Evaluation of Pulmonary Hypertension Using the Right to Left Ventricular Diameter Ratio on Contrast-Enhanced Computed Tomography

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ICHINOSE ET AL.: *Evaluation of Pulmonary Hypertension Using the Right to Left Ventricular Diameter Ratio on Contrast-Enhanced Computed Tomography*. Objective: *To assess the severity of a right heart overload due to pulmonary hypertension (PH), the estimated right ventricular systolic pressure (RVSP) determined by echocardiography has generally been measured. The purpose of the present study was to evaluate the correlation between the right to left ventricular diameter (RV/LV) ratio determined with contrast-enhanced computed tomography (CE-CT) and the RVSP by echocardiography.* **Methods and Materials:** *63 patients were enrolled and placed in two groups consisting of those with or without a right heart overload that was defined as an RV pressure of more than 40 mmHg on echocardiography. PH was observed in 31 patients (PH group) and the remaining 32 patients exhibited no PH (control group). In both groups, the RV and LV diameters were measured as the maximum inner diameter of each heart chamber in the axial image obtained from the CE-CT.* **Results:** *The RVSP of the PH and control groups was 58.5±20.7 mmHg and 26.1±0.4 mmHg, respectively. The RV/LV ratio for the PH group was significantly greater than that of the control group (1.1±0.4 and 0.8±0.1, $p<0.05$). In both groups, the RV/LV ratio was correlated ($r^2=0.21$, $p<0.05$) with the RVSP. An optimal cut off value of the diagnostic value of the RV/LV ratio of above 1.0 in the PH group had a sensitivity of 64.5%, specificity of 100%, positive predictive value of 100% and negative predictive value of 74.4%.* **Conclusion:** *The RV/LV ratio significantly correlated with the RVSP and that ratio was a useful parameter for diagnosing a right heart overload. (J HK Coll Cardiol 2010;18:44-52)*

Computed tomography, Echocardiography, Estimated right ventricular systolic pressure, Pulmonary hypertension, Right and left ventricular diameter

摘要

目的：超聲心動圖的右室收縮壓（RVSP）廣泛用於評估肺動脈高壓引起的右室超負荷嚴重程度。本研究的目的是評估增強–電腦掃描（CE-CT）測量的右/左室直徑比（RV/LV）和超聲心動圖的右室壓之間的關係。**方法與材料：**本研究共納入63例患者。以超聲心動圖的右室壓超過40 mmHg爲標準，分爲右室超負荷組及非右室超負荷組。其中31例爲肺動脈高壓組，32例爲非肺動脈高壓組（對照組）。以增強CT測量心臟搏動週期內軸向最大內徑爲右室和左室直徑。**結果：** 肺動脈高壓組和對照組的右室收縮壓分別爲58.5±20.7 mmHg 和26.1±0.4 mmHg。肺動脈高壓組RV/LV比

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顯著高於對照組（1.1±0.4 vs 0.8±0.1，p<0.05）。兩組內RV/LV比與RVSP有顯著相關性（r^2=0.21, p<0.05）。肺動脈高壓組內RV/LV>1.0爲最優診斷意義值，敏感度64.5%，特異性100%，陽性預測率100%，陰性預測率74.4%。**結論**：RV/LV值與RVSP顯著相關，可作爲診斷右室超負荷的有效指標。

關鍵詞：電腦掃描　超聲心動圖　估計右室測量壓　肺動脈高壓　右室左室直徑

Introduction

Echocardiography has been recognized as a rapid and non-invasive method for evaluating the right heart overload. Using Doppler echocardiography, the right ventricular systolic pressure (RVSP) has been shown to be highly correlated with the pulmonary artery pressure during right heart catheterization.[1,2] The assessment of pulmonary hypertension which suggests a right heart overload has been performed by measuring the estimated RVSP using echocardiography. However, some studies[3-6] have reported that the right to left ventricular diameter (RV/LV) ratio determined with contrast-enhanced computed tomography (CE-CT) is useful for assessing the severity of pulmonary thrombo-embolisms (PTEs). The purpose of the present study was to evaluate the correlation between the RV/LV ratio determined by CE-CT and the RVSP by echocardiography.

