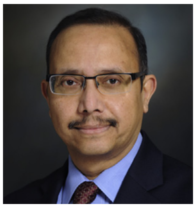
JACC: CARDIOVASCULAR IMAGING VOL. 13, NO. 1, 2020

iVIEW

SPECIAL ISSUE: NONINVASIVE ASSESSMENT OF LEFT VENTRICULAR DIASTOLIC FUNCTION

EDITOR'S PAGE

Noninvasive Imaging for the Evaluation of Diastolic Function

Promises Fulfilled

Sherif F. Nagueh, MD,[a] Y. Chandrashekhar, MD[b]

"Everything should be made as simple as possible, but no simpler."

—Albert Einstein

Left ventricular (LV) diastolic function determines LV filling and diastolic pressures. It is a complex process that depends on many factors, including LV end diastolic and end systolic volumes and pressures, LV systolic properties, elastic recoil, rate and extent of LV relaxation, LV chamber and myocardial stiffness, pericardial and LV/right ventricular (RV) interactions, and left atrium (LA) systolic, reservoir, and conduit functions. Given the complexity, it is challenging to simplify the evaluation and limit it to few measurements. The gold standard is invasive measurements of LV relaxation rate and chamber stiffness. Both require the use of high-fidelity catheters and are difficult to apply for the routine evaluation of patients with cardiovascular disease. Some emerging techniques might make it possible to get an idea of central elements such as myocardial stiffness (1,2), but many mechanisms are difficult to measure accurately in patients with traditional noninvasive imaging. Therefore, noninvasive imaging has been increasingly used to identify the presence of diastolic dysfunction and to estimate LV diastolic pressures using a multiparametric approach with significant success (3-5). However, as expected, these criteria also have some limitations, such as a higher proportion of indeterminate cases and possibly identifying the more advanced cases (5); newer strategies may show some additional promise – these include using LA parameters which could be the A1c-like surrogate of diastolic dysfunction (6), using stress testing to uncover subclinical diastolic dysfunction (7), and invoking complex computational strategies (8) or using artificial intelligence (9) to estimate filling pressures. Such strategies may offer better parsing of prediction of future heart failure (HF) events (10) and outcomes (11).

It may be time to compile a summary of such new developments in this space, and this issue of *JACC: Cardiovascular Imaging* showcases several interesting contributions that tackle different aspects of the noninvasive evaluation of LV diastolic function and its clinical relevance. Nagueh (12) discusses the role of echocardiography, which is particularly capable of looking at many aspects that affect LV filling, as well as filling rates and surrogates of LV relaxation, filling pressures, and chamber stiffness. The review delves into an in-depth analysis of recent publications on this topic, including a meta-analysis on the application of E/e′ ratio to the estimation of LV filling pressures in patients with normal ejection fraction (12). In addition to evaluating LV function, the underlying pathology for diastolic dysfunction can now be examined. Cardiac magnetic resonance (CMR)

From the [a]Methodist DeBakey Heart and Vascular Center, Houston, Texas; and the [b]Division of Cardiology, University of Minnesota and Veterans Affairs Medical Center, Minneapolis, Minnesota. Both authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ISSN 1936-878X/$36.00 https://doi.org/10.1016/j.jcmg.2019.12.006

imaging provides unique insights into myocardial structure including LV geometry, as well as the presence of replacement and interstitial fibrosis that is an important tissue signature of hearts with diastolic dysfunction. In addition, indices looking at this, such as extracellular volume seem to be able to differentiate HF with preserved ejection fraction (HFpEF) from its mimics (13). Chamsi-Pasha et al. (14) summarize the role of CMR imaging and provide future perspectives. They draw attention to the importance of using data from CMR images to identify alternative pathology in patients with HFpEF diagnosis, for example, cardiac amyloidosis.

Diastolic dysfunction is present in many patients with HFpEF. Obokata et al. (15) comment on the role of echocardiographic imaging in the diagnosis of these patients. Importantly, the evaluation of LV diastolic function is only 1 of the parameters needed for phenotyping. Many patients with HFpEF have abnormal LV systolic properties as well as pulmonary hypertension, abnormal LA mechanics, and RV disease with systemic congestion at times. Given the heterogeneous phenotypes in HFpEF, there is a good argument to tailor treatment based on the pathophysiology identified by imaging in a given patient. For example, some therapies may be better suited for patients with low normal ejection fraction (EF) as opposed to those with hyperdynamic LV, even though both meet the diagnostic criteria for HFpEF (16). The evolutionary changes in abnormal myocardial mechanics for the LV, RV, and LA in HFpEF are nicely reviewed by Bianco et al. (17), for patients progressing from HF stages A and B to stages C and D. They draw attention to the role of exercise in identifying abnormal myocardial reserve, and comment on the promising role of machine learning in diagnosing HFpEF (17).

