Power loss and right ventricular efficiency in patients after tetralogy of Fallot repair with pulmonary insufficiency: Clinical implications

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Objectives: To quantify right ventricular output power and efficiency and correlate these to ventricular function in patients with repaired tetralogy of Fallot. This might aid in determining the optimal timing for pulmonary valve replacement.

Methods: We reviewed the cardiac catheterization and magnetic resonance imaging data of 13 patients with tetralogy of Fallot (age, 22 ± 17 years). Using pressure and flow measurements in the main pulmonary artery, cardiac output and regurgitation fraction, right ventricular (RV) power output, loss, and efficiency were calculated. The RV function was evaluated using cardiac magnetic resonance imaging.

Results: The RV systolic power was 1.08 ± 0.62 W, with $20.3\% \pm 8.6\%$ power loss owing to $41\% \pm 14\%$ pulmonary regurgitation (efficiency, $79.7\% \pm 8.6\%$; 0.84 ± 0.73 W), resulting in a net cardiac output of 4.24 ± 1.82 L/min. Power loss correlated significantly with the indexed RV end-diastolic and end-systolic volume ($R = 0.78$, $P = .002$ and $R = 0.69$, $P = .009$, respectively). The normalized RV power output had a significant negative correlation with RV end-diastolic and end-systolic volumes (both $R = -0.87$, $P = .002$ and $R = -0.68$, $P = .023$, respectively). A rapid decrease occurred in the RV power capacity with an increasing RV volume, with the curve flattening out at an indexed RV end-diastolic and end-systolic volume threshold of 139 mL/m^2 and 75 mL/m^2 , respectively.

Conclusions: Significant power loss is present in patients with repaired tetralogy of Fallot and pulmonary regurgitation. A rapid decrease in efficiency occurs with increasing RV volume, suggesting that pulmonary valve replacement should be done before the critical value of 139 mL/m^2 and 75 mL/m^2 for the RV end-diastolic and end-systolic volume, respectively, to preserve RV function. (J Thorac Cardiovasc Surg 2012;143:1279-85)

The repair of tetralogy of Fallot (TOF),¹ which has pulmonary stenosis present, consists of placing a transannular patch across the right ventricular (RV) outflow tract to relieve the obstruction that results in pulmonary regurgitation (PR) and imposes a volume load on the RV.^{2,3} This RV volume load affects the RV function at rest as well as at exercise, and has been correlated with the degree of PR.⁴⁻⁶ Once the PR is abolished by placement of a competent pulmonary valve, exercise tolerance improves.^{7,8}

We hypothesized that parameters such as RV volume, RV mass, and PR, which have been previously characterized in TOF, are surrogates to what is at the root of ventricular

performance—RV power output. Because the right ventricle must pump the regurgitant as well as the net stroke volume, we further hypothesized that this results in wasted power by the heart. The increased power needed might be a significant contributor to the etiology of ventricular dysfunction,^{5,6} exercise intolerance,^{4,5} and dysrhythmias that these patients experience. The quantification of this “wasted” power and its association with other parameters of ventricular performance might be the key toward understanding the limitations in patients with TOF and toward improving the medical, surgical, or catheter (eg, pulmonary valve replacement) management.

Cardiac magnetic resonance (CMR) cine imaging⁶ and phase contrast-CMR (PC-CMR)⁹ can accurately quantify the ventricular volume, cardiac index, and PR. Combined with measures of right-sided pressures by cardiac catheterization, power output, and power loss (PL) associated with PR and their association with standard measures of ventricular performance can be quantified. The hypothesis of the present study was twofold: significant PL is present in patients with TOF with PR; and that the PL has a significant effect on global ventricular function. We speculated that PL might be the global parameter that can explain decreasing RV function, could be the sentinel of deteriorating cardiorespiratory performance

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Abbreviations and Acronyms

CMR	= cardiac magnetic resonance
TOF	= tetralogy of Fallot
PC-CMR	= phase contrast-CMR
PL	= power loss
RV	= right ventricular
RVEDVI	= right ventricular end-diastolic volume indexed to standard clinical form
RVEDV _{Normalized}	= “normalized” right ventricular end-diastolic volume
RVESVI	= right ventricular end-systolic volume indexed to standard clinical form
RVESV _{Normalized}	= “normalized” right ventricular end-systolic volume
RVOT	= right ventricular outflow tract
PR	= pulmonary regurgitation

and aid in determining the timing for pulmonary valve replacement.

