Assessment of Systemic Right Ventricular Function in Patients With Transposition of the Great Arteries Using the Myocardial Performance Index

Comparison With Cardiac Magnetic Resonance Imaging

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Background—Assessment of systemic right ventricular (RV) function is a key point in the follow-up of patients with transposition of the great arteries (TGA). Current echocardiographic assessment of RV function is at best an estimate, and cardiac magnetic resonance (CMR) is considered the gold standard. However, this technique is expensive, has limited availability, and requires significant expertise to acquire and interpret the images. The myocardial performance index (MPI) has recently been studied for assessment of pulmonary RV function and shows promise as a simple yet powerful tool for assessing patients with RV dysfunction of various origins. We set out to compare MPI and CMR assessment of systemic RV function in patients with TGA.

Methods and Results—Data from patients with TGA (11 with congenitally corrected TGA, 18 with surgically corrected TGA) who had CMR within 6 months of their echocardiogram were reviewed. The average systemic RV ejection fraction (RVEF) by CMR was 39.4 ± 11.4%, and the systemic RV MPI for this group was 0.56 ± 0.21. There was a strong negative correlation between the systemic RV MPI and systemic RVEF by CMR (r = -0.82, P < 0.01). The systemic RVEF can be estimated from this formula: RVEF = 65% - (45.2 × MPI).

Conclusions—MPI can be used in patients with systemic RVs to assess global function and to estimate an EF with good accuracy. (Circulation. 2004;110:3229-3233.)

Key Words: echocardiography • heart defects, congenital • magnetic resonance imaging • transposition of great vessels • ventricles

In patients with both congenitally corrected transposition of the great arteries (CCTGA) and surgically corrected TGA (D-TGA) via a Mustard or Senning procedure,1 the morphological right ventricle (RV) is the systemic ventricle. Long-term follow-up of these patients shows that reduced function of the systemic RV is associated with increased mortality.2,3 The exact pathogenesis of systemic RV dysfunction has yet to be elucidated. Abnormal pressure loading conditions of the systemic RV,4 the imbalance in myocardial oxygen supply and demand leading to ischemia,5,6 and the increased preload associated with substantial systemic AV valve regurgitation (AVVR)7 have all been implicated. Therefore, assessment of systemic RV function and evaluation of the degree of systemic AVVR are 2 key points during follow-up of patients with TGA. Although the definition of “normal” systemic RV ejection fraction (EF) remains somewhat problematic, most authorities agree that an EF >50% can be considered normal.8,9

Assessing the function of the morphological RV is challenging because of its complex anatomy. Difficulties are compounded by irregularities in the ventricular cavities and abnormalities in wall motion in patients with congenital heart lesions. None of the geometric assumptions used to assess left ventricular (LV) function hold true for the systemic RV. The complex shape of the RV makes quantification difficult.10 Thus, in clinical scenarios, many centers rely on visual estimation of RV systolic function, which is then subject to variability because of incomplete visualization of the entire RV and the experience of the observer. Therefore, cardiac magnetic resonance (CMR) has evolved to be a better quantitative standard, especially for serial comparisons.8 However, this technique, which is contraindicated in some patients, is expensive, has limited availability, and requires significant resources and expertise to acquire and interpret the images.
Myocardial performance index (MPI) was first described by Tei and colleagues as a measure of combined systolic and diastolic function of the LV. This index has since been studied in a wide array of disease states involving the LV. The index has also been used to assess RV function. An advantage of MPI is that, because it is independent of geometric assumptions, it can be used to assess the performance of the RV and other ventricles with unusual geometry. Although MPI has been used in patients with congenital heart lesions such as those with Ebstein’s anomaly, there are few data demonstrating its utility in assessing systemic RV function. The goals of this study were to compare qualitative echocardiographic assessment of systemic RV function with CMR and, more importantly, to evaluate MPI as a method for assessing systemic RV function by comparing it with the gold standard, CMR.

