JACC: CARDIOVASCULAR IMAGING
VOL. 10, NO. 10, 2017

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcmg.2016.10.006

EDITORIAL COMMENT

Understanding the Role of the LA in Functional Responses to Heart Failure*

Thomas H. Marwick, MBBS, PhD, MPH, David Kaye, MBBS, PhD

Although the contribution of left atrial (LA) contractile function to the ventricular stroke volume is well-understood, the role of this chamber as a capacitor between the left ventricle (LV) and the pulmonary circulation is often neglected. Previous experimental models have shown augmentation of LA reservoir and pump function with exercise, without alteration of conduit function in normal hearts (1) and mild diastolic dysfunction (2). The reservoir facilitates LV filling by maintaining a high AV pressure gradient throughout diastole, and may be especially important in heart failure (HF) with preserved ejection fraction (HFpEF) (3).

SEE PAGE 1253

The paper by Sugimoto et al. (4) in this issue of *iJACC* adds further interesting insight into the role of the LA in the association between LV pathology, pulmonary congestion with exercise intolerance, and right ventricular (RV) dysfunction. It does so by studying the LA strain response to exercise in 76 HF patients, 69 of whom had interpretable responses (20 of whom had HFpEF) and 32 control subjects with normal LA. Lung mechanics, ventilation, and gas exchange were used to identify ventilatory inefficiency. In general, impaired LA strain (<23%) was associated closely with LA enlargement (>34 ml/m^2). The cardiac output response to exercise was blunted in HF with reduced ejection fraction (HFrEF), with an intermediate response in HFpEF. As expected, HF patients had an increase in E/e' with exercise, but significant exercise mitral regurgitation was only detected in HFrEF. Of relevance to understanding the role of the LA in the hemodynamic response to exercise, the stroke volume augmentation was modest and lowest in HFrEF. The normal increment of atrial strain rate (a marker of atrial contraction) in recovery did not occur in HF, and atrial strain reserve (reflecting the expected increment in reservoir function) was exhausted in HFrEF and reduced to a lesser degree in HFpEF. Interestingly, the investigators also found relationships between minute ventilation and carbon dioxide production (VE/VCO_2) slope, a marker of excessive ventilation that has been associated with a poor prognosis in HF. This parameter corresponds with the rate and magnitude of the rise in LA pressure, so pulmonary pressures are key to the relationship between LA strain and VE/VCO_2 (5).

Because the function of the RV is exquisitely linked to afterload, the investigators assessed RV-pulmonary artery (PA) coupling as the ratio between PA systolic pressure and tricuspid annular systolic excursion. This ratio increased in HF patients more than controls, and increased especially in HFrEF. Although only a handful of participants had an enlarged LA with normal function, or impaired LA function with normal left atrial volume (LAV), the latter groups tended to increase PA systolic pressure/tricuspid annular systolic excursion with exercise. The interpretation of these observations is complex and must be considered in the context of differences in the RV function exercise response, together with the temporal pattern of changes in LA pressure. Both pulmonary hypertension and RV dysfunction are well-recognized and associated with adverse outcome in HFpEF and HFrEF. The pathogenesis of pulmonary hypertension in HF is complex, but the RV adaptation to chronic pressure overload is related to LA function (6). In pulmonary hypertension, not only PA stiffness (pulsatile load), but also vascular resistance (steady afterload) are independently associated with the degree of RV dysfunction, dilation, and hypertrophy. In HF patients, pulmonary congestion is correlated inversely

*Editorials published in *JACC: Cardiovascular Imaging* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Imaging* or the American College of Cardiology.

From the Baker-IDI Heart and Diabetes Institute, Melbourne, Australia. Dr. Marwick has received research grants from General Electric Medical Systems. Dr. Kaye has reported that he has no relationships relevant to the contents of this paper to disclose.

JACC: CARDIOVASCULAR IMAGING, VOL. 10, NO. 10, 2017
OCTOBER 2017:1265–7

with PA compliance ($p < 0.001$), and was associated with reduced survival ($p < 0.0001$), independent of PA wedge pressure and type B-natriuretic peptide. Indeed, patients with pulmonary congestion have only slightly greater PA wedge pressure (22 vs. 19 mm Hg; $p = 0.002$) than those with dry lungs, but have a 25% lower PA compliance and >25% higher pulmonary resistance, transpulmonary gradients, and PA pressures, with greater RV dilatation and dysfunction (7). Moreover, a sustained reduction in LV filling pressures with LV assist device implantation in HFrEF is associated with a reduction in both PA pressure and pulmonary vascular resistance, the latter likely reflecting reverse vascular remodeling (8). The influence of RV afterload in influencing RV function has recently been established in HFpEF (9), and impaired atrial reservoir function is associated with this loss of pulmonary vascular compliance.

