Evaluation of the hemodynamics and right ventricular function in pulmonary hypertension by echocardiography compared with right-sided heart catheterization

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Abstract. The present study aimed to evaluate hemodynamics and right ventricular function in patients with pulmonary hypertension (PH) using transthoracic echocardiography and to compare these results with measurements obtained using right-sided heart catheterization (RHC). A total of 75 patients with PH were examined using echocardiography and RHC. Patients were divided into the following two groups according to their difference between $SPAP_{echo}$ and $SPAP_{RHC}$ measurement: The overestimated group and underestimated group. The overestimated group included the subgroups $group_{over-A}$ (difference <20 mmHg) and $group_{over-B}$ (difference ≥20 mmHg), and the underestimated group included $group_{under-A}$ (absolute value of the difference <20 mmHg) and $group_{under-B}$ (absolute value of the difference ≥20 mmHg). $SPAP_{echo}$ measurements were revealed to be significantly positively correlated with $SPAP_{RHC}$ measurements (r=0.794; P<0.01). Among all echocardiographic measurements, only tricuspid annular plane systolic excursion (TAPSE) was significantly different between groups; it was increased in $group_{over-A}$ and $group_{under-A}$ compared with $group_{over-B}$ (P<0.01). Although SPAP measurements obtained using echocardiography were significantly positively correlated with those obtained using RHC, a high proportion of overestimation or underestimation of SPAP by echocardiography remained.

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Introduction

Pulmonary hypertension (PH) is characterized by an increased pressure in the pulmonary arteries, leading to increased right-sided heart load and dysfunction (1-3). PH is diagnosed by a mean pulmonary artery pressure (mPAP) ≥25 mmHg measured during right-sided heart catheterization (RHC) at rest whilst at sea level (4). PH is a hemodynamic condition caused by a variety of diseases of the lungs and heart, or other systemic diseases (5-8). RHC remains the primary standard for the evaluation of PH, with the ability to exclude left-to-right cardiac shunt and other severe left-sided heart conditions (9,10). However, RHC is invasive and has potentially fatal complications (11). Therefore, various noninvasive methods have been used to diagnose PH, including echocardiography, magnetic resonance imaging and nuclear imaging (12-19). Transthoracic echocardiography is a promising method for the evaluation of PH, and right-sided heart structure and function (20,21). A previous study demonstrated that systolic pulmonary arterial pressure (SPAP) and mPAP measured during RHC are similar to measurements obtained by echocardiography (22). However, concerns regarding the accuracy of echocardiography for measuring SPAP remain (23-26).

In the present study, the clinical data of 75 patients with PH were enrolled and the results of echocardiography were compared with those of RHC. Factors that affect the accuracy of echocardiography in the evaluation of PH were analyzed and discussed.

Materials and methods

Patients. Between August 2011 and December 2014, a total of 92 patients with clinical manifestations of PH were enrolled in the present study, recruited from the Heart Center of Beijing Chao Yang Hospital (Beijing, China). Among these patients, 17 were excluded due to contraindications such as severe arrhythmias, renal inadequacy, and serious heart failure. Therefore, a total of 75 patients with PH were included in the present study. Among these 75 patients, 22 were male and 53 were female, with a mean age of 46.8±12.5 years. The present study followed the guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of Beijing Chao

Yang Hospital (Beijing, China). Written informed consent was obtained from all participants.

Echocardiographic measurements. Echocardiography to measure SPAP ($SPAP_{echo}$) was performed using Philips iE33 (Philips Healthcare, DA Best, The Netherlands) and Toshiba Artida (Toshiba Medical Systems, Tochigi, Japan) Doppler ultrasound machines with S4 and PST-30SBT transducers, respectively (2.5-3.5 MHz). The lead II electrocardiogram was recorded synchronously. The patients were placed into a left lateral position or supine position for measurements. The inner diameter of the main pulmonary artery was measured in the short axis view of the great vessels. Left ventricular ejection fraction was measured using the Simpson's method (27). The tricuspid regurgitation area was measured in an apical four chamber view. To evaluate RV function, the RV index of myocardial performance (RIMP), tricuspid annular plane systolic excursion (TAPSE), RV fractional area change (RVFAC), and tricuspid annular systolic velocity (s') were included. Images of the RV-focused apical four-chamber view were obtained for further analysis, and TAPSE was acquired in M-mode. Systolic displacement was measured from end-diastole to end-systole. Furthermore, RV end-diastolic area (RV EDA) and RV end-systolic area (RV ESA) were obtained by two-dimensional echocardiography. The RVFAC was calculated as: (RV diastolic area-RV systolic area)/RV diastolic area x100%. The tricuspid s' was measured by tissue Doppler imaging in the apical four-chamber view. RIMP was calculated as the ratio of isovolumic time to ejecting time, which was measured during pulsed tissue Doppler imaging. The ratio of the RV transverse diameter to the left ventricular transverse diameter was obtained at the end of diastole using the apical four chamber view.