Methods

Population
After approval was obtained from the university research ethics board, adult patients with systemic RVs and the diagnosis of D-TGA or CCTGA were identified from the Toronto Congenital Cardiac Center for Adults database. Routine care for patients with a systemic RV in the adult congenital clinic includes surveillance with CMR every 3 to 5 years and annual clinical evaluation and echocardiographic assessment. All patients who had an echocardiographic assessment within 6 months of their CMR examination were selected. Patients were excluded if they were clinically unstable, were not in sinus rhythm, had a prosthetic systemic AV valve, or had incomplete 2D and Doppler echocardiographic assessment. Patients’ medical records were reviewed to gather demographic information, previous surgical history, and clinical status (NYHA functional class).

Echocardiography
Echocardiograms were performed with commercially available machines by experienced sonographers. Complete 2D, conventional color-flow, and spectral Doppler studies were performed in the usual manner. Doppler recordings of systemic RV inflow and outflow were used to measure the parameters required for the calculation of MPI (Figure 1). Measurements of systemic AVVR Doppler signal duration (interval a) and the duration of the systemic outflow Doppler signal (interval b) were made on 4 consecutive beats to account for slight variation in the R-R cycle length. MPI was calculated from the average values with this formula: MPI=(a−b)/b.

Echocardiograms were examined by the primary reader (O.S.) who was blinded to CMR data. Qualitative assessment of the global systemic RV function was performed with the visual grading system (1=mild, 2=mild to moderate, 3=moderate, and 4=severe). Severity of systemic AVVR was graded qualitatively following the American Society of Echocardiography guidelines for native valve regurgitation and reported as follows: 1=mild, 2=moderate, 3=moderate to severe, and 4=severe.

Reproducibility
Intraobserver variability for MPI measurements was assessed in a randomly selected subset of 10 patients by repeating the measurements. To test the interobserver variability, measurements were performed offline by a second observer (J.T.) who was blinded to both the initial echocardiographic examination and the CMR data.

CMR Scans
CMR scans were performed as previously described with a 1.5-T system with an ECG gated spin-echo images. Systemic RV

Figure 1. A, Continuous-wave Doppler recordings of systemic AV valve in patient with D-TGA and previous Mustard operation. B, Pulsed-wave Doppler recording in same patient across systemic RV outflow. A represents interval from onset of systemic AVVR to its cessation; b, systemic RV ejection time; ICT, isovolumetric contraction time; and IRT, isovolumetric relaxation time.

end-diastolic volume (EDV) and end-systolic volume (ESV) were determined from multisection cine CMR images in which the RV cavity area was manually traced at multiple levels from the base of the heart to the RV outflow. Systemic RVEF was estimated from the following formula: EF= [(EDV−ESV)/EDV]×100%.

Statistical Analysis
All statistical analyses were done with SPSS 12.0. Data are expressed as mean±SD. Spearman’s correlation was used to determine the relationship between RVEF by CMR and RVMPI by echocardiography. The Kruskal-Wallis test was used for multiple sample comparisons, and the Mann-Whitney test was used for 2-sample comparisons. Intraobserver and interobserver variabilities were calculated as the mean percentage error, derived as the difference between the 2 sets of measurements, divided by the mean observations. Cohen’s κ was used for interobserver variability of qualitative grading of global systemic RV function and systemic AVVR.

Results
Demographics and Surgical History
A total of 39 patients who had an echocardiogram within 6 months of their CMR study were identified from the database (Table). Ten patients were excluded (6 had incomplete Doppler data, 2 had previous systemic AV valve replacements, and 2 were not in sinus rhythm). The remaining 29 eligible patients (72.4% male) were on average 32.2±9.6 years of age. Eighteen patients (62%) had D-TGA by either a Mustard (n=17) or Senning (n=1) operation at an average of 1.6±1.9 years of age. The average length of time between the initial surgery and the CMR study was 26.7±7.9 years. Of the patients with CCTGA (n=11), 7 had previous surgeries (2 ventricular septal defect closures, 5 with LV to pulmonary artery conduit combined with ventricular septal defect closure) at an average of 18.3±10.4 years of age. The average length of time between the initial surgery and the CMR assessment was 19.9±5.7
Ventricular dysfunction (grade 2) were compared with those with moderate (grade 3) and severe (grade 4) ventricular dysfunction, there was a statistically significant difference in systemic RVEF between the 2 groups (44.6±9.8% versus 34.4±11%; \( P=0.004 \)), although there was considerable overlap.

