Evaluation of Regional Differences in Right Ventricular Systolic Function by Acoustic Quantification Echocardiography and Cine Magnetic Resonance Imaging

Tal Geva, MD; Andrew J. Powell, MD; Elizabeth C. Crawford; Taylor Chung, MD; Steven D. Colan, MD

Background—Accurate quantitative evaluation of right ventricular (RV) function has been limited by its complex structural geometry. Although embryological and anatomic observations suggest that the RV is composed of 2 distinct components, the RV sinus and infundibulum, most studies on RV dimensions and function viewed it as a single chamber. This study was designed to determine the volumes, relative contribution to global systolic function, and temporal course of contraction and relaxation of the RV sinus and infundibulum.

Methods and Results—Thirty-one individuals without heart disease (aged 1 month to 17 years, 16 boys and 15 girls) participated in this study. Instantaneous area over time, its derivatives, and the temporal course of contraction and relaxation were studied by acoustic quantification echocardiography and phonocardiography in 20 individuals. Global and regional RV volumes and ejection fraction were determined by cine MRI in 11 individuals. The RV sinus made up 81% of the combined RV end-diastolic volume and 87% of the combined stroke volume. The infundibulum accounted for the remaining 19% and 13% of the combined stroke volume. The RV sinus fiber shortening was significantly greater than the infundibulum for ejection fraction (56% versus 38%, $P<0.001$), fractional area change (42% versus 28%, $P<0.0001$), and dA/dt (27% versus 13%, $P<0.0001$). Analysis of temporal course of contraction and relaxation (expressed as percentage of the cardiac cycle to adjust for differences in heart rate) showed that the infundibulum follows the RV sinus: onset of contraction 53% versus 19% of systole, time to peak systole 115% versus 97% of systole, time to peak systole 115% versus 97% of systole ($P<0.01$), indicating a peristalsis-like pattern of contraction and relaxation.

Conclusions—The results of this study demonstrate significant regional differences between the sinus and infundibulum components of the RV with regard to contribution to stroke volume, extent of fiber shortening, and sequence of mechanical activation. These data from normal individuals can be used in future research on RV function in pathological conditions.

Key Words: ventricles ■ magnetic resonance imaging ■ echocardiography

A ccurate quantitative evaluation of right ventricular (RV) function has remained an elusive clinical challenge. Most investigators attribute the difficulties in finding a reproducible method to assess RV function to its complex structural geometry. Most studies on RV function regarded the RV as a single anatomic and functional unit and attempted to evaluate its function as 1 chamber. The RV, however, is composed of several anatomic segments that can be divided into 2 major components: the RV sinus, which extends from the tricuspid valve annulus to the proximal os infundibulum, and the infundibulum, which extends from the proximal os infundibulum to the pulmonary valve (distal os infundibulum). In the normal heart, both components are well integrated and are viewed by most observers as a single functional unit. Data from embryological, anatomic, and molecular observations suggest that the RV sinus and the infundibulum are distinct chambers that evolved from different parts of the embryonic heart. Electrophysiological studies indicate that activation of the RV outflow tract (eg, infundibulum) occurs relatively late in systole and that this part of the heart is the last to be activated, possibly leading to asynchronous contraction and relaxation of the sinus and infundibulum components of the RV. Little is known about regional differences between the RV sinus and the infundibulum with regard to their relative contribution to global RV systolic function and with regard to timing of mechanical contraction and relaxation during the cardiac cycle.

This study was designed to determine the relative contribution of the sinus and infundibulum components to global RV systolic function in children without heart disease. It also
examines the temporal course of contraction and relaxation of the two components of the RV. Such data can improve understanding of regional and global RV function and are essential for future studies in patients with congenital heart disease involving the RV.

**Methods**

**Patients**

Thirty-one individuals with structurally normal heart participated in this study. Twenty infants and children who have undergone a complete echocardiographic examination in our laboratory for evaluation of a heart murmur or chest pain and were found to have no significant heart disease were included in the echocardiographic component of the study. Another 11 subjects who have undergone cardiac MRI study at Children’s Hospital to rule out cardiac tumor or other structural abnormalities and were found to have structurally normal heart were also included. Patients’ age, sex, height, weight, and body surface area were recorded.

