

EACVI survey on the evaluation of left ventricular diastolic function

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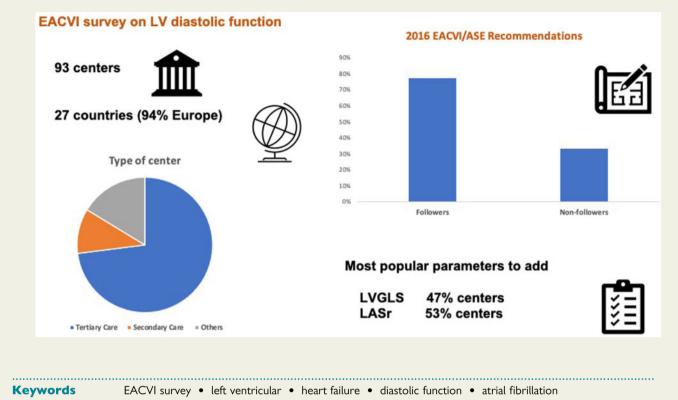
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Aims	The aim of this study is to analyse how current recommendations on left ventricular (LV) diastolic function assessment have been adopted. Identifying potential discrepancies between recommendations and everyday clinical practice would enable us to better understand and address the remaining challenges in this controversial and complex field.
Methods and results	A total of 93 centres, mainly from tertiary care settings, responded to the survey. More than three-quarters (77%) of centres follow the 2016 ASE/EACVI recommendations for LV diastolic function evaluation in patients with pre- served ejection fraction based upon e', <i>E/e'</i> , tricuspid regurgitation velocity, and left atrial (LA) volume. These rec- ommendations were generally preferred to the previous 2009 version. Many centres also consider strain assess- ments in the LV (48%) and left atrium (53%) as well as diastolic stress echocardiography (33%) to be useful as additional assessments of LV diastolic function. Echocardiographic assessments of LV diastolic function were used frequently to guide therapy in 72% of centres.
Conclusion	There is widespread adoption of current recommendation on the evaluation of LV diastolic function and these are frequently used to guide patient management. Many centres now also consider LV and LA strain assessments useful in the clinical assessment of diastolic function. These may be considered in future recommendations.

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Introduction

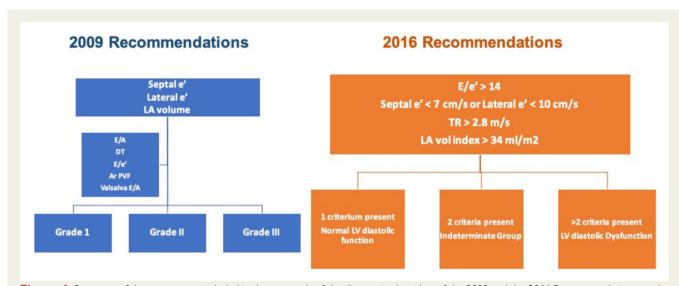
The echocardiographic assessment of left ventricular (LV) diastolic function is integral to the routine evaluation of patients presenting with dyspnoea or other features of heart failure. Indeed, the diagnosis of heart failure with preserved ejection fraction (HFpEF) is based on evidence of heart failure, preserved ejection fraction, and evidence of LV diastolic dysfunction.¹

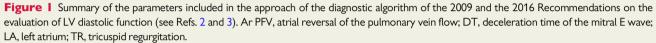
Evaluation of LV diastolic function by echocardiography is challenging and particularly difficult to apply in several subgroups of patients, such as those with atrial fibrillation, significant mitral valve disease, or paced rhythms. International guideline recommendations for the clinical evaluation of diastolic dysfunction have undergone two iterations in the last decade. In an attempt to standardize the assessment of diastolic function, the American Society of Echocardiography (ASE) and European Association of Echocardiography (EAE) jointly released a document in 2009, which embedded a comprehensive range of traditionally used diastolic parameters in a number of diagnostic algorithms to classify patients into three different grades of diastolic dysfunction.² Limitations of those recommendations included their perceived complexity, problems with reconciling discordant data (when different approaches do not agree in their assessment of diastolic function) and the large number of included variables considered difficult to apply in clinical practice.