PATIENTS AND METHODS**Patients**

Thirteen consecutive patients with repaired TOF and PR who underwent CMR and catheterization were enrolled in the present retrospective study, which was approved by the institutional review board. These patients underwent catheterization for possible interventional procedures (eg, stent placement, electrophysiologic testing). The patients with a peak velocity across the RV outflow tract (RVOT) of >3 m/s by echocardiography were excluded. The average interval between CMR and catheterization was 2 ± 3 months. All patients, except for 1, underwent transannular patch repair of the RVOT; that patient underwent conduit placement. None underwent monocusp RVOT reconstruction or another valved type of intervention. Eight patients without right-sided lesions and normal right ventricles (5 with coarctation and 3 with aortic valve disease) were included as controls.

CMR Imaging Protocol

A standard electrocardiographic-gated CMR examination was performed on a 1.5-Tesla Siemens Avanto magnetic resonance system (Siemens Medical Solutions, Malvern, Pa). This consisted of static, steady-state, free precession for anatomy, cine CMR imaging for ventricular performance parameters (volumes), delayed enhancement to discern myocardial scarring, and PC-CMR for evaluation of the pulmonary flow. From PC-CMR imaging, the cardiac index was obtained. From cine CMR imaging, the ventricular function parameters such as RV end-diastolic volume, ejection fraction, and cardiac index were evaluated. Delayed enhancement imaging was used to determine myocardial scarring.

Cardiac Catheterization

Standard catheterization for TOF was performed. The oxygen saturation and pressure were obtained from both right- and left-sided structures

according to the routine protocol. Catheterizations were performed for diagnostic reasons and intervention (stent placement) under sedation.

Other Clinical Data

Routine echocardiographic data were collected to determine the grade of tricuspid insufficiency and the assessment of the RVOT. Electrocardiograms were obtained to assess the QRS duration.

Data Processing

Ventricular function. The ARGUS software (ARUGUS Software, Houston, Tex), resident on Siemens workstations, was used to evaluate ventricular function. The endocardial borders were traced (semiautomatically) by an expert observer. The segmented CMR slices were integrated along the long axis using Simpson's rule to extract the total ventricular volumes.

Flow quantification. An in-house program using Matlab (MathWorks, Natick, Mass), described previously,¹⁰ was used to process the PC-CMR images. The regurgitant fraction is the reverse flow divided by the forward flow multiplied by 100.

Evaluation of power output. Flow waveforms from PC-CMR and the systolic and diastolic pressures from catheterization were used to quantify the power output according to following equation:

$$\text{Power} = (0.5 \cdot \rho \cdot v_{\text{mean}}^2 + P_{\text{mean}}) \cdot Q_{\text{mean}}$$

where ρ is the blood density (a constant value of 1060 kg/m^3), v is the mean systolic velocity calculated in the systolic phase from PC-CMR ($Q_{\text{mean}}/\text{Area}_{\text{mean}}$), P_{mean} is the mean static systolic pressure measured in the main pulmonary artery during cardiac catheterization, and Q_{mean} is the mean flow rate in the systolic phase (forward flow, Figure 1) calculated from PC-CMR. The power output thus calculated is the mean power generated by the right ventricle in systole. This method has been used previously to evaluate the ventricular power output in single ventricle physiology.¹⁰

Evaluation of power loss. Similar to the power output, the PL due to PR was also evaluated using the previous equation. The mean diastolic pressure in the main pulmonary artery measured from catheterization was used as the P_{mean} , the mean flow in the diastolic phase (backward flow, Figure 1) was used as the Q_{mean} , and the mean backward velocity was used as the v_{mean} , all derived from PC-CMR. The net efficiency was as follows:

$$\text{Efficiency}(\%) = 100 \cdot \frac{\text{Power}_{\text{Total}} - \text{Power}_{\text{Loss}}}{\text{Power}_{\text{Total}}}$$

