

Clinical update

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

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Left ventricular ejection fraction (LVEF) has been the central parameter used for diagnosis and management in patients with heart failure. A good predictor of adverse outcomes in heart failure when below ~45%, LVEF is less useful as a marker of risk as it approaches normal. As a measure of cardiac function, ejection fraction has several important limitations. Calculated as the stroke volume divided by end-diastolic volume, the estimation of ejection fraction is generally based on geometric assumptions that allow for assessment of volumes based on linear or two-dimensional measurements. Left ventricular ejection fraction is both preload- and afterload-dependent, can change substantially based on loading conditions, is only moderately reproducible, and represents only a single measure of risk in patients with heart failure. Moreover, the relationship between ejection fraction and risk in patients with heart failure is modified by factors such as hypertension, diabetes, and renal function. A more complete evaluation and understanding of left ventricular function in patients with heart failure requires a more comprehensive assessment: we conceptualize an integrative approach that incorporates measures of left and right ventricular function, left ventricular geometry, left atrial size, and valvular function, as well as non-imaging factors (such as clinical parameters and biomarkers), providing a comprehensive and accurate prediction of risk in heart failure.

## Keywords

Heart failure • Ejection fraction • Outcomes • Risk assessment • Echocardiography • Deformation imaging

## Introduction

In 1962, Folse and Braunwald published a seminal article describing the use of a radioisotope indicator dilution technique to assess the 'fraction of left ventricular volume ejected per beat'.<sup>1</sup> This first description of a technique to measure what has subsequently been coined 'ejection fraction' heralded an era in which this single measure has become the most important metric of cardiac function utilized by clinicians. Clinical decision-making and patient management in a number of cardiovascular conditions largely rely on left ventricular ejection fraction (LVEF) as the primary measure of left ventricular (LV) function. Left ventricular ejection fraction is considered to be an essential measurement in heart failure (HF); in addition to typical signs and symptoms, determining the LVEF value is critical for the diagnosis of HF and distinguishing between HF with reduced LVEF and preserved LVEF

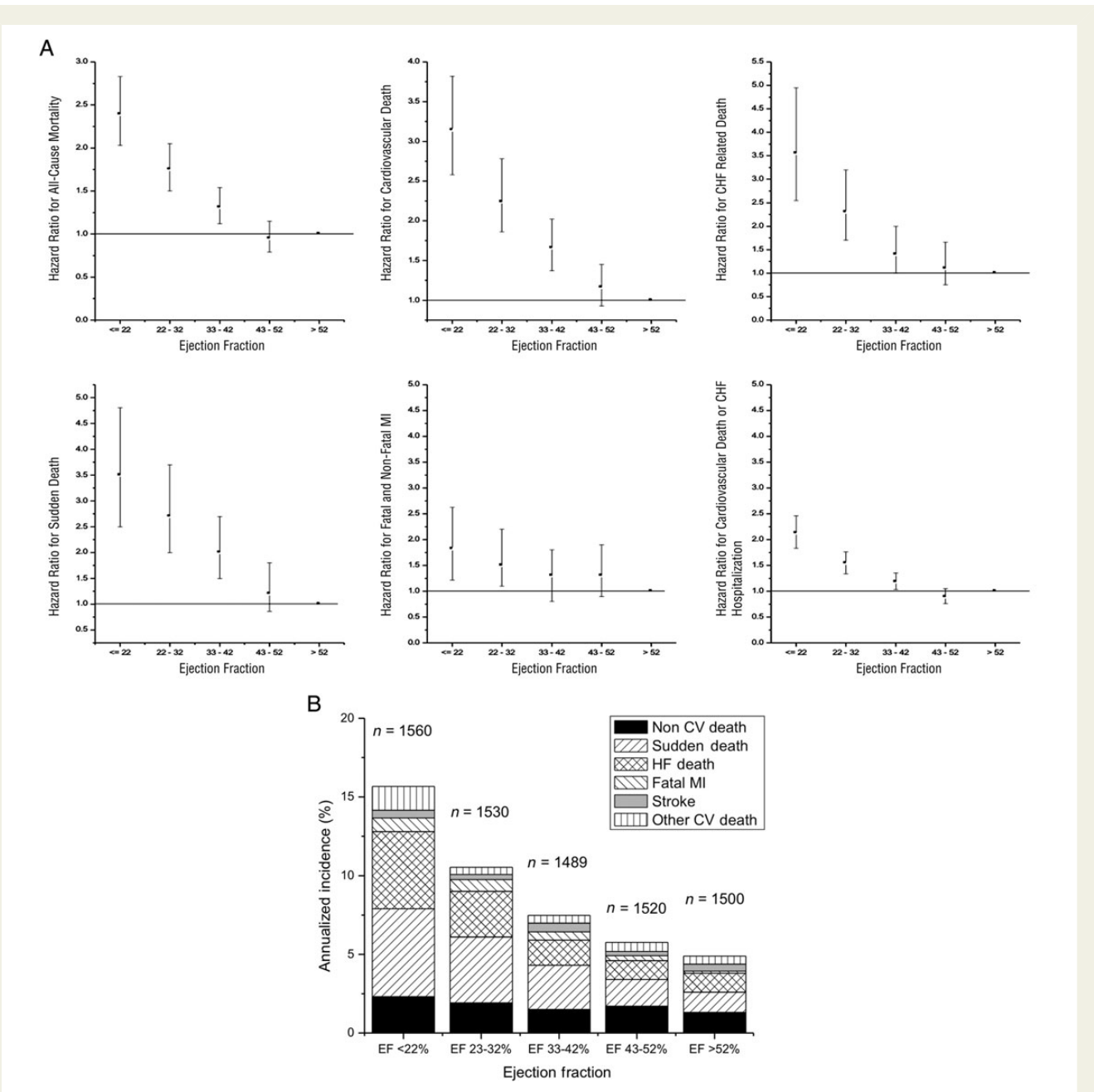
(HFpEF).<sup>2,3</sup> While the exact definitions of HF with reduced LVEF and HFpEF are controversial, effective therapies have only been proved for patients with the former form based on the definition of LVEF  $\leq 40\%$ .<sup>2</sup> In patients with HF with reduced LVEF, ejection fraction has proved to be an accurate predictor of clinical outcome (Figure 1A).<sup>4–6</sup>