Thereafter, the ASE and EACVI jointly released a second set of recommendations in 2016 that sought to simplify the assessment of

LV diastolic function in clinical practice by adopting algorithms that avoided problems with discordance.³ In patients with normal LV ejection fraction this focused upon four key echo variables: mitral annular e' velocities, average E/e' ratio, peak tricuspid regurgitation velocity and left atrial (LA) volume.³ Patients with zero or one positive criteria have normal diastolic function, whilst those with three or four criteria have diastolic dysfunction. Moreover, they suggested that patients classified with indeterminate LV diastolic function (two positive and two negative criteria) might represent an opportunity, rather than a limitation, by identifying a new subgroup of patients at intermediate risk. Figure 1 summarizes the main differences in the parameters included in the approach of the 2009 and 2016 algorithm. Of note, the 2016 ASE/EACVI document recommended a different approach to the assessment of LV filling pressures and grading diastolic dysfunction in patients with known myocardial disease and normal ejection fraction and in patients with a low ejection fraction, but this algorithm was not assessed in the present survey. Furthermore, the exclusion of underlying myocardial injury (e.g. storage disease or inflammatory disorder) by cardiovascular magnetic resonance was also recommended in the 2016 consensus.

The EACVI Scientific Initiatives Committee developed this survey to analyse how the 2016 ASE/EACVI recommendations have been adopted and how LV diastolic function is evaluated across Europe and beyond. The purpose is to obtain real-world data on the current assessment of LV diastolic function with a particular focus on patients with HFpEF. Identification of potential discrepancies between





guideline recommendations and everyday clinical practice would enable us to better understand and address the remaining challenges in this controversial and complex field.

Methods

The present survey was conducted by the EACVI Scientific Initiatives Committee from November 2020 to January 2021 according to published criteria (www.escardio.org/eacvi/surveys).⁴ Cardiology Units across Europe and beyond were invited to complete an easily accessible online survey to describe their contemporary local approach to the evaluation of left ventricular diastolic function among patients with heart failure. The survey was also disseminated via social media. The survey consisted of 21 questions aimed at understanding the available facilities and workload of each centre, and the key measurements implemented in their routine clinical practice to assess LV diastolic function. A number of questions incorporating clinical vignettes were included to gain a better understanding of clinical management in challenging scenarios. The 21 survey questions were designed based on the current 2016 ASE/EACVI recommendations on the assessment of LV diastolic function.

Results

Characteristics of responding centres

A total of 93 worldwide centres in 27 countries (n = 88, 95% from Europe), answered the survey. Among them, 68 (73%) were tertiary care facilities, 10 (11%) secondary or district care hospitals, 8 (9%) primary care centres, and 6 (6.45%) private clinics. Forty percent of centres were high-volume centres as defined by performing >250 transthoracic echocardiographic studies/week.; 19% performed 151–250 transthoracic echocardiograms/week, whilst 26% did 101–150/ week. Only 15% of the responding centres were low volume centres with <100 echocardiograms/week.

The majority of centres (n = 51, 55%) reported using the 2016 ASE/EACVI recommendations on the assessment of LV diastolic function either all (n = 21, 23%) or most of the time (n = 30, 32%). Only 6 (7%) centres reported never following these recommendations whilst 15 (16%) reported doing so only occasionally (*Figure 2A*). When asked about alternative algorithms used to evaluate LV diastolic function, 15 (16%) centres reported using the 2009 ASE/EAE recommendations, 8 (9%) centres used national recommendation, and 8 (9%) followed local institutional protocols.

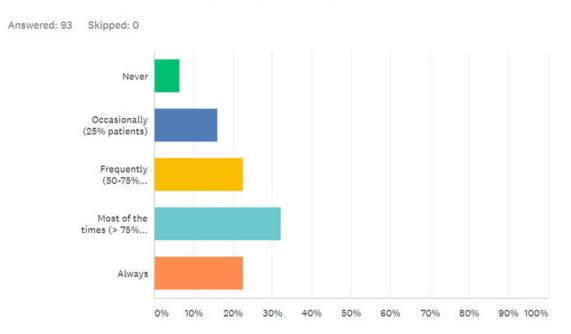
The respondents reported wide variability when asked about their opinion on the current 2016 ASE/EACVI recommendations in comparison to the previous 2009 recommendations, although generally the 2016 recommendations were preferred (*Figure 2B*). Fifty-five percent of centres reported the 2016 recommendations to be easier to use while 28% found them harder; 17% did not answer. Thirty-nine percent felt the 2016 version was more accurate with less indeterminate evaluations, whilst 21% felt them less accurate than the 2009 version. Forty-seven percent found the 2016 recommendations to have more clinical impact, compared with 10% who preferred the 2009 recommendations in this regard.

Reporting of LV diastolic function

In terms of describing LV diastolic function in echo reports, most centres (84%) report diastolic function routinely, whilst 10% of centres only report it in patients referred with dyspnoea or suspected heart failure. Half of the centres (53%) describe mitral annulus e' and E/e' in all patients with LV ejection fraction >50%, a third (31%) report them in most patients, whilst only seven centres either never report them or just report them in very few cases.