**Anatomic Definitions**

The boundary between RV sinus and infundibulum is delineated by a muscular ring within the RV that includes the parietal band (PB), infundibular septum (IS), septal band (SB), moderator band (MB), and the anterior papillary muscle of the tricuspid valve. RV sinus is the chamber that lies proximal (or “upstream”) to the proximal os infundibulum, and the infundibulum is the chamber that lies between the proximal os infundibulum and the pulmonary valve (distal os infundibulum). The parietal, septal, and moderator bands are included in the infundibulum. Two representative cross-sectional spin-echo MR images in the transverse plane are shown. Broken lines represent additional sections across the RV. Ao indicates aorta; LA, left atrium; LV, left ventricle; RA, right atrium; and S, spine.

**Echocardiographic Data Acquisition**

All echocardiographic examinations were performed with a Hewlett Packard 2500 cardiac scanner equipped with transducers ranging in frequency from 3.5 to 7.5 MHz. Transducer frequency and focus were chosen on the basis of the patient’s size and acoustic window. Patients were examined in the left lateral decubitus or supine position. Each chamber was imaged from two orthogonal views. The long-axis plane of the RV sinus (from the plane of the tricuspid valve annulus to the RV apex) was imaged from the apical 4-chamber view. The short-axis plane of the RV sinus was imaged from the parasternal or subxiphoid short-axis views (according to patient’s size and acoustic windows) at the level of the tricuspid valve leaflets tips. The infundibulum was evaluated from a modified high parasternal short-axis view under the pulmonary valve and from a parasternal long-axis view angled leftward and superiorly toward the RV outflow tract (Figure 2).

For each chamber, the 2-dimensional imaging, acoustic quantification (AQ) waveform, ECG, and phonocardiogram (PCG) were simultaneously obtained. The AQ system used in this study has been described in detail and is commercially available. After optimizing the 2-dimensional image of the examined chamber, the region of interest was defined using the scanner’s trackball. The overall transmit gain control, temporal, and lateral gain compensations were adjusted to optimize the echocardiographic signal and to achieve clear and continuous endocardial definition as described by Bednarz et al. The AQ-derived instantaneous area and $dA/dt$ dual waveform display were viewed together with the ECG and PCG. The display’s sweep rate was set at 100 mm/s. PCG was obtained from the left lower sternal border with the use of a commercially available transducer (Hewlett Packard Co, model 21050A) interfaced with the cardiac scanner. The position of the PCG transducer, gain, and filter settings were adjusted to obtain a clear recording of the first and second heart sounds. Once a stable reading was obtained, the data were recorded on a 1.27 cm (0.5 inch) super VHS videocassette tape, and hard copies were printed for subsequent off-line analysis.
Echocardiographic Data Analysis

The following parameters were obtained for the RV sinus and infundibulum by averaging 3 consecutive cardiac cycles: (1) maximal area (A_{max}) (in cm^2); (2) minimal area (A_{min}) (in cm^2); (3) fractional area change was calculated as (A_{max} - A_{min})/A_{max}; (4) peak filling rate (or peak rate of area increase) (dA/dt)_max /A_max (in cm^2/s); (5) time to peak filling rate was measured from the time of minimal area to the time of peak filling rate (in milliseconds); (6) peak ejection rate (or peak rate of area decrease) (~dA/dt)_max, in cm^2/s; (7) to adjust for differences in chamber size, the peak filling and ejection rates were divided by the end-diastolic area yielding normalized peak filling rate (PFR)=(dA/dt)_max/A_{max} and normalized peak ejection rate (PER)=(~dA/dt)_max/A_{max} (in s^{-1}); (8) cardiac cycle length (in milliseconds) was measured from the RR interval by ECG; (9) duration of systole was measured from the PCG between the first high frequency component of the first heart sound (S_1) to the first high frequency component of the second heart sound (S_2); (10) duration of diastole was similarly measured from S_1 to S_2; (11) time to onset of contraction was measured from S_1 to onset of ejection (defined as the point when the dA/dt tracing first crosses the baseline after onset of the QRS); (12) time to peak systole was measured from S_1 to A_{max}; (13) time to onset of diastole was measured from S_1 to onset of relaxation (defined as the second baseline crossing of the dA/dt tracing after onset of the QRS); (14) time to peak diastolic area was measured from S_1 to A_{max}, and (15) to allow comparison between patients with different heart rates, all time intervals were expressed as percent of cardiac cycle. To adjust for differences in body size, A_{max} and A_{min} were indexed to body surface area.

