Congenital Heart Disease

Restrictive Right Ventricular Physiology

Its Presence and Symptomatic Contribution in Patients With Pulmonary Valvular Stenosis

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Objectives	The aim of this study was to examine whether restrictive right ventricular (RV) physiology (the presence of ante-grade pulmonary arterial flow in late diastole) occurred in patients with moderate to severe isolated pulmonary valvular stenosis (PVS) and to estimate its prevalence and relationship to RV function and patient symptoms.
Background	Little is published about RV diastolic performance in adult patients with PVS.
Methods	A total of 43 consecutive patients (age 44 ± 10 years) with moderate to severe PVS referred to Royal Brompton Hospital from 2002 to 2005 were retrospectively studied. Patient New York Heart Association (NYHA) functional class was recorded. The RV (lateral tricuspid annulus motion) long-axis movement was measured by M-mode and pulsed-wave (PW) tissue Doppler imaging (TDI). Restrictive RV physiology was assessed by PW Doppler echocardiography.
Results	Eighteen patients (42%) had restrictive RV physiology. They were more symptomatic (NYHA functional class 1.8 ± 0.5 vs. 1.3 ± 0.5; p < 0.001) and had poorer RV long-axis function (TDI peak systolic velocity 7.3 ± 2.1 cm/s vs. 9.7 ± 2.7 cm/s; TDI early diastolic velocity 6.6 ± 1.6 cm/s vs. 8.5 ± 2.4 cm/s; RV long-axis systolic amplitude 1.3 ± 0.2 cm vs. 1.5 ± 0.3 cm; p < 0.01 for all) compared with other PVS patients despite similar RV ejection fraction, myocardial performance index, and RV systolic pressure. The presence of restrictive RV physiology (odds ratio [OR] 6.05, 95% confidence interval [CI] 1.45 to 10.29; p = 0.01) and peak pulmonary valve pressure gradient (OR 1.07, 95% CI 1.01 to 1.13; p = 0.04) were the 2 independent echocardiographic predictors for decreased exercise tolerance in patients on multivariate analysis.
Conclusions	Restrictive RV physiology is common in PVS patients. Its presence is related to a worse deterioration in RV long-axis function and decreased exercise tolerance in patients. (J Am Coll Cardiol 2007;50:1491–7) © 2007 by the American College of Cardiology Foundation

Isolated pulmonary valvular stenosis (PVS) occurs in 7% to 10% of patients with adult congenital heart disease, and balloon dilation is the mainstay of treatment in anatomically suitable lesions (1). Current recommendations for the timing of intervention depend on the severity of outflow tract obstruction and the presence of symptoms (2). Data are scant to address the impact of chronic increase in right ventricular (RV) outflow resistance on RV diastolic performance. The RV filling indexes measured by pulsed-wave (PW) Doppler (peak E- and A-wave velocities, E-wave

deceleration time and isovolumic relaxation time) have the drawbacks of heart rate and load dependency as well as the lack of generally acceptable reference values, particularly for different age groups. Our center has previously reported that the RV restrictive filling pattern (antegrade pulmonary arterial flow in late diastole) (3) predicted postoperative outcomes (4,5) and long-term RV restriction (6) in repaired tetralogy of Fallot (TOF) as a result of long-standing pressure overload. This late diastolic forward flow in the pulmonary artery coincided with premature pulmonary valve opening (3). Simultaneous catheter pressure monitoring demonstrated that this flow occurred when RV end-diastolic pressure equaled or exceeded pulmonary arterial diastolic pressure (3,7). Such findings suggested that RV compliance fell and the cavity became stiff and, therefore, acted as a passive conduit between the right atrium and the pulmonary artery during atrial systole. This Doppler finding of RV restriction reported in children was different from the

