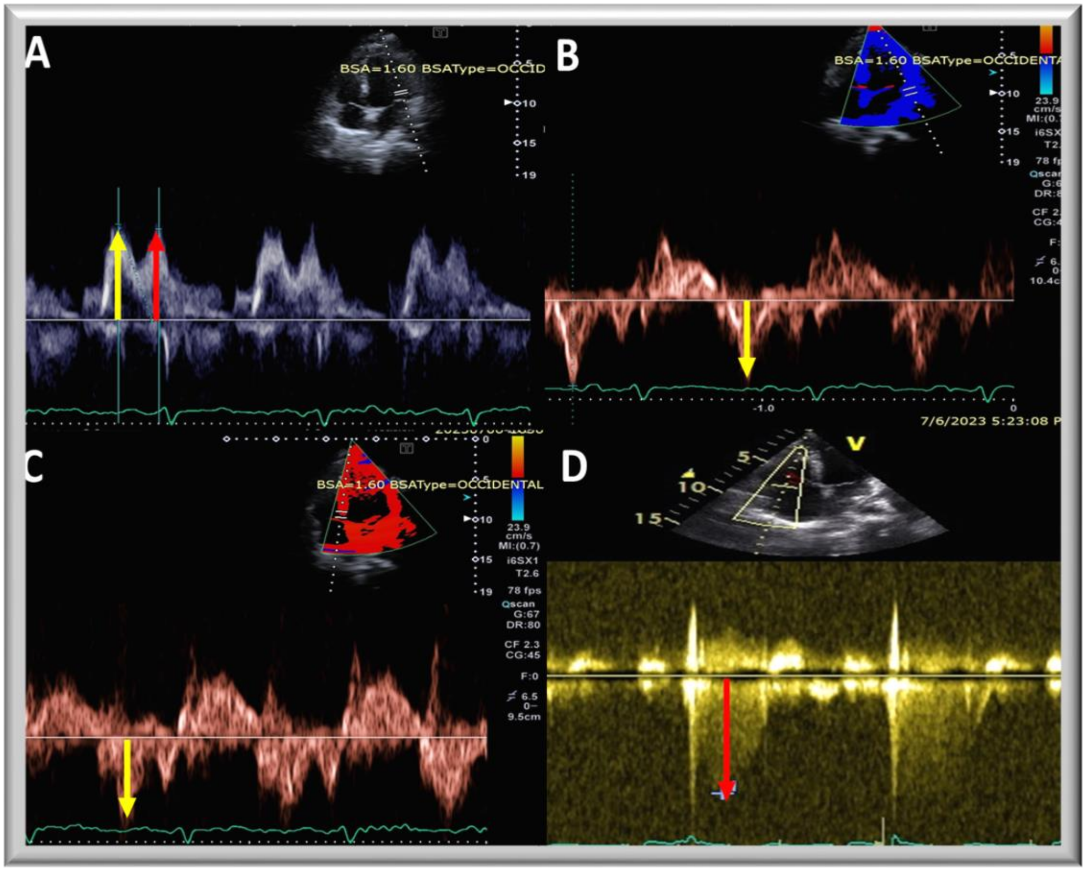

Figure 8. Diastolic function parameters on echocardiography. A- mitral E and A wave, B and C- lateral wall and septal e' and D- TR velocity.

Zamfirescu et al, in 91 patients (first HF admissions) with HFpEF, found that E/e' (cutoff point 13.8) has prognostic value for HF re-admissions at 6-months but is not associated with mortality. This ratio supersedes other echo parameters in this regard showing the best values for AUC = 0.693, sensitivity = 78.6%, specificity = 55%, $p < 0.004$.[61]

Of the five parameters used for diastolic function assessment viz, LVMI, LAVI, TRV, e' and E/e' in a meta-analysis of 27 studies noting correlation of these parameters with invasively determined filling pressure (nine studies) and prognostic assessment (eighteen studies), only E/e' showed prognostic importance in HFpEF for mortality and HF hospitalization (HR 1.05, 95% CI: 1.03-1.06 per unit increase in E/e') for the combined outcome.[62] E/e' has good correlation in HFpEF but only moderate in HFrEF with invasively determined LVFP.

III. RIGHT VENTRICLE PARAMETERS

Different parameters of RV function have been assessed for prognosis across HF spectrum, figure 9. These include RV fractional area change (RV FAC), tricuspid regurgitation (TR), TDI parameters (isovolumic acceleration time, S' velocity, early diastolic velocity, and Tei index) and RV-PA uncoupling by TAPSE/TR velocity ratio.

