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Improvement in the electrocardiograms associated with right ventricular hypertrophy after balloon pulmonary angioplasty in chronic thromboembolic pulmonary hypertension

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ABSTRACT

Background: Balloon pulmonary angioplasty (BPA) is a treatment option for patients with chronic thromboembolic pulmonary hypertension (CTEPH).

Methods and results: In 60 patients with CTEPH, we examined the hemodynamic data before and after BPA. In addition, the sequential ECG findings for right ventricular hypertrophy (RVH) were assessed. The mean pulmonary arterial pressure (mPAP) decreased from 38 ± 11 to 20 ± 4 mm Hg ($p < 0.05$). The ROC analysis showed that the S waves in V5, R waves in V1 + S waves in V5, S waves in I, and QRS axis were significant predictors of an mPAP ≧ 30 mm Hg (AUC > 0.75, $p < 0.01$). The predictive values for the mPAP before the BPA were the S and R waves in lead V6, and P waves in lead II ($33.417 + 0.078 \times P$ in II $- 0.10 \times R$ in V6 $+ 0.012 \times S$ in V6). The change in the mPAP (ΔmPAP) correlated with the change in the amplitudes of the ECGs: ΔS wave in lead I ($R = 0.544$, $p < 0.001$), ΔR in V1 + S in V5 ($R = 0.476$, $p < 0.001$), and ΔP wave in II ($R = 0.511$, $p < 0.001$). At 6 months of follow-up, the improvement in an R in V1 + S in V5 of ≧10 mm implied a better functional status.

Conclusion: BPA therapy reduced the pulmonary arterial pressure in patients with CTEPH and was associated with an improvement in the ECG findings related to RVH.

1. Introduction

In chronic thromboembolic pulmonary hypertension (CTEPH), the obstruction of the vascular bed due to organized thrombi causes an elevation in the pulmonary artery pressure (PAP) [1]. CTEPH has a poor outcome because of right heart failure with progressive right ventricular (RV) dysfunction, dilatation, and severe tricuspid regurgitation caused by a chronic pressure overload [2,3]. A pulmonary endarterectomy (PEA) is a surgical treatment for CTEPH, and has been proven to improve the prognosis [4,5], which is, however, hardly applied in patients with distal obstructions or significant comorbidities.

Balloon pulmonary angioplasty (BPA) is an alternative therapy for patients with CTEPH [6]. BPA may improve the pulmonary hemodynamics associated with the amelioration of symptoms and the RV function [7,8]. The RV function is known as an important prognostic factor in patients with CTEPH [9]. To evaluate the RV hemodynamics by right heart catheterization (RHC) is feasible but invasive. Previous studies showed a significant improvement in the functional parameters of the RV by echocardiography after BPA [10–12]. Echocardiographic methods including 3-dimentional transthoracic echocardiography and speckled tracking also provide a precise evaluation of the RV function [13]. The 12-lead electrocardiogram (ECG) is easily available and inexpensive. The predictive values of the ECG patterns suggestive of right ventricular hypertrophy (RVH) are investigated in diagnosing pulmonary hypertension (PH) [14–16]. However, whether the parameters of the ECG respond to treatment in patients with CTEPH after BPA has not been fully investigated. We evaluated the relationship between the improvement in the ECG and RV function in patients with CTEPH who underwent BPA treatment.

2. Methods

2.1. Study population

This study was approved by our Institutional Review Board based on the ethical guidelines of the Declaration of Helsinki. All patients

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provided their written informed consent before the procedure. A series of 66 patients were enrolled, but 4 patients with complete right bundle branch block (CRBBB) and 2 patients with atrial fibrillation (AF) were excluded. There were no patients classified to a PEA. Sixty patients with CTEPH (65 ± 14 years old, 21 male) at a single center were included in this study. The diagnosis of CTEPH was defined as follows. 1) A mean pulmonary arterial pressure (mPAP) >25 mm Hg measured by RHC. 2) The recognition of pulmonary thromboembolisms using contrast-enhanced lung computed tomography, perfusion lung scintigraphy, or pulmonary angiography. 3) Collagen vascular disease, parenchymal lung disease, left heart abnormality, and other systemic diseases, were ruled out by blood tests and echocardiography. We also defined severe PH as an mPAP >40 mm Hg. We excluded any patients who had pulmonary artery hypertension, lung disease, primary left ventricular systolic dysfunction, and aortic and/or mitral valvular heart disease, and who were suitable for the PEA. The indication of the BPA was decided according to the Guidelines for Treatment of Pulmonary Hypertension (JCS2012) [17], on the basis of the inoperability and surgical accessibility of the thrombi.