Abbreviations and Acronyms

Ea = pulsed-wave tissue Doppler imaging early diastolic velocity

MPI = myocardial performance index

NYHA = New York Heart Association

PASP = pulmonary arterial systolic pressure

PV = pulmonary valve

PVS = pulmonary valvular stenosis

RAP = right atrial pressure

RV = right ventricular

RVSP = right ventricular systolic pressure

Sa = pulsed-wave tissue Doppler imaging peak systolic velocity

TDI = tissue Doppler imaging

TOF = tetralogy of Fallot

restrictive filling pattern of the left ventricle (LV) in adults, which was well characterized by a large E/A ratio (>2), a short E-wave deceleration time (<160 ms), and a short isovolumic relaxation time (<70 ms) (8). The clinical implication of restrictive RV filling pattern in adult PVS patients was unknown. The present study aimed to investigate the prevalence of restrictive RV physiology in adult PVS patients and its relationship to RV function and symptoms.

Methods

Study population. We retrospectively studied 43 consecutive patients with moderate to severe isolated PVS who were followed up in an adult congenital heart disease clinic and received transthoracic echocardiographic examination between 2002 and 2005. Patient blood pressure was measured supine at the same time. Significant PVS was defined as continuous-wave (CW) Doppler-derived peak pulmonary valve (PV) gradient >40 mm Hg (2). The New York Heart Association (NYHA) functional class, other cardiovascular symptoms, and comorbidities were recorded. Patients with Noonan's syndrome, suboptimal echocardiographic windows, pacemakers, atrial fibrillation, bundle branch block, previous surgical pulmonary valvotomy, and/or other significant cardiac lesions (especially more than a mild degree of pulmonary regurgitation) were excluded from the study. Included results were compared with 27 age- and gender-matched healthy subjects, randomly sampled from our database, with a structurally normal heart and without a history of cardiovascular diseases.

Echocardiography. Echocardiograms were obtained using a Philips Sonos 5500 system (Philips, Andover, Massachusetts). At least 3 consecutive beats in sinus rhythm were recorded, and the average values were taken.

Peak and mean PV gradients were measured from CW Doppler recordings from parasternal short-axis view at aortic valve level by modified Bernoulli equation (9,10). A pulsed-wave (PW) Doppler of pulmonary arterial flow was obtained with the sample volume 1 cm distal to the pulmonary valve (3,4,7). Restrictive RV physiology was defined as the presence of antegrade pulmonary arterial flow in late diastole throughout the respiratory cycle (3,7). Prominent hepatic vein and superior vena cava diastolic flow reversals, if any, were recorded by PW Doppler and color M-mode techniques (4,8). The LV and RV filling indexes

were obtained by placing a 2-mm PW Doppler sample volume at the tip of mitral valve and tricuspid valve leaflets, respectively, from an apical 4-chamber view. Peak E- and A-wave velocities, E/A ratio, E-wave deceleration time and isovolumic time were then measured. The LV and RV myocardial performance indexes (MPI) were calculated (11,12). The LV and RV ejection fractions were measured using Simpson volume estimates. Tricuspid regurgitation was assessed by color-flow and CW Doppler. Pulmonary arterial systolic pressure (PASP) was calculated by the following formulas (13):

$$RVSP = 4 \times (\text{peak tricuspid regurgitation velocity})^2 + RAP$$

$$PASP = RVSP - \text{peak PV gradient}$$

where RVSP = right ventricular systolic pressure, and RAP = right atrial pressure (assessed by inferior vena cava size and collapsibility) (14).

Segmental myocardial function was assessed by recording long-axis motions at lateral tricuspid and septal annular sites with M-mode and PW tissue Doppler imaging (TDI) techniques (15). Long-axis systolic amplitude and peak systolic (Sa), early diastolic (Ea), and late diastolic velocities were all measured. All recordings were made using a sweep speed of 100 mm/s, with an electrocardiogram (lead II) and a phonocardiogram superimposed.

Reproducibility. Intraobserver and interobserver variability were assessed in 18 randomly chosen patients. Variability was calculated as the percentage error, derived as the absolute difference between 2 sets of measurements, divided by the mean of the observations.