Ejection fraction is used to assess LV function in more situations than just treatment of cardiovascular diseases—the administration of several potent chemotherapeutic agents is largely guided by the potential occurrence of cardiotoxicity, mainly defined by decrementing LVEF values;<sup>7</sup> indeed, ~14% of patients are withheld further treatment with potentially life-saving therapies such as trastuzumab based on asymptomatic reduction in LVEF alone.<sup>8</sup>

However, LVEF as a measure of LV function has some important limitations. In this review, we summarize the current knowledge on the relation between LVEF and cardiovascular risk, describe the

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**Figure 1** Left ventricular ejection fraction (LVEF) as a predictor of cardiovascular outcomes at values below 45%. (From Ref. 4). (A) Hazard ratio for all-cause mortality (top left), cardiovascular death (top middle), heart failure (HF)-related death (top right), sudden death (bottom left), fatal and non-fatal myocardial infarction (bottom middle), and cardiovascular death or hospitalization for heart failure (bottom right), based on LVEF. At LVEF values below 45%, each 10% reduction in LVEF was independently associated with a significant increased risk of death due to any cause, cardiovascular death, sudden death, death due to heart failure, death due to myocardial infarction, and other/ procedure-related cardiovascular death but not death due to stroke or due to non-cardiovascular causes. CHF, chronic heart failure. (B) The relationship between LVEF and risk of death, including individual modes of death. The risk of cardiovascular death and the components of cardiovascular death, except fatal stroke, declined with increase in LVEF up to the approximate value of 45%. Left ventricular ejection fraction did not influence the rate of non-cardiovascular death. CV, cardiovascular; MI, myocardial infarction; EF, ejection fraction.

assessment of LV function by LVEF, including the pitfalls and alternatives to this method, and discuss other imaging-based measures of risk and modifiers of risk assessment and prognostication

in HF. Finally, we propose a more comprehensive, integrative approach to the assessment of LV function in patients with heart failure.

## The predictive value of left ventricular ejection fraction in heart failure

### Left ventricular ejection fraction as a predictor of outcomes in heart failure

Ejection fraction has proved to be a good predictor of incident HF. In the CARE trial, with the exception of patient age, LVEF was the most relevant predictor of HF occurrence in 3860 long-term survivors of myocardial infarction without prior history of HF, with a 4% increase in the risk of HF for every 1% decrease in baseline LVEF, over a 5-year follow-up period, adjusting for other covariates.<sup>9</sup> Similarly, LVEF has proved to be a predictor of outcomes in patients with prevalent HF and following myocardial infarction.<sup>4,5,10,11</sup> In the VALIANT echocardiography study, which studied 610 patients with HF, LV dysfunction, or both following myocardial infarction, LVEF and LV volumes at baseline were powerfully and independently predictive of adverse clinical outcomes including total mortality, cardiovascular mortality, resuscitated sudden death, hospitalization for HF, and stroke.<sup>5</sup> Likewise, data from the CHARM programme, enrolling 7599 patients with symptomatic HF over a broad spectrum of LVEF, confirmed LVEF as a powerful predictor of cardiovascular outcomes, including all-cause death, cardiovascular death, HF-related death, myocardial infarction, and HF hospitalization, such that every 10% reduction in LVEF below 45% was independently associated with a 39% increase in the risk of all-cause mortality. However, the discriminatory value of LVEF in predicting morbidity and mortality was limited above an LVEF of 45%, suggesting that in patients with HFpEF, LVEF is a poor overall predictor of risk and that factors other than ventricular systolic function expressed by LVEF contribute to cardiovascular risk.<sup>4</sup> A similar finding of a linear decrease in mortality up to an LVEF of ~45% was found in the DIG trial that studied a similar number of stable HF patients, however, without data on morbidity.<sup>11</sup> Both of these trials have also provided data on specific causes of death with respect to LVEF subgroups (Figure 1B).<sup>4,11</sup>

### Left ventricular ejection fraction as a predictor of sudden cardiac death

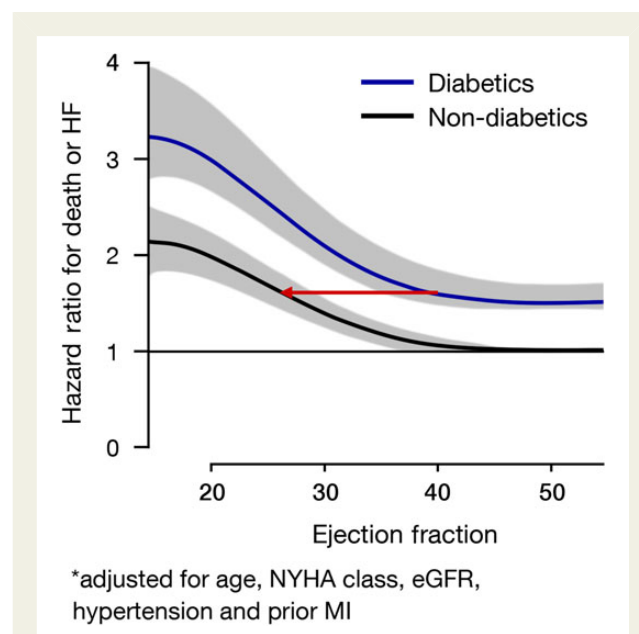
Left ventricular ejection fraction, a predictor of sudden cardiac death (SCD), is currently the primary metric by which decisions regarding ICD placement are made. An LVEF  $\leq 35\%$  is the currently recommended treatment cut-off for ICD implantation for the primary prevention of SCD,<sup>1</sup> primarily based on studies that utilized LVEF as the only common entry criterion and have only included patients with such low LVEF values.<sup>12,13</sup> However, previous studies have shown that the majority of SCD victims have had no known history of heart disease, or have had heart disease with normal or only mildly impaired LV function, constituting a group of patients in which predictors of SCD are still sought for.<sup>14–16</sup> Recently, a community-based prospective study identified SCD subjects eligible for primary ICD implantation based on echocardiograms performed prior to the SCD event in conjunction with guideline criteria relevant at the time of the echocardiogram and found that only 20.5% would have been guideline-eligible for a primary prevention ICD