2.2. Right heart catheterization and BPA

All patients underwent standard RHC using a 6 Fr or 7 Fr Swan-Ganz catheter (Swan-gantz CCO CEDV, Edwards Lifescience, Irvine, CA, USA) before the first BPA procedure. The follow-up RHC was performed within 2 weeks after the final procedure. The cardiac output (CO) was calculated by the direct Fick method. The procedural details of the BPA were previously described [13]. The BPA was performed through the right jugular vein or femoral vein. Selection of the pulmonary artery segment for dilation was determined and measured by intravascular ultrasound or optical coherence tomography. After a 0.014-inch wire was crossed across the targeted lesions, we evaluated and measured the target vessel characteristics and diameter by pulmonary angiography in all lesions. After determination of the vessel diameter, we dilated the vessel using balloon catheters of an appropriate size (1.25 to 8 mm). The balloon was inflated by hand until the indentation disappeared or until the balloon had fully expanded (2 to 22 atm). Each session was limited by an X-ray time of 60 min and a contrast agent of 300 ml. To achieve an mPAP of <25 mm Hg, repeated sessions were performed.

2.3. Electrocardiography

The standard 12-lead ECG was performed using a cardiofax V ECG-1550 (Nihon Kohden, Tokyo, Japan) by trained technicians. The ECG calibration was 25 mm/s and 10 mm/mV. The amplitudes of the R and S waves in leads I, V1, V5, and V6, P wave amplitude in lead II, and T wave amplitude in leads V1, V2, and V3 were measured before and after the BPA. An ECG after each BPA session was recorded 2 weeks later to avoid any effects of therapy such as acute pulmonary edema. Several parameters associated with RVH, such as the basal rhythm, frontal axis, P wave in II ≧ 2.5 mV, R wave in I ≦ 2 mm, R wave in V1 ≧ 7 mm, R/S in V1 ≧ 1, R/S in V6 ≦ 1, R wave in V1 + S wave in V5 ≧ 10 mm, and T wave inversion in all of V1-V3 were evaluated [14]. We assessed the amplitude of the ECG electronically. Every ECG analyzed was checked by an expert cardiologist to confirm the automatic analysis.

2.4. Echocardiography

Experienced personnel in our echocardiography laboratory performed all the echocardiographic examinations using Vivid E9 scanners (GE Healthcare, Horten, Norway). The examinations were performed according to the current recommendations, including dedicated RV views [18]. The RV size and function were estimated as recommended by the American Society of Echocardiography [19]. The RV diameters at the basal and middle cavity of the minor and longitudinal dimension were calculated in the 4-chamber view. Doppler measurements of the tricuspid regurgitation pressure gradient (TRPG) were performed in at least two different views, with the most commonly used views being the 4-chamber and parasternal short axis views. The right atrial pressure was estimated by the dimension and respiratory variation of the inferior vena cava.

2.5. R in V1 + S in V5 ≧ 10 mm for correlating the functional status at 6 months follow-up

We classified the patients with criteria of an R in V1 + S in V5 of ≧10 mm before the BPA into 2 groups as follows according to the change in that parameter after the BPA: improved (improved group) and not improved (unchanged group). We compared the functional characteristics among those groups at 6 months of follow-up.

2.6. Statistical analysis

The continuous variables were expressed as the mean ± standard deviation and categorical variables as numbers and proportions. The continuous variables were compared using a *t*-test or Mann-Whitney *U* test. A receiver-operating characteristic (ROC) curve was created and the area under the curve (AUC) was calculated to determine the significance of the ECG criteria for an mPAP ≧ 30 mm Hg. We chose the parameters that had an AUC > 0.75. A multiple regression analysis was performed to evaluate the independent predictors of the mPAP before the BPA therapy. The correlations of the improvement between the mPAP and ECG parameters were assessed by a Pearson's correlation coefficient (R). A p value < 0.05 was considered statistically significant. The statistical analyses were performed using IBM SPSS Statics software version 22 (IBM, Armonk, NY).

3. Results

3.1. Patient characteristics

A series of 60 patients were included in this study. The baseline clinical characteristics are summarized in Table 1. The mean age was 65 ± 14 years old and 35% of the patients were men.

3.2. Hemodynamic data

The hemodynamic data are summarized in Table 2. Twenty-four patients had severe PH before the BPA therapy. The values obtained by catheterization, except for the systemic vascular resistance, improved after the BPA therapy (averaged 6 ± 2 procedures). The mPAP

Table 1
Baseline patient characteristics.

