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Quantification of Myocardial Stiffness using Magnetic Resonance Elastography in Right Ventricular Hypertrophy: Initial Feasibility in Dogs

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Abstract

Introduction—Myocardial stiffness is an important determinant of cardiac function and is currently invasively and indirectly assessed by catheter angiography. This study aims to demonstrate the feasibility of quantifying right ventricular (RV) stiffness noninvasively using cardiac magnetic resonance elastography (CMRE) in dogs with severe congenital pulmonary valve stenosis (PVS) causing RV hypertrophy, and compare it to remote myocardium in the left ventricle (LV). Additionally, correlations between stiffness and selected pathophysiologic indicators from transthoracic echocardiography (TTE) and cardiac magnetic resonance imaging were explored.

Methods—In-vivo CMRE was performed on nine dogs presenting severe congenital PVS using a 1.5T MRI scanner. T1-MOLLI, T2-prepared-bSSFP, gated-cine GRE-MRE and LGE (PSIR) sequences were used to acquire a basal short-axis slice. RV and LV-free-wall (FW) stiffness measurements were compared against each other and also correlated to ventricular mass, RV and LV FW thickness, T1 and T2 relaxation times, and extracellular volume fraction (ECV). Peak transpulmonary pressure gradient and myocardial strain were also acquired on eight dogs by TTE and correlated to RV-FW systolic stiffness. Potential correlations were evaluated by Spearman's rho (r_s).

Results—RV-FW stiffness was found to be significantly higher than the LV-FW stiffness both during end-systole (ES) ($p=0.002$) and end-diastole (ED) ($p=0.029$). Significant correlations were observed between RV-FW ES and LV-FW ED stiffness versus ECV ($r_s=0.75$; $p\text{-value}=0.05$). Non-significant moderate correlations were found between LV-FW ES ($r_s=0.54$) and RV-FW ED ($r_s=0.61$) versus ECV. Furthermore, non-significant correlations were found between RV or LV-FW stiffness and the remaining variables ($r_s<0.54$; $p\text{-value}>0.05$).

Conclusion—This study demonstrates the feasibility of determining RV stiffness. The positive correlations between stiffness and ECV might indicate some interdependence between stiffness and myocardial extracellular matrix alterations. However, further studies are warranted to validate our initial observations.

Keywords

Elasticity imaging techniques; Cardiac magnetic resonance elastography; Myocardial intrinsic properties; T2-mapping; T1-mapping; ECV; Echocardiography; Speckle tracking

1. Introduction

Myocardial stiffness is an important marker of myocardial performance in a variety of cardiac diseases [1–3]. To date, myocardial stiffness has been clinically assessed by catheter angiography using pressure-volume (P-V) measurements [2, 4]. However, cardiac catheterization is an expensive and invasive procedure, with risk of complications, which limits its regular use in daily clinical practice [5]. For this reason, the development of noninvasive methods to accurately estimate intrinsic stiffness of the myocardium would be of great clinical interest.

Two-dimensional and Doppler echocardiography is the primary noninvasive imaging modality used for evaluation of cardiac function and anatomy [6]. Several echocardiographic parameters are clinically accepted as surrogates of intrinsic myocardial properties, for example, estimation of pressure gradients between cardiac chambers or through stenotic valvular lesions, and myocardial deformation analysis using tissue Doppler or speckle tracking imaging [7].

Magnetic resonance elastography (MRE) is a novel noninvasive imaging technique that has been used to map the shear stiffness of soft tissues in different organs [8–11]. In MRE [12], cyclic mechanical waves are introduced in the region of interest, which are then tracked using a phase-contrast MR sequence. Subsequently, these wave images are mathematically processed to obtain spatial stiffness maps using an inversion algorithm [13]. Previous studies applying this technique to the heart have demonstrated changes in left ventricular (LV) stiffness over the cardiac cycle, showing good correlation with invasive pressure measurements [14, 15]. The application of Cardiac MRE (CMRE) to measure myocardial elastic properties has the potential to facilitate noninvasive assessment of myocardial dysfunction and relaxation abnormalities related to increased myocardial stiffness [16].

