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Overestimation by echocardiography of the peak systolic pressure gradient between the right ventricle and right atrium due to tricuspid regurgitation and the usefulness of the early diastolic transpulmonary valve pressure gradient for estimating pulmonary artery pressure

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ABSTRACT

We investigated the influence of tricuspid regurgitation (TR) severity on the echocardiographic peak systolic transtricuspid pressure gradient (TRPG) and evaluated the usefulness of the peak early diastolic transpulmonary valve pressure gradient (PRPG) for estimating pulmonary artery (PA) pressure. In 55 consecutive right heart-catheterized patients, we measured the peak systolic right ventricular (RV)-right atrial (RA) pressure gradient (RV-RA_{CATH}), peak early diastolic PA-RV pressure gradient (PA-RV_{CATH}), and mean PA pressure (MPAP_{CATH}). Using echocardiography, we obtained the TRPG, PRPG and an estimate of the mean PA pressure (EMPAP) as the sum of PRPG and the estimated RA pressure, and measured the vena contracta width of TR (VC_{TR}). The difference between the TRPG and RV-RA_{CATH} was significantly greater in the very severe TR group (VC_{TR} >11 mm) than in the mild, moderate, and severe TR groups, and significantly greater in the severe TR group (7 < VC_{TR} ≤ 11 mm) than in the mild TR group. The overestimation of the pressure gradient >10 mmHg by TRPG was not seen in the mild or moderate TR groups, but was observed in the severe and very severe TR groups (22% and 83%, respectively). In ROC analysis, EMPAP could distinguish patients with MPAP_{CATH} ≥25 mmHg with the area under the curve of 0.93, 100% sensitivity and 87% specificity. In conclusion, TRPG frequently overestimated RV-RA_{CATH} when VC_{TR} was >11 mm and sometimes did when VC_{TR} was >7 mm, where EMPAP using PRPG was useful for estimating PA pressure.

Key words: echocardiography, pulmonary artery pressure, tricuspid regurgitation, pulmonary regurgitation

INTRODUCTION

In the diagnosis and pathophysiological assessment of patients with cardiopulmonary diseases, the assessment of pulmonary artery pressure plays an important role [1]. The peak systolic pressure gradient between the right ventricle (RV) and the right atrium (RA) can be estimated by using the peak systolic transtricuspid pressure gradient (TRPG) calculated from the peak velocity of the tricuspid regurgitation (TR) measured by continuous-wave Doppler echocardiography, using the simplified Bernoulli equation [1-5]. The pulmonary artery (PA) systolic pressure is usually estimated by adding the TRPG to the echocardiographically estimated RA pressure. This technique is the most widespread and well-recognized method of assessing PA pressure noninvasively.

Although echocardiography-derived PA systolic pressure was reported to correlate well with catheterization-derived PA systolic pressure, there have been some controversies about the reliability of Doppler echocardiography for this purpose [6-11]. Fisher et al. [6] reported that echocardiography overestimates PA systolic pressure because of an inaccurate echo-derived right atrial pressure. Groh et al. [10] suggested that both the overestimation and underestimation of PA systolic pressure can occur, because viscous losses or inertial forces are ignored in the simplified Bernoulli equation. In addition, the 2014 American Heart Association/American College of Cardiology (AHA/ACC) guideline [12] suggested that the accuracy of the Doppler-derived technique can be compromised by the potential inaccuracies of applying the simplified Bernoulli equation to laminar flow, which is frequently seen in patients with severe TR. A very wide regurgitant orifice, which may be most frequently seen in the tricuspid valve among the four cardiac valves, will lead to laminar regurgitant flow [12-14]. In the presence of such a laminar TR flow, the TRPG calculated using the simplified Bernoulli equation should overestimate the true RV-RA pressure gradient due to the pressure recovery phenomenon [15-17]. So far, however, the error in the TRPG caused by this

phenomenon has not been substantially studied in a clinical setting, and we do not have any useful information regarding how severe TR induces this type of error.

Several studies have reported that the PA-RV pressure gradient estimated from pulmonary regurgitation (PR) is also useful for estimating PA pressure [18-20]. The purposes of the present study were to (1) determine the influence of the severity of TR on the Doppler-derived peak systolic RV-RA pressure gradient based on a comparison with the peak systolic pressure gradient derived from right heart catheterization, and (2) evaluate the usefulness of the Doppler flow velocity measurement of PR for the noninvasive estimation of PA pressure as an alternative to TR velocity measurement.

SUBJECTS and METHODS

Subjects

The study population consisted of 55 consecutive patients (35 men and 20 women, 67 ± 14 years) who were admitted to Hokkaido University Hospital from January to December 2013 and underwent echocardiographic examination and right heart catheterization under stable clinical condition within 4 weeks. We carefully excluded patients with changes in clinical condition, such as symptoms and signs of heart failure, body weight, and plasma BNP level, or in cardiovascular medications between echocardiography and catheterization. Among the initial 123 patients, 26 patients were excluded because of the unstable clinical condition. Fourteen of the remaining 97 patients were excluded because of missing or inadequate pressure record, and then 28 of the remaining 83 were excluded because of insufficient quality of the continuous-wave Doppler TR velocity tracing. The underlying diseases of the study patients were valvular disease in 22 patients, cardiomyopathy in 14, ischemic heart disease in 12, congenital heart disease in 4, idiopathic arrhythmia in 2, and pericardial disease in 1. They

did not include patients with pulmonic stenosis, right ventricular outflow obstruction, double outlet right ventricle, or respiratory assist device.

This study was approved as a retrospective observational study both by the Research Ethics Committee of Hokkaido University Hospital and by the Ethics Committee of Faculty of Health Sciences in Hokkaido University.

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 with an M3S/M4S probe (GE Healthcare, Little Chalfont, UK), or a iE33/Sonos 5500 with an S3/S4 probe (Philips Medical Systems, Eindhoven, The Netherlands). The left ventricular (LV) end-diastolic dimension and the left atrial end-systolic dimension were measured in the parasternal long-axis image. The LV ejection fraction was calculated from the apical two-chamber and four-chamber images using the biplane disk-summation method, and the LV mass index was calculated from two-dimensional linear measurements of LV end-diastolic dimension and thicknesses of interventricular septum thickness and LV posterior wall in accord with the guidelines of the American Society of Echocardiography [21]. The basal RV dimension at end-diastole and the RA minor axis dimension at end-systole were measured in the apical four-chamber image. The inferior vena cava (IVC) dimension was measured in the epigastric long-axis image.