Age (years)	65 ± 14
Male, n = (%)	21 (35)
Height (cm)	160.1 ± 9.7
Body weight (kg)	62.0 ± 16.7
WHO functional class	
I/II/III/IV, n	0/13/43/4
6 minute walk distance (m)	313 ± 102
Systolic blood pressure (mm Hg)	117 ± 16
Diastolic blood pressure (mm Hg)	70 ± 14
Cr (mg/dl)	0.9 ± 0.2
BNP (pg/ml)	232.4 ± 595.7
UA (mg/dl)	6.3 ± 1.9
Medication	
Soluble guanylate cyclase stimulator, n = (%)	2 (3)
Phosphodiesterase type-5 inhibitor, n = (%)	36 (60)
Endothelin receptor antagonist, n = (%)	24 (40)
Prostanoid, n = (%)	21 (35)
Calcium channel blocker, n = (%)	12 (20)
Vitamin K antagonist, n = (%)	54 (90)

Table 2
The changes in the hemodynamic data.

Hemodynamic data	Before	After	Δpost-pre	p
Systolic right ventricular pressure (mm Hg)	63.5 ± 19.6	33.3 ± 7.3	−30.3 ± 17.8	<0.01*
Mean right atrial pressure (mm Hg)	6.8 ± 2.9	2.2 ± 1.7	−4.3 ± 3.7	<0.01*
Mean pulmonary artery pressure (mm Hg)	38.0 ± 10.7	19.4 ± 4.1	−18.6 ± 9.8	<0.01*
Mean pulmonary capillary wedge pressure (mm Hg)	9.3 ± 2.9	7.1 ± 3.4	−2.2 ± 3.8	<0.01*
Cardiac output (Fick) (L/min)	3.5 ± 1.1	3.7 ± 0.9	0.2 ± 1.0	0.03*
Cardiac index (Fick) (L/min/m^2)	2.1 ± 0.5	2.3 ± 0.4	0.2 ± 0.6	0.03*
Pulmonary vascular resistance (dyne·sec·cm^{-5})	714 ± 524	263 ± 101	−458 ± 500	<0.01*
Systemic vascular resistance (dyne·sec·cm^{-5})	1878 ± 792	1670 ± 498	−230 ± 1001	0.31

* P value < 0.05.

decreased from 38 ± 11 to 20 ± 4 mm Hg ($p < 0.05$). The average period between the initial and last procedures was 216 ± 120 days.

3.3. The correlation between the ECG parameters and mPAP before the BPA

On the basis of the ECG and RHC data before the BPA, the correlation between the ECG parameters and mPAP was assessed.

The ROC analysis for an mPAP ≧ 30 mm Hg is shown in Fig. 1. The S wave in V5 (AUC 0.809, 95% CI 0.712–0.906, $p < 0.01$), R wave in V1 + S wave in V5 (AUC 0.804, 95% CI 0.711–0.897, $p < 0.01$), S wave in I (AUC 0.776, 95% CI 0.673–0.879, $p < 0.01$), and QRS axis (AUC 0.771, 95% CI 0.667–0.874, $p < 0.01$) were significant predictors.

Before the BPA, the ECG parameters indicating an mPAP ≧ 30 mm Hg were investigated using a multiple regression analysis. The S and R waves in V6, and P waves in II significantly correlated with a higher mPAP (33.417 + 0.078 × P in II-0.10 × R in V6 + 0.012 × S in V6).

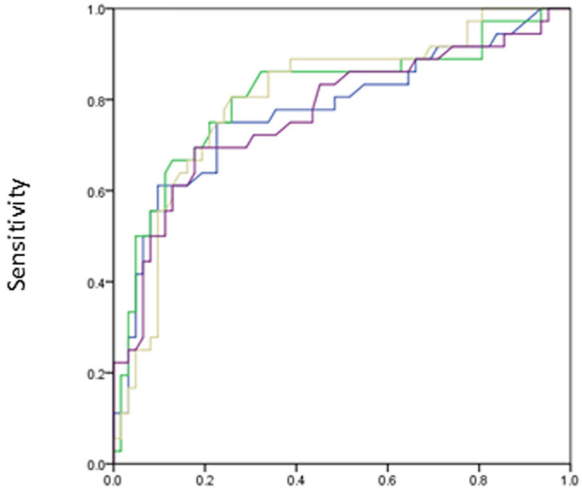
3.4. The prevalence of ECG findings associated with RVH

