Eur Radiol (2014) 24:52–59
DOI 10.1007/s00330-013-2976-x

CARDIAC

Cardiovascular magnetic resonance imaging assessment of diastolic dysfunction in a population without heart disease: a gender-based study

Bruno Graça · Maria João Ferreira · Paulo Donato · Miguel Castelo-Branco · Filipe Caseiro-Alves

Received: 23 June 2013 / Accepted: 27 June 2013 / Published online: 3 August 2013

Abstract

Objectives Asymptomatic left ventricular (LV) diastolic dysfunction is increasingly recognised as an important diagnosis. Our goal was to study the prevalence and gender differences in subclinical LV diastolic dysfunction, using cardiovascular magnetic resonance imaging (CMR) at 3 T.

Methods We prospectively studied 48 volunteers (19 male and 29 female, mean age 49±7 years) with no evidence of cardiovascular disease. We used CMR to measure left atrium (LA) and LV volumes, LV peak filling rate and transmitral flow.

Results The overall prevalence of LV diastolic dysfunction in our cohort varied between 20 % (based on evaluation of LV filing profiles) and 24 % (based on the evaluation of the transmitral flow). The prevalence of diastolic dysfunction was higher in men than in women, independently of the criteria used (P between 0.004 and 0.022). Indexed LV end-diastolic volume, indexed LV stroke volume, indexed LV mass, indexed LA minimum volume and indexed LA maximum volume were significantly greater in men than in women ($P<0.05$). All the subjects had LV ejection fractions within the normal range.

Conclusions It is clinically feasible to study diastolic flow and LV filling with CMR. CMR detected diastolic dysfunction in asymptomatic men and women.

Key Points

- *CMR imaging offers new possibilities in assessing left ventricular diastolic function.*
- *The prevalence of diastolic dysfunction is higher in men than in women.*
- *The prevalence of some diastolic dysfunction in a normal population is 24 %.*

Keywords Cardiac imaging techniques · Magnetic resonance imaging · Transmitral flow · Peak filling rate · Diastolic function

B. Graça (✉)
Medical Imaging Department, University Centre Hospitals of Coimbra, Faculty of Medicine, University of Coimbra, Praceta Mota Pinto/Av. Bissaya Barreto, 3000-075 Coimbra, Portugal
e-mail: brunomgraca@gmail.com

M. J. Ferreira
Cardiology Department, University Centre Hospitals of Coimbra, Faculty of Medicine, University of Coimbra, Coimbra, Portugal

P. Donato
Medical Imaging Department, University Centre Hospitals of Coimbra, Faculty of Medicine, University of Coimbra, Coimbra, Portugal

M. Castelo-Branco
Institute for Biomedical Imaging and Life Sciences, Faculty of Medicine, University of Coimbra, Coimbra, Portugal

F. Caseiro-Alves
Medical Imaging Department, University Centre Hospitals of Coimbra, Faculty of Medicine, University of Coimbra, Coimbra, Portugal

Abbreviations

LA	left atrium
LV	left ventricle
PFR	peak filling rate
TMF	transmitral flow
VENC	velocity encoded

Introduction

Diastolic heart failure (HF) is a progressive disorder characterised by impaired left ventricular (LV) relaxation, increased LV stiffness, increased interstitial deposition of collagen, and modified extracellular matrix proteins. Diastolic HF, also referred to as HF with normal ejection fraction, currently accounts for 40–50 % of all HF cases and has a prognosis which is as ominous as that of systolic HF. Clinical consensus places special emphasis on the detection of subclinical LV systolic and diastolic dysfunction and the timely identification of risk factors for heart failure [1]. Fundamental structural and functional properties of the left ventricle (LV) and of the left atrium (LA) including parameters of diastolic function are often assessed in the clinical setting using two-dimensional and tissue Doppler echocardiography. Over the last decade, cardiovascular magnetic resonance (CMR) imaging has been widely accepted as the "gold standard" for the assessment of cardiac structure and function because of its high spatial and temporal resolution, excellent image quality and lack of geometric assumptions [2]. CMR offers a variety of alternative approaches for evaluating diastolic function [3].

So far, few MRI-based studies of left ventricular diastolic dysfunction have been carried out. Several studies have defined CMR normal ranges of LV volumes and systolic function [4–11] but none has assessed the prevalence of left ventricular diastolic dysfunction in healthy adult individuals.

The aim of the study was, therefore, to evaluate the prevalence of diastolic dysfunction in a normal population and to determine gender-specific differences for left heart volumes and function, using CMR at 3 T.

Materials and methods

Study population

Forty-eight healthy volunteers (19 male and 29 female, mean age 49±7 years, mean height 165±8 cm, mean weight 68±11 kg, with normal left ventricular ejection fraction, no history of cardiac disease, hypertension or other cardiac risk factors and a normal baseline electrocardiogram (ECG) were recruited. Exclusion criteria included a personal history of any condition that might be associated with systemic inflammation (such as systemic inflammatory arthritis or chronic chest disease) and signs of valvular disease in cine CMR imaging. Volunteers with contraindications to CMR were not enrolled. The study was approved by our institutional ethics committee. Each subject gave written informed consent.

