Normal Human Right and Left Ventricular Mass, Systolic Function, and Gender Differences by Cine Magnetic Resonance Imaging

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ABSTRACT

Our objective was to establish normal ranges of left and right ventricular mass and function with cine magnetic resonance imaging (MRI) and to determine gender differences. Seventy-five healthy subjects (age range 8–55, mean 28 yr) were studied with cine MRI. Ten dogs were imaged for autopsy validation with a mean difference between actual and MRI-determined mass of $0.2 \text{ A} \pm 8.4 \text{ g}$. Intraobserver and interobserver variability and interstudy variability were 5–6%. All parameters were significantly different between males and females except ejection fraction and the left ventricular mass to end-diastolic volume ratio. Agreement with published autopsy series, including gender differences, was excellent. This study presents normative MRI data that can be used for comparing individual patients and for further study of right and left ventricular interaction.

KEY WORDS: Left ventricle; Magnetic resonance imaging; Normative values; Right ventricle; Ventricular function.

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INTRODUCTION

Several recent studies showed that cine magnetic resonance imaging (MRI) is accurate and reproducible for estimation of both left and right ventricular mass and function (1-9). Left ventricular mass and function parameters are available from large numbers of normal subjects using echocardiography, and similar normal data from smaller series have been published using MRI (2,6–9). With the exception of autopsy studies, however, there are only a few studies to date on normal right ventricular mass and function in humans (10,11).

The right ventricle (RV) is difficult to assess quantitatively with echocardiography, and projection techniques such as radionuclide ventriculography and cine angiography are limited for this role because of overlap of structures and assumptions concerning right ventricular geometry (11-14). In part because of its tomographic nature, MRI has the potential for being more accurate in evaluation of right heart abnormalities than echocardiography (3,15-17). Congenital heart disease, pulmonary disease, and pulmonary vascular disease all frequently cause abnormalities of right heart mass and function. In addition, acute or chronic left heart failure can lead to right ventricular dysfunction, particularly when left ventricular dysfunction is severe. Thus, normal values for right ventricular mass and function by a noninvasive method should prove extremely useful to aid in management of patients with diverse types of heart disease.

In this study, we sought to establish a normative database of both right and left ventricular function and mass. This database can be used to establish confidence limits of normal mass and function by MRI and to establish the dependence of these parameters on height, weight, body surface area (BSA), and gender.

MATERIALS AND METHODS

Study Population

Seventy-five subjects with no previous history of cardiovascular disease were recruited (28 females, 47 males). Age of the subjects ranged from 8 to 55 yr (mean 28 ± 9 yr). All gave informed consent for the MRI protocol. No subjects were sedated. Table 1 describes the subject characteristics.

Image Acquisition

A protocol for cine slice selection that could be reproduced easily from subject to subject was developed

(17,18). Short-axis views were used to minimize partial volume effects. The protocol began with ungated sagittal spin-echo scout images (TE 15 msec, TR 200 msec, slice thickness 10 mm, field of view 400 mm, acquisition matrix 128×256). Based on these images, either an electrocardiogram- (ECG) triggered T1-weighted axial series of images or another ungated axial scout series is acquired. Typical parameters for the ECG-triggered T1-weighted scan are TE 15 msec, TR 80-90% of the subject's RR interval, slice thickness 7 mm, and slice gap 1.4 mm. These axial images are used to define the vertical long axis of the left ventricle (LV). Ungated scout images are acquired parallel to the long axis of the LV, bisecting the mitral valve orifice and passing through the LV apex. Based on the resulting vertical long axis images, another series of ungated scout images is acquired in the horizontal long-axis plane. These images bisect the mitral valve orifice and pass through the tip of the LV apex. A gradient-echo cine sequence is then performed in the horizontal long-axis view so that the atrioventricular valve plane can be localized. Short-axis cine loops are then acquired in contiguous 7-mm slices from base to apex starting with the most basal slice positioned across the atrioventricular valve plane. Cine loops are acquired at either one or two short-axis levels per acquisition.

The pulse sequence used is a fast-imaging at steadystate precession sequence with velocity compensation in the slice selection and frequency encoding axes. Imaging parameters are TR 50 msec, TE 12 msec, acquisition matrix 128×256 , two signal averages, FOV 275-350 mm, and slice thickness 7 mm. Flip angle is 30° in the horizontal long-axis plane and 60° in the short-axis plane. The number of cardiac phases per acquisition is determined as 80-90% of the RR interval divided by 50 msec (the TR per image). For subjects with steady heart rates, 90% of the RR interval was used, whereas in subjects with varying heart rates, 80% of the average RR interval was used to allow for changes in RR interval during scanning. All imaging was performed at either 1.0 or 1.5 T (Siemens SP 4000 1.5T scanner, Siemens 1.0 T mobile scanner, Iselin, NJ; and Philips Gyroscan ACS-NT15, Best, The Netherlands). Total imaging and subject setup time was approximately 1 hr, depending on heart rate. Typically, 12-14 slices were required to cover the ventricles.

Image Analysis and Determination of Ventricular Parameters

The images were transferred to an independent workstation (MaxiView, Dimensional Medicine, Inc., Minnetonka, MN; or SPARCstation 20, Sun Microsystems,

Study Population				
	All $(n = 75)$	Males $(n = 47)$	Females $(n = 28)$	
Height (cm)	172.5 ± 12.4	178.8 ± 8.5	169.6 ± 22.7	
Weight (kg)	69.0 ± 18.5	77.2 ± 15.7	68.0 ± 19.5	
BSA (m ²)	1.81 ± 0.30	1.95 ± 0.23	1.78 ± 0.35	
HR (bpm)	64 ± 9	63 ± 9	63 ± 11	

HR, heart rate.

Mountain View, CA) for analysis. The cine loops were viewed, and end-diastolic (ED) and end-systolic (ES) frames were chosen for each short-axis slice position. The first frame in each series was selected as the ED image. The ES image was chosen as the image with the smallest left and right ventricular blood pools before opening of the mitral valve.

