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Short communication

Normal values for myocardial deformation within the right heart measured by feature-tracking cardiovascular magnetic resonance imaging☆

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ABSTRACT

Background: Reproducible and repeatable assessment of right heart function is vital for monitoring congenital and acquired heart disease. There is increasing evidence for the additional value of myocardial deformation (strain and strain rate) in determining prognosis. This study aims to determine the reproducibility of deformation analyses in the right heart using cardiovascular magnetic resonance feature tracking (FT-CMR); and to establish normal ranges within an adult population.

Methods: A cohort of 100 healthy subjects containing 10 males and 10 females from each decade of life between the ages of 20 and 70 without known congenital or acquired cardiovascular disease, hypertension, diabetes, dyslipidaemia or renal, hepatic, haematologic and systemic inflammatory disorders underwent FT-CMR assessment of right ventricular (RV) and right atrial (RA) myocardial strain and strain rate.

Results: RV longitudinal strain (Ell) was $-21.9 \pm 3.24\%$ (FW + S Ell) and $-24.2 \pm 3.59\%$ (FW-Ell). Peak systolic strain rate (S′) was $-1.45 \pm 0.39\ s^{-1}$ (FW + S) and $-1.54 \pm 0.41\ s^{-1}$ (FW). Early diastolic strain rate (E′) was $1.04 \pm 0.26\ s^{-1}$ (FW + S) and $1.04 \pm 0.33\ s^{-1}$ (FW). Late diastolic strain rate (A′) was $0.94 \pm 0.33\ s^{-1}$ (FW + S) and $1.08 \pm 0.33\ s^{-1}$ (FW). RA peak strain was $-21.1 \pm 3.76\%$. The intra- and inter-observer ICC for RV Ell (FW + S) was 0.92 and 0.80 respectively, while for RA peak strain was 0.92 and 0.89 respectively.

Conclusions: Normal values of RV & RA deformation for healthy individuals using FT-CMR are provided with good RV Ell and RA peak strain reproducibility. Strain rate suffered from sub-optimal reproducibility and may not be satisfactory for clinical use.

1. Introduction

Reproducible and repeatable quantification of right heart function is vital for monitoring patients, yet volume-based measurements are time-consuming, difficult and require meticulous care even in the era of semi-automated boundary detection [1]. Although there is extensive evidence that left ventricular (LV) and right ventricular (RV) ejection fraction are of prognostic importance, there is increasing evidence for the incremental value of myocardial deformation (strain and strain rate) imaging in both congenital [2,3] and acquired cardiovascular disease [4]. Strain measured by cardiovascular magnetic resonance imaging (CMR) has been shown to be both a more sensitive and earlier marker of contractile dysfunction in multiple studies but until the development of feature-tracking, has not gained wide popularity in routine clinical practice due to the time needed for additional acquisition and time required for analysis [5]. Feature-tracking CMR (FT-CMR) of the RV and right atrium (RA) offers the potential for rapid and sensitive quantification of function, with the advantage of high image quality unlimited by the availability of an adequate acoustic window. Normal ranges are available for LV strain and strain rate by FT-CMR [6]. Data for the right heart are limited and knowledge of reproducibility is particularly important in the RV due to the potential adverse effects of through plane motion, with loss of features leaving the image plane, and needs to be known to ensure clinical utility [7]. Therefore, the aims of this study were: firstly, to establish normal ranges for RV and RA peak longitudinal strain and strain rate within an

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adult population that can be used for future comparative studies; secondly, to determine reproducibility of analysis of deformation of the RV and RA using FT-CMR.

2. Methods

2.1. Study population

A cohort of 100 normal healthy subjects, with 10 men and 10 women in each of 5 age deciles from 20 to 70 years was constructed. Subjects were recruited from control participants of an on-going research study within the Department of Cardiology, University Hospital Birmingham and the Institute of Cardiovascular Science, University of Birmingham (CRIB-Donor NCT01769924). Self-report history was taken to exclude subjects with chest pain, breathlessness or other cardiac symptoms, and those with a history of hypertension, diabetes, dyslipidaemia, or any cardiovascular, renal, hepatic, haematological and systemic inflammatory disease. Clinical examination was performed, including office blood pressure (normal <140/90 mm Hg). Blood samples were taken to confirm normal range full blood count, serum electrolytes, and random glucose. All subjects had a normal resting 12 lead ECG and either negative (maximal >85% maximum predicted heart rate) exercise stress echocardiography or exercise ECG. Demographic data were collected and informed consent was obtained from each patient but ethnicity was not recorded. The QRISK®2 score is widely used within the National Health Service to predict the risk of an individual developing cardiovascular disease over the next 10 years [8]; this was calculated for each patient using the QRISK®2-2017 calculator. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

2.2. CMR acquisition

CMR imaging was conducted using a 1.5-T scanner (Magnetom Avanto, Siemens, Germany). Cardiac morphology and function were studied using standard CMR protocols, with steady state free precession (SSFP) cine images (typical parameters: resolution 40–50 ms, repetition time 3.2 ms, echo time 1.7 ms, flip angle 60, field of view 300 mm, in-plane resolution 1.5 × 1.5 mm^2, slice thickness 7 mm with 3 mm gap, minimum 25 phases per cardiac cycle) in accordance with previously validated methodology [9].

2.3. CMR analysis

Image analysis was performed off-line using a standardized approach by trained cardiologists (AD; BL) with delineation of papillary muscles and trabeculations using thresholding (version 5.3.4 cvi42, Circle Vascular Imaging, Canada).

