Indian Heart Journal xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Original Article

Left ventricular structure and diastolic function by cardiac magnetic resonance imaging in hypertrophic cardiomyopathy

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ARTICLE INFO

Article history:
Received 12 August 2016
Accepted 28 December 2016
Available online xxx

Keywords:
Diastolic function
Hypertension
Hypertrophic cardiomyopathy
Left ventricle
Magnetic resonance imaging

ABSTRACT

Objective: Diastolic dysfunction is common in hypertrophic cardiomyopathy (HCM) and hypertensive heart disease (HHD), but its relationships with left ventricular (LV) parameters have not been well studied. Our objective was to assess the relationship of various measures of diastolic function, and maximum left ventricular wall thickness (MLVWT) and left ventricular mass index (LVMI) in HCM, HHD and normal controls using cardiac magnetic resonance imaging (CMR). We also assessed LV parameters and diastolic function in relation to late gadolinium enhancement (LGE) and right ventricular (RV) hypertrophy in HCM.

Methods: 41 patients with HCM, 21 patients with HHD and 20 controls were studied. Peak filling rate (PFR), time to peak filling (TPF), MLVWT and LVMI were measured using CMR. LGE and RV morphology were assessed in HCM patients.

Results: MLVWT correlated with TPF in HCM ($r = 0.38$; $p = 0.02$), HHD ($r = 0.58$; $p = 0.01$) and controls ($r = 0.54$; $p = 0.01$); correlation between MLVWT and TPF was weaker in HCM than HHD. LVMI did not correlate with diastolic function. In HCM, LGE extent correlated with MLVWT ($\tau = 0.41$; $p = 0.002$) and with TPF ($\tau = 0.29$; $p = 0.02$). The HCM patients with RV hypertrophy had higher MLVWT ($p < 0.001$) and TPF ($p = 0.03$) than patients without RV hypertrophy.

Conclusion: MLVWT correlates with diastolic function (TPF) in HCM, HHD and controls. LVMI did not show significant correlation with TPF. The diastolic dysfunction in HCM is not entirely explained by wall thickening. LGE and RV involvement are associated with worse LV diastolic function, suggesting that these may be markers of more severe underlying myocardial disarray and fibrosis that contribute to diastolic dysfunction.

1. Introduction

Diastolic dysfunction indicates abnormal mechanical properties of the myocardium and includes slow or delayed myocardial relaxation, abnormal left ventricular distensibility and impaired left ventricular filling.[1] Diastolic dysfunction is one of the early manifestations in hypertrophic cardiomyopathy (HCM) and hypertensive heart disease (HHD), which could be subclinical. Diastolic dysfunction with preserved ejection fraction accounts for approximately 50% of patients with heart failure[2] with substantial morbidity and mortality. Accurate non- invasive assessment of diastolic function could be helpful in elucidating pathophysiology, predicting adverse outcome, patient monitoring, and assessing treatment response. For these reasons, there exist several measures of left ventricular diastolic function that are used in clinical practice and research. Cardiac magnetic resonance imaging (CMR) provides excellent assessment of maximum left ventricular wall thickness (MLVWT), left ventricular mass (LVM) and focal

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http://dx.doi.org/10.1016/j.ihj.2016.12.021

fibrosis shown as late gadolinium enhancement (LGE). Recent advances in image-processing software have facilitated measurements of left ventricular (LV) filling parameters and diastolic function. However, the relationships between diastolic function and left ventricular structural parameters in HCM and HHD have not been well studied. Therefore, the objective of our study was to assess the relationship between various measures of diastolic function, and MLVWT and left ventricular mass index (LVMI) in HCM, HHD and normal controls. We also assessed diastolic function in relation to LGE and right ventricular (RV) hypertrophy in HCM.

2. Methods

2.1. Study population

This is a retrospective study of 41 patients with HCM, 21 patients with HHD, and 20 control subjects. The study population were from cardiac MRI database of our tertiary care hospital during the time period January 2006 to November 2013. The study protocol was approved by our institutional research ethics board (Medical Research Ethics Committee number #12-389). All the patients in the HCM group had a confirmed diagnosis of HCM based on CMR morphological features, in addition to other clinical information (previous echocardiography, ECG, or family history). CMR diagnosis of HCM was based on the definition of LV wall thickness $\geq$15 mm at end-diastole or septal to lateral wall thickness ratio higher than 1.3 in a non-dilated LV, in the absence of a loading condition sufficient to cause the observed abnormality or a ratio between apical to basal LV wall thicknesses $\geq$1.3.[3] Genetic mutations were not assessed. All patients in the HHD group had hypertension diagnosed by the treating physicians. Those with coexisting severe chronic kidney disease in the HHD group did not undergo late enhancement imaging. Control subjects consisted of patients with normal CMR (including late enhancement imaging) and no history of hypertension, heart failure, angina, myocardial infarction, coronary revascularization or cardiomyopathy. Subjects in the control were referred for CMR by cardiologists to exclude structural heart disease for symptoms such as palpitations, syncope, or family history of sudden cardiac death. All the patients were in sinus rhythm and had left ventricular ejection fraction $\geq$50%. Patients with other coexisting diseases (e.g. pericardial disease, significant primary valvular disease) and patients with suspected amyloidosis (based on other clinical findings) and any CMR findings suggestive of cardiac amyloidosis (e.g. abnormal gadolinium kinetics and diffuse subendocardial LGE) which could potentially affect diastolic filling parameters were excluded from our study.