Parameter Normalization

Proper normalization of the parameters to account for patient-to-patient variability is necessary. The normalizing/indexing power using cardiac output or body surface area (BSA) assumes a linear relationship that might not be true because power is not linearly related to cardiac output or BSA. Dasi

and colleagues¹¹ have recently shown that $\rho \frac{Q^3}{\text{BSA}^2}$ (where Q is the mean flow rate or cardiac output, and ρ is the blood density) has the same dimension as power (Watts or $\text{kg} \cdot \text{m}^2/\text{s}^3$), and provides the appropriate normalizing parameter for power output, which transforms it to a dimensionless parameter (ie, dividing power by this parameter cancels out the dimensions, making the quotient dimensionless). Similarly, a dimensionless form of ventricular volumes was obtained by normalizing to $\text{BSA}^{1.5}$, instead of the BSA alone. This is because the unit of measure for $\text{BSA}^{1.5}$ is meters cubed, the same as for the ventricular volume. The dimensionless form of the ventricular volume is referred to as the “normalized” volume (RV end-diastolic volume [RVEDV_{Normalized}] and RV end-systolic volume). The present study also indexed the ventricular volumes to their standard

FIGURE 1. A, Typical main pulmonary artery (MPA) flow waveform in patients with tetralogy of Fallot (TOF) with pulmonary regurgitation (PR) (top curve). The waveform is divided into forward and backward phases to evaluate the total right ventricular (RV) power generated and power loss (PL) due to pulmonary regurgitation (PR). B, The images represent how the RV function and flow were obtained. Left, A 4-chamber view and short-axis views (rectangle on 4-chamber view) at end diastole and end systole (from left to right). C, Velocity map plane was obtained in the MPA (top) and an example of a velocity map (bottom).

clinical forms using just the BSA (mL/m^2), referred to as RVEDVI and RVESVI, respectively. The percentage of PL, percentage of ejection fraction, and percentage of power efficiency are dimensionless and do not require any additional normalization.

Statistical Analysis

All values are presented as the mean $\pm$ standard deviation. Descriptive statistics were used for general characteristics of the population. The relationships between the power output and ventricular volumes were established using their normalized dimensionless forms. PL, hydraulic efficiency, PR, and QRS duration were correlated with the clinical indexes of RVEDVI and RVESVI, respectively. Statistical significance was set at $P < .05$. Correlations between different parameters were evaluated using Microsoft Excel (Microsoft, Redmond, Wash) and Systat (Cranes Software, Chicago, Ill). The Pearson coefficient of correlation was used to describe the nature of the parametric relationship.

RESULTS

Baseline Characteristics and Standard Measures of Hemodynamics and Function

The baseline characteristics and standard measures of hemodynamics and ventricular performance are listed in Table 1. The right ventricle was dilated with a normal RV ejection fraction, and the LV size, ejection fraction, and cardiac output were normal. The QRS duration was prolonged (137 ± 33 ms) and the mean PR was $41\% \pm 14\%$. The mean gradient across the RVOT was 12 ± 21 mm Hg. Tricuspid insufficiency was trivial in 6 of 13 patients and mild in 6 patients. No significant aortic or mitral regurgitation was present. No myocardial scarring was noted in any of the patients; the RVOT patch demonstrated delayed enhancement in all patients. The control patient age was 12 ± 6.7 years, with a body surface area of 1.37 ± 0.64 m^2 and 0.21 ± 0.26 years from catheterization to CMR; none had PR.