implantation, while 32.1% of SCD victims had an LVEF  $\leq 35\%$ .<sup>17</sup> Moreover, the limited predictive accuracy of LVEF for serious arrhythmic events has been demonstrated in a meta-analysis of 20 studies including a total of 7294 patients: the sensitivity of LVEF for major arrhythmic events post-myocardial infarction was 59% and its specificity reached 78%.<sup>18</sup> Several clinical factors are recognized as modifiers of the relationship between LVEF and risk of SCD in particular, including symptomatic HF or history of HF, documented non-sustained ventricular tachycardia or ventricular tachycardia induced by programmed electrical stimulation, QRS interval  $\geq 120$  ms, or LVEF deterioration over time.<sup>19</sup>

### Left ventricular ejection fraction and other metrics of risk

Although LVEF is well established as an independent predictor of outcomes in HF, its prognostic significance should be interpreted in the context of other measures of risk. Various co-morbidities often present in patients with HF, such as diabetes and chronic kidney disease, convey an increased risk, regardless of the underlying LVEF.<sup>6,20,21</sup>

In the CHARM programme, age  $>60$  years, diabetes, and LVEF  $<45\%$  were recognized as the three most powerful independent predictors of all-cause mortality or the composite of cardiovascular death and HF hospitalization in patients who have already developed HF.<sup>6</sup> In CHARM, the presence of diabetes would increase a patient's risk of death or development of HF such that a diabetic patient with an LVEF of 40% had the equivalent risk of a non-diabetic patient with an LVEF of 25% (Figure 2). Similar to diabetes, chronic kidney disease



**Figure 2** The altered relationship between left ventricular ejection fraction (LVEF) and death or heart failure in patients with diabetes. An equivalent risk for death or heart failure in a diabetic patient with an LVEF of 40% and in a non-diabetic patient with an LVEF of 25%. HF, heart failure; NYHA, New York Heart Association; eGFR, estimated glomerular filtration rate; MI, myocardial infarction. (Modified from Ref. 22).

is well recognized as a co-morbidity contributing to increased risk for cardiovascular outcomes in patients with HF.<sup>20</sup> Data from a pooled analysis of four Danish myocardial infarction and HF patient registries including >18 000 patients followed over 10 years have shown a significant interaction between estimated glomerular filtration rate and LVEF (measured as the wall motion index), with each of these parameters becoming relatively more important with low values of the other; the combination of LV systolic dysfunction and chronic kidney disease was associated with a two-fold 10-year mortality risk.<sup>21</sup>

## The pitfalls of ejection fraction measured by echocardiography

Left ventricular ejection fraction is measured indirectly by most imaging techniques, including echocardiography, which calculate ejection fraction from estimations of LV volume. While tomographic techniques such as cardiac MRI or CT can calculate ventricular volumes by summing multiple equally spaced slices in end-diastole or end-systole, requiring no geometric assumptions, two-dimensional echocardiography requires inferences about ventricular shape in order to estimate a three-dimensional volume from a two-dimensional image. Various technical limitations, partly inherent to echocardiography as a non-tomographic technique, hamper the calculated LVEF values: poor image quality, anatomy difficult to scan often leading to foreshortened ventricles, the tedious and time-consuming process of manual delineation of the endocardium with boundary continuity often out-of-plane, being prone to inter- and intra-observer variability as well as shortcomings of novel, semi-automatic delineation applications dealing with similar issues, in particular lack of standardization and reproducibility.<sup>23,24</sup> Moreover, as a volume-derived index, LVEF often relies on geometric assumptions (particularly in one- and two-dimensional echocardiography) and is extremely load-dependent. These limitations lead to substantial loss of reproducibility, and even repeated measures of ejection fraction in the same individual over a brief time period can result in a 5- to 7-point variability. The measurements of LVEF may be influenced by changes in LV geometry and not correspond to true LV contractility: in athletes with an enlarged LV cavity marginally lower LVEF values may be obtained,<sup>25</sup> supranormal LVEF values are often measured in various forms of LV hypertrophy<sup>24</sup>, while in dyssynchronous ventricles such as in left bundle branch block, the largest LV volume is not necessarily correspondent to the end-diastolic volume, which may impede the performed LVEF measurement. Finally, certain factors such as high heart rate may impact LVEF values, which will typically be reduced in tachycardic states, even in cases of clearly increased contractility such as by the administration of dobutamine.

