

## Correlation of Right Ventricular dP/dt with Functional Capacity and RV Function in Patients with Mitral Stenosis

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**Background:** Evaluation of right ventricular (RV) contractility and systolic function in patients with right sided heart disease is an essential component of clinical management. The aim of this study was to assess RV systolic function by qualitative and quantitative methods and compare it to rate of ventricular pressure change during the isovolumic contraction period (dP/dt) as RV contractility index in patients with rheumatic mitral stenosis.

**Patients and Methods:** In 56 consecutive patients with moderate to severe mitral stenosis, RV systolic function, RV dP/dt and dP/dt/Pmax, were calculated and compared.

**Results:** There was significant correlation between RV dP/dt and RV function ( $P < 0.001$ ) and between RV dP/dt and New York Heart Association (NYHA) functional capacity ( $P < 0.001$ ). The mean of dP/dt was decreased with increasing severity of RV dysfunction (mean dP/dt was  $648 \pm 159$  for normal RV function,  $592 \pm 126$  for mild RV dysfunction,  $319 \pm 146$  for moderate RV dysfunction and  $166 \pm 150$  for severe RV dysfunction) Severity of tricuspid regurgitation and pulmonary hypertension had no significant effect on RV dP/dt and RV function. RV dP/dt/Pmax had also significant relationship with RV function and functional capacity ( $P < 0.001$ ).

**Conclusion:** Measurements of dP/dt and dP/dt/Pmax, are practical methods for estimating RV contractility and results have a good correlation with RV systolic function and functional capacity.

**Keywords:** Right ventricles, contractility, mitral stenosis

### Introduction

Echocardiographic assessment of right ventricular (RV) systolic function is challenging. Although originally RV was not considered much more than a conduit and reservoir, its importance in both acquired as well as congenital heart disease has become increasingly clear. RV function has an important role in determining cardiac output and functional capacity,<sup>1-8</sup> and estimation of right ventricular function is help-

ful to predict prognosis in various clinical situations such as primary pulmonary hypertension and dilated cardiomyopathy.<sup>9-13</sup> A qualitative assessment of the right ventricle is a routine part of echocardiography,<sup>1-3</sup> but visual assessment of RV function is suboptimal, and the complex shape of the right ventricle greatly complicates volume quantification and quantitative assessments such as ejection fraction and other indices that are used for the left ventricle. There are few clinically applicable quantitative methods to assess RV function and most of them depend on loading conditions.<sup>2</sup> The rate of ventricular pressure change during the isovolumic

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contraction period,  $dP/dt$ , is a well-established index of myocardial contractility, and is among the most widely used measurements of left ventricular (LV) contractility. Little data is available for RV  $dP/dt$ , and it had not been used routinely in clinical practice. Some authors suggested that RV  $dP/dt$  is a more accurate measurement of RV contractility, but no study has compared it to other RV systolic function indices such as tricuspid annular plane systolic excursion (TAPSE) or RV tissue Doppler imaging (TDI) S velocity.<sup>15-16</sup>

The aim of this study was to evaluate the correlation of RV  $dP/dt$  (as a contractility index) and RV systolic function (by qualitative and quantitative measurements) in patients with moderate to severe mitral stenosis (MS).

## **Patients and Methods**

### **Population**

We enrolled 56 consecutive patients with moderate to severe MS (by definition MV area < 1.5 cm<sup>2</sup>) who had a detectable tricuspid regurgitation (TR) jet and were referred to our center for percutaneous mitral commissurotomy. Patients with concomitant coronary artery disease, congenital heart disease, and severe rheumatic involvement of the aortic or tricuspid valves were excluded.

### **Echocardiographic evaluation**

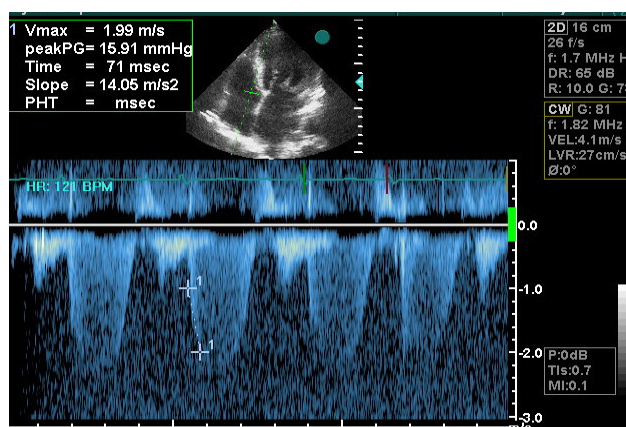
All patient underwent a clinical assessment and comprehensive two dimensional and Doppler echocardiography study with a commercially available ultrasound system (Vivid 3, GE ultrasound), equipped with a 2.5-MHz transducer. LV size and function was graded based on the American Society of Echocardiography