Power Evaluation

The total RV power output was 1.08 ± 0.62 W. PR resulted in a PL of 0.24 ± 0.18 W, with a net RV power generation of 0.84 ± 0.48 W. This yielded an RV efficiency of $79.7\% \pm 8.6\%$. The total RV power output of the control patients was 0.8 ± 0.6 W, which appeared smaller than the total RV power output of the patients with TOF, although the difference was not statistically significant ($P = .32$). It was similar to the net RV power generation of the patients with TOF ($P = .87$). Figures 2 and 3 demonstrate the effect of PL on clinical indexes of RVEDVI and RVESVI, respectively. Significant positive correlations ($R = 0.78$ and $R = 0.69$) were noted between PL and RVEDVI and RVESVI, respectively (Figure 2). The RV power efficiency, which takes into account the PL indexed to the total power output, was plotted against the RV volumes in Figure 3. A significant inverse relationship was noted between the efficiency and ventricular volumes ($R = -0.78$ and $R = -0.69$ for RVEDVI and RVESVI, respectively).

TABLE 1. Baseline characteristics

Parameter	Value
Age (y)	21.9 ± 16.9
Body surface area (m^2)	1.34 ± 0.6
RV end-diastolic volume index (mL/m^2)	142 ± 48
RV end-systolic volume index (mL/m^2)	66 ± 37
RV ejection fraction (%)	56 ± 11
RF (%)	40.5 ± 13.8
LV end-diastolic volume index (mL/m^2)	72 ± 9
LV end-systolic volume index (mL/m^2)	26 ± 5
LV ejection fraction (%)	63 ± 5
Systemic flow (Q_s) (L/min) (CMR/catheterization)	$4.68 \pm 2.9/4.28 \pm 3.3$
Q_p (L/min)	4.24 ± 1.8
Systemic vascular resistance (Wood units)	26.2 ± 9.7
Pulmonary vascular resistance (Wood units)	2.54 ± 0.94
RV end-diastolic pressure (mm Hg)	4.3 ± 3.6
RV peak-systolic pressure (mm Hg)	49.3 ± 20.3
RV mean systolic pressure (mm Hg)	10.77 ± 6.1
LV end-diastolic pressure (mm Hg)	6.7 ± 4.8
LV peak-systolic pressure (mm Hg)	102.5 ± 22.0
LV mean systolic pressure (mm Hg)	10.62 ± 5.30
Systolic pulmonary artery pressure (mm Hg)	36.5 ± 11.3
Diastolic pulmonary artery pressure (mm Hg)	9.4 ± 4.5
Systolic systemic blood pressure (mm Hg)	102.6 ± 18.4
Diastolic systemic blood pressure (mm Hg)	62.8 ± 11.9
QRS duration (ms)	137 ± 33
Tricuspid regurgitation	
None	1
Trivial	6
Mild	6
RV power output (W)	1.08 ± 0.62
Power loss (W)	0.24 ± 0.18
Net efficiency (%)	79.75 ± 8.6

RV, Right ventricular; RF, regurgitant fraction; LV, left ventricular; CMR, cardiac magnetic resonance.

Figure 4 shows the relationship between the normalized RV total power output and the normalized RV volumes. A strong significant negative correlation was found between the normalized RV output power and $\text{RVEDV}_{\text{Normalized}}$. The RV power capacity decreased drastically as the $\text{RVEDV}_{\text{Normalized}}$ increased from 50 and 120 (120 is the inflection point at which the slope of the curve increases from < -1 to > -1 and at which the second derivative of this curve becomes 0). After 120, the curve flattens out, suggesting a possible critical state, after which the RV's ability to pump with adequate power diminishes. Because the mean BSA of the study population was 1.34 ± 0.6 m^2 , the RVEDVI can be estimated to be 139 mL/m^2 (120 $\text{mL}/\text{m}^2 \times 1.34^{0.5}$ m). Similarly, the RV power capacity decreased rapidly as the RVESVI increased, with an inflection point at a $\text{RVESV}_{\text{Normalized}}$ of 65 (corresponding to a clinical RVESVI of 75 mL/m^2).

The mean LV power was 1.82 ± 0.76 W. Mitral and aortic valve regurgitation was absent or trivial in all patients;

FIGURE 2. Relationship of right ventricular (RV) power loss (PL) with right ventricular end-diastolic volume index (RVEDVI) and right ventricular end-systolic volume index (RVESVI).

hence, all LV power was transferred to aortic flow (ie, PL on the left side was minimal).

