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SPECIAL ISSUE: NONINVASIVE ASSESSMENT OF LEFT VENTRICULAR DIASTOLIC FUNCTION

EDITORIALS AND VIEWPOINTS: DEBATES IN IMAGING

The 2016 Diastolic Function Guideline

Is it Already Time to Revisit or Revise Them?

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A Proposal For Modifications To The Current Diastolic Function Guideline

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Determination of diastolic function is an integral part of an echocardiography examination, especially in patients with symptoms of heart failure. To standardize the evaluation of diastolic function, the American Society of Echocardiography (ASE)/European Association of Cardiovascular Imaging (EACVI) diastolic function working group published recommendation guidelines in 2009 and 2016 (1). In the 2009 guideline, 9 parameters were listed in 3 algorithms; and in the 2016 guideline document, 4 primary parameters were recommended for initial evaluation: early diastolic mitral annulus velocity (e'), ratio between early diastolic mitral inflow velocity (E) and e' (E/e'), left atrial volume index (LAVI), and tricuspid regurgitation (TR) velocity. The 2016 guideline recommended 2 separate algorithms: algorithm A for patients with preserved left ventricular ejection fraction (LVEF) (≥50%) and unknown diastolic function, primarily for separating normal from abnormal diastolic function; and algorithm B for patients with reduced LVEF (<50%) or with preserved LVEF and known or suspected diastolic dysfunction (DD), designed for estimating left ventricular (LV) filling pressure and grading diastolic function. The 2016 guideline emphasized the specificity for detecting DD. In selected patients who were referred to cardiac catheterization, assessment of filling pressure according to the 2016 guideline was shown to be reliable and interobserver variability was excellent (2). However, its sensitivity for detecting DD (especially grade 1) markedly decreased. Almeida et al. (3) showed that the incidence of DD in 1,000 individuals (mean age of 62 years) was 1.4% based on the 2016 guideline compared to 38.1% based on the 2009 guideline.

In addition, the 2016 guideline recommended adjudication of DD based on clinical history or imaging data in the algorithm B. However, individuals with those predisposing conditions (hypertension, diabetes mellitus, and coronary artery disease) can have normal diastolic function especially when they are young. The 2016 guideline was carefully crafted and reviewed additionally by an external group, but our clinical experience with the 2016 guideline for the last 3 years has identified several areas which can be improved. Herein, we propose the combination of 2 algorithms to 1 unified algorithm with several modifications to make it easier to assess diastolic function without changing the basic parameters.

ISSUES WITH THE 2016 GUIDELINE. Although the 2016 guideline attempted to simplify the assessment

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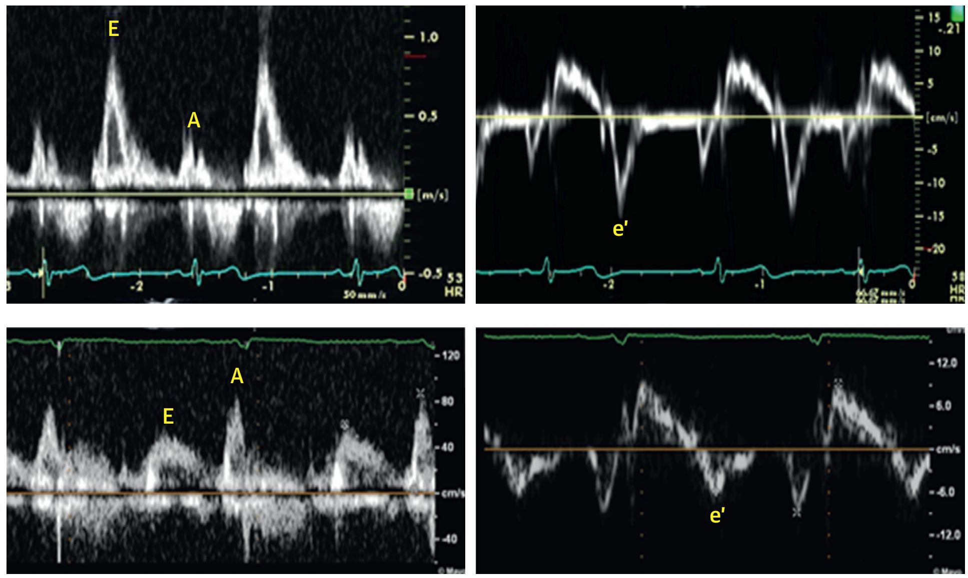
FIGURE 1 **Normal Diastolic Function of 2 Different Mitral Inflow and Annulus Velocity Patterns**