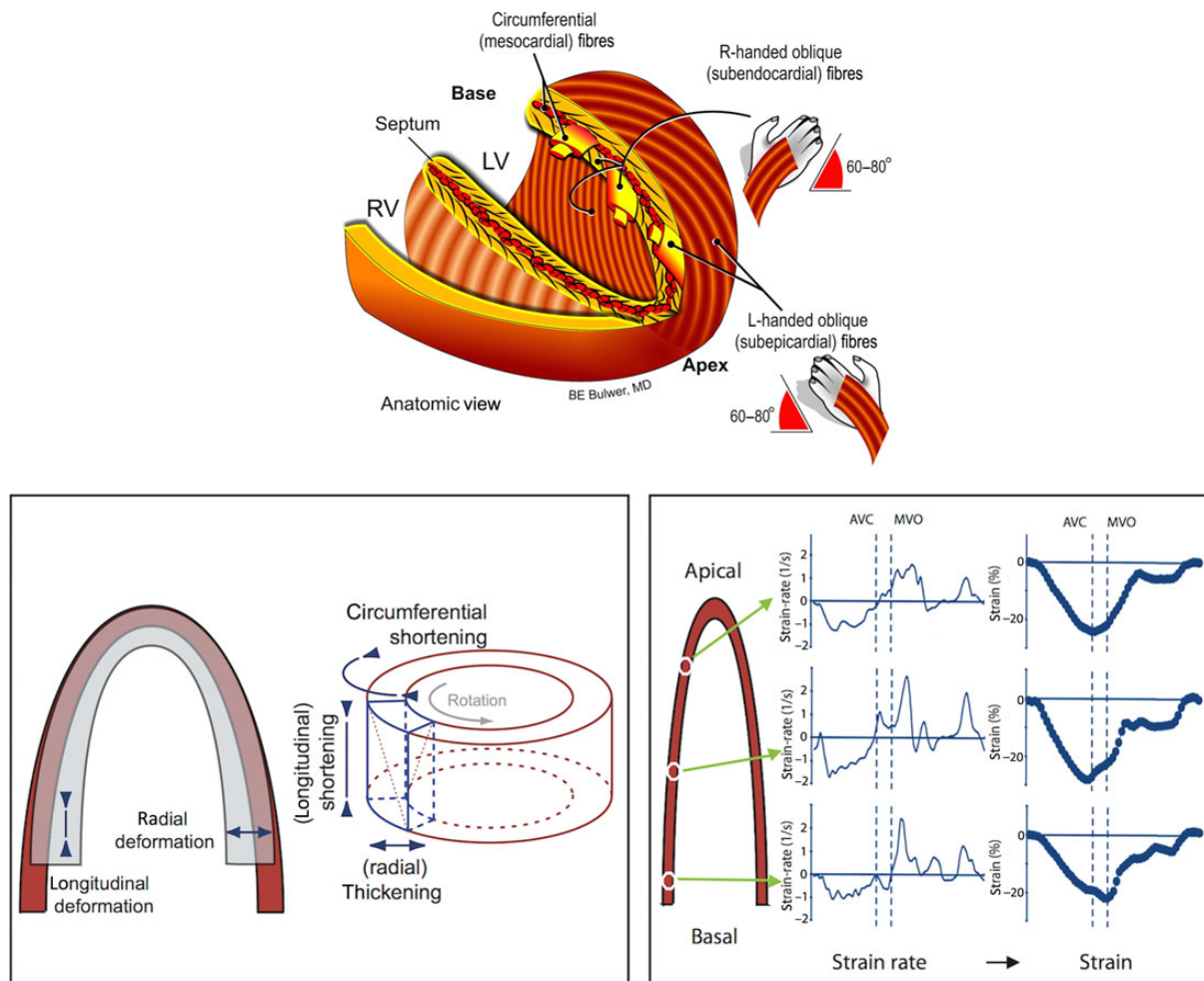
True three-dimensional echocardiography offers several advantages to two-dimensional techniques; the acquisition of real-time volumetric data obviates the reliance on geometrical assumptions and may provide a more integrative view of regional myocardial mechanics, though current three-dimensional technology has other limitations including reduced image quality and lower frame rate than two-dimensional echocardiography.

## Assessment of left ventricular systolic function by myocardial deformation imaging

Myocardial fibre architecture of the LV consists of endo- and epicardial layers composed of longitudinal fibres, and mid-myocardial layers formed by circumferential fibres (Figure 3).<sup>27</sup> In systole, the shortening of longitudinal fibres causes the displacement of the LV basal plane towards the more stationary apex, while the shortening of circumferential fibres induces an inward deformation (towards the LV cavity) of the LV myocardium (radial thickening) (Figure 3). Deformation in both of these planes reduces LV volume during systole; thus if measured by volumetric techniques, LVEF reflects the function of both longitudinal and circumferential LV fibres, without the ability to distinguish functional impairment of one of these components. However, in various cardiac pathologies, impairment in longitudinal function precedes the reduction in circumferential indices, giving rise to subclinical impairment of LV pump function.<sup>24,28–32</sup> As circumferential function can even to a certain extent compensate for the initial reduction in longitudinal function, both LVEF and fractional shortening are often above normal in, e.g. hypertrophic hearts, despite the fact that longitudinal function can be significantly impaired (Figure 4).

The assessment of myocardial deformation in different planes corresponding to LV fibre orientation has been enabled by the development of several advanced echocardiographic methods (Figure 3). Doppler myocardial imaging (or Doppler tissue imaging) and the more recent method of two- and three-dimensional speckle-tracking echocardiography based on grey-scale imaging provide data on myocardial deformation by measuring strain and strain rate (Figure 3). Strain is defined as the change in length of a myocardial segment relative to its resting length (for example, the shortening of longitudinal myocardial fibres during systole). Strain rate is defined as the rate of such deformation ( $s^{-1}$ ), and can provide data on both systolic and diastolic events. During systole, longitudinal shortening (resulting in negative strain values) can be evaluated from apical views. The parasternal short- and/or long-axis views provide assessment of circumferential shortening (negative strain values) and inward radial thickening (positive strain values) of the myocardium.<sup>23,24</sup> Conversely, longitudinal and circumferential lengthening and radial shortening will occur in diastole.