On each ED frame, both endocardial and epicardial borders of each ventricle were defined for mass and volume determination. On each ES frame, the endocardial border of each ventricle was defined for volume determination. The interventricular septum was also outlined separately at ED. The ED frame was selected for mass determination because partial volume effects are likely to be less of a problem when the ventricle is relaxed, especially for the RV. Additionally, it is easier to determine the border between atrium and ventricle at ED than at ES. In total, seven ventricular tissue or blood volumes were determined per subject: LV free wall, interventricular septum, RV free wall, LV ED volume, RV ES volume, LV ES volume, and RV ES volume. Analysis time averaged between 20 and 30 min per subject.

Border definition was accomplished by either manual tracing using a mouse or by using a semiautomatic edge detection technique with user correction. The semiautomatic technique allows the user to select a range of image intensities to be considered blood. The pixels that fall within this intensity range are displayed in color. By placing a seed point in the colored area, the edges of the colored area are automatically detected and outlined. The user may then switch back to a pure grayscale image and edit the borders.

The borders marked for each of the seven volumes over the stack of contiguous slices are used to create a three-dimensional surface rendering of the volume. The rendering algorithm smooths the borders between slices and calculates the volume contained within the borders. Myocardial mass is determined by multiplying the myocardial tissue volume by an assumed density of 1.05 g/cm³. Stroke volume was calculated as the difference between ED and ES volumes, and ejection fraction was calculated as the stroke volume multiplied by 100 and divided by the ED volume. The LV-to-RV mass ratio and ED volume-to-mass ratios for each ventricle were calculated.

Because border identification is subjective, we used a fixed set of criteria for determination of borders to minimize interobserver and intraobserver variability. In the following sections, the criteria used to establish each of the seven measurements are presented.

LV ED Volume

The grayscale is adjusted so that no pixels are saturated at the peak image display intensity of 255 (8-bit display) and so that variations in intensity in the LV blood pool and at the blood pool-myocardium interface are seen. At the base of the LV, the aorta is included in the LV volume below the aortic valve. If the slice contains part of the aorta above the valve, only the remainder of the blood volume of the slice (mitral valve plane) is included as LV volume, as shown in Fig. 1(A). Additionally, if the myocardial wall surrounding this blood volume is thin, the volume is considered to be in the left atrium and is not included in the LV ED volume.

If the blood signal is uniform and the blood-myocardium contrast is high, the semiautomatic thresholding technique can be used on some slices. At the apex, the blood-myocardium contrast is often poor because of partial volume effects and slow flow. If the border is not clearly seen, the borders marked on slices above are used to guide identification, and the borders are marked manually. The papillary muscles are included as LV mass and excluded from LV volume. To accomplish this, taking into consideration the partial volume effects of 7-mmthick slices, the papillary muscles are included as mass only on the slices where they appear attached to the ventricular wall.



Figure 1. These images depict some of the criteria used to determine ventricular borders. (A) The aortic outflow region below the valve plane is included at ED for determination of LV volume. (B) The RV-LV junctions are used to divide the septum from the left ventricular free wall for mass determination. (C) If the pulmonic valve is seen at the top of the RV volume, the portion of the volume above the valve is excluded. (D) Identification of the RV free wall endocardial border.

Normal RV and LV Mass and Function

LV Free Wall Mass

The grayscale contrast is adjusted as described above for LV volume, with special attention to the myocardium-lung/liver border. The LV volume border is left in place and edited to enclose the LV free wall border. The LV free wall border extends from the RV-LV junction in the anterior wall to the RV-LV junction in the inferior wall, as shown in Fig. 1(B). The same criteria for determination of the most basal slice are used. Epicardial fat and pericardium are excluded from LV mass. If the livermyocardium border is not clear, the curvature of the lateral wall and septum are used to guide manual placement of the border. The papillary muscles are included as mass as described above.

Interventricular Septal Mass

The LV free wall borders are used to guide placement of the interventricular septum. Borders are placed to contain the septum and are limited by the edges of the free wall borders at the RV-LV junctions, as shown in Fig. 1(B). The upper portion of the membranous septum is not included.

RV ED Volume

The grayscale contrast is adjusted to maximize the RV free wall-blood pool contrast and so that no pixels exceed the maximum displayed signal intensity. If the pulmonic valve is seen at the top of the right ventricular volume, the portion of the volume above the valve is excluded [Fig. 1(C)]. If the moderator band is prominent, it is excluded from the RV volume and included as mass.

RV Free Wall Mass

The grayscale is adjusted so that the epicardial border of the RV free wall is well seen. The RV endocardial border is left in place and edited to enclose the RV free wall. Care is taken to exclude epicardial fat and pericardium [Fig. 1(D)].

LV ES Volume

Partial volume is more of a problem at ES because of the smaller ventricular cavity. The grayscale is adjusted so that no pixels exceed the maximum intensity and so that subtle grayscale variations near the endocardial border can be seen. The endocardial border is then traced, excluding the papillary muscles. At the base, slices that contain solely left atrium are excluded from analysis. Occasionally, a slice contains both atrium and ventricle. In these cases, only the portion of the image that can be identified as ventricle by inspection of the cine loops is included.

RV ES Volume

The grayscale is adjusted as described for the left ventricular ES volume. The endocardial border is traced, taking care to exclude trabeculae. At the base, slices that contain right atrium are excluded. As for the LV at ES, slices may contain a mix of ventricle and atrium. The atrial portions of these images are excluded. As at ED, only the portion of the volume below the level of the pulmonic valve is included.