guidelines.<sup>17</sup> TR severity was visually assessed from multiple views. Jet area (percentage of right atrium area) and PISA radius with aliasing velocity of 28 cm/s were obtained for determining TR severity, which was graded as mild, moderate and severe according to the American Society of Echocardiography guidelines.<sup>18</sup>

TR velocity was recorded by Continuous wave (CW) Doppler echocardiography, with the aid of color Doppler echocardiography, to obtain the highest jet velocity of adequate quality and was recorded on a strip chart recorder at a paper speed of 100 mm/s. RV  $dP/dt$  was calculated from the interval between 1 m/s and 2 m/s velocity spectrum on the TR ( Fig. 1), therefore  $RV\ dP/dt = 12000 / \text{time}$  (in millisecond) was obtained by averaging 3 cycles in sinus rhythm and 5 cycles in atrial fibrillation. RV systolic function was graded as mild, moderate and severe by visual assessment and two other quantitative methods: tricuspid annular plane systolic excursion (TAPSE) and tissue Doppler imaging (TDI) tricuspid annulus S velocity. Given a reference value of 20 mm for TAPSE and 12 cm/sec for TDI, the RV was considered mildly impaired when TAPSE was between 15-20 mm and severely impaired when TAPSE was less than 10 mm.<sup>19-20</sup> The RV pressure was calculated from the sum of the TR pressure gradient and estimated RA pressure based on inferior vena caval (IVC) diameter.

Patient symptoms were classified according to the New York Heart Association (NYHA) functional classes (FC) I-IV.

To decrease variability of the echocardiographic measurements, all measurements were prospectively performed by a cardiologist with



**Figure 1:** RV dP/dt showing calculation of the interval between 1 m/s and 2 m/s velocity on the TR spectrum.

a level III training in echocardiography, and RV systolic function was assessed by another echocardiologist who was blinded to other measurements.

### Statistical Analysis

Interval data was expressed as means (SD) and categorical data was expressed as count (relative frequency). Statistical analysis was performed by using one-way analysis of variance (ANOVA) and its non-parametric equivalent, Kruskal-Wallis tests. Independent sample t and Chi-square tests were also used. P value less than 0.05 was considered significant.

Multiple analysis was performed, using ordinal logistic regression models between RV function and dP/dt and also RV function and dP/dt/  $P_{max}$ , adjusted for TR severity, Pulmonary artery hypertension (PAH), FC and LV ejection fraction (EF). SPSS 15 for Windows (SPSS Inc., Chicago, Illinois, USA) was used for statistical analysis.

### Reliability

Intra-observer variability was measured

by random selection of 20 echocardiographic records and reassessment dP/dt index. No significant difference was observed between two measurements (paired t test,  $p = 0.06$ ). Pearson's correlation coefficient  $r$  was 0.79, which suggest a good correlation among data. Bland-Altman plot showed that only one out of 20 (0.05) measurement was beyond the mean  $\pm 1.96$  SD range. This meant that there was a good agreement between two set of observations and therefore, acceptable intra-observer reliability.

## Results

### Baseline characteristics

56 patients (28 women), with a mean (SD) age of 54 (13.5) years (range 22 to 88 years) participated in the study. 48 cases (0.85) had sinus rhythm, 7 (0.13) had atrial fibrillation and 1 patient (0.02) had atrial flutter.

Estimated mean (SD) for left ventricular ejection fraction (LVEF) was 43.6 (9) percent. Mean heart rate (SD) was 76 (14.7) beat/min. LV size was in normal range mean (SD) of diastolic dimension was 5.1 (1) cm. We observed 2 patients (0.04) in NYHA functional class (FC) I, 28 (0.50) in FC II, 24 (0.42) in FC III and 2 (0.04) in FC IV.