Other cardiac magnetic resonance (CMR) methods have recently been developed to allow quantitative analysis of myocardial T1 and T2 relaxation times [17, 18]. An imaging-based measurement of extracellular volume fraction (ECV) using T1 relaxation times has also

been proposed [19]. These intrinsic relaxation times and ECV measurements are altered in the presence of myocardial extracellular space modifications [18, 20], with changes developing in proportion to connective tissue variation in the setting of myocardial infarction, hypertrophic cardiomyopathy, non-ischemic cardiomyopathy, aortic stenosis, and other pathologies causing focal and diffuse fibrosis [20–22]. T2 relaxation times are prolonged in conditions culminating with myocardial edema, such as from acute myocarditis or acute myocardial ischemic injury [23, 24]. While previous studies have demonstrated that excess myocardial interstitial fluid or fibrosis cause increased myocardial stiffness [25, 26], T1 and T2 relaxation times have not yet been correlated with either invasive or noninvasive measures of myocardial stiffness.

To the best of our knowledge, there have been no studies applying CMRE to quantitation of right ventricular (RV) stiffness. This is because the normal RV walls, in contrast to the LV, have just a few millimeters of thickness, precluding CMRE derived stiffness quantification using current techniques. To overcome this restriction, we enrolled a specific cohort of client-owned dogs diagnosed with congenital pulmonary valve stenosis (PVS), leading to prominent concentric RV hypertrophy (RVH) [27, 28]. Since pathophysiological consequences related to PVS have been described in both humans and dogs, a naturally occurring animal model such as this might provide insight into the human disorder [27, 29].

The aim of our study was to demonstrate the feasibility of quantifying RV free-wall (FW) stiffness using CMRE and correlate it against selected pathophysiologic indicators from echocardiography and CMR, in dogs with severe congenital pulmonary stenosis causing concentric RVH. In addition, we determine any significant difference in stiffness measurements between RV and LV-FW, where LV-FW is used as a remote myocardium for comparison.

2. Materials and methods

2.1. Animal Preparation

In-vivo imaging was performed on nine client-owned dogs of different breeds presenting with severe congenital pulmonary stenosis (6 males and 3 females, age: 4 to 59 months, weight: 4 to 34 kg), in compliance with the Institutional Animal Care and Use Committee. All dogs were premedicated with acepromazine (0.04 to 0.10 mg/kg) and butorphanol (0.20 to 0.40 mg/kg) subcutaneously. A peripheral intravenous catheter was inserted into a cephalic vein and anesthesia was induced with an intravenous injection of ketamine (2.0 to 2.5 mg/kg) and propofol (2.0 to 2.5 mg/kg). The animals were orotracheally intubated and maintained under anesthesia using inhaled isoflurane (1.0% to 2.0%) in 100% oxygen with mechanical ventilation until the recovery phase. Transthoracic 2-dimensional and Doppler echocardiography (TTE) was performed under an identical anesthesia protocol in eight of these dogs within 24 hours of the CMR study. Breath-holds were performed during image acquisition by suspending mechanical ventilation.

2.2 TTE Acquisition & Analysis

TTE was performed using a digital cardiac ultrasound system (Vivid 7 Dimension with EchoPac software package, version BT09, GE Medical Systems, Waukesha, WI, USA) with

transducer selection (4, 7, or 10 MHz nominal frequency) matched to the size of the dog and preset for optimal canine imaging. The dogs were positioned in right and left lateral decubitus and two-dimensional cine loops and Doppler echocardiography tracings were acquired with a simultaneous ECG by a single observer (BAS); all raw data were captured digitally for off-line analysis at a digital workstation. A TTE study was not performed in one dog due to concerns of anesthetic duration.