The prevalence of ECG patterns suggestive of RVH in all patients before and after the BPA is summarized in Fig. 2. The prevalence of each parameter ranged from 5% to 56% before the BPA and from 0% to 30% after the BPA. The highest was 56% for a T wave inversion in all of V1-V3 before the BPA. After the BPA, the highest was 30% for an R/S in V1 ≧ 1. In contrast, the lowest before and after the BPA was 5% for a P wave in II ≧ 2.5 mV, and 0% for an R/S in V6 ≦ 1 and P wave in II ≧ 2.5 mV, respectively. The prevalence of the following parameters decreased significantly: R wave in V1 ≧ 7 mm (23% vs. 8%, $p = 0.024$), R/S in V6 ≦ 1 (18.3% vs. 0%, $p < 0.01$), R wave in V1 + S wave in V5 ≧ 10 mm (46.7% vs. 18.3%, $p < 0.01$), qR in V1 (8.3% vs. 1.7%, $p < 0.01$), QRS axis ≧ 110° (18.3% vs. 3.3%, $p < 0.01$), and T wave inversion in all of V1-V3 (56.7% to 8.3%, $p < 0.01$).

Supplemental Table 1 shows that each amplitude of the ECG parameters improved significantly before the BPA than that after the BPA except for an S wave in V1 and R/S in V1. The correlation between the changes in the amplitudes of the ECG parameters and changes in the mPAP (ΔmPAP) were also estimated (Table 3). The change in the S waves in I (ΔS wave in I) correlated with the ΔmPAP ($R = 0.544$, $p < 0.001$). In addition, the ΔR in V1 + S in V5 ($R = 0.476$, $p < 0.001$) and ΔP wave in II ($R = 0.511$, $p < 0.001$) had a good correlation (Fig. 3).

3.5. The improvement in the echocardiographic data

The echocardiographic parameters reflecting the RV size and function at baseline and during the follow-up after the BPA are shown in Supplemental Table 2. All diameters of the RV were significantly



	AUC	Cut-off	Sens	Spec
S wave in I	0.766*	295	0.750	0.774
S wave in V5	0.809*	578	0.861	0.677
R wave in V1 + S wave in V5	0.804*	930	0.806	0.742
QRS axis	0.771*	79.5	0.694	0.823

Fig. 1. Receiver-operating characteristics curves for the ECG parameters for predictors of pulmonary hypertension. The area under the curve (AUC), cut-off level, sensitivity, and specificity are shown. *$p < 0.01$ vs. AUC = 0.5.

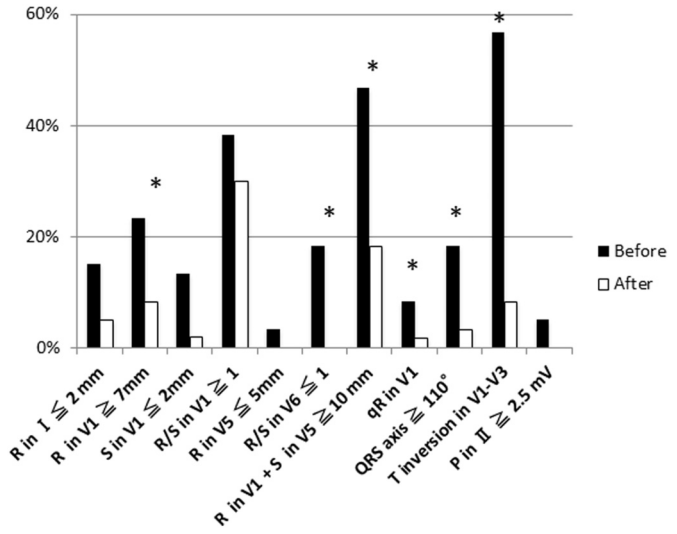


Fig. 2. The prevalence of the ECG parameters. The prevalence before and after the BPA are shown, respectively. The asterisk shows the different between that before and after the BPA ($p < 0.05$).

decreased. The tricuspid annular plane systolic excursion was also increased. Both the LV systolic and diastolic diameters were enlarged after the treatment.