Statistics. The software used was SPSS version 13 (SPSS Inc., Chicago, Illinois). All continuous variables were analyzed using the Kolmogorov-Smirnov test for normality and were expressed as mean $\pm$ SD or median and range as appropriate. Differences between 3 groups (control and 2 patient groups) were evaluated by 1-way analysis of variance with Bonferroni or Kruskal-Wallis with Mann-Whitney U test (Bonferroni adjustment) according to data distributions. Categoric variables were expressed as frequency and compared by chi-square test. Correlations were tested with Pearson coefficients. Echocardiographic predictors (global and segmental indexes for RV function, estimated pressures, and the presence of RV restriction) for symptom (decreased exercise tolerance) were identified with univariate analysis, and multivariate logistic regression was performed by the stepwise method. A significant difference was defined as $p < 0.05$ (2-tailed).

Results

Table 1 lists patients' clinical data. The patients had similar age, gender prevalence, heart rate, and systemic blood pressure as the control subjects. No other cardiovascular comorbidities or medications were recorded in PVS pa-

Table 1	Patient Characteristics		
Variables	Control Subjects (n = 27)	PVS Without Restrictive RV Physiology (n = 25)	PVS With Restrictive RV Physiology (n = 18)
Demographics			
Age (yrs)			
At presentation		21 ± 7	23 ± 8
At echocardiographic examination	38 ± 7	37 ± 9	38 ± 9
Gender (M/F)	13/14	11/14	8/10
Heart rate (beats/min)	70 ± 7	68 ± 6	68 ± 9
Blood pressure (mm Hg)			
Systolic	121 ± 10	119 ± 10	122 ± 12
Diastolic	69 ± 9	70 ± 10	68 ± 11
History of balloon valvuloplasty		6/25 (24%)	5/18 (28%)
Hepatic vein/superior vena cava diastolic reversal		7/23 (30%)	16/18 (89%)*
NYHA functional class	1.0 ± 0	1.3 ± 0.5†	1.8 ± 0.5†‡
Symptoms			
Decreased exercise tolerance	—	8/23 (35%)	13/18 (72%)*
Palpitation	—	2/23 (9%)	4 (22%)
Chest pain	—	1/23 (4%)	2 (11%)
Comorbidities/medications	—	—	—
Echocardiographic evaluation of PVS severity			
Peak PV gradient (mm Hg)	2.7 ± 0.7	60.3 ± 13.9†	62.3 ± 12.8†
Mean PV gradient (mm Hg)	1.8 ± 0.5	40.5 ± 9.2†	41.8 ± 7.8†
RV systolic pressure (mm Hg)	22.0 ± 4.1	80.6 ± 15.8†	82.4 ± 13.7†
Right atrial pressure (mm Hg)	5.7 ± 1.8	10.6 ± 2.4†	15.6 ± 2.4†‡
Pulmonary arterial systolic pressure (mm Hg)	19.4 ± 4.2	20.3 ± 4.2	20.2 ± 4.3

*p < 0.05, comparison between patient groups; †p < 0.001 versus control; ‡p < 0.001, comparison between patient groups.
NYHA = New York Heart Association; PV = pulmonary valve; PVS = pulmonary valvular stenosis; RV = right ventricular.

tients. Eighteen of the 43 PVS patients (42%) had restrictive RV physiology. The 2 patient groups were of similar age at initial presentation and prevalence of balloon valvuloplasty. Patients with RV restriction had a higher prevalence of prominent diastolic flow reversal in the hepatic vein or superior vena cava (89% vs. 30%, p < 0.05), were more symptomatic (NYHA functional class 1.8 ± 0.5 vs. 1.3 ± 0.5; p < 0.001; decreased exercise tolerance 72% vs. 35%; p < 0.05), had higher RAP (15.6 ± 2.4 mm Hg vs. 10.6 ± 2.4 mm Hg; p < 0.001) despite similar RV outflow resistance (peak PV gradient 62.3 ± 12.8 mm Hg vs. 60.3 ± 13.9 mm Hg; RVSP 82.4 ± 13.7 mm Hg vs. 80.6 ± 15.8 mm Hg; and PASP 20.2 ± 4.3 mm Hg vs. 20.3 ± 4.2 mm Hg; p = NS for all comparisons) compared with other PVS patients.