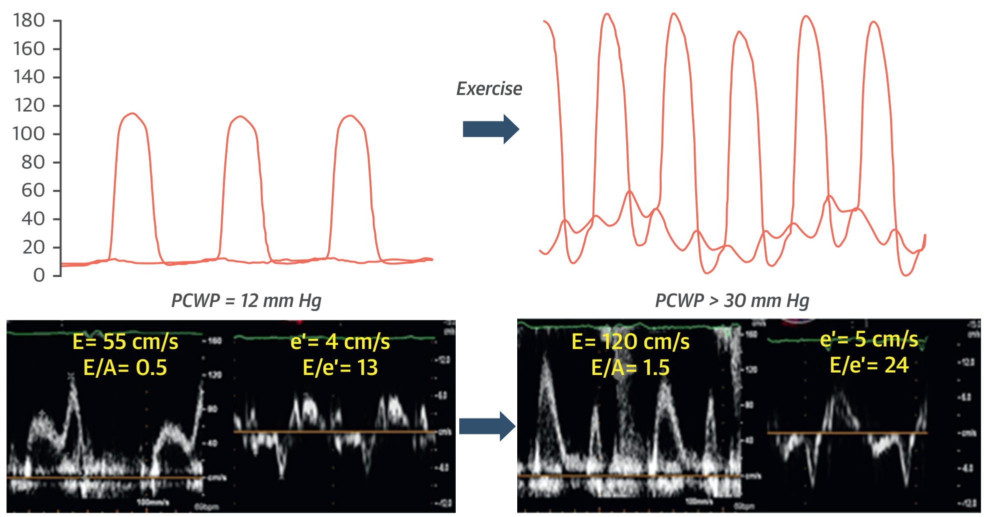


Mitral inflow **(left)** and septal mitral annulus **(right)** velocities from 2 individuals with normal diastolic function according to the 2016 guideline. The **upper panel** was from a healthy 23-year-old patient with a predominant early diastolic filling (E/A = 3) and normal e' of 14 cm/s and E/e' of 6.4 cm/s. The **lower panel** was from 77-year-old asymptomatic woman with a predominant late filling (E/A= 0.5) and abnormal relaxation with e' of 6 cm/s and E/e' of 6.7. If the latter patient has a condition labeled as a risk for diastolic dysfunction, the same echo-Doppler findings are classified as grade 1 dysfunction.

of diastolic function, the following issues and consequences have emerged:

1. In algorithm A for the patients with preserved LVEF and uncertain diastolic function, the normal diastolic function category can include both the truly normal population and patients with reduced myocardial relaxation with normal filling pressure, previously categorized as grade 1 dysfunction (**Figure 1**). The 2016 guideline adopted normal diastolic function values from the oldest asymptomatic group in the NORRE study (4) and advocated that the aging-related diastolic pattern with reduced LV relaxation should be graded as normal as long as there is no underlying condition predisposing to DD. A substantial subset of patients with heart failure with preserved ejection fraction has increased diastolic filling pressure only with exertion (**Figure 2**) (5,6). In these patients, the only abnormal parameter at rest may be reduced e' velocity with grade 1 pattern, which has increased mortality, but can be classified as normal (7,8). Moreover, younger patients with an early stage of cardiomyopathy can be classified as normal when there is clearly grade 1 dysfunction (**Figure 3**).
2. Three of 4 parameters (increased E/e', LAVI, and TR velocity) in algorithm A are associated not only with DD, but also with increased LV filling pressure. However, the 2016 guideline classifies patients with ≥3 abnormal parameters as abnormal diastolic function, and algorithm B is used for assessing filling pressure.
3. Adjudication of DD by clinical and/or 2-dimensional (2-D) echocardiographic data (LVEF < 50%, hypertension, diabetes mellitus, coronary artery disease, or increased wall thickness) may not be reliable or available. This approach has a potential for falsely making one's diastolic function worse than what truly is since some (especially young) subjects with those conditions associated with DD can have normal diastolic function (**Figure 4**). This potential false-positive assessment when E/A >2 in young individuals was alerted in the 2016 guideline which recommended to verify the presence of normal diastolic function by e' velocity (1). It is more reliable and standardized to define the basic component of DD as reduced or impaired myocardial relaxation, using mitral annulus e' velocity as a screening for relaxation status in most patients without exceptions listed below.

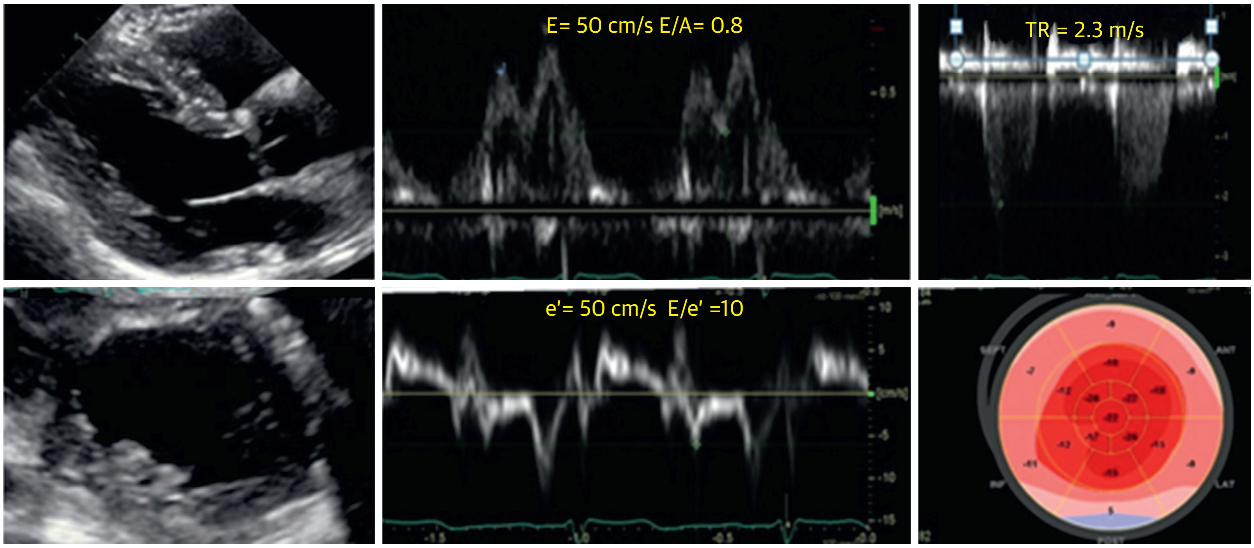
FIGURE 2 **Invasive and Echocardiography Diastolic Exercise Tests**



