The right ventricle under acute and chronic overload: early detection of right ventricular dysfunction

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Introduction and Outline

**QUANTITATIVE ASSESSMENT OF THE PRESSURE AND VOLUME OVERLOADED RIGHT VENTRICULAR FUNCTION: IMAGING IS A REAL CHALLENGE**

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INTRODUCTION

Physicians are facing an increasing number of patients with right ventricular (RV) overload due to congenital heart disease. Adult patients with congenital heart disease are emerging as a new and continuously growing population. Improvements in medical care, surgical techniques, and closer follow-up have dramatically improved life expectancy in this group of patients. However, in a substantial part of these patients, the RV is or has been subjected to chronic pressure and/or volume overload (Figure 1). The long-term prognosis of these patients is unknown and mainly dependent on factors such as RV (dys)function, the occurrence of RV failure\(^1\), and rhythm disorders\(^2,4\). There is much controversy regarding the long-term outcome of RV function under these circumstances\(^4,6\). Some patients are asymptomatic\(^3,7,8\), while others are in need of frequent medical care\(^9\). Accordingly, their life expectancy is highly variable and expressed over a wide range\(^10,13\). Because assessment of RV function is a difficult task, current evaluation of these patients is mainly based on qualitative parameters\(^14\). The lack of quantitative determinants for RV function hampers physicians to estimate the appropriate time for surgical or medical intervention in order to prevent irreversible RV failure.

Management of these patients would be improved by establishing accurate noninvasive quantitative RV function determinants and to relate them to the already existing qualitative RV function determinants. The combined information could thus be implemented in daily clinical practice.

This paper will review the imaging modalities for RV function determination in congenital heart disease.

RV PHYSIOLOGY UNDER PRESSURE AND VOLUME OVERLOAD

The muscle mass of RV is approximately one-sixth of left ventricle (LV). Because of its thin muscular, the wall RV is more compliant than the LV and able to accommodate acute large increments of volume rather than acute pressure overload. However, exposure to chronic pressure overload and increased wall stress will stimulate RV hypertrophy in order to decrease wall stress and to enhance functional performance\(^15\). Increased volume load will result in RV dilatation and, according the Frank-Starling mechanism, increased RV contractility. The pressure-volume relation differs considerably between RV and LV. The normal RV ventricular pressure-volume loop is triangular while the normal LV ventricular pressure-volume loop has a square or rectangular form\(^16\). However in patients with morphologic RV in systemic position, the pressure-volume diagrams obtained from the RV are almost indistinguishable from a normal LV\(^17\). RV stroke work can be increased manifolds with well-maintained systolic performance using the huge contractile reserve of the RV\(^17\). Heart failure becomes imminent when the compensating mechanisms are exceeded and RV is no longer able to cope with the pressure or volume load.

Deterioration of RV function under chronic pressure/volume overload with time has been a common finding in few studies\(^16,7\), but not in all. In a population of 18 patients with ccTGA after a mean of 10 years of follow-up, Dimas et al.\(^4\) found that RV ejection fraction (EF) was essentially unchanged (Figure 2). These conflicting reports are highlighting the need for established reproducible quantitative parameters for determination of RV (dys)function and their integration in clinical practice.
RV SYSTOLIC FUNCTION

EF is the most commonly used parameter for RV systolic function in clinical practice. Normal RVEF appears to vary depending on the technique used. Angiographic measurements tend to be somewhat higher than those obtained by radionuclide angiography or echocardiography. RVEF values between 51% and 68% have been reported\(^{19,20}\). However, assessment of systolic function of RV in systemic position may be more complex, particularly when normal values have not been established\(^1\). No matter which method is chosen, the interpretation of these results is difficult. Helbing et al.\(^21\) suggested that RVEF should be interpreted as a measure of global ventricular performance considering that RVEF is an outcome of the different variables (preload, afterload, contractility and heart rate) present in a given disease state. Experimental evidence suggests that RVEF is at least twice as sensitive as LVEF to changes in ventricular afterload\(^22\).