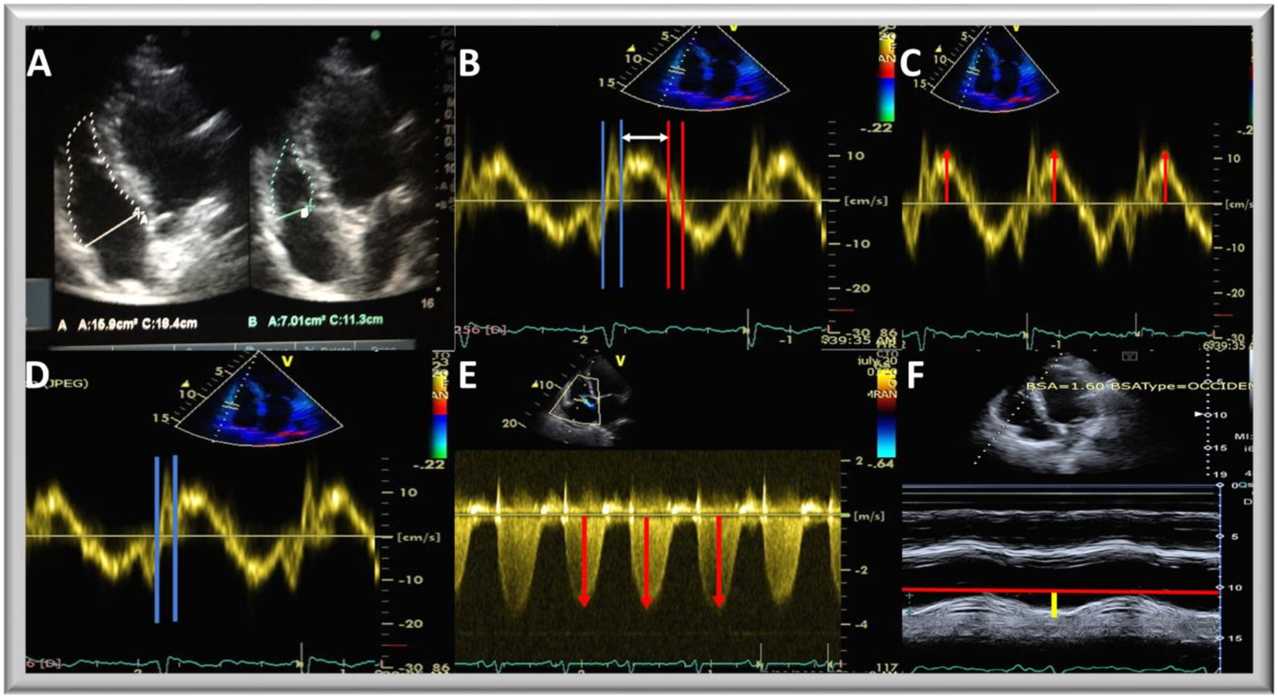

Figure 9. RV function parameters: A-RV FAC. B-Tei index, C- S' velocity, D- Iso-volumic acceleration time, E- TR velocity and F- TAPSE.

In HFpEF, function of right ventricle deteriorates more rapidly than left. This has been aptly demonstrated by Obokata M et al in 271 subjects of HFpEF by longitudinal studies 6 months apart with median FU of 4 Years after the second exam. Right ventricular fractional area change (decrease 10%) and RV diastolic area (increase 21%) were noted, both p <.001. Tricuspid regurgitaion incidence increased by 45%. In an unadjusted Cox model, RV dysfunction was associated with an 80% increased risk of mortality, (HR 1.82, 95% CI 1.01–3.19, p= 0.04).[63] Reduction in function of RV supersedes the corresponding reduction in LV function.

Systolic BP (SBP) at admission has shown prognostic importance in patients of HF. Parameters for difference in prognosis have been assessed so that HFpEF patients can be pheno-typed at first admission. Nakagawa A et al studied 1008 HFpEF patients (stratified according to BP at admission; reduced < 100 mmHg, preserved 100-140 mmHg and elevated > 140 mmHg) with a FU of 374 ± 360 days for the parameters showing prognostic importance with primary endpoint a composite of mortality and HF re-admission and secondarily for individual endpoints. The last group was not considered in statistical calculation due to very small number of patients (only 4). Prognostically, echo parameters differed in the two groups with left ventricular SV and TAPSE being significantly higher in elevated SBP patients, and PASP was higher and TAPSE/PASP was lower in preserved SBP patients. They found right ventricular-pulmonary artery uncoupling, a ratio of TAPSE and PASP at discharge as the only co-variate of prognostic significance in preserved SBP patients (HR 0.19, 95% CI 0.05–0.65, P = 0.0075).[64] Nagakawa A et al showed (655 HFpEF patients) even with a higher cutoff of 0.48 this parameter demonstrated prognostic value for primary endpoints (all-cause mortality, HF rehospitalization, and cerebrovascular events) HR:1.77, 95% CI, 1.34–2.32, P<0.0001 and also for secondary endpoints (all-cause death and HF rehospitalization) HR 2.75, 95% CI, 1.77–4.33, P < 0.0001.[65]