There was a significant negative correlation between systemic RVMPI and systemic RVEF determined by CMR (\( r=-0.82, P<0.01 \)) (Figure 3). This correlation was significant in both D-TGA patients (\( n=18 \)) with a Mustard or Senning procedure (\( r=-0.82, P<0.01 \)) and CCTGA patients (\( n=11; r=-0.85, P<0.01 \)). Secondary analysis revealed that the correlation remained significant when the 4 patients with severe systemic AVVR were excluded (\( r=-0.78, P<0.01 \)). A regression equation for estimating EF was derived from this correlation: \( \text{EF} = 65 - (45.2 \times \text{MPI}) \). Patients were divided into 3 groups on the basis of their CMR-assessed systemic RVEF: EF <30% (\( n=6 \)), EF between 30% and 50% (\( n=18 \)), and EF >50% (\( n=5 \)). There was a statistically significant difference between the systemic RVMPIs of the 3 groups (Figure 4). When patients with grade 1 through 3 AVVR (\( n=25 \)) were compared with

### CMR Scans

Mean systemic RVEDV corrected for body surface area was \( 137.8±82.1 \text{ cm}^2/\text{m}^2 \), and mean ESV corrected for body surface area was \( 85.1±69.7 \text{ cm}^2/\text{m}^2 \). The average systemic RVEF was \( 39.4±11.4\% \) (range, 20% to 66%).

### Echocardiographic Findings: Qualitative and Quantitative

The average time interval between the CMR and echocardiographic assessment was \( 65.6±4.0 \) days (range, 0 to 180 days). Qualitative assessment of global systemic RV function revealed 4 patients (13.8%) with grade 1, 11 patients (37.9%) with grade 2, 8 patients (27.6%) with grade 3, and 6 patients (20.7%) with grade 4 ventricular function (Figure 2). Nine patients (31%) had grade 1 systemic AVVR, 7 (24.1%) had grade 2, 9 (31%) had grade 3, and 4 (13.8%) had grade 4 regurgitation. The average MPI for the systemic RV for the entire group was \( 0.56±0.21 \) (range, 0.21 to 0.95).

### Comparison of Echocardiography with CMR

There was a statistically significant negative correlation between qualitative echo-based global systemic RV function and CMR-derived EF (\( r=-0.71, P<0.01 \)). When patients with visually graded normal ventricular function (grade 1) and those with mild normal ventricular function (grade 1) and those with mild ventricular function (grade 1) and those with mild...
AVVR, Cohen’s interobserver variability for qualitative echocardiographic comparisons between mild and severe impairment. Furthermore, function by echocardiography correlated relatively well with LV angiography and radionuclide angiography, is used Although echocardiography, which has good correlation with CMR-derived systemic RVEF.

Intraobserver and Interobserver Variabilities
For qualitative grading of global systemic RV function, Cohen’s κ correlation for the 2 readers was 0.70; for grading of systemic AVVR, Cohen’s κ correlation for the 2 readers was 0.75. For MPI measurements, the intraobserver and interobserver variabilities were 3.1±2.4% and 6.2±3.1%, respectively.

Discussion
Our study is the first to demonstrate that MPI is a robust surrogate for CMR-derived EF in the evaluation of systemic RV function in patients with TGA.

Qualitative Assessment of Systemic RV Function
Although echocardiography, which has good correlation with LV angiography and radionuclide angiography, is used everyday in clinical practice to quantitatively assess LV function, it has previously been considered an inaccurate tool to quantitatively assess RV function because of a lack of an ideal geometric model for evaluation of ventricular volumes. More recently, in children, 3D echocardiography has been found to have an excellent correlation with CMR in the assessment of RV volumes and function. However, questions remain about the accuracy in adults because of inadequate windows and larger RV volumes. Because of a lack of any other suitable noninvasive method, qualitative assessment of the systemic RV has been used for surveillance of function reported in number of studies for both D-TGA with atrial baffle surgery and CCTGA.

Our results show that qualitative estimation of systemic RV function by echocardiography correlated relatively well with CMR-derived EF, although the best results were found in comparisons between mild and severe impairment. Furthermore, interobserver variability for qualitative echocardiographic assessment was quite wide.