(Upper) Left ventricular and pulmonary capillary wedge pressure (PCWP) tracing at rest **(left)** and with exercise **(right).** PCWP was normal at rest and increased markedly with exercise. **(Lower)** Mitral inflow and annulus velocities at rest **(left)** and with exercise **(right).** E/e' was upper normal at rest and rose from 13 to 24 with a minimal increase in e' velocity, indicating marked elevation of filling pressure with exercise.

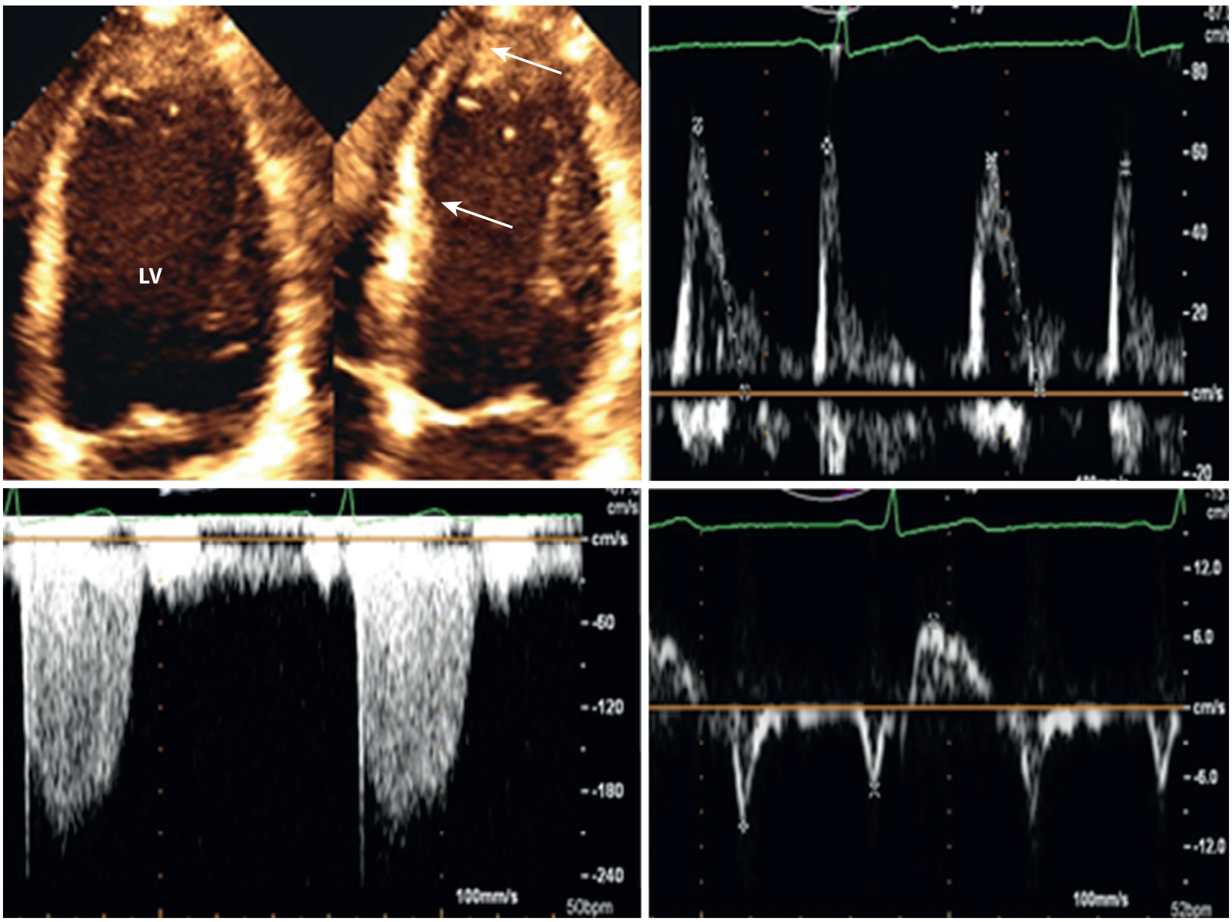
4. Averaging of the lateral and the septal e' velocities was recommended since they are significantly different in certain situations such as left bundle branch block, regional wall motion abnormality, or significant right ventricular dysfunction (as seen with primary pulmonary hypertension). However,