Meluzin J et al studied the prognostic power of RV parameters by TDI in 140 patients of HFrEF for endpoints of death, hospitalization for HF and heart transplant. Parameters studied were isovolumic acceleration time, systolic (S') velocity, early diastolic velocity and Tei index. An association for prognostic endpoints was noted for every parameter but the effect became more marked when cumulative effect of these parameters was studied. Combination of peak tricuspid annular systolic velocity (≤10.8 cm/s), early diastolic tricuspid annular velocity (≤8.9) cm/s and tricuspid annular acceleration during isovolumic contraction (IVA, ≤ 2.52 m/s^2) showed worst relative risk of 6.17, p < .001 for survival. The worst event-free survival was noted when, in this model, Doppler RV index (Tei index ≥1.2) was replaced for IVA (relative risk 3.62, P < .001).[66]

IV. PULMONARY ARTERY HYPERTENSION

Presence of PAH in HFpEF and HFrEF patients entails different prognostic significance as exemplified by Salamon JN et al in 650 patients (HFpEF, n=373, and HFrEF, n=277) with Type II PAH (PAP > 65mmHg). Five-year mortality was higher in HFpEF-PH group (HR: 1.72, p <0.012) but HF hospitalization rates were higher in HFrEF-PH group ((28.6% vs 15% p=0.003), more so during the first year (9.1% vs 1.7%, p=0.005).[67]

Zafrir B et al demonstrated the differential prognostic power of severe PAH across the spectrum of HF patients. They studied 372 HF patients (HFrEF; n = 159, HFmrEF; n = 50, HFpEF; n = 163) for a mortality follow-up of 24 months. On univariate and multivariate analysis, severe PAH (PAP ≥ 65 mmHg) was significantly associated with mortality only in HFpEF group and not with the other two groups (HR 2.99, 95%CI 1.29-6.91, p = 0.010).[68]

V. VALVE REGURGITATION PARAMETERS:

Regurgitation of mitral and tricuspid valves in HF should be taken seriously as both of them have demonstrated prognostic significance across the spectrum.

Functional mitral regurgitation (FMR) is commonly seen in HFrEF. Thirty percent of HF patients show moderate to severe FMR. Severe FMR is associated with a worse prognosis as demonstrated by Rossi A in a large prospective study of 1256 patients with HFrEF (HR=2.0, 95% CI 1.5 to 2.6; p<0.0001).[69]
In a recent study, significant MR at rest was noted in 15% of patients with HFpEF, 27% in HFmrEF, and 47% with HFrEF. Importantly, exercise elicited worsening of FMR, was noted in 35, 41, and 60% of HFpEF, HFmrEF, and HFrEF patients respectively. Presence of secondary MR increases mortality across all groups of HF.[70]

Presence of FMR perse may not be predictive of prognosis if NYHA class of patients is not considered. Interestingly, prognostic value of FMR has been noted in cases with less severe FC (NYHA class I-II). This has been demonstrated by Bursi F et al in 469 patients with FMR and EF below 50%. On a mean FU of 5.1 ± 3.5 years, only patients with better NYHA class (I-II) showed prognostic value of FMR on multivariate analysis, not seen in patients with worse NYHA class (III-IV).[71]

Goliasch G et al also noted (576 HFrEF patients) that severity of FMR is significant prognostically (HF hospitalization and mortality) only in intermediate cases of NYHA i.e., classes II (p-0.03) and III (p=0.008) and not with classes I (p=0.73) and IV (p=o.71). This association was also seen in moderately reduced LVEF (p=0.002) and not with severe reduction in EF (p=0.1). Other parameters showing prognostic significance were smaller LV size (males < 69mm and < 62 mm in females), smaller LA size (< 64 mm) and non-severe TR.[72]

