New Diastology Guidelines: Evolution, Validation and Impact on Clinical Practice

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The 2016 American Society of Echocardiography/European Association of Echocardiography (ASE/EACVI) guidelines on the assessment of diastolic function sought to simplify the assessment of diastolic function by recommending a streamlined, stepped approach with a focus on four key variables. Haemodynamic validation using simultaneous cardiac catheterisation and echocardiographic assessment of diastolic function have shown robust prediction of left ventricular filling pressure (LVFP) using the streamlined 2016 algorithms, with favourable comparisons to the 2009 guidelines. Similarly, prognostic validation data demonstrates that the 2016 algorithms are easier to implement in clinical practice, have superior interobserver reliability across a broad range of observer experience, and are better at predicting clinical outcomes. Furthermore, published data show improved classification of clinical heart failure patients. However, increased specificity of the updated 2016 guidelines results in a lower prevalence of diastolic dysfunction compared to the 2009 recommendations. Further refinement of guidelines for the identification and diagnosis of diastolic dysfunction is possible through incorporation of new diastolic parameters.

Keywords   Diastolic • Echocardiography • Doppler • Left ventricular filling pressure • E/e' ratio • Stress
• Exercise • Heart failure with preserved ejection fraction • HFpEF

Introduction

The guidelines for the evaluation of diastolic dysfunction in clinical practice have undergone two iterations in the last decade. In an attempt to simplify and standardise the assessment of diastolic function, the American Society of Echocardiography (ASE) and European Association of Echocardiography (EAE) released the first guidelines document in 2009, which embedded a comprehensive range of traditionally used diastolic parameters in a number of diagnostic algorithms [1]. Despite subsequent haemodynamic validation data which showed that the 2009 ASE/EAE algorithms had a good sensitivity and specificity for elevated filling pressures [2], and evidence of reasonable interobserver concordance [3], problems with reconciling discordant data emerged. In addition, the diastolic guidelines committee of the ASE and European Association of Cardiovascular Imaging (EACVI) criticised the 'complexity' of the 2009 algorithms, with the large number of included variables considered not conducive for easy and practical application

in routine clinical practice [4]. For this reason, the ASE and EACVI jointly released new guidelines in 2016 which sought to simplify the assessment of left ventricular (LV) diastolic function in clinical practice by focussing on four key variables only and adopting algorithms that avoided problems with discordance [4]. The purpose of this review is to briefly review the evolution of the guidelines between the 2009 and 2016 versions, review the haemodynamic and prognostic validation data relevant to the contemporary guidelines, and explore potential clinical implications.

Traditional 'Comprehensive' Approach to Assessing Diastolic Function

Traditional approaches to the assessment of LV diastolic function used various measures of LV filling and required a thorough knowledge of the strengths and limitations of a comprehensive range of diastolic parameters, which were then applied to the assessment of LV diastolic function in individual patients taking into account the unique characteristics (including associated measures such as ejection fraction and clinical presentation) of that particular patient [5]. Most standard echocardiography textbooks recommend a thorough assessment of parameters obtained with Doppler echocardiography and two dimensional (2D) measurements as summarised in Table 1. This approach inherently requires a high level of knowledge and understanding, coupled with expert training in the assessment of diastolic function. However, due to its reliance on the observer's 'expertise' in diastology, and the large variations in levels of training of sonographers who collect the parameters, and cardiologists, intensivists, anaesthetists and emergency physicians who report echocardiograms at the clinical interface, this represents a 'non-standardised' approach and is open to subjectivity as well as a high degree of inter-observer variability. Importantly, published data demonstrating intra- and inter-observer variabilities using this traditional 'comprehensive' approach are lacking.

ASE/EAE Guidelines: Adopting an Algorithmic Approach

In a step towards a more standardised approach, the ASE/EAE guidelines recommended an algorithmic approach with a comprehensive range of echo-determined parameters (Figures 1–3) [1]. These three algorithms, based on different clinical presentations, suggested assessment of 10 individual components of diastolic function. The strength of this approach was greater standardisation, and ease of use by practitioners with a broad range of training in echocardiography. The haemodynamic validation of this algorithm-based approach was explored in two studies. Nagueh et al. studied 79 patients with decompensated heart failure and using simultaneous Doppler echocardiography and right heart catheterisation demonstrated

that the 2009 ASE/EAE guideline recommended algorithms for diagnosing elevated left ventricular filling pressures (LVFP) (defined as pulmonary capillary wedge pressure [PCWP] >15 mmHg) had a sensitivity of 98% with a corresponding specificity of 91% [6]. Dokainish et al. studied 62 patients with near-simultaneous Doppler echocardiography and left heart catheterisation and showed a sensitivity of 84% and a specificity of 80% for elevated LVFP (defined as LV pre-atrial contraction pressure of >15 mmHg) [2].

However, assigning specific values of the diastolic parameters to different categories inevitably gave rise to discordance, where values obtained in the same patient were not confined to a single category. A rigid application of the algorithms thus became problematic as diastolic function could not be reliably categorised. Moreover, specific rules for dealing with discordant parameters were not specified in the guidelines document.