The control subjects and PVS patients had similar LV ejection fractions, filling indexes, and MPI (Table 2). The PVS patients with RV restriction, however, had a higher tricuspid inflow A-wave velocity and a shorter E-wave deceleration time than control subjects (A-wave velocity 52 ± 18 cm/s vs. 39 ± 16 cm/s; p < 0.01; E-wave deceleration time 166 ± 28 ms vs. 184 ± 25 ms; p < 0.05) despite similar RV ejection fractions and MPI. These patients also had a shorter tricuspid inflow E-wave deceleration time than other PVS counterparts (p < 0.01).

Table 3 shows segmental function of all subjects. The RV (lateral tricuspid annulus) and septal long-axis systolic ampli-

tudes were reduced in the 2 patient groups compared with control subjects (p < 0.01 for all). Patients also had lower Sa and Ea velocities and higher E/Ea ratios at both sites than control subjects (p < 0.05 for all).

Patients with restrictive RV had lower RV and septal systolic amplitudes and Sa and Ea velocities and higher E/Ea ratios compared with other nonrestrictive PVS patients (p < 0.05 for all). A significant relation was also found between RAP and RV E/Ea ratio in PVS patients (r = 0.54; p = 0.002), indicating that RV E/Ea could be a potential surrogate for assessing RV filling pressure in these patients. The difference in segmental myocardial function between patient groups was independent of RV ejection fraction and MPI. A significant moderate inverse relation was found between RV long-axis velocities (Sa, Ea) and RVSP in patients without restrictive RV physiology (Figs. 1A and 1B). Such close coupling between RV long-axis function and outflow resistance, however, was not observed in patients with RV restriction. (Figs. 1C and 1D).

Predictors for symptoms. We identified several univariate predictors of decreased exercise tolerance in patients: peak PV gradient, the presence of restrictive RV physiology, RV E-wave deceleration time, long-axis systolic amplitude, and Sa and Ea velocities (p < 0.05 for all). Only the presence of restrictive RV physiology (odds ratio [OR] 6.05, 95% confidence interval [CI] 1.45 to 10.29; p = 0.01) and peak PV gradient (OR 1.07, 95% CI 1.01 to 1.13; p = 0.04) were

Table 2	Global Biventricular Function		
Variables	**Control Subjects (n = 27)**	**PVS Without Restrictive RV Physiology (n = 25)**	**PVS With Restrictive RV Physiology (n = 18)**
Left ventricle			
Ejection fraction (%)	69 ± 6	66 ± 8	68 ± 6
Myocardial performance index	0.34 ± 0.06	0.35 ± 0.06	0.33 ± 0.06
E-wave (cm/s)	72 ± 15	72 ± 18	71 ± 18
A-wave (cm/s)	51 ± 10	57 ± 13	58 ± 14
E/A ratio	1.4 ± 0.2	1.3 ± 0.5	1.3 ± 0.4
E-wave deceleration time (ms)	200 ± 22	194 ± 43	194 ± 36
Isovolumic relaxation time (ms)	66 ± 15	70 ± 13	68 ± 8
Right ventricle			
Ejection fraction (%)	58 ± 13	55 ± 12	57 ± 14
Myocardial performance index	0.29 ± 0.07	0.31 ± 0.05	0.32 ± 0.08
E-wave (cm/s)	53 ± 13	55 ± 12	57 ± 14
A-wave (cm/s)	39 ± 16	46 ± 17	52 ± 18*
E/A ratio	1.4 ± 0.3	1.3 ± 0.5	1.3 ± 0.6
E-wave deceleration time (ms)	184 ± 25	187 ± 32	166 ± 28†‡
Isovolumic relaxation time (ms)	62 ± 18	65 ± 14	63 ± 12

*$p < 0.01$ versus control; †$p < 0.01$, comparison between patient groups; ‡$p < 0.05$ versus control.
Abbreviations as in Table 1.

independent predictors of symptoms after multivariate analysis.