Materials and Methods

1) Patient Characteristics

In this retrospective study, from December 2008 to March 2009, consecutive 63 patients were divided into two groups consisting of those with or without a right heart overload. In standard echocardiographical definition of pulmonary hypertension (PH), maximum flow velocity and pressure gradient of a tricuspid regurgitation considered as more than 2.8 m/second and 30 mmHg at a rest.[7] If a right atrial pressure estimate of more than 10 mmHg is used for PH, estimated RVSP of more than 40 mmHg is reasonable to consider PH. So the pulmonary hypertension group consisted of those diagnosed with an estimated RVSP of more than 40 mmHg on the echocardiography, and the control group as those diagnosed with an estimated RVSP of less than 39 mmHg. Those with an acute or active stage of PH were excluded from this study. Other exclusion criteria included (i) dilatation of the thickness or lumen such as with a myocardial infarction, pacemaker implantations, left bundle branch block, left ventricular hypertrophy, or dilated and hypertrophic cardiomyopathy, and (ii) pericardial involvement such as a pleural effusion or pericarditis.

The baseline patient characteristics and comorbidities are presented in Table 1. Sixty-three patients (29 males and 35 females) were included in this study. Thirty-one patients (mean age, 60.5±20.8, 13 males sand 18 females) were enrolled in the PH group and the remaining 32 (mean age, 59.8±13.6, 16 males and 17 females) in the control group. The clinical pathogenesis of the PH was as follows; 9 patients with congestive heart failure (6 with valvular disease, 1 with hypertensive heart disease, 1 with atrial septal defect and 1 with ischemic heart disease), 6 with malignant disease, 5 with chronic obstructive pulmonary disease, 4 with pulmonary PTEs, 3 with primary pulmonary hypertension and 4 with collagen disease. Maximum pressure gradient of a tricuspid regurgitation in the PH group and the control group were 3.5±0.6 mmHg and 2.2±0.3 mmHg (p<0.001), respectively. And its severity were as follows, 49 with mild tricuspid regurgitation (PH group, n=17, control group, n=32), 5 with moderate tricuspid regurgitation (PH group, n=5) and 4 with severe tricuspid regurgitation (PH group, n=4). The patients received warfarin potassium (PH group, n=11; control group, n=3), Beraprost sodium (PH group, n=5), Bosentan hydrate (PH group, n=2), Sildenafil citrate (PH group, n=3), diuretics (PH group, n=9; control group, n=2) and depressors (calcium channel antagonists, n=8, angiotensin converting enzyme inhibitors (ACE-Is) and angiotensin II receptor blockers

Table 1. Clinical basis of the disease in the 63 patients

	PH group (*n*=31)			Control group (*n*=32)		*P* value
Age (years)	60.5±20.8			59.8±13.6		NS
Male/Female	13/18			16/17		NS
BMI (kg/m^2)	21±5.4			23±3.7		NS
Comorbidities						NS
Diabetes mellitus	7			2		NS
Hypertension	14			15		NS
Hyperlipidemia	7			5		NS
Hyperuricemia	5			1		NS
	CHF	9		Malignancy	15	
	Malignancy	6		Vascular disease	5	
	COPD	5		Collagen disease	6	
	PTEs	4		IHD	2	
	IPAH	3		COPD	2	
	Collagen disease	4		PTE	1	
				Infectious disease	1	

All continuous variables are presented as mean±S.D.

BMI, body mass index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; IHD, ischemic heart disease; IPAH, idiopathic pulmonary arterial hypertension; PH, pulmonary hypertension; PTE, pulmonary thrombo-embolism.

(ARBs), n=14) and home oxygen therapy (PH group, n=9). Four patients died from cancer (3) or a PH crisis (1) after 7 months.