Deformation imaging (in particular strain rate) has shown good correlation with sonomicrometry data, is somewhat less load-dependent than LVEF,<sup>33,34</sup> and may provide better insight into myocardial dysfunction in patients with preserved LVEF.<sup>35,36</sup> Although the learning curve for Doppler-based deformation analysis is longer compared with LVEF, speckle tracking can be mastered faster; the obtained deformation curves are much easier to interpret, mainly as a consequence of spatial smoothing. The currently available applications for speckle tracking-based deformation analysis predominantly rely on semi-automatic image segmentation (delineation) and quantification techniques, providing a reproducible platform. However, the reproducibility of myocardial deformation imaging data among vendors may be jeopardized by the use of different analysis algorithms, while recent agreements among several vendors to standardize deformation imaging should improve the robustness of the technique.<sup>37</sup>



**Figure 3** Normal myocardial fibre orientation, deformation planes and typical longitudinal strain rate and strain traces. Upper panel: Left ventricular endo- and epicardial longitudinal fibres and their opposing oblique directions, mid-myocardial circumferential fibres. (From Ref. 26, with permission). Lower panel, left: The three planes of myocardial motion and deformation at systole: longitudinal shortening, radial thickening, and circumferential shortening. Lower panel, right: Typical traces of longitudinal strain rate and strain from a healthy adult. AVC, aortic valve closure; AVO, aortic valve opening; MVO, mitral valve opening. (From Ref. 24).

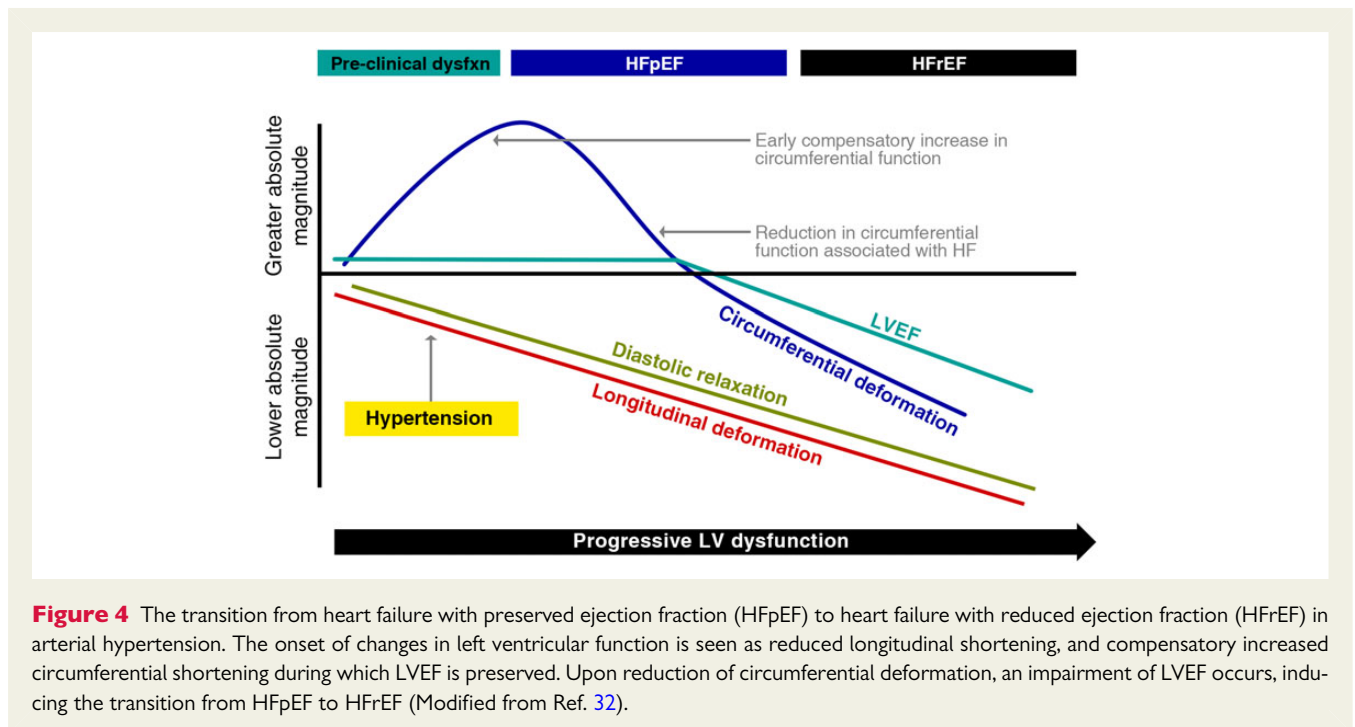
### The prognostic value of myocardial deformation imaging in the post-myocardial infarction setting and with valvular disease

The correlation between impaired myocardial deformation and underlying disease severity has been shown in various cardiac pathologies.<sup>24,38,39</sup> The prognostic value of deformation imaging for death or HF was studied in VALIANT at a mean time of 5 days after high-risk myocardial infarction.<sup>40</sup> Both reduced longitudinal and circumferential LV function evaluated by speckle tracking were independently associated with all-cause mortality and combined death or HF hospitalization. Reduced longitudinal strain rate added significant incremental value in the prediction of all-cause mortality when added to LVEF and relevant clinical variables, and circumferential strain rate was shown to be a good predictor of LV remodelling.<sup>40</sup> Furthermore, the patients with the greatest

degree of dyssynchrony, measured as the standard deviation of time to peak velocity and to strain rate for 12 LV segments, had an increased risk of all-cause mortality or HF hospitalization, even after adjusting for various relevant covariates including LVEF.<sup>41</sup> This finding suggests that the pattern of contraction might also be important in the evolution of HF, independently of global and regional systolic function. Strain can also be used to calculate mechanical dispersion, as the standard deviation of the time to peak strain.<sup>42</sup> Mechanical dispersion has been shown to be a predictor of arrhythmias in ischaemic and other forms of cardiomyopathies.

