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ORIGINAL PAPER

Simple and noninvasive method to estimate right ventricular operating stiffness based on echocardiographic pulmonary regurgitant velocity and tricuspid annular plane movement measurements during atrial contraction

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Abstract
It was recently shown that invasively determined right ventricular (RV) stiffness was more closely related to the prognosis of patients with pulmonary hypertension than RV systolic function. So far, a completely noninvasive method to access RV stiffness has not been reported. We aimed to clarify the clinical usefulness of our new echocardiographic index of RV operating stiffness using atrial-systolic descent of the pulmonary artery-RV pressure gradient derived from pulmonary regurgitant velocity ($PRPGD_{AC}$) and tricuspid annular plane movement during atrial contraction ($TAPM_{AC}$). We studied 81 consecutive patients with various cardiac diseases who underwent echocardiography and cardiac catheterization. We measured $PRPGD_{AC}$ and $TAPM_{AC}$ using continuous-wave Doppler and M-mode echocardiography, respectively, and calculated $PRPGD_{AC}/TAPM_{AC}$. RV end-diastolic pressure (RVEDP) and RV pressure increase during atrial contraction (ΔRVP_{AC}) were invasively measured, and RV volume change during atrial contraction (ΔV_{AC}) was calculated from echocardiographic late-diastolic transtricuspid flow time-velocity integral and tricuspid annular area; thus $\Delta RVP_{AC}/\Delta V_{AC}$ was used as the standard index for RV operating stiffness. $PRPGD_{AC}/TAPM_{AC}$ well correlated with $\Delta RVP_{AC}/\Delta V_{AC}$ ($r = 0.84$, $p < 0.001$) and RVEDP ($r = 0.80$, $p < 0.001$), and the area under the receiver operating characteristic curve to discriminate RVEDP > 12 mmHg was 0.94. Multivariate regression analysis revealed that $PRPGD_{AC}/TAPM_{AC}$ was the single independent determinant of $\Delta RVP_{AC}/\Delta V_{AC}$ ($\beta = 0.86$, $p < 0.001$). $PRPGD_{AC}/TAPM_{AC}$ is useful to estimate RV operating stiffness and a good practical indicator of RVEDP.

Keywords Echocardiography · Pulmonary regurgitation · Right ventricular stiffness · Right heart failure

Abbreviations

CMR	Cardiac magnetic resonance
ΔP	Pressure change
ΔRVP_{AC}	RV pressure increase during the atrial contraction
ΔV	Volume change
ΔV_{AC}	Right ventricular volume change during atrial contraction
EDPVR	End-diastolic pressure–volume relation
LV	Left ventricular
PA	Pulmonary artery
PAH	Pulmonary arterial hypertension
PR	Pulmonary regurgitant
$PRPGD_{AC}$	The descent of pulmonary regurgitant pressure gradient during atrial contraction
RV	Right ventricular
RVEDP	Right ventricular end-diastolic pressure
$TAPM_{AC}$	Tricuspid annular plane movement during atrial contraction
TAPSE	Tricuspid annular plane systolic excursion

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Introduction

In recent years, the prognosis of patients with left heart disease and pulmonary arterial hypertension (PAH) has been shown to be associated with right ventricular (RV) systolic function assessed by various parameters, such as the tricuspid annular plane systolic excursion (TAPSE), RV fractional area change, RV ejection fraction, tissue Doppler-derived peak systolic tricuspid annular velocity and speckle tracking-derived RV longitudinal strain [1–4]. A more recent study by Trip et al. highlighted that the RV diastolic stiffness measured by single-beat RV pressure–volume analysis using a right heart catheter and cardiac magnetic resonance (CMR) was more closely related to patient's prognosis than the RV systolic function at both baseline and in treated patients with idiopathic and heritable PAH [5].

Generally, the assessment of ventricular operating stiffness requires both the ventricular pressure change (ΔP) and volume change (ΔV) [6]. However, the RV pressure is usually measured using an invasive catheterization procedure and the accurate measurement of RV volume is not easy because of its complex geometry [7–9]. Trip et al. [5, 10] employed CMR RV volumetry to analyze the RV pressure–volume relationship. However, CMR volumetry is a time-consuming procedure, and the inadequate time resolution and difficulty in late-diastolic imaging of CMR may compromise its accuracy [11]. Instead of the direct measurement of RV volume, Otsuji et al. [12] estimated the RV ΔV due to right atrial (RA) contraction using echocardiography by multiplying the tricuspid annular area and the velocity–time integral during atrial-systole. However, their method was also somewhat complex and time-consuming, and still required an invasive measurement of the RV pressure. There is thus need of a completely noninvasive method to assess RV operating stiffness.