The vena contracta width of TR was measured in the right ventricular inflow and the parasternal four-chamber color Doppler images, and the greater value of the two measurements (VC_{TR}) was used as the index of the severity of TR. The severity of TR was classified according to the VC_{TR} : the mild TR group was defined as $VC_{TR} \leq 3$ mm (29 patients), the moderate TR group as $3 \text{ mm} < VC_{TR} \leq 7$ mm (11 patients), the severe TR group as $7 \text{ mm} < VC_{TR} \leq 11$ mm (9 patients), and the very severe TR group as $VC_{TR} > 11$ mm (6

patients) [12,22]. Severe PR was defined as the PR with a color jet filling RV outflow tract, a dense laminar flow velocity pattern with a steep deceleration slope, RV enlargement, and paradoxical interventricular septal motion [12].

Using continuous-wave Doppler echocardiography, we measured the peak systolic TR velocity to calculate TRPG (Fig. 1A). We also measured the peak early diastolic velocity of PR to calculate the peak early diastolic PA-RV pressure gradient (PRPG) (Fig. 1B). To minimize the incident angle of the beam to the TR and PR jets, the color flow signal of a jet was visualized in two mutually orthogonal planes from several different echocardiographic windows, and the flow velocity was recorded from the window providing the least incident angle and the greatest velocity [23]. The interobserver variability was tested each for TRPG and PRPG by two independent observers (T. H. and S. K.), and we found excellent agreement between the two observers with an interclass correlation coefficient of 0.96 for TRPG in all the 55 patients and that of 0.98 for PRPG in 45 patients whose PR velocity could be recorded.

Based on the IVC dimension and its respiratory change, we estimated the mean RA pressure (EMRAP) as 3 mmHg when the IVC diameter was ≤ 19 mm and collapsed $> 20\%$ with quiet inspiration, and as 15 mmHg when the IVC diameter was > 19 mm and collapsed $< 20\%$ with quiet inspiration. In indeterminate cases in which the IVC diameter and collapse did not fit this paradigm, EMRAP was estimated as 8 mmHg. These criteria were almost in agreement with the guidelines of the American Society of Echocardiography [24], but we modified the cut-off value of the IVC diameter from 21 to 19 mm in light of the different body sizes between Asian and Western populations [25]. We used the sum of the PRPG and the EMPAP as an echocardiographic estimate of the mean PA pressure (EMPAP) [19,24].

Right heart catheterization

Right heart catheterization was performed using fluid-filled catheters, and the systolic and end-diastolic PA pressures, mean PA pressure ($MPAP_{CATH}$), systolic and end-diastolic RV

pressures, and mean RA pressure were measured. The peak systolic pressure gradient between the RV and RA ($\text{RV-RA}_{\text{CATH}}$) was calculated as the difference between the peak systolic RV pressure and the RA pressure at that timing. We calculated the peak early diastolic pressure gradient between the PA and the RV ($\text{PA-RV}_{\text{CATH}}$) by subtracting the lowest early diastolic RV pressure from the PA pressure at that timing (Fig. 2).

Statistical analyses

Standard statistical software (SPSS version 23 for Windows, SPSS, Chicago, IL, USA) was used for the statistical analyses. Pearson's linear correlation and a regression analysis, and a Bland-Altman analysis were used to compare the catheter and Doppler data [26]. Differences in continuous variables among the four TR groups were first examined by a one-way analysis of variance (ANOVA), and when a significant difference was detected, each difference between pairs of groups was tested using Fisher's LSD test. A receiver operating characteristic (ROC) curve was constructed to evaluate the ability of EMPAP to predict the presence of pulmonary hypertension ($\text{MPAP}_{\text{CATH}} \geq 25 \text{ mmHg}$). For all statistical tests, a p-value < 0.05 was used to indicate significance.

RESULTS

Relationship between TRPG and $\text{RV-RA}_{\text{CATH}}$

The TRPG was significantly correlated with $\text{RV-RA}_{\text{CATH}}$ ($r=0.73$, $p<0.001$) (Fig. 3A). In the Bland-Altman analysis, there was direct fixed bias (mean 2.52 mmHg, 95% confidence interval 0.70 to 4.34 mmHg, limits of agreement -11.27 to 16.31 mmHg) showing an overestimation of the RV-RA pressure gradient by echocardiography (Fig. 3B).

Relationship between errors of TRPG and severity of TR

Table 1 summarizes the clinical characteristics and echocardiographic and catheterization data of the study patients classified according to the severity of their TR. The difference between the TRPG and the RV-RA_{CATH} ([TRPG – RV-RA_{CATH}]) was significantly greater in the very severe TR group (14.1 ± 8.1 mmHg) than in the mild TR group (-0.4 ± 4.5 mmHg; $p<0.001$), the moderate TR group (2.0 ± 4.6 mmHg; $p<0.001$) and the severe TR group (4.9 ± 6.6 mmHg; $p=0.002$), and also significantly greater in the severe TR group than in the mild TR group ($p=0.013$) (Fig. 4). No significant difference was observed between the mild TR group and the moderate TR group, in which the [TRPG – RV-RA_{CATH}] value was nearly 0. An overestimation of the pressure gradient > 10 mmHg was observed in 7 of the 55 patients (13%). Such an overestimation was not seen in the mild or moderate TR groups, but was seen in 2 of 9 patients (22%) with severe TR, and 5 of 6 patients (83%) with very severe TR. An underestimation of the pressure gradient > 10 mmHg was seen in only one patient (2%) in the mild TR group. The degree of overestimation of RV-RA_{CATH} by TRPG (%), that is, [(TRPG – RV-RA_{CATH})/RV-RA_{CATH}*100], was also significantly greater in the very severe TR group (56 ± 46 %) than in the mild TR group (1 ± 19 %; $p<0.001$), the moderate TR group (8 ± 22 %; $p<0.001$) and the severe TR group (23 ± 28 %; $p=0.016$), and significantly greater in the severe TR group than in the mild TR group ($p=0.028$). No significant difference was observed between the mild TR group and the moderate TR group.