Furthermore, the superiority of deformation parameters in risk assessment has also been demonstrated in patients with valvular disease: a study of 157 elderly patients with advanced stages of aortic stenosis demonstrated that only longitudinal strain rate and mitral annular displacement were strong predictors of risk of all-cause and cardiac death, unlike LVEF or EuroSCORE.<sup>43</sup>





**Figure 4** The transition from heart failure with preserved ejection fraction (HFpEF) to heart failure with reduced ejection fraction (HFrEF) in arterial hypertension. The onset of changes in left ventricular function is seen as reduced longitudinal shortening, and compensatory increased circumferential shortening during which LVEF is preserved. Upon reduction of circumferential deformation, an impairment of LVEF occurs, inducing the transition from HFpEF to HFrEF (Modified from Ref. 32).

## Myocardial deformation imaging in heart failure with preserved left ventricular ejection fraction

That ejection fraction has limited ability to predict risk in patients with heart failure and relatively preserved LVEF suggests a potential role for myocardial deformation imaging in the assessment of patients with HFpEF. Several studies have suggested that LV longitudinal function might be impaired in HFpEF.<sup>44–48</sup> In the PARAMOUNT trial of patients with HFpEF, longitudinal strain was reduced compared with normal controls or patients with hypertensive heart disease.<sup>29</sup> Circumferential function and LVEF were maintained in hypertensive patients, suggesting that this may be a compensatory mechanism for impaired longitudinal function, a finding that has been previously reported in diabetic patients.<sup>30,31</sup> Worse circumferential strain in the HFpEF group was associated with lower systolic blood pressure and stroke volume, suggesting that the impairment of circumferential function, in conjunction with impaired longitudinal function, appears to be a mechanism relevant to the development of HFpEF.<sup>24,29,32</sup> Similarly, patients with HFpEF enrolled in the TOP-CAT trial also showed substantial reduction in longitudinal strain, which was shown to be the most important echocardiographic predictor of cardiovascular death or HF.<sup>49</sup>

## Incorporating additional echocardiographic measures of risk

While LVEF remains the single most utilized metric of cardiac function, echocardiography provides substantial additional information regarding cardiac structure and function that can aid in the management of HF patients, including chamber volumes, wall thickness/

myocardial mass, LV filling pressures, right ventricular function, and evaluation of valvular disease.

## Left ventricular geometry predicts the risk of adverse cardiovascular events

Left ventricular geometry has been shown to be predictive of outcomes in HF even beyond traditional measures of size and function. In VALIANT, the risk of adverse cardiovascular events was increased with concentric remodelling and eccentric hypertrophy and was the greatest for concentric hypertrophy, after adjusting for baseline covariates such as history of diabetes, hypertension, congestive HF, COPD, prior myocardial infarction, and LVEF.<sup>50</sup> Similarly, a high prevalence of concentric remodelling and LV hypertrophy was found in HFpEF patients enrolled in the iPRESERVE trial, and was associated with an increased risk of morbidity and mortality, after adjusting for relevant covariates.<sup>51</sup>

## Right ventricular dysfunction significantly impacts outcomes in heart failure

Adequate preload provided by a well-functioning right ventricle (RV) may be crucial for the failing LV. Right ventricular function can be impaired in patients with HF by the same aetiologic processes causing LV failure, or by increased RV afterload owing to secondary pulmonary hypertension in the setting of high LV filling pressures. RV function has been shown to be an important determinant of outcome in HF patients<sup>52,53</sup> and in patients following myocardial infarction,<sup>54,55</sup> while elevated right atrial pressure has been associated with hepatic and renal dysfunction and malnutrition.<sup>56</sup> RV function has also been shown to be prevalent and predict outcomes in HFpEF, even after adjustment for pulmonary hypertension.<sup>57</sup>

Right ventricular function is difficult to assess routinely by echocardiography due to its complex crescent-shaped geometry. Several

methods have been proposed for assessment of RV function.<sup>58</sup> Right ventricular fractional area change (RVFAC), tricuspid annular plane systolic excursion (TAPSE), and tissue Doppler-derived tricuspid lateral annular systolic velocity (S') have all been proposed as methods to evaluate RV function echocardiographically. Right ventricular fractional area change is in practice easy to perform and has been validated against cardiac MRI measurements of RV ejection fraction.<sup>59</sup>