Recently, we reported that the pulmonary regurgitant (PR) velocity waveform derived from continuous-wave Doppler echocardiography can reflect the late-diastolic RV pressure curve [13]. We assumed that the rise in atrial-systolic RV pressure may be estimated from the descent of the pulmonary artery (PA)-RV pressure gradient during atrial contraction derived from PR velocity ($PRPGD_{AC}$). We also speculated that a tricuspid annular plane movement during atrial contraction ($TAPM_{AC}$) could be used as a surrogate for the RV ΔV due to atrial contraction. Thus, the aim of this study was to determine the clinical usefulness of the $PRPGD_{AC}$ divided by $TAPM_{AC}$ ($PRPGD_{AC}$/$TAPM_{AC}$) as a simple and noninvasive index of RV operating stiffness by comparing it with the RV operating stiffness measured using Otsuji's method and RV end-diastolic pressure (RVEDP).

Methods

Subjects

Among 146 consecutive patients who were admitted to Hokkaido University Hospital from January 2013 to December 2015 and underwent an echocardiographic examination and right heart catheterization within a 1-week interval under stable clinical conditions, we excluded 30 patients with atrial fibrillation and 12 with tachycardia (heart rate ≥ 100 bpm). Of the remaining 104 patients, an adequate Doppler flow velocity waveform of PR could not be obtained in 18 patients, and $TAPM_{AC}$ could not be measured due to an insufficient echocardiographic image of the anterior tricuspid annulus in other 5 patients. Thus, the measurement of $PRPGD_{AC}$/$TAPM_{AC}$ was successful in 81 of the 104 patients (78%). The underlying diseases were ischemic heart disease in 35 patients, cardiomyopathy in 18, valvular heart disease in 16, congenital heart disease in 3, hypertensive heart disease in 3, idiopathic arrhythmia in 2, and other in 4. Among the 81 patients, 16 had pulmonary hypertension defined as mean PA pressure ≥ 25 mmHg [14]. Causes of pulmonary hypertension were left heart diseases in 15 and congenital heart disease in 1.

This study was approved as a retrospective observational study by the Research Ethics Committee of Hokkaido University Hospital and the Ethics Committee of the Faculty of Health Sciences in Hokkaido University. Instead of obtaining informed consent, the program of the present study had been open to the public both through the home page and on the bulletin board of Hokkaido University Hospital.

Echocardiographic measurements

Echocardiography was performed using an Aplio XG/Artida system equipped with a 2.5/3.0 MHz probe (Toshiba Medical Systems, Otawara, Japan), a Vivid E9 ultrasound system with an M5S probe (GE Healthcare, Little Chalfont, UK), or an iE33 ultrasound system with an S5-1 probe (Philips Medical Systems, Eindhoven, The Netherlands).

Basic echocardiographic parameters were measured according to the guidelines of the American Society of Echocardiography [15–17]. TAPSE was measured by placing an M-mode cursor through the tricuspid annulus of the RV free wall in the apical 4-chamber image [1, 15, 18]. We also measured $TAPM_{AC}$ as a surrogate for the RV ΔV during atrial contraction (Fig. 1a). To determine the RV ΔV during atrial contraction (ΔV_{AC}) by Otsuji's method, we measured the tricuspid annular diameters in the RV inflow tract and the apical 4-chamber views, calculating the tricuspid annular area as an ellipse under the assumption that these diameters represent the major and minor axes. We measured