MRI Protocol and Data Analysis

Cine MRI was used to measure the maximal (diastolic) and minimal (systolic) volumes of the RV sinus and infundibulum and to calculate their relative contributions to RV stroke volume. All MRI studies were performed with a General Electric Signa Advantage 1.5 T scanner, versions 5.5 and 5.6. In both versions, the maximal gradient is 10 mT/m and the slew rate is 16.7 T/m per second. A general-purpose 5-inch surface coil was used for studies of the RV and either a body or a torso array coil was used when imaging deeper structures. After obtaining localizing sequences, multislice ECG-triggered spin-echo images of the RV were obtained in the axial plane (slice thickness=3 to 6 mm; skip=1 to 1.5 mm; image matrix size=256 to 512×160 to 192; echo time [TE]=20 ms; repetition time [TR]=RR interval; field of view 20 to 40 cm; number of excitations=2 to 4). Cine MRI sequences were then obtained in multiple locations covering the RV by using segmented k-space cine–fast gradient echo (FASTCARD) sequence (phases per cardiac cycle=15 to 17; lines per segment=6 to 10; slice thickness=6 to 10 mm; skip=0 mm; image matrix size=256×128; TE=3 to 5 ms; TR=10 to 15 ms; flip angle=20 degrees; field of view=20 to 40 cm; number of excitations=4). Given these parameters, scan time for each location varies according to the RR interval (~1 minute per location when the heart rate is 60 bpm). Off-line analysis was performed on a General Electric Advantage Windows workstation with software version 2.0. First, the endocardial borders of the RV were traced, slice volume was computed, and RV volume was calculated by summation of all slice volumes. The process was then repeated by tracing the endocardial borders of the RV sinus and infundibulum according to the above-described anatomic landmarks. The boundary between the RV sinus and infundibulum was drawn along the proximal os infundibulum so that the parietal, septal, and moderator bands were included in the infundibulum (Figure 1). Diastolic volume was considered maximal volume and systolic volume was considered minimal volume. Stroke volume was calculated as the difference between diastolic volume and systolic volume. Ejection fraction was calculated as stroke volume/diastolic volume. Given the wide range of subject age and body size of individuals included in this study, both indexed and absolute values of RV volumes are reported. RV volumes were indexed to BSA raised to the 1.3 power.

Statistical Analysis

Data are reported as mean value±SD for each group of measurements. Two-tailed paired Student’s t test was used to compare...
measurements of RV sinus to RV infundibulum. To determine interobserver variability in measuring RV volume by MRI and onset of contraction (percentage of systole) by AQ echocardiography, the data were measured by two investigators who were unaware of each other’s measurements. Simple linear regression analysis was used to calculate the correlation of measurements by the two observers. The absolute difference between observers’ measurements was divided by the mean value of measurements and expressed as a percentage. Interobserver variability was expressed as the mean value (±SD) of these percentages. Data analysis was performed with commercially available statistical packages (StatView 4.1, Abacus Concepts Inc). For all tests, a probability value of <0.05 was considered statistically significant.

Results

Patients

The echocardiographic study included 20 children 1 month to 15.4 years of age (mean ± SD 5.2 ± 5.3 years, median 2.95 years). There were 11 boys and 9 girls whose weight ranged from 3.9 to 69.4 kg (mean 23 ± 20.3, median 13.4 kg) and their body surface area ranged from 0.24 to 1.82 m² (mean 0.76 ± 0.5, median 0.56 m²). Chloral hydrate (80 mg/kg) sedation was used in 10 infants according to clinical practice in our laboratory. The MRI studies of 11 individuals, 5 male and 6 female, were analyzed. Their age ranged from 11 to 28 years (median 15.5 years) and their body surface area ranged from 1.19 to 2.03 m² (mean 1.6 ± 0.29, median 1.41 m²). No sedation was used in any of these patients.

Regional RV Dimensions and Function

The data regarding dimensions and function of the RV sinus and infundibulum are summarized in the Table and Figure 3. The combined RV sinus and infundibular end-diastolic volume by MRI ranged from 47.4 to 157.7 mL, end-systolic volume ranged from 41.7 to 116.2 mL, and stroke volume ranged from 28.2 to 67.3 mL. When the combined RV sinus and infundibulum volumes were indexed to body size, the mean (± SD) end-diastolic volume was 47.1 ± 11.5 mL/BSA and the end-systolic volume was 24.8 ± 11.6 mL/BSA. The RV sinus composed 81.3 ± 6.1% of the combined RV end-diastolic volume and the infundibulum occupied 18.7 ± 6.1%. Of the combined RV stroke volume, the RV sinus contributed 86.6 ± 4.2% and the infundibulum 13.2 ± 4.2% (P < 0.0001). Global RV ejection fraction was 56 ± 11% and infundibular ejection fraction was 38 ± 13% (P < 0.0001). Global RV ejection fraction (RV sinus and infundibulum) was 53.6 ± 10%.