RHC procedure. A Swan-Ganz catheter (Edwards Lifesciences, Irvine, CA, USA) was inserted through the internal jugular vein into the right inferior pulmonary artery. The following parameters were measured after hemodynamics had stabilized: SPAP ($SPAP_{RHC}$), mPAP, central venous pressure (CVP) and pulmonary vascular resistance. For each patient, echocardiography and RHC were performed with an interval of <48 h. All echocardiography and RHC measurements were repeated three times, and the mean value was calculated.

Patients were divided into two groups according to the difference between $SPAP_{echo}$ and $SPAP_{RHC}$, an overestimated group and underestimated group. The overestimated group included the subgroups $group_{over-A}$ (difference, <20 mmHg) and $group_{over-B}$ (difference, ≥20 mmHg). The underestimated group included the subgroups $group_{under-A}$ (absolute value of the difference <20 mmHg) and $group_{under-B}$ (absolute value of the difference ≥20 mmHg).

Statistical analysis. All data are presented as the mean ± standard deviation. Comparisons between groups were made using independent sample t-tests and comparison between the overestimated and underestimated subgroups were made using one-way analysis of variance followed by a Fisher's least significant difference test. $SPAP_{echo}$ and $SPAP_{RHC}$ were analyzed using Pearson correlation coefficient analysis and a Bland-Altman plot. All statistical analyses were performed

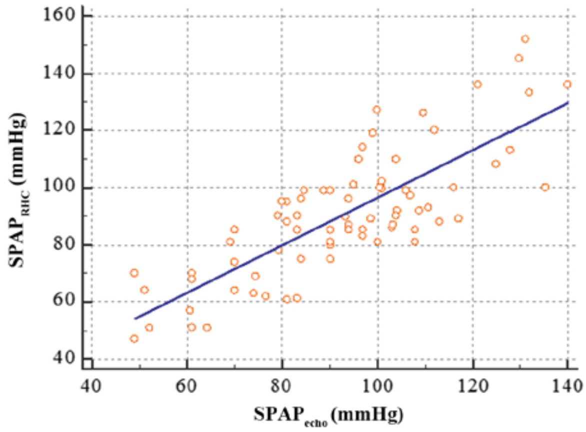

Figure 1. $SPAP_{echo}$ measured using echocardiography revealed a strong correlation with $SPAP_{RHC}$ measured using RHC. $r=0.794$; P<0.01. SPAP, systolic pulmonary arterial pressure; RHC, right heart catheterization.

using SPSS software (version 17.0; SPSS, Inc., Chicago, IL, USA). P<0.05 was considered to indicate a statistically significant difference.

Results

Patient clinicopathological characteristics. According to the 2003 World Health Organization PH classification criteria (28), there were 39 cases of pulmonary arterial hypertension (PAH) and 36 cases of chronic thromboembolic pulmonary hypertension in the present study (Table I). The etiologies of PAH included idiopathic PAH in 26 cases, connective tissue disease in 9 cases, congenital heart disease in 2 cases, portal hypertension in 1 case and hereditary PAH in 1 case, data not shown.

Positive correlation between RHC and echocardiography measurements. There was a significant positive correlation between $SPAP_{echo}$ measured using tricuspid regurgitation and $SPAP_{RHC}$ measured using RHC (r=0.794; P<0.01; Fig. 1). In addition, a Bland-Altman plot revealed agreement between $SPAP_{echo}$ and $SPAP_{RHC}$ measurements (Fig. 2). Compared with $SPAP_{RHC}$, $SPAP_{echo}$ was overestimated in 23 patients (overestimated group, 30.7%), in which 16 patients were in $group_{over-A}$ and 7 patients were in $group_{over-B}$ (Table II). $SPAP_{echo}$ was underestimated in 18 patients (underestimated group, 24%) compared with $SPAP_{RHC}$, with 14 patients in $group_{under-A}$ and 4 patients were in $group_{under-B}$ (Table II).