MPI Assessment of Ventricular Function
MPI has been used extensively in the assessment of LV function. The normal value for LVMPI in the adult population is between 0.34 and 0.40, with some age dependency. Numerous studies have documented the utility of MPI in assessing patients with LV dysfunction of various causes. Only a few studies have assessed pulmonary RV function by MPI and found that the average normal value in the adult population ranges from 0.26 to 0.28. These studies also show that measurement of MPI is fairly reproducible, with an intraobserver variability of 2% to 5% and an interobserver variability of 4% to 7%. Similar variability is seen in our study, which had an intraobserver variability of 3.1±2.4% and an interobserver variability of 6.2±3.1% for the measurement of MPI.

Currently, there are no known values for MPI in patients with systemic RV presumed to be functioning normally. Because the systemic RV behaves more like a morphological LV than an RV, one could logically assume that it should have an MPI value similar to that of a morphological LV. In our study, 4 of the 5 patients with EF values >50% had MPI values <0.4 (0.29±0.08; range, 0.21 to 0.43).

The increased preload associated with systemic AVVR is thought to be partially responsible for the systemic RV dysfunction. Increased preload has been shown to cause increases in LVMPI mainly as a result of shorter ejection time. The higher systemic RVMPI seen in the subset of our patients with severe systemic AVVR likely represents the effect of increased preload by similar mechanisms because we see shorter ejection times in the 4 patients with severe AVVR compared with the rest (236.9±31.3 versus 293±34.8 ms), although other factors such as the associated systemic RV dysfunction are likely contributory.

Lax et al found LVEF and LVMPI to have a good correlation. They constructed a regression equation from the data to convert MPI to LVEF: \[ \text{LVEF} = 60 - 34 \times \text{MPI} \]. They argued that although MPI is an easily measured, reproducible value, it is not a measurement with which clinicians are familiar, so converting it to the more standard EF would yield more clinically useful information. We found the relationship between systemic RVMPI and EF \[ \text{EF} = 65\% - (45.2 \times \text{MPI}) \] to be very similar to the above relationship for LV.

More recently, MPI has been used to assess RV function in patients with a variety of congenital heart defects. Eidem and colleagues used only echocardiography to study the RVMPI in both children and adults with variety of congenital heart defects affecting the RV. The average systemic RVMPI in 27 patients with CCTGA was 0.72±0.17. Twenty-three of these patients (85%) had moderate or severe global systemic RV dysfunction, and all had moderate or severe systemic AVVR. In contrast, in our population of patients with CCTGA \( n = 11 \), only 6 (54%) had moderate or severe systemic RV dysfunction, and 6 (54%) had moderate or severe systemic AVVR. Our systemic RVMPI value was 0.55±0.20. Another study by Williams and colleagues reports an average MPI of 0.72±0.19 in children with single ventricles of RV morphology \( n = 9 \). No comparison was made with any other form of evaluation of ventricular function. The fact that this was a study in a pediatric population (average age, 11 months) and the patients had univentricular morphology might explain the difference seen in the values for MPI compared with our study.
Study Limitations
Several potential study limitations should be examined. Ideally, CMR and echocardiographic assessment would have been performed on the same day to eliminate the possibility of changes in systemic ventricular function with time. However, we chose 6 months as a reasonable time between CMR and echocardiographic assessment on the basis of our clinical experience and a previous report. During the interval between CMR and echocardiographic assessment, 0 of the 29 patients had hospital admissions or change in their clinical status. Analysis of data from patients who had their echocardiograms within 90 days of the CMR study (n=22) showed a similar correlation between MPI and systemic RV EF (r=−0.80, P<0.01).

Although systemic RV MPI is a good quantitative measure of systemic RV function, it does not provide information about ventricular volumes. Finally, our study was retrospective with a relatively small sample size. A larger prospective study to validate our findings would be welcome.

Conclusions
Quantitative echocardiographic assessment of global systemic RV function by MPI in patients with TGA highly correlates with RV EF obtained by CMR. This simpler, more available, yet accurate and reproducible measurement may facilitate serial follow-up of RV function in these patients.

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References
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