FIGURE 3 **Normal Diastolic Function With Cardiac Amyloidosis**



(Left) 2-Dimensional parasternal long **(upper)** and short axis **(lower)** views from a 58-year-old male with multiple myeloma and no symptoms. Left ventricular wall thickness and left atrial volume are normal. He was referred to echocardiography for evaluation of possible cardiac amyloidosis. **(Middle)** Mitral inflow **(upper)** and septal annulus **(lower)** velocities show reduced e', but normal E/e'. **(Right)** Tricuspid regurgitation velocity **(upper)** was normal, indicating that 3 of 4 diastolic function parameters were normal. According to the 2016 guideline, his diastolic function was graded as normal. However, the longitudinal strain **(lower)** showed a characteristic pattern for cardiac amyloidosis, which was subsequently confirmed.

FIGURE 4 Normal Diastolic Function With Myocardial Infarction and Reduced LVEF



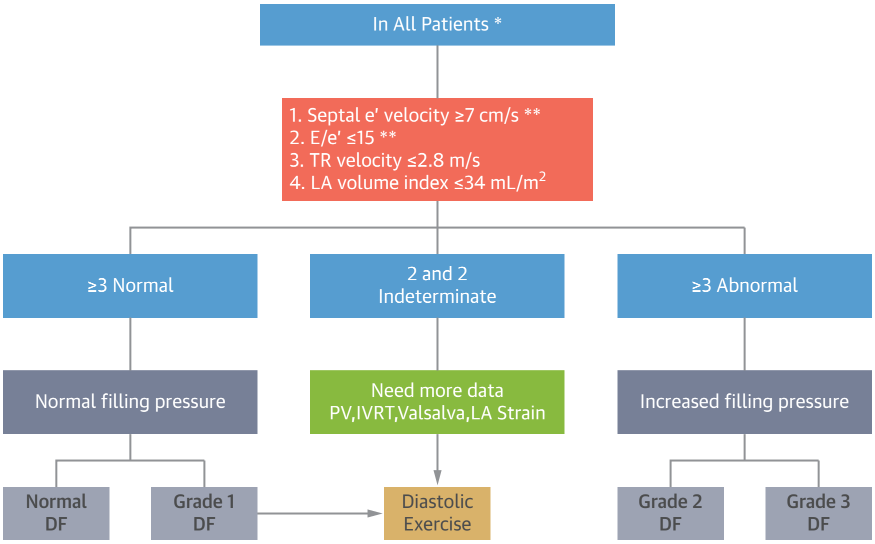
(Upper Left) Apical 4-chamber view showing diastolic **(left)** and systolic frame **(right)** with akinetic apical septum **(arrows)** with left ventricular ejection fraction (LVEF) of 40% in a 45-year-old male who had anteroapical myocardial infarction. Mitral inflow **(upper right)** and mitral annulus velocity **(lower right)** show E = 60 cm/s, E/A = 1, e' = 10 cm/s, and E/e' = 6 indicating normal diastolic function along with normal pulmonary artery systolic pressure **(lower left)**. In the 2016 guideline, normal diastolic function cannot be assigned to a subject who had myocardial infarction with reduced LVEF. LV, left ventricle.

under most other clinical situations, there is no evidence that averaging of e' velocities provides a more reliable assessment of diastolic function. Septal e' velocity is more parallel with the direction of the ultrasound beam and also recommended for atrial fibrillation or constrictive pericarditis. Moreover, septal E/e' was found to be associated with a poor outcome in TOPCAT (9), whereas lateral E/e' did not differ between patients with heart failure with preserved ejection fraction who were and were not hospitalized in I-Preserve (10).

PROPOSED MODIFICATIONS TO THE 2016 GUIDELINE. The issues stated above could be addressed by integrating 2 algorithms to 1 merged algorithm with following modifications (Figure 5):

1. Initial assessment based on the 4 parameters (septal e', E/e', LAVI, and TR velocity) is to determine diastolic filling pressure, not normal or abnormal diastolic function. When 3 or more are normal, filling pressure is normal and when 3 or more are abnormal, filling pressure is abnormal.
2. After filling pressure assessment, diastolic grading can be assigned based on E/A ratio. Normal or grade 1 diastolic function is assigned to the subject with normal filling pressure with E/A > 0.8 and ≤ 0.8, respectively, and grade 2 or 3 to the group with increased filling pressure with E/A < 2 and ≥ 2.
3. When diastolic function is indeterminate based on the 4 variables, additional parameters including pulmonary vein velocities, Valsalva maneuver, isovolumic relaxation time, or strain imaging

FIGURE 5 A Proposed Revised Unified Algorithm for Assessment of Diastolic Filling Pressure and Function



Proposed revised integrated algorithm using the same 4 basic parameters for assessing diastolic filling pressure and function for all patients except for (as noted with an asterisk) those with at least moderate mitral annulus calcification, left bundle branch block, pacemaker rhythm, or severe primary pulmonary hypertension. In this algorithm, the septal mitral annulus e' velocity is recommended (as noted with the double asterisks). When diastolic function assessment is indeterminate or uncertain as in the green box, use additional parameters. Diastolic exercise test **(in yellow box)** is helpful in symptomatic patients with grade 1 or indeterminate diastolic function. See text. DF = diastolic function; LA = left atrium; TR = tricuspid regurgitation.

should be used as described in the 2016 guideline (1,2).

