Scholars LITERATURE

International Journal of Integrative Cardiology

Short Communication

DOI: https://doi.org/10.47275/2690-862X-125
Volume 3 Issue 2

Can Left Atrial Function be used as a Marker for Evaluating the Severity of Heart Failure with Preserved Ejection Fraction?

Li Liu[1]* and Mingxue Sun[2]

[1]Department of Cardiology, Affiliated Zhongshan Hospital of Dalian University, China

[2]Department of Cardiology, The People's Hospital of Sanya City, China

Abstract

Heart failure with preserved ejection fraction (HFpEF) is a common clinical syndrome with increasing prevalence. Patients with HFpEF experience similar patterns of morbidity and functional decline as do those with heart failure and reduced ejection fraction, but effective treatments for HFpEF are lacking. The pathophysiology of HFpEF is complex and the major gaps are still present today in our understanding of HFpEF pathophysiology and managing patients. Recent studies revealed that left atrial (LA) dysfunction may be an important player in the pathophysiology of HFpEF. LA function assessed with the novel technique of 2D speckle tracking echocardiography (2D-STE) is able to provide critical information about the status of cardiac function, therefore could be used as a marker for the severity of HFpEF. LA dysfunction may represent a potential therapeutic target for patients with HFpEF.

Correspondence to: Li Liu, Department of Cardiology, Affiliated Zhongshan Hospital of Dalian University, Dalian, Liaoning Province, 116001, China; E-mail: lbeilliun@yahoo.com

Citation: Liu L, Sun M (2021) Can Left Atrial Function be used as a Marker for Evaluating the Severity of Heart Failure with Preserved Ejection Fraction?. Int J Integr Cardiol, Volume 3:2. 125. DOI: https://doi.org/10.47275/2690-862X-125

Received: June 23, 2021; **Accepted:** July 12, 2021; **Published:** July 19, 2021

Introduction

Heart failure (HF) with preserved ejection fraction (HFpEF) is a complex syndrome characterized by heart failure symptoms and signs, but normal or near-normal left ventricular ejection fraction (LV-EF) [1]. Epidemiological studies indicated that the prevalence of HFpEF within the population varies from 1.14% to 5.5%, and appears to be rising [1-4]. At least one-half of patients with HF indeed have preserved ejection fraction, and it is more likely seen in women, the elderly, people with a history of hypertension, obesity, and other cardiovascular risk factors [2,4 and 5]. Patients with HFpEF experience similar patterns of morbidity and functional decline as do those with heart failure and reduced ejection fraction (HFrEF) [4,5], but different from HFrEF which has classes of drugs to improve patients' symptoms and outcome, the effective treatments for HFpEF are lacking [5,6]. One of the reasons is thought to be due to incomplete understanding of its pathophysiology therefore poor matching of therapeutic mechanisms and primary pathophysiological processes.

The diagnosis, classification of its severity, and management of HFpEF remain challenging due to the complicated pathophysiological processes, phenotypic manifestations, and frequent multiple concomitant illnesses [4,7]. In the clinical setting, echocardiography plays a key role in the evaluation and management of HFpEF. However, currently used techniques, Two dimensional (2D) and Doppler echocardiography have shown several limitations [7,8]. 2D speckle tracking echocardiography (2D-STE) is a novel technique that has been shown a feasible and sensitive method for evaluating the left atrial (LA) deformation in patients with HFpEF. In this review, we will address the potential role of left atrial dysfunction assessed with 2D-STE in the diagnosis and clarification of the severity in patients with HFpEF according to our study and existing literature.