Prognostic value of FMR differs in HFpEF and HFrEF. Kajimoto K et al in ATTEND (Acute Decompensated Heart Failure Syndromes registry) study (3357 patients, mean FU = 530 days) demonstrated that whereas FMR is significant across all grades of severity in HFpEF (p=0.001 and 0.009 for mild and moderate/severe MR respectively) but not in mild cases in HFrEF (P = 0.510) although significant in moderate/severe cases (p=0.015).[73]

In HFpEF, mild to moderate FMR is ignored as innocent bystanders considered to be due to LV factors (tethering of chordae) although it is usually not much enlarged. Tamargo M et al, in 280 patients of HFpEF with and without FMR, found that presence of mild to moderate MR is due to atrial myopathy evidenced by enlarged mitral valve annulus size, LA reverse remodeling and reduced LA strains. These changes correlated strongly with LA dilatation (r = 0.63, P < .0001) and only weekly with LV remodeling (r=0.37). Prognostically, on a median FU of 5.4 years (IQR: 3.7–7.5), LA dysfunction was highly significant for the composite and individual outcome of hospitalizations (HR 3.93, 95% CI 1.55–10.0; p =0.004) and deaths (HR 1.79, 95% CI 1.02–3.15; p =0.04).[74] Presence of even such degrees of MR shouldn't be ignored.

Many features of TR (velocity, regurgitant area, severity etc.) have prognostic value. Shahim A et al, in a 10-year long (median FU 5.44 years) study of 536 patients with HFpEF, found that amongst echocardiographic parameters, only TR velocity had a predictive value (HR 1.87 95% CI 1.34–2.62; p < 0.001) for a combined endpoint of mortality and HF hospitalization in multivariate analysis, as a long-term prognostic parameter. E/e' showed such predictive value in univariate analysis only.[75]

Topilsky Y et al found an association of effective regurgitant orifice area (EROA) of TR with clinical endpoints. In 291 patients with EF <50%, EROA ≥0.4 cm^2 was associated with increased mortality (HR: 1.8, p = 0.009) and cardiac events (HR: 2.2, p = 0.02), both outcomes after comprehensive adjustment.[76]

In 11507 patients (mean EF =36±10%), severity of TR (trivial=33%, mild=32%, moderate=17%, and severe=6%) was correlated with mortality (median FU =4.02 years) by Benfari G et al. Higher grade of TR was associated with increasing mortality and the 5-year survival rate was trivial =68±1%, mild =58±2%, moderate =45±2%, and severe =34±4%.[77]

Zeitoun DM et al, in 435 679 patients, studied the association of baseline (at the time of inclusion) or developing TR (during a follow-up of 1.5 years) with mortality. At baseline 10.1%, 5.1% and 1.4% showed mild, moderate, and severe TR respectively, whereas 12.1%, 5.1% and 1.1% of the subjects developed the three grades of TR during follow-up. Presence of TR reduced survival for all grades in both the groups with significant HRs, and this was noted in all types of HF across the spectrum.[78] This demonstrates the significance of TR as an isolated finding for mortality in HF, more so with increasing grade.

Simple parameters of TR have also shown prognostic value as demonstrated by Xu B et al in 45 patients with DCM for the endpoints of mortality or transplant. They measured the systolic and diastolic durations of TR, and found that S/D ratio, (cutoff value >1.2) was higher in patients with events (1.8±0.8 vs 1.2±0.5, $p = 0.008$).[79]

VI. COMBINED PARAMETERS:

Compared to individual echo parameters, combination shows greater prognostic power. Various combinations have been studied in clinical trials. LV diastolic dimension, diastolic function, filling pressure, cardiac output, valvular regurgitation (tricuspid or mitral), pulmonary artery systolic pressure and strain have been evaluated by echocardiography in different combinations.

Huttin O et al devised (515 patients with HFpEF, with a median FU of 361 days) an echo score, in MEtabolic Road to DIAstolic Heart Failure (MEDIA) trial, based on four variables showing greater prognostic value over clinical variables alone and combined with NT Pro-BNP levels by net reclassification index (NRI) and C-statistic. The four parameters assessed were S' (< 7 cm/s), E/e' (>9), PASP (>40 mmHg) and respiratory variation in IVC size (<50%). At 1 year, patients with echo score ≥3 and those with score ≤1, the risk of endpoints was > 35% vs <10% of patients. The NRI (33.8%, $p < 0.0001$) and C-index (5.3% $P = 0.015$) improved significantly when score was added to biochemical and clinical markers. Echo MEDIA score when applied to KaRen cohort (also with HFpEF) showed similar improvement in the two statistics, NRI (22.3%, $p = 0.014$) and C-index (4.0%, $p = 0.029$). [80]