Interstudy and Inter/Intraobserver Variation

To assess the magnitude of variability in each of the calculated parameters due to subjectivity in image analysis and due to reproducibility in scanning, both imaging and analysis were repeated in a series of volunteers. To assess intraobserver variability, one observer reanalyzed the studies of six subjects. The observer was blind to the results of the previous analysis, and the time between analyses was more than 2 weeks. To assess interobserver variability, a second observer analyzed the same six studies. To assess interstudy variation, eight subjects were imaged twice in sessions 8–24 weeks apart.

All ventricular parameters were calculated in each case. The mean difference between observers and repeat studies and the variability (SD of the differences) were computed according to the method of Bland and Altman (19). In addition, the results for all parameters of each pair of compared data were plotted against one another, and linear regression analysis was performed to assess the degree of correlation between observers and repeat studies.

Autopsy Validation of Method

Ten mongrel dogs were studied to validate measurement of left and right ventricular mass. A similar MR acquisition protocol as the one described above was used but with a slice thickness of 5 mm to compensate for the smaller heart size of dogs. After imaging, the heart was excised, and the ventricles were separated and weighed. The differences between MRI-determined and actual mass were computed for both the RVs and LVs. Interobserver and intraobserver variability was also assessed.

Statistical Analysis

Comparisons were made for each ventricular parameter between males and females using analysis of variance. Comparisons were made using the unnormalized data and again using the data normalized to BSA, height, and weight. Power calculations were performed to ensure that population sampling was sufficient to detect gender differences in ventricular parameters. In addition to presenting normal ranges for each parameter, the data were fit to a linear model using least-squares analysis describing the relationship between BSA, height, and weight and LV ED volume, RV ED volume, LV mass, and RV mass. A polynomial model of the form parameter = $a \times$ $BSA + b \times BSA^2 + c$ was also fit to the ED volume and mass data to determine whether this approach could better characterize the dependence on BSA than a linear model.

RESULTS

For the validation study in dogs, the mean difference between actual and MRI-determined mass was 0.2 ± 8.4 g ($0.3 \pm 12.8\%$) for both ventricles combined (4.6 ± 6.3 g [$13.2 \pm 18.1\%$] for RV mass and -5.0 ± 7.7 g [$5.2 \pm 8.0\%$] for LV mass). Actual mean mass of the RV was 35 ± 18 g (range 18-62 g) and mean mass of the LV was 98 ± 46 g (range 52–186 g). Left and right ventricular stroke volumes agreed within 6 ml, and there was no significant difference in actual versus MRI-determined mean mass. Intraobserver and interobserver correlation was excellent (r = 0.98). The mean interobserver difference was 2.5 ± 2.0 g (7.1 ± 5.7%) for the RV and 7.6 ± 5.8 g (7.8 ± 5.9%) for the LV. The mean intraobserver difference was 5.1 ± 1.2 g (14.6 ± 3.4%) for the RV and 9.1 ± 3.3 g (9.3 ± 3.4%) for the LV.

Table 2 shows the results for all parameters for the entire group of 75 human subjects and separately for the male and female groups. Tables 3–5 show the ventricular parameters normalized to BSA, weight, and height. Summaries of the relationships between the ventricular parameters and BSA, height, and weight are presented in Tables 6 and 7.

With the sample size used in this study, all predicted ventricular parameters had a power greater than 90% for detecting differences between males and females except for heart rate (power 50%), LV and RV stroke volume normalized to BSA (power 85–90%), and RV free wall mass normalized to height (power 88%).

Ventricular Volume

Right ventricular volume was greater than left ventricular volume for all groups. In males, LV ED volume

Ventricular Farameters (mean \pm 1 SD) with 95% Confidence Intervals (1.90 SD) in Farentineses									
		All (n	= 75)		Males ((n = 47)		Females	(n = 28)
LV ED volumes (ml)	121	± 34	(55–187)	136	± 30	(77–195)	96	± 23	(52-141)
RV ED volumes (ml)	138	± 40	(59–217)	157	± 35	(88-227)	106	± 24	(58–154)
LV ES (ml)	40	± 14	(13–67)	45	± 14	(19-72)	32	± 9	(13–51)
RV ES (ml)	54	± 21	(12-96)	63	± 20	(23-103)	40	± 14	(12-68)
IVSM (g)	54	± 13	(28-80)	61	± 11	(40-82)	42	± 8	(26–58)
LVFWM (g)	104	± 27	(44–150)	117	± 22	(75–159)	82	± 19	(46–119)
LVTM (g)	158	± 39	(82–234)	178	± 31	(118-238)	125	± 26	(75–175)
RVFWM (g)	46	± 11	(25–67)	50	± 10	(30–70)	40	± 8	(24–55)
LV EF (%)	67	± 5	(57–78)	67	± 5	(56-78)	67	± 5	(56-78)
RV EF (%)	61	± 7	(47-76)	60	± 7	(47-74)	63	± 8	(47-80)
LVSV (ml)	82	± 23	(36–127)	92	± 21	(51-33)	65	± 16	(33–97)
RVSV (ml)	84	± 24	(37–131)	95	± 22	(52-138)	66	± 16	(35–98)
LVTM/LVEDV (g/ml)	1.3	3 ± 0.18	(0.98-1.68)	1.34	± 0.19	9 (0.96–1.71)	1.3	1 ± 0.1	6 (0.99-1.63)
RVFWM/RVEDV (g/ml)	0.3	5 ± 0.06	6 (0.23-0.47)	0.33	3 ± 0.00	6 (0.21–0.44)	0.3	8 ± 0.0	5 (0.28-0.48)
LVTM/RVM	3.4	6 ± 0.66	6 (2.16-4.76)	3.64	± 0.72	2 (2.23–5.04)	3.1	7 ± 0.4	3 (2.33-4.01)
CO (l/min)	5.2	± 1.4	(2.42-8.05)	5.8	± 3.0	(2.82-8.82)	4.3	± 0.9	(2.65–5.98)

 Table 2

 Ventricular Parameters (mean + 1 SD) with 95% Confidence Intervals (1.96 SD) in Parentheses

EF, ejection fraction; CO, cardiac output; LVEDV, RVEDV, left and right ventricular end diastolic volume; LVES, RVES, left and right ventricular end systolic volume; IVSM, interventricular septal mass; LVFWM, RVFWM, left and right ventricular free wall mass; LVSV, RVSV, left and right ventricular stroke volume; LVTM, left ventricular total mass; RVM, right ventricular mass.