2) CE-CT Acquisition and Image Analysis

CE-CT was performed using a multi-detector row helical CT scanner (Aquilion TSX-101A, Toshiba Medical Systems Co. Ltd., Japan). The scanning parameters were 120 kV, and 150~300A with 0.5 mm thick sections. A nonionic iodinated contrast medium (Iopamidol 612 mg/ml) was intravenously administered at a total dose of 2 ml/kg and injection rate of 1.5 ml/second, and the CT data were available after 70 seconds from the start of the contrast medium injection. The scanned images were retrospectively reviewed with a DICOM viewer (ExaVision LITE, Ziosoft Inc., Japan). The RV/LV ratio was evaluated by measuring the right and left ventricular diameters of the heart in the axial view of the transverse plane at the maximum point between the inner surfaces of the lumen (Figure 1A). The pulmonary artery trunk diameter (PA) and ascending aorta diameter (Ao) were measured at the maximum inner diameter of the transverse plane (Figure 1B).

3) Echocardiographic Data

Standard two-dimensional and Doppler echocardiography were performed with a SONOS 5500 (Phillips Medial Systems Inc., USA) standard ultrasound system with a 1 to 3 MHz wideband transducer. The left ventricular diastolic dimension and systolic dimension, left atrium dimension, ascending aorta dimension, pulmonary artery dimension and inferior vena cava dimension (IVC) were obtained in a left parasternal, apical, and subxiphoid approach. The estimated RVSP was calculated using the following formula:

Estimated RVSP=4 × $v^{2\,\#}$ + Estimated RAP

#, Bernoulli's formula; v, maximum flow velocity of the tricuspid regurgitation; RAP, right atrium pressure. The RAP was calculated as in Table 2.

A echocardiographic examination was performed within 4 weeks of the CE-CT examination. Two-experienced sonographers without any knowledge of the CE-CT examination reviewed the patients undergoing the echocardiography.