Conventional echocardiographic indices of LA function used the Doppler signal of transmitral and pulmonary venous flow to define reservoir, conduit, and active phases of atrial function (10). The development of global LA strain has provided a simpler, single step for measuring these parameters. However, despite research interest, this measurement has not enjoyed much clinical uptake. Although the lack of a consensus approach to its measurement has been unhelpful (11), the interested clinician might reasonably ask whether adding the analysis of atrial function to standard echocardiography is a justifiable increment in complexity. Indeed, LAV is well-accepted as a simple marker of the role of the left atrium. LAV has become a cornerstone of diastolic evaluation (12), effectively providing a time-averaged marker of elevated LV diastolic pressure. Although this parameter is imperfect—for example, the left atrium may not reverse remodel very effectively (13)—it is clearly a predictor of adverse outcomes in a variety of situations (14). Despite this, the assessment of atrial function, both using conventional Doppler techniques and atrial strain, has been shown to add incremental information to the structural information provided by LAV (14). In the absence of specific software for LA deformation, investigators have generally performed these measurements by applying the LV strain software to the atrium (11). Measuring the LA response to exercise using speckle tracking is technically challenging. Indeed, because of the challenges of post-stress imaging, only the 4-chamber view was used in this study. This may be important, because the evaluation of global LA strain makes an assumption that the regional response is uniform, which seems unlikely, given the presence of fibrous tissue between the pulmonary veins. The inability to average across multiple views may therefore be important. Some other potential limitations have been well-defended by the authors. Mitral regurgitation is a potential confounder, because it would both influence atrial strain as well as outcome, without being related to atrial function. Fortunately, mitral regurgitation is an accompaniment to HFrEF rather than HFpEF. Second, although some investigators have questioned whether LA reservoir function is simply the mirror image of LV diastolic dysfunction, these investigators show that it is actually independent of LA contractile function.

To develop an integrated understanding of the pathophysiologic basis of HF symptoms (i.e., breathlessness, fatigue, and congestion), one can conceptually parse the physiologic contributors into left and RV filling pressures, left and right heart output, and their relevant determinants, including afterload and renal function. Added factors such as skeletal muscle function and endothelial function are also relevant. The development and application of newer approaches such as LA strain analysis, particularly with regard to exercise limitation, will aid in our treatment of HF. The results of this study provide a convincing argument that LA function is a critical link between the dysfunctional LV and its pulmonary and RV consequences. Clearly, atrial image quality after exercise can be challenging, so the protocol provides a new level of complexity in atrial assessment, and it is unclear that the atrial strain response to exercise stress will become a useful clinical tool. If the current generation of devices to “unload” the LA by permitting shunting to the RA are successful, then such a test could be helpful to better understand which patients are likely to respond, and perhaps how to tailor the device to the severity of the problem.

ADDRESS FOR CORRESPONDENCE: Dr. Thomas H. Marwick, Baker-IDI Heart and Diabetes Institute, 75 Commercial Road, Melbourne, Vic 3004, Australia. E-mail: tom.marwick@bakeridi.edu.au.

REFERENCES

1. Nishikawa Y, Roberts JP, Tan P, Klopfenstein CE, Klopfenstein HS. Effect of dynamic exercise on left atrial function in conscious dogs. J Physiol 1994; 481:457–68.

2. Prioli A, Marino P, Lanzoni L, Zardini P. Increasing degrees of left ventricular filling impairment modulate left atrial function in humans. Am J Cardiol 1998;82:756–61.

3. Guazzi M, Borlaug BA. Pulmonary hypertension due to left heart disease. Circulation 2012;126:975–90.

4. Sugimoto T, Bandera F, Generati G, et al. Left atrial function dynamics during exercise in heart failure: pathophysiological implications on the right heart and exercise ventilation inefficiency. J Am Coll Cardiol Img 2017;10:1253–64.

5. Maeder MT, Thompson BR, Htun N, Kaye DM. Hemodynamic determinants of the abnormal cardiopulmonary exercise response in heart failure with preserved left ventricular ejection fraction. J Card Fail 2012;18:702–10.

6. Stevens GR, Garcia-Alvarez A, Sahni S, Garcia MJ, Fuster V, Sanz J. RV dysfunction in pulmonary hypertension is independently related to pulmonary artery stiffness. J Am Coll Cardiol Img 2012;5:378–87.

7. Melenovsky V, Andersen MJ, Andress K, Reddy YN, Borlaug BA. Lung congestion in chronic heart failure: haemodynamic, clinical, and prognostic implications. Eur J Heart Fail 2015;17:1161–71.

8. Salzberg SP, Lachat ML, von Harbou K, Zund G, Turina MI. Normalization of high pulmonary vascular resistance with LVAD support in heart transplantation candidates. Eur J Cardiothorac Surg 2005;27:222–5.

9. Andersen MJ, Hwang SJ, Kane GC, et al. Enhanced pulmonary vasodilator reserve and abnormal right ventricular: pulmonary artery coupling in heart failure with preserved ejection fraction. Circ Heart Fail 2015;8:542–50.

10. Vieira MJ, Teixeira R, Goncalves L, Gersh BJ. Left atrial mechanics: echocardiographic assessment and clinical implications. J Am Soc Echocardiogr 2014;27:463–78.

11. Mor-Avi V, Lang RM, Badano LP, et al. Current and evolving echocardiographic techniques for the quantitative evaluation of cardiac mechanics: ASE/EAE consensus statement on methodology and indications endorsed by the Japanese Society of Echocardiography. J Am Soc Echocardiogr 2011; 24:277–313.

12. 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.

13. Huynh QL, Kalam K, Iannaccone A, Negishi K, Thomas L, Marwick TH. Functional and anatomic responses of the left atrium to change in estimated left ventricular filling pressure. J Am Soc Echocardiogr 2015;28: 1428–33.e1.

14. Hoit BD. Left atrial size and function: role in prognosis. J Am Coll Cardiol 2014;63: 493–505.

KEY WORDS heart failure preserved ejection fraction, heart failure reduced ejection fraction, left atrial function