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Ventricular Parameters Normalized to BSA (95% Confidence Interval [1.96 SD] in Parentheses)

	All $(n = 75)$	Males $(n = 47)$	Females $(n = 28)$
LV ED volume/BSA (ml/m ²)	66 ± 12 (44-89)	69 ± 11 (47-92)	$61 \pm 10 (41-81)$
RV ED volume/BSA (ml/m ²)	75 ± 13 (49–101)	$80 \pm 13 (55-105)$	$67 \pm 10 (48-87)$
LVTM/BSA (g/m ²)	$87 \pm 12 (64-109)$	$91 \pm 11 (70-113)$	79 ± 8 (63-95)
LVFWM/BSA (g/m ²)	57 ± 8 (40-73)	$60 \pm 8 (44-76)$	$52 \pm 6 (40-64)$
IVSM/BSA (g/m ²)	$30 \pm 4 (21-38)$	$31 \pm 4 (23-39)$	$27 \pm 4 (20-34)$
RVFWM/BSA (g/m ²)	$26 \pm 5 (17-34)$	$26 \pm 5 (16-36)$	$25 \pm 4 (18-33)$
LVSV/BSA (ml/m ²)	45 ± 8 (29-61)	47 ± 8 (32–62)	41 ± 8 (26-56)
RVSV/BSA (ml/m ²)	46 ± 8 (30-62)	48 ± 8 (32-64)	42 ± 8 (27-57)
$CO/BSA (1/min/m^2)$	2.9 ± 0.6 (1.74–4.03)	$3.0 \pm 0.6 (1.74 - 4.20)$	$2.8 \pm 0.5 (1.75 - 3.80)$

CO, cardiac output; IVSM, interventricular septal mass; LVFWM, RVFWM, left and right ventricular free wall mass; LVSV, RVSV, left and right ventricular stroke volume; LVTM, left ventricular total mass.

Table 4

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Ventricular Parameters Normalized to Weight (95% Confidence Interval in Parentheses)				
	All $(n = 75)$	Males $(n = 47)$	Females $(n = 28)$	
LV ED volume/WT (ml/kg)	$1.8 \pm 0.3 (1.2 - 2.4)$	$1.8 \pm 0.3 (1.2 - 2.3)$	$1.8 \pm 0.2 \ (1.2 - 2.4)$	
RV ED volume/WT (ml/kg)	$2.0 \pm 0.3 (1.4 - 2.6)$	$2.0 \pm 0.3 (1.5 - 2.6)$	$2.0 \pm 0.3 (1.3 - 2.6)$	
LVTM/WT (g/kg)	$2.4 \pm 0.3 (1.8 - 2.9)$	$2.4 \pm 0.3 (1.9 - 3.0)$	$2.3 \pm 0.3 (1.8 - 2.8)$	
LVFWM/WT (g/kg)	$1.6 \pm 0.2 (1.2 - 1.9)$	$1.6 \pm 0.2 (1.2 - 2.0)$	$1.5 \pm 0.2 (1.2 - 1.9)$	
IVSM/WT (g/kg)	$0.8 \pm 0.1 \ (0.6 - 1.1)$	$0.8 \pm 0.1 \ (0.6 - 1.0)$	$0.8 \pm 0.1 \ (0.5 - 1.0)$	
RVFWM/WT (g/kg)	$0.7 \pm 0.1 \ (0.5 - 1.0)$	$0.7 \pm 0.1 \ (0.5 - 0.9)$	$0.7 \pm 0.1 \ (0.5 - 1.0)$	
LVSV/WT (ml/kg)	$1.2 \pm 0.2 \ (0.8 - 1.6)$	$1.2 \pm 0.2 \ (0.8 - 1.6)$	$1.2 \pm 0.2 (0.7 - 1.7)$	
RVSV/WT (ml/kg)	$1.2 \pm 0.2 \ (0.8-1.7)$	$1.2 \pm 0.2 \ (0.8 - 1.6)$	$1.2 \pm 0.2 (0.8 - 1.7)$	

WT, weight; IVSM, interventricular septal mass; LVFWM, RVFWM, left and right ventricular free wall mass; LVSV, RVSV, left and right ventricular stroke volume; LVTM, left ventricular total mass.

Table 5

Ventricular Parameters	Normalized to	Height (9	5% Confidence	Interval in	Parentheses)
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-	All $(n = 75)$	Males $(n = 47)$	Females $(n = 28)$
LV ED volume/HT (ml/cm)	$0.7 \pm 0.1 \ (0.4 - 1.0)$	$0.7 \pm 0.1 \ (0.5 - 1.0)$	$0.6 \pm 0.1 \ (0.4 - 0.8)$
RV ED volume/HT (ml/cm)	$0.8 \pm 0.2 \ (0.4 - 1.1)$	$0.8 \pm 0.2 \ (0.5 - 1.2)$	$0.6 \pm 0.1 \ (0.4 - 0.9)$
LVTM/HT (g/cm)	$0.9 \pm 0.1 \ (0.8 - 1.0)$	$1.0 \pm 0.1 \ (0.7 - 1.3)$	$0.8 \pm 0.1 \ (0.5 - 1.0)$
LVFWM/HT (g/cm)	$0.6 \pm 0.0 \ (0.6-0.6)$	$0.7 \pm 0.1 \ (0.4-0.9)$	$0.5 \pm 0.1 \ (0.3-0.7)$
IVSM/HT (g/cm)	$0.3 \pm 0.1 \ (0.2-0.4)$	$0.3 \pm 0.1 \ (0.2 - 0.4)$	$0.3 \pm 0.0 \ (0.2-0.3)$
RVFWM/HT (g/cm)	0.3 ± 0.1 (0.2–0.4)	$0.3 \pm 0.0 \ (0.2 - 0.4)$	$0.3 \pm 0.0 \ (0.2 - 0.3)$
LVSV/HT (ml/cm)	$0.5 \pm 0.1 \ (0.3-0.7)$	$0.5 \pm 0.1 \ (0.3 - 0.7)$	$0.4 \pm 0.1 \ (0.2-0.6)$
RVSV/HT (ml/cm)	$0.5 \pm 0.1 (0.3-0.7)$	$0.5 \pm 0.1 \ (0.3-0.7)$	$0.4 \pm 0.1 \ (0.2-0.6)$