For evaluation of congenital pulmonary stenosis, continuous-wave Doppler tracings were recorded across the pulmonary valve from a right parasternal short-axis imaging plane and an average of 3 to 5 velocity profiles were measured for peak transpulmonary pressure gradient (PTPG) estimations using the modified Bernoulli equation ($P=4V^2$) [30]. Particular attention was paid to correctly align the ultrasound beam parallel to flow direction to avoid underestimation of the PTPG.

Speckle tracking myocardial deformation analysis of the RV-FW was performed with proprietary speckle-tracking software (EchoPAC 2D Strain software, Q-Analysis (strain module), version 6.1, GE Medical Systems, Waukesha, WI, USA) using the left ventricular 2-chamber algorithm as recently reported in normal dogs [31]. Event timing for pulmonary valve opening and closure relative to the ECG was determined individually for each study by measuring a continuous wave Doppler recording of RV outflow ejection velocity. The region of interest for strain and strain rate measurement was defined by manually tracing the RV-FW endocardial border from the level of the tricuspid valve annulus to the RV apex with manual adjustments to incorporate the entire RV-FW myocardial thickness. Individual RV-FW segments (basilar, mid, apical) were then visually analyzed to assure adequate myocardial tracking by the software and manually adjusted if necessary. Global peak longitudinal strain and strain rate from the entire RV-FW (considered as a single segment and not a mean of the 3 segments) were then recorded as the maximal (most negative) systolic point on the respective global strain or strain rate curve prior to pulmonary valve closure. Each measurement for each dog was repeated in triplicate from 3 separate stored images and the average recorded (Figure 1).

2.3. CMR Acquisition & Analysis

2.3.1 CMR Acquisition—CMR was performed using a 1.5-Tesla MRI scanner (Avanto, Siemens Healthcare; Erlangen, Germany), and a 12-channel phased-array coil (6 anterior elements plus 6 spine coil elements). Animals were placed into the scanner in the supine feet-first position. The following protocol was executed, with the imaging parameters for the sequences outlined in table 1:

1. Breath-hold segmented balanced steady-state free precession (b-SSFP) cine imaging was performed in 8 to 12 contiguous short-axis planes to cover the RV.
2. ECG-gated gradient-recalled echo cine MRE sequence [32] was performed in a single basal short-axis slice. Mechanical waves were introduced into the heart using a pneumatic driver system [15, 33] by placing the passive driver on the dog's anterior chest wall (Figure 2). Motion-encoding gradients were applied separately

in the x, y and z directions to encode the motion in all directions during suspended breathing.

3. T1 modified Look-Locker inversion recovery (MOLLI) and T2-prepared b-SSFP sequences were also applied before contrast to acquire a single basal short-axis slice, matching the slice position used to acquire the MRE images [17, 18]. T1 post-contrast maps were obtained 10 minutes after injection of the contrast agent. However, T1 MOLLI was not performed in the first two dogs.
4. Late gadolinium enhancement (LGE) imaging was performed using a T1- weighted phase-sensitive inversion recovery (PSIR) sequence 10 to 15 min after administration of the contrast agent in all dogs [34]. Post-contrast images were acquired after manual injection of a rapid bolus of Gadoteridol (ProHance, Bracco Diagnostics, Princeton, NJ) at total dose of 0.2 mml/kg, followed by a 10 ml saline flush.

2.3.2 Image Analysis

RV Mass and Thickness Measurements: Global RV and left ventricular (LV) mass were determined by Simpson's rule using b-SSFP images at end-diastole. Mass was calculated by computer assisted endocardial and epicardial border definition on an advanced Leonardo workstation (Siemens Medical Solutions, Erlangen, Germany). Wall trabeculations were included as part of the RV cavity volume and interventricular septum as part of the LV. Results were then normalized to body surface area, which was calculated using the formula $BSA (m^2) = ((10.1 \times (\text{body weight in grams})^{2/3} / 10,000))$ [35]. The thickness of the RV and LV-FW were obtained from CMRE-derived stiffness maps using a custom built software in Matlab (The Mathworks, Natick, MA, USA), as described later, so that the stiffness and thickness measurements can be compared in the same region of interest.