Relationship between PRPG and PA-RV_{CATH}

The PRPG could be measured in 45 of the 55 (82%) study patients. In these patients, the PRPG was significantly correlated with the PA-RV_{CATH} ($r=0.73$, $p<0.001$), and the correlation coefficient was nearly equal to that between the TRPG and RV-RA_{CATH} (Fig. 5A). In the Bland-Altman analysis, there was no fixed bias (mean -1.45 mmHg, 95% confidence interval -2.93 to 0.04 mmHg, limits of agreement -11.61 to 8.72 mmHg) (Fig. 5B).

Relationship between the difference between PRPG and RV-RA_{CATH} and the severity of TR

The differences between the PRPG and PA-RV_{CATH} ([PRPG – PA-RV_{CATH}]) were not significantly different among the mild TR (-0.8 ± 4.4 mmHg), moderate TR (-3.4 ± 6.3 mmHg), severe TR (-3.1 ± 5.9 mmHg) and very severe TR groups (0.9 ± 4.8 mmHg). Severe PR was observed only in one of the 45 patients (2%) who belonged to the mild TR group and whose [PRPG – PA-RV_{CATH}] value was high at 7.0 mmHg. The percent difference between PRPG and the actual value (%), that is, [(PRPG – PA-RV_{CATH})/PA-RV_{CATH} × 100], also did not show any significant difference among the 4 groups (0 ± 38 %, -9 ± 33 %, -12 ± 32 % and 1 ± 25 %, respectively).

Estimation of the mean pulmonary artery pressure using the PRPG

The EMPAP was significantly correlated with the MPAP_{CATH} ($r=0.76$, $p<0.001$) (Fig. 6A), and no fixed bias was detected in the Bland-Altman analysis (mean 1.76 mmHg, 95% confidence interval -0.12 to 3.65 mmHg, limits of agreement -11.15 to 14.68 mmHg) (Fig. 6B). The ROC analysis to determine patients with MPAP_{CATH} ≥ 25 mmHg by EMPAP revealed that the area under the curve was 0.93 and the sensitivity and specificity were 100% and 87%, respectively when using the cut-off value of 24.9 mmHg (Fig. 7).

DISCUSSION

It has been suggested that the Doppler estimation of the peak systolic RV-RA pressure gradient based on TR velocity measurement may be inaccurate in patients with severe TR because of the theoretical irrelevance of the simplified Bernoulli equation [12]. However, no

clear evidence of this type of error has been provided in a clinical setting. Moreover, we do not have any guidance to avoid such an error; in other words, there has not been any evidence showing how severe TR interferes with the accurate evaluation of the RV-RA pressure gradient. The results of this study clarified that echocardiography increasingly overestimates the RV-RA pressure gradient with the advance of TR severity, as was theoretically predicted by the pressure recovery phenomenon associated with the laminar regurgitant flow. Our study results also suggested that the risk of the overestimation due to this mechanism could occur in patients with $VC_{TR} > 7$ mm (the “severe TR group”) and was very frequently seen in those with $VC_{TR} > 11$ mm (the “very severe TR group”). We also observed that the PRPG and EMPAP derived from the PRPG properly reflect the PA-RV_{CATH} and MPAP_{CATH}, respectively, suggesting usefulness of PRPG measurement as an alternative in such patients.

Fisher et al. [6] reported that an echocardiographic estimate of the PA systolic pressure underestimates the actual value measured by right heart catheterization by > 10 mmHg in 20% of patients (12/59) and overestimates by > 10 mmHg in 27% (16/59). Rich et al. [7] reported that the PA systolic pressure by echocardiography underestimated an actual value by > 10 mmHg in 30% of their patients (48/160) and overestimated it by > 10 mmHg in 21% (33/160). Testani et al. [8] reported that a misclassification occurred on a four-point scale of clinical categories of PA systolic pressure by echocardiography in 54% of their patients, and Farber et al. [9] also reported that the echocardiographic estimate of the PA systolic pressure was inaccurate in 57% of their patients by > 10 mmHg higher or lower than the value obtained by right heart catheterization. These researchers all suggested that the underestimation might have been caused by an inadequate quality of Doppler recording and an incorrect angle between the Doppler beam and the TR jet, and the overestimation was attributed to the incorrect echocardiographic estimate of the RA pressure. However, none of the above studies examined the error of the TRPG or the influence of TR severity on the TRPG or the estimated PA systolic pressure, and they did not discuss the possibility of the

overestimation due to the pressure recovery phenomenon.

Groh et al. [10] compared the echocardiographic estimates of the RV-RA pressure gradient and the values obtained by right heart catheterization in children, and they reported that 8 of the 80 patients (10%) were underclassified and another 8 of the 80 (10%) were overclassified by echocardiography. They noted that viscous losses can lead to the underestimation of RV pressure. They also proposed that the small RA size in children may induce the pressure recovery phenomenon, leading to an overestimation of RV pressure by echocardiography, but they did not assess the relationship between the overestimation and TR severity.

Alone among the previous reports, Özpelit et al. [11] examined the relationship between the severity of TR and the error in estimated PA systolic pressure by echocardiography, and they found that the echocardiographic overestimation of PA systolic pressure was more frequently seen in patients with severe TR than in those with mild-to-moderate TR. However, they did not examine the relationship between echocardiographic and catheter pressure gradients, and they again attributed the cause of the error to an inaccurate RA pressure estimation due to TR.

In this study, we compared the TRPG with $\text{RV-RA}_{\text{CATH}}$ to exclude the influence of echo-derived RA pressure. Nevertheless, we found that echocardiography overestimated the $\text{RV-RA}_{\text{CATH}}$ in the patients with severe or very severe TR. In our series, underestimation of an actual value by $> 10 \text{ mmHg}$ was seen in only one of the 55 patients (2%), which might have occurred because we more strictly excluded patients with inadequate Doppler recording image quality. On the other hand, the overestimation of an actual value by $> 10 \text{ mmHg}$ was seen in 7 of the 55 patients (13%). Two of these 7 patients had severe TR ($7 \text{ mm} < \text{VC}_{\text{TR}} \leq 11 \text{ mm}$) and the other 5 had very severe TR ($\text{VC}_{\text{TR}} > 11 \text{ mm}$). Thus, this is the first study to clarify that the TRPG overestimates the systolic RV-RA pressure gradient due to TR, and the overestimation very frequently occurs when the VC_{TR} is $> 11 \text{ mm}$. From a more practical viewpoint, it would

be safe not to use the TRPG for PA pressure estimations when the VC_{TR} is > 7 mm.