Cardiovascular magnetic resonance protocol

CMR imaging was performed at 3.0 T (Magnetom Trio; Siemens, Erlangen, Germany). Cardiac cine images were acquired by using steady-state free-precession sequences with retrospective electrocardiographic gating. Participants were imaged in the supine position and performed a breath-hold at end expiration for each image acquisition to eliminate respiratory motion artefacts. After scout images were obtained, cine imaging was performed in four-chamber, three-chamber and two-chamber long- and short-axis views with the use of the following parameters: 8-mm-thick sections with a 2-mm gap between sections, repetition time 59.04 ms, echo time 1.45, number of segments 18; 50° flip angle, 256×156-mm matrix, 2.1×1.6-mm pixel size, acquired temporal resolution 25–40 ms; and number of reconstructed cardiac phases, 25.

A breath-held, retrospectively vector-ECG gated, two-dimensional flow-sensitive phase-contrast gradient-echo sequence was used for velocity-encoded (VENC) MRI flow measurements perpendicular to the orifice of the mitral valve. VENC-MRI slices were positioned in early diastole at the tip of the mitral valve leaflets. Typical imaging parameters of VENC-MRI were as follows: slice thickness 6 mm, repetition time 35.6 ms, echo time 2.33 ms, number of segments 3, acquired temporal resolution 24–56 ms, 20° flip angle, 25 calculated phases and pixel spacing 4.5×3.1 mm. Encoding velocity was set to 130 cm/s [12].

MR image analysis

Quantitative image data analysis was performed by using dedicated software (Segment, Medviso, Lund, Sweden) [13]. All functional evaluation was performed within 25 min per patient.

Tracing of endocardial and epicardial contours

All measurements were undertaken semi-automatically. End-diastolic and end-systolic frames were identified according to the ventricular blood pool area. In all LV short-axis slices across all temporal phases (200–250 images) endocardial and epicardial contours were semi-automatically drawn and manually corrected (Fig. 1). This segmentation took about 3–5 min. At the base of the LV, the aortic outflow tract below the valve was included in volume measurements. The free papillary muscles were included for LV mass assessment and excluded for left ventricular volume assessment. In the basal region of the heart where the LA was seen, only the portion of the slice that could be identified as the LV was included for measurement.

This analysis provided the time-varying course of the LV volume during the cardiac cycle. The peak filling rate (PFR) is the steepest tangent to the first part of the filling curve (Fig. 2). Segment software automatically determines this parameter.

LA volume measurements were performed in the four- and two-chamber orientations by the biplane area–length methods. The following parameters of LA size and function were included in our analyses:

– LA minimum volume (LAVmin): LA end-diastolic volume at the first frame after mitral valve closure