CMRE Stiffness Analysis: MRE wave images were masked with RV and LV epicardial and endocardial contours and analyzed with MRE Lab (Mayo Clinic, Rochester, MN, USA) using 2D local frequency estimation algorithm [13, 36] to report shear stiffness measurements. First, wave images were directionally filtered in 8 directions to remove reflected waves, and band-pass filtered (0.4m (1 Wave/FOV) to 0.01m (40 Waves/FOV) as cutoffs) to remove longitudinal waves. Then, a temporal Fourier transform was performed to obtain the first harmonic displacement field in each encoding direction. The first harmonic displacement fields are further processed to estimate weighted stiffness map. Mean RV and LV-FW myocardial effective shear stiffness were obtained using a custom built analysis tool in Matlab (The Mathworks, Natick, MA, USA). The tool was set to automatically quantify stiffness within a 135° segment by eroding 3 and 2 pixels from RV and LV FWs respectively, to remove edge effects stemming from the inversion algorithm. Multiple thickness values were also automatically obtained from the same RV and LV-FW segments without pixel erosion using the aforementioned custom built tool, and average thickness was recorded (Figure 3).

T1, T2, and ECV Measurements: T1 and T2 values were recorded from quantitative T1 and T2 maps by manually drawing regions of interest (ROIs) encompassing the RV and LV-

FW regions used to determine the MRE effective shear stiffness (Figure 4). Care was taken to avoid inclusion of blood pool (including RV trabeculations) within the ROIs. Blood pool T1 relaxation times were also calculated before and after contrast administration by placing ROIs in the center of the RV and LV lumens. Extracellular volume (ECV) fraction was calculated as the change in myocardium and blood relaxation rates $R1$ (where $R1 = 1/T1$ post-contrast - $1/T1$ pre-contrast) and calibrated by blood hematocrit using the following formula: $ECV = (R1 \text{ myocardium} / R1 \text{ blood}) \times (1 - \text{hematocrit})$ [37]. Pre-contrast T1 values were then corrected for heart rate using the formula described elsewhere [38]: $T1_{\text{corr}} = T1_{\text{raw}} - ((2.7 \times (HR - 88)))$, where 2.7 is a constant that describes the relationship between corrected T1 ($T1_{\text{corr}}$) and uncorrected T1 ($T1_{\text{raw}}$), and 88 is the average heart rate recorded by pooling all dogs undergoing T1 quantification.

LGE analysis: LGE images were independently reviewed by two experienced radiologists (J.S.S. and R.D.W.) who qualitatively assessed the presence of delayed myocardial enhancement in the RV and LV basal segments. For each data set, the presence of LGE was assessed by a dichotomous yes or no question and segments with consensus were considered positive for fibrosis.

2.4. Statistical Analysis

Exploratory correlation was performed between estimates of mean RV and LV-FW stiffness and selected TTE and CMR variables. For each comparison, scatterplots were generated and inspected for a linear relationship between the variables. Due to the small number of data pairs, and probable lack of normal distribution, the nonparametric correlation coefficient, Spearman's rho (r_s), was calculated. Correlations between end-systolic mean RV-FW stiffness were explored against TTE derived PTPG and RV-FW longitudinal strain and strain rate. Additionally, both RV and LV-FW end-diastolic and end-systolic stiffness were correlated against selected CMR variables (RV and LV-FW thickness, global ventricular mass, intrinsic myocardial relaxation times and ECV). Correlation coefficients with (unadjusted, two-tail) p-values and bivariate scatterplots were generated using commercial software (JMP 9.0, SAS Institute Inc; and IBM-SPSS version 21, IBM Inc.). Student's paired T-test was also performed to determine significant differences in stiffness estimates between RV and LV. Statistical significance was set at $p < 0.05$.