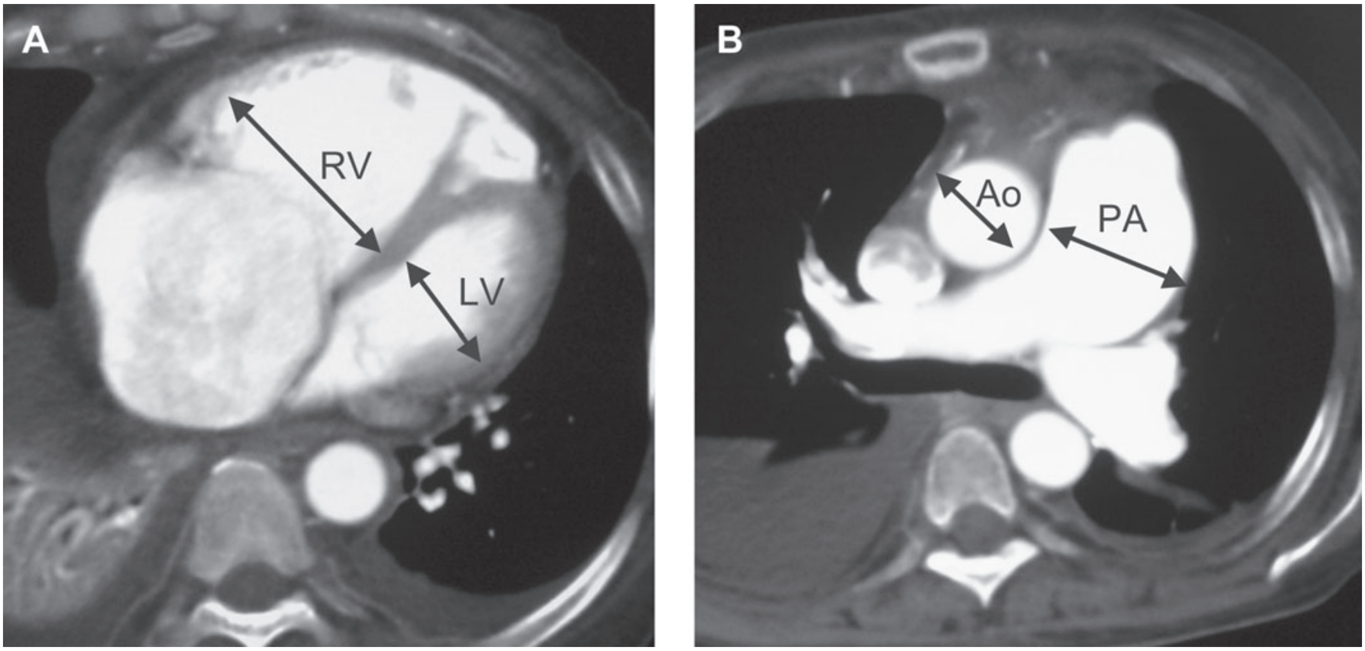


Figure 1. *Axial image of the contrast-enhanced computed tomography. (A) Measurement of the RV/LV ratio. LV, left ventricle inner maximum lumen diameter; RV, right ventricle inner maximum lumen diameter. The scan shows the measurements of the maximum inner lumen diameter of the left and right ventricles. (B) Measurement of the PA/Ao ratio. PA, pulmonary artery inner lumen diameter; Ao, ascending aorta inner lumen diameter. This scan shows the measurement of the ascending aortic inner diameter and maximum pulmonary artery trunk inner diameter.*

Table 2. Estimation of the right atrial pressure

IVC diameter (mm)	Respiratory variation*	Estimated RAP (mmHg)
12~15	+	0~5
12~15	-	5~10
15<	+	10~20
15<	-	15~25

IVC, inferior vena cava; RAP, right atrial pressure.
*respiratory variations were positive when there was a greater than 50% variation of the minimum to maximum diameters of the IVC and negative when there was less than a 50% variation in those diameters.

4) Statistical Analysis

The results are expressed as the mean ± the standard deviation (S.D.). The qualitative parameters were compared by means of a t-test or Fisher's exact test. A p value <0.05 was considered to indicate statistically significant differences. A statistical analysis was performed with a statistical software system (Stat Mate III, ATMS Tokyo, Japan)