HT, height; IVSM, interventricular septal mass; LVFWM, RVFWM, left and right ventricular free wall mass; LVSV, RVSV, left and right ventricular stroke volume; LVTM, left ventricular total mass.

	Equation	Correlation Coefficient	SE of y-estimate
Normalization to BSA (m ²)	LV ED volume = 91 BSA - 43	0.89	21 ml
	RV ED volume = 114 BSA - 67	0.84	22 ml
	LVTM = 112 BSA - 45	0.86	20 g
	LVFWM = 76 BSA - 33	0.84	14 g
	IVSM = 37 BSA - 12	0.82	8 g
	RVFWM = 21 BSA + 7	0.59	9 g
Normalization to height (cm)	LV ED volume = 2.0 HT $- 227$	0.74	23 ml
_	RV ED volume = 2.5 HT $- 298$	0.78	25 ml
	LVTM = 2.6 HT - 290	0.83	22 g
	LVFWM = 1.7 HT - 195	0.81	16 g
	IVSM = 0.9 HT - 95	0.80	8 g
	RVFWM = 0.6 HT - 54	0.67	8 g
Normalization to weight (kg)	LV ED volume = 1.4 WT + 24	0.77	22 ml
	RV ED volume = 1.8 WT + 17	0.81	24 ml
	LVTM = 1.7 WT + 40	0.82	- 22 g
	LVFWM = 1.2 WT + 24	0.80	16 g
•	IVSM = 0.6 WT + 16	0.77	9 g
-	RVFWM = 0.3 WT + 25	0.52	9 g

Linear Model of Dependence on BSA of Ventricular Parameters

IVSM, interventricular septal mass; LVFWM, RVFWM, left and right ventricular free wall mass; LVTM, left ventricular total mass.

averaged 136 \pm 34 ml versus 96 \pm 23 ml in females. RV ED volume averaged 157 \pm 40 ml in males versus 106 \pm 24 ml in females. The RV volume was 14% larger than the LV volume in the composite group; 15% larger in males but only 10% larger in females (p < 0.05). The differences between males and females were significant for all right and left ventricular parameters except ejection fraction and the LV total mass-to-LV ED volume ratio. When normalized to BSA (ventricular parameter divided by BSA), significant differences remained between males and females in all parameters except RV mass. Normalization to height yielded similar results, with all parameters significantly different between males and females. Normalization to weight yielded no significant differences between groups for any of the volume parameters.

Ventricular Ejection Fraction, Stroke Volume, and Output

The average LV and RV ejection fractions were $67 \pm 5\%$ and $61 \pm 7\%$, respectively, for the composite group (Table 2). Left and right ventricular stroke volumes were equal in all groups, consistent with the lack of significant valvular regurgitation in this population. The finding of equal stroke volumes also served as an internal validation of the methods used. Stroke volume was significantly higher in males than in females (92 versus 65 ml, p <

Equation	Correlation Coefficient	SE of y-estimate
$LV ED volume = 144.5 BSA - 0.2 BSA^2 - 137.8$	0.80	26 ml
$RV ED volume = 175.3 BSA - 3.6 BSA^2 - 166.6$	0.84	26 ml
$LVTM = 333.1 BSA - 51.1 BSA^2 - 272.8$	0.87	22 g
$RV mass = 253.2 BSA - BSA - 56.0 BSA^2 - 223.7$	0.65	13 g

Polynominal Model of Dependence on BSA of Ventricular Parameters

LVTM, left ventricular total mass.

0.01), indicative of higher cardiac outputs in males (5.8 \pm 1.4 versus 4.3 \pm 0.9 l/min). This gender difference was removed with normalization to BSA.

Ventricular Mass

RV free wall mass averaged 50 ± 10 g in males and 40 ± 8 ml in females. Mean LV total mass was 178 ± 31 g in males and 125 ± 26 g in females. Differences between males and females were significant for all mass parameters. When normalized to BSA, all parameters except right ventricular mass were significantly different between groups.

The mass-to-ED volume ratio for the LV did not differ between males and females. For the RV, the mass to ED volume ratio was significantly different between males and females (0.33 \pm 0.06 versus 0.38 \pm 0.06 g/ml, p <0.05). The ratio of LV total mass-to-RV mass was significantly different (p < 0.01) between males and females (3.64 \pm 0.72 for males, 3.17 \pm 0.43 for females, and 3.46 \pm 0.66 for the composite group).

Inter/Intraobserver and Interstudy Variation

For the intraobserver and interobserver studies of six subjects and the interstudy comparison, the mean difference and variability in each measured parameter between trials is shown in Table 8. Pooling all ventricular volume parameters together, the mean difference between trials for the intraobserver study was 0.46 ± 4.30 ml ($0.6 \pm 5.4\%$). The pooled interobserver data resulted in a mean difference of 0.55 ± 4.64 ml ($0.7 \pm 5.9\%$). For the

interstudy evaluation, the mean difference between trials was 0.34 ± 4.76 ml ($0.4 \pm 6.0\%$). The results from the linear regressions for the intraobserver and interobserver studies were as follows: observer $2 = 0.99 \times$ observer 1 + 2.65, r = 0.99, SEE = 4.45 ml; and observer 1-trial $2 = 0.97 \times$ observer 1-trial 1 + 1.95, SEE = 4.12 ml, r = 0.99. For the interstudy comparison, the linear regression results were study $2 = 0.98 \times$ study 1 + 1.77, SEE = 4.74 ml, r = 0.99.