3. Results

3.1 Echocardiography

Peak transpulmonary pressure gradients under anesthesia ranged from 48 to 107 mm Hg, RV-FW peak longitudinal systolic strain ranged from -12 to -26%, and RV-FW peak longitudinal strain rate ranged from -1.0 to -1.9 s^{-1} . No significant correlations were found between end-systolic RV-FW stiffness and any of the following: PTPG ($r_s = -0.07$, p-value=0.87), RV-FW peak longitudinal systolic strain ($r_s = -0.29$, p-value=0.96), or RV-FW peak longitudinal strain rate ($r_s = 0.31$, p-value=0.87) (Table 2). Scatterplots are shown in Figure 5.

3.2 MRI

In all animals, there was excellent detection of wave displacements in the x, y and z directions within the ventricular walls across the cardiac cycle. An example snapshot of wave propagation and the corresponding stiffness map with automated contours to obtain the mean stiffness and thickness is shown in Figure 3. RV-FW stiffness in all animals was higher at end-systole (5.9 to 13.5 kPa) in comparison to end-diastole (3.3 to 6.8 kPa). LV-FW effective stiffness also varied with the cardiac cycle, but was lower at both end-systole (3.5 to 12.1 kPa) and end-diastole (2.2 to 5.4 kPa), when compared to the RV-FW results. There was a statistically significant difference between RV and LV-FW stiffness both during end-systole ($p=0.002$) and end-diastole ($p=0.029$).

As expected, normalized RV mass and RV-FW thickness were increased in comparison to reference values in healthy dogs [39, 40]. RV mass ranged from 41 to 167 g/m² and RV-FW thickness ranged from 11 to 20 mm at end-systole and 9 to 19 mm at end-diastole. Normalized LV mass and LV-FW thickness were in the normal range except in one animal, with LV mass ranging from 51 to 91 g/m², and thickness ranging from 9 to 19 mm at end-systole and 7 to 16 mm at end-diastole.

RV and LV-FW pre-contrast T1 values (heart rate corrected) were in the range of 704 – 964 ms and 700 – 976 ms, while T2 values ranged from 36 to 53 ms and 34 to 52 ms, respectively. RV-FW ECV ranged from 13% to 34% and LV-FW ECV ranged from 12 to 27%. No reference values for myocardial relaxation times and ECV were found in the literature for the RV.

On LGE imaging, enhancement in the RV insertion point of the interventricular septum was observed in three dogs and patchy antero-septal or infero-septal enhancement in proximity to the insertion areas was observed in two dogs. There was absolute agreement between the readers that no delayed enhancement was present in either the RV or in the LV-FW segments used to quantify the RV and LV selected variables (Figure 4).

Scatterplots of mean end-diastolic and end-systolic RV-FW stiffness versus end-diastolic and end-systolic RV-FW thickness, RV mass index, T1, T2, and ECV are shown in Figure 6. Of these, only ECV showed a significant correlation to RV-FW end-systolic stiffness with an $r_s = 0.75$ ($p = 0.05$). At end-diastole, moderate correlation of ECV to RV-FW stiffness was found ($r_s = 0.61$), but with a non-significant p value ($p = 0.14$). Moderate to poor correlations were present between mean end-diastolic and end-systolic RV-FW stiffness and thickness, normalized RV mass, T1 and T2 relaxation times, with correlation coefficients lower than 0.70 and non-significant p-values. Summary of correlation coefficients found between mean RV-FW stiffness and RV variables is listed in Table 2.

Similar scatterplots of mean end-diastolic and end-systolic LV-FW stiffness vs. LV-FW thickness, LV mass index, T1, T2, and ECV are shown in Figure 7. Correlation coefficients found between mean LV-FW stiffness and the selected variables are listed in Table 3. ECV showed a positive correlation to mean end-diastolic LV-FW stiffness ($r_s = 0.75$, $p = 0.05$). However, at end-systole, moderate correlation of ECV to LV-FW stiffness was observed ($r_s = 0.54$), with a non-significant p-value of 0.22. Moderate to poor correlations were present

between mean LV-FW stiffness and the remaining LV variables, with correlation coefficients lower than 0.70 and non-significant p-values.

