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Simultaneous Measurement of Left and Right Ventricular Volumes and Ejection Fraction During Dobutamine Stress Cardiovascular Magnetic Resonance

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Abstract

Objective—During cardiovascular stress, if right ventricular (RV) exceeds left ventricular (LV) stroke volume, then a large volume of blood is displaced into the pulmonary circulation that may precipitate pulmonary edema. We sought to determine the metrics by which cardiovascular magnetic resonance (CMR) could measure simultaneous displacement of right and LV stroke volume during dobutamine stress.

Methods—Thirteen healthy subjects (5 women) aged 53 ± 10 years without medical conditions and taking no medications underwent 2 CMR exams at 1.5 T separated by 4 to 8 weeks in which right and LV stroke volume were determined during intravenous dobutamine and atropine infused to achieve 80% of the maximum predicted heart rate response (MPHRR) for age.

Results—The right and LV stroke volume were highly correlated at each level of stress (rest, $r=0.98$, $p=0.007$; low stress, $r=0.87$, $p=0.001$; and peak stress, $r=0.88$, $p=0.001$), and the mean difference in SV at each level of stress (rest, low stress, and peak stress was 0 to 2 ml on both exam 1 and 2.

Conclusions—Simultaneous change in right and left ventricular stroke volume can be assessed in a highly reproducible manner throughout the course of dobutamine CMR stress administered to achieve 80% of MPHRR for age. This technology may help identify discrepancies in right and LV stroke volume during cardiovascular stress that are associated with the development of pulmonary edema.

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Conflict of Interest: None

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Introduction

Appropriate displacement of blood volume from the right into the left ventricle via the pulmonary circulation is necessary to maintain forward cardiac output during stress.^{1,2} In the setting of impaired left ventricular (LV), but normal right ventricular (RV) systolic and diastolic function, the inappropriate displacement of blood into the lungs may contribute to the development of pulmonary edema.^{3,4} During elevated heart rates that occur with exercise, emotional, mental, or pharmacologic induced stress, discrepancies in right (elevated) versus left (reduced) stroke volume become more problematic and can increase the likelihood of pulmonary edema.^{4,5}

At present, cardiovascular magnetic resonance (CMR) has been used to quantify right and LV volumes at rest.^{6,7} The ability of CMR to accurately assess ventricular shape in 3-dimensions makes the technique well suited to assess the volume of the irregularly shaped right ventricle.⁶ To date, however, the utility of CMR to quantify simultaneous measures of right and LV stroke volume (SV) throughout cardiovascular (CV) stress in humans is unknown. This study was performed to determine the association and correlation between right and LV SV at various levels of stress in middle-aged healthy subjects. In addition, we sought to determine the reproducibility of these measures so that sample sizes could be estimated for future trials designed to examine the relationship between right and LV stroke volume interdependence and the onset of pulmonary edema.

Materials and Methods

Study Population and Design

This study was approved by the Institutional Review Board of the home institution and all participants provided witnessed informed consent. Thirteen healthy subjects (5 women), aged 53 ± 10 (range 36 to 64) years were enrolled into the study. Participants had no medical conditions and were receiving no medications.

According to previously published techniques,^{8,9} each participant underwent a dobutamine-atropine CMR stress test on 2 separate occasions separated by 2 - 4 months without a change in the participant's state of health. During each stress test, dobutamine and atropine were administered to increase the heart rate to a peak level defined as 80% of the maximum predicted heart rate response (MPHRR) for age.⁹ Levels similar to this are used during exercise and pharmacologic induced stress tests designed to identify inducible ischemia and assess cardiac prognosis. Throughout the CMR procedure, nursing and physician personnel were present, and heart rate, brachial forearm blood pressure, and oxygen saturation were continuously monitored and recorded.⁸

CMR Imaging Technique

Images were collected on a 1.5 T Excite (General Electric Medical Systems, Waukesha, Wisconsin) scanner with a phased array cardiac surface coil (MedRad, Incorporated, Pennsylvania) on the chest.¹⁰ Multi-slice, multi-phase, cine white blood images were acquired using steady state free precession to assess right and LV volumes. These scans were positioned in short axis planes perpendicular to the long axis of the left ventricle, and encompass the entire right and left ventricle from the cardiac base to its apex. Slices were 8 mm thick with 2 mm of interposed gap. Other image parameters included a 10 msec repetition time, a 3 msec echo time, a 45 cm field of view, a 224×160 matrix, a band width of 125 hztz/pixel, a flip angle of 50 degrees, and a temporal resolution of 20 msec.