Among all echocardiographic measurements taken in the present study, only TAPSE was significantly increased in $group_{over-A}$ and $group_{under-A}$ compared with $group_{over-B}$ (P<0.01; Table II). Among the RHC measurements, CVP was significantly decreased in $group_{over-A}$ compared with $group_{over-B}$ (P<0.05), while mPAP was significantly increased in $group_{under-A}$ (P<0.01) and $group_{under-B}$ (P<0.05) compared with $group_{over-A}$ (Table III). An electrocardiography SPAP cut-off value of ≥50 mmHg demonstrated good sensitivity (98.64%) and specificity (100%) for PH, in addition to a good positive (100%) and negative (50%) predictive value (Table IV).

A 36-year-old female with pulmonary hypertension was presented, in which tricuspid regurgitation velocity was from

Table I. Patient characteristics.

Clinical characteristics	Type of PH		P-value
	CTEPH (n=36)	PAH (n=39)	
General information			
Age, years	52.03±12.33	42.03±10.72	0.001
Body mass index, kg/m^2	25.89±4.88	23.26±3.82	0.011
Heart rate, beats/min	79.14±18.81	81.29±11.04	0.702
SBP, mmHg	117.71±15.12	109.61±21.65	0.094
DBP, mmHg	76.48±10.25	70.01±15.74	0.074
6 min walk distance, m	378.09±90.89	360.60±102.37	0.030
Hemodynamic parameters			
$SPAP_{RHC}$	90.28±12.13	90.33±28.52	0.992
mPAP, mmHg	49.61±9.72	54.21±18.48	0.188
PCWP, mmHg	9.22±4.82	8.51±4.77	0.524
PVR, dyn·S·cm^{-5}	1,046.00±394.87	1,227.40±616.78	0.141
Echocardiographic structure			
RVTD	48.75±10.11	45.70±8.80	0.180
LVTD	31.51±4.13	30.28±6.11	0.359
D_{MPA}	31.75±3.91	32.19±4.79	0.669
D_{RPA}	23.28±3.00	21.17±2.63	0.003
D_{LPA}	22.02±2.56	20.30±3.52	0.029
Echocardiographic function			
LVEF	72.29±6.99	73.36±6.45	0.502
$SPAP_{echo}$	92.99±17.09	92.35±24.47	0.896
TAPSE	13.18±2.72	14.275±1.95	0.124
RIMP	0.92±0.27	0.91±0.29	0.925
FAC	26.68±6.95	26.53±7.81	0.942
s'	9.57±1.75	10.41±2.25	0.198

CTEPH, chronic thromboembolic pulmonary hypertension; PAH, pulmonary arterial hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure; SPAP, systolic pulmonary arterial pressure; RHC, right heart catheterization; mPAP, mean pulmonary arterial pressure; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; RVTD, right ventricular transverse diameter; LVTD, left ventricular transverse diameter; D_{MPA}, diameter of main pulmonary artery; D_{LPA}, diameter of left arterial branch; D_{RPA}, diameter of right pulmonary arterial branch; LVEF, left ventricular ejection fraction; echo, echocardiography; TAPSE, tricuspid annular plane systolic excursion; RIMP, RV index of myocardial performance; FAC, right ventricular fractional area change; s', tissue Doppler-derived tricuspid lateral annular systolic velocity.

Table II. Comparison of echocardiographic measurements between groups.

Group	No. of patients	TAPSE, mm	FAC, %	RIMP	s', cm/sec	A_{TR}, cm^2	$SPAP_{echo}$, mmHg
$Group_{over-A}$	16	14.11±2.15[a]	24.46±6.74	0.87±0.21	10.33±1.94	8.20±5.84	96.33±19.82
$Group_{over-B}$	7	10.41±2.07	29.31±2.09	0.80±0.16	9.33±2.16	13.25±5.58	93.01±16.94
$Group_{under-A}$	14	14.81±2.51[a]	28.26±11.02	0.88±0.32	10.98±1.91	5.53±2.75	83.91±20.92
$Group_{under-B}$	4	13.30±1.93	27.73±4.24	1.02±0.19	9.47±3.42	10.53±7.59	93.00±26.39

[a]$P<0.05$ vs. $group_{over-B}$. TAPSE, tricuspid annular plane systolic excursion; FAC, right ventricular fractional area change; RIMP, RV index of myocardial performance; s', tissue Doppler-derived tricuspid lateral annular systolic velocity; A_{TR}, tricuspid regurgitation area; SPAP, systolic pulmonary arterial pressure; echo, echocardiography.