Intraobserver and interobserver variability. Intraobserver and interobserver variability for conventional Doppler and TDI-derived variables (LV and RV E-wave deceleration time, Sa, Ea) ranged from 1% to 6%. Reproducibility of long-axis measurements has been published previously (15).

Discussion

This was the first study that examined the potential existence of restrictive RV physiology in adults with isolated PVS and compared them with other PVS patients and normal control subjects. We demonstrated that restrictive RV physiology was common and occurred in as many as 42% patients with moderate to severe PVS. Furthermore, its presence was related to more RV long-axis dysfunction and the loss of close coupling between RV long-axis function and outflow resistance. Lastly, the presence of restrictive RV physiology was a strong determinant of decreased exercise tolerance in patients.

Characterization of diastolic performance in PVS patients. Pulmonary valve stenosis is a common adult congenital heart disease that can be treated effectively with balloon dilation or surgery (1). Decision for intervention based on Doppler-derived peak PV gradient (2) has the drawback of overestimating the disease severity, and con-

Table 3	Segmental Myocardial Function					
Variable	**Group 1: Control (n = 27)**	**Group 2: PVS Without Restrictive RV Physiology (n = 25)**	**Group 3: PVS With Restrictive RV Physiology (n = 18)**	**p Value (1 vs. 2)**	**p Value (1 vs. 3)**	**p Value (2 vs. 3)**
Septal annular long-axis systolic amplitude (cm)	1.4 ± 0.2	1.2 ± 0.3	1.0 ± 0.2	0.002	<0.001	0.010
TDI						
Sa (cm/s)	9.1 ± 2.0	6.8 ± 1.5	5.7 ± 1.3	<0.001	<0.001	0.026
Ea (cm/s)	10.8 ± 2.0	7.8 ± 1.8	6.4 ± 2.4	<0.001	<0.001	0.030
Aa (cm/s)	7.1 ± 2.3	6.4 ± 1.4	7.3 ± 2.0	0.397	0.627	0.189
E/Ea	6.8 ± 1.4	9.7 ± 2.9	11.0 ± 3.5	<0.001	<0.001	0.115
RV (lateral tricuspid annular) long-axis systolic amplitude (cm)	2.4 ± 0.4	1.5 ± 0.3	1.3 ± 0.2	<0.001	<0.001	0.027
TDI						
Sa (cm/s)	11.0 ± 2.0	9.7 ± 2.7	7.3 ± 2.1	0.039	<0.001	0.001
Ea (cm/s)	9.9 ± 3.1	8.5 ± 2.4	6.6 ± 1.6	0.049	<0.001	0.015
Aa (cm/s)	8.1 ± 2.5	8.2 ± 2.8	8.4 ± 2.4	0.774	0.641	0.753
E/Ea	5.8 ± 2.2	7.0 ± 2.7	9.2 ± 3.1	0.049	<0.001	0.009