Clinically, one is faced with the question of which is more important from a patient management perspective: diagnosing the presence of diastolic dysfunction or estimating LA mean pressure. Litwin and Zile (18) answer this question and argue that estimating mean LA pressure is the more important because it can inform the administration of diuretic agents. Patients often come to us with symptoms on exertion before experiencing them at rest, and stress testing might show promise — it indeed allows diagnosis as well as prognostication better than resting indices (19). Ha et al. (20) answer the question of how to evaluate symptomatic patients who have normal LV diastolic pressures at rest. The authors present the conceptual background and the invasive and noninvasive clinical application of diastolic stress testing (20).

Preclinical diagnosis of cardiac disease, if successful, can lead to early treatment provided such treatment is available, safe, and effective. Four articles in this issue describe the use of echocardiography to identify the presence of diastolic dysfunction and the likelihood of subsequent HF-related events. Kosmala et al. (21) show that apical, but not basal, untwisting provides incremental information that can identify new-onset HF and cardiovascular death. They evaluated apical and basal untwisting in addition to other echocardiographic variables in 465 asymptomatic patients who were ≥65 years of age, and had at least 1 risk factor for HF (diabetes, hypertension, or obesity). In another study, Upshaw et al. (22) evaluated diastolic function in 362 patients undergoing chemotherapy using a doxorubicin-containing regimen, with some patients also on trastuzumab. Diastolic dysfunction occurred based on reduction in the mitral E/A ratio, decrease in mitral annulus septal and lateral e′ velocities, and increase in E/e′ ratio. The changes were observed in patients who received doxorubicin alone or doxorubicin followed by trastuzumab but not those who received only trastuzumab. Importantly, diastolic dysfunction was associated with subsequent decrease in LV EF and deterioration in LV global longitudinal strain (GLS) (22), suggesting that diastolic dysfunction may precede GLS reduction in this cascade and the current emphasis on identifying abnormal GLS in the guidelines and in currently ongoing randomized controlled trials (23) might inadvertently overshadow the need to also look at an important parameter such as diastolic dysfunction. The third article dealing with asymptomatic patients with diastolic dysfunction is a State-of-the-Art review by Kosmala and Marwick (24) who advocate for including diastolic dysfunction in the definition of preclinical stage B HF, along with a discussion of the therapeutic implications. The fourth article by Chetrit et al. (25) summarizes the published epidemiologic studies that reported on noninvasive assessment of diastolic function, including the definitions used in each of these studies, the prevalence of diastolic dysfunction based on the definition adopted, and the association of diastolic dysfunction with clinical events. Their review article addresses, in addition, the use of diastolic function parameters in clinical trials for treatment of patients with HFpEF (25).

For readers interested in viewpoints and counterpoints, the issue contains a debate between Oh and Nagueh (26) on using different criteria to diagnose diastolic dysfunction and estimate mean LA pressure. Oh call for simplicity and limiting the number of variables, whereas Nagueh (26) argues for the satisfactory performance of the existing guidelines based on validation and outcome studies, among other considerations.

While *JACC: Cardiovascular Imaging* is primarily focused on presenting the best in the imaging sciences, the ultimate goal is always to improve patient care—this can only happen if front-line clinicians can translate these advances into high-quality imaging for their patients. Therefore, we are very much dedicated to educating our front-line clinician readers on understanding seminal concepts and using these to best diagnose and treat their patients. In this regard, we are excited to launch a new category geared toward the practicing clinicians that focuses on practical aspects of the day-to-day application of noninvasive cardiovascular imaging. This new multimedia series, the "Case-Based Imaging Curriculum," is a new take on the traditional iPix that is so popular in *JACC: Cardiovascular Imaging*. First, it will be entirely case-based and will cover all the necessary salient features of any disease condition in just 7 to 10 illustrative cases. Second, it will, to start with, be video-based but with the added bonus of narration—the expert narrator will indicate specific features in each case and highlight evidence-based nuggets that we believe to be crucial for good patient care in that particular condition—this will be just like attending a high-quality conference, except that it is free and the expert is coming to you! Third it will, have interactivity—initially in the form of quizzes and the answers that will be linked to a SCORM platform in the near future—this will allow us to collect anonymized data about which areas and concepts our readers find useful or difficult and will allow us to define where we need to better focus our efforts to improve the educational experience for our readers. Finally, there are some exciting developments in the offing that will allow our readers to take this information directly into their imaging laboratories for quality assurance and standardizing their practice patterns as well as earn continuing medical education credits. This January 2020 issue inaugurates this feature by addressing a common topic that we see in our day-to-day practice—nuances of diastolic function assessment by echocardiography through several narrated cases that cover a wide spectrum of pathology and pathophysiology. We hope you will enjoy these real-patient scenarios, and we eagerly look forward to your feedback. Stay tuned for more exciting features to come in the next few months.

ADDRESS FOR CORRESPONDENCE: Dr. Y. Chandrashekhar, Division of Cardiology, Mail Code: 111c, University of Minnesota/VA Medical Center, 1 Veterans Drive, Minneapolis, Minnesota 55417. E-mail: shekh003@umn.ed.

REFERENCES

1. Villemain O, Correia M, Mousseaux E, et al. Myocardial stiffness evaluation using noninvasive shear wave imaging in healthy and hypertrophic cardiomyopathic adults. J Am Coll Cardiol Img 2019;12:1135–45.