Several centers have reported normal resting and exercise RV function in some\(^{18,23,24}\) or even in all asymptomatic patients with surgically corrected TGA\(^25\). Graham et al.\(^18\) and Conelly et al.\(^3\) presented evidence suggesting that systemic RV function may gradually deteriorate with age, in contrast to the findings reported by Hochreiter et al.\(^25\) and Dimas et al.\(^4\) showing no deterioration of RV function in longitudinal studies. However, reduced RVEF in chronic elevation of afterload (Mustard, Senning, Fallot) is certainly sustainable for many years, but important questions as to its implications or its adaptive responses still remain unanswered. These controversies concerning the clinical interpretation of RV systolic function are in accordance with Redington’s\(^26\) statement: “We are a long way from being able to assess RV contractility with the currently measurable noninvasive indices.”

RV DIASTOLIC FUNCTION

Noninvasive evaluation of LV diastolic function has gained widespread attention and is usually performed on a routine basis\(^27,28\). However, limited data have been reported concerning RV inflow characteristics and diastolic function\(^29,31\). RV diastolic filling abnormalities may be a matter of concern especially in patients with chronic pressure and volume overload and postoperative congenital heart disease\(^32,33\). Since diastolic filling abnormalities may precede systolic dysfunction\(^34\), assessment of diastolic performance may provide early information on the development of RV dysfunction. Among the methods presently available, Doppler-echocardiography has gained the widest acceptance in the study of RV diastolic dysfunction\(^34\). Diastolic function of RV is best assessed by a combination of Doppler examination of the flow through tricuspid valve, hepatic veins, inferior and superior caval veins, and pulmonary arteries\(^26\) However it is often difficult to obtain satisfactory measurements of tricuspid flow by means of Doppler-echocardiography. Magnetic resonance imaging (MRI) has the possibility to assess RV diastolic function and it enables calculation of the volume patterns over the tricuspid valve\(^35,36\). Rebergen et al performed MRI measurements of tricuspid flow and found them feasible and accurate in healthy children and in patients after a Mustard or Senning operation\(^35\). Abnormal tricuspid flow patterns after a Mustard or Senning repair, demonstrated with Doppler echocardiography, have been attributed to reduced compliance, impaired relaxation of the hypertrophied RV\(^33\) or rigid baffles\(^37,38\). Using MRI velocity mapping in a group of corrected Fallot patients with important pulmonary regurgitation, Helbing et al. have established impaired RV relaxation and restriction to RV filling in these patients\(^29\). The assessment of RV diastolic function is a real challenge. Comparison between groups can only be made when measurements are taken in reproducible fashion. Even
than the variable effects of loading conditions, respiration, geometry, and natural history must all be taken into account.

**DIAGNOSTIC METHODS**

Estimation of RV volume and function are more difficult to obtain than similar measurements of LV mainly because the configuration of the RV is far more complex and not well approximated by simple geometric formulas\(^3\). Consequently, in clinical practice, the increasing interest in the evaluation of RV function has not been matched by an increase in the spectrum of diagnostic noninvasive modalities. New techniques for studying ventricular function are therefore increasingly being applied to RV.

**IMAGING**

With ongoing technical advances and an increased interest in the role of the RV, accurate estimation of anatomy and function is not only possible but should be essential. Evaluation of RV function is confounded by the complex geometry, which makes mathematical assumption of RV volumes fairly inaccurate. The most effective method for quantification of the volume of an unknown shape such as the RV is the application of a multislice technique using Simpson's rule\(^3\). Multislice technique divides the ventricle into multiple thin slices where after the volume of each slice is calculated and summed to provide the total RV volume. Conventional imaging methods such as angiography, echocardiography and radionuclide ventriculography have given some insight into the importance of the various determinants of RV pump function. These imaging modalities have their advantages and disadvantages. The RV is difficult to assess quantitatively with echocardiography. Projection techniques such as radionuclide ventriculography and cine angiography have a limited role because of overlapping of structures and assumptions concerning RV geometry\(^3\). Relatively new techniques for studying RV function and anatomy like MRI are increasingly being applied in clinical practice.
ECHOCARDIOGRAPHY

Echocardiography is the most used imaging technique for the RV, supplementing and often replacing the traditional approach using selective RV contrast angiography. Doppler echocardiography can provide morphologic and hemodynamic information through segmental analysis of most congenital heart defects. Also, echocardiography provides indirect documentation of pulmonary artery hypertension and estimation of severity by the presence of RV dilatation and/or hypertrophy, the presence of tricuspid or pulmonary valvular regurgitation, and by Doppler estimation of RV systolic pressure.