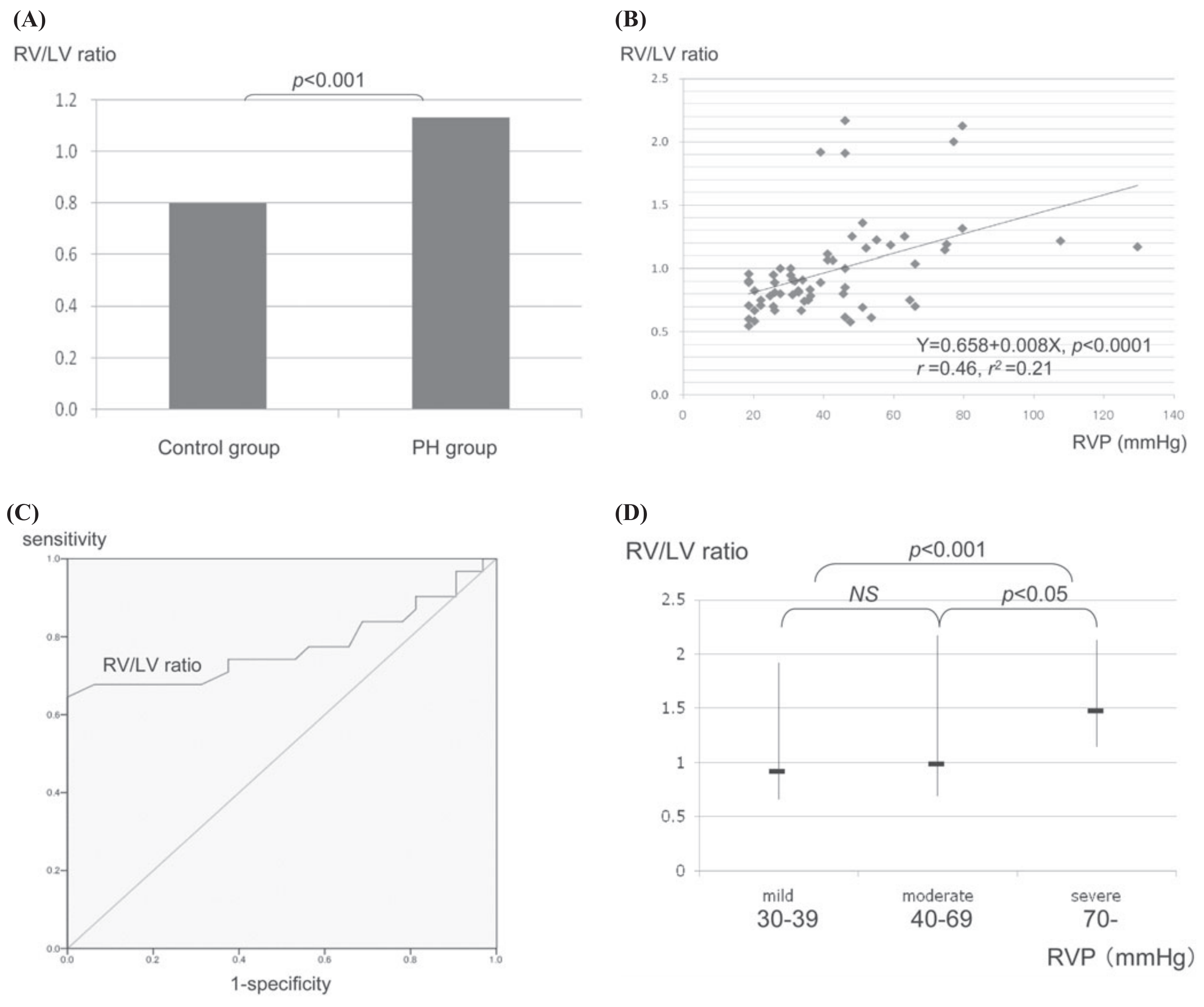
Results

1) RV/LV Ratio

The estimated RVSP in the PH and control groups were 58.5±20.7 mmHg and 26.1±0.4 mmHg, respectively. The mean RV/LV ratio in the PH group was 1.1±0.3, and differed statistically significantly (p<0.05) from that in the control group (0.8±0.3)

(Figure 2A).

In both groups, the RV/LV ratio correlated ($r=0.46$, $r^2=0.21$, $p<0.05$) with the estimated RVSP (Figure 2B). In a calculation from the receiver operating characteristics (ROC) curve, an optimal RV/LV ratio of more than 1.0 diagnosed PH with a sensitivity of 65%, specificity of 100%, positive predictive value (PPV) of 100% and negative predictive value (NPV) of 74% (Figure 2C).



RV/LV ratio, right ventricular to left ventricular ratio; RVP, right ventricular pressure; PH, pulmonary hypertension.

Figure 2. *(A) The RV/LV ratios between the PH and control groups. The estimated RVP in the PH and control groups from the echocardiogram were 58.5±20.7 mmHg and 26.1±0.4 mmHg, respectively. The mean RV/LV ratio was significantly higher in the PH group than in the control group (p<0.0001, t-test). (B) Scattergram illustrating the correlation between the right ventricular to RV/LV ratio and estimated RVP in the PH and control groups. There was a significant correlation between the RV/LV ratio and estimated RVP. The regression equation was determined as follows: RV/LV ratio=0.0077× estimated RVP+0.66 (r=0.46, r^2=0.21, p<0.0001 Fisher's test). (C) Receiver operating characteristic curve for the RV/LV ratio which diagnosed PH (RVP≧40 mmHg). (D) Relationship between the RV/LV ratio and severity of the RVP. Moderate and severe RVP had a statistically higher RV/LV ratio than that of mild RVP.*

2) Other Parameters

The mean value of the PA/Ao ratios other than for thoracic aortic aneurysms was 1.04±0.36 in the PH group and 0.86±0.24 in the control group. The PA/Ao ratio in the PH group was significantly higher (p<0.05) than that in the control group (Table 3) and that ratio statistically correlated with the RVSP (r^2=0.23, p<0.001). An optimal PA/Ao ratio threshold of more than 0.9 calculated from the ROC curve diagnosed PH with a sensitivity of 74%, specificity of 62%, PPV of 68%, and NPV of 69% (Figures 3A & 3B).