415.9-482.7 cm/sec and the PG was from 69.2-93.2 mmHg as measured by contrasted echocardiography. A low level of tricuspid regurgitation may lead to an incomplete Doppler spectrum and underestimation of SPAP, and may be solved by using contrast bubbles in the right side of the heart (Fig. 3). A 61-year-old female with pulmonary hypertension was also

Table III. Comparison of right-sided heart catheterization measurements between groups.

Group	n	CVP, mmHg	$SPAP_{RHC}$, mmHg	mPAP, mmHg	PVR, dyn·S·cm^{-5}
$Group_{over-A}$	16	4.38±3.48	80.81±19.70	44.94±9.06	1,081.25±492.65
$Group_{over-B}$	7	9.71±6.37[a]	71.43±16.38	43.71±11.10	933.29±389.24
$Group_{under-A}$	14	7.71±5.12	98.79±21.70[a]	62.29±20.46[b]	1,367.50±670.31
$Group_{under-B}$	4	9.25±8.77	117.25±24.49[b]	61.75±15.09[a]	1,260.25±416.64

[a]$P<0.05$, [b]$P<0.01$ vs. $group_{over-A}$. CVP, central venous pressure; SPAP, systolic pulmonary arterial pressure; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance.

Table IV. Sensitivity, specificity and diagnostic accuracy of noninvasive assessment of pulmonary hypertension by Doppler echocardiography at various cut-off levels.

Cut-off SPAP, mmHg	Specificity, %	Specificity, %	PPV, %	NPV, %
≥50	98.64	100	100	50.00
≥70	95.16	53.85	90.77	70.00
≥90	80.00	57.50	62.22	76.67

SPAP, systolic pulmonary arterial pressure; PPV, positive predictive value; NPV, negative predictive value.

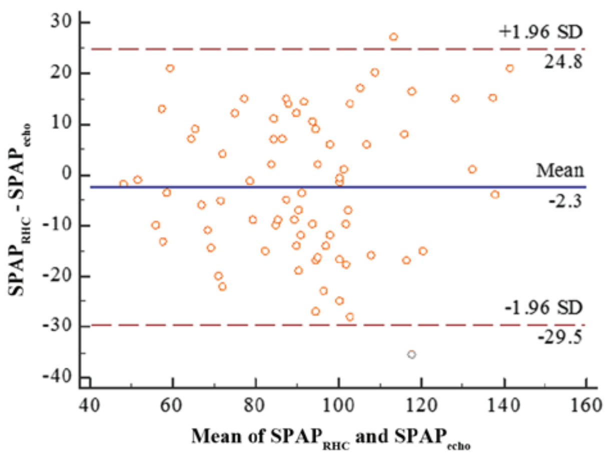

Figure 2. Bland-Altman plot of $SPAP_{echo}$ measured using echocardiography and $SPAP_{RHC}$ measured using RHC. SPAP, systolic pulmonary arterial pressure; RHC, right heart catheterization; SD, standard deviation.

presented; echocardiography revealed intermediate to severe tricuspid regurgitation with a velocity of 500 cm/sec and a PG of 99.8 mmHg. Follow up 3 years later, revealed severe tricuspid regurgitation with a velocity of 232 cm/sec and a PG of 21.6 mmHg (Fig. 4). Finally, a 33-year-old male with pulmonary hypertension was presented. During inspiration, tricuspid regurgitation velocity was 480.4 cm/sec with a PG of 92.3 mmHg. During expiration, the tricuspid regurgitation velocity was 584.9 cm/sec with a PG of 136.8 mmHg. At the end of expiration, tricuspid regurgitation velocity was 496.7 cm/sec with a PG of 98.7 mmHg. (Fig. 5).

Discussion

RHC is the reference method and 'gold standard' for the quantification of SPAP; however, the noninvasive assessment of SPAP by Doppler echocardiography is feasible and represents a potential examination to conduct in patients with suspected PH. Conclusions derived from an echocardiographic examination should aim to assign a level of probability to a diagnosis of PH. Echocardiography may also aid in detecting the cause of suspected or confirmed PH (29). The present study demonstrated a significant positive correlation and good agreement between Doppler echocardiography and RHC measurements. A detailed literature analysis by Finkelhor *et al* (30) demonstrated that the $SPAP_{echo}$ correlates well with $SPAP_{RHC}$ values in patients with left-sided heart pathology, whereas it does not correlate as well in right-sided heart pathology. Further information is required to explain these disparate results.