Techniques used for estimating RVEF rely on models that assume a specific geometric shape to calculate ventricular volumes. The complex geometry of the RV, especially in congenital heart disease, makes application of geometric models for determination of RV function by means of two-dimensional echocardiography virtually impossible. Frequent coexistence of tricuspid regurgitation also confounds accurate RVEF determination.

Limitations of two-dimensional echocardiography in quantifying RV function can be overcome by three-dimensional echocardiography. The technique of three-dimensional echocardiographic assessment of the RV is an accurate method, because the images acquired with this technique can be analyzed according to Simpson’s rule. The limitation of the system is that only a limited sector is imaged with the probe. In dilated right ventricles, the margins of the cardiac chamber often fall outside these angles and therefore an incomplete data set is rendered. More recently, an echocardiographic machine has become available that uses a digital beamformer system, which has improved by the imaging characteristics of the probe. Manual tracing of the RV cavity is required at the present time and this is continually verified by comparison with the two-dimensional images to ensure that errors are avoided and this process is time consuming.

Reliable estimates of ventricular function, independent of ventricular geometry can be obtained by the estimation of the first derivative of pressure rise, or dP/dt. The peak dP/dt is considered as a reliable parameter of ventricular function, but it is believed to be preload dependent. This parameter was usually obtained via micromanometer catheters, but in the presence of atrioventricular valve regurgitation it can be estimated using Doppler echocardiography showing good correlation with catheter-derived values.

More recently the myocardial performance index has been proposed as a geometry-independent index for global RV function. Myocardial performance index is derived from the time intervals obtained via Doppler echocardiography of the inflow and outflow of either ventricle. It reflects the isovolumetric activity of the ventricle in relation to the ejection time, and shows a good correlation with catheter-derived parameters of ventricular function such as peak dP/dt and Tau. This index does not distinguish between systolic and diastolic function, but rather reflects global performance. Because of variations during respiration, tricuspid inflow is less useful in determining diastolic function than mitral inflow. In combination with tissue-Doppler it may be an excellent indicator for RV diastolic function.

In the clinical practice cardiologists and echocardiographic technicians are faced with wide variety of RV lesions, caused by congenital heart disease. It is likely that they might recognize something abnormal but they might not recognize all the characteristics of the congenital heart lesion. For that reason and considering that the echocardiography is still the first diagnostic choice in patients with congenital heart disease it is necessary that both the interpreting cardiologist and the echocardiographic technician have special competencies in congenital heart disease.
ANGIOGRAPHY

RV function can be quantitatively assessed by RV angiography, whereby RV pressures are directly measured and accurate volumetric analysis can be performed. Graham et al. first reported on the angiographic application of both the biplane area length method and Simpson’s rule for volumetric assessment of the RV in normal children and they found good correlation between both methods. Angiographic volumes are normally calculated using geometric assumptions but they tend to be inaccurate. Such techniques do not allow the real time measurement of changes in volume during periods of changing function, and emphasis has therefore shifted towards the use of other imaging techniques, such as echocardiography, scintigraphic methods and MRI. Angiographic studies of RV function are less useful because of the invasive nature of the study and certain structures overlapping in these images. The fact that noninvasive studies like MRI and echocardiography can yield all the necessary morphological and hemodynamic information makes the role of cardiac catheterization less prominent.

Figure 3. 3D reconstruction of the Left and Right Ventricle.

MR IMAGING

MRI provides the diagnostic noninvasive technique of choice for the evaluation of RV function by its potential to obtain both anatomic detail and flow quantification. Good accuracy and superior reproducibility of MRI are setting a new gold standard for the quantification of RVEF, cardiac output (systolic function), myocardial mass and wall thickness. MRI in comparison with other techniques are the excellent spatial resolution, the characterization of myocardial tissue, any imaging plane is possible in any direction and the potential for three-dimensional imaging. No ionizing radiation or harmful contrast agents are generally being used during MRI examination. MRI is also a useful tool in the follow-up of patients with (postoperative) congenital heart disease that may be associated with various anatomical and functional abnormalities of the RV (Figure 4).
This is because of its noninvasive nature, the unlimited access to the chest, and the ability to provide detailed anatomic images and functional information from the heart obtained with a single examination. MRI can easily provide multiple tomographic sections of the entire RV in patients with cardiac deformities, without making geometric assumptions concerning ventricular shape. MRI can also be used to detect intracardiac and homograft conduit obstruction following cardiac surgery in complex congenital heart disease. Further specialized MRI pulse sequences such as SPAMM (spatial modulation of magnetization) can be used to noninvasively determine regional strain and motion. 