A wide variety of methods are used to measure LA size, although most of the measurements used [diameters or area derived from apical four chamber view (24%), single plane volume (35%), or biplane volumes (68%)] were made from the four-chamber apical view and

A At your centre, do you follow the currently recommended algorithm for assessing LV diastolic dysfunction (ASE/EACVI 2016 Recommendations)? (Single choice)



How do you think the 2016 ASE/EACVI recommendations for LV diastolic function assessment are compared to the previous 2009 version: (Multiple choice, one for each of the 3 items: complexity / accuracy / clinical impact)

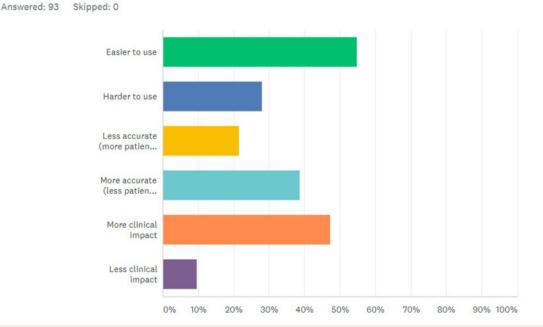


Figure 2 (A) Responses regarding the used algorithm for assessing LV diastolic dysfunction. (B) Answer on the comparison of the current 2016 Recommendations and the previous 2009 version. LV, left ventricular.

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the large majority reported indexed (84%) rather than non-indexed values of LA size (16%). Nine centres (10%) reported using 3D LA volumes.

Routine reporting of pulmonary vein flow velocities is done in seven centres (8%), whilst 72% centres never or only occasionally report them.

Most centres (75%) do not use agitated saline contrast to improve the detection of tricuspid regurgitation and the estimation of pulmonary pressures. Fifty-six percent of centres reported occasionally using a right heart catheterization to measure the pulmonary artery pressure when this cannot be estimated by echocardiography. Only 11% do it frequently (>50% patients), whilst a third of centres never use it.

Additional assessments of LV diastolic function

The approach to patients with intermediate diastolic function (two positive 2016 criteria and two negative) varied widely across our survey (*Figure 3A*). In particular, there was low agreement as to which parameters respondents would use next to help adjudicate diastolic function. Based on a multiple-choice option, the most frequent selected parameters were LV global longitudinal strain (47% of responses), mitral inflow assessment during a standardized Valsalva manoeuver (40% of responses), pulmonary vein flow velocities (37% of responses), LA longitudinal strain (34% of responses), and diastolic stress echo testing (24%). LV propagation velocity using colour Doppler M-mode was less popular (only 12% of centres reported its use). Nearly two-thirds of centres (63%) reported performing stress echo to assess LV diastolic function in their clinical practice, although only a quarter (23%) reported using it routinely (>5 cases/month).

When respondents were asked to propose the most useful novel markers of diastolic dysfunction in clinical practice and which markers should be incorporated in future recommendations, the most frequent proposals were LA longitudinal strain (53%), LV longitudinal global strain (49%), and diastolic echo stress testing (34%) (*Figure 3B*).

Diastolic function evaluation in difficult scenarios

LV diastolic function evaluation in challenging scenarios was also surveyed. In patients with atrial fibrillation, 20 (22%) responded they would not attempt the evaluation of diastolic function, whilst 12 (13%) use the same assessments as patients in sinus rhythm. Thirty-seven (40%) centres said they would assess diastolic function in patients with atrial fibrillation by averaging at least five beats for each parameter. Seven (8%) centres stated they would exclude LA volume as a criterion for LV diastolic dysfunction diagnosis in the context of atrial fibrillation.

In patients with severe mitral regurgitation, 27 (29%) of centres would assess diastolic function in the same way as in patients without, whilst 32 (35%) centres would not measure it at all. Twelve (13%) centres stated that they would exclude LA volume and E/e' as criteria for diagnosing LV diastolic dysfunction in patients with severe mitral regurgitation, whilst 7 (8%) centres said they would assess the isovolumic relaxation time in these patients.

Clinical implications of diastolic function assessments

Regarding follow-up of patients with HFpEF and elevated LV filling pressures, the majority of centres (n = 53, 57%) would repeat LV diastolic assessments in response to a change in symptomatic status, whilst 28 centres (30%) would routinely repeat this form of imaging on a yearly basis. Echocardiographic assessments of LV diastolic function were used frequently (>50% of patients) to guide therapy in the large majority of centres (n = 67, 72%).