Among the four cardiac valves, a wide regurgitant orifice may be most frequently seen in the tricuspid valve, probably because of easy distensibility of right heart structures around the tricuspid annulus [27,28]. A very wide regurgitant orifice leads to laminar regurgitant flow instead of turbulent flow [12-14]. The simplified Bernoulli equation hypothesizes the presence of strongly turbulent flow in which the kinetic energy is completely depleted due to the turbulence. However, in a laminar TR flow, the kinetic energy is preserved and converted into static pressure, which is denoted as a pressure recovery phenomenon. Thus, the peak systolic RV-RA pressure gradient can be overestimated by the simplified Bernoulli equation, as may be frequently seen in transaortic valve pressure gradient of patients with relatively mild aortic stenosis [29-31]. Because our study subjects were adult patients and the RA dimension was very enlarged in our severe and very severe TR patients (52.9 ± 9.9 mm), an overestimation due to small RA size, as Groh et al. described, is very unlikely. Thus, we considered that the laminar TR flow may be the predominant cause of the overestimation of the RV-RA pressure gradients in patients with severe or very severe TR.

This study also showed fairly good correlations between the EMPAP and the $MPAP_{CATH}$. Although an overestimation of pressure gradients can also occur in patients with severe PR, such patients may be virtually limited to those after surgery for tetralogy of Fallot, who would be far less frequent than patients with severe TR. Thus, the EMPAP derived from the PRPG may be useful as an alternative method to estimate PA pressure, especially in patients with severe or very severe TR whose TRPG will be inaccurate.

There are several limitations in this study. First, the sample size was relatively small in a single hospital, and the study subjects included only adult patients. These might have led to some bias and influenced the results. In pediatric cardiology, for example, more caution may be required to use the PRPG for the assessment of PA pressure because patients with severe PR might be more frequent [32]. Only 17 of our 55 patients had pulmonary

hypertension defined as $\text{MPAP}_{\text{CATH}} \geq 25 \text{ mmHg}$, and this may have worsened the correlations of pressures between echocardiography and catheterization in this study. In addition, the small number of patients with very severe TR might have led to a type 2 error, that is, overlooking statistical differences among the groups classified according to TR severity. Second, right heart catheterization and echocardiography were not performed simultaneously; there was a time difference of 6.8 ± 6.8 days (0–23 days). Although we carefully excluded patients with obvious changes in clinical condition and/or cardiovascular medications between echocardiography and catheterization, the possibility of minor alternation in loading condition can not be excluded. Third, we employed a semi-quantitative approach, i.e., the VC_{TR} , for the assessment of TR severity. The proximal isovelocity surface area method is one of the available quantitative methods, but there have been reports suggesting inaccuracy of regurgitant volume by this method in patients with very severe TR [33,34]. The TR volume can be quantified based on the forward flow volume measurements in the tricuspid and pulmonary valve orifices, but this method may be too complex to be performed during daily echocardiographic examinations to judge whether TRPG measurement is feasible or not. Forth, the echocardiographic EMPAP was significantly greater in our very severe TR group than in the other 3 groups without any significant difference in the PRPG or catheterization $\text{MPAP}_{\text{CATH}}$ among the 4 groups. We think that the discrepancy between the EMPAP and $\text{MPAP}_{\text{CATH}}$ in patients with very severe TR may come from an inaccuracy of the echocardiographic EMRAP and, more importantly, the exaggerated difference between mean RA pressure and early diastolic RA pressure due to a large v wave in this situation.

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Table 1. Clinical characteristics of the study patients

Variable	Mild TR	Moderate TR	Severe TR	Very severe TR	Overall p-value
	n=29	n=11	n=9	n=6	
Baseline characteristics:					
Age (years)	67±13	68±15	64±11	64±20	0.831
HR (beats/min)	70±15	69±15	66±7	65±9	0.734
BSA (m^2)	1.60±0.17	1.63±0.21	1.68±0.30	1.50±0.20	0.394
SBP (mmHg)	118±22	121±25	106±18	113±20	0.421
DBP (mmHg)	62±12	67±16	65±11	62±13	0.707
Echocardiographic parameters:					
LVDd (mm)	49.8±8.9	51.6±12.4	58.0±15.0	47.2±7.3	0.185
LVEF (%)	55.5±15.0	55.8±15.9	49.4±21.2	53.7±15.9	0.786
LVMI (g/m^2)	102±45	126±47	147±43	106±30	0.069
LAD (mm)	42.7±13.1	43.4±10.5	54.1±11.3 [†]	53.3±11.4	0.042
RVDd (mm)	39.5±9.6	42.2±4.0	47.0±6.7	50.4±8.4 ^{**}	0.012
RAD (mm)	40.2±8.1	43.8±5.4	49.0±8.5 ^{**}	58.8±9.5 ^{*** ††† §}	<0.001
IVCD (mm)	14.9±4.5	16.3±4.8	17.1±4.1	24.7±3.1 ^{*** ††† §§}	<0.001
VC _{TR} (mm)	2.3±0.6	5.1±1.3 ^{***}	8.9±1.2 ^{*** †††}	14.0±2.2 ^{*** ††† §§§}	<0.001
TRPG (mmHg)	23.9±5.5	26.4±12.2	30.0±8.3	39.7±15.2 ^{*** †§}	0.002
PRPG (mmHg)	14.2±6.3	14.7±4.7	15.5±7.3	21.4±9.5	0.201
EMRAP (mmHg)	6.2±4.2	8.7±5.4	7.7±3.5	13.8±2.9 ^{*** † §§}	0.002
EMPAP (mmHg)	20.7±8.4	23.5±9.3	23.2±8.4	35.0±9.1 ^{** † §}	0.017
Catheterization parameters:					
RV-RA _{CATH} (mmHg)	24.3±7.0	24.4±9.5	25.1±8.4	25.7±9.6	0.979
PA-RV _{CATH} (mmHg)	14.8±5.5	17.3±8.9	18.6±7.4	22.3±7.2	0.081
PCWP (mmHg)	12.0±7.2	12.5±7.6	15.7±8.0	16.7±6.0	0.367
PASP (mmHg)	29.0±10.8	30.5±13.1	35.4±13.0	39.0±8.3	0.181
PADP (mmHg)	13.3±6.2	13.1±7.5	16.7±8.0	17.3±4.7	0.354
MPAP (mmHg)	19.2±7.7	19.5±10.1	24.0±10.5	24.8±4.9	0.284
RVSP (mmHg)	30.0±9.6	30.1±12.6	33.8±11.3	40.3±6.7	0.148
RVEDP (mmHg)	8.4±4.4	8.9±5.4	9.5±5.9	13.2±3.6	0.188
MRAP (mmHg)	6.7±5.2	7.2±6.1	8.7±5.8	12.8±3.9	0.091