Aa = pulsed-wave tissue Doppler imaging late diastolic velocity; Ea = pulsed-wave tissue Doppler imaging early diastolic velocity; PVS = pulmonary valvular stenosis; RV = right ventricular; Sa = pulsed-wave tissue Doppler imaging peak systolic velocity; TDI = tissue Doppler imaging.
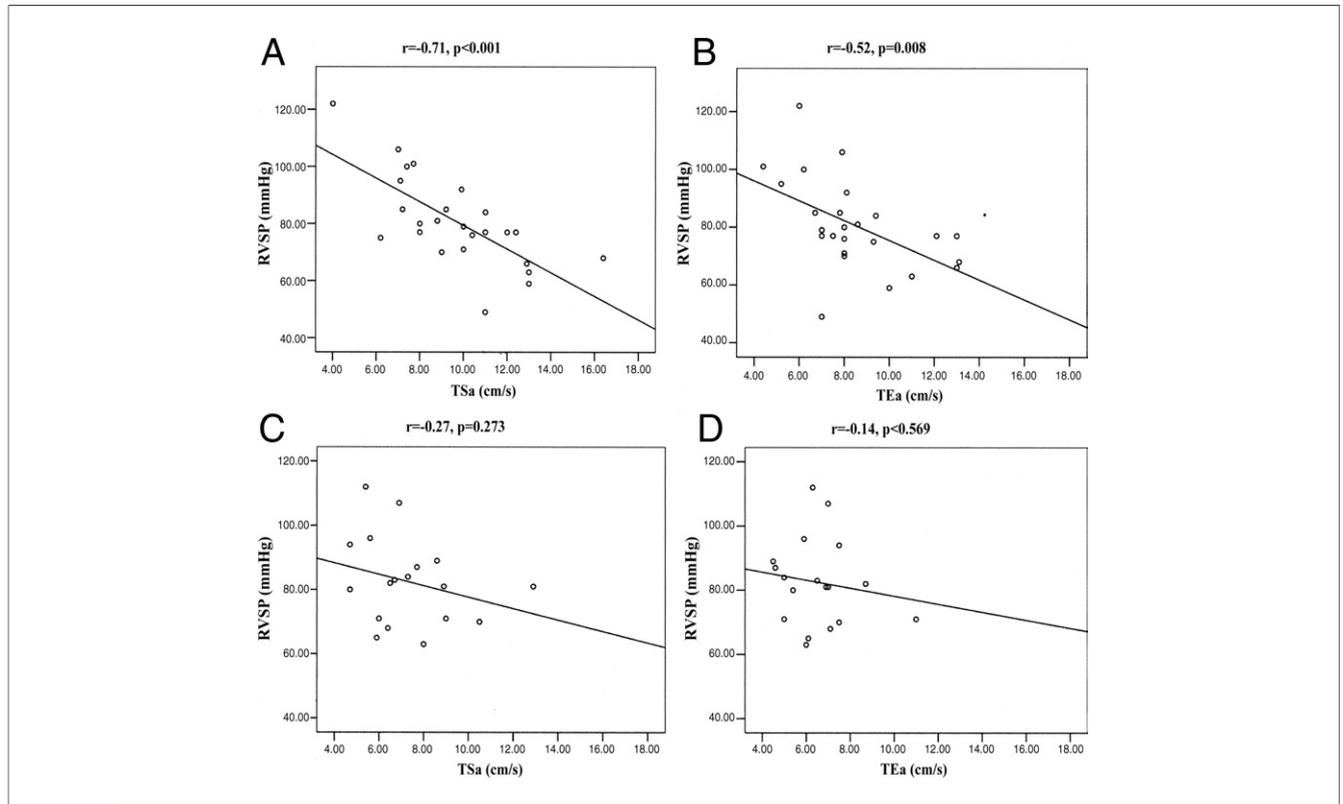
Figure 1 Relationship Between RVSP and Long-Axis Velocities (TSa, TEa) in Patients Without and With Restrictive RV Physiology

(A,B) Patients without restrictive right ventricular (RV) physiology; (C,D) patients with restrictive RV physiology. RVSP = right
ventricular systolic pressure; TSa, TEa = tissue Doppler imaging lateral tricuspid annular peak systolic and early diastolic velocity, respectively.