2.4. CMR RV feature tracking

Cvi42 is based upon an incompressible volume-based algorithm, which has been previously validated to produce accurate biventricular anatomical tracking [10]. From the horizontal long axis view, right ventricular 2D longitudinal (Ell) strain as well as strain rates (peak systolic strain rate SR_S; peak early diastolic strain rate SR_E; peak late diastolic strain rate SR_A) were defined in the region of interest between the endocardial and epicardial borders (Fig. 1) drawn in the end-diastolic frame (defined as phase 1 out of 25). Beginning of systole is defined as phase 2 out of 25; end-systole is defined as peak RV contraction with the smallest RV area. RV peak strain was taken as the highest strain irrespective of time during systole. Two datasets were produced with inclusion (free wall plus septum Ell, FW + S Ell) [11] and exclusion (free wall Ell, FW-Ell) [12] of the septum to reflect different approaches to the contribution of the septum to RV function. The accuracy of feature tracking for both endocardial and epicardial RV borders was visually checked following automated strain analysis on the CMR model, and good quality tracking was obtained in all subjects following a maximum of two user adjustments. Endocardial and epicardial borders were drawn around the largest RA area to coincide with the RV end-systolic phase.

2.5. Reproducibility

All CMR studies were anonymized prior to strain analysis. For intra-observer variability, observer 1 (AD) performed tissue tracking analysis for all 100 subjects, with a second analysis repeated in a randomly generated subset of 10 patients after a 1-month interval. For inter-observer variability, observer 2 (BL) independently feature tracked the randomly generated set of 10 scans.

2.6. Statistical analysis

Data are presented as mean ± standard deviation. Data distribution for continuous variables was assessed using normality plots and the Kolmogorov–Smirnov test. Independent *t*-tests were used to compare inter-gender differences. Correlations were assessed with Pearson's correlation coefficient. Intra- and inter-observer agreement was tested by calculating mean absolute bias and 95% limits of agreement (confidence intervals, CI) from Bland–Altman analyses and intraclass correlation coefficient (ICC). A *P*-value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS v24.0 (SPSS, Inc., Chicago, IL, USA).

3. Results

3.1. Baseline demographics

Full demographic data are available within the 'data in brief' article [13]. All participants had a 10-year QRISK-2 score of <20% [8]. There were 8 current smokers and 19 ex-smokers. No patient had a clinical history of COPD. Indexed cardiac volumes, mass, and ejection fraction were within normal limits for all participants for both the LV (LVEF 70.6 ± 6.6%) and RV (RVEF 66.9 ± 7.7%) [14]. There was a weak correlation between age and increasing LVEF ($r = 0.4$, $P < 0.001$), RVEF ($r = 0.2$, $P = 0.03$), and decreasing indexed biventricular volumes (LVEDVi $r = -0.4$, $P < 0.001$; LVESVi $r = -0.45$, $P < 0.001$; RVEDVi $r = -0.3$, $P = 0.001$; RVESVi $r = -0.3$, $P = 0.001$).

3.2. Reference values for RV strain and strain rate

Good quality tracking was obtained in all subjects following a maximum of two editions. Normal RV strain and strain rates are shown in Table 1. FW-Ell (−24.2 ± 3.59) was significantly higher than FW + S Ell (−21.9 ± 3.24). There were no gender differences in strain (Table 3, 'data in brief') [13]. For both FW and FW + S techniques, there were no clear relationships between strain or strain rates and increasing age on linear regression analysis. However, with inclusion of the septum, increasing age was associated with a linear decrease in early diastolic strain rate (SR_E, falling from a mean of 1.18 ± 0.24 s^{-1} to 0.92 ± 0.25 s^{-1} with advancing age from 20 to 70 years of age, $r = -0.30$, $P = 0.002$) and an increase in late diastolic strain rate (SR_A, $r = 0.24$, $P = 0.018$) [13]. Considering the absence of a consistent impact of age and gender on strain and strain rate, the normal range values of the overall cohort are presented (Table 1) with individual decile values presented in the associated 'data in brief' article [13].

3.3. Reference values for RA strain

Mean RA Ell was −21.1 ± 3.76 and was unaffected by age or gender [13].

3.4. Reproducibility

Intra- and inter-observer reproducibility for RV and RA Ell was consistently high (ICC range 0.80–0.92) but worse for strain rate whether analyzed with inclusion or exclusion of the septum. Full reproducibility data are presented in the associated 'data in brief' article [13].

4. Discussion

This is the first study to report reference values for RV and RA myocardial Ell using FT-CMR from a group of healthy volunteers across a balanced stratification of age and sex. No consistent relationship between RV Ell, RA Ell or strain rate parameters and either age or sex was found, despite the relationship between baseline biventricular volumes and age being similar to that observed in the general population [14]. The reproducibility of RV and RA Ell was satisfactory but poor for RV strain rate, which are differential quantities that are derivatives of the former.

In contrast to studies that have demonstrated an association between age and LV Ell and strain rate [6], no such relationship was found in our study between age and RV Ell. It is interesting to note that our study found the same relationship between increasing age and conventional measures of chamber size and function as previous research, demonstrating decreasing RV volumes with increasing RV ejection fraction [14]. There is one other small study of longitudinal free wall RV Ell using FT-CMR [12], and one study of 219 healthy subjects using speckle tracking echocardiography that found no relationship with age [15]. While results using pulsed Tissue Doppler are discordant, the

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