Title Page

Article Title

Left atrial dilation in patients with heart failure and preserved ejection fraction: Insights from Cardiovascular Magnetic Resonance

Author names

Vassilios S Vassiliou*[1,2], Hitesh C Patel*[1], Stuart D Rosen[1], Dominique Auger[2], Carl Hayward[1], Francisco Alpendurada[2], Alexander R Lyon[1], Dudley J Pennell[1,2], Carlo Di Mario[1], Sanjay K Prasad[1,2]

Affiliations

1- NIHR Biomedical Research Unit, Royal Brompton and Harefield NHS Trust and Imperial College London, UK

2- CMR Unit, Royal Brompton Hospital, London, UK

Corresponding author

Dr Vassilios S Vassiliou, CMR Unit, Royal Brompton Hospital, Sydney Street, London, SW3 6NP, UK. Email: v.vassiliou@rbht.nhs.uk

*Dr Vassiliou and Dr Patel contributed equally.

Keywords:

HFpEF, Atrial volume, CMR, echocardiography

Left atrial dilation in patients with heart failure and preserved ejection fraction: Insights from Cardiovascular Magnetic Resonance

Vassilios S Vassiliou*, Hitesh C Patel*, Stuart D Rosen, Dominique Auger, Carl Hayward, Francisco Alpendurada, Alexander R Lyon, Dudley J Pennell, Carlo Di Mario, Sanjay K Prasad

*VSV and HCP contributed equally

Keywords: HFpEF, Atrial volume, CMR, echocardiography

The left atrium (LA) is an important load-independent barometer of left ventricular filling pressure and diastolic dysfunction. In heart failure with preserved ejection fraction (HFpEF) measuring left atrial volume has come into vogue not least because LA dilatation forms part of the diagnostic criteria[1] but also as increased size is associated with worse outcomes[2]. Moreover, atrial reverse remodelling has been used as a surrogate marker of therapeutic success in clinical trials.

Volumetric short axis Simpson's methods using cardiovascular magnetic resonance (CMR)[3,4] is widely considered gold-standard technique for calculating left atrial volume. Echocardiography is an alternative modality and, though more widely available and versatile than CMR, it has poorer spatial resolution and generally underestimates the true volume compared to CMR[3,5]. Multiple validation studies comparing the two modalities have focused on healthy volunteers alone. We sought to investigate whether LA volume calculated by 2D transthoracic echocardiography (biplane area-length [BAL] method) and CMR (BAL and gold standard volumetric Simpson's methods [CMR GS]) were comparable in a cohort of patients with HFpEF.

We analysed 72 paired studies - echocardiograms (using a Philips iE33 machine with a S5-1 transducer) and CMR (1.5T Siemens Avanto Healthcare, Erlangen, Germany and analysed on CMRtools, Cardiovascular Imaging Solutions, London, UK) from 25 patients (age 74±6 years, 15 male) with HFpEF who participated in the Renal Denervation in HFpEF (RDT-PEF) study at our institution (Clinicaltrials.gov identifier: NCT01840059), three patients only had two CMR studies. The study protocol conformed to 1975 Helsinki guidelines, had been given regional ethical approval and all patients provided written informed consent.

CMR and echocardiography studies were undertaken on the same day on three different occasions more than 90 days apart. For the CMR GS method, steady-state free precession (SSFP) cine imaging with contiguous stack of short-axis images across the LA was taken to calculate LA volume using the Simpson's method as previously described by our group[6]. For the BAL method, both for echo and CMR standard 2 chamber and 4 chamber views were also obtained to calculate LA volume as previously described[6].

In total 43 studies were performed in atrial fibrillation (AF), and 29 in sinus rhythm (SR). The absolute LA volumes using the three methods were analysed by two blinded experienced level

3 accredited observers (HP/ VV). LA volumes calculated from echocardiography using the BAL method were significantly lower than the CMR GS in the overall cohort (48.8±18.9mL/m^2 vs 68.6± 29.3mL/m^2, p <0.0001) likely due to lower spatial resolution for detecting myocardial-chamber borders[7] and foreshortening[8] (Table 1A).

This difference was driven mainly by the presence of AF. Echo BAL vs CMR GS mean LA volume in SR was similar (39.5mL/m^2 vs 41.6mL/m^2, p=0.60) but different in AF (54.6mL/m^2 vs 72.6mL/m^2, p<0.0001). However, comparison of the volumes derived from echocardiography BAL with the CMR GS method suggested good agreement when the LA volume was normal but a trend to systematic underestimation by echocardiography in patients with pathological LA enlargement (Figure 1A). This was more pronounced in patients with an LA volume >60mL/m^2 and the effect was compounded by presence of AF (Figure 1C and 1D). This phenomenon has been reported for dilated cardiomyopathy patients in sinus rhythm previously[9] but this is the first study to report this phenomenon in patients with HFpEF and AF.

There was no difference between the CMR GS and CMR BAL values (68.6±29.3mL/m^2 vs 64.7mL±29.4mL/m^2, p=0.43)(Figure 1B).