Right ventricle (RV) function was normal in 10 (0.18), mild dysfunction in 12 (0.21), moderate dysfunction in 24 (0.43) and severe dysfunction in 10 (0.18) patients. Mean (SD) RV dP/dt was 408 (220) mmHg/s (range 94 to 1000 mmHg/s); also, RV dP/dt/ $P_{max}$  was estimated with a mean (SD) of 11.7(7.8) /s (range 1.81 to 31.96 /s)

Severity of tricuspid valve regurgitation (TR) was mild in 32(0.57), moderate in 14(0.25) and severe in 10 (0.18) patients. Mean (SD)

of pulmonary artery pressure (PAP) was 47.75 (21.04) mmHg. Twenty-five (0.45) patients had mild, 22 (0.39) moderate and 9 (0.16) severe pulmonary arterial hypertension (PAH).

### Relationships between RV function, dp/dt and dp/dt/p<sub>max</sub>

A statistically significant negative association was found between the state of RV function (as ordinal data) and dP/dt ( $P < 0.001$ ). Bonferroni post-hoc test revealed a statistically significant difference in mean of dP/dt in any subgroup of RV function, except the mean in normal RV function and mild RV dysfunction subgroups (Fig. 2-a). The mean of dP/dt decreased with increasing RV dysfunction.

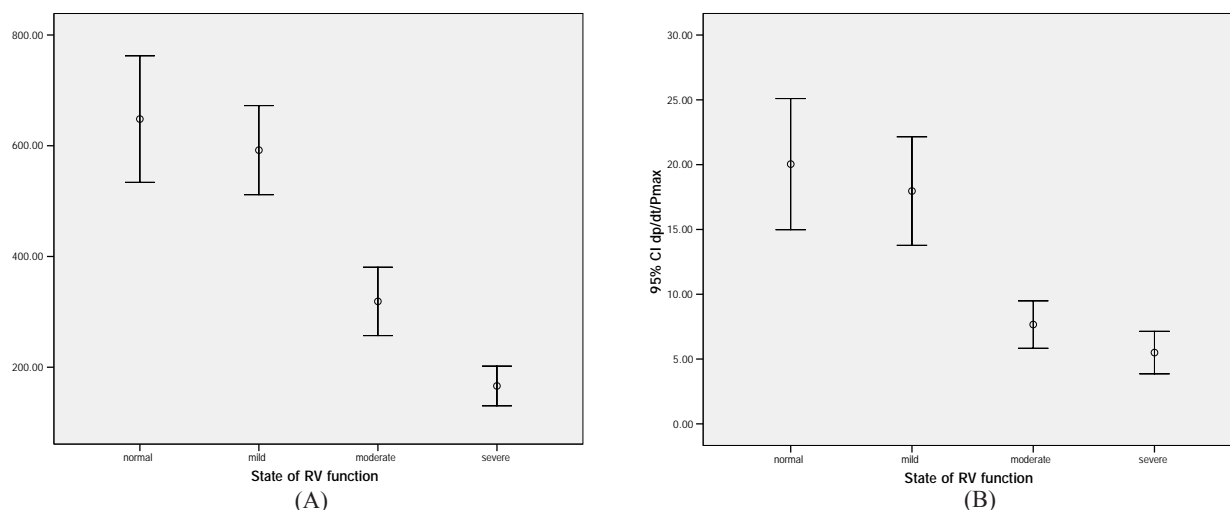
RV dP/dt ranged from 94 to 1000 mmHg/s; mean  $408 \pm 220$  mmHg/s. In normal RV function, mean dP/dt was  $648 (\pm 159)$ , in mild RV dysfunction, mean dP/dt was  $592 (\pm 126)$ , in moderate RV dysfunction, mean dP/dt was  $319 (\pm 146)$  and in severe RV dysfunction, mean dP/dt was  $166 (\pm 150)$ . There were significant correlation between RV dp/dt and RV function ( $P < 0.001$ ) and between RV dP/dt and NYHA functional capacity ( $P < 0.001$ ).

There was a significant difference between RV function and dP/dt/P<sub>max</sub> ( $P < 0.001$ ) and the results of Bonferroni post-hoc test was in agreement with those of dp/dt (Table 1, Fig. 2-b); RV dP/dt/Pmax showed significant relationship with RV function and functional capacity ( $P < 0.001$ ).