Discussion

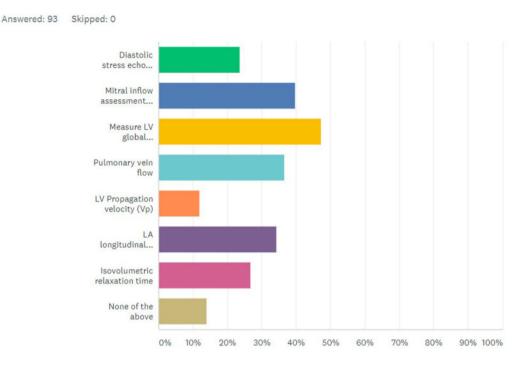
This global survey provides new insight into the contemporary evaluation of LV diastolic function, focusing upon the application of the 2016 ASE/EACVI Recommendations and opinions regarding its approach. We observed good general adoption of these recommendations and a general preference for them in comparison to the 2009 iteration. Seventy-seven percent of the centres followed the 2016 recommendations in >50% of patients, and 54% of them did so in >75% of patients.

The 2016 approach is based on the assessment of e', E/e', tricuspid regurgitation velocity, and LA size. The role of the E/e' ratio has been widely discussed and its accuracy in estimating LV filling pressures is still a matter of controversy with reported reduced accuracy in normal subjects, in patients with heavy mitral annulus calcification or significant mitral regurgitation, and with conflicting results in haemodynamic validation studies.^{5,6} Nevertheless e' and E'/e remain cornerstones of the 2016 recommendations for evaluation of diastolic function and reported in the vast majority of responding centres.

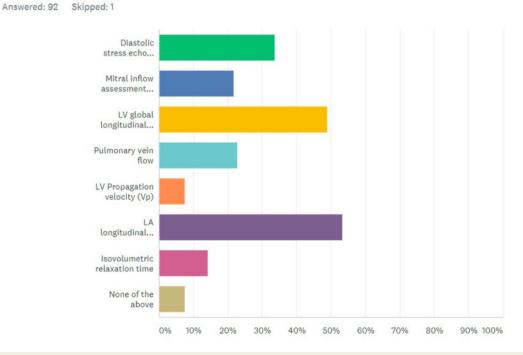
Similarly, the assessment of LA size is widely performed among responding centres with good progress having been made in evaluating LA size beyond traditional anteroposterior LA diameters. Indeed, most centres (70%) reported measuring indexed LA area or volumes based on 2D apical views. Further work needs to be done to incorporate 3D echocardiography measurements of LA volume, which were only used in 10% of participating centres, despite being considered the reference method for the assessment of LA size.⁷ The reported low use of 3D echocardiography to describe LA size is in keeping with a previous survey on chamber quantification where also only 10% of centres used 3D echocardiography to assess LA volume.⁸ The development of dedicated commercialized software available on standard acquisition echo systems should improve adoption in the future.

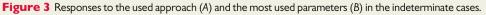
The final parameter of LV diastolic dysfunction recommended for routine evaluation in the 2016 Recommendations is the assessment of pulmonary artery pressures. This is a routine measurement made on standard echocardiographic assessments, the estimation of which can be improved using echo contrast. However, in this survey, only few centres reported the use of such contrast despite its proven efficacy.^{9,10} Similarly, only a minority of centres would consider right heart catheterization for the measurement of pulmonary artery pressures when echocardiographic assessments are not available despite its clear indication according to current Guidelines in the management of heart failure.¹

A Which parameters do you perform in indeterminate cases in order to improve classification within the indeterminate group? (multiple choice)



Which of the following do you find most useful in clinical practice and would you like to see incorporated in the new recommendations on diastolic function assessment? (Multiple choice)





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Many centres reported the use of additional parameters to assess LV diastolic function, particularly in indeterminate group patients and also in difficult clinical situations such as atrial fibrillation and mitral regurgitation. Among these added parameters the most frequently used and proposed were LV global longitudinal strain and LA strain, with most centres agreeing that these are useful parameters in the evaluation of LV diastolic function. Education of sonographers and cardiologists in appropriate image acquisition and analysis, automatization of measurements in order to facilitate fast and reproducible daily use, as well as the establishment of robust standardized reference values between different vendors will help in the widespread adoption of these advanced measurements. This work is currently underway and related evidence is growing.^{11,12} Future recommendations on the assessment of diastolic function may need to consider incorporation of strain assessment.

The use of diastolic stress echocardiography appears to be controversial according to our survey results. Whilst a majority of respondents believe in the potential utility of this test (up to 63%), its current performance in clinical practice was low with most centres (76%) not performing diastolic stress echo or performing <5 cases per month. Diastolic stress echocardiography has been proposed as a useful tool to further evaluate LV diastolic function. Several studies have demonstrated its diagnostic and prognostic value, in particular in patients with exertional symptoms but normal or indeterminate diastolic function at rest.^{13,14} However, it does require an additional test and the administration of a stressor.