2. Petrescu A, Santos P, Orlowska M, et al. Velocities of naturally occurring myocardial shear waves increase with age and in cardiac amyloidosis. J Am Coll Cardiol Img 2019;12:2389–98.

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

4. Lancellotti P, Galderisi M, Edvardsen T, 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.

5. Almeida JG, Fontes-Carvalho R, Sampaio F, 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.

6. Morris DA, Belyavskiy E, Aravind-Kumar R, et al. Potential usefulness and clinical relevance of adding left atrial strain to left atrial volume index in the detection of left ventricular diastolic dysfunction. J Am Coll Cardiol Img 2018;11:1405–15.

7. Kosmala W, Przewlocka-Kosmala M, Rojek A, Marwick TH. Comparison of the diastolic stress test with a combined resting echocardiography and biomarker approach to patients with exertional dyspnea: diagnostic and prognostic implications. J Am Coll Cardiol Img 2019;12:771–80.

8. Selmeryd J, Henriksen E, Dalen H, Hedberg P. Derivation and evaluation of age-specific multivariate reference regions to aid in identification of abnormal filling patterns: the HUNT and VaMIS studies. J Am Coll Cardiol Img 2018;11:400–8.

9. Salem Omar AM, Shameer K, Narula S, et al. artificial intelligence-based assessment of left ventricular filling pressures from 2-dimensional cardiac ultrasound images. J Am Coll Cardiol Img 2018;11:509–10.

10. Wang Y, Yang H, Huynh Q, Nolan M, Negishi K, Marwick TH. Diagnosis of nonischemic stage B heart failure in type 2 diabetes mellitus. J Am Coll Cardiol Img 2018;11:1390–400.

11. Lancaster MC, Salem Omar AM, Narula S, Kulkarni H, Narula J, Sengupta PP. Phenotypic clustering of left ventricular diastolic function parameters: patterns and prognostic relevance. J Am Coll Cardiol Img 2019;12:1149–61.

12. Nagueh SF. Left ventricular diastolic function: understanding pathophysiology, diagnosis, and prognosis with echocardiography. J Am Coll Cardiol Img 2019;13:228–44.

13. Mordi IR, Singh S, Rudd A, et al. Comprehensive echocardiographic and cardiac magnetic resonance evaluation differentiates among heart failure with preserved ejection fraction patients, hypertensive patients, and healthy control subjects. J Am Coll Cardiol Img 2018;11:577–85.

14. Chamsi-Pasha M, Zhan Y, Debs D, Shah DJ. Role of CMR in the evaluation of LV diastolic function: current role and future perspectives. J Am Coll Cardiol Img 2020;13:283–96.

15. Obokata M, Reddy YNV, Borlaug BA. Echocardiography in heart failure with preserved ejection fraction: pathophysiology, diagnosis and phenotyping. J Am Coll Cardiol Img 2019;12:2098–9.

16. Solomon SD, McMurray JJV, Anand IS, et al. angiotensin-neprilysin inhibition in heart failure with preserved ejection fraction. N Engl J Med 2019;381:1609–20.

17. Bianco CM, Farjo PD, Ghaffar YA, Sengupta PP. Myocardial mechanics in patients with normal LVEF and diastolic dysfunction. J Am Coll Cardiol Img 2020;13:258–71.

18. Litwin SE, Zile MR. Should we test for diastolic dysfunction? How and how often? J Am Coll Cardiol Img 2020;13:297–308.

19. 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. J Am Coll Cardiol Img 2018;11:1737–46.

20. Ha J-W, Andersen OS, Smiseth OA. Diastolic stress test: Invasive and noninvasive testing. J Am Coll Cardiol Img 2020;13:272–82.

21. Kosmala MP, Marwick TH, Yang H, Wright L, Negishi K, Kosmala W. Association of reduced left ventricular apical untwisting with incident heart failure in asymptomatic patients with heart failure risk factors. J Am Coll Cardiol Img 2020;13:187–94.

22. Upshaw J, Finkelman B, Hubbard RA, et al. Comprehensive assessment of changes in left ventricular diastolic function with contemporary breast cancer therapy. J Am Coll Cardiol Img 2020;13:198–210.

23. Negishi T, Thavendiranathan P, Negishi K, Marwick TH. Rationale and design of the strain surveillance of chemotherapy for improving cardiovascular outcomes: the SUC-COUR trial. J Am Coll Cardiol Img 2018;11:1098–105.

24. Kosmala W, Marwick TH. Asymptomatic left ventricular diastolic dysfunction: predicting progression to symptomatic heart failure. J Am Coll Cardiol Img 2020;13:215–27.

25. Chetrit M, Cremer PC, Klein AL. Imaging of diastolic dysfunction in community-based epidemiologic studies and randomized controlled trials. J Am Coll Cardiol Img 2020;13:310–27.

26. Oh JK, Miranda WR, Bird JG, Kane GC, Nagueh SF. The 2016 Diastolic Function Guideline: Is it Already Time to Revisit or Revise Them? J Am Coll Cardiol Img 2020;13:328–36.