MRI Image Analysis

According to previously published techniques, right and LV volumes (end diastolic volume [EDV], end systolic volume [ESV], and SV) and ejection fraction (EF) were determined using a Simpson's Rule technique at each level of stress: rest, low level stress (7.5 mcg/kg/min of dobutamine), and peak infusion.^{6,10} Papillary muscles were included within the right and LV cavities. At the base of the left ventricle, the boundary of the left atrium was taken as the slice in which the wall thickness of the left ventricle remained for 50% of the circumference of the left sided cardiac chambers.^{6,10} The base of the right ventricle was observed at the juncture of the right ventricular infundibulum with the pulmonic valve.^{6,10} On each slice, the endocardial surface was identified at end diastole and end systole. The end diastolic and end systolic areas of the series of endocardial slices for the respective cardiac chambers (right and left ventricle) were determined and then multiplied by the slice and gap thickness to derive ventricular volumes. The stroke volume for each ventricle was calculated as EDV - ESV. Ejection fractions were calculated as $SV/EDV \times 100\%$.

Statistical Analyses

All data are represented as mean $\pm$ the standard deviation. Associations between values identified on exam 1 and exam 2 were estimated by Pearson's correlation coefficients. Regression analysis was used to test the association between right and LV volumes after controlling for subject characteristics. Differences between the right and LV values were tested for differences with a paired sample Student's t-test.

Results

The demographic data for the participants in this study are displayed in Table 1. Ninety-two percent of the participants were Caucasian. Hemodynamic data for the participants at each level of stress on both the first and second exam are displayed in Table 2. There were no significant differences in heart rate or blood pressure responses for the participants in exam 1 versus exam 2. Importantly, all participants achieved 80% of MPHRR for age during testing.

The right and LV volumes as well as ejection fractions for all of the participants are displayed in Table 3. As shown, there were no important differences in right or LV stroke volume as assessed between exam 1 and exam 2.

Additional analyses were performed to determine the association between right and LV stroke volume at each level of stress. As shown in Table 4, right and LV stroke volumes were highly correlated at each level of stress. These factors remained significant at all levels of stress after adjusting for age, gender, heart rate, and systolic blood pressure ($p = 0.001$ for all).

An important consideration for this work was to provide estimates for determining sample sizes to detect differences in right and LV stroke volumes between individuals randomized into 2 separate arms of a research study. The sample sizes to detect differences in a study between right and LV stroke volumes with 90% power at rest and during low and high dose dobutamine infusions are shown in Table 5.

Discussion

The results of this study indicate that CMR can be performed to assess right and LV end-diastolic, end-systolic, and stroke volume as well as ejection fraction throughout the course of a cardiovascular stress test performed to achieve 80% of the maximum predicted heart rate response for age (Tables 1-3). In addition, in healthy individuals without any

intracardiac shunting and no history of CV disease, right and LV stroke volumes measured by CMR throughout the course of a stress test are similar (Table 3) and highly correlated (Table 4). Importantly, in healthy individuals, relatively small numbers of subjects could be enrolled into a future study to detect stress induced differences in stroke volume between the right and left ventricle (Table 5).