4. Discussion

In this study, we evaluated the feasibility of measuring effective RV-FW stiffness in RVH using CMRE. To this end, we utilized a unique cohort of dogs presenting with naturally occurring PVS and consequent RVH. As the first study of the kind, findings reported here require further validation. As we expected, there was increased myocardial stiffness in the hypertrophic RV-FW in comparison to the remote myocardium in the LV-FW. We have detected positive correlations between RV and LV-FW effective stiffness and ECV, while no significant correlations were found between RV or LV-FW effective stiffness and FW thickness, global normalized ventricular mass, T1 or T2 relaxation times. Also, no significant correlations were observed between RV-FW effective stiffness and TTE derived systolic parameters (i.e. PTPG, RV-FW peak longitudinal systolic strain and strain rate).

The positive correlations between stiffness and ECV might indicate some interdependence between changes in extracellular matrix and the mechanical properties of the heart. Despite the fact that LGE was negative and T1 correlations were not significant, pressure overload is known to induce increased connective tissue elements resulting from delayed collagen deposition and accumulation within the myocardial interstitium [41, 42]. The likelihood of some degree of RV extracellular matrix remodeling secondary to elevated chronic afterload could account for the positive correlation between CMRE derived effective shear stiffness and the corresponding ECV. Nonetheless, those potential extracellular matrix alterations were probably mild and/or scattered throughout the tissue, with no evident signs of localized fibrosis present on the LGE imaging.

A cause for the absence of correlation between RV-FW end-systolic stiffness and TTE derived systolic parameters is unclear. Correlation was expected between RV-FW end-systolic stiffness and TTE derived PTPG, RV-FW peak longitudinal systolic strain and strain rate. However, no significant correlations were found. The lack of correlation may be explained by a variation in anesthetic depth between TTE and CMRE acquisitions. Despite our efforts to match TTE and CMRE anesthetic level and timing of imaging, the imaging was performed in two physically separate facilities and required 2 separate periods of anesthesia; variation in cardiac function between the two imaging sessions could have potentially affected the data. If different degrees of cardiac depression occurred between TTE and CMRE secondary to variable levels of sedation, our ability to demonstrate significant correlations between those variables could have been affected. Also, the age of the dogs and consequent duration of RVH and time for development of altered RV myocardium varied. It is possible that the intrinsic systolic performance of the RV differed between dogs based on duration of RVH and degree of pathologic remodeling; such animals may have had increased RV stiffness and altered ECV, while PTPG may not accurately reflect the degree of stenosis due to reduced RV systolic function. The duration of therapy was also non-standardized between dogs, with some dogs receiving chronic beta-blockade for their disease, which may have altered TTE or CMR derived variables.

The absence of correlation between ventricular FW effective stiffness and either ventricular mass or wall thickness suggests that thickness and mass may not be used as surrogates of myocardial stiffness. Prior reports have already recommended that neither ventricular mass nor wall thickness should be used as a substitute for estimating myocardial stiffness, thus corroborating our findings [1, 43, 44].

The absence of correlation between CMRE derived effective shear stiffness and T2 relaxation time could be attributed to an absence of acute myocardial injury with edema at the time of the imaging. T2 myocardial relaxation times were not elevated in our study, suggesting that myocardial edema probably did not contribute to myocardial stiffness in these canine hearts [23, 24].