Diagnostic Criteria for HFpEF

The diagnosis of HFpEF is challenging. The guidelines for diagnosing HFpEF have been proposed by the American Society of Echocardiography and the European Association of Cardiovascular Imaging (ASE/EACVI) and the European Society of Cardiology (ESC) respectively [10,11]. In the guideline proposed by ASE/EACVI, the key functional alteration is the elevated left ventricular filling pressures (LVFP) in patients with signs and symptoms of heart failure and with the myocardial disease [10], while in the ESC guideline, the key functional alterations are the ratio of early diastolic transmitral inflow velocity to mitral annular tissue velocity (E/e') ≥13 and an average septal-lateral e' velocity < 9 cm/s. In addition, LV mass > 115g/m2 (men)/95g/m2 (women) or LAVI > 34mL/m2 was considered as key structural alterations [11]. The determination of elevated LVFP is mainly based on the mitral E/A ratio. If E/A ratio ≥ 2, the patients are considered as having elevated LV filling pressures. In patients with mitral E/A ratio between 0.8 and 1.9, further criteria (including left atrial volume index, peak velocity of tricuspid regurgitation, and E/e') should be considered

for finally determining elevated LVFP **(Figure)**. Briefly, the diagnosis of HFpEF can be established if the following criteria were met [10]: (1) symptoms and/or signs of heart failure; (2) LV-EF ≥50%; (3) elevated brain natriuretic peptide levels; (4) At least one of the following: 1) Associated structural heart disease (left ventricular hypertrophy and/or left atrial hypertrophy); 2) Elevated LVFP or diastolic dysfunction. Moreover, both guidelines also highlighted the potential role of diastolic stress test for those patients with suspected HFpEF despite negative functional or structural criteria. Recently, several new algorithms were proposed for diagnosing HFpEF, such as diastolic stress test [10,11], HFA-PEFF score from Heart Failure Association [1], and H2FPEF score from the Mayo Clinic group [12].

Transthoracic 2D and Doppler echocardiography play a key role in the evaluation and management of HFpEF in the clinical setting. LV-EF (≥50%) measured using 2D-echocardiography is used as a cut-off for inclusion/exclusion criteria [10]. However, some limitations were present regarding these quantitative methods [7,8 and 13-15]. And also, the accuracy of the E/e' ratio in HFpEF has recently reported only a modest correlation between E/e' and invasively obtained resting filling pressures (pooled r = 0.56) [16]. Therefore, along with the further understanding of this disorder, the diagnostic criteria for HFpEF will likely continue to evolve.

The Pathophysiological Mechanisms

HFpEF was not caused simply by LV diastolic dysfunction, its pathophysiology is much more complex which is related to cardiac structural and functional alterations, and systemic and pulmonary vascular abnormalities. The essence of the pathophysiology of HFpEF is an increase of LVFP due to delayed active relaxation, intrinsic ventricular stiffness, or a combination of these factors [11,17]. Elevation in LVFP alters the Starling forces across the pulmonary capillaries through the left atrium, favoring filtration of water out of the vascular space and into the interstitium of lungs [18,19], induces alterations in gas exchange and pulmonary ventilation, and therefore reductions in aerobic capacity [20,21]. These factors prompt patients' symptoms of dyspnea, especially during the stress of exercise. HFpEF is believed to be a heterogeneous entity. The majority of HFpEF patients do not have any known specific genetic, pericardial, myocardial, or valvular etiology. However, most patients have one or more comorbidities

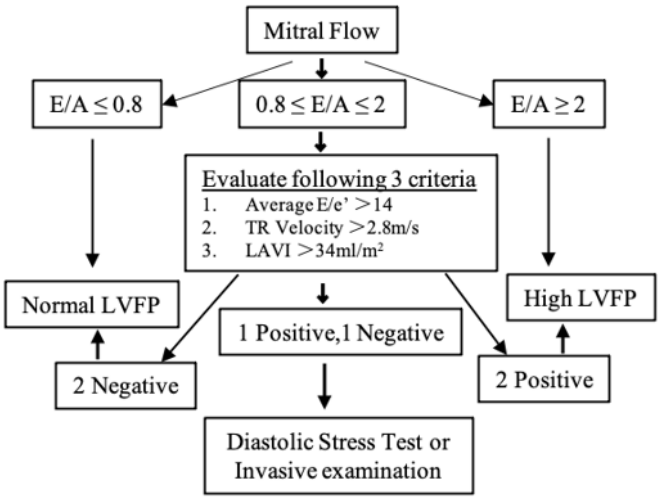

Figure: Algorithm for Estimation of LV Filling Pressure (LVFP).
Note: Adapted from Dzhioeva O, et al. (7).

that may worsen HFpEF, such as hypertrophic cardiomyopathy, hypertension, diabetes, chronic kidney disease, obesity, and chronic obstructive pulmonary disease [22-25].