By echocardiography, the maximal and minimal area of the RV sinus were approximately twice that of the infundibulum. The fractional area change of the RV sinus was also significantly higher than that of the infundibulum. Regional RV ejection fraction was 11% and infundibular ejection fraction was 4.2% (P < 0.0001). Of the combined RV stroke volume, the RV sinus contributed 86.6 ± 4.2% and the infundibulum 13.2 ± 4.2% (P < 0.0001). Regional RV ejection fraction was 56 ± 11% and infundibular ejection fraction was 38 ± 13% (P < 0.0001). Similarly, the peak rate of change in chamber area with respect to change in time during

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RV indicates right ventricular.
systole and diastole (dA/dt and −dA/dt) were significantly greater for the RV sinus compared with the infundibulum. The normalized peak filling rate, peak emptying rate, and time to peak filling rate did not differ significantly between the two components of the RV.

Sequence of Activation
Analysis of temporal course of contraction and relaxation with respect to the cardiac cycle revealed that the infundibulum lags behind the RV sinus. Onset of RV sinus contraction occurs at 19.3±10.6% of systole, whereas onset of infundibular contraction occurs 52.6±13.7% of systole (P<0.0001). Minimal RV sinus area occurs at end systole (onset of the second heart sound), whereas minimal infundibulum area occurs at 115.5±16% of systole (P=0.01). The onset of infundibular relaxation and time to maximal area were also delayed compared with the RV sinus (Table and Figure 3).

Interobserver Variability
The mean interobserver variability for RV volume measurements by MRI was 4±5.5% (4.1±5.6 mL) and the correlation coefficient was 0.98 (P<0.0001). The mean interobserver variability for onset of contraction (percentage of systole) by AQ echocardiography was 5.2±8.5% and the correlation coefficient was 0.94 (P<0.0001).

Discussion
It has long been recognized by embryological and anatomic observations that the RV is composed of two distinct anatomic units—the sinus and the infundibulum. The results of this study provide several new quantitative and functional observations: (1) the sinus component comprises >80% of the total RV volume and the infundibulum comprises <20%; (2) from a functional standpoint, the sinus portion contributes >85% of the total RV stroke volume, whereas <15% is ejected by the infundibulum; (3) the extent of infundibular myocardial contraction is substantially less compared with that of the RV sinus; and (4) the sequence of chamber contraction and relaxation is peristaltic in nature with the infundibulum following the RV sinus by >15% of the cardiac cycle. In fact, the infundibulum continues to decrease in dimension after the second heart sound and continues to increase in dimension after the RV sinus begins to contract and the pulmonary valve opens. The normative data provided in this study can be used as a foundation for future studies on assessment of RV dimensions and function in surgical and nonsurgical patients with pathological conditions involving the RV.

Developmental and Anatomic Considerations
Phylogenetic observations suggest that the infundibulum is the muscularized outlet from the heart, which can be found as early as in the early chordates (such as the jawless fish, traced to the Silurian period in the Paleozoic era 435 million years ago). The RV sinus, however, is found quite later (in evolutionary terms) in vertebrates, which can be traced to the Carboniferous period some 275 million years ago. Hence, the RV sinus developed approximately 160 million years after the infundibulum, presumably as an adaptation of the cardiovascular system to air breathing. Specifically, the RV sinus developed as a specialized lung pump to improve the efficacy of the cardiorespiratory unit in air breathing creatures. Ontogenetic observations suggest that the infundibulum is present in very early stages of mammalian embryonic development, as early as in the straight heart tube stage (20 days after ovulation). The RV sinus develops later as an outpouching from the region of the proximal bulbus cordis (infundibulum), starting approximately 22 to 24 days after ovulation. The rapidly expanding RV sinus becomes the main pump of the right heart while the infundibulum continues to function as a muscularized exit from the ventricles.