2.2. Cardiac magnetic resonance imaging

All the scans were performed with a 1.5 T MR scanner (Intera, Philips Medical systems). The imaging protocol consisted of standard 2-chamber, 3-chamber, 4-chamber and short-axis steady state free precession (SSFP) cine imaging and LGE imaging. Contiguous short axis SSFP cine images were obtained from apex to base of left ventricle with 8 mm slice thickness (no interslice gap), 3.6–3.9/1.9 ms TR/TE, 60° flip angle, 11–16 turbofactor, 28–34 × 28–34 cm field of view, 256 × 256 acquisition matrix and 25 phases. The temporal resolution was approximately 50 ms. LGE imaging was performed 8–15 min after intravenous gadolinium-DTPA (Magnevist, Bayer) or gadobenate dimeglumine (Multihance, Bracco) contrast administration (0.2 mmol/kg). Inversion recovery prepared breath hold images were obtained with 8 mm slice thickness, 3.8/1.3 ms TR/TE, 15° flip angle,180 × 160 acquisition matrix and 28–34 × 28–34 cm field of view.

2.3. Image analysis

Semi-automated endocardial contouring of the left ventricular slices from apex to base was performed using commercially available software (CVi 42; Circle Cardiovascular Imaging) to generate left ventricular time-volume curve (TVC) and its first derivative curve to obtain early peak filling rate (PFR), PFR/end-diastolic volume (PFR/EDV) and time to early peak filling rate (TPF) for assessment of diastolic function.[4,5] A radiologist with two years of dedicated cardiac radiology experience reviewed all contours and revised them if required. TVC (Fig. 1A) is a graphic representation of the change in the LV volume during cardiac cycle plotted against time. The first derivative of TVC (Fig. 1B) is a graphic representation of the instantaneous filling rates during cardiac cycle plotted against time. The PFR is the maximal change in LV volume per unit time, which is the highest positive slope in the volume curve (Fig. 1A and B). PFR occurs during early ventricular diastole. Time to peak filling rate is the time interval from end systole to peak filling rate (Fig. 1A and B). Diastolic

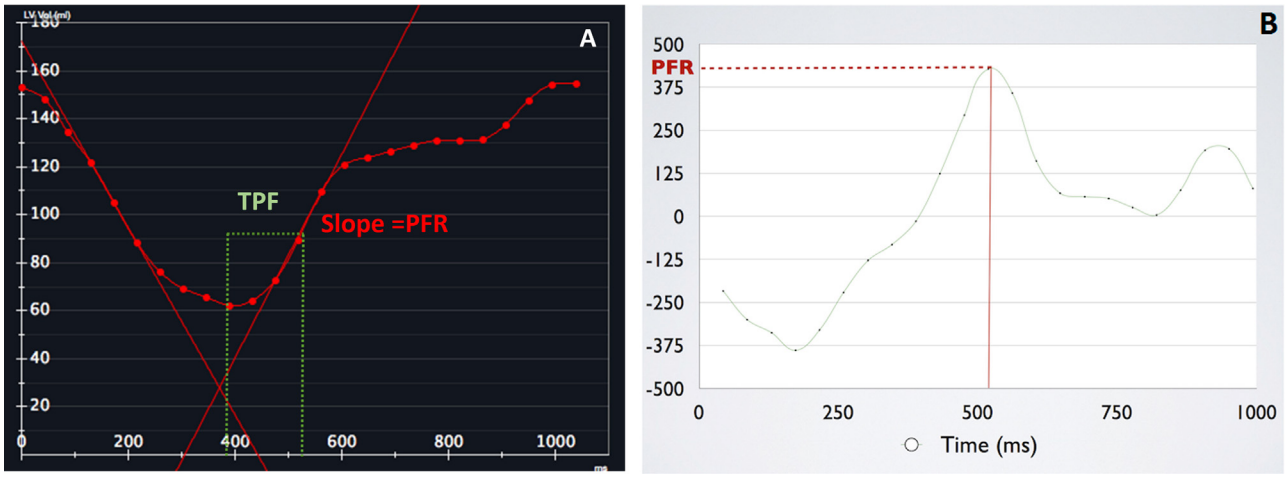

Fig. 1. Time-volume curve (A) and its first derivative curve (B) of a control subject. These demonstrate peak filling rate and time to peak filling rate. PFR is the highest upward slope of TVC. TPF is the time interval between end systole and PFR.

Please cite this article in press as: B.R. Chacko, et al., Left ventricular structure and diastolic function by cardiac magnetic resonance imaging in hypertrophic cardiomyopathy, Indian Heart J (2017), http://dx.doi.org/10.1016/j.ihj.2016.12.021