Prognostication of HFrEF patients on hemodynamic variables defined by echocardiography not only facilitated this goal but also helped in selecting newer treatment strategies [Angiotensin- Neprisylin inhibitors (ARNI)] and also defined the dosages. A cohort of 717 ambulatory HFrEF subjects were followed for composite of death and HF rehospitalization (median 12.3 months). Based on cardiac index and LV filling pressure, four groups were defined, profile-A normal-flow and normal-pressure, profile-B low-flow, normal pressure, profile-C normal flow, high-pressure and profile-D low-flow, high-pressure. Events escalated progressively from profile -A to D (12.0%, 16.4%, 22.9%, and 35.2%, respectively, $p < 0.0001$). Dose of ARNI was significantly related to group (Spearman's rho = -0.12, $p = 0.0009$), with progressive decrease noted from profile A to D. In group D, low dose was most prevalent ($p < 0.0009$) and highest rate of withdrawals ($P < 0.0001$).[81] Thus, echo determined variables not only show prognostic importance but also give clue for most effective drug dose in various hemodynamic phenotypes of HFrEF.

Echo signs of congestion in HFpEF patients indicate prognostic value in patients with sinus rhythm and atrial fibrillation (AF). Abe H et al studied 505 HFpEF patients (median FU 373 days) for three signs of congestion viz, E/e', TR gradient and IVC size, dividing the patients into three grades as the number of signs increase. Grade C patients showed the highest HR for endpoint of HF hospitalizations and deaths as compared to the other two groups (log rank $p<.0001$). Adding congestion to a base model (age, gender, NYHA class and NT pro BNP), the prognostic prediction ability increased in both groups.[82]

Various parameters of right ventricular function are associated with prognosis in both types of HF i.e., HFpEF and HFrEF. Bosch L et al, in a study of 657 patients with a median follow-up of 715 days, assessed TAPSE/PASP, and RV longitudinal strain (RVLS)/PASP for composite end points of all-time deaths and heart failure hospitalizations. Both ratios were related to the endpoint (TAPSE/PASP HR: 0.33; 95% CI 0.14–0.74 and RVLS/PASP HR 3.09; 95% CI 1.52–6.26) with no difference between the two groups.[83]

Chen JS et al studied multiple echo parameters as an index called "heart failure echocardiography index" (HFEI) in HF patients (n=489) of three categories, HFpEF (n=148), HFmrEF (n=170) and HFrEF (n=171) for one-year mortality. Parameters assessed were: PASP, LVEF or wall motion abnormality, LV diastolic function, atrioventricular remodeling, and valvular regurgitation or stenosis. A value of 3.5 was calculated to show adverse events with AUC= 0.712 with a sensitivity of 64% and a specificity of 75%. A higher score was associated with adverse prognosis and the score was highest in HFrEF (5.54 ± 1.20), intermediate for HFmrEF (4.12 ± 1.52) and lowest for HFpEF (2.45 ± 1.16) patients. When the scoring was combined with NT-ProBNP levels, the prognostic yield enhanced further.[84]

Although used for the diagnosis of HFpEF, H2FPEF score [incorporating two echo parameters (E/e' > 9 and PASP > 35 mmHg)], has shown prognostic significance also as demonstrated by Sun Yuxi et al in 479 patients as an independent predictor of mortality (AUC 0.67, 95%CI: 0.6-0.73, p <0.0001) and re-hospitalization (AUC 0.59, 95%CI: 0.54-0.65, p< 0.001).[85] The score has shown prognostic importance with regard to readmission as well, in other studies.

In the echocardiographic sub-study of TOPCAT (Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist) trial, 935 patients of HFpEF were assessed for a median follow-up of 2.9 years for composite endpoint of deaths, hospitalizations and aborted cardiac arrests. LVH, E/e', and higher tricuspid regurgitation velocity were significantly associated with endpoint.[86]

VII. EPICARDIAL FAT

Epicardial adiposity around the right ventricle increases RV filling pressures by virtue of pressure effects, infiltration, and secretion of pro-inflammatory cytokines, significantly lowering exercise capacity. This detrimental effect is not seen in left-sided filling pressures.[87] Adverse prognosis of Epicardial adiposity in HFmrEF and HFpEF patients has also been demonstrated by CMR.[88]

VIII. STRAIN PARAMETERS

Strain is a relatively new method of myocardial performance assessment. The significance of strain analysis lies in detection of myocardial dysfunction much before a decline in EF. For left ventricle, global longitudinal strain (GLS), for atria, peak atrial longitudinal strain (PALS) and for right ventricle, free wall strain (RVFWS) are employed, figure 10.