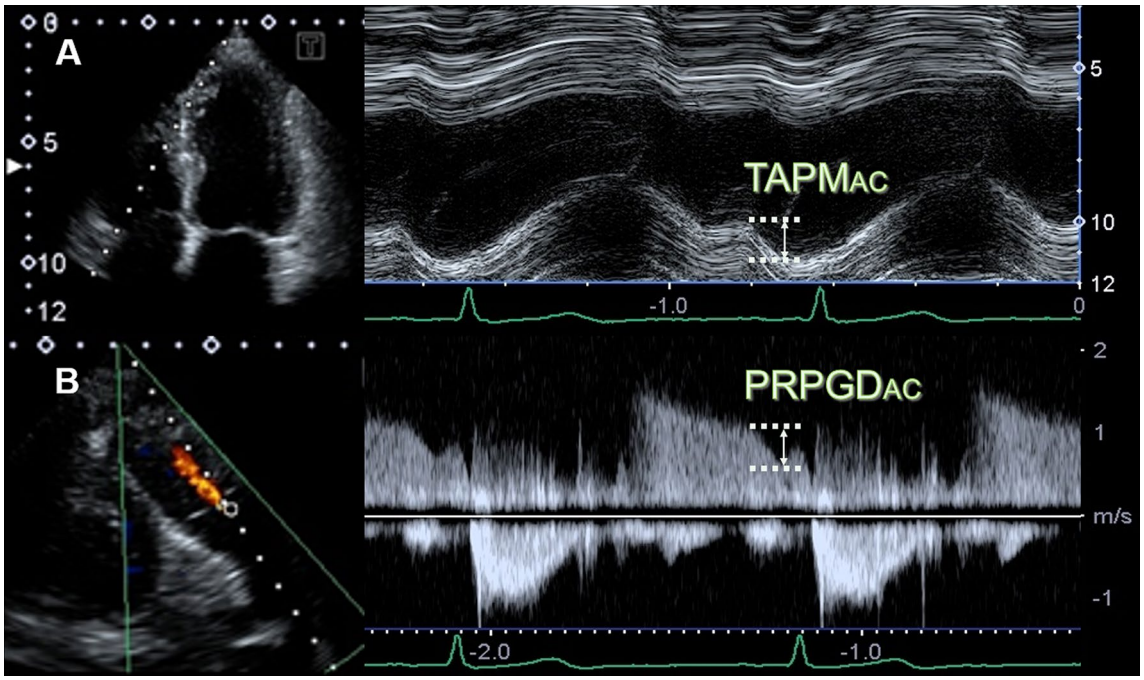

Fig. 1 Our method for echocardiographic estimation of right ventricular operating stiffness. **a** M-mode echocardiographic measurement of the tricuspid annular plane movement during atrial contraction ($TAPM_{AC}$). **b** Continuous-wave Doppler measurements of the descent of pulmonary regurgitant pressure gradient during atrial contraction ($PRPGD_{AC}$). The ratio of $PRPGD_{AC}$ to $TAPM_{AC}$ was calculated as a new echocardiographic index of right ventricular operating stiffness

the velocity–time integral of the late-diastolic transtricuspid flow, and obtained ΔV_{AC} by calculating the product of the velocity–time integral and the tricuspid annular area [12].

The PR flow velocity was recorded using continuous-wave Doppler echocardiography during a breath-hold at shallow expiration or at the intermediate expiratory position under quiet respiration [19]. In order to minimize the incident angle of the beam to the PR jets, the color flow signal of a jet was visualized in two mutually orthogonal planes, and the flow velocity was recorded from the window providing the least incident angle and the greatest PR velocity [19, 20]. We measured the PR velocities just before RA contraction and at bottom of the dip during RA contraction to calculate the PA-RV pressure gradients at both timings. Then, $PRPGD_{AC}$ was determined by subtracting the latter from the former (Fig. 1b). When the dip was very small, the time just before RA contraction was assumed to be 0.11 s after the onset of the electrocardiographic P wave based on our previous study [13]. In addition, the ratio of $PRPGD_{AC}$ to $TAPM_{AC}$ was calculated as our new echocardiographic index of the RV operating stiffness.

Measurements of RVEDP and RV operating stiffness

Right heart catheterization was performed using a Swan-Ganz catheter. From the pressure records, we measured the mean RA pressure, RV pre-atrial contraction pressure, RV pressure increase during the atrial contraction (ΔRVP_{AC}), RVEDP, mean PA pressure, and mean PA wedge pressure (Fig. 2). Pulmonary vascular resistance was calculated as the difference between the mean PA pressure and mean PA wedge pressure divided by cardiac output measured using the thermodilution method. Averaged values of five consecutive beats during end-expiratory breath-holding were used for the analysis. Using the catheterization ΔRVP_{AC} and echocardiographic ΔV_{AC}, we calculated the $\Delta RVP_{AC}/\Delta V_{AC}$ ratio as a standard index for RV operating stiffness during late-diastole [6, 12]. Because the ΔV_{AC} was not clearly recorded in 4 subjects, the $\Delta RVP_{AC}/\Delta V_{AC}$ could be calculated in the remaining 77 subjects.