4. One of the main reasons for the indeterminate grading is the discordance among the diastolic parameters. LAVI is the most discordant parameter and its measurement can be challenging. There is also a significant overlap in LAVI among different groups. Left atrial (LA) volume may be increased in individuals with high stroke volume such as athletes. It has been shown that when LA pressure normalizes, E/e' and LA strain values also did, but LAVI remained elevated (11). LA systolic strain has been shown to decrease gradually as diastolic function worsens (12). Further studies are needed to assess whether diastolic function assessment can be better optimized by eliminating LAVI or by using LA strain instead of LAVI (13).

This proposed algorithm may not be applicable for the patients with mitral annulus calcification, left bundle branch block, regional wall motion abnormality, or significant primary pulmonary hypertension. This revised algorithm is intended for most of patients without conditions affecting mitral annulus velocity by factors not intrinsically related to LV DD, such as primary electric or right heart abnormalities. For these groups of patients, diastolic function and filling pressure assessment must be based on E/A, isovolumic relaxation time, TR velocity, pulmonary vein, LA strain, and Valsalva maneuver (1,2,13,14). The revised algorithm can be also used for patients with atrial fibrillation to assess filling pressure, but not grading, with the different E/e' cutoff value of 11.

SUMMARY. With its emphasis on specificity and dependence on clinical information for adjudicating the presence of DD, the 2016 guideline can underestimate the significance of early DD in asymptomatic individuals or in early myocardial disease, while it can also overestimate DD in the young with associated risk factors. A more practical and simpler modified algorithm for assessing diastolic filling pressure first and subsequent determination of its grading is proposed using the same 4 initial parameters recommended in the 2016 guideline. We also emphasize that the most important and efficient algorithm is our comprehensive understanding of mechanism and hemodynamics of DD in comprehensive clinical context. The proposed algorithm must be further validated by correlating with simultaneous invasive hemodynamics and clinical outcomes.

No Need for Modifications But a Need for Careful Application of the Diastolic Function Guidelines

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The diagnosis and grading of DD is an integral component in the comprehensive evaluation of patients with cardiovascular disease (1,2). The writing group of the 2016 ASE/EACVI diastolic function guidelines was tasked with developing algorithms that simplify the evaluation. The drafted guidelines were then reviewed by ASE and EACVI standards committees, ASE and EACVI boards of directors, and outside reviewers, all of whom contributed to the final version that was published in April 2016.

While emphasizing the consideration of 4 to 5 key variables, the 2016 guidelines advocate careful consideration of all clinical, 2-D, and Doppler data in drawing conclusions about diastolic function. The statement that only 4 variables (septal/lateral e' velocities, average E/e' ratio, LA or LA maximum volume index and peak TR or TR velocity) are recommended is incorrect. The presence of systolic dysfunction (reduced LVEF, reduced LV long axis function based on mitral annulus s' velocity, mitral annulus systolic descent, or LV global longitudinal strain [GLS]), pathological LV hypertrophy, pathological "L" velocity in mitral inflow, abnormally increased amplitude or prolonged duration of atrial reversal velocity in pulmonary vein flow, and a shift to an impaired relaxation pattern in mitral inflow with Valsalva were explicitly declared in the guidelines' indicators of abnormal diastolic function (not only the 4 variables). Clinical data are also emphasized (1). Consideration of clinical findings is a simple application of common sense. For example, an enlarged LA in an athlete with no risk factors for cardiac disease does not indicate DD. On the other hand, an enlarged LA in a patient with hypertension is diagnostic of DD because DD leads to chronically elevated LA pressure, and over time, LA enlargement. Similar to all echocardiographic diagnoses, clinical context is essential for the diagnosis of DD. With the availability of electronic health records, there is no good reason why the interpreting physician should not seek clinical data before interpreting the echocardiographic study. The low prevalence of DD in the study from Almeida et al. (3) based on the 2016 guidelines may be explained by many issues (**Table 1**). Before accepting the conclusions of studies trying to apply the guidelines to retrospectively acquired data, one must look at the rigor and quality of data acquisition as well as whether the guidelines were correctly applied.

PERCEIVED ISSUES WITH 2016 GUIDELINES. The viewpoint comments on 4 perceived limitations in the guidelines. First, is the issue of diagnosing grade 1 DD. The guidelines advocate an algorithm based on the 4 variables mentioned above to diagnose DD, but only in subjects with normal ejection fraction and absent clinical/2-D/Doppler data of myocardial disease. The objective is to avoid false-positive calls of DD in the absence of cardiovascular risk factors and with structurally normal LV which may happen if one relies only on a single parameter. The guidelines recommend consideration of several other variables to diagnose DD as LV systolic dysfunction and pathological LV hypertrophy in patients with risk factors for DD as hypertension and diabetes mellitus. Therefore, the correct application of the guidelines does not lead to a low prevalence of grade 1 DD.