Normalization to BSA, Height, and Weight

The linear model of the relationship between ventricular parameters and BSA resulted in slightly lower SE than did the polynomial model (Tables 6 and 7). the correlation coefficient ranged from 0.82 to 0.86 for dependence on BSA with the exception of RV free wall mass, which yielded a correlation coefficient of only 0.59. Normalization to BSA yielded slightly better SEs errors than did normalization to either height or weight for all parameters and slightly better correlation coefficients. Figures 2-5 show the dependence of left and right ED volume and mass on BSA.

DISCUSSION

Comparison with Other Studies

The results of this study compare favorably with other imaging studies and autopsy studies as outlined below and summarized in Table 9. The validation study in dogs yielded similar correlations with actual mass, as have other animal validation studies (20).

Inter/Intraobserver and Interstudy Variation				
***	Interobserver (ml)	Intraobserver (ml)	Interstudy (ml)	
LV ED volume	3.4 ± 3.5	4.2 ± 3.8	1.4 ± 5.9	
RV ED volume	0.2 ± 5.6	-0.0 ± 4.2	-0.9 ± 4.0	
LVFW volume	4.9 ± 6.5	-1.7 ± 4.0	0.7 ± 5.6	
IVS volume	-0.1 ± 2.7	-3.6 ± 2.2	1.5 ± 2.0	
RVFW volume	-4.4 ± 2.5	0.4 ± 1.3	-2.1 ± 4.0	
LVES	0.6 ± 2.6	0.9 ± 2.3	2.1 ± 5.0	
RVESV	-0.7 ± 2.6	3.0 ± 6.5	-0.3 ± 6.0	
All parameters	0.6 ± 4.6	0.5 ± 4.3	0.3 ± 4.8	

Table 8

Values are mean differences \pm variability.

LVES, left ventricular end systolic volume; IVS, interventricular septal; LVFW, RVFW, left and right ventricular free wall.



Figure 2. Left ventricular end-diastolic volume (LVEDV) is plotted versus BSA. Female and male groups are represented with different symbols to illustrate that although males and females appear to have the same dependence on BSA, the female group has generally smaller values of both BSA and LV volume.

Autopsy

An autopsy study of 300 subjects by Hangartner et al. (20) showed similar values of LV and RV mass and emphasized the differences between males and females in both-the magnitude of each parameter and the dependence of each parameter on body size. In agreement with



Figure 4. Left ventricular total mass is plotted versus BSA with different symbols for the female and male groups.

our results, Hangartner et al. found that body weight was a better predictor of isolated ventricular weights, for both sexes, than height.

Another autopsy study (n = 43) by Fulton et al. (21) did not separate results by gender and reported a mean subject age greater than that of our study (mean age 49)



Figure 3. Right ventricular end-diastolic volume (RVEDV) is plotted versus BSA. Female and male groups are represented with different symbols.



Figure 5. Right ventricular total mass is plotted versus BSA with different symbols for the female and male groups.