Several anatomic observations also illustrate that the sinus and infundibulum are distinct components of the RV. Double-chambered RV is a lesion characterized by progressive stenosis of the proximal os infundibulum, leading to obstruction between the sinus and the infundibulum. In double-inlet left ventricle, the most common form of single ventricle, the RV sinus is absent but the infundibulum is always present. Two other congenital cardiac anomalies demonstrate that the infundibulum may be dissociated from the RV sinus and associated with the left ventricle. In anatomically corrected malposition of the great arteries, the infundibulum becomes part of the left ventricle and supports the aorta. The pulmonary artery in this condition arises directly from the RV sinus with direct fibrous continuity between the tricuspid and pulmonary valves. In transposition of the great arteries with a posterior aorta, the infundibulum is also associated with the left ventricle. In contrast to anatomically corrected malposition, however, the main pulmonary artery arises from the left ventricular infundibulum and the aorta arises directly from the RV sinus with fibrous continuity between the aortic and tricuspid valves. These observations on evolution, embryology, and pathology support the contention that the RV sinus and infundibulum are distinct components of the heart.

Functional Considerations
This study shows that the RV sinus performs most of the pump function of the right heart and the infundibulum serves mostly as a pulsatile conduit, ejecting only 13±4% of the combined RV stroke volume. The peristaltic motion demonstrated here is compatible with the evolutionary, anatomic, and functional findings discussed above. These findings support the hypothesis that the infundibulum functions as a propulsive exit from the RV, or in some instances, from the left ventricle. The relatively small volume and limited ejection capability may explain why attempts to utilize the infundibulum as a pumping chamber in patients with single left ventricle have failed. Such attempts included partitioning of single left ventricle and modifications of the Fontan operation with a right atrium–to–right ventricle connection. The results of these operations may have been suboptimal in part because the “small RV” was in fact an infundibulum, which is not an effective pump. These findings may also explain why operations in which a portion of the infundibular free wall...
is sacrificed are well tolerated. Examples include repair of tetralogy of Fallot and pulmonary atresia with intact ventricular septum in which a portion of the infundibular free wall is replaced by a patch as well as most other surgical procedures in which a conduit is used to connect the RV to the pulmonary arteries. Follow-up data of up to 34 years suggest good functional outcome in the majority of patients in whom an infundibular patch was used as part of their tetralogy of Fallot repair. Future research on RV function in patients who have undergone RV outflow tract procedures may examine the effects of prosthetic material in the infundibular free wall on global and regional RV function.

The anatomic and functional findings discussed above explain some of the difficulties encountered by researchers who used cross-sectional imaging techniques to assess RV volume, mass, and function. The sinus and infundibulum components have different shape, extent of fiber shortening, and timing of contraction and relaxation. Future research on RV structure and function should use methods that are inherently 3-dimensional and capable of resolving time. Currently, these methods include multidimensional echocardiography (time-resolved 3-D echo) and multislice cine-MRI techniques. These techniques do not rely on any geometrical assumptions or extrapolations and have been shown to be accurate. Echocardiographic techniques are limited by acoustic windows that hinder imaging of parts of the RV free wall. This limitation is particularly significant in adolescents and adults as well as in patients who have undergone cardiac surgery. Further research is needed to refine these evolving imaging techniques and to develop reliable and accurate algorithms for automated border detection. This will facilitate rapid and accurate assessment of RV dimensions and function.

Study Limitations

The AQ echocardiographic technique has a number of potential pitfalls because of the necessity for manual setting of the gain controls based on qualitative evaluation of the echocardiographic images by the operator. To circumvent these limitations, the technical guidelines published by Bednarz et al were carefully followed. Furthermore, the AQ data were used primarily to study the temporal sequence of mechanical contraction and relaxation of the RV. Gain control settings have little or no effect on these measurements, which were highly reproducible as evident by the small interobserver variability. With regard to measurements of RV and infundibular area by AQ, the echocardiographic data are highly consistent with the MRI data. MRI also has known technical limitations but the accuracy of gradient cine-MRI in the evaluation of RV volume has been demonstrated to be good.

Conclusions

The results of this study demonstrate significant regional differences between the sinus and infundibulum components of the RV with regard to contribution to stroke volume, extent of fiber shortening, and sequence of mechanical activation. These data from normal individuals can be used in future research on RV function in pathological conditions.

Acknowledgments

We thank Emily Flynn-McIntosh for artwork and Bil McIntosh for photography.

References


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Circulation. 1998;98:339-345
doi: 10.1161/01.CIR.98.4.339
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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