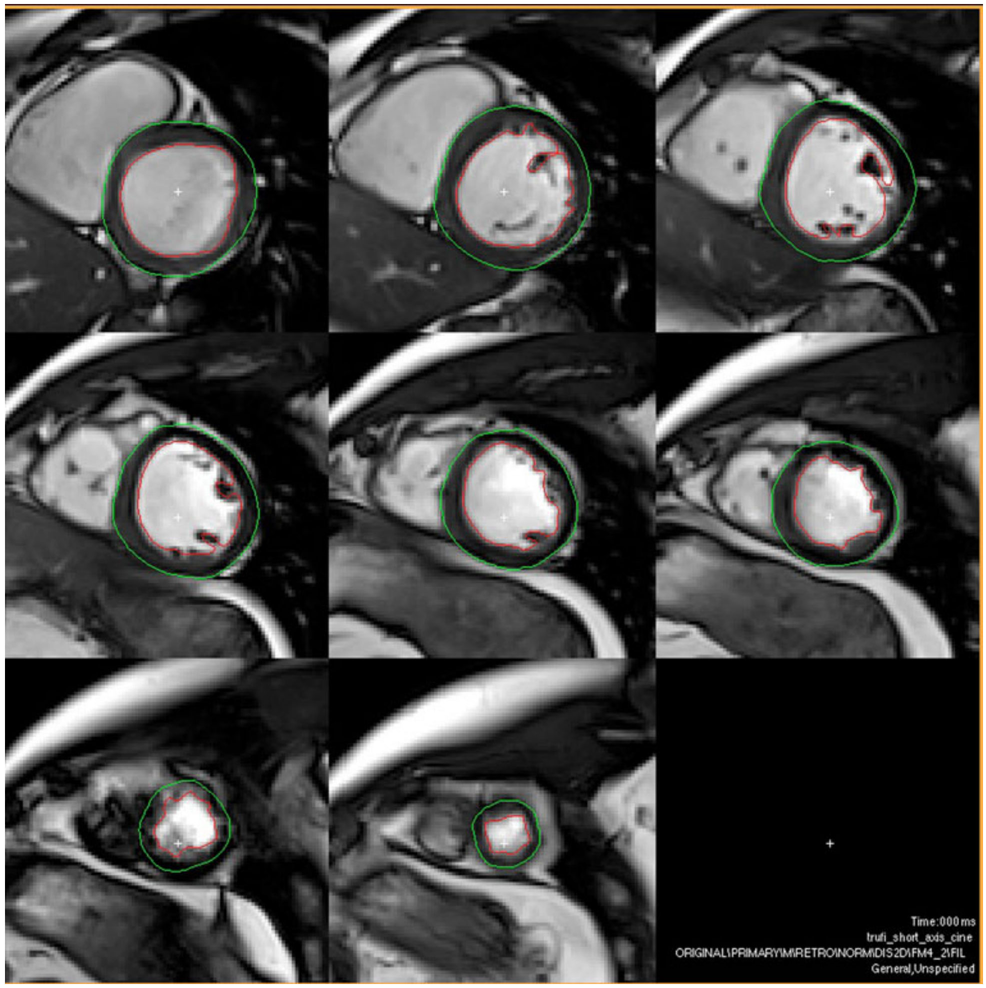

Fig. 1 Semi-automatic left ventricular (LV) segmentation performed on short-axis views obtained with cine sequences for volumetric assessment of global LV filling

– LA maximum volume (LAVmax): LA end-systolic volume right before mitral valve opening
– LA total emptying volume (LAEV): LAVmax - LAVmin
– LA total emptying fraction (LAEF): 100×(LAVmax - LAVmin)/LAVmax
– LA conduit volume (LACV): LV stroke volume - LAEV

Analysis of the transmitral flow (TMF)

In the flow-sensitive sequence, a round region of interest with a minimum of 1 cm^2 was placed at the centre of the mitral valve orifice (Fig. 3) and propagated to other phases to obtain the TMF curve (Fig. 4). From the analysis of the TMF curve,

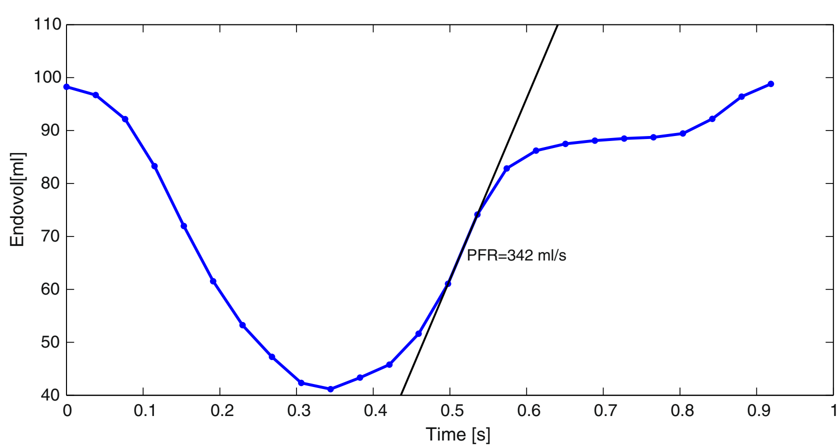

Fig. 2 Left ventricular (LV) filling volume versus time curve and its first derivative, the peak filling rate curve. The LV volume versus time curve and its first derivative (LV d*V*/d*t*) are obtained after the endocardial delineation of all LV short-axis slices across all temporal phases. The peak filling rate is the steepest tangent to the first part of the filling curve and represents the most rapid ventricular filling

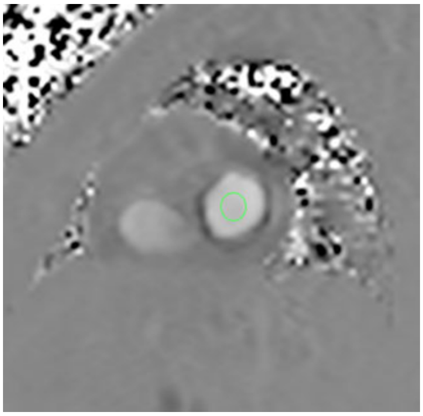

Fig. 3 Measurement of transmitral flow. Phase-encoded MRI obtained with a phase-contrast sequence shows a region of interest placed at the centre of the mitral orifice. The transmitral flow curve is obtained from this region of interest

the following measurements were performed: E and A mean peak velocities (in centimetres per second), E/A ratio, and mitral deceleration time (MDT) (measured from the E peak to the baseline).

Statistical analysis

All data were subjected to Shapiro–Wilk tests to establish normal distribution of the data. All normally distributed data are expressed as means±standard deviations. Differences between means of women and men were assessed using Student's *t* test for independent samples. The chi-squared test (Fischer's exact test) was used to determine a relation between the parameters diastolic dysfunction and gender. *P* values of less than 0.05 were considered statistically significant. All computations were performed using software (SPSS, version 20.0; SPSS, Chicago, IL, USA).

Results

This study included 48 (19 male and 29 female) subjects. Table 1 displays the baseline characteristics for the current study population.

Gender differences in left ventricular measures

Table 2 lists the values obtained for LV mass, end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV) and ejection fraction (EF), according to gender.