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		Comparison with Results of Other	Studies	
Reference	Modality	Parameter	Literature Value	Present Study
Hajduczok (37)	Ultrafast CT	RV mass (male, $n = 7$) I V mass (DV mass (male $n = 7$)	$55 \pm 3g$ 37 ± 02	50 ± 10 g 364 ± 072
Wachspress (40)	Ultrafast CT $(n = 10)$	LV ED volume/BSA	5.4 ± 0.4 61 \pm 15 ml/m ²	$566 \pm 12 \text{ m/m}^2$
•		RV ED volume/BSA	$76 \pm 19 \text{ m}/\text{m}^2$	$75 \pm 13 \text{ ml/m}^2$
		LV ES volume/BSA	$19 \pm 7 \mathrm{ml/m^2}$	$21 \pm 10 \text{ m}/\text{m}^2$
		RV ES volume/BSA	$35 \pm 13 \mathrm{ml/m^2}$	$29 \pm 10 \text{ m}/\text{m}^2$
		LV EF	, 70 ± 7	67 ± 5
		RV EF	55 ± 6	61 ± 7
Katz (15)	MRI	RV mass/BSA ($n = 10$)	$23.3 \pm 1.4 \text{ g/m}^2$	$26.1 \pm 7.7 \mathrm{g/m^2}$
Doherty (16)	MRI	RV mass (male, $n = 10$)	45 ± 8 g	$46 \pm 11 \text{ g}$
Daniels (33)	Echocardiography (age 12.6	LV mass/BSA (males, $n = 167$)	70.4 g/m ²	91 \pm 11 g/m ² (mean BSA 1.81 m ²)
	yr, range 6–23 yr, mean BSA 1.38 m ²)			79 g/m ² pred. by regression
		LV mass/BSA (females, $n = 167$)	60.7 g/m ²	$79 \pm 8 \text{ g/m}^2$
				78 g/m ² pred. by regression
		LV mass (males, $n = 167$)	$100 \pm 42 \text{ g}$	$178 \pm 31 \text{ g}$
				110 g pred. by regression
		LV mass (females, $n = 167$)	81 ± 29 g	125 ± 26 g
				103 g pred. by regression
Verdecchia (26)	Echo ($n = 496$)	Upper limit LV mass/BSA	125 g/m ²	109 g/m ²
Fazio (28)	Echo $(n = 31)$	LV mass	$80 \pm 18 \text{ g/m}^2$	$87 \pm 12 {\rm g/m^2}$
Mohan (29)	Echo (race, Indian)	LV mass (male)	$171 \pm 52 \text{ g}$	178 ± 31 g
	•	LV mass (female)	131 ± 43 g	$125 \pm 26 g$
Devereux (30)	M-mode echo	Upper limit LV mass/BSA (male)	134 g/m ²	113 g/m ²
		Upper limit LV mass/BSA (female)	110 g/m ²	95 g/m ²
Douglas (31)	Echo $(n = 17)$	LV mass	$143 \pm 54 \text{ g}$	$158 \pm 39 g$
Byrd (32)	Echo $(n = 84)$	LV mass (male)	148 g	$178 \pm 31 \text{ g}$
		LV mass (female)	108 g	$125 \pm 26 \text{ g}$
Fulton (21)	Autopsy	RV mass (male and female)	46 g (23–68 g)	46 ± 11 (25–67)
		LV free wall mass (male and female)	86 g (48–123 g)	97 (44–150)
Hangartner (20)	Autopsy	LV mass (males)	164 ± 38 (92–256)	$178 \pm 31 \ (118-238)$
		RV mass (males)	56 ± 14 (34-87)	50 ± 10 (30-70)
		LV mass (females)	122 ± 26 (50–165)	125 ± 26 (75–175)
		RV mass (females)	40 ± 8 (26–57)	$40 \pm 8 (24-55)$
Bove (35)	X-ray angiography ($n = 20$)	LV mass/BSA	$97 \pm 6 {\rm g/m^2}$	$87 \pm 12 \text{ g/m}^2$
		LV ED volume	82 ± 3 ml	$121 \pm 34 \text{ ml}$
		LV EF	60 ± 2	67 ± 5
O'Keefe (34)	X-ray angiography $(n = 13)$	LV mass/BSA	88 \pm 7 g/m ²	$87 \pm 12 \text{ g/m}^2$
Pietras (11)	X-ray angiograpy	RV ED volume/BSA	$76 \pm 14 \text{ ml/m}^2$	$75 \pm 13 \text{ ml/m}^2$
		RV ES volume/BSA	$33 \pm 8 \mathrm{ml/m^2}$	$29 \pm 10 \text{ m}/\text{m}^2$
		RV EF	57 ± 4	61 ± 7
		LV ED volume/BSA	$70 \pm 12 \text{ ml/m}^2$	$66 \pm 12 \text{ m}/\text{m}^2$
		LV ES volume/BSA	$22 \pm 5 \text{ ml/m}^2$	$21 \pm 10 \text{ m}/\text{m}^2$
		LVEF	68 ± 7	67 ± 5

Normal RV and LV Mass and Function

CT, completed tomography: EF, ejection fraction.

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yr). Nonetheless, the magnitude and range of parameters for their study are similar to those found in the present study. For RV free wall mass, the mean mass was 46 g (range 23-68 g, upper limit of normal 65 g). For LV free wall mass, the mean mass was 86 g (range 48-123 g, upper limit of normal 125 g). For the interventricular septal mass, the mean value was 39 g (range 17-61 g, upper limit of normal 60 g). Other autopsy studies in the first half of the 20th century showed similar values for RV, LV, and interventricular septal mass (22,23).

Scholz et al. (24), in an autopsy study of 200 subjects (aged 0–9 yr), concluded that weight and BSA were superior to height for normalization but found no significant difference between using BSA or weight. Kitzman et al. (25), in another autopsy study of 765 subjects (aged 20– 99 yr), found weight to be better than either BSA or height for predicting total heart weight.

Echocardiography

Many studies have used two-dimensional and Mmode echocardiography to estimate normal values of left ventricular parameters. Some of these results are summarized in Table 9 (26–33). Most were in good agreement with the results found in this study. Where differences occurred, generally MRI values were slightly larger than echo values. Upper limits for LV mass and BSA for echo were slightly larger than those determined in this study where we used mean + 1.96 SDs as the 95th percentile.

Daniels et al. (33) performed a study of 334 young normal volunteers (aged 6–23 yr, mean 12.6 yr) using echocardiography to determine LV mass normalized to either BSA or height. Correlation coefficients for the dependence of mass on either parameter ranged from r =0.71 to r = 0.83. As in our study, gender differences persisted even with normalization to BSA or height. Normalization to weight was not performed in Daniels et al.'s study. The magnitudes of ventricular parameters were consistently lower than in our study, even when normalized to BSA, consistent with the fact that the mean BSA of our population was larger than that of Daniels et al. However, when the linear regression for mass versus BSA was used, the predicted values obtained in this study were closer to those found by Daniels et al. (Table 9).

X-ray Angiography

Pietras et al. (11) measured normal right and left ventricular volumes using angiography and found both ED and ES values very close to those obtained in the current study (RV ED volumes 76 \pm 14 ml/m², Pietras et al. versus 75 \pm 13 ml/m² in this study). RV EF and LV EF were also very similar to the values obtained in the current study.

O'Keefe et al. (34) studied LV mass using angiography and also found normal values close to those obtained here (88 \pm 7 versus 87 \pm 12 g/m²). In another older angiography study (1978) in 20 normal volunteers (35), however, slightly different values were found (Table 9).

Magnetic Resonance Imaging

In a study of normal RV mass measured with MRI in 10 volunteers, Doherty et al. (16) found RV mass to average 45 \pm 8 g. In this study, RV mass was 46 \pm 11 g. Interobserver and intraobserver variability was comparable with that found in the present study.

In a study of RV mass using MRI in 10 normal volunteers, Katz et al. (15) found RV mass normalized to BSA to be 23.3 \pm 1.4 g/m², whereas in this study, we found a value of 26.1 \pm 7.7 g/m². The mean values between the two studies are not likely to be significantly different because of the larger number of subjects and larger variability in the present study.