In the present study, PH with a systolic pulmonary artery pressure ≥50 mmHg was estimated invasively by RHC, confirming that tricuspid regurgitation could exclude PH. SPAP may be evaluated using echocardiography and tricuspid regurgitation according to the simplified Bernoulli equation (31) (tricuspid regurgitation pressure gradient+right atrium pressure). A low level of tricuspid regurgitation may lead to an incomplete Doppler spectrum and underestimation of SPAP (31,32). This problem may be solved by using contrast bubbles in the right side of the heart. A study by Jeon *et al* (32) demonstrated that contrasted echocardiography using a 10% air, 10% blood and 80% saline mixture had a high correlation with RHC measurements. By contrast, in patients with severe tricuspid regurgitation or right-sided heart failure, evaluation of SPAP using tricuspid regurgitation is prone to underestimation. Under these conditions, due to the neglect of inertial factors in the simplified Bernoulli equation, the pressure gradient between the right atrium and ventricle is underestimated, causing truncation of the tricuspid regurgitation spectrum.

Intrathoracic pressure and respiration affects the accuracy of tricuspid regurgitation pressure gradient measurement (33). During inspiration, RV pressure is decreased, leading to increased blood return and filling of the RV in diastole. This increases RV contraction and tricuspid regurgitation velocity. However, in patients with right-sided heart failure, increased filling of the right side of the heart during diastole does not increase RV contraction; therefore, the regurgitation velocity

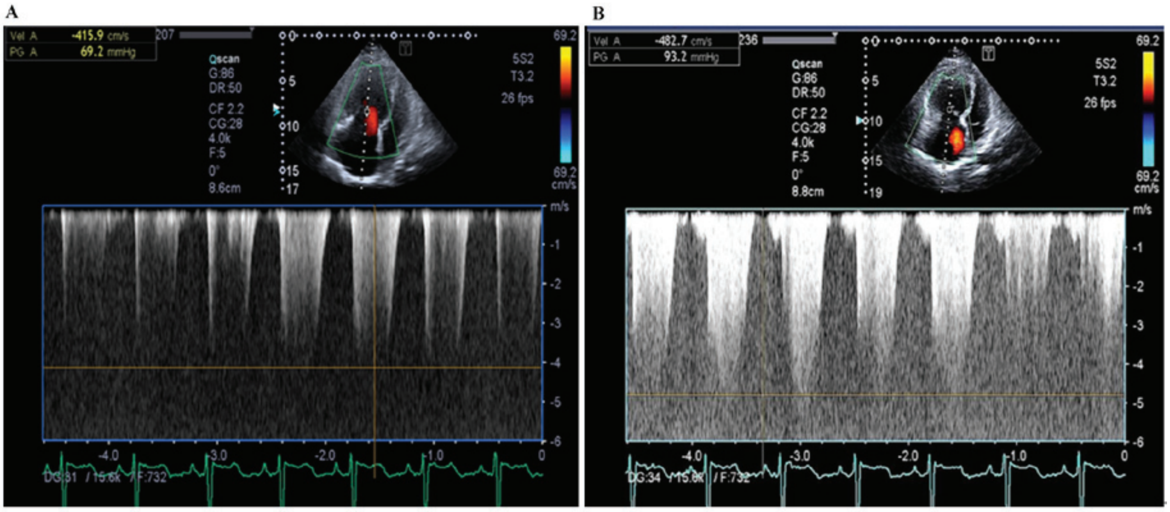

Figure 3. Echocardiography performed on a 36-year-old female with pulmonary hypertension. (A) Tricuspid regurgitation Vel was 415.9 cm/sec and the PG was 69.2 mmHg. (B) Contrasted echocardiography of the right side of the heart revealed a tricuspid regurgitation Vel of 482.7 cm/sec with a PG of 93.2 mmHg. Vel, velocity; PG, pressure gradient.