Retrospectively 468 patients of HF were assessed for the endpoint of death or readmission 30 days after discharge in three models. Model 1 included clinical parameters, model 2 consisted of clinical and baseline echocardiographic parameters and model 3 comprised of the previous two groups along with GLS. Model 3 showed incremental prognostic importance for endpoints (HR 1.16; 95% CI 1.07–1.26; P < .01). GLS ≤ 10.5 and GCS ≤ 14.9% (entire cohort) were associated with endpoints. GLS ≤ 14.8 (in HFpEF cases) and ≤ 7.2 (in HFrEF cases) discriminated the two groups.[89]

Park JJ et al, in a longitudinal study of 2104 patients (acute HF), showed that subjects categorized as HFpEF (974 patients) or HFrEF (1130 patients) behaved as different phenotypes on a median follow-up of 1304 days. Left ventricular strain can predict to which phenotype a patient will end (declined or improved). In HFpEF, 10.5% declined their EF whereas, of HFrEF subjects, 45.8% showed improvement. In baseline echo, LVEDD and GLS in HFpEF patients and these two along with LAD in HFrEF patients were significantly different. Multivariate analysis showed that in HFrEF, each 1% increase in GLS was associated with 10% increased odds for improved EF and, in HFpEF, 7% reduced odds for declined EF. In HFrEF with GLS above the median, the odds for improved EF were 49% P<.001, whereas, in HFpEF, GLS less than the median showed 2.12-fold increased odds for decline (p=0.008).[90]