Second, the viewpoint deals with drawing conclusions about diastolic function and LV filling pressure based on the 2 algorithms in the guidelines [Figures 8A and 8B in the guidelines document in Nagueh et al. (1)] arguing for the difference between DD and elevated LV filling pressure. I agree that a patient with 3 or 4 abnormal variables in algorithm A has elevated LV filling pressure which is usually the result of DD. Algorithm B, which is needed to grade diastolic dysfunction, calls for the evaluation of average E/e' ratio, LA maximum volume index, and peak TR velocity in patients with intermediate values of E/A ratio and mitral peak E velocity. The writing group believed it is reasonable to infer the presence of DD with elevated LV filling pressure in most clinical scenarios as subjects with normal diastolic function do not develop elevated LA pressure except under unusual circumstances as in rapid volume infusion with leg raising and measuring LA pressure before the kidney excretes the infused fluids. Isolated constrictive pericarditis is another exception as patients usually have increased LV diastolic pressures in the absence of myocardial disease. Conversely, some patients with systolic dysfunction have impaired LV relaxation but normal LV filling pressure. In the latter situation, the first algorithm is bypassed altogether and only the second algorithm (for estimation of LV filling pressure and grading diastolic dysfunction) is needed. The argument is made that second algorithm is therefore not needed when 3 or 4 variables are abnormal. However, the mere presence of elevated LV filling pressure is not enough to differentiate

TABLE 1 Limitations of the Study From Almeida et al. (3)

1. Guidelines were incorrectly applied as clinical, 2-dimensional data, and specific Doppler signals were not considered
2. Retrospective dataset was collected before publication of guidelines; no mention of frequency of satisfactory TR jet
3. Pulmonary vein flow, Valsalva induced changes in mitral inflow not obtained
4. Mitral annulus e′ velocity only at lateral side
5. Investigators did not look for L velocity in mitral inflow
6. No gold standard against which diagnosis of diastolic dysfunction can be compared
7. No prediction of outcome events

grade 2 from grade 3 DD, hence the need for mitral inflow for the latter objective. Further, mitral inflow by itself in patients with DD provides incremental prognostic information above and beyond LVEF.

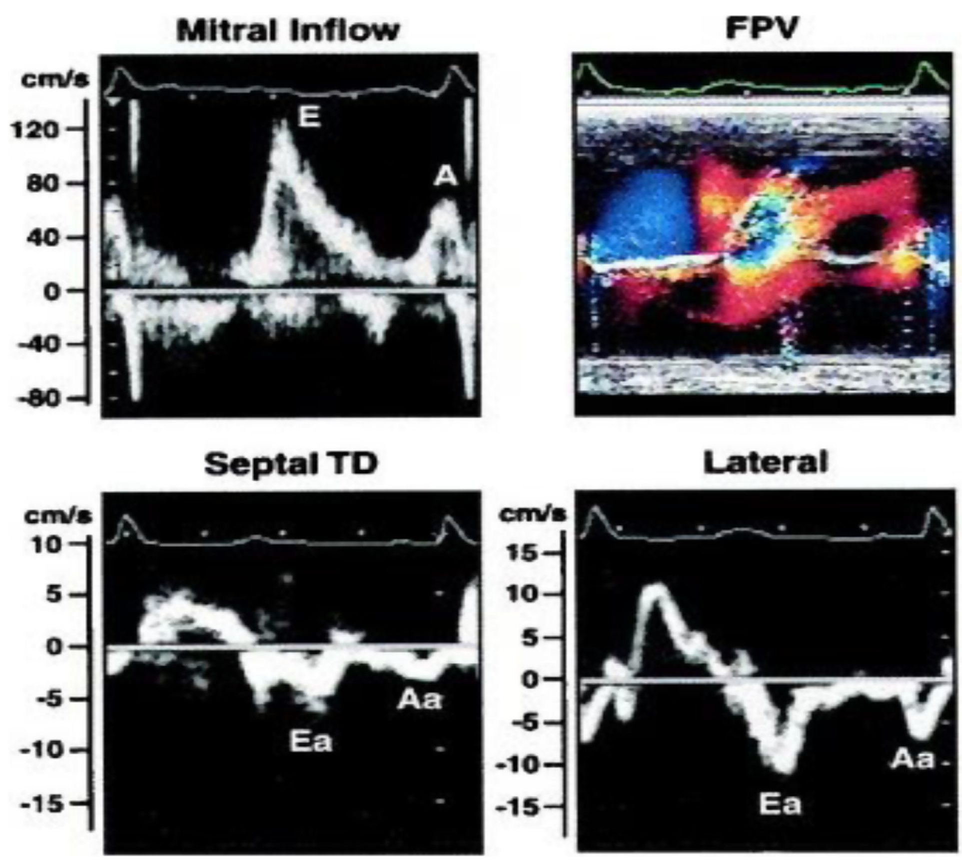
Third, Oh and colleagues introduce the idea that patients with LV systolic dysfunction or pathological LV hypertrophy have normal diastolic function. To my knowledge, this idea is not supported by invasive data. On the contrary, there are several invasive studies with high-fidelity catheters in these patients showing abnormal LV relaxation and increased LV chamber stiffness. Outcome studies have likewise convincingly shown that patients with myocardial disease have abnormally reduced exercise tolerance, abnormally elevated natriuretic peptide levels reflecting LV end diastolic pressure and wall stress, as well as worse outcomes (1). Relying on apparently normal Doppler velocities to support the presence of normal diastolic function in patients with LV structural abnormalities is problematic given the multiple hemodynamic determinants of Doppler velocities.