**Table 1.** Associations between the state of right ventricle function and other variables

	State of RV Function				P value
	Severe Dysfunction (n=10)	Moderate Dysfunction (n=24)	Mild Dysfunction (n=12)	Normal Function (n=10)	
<b>dP/dt mmHg/s *</b>	648 (159.7)	592 (126.6)	319 (146.3)	166 (150.1)	< 0.001
<b>dP/dt/P<sub>max</sub> /s *</b>	20 (7.1)	18 (6.6)	8 (4.3)	5 (2.3)	< 0.001
<b>LVEF percent *</b>	48 (10.2)	50 (4.9)	40 (8.8)	38 (7.8)	0.001
<b>FC †</b>					
<b>Class I</b>	2 (0.20)	0	0	0	0.002
<b>Class II</b>	7 (0.70)	9 (0.67)	10 (0.42)	2 (0.20)	
<b>Class III</b>	1 (0.10)	3 (0.33)	12 (0.50)	8 (0.80)	
<b>Class IV</b>	0	0	2 (0.08)	0	
<b>PAH†</b>					
<b>Mild</b>	5 (0.50)	8 (0.67)	6 (0.25)	6 (0.60)	0.038
<b>Moderate</b>	5 (0.50)	3 (0.25)	11 (0.46)	3 (0.30)	
<b>Severe</b>	0	1 (0.08)	7 (0.29)	1 (0.10)	
<b>TR Severity †</b>					
Mild	8 (0.80)	9 (0.75)	11 (0.46)	4 (0.40)	0.080
Moderate	2 (0.20)	2 (0.17)	7 (0.29)	3 (0.30)	
Severe	0	1 (0.8)	6 (0.25)	3 (0.30)	

RV: right ventricle; LVEF: left ventricle ejection fraction; FC: NYHA functional class; PAH: pulmonary artery hypertension; TR: tricuspid regurgitation. \* Numbers in the parentheses represent standard deviations. † Numbers in the parentheses represent relative frequency in each RV function subgroup.



**Figure 2:** Error bars show the relationship between the state of RV function and A) dp/dt; B) dp/dt/p<sub>max</sub>

### Relationships between RV function and other determinants

Bivariate associations between the state of RV function (as ordinal data) and TR severity, PAH (as ordinal data), FC and LVEF are shown in Table 1. LVEF had a significant association with the state of RV function ( $P=0.001$ ). There were significant differences between the mean values of LVEF in the subgroup with mild degrees of RV dysfunction and moderate and severe RV dysfunction ( $P < 0.01$ ). There was significant association between FC ( $P=0.002$ ) and PAH ( $P=0.038$ ) and RV function. No significant result was observed regarding TR se-

verity ( $p=0.08$ ). Also, age and gender did not have significant difference among subgroups ( $P=0.91$ ).

### Multiple analysis

Considering the state of RV function as an ordinal variable with 4 subgroups, we used two ordinal logistic regression models to determine the associations between RV function and dp/dt and also RV function and dp/dt/p<sub>max</sub>, adjusted for TR severity, PAH, FC, and LVEF. The results are presented in Table 2 and 3.

The first model showed a weak, reverse but statistically significant association between RV [0.983 - 0.993];  $P < 0.001$ ). No significant association remained among other variables (Table 2).

In the second model (Table 3), there was a reverse association between RV function and dp/dt/p<sub>max</sub> (odds ratio= 0.73, CI 95%: 0.64 - 0.84);  $P < 0.001$ ). Besides, FC and PAH had significant adjusted relationship with the state of RV function.

**Table 2.** Associations between the state of right ventricle function and dp/dt, adjusted for other determinants.

	Odds Ratio [CI 95%]	P value*
<b>dp/dt</b>	0.988 [0.983 - 0.993]	< 0.001
<b>LVEF</b>	0.94 [0.87 - 1.01]	0.110
<b>FC</b>	1.84 [0.56 - 6.12]	0.321
<b>PAH</b>	1.76 [0.76 - 4.07]	0.187
<b>TR Severity</b>	0.85 [0.33 - 2.15]	0.726

LVEF: left ventricle ejection fraction; FC: NYHA functional class; PAH: pulmonary artery hypertension; TR: tricuspid regurgitation.

\* Based on Wald test; values < 0.05 considered significant.



**Table 3.** Associations between the state of right ventricle function and  $dp/dt/p_{max}$ , adjusted for other determinants.