### Left atrial size—the 'barometer' of left ventricular pressures

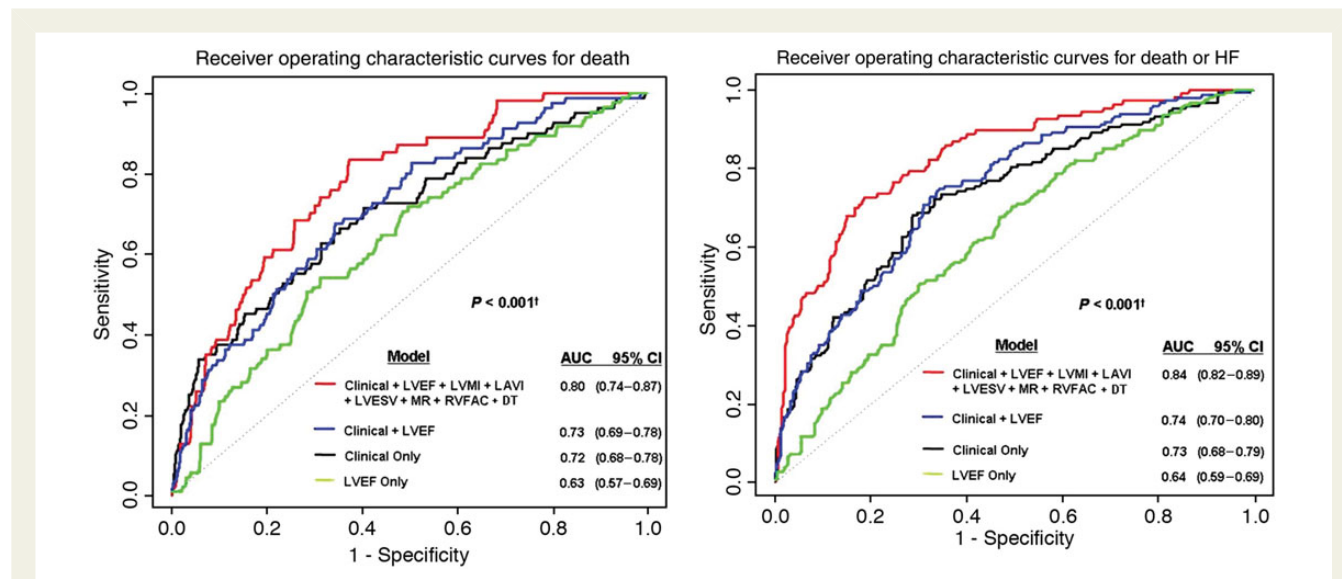
An increase in left atrial (LA) volume and pressure leads to increased LA size, initially associated with enhanced contractile shortening. Further LA dilatation will, however, ultimately lead to a threshold fibre length, precipitating a reduction in atrial contractility, while further atrial enlargement would induce the impairment of LA function.<sup>60</sup> Such a 'vicious circle' of LA remodelling and dysfunction is frequently observed in HF, and while LA enlargement appears to occur early after HF onset and continues subsequently,<sup>61</sup> LA shortening, i.e. function, may be both increased or decreased, depending on the stage of disease. Acting as a 'transducer' between LV filling pressures and the alveocapillary membrane, it is not surprising that LA dysfunction can actively contribute to HF symptoms,<sup>62–65</sup> while the combination of increased LA size and impaired function has a highly predictive value for the diagnosis of HF.<sup>65</sup>

The association between LA remodelling and adverse cardiovascular outcomes is well established.<sup>66–68</sup> Data from the VALIANT echocardiographic study have confirmed that baseline LA size as

well as early post-infarct LA remodelling are predictive of mortality and cardiovascular morbidity.<sup>61</sup> The prognostic relevance of LA remodelling seems to be crucial in patients with HFpEF in which impairment in all phases of LA function has been observed and likely contributes to risk.<sup>69</sup> Data from 745 HFpEF patients enrolled to the I-PRESERVE trial have confirmed the presence of LA enlargement in 66% of these patients, while increased LA area was associated with an increased rate of HF and cumulative event rate of death or cardiovascular hospitalization. Left ventricular mass and LA size were independently associated with increased risk of morbidity and mortality.<sup>51</sup>

### Mitral regurgitation: an integral component of the heart failure syndrome

Functional mitral regurgitation due to LV remodelling and/or papillary muscle displacement is a frequent finding in HF patients, and if developed during the acute or chronic phases following myocardial infarction is associated with an increased risk of mortality and HF occurrence.<sup>68,70</sup> The presence and degree of mitral regurgitation in patients with LV dysfunction and/or HF were also shown to be independently associated with death and other adverse outcomes, while an increase in mitral regurgitation severity over a 20-month follow-up led to an increased number of HF hospitalizations.<sup>71</sup> It should be emphasized that patients with severe mitral regurgitation causing significant LV volume overload will have artificially augmented LVEF, which may conceal an underlying severe reduction in pump function.



**Figure 5** Receiver operating characteristic curves in the assessment of the added predictive value of echocardiography on top of clinical assessment. Clinical assessment alone provided good discrimination of 17-month survival (left), while adding LVEF alone did not substantially improve discrimination – neither for survival (left), nor survival free of heart failure (right). However, adding multiple echocardiographic markers significantly improved discrimination of survival (left) and survival free of heart failure (right). †*P*-value comparing the added value of further echocardiographic assessment beyond LVEF (<0.001 for both comparisons). (From Ref. 72, with permission). LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; LAVI, left atrial volume index; LVESV, left ventricular end-systolic volume; MR, mitral regurgitation; RVFAC, right ventricular fractional area change; DT, deceleration time.

## Can echocardiographic multivariable models improve the prognostic value of clinical assessment in heart failure?

While a number of echocardiographic measures individually predict outcomes in patients with heart failure, risk assessment might benefit from a more comprehensive echocardiographic approach to heart failure patients. A further analysis of VALIANT assessed the individual predictive value of echocardiographic parameters such as LV mass index, LVEF, LV volumes, LA volume index, RVFAC, mitral regurgitation, and deceleration time significantly improved the predictor of survival free of HF, adjusting for confounders.<sup>72</sup> Indeed, the added prognostic value of LVEF to clinical assessment was minimal; nonetheless, additional echocardiographic measures added to the multivariable model significantly improved the prediction of 17-month survival free of HF (Figure 5).