The viewpoint recommends relying on mitral e′ velocity only to reach conclusions about abnormal LV relaxation. There are problems with this proposal. The e′ velocity in normal subjects depends on LV relaxation and LV filling pressure. Normal subjects can have reduced e′ velocity despite normal LV relaxation if they are dehydrated, thus the challenge of relying exclusively on e′ velocity in drawing conclusions about diastolic function. The viewpoint incorrectly states that the guidelines relied on e′ velocity values in the oldest age group in the NORRE study. However, reduced septal e′ velocity was reported in 20% of normal subjects 40 to 60 years of age in the NORRE study (not just the oldest age group), and in many normal subjects in Olmstead county in age groups of 45-49, 50-54, and 55-59 years (4,15). Importantly, in a recent analysis from the ARIC study, a septal e′ velocity of 7 cm/s was not associated with incident heart failure (16).

Fourth, the viewpoint mentions using septal e′ velocity only and not the average as they say there are no data to show higher accuracy with the average of septal and lateral e′ velocities. Mitral annulus e′ velocity is measured as an index of LV global relaxation. However, limiting the measurement to 1 site only is not representative of global annulus early diastolic recoil. There are differences between septal and lateral velocities (from 2 to 8 cm/s) not only in normal subjects but also in patients with cardiac diseases. For example, patients with anteroseptal myocardial infarction (Figure 6) usually have a markedly reduced septal e′ velocity and increased lateral velocity with hyperdynamic basal lateral wall. One would arrive at very different conclusions not only about LV relaxation but also about filling pressures by relying on the septal velocity only, whereas using the average results in a more accurate estimation of filling pressure. This is supported by observational studies where cardiac catheterization and echocardiographic imaging were simultaneously performed (17). In addition, patients with group I and group III pulmonary hypertension usually have reduced septal e′ velocity due to right ventricular diastolic dysfunction and septal E/e′ ratio that is abnormally elevated and if used would lead to erroneous conclusions about LV filling pressure. In these patients, lateral e′ velocity is normal as is the lateral E/e′ ratio and results in an accurate reflection of LA pressure (1).

LA MAXIMUM VOLUME INDEX AND LA STRAIN. Oh and colleagues raise concerns with the reliance on LA volume in trying to gain insight into LA pressure. There can be challenges in few patients to satisfactorily image the LA. Nevertheless, the vast majority of sonographers and well-trained echocardiographers can readily obtain and measure biplane LA volumes which are an integral component of all echocardiographic studies. To say that satisfactory LA volumes cannot be relied on for the evaluation of LV diastolic function is to accept that such a valuable measurement, which can contribute to the diagnosis and prognosis in many cardiovascular diseases (mitral regurgitation, heart failure, hypertensive heart disease, and atrial arrhythmias to mention a few), should be abandoned. On the other hand, I agree that LA strain can provide incremental information in the evaluation of diastolic function, but its utility must be shown not only in the research setting but also in the real world as it is highly doubtful that a lab struggling to get an accurate measurement of LA volume will do a much better job in measuring LA strain. Further, there is no reason to believe that LA strain values would be accurate when obtained from a foreshortened LA.

FIGURE 6 Impact of Segmental Dysfunction on Mitral Annulus Early Diastolic Velocity



Mitral inflow **(upper left),** flow propagation velocity (FPV), and tissue Doppler velocities at septal and lateral sides of the mitral annulus in a patient with post infarction cardiomyopathy and LVEF of 20%. Septal infarction was present and the basal segment of the lateral wall had normal function. Mean wedge pressure was 20 mm Hg. The average of septal and lateral e' velocities is 8.25. Average E/e' ratio at 14.5 provided the best estimate of wedge pressure. Reproduced with permission from Rivas-Gotz et al. (17).

IMPORTANCE OF CORRECT APPLICATION OF THE GUIDELINES. In Figure 1, an e' of 6.7 cm/s in an asymptomatic 77-year-old woman can be normal in elderly patients without cardiovascular risk factors. The reader is not provided with clinical data or LA volume data which are essential given the limitations of septal e' velocity as detailed above. For the second example, the patient with amyloidosis and abnormally reduced GLS has DD based on the 2016 guidelines despite the normal values of LA volume and apparently normal LV wall thickness. Figure 2 highlights the importance of considering LV long axis function in diagnosing myocardial disease as recommended in the guidelines (1).

MODIFIED ALGORITHM IN THE VIEWPOINT. There are no major differences between the modified algorithm and the 2016 guidelines' recommendations. It largely appears as a different read of the recommendations in the 2016 guidelines. Four variables are still recommended as the starting point but apparently without consideration of clinical and 2-D data. Septal e' and E/e' ratios are used instead of an average E/e' ratio. The mitral E/A ratio is then used when elevated LV filling pressure is concluded for grading. Of note, the modified algorithm, similar to the 2016 guidelines, still advocates for other variables for cases with indeterminate diastolic function. For the reasons mentioned above, there are major limitations in relying on a single value of septal e' velocity and septal E/e' ratio.