HFpEF and LA Function

The left atrium plays an important role in ensuring the proper performance of left ventricular function and systemic circulation [26]. It is not just simply a conduit for LV filling. From a hemodynamic perspective left atrium is divided into three phases, LA reservoir, conduit, and pump function, all of which contribute to LV filling [13,26 and 27]. Conversely, LV function influences LA function. LA reservoir function is affected by LV contraction and LA compliance. LA pump function is influenced by LV end-diastolic pressure, LV compliance, and LA contractile properties, while LA conduit function is dependent on LV diastolic properties [27,28]. In patients with HFpEF, as LV diastolic filling pressures are elevated intermittently over time, there is secondary remodelling and dysfunction that develops in the left atrium, therefore, LA dysfunction is common in patients with HFpEF [9,29-31]. Studies have indicated that LA structure and functions provide incremental clinical and prognostic information in patients with HFpEF [8,13,14,27, and 32], it is associated with worse symptoms, more severe pulmonary vascular disease, greater right ventricular (RV) dysfunction, depressed exercise capacity, and increase mortality [29-32,33 and 34].

Accurate evaluation of LA function has important significance. In clinical practice, LA function is usually assessed by 2D and Doppler echocardiography through analysis of pulmonary venous and transmitral flows, and LA myocardial velocities by tissue-Doppler echocardiography. However, these quantitative methods are affected by myocardial tethering, hemodynamic loading, and acquisition angle [7,8, and 13-15]. 2D-STE is a relatively new echocardiographic technique that tracks the spatial dislocation of speckles (natural acoustic reflections) for regional and global myocardial function analysis, it gives an excellent assessment of the atrial deformation profile during an entire cardiac cycle, closely following the LA physiology [35-37]. In contrast to Doppler-derived parameters, speckle tracking has the advantages of being angle-independent, less load-dependent, less affected by reverberations, side lobes, and drop-out artifacts. 2D-STE was found to be a feasible, reproducible, and sensitive method to assess LA function [37-39]. Several studies have shown that strain imaging can detect LA dysfunction before the manifestation of LA structural changes [40-42]. Reduction in LA strain was found to be an important predictor in separating patients with clinical HFpEF and asymptomatic diastolic dysfunction [29].

In our current study [43], we observed significant impairment of LA functions assessed with 2D-STE, including reservoir function, conduct function, and pump function in patients with HFpEF. With the cardiac functions further worsening (NYHA class II to class IV), the LA triphasic functions become even worse although the size of LA (LAD) has no significant changes. Correlation analysis indicated that LA triphasic function has a strong correlation with LV systolic function (LV-GLS %), and modest correlation with the LV diastolic function (E/e'), suggesting that LA function can be used as a sensitive marker for scaling the severity of HFpEF [43]. Our study is consistent with an important study conducted by Telles and colleagues [44], they also observed that patients with HFpEF displayed reduced LA reservoir and pump function assessed by longitudinal strain, strain rate, and LA ejection fraction, with increased LA stiffness, while the LA volume/LA volume index has no difference compared to control group, meaning

that LA function was the greater correlate of abnormal hemodynamic rather than structure.

Conclusion

In conclusion, patients with HFpEF displayed significant impairment of LA function assessed with 2D-STE, which may be an important player in the pathophysiology of HFpEF rather than simply a secondary consequence of LV diastolic dysfunction. LA triphasic functions are a sensitive marker for evaluating the severity of HFpEF, however, the cut-off value of LA function needs to be determined from large-scale studies. LA dysfunction may represent a potential therapeutic target for patients with HFpEF, warranted further investigation.

Conflict of Interest

The author has no conflict of interest to disclose.

Consent for Publication

All authors have read and agreed to the published version of the manuscript.

Funding

No.