There are several limitations in our study. First, the study was conducted on a relatively small cohort of dogs that spontaneously presented with pulmonary stenosis. Second, age, duration and severity of pressure overload could not be controlled. Third, the animals studied were clinical veterinary patients, and could not be euthanized in order to gather histological evidence. Fourth, these are veterinary patients with variable duration of medical therapy and prior treatments. Hence, differing clinical courses may have prevented us from finding strong correlations between myocardial stiffness and CMR or TTE derived variables. Finally, the stiffness values obtained are not absolute and are therefore termed to be “effective” as explained in previous work [15]. Given that our findings are based on a limited number of observations, results should be interpreted with care as the small sample size may have impacted the ability to find statistical significance between some variables. However, this was a feasibility study and is the first of its kind to estimate RV stiffness noninvasively and demonstrated that RV-FW stiffness is significantly higher than LV-FW stiffness in dogs with PVS. Additionally, it is important to note that this report comprises a hypothesis-driven study, and results should be explored in further research.

Future studies integrating non-invasive CMRE effective stiffness with simultaneous invasive chamber pressure quantification, myocardial biopsy and/or post-mortem histological analysis could potentially clarify the degree of interdependence between MRE derived effective shear stiffness and the underlying extracellular matrix alterations and intracellular/extracellular edema. Also, the development of new respiratory navigator based CMRE sequences using faster acquisition strategies and incorporating higher temporal and spatial resolution could allow 3D imaging acquisition and better cardiac anatomic coverage.

5. Conclusion

In conclusion, we demonstrated the feasibility of CMRE for determination of effective myocardial shear stiffness in the RV, a challenging task compared to assessing the LV. CMRE is a potential modality for an elasticity-based evaluation of the myocardium, and may be used in combination with other CMR imaging techniques to noninvasively investigate focal and global myocardial abnormalities in hypertrophic diseases. Our results suggest a potential interdependence between changes in extracellular matrix and the mechanical properties of the heart. Further studies integrating myocardial histological

assessment are warranted to explore the association between myocardial stiffness and extracellular matrix remodeling in cardiac hypertrophic conditions.

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Figure 1.

Representative echocardiographic images from the dogs. Panel A shows the degree of right ventricular hypertrophy present in these dogs, recorded from an apical imaging plane. Panel B shows a continuous wave Doppler tracing recorded across the pulmonary valve for determination of PTPG. Panels C and D show tracings recorded from speckle tracking analysis of RV-FW peak longitudinal systolic strain (C) denoted by the arrow and RV-FW peak longitudinal systolic strain rate (D) denoted by the arrowhead.

Figure 2. Shows the experimental setup in one of the dogs. The passive driver was placed on the dog's anterior chest wall to induce the vibrations.

Figure 3.

Example of MRE images in a dog during end-systole. Short-axis magnitude image with hypertrophic RV indicated (asterisk) (A), snap-shots of wave images in the x, y and z motion sensitization directions (B,C,D), and the corresponding stiffness map (E). RV and LV-FW mean stiffness and thickness were obtained using the automated tool by drawing the spokes in the region of interest (F,G). The mean RV and LV-FW stiffness was 6.8 and 3.5 kPa, while average FW thickness was 19 and 9 mm, respectively.

Figure 4.

Example of pre-contrast and post-contrast T1 maps (A, B), as well as pre-contrast T2 map (C), and LGE imaging (D) in a dog. The mean RV-FW T1 (pre and post-contrast) and T2 values in the region of interest are found to be 856, 509 and 47ms respectively for the RV (solid contour line) and 887, 527 and 46 ms for the LV (dashed contour line). No enhancing areas of focal scar are observed either in the RV or in the LV walls on LGE images.

RV: Right ventricle, ES: end-systole, PTPG: Peak transpulmonary pressure gradient,
Strain: Peak systolic strain, SR: Peak systolic strain rate.

Figure 5.

Scatterplots illustrate the absence of correlation between mean RV end-systolic stiffness and TTE derived peak transpulmonary pressure gradient, RV-FW longitudinal systolic strain, and strain rate.

Figure 6.

Scatterplots of mean RV end-diastolic and end-systolic stiffness plotted against selected RV variables. Significant correlation was evident between mean RV-FW stiffness versus extracellular volume fraction at end-systole ($r_s > 0.75$; $p = 0.05$).