3.6. R in V1 + S in V5 is an important factor for the functional status at 6 months of follow-up

We focused on the parameter involving an R in V1 + S in V5 of ≧10 because of the good correlation with the change in the PAP in addition to the baseline PH. Further, it was observed in approximately half of the patients before the BPA. The differences in the hemodynamic and echocardiographic data between the patients with and without meeting the criteria of an R in V1 + S in V5 ≧10 mm after the BPA were assessed (Table 4 and Supplemental Fig. 1). The criteria of an R in V1 + S in V5 ≧10 mm were met in 28 patients before the BPA, among whom an improvement in that parameter was observed in 17 patients after the BPA (improved group) and was not observed in the remaining 11 patients (unchanged group). The amplitude of the R in V1 + S in V5 of the unchanged group was larger than that of the improved group both before and after the BPA (1383 ± 261 vs. 2366 ± 937 μV, 794 ± 151 vs. 1688 ± 550 μV, $p < 0.01$), however, the Δpost-pre did not differ (−588 ± 263 vs. −678 ± 542 μV, $p < 0.05$). The hemodynamic data before the BPA showed that the systolic RV pressure in the unchanged group was higher (69.4 ± 18.7 vs. 82.2 ± 15.7 mm Hg, $p < 0.05$). All hemodynamic data after the BPA did not statistically differ between the two groups. In the echocardiographic data, the diameters of the RV (base and middle), LV end-systolic diameter, TRPG, and estimated systolic PAP were worse in the unchanged group. After the BPA, only the middle diameter of the RV was larger in the unchanged group (27.6 ± 3.6 vs. 30.9 ± 3.3 mm, $p < 0.05$).

At 6 months of follow-up, the mPAP using RHC, 6 minute walk distance (6MWD), WHO functional class (FC), and BNP were evaluated in both groups. As a result, the 6MWD (483 ± 85 vs. 411 ± 97 m, $p < 0.05$) and WHO FC class (1.2 ± 0.4 vs. 1.7 ± 0.5, $p < 0.05$) were significantly ameliorated in the patients with an improvement in the R in V1 + S in V5 (Fig. 4). The BNP (34.1 ± 32.9 vs. 46.9 ± 48.6 pg/μl, $p = 0.249$) was also lower in this group, and mPAP (18.9 ± 3.4 vs. 18.7 ± 4.4 mm Hg, $p = 0.464$) was not different statistically.

Table 3
Correlation between the change in the mean pulmonary artery pressure and changes in the parameters of the ECG.

ΔmPAP vs.	R	p
ΔR wave in I	−0.281	0.034*
ΔS wave in I	0.544	<0.001*
ΔR wave in V1	0.292	0.027*
ΔS wave in V1	−0.281	0.034*
ΔR/S in V1	0.228	0.089
ΔR wave in V5	−0.263	0.048*
ΔS wave in V5	0.404	0.002*
ΔR wave in V6	−0.42	0.001*
ΔS wave in V6	0.344	0.01*
ΔR/S in V6 ≦ 1	−0.176	0.193
ΔR in V1 + S in V5	0.476	<0.001*
ΔQRS axis	0.225	0.093
ΔT inversion in V1	−0.021	0.876
ΔT inversion in V2	−0.2	0.135
ΔT inversion in V3	−0.216	0.107
ΔP wave in II	0.511	<0.001*

mPAP = mean pulmonary artery pressure.
* P value < 0.05.

4. Discussion

To the best of our knowledge, this is the first study to evaluate the ECG and echocardiographic changes in patients with CTEPH undergoing BPA, and the correlation of the ECG parameters related to the hemodynamic findings. Those patients are a suitable clinical model for estimating the ECG markers of RV reverse remodeling. The 12-lead ECG may be useful to guide the clinicians in judging the treatment effect.

5. The prevalence of ECG parameters

In a previous study, the ECG parameters related to RVH were observed exclusively in patients with CTEPH. In particular, negative T waves in the V1-V5 precordial leads, negative T waves in II, III, and aVF, pulmonary P waves, and a right axis deviation >90° were observed with the highest incidence (43%, 32%, 30%, and 30%, respectively) [16]. In our study, negative T waves in all of V1–V3 were also detected in 56.7% of the patients with CTEPH.

With the progress of PAH, RV dilatation and heart failure will develop. The RV function is one of the major prognostic determinants of survival from PAH. It has been reported that a qR in V1 reflects RV dilatation and interventricular septum flattening, and it is also a predictor of death in the PAH population [20]. The prevalence of a qR in V1 declined from 8.3% to 1.7% ($p < 0.01$) in our study. ECG patterns suggestive of RVH are observed for PAH with a positive predictive value of >80% [14]. The ECG patterns focusing on the R and S amplitudes and R/S ratio in lead V1 are more predictive [14]. In our study, these parameters were also observed frequently. In particular, an R/S in V1 ≧ 1 was recognized in 38.3% and 30% before and after BPA, respectively. The amplitude of the R wave in V1 was significantly decreased, but that of the S wave in V1 and R/S ratio did not change significantly. That meant that an R/S in V1 of ≧1 could be frequently observed with an improved hemodynamic condition in patients with CTEPH.