	Odds Ratio [CI 95%]	P value*
$dp/dt/p_{max}$	0.73 [0.64 - 0.84]	< 0.001
LVEF	0.94 [0.88 - 1.02]	0.127
FC	4.08 [1.27 - 13.16]	0.018
PAH	0.31 [0.12 - 0.78]	0.014
TR Severity	0.67 [0.28 - 1.61]	0.369

LVEF: left ventricle ejection fraction; FC: NYHA functional class; PAH: pulmonary artery hypertension; TR: tricuspid regurgitation.

\* Based on Wald test; values < 0.05 considered significant.

## Discussion

The evaluation of right ventricular (RV) systolic function is important for its clinical and prognostic value but difficult to obtain due to complex RV geometry. The instantaneous pressure-volume relationship of the RV may provide a more accurate measurement of RV contractility,<sup>21-24</sup> however, it is too invasive and is not suitable for a routine assessment. RV  $dP/dt$  which is a well-validated index of ventricular systolic performance is not dependent on RV geometry and can be easily estimated in any patient with TR jet. We selected RV  $dP/dt$  and RV  $dP/dt/P_{max}$  as RV contractility indices in patients with significant MS who had a detectable TR jet.

In this study we calculated RV  $dP/dt$  and RV  $dP/dt/P_{max}$  using Doppler echocardiography and demonstrated that these indices have a good correlation with both qualitative and quantitative assessment of RV function and the patient's functional capacity.

It has been suggested that RV  $dP/dt$  is less dependent on afterload<sup>4,21,25</sup> but dependent on preload; in contrast,  $dP/dt/P_{max}$  is considered to

be relatively insensitive to both preload and afterload, both theoretically and experimentally<sup>4</sup>. Using RV TDI S velocity and TAPSE for assessment RV systolic function, Saxena et al have demonstrated that RV systolic function had an excellent correlation with RV fractional area change regardless of the degree of PAH.<sup>26</sup> In our study we found no significant difference between patients with different TR severity and PAH when we adjusted them for evaluating associations between RV function and  $dP/dt$  and  $dP/dt/P_{max}$ . We therefore concluded that TR severity and PAH are not major confounding factors, and that RV  $dP/dt$  and  $dP/dt/P_{max}$  were relatively after load and pre-load independent.

We found a significant association between the state of RV function and LVEF, and other authors have suggested that there is a good correlation between TAPSE and LV systolic function.<sup>27</sup>

We also found a significant association between FC and PAH.

Kanzaki et al, found only a weak correlation between RV  $dP/dt$  and NYHA functional capacity.<sup>2</sup> Their study population was patients with dominant RV failure and they concluded that RV  $dP/dt/P_{max}$ , but not RV  $dP/dt$ , was a clinically useful index, whereas in our patients, both indices correlated significantly with NYHA FC. This difference might be due to the patient population selection. Our patients were in the entire spectrum of RV dysfunction, but they had only selected patients with severe RV dysfunction.

Our study showed a mean value of RV  $dP/dt$  for the spectrum of RV function (Table 1), although we could not find a significant difference between normal RV function and mild RV

dysfunction.

To our knowledge there is no documented normal value for RV dP/dt, and we demonstrated that there is some overlap between RV dP/dt value in patients with normal RV function and mild RV dysfunction. This could be due to a relatively small sample selection of these patients. Although we found a significant difference between moderate and severe RV dysfunction, more studies are needed to substantiate these values.

RV dP/dt and  $RV\ dP/dt/P_{max}$  are contractility indices of the isovolumic contraction time, and in the presence of TR there is no actual isovolumic time. It has been shown that MR per se had little effect on LV dP/dt,<sup>3, 4</sup> and although there is no similar data available, we hypothe-

size that TR also has little effect on RV dP/dt.

Although magnetic resonance imaging (MRI) is considered as the gold standard for quantization of ventricular volumes and systolic function, subjective assessment, eyeballing, by echocardiography is the modality most often used for the RV.<sup>14</sup> We selected quantitative methods that are clinically applicable and have a high specificity and negative predictive value for detecting abnormal RV systolic function.<sup>19</sup>

Measurements of RV dP/dt, and  $dP/dt/P_{max}$ , are practical methods for estimating RV contractility and have a good correlation with RV systolic function and functional capacity.

**Conflicts of Interest** no declare.

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