Doherty et al. (36) in an MRI study of dilated cardiomyopathy presented interobserver reproducibility of 7.9– 10.6 ml on volume and 14.6–15.4 g on mass measurements. Pattynama et al. (3) also studied reproducibility of MRI-determined ventricular parameters and found somewhat higher interobserver and intraobserver variability than either the Doherty study or the present study. These findings underscore the need for strict criteria for data acquisition and determining ventricular borders on MR images to provide reproducible results. Work is underway by several groups to develop semiautomated techniques for determining ventricular borders in MRI, which in principle should reduce variability.

Computed Tomography

A study using ultrafast computed tomography in seven male volunteers found RV mass to average 55 ± 2.8 g and an LV mass-to-RV mass ratio of 3.2 ± 0.2 (37). In the present study, we found RV mass to average $50 \pm$ 10 g for males and LV mass-to-RV mass ratio equal to 3.64 ± 0.72 . Other work cited by Hajduczok (37) report normal male RV mass as 46 g and LV mass-to-RV mass ratio to be 3.4. Wachspress et al. (40) used ultrafast computed tomography in 10 normal subjects and also found LV and RV parameters similar in magnitude to ours as shown in Table 9 (40).

In general, excellent agreement with normative values found by autopsy and tomographic imaging modalities was found. Excellent agreement was also attained with some echocardiographic and x-ray angiography studies, but not as good with others. These differences likely reflect differences in the methods and assumptions used in the echocardiography and angiography studies to estimate ventricular parameters from projections or limited imaging planes.

Gender Differences

Gender differences were apparent in all ventricular parameters measured, except for ejection fraction, cardiac index, and the LV mass-to-ED volume ratio. Power calculations indicated that the sample sizes used in this study were sufficient for detecting these gender differences with a power greater than 90%. All mass and volume parameters were smaller in females than males, and normalization to BSA did not remove these gender differences except in the case of RV mass. Only normalization to weight removed the gender dependence. These findings are consistent with those found by other researchers in autopsy and echocardiographic studies (20,24,33). The physiologic significance of these differences is not known and awaits further study. The results of this study indicate that when determining whether an individual's ventricular parameters fall into normal ranges, parameters related to function and relative LV hypertrophy are relatively gender independent (LV mass/LV ED volume, ejection fraction, cardiac output), whereas parameters related to morphology should be compared to differentiate male and female groups.

Potential Utility

The results of this study can be used to determine whether individual patient's ventricular size and function fall in normal ranges. In addition, this MRI database serves as a basis for determining normal ranges of left and right ventricular relationships and interventricular dependence, something that is not easily possible with other currently used modalities.

For example, in this study, we chose to separate the interventricular septum from the LV free wall mass. In studies of right ventricular hypertrophy due to atrial repair of transposition of the great arteries (17), we found that the interventricular septum does not hypertrophy along with the RV. Establishing normative values for each of these components of LV mass separately will allow further study of the role of the septum in ventricular interaction.

The regression equations determined in this study are only valid for the range of age, weight, height, or BSA found in our subject population. Although we attempted to study individuals with a wide range of heart sizes over a wide range of ages, it is not possible to extend the results of this study to all possible cases. Further study is required to determine age-dependent changes in ventricular function and size with MRI. As shown in the study by Daniels et al. (33), normal values for children (mean age 12.6 yr), even when normalized to BSA, are different from those of adults. Determination of normal mass by use of the regression equation improved the estimate, but some gender differences remained.

An additional limitation is that only systolic function was evaluated in this study. Future work should also include determination of normal diastolic function by MRI.

Overall, normalization to BSA provided the lowest SE. However, the normalization to height and weight provided similar SEs. Although normalization to body size provides a good basis for comparison of different subjects, it does not take into account other factors that affect ventricular function, such as physical fitness. Studies by Milliken et al. (41) and Riley-Hagen et al. (42) showed that both male and female endurance athletes have higher LV volume and mass than control subjects, even when normalized to BSA and lean body mass. Interestingly, in the current study, RV mass was relatively more independent of body size, indicating that other factors, not measured in this study, may affect RV mass.

Sources of error in ventricular volume and mass estimates involve errors introduced both during the acquisition process and errors introduced during the analysis process. Because the period of cine image acquisition is generally 30–40 min, the ventricular parameters derived from these images represent an average value over the acquisition period, which will be affected if heart rate varies significantly during this period. Another potential source of error during the image acquisition is patient motion because the three-dimensional reference frame for the short-axis cine acquisitions is set at the beginning of the acquisition and is assumed constant during the examination. By visual inspection, none of the subjects scanned for the study shifted. As MRI acquisition times become shorter, these sources of error will be minimized.

During the analysis, one source of error is definition of the endocardial and epicardial borders based on grayscale intensity. In some cases, border definition was difficult because of respiratory and pulsatility artifacts, and display of the cine loops was needed to visually differentiate moving blood from myocardium to identify portions of some of the borders.

Because of the small size of the RV in the dogs studied in the validation study, 35 ± 18 g, an uncertainty of only 4.6 ± 6.3 g resulted in a somewhat large percentage uncertainty ($13 \pm 18\%$). However, if as a worse case a similar magnitude uncertainty in humans was assumed, the uncertainty would be less than 10%, sufficient for clinical studies.

Despite the subjective nature of the border identification, the analysis is reproducible. The mean difference, which is an indicator of the bias between two measurements, was less than 1 ml for all ventricular measurements made. The variability was less than 6 ml (7.5%), indicating that MRI has the potential to provide highly reproducible measurements of both left and right ventricular parameters.

CONCLUSIONS

This study yields a range of normal ventricular parameters for both females and males that can be used to identify abnormal function or mass in either ventricle and the relationship between ventricles. In general, functional parameters are gender independent, whereas morphologic parameters remain gender dependent, even with normalization to BSA. These results can serve as a reference for studying diseases that affect both ventricles in addition to supplementing left and right ventricular data obtained by other investigators.

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