The RV and PA diameters were significantly increased in the PH group (p<0.01 and p<0.001, respectively). The LV and Ao diameters did not statistically differ in the two groups (Table 3).

Discussion

Echocardiography is a non-invasive and rapid imaging technique for demonstrating the signs of PH, such as RV dilatation, leftward bowing of the intraventricular septum (IVS), collapse of the LV and the estimated RVSP. However, this examination has an operator-dependent bias and the need for special echocardiographic techniques. On the other hand, CT is an objective examination. The purpose of this study was to determine whether the RV/LV ratio of the CT parameters could predict PH when compared with the RVSP of the echocardiographic parameters.

1) RV/LV Ratio

For PTEs, some literature[3-6] has been available for assessing the severity of the PH using CE-CT. Those studies estimated that an RV/LV ratio of >1.5 indicated the severity and the potential of dying from the PTE within 30 days. Collomb et al.[3] reported the severity assessment of acute PTEs using CT. In their study, the clinically severe PTE group had a statistically larger RV/LV ratio than the non-severe PTE group (1.63 vs. 1.09, p<0.0001). Further, the diagnostic accuracy of an RV/LV ratio of greater than 1.5 as a sign of a severe PTEs occurrence had a sensitivity of 60%, specificity of 83%, PPV of 83% and NPV of 76%. In our study, clinically severe PH was defined as a patient death due to PH, state of shock (systolic blood pressure of greater than 80 mmHg) or New York Heart Association (NYHA) class III-IV. In the ROC curve, if using an optimal RV/LV ratio of more than 1.1, severe PH could be accurately diagnosed with a sensitivity, specificity, PPV and NPV of 79%, 88%, 65% and 94%, respectively, which was comparable to the prior study. However, the optimal cut off value of the RV/LV ratio differed between our study and that of the previous study done by Collombo et al. The reason was considered as follows; in the acute phase of a severe PTE, the RV chamber is enlarged and the LV collapses. However, our study included all causes or stages of PH such as right sided heart failure, and a chronic state of PH. Therefore, the LV chamber size became compensated to some degree and it was not necessary complicated

Table 3. Results of the contrast-enhanced computed tomography parameters in the pulmonary hypertension and control groups