Surprisingly low use of pulmonary vein flow measurements was also noted in this study. With contemporary echocardiographic technology, scanners provide sufficient quality of Doppler to obtain accurate pulmonary vein flow velocities, in most transthoracic studies. Pulmonary vein flow particularly combined with mitral inflow, still provides an important insight into LV filling pressure if A flow reversal can be properly recorded.¹⁵ Further education is required to increase the use of both diastolic stress echocardiography and pulmonary vein flow measurements in the assessment of LV diastolic function. Of note, the use of velocity flow propagation from colour M-mode was testimonial. Whilst providing a potential measure of LV intraventricular gradients,¹⁶ this approach still requires commercialization and automatization before it is likely to be widely adopted in clinical practice.¹⁷

Finally, it is important to note that nearly three-quarters of respondents felt that their assessments of LV diastolic function had a frequent impact on clinical decision making and therapy. This proportion is likely to improve further as new therapies for HPpEF are developed and become available.

Limitations

The overall number of survey respondents is relatively low, and the majority worked in tertiary care centres with a high volume of patients. The findings of this survey may therefore not be generalizable to other clinical environments.

Conclusions

Most of the surveyed centres follow current 2016 ASE/EACVI recommendations for the assessment of LV diastolic function and these diastolic assessments frequently impact clinical decision making and therapy. Furthermore, many centres consider strain assessments useful in the clinical assessment of diastolic function. These should be considered in future recommendations.

Conflict of interest: none declared.

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References

- Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, ESC Scientific Document Group *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.
- 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. *Eur J Echocardiogr* 2009;**10**:165–93.
- Nagueh SF, Smiseth OA, Appleton CP, Byrd BF III, 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;17:1321–60.
- Haugaa KH, Marsan NA, Cameli M, D'Andrea A, Dweck MR, Carvalho RF et al. Criteria for surveys: from the European Association of Cardiovascular Imaging Scientific Initiatives Committee. Eur Heart J Cardiovasc Imaging 2019;20:963–6.
- Mullens W, Borowski AG, Curtin RJ, Thomas JD, Tang WH. Tissue Doppler imaging in the estimation of intracardiac filling pressure in decompensated patients with advanced systolic heart failure. *Circulation* 2009;119:62–70.
- 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.
- Thomas L, Muraru D, Popescu BA, Sitges M, Rosca M, Pedrizzetti G et al. Evaluation of left atrial size and function: relevance for clinical practice. J Am Soc Echocardiogr 2020;33:934–52.
- Ajmone Marsan N, Michalski B, Cameli M, Podlesnikar T, Manka R, Sitges M et al. EACVI survey on standardization of cardiac chambers quantification by transthoracic echocardiography. Eur Heart J Cardiovasc Imaging 2020;21:119–23.
- Senior R, Becher H, Monaghan M, Agati L, Zamorano J, Vanoverschelde JL et al. Contrast echocardiography: evidence-based recommendations by European Association of Echocardiography. *Eur J Echocardiogr* 2009;**10**:194–212.
- Galiè N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, ESC Scientific Document Group et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: the Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): endorsed by: association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J 2016;37:67–119.
- Voigt JU, Mălăescu GG, Haugaa K, Badano L. How to do LA strain. Eur Heart J Cardiovasc Imaging 2020;21:715–7.
- Cameli M, Miglioranza MH, Magne J, Mandoli GE, Benfari G, Ancona R et al. Multicentric Atrial Strain COmparison between Two Different Modalities: MASCOT HIT Study. *Diagnostics* (*Basel*) 2020;**10**:946.
- 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.

- Prasad SB, Holland DJ, Atherton JJ. Diastolic stress echocardiography: from basic principles to clinical applications. *Heart* 2018;**104**:1739–48.
- Rossvoll O, Hatle LK. Pulmonary venous flow velocities recorded by transthoracic Doppler ultrasound: relation to left ventricular diastolic pressures. J Am Coll Cardiol 1993;21:1687–96.
- Yotti R, Bermejo J, Benito Y, Antoranz JC, Desco MM, Rodríguez-Pérez D et al. Noninvasive estimation of the rate of relaxation by the analysis of intraventricular pressure gradients. *Circ Cardiovasc Imaging* 2011;4:94–104.
- Thomas JD. Flow propagation analysis computer or eyeball? JACC Cardiovasc Imaging 2011;4:47–9.