Statistical analysis

The statistical analysis was performed using standard statistical software (IBM SPSS ver. 25 for Windows, IBM Co., Armonk, NY, USA). All numerical data are presented as means ± SD. Relationships between two parameters were assessed by the linear correlation and regression analysis. The prediction interval was calculated and displayed on a scatter plot. A receiver operating characteristic curve analysis was performed to evaluate the ability to predict the elevation of the catheterization

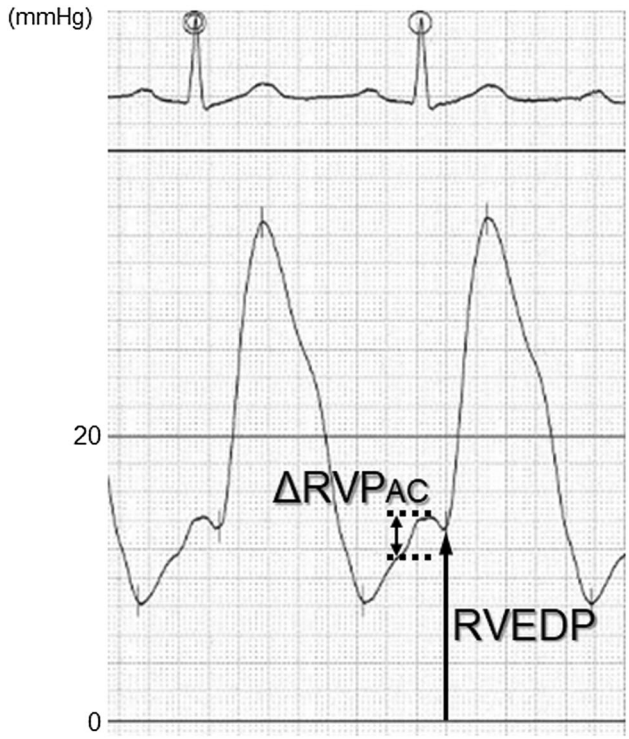

Fig. 2 Catheterization measurements of right ventricular pressure increase during atrial contraction (ΔRVP_{AC}) and right ventricular end-diastolic pressure (RVEDP)

RVEDP (> 12 mmHg). A stepwise multivariate regression analysis was performed to find independent determinants of $\Delta RVP_{AC}/\Delta V_{AC}$ among multiple echocardiographic parameters including $PRPGD_{AC}/TAPM_{AC}$. For all statistical tests, a $p < 0.05$ was used to indicate significance. Intraobserver and interobserver variabilities for $PRPGD_{AC}/TAPM_{AC}$ were assessed in 20 randomly selected patients from the present study between two measurements by one observer (M. M.) and between two observers (M. M. and K. O.).

Results

Patient characteristics

The clinical, echocardiographic and catheterization data of the patients are summarized in Table 1. Among the 81 study patients, RV dilatation (RV basal dimension > 42 mm) was present in 21 patients (26%), reduced RV systolic function (TAPSE < 16 mm) in 21 (26%), elevated RVEDP (> 12 mmHg) in 16 (20%) and elevated mean RA pressure (> 8 mmHg) in 23 (28%). Data associated with RV operating stiffness are summarized in Table 2.

Comparison between our new echocardiographic parameters and the conventional ones

The Doppler-derived $PRPGD_{AC}$ was significantly and well correlated with the catheterization ΔRVP_{AC} ($r = 0.77$, $p < 0.001$) (Fig. 3a). The echocardiographic $TAPM_{AC}$ was also significantly and fairly well correlated with the conventional echo-Doppler derived ΔV_{AC} ($r = 0.69$, $p < 0.001$) (Fig. 3b).

Our new echocardiographic parameter for RV operating stiffness, $PRPGD_{AC}/TAPM_{AC}$, was significantly and excellently correlated with the conventional one, $\Delta RVP_{AC}/\Delta V_{AC}$ ($r = 0.84$, $p < 0.001$) (Fig. 4a). The $PRPGD_{AC}/TAPM_{AC}$ was also significantly and very well correlated with RVEDP ($r = 0.80$, $p < 0.001$) (Fig. 4b).

In the receiver operating characteristic analysis to identify the patients with abnormal elevation of RVEDP (> 12 mmHg), the area under the curve was 0.94 for $PRPGD_{AC}/TAPM_{AC}$ (Fig. 5), which had 81% sensitivity and 92% specificity at the optimal cut-off value of 0.6.

Multivariate regression analysis

The relationships of the $\Delta RVP_{AC}/\Delta V_{AC}$ to age and the echocardiographic parameters including $PRPGD_{AC}/TAPM_{AC}$ are summarized in Table 3. Stepwise multivariate regression analysis to find the determinant of the $\Delta RVP_{AC}/\Delta V_{AC}$ using age, RV basal dimension, RA minor-axis dimension, inferior vena cava dimension, TAPSE, systolic peak gradient across the tricuspid valve derived from tricuspid regurgitant velocity and $PRPGD_{AC}/TAPM_{AC}$ as explanatory variables revealed that the $PRPGD_{AC}/TAPM_{AC}$ was the single independent determinant for $\Delta RVP_{AC}/\Delta V_{AC}$.