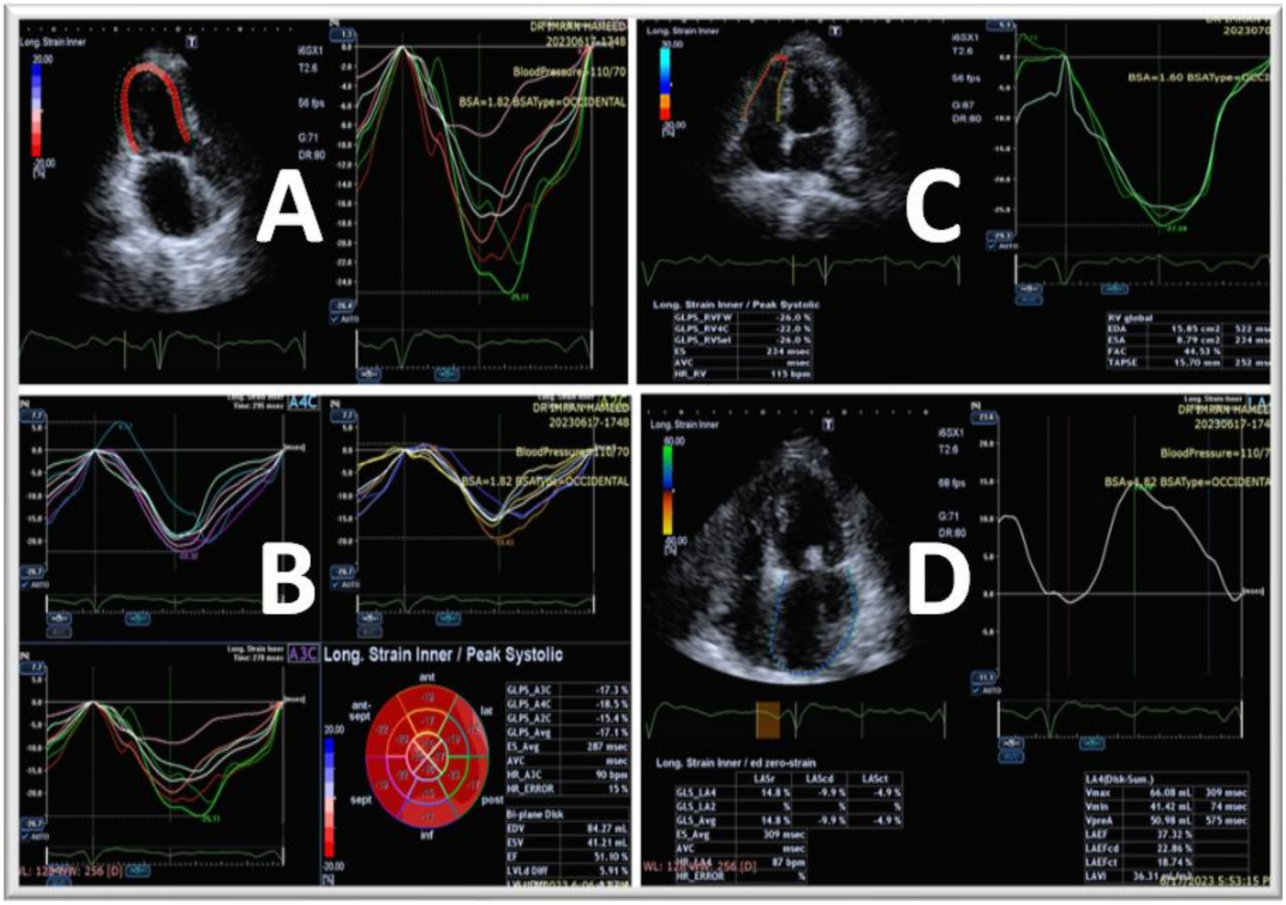

Figure 10. Strain parameters. A- Longitudinal strain 3-chamber, B- Strain graphs with Bulls's eye view, C- Right Ventricular strain and D- Left atrial strain.

Left ventricular longitudinal function is assessed by MAPSE, S'velocity, and LV GLS. Strain parameters (LV GLS at rest and exercise and LV GLSR after exercise) have shown significantly superior prognostic power than the other two. This has been documented by Gozdzik A et al in 201 HFpEF patients with a FU of 48 months (12-60) for endpoints of mortality and HF re-hospitalization. Over a baseline model of MAGGIC score, BNP and peak VO2, the addition of these strain parameters showed a significant net reclassification index (NRI = 49%, P < 0.001; NRI = 42%, P = 0.004; and NRI = 38%, P = 0.009, for GLS at rest and exercise and GLSR at exercise respectively), feature not noted for non-strain parameters.[91] Special prognostic power has been shown by GLS in HFmrEF and HFpEF subjects as LVEF loses its predictive power in these subsets of HF patients.[92]

Per 1% decrease in GLS stood out as the best prognostic indicator amongst the echo variables (LVEF, LVMI, LAVI, TAPSE, E, DT, E/A, E/e') in a cohort of HFrEF (n=1065) followed up for 40 months (HR 1.15 (95% CI: 1.04 to 1.27), p = 0.008).[93]

Left atrial strain analysis is easy to apply with good reproducibility. In a sub-study of TOPCAT trial, Angela B found significant prognostic value (for mortality and HF hospitalization) of PALS in 357 patients on a mean follow-up of 31 months.[94] Similarly, it has shown excellent prognostic value in HFrEF patients. On multivariate analysis, a study involving 286 patients, the primary outcome MACEs occurred in 34% of patients over a follow-up of 48 ± 11 months with increasing events in subjects showing worse PALS. Atrial fibrillation also occurred more frequently with worse global PALS i.e., in lowest quartile (HR, 0.94; 95% CI, 0.90–0.98; P = .01).[95] Addition of PALS to a baseline risk model (comprising of age, gender, LAV, EF, E/E' ratio, and GLS) increased the predictive value (NRI, 0.449; p=0.0009).[96]

Sanchis L et al, in 144 patients with initial diagnosis of HF, assessed the utility of LA contractile strain rate (LASRa) for endpoints of all-cause deaths or hospitalizations. Of these, 70.1% confirmed to have HF whereas rest served as controls. LASRa correlated best with events compared to LA strain (3 types), average LA strain, LV strain, and LAVI.

Patients were compared by LASRa in groups of HF vs non-HF, non-HF vs HFpEF, non-HF vs HFrEF, and HFpEF vs HFrEF. HF subjects were divided into tertiles of LASRa. Patients in the lowest tertile and those in AF had the lowest event-free survival, the difference between the two was not statistically different. Significant difference was noted in LASRa in HF vs non-HF group but not between HFpEF and HFrEF.[97]

Left atrial strain showed superiority over other echocardiographic parameters for correlation with exercise capacity. Evidence for this has been provided by Maffies C et al in 65 patients (HFpEF and HEmrEF) with regard to a peak VO2. Patients with value > 14 mL/kg/min showed significantly better LA strain values (reservoir strain, $p = 0.002$; conduit strain, $p = 0.001$; contractile strain, $p = 0.02$). LA reservoir strain added value to predict lower pVO2 independently of age, sex, BMI, rhythm, and NT-proBNP levels. Moreover, LA reservoir strain $< 22\%$ can predict pVO2 < 14 mL/kg/min with 93% sensitivity and 49% specificity (AUC 0.69, $P = 0.008$, 95% CI 0.56–0.82). No other echo parameter demonstrated such predictive ability for exercise capacity.[98]