Indexed LV end-diastolic and stroke volumes were significantly greater in men than in women ($P=0.007$ and $P=0.005$, respectively). The indexed LV myocardial masses at end diastole were significantly greater in male than in female volunteers ($P=0.038$).

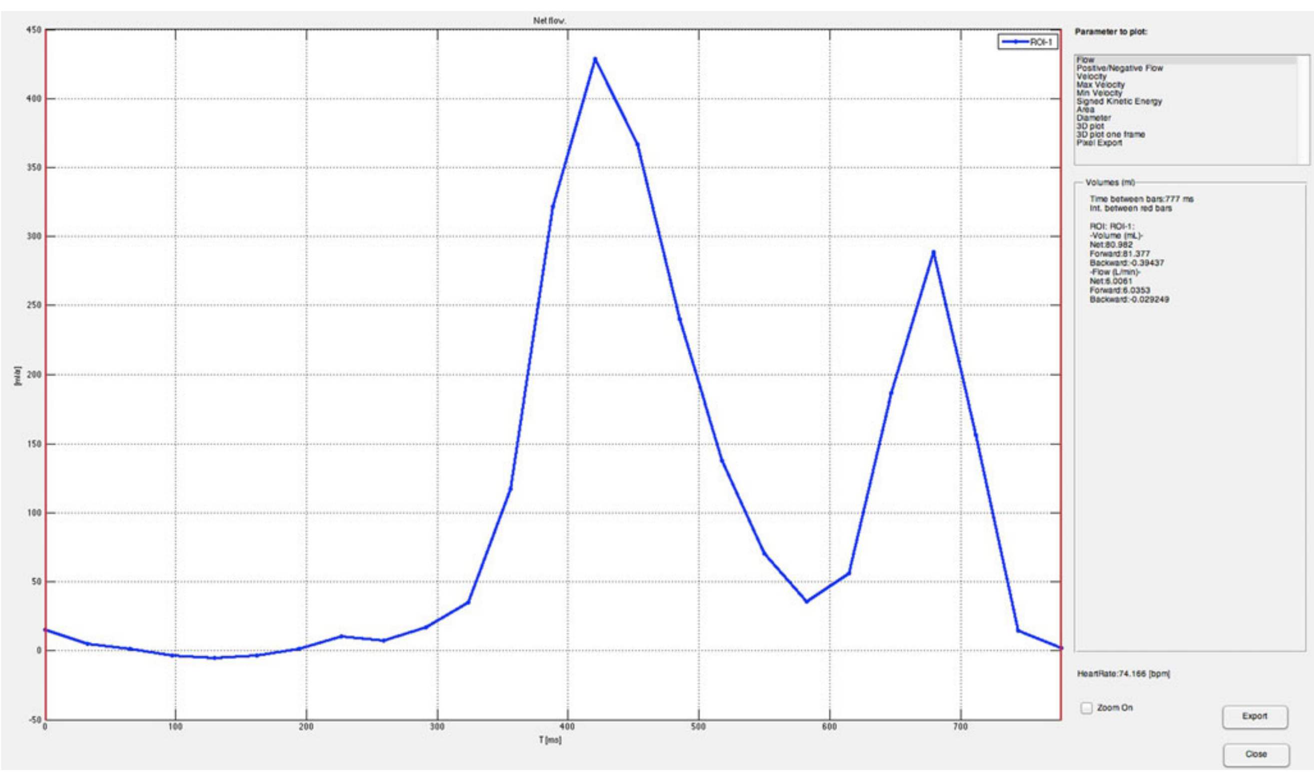

Fig. 4 Cardiac MR findings of the transmitral flow. The transmitral flow curve is composed of two peaks. The first one is the E wave and second one is the A wave. The E wave corresponds to rapid LV filling at early diastole; the A wave corresponds to late LV filling during end-diastole, secondary to LA contraction

Table 1 Baseline characteristics of the study population according to gender

	Female (*n*=29)	Male (*n*=19)	*P*
Age (years)	47±6	52±8	0.018
Height (cm)	160.4±5	172.9±5.3	<0.001
Weight (kg)	62.9±8.7	76.6±9.8	<0.001
BSA (m^2)	1.67±0.13	1.92±0.14	<0.001
BMI (kg/m^2)	24.4±3.2	25.6±2.4	0.175

BSA body surface area, *BMI* body mass index

All the subjects had LV EFs within the normal range (male, range 55–85 %; female, range 56–85 %) published for healthy individuals at MRI and no significant gender differences were noted in this parameter.

Gender differences in left auricular measures

Table 3 lists the values obtained for LA volumes and reservoir function, according to gender.

Indexed LA minimum and maximum volumes were significantly greater in men than in women (*P*=0.046; *P*=0.032, respectively). Although absolute values of LA total emptying and conduit volumes were significantly greater in men than in women (*P*=0.01; *P*=0.016, respectively), the respective indexed volumes were comparable (*P*=0.176; *P*=0.235). Values of LAEF were similar in both genders (*P*=0.698)

Gender differences in left ventricular diastolic measures

Table 4 lists the values obtained for LV parameters of diastolic function, according to gender. Two subjects were excluded from the study because of intense motion artefacts during the flow-sensitive acquisition.