Another study described a strong linear relation between the amplitude of the P waves in lead II and PVR in evaluations regarding a treatment response [21]. Further, the amplitude of the P waves in lead II had a prognostic value in patients with PAH. An elevated P wave amplitude in lead II is associated with changes in the QRS axis, which could be an important determinant of a treatment response in PAH patients [21]. In this study, the parameters that were associated with the mPAP were the amplitude of the S and R waves in lead V6 and the P wave in lead II. The amplitude of the S and R waves in lead V6 referred to a clockwise rotation of the heart. A clockwise rotation was associated with a higher incidence of cardiovascular risk factors and higher rates of heart failure, cardiovascular disease, and death [22].

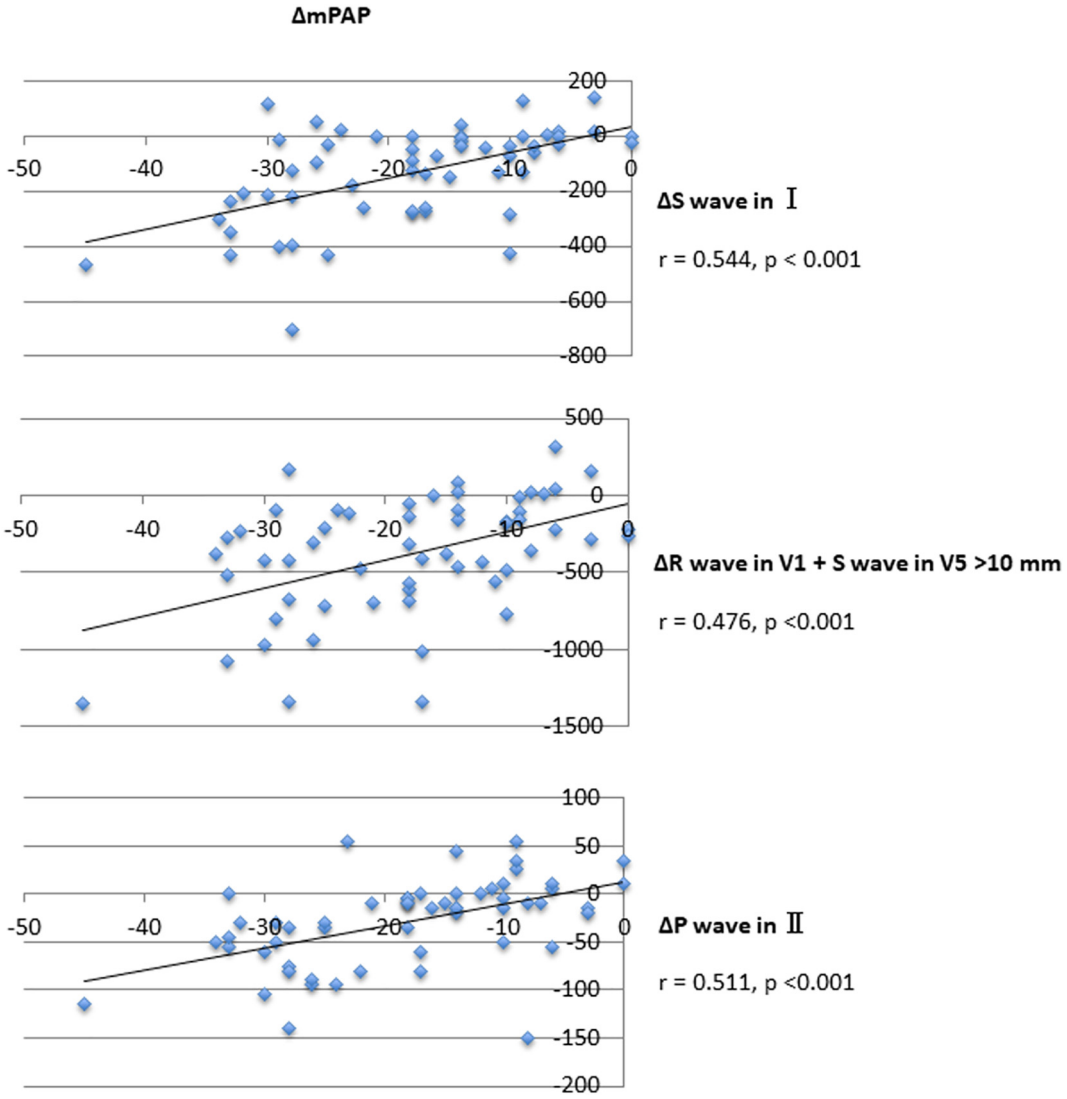


Fig. 3. Association between the changes in the mean pulmonary artery pressure and changes in the electrocardiogram parameters.