References

1. Pieske B, Tschöpe C, De Boer RA, Fraser AG, Anker SD, et al. (2019) How to diagnose heart failure with preserved ejection fraction: the HFA–PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). Eur Heart J 40: 3297-3317. https://doi.org/10.1093/eurheartj/ehz641
2. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, et al. (2006) Trends in prevalence and outcome of heart failure with preserved ejection fraction. N Engl J Med 355: 251-259. https://doi.org/10.1056/NEJMoa052256
3. Senni M, Paulus WJ, Gavazzi A, Fraser AG, Díez J, et al. (2014) New strategies for heart failure with preserved ejection fraction: the importance of targeted therapies for heart failure phenotypes. Eur Heart J 35: 2797-2815. https://doi.org/10.1093/eurheartj/ehu204
4. Andersen MJ, Borlaug BA (2014) Heart Failure with preserved ejection fraction: Current understandings and challenges. Curr Cardiol Rep 16: 501-522. https://doi.org/10.1007/s11886-014-0501-8
5. Becher PM, Fluschnik N, Blankenberg S, Westermann D (2015) Challenging aspects of treatment strategies in heart failure with preserved ejection fraction: "why did recent clinical trials fail?". World J Cardiol 7: 544-554. https://doi.org/10.4330/wjc.v7.i9.544
6. Pfeffer MA, Shah AM, Borlaug BA (2019) Heart failure with preserved ejection fraction: in perspective. Circ Res 124: 1598-1617. https://doi.org/10.1161/CIRCRESAHA.119.313572
7. Dzhioeva O, Belyavskiy E (2020) Diagnosis and management of patients with heart failure with preserved ejection fraction (HFpEF): current perspectives and recommendations. Ther Clin Risk Manag 16: 769-785. https://doi.org/10.2147/TCRM.S207117
8. Sharifov OF, Schiros CG, Aban I, Denney TS, Gupta H (2016) Diagnostic accuracy of tissue Doppler index E/e' for evaluating left ventricular filling pressure and diastolic dysfunction/heart failure with preserved ejection fraction: a systematic review and meta-analysis. J Am Heart Assoc 5: e002530. https://doi.org/10.1161/JAHA.115.002530
9. Santos A, Kraigher-Krainer E, Gupta DK, Claggett B, Zile MR, et al. (2014) Impaired left atrial function in heart failure with preserved ejection fraction. Eur J Heart Fail 16: 1096-1103. https://doi.org/10.1002/ejhf.147
10. Ponikowski P, Voors AA, Anker SD, Bueno H, Cle JGF, et al. (2016) 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 J Heart Fail 18: 891-975. https://doi.org/10.1093/eurheartj/ehw128
11. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, et al. (2009) 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 17: 1321-1360. https://doi.org/10.1093/ejechocard/jep007
12. Reddy YNV, Carter RE, Obokata M, Redfield MM, Borlaug BA, et al. (2018) A Simple, Evidence-based approach to help guide diagnosis of heart failure with preserved ejection fraction. Circulation 138: 861- 870. https://doi.org/10.1161/CIRCULATIONAHA.118.034646
13. Hoit BD (2014) Left atrial size and function: role in prognosis. J Am Coll Cardiol 63: 493-505. https://doi.org/10.1016/j.jacc.2013.10.055
14. Leung DY, Boyd A, Ng AA, Chi C, Thomas L, et al. (2008) Echocardiographic evaluation of left atrial size and function: current understanding, pathophysiologic correlates, and prognostic implications. Am Heart J 156: 1056-1064. https://doi.org/10.1016/j.ahj.2008.07.021