Absolute values of PFR were significantly greater in men than in women (*P*=0.043). The PFR indexed values (to EDV and SV) in women and men subjects were comparable (*P*=0.246; *P*=0.208). The analysis of transmitral parameters showed no gender differences. Mitral peak E (*P*=0.164) and peak A (*P*=0.446) velocities were comparable in women and men. Values of the E/A ratio (*P*=0.147) and MDT (*P*=0.176) were also similar in both genders.

Table 2 Left ventricular (LV) measurements according to gender

	Female (*n*=29)	Male (*n*=19)	*P*
LV EDV (mL)	103.0±17.0	136.3±24.4	<0.001
LV EDV/BSA (mL/m^2)	61.9±10.8	71.0±10.9	0.007
LV ESV (ml)	35.9±11.7	46.4±12.5	0.006
LV ESV/BSA (mL/m^2)	21.6±6.6	24.1±6.1	0.178
LV SV (ml)	67±10.4	90±16.4	<0.001
LV SV/BSA (mL/m^2)	40.4±7.1	47.0±7.9	0.005
LV EF (%)	66±5.6	66.6±5.7	0.693
LV mass (g)	107.8±14.7	134.7±18.6	<0.001
LV mass/BSA (g/m^2)	65.1±7.7	70.4±8.9	0.038

LV left ventricle, *EDV* end-diastolic volume, *BSA* body surface area, *ESV* end-systolic volume, *SV* stroke volume, *EF* ejection fraction

Table 3 Left atrium (LA) measurements according to gender

	Female (*n*=29)	Male (*n*=19)	*P*
LAVmin (mL)	26.3±8.2	36.9±11.7	0.002
LAVmin/BSA (mL/m^2)	15.7±4.8	19.2±6.2	0.046
LAVmax (mL)	62.7±16.4	84.0±21.1	0.001
LAVmax/BSA (mL/m^2)	37.5±9.3	43.8±10.1	0.032
LAEV (mL)	36.4±11.6	47.2±14.4	0.010
LAEV/BSA (mL/m^2)	21.8±6.6	24.5±6.8	0.176
LACV (mL)	30.9±13.2	42.2±16.0	0.016
LACV/BSA (mL/m^2)	18.7±8.4	21.8±8.8	0.235
LAEF (%)	57.4±9.3	56.4±8.9	0.698

LAVmin left atrium minimum volume, *LAVmax* LA maximum volume, *LAEV* LA total emptying volume, *LACV* LA conduit volume, *LAEF* LA total emptying fraction, *BSA* body surface area

Prevalence of diastolic dysfunction

A PFR normalised to EDV of less than 2.5 EDV/s was considered abnormal [14–16]. This analysis was repeated using a PFR normalised to the stroke volume (SV), with a PFR less than 4 SV/s considered abnormal [17, 18].

The criteria for diastolic dysfunction from the analysis of the TMF curve were established according to published data [12]. Normal diastolic function was defined as an E/A between 1 and 2 and MDT between 150 and 220 ms. In grade I dysfunction, E/A decreases below 1. In grade II, E/A moves back into the normal range of 1–2, MDT is also normal, but there is LA dilatation (LAVmax/body surface area (BSA) (millilitres per square metre) greater than 52 in women or greater than 53 in men). In grades III and IV, E/A increases to a value above 2 and

Table 4 LV diastolic function measurements according to gender

	Female (*n*=27)	Male (*n*=19)	*P*
LV PFR (mL/s)	360.9±84.0	429.6±139.7	0.043
LV PFR/EDV (mL/s)	3.58±0.8	3.22±1.2	0.246
LV PFR/SV (mL/s)	5.51±1.4	4.9±1.8	0.208
Mitral peak E velocity (cm/s)	51.8±8.3	47.7±10.2	0.164
Mitral peak A velocity (cm/s)	39.5±8.2	41.6±9.7	0.446
Mitral E/A ratio	1.35±0.4	1.19±0.3	0.147
Mitral deceleration time (ms)	164±31	181±48	0.176

LV left ventricle, *PFR* peak filling rate, *EDV* end-diastolic volume, *SV* stroke volume

MDT drops below 150 ms. One male patient of 70 years of age with a mitral E/A ratio of 0.74 and MDT of 162 ms was established as a normal subject. We maintained the diagnosis of diastolic dysfunction in a 63-year-old man with a mitral E/A ratio of 0.68 and MDT of 234 ms [19].

Table 5 lists the prevalence of LV diastolic dysfunction, according to gender and the criteria used.

When patients were classified as having normal and abnormal PFR on the basis of a threshold of 2.5 EDV/s, 9 (7 male and 2 female, $P=0.022$) patients were found to have diastolic dysfunction. When the PFR was normalised to the SV and analyses were repeated using a PFR less than 4 SV/s as abnormal, the number of patients with diastolic dysfunction was also 9 (7 male and 2 female, $P=0.022$).

When the patients were classified as having diastolic dysfunction on the basis of TMF analysis and LA size, 11 (9 male and 2 female, $P=0.004$) patients were found to have grade I or grade II diastolic dysfunction. None of the subjects showed grade III diastolic dysfunction.