ASE/EACVI Guidelines: Simplifying the Algorithms

The 2016 guidelines streamlined the algorithms by restricting the number of variables used to assess diastolic function to four key variables: early diastolic tissue velocity (septal and lateral e'), the average E/e' ratio (from septal and lateral e'), left atrial volume indexed to body surface area (LAVI), and tricuspid regurgitation velocity (TRV) [4]. These are embedded in the two-step algorithms shown in Figures 4 and 5. The first algorithm (Figure 4) is used to 'screen' for diastolic dysfunction in patients with normal LV ejection fraction (LVEF) and no evidence of underlying myocardial disease. If more than 50% of criteria are positive (three out of four available variables; or two out of three available variables), the patient is determined to have diastolic dysfunction and the second algorithm is then used to grade the diastolic dysfunction (Figure 5). The second algorithm utilises two additional parameters in the form of the mitral inflow E/A ratio as well as the mitral inflow E-wave velocity (Figure 5). Briefly, if patients have an 'abnormal relaxation' mitral inflow pattern (E/A ratio <0.8 and E-wave <50 cm/s), they are determined to have grade I diastolic dysfunction with normal LVFP. If patients have a 'restrictive' pattern (E/A ratio >2), they are graded as grade III diastolic dysfunction with increased LVFP. For patients in between with E/A ratio >0.8 and <2 (and, also including E/A ratio <0.8 and E-wave >0.5 m/s), a second step is recommended with consideration of three criteria (average E/e' >14, TRV >2.8 m/s and LAVI >34 mL/m^2). If at least two criteria are met, subjects are deemed to have grade II diastolic dysfunction with increased LVFP. In the case of one positive and one negative criteria, the assessment of diastolic dysfunction is indeterminate, and if both are negative, an assessment of grade I diastolic dysfunction with normal LVFP is made. Importantly, these new algorithms avoid problems with discordance by classifying individual patients into specific categories using a simple majority of available variables, rather than assigning individual variables to rigid grades of dysfunction [4].

Table 1 Comprehensive Range of Diastolic Parameters for Evaluation of Diastolic Function with Echocardiography.

Parameter	Acquisition/Analysis	Advantages	Disadvantages
Mitral inflow E-wave	- Apical four-chamber view - Use colour flow mapping for optimal alignment with blood flow. - PW Doppler sample volume 1–3 mm between mitral leaflet tips. - Optimise filter/gain to minimise spectral broadening - Measure peak modal velocity in early diastole at leading edge of spectral waveform	- Highly feasible and reproducible	- E/A fusion at high heart rates (ideally sample when heart rate 100–120 bpm) - Decreases with age
Mitral inflow A-wave	- As above for acquisition of mitral inflow E-wave - Measure peak modal velocity in late diastole at leading edge of spectral waveform	- Highly feasible and reproducible	- E/A fusion at high heart rates (ideally sample when heart rate 100–120 bpm) - Increases with age - Not applicable in atrial fibrillation or flutter
Mitral E/A ratio	Mitral E-wave velocity divided by A-wave velocity	- As above for acquisition of E and A wave	- E/A fusion at high heart rates (ideally sample when heart rate 100–120 bpm) - Pseudonormalisation with moderate diastolic dysfunction - Decreases with age - Not applicable in atrial fibrillation or flutter
Mitral E wave deceleration time (DT)	- As above for acquisition of mitral inflow profile - Measure time from peak E wave along leading edge of spectral waveform to zero baseline	- Highly feasible - Established and familiar parameter in clinical practice - Large database of haemodynamic and prognostic validation	- Variable inter- and intra-observer variability - E/A fusion at high rates - Confounded/influenced by mitral valve disease and preload
Early diastolic tissue velocity (e′)	- Apical four-chamber view - 5–10 mm PW Doppler sample volume at lateral and septal basal segments - Optimise gain/filter to minimise spectral broadening signal gain.	- Highly feasible and reproducible. - Less load dependent than other Doppler parameters	- Fusion with late tissue velocities at high heart rates - Limited accuracy in patients with regional dysfunction in the sampled segments, MAC, surgical rings or prosthetic mitral valves and pericardial disease. - Need to sample at least two sites - Different cut-offs depending on sampling site - Decreases with ageing.
Mitral E/e′ ratio	MV E velocity divided by mitral annular e′ velocity	- Feasible and reproducible. - Haemodynamic validation against invasively measured LVFP at rest and post exercise demonstrated in several studies	- Reduced accuracy in normal subjects, patients with heavy MAC, significant mitral valve and pericardial disease, regional dysfunction in sampled segments. - ''Grey zone'' of values in which LV filling pressures are indeterminate. - Different cut-offs depending on sampling site. - Conflicting results in haemodynamic validation studies
Tricuspid Regurgitation Velocity (TRV)	- Parasternal RV inflow view and apical four-chamber view	- Systolic PASP useful as an adjunctive indirect measure of LVFP.	- Indirect estimate of LVFP. - Elevation with exercise can be caused by lung disease

Table 1. (continued).

Parameter	Acquisition/Analysis	Advantages	Disadvantages
	- Highest Doppler velocity obtained with CW. - Optimise gain and contrast to display complete spectral envelope without spectral broadening	- Evidence of pulmonary hypertension has prognostic implications.	- Complete TR signal not feasible in around 1/3 of patients - Increase in TRV normal physiological response in healthy athletes - Less reliable in severe TR
Pulmonary Venous Inflow velocities (S/D/Ar)	- Apical four-chamber with colour flow imaging to help position pulsed Doppler sample volume (1–3 mm axial size). - Sample volume placed at 1–2 cm depth into right (or left) upper PV. - Use low wall filter setting (100–200 MHz) and low signal gain. - Optimised spectral waveforms should not display signal spikes or feathering.	- Reasonably feasible and reproducible - Increasing feasibility with modern machines - Established and familiar parameter in clinical practice	- Low feasibility on older machines - Confounded/ influenced by mitral regurgitation and atrial fibrillation
Pulmonary Venous Inflow A reversal velocity and duration (PV Adur)	- As above for pulmonary venous inflow velocities	- Sensitive marker of elevated end-diastolic pressure - Useful as early marker of elevated LVFP	- Low feasibility - Variability in measurement - Not available in atrial fibrillation
Left Atrial Volume Indexed to body surface area (LAVI)	- Apical four and two chamber views - Measured at end ventricular systole - LA endocardium traced out excluding pulmonary vein orifices, left atrial appendage, mitral valve inlet - Simpson's biplane volumes derived by on-cart disc summation algorithm	- Highly feasible and reproducible - Large body of supporting literature for cut-offs - Large body of prognostic validation data	- May be underestimated - Confounded/influenced by mitral valve disease, atrial cardiomyopathies

Abbreviations: RV, right ventricular; LVFP, left ventricular filling pressure; TR, tricuspid regurgitation; PASP, pulmonary artery systolic pressure; MV E, mitral valve E-wave velocity; MAC, mitral annular calcification; PW, pulsed-wave.