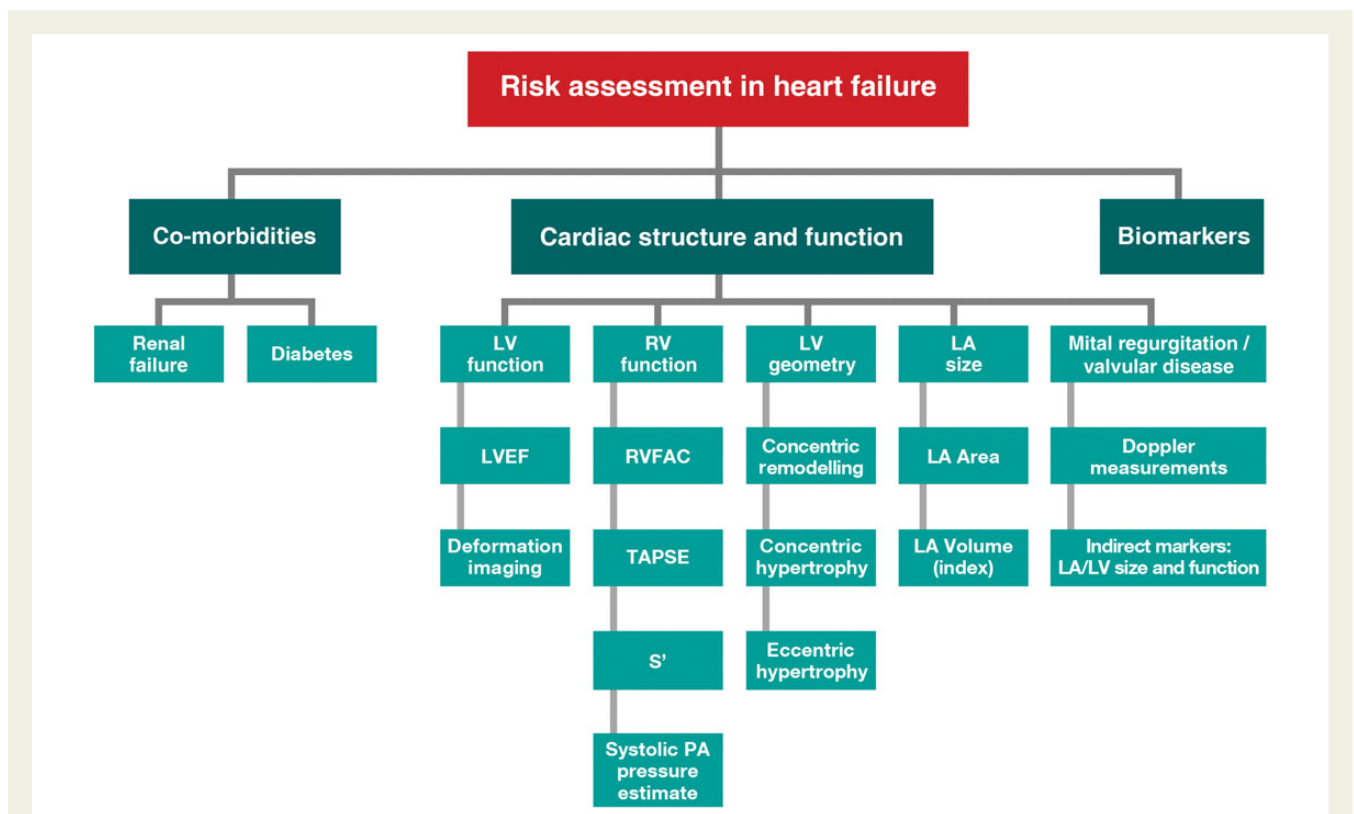
The measures of cardiac morphology and function relevant for the prognosis of cardiovascular morbidity and mortality are still a matter of debate within the heterogeneous syndrome of HFpEF. However, a recent analysis of the TOPCAT trial has determined the prognostic relevance of three easily obtainable parameters:<sup>73</sup> the presence of LV hypertrophy, elevated LV filling pressures, and high pulmonary artery pressures, which were predictive of the composite outcome of cardiovascular death, aborted cardiac arrest or HF hospitalization, or HF hospitalization alone even adjusting for clinical and laboratory characteristics, while neither LV volumes

nor LVEF predicted worse outcomes. These measures were increasingly important in the risk model.

## Conclusion

In daily cardiology practice, patient management decisions are an integration of readily available clinical parameters and values obtained by various diagnostic techniques, proved to be of prognostic relevance. Although LVEF is a well-established prognosticator in heart failure, it has several limitations, such as the quantification of LV function based on volumetric measures from a two-dimensional non-tomographic technique. Advanced imaging technologies as speckle-tracking echocardiography can provide data on regional myocardial function and its specific components, in particular longitudinal myocardial function, which is often the earliest component to be affected by disease. Longitudinal strain by speckle-tracking echocardiography has been shown to be an excellent metric of risk in HF, particularly HFpEF, where reduced longitudinal strain is the earliest marker of reduced LV function, in addition to LA size, which can be regarded as a marker of severity and chronicity of elevated LV filling pressures.

No single parameter can replace the multitude of valuable data that echocardiography can provide in the assessment of a patient with heart failure; nonetheless, the plethora of numbers often generated in an echocardiographic report can be confusing and



**Figure 6** An integrated approach to risk assessment in heart failure. The integration of clinical parameters such as age and co-morbidities, easily obtainable echocardiographic features of cardiac structure and function as well as biomarkers -towards a superior risk assessment to the left ventricular ejection fraction (LVEF) alone. LV, left ventricular; RV, right ventricular; RVFAC, right ventricular fractional area change; TAPSE, tricuspid annular plane systolic excursion;  $S'$ , tissue Doppler-derived tricuspid lateral annular systolic velocity; LA, left atrial.



misleading. An integration of clinical parameters and biomarkers with several easily obtainable echocardiographic measures in addition to LVEF such as LV mass, LA size, RV function, and the presence of significant valvular disease should provide a comprehensive measure to inform patient-care diagnostic decisions and management strategies, providing much better predictive ability than LVEF alone (Figure 6).

**Conflict of interest:** none declared.

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