HR, heart rate; BSA, body surface area; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVDd, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; LAD, left atrial diameter; RVDd, right ventricular end-diastolic diameter; RAD, right atrial diameter; IVCD, inferior vena cava diameter; VC_{TR}, vena contracta of tricuspid regurgitation jet; TRPG, peak systolic pressure gradient of tricuspid valve measured by echocardiography; PRPG, peak early diastolic pressure gradient of pulmonary valve measured by echocardiography; EMRAP,

echocardiographic estimate of mean right atrial pressure; EMPAP, echocardiographic estimate of mean pulmonary artery pressure; RV-RA_{CATH}, peak systolic right ventricular-right atrial pressure gradient; PA-RV_{CATH}, peak early diastolic pulmonary artery-right ventricular pressure gradient; PCWP, pulmonary capillary wedge pressure; PASP, systolic pulmonary artery pressure; PADP, end-diastolic pulmonary artery pressure; MPAP, mean pulmonary artery pressure; RVSP, peak systolic right ventricular pressure; RVEDP, end-diastolic right ventricular pressure; MRAP, mean right atrial pressure. Data are mean \pm SD. * $p<0.05$, ** $p<0.01$, *** $p<0.001$ vs. mild TR group; $^{\dagger}p<0.05$, $^{+\dagger}p<0.01$, $^{+\ddagger}p<0.001$ vs. moderate TR group; $^{\S}p<0.05$, $^{\S\S}p<0.01$, $^{\S\S\S}p<0.001$ vs. severe TR group.

FIGURE LEGENDS

Fig. 1. Continuous-wave Doppler measurement of the peak systolic tricuspid regurgitant velocity (A) and the peak early diastolic pulmonary regurgitant velocity (B).

Fig. 2. Measurements of pressure gradients from catheterization pressure recordings.

The peak systolic right ventricular pressure and the right atrial pressure at the timing were measured, and their difference was calculated. Similarly, the lowest early diastolic right ventricular pressure and the pulmonary artery pressure at the timing were measured, and their difference was calculated. The mean pulmonary artery pressure was also measured.

Fig. 3. The relationship between the peak systolic right ventricular-right atrial pressure gradient derived by echocardiography (TRPG) and that measured by right heart catheterization (RV-RA_{CATH}).

The results of the correlation and regression analysis (A) and Bland-Altman analysis (B) are shown.

Fig. 4. The difference between the echocardiography-derived peak systolic right ventricular-right atrial pressure gradient (TRPG) and the catheterization-derived one (RV-RA_{CATH}) in relation to the severity of tricuspid regurgitation.

Fig. 5. The relationship between the peak early diastolic pulmonary artery-right ventricular pressure gradient derived by echocardiography (PRPG) and that measured by right heart catheterization (PA-RV_{CATH}).

The results of the correlation and regression analysis (A) and Bland-Altman analysis (B) are shown.

Fig. 6. Relationship between the mean pulmonary artery pressure estimated by echocardiography (EMPAP) and the mean pulmonary artery pressure measured by right heart catheterization (MPAP_{CATH}).

The results of correlation and regression analysis (A), and Bland-Altman analysis (B) are shown.

Fig. 7. Receiver operating characteristic curve showing the ability of the mean pulmonary artery pressure estimated by echocardiography to predict pulmonary hypertension defined by the catherterizaiton-derived mean pulmonary artery pressure ≥ 25 mmHg.

Figure 1

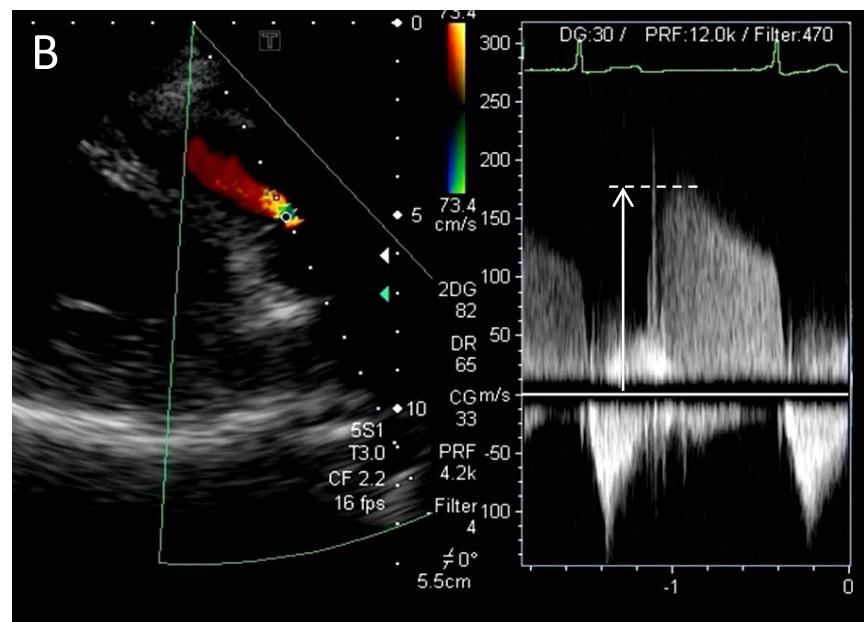
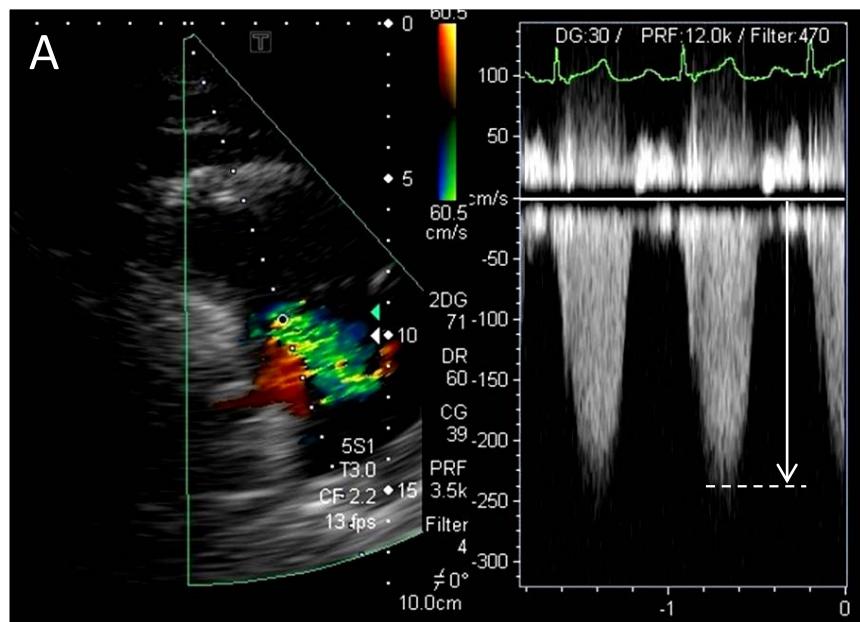