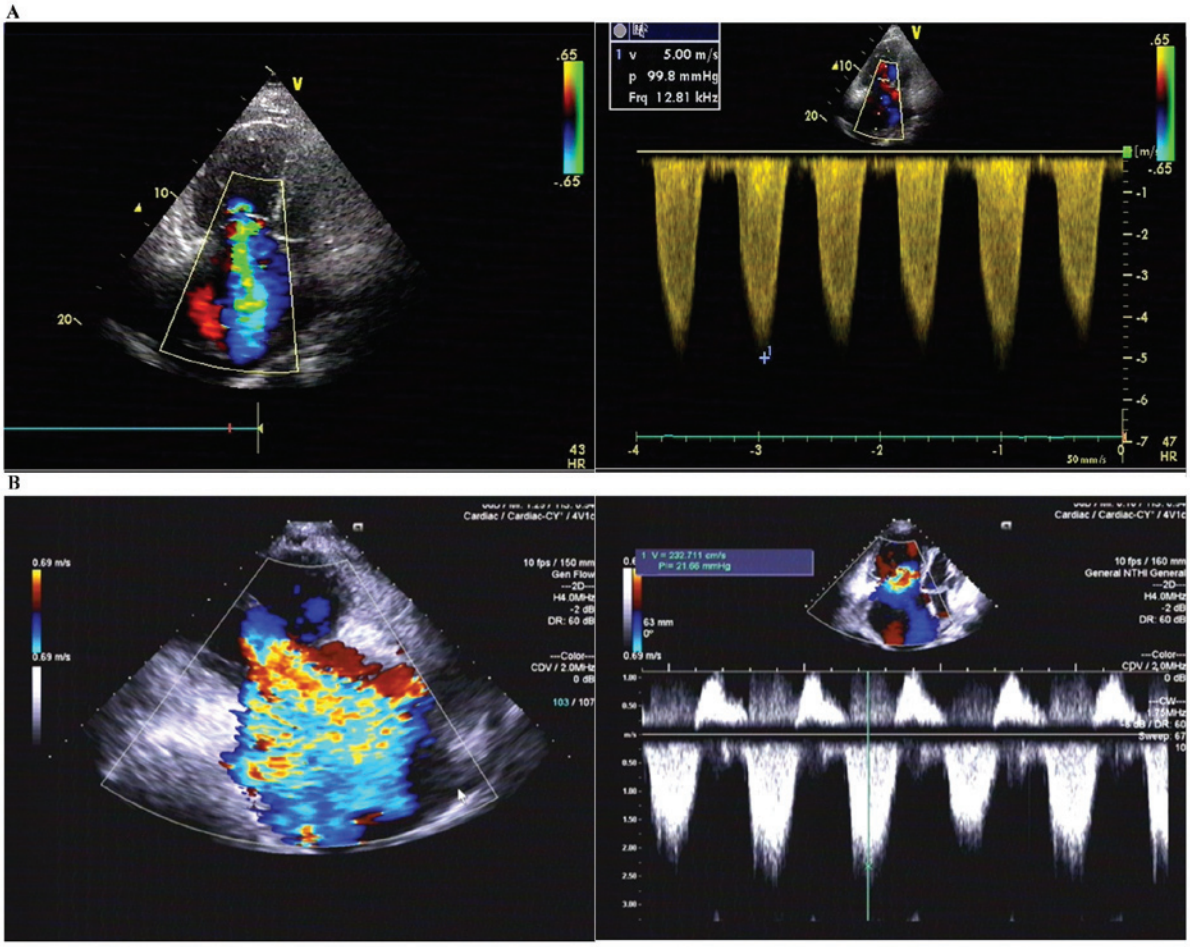

Figure 4. Echocardiography performed on a 61-year-old female with pulmonary hypertension. (A) Echocardiography revealed intermediate to severe tricuspid regurgitation with a Vel of 500 cm/sec and a PG of 99.8 mmHg in August 2011. (B) Echocardiography, performed 3 years later, revealed severe tricuspid regurgitation with a Vel of 232 cm/sec and a PG of 21.6 mmHg. Vel, velocity; PG, pressure gradient.

remains low (34,35). Thus, SPAP measurements using echocardiography should be performed at the end of inspiration or at the end of expiration whilst the patient holds their breath.