15. Teske AJ, De Boeck BW, Melman PG, Sieswerda GT, Doevendans PA, et al. Echocardiographic quantification of myocardial function using tissue deformation imaging, a guide to image acquisition and analysis using tissue doppler and speckle tracking. Cardiovasc Ultrasound 5: 27. https://doi.org/10.1186/1476-7120-5-27
16. Nauta JF, Hummel YM, van der Meer P, Lam CSP, Voors AA, et al. (2018) 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 20: 1303-1311. https://doi.org/10.1002/ejhf.1220
17. Borlaug BA (2014) The pathophysiology of heart failure with preserved ejection fraction. Nat Rev Cardiol 11: 507-515. https://doi.org/10.1038/nrcardio.2014.83
18. Melenovsky V, Andersen MJ, Andress K, Reddy YN, Borlaug BA (2015) Lung congestion in chronic heart failure: haemodynamic, clinical, and prognostic implications. Eur J Heart Fail 17: 1161-1171. https://doi.org/10.1002/ejhf.417
19. Thompson RB, Pagano JJ, Chow K, Sekowski V, Ezekowitz J, et al. (2017) Subclinical pulmonary edema is associated with reduced exercise capacity in HFpEF and HFrEF. J Am Coll Cardiol 70: 1827-1838. https://doi.org/10.1016/j.jacc.2017.07.787
20. Obokata M, Olson TP, Reddy YN, Melenovsky V, Kane GC, et al. (2018) Hemodynamics, dyspnea, and pulmonary reserve in heart failure with preserved ejection fraction. Eur Heart J 39: 2810-2821. https://doi.org/10.1093/eurheartj/ehy268
21. Reddy YNV, Olson TP, Obokata M, Melenovsky V, Borlaug BA (2018) Hemodynamic correlates and diagnostic role of cardiopulmonary exercise testing in heart failure with preserved ejection fraction. JACC Heart Fail 6: 665-675. https://doi.org/10.1016/j.jchf.2018.03.003
22. Chioncel O, Lainscak M, Seferovic PM, Anker SD, Crespo-Leiro MG, et al. (2017) Epidemiology and one-year outcomes in patients with chronic heart failure and preserved, mid-range and reduced ejection fraction: an analysis of the ESC heart failure long-term registry. Eur J Heart Fail 19: 1574-1585. https://doi.org/10.1002/ejhf.813
23. Triposkiadis F, Giamouzis G, Parissis J, Starling RC, Boudoulas H, et al. (2016) Reframing the association and significance of comorbiditiesin heart failure. Eur J Heart Fail 18: 744-758. https://doi.org/10.1002/ejhf.600
24. Beale AL, Meyer P, Marwick TH, Lam CS, Kaye DM (2018) Sex differences in cardiovascular pathophysiology: why women are overrepresented in heart failure with preserved ejection fraction. Circulation 138: 198-205. https://doi.org/10.1161/CIRCULATIONAHA.118.034271
25. Borlaug BA, Olson TP, Lam CS, Flood KS, Lerman A, et al. (2010) Global cardiovascular reserve dysfunction in heart failure with preserved ejection fraction. J Am Coll Cardiol 56: 845-854. https://doi.org/10.1016/j.jacc.2010.03.077
26. Hoit BD (2005) Assessing atrial mechanical remodeling and its consequences. Circulation 112: 304-306. https://doi.org/10.1161/CIRCULATIONAHA.105.547331
27. Thomas L, Marwick TH, Popescu BA, Donal E, Badano LP (2019) Left atrial structure and function and left ventricular diastolic dysfunction: JACC state-of-the-art review. J Am Coll Cardiol 73: 1961-1977. https://doi.org/10.1016/j.jacc.2019.01.059
28. Barbier P, Solomon SB, Schiller NB, Glantz SA (1999) Left atrial relaxation and left ventricular systolic function determine left atrial reservoir function. Circulation 100: 427-436. https://doi.org/10.1161/01.CIR.100.4.427
29. Melenovsky V, Hwang SJ, Redfield MM, Zakeri R, Lin G, et al. (2015) Left atrial remodeling and function in advanced heart failure with preserved or