Figure 2

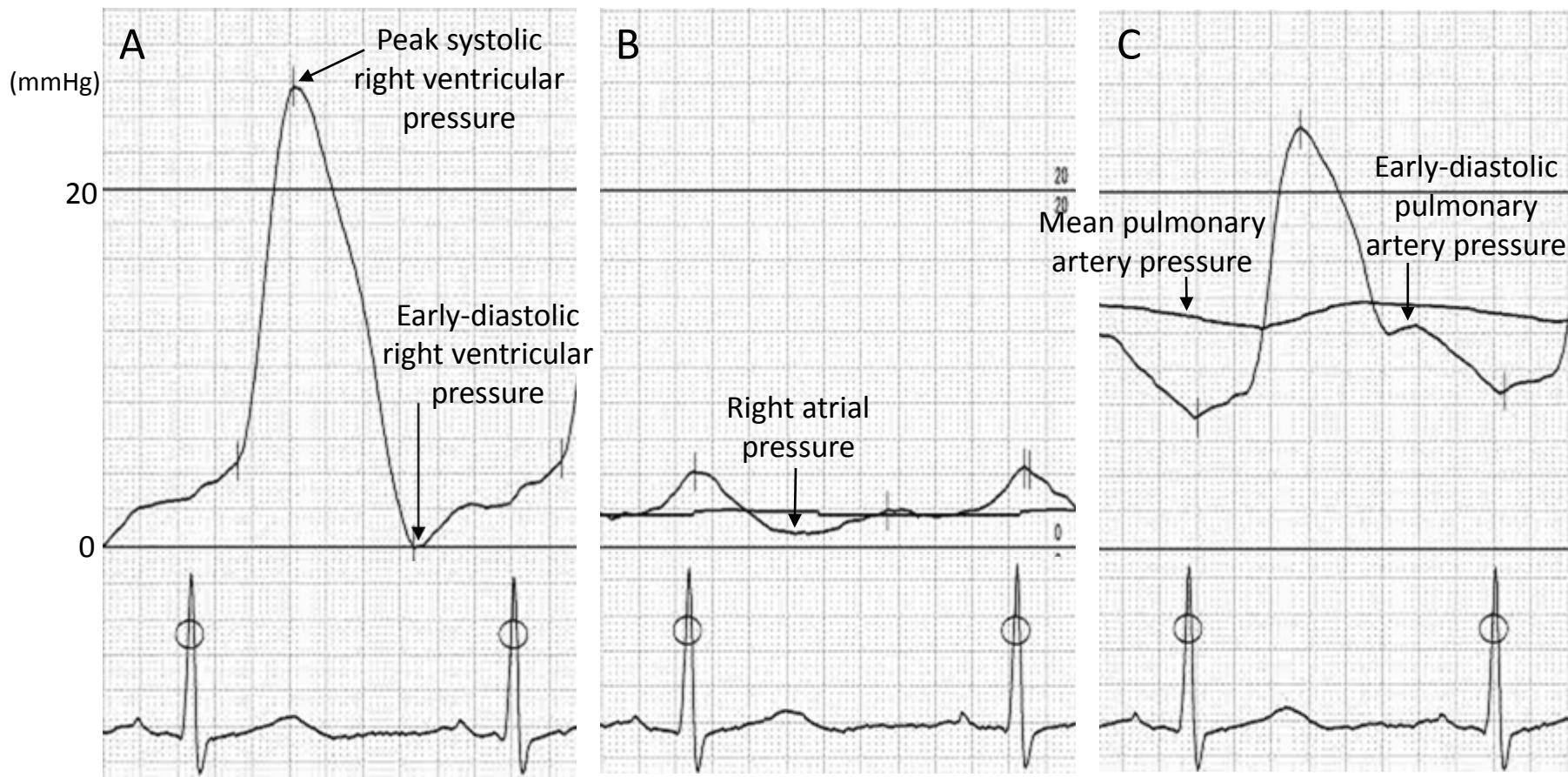


Figure 3

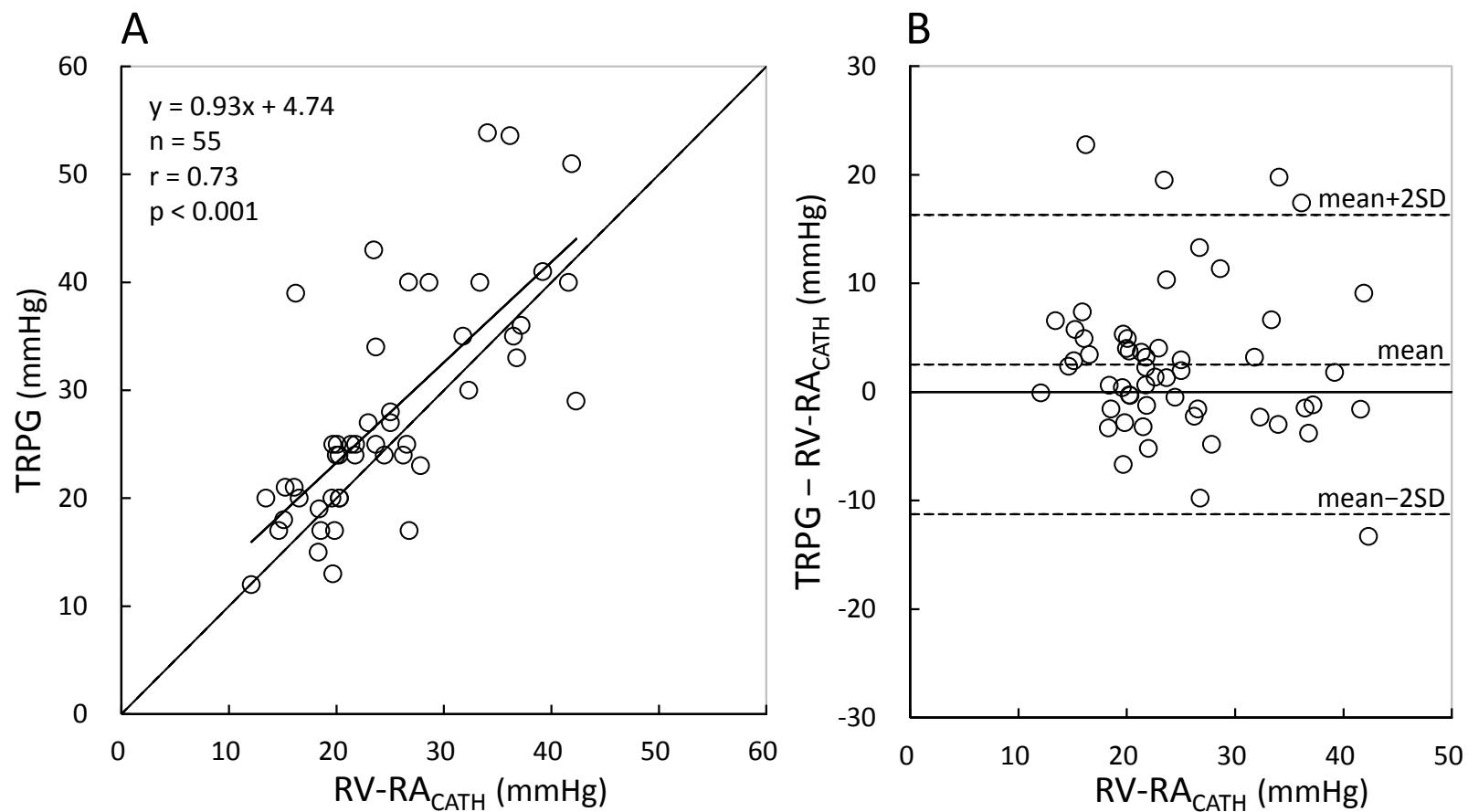