There are still some difficulties to overcome in the assessment of the systolic RV function with MRI. Images around the tricuspid valve are not easily interpreted whether they belong to the ventricle or to the atrium. Valve motion during the cardiac cycles makes the assessment of the RV end systolic and end diastolic volumes more complicated due to a certain overlap between the right atrium and RV. However, new techniques with valve tracing possibility are emerging to overcome this problem.

Presence of valvular dysfunction or septal defects influences the RV function and its assessment. Additional flow measurements in the outflow tract of the RV, LV, aorta, or in the pulmonary artery are needed for accurate RV function determination. There have been several potential clinical applications of MR velocity mapping (velocity encoded cine MRI) that can provide measurements of flow through the atrioventricular valves (AV), aorta and pulmonary artery. This allows assessment of valvular stenosis, regurgitation and diastolic function.

Although real-time image acquisition with sufficient spatial and temporal resolution has recently become feasible, cardiac gating using the ECG is still being used for most cardiovascular applications. With cardiac gating, the images are acquired in small parts during each heart cycle at a fixed time frame relative to the QRS complex of the ECG until the entire image is acquired. Hence, a cardiovascular MR image reflects the average cardiac condition at a certain time and thus requires a regular heart rate, which is not always present in patients with RV overload. Irregular heart rate has negative effect on the quality of MR imaging causing blurred images.

Analysis of RV function is time-consuming. In particular, RV function in patients with congenital heart defects using MRI requires highly trained personnel, both to obtain and to analyze the images. To date there is no automatic contour detection software commercially available, and the analysis requires hand drawing of the RV contours, which is time-consuming.
(Figure 5). This problem should be soon resolved with the development of new automatic contour detection software.

Problems in differentiating epicardial fat, papillary muscles and interventricular septum are common to both in-vitro and in-vivo determinations of RV myocardial mass. The results of these determinations should therefore be interpreted as the minimum volume errors that can be achieved using MRI methods with the specified image resolution and slice thickness for ventricular volume estimates\(^\text{61}\).

Mismatch between resting functional parameters and symptomatology have emphasized the need for exercise studies to monitor RV function in patients with TGA\(^\text{8}\), and more generally, in patients with RV functioning under pressure and/or volume overload. Exercise studies, apart from their fundamental relevance to understanding various physiological adaptation mechanisms in health and in disease, have provided objective clinical hallmarks during evolution of clinical/surgical management programs for congenital heart lesions\(^\text{8}\). Several studies, using a wide range of approaches towards exercise testing, have been performed but these studies yielded conflicting results regarding cardiac reserve\(^\text{8}\). Patients with surgically corrected TGA generally show reduced exercise tolerance, which has been attributed to factors such as abnormally low heart rate response, filling abnormalities of the RV\(^\text{8,21,35}\) and systolic dysfunction\(^\text{35}\). Derrick et al. found reduced diastolic filling and decreased stroke volumes during dobutamine stress testing in patients after Mustard repair. The authors are assuming that the capacitance and conduit function of the abnormal, often calcified, intra-atrial pathways may be responsible for the failure of stroke volume augmentation during exercise\(^\text{37}\).

Dobutamine, a relatively selective beta-1-adrenoreceptor agonist, can be used as a pharmacological stress agent during MRI investigation\(^\text{62,63}\) (Figure 6). Although the positive inotropic action of dobutamine on RV function seems clinically evident\(^\text{64,65}\), few data are available regarding contractile reserve of the RV following beta-adrenergic stimulation\(^\text{24,46-48}\). Data from our institution have shown the usefulness of MRI in determining RV and LV contractility in patients with surgically corrected TGA\(^\text{24}\). This imaging method can also be applied to other patient groups with RV overload for quantitative determination of their cardiac reserve.

Cardiac MRI allows an accurate noninvasive functional assessment of the RV. Further development of this diagnostic method needs to be done in a multidisciplinary fashion between cardiologists, radiologists, physicists, software scientists and MRI producers.

![Figure 6. End systolic frame of midventricular slice during baseline and stress in patient with TGA.](image-url)
Table 2. Indications for imaging techniques in patients with known or suspected congenital heart disease.