troversy exists on whether peak or mean pressure gradients would be more accurate (9,10,16,17). Unlike aortic stenosis, in which the occurrence of LV diastolic dysfunction has been well characterized and is related to the development of symptoms (18), little is known about that in PVS patients. Because RV systolic function is generally preserved in PVS patients, characterization of RV diastolic performance and its relation to symptoms is important. The present study observed a relatively high prevalence of restrictive RV filling (42%) in PVS patients. Such a restrictive filling pattern is associated with elevation of RAP, a shorter tricuspid E-wave deceleration time, and more RV long-axis dysfunction compared with other PVS patients and normal control subjects. Interestingly, we also demonstrated a trend of progressive fall in long-axis systolic amplitudes as well as Sa and Ea velocities from control subjects to patients without restrictive physiology to those with restrictive RV physiology. These findings were in contrast to the RV ejection fraction and MPI, which were similar in the 3 groups. Both RV long-axis systolic amplitudes and TDI velocities have been validated as surrogate markers for RV function (19,20). Because RV long-axis impairment could also be affected by cardiopulmonary bypass (21), interventricular conduction abnormalities (22), and cardiac lesions in addition to RV outflow tract obstruction, patients with previous surgical valvotomy, bundle branch block, and significant pulmonary regurgitation were excluded from the present study. Thus our data confirmed the selective sensitivity of long-axis function, which was previously documented in patients with LV outflow tract obstruction (15,23), in unveiling RV myocardial dysfunction in RV outflow tract obstruction as well.

Furthermore, we reported that patients with RV restriction were more likely to experience exercise intolerance. Among all echocardiographic variables, the presence of restrictive RV physiology (p = 0.01) and peak PV gradient (p = 0.04) were the only 2 independent determinants for decreased exercise tolerance on multivariate analysis. It seems that the development of restrictive physiology might herald a "sicker" RV as a result of chronic increase in afterload irrespective of preserved systolic function as measured by ejection fraction. Such postulation was evident by its association with a worse deterioration in RV long axis function and it being the strongest determinant of patient symptoms.

Mechanism of restrictive RV physiology in PVS patients. The fundamental abnormality of restrictive RV physiology is reduced RV compliance as a result of a chronic increase in afterload. In essence, the RV end-diastolic pressure increases and the cavity becomes unfillable during atrial systole and acts as a passive conduit. Thus, some or all of the
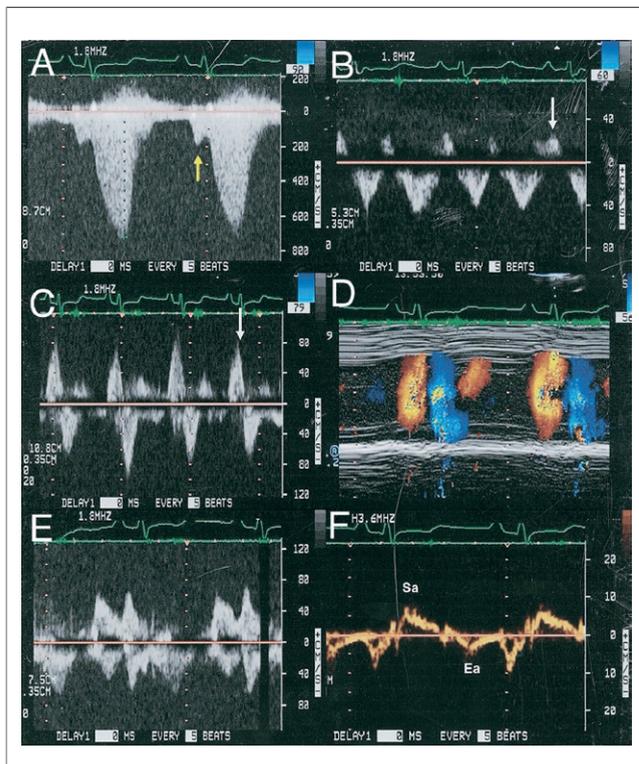
Figure 2   **Example of a Pulmonary Valvular Stenosis Patient With Restrictive RV Physiology**