6. Reverse remodeling

In this study, the effectiveness of the ECG as a maker reflecting RVH and reverse remodeling was elucidated. Most of the parameters related to RVH significantly improved after the BPA procedures, such as a right axis deviation, clockwise rotation, parameters including the R wave in V1, and T wave inversion in leads V1-V3. Further, in addition to the ΔS wave in leadI, ΔP amplitude in lead II, and ΔR in V1 + S in V5 were linked to a reduction in the mPAP. In particular, the prevalence of an R in V1 + S in V5 of ≧10 mm changed significantly, and this parameter was a predictive factor for an mPAP of ≧30 mm Hg before the BPA. We estimated the differences between the patients with and without an improvement in this parameter. As a result, the middle diameter of the RV in the unchanged group was larger than that in the improved group, even though the pulmonary hemodynamic conditions were the same. That meant that an improvement in this parameter was important for reverse remodeling of the RV. Indeed, the groups with an improvement had better results of the 6MWD and WHO FC at 6 months of follow-up. The R in V1 + S in V5 ≧ 10 parameter also suggested the functional status.

In another study, the amplitude of the S waves in V1, R/S ratio in lead V6, and prevalence of an SIQIII pattern significantly improved after the PEA, in parallel with the remodeling of the RV observed by echocardiography [23]. The remodeling of the RV was associated with the prognosis in patients with PAH [24,25]. A size reduction of the RV may correlate with the changes in the rotation and axis. Horizontal plane loop vectorcardiography in RVH exhibits a rightward and anterior deviation [26,27]. It was considered that the BPA therapy improved the deviation of the horizontal loop.

However, it remains unclear whether those parameters could really be used to distinguish patients and the clinical follow-up. A study is needed to investigate the correlation between these ECG parameters and the RV function assessed by cardiac magnetic resonance imaging (CMRI) or 3D echocardiography.

7. Limitations

The limitation of this study was the retrospective nature and relatively small group of patients. CMRI was the best examination for an assessment of the RV function and structure, but it was not performed in this study. The RV volume and mass were not investigated by echocardiography. Further, vectorcardiography was not performed in this study.

8. Conclusion

The BPA therapy ameliorated the pulmonary hemodynamics in patients with CTEPH and caused an improvement in the ECG parameters

Table 4
The differences between the patients with and without an improvement in R in V1 + S in V5 of ≧10 mm.