Left atrial strain parameters have shown prognostic value in patients of HFpEF for the development of atrial fibrillation. Jazik-Zspak et al, in 103 patients (median FU = 49 months), demonstrated PALS $\leq 29.4\%$, PACS $\leq 12.7\%$, and LAVI > 34.3 ml/m^2 as discriminatory nodes for atrial fibrillation, with a 33-fold risk ($p < 0.001$) in high-risk patients.[99]

Left atrial stiffness increases pulmonary vascular resistance and pressure and has prognostic importance. Non-invasively determined LA stiffness (in 215 patients with HFrEF and HFmrEF) by calculating the ratio of E/e' and PALS was the most significant parameter ($p = 0.001$), a composite of HF and death compared to E/e', mitral restrictive filling pattern, and PASP on multivariate analysis.[100] Right ventricle demonstrates longitudinal, radial, and circumferential strains. Longitudinal strain is responsible for 80% of function. RV strain is affected by LV contractility hence, ASE/EACVI guideline provided values for assessment of RV free wall only.[101] In a cohort of 148 patients of HFpEF, Lejuene S et al demonstrated RV global strain (RVGLS) as the best parameter which provided additional prognostic value (x^2 to enter 7.85, $p = .005$) over a base model comprising of NYHA class III/IV, eGFR, hemoglobin level and TR severity for the primary endpoint of death or first HF hospitalization. FAC and TAPSE did not.[102]

Right ventricular strain provides better prognostic information as compared to clinical features (age, gender, and ischemic etiology), other echo parameters (measures of LV and RV systolic and diastolic function including LVEF, RV s', E/e' septal, and RA volume index) and LVEF $< 35\%$. On a 5 year-FU of 171 patients, RV strain worse than -14.8% was significantly more associated with clinical endpoints (death, hospitalization, and heart transplant (HR, 1.30; 95% CI 1.02–1.70; $p = .037$)).[103]

Amongst the numerous echo variables for prognostic assessment (primary endpoint overall death and secondary endpoint cardiovascular death), RVGLS and free wall strain (RVFWS) surpassed all including CMR derived RVEF, FT-GLS, TAPSE, and RV-FAC. This has been demonstrated by Houard L et al in 266 patients of HFrEF (median FU 4.7 years). Over a baseline clinical model, they calculated the chi-square to enter for every additional RV functional parameter and found RV strain to have the highest value, 10.8 ($p < 0.001$) significantly higher ($p < 0.05$) than other variables.[104]

Septum and free wall make up RV. Strain of septum is mainly due to the mid-layer, an indicator of LV function. To know the relative contribution of RVGLS and RVFWS with regard to prognosis, Carluccioe E et al studied 288 HFrEF patients (FU 30.2 ± 23.0 months) for clinical and other echo parameters (LVEF, LVGLS, LAVI, diastolic dysfunction, PASP, and severity of MR). Right ventricular global (HR 1.60; 95% CI, 1.29-1.99; $P < .0001$) and RVFWS (HR, 1.82; 95% CI, 1.45-2.29; $P < .0001$) were associated with endpoints (mortality and HF re-admission). However, only RVFWS remained significantly associated with outcome ($P < .01$) when LV function parameters (RF and LVGLS) were added to the base model showing net reclassification improvement 0.390; $P < .05$, not noted on addition of RVGLS.[105]

Incremental diagnostic ability of right atrial strain has been shown in clinical studies but regarding prognosis no research has been done for strain parameters.[106]

Conclusion

Heart failure is a rampant disease, especially affecting the elderly. Although diagnosed clinically, its classification according to EF constituting a '**spectrum**' revolves around echocardiography. The three classes of HF not only differ in their etiology, pathogenesis, and risk factors but also in prognosis.

This prognostic assessment can be done by many parameters, but routine trans-thoracic echocardiography provides important markers which differ for the three types of HF. Prognostic assessment has been done mostly for mortality and re-hospitalization risks. Left ventricular ejection fraction and diastolic dysfunction are not the only criteria in this regard as echo parameters of RV function, valve regurgitation, PAH and strain measures provide great information. No single echo parameter serves as a fit for the entire spectrum and a combination of parameters provides more robust prognostic data, especially if strain measures are included. Future studies are needed to evaluate all the echo parameters in all types of heart failure.

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Conflict of Interest

None.

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