reduced ejection fraction. Circ Heart Fail 8: 295-303. https://doi.org/10.1161/CIRCHEARTFAILURE.114.001667

30. Freed BH, Daruwalla V, Cheng JY, Aguilar FG, Beussink L, et al. (2016) Prognostic utility and clinical significance of cardiac mechanics in heart failure with preserved ejection fraction: importance of left atrial strain. Circ Cardiovasc Imag 9: e003754. https://doi.org/10.1161/CIRCIMAGING.115.003754

31. Kurt M, Wang J, Torre-Amione G, Nagueh SF (2009) Left atrial function in diastolic heart failure. Circ Cardiovasc Imaging 2: 10-15. https://doi.org/10.1161/CIRCIMAGING.108.813071

32. Santos AB, Roca GQ, Claggett B, Sweitzer NK, Shah SJ, et al. (2016) Prognostic relevance of left atrial dysfunction in heart failure with preserved ejection fraction. Circ Heart Fail 9: e002763. https://doi.org/10.1161/CIRCHEARTFAILURE.115.002763

33. Melenovsky V, Borlaug BA, Rosen B, Hay I, Ferruci L, et al. (2007) Cardiovascular features of heart failure with preserved ejection fraction versus nonfailing hypertensive left ventricular hypertrophy in the urban Baltimore community: the role of atrial remodeling/dysfunction. J Am Coll Cardiol 49: 198-207. https://doi.org/10.1016/j.jacc.2006.08.050

34. Sugimoto T, Bandera F, Generati G, Alfonzetti E, Bussadori C, et al. (2017) Left atrial function dynamics during exercise in heart failure: pathophysiological implications on the right heart and exercise ventilation inefficiency. JACC Cardiovasc Imaging 10: 1253-1264. https://doi.org/10.1016/j.jcmg.2016.09.021

35. Mondillo S, Galderisi M, Mele D, Cameli M, Lomoriello VS, et al. (2011) Echocardiography study group of the Italian society of cardiology: speckle tracking echocardiography: a new technique for assessing myocardial function. J Ultrasound Med 30: 71-83. https://doi.org/10.7863/jum.2011.30.1.71

36. Gan GCH, Ferkh A, Boyd A, Thomas L (2018) Left atrial function: evaluation by strain analysis. Cardiovasc Diagn Ther 8: 29-46. https://doi.org/10.21037/cdt.2017.06.08

37. Cameli M, Lisi M, Righini FM, Mondillo S (2012) Novel echocardiographic techniques to assess left atrial size, anatomy and function. Cardiovasc Ultrasound 10: 4. https://doi.org/10.1186/1476-7120-10-4

38. Cameli M, Caputo M, Mondillo S, Ballo P, Palmerini E, et al. (2009) Feasibility and reference values of left atrial longitudinal strain imaging by two-dimensional speckle tracking. Cardiovasc Ultrasound 7: 6. https://doi.org/10.1186/1476-7120-7-6

39. Vianna-Pinton R, Moreno CA, Baxter CM, Lee KS, Tsang TSM, et al. (2009) Two-dimensional speckle-tracking echocardiography of the left atrium: Feasibility and regional contraction and relaxation differences in normal subjects. J Am Soc Echocardiogr 22: 299-305. https://doi.org/10.1016/j.echo.2008.12.017

40. Nagao M, Tsuzuki C, Wakabayashi K, Hashimoto A, Nakata T, et al. (2007) Noninvasive assessment of left atrial function by strain rate imaging in patients with hypertension: a possible beneficial effect of renin-angiotensin system inhibition on left atrial function. Hypertens Res 30: 13-21. https://doi.org/10.1291/hypres.30.13

41. Yan P, Sun B, Shi H, Zhu W, Zhou Q, et al. (2012) Left atrial and right atrial deformation in patients with coronary artery disease: a velocity vector imaging-based study. PLoS One 7: e51204. https://doi.org/10.1371/journal.pone.0051204

42. Wang Y, Zhang Y, Ma C, Guan Z, Liu S, et al. (2016) Evaluation of left and right atrial function in patients with coronary slow-flow phenomenon using two-dimensional speckle tracking echocardiography. Echocardiography 33: 871-880. https://doi.org/10.1111/echo.13197

43. Sun M, Shui Z, Wang Y, Gao Y, Liang S, et al. (2021) The left atrial function as a marker for the severity of heart failure and preserved ejection fraction. Cardiol and Cardiovasc Med 5: 280-293. https://doi.org/10.26502/fccm.92920203

44. Telles F, Nanayakkara S, Evans S, Patel HC, Mariani J, et al. (2019) Impaired left atrial strain predicts abnormal exercise hemodynamics in heart failure with preserved ejection fraction. Eur J Heart Fail 21: 495-505. https://doi.org/10.1002/ejhf.1399