Previous studies have reported right and LV volumes and ejection fractions at rest. For example, Chahal, et al. reported that in general, RVEDV and RVESV are larger than LVEDV or ESV, but that SV is similar between the 2 chambers.⁶ Consequently, the LVEF is generally higher than the RVEF.^{6,11} In our study, the resting right and LV mean end diastolic and systolic volumes ranged from 99 to 125 ml, and 40 to 63 ml, respectively (Table 3) resting before stroke volumes and ejection fraction averages ranged from 59 to 63 ml, and 49% to 61%, respectively. The volume data from the resting component of this study are similar to those reported in other studies involving participants of similar age and gender.

A potential cause of pulmonary edema relates to the inappropriate displacement of right volume into the pulmonary circulation when LV stroke volume is not maintained.¹⁻⁴ This is particularly true during heightened emotional, mental, or physical stress when the heart rate response is elevated.¹⁻⁴ As shown in Tables 3 and 4, the results of this study indicate that CMR is a highly reproducible method for defining similarities in right and LV stroke volumes throughout the course of a stress test in which pharmacologic agents are administered to achieve 80% of the maximum predicted heart rate response for age (Tables 3 and 4).

An important aspect of data such as these are to provide estimates for sample sizes needed to identify a discrepancy in right and LV stroke volume when potential study participants are randomized to receive therapy designed to modify right (administration of nitrates that reduce preload) or left (administration of beta blockers that reduce contractility) ventricular stroke volume.^{12,13} Although a preserved or elevated RV SV in the setting of an impaired LV SV is associated with displacement of blood into the lungs and an increased chance of pulmonary edema and congestion, previous to this report, noninvasive methods to identify these associations have not been available. As shown in Table 5, 99 participants per group are needed to determine whether a 2 ml difference, and 26 per group to detect a 5 ml difference in right and LV stroke volume exists at peak stress in a randomized, blinded trial of therapies that could influence ventricular volumes.

There are limitations to the study. First, all of the individuals selected for study were relatively healthy. This study has little data to identify changes in right and LV volumes in individuals with abnormal resting right or LV function. Second, all individuals achieved 80% of the maximum predicted heart rate response for age during testing. We are uncertain of results in younger individuals with heart rates that approach 160 -200 bpm (at 90% to 100% of their MPHRR for age. Finally, our sample size is small, and we are unable to comment on potential differences in right and LV stroke volume that may be related to differences in gender, race, or ethnicity.

In conclusion, simultaneous change in right and LV stroke volume can be assessed in a highly reproducible manner throughout the course of pharmacologic stress administered to achieve 80% of the maximum predicted heart rate response for age. This noninvasive CMR methodology will be useful to further study the interdependence of right and LV stroke volume during various forms of stress, and may identify inappropriate displacement of blood flow into the lungs that predispose patients to developing pulmonary edema.

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Abbreviations

CMR	cardiovascular magnetic resonance
EDV	end diastolic volume
EF	ejection fraction

ESV	end systolic volume
LV	left ventricular
LV EDV	left ventricular end diastolic volume
LVEF	left ventricular ejection fraction
LV SV	left ventricular stroke volume
MPHRR	maximum predicted heart rate response
RV	right ventricular
RV EDV	right ventricular end diastolic volume
RVEF	right ventricular ejection fraction
RV ESV	right ventricular end systolic volume
SV	stroke volume

Table 1
Demographic data from 13 participants (mean $\pm$ standard deviation)

Variable	Characteristics
Age (yrs)	53 $\pm$ 10
Gender	
Male	8
Female	5
Race	
White	12
Black	1
Height (cm)	175 $\pm$ 10 cm
Weight (kg)	82 $\pm$ 17 kg

Table 2
Hemodynamics variables during stress (mean $\pm$ standard deviation)

Variables	Exam 1	Exam 2
Rest		
Heart Rate	64 $\pm$ 10	65 $\pm$ 10
Systolic Blood Pressure	139 $\pm$ 16	137 $\pm$ 16
Diastolic Blood Pressure	80 $\pm$ 12	83 $\pm$ 15
Low		
Heart Rate	81 $\pm$ 13	81 $\pm$ 13
Systolic Blood Pressure	141 $\pm$ 16	139 $\pm$ 18
Diastolic Blood Pressure	80 $\pm$ 8	78 $\pm$ 13
Peak *		
Heart Rate	133 $\pm$ 11	134 $\pm$ 13
Systolic Blood Pressure	155 $\pm$ 20	151 $\pm$ 18
Diastolic Blood Pressure	78 $\pm$ 11	80 $\pm$ 11