Figure 1 2009 ASE/EAE Guidelines: Estimation of Filling Pressures in Patients with Normal EF.
Abbreviations: LA, left atrial; PAS, pulmonary artery systolic pressure; LAP, left atrial pressure; EF, ejection fraction; ASE, American Society of Echocardiography; EAE, European Association of Echocardiography.
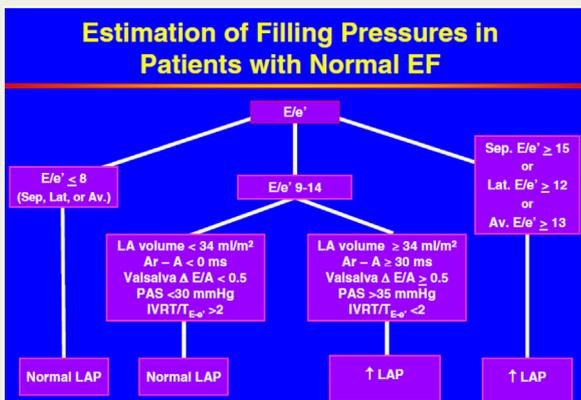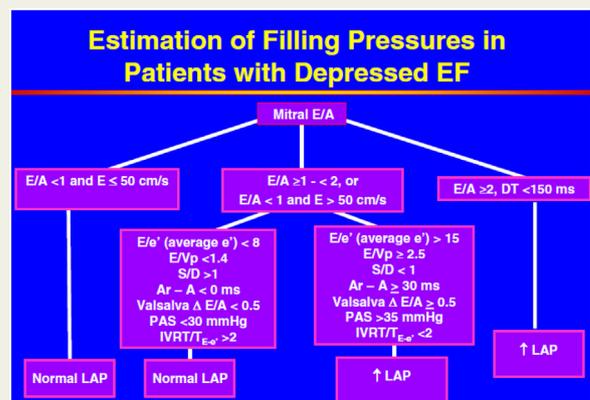

Figure 2 2009 ASE/EAE Guidelines: Estimation of Filling Pressures in Patients with Reduced EF.
Abbreviations: LAP, left atrial pressure, IVRT/T; ASE, American Society of Echocardiography; EAE, European Association of Echocardiography; EF, ejection fraction; IVRT/T, isovolumic relaxation time.
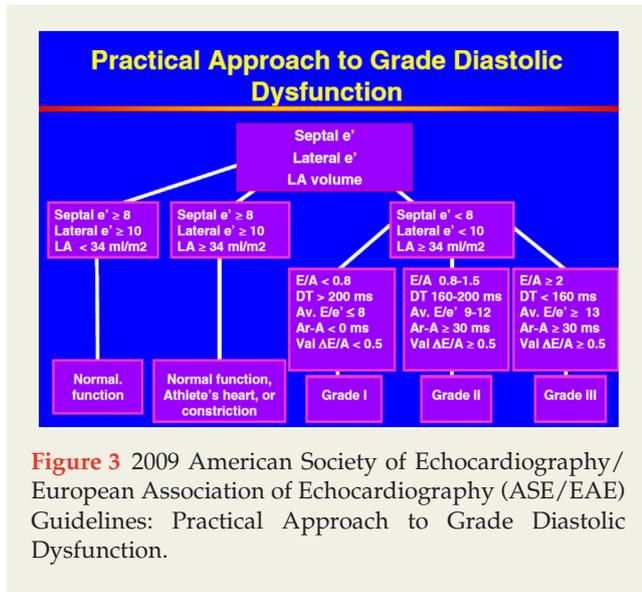
Figure 3 2009 American Society of Echocardiography/ European Association of Echocardiography (ASE/EAE) Guidelines: Practical Approach to Grade Diastolic Dysfunction.
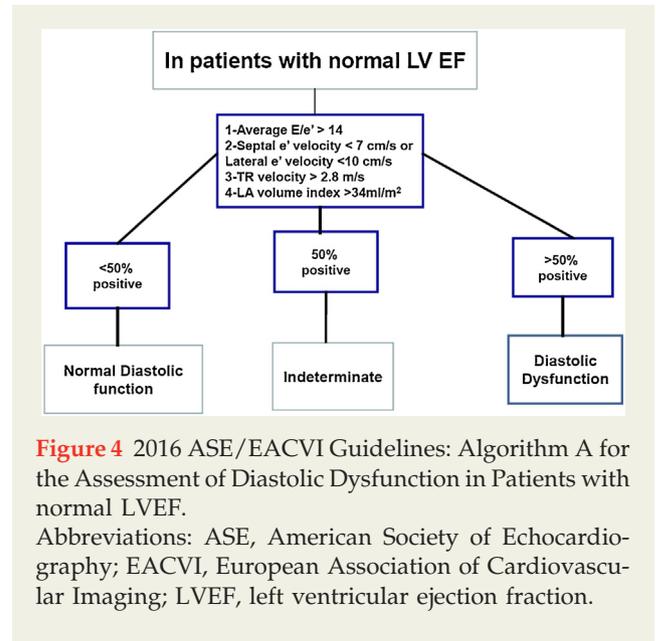

Figure 4 2016 ASE/EACVI Guidelines: Algorithm A for the Assessment of Diastolic Dysfunction in Patients with normal LVEF.
Abbreviations: ASE, American Society of Echocardiography; EACVI, European Association of Cardiovascular Imaging; LVEF, left ventricular ejection fraction.