Reproducibility of measurements

Intraobserver and interobserver measurements for $PRPGD_{AC}/TAPM_{AC}$ showed interclass correlation coefficients of 0.93 and 0.86, respectively, indicating satisfactory reproducibility of the measurement of $PRPGD_{AC}/TAPM_{AC}$.

Discussion

The present study demonstrated that our new echocardiographic parameter for RV operating stiffness, $PRPGD_{AC}/TAPM_{AC}$, correlated well with that determined using

Table 1 Patient characteristics

Variable	Mean ± SD	Range
Baseline characteristics		
Age (years)	63 ± 16	20–88
Male/female	53/28	
Heart rate (bpm)	64 ± 10	47–93
Body surface area (m^2)	1.64 ± 0.91	1.18–2.05
Systolic blood pressure (mmHg)	115 ± 22	74–164
Underlying heart disease, n (%)		
Ischemic heart disease	35 (43%)	
Cardiomyopathy	18 (22%)	
Valvular heart disease	16 (20%)	
Hypertensive heart disease	3 (4%)	
Congenital heart disease	3 (4%)	
Idiopathic arrhythmia	2 (2%)	
Others	4 (5%)	
Medications, n (%)		
ARBs and/or ACEIs	39 (48%)	
β-blockers	36 (44%)	
Calcium-channel blockers	10 (12%)	
Diuretics	35 (43%)	
Digitalis	4 (5%)	
Statins	24 (30%)	
Antiplatelet agents	22 (27%)	
Echocardiographic parameters		
Left ventricular end-diastolic dimension (mm)	56.6 ± 14.3	31.0–95.0
Left ventricular mass index (g/m^2)	126 ± 47	45–256
Left ventricular ejection fraction (%)	48.7 ± 19.5	12–83
Left atrial volume index (ml/m^2)	51.4 ± 29.4	10.5–139.1
E (cm/s)	72.8 ± 23.4	30.7–136.5
A (cm/s)	66.4 ± 27.8	13.3–136.5
E/A	1.5 ± 1.2	0.5–5.5
Right ventricular basal dimension (mm)	38.5 ± 7.9	26.0–62.0
Right atrial minor-axis dimension (mm)	40.6 ± 7.7	25.0–63.0
Inferior vena cava dimension (mm)	14.3 ± 4.6	6.0–30.0
Tricuspid annular plane systolic excursion (mm)	18.1 ± 4.3	8.0–28.0
Right heart catheterization parameters		
Pulmonary arterial wedge pressure (mmHg)	13.2 ± 8.0	4.0–38.0
Mean pulmonary arterial pressure (mmHg)	20.6 ± 9.8	9.8–52.0
Pulmonary vascular resistance (WU)	2.1 ± 1.8	0.0–13.5
Right ventricular pre-atrial contraction pressure (mmHg)	6.9 ± 3.2	0.1–17.3
Right ventricular end-diastolic pressure (mmHg)	8.7 ± 3.8	0.7–19.4
Mean right atrial pressure (mmHg)	6.3 ± 3.7	0.0–18.0

Data are mean ± SD or number of patients

ARB angiotensin II receptor-blocker, *ACEI* angiotensin-converting enzyme inhibitor, *E* peak early diastolic transmitral flow velocity, *A* peak late diastolic transmitral flow velocity

Otsuji's partially invasive method, $\Delta RVP_{AC}/\Delta V_{AC}$, and the catheterization RVEDP, and could readily distinguish the patients with elevated RVEDP (> 12 mmHg) from those without. The $PRPGD_{AC}/TAPM_{AC}$ can be measured noninvasively and simply using only echocardiography. The present study is the first to report the usefulness of a noninvasive method for estimating RV operating stiffness.

Table 2 Parameters associated with right ventricular operating stiffness

Parameters	Mean ± SD	Range
Echocardiographic parameters		
$TAPM_{AC}$ (mm)	9.3 ± 3.4	3.2–19.0
ΔV_{AC} (ml)	51.3 ± 15.4	18.5–94.5
$PRPGD_{AC}$ (mmHg)	3.4 ± 1.6	1.1–9.7
Right heart catheterization parameter		
ΔRVP_{AC} (mmHg)	2.0 ± 1.3	0.4–6.9
Right ventricular operating stiffness parameters		
$PRPGD_{AC}/TAPM_{AC}$ (mmHg/mm)	0.4 ± 0.3	0.1–1.4
$\Delta RVP_{AC}/\Delta V_{AC}$ (mmHg/ml)	0.04 ± 0.04	0.01–0.17