Correlations of RV Volumes and Power With Other Measures

PR correlated well with both RVEDVI ($R = 0.79$) and RVESVI ($R = 0.72$). The QRS duration did not correlate with RVEDVI ($P = .806$) or RVESVI ($P = .482$). A relationship between the RVOT gradient and RV power output ($P = .35$) and PL ($P = .24$) was not present. Age also did not correlate with RV power output ($P = .27$); however, it did correlate with PL ($R = 0.57$, $P = .04$).

DISCUSSION

Power is simply energy per unit of time, and it would make sense that a heart that is required to pump a larger volume of blood must also expend more energy per unit of time to do so. The present study demonstrated that PL (average PL of 0.24 W in patients with TOF) can be assessed using a combination of CMR and catheterization. The mean value of the total RV power output of the patients with TOF was 1.08 W compared with 0.8 W in the control group. As expected, PL positively correlated with increasing RVEDVI,

FIGURE 3. Relationship between total right ventricular (RV) power efficiency and right ventricular end-diastolic and end-systolic volume indexes (RVEDVI and RVESVI, respectively).

RVESVI, and age. In addition, as the RVEDVI increased, a linear decrease occurred in RV efficiency, but a precipitous decrease occurred in the RV power output in an exponential fashion. The inflection point of the curve of RV power output versus $RVEDV_{\text{Normalized}}$ was 120 mL/m³, corresponding to an estimated RVEDVI of 139 mL/m².

Multiple studies have used routine parameters of ventricular function or flow to assess the postoperative TOF patient with PR. Nearly all have shown that depressed biventricular function is present at rest and during exercise using a number of different techniques such as CMR and radionuclide angiography.^{5,12} PR was correlated with a depressed LV ejection fraction ($r = -0.68$) and exercise tolerance ($r = -0.50$) by Niezen and colleagues.¹² Wessel and Paul¹³ performed a review of 22 exercise studies from 1990 onward and found that 14 had found a significant relationship of the degree of PR with abnormal RV function and decreased exercise capacity.

There have also been attempts to correlate ventricular performance and clinical status. Knauth and colleagues,¹⁴ in a follow-up period of just longer than 4 years, found that a greater RVEDVI (> 7 standard deviations) and a lower RV ejection fraction ($< 45\%$) correlated with an increasing

FIGURE 4. Relationship between normalized right ventricular (RV) power output and normalized RV end-diastolic and end-systolic volume indexes ($RVEDV_{Normalized}$ and $RVESV_{Normalized}$, respectively). Two sets of points (108.8 and 94.1 and 108.3 and 94.0) are right on top of each other and seem to appear as a single point.

probability of adverse events. An increasing New York Heart Association class has been found to be associated with lower LV ejection fraction (odds ratio, 3.88 for a 10% decrease; $P = .002$) and lower RV ejection fraction (odds ratio, 2.41 for a 10% decrease; $P = .01$).⁶ The regurgitant fraction, RVEDVI, and all the mentioned parameters result from the RV volume load due to the PR. These parameters are surrogates for the effect of the RV volume load on RV energetics, which is a more integrated assessment of function, drills down to ventricular performance on a more basic level and has been correlated with myocardial oxygen consumption.¹⁵ It could serve as a useful tool in predicting the clinical outcome and be a sentinel for deteriorating cardiorespiratory status.

Although this is the first study to demonstrate PLs in patients with TOF and its association with RV volumes, this is not the first study of power output or PL in congenital heart disease. Sundareswaran and colleagues¹⁰ demonstrated that patients with hypoplastic left heart syndrome had a much lower power capacity than patients with other forms of

single-ventricle morphology. In patients with Fontan circulation, Pekkan and colleagues¹⁶ demonstrated that a 7% decrease in energy losses corresponded with an 11% increase in cardiac output. Our laboratory has also shown a nonlinear, almost exponential increase in energy losses in the systemic venous pathway with increasing cardiac output.¹⁷

The findings of the present study, however, have implications beyond the realm of TOF and can be applied to other forms of heart disease. For example, repair of truncus arteriosus results in PR. Furthermore, the concept of PL in regurgitant lesions can be applied to adult valvular disease such as aortic or mitral insufficiency. PL could be a unifying concept and could possibly find utility as a predictor of outcomes; our findings might be the groundwork to investigate this concept in more detail.