Discussion

Gender differences in left ventricular measures

Gender-specific differences include all absolute functional and morphological values except for EF. Normalisation to BSA eliminated differences in LV ESV. Several studies [5–11] have described overall values of EDV, ESV, SV, LV mass and EF, which are consistent with findings from other imaging techniques and are broadly consistent with the findings in this study. Regarding the use of 3-T equipment in our study, published data suggest that field strength does not have an influence on the quantification of cardiac volume or mass, and normal values for cardiac volumes and mass established at 1.5 T can be applied to images obtained at 3 T [20].

Table 5 Prevalence of LV diastolic dysfunction diagnoses according to gender

Criteria	All (n=46)	Female (n=27)	Male (n=19)	P
LV PFR/EDV (mL/s) <2.5	9 (20 %)	2 (7 %)	7 (37 %)	0.022
LV PFR/SV (mL/s) <4	9 (20 %)	2 (7 %)	7 (37 %)	0.022
Transmitral flow analysis	11 (24 %)	2 (7 %)	9 (47 %)	0.004
Mitral E/A ratio <1	6 (13 %)	2 (7 %)	4 (21 %)	0.213
Mitral E/A ratio 1–2 and LAVmax/BSA (mL/m^2) >52 in women or >53 in men	5 (11 %)	0 (0 %)	5 (26 %)	0.008

LV left ventricle, *PFR* peak filling rate, *EDV* end-diastolic volume, *SV* stroke volume, *LAVmax* left atrium maximum volume, *BSA* body surface area

Gender differences in left atrial measures

We observed that nearly all non-indexed LA volumes were significantly higher in men, except for the left atrial emptying fraction. While these differences disappeared in most normalised parameters, indexed LA minimum and maximum volumes remained higher in men. Hudsmith et al. [6, 21] also reported higher absolute LA volumes in male patients with similar ejection fraction in patients of both genders. Regarding indexed LA volumes, our findings are broadly consistent with those reported by Maceira et al. [4]. The effect of age may explain the greater indexed LA maximum volumes observed in men. Gender differences in the indexed LA minimum volume may be due to the decreased ejection force of the atrial pump in men, in a Frank Starling-like mechanism [22]. This could be further clarified by the analysis of LA active pumping volume and index, which we did not perform.

Gender differences in left ventricular diastolic measures

Although absolute LV PFR values were significantly higher in men, the parameter indexed for EDV or SV was higher in women, but not significantly so.

Regarding the evaluation of the TMF, there were no gender differences.

One of the largest cohort studies with mitral flow-derived indices published [23] also showed no gender difference in E/A ratio. Previous studies have demonstrated a good correlation between cardiac MRI and Doppler echocardiography for measurement of flow velocities [2, 24, 25]. Nevertheless there are no significant data from cardiac MR studies in a general population.

Prevalence of diastolic dysfunction

The proportion of patients with an abnormal diastolic function is variable in the population depending on the criteria used. The prevalence reported here (between 20 % and 24 %) is consistent with larger population studies [26–29].

The gold standard for assessing diastolic function remains the pressure–volume relationship, but this requires an invasive approach. Conventionally, Doppler echocardiography measurements of MV flow conditions are used to assess diastolic function. CMR is a valid alternative for those patients who do not have adequate echocardiographic image quality to reliably obtain these parameters [1].

Flow analysis with CMR allows the quantitative assessment of blood velocity, with the advantage that the tomographic plane of interest can be positioned optimally in a larger area than in Doppler echocardiography. CMR provides velocities (metres per second) as well as volume flow (millilitres per second) [30] and is less operator and angle dependent [31]. Lower transmitral E/A ratios reflect impaired myocardial relaxation, characterised by decreased early, but enhanced atrial filling of the LV. In subjects with transmitral E/A ratio between 1 and 2, to establish a diagnosis of grade II diastolic dysfunction, we used the criterion of increased LA maximum volume, as it often reflects the cumulative effects of filling pressures over time [1].

Left ventricular filling profiles have been used to assess diastolic function by other imaging investigations, such as radionuclide cineangiography and SPECT. Similar applications for CMR imaging have been impractical because manual planimetry of all LV images across all temporal phases would typically require tracing of more than 200 images per patient. With the improvements in post-processing tools it is now possible to semi-automatically segment all phases and quickly provide the time-varying course of the LV volume during the cardiac cycle. The ventricular relaxation abnormalities can be diagnosed by a low PFR. This evaluation is based on conventional short-axis sequences, without the necessity to perform a dedicated acquisition. The cut-off used to define the abnormal PFR has been applied to nuclear medicine tests. The use of indexed values of PFR to EDV and SV minimises the dependency of PFR from EDV and heart rate. We demonstrated that the left ventricular PFR can be easily obtained as an addition to the assessment of LV systolic function with semi-automatic contour detection and it may become a valuable asset to the evaluation of LV diastolic function.

Gender differences in the prevalence of diastolic dysfunction

The effects of age and hormonal protection may explain the lower prevalence of diastolic dysfunction in women.