Data are mean ± SD or number of patients

$TAPM_{AC}$ tricuspid annular movement during atrial contraction, ΔV_{AC} right ventricular volume change during atrial contraction, $PRPGD_{AC}$ the descent of pulmonary regurgitant pressure gradient during atrial contraction, ΔRVP_{AC} right ventricular pressure increase during atrial contraction

Appropriate timing to measure ventricular operating stiffness in a clinical setting

The most comprehensive and specific means of characterizing ventricular passive diastolic properties is the end-diastolic pressure–volume relation (EDPVR) obtained from the pressure–volume loop [8, 21]. However, it is difficult to assess EDPVR in clinical patients because it requires intentional stepwise preload alteration, which is invasive and may even be hazardous to the patients. To estimate ventricular operating stiffness in a clinical setting, the ΔP/ΔV at atrial-systole has been considered a more practical substitute for EDPVR than the ΔP/ΔV during earlier diastole, which may be more strongly influenced by ventricular relaxation and viscous and inertial properties of the ventricular myocardium [22]. In fact, in several previous clinical studies, the left ventricular (LV) operating stiffness was estimated from the ΔP/ΔV during atrial contraction [22–25].

Otsuji et al. [12] reported the usefulness of the RV ΔP/ΔV during atrial contraction to obtain RV operating stiffness. They obtained the RV operating stiffness as the ratio of the micromanometer-derived RV ΔP to the echocardiographically derived RV ΔV during atrial-systole. We think that their method is reasonable because they used Doppler flowmetry, which is suited for the accurate measurement of minute and quick RV volume changes during atrial contraction. In the clinical context, however, their approach had some drawbacks, such as the invasiveness of the RV pressure measurement, and the somewhat complex and time-consuming process of the RV ΔV measurement. For these reasons, their method has not been widely adopted for routine clinical practice.

Previous challenges to the estimation of elevated RV stiffness by echocardiography

Sakai et al. [26] showed that the hepatic vein flow pattern, i.e., the velocity of the systolic wave divided by that of the diastolic wave using pulse-wave Doppler, correlated relatively well with RVEDP (r = − 0.64) in 60 patients with

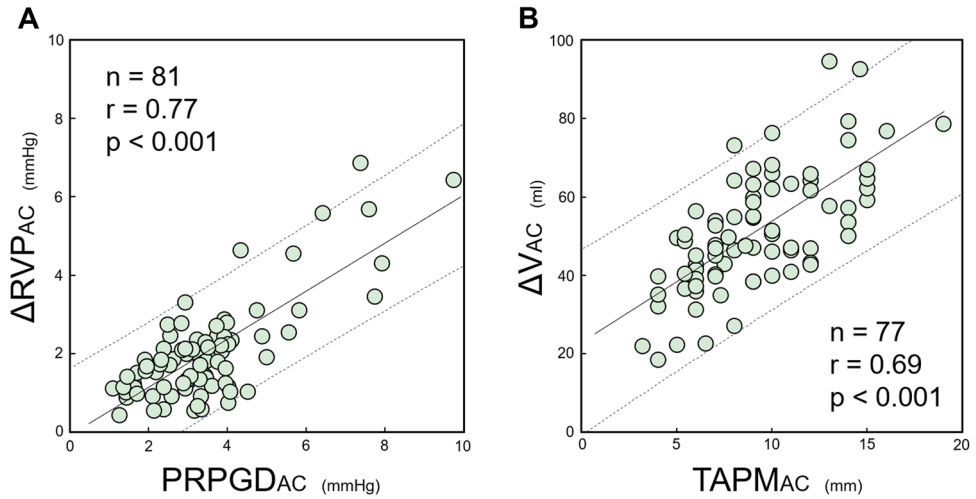

Fig. 3 Comparison between echocardiographic parameters used to calculate our new index for right ventricular operating stiffness and the standard ones. Correlation between the parameters of pressure increase during atrial-systole (**a**) and that between the parameters of volume increase during atrial-systole (**b**) are shown. The regression lines (solid line) and 95% prediction intervals (dashed line) are provided. $PRPGD_{AC}$ the descent of pulmonary regurgitant pressure gradient during atrial contraction, ΔRVP_{AC} right ventricular pressure increase during the atrial contraction, $TAPM_{AC}$ the tricuspid annular plane movement during atrial contraction, ΔV_{AC} right ventricular volume change during atrial contraction