Figure 4

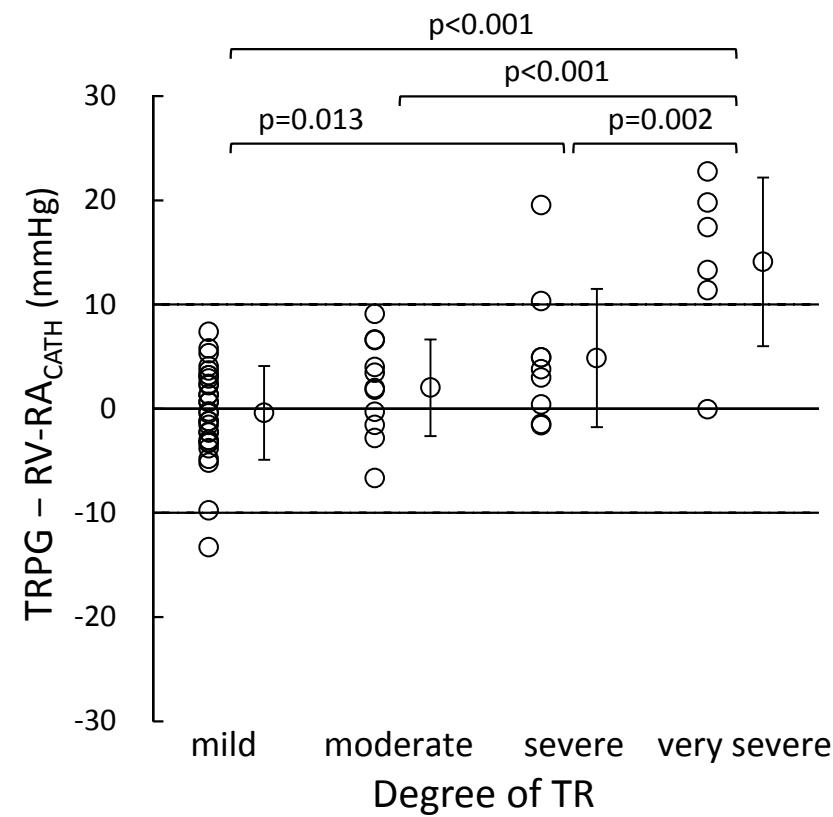


Figure 5