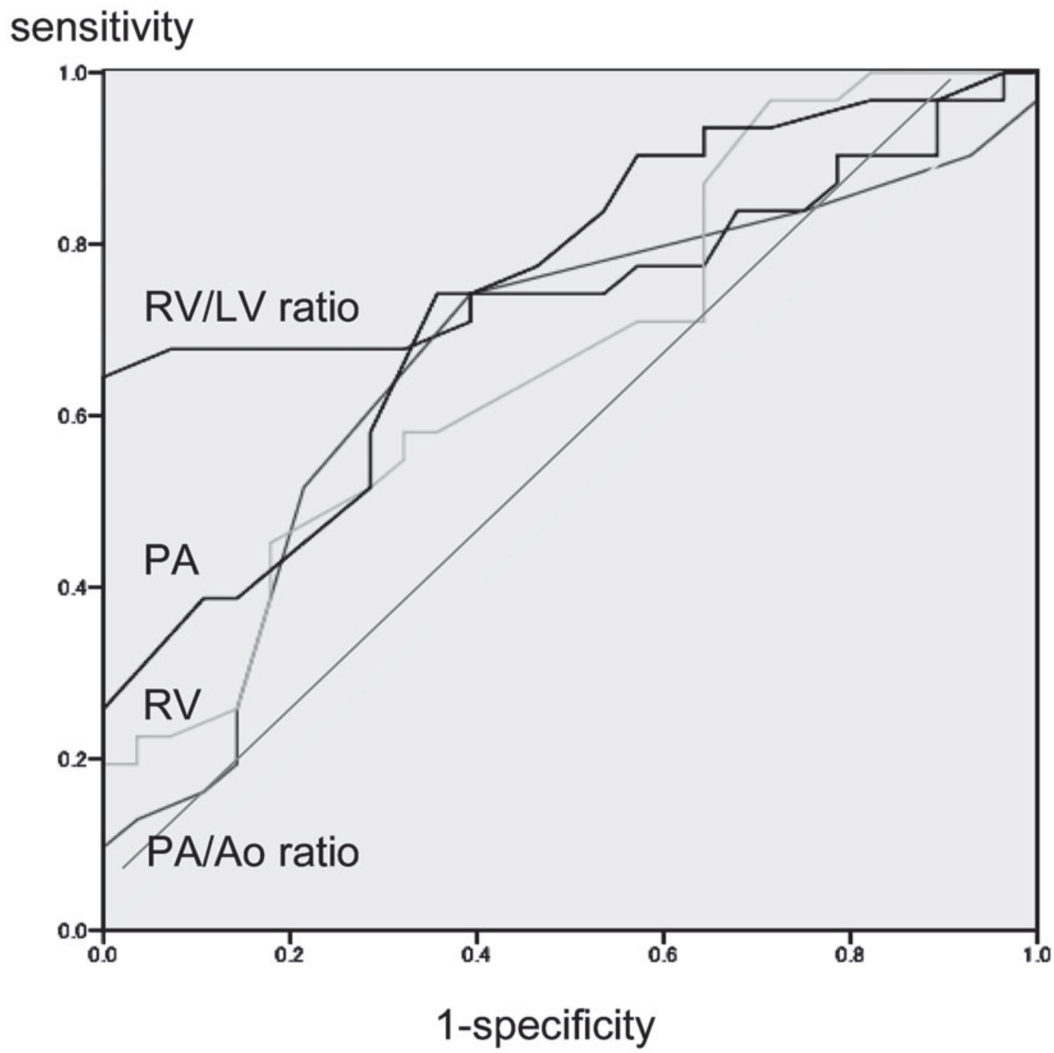
Parameters	PH group	Control group	*P* value*
Maximum diameter			
RV (mm)	38.7±9.6	32.3±6.5	<0.05
LV (mm)	38.2±12.0	40.2±5.1	NS
PA (mm)	31.6±5.9	26.5±5.6	<0.05
Ao (mm)	32.7±9.3	32.6±9.0	NS
RV/LV ratio	1.16±0.44	0.80±0.12	<0.05
PA/Ao ratio	1.04±0.36	0.86±0.24	<0.05

All continuous variables are presented as mean±S.D.

PA, pulmonary artery diameter; PA/Ao ratio, pulmonary artery diameter to aortic diameter ratio; PH, pulmonary hypertension; LV/RV ratio, left ventricle to right ventricle diameter ratio. RV, right ventricular.

*The LV/RV ratio, PA/Ao ratio, PA, and RV significantly differed between the two groups (p<0.05).

(A)



(B)

	AUC	Cut off value*	sensitivity	specificity	PPV	NPV
RV/LV ratio	0.77	1.0	0.65	1.00	1.00	0.74
PA/Ao ratio	0.66	0.9	0.74	0.61	0.68	0.68
RV diameter	0.68	38.5 mm	0.45	0.84	0.73	0.61
PA diameter	0.74	28.5 mm	0.74	0.65	0.68	0.71

AUC, area under the curve; NPV negative predictive value; PH, pulmonary hypertension; PPV, positive predictive value; RVP, right ventricular pressure.

Figure 3. *(A) Receiver operating characteristic curve for all the parameters for diagnosing PH (RVP≧40 mmHg). (B) The accuracy of the parameters for predicting an echocardiographic diagnosis of PH (RVP≧40 mmHg).*

**the optimal cutoff levels were made available with a Youden index.*

by an LV collapse. In addition, the RV dimension was enlarged with an increasing RVSP, however, the LV dimension was not. That might demonstrate that the optimal cut off value in our study was low compared with the previous data. Nevertheless, the RV/LV ratio was correlated with the estimated RVSP. If the patients were divided into three groups based on the severity of the RVSP with mild PH (30-39 mmHg), moderate PH (40-69 mmHg) and severe PH (above 70 mmHg), the RV/LV ratio for severe PH was significantly higher than that for the moderate ($p<0.05$) and mild PH ($p<0.001$). To the best of our knowledge there have been no previous studies which have demonstrated a correlation between the RV/LV ratio of the CE-CT and the severity of the RVSP.