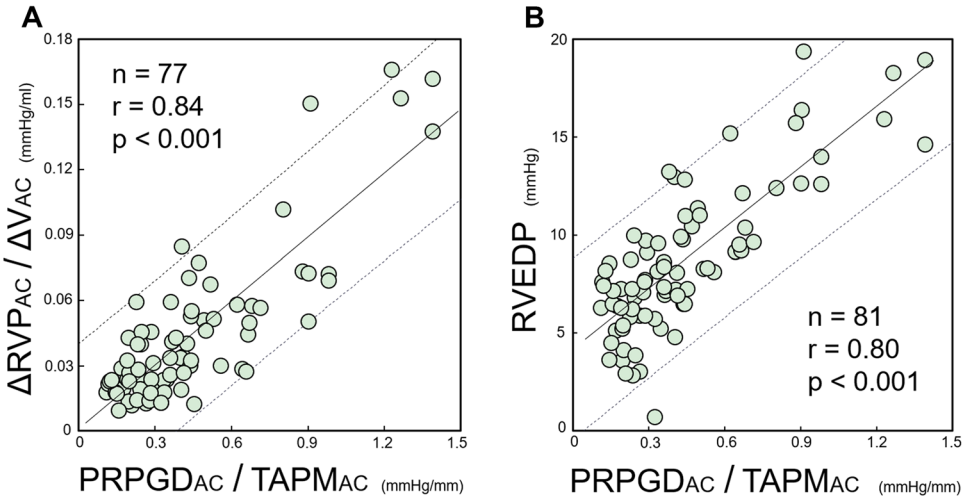

Fig. 4 Relationship of our new echocardiographic index for right ventricular operating stiffness ($PRPGD_{AC}/TAPM_{AC}$) to the invasively determined stiffness ($\Delta RVP_{AC}/\Delta V_{AC}$) (**a**) and right ventricular end-diastolic pressure (RVEDP) (**b**). The regression lines (solid line) and 95% prediction intervals (dashed line) are provided

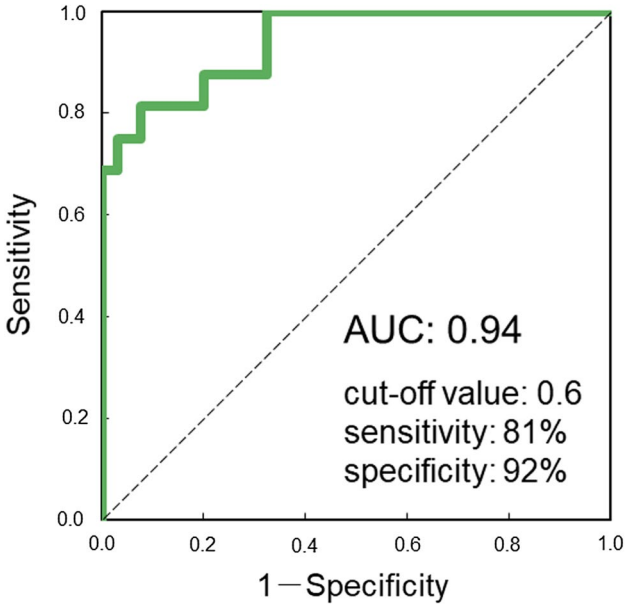

Fig. 5 Receiver operating characteristic curves for the echocardiographically estimated right ventricular (RV) operating stiffness ($PRPGD_{AC}/TAPM_{AC}$) to distinguish patients with RV end-diastolic pressure > 12 mmHg

Table 3 Stepwise multivariate regression analysis to find the determinants of the $\Delta RVP_{AC}/\Delta V_{AC}$ among age, RVD, RAD, IVCD TAPSE, TRPG and $PRPGD_{AC}/TAPM_{AC}$ as explanatory variables

	Univariable		Multivariable	
	r	p value	β	p value
Age	− 0.01	0.25		
RVD	0.40	< 0.001		
RAD	0.26	< 0.05		
IVCD	0.47	< 0.001		
TAPSE	− 0.37	< 0.01		
TRPG	0.50	< 0.001		
$PRPGD_{AC}/TAPM_{AC}$	0.86	< 0.001	0.86	< 0.001

RVD right ventricular basal dimension, *RAD* right atrial minor-axis dimension, *IVCD* inferior vena cava dimension, *TAPSE* tricuspid annular plane systolic excursion, *TRPG* systolic peak gradient across the tricuspid valve derived from tricuspid regurgitant velocity

Other abbreviations are the same as those listed in the Table 2 footnotes

valvular heart disease. Zhang et al. [27] also evaluated the flow pattern of the hepatic vein by pulse-wave Doppler, and reported that the peak velocity of the A-wave during the active RA contraction was weakly correlated with the RVEDP (r = 0.45). Do et al. [28] stated that the RA area from the apical 4-chamber window was strongly correlated to invasive RVEDP (r = 0.79) and could predict high RVEDP in 31 adult patients with congenital heart disease. These investigators attributed such abnormal echocardiographic findings to the reduced RV chamber compliance or increased RV chamber stiffness. However, the direct relationship between these echocardiographic parameters and RV chamber stiffness has not been investigated. Thus, there has been no systematic clinical study assessing the RV operating stiffness in a completely noninvasive manner.