PLs in the patient with TOF could have a clinical effect with regard to the timing of pulmonary valve replacement. RV volumes have been used as the key parameter in the past. Therrien and colleagues¹⁸ studied 17 patients with TOF using CMR before and after pulmonary valve replacement and found that the RVEDVI and RVESVI decreased 34% and 37%, respectively. Importantly, no patient achieved a normal RVEDVI and RVESVI after pulmonary valve competency if their RVEDVI before surgery was $>170 \text{ mL/m}^2$ and their RVESVI was $>85 \text{ mL/m}^2$. Valsangiacomo Buechel and colleagues¹⁹ performed a prospective study with CMR in patients with TOF of approximately 14 years with pulmonary valve replacement at an RVEDVI of greater than 150 mL/m^2 . They found a significant decrease in the RV volumes and mass after valve replacement and significant remodeling 6 months after surgery, concluding that an RVEDVI of 150 mL/m^2 was a good clinical cutoff to undergo pulmonary valve repair. These studies corroborate our findings of using an RVEDVI of 139 mL/m^2 for pulmonary valve replacement, which is close to the cutoff from the study by Valsangiacomo Buechel and colleagues.¹⁹ After this point, a greater than 1 unit of volume change must occur in the reverse direction along the curve shown in Figure 4 to elicit a 1-unit change in power capacity. Hence, if valve replacement is performed before the cutoff, a greater improvement in ventricular power capacity can be achieved with ventricular remodeling. RV volumes greater than these values are operating on the flat part of the RV power output–RVEDVI curve, where the right ventricle has less power output and its energetics are least favorable. The importance of the timing of pulmonary valve replacement in patients with TOF should not be underestimated. Studies in the past decade have shown that once the right ventricle becomes too dilated, functional recovery is lacking.^{20,21}

Our study is complementary to the recent report by Frigiola and colleagues,²² who had an aggressive pulmonary valve replacement strategy by operating on patients with an average RVEDVI of $142 \pm 43 \text{ mL/m}^2$, again very close

to our value of 139 mL/m². They found that replacing the pulmonary valve early led to RVEDVI normalization, improvement in biventricular function, and much improved submaximal exercise capacity. It could be that because this group had a much lower RVEDVI threshold to operate, they were intervening at the steep part of the RV power output curve delineated in our study, preserving RV function and exercise capacity and facilitating improvement in RV power capacity.

Study Limitations

This was a retrospective study with all the inherent biases accompanying this type of investigation. We also studied a small group of patients. A prospective study is needed to determine whether an RVEDVI of 139 mL/m² and an RVESVI of 75 mL/m² should be used as the cutoff values to replace the pulmonary valve. CMR and cardiac catheterization occurred approximately 2 months apart and were not simultaneous with each other. No change in clinical status was noted between these 2 examinations, and it is unlikely that the interval in between these studies significantly affected our results. In addition, the light, conscious sedation used for catheterizations (ie, diazepam, meperidine, midazolam, and fentanyl in some combination) in the doses given generally have little effect on systemic and pulmonary vascular resistance. The catheterization team would not want to obtain data that were not reflective of the patient's true physiology. Therefore, we believe that this did also not significantly affect the results.

CONCLUSIONS

Patients with TOF after repair with PR experience PLs due to the regurgitant volume of just more than 20% on average, despite a regurgitant fraction of 41%. The power output of the right ventricle decreases in an exponential fashion as the RV volume increases, with the curve flattening above an RVEDVI of 139 mL/m² and an RVESVI of 75 mL/m². The PL increases and RV power efficiency decreases with an increasing RV volume. This has implications for the timing of pulmonary valve replacement and could contribute to the decreased exercise performance in these patients. A prospective study is warranted.

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