ASE/EACVI Guidelines: Variation from Previous Approaches

As illustrated in the preceding discussion, the 2016 ASE/ EACVI guidelines represent a significant variation from the traditional comprehensive approach as well as the 2009 ASE/ EAE guidelines [1,4]. Compared to 2009 guidelines, the 2016 guidelines omit a number of previously validated parameters, many of which were linked to prognosis, with a reduction in the number of included variables from 10 in the 2009 guidelines to four in algorithm A and six in algorithm B by using a stepped approach. Many commonly measured and validated variables such as mitral inflow E-wave

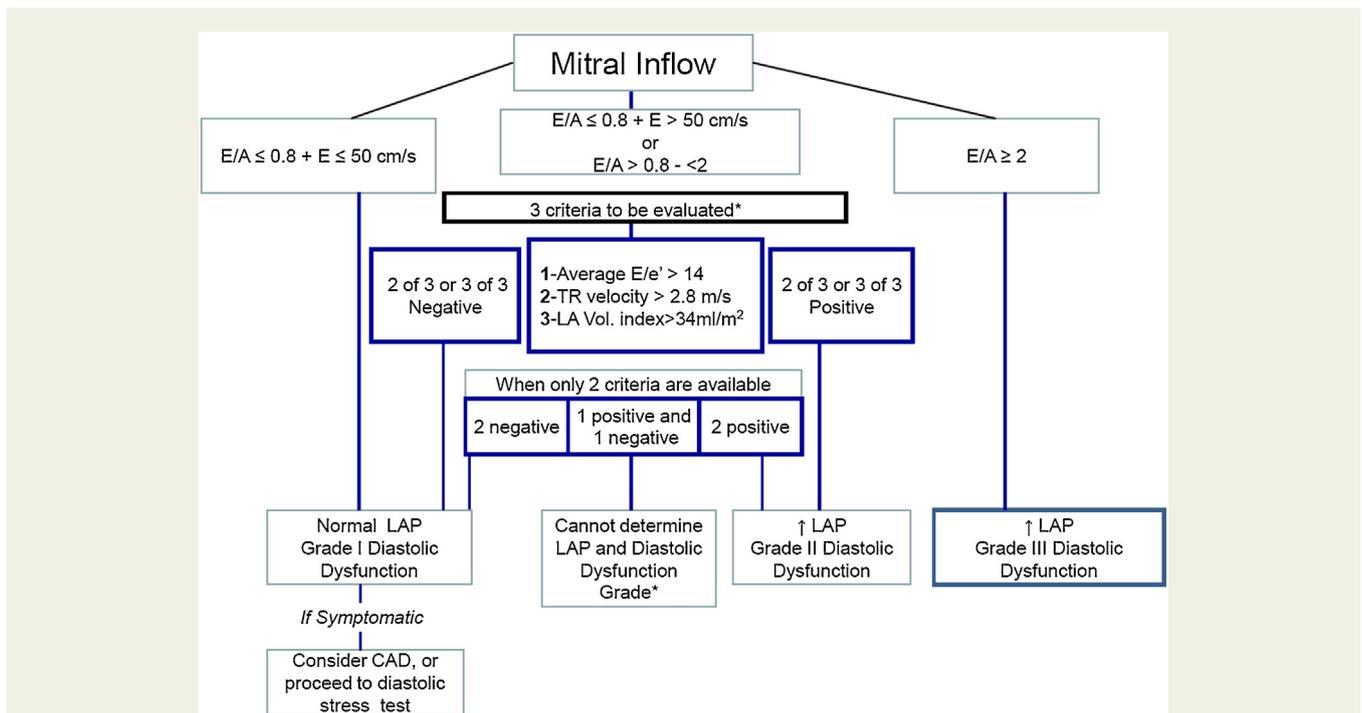**Figure 5** 2016 ASE/EACVI Guidelines: Algorithm B for estimation of LV filling pressures and grading LV diastolic function in patients with depressed LVEFs and patients with myocardial disease and normal LVEF after consideration of clinical and other 2D data.
Abbreviations: ASE, American Society of Echocardiography; EACVI, European Association of Cardiovascular Imaging; LV, left ventricular; LVEF, left ventricular ejection fraction.

deceleration time, mitral inflow A wave duration, as well as pulmonary venous inflow velocities and derivative data (S, D and A waves, S/D ratio, pulmonary A wave duration and the derived mitral to pulmonary A duration difference) have been removed. The Valsalva manoeuvre to distinguish normal from pseudonormal filling patterns, or to further evaluate restrictive filling, has also been omitted. Other parameters that were less commonly used in routine clinical practice but were included in the 2009 algorithms have also been removed, including flow propagation velocity (Vp) as well as the ratio of the isovolumic relaxation time to times to onset of mitral annular e' wave (Te') and times to onset of mitral E wave (T-E) (IVRT/Te'–E). The assessment of right heart haemodynamics has been downgraded from a formal assessment of right ventricular systolic pressure (RVSP) to simply evaluating TRV.