SUMMARY. The 2016 ASE/EACVI guidelines have been validated and had good accuracy in a large multicenter study with 450 patients, irrespective of LVEF (18). The good accuracy was noted in obese patients and in patients with pulmonary disease (18). Further, the 2016 guidelines have excellent interobserver accuracy (against invasive LV filling pressure as the gold standard) and reproducibility, irrespective of the experience level of the observer (19). Finally, there are growing data showing the incremental prognostic value of diastolic function assessment by 2016 ASE/EACVI guidelines in several patient populations (20-22). Importantly, 1 of these prognostic studies showed low event rate in patients classified with normal diastolic function based on the 2016 guidelines who would have been diagnosed with grade 1 DD based on earlier recommendations (21), a further attestation to the low rate of false-negative calls of grade 1 DD by the 2016 guidelines.

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REFERENCES

1. Nagueh SF, Smiseth OA, Appleton CP, 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.

2. Nagueh SF. Left ventricular diastolic function: understanding pathophysiology, diagnosis, and prognosis with echocardiography. J Am Coll Cardiol Img 2020;13:228–44.

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

4. Caballero L, Kou S, Dulgheru R, Gonjilashvili N, et al. Echocardiographic reference ranges for normal cardiac Doppler data: results from the NORRE Study. Eur Heart J Cardiovasc Imaging 2015;16:1031–41.

5. Ha J-W, Oh J, Pellikka P, et al. Diastolic stress echocardiography: a novel noninvasive diagnostic test for diastolic dysfunction using supine bicycle exercise Doppler echocardiography. J Am Soc Echocardiogr 2005;18:63–8.

6. Obokata M, Kane GC, Reddy YN, et al. role of diastolic stress testing in the evaluation for heart failure with preserved ejection fraction: a simultaneous invasive-echocardiographic study. Circulation 2017;135:825–8.

7. Redfield MM, Jacobsen SJ, Burnett JC Jr., et al. Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. JAMA 2003;289:194–202.

8. Kane GC, Karon BL, Mahoney DW, et al. Progression of left ventricular diastolic dysfunction and risk of heart failure. JAMA 2011;306:856–63.

9. Shah AM, Claggett B, Sweitzer NK, et al. Cardiac structure and function and prognosis in HFPEF: findings from the echocardiographic study of the TOPCAT Trial. Circ Heart Fail 2014;7:740–51.

10. Carson PE, Anand IS, Win S, et al. The hospitalization burden and post-hospitalization mortality risk in heart failure with preserved ejection fraction: results from the I-PRESERVE trial. J Am Coll Cardiol HF 2015;3:429–41.

11. Huynh QL, Kalam K, Iannaccone A, et al. Functional and anatomic responses of the left atrium to change in estimated left ventricular filling pressure. J Am Soc Echocardiogr 2015;28:1428–33.

12. Singh A, Addetia K, Maffessanti F, et al. LA strain for categorization of LV diastolic dysfunction. J Am Coll Cardiol Img 2017;10:735–43.

13. Thomas L, Marwick TH, Popescu BA, Donal E, Badano LP. Left atrial structure and function, and left ventricular diastolic dysfunction: JACC State-of-the-Art Review. J Am Coll Cardiol 2019;73:1961–77.

14. Abudiab MM, Chebrolu LH, Schutt RC, et al. Doppler echocardiography for the estimation of LV filling pressure in patients with mitral annular calcification. J Am Coll Cardiol Img 2017;10:1411–20.

15. Munagala VK, Jacobsen SJ, Mahoney DW, Rodeheffer RJ, Bailey KR, Redfield MM. Association of newer diastolic function parameters with age in healthy subjects: a population-based study. J am Soc Echocardiogr 2003;10:1049–56.

16. Shah AM, Claggett B, Kitzman D, et al. Contemporary assessment of left ventricular diastolic function in older adults: the Atherosclerosis Risk in Communities Study. Circulation 2017;135:426–39.

17. Rivas-Gotz C, Manolios M, Thohan V, Nagueh SF. Impact of left ventricular ejection fraction on estimation of left ventricular filling pressures using tissue Doppler and flow propagation velocity. Am J Cardiol 2003;91:780–4.

18. Andersen OS, Smiseth OA, Dokainish H, et al. Estimating left ventricular filling pressure by echocardiography. J Am Coll Cardiol 2017;69:1937–48.

19. Nagueh SF, Abraham TP, Aurigemma GP, et al., for Diastolic Function Assessment Collaborators. 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:e008122.

20. Prasad SB, Lin AK, Guppy-Coles KB, et al. Diastolic dysfunction assessed using contemporary guidelines and prognosis following myocardial infarction. J Am Soc Echocardiogr 2018;31:1127–36.

21. Sanchis L, Andrea R, Falces C, Poyatos S, Vidal B, Stiges 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.

22. Tennøe AH, Murbræch K, Andreassen JC, et al. Left ventricular diastolic dysfunction predicts mortality in patients with systemic sclerosis. J Am Coll Cardiol 2018;72:1804–13.

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