When compared to the CMR GS , echocardiography BAL incorrectly classified 4/14 (29%) patients as having normal LA volume when it was dilated on the CMR GS, and 16/58 as dilated (28%) when it was normal on the CMR GS (Table 1B) if upper limit of normal was taken as 34mL/m^2 for echocardiography and 53mL/m^2 for CMR[4,10]. Likewise, when compared to the CMR GS the CMR BAL method incorrectly classified 3/23 (16%) as normal size and 6/43(14%) as dilated (table 1B).

The main limitation of our study is that we only used 2D echocardiography. 3D echocardiography may show better agreement with the CMR GS but this was not investigated. Also, our number of subjects (n=25) was relatively small however with 72 studies this represents the largest HFpEF population studied to date with CMR.

In conclusion, this is the first study to investigate patients with HFpEF with both CMR and 2D echocardiography for LA volume calculation. We have shown that CMR BAL method for estimating LA volume in both SR and AF correlated and agreed well with the gold standard volumetric short axis Simpson's method. This suggests that in patients with HFpEF BAL volume calculation of LA with CMR BAL is reliable and can be considered to shorten scan duration. 2D echocardiographic data in patients with LA volume >60 mL/m^2 appeared less accurate and measurements should be interpreted with caution, both in patients in SR and especially in AF.

Acknowledgements: This work was funded by the NIHR Cardiovascular Biomedical Research Centre of Royal Brompton and Harefield NHS Foundation Trust and Imperial College, London UK and Rosetrees Trust, UK.

References:

1. McMurray JJ V, Adamopoulos S, Anker SD, Auricchio A, Böhm M, Dickstein K, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart. Eur Heart J. 2012 Jul;33(14):1787–847.

2. Rossi A, Cicoira M, Florea VG, Golia G, Florea ND, Khan AA, et al. Chronic heart failure with preserved left ventricular ejection fraction: diagnostic and prognostic value of left atrial size. Int J Cardiol. 2006 Jun 28;110(3):386–92.

3. Artang R, Migrino RQ, Harmann L, Bowers M, Woods TD. Left atrial volume measurement with automated border detection by 3-dimensional echocardiography: comparison with Magnetic Resonance Imaging. Cardiovasc Ultrasound. 2009 Jan;7:16.

4. Maceira AM, Cosín-Sales J, Roughton M, Prasad SK, Pennell DJ. Reference left atrial dimensions and volumes by steady state free precession cardiovascular magnetic resonance. J Cardiovasc Magn Reson. 2010 Jan;12:65.

5. Shimada YJ, Shiota T. Underestimation of left atrial volume by three-dimensional echocardiography validated by magnetic resonance imaging: a meta-analysis and investigation of the source of bias. Echocardiography. 2012 Apr;29(4):385–90.

6. Gulati A, Ismail TF, Jabbour A, Ismail NA, Morarji K, Ali A, et al. Clinical utility and prognostic value of left atrial volume assessment by cardiovascular magnetic resonance in non-ischaemic dilated cardiomyopathy. Eur J Heart Fail. 2013 Jun;15(6):660–70.

7. Bank A, Wickstrom K, Handran C, Burkhoff D, Lesser JR, Schwartz RS. Modeling left atrial volume, shape, and contraction patterns in normal subjects by cardiac magnetic resonance imaging. Int J Cardiol. 2013 Oct 9;168(4):3348–50.

8. Whitlock M, Garg A, Gelow J, Jacobson T, Broberg C. Comparison of left and right atrial volume by echocardiography versus cardiac magnetic resonance imaging using the area-length method. Am J Cardiol. 2010 Nov 1;106(9):1345–50.

9. Maddukuri P V, Vieira MLC, DeCastro S, Maron MS, Kuvin JT, Patel AR, et al. What is the best approach for the assessment of left atrial size? Comparison of various unidimensional and two-dimensional parameters with three-dimensional echocardiographically determined left atrial volume. J Am Soc Echocardiogr. 2006 Aug;19(8):1026–32.

10. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2015 Mar;16(3):233–70.

Legend for Table 1

Table 1. Panel A showing the absolute indexed LA volume values obtained with echocardiography BAL method, the CMR BAL method and the CMR GG. Echocardiography underestimated the true volume compared to the CMR GG, especially in pathological dilation and AF. There was no significant difference between the CMR BAL and CMRGG. Panel B demonstrating that atrial volumes calculated by echocardiography can classify patients incorrectly in 15/72 (21%) of the cases, whereas for CMR BAL method this is 9/72 (13%).

BAL= Biplane Area Length method
GG= Volumetric Simpson gold standard
AF= Atrial Fibrillation

Legend for Figure 1

Figure 1. Panel A showing a Bland-Altman plot of the echocardiographic BAL LA volume compared to the CMR GS showing that at normal volumes echocardiography performs well. However at higher LA volumes (~>60mL/m^2) echocardiography systematically underestimates compared to the gold standard. Panel B showing a Bland-Altman plot of the CMR BAL compared to the CMR gold standard indicating good agreement independently of LA volume. Panel C showing echocardiographic BAL LA volume compared to the CMR GS in patients with SR suggesting that underestimation is present at pathological volumes even in SR, however panel 1D shows that this is more pronounced in AF.

BAL= Biplane Area Length method
GG= Volumetric Simpson gold standard
LA= Left atrium
AF= Atrial Fibrillation
SR= Sinus rhythm