Haemodynamic Validation of 2016 ASE/EACVI Guidelines

Following the release of the 2016 guidelines, four well designed studies have provided haemodynamic validation of the proposed algorithms [7–10]. The primary results of these are summarised in Table 2, and key points highlighted below. In the multicentre EACVI Euro-Filling study, Lancellotti et al. examined the correlation between simultaneously measured LV end-diastolic pressure (LVEDP) and diastolic function assessed by echocardiography in 159 patients [8]. Using an LVEDP >15 mmHg to signify raised LVFP, the 2016

algorithms were shown to be superior to the 2009 algorithms, having a sensitivity of 75% and a specificity of 74%, compared to the 2009 approach which had a sensitivity of 43% and specificity of 75%. In another multicentre study, Andersen et al. reviewed the accuracy and incremental value of diastolic dysfunction and LVFP assessed using the 2016 ASE/EACVI algorithms against invasively measured LVFP (pulmonary capillary wedge pressure in the majority) [10]. Aggregate assessment of diastolic function using the 2016 algorithms had a sensitivity of 87%, specificity of 88% and overall accuracy of 87% for predicting raised LVFP, and were superior to clinical assessment for detecting elevated LVFP [10]. Sato et al. studied the reliability of updated 2016 algorithms for predicting LVFP in 460 patients who underwent echocardiography and subsequent left heart catheterisation for determination of LVEDP within 24 hours [9]. The 2016 ASE/EACVI algorithms were shown to have better discriminatory power for predicting LVEDP (p < 0.001) than the 2009 ASE/EAE algorithms as measured by net reclassification index and area under the curve for receiver operating curves [9]. More recently, Balaney et al. performed a head-to-head comparison between the 2009 ASE/EAE guidelines and 2016 ASE/EACVI guidelines for correlation with invasively measured LVFP in 90 patients [7]. A LV pre-atrial contraction pressure of >12 mmHg was defined as elevated. The 2016 algorithms had a sensitivity of 69% and a specificity of 81%, compared to the 2009 algorithms which had a sensitivity of 79% and a specificity of 70%. The authors concluded that the increased simplicity and ease of use of the new guidelines did not compromise accuracy compared to the 2009 guidelines

Table 2 Haemodynamic validation studies of 2016 ASE/EACVI Guidelines using correlation between invasive measures obtained at cardiac catheterisation and Doppler echocardiography.

Study	N	Invasive LVFP measure	Sens	Spec	PPV	NPV	Accuracy	Conclusions
Lancellotti et al. [8]	159	LVEDP >15 mmHg	75%	74%	39%	93%	-*	2016 ASE/EACVI algorithms superior to 2009 ASE/EAE algorithms in head to head comparison
Andersen et al. [10]	450	PCWP or Pre-A Pressure >12 mmHg	87%	88%	91%	83%	87%	Echocardiographic assessment of diastolic function and LVFP with 2016 ASE/EACVI algorithms are highly feasible and accurate, and incremental to clinical assessment.
Balaney et al. [7]	90	Pre-A Pressure >12 mmHg	69	81	77	77	75%	2016 ASE/EACVI algorithms comparable to 2009 ASE/EAE algorithms in head to head comparison despite simplification.
Sato et al. [9]	460	LVEDP > 16 mmHg	-*	-*	-*	-*	-*	2016 ASE/EACVI algorithms had greater discriminatory power for elevated LVEDP > 16 mmHg as measured by net reclassification index and area under curve of receiver operating curves.

Pre-A: left ventricular pre-atrial contraction pressure.

Abbreviations: LVEDP, left ventricular end-diastolic pressure; PCWP, pulmonary capillary wedge pressure; ASE, American Society of Echocardiography; EACVI, European Association of Echocardiography Imaging.

*not reported.

[7]. Of note, all studies uniformly demonstrated that not all guideline recommended parameters have an equal correlation with LVFP, and the aggregate assessment with guideline recommended algorithms outperforms individual parameters.

Prognostic Validation of 2016 ASE/EACVI Guidelines

A number of studies have also reported on the prognostic significance of adopting the current guideline recommendations, as summarised in Table 3 [9]. Sato et al., in addition to examining the correlation with LVFP as discussed in the preceding section, also studied the relative prognostic value of diastolic dysfunction grading using the 2016 ASE/EACVI algorithms compared to the 2009 ASE/EAE algorithms and demonstrated superior correlation with all-cause mortality at a median follow-up of 416 days using the 2016 algorithms [9]. Prasad et al. compared the prognostic value of significant diastolic dysfunction (grade II or III diastolic dysfunction) assessed by the 2016 guidelines compared to the 2009 guidelines in 419 consecutive patients with a first presentation of myocardial infarction (MI) [11]. The primary outcome measure was composite major adverse cardiac events comprising

death, myocardial infarction and heart failure. On multivariate Cox proportional hazards analysis that incorporated significant clinical predictors and LVEF, significant diastolic dysfunction assessed with the 2016 algorithms was the strongest independent predictor of outcome (HR 2.22 [CI 1.25–3.98]; p = 0.007), whereas significant diastolic dysfunction assessed using the 2009 algorithms was not an independent predictor (HR 1.63 [CI 0.95–2.80]; p = 0.074) [11]. Sanchis et al. studied 157 patients with suspected heart failure attending a heart failure clinic with echocardiography and serum BNP performed at first evaluation, and showed that reclassification of these patients using the 2016 ASE/EACVI guideline resulted in a significantly better prognostic stratification compared to the 2009 guidelines by Kaplan-Meier analysis [12]. Asami et al. studied the impact of diastolic dysfunction graded using the 2016 ASE/EACVI algorithms on clinical outcomes in 777 patients with aortic stenosis after transcatheter aortic valve replacement and demonstrated a graded influence on 12-month mortality of different diastolic dysfunction grades: grade I HR 2.36 [CI 1.17–4.74], grade II HR 2.58 [CI 1.42–4.66], and grade III HR 4.41 [CI: 2.37–8.20] [13].