In two studies on massive PTEs, Contractor et al.[8] and Lim et al.[9] reported that CT signs of RV dysfunction (such as an RV/LV ratio>1.0, and leftward bowing of the IVS) had a sensitivity of 78-92%, specificity of 100% and PPV of 100%, as compared to the echocardiographic findings of RV dysfunction (RV dilatation, leftward bowing or paradoxical motion of the IVS). In our study, using similar criteria, CT demonstrated a sensitivity, specificity, PPV and NPV of 50%, 100%, 100% and 79%, respectively for the diagnosis of RV dysfunction. Only the sensitivity was lower than that of those two studies despite the similar specificity and PPV.

The CT images obtained in the axial view were not similar to those in the four-chamber view. Quiroz et al.[10] reported that the CT measurements obtained from the four chamber view images differed from those in the axial view images. In acute PTEs, the RV/LV ratio determined by the four-chamber view is more correlative than that of the axial view with the clinical adverse events including the mortality, necessity for cardiopulmonary resuscitation, hypotension and rescue thrombolysis. In our study, the RV/LV ratio was analyzed by the axial view because of the advantage of rapidly obtainable results without any reconstruction-imaging process. However, if we had performed a reconstruction from the four-chamber view, more accurate data might have been obtained.

2) Other Parameters

The RV diameter and RV/LV ratio determined by CT have demonstrated a significant positive correlation with the severity of PTEs or fatal outcomes, whereas the LV diameter has shown a negative correlation.[3-6] In our study, the RV, RV/LV, PA, and PA/Ao ratios exhibited a positive correlation to the RVSP (the individual r indexes were 0.44, 0.46, 0.45 and 0.48 and r^2 indexes 0.19, 0.21, 0.20 and 0.23, respectively. All p values were <0.001). On the other hand, there was no correlation between the LV and RVSP. The ROC curve for the RV/LV ratio, PA/Ao ratio, RV and PA are demonstrated in Figure 3A and the optimal cut off value is demonstrated Figure 3B.

In Ng[11] and colleagues reported the correlation between the PA/Ao ratio determined by CT and the right atrial pressure (RAP) measured by right heart catheterization in chronic PH patients with cardiovascular and pulmonary disease. The PA diameter and PA/Ao ratio were also correlated with the systolic pulmonary artery pressure (PAP) (the individual r indexes were 0.75 and 0.72, respectively, $p<0.0005$). In the patients with the mean PAP measured by catheterization, the accuracy values (sensitivity, specificity, PPV and NPV) of a PA/Ao ratio of >1.0 in predicting a diagnosis of PH, were 68%, 100%, 100% and 52%, respectively. Those values for a PA diameter of >30 mm were 70%, 92%, 96% and 52%, respectively. Our data of the optimal cut off value for the PA/Ao ratio and PA diameter are shown in Figure 3A. Although the definition of PH and cut off value for the indices differed, the PA/Ao ratio and PA diameter from our study were less accurate in diagnosing PH than that in Ng's study. The RV/LV ratio had the highest accuracy among the four parameters constructing the area under the curve (AUC) (Figures 3A & 3B). To the best of our knowledge, no previous studies have demonstrated the relationship between the RV/LV ratio and estimated RVSP in PH due to various diseases. Our study was the first to demonstrate that the RV/LV ratio had a good correlation to the RVSP, and that an RV/LV ratio of >1.0 was the most powerful index for diagnosing PH.

Study Limitations

The patient background in this study consisted of the chronic stage of PH, because the CE-CT examination was hard to perform during the active stage of PH, particularly with congestive heart failure. This evaluation may be useful for only patients in the chronic stage of PH. Second, the end-diastolic ventricular diameter may be obtained if an electrocardiogram-synchronized gating system is used together with CE-CT. However that technique increases the radiation exposure and requires a specific gating system. Third, in our study, right heart catheterization was not performed, however the RVSP has been recognized to have a good correlation to the PAP in previous studies[1,2] More accurate results might have been obtained if the PAP was measured by a right heart catheterization.

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