Methodological considerations of $PRPGD_{AC}/TAPM_{AC}$

Recently, we reported that the late-diastolic PR velocity pattern was distinctly modified by the late-diastolic RV pressure rise associated with RA contraction [13]. We considered that the measurement of the atrial-systolic descent of PR velocity could be useful for noninvasive estimation of the RV pressure increase during atrial contraction. Actually, in the present study, $PRPGD_{AC}$ was well correlated with ΔRVP_{AC} (Fig. 3a), and the mean difference between $PRPGD_{AC}$ and ΔRVP_{AC} was only 1.4 mmHg (Table 2). These findings

indicated that $PRPGD_{AC}$ correctly reflects the late-diastolic RV pressure increase without the extremely severe PR, which impedes estimation of the RV diastolic pressure curve from the PR velocity due to the huge, steep decline in the diastolic PA pressure.

We think that the ΔV_{AC} in the Otsuji's method is suitable to measure quick and minute RV volume change during atrial-systole [12], and we employed their method as a standard. However, as described above, their method was complex and time-consuming. The direct measurement of RV volume may not be easy even using the 3-dimensinal echocardiography or CMR. Especially, these methods do not suit to measure the RV volume change during atrial-systolic period due to inadequate time resolution. The planimetry of RV areas has also several limitations including low feasibility owing to the difficulty in tracing endocardial border [29]. In the present study, we employed tricuspid annular plane movement during atrial contraction to estimate the atrial-systolic RV ΔV. TAPSE has been widely used for the evaluation of RV systolic function [15]. RV longitudinal shortening has been recognized as an important factor determining RV contraction [30]. We conjectured that the atrial-systolic movement of the base of the RV free wall may reflect a passive increase in the RV volume due to RA contraction. In fact, in this study, $TAPM_{AC}$ was well correlated with ΔV_{AC} (Fig. 3b). Although M-mode echocardiography-derived $TAPM_{AC}$ has a limitation as a 1-dimensional parameter, it has a great advantage in terms of its very high sampling rate, which enables a very good time resolution suitable for measuring a quick but fine movement such as RV ΔV during atrial-systole. In addition, $TAPM_{AC}$ can be easily measured in a clinical setting because of its methodological simplicity, lower dependence on optimal image quality and better reproducibility.

Clinical implications

A pathological increase in LV operating stiffness, usually in association with a prominent A-wave and elevated LV end-diastolic pressure, may precede an elevation of mean left atrial pressure [16, 25]. Thus, even in patients without apparent symptoms of left heart failure, the detection of increased LV operating stiffness and elevated LV end-diastolic pressure may play a key role in managing patients with potential heart failure in order to prevent the development of overt left heart failure [16, 25]. Also in the RV, the measurement of ventricular operating stiffness may have utility for stratifying cardiac patients for the risk of right heart failure before a clear rise in the mean RA pressure. In previous studies of PAH patients, invasively determined RV stiffness was more closely associated with the disease severity and better related to prognosis than the RV systolic function [5, 10]. Our simple and noninvasive parameter of RV operating stiffness may have utility for predicting the outcome in patients with secondary pulmonary hypertension due to organic left-sided heart diseases as well as the outcome in PAH patients.

Limitations

There were several limitations in this study. First, the study population was small for a retrospective study, and might have led to some bias and influenced the results thorough type 2 errors. Second, right-sided heart catheterization and echocardiography were not performed simultaneously; there was a mean time difference of 2.5 days (range 0–7 days). Although we excluded patients with unstable hemodynamics and/or loading conditions between catheterization and echocardiography, the possibility of hemodynamic changes could not be completely excluded. Third, our method cannot be applied to patients lacking synchronized atrial activity due to arrhythmias such as atrial fibrillation, atrial flutter and complete atrioventricular block. Forth, our method also cannot be applied to patients with tachycardia owing to the summation of the rapid filling flow and atrial contraction flow. Finally, we could not test re-acquisition variability due to the retrospective nature of this study. Re-acquisition variability might be higher than the re-measurement variability written in this text.

Conclusion

Our novel, simple and completely noninvasive index, $PRPGD_{AC}/TAPM_{AC}$, will be useful to estimate RV operating stiffness and can be a good practical marker of RVEDP elevation in routine echocardiographic examinations.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Instead of obtaining informed consent, the program of the present study had been open to the public both through the home page and on the bulletin board of Hokkaido University Hospital.

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