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

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Objective: During cardiovascular stress, if right ventricular (RV) stroke volume 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 RV and LV stroke volumes during dobutamine stress.

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

Results: The RV and LV stroke volumes 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 stroke volume was 0 to 2 mL on examinations 1 and 2.

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

Key Words: cardiovascular magnetic resonance, dobutamine stress, stroke volume

(J Comput Assist Tomogr 2011;35: 614–617)

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. 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. During elevated heart rates that occur with exercise-, emotional-, mental-, or pharmacologically induced stress, discrepancies in right (elevated) versus left (reduced) stroke volume (SV) become more problematic and can increase the likelihood of pulmonary edema.

At present, cardiovascular magnetic resonance (CMR) has been used to quantify RV and LV volumes at rest. 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. To date, however, the use of CMR to quantify simultaneous measures of RV and LV throughout cardiovascular (CV) stress in humans is unknown. This study was performed to determine the association and correlation between RV 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 RV and LV SV 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 years (range, 36–64 years) were enrolled into the study. Participants had no medical conditions and were receiving no medications.

According to previously published techniques, each participant underwent a dobutamine-atropine CMR stress test on 2 separate occasions separated by 2 to 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. Levels similar to this are used during exercise and pharmacologically 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.

CMR Imaging Technique

Images were collected on a 1.5-T Excite (General Electric Medical Systems, Waukesha, Wis) scanner with a phased array cardiac surface coil (MedRad Inc, Pittsburgh, Pa) on the chest. Multislice, multiphase, cine white blood images were acquired using steady-state free precession to assess RV 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-millisecond repetition time, a 3-millisecond echo time, a 45-cm field of view, a 224 × 160 matrix, a band width of 125 Hz/pixel, a flip angle of 50 degrees, and a temporal resolution of 20 milliseconds.
MRI Image Analysis

According to previously published techniques, RV and LV volumes (end diastolic volume [EDV], end systolic volume [ESV], and SV) and ejection fraction (EF) were determined using a Simpson Rule technique at each level of stress: rest, low-level stress (7.5 μg/kg per minute of dobutamine), and peak infusion. Papillary muscles were included within the RV 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-sided cardiac chambers remained for 50% or greater of the circumference of the left-sided cardiac chambers. The base of the right ventricle was observed at the juncture of the RV infundibulum with the pulmonic valve. 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 ventricles) were determined and then multiplied by the slice and gap thickness to derive ventricular volumes. The SV for each ventricle was calculated as EDV - ESV. Ejection fractions were calculated as SV/EDV × 100%.

Statistical Analyses

All data are represented as mean ± SD. Associations between values identified on examinations 1 and 2 were estimated by Pearson correlation coefficients. Regression analysis was performed.
used to test the association between the RV and LV volumes after controlling for subject characteristics. Differences between the RV and LV values were tested for differences with a paired sample Student t-test.

## RESULTS

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

The RV and LV volumes and EFs for all of the participants are shown in Table 3. As shown, there were no important differences in the RV or LV SV as assessed between examinations 1 and 2.

Additional analyses were performed to determine the association between the RV and LV SVs at each level of stress. As shown in Table 4, RV and LV SVs were highly correlated at each level of stress. These factors remained significant at all levels of stress after adjusting for age, sex, 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 the RV and LV SVs between individuals randomized into 2 separate arms of a research study. Sample sizes to detect differences in a study between RV and LV SVs 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 RV and LV EDV, ESV, and SV as well as EF throughout the course of a cardiovascular stress test performed to achieve 80% of the MPHRR for age (Tables 1–3). In addition, in healthy individuals without any intracardiac shunting and no history of CV disease, RV and LV SVs 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 SV between the right and left ventricles (Table 5).

Previous studies have reported RV and LV volumes and EFs at rest. For example, Chahal et al. reported that in general, RV EDV and RV ESV are larger than LV EDV or ESV but that SV is similar between the 2 chambers. Consequently, the LV EF is generally higher than the RV EF. In our study, the resting RV and LV mean EDV and ESV ranged from 99 to 125 mL and 40 to 63 mL, respectively (Table 3); resting before SVs and EF 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 sex.

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

An important aspect of data such as these is to provide estimates for sample sizes needed to identify a discrepancy in RV and LV SVs when potential study participants are randomized to receive therapy designed to modify right (administration of nitrates that reduce preload) or left (administration of β-blockers that reduce contractility) ventricular SV. 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 RV and LV SVs 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 RV and LV volumes in individuals with abnormal resting RV or LV function. Second, all individuals achieved 80% of the MPHRR for age during testing. We are uncertain of results in younger individuals with heart rates that approach 160 to 200 beats per minute (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 RV and LV SV that may be related to differences in sex, race, or ethnicity.

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

## REFERENCES


### TABLE 5. Sample Sizes for Each of 2 Groups With 90% Power

<table>
<thead>
<tr>
<th>Difference Between RV and LV SVs</th>
<th>No. Participants</th>
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<td>Low-Level Stress</td>
<td>peak-Level Stress</td>
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<tr>
<td>Rest</td>
<td>Rest</td>
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