Of note, not all guideline recommended parameters have an equal correlation with outcomes, and the aggregate assessment with guideline recommended algorithms outperforms individual parameters in all the studies discussed

Table 3 Studies investigating relationship between diastolic dysfunction assessed by 2016 ASE/EACVI diagnostic algorithms and outcomes.

Study	N	Study Population	Main outcome measure	Median follow-up	Results
Sato et al. [9]	460	Patients undergoing elective cardiac catheterisation and echocardiography within 24 hours	All-cause mortality	419 days	2016 ASE/EACVI guideline algorithms better predictor of all-cause mortality than either the 2009 ASE/EAE algorithms or individual guideline recommended parameters
Prasad et al. [11]	419	Patients with first-ever myocardial infarction; echocardiography within 24 hours of admission	MACE (death/MI/HF)	2 years	2016 ASE/EACVI guideline algorithms better predictor of MACE (and all-cause mortality) than either the 2009 ASE/EAE algorithms or individual guideline recommended parameters
Sanchis et al. [12]	157	Patients with suspected heart failure attending a 'one stop' heart failure clinic	MACE (death/ HF readmission)	65 months	Higher event rates with classification with 2016 ASE/EACVI guidelines compared to 2009 ASE/EAE guidelines. Kaplan-Meier curves showed significant differences in survival curves with 2016 classification but not 2009 classification.
Asami et al. [13]	777	Patients with severe aortic stenosis undergoing TAVR	All-cause mortality	12 months	Diastolic dysfunction grades I-III according to 2016 ASE/EACVI guidelines were independent predictors of 1-year mortality, with increasing hazard with increasing grade of diastolic dysfunction.

Abbreviations: Ex E/e', exercise E/e'; HFpEF, heart failure with preserved ejection fraction; CV, cardiovascular; AF, atrial fibrillation; MACE, major adverse cardiac events; TAVR, transcatheter aortic valve replacement; EAE, European Association of Cardiography; ASE, American Society of Echocardiography; EACVI, European Association of Cardiovascular Imaging.

above. Subsequently, Nauta et al. performed a systematic review of the correlation between guideline recommended diastolic parameters and outcomes in patients with heart failure with preserved ejection fraction (HFpEF), and showed that the E/e' was the most predictive parameter in these patients [14].

Clinical Impact of 2016 ASE/EACVI Guidelines

The clinical impact of the new guidelines has been examined in a few studies focussed on prevalence of diastolic function with new algorithms, improvements in inter-observer variability, and classification of heart failure patients. Almeida et al. studied the impact of the 2016 ASE/EACVI recommendations compared with the 2009 guidelines on the prevalence and grades of diastolic dysfunction in a general population cohort (n = 1,000) with preserved systolic function (LVEF > 50%) and found that the prevalence of diastolic dysfunction was only 1.6% using the 2016 guidelines compared to 38.1% using the 2009 guidelines [15]. The concordance between the two guidelines was also noted to be poor, and the authors raised the concern that the updated algorithms might only diagnose the most advanced cases. Huttin et al. also reported on the impact of changes in consensus diagnostic recommendations on the echocardiographic prevalence of diastolic dysfunction by reclassifying 1,485 patients with LVEF > 50% in a community-based cohort according to both the 2009 and 2016 recommendations [16]. Only 1.3% were classified as having diastolic dysfunction using the 2016 criteria, whereas 5.9% had diastolic dysfunction according to the 2009 guidelines, raising further concerns about variability in the calculated prevalence of diastolic dysfunction between the 2009 and 2016 recommendations.

With respect to inter-observer variability in clinical practice, the Diastolic Function Assessment Collaborators investigated the impact of applying the new 2016 guidelines on accuracy and interobserver variability in four groups of assessors, including senior cardiologists, fellows in training, experienced sonographers, and general cardiology fellows [17]. Invasively measured filling pressures were used as the gold standard. A high level of sensitivity for elevated LVFP using the 2016 algorithms was noted with values of 92% for senior cardiologists, 91% for fellows in training, 88% for experienced sonographers, and 91% for general cardiology fellows. High levels of inter-observer agreement were also noted for the four groups, with Fleiss K-values of 0.80, 0.94, 0.76 and 0.89 respectively. This data suggests a high level of inter-observer agreement and accuracy with assessment of LV diastolic function using the 2016 ASE/EACVI guidelines, irrespective of the experience level of the observer [17].

In addition to examining the prognostic value of the classification of patients with suspected heart failure with the 2009 and 2016 diagnostic algorithms as discussed above, Sanchis et al. also investigated the impact of utilising the 2016 diagnostic algorithms on B-type natriuretic peptide (BNP) levels and the final proportion of patients with a clinical heart failure diagnosis [12]. Patients with suspected heart failure attending a heart failure clinic were screened with echocardiography and serum BNP levels at the initial evaluation [12]. A majority of patients were initially classified as grade I diastolic dysfunction using the 2009 algorithms, but 49% of these were reclassified as having normal diastolic function using the 2016 diagnostic algorithms. The patients reclassified as having normal diastolic function using the 2016 algorithms were noted to have lower BNP levels and a lower proportion of clinical heart failure diagnosis. The authors concluded that classification of suspected heart failure patients using the 2016 ASE/EACVI guideline algorithms achieved a more accurate classification of patients in relation to BNP levels and heart failure diagnosis compared to the 2009 ASE/EAE guidelines [12]. Although compelling, it should be noted that BNP is a measure of heart failure, which is not the equivalent of diastolic dysfunction, although clearly may be the clinical consequence of diastolic dysfunction.