The incidence of diastolic dysfunction increases with age [26] and seems to be affected by the postmenopausal state. Hormone replacement therapy may improve LV diastolic function as one of the mechanisms of its cardioprotective effects [32].

Although we did not find any gender differences regarding body mass index (BMI), the increased weight and BSA of men compared with women may also be related to the higher prevalence of diastolic dysfunction in this gender.

We recognise the limitations of our study. The sample size of the study is modest and our findings need to be validated in a larger population.

The normal controls did not undergo a stress test to rule out latent ischaemia. However, none of the controls had significant cardiac risk factors.

We considered that the analysis of cine and TMF images was sufficient to exclude left-sided valvular disease. Regarding the exclusion of infiltrative myocardial disease, we did not study myocardial delayed enhancement nor did we perform endomyocardial biopsy. Nevertheless, none of our subjects had increased LV myocardial end-diastolic thickness, pericardial thickening, pericardial effusion or pleural effusion.

Cardiac catheterisation was not performed to evaluate LV diastolic function.

The use of another imaging technique such as Doppler echocardiography to study TMF and to assess LA size and function was considered beyond the scope of the present study.

Although good correlation between Doppler echo studies and MRI has been reported, the cut-off values used in echocardiography cannot simply be translated to these MRI-assessed indices based on the time–flow rate curves.

Normalising early mitral velocity (E) for the influence of myocardial relaxation by combining E with early diastolic mitral septal tissue velocity (Ea) may be performed by MR tissue phase contrast imaging, and this is an important criterion that has been established [19]. On the other hand there are still conflicting data regarding the relation between E/Ea ratio and LV filling pressure [33, 34].

It is demonstrated that an LA volume index greater than 34 mL/m^2 is an independent predictor of death, heart failure, atrial fibrillation, and ischaemic stroke. However, we recognise that dilated left atria may be seen in patients with bradycardia and four-chamber enlargement, anaemia and other high-output states, atrial flutter or fibrillation, and significant mitral valve disease, in the absence of diastolic dysfunction. We used a cut-off that was clearly higher (LAVmax/BSA (millilitres per square metre) greater than 52 in women or greater than 53 in men subjects) and we think that this eliminated most if not all of these potential confounding conditions.

This study highlights certain key points for the routine use of CMR to study diastolic function. Firstly, it is clinically feasible to study left heart volumes and function, including diastolic flow and LV filling data, in a single CMR examination. Secondly, the prevalence of diastolic dysfunction in a normal adult population has clinical importance in view of the high risk in patients with impaired LV diastolic function.

In conclusion, our observations provide promising initial results for the routine use of CMR to study the prevalence and gender differences in subclinical LV diastolic dysfunction.

Acknowledgements We thank Miguel Patrício for statistical advice. This research was financially supported by project “DoIT”, co-financed by the European Community Fund FEDER through COMPETE – Programa Operacional Factores de Competitividade.

References

1. Paulus WJ, Tschöpe C, Sanderson JE et al (2007) How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. Eur Heart J 28:2539–50
2. Grothues F, Smith GC, Moon JCC et al (2002) Comparison of interstudy reproducibility of cardiovascular magnetic resonance with