(A) Continuous-wave (CW) Doppler recording showed the antegrade pulmonary flow in late diastole **(yellow arrow)** which was coincident with premature pulmonary valve opening during atrial systole (indicated by P-wave of electrocardiographic tracing). A CW Doppler instead of pulsed-wave (PW) Doppler recording was shown to illustrate severe pulmonary stenosis (estimated peak pulmonary valve gradient >100 mm Hg). **(B, C)** Prominent diastolic flow reversals **(white arrows)** seen after atrial systole in hepatic vein **(B)** and superior vena cava **(C)**. **(D)** Prominent diastolic flow reversal **(red)** in the hepatic vein could be better visualized with color M-mode technique. **(E)** A PW Doppler recording of tricuspid inflow showed a short E-wave deceleration time with a high A-wave velocity. **(F)** A PW tissue Doppler imaging trace at the lateral tricuspid annulus showed depressed peak systolic (Sa) and early diastolic (Ea) velocities. RV = right ventricular.

transtricuspid atrial systolic flow, demonstrable by Doppler, results in antegrade pulmonary blood flow (3,4). The findings of a higher prevalence of diastolic flow reversal in the hepatic vein or superior vena cava, a shorter E-wave deceleration time, and a higher E/Ea ratio and RAP observed in these patients were consistent with restrictive RV with significant elevation of RV filling pressure (Fig. 2). We previously addressed reduced long-axis velocity in hypertrophic cardiomyopathy patients that could be secondary to underlying myocardial fiber disarray or fibrosis (24). In the present study we demonstrated a significant inverse relationship between the degree of outflow obstruction (indicated by RVSP) and RV long-axis motion in PVS patients without RV restriction. Such close coupling was lost in patients with restrictive RV physiology, suggesting that factors other than afterload increase itself were involved in the cavity physiology. Recent histologic studies reported a higher collagen load in LV myocardium in aortic stenotic

patients with severe diastolic dysfunction (25). If we allow the same pathologic interpretations to be applied in our patients with PVS, then the profound RV myocardial fibrosis explains the diastolic restrictive RV physiology. Earlier studies reported a higher prevalence of RV restriction in TOF patients who received transannular patch repair, because of its greater association with more RV scarring than transatrial repair (26). Early repair of TOF to relieve RV outflow tract obstruction was shown to prevent subsequent development of RV restriction (27). Our center, using cardiac magnetic resonance with the late gadolinium enhancement technique, further demonstrated that RV restriction in repaired TOF patients was related to more RV myocardial fibrosis and a worse clinical outcome (28). Taking all of the above together, it seems that PVS patients with RV restriction are likely to have higher collagen deposition in the RV myocardium, which subsequently contributes to the increase in RV stiffness, impairment of RV long-axis function, and development of exercise intolerance.

Study implications. Adult patients with restrictive RV complicating PVS had more RV dysfunction and symptoms. We therefore suggest including assessment of restrictive RV physiology in future studies that may shed further light on the mechanism of myocardial damage in pressure-overloaded RV and predict potential reversibility of long-axis function in a fashion similar to what we previously addressed in patients with raised LV afterload caused by peripheral vascular disease (29). Regular follow-up of adult PVS patients using RV Doppler echocardiographic measurements should guide toward early identification of myocardial dysfunction and the need for removal of outflow tract obstruction before irreversible damage occurs.

Study limitations. Most limitations were inherent to the retrospective design and the small sample size. However, the study included a respectable contemporary cohort of PVS patients, given that it is a rare disorder. The current state-of-the-art machine with myocardial tissue Doppler imaging and speckle tracking techniques may provide in-depth regional quantitative assessment of RV dysfunction. Furthermore, invasive data were not available, particularly on absolute pulmonary artery pressure, which might have explained some other contributing factors. Finally, we did not have objective exercise tolerance and cardiac magnetic resonance imaging data to validate patients' symptoms and the degree of RV fibrosis, which may have further consolidated our hypothesis.

Conclusions

The RV diastolic function characteristic of restrictive physiology occurs in a significant proportion of PVS patients and is related to a worse deterioration of RV long-axis function and decreased exercise tolerance in these patients.

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