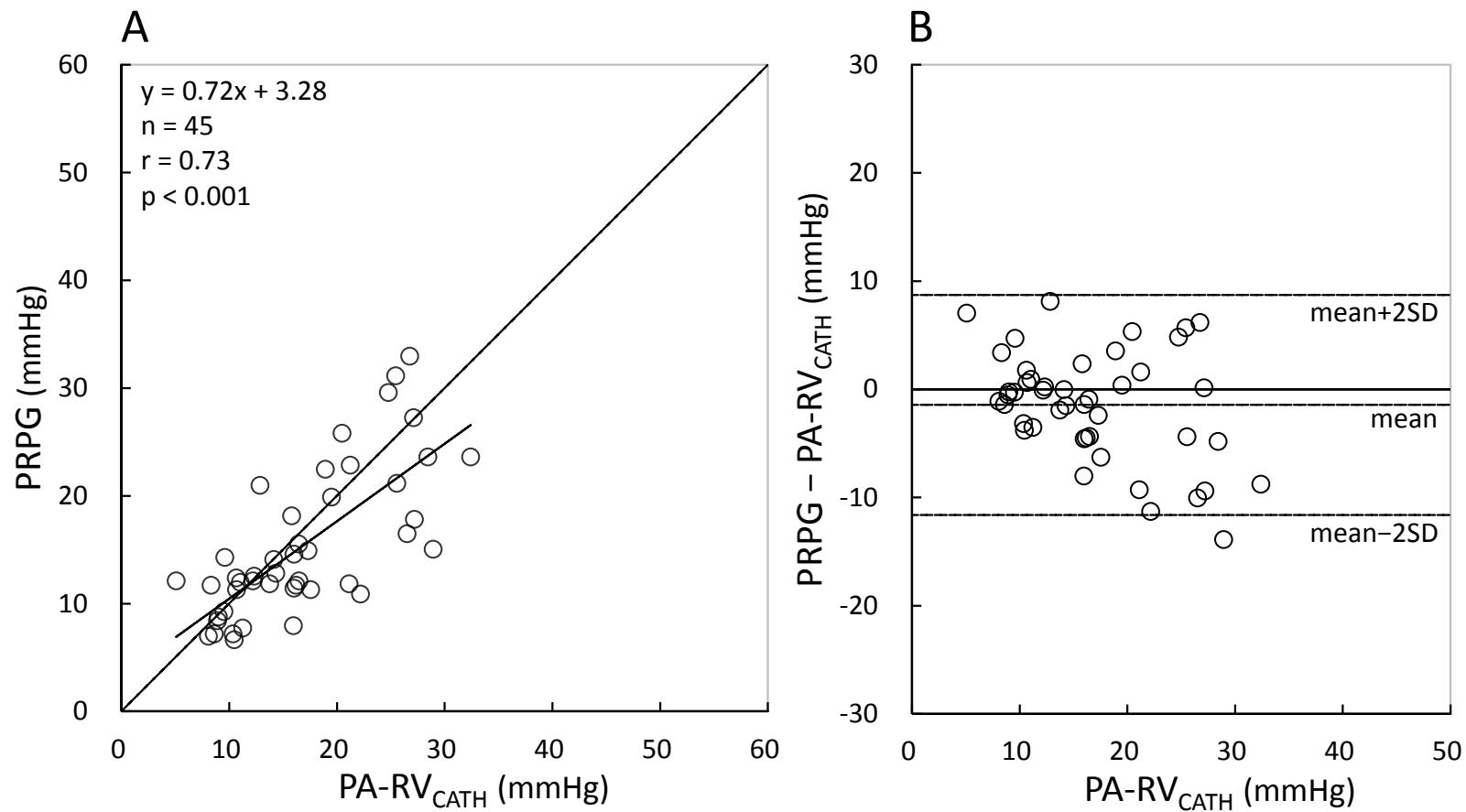


Figure 6

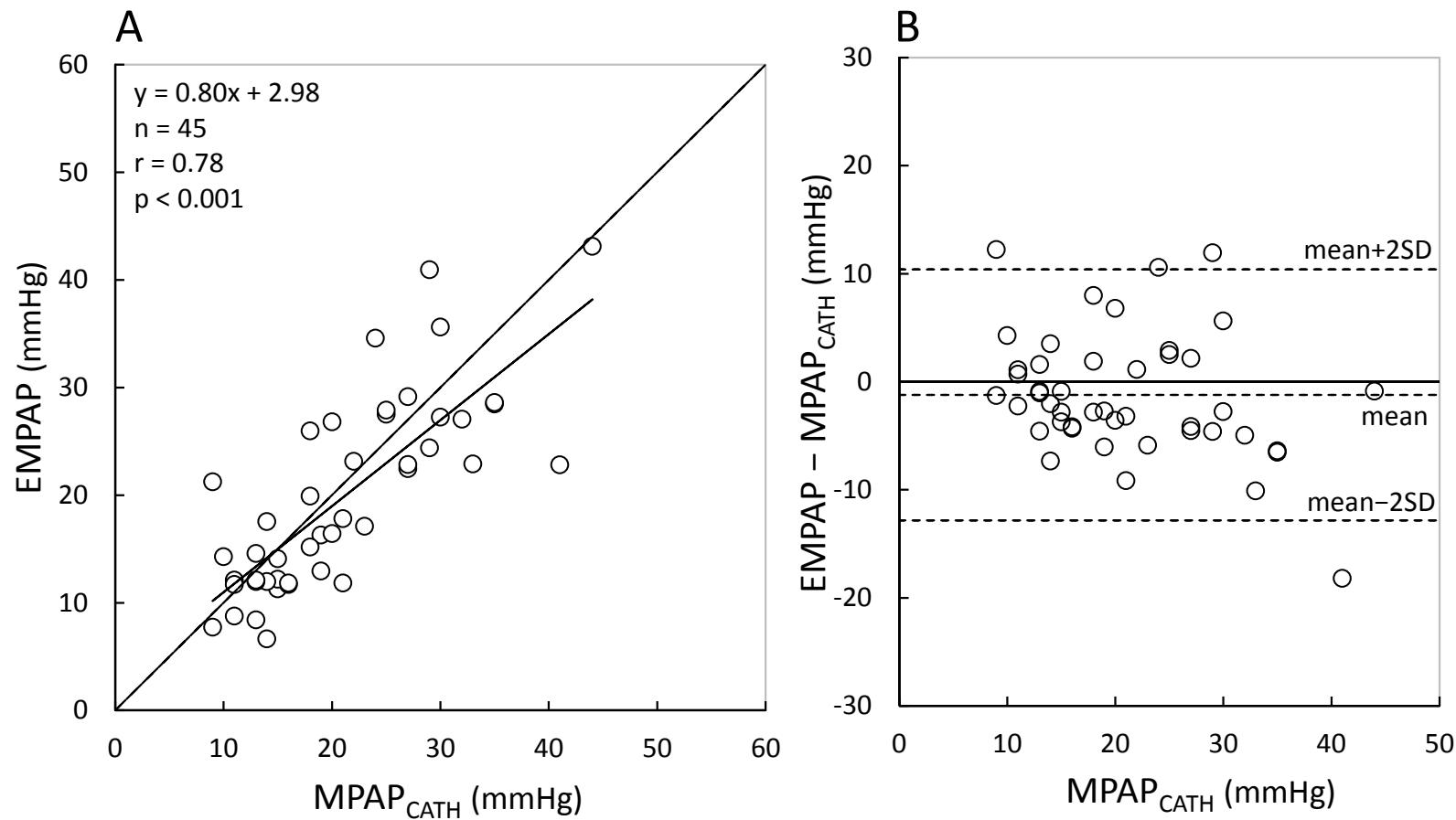


Figure 7