This may avoid the inaccuracy of overestimation or underestimation. Right atrium pressure also affects the accuracy of SPAP measurement. In the patients included in the the present

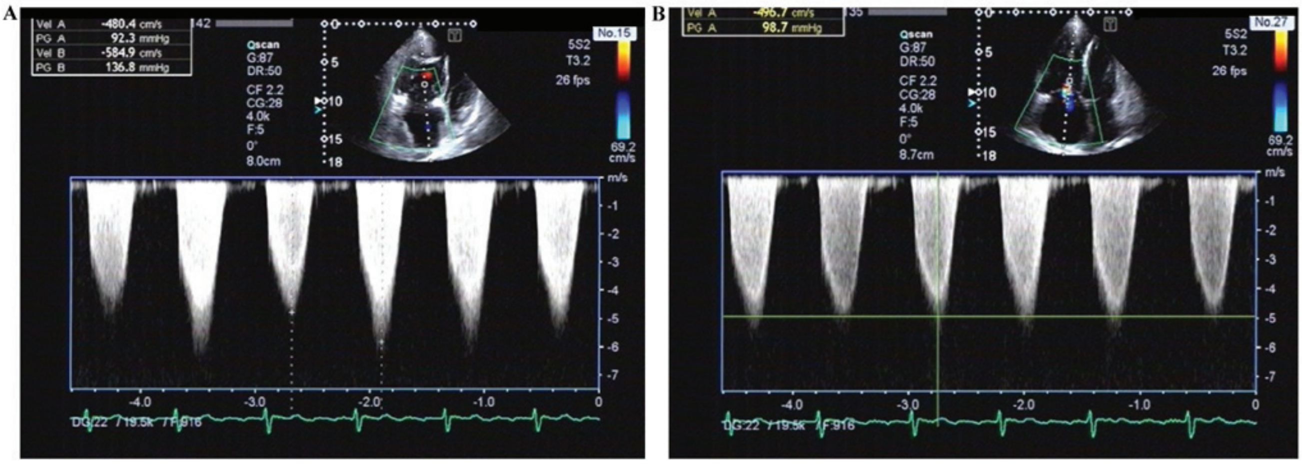

Figure 5. Echocardiography performed on a 33-year-old male with pulmonary hypertension. (A) During inspiration, tricuspid regurgitation Vel was 480.4 cm/sec with a PG of 92.3 mmHg. During expiration, tricuspid regurgitation Vel was 584.9 cm/sec with a PG of 136.8 mmHg. (B) At the end of expiration, tricuspid regurgitation Vel was 496.7 cm/sec with a PG of 98.7 mmHg. Vel, velocity; PG, pressure gradient.

study, the mean CVP was 6.38±5.12 mmHg, suggesting that overestimation of right atrium pressure may be a reason for the overestimation of SPAP. In addition, it has been demonstrated that increased right atrium pressure is associated with patient prognosis in PAH (36). Therefore, the accurate measurement of right atrium pressure is important in the diagnosis and prognosis of PH.

The present study demonstrated that only TAPSE and CVP measurements were significantly different between the groups with overestimation or underestimation of SPAP by echocardiography. It has been suggested that right-sided heart function is not a dominant factor affecting SPAP; however, it may affect the accuracy of the measurement (30,35). A previous meta-analysis revealed that the correlation coefficient between SPAP measurements obtained using Doppler echocardiography and those obtained using RHC ranged from 0.65-0.97, and that the sensitivity, specificity and diagnostic accuracy of Doppler echocardiography was 88, 56 and 63%, respectively (37). The present study indicated that non-invasive echocardiography is a reliable method for the classification of normal, increased and significantly increased pulmonary arterial pressure. However, measurement results of echocardiography should be verified by using RHC. A study by Greiner *et al* (38) indicated that near simultaneous Doppler echocardiography examinations within 24 h demonstrated a closer correlation compared with examinations with an interval of >24 h. In addition, Doppler echocardiography examinations that were performed prior to RHC were more correlated compared with those performed after RHC (38).

The primary limitation of the present study was the small sample size. Further studies using a larger cohort are required to investigate the application of echocardiography in different pathologic groups, such as PAH and chronic thromboembolic pulmonary hypertension. Right heart catheterization parameters in the normal control group require further study. Another limitation of the current study was that the SPAP measured by echocardiography and RHC were not conducted simultaneously.

In conclusion, the present study demonstrated that SPAP measured using echocardiography is significantly positively correlated with SPAP measured using RHC, and that only TAPSE and CVP measurements were significantly between patient with PH patients with overestimation and underestimation of SPAP by echocardiography. However, due to the small sample size used, further investigations are required to determine the specific reasons for the overestimation or underestimation of SPAP measurement by echocardiography.

Acknowledgements

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