	Improved (n = 17)	Not improved (n = 11)	p
Age (years)	62 ± 14	65 ± 14	0.255
Male, n = (%)	4 (24)	4 (36)	0.184
Height (cm)	160.0 ± 7.9	160.1 ± 7.1	0.469
Body weight (kg)	64.1 ± 16.6	56.3 ± 10.5	0.071
WHO functional class before BPA	2.9 ± 0.4	3.2 ± 0.4	0.07
6 minute walk distance before BPA (m)	297 ± 94	265 ± 90	0.194
Amplitude of R in V1 + S in V5 before BPA (μV)	1383 ± 261	2366 ± 937	<0.01*
Amplitude of R in V1 + S in V5 after BPA (μV)	794 ± 151	1688 ± 550	<0.01*
Δpost-pre (μV)	−588 ± 263	−678 ± 542	0.327
Hemodynamic data			
Before BPA			
Systolic right ventricular pressure (mm Hg)	69.4 ± 18.7	82.2 ± 15.7	0.034*
Mean right atrial pressure(mm Hg)	6.5 ± 2.9	7.8 ± 3.5	0.166
Mean pulmonary artery pressure(mm Hg)	40.8 ± 9.4	46.8 ± 12.2	0.102
Mean pulmonary capillary wedge pressure (mm Hg)	8.8 ± 28	8.3 ± 3.9	0.369
Cardiac output (Fick) (L/min)	3.5 ± 0.9	3.3 ± 1.1	0.388
Cardiac index (Fick) (L/min/m^2)	2.1 ± 0.5	2.0 ± 0.6	0.478
Pulmonary vascular resistance (dyne·sec·cm^{-5})	850 ± 447	1172 ± 857	0.145
Systemic vascular resistance (dyne·sec·cm^{-5})	2161 ± 906	2207 ± 1073	0.459
After BPA			
Systolic right ventricular pressure (mm Hg)	32.6 ± 6.9	33.9 ± 8.1	0.337
Mean right atrial pressure(mm Hg)	2.4 ± 1.8	2.1 ± 1.7	0.359
Mean pulmonary artery pressure(mm Hg)	19.3 ± 3.5	19.9 ± 4.9	0.369
Mean pulmonary capillary wedge pressure (mm Hg)	7.4 ± 3.0	6.6 ± 3.4	0.284
Cardiac output (Fick) (L/min)	3.9 ± 0.8	3.8 ± 2.3	0.336
Cardiac index (Fick) (L/min/m2)	2.3 ± 0.4	2.3 ± 0.4	0.473
Pulmonary vascular resistance (dyne·sec·cm^{-5})	249 ± 84	300 ± 127	0.141
Systemic vascular resistance (dyne·sec·cm^{-5})	1764 ± 513	1639 ± 443	0.255
Echocardiography			
Before BPA			
Left ventricular end-diastolic diameter (mm)	42.2 ± 5.7	37.9 ± 7.6	0.07
Left ventricular end-systolic diameter (mm)	26.5 ± 3.2	20.8 ± 3.9	<0.01*
Left ventricular ejection fraction (%)	67.6 ± 8.5	77.6 ± 4.6	<0.01*
Right ventricular diameter (base) (mm)	43.4 ± 5.7	51.0 ± 6.6	<0.01*
Right ventricular diameter (middle) (mm)	34.3 ± 4.9	44.5 ± 4.8	<0.01*
Right ventricular diameter (long) (mm)	61.6 ± 7.4	62.4 ± 7.5	0.393
Mitral inflow velocity, E wave (cm/s)	58.1 ± 14.3	54.5 ± 18.2	0.302
Mitral inflow velocity, A wave (cm/s)	75.3 ± 16.0	71.2 ± 14.1	0.242
Tricuspid regurgitation pressure gradient (mm Hg)	61.2 ± 15.9	73.6 ± 1269	0.025*
Pulmonary regurgitation pressure gradient (mm Hg)	15.0 ± 17.2	13.4 ± 6.4	0.374
Estimated systolic pulmonary artery pressure (mm Hg)	63.3 ± 22.2	82.7 ± 15.1	0.010*
Estimated diastolic pulmonary artery pressure (mm Hg)	17.3 ± 7.4	22.5 ± 10.2	0.098
Tricuspid annular plane systolic excursion (mm)	17.4 ± 3.4	16.8 ± 3.7	0.338
Peak systolic tricuspid annular velocity (cm/s)	10.2 ± 3.2	10.5 ± 1.7	0.405
After BPA			
Left ventricular end-diastolic diameter (mm)	45.2 ± 4.8	44.4 ± 4.5	0.327
Left ventricular end-systolic diameter (mm)	28.0 ± 2.3	27.0 ± 4.1	0.244
Left ventricular ejection fraction (%)	67.8 ± 5.2	69.9 ± 5.7	0.175
Right ventricular diameter (base) (mm)	33.4 ± 3.0	35.7 ± 5.3	0.115
Right ventricular diameter (middle) (mm)	27.6 ± 3.6	30.9 ± 3.3	0.0140*
Right ventricular diameter (long) (mm)	59.2 ± 8.0	57.9 ± 6.4	0.319
Mitral inflow velocity, E wave (cm/s)	69.6 ± 19.0	59.5 ± 17.0	0.085
Mitral inflow velocity, A wave (cm/s)	72.2 ± 17.5	69.3 ± 16.1	0.331
Tricuspid regurgitation pressure gradient (mm Hg)	33.3 ± 9.6	31.6 ± 9.1	0.323
Pulmonary regurgitation pressure gradient (mm Hg)	6.1 ± 2.4	7.6 ± 3.5	0.1156
Estimated systolic pulmonary artery pressure (mm Hg)	32.3 ± 14.6	35.3 ± 9.8	0.273
Estimated diastolic pulmonary artery pressure (mm Hg)	7.9 ± 3.3	10.3 ± 5.1	0.102
Tricuspid annular plane systolic excursion (mm)	19.3 ± 3.2	18.6 ± 3.4	0.304
Peak systolic tricuspid annular velocity (cm/s)	11.3 ± 2.0	11.4 ± 2.2	0.471
Δpost-pre			
Left ventricular end-diastolic diameter (mm)	3.1 ± 4.5	6.5 ± 8.5	0.129
Left ventricular end-systolic diameter (mm)	1.4 ± 2.8	6.2 ± 5.7	0.015*
Left ventricular ejection fraction (%)	0.2 ± 8.6	−7.7 ± 8.2	0.014*
Right ventricular diameter (base) (mm)	−10.1 ± 6.2	−15.3 ± 4.1	<0.01*
Right ventricular diameter (middle) (mm)	−6.4 ± 6