Diastolic Stress Echocardiography

The 2016 ASE/EACVI guidelines provide the strongest recommendations and guidance to date about the use of diastolic stress echocardiography in patients with suspected heart failure with preserved ejection fraction [18]. Whilst there are no published data on the increased uptake of this technique following the publication of the 2016 guidelines, it is worth noting that the European Society of Echocardiography guidelines for the diagnosis and treatment of acute and chronic heart failure [19], as well as the National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand guidelines for the prevention, detection, and management of heart failure, both provide positive recommendations about using diastolic stress echocardiography in clinical practice in line with the 2016 ASE/EACVI diastology guidelines [20]. Diastolic stress echocardiography has diagnostic [21] and prognostic value [22,23], and is of particular use in patients with exertional symptoms but normal or indeterminate diastolic function at rest [24]. The incorporation of diastolic exercise testing in future guidelines may assist in the diagnosis and identification of select patients who do not meet criteria for haemodynamically significant diastolic dysfunction at rest.

Limitations of 2016 ASE/EACVI Guidelines

The latest iteration of the guidelines is limited by a number of issues. Using the algorithms proposed, around 10–30% of patients have 'indeterminate' diastolic function [4]. This occurs when only two (of three) criteria are available for the second step in the diagnostic algorithm, with one positive and one negative criteria. Whilst the four key parameters

have been assigned equal weight in determining diastolic function, a number of recent studies have shown that the four key criteria do not have an equal correlation with either LVFP or with outcomes [8,11]. Future iterations of guidelines will have to consider weighted scores with more emphasis on parameters with more robust haemodynamic and prognostic associations such as the E/e' ratio, which appears to have the greatest non-invasive prediction of invasively-determined LVFP.

It is worth noting that TRV is an excellent surrogate for pulmonary hypertension, but pulmonary hypertension is not a surrogate of diastolic dysfunction. Pulmonary hypertension may arise as a result of diastolic dysfunction, but it may also arise in other pathologies such as mitral valve disease or pulmonary pathology. Furthermore, TRV is not available in 30–50% of unenhanced transthoracic echocardiograms, which limits the full application of the algorithms in a significant proportion of patients. Thus, using TRV as a significant marker of diastolic dysfunction is complicated.

The 'old' way of assessing diastolic function was to consider the filling pattern (based on E:A ratio and deceleration time with Valsalva if needed) and the filling pressure (based on E/e') and the chronicity of diastolic dysfunction (based on left atrial volume). Both filling pattern and E/e' are somewhat labile, however, and affected by clinical and fluid status. An additional omission is the removal of grade Ib diastolic dysfunction from the 2016 guidelines, which previously identified abnormal relaxation with elevated left ventricular end diastolic pressure, which is potentially identifying at-risk unstable patients transitioning between mild and moderate diastolic dysfunction. Furthermore, an E/A ratio >2 is previously used as the sole arbiter of severe diastolic dysfunction based on many studies showing it is an independent prognostic marker, but studies have shown that, whilst this has a high specificity for elevated LVFP, this comes at the cost of a reduced sensitivity [25] and is outperformed by more modern markers. Despite established data demonstrating age-dependent deterioration in diastolic dysfunction [26], standardised cut-offs for specific age groups have not been employed in current guidelines, adopting a 'one size fits all' approach to the way diastolic parameters and algorithms are applied. Furthermore, novel resting diastolic parameters have not been incorporated into the diagnostic algorithms. In particular, left atrial strain and global longitudinal strain have shown promise as parameters for future clinical application [27–29].

Conclusions

The 2016 ASE/EACVI guidelines on the assessment of diastolic function sought to simplify the determination of diastolic dysfunction by recommending a streamlined approach with a focus on four key variables. Haemodynamic validation using simultaneous cardiac catheterisation and echocardiographic assessment of diastolic function have shown robust prediction of LVFP using the streamlined 2016

ASE/EACVI algorithms, with favourable comparisons to the 2009 algorithms. Similarly, prognostic validation data demonstrates that the 2016 algorithms are favourable for prediction of clinical outcomes. Furthermore, the updated guidelines are easier to use in clinical practice, have improved inter-observer agreement across a broad range of observer experience, and improve classification of heart failure patients. Although this simpler approach is useful and more reproducible, this simplicity has, by necessity, excluded some of the more advanced understanding and differentiation of diastolic physiology. Of note, the higher specificity of these guidelines has led to a lower calculated prevalence of diastolic dysfunction in large community-based cohorts and the impact of this will only be determined in longitudinal studies. Further refinement of the updated 2016 guidelines by inclusion of new diastolic parameters and assessments involving exercise echocardiography are encouraged based on the evidence-base.

Acknowledgements

References

[1] Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr 2009;22:107–33.

[2] Dokainish H, Nguyen JS, Bobek J, Goswami R, Lakkis NM. Assessment of the American Society of Echocardiography-European Association of Echocardiography Guidelines for diastolic function in patients with depressed ejection fraction: an echocardiographic and invasive haemodynamic study. Eur J Echocardiogr 2011;12:857–64.

[3] Unzek S, Popovic ZB, Marwick TH. Diastolic Guidelines Concordance Investigators. Effect of recommendations on interobserver consistency of diastolic function evaluation. JACC Cardiovasc Imaging 2011;4:460–7.

[4] Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, Dokainish 3rd H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2016;29:277–314.

[5] Oh JK, Appleton CP, Hatle LK, Nishimura RA, Seward JB, Tajik AJ. The noninvasive assessment of left ventricular diastolic function with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 1997;10:246–70.

[6] Nagueh SF, Bhatt R, Vivo RP, Krim SR, Sarvari SI, Russell K, et al. Echocardiographic evaluation of hemodynamics in patients with decompensated systolic heart failure. Circ Cardiovasc Imaging 2011;4:220–7.