LV: Left ventricle, ED: end-diastole, ES: end-systole, T1: T1 relaxation time; T2: T2 relaxation time; ECV: extracellular volume fraction.

Figure 7.

Scatterplots of mean LV end-diastolic and end-systolic stiffness plotted against selected LV variables. Significant correlation was observed between mean LV-FW stiffness and extracellular volume fraction at end-distole ($r_s > 0.75$; $p = 0.05$).

Table 1

Image acquisition parameters for all sequences performed.

Sequence	B-SSFP Cine	Cine GRE MRE	T1-MOLLI	T2 Prep B-SSFP	PSIR
Parallel acceleration	GRAPPA rate 2	GRAPPA rate 2	GRAPPA rate 2	GRAPPA rate 2	-
Acquisition matrix	256 × 128	128 × 64	192 × 124	192 × 126	192×140
FOV, mm	240–320 *	240–320 *	240–300 *	240–340 *	240–320 *
Slice thickness, mm	5–8 *	5–8 *	5–8 *	5–8 *	5–8 *
TR/TE, ms	3.1/1.3	12.5/9.0	2.5/1.0	3 × R-R/0.24,55	9.5/4.3
Band width, Hz/pixel	868	501	930	930	130
Flip angle, °	46	30	35	70	25
MRE time Offsets	-	4	-	-	-
MEG/Excitation frequency, Hz	-	160/80	-	-	-
Acquisition Heartbeats	-	-	3,3,5	-	-
TI/TT increment, ms	-	-	100/80	-	200–270

B-SSFP indicates balanced steady state free precession; GRE, cine gradient echo; MRE, magnetic resonance elastography; MOLLI, Modified Look-Locker inversion recovery; PSIR, Phase-sensitive inversion recovery; GRAPPA, generalized auto calibrating partially parallel acquisitions; TR, repetition time; TE, echo time, MEG, motion encoding gradients.

* Slice thickness and FOV varied accordingly to the size of the dog.

Table 2

Exploratory correlations of MRI-derived myocardial effective stiffness to right ventricular variables.

RV stiffness	RV variable	r_s	p^*
ED	ED thickness	-0.38	0.31
ES	ES thickness	-0.23	0.55
ED	RV mass	0.13	0.73
ES	RV mass	-0.23	0.55
ED	T1	0.36	0.43
ES	T1	0.43	0.34
ED	T2	0.53	0.14
ES	T2	0.18	0.64
ED	ECV	0.61	0.15
ES	ECV	0.75	0.05
ES	PTPG	-0.07	0.87
ES	Strain	-0.29	0.49
ES	Strain rate	0.31	0.46

RV: right ventricular; ED: end-diastole; ES: end-systole; T1/T2: T1 and T2 relaxation times; ECV: extracellular volume fraction; PTPG: peak transpulmonary pressure gradient; Strain: peak longitudinal systolic strain; Strain rate: peak longitudinal systolic strain rate;

* Probability derived from Spearman Rank Correlation; Coefficients $r_s > 0.7$ are indicated in bold.

Table 3

Exploratory correlations of MRI-derived myocardial effective stiffness to left ventricular variables.

LV stiffness	LV variable	r_s	p^*
ED	ED thickness	0.38	0.31
ES	ES thickness	-0.22	0.58
ED	RV mass	0.02	0.97
ES	RV mass	-0.38	0.31
ED	T1	0.57	0.18
ES	T1	0.50	0.25
ED	T2	0.15	0.70
ES	T2	-0.07	0.86
ED	ECV	0.75	0.05
ES	ECV	0.54	0.21

LV: Left ventricular; ED: end-diastole; ES: end-systole; T1/T2: T1 and T2 relaxation times; ECV: extracellular volume fraction.

* Probability derived from Spearman Rank Correlation; Coefficients $r_s > 0.7$ are indicated in bold.