two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. Am J Cardiol 90:29–34
3. Rathi VK, Doyle M, Yamrozik J et al (2008) Routine evaluation of left ventricular diastolic function by cardiovascular magnetic resonance: a practical approach. J Cardiovasc Magn Reson 10:36
4. Maceira AM, Cosín-Sales J, Roughton M et al (2010) Reference left atrial dimensions and volumes by steady state free precession cardiovascular magnetic resonance. J Cardiovasc Magn Reson 12:65
5. Maceira AM, Prasad SK, Khan M, Pennell DJ (2006) Normalized left ventricular systolic and diastolic function by steady state free precession cardiovascular magnetic resonance. J Cardiovasc Magn Reson 8:417–26
6. Hudsmith LE, Petersen SE, Francis JM et al (2005) Normal human left and right ventricular and left atrial dimensions using steady state free precession magnetic resonance imaging. J Cardiovasc Magn Reson 7:775–82
7. Alfakih K, Plein S, Thiele H et al (2003) Normal human left and right ventricular dimensions for MRI as assessed by turbo gradient echo and steady-state free precession imaging sequences. J Magn Reson Imaging 17:323–9
8. Salton CJ, Chuang ML, O'Donnell CJ et al (2002) Gender differences and normal left ventricular anatomy in an adult population free of hypertension. A cardiovascular magnetic resonance study of the Framingham Heart Study Offspring cohort. J Am Coll Cardiol 39:1055–60
9. Sandstede J, Lipke C, Beer M et al (2000) Age- and gender-specific differences in left and right ventricular cardiac function and mass determined by cine magnetic resonance imaging. Eur Radiol 10:438–42
10. Lorenz CH, Walker ES, Morgan VL et al (1999) Normal human right and left ventricular mass, systolic function, and gender differences by cine magnetic resonance imaging. J Cardiovasc Magn Reson 1:7–21
11. Hees PS, Fleg JL, Lakatta EG, Shapiro EP (2002) Left ventricular remodeling with age in normal men versus women: novel insights using three-dimensional magnetic resonance imaging. Am J Cardiol 90:1231–6
12. Caudron J, Fares J, Bauer F, Dacher JN (2011) Evaluation of left ventricular diastolic function with cardiac MR imaging. Radiographics 31:239–59
13. Heiberg E, Sjögren J, Ugander M et al (2010) Design and validation of Segment–freely available software for cardiovascular image analysis. BMC Med Imaging 10:1
14. Bonow RO, Bacharach SL, Green MV et al (1981) Impaired left ventricular diastolic filling in patients with coronary artery disease: assessment with radionuclide angiography. Circulation 64:315–23
15. Aggarwal A, Brown KA, LeWinter MM (2001) Diastolic dysfunction: pathophysiology, clinical features, and assessment with radionuclide methods. J Nucl Cardiol 8:98–106
16. Zeidan Z, Erbel R, Barkhausen J et al (2003) Analysis of global systolic and diastolic left ventricular performance using volume-time curves by real-time three-dimensional echocardiography. J Am Soc Echocardiogr 16:29–37
17. Poppe KK, Doughty RN, Whalley GA (2013) Redefining normal reference ranges for echocardiography: a major new individual person data meta-analysis. Eur Heart J Cardiovasc Imaging 14:347–8
18. Bowman LK, Lee FA, Jaffe CC et al (1988) Peak filling rate normalized to mitral stroke volume: a new Doppler echocardiographic filling index validated by radionuclide angiographic techniques. J Am Coll Cardiol 12:937–43
19. Nagueh SF, Appleton CP, Gillebert TC et al (2009) Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr 22:107–33
20. Hudsmith LE, Petersen SE, Tyler DJ et al (2006) Determination of cardiac volumes and mass with FLASH and SSFP cine sequences at 1.5 vs. 3 Tesla: a validation study. J Magn Reson Imaging 24:312–8
21. Hudsmith LE, Cheng ASH, Tyler DJ et al (2007) Assessment of left atrial volumes at 1.5 Tesla and 3 Tesla using FLASH and SSFP cine imaging. J Cardiovasc Magn Reson 9:673–9
22. Anwar AM, Geleijnse ML, Soliman OII et al (2007) Left atrial Frank-Starling law assessed by real-time, three-dimensional echocardiographic left atrial volume changes. Heart 93:1393–7
23. Schirmer H, Lunde P, Rasmussen K (2000) Mitral flow derived Doppler indices of left ventricular diastolic function in a general population; the Tromso study. Eur Heart J 21:1376–86
24. Mohiaddin RH, Gatehouse PD, Henien M, Firmin DN (1997) Cine MR Fourier velocimetry of blood flow through cardiac valves: comparison with Doppler echocardiography. J Magn Reson Imaging 7:657–63
25. Karwatowski SP, Brecker SJ, Yang GZ et al (1995) Mitral valve flow measured with cine MR velocity mapping in patients with ischemic heart disease: comparison with Doppler echocardiography. J Magn Reson Imaging 5:89–92
26. Kuznetsova T, Herbots L, López B et al (2009) Prevalence of left ventricular diastolic dysfunction in a general population. Circ Heart Fail 2:105–12
27. Fischer M, Baessler A, Hense HW et al (2003) Prevalence of left ventricular diastolic dysfunction in the community. Results from a Doppler echocardiographic-based survey of a population sample. Eur Heart J 24:320–8
28. Abhayaratna WP, Marwick TH, Smith WT, Becker NG (2006) Characteristics of left ventricular diastolic dysfunction in the community: an echocardiographic survey. Heart 92:1259–64
29. Redfield MM, Jacobsen SJ, Burnett JC et al (2003) Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. JAMA 289:194–202
30. Bowman AW, Frihauf PA, Kovács SJ (2004) Time-varying effective mitral valve area: prediction and validation using cardiac MRI and Doppler echocardiography in normal subjects. Am J Physiol Heart Circ Physiol 287:H1650–7
31. Fyrenius A, Wigström L, Bolger AF et al (1999) Pitfalls in Doppler evaluation of diastolic function: insights from 3-dimensional magnetic resonance imaging. J Am Soc Echocardiogr 12:817–26
32. Duygu H, Akman L, Ozerkan F et al (2009) Comparison of the effects of new and conventional hormone replacement therapies on left ventricular diastolic function in healthy postmenopausal women: a Doppler and ultrasonic backscatter study. Int J Cardiovasc Imaging 25:387–96
33. Bhella PS, Pacini EL, Prasad A et al (2011) Echocardiographic indices do not reliably track changes in left-sided filling pressure in healthy subjects or patients with heart failure with preserved ejection fraction. Circ Cardiovasc Imaging 4:482–9
34. Kumar K, Nepomuceno RG, Chelvanathan A et al (2012) The role of tissue doppler imaging in predicting left ventricular filling pressures in patients undergoing cardiac surgery: an intraoperative study. Echocardiography 30:271–278