<table>
<thead>
<tr>
<th>General</th>
<th>Echo Doppler</th>
<th>Angiography</th>
<th>MRI</th>
<th>Radiouclide imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anatomy</td>
<td>1</td>
<td>III</td>
<td>1</td>
<td>IV</td>
</tr>
<tr>
<td>Preoperative (catheterization)</td>
<td>1</td>
<td>I</td>
<td>1</td>
<td>IV</td>
</tr>
<tr>
<td>Follow-up</td>
<td>I</td>
<td>III</td>
<td>1</td>
<td>II</td>
</tr>
<tr>
<td>Specific</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Viscero-atrial sites</td>
<td>1</td>
<td>II</td>
<td>1</td>
<td>III</td>
</tr>
<tr>
<td>ASD</td>
<td>1</td>
<td>II</td>
<td>1</td>
<td>IV</td>
</tr>
<tr>
<td>Anomalous pulmonary/venous return</td>
<td>1</td>
<td>II</td>
<td>1</td>
<td>IV</td>
</tr>
<tr>
<td>Atrioventricular valves</td>
<td>1</td>
<td>II</td>
<td>1</td>
<td>IV</td>
</tr>
<tr>
<td>VSD</td>
<td>1</td>
<td>II</td>
<td>1</td>
<td>III</td>
</tr>
<tr>
<td>RV/LV function</td>
<td>1</td>
<td>III</td>
<td>1</td>
<td>III</td>
</tr>
<tr>
<td>The semilunar valves</td>
<td>1</td>
<td>III</td>
<td>1</td>
<td>III</td>
</tr>
<tr>
<td>Malposition of the GA</td>
<td>1</td>
<td>II</td>
<td>1</td>
<td>III</td>
</tr>
<tr>
<td>Pulmonary atresia</td>
<td>1</td>
<td>II</td>
<td>1</td>
<td>III</td>
</tr>
<tr>
<td>Central pulmonary stenosis</td>
<td>1</td>
<td>II</td>
<td>1</td>
<td>III</td>
</tr>
<tr>
<td>Pulmonary artery pressure</td>
<td>1</td>
<td>II</td>
<td>1</td>
<td>IV</td>
</tr>
</tbody>
</table>

Class I – provides clinically relevant information and is usually appropriate; may be used as a first line imaging technique.
Class II – provides clinically relevant information and is frequently useful, but similar information may be provided by other imaging techniques.
Class III – may provide clinically relevant information but is infrequently used because information from other imaging techniques is usually adequate.
Class IV – does not provide clinically useful information.

DISCUSSION

Many authors have used different techniques to evaluate RV function in patients with congenital heart disease, but the practical value of these data is questionable. As already stated, there is a structural difference between the techniques used, the series of patients included are often too small and heterogeneous, and therefore these studies are not always representative. Considering that current clinical practice is falling short of reliable quantitative parameters to assess RV function under chronic overload, the central question is: to which extent are normal RV or LV function parameters applicable for RV in systemic position? Is this a valid comparison? In the normal heart, RV end-diastolic volume is higher, RVEF is lower, and pressure-volume characteristics are substantially different from those of the LV\textsuperscript{15}. Indeed these differences have been highlighted as reasons why it may be invalid to use indices of LV function to assess RV function\textsuperscript{3,38}. The situation in patients with TGA is somewhat different. Under these circumstances, the systemic RV is expected to perform the same function as the LV. Indeed, some studies\textsuperscript{34,38,69} have shown that RV function in some patients with transposition of the great arteries may be comparable to that of normal LV, but often this is not the case\textsuperscript{3,70,71}. Uncertainty about deteriorating RV function should best be confirmed by noninvasive quantitative studies that will allow optimal timing in the decision-making process tailored to the individual patient. There is no doubt that timely detection and identification of high risk patients who might derive survival benefit from more aggressive medical and or surgical therapy becomes the cornerstone for improving life expectancy of patients with a RV under chronic pressure/volume overload. Considering the complexity of RV heart failure as a syndrome, it is unwise to look after a single parameter to reveal either the severity of heart failure or its prognosis. We strongly believe in a comprehensive approach and combination of the imaging, quantitative and noninvasive diagnostic methods to establish practical and useful relation between the quantitative determinants and patients.
REFERENCES