[7] Balaney B, Medvedofsky D, Mediratta A, Singh A, Ciszek B, Kruse E, et al. Invasive validation of the echocardiographic assessment of left ventricular filling pressures using the 2016 diastolic Guidelines: head-to-head comparison with the 2009 Guidelines. J Am Soc Echocardiogr 2018;31:79–88.

[8] Lancellotti P, Galderisi M, Edvardsen T, Donal E, Goliasch G, Cardim N, et al. Echo-Doppler estimation of left ventricular filling pressure: results of the multicentre EACVI Euro-Filling study. Eur Heart J Cardiovasc Imaging 2017;18:961–8.

[9] Sato K, Grant ADM, Negishi K, Cremer PC, Negishi T, Kumar A, et al. Reliability of updated left ventricular diastolic function recommendations in predicting elevated left ventricular filling pressure and prognosis. Am Heart J 2017;189:28–39.

[10] Andersen OS, Smiseth OA, Dokainish H, Abudiab MM, Schutt RC, Kumar A, et al. Estimating left ventricular filling pressure by echocardiography. J Am Coll Cardiol 2017;69:1937–48.

[11] Prasad SB, Lin AK, Guppy-Coles KB, Stanton T, Krishnasamy R, Whalley GA, et al. Diastolic dysfunction assessed using contemporary guidelines and prognosis following myocardial infarction. J Am Soc Echocardiogr 2018;31:1127–36.

[12] Sanchis L, Andrea R, Falces C, Poyatos S, Vidal B, Sitges M. Differential clinical implications of current recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr 2018;31:1203–8.

[13] Asami M, Lanz J, Stortecky S, Räber L, Franzone A, Heg D, et al. The impact of left ventricular diastolic dysfunction on clinical outcomes after transcatheter aortic valve replacement. J Am Coll Cardiol Cardiovasc Interv 2018;26:593–601.

[14] Nauta JF, Hummel YM, van der Meer P, Lam CSP, Voors AA, van Melle JP. Correlation with invasive left ventricular filling pressures and prognostic relevance of the echocardiographic diastolic parameters used in the 2016 ESC heart failure guidelines and in the 2016 ASE/EACVI recommendations: A systematic review in patients with heart failure with preserved ejection fraction. Eur J Heart Fail 2018;20:1303–11.

[15] Almeida JG, Fontes-Carvalho R, Sampaio F, Ribeiro J, Bettencourt P, Flachskampf FA, et al. Impact of the 2016 ASE/EACVI recommendations on the prevalence of diastolic dysfunction in the general population. Eur Heart J Cardiovasc Imaging 2018;19:380–6.

[16] Huttin O, Fraser AG, Coiro S, Bozec E, Selton-Suty C, Lamiral Z, et al. Impact of changes in consensus diagnostic recommendations on the echocardiographic prevalence of diastolic dysfunction. J Am Coll Cardiol 2017;69:3119–21.

[17] Nagueh SF, Abraham TP, Aurigemma GP, Bax JJ, Beladan C, Browning A, et al. Interobserver variability in applying American Society of Echocardiography/European Association of Cardiovascular Imaging 2016 Guidelines for estimation of left ventricular filling pressure. Circ Cardiovasc Imaging 2019;12.

[18] Nagueh SF, Smiseth OA, Appleton CP, Byrd BFr, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 2016;17:1321–1360.

[19] Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016;37:2129–200.

[20] Atherton JJ, Sindone A, De Pasquale CG, Driscoll A, MacDonald PS, Hopper I, et al. National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand: guidelines for the prevention, detection, and management of heart failure in Australia 2018. Heart Lung Circ 2018;27:1123–208.

[21] Holland DJ, Prasad SB, Marwick TH. Contribution of exercise echocardiography to the diagnosis of heart failure with preserved ejection fraction (HFpEF). Heart 2010;96:1024–8.

[22] Holland DJ, Prasad SB, Marwick TH. Prognostic implications of left ventricular filling pressure with exercise. Circ Cardiovasc Imaging 2010;3:149–56.

[23] Kosmala W, Przewlocka-Kosmala M, Rojek A, Mysiak A, Dabrowski A, Marwick TH. Association of abnormal left ventricular functional reserve with outcome in heart failure with preserved ejection fraction. JACC Cardiovasc Imaging 2017;11:1747–9.

[24] Prasad SB, Holland DJ, Atherton JJ. Diastolic stress echocardiography: from basic principles to clinical applications. Heart 2018;104:1739–48.

[25] Giannuzzi P, Imparato A, Temporelli PL, de Vito F, Silva PL, Scapellato F, et al. Doppler-derived mitral deceleration time of early filling as a strong predictor of pulmonary capillary wedge pressure in postinfarction patients with left ventricular systolic dysfunction. J Am Coll Cardiol 1994;23:1630–7.

[26] Klein AL, Burstow DJ, Tajik AJ, Zachariah PK, Bailey KR, Seward JB. Effects of age on left ventricular dimensions and filling dynamics in 117 normal persons. Mayo Clinic Proceedings 1994;69:212–24.

[27] Singh AAK, Maffessanti F, Mor-Avi V, Lang RM. LA strain for categorization of LV diastolic dysfunction. JACC Cardiovasc Imaging 2017;10:735–43.

[28] Wang J, Khoury DS, Thohan V, Torre-Amione G, Nagueh SF. Global diastolic strain rate for the assessment of left ventricular relaxation and filling pressures. Circulation 2007;115:1376–83.

[29] Tan YTWF, Lee E, Heatlie G, Leyva F, Patel K, Frenneaux M, et al. The pathophysiology of heart failure with normal ejection fraction: exercise echocardiography reveals complex abnormalities of both systolic and diastolic ventricular function involving torsion, untwist, and longitudinal motion. J Am Coll Cardiol 2009;54:36–46.