* All subjects achieved 80% of the maximum predicted heart rate response for age

Table 3
Ventricular Volume Measures (mean $\pm$ standard deviation)

Variables	RV				LV			
	Diff		Exam		Diff		Exam	
	Exam 1	Exam 2	1 & 2	Abs	Exam 1	Exam 2	1 & 2	Abs
Rest								
EDV (ml)	125 $\pm$ 19	122 $\pm$ 16	3 $\pm$ 7	6	103 $\pm$ 18	99 $\pm$ 15	4 $\pm$ 12	8
ESV (ml)	63 $\pm$ 11	62 $\pm$ 12	1 $\pm$ 3	3	40 $\pm$ 11	40 $\pm$ 9	1 $\pm$ 7	5
SV (ml)	62 $\pm$ 10	59 $\pm$ 7	2 $\pm$ 7	4	63 $\pm$ 11	59 $\pm$ 8	3 $\pm$ 9	6
EF (%)	50 $\pm$ 4	49 $\pm$ 4	1 $\pm$ 3	2	61 $\pm$ 5	60 $\pm$ 4	1 $\pm$ 5	3
Low								
EDV (ml)	106 $\pm$ 19	107 $\pm$ 15	-1 $\pm$ 6	5	91 $\pm$ 16	90 $\pm$ 12	1 $\pm$ 13	8
ESV (ml)	40 $\pm$ 13	42 $\pm$ 10	-2 $\pm$ 7	5	25 $\pm$ 8	25 $\pm$ 6	0 $\pm$ 7	4
SV (ml)	66 $\pm$ 10	65 $\pm$ 7	1 $\pm$ 5	4	66 $\pm$ 12	65 $\pm$ 9	2 $\pm$ 10	6
EF (%)	63 $\pm$ 7	61 $\pm$ 4	2 $\pm$ 6	4	73 $\pm$ 7	72 $\pm$ 5	1 $\pm$ 5	4
Peak								
EDV (ml)	95 $\pm$ 16	94 $\pm$ 14	1 $\pm$ 8	6	88 $\pm$ 13	85 $\pm$ 9	3 $\pm$ 11	8
ESV (ml)	25 $\pm$ 10	25 $\pm$ 11	0 $\pm$ 7	5	17 $\pm$ 5	16 $\pm$ 5	1 $\pm$ 6	4
SV (ml)	70 $\pm$ 9	70 $\pm$ 7	1 $\pm$ 5	4	71 $\pm$ 11	69 $\pm$ 7	2 $\pm$ 9	7
EF (%)	75 $\pm$ 6	74 $\pm$ 7	1 $\pm$ 6	4	81 $\pm$ 5	81 $\pm$ 5	0 $\pm$ 5	3

Abbreviations: Abs = absolute; Diff = difference; EDV = end-diastolic volume; EF = ejection fraction; ESV = end-systolic volume; SV = stroke volume; RV = right ventricle; LV = left ventricle

Table 4
Correlation between right and left ventricular stroke volume

Variables	All	Exam 1	Exam 2
Rest	0.98 [*]	0.99 [*]	0.97 [*]
Low Dose	0.87 [*]	0.83 [*]	0.93 [*]
Peak Stress	0.88 [*]	0.85 [*]	0.96 [*]

^{*} p = 0.001

Table 5

Sample sizes for each of 2 groups with 90% power.

Difference between right and left ventricle SV ml	Number of participants		
	Rest	Low Level Stress	Peak Level Stress
2	25	165	100
3	12	74	45
4	7	42	26
5	5	28	17
6	4	20	12
8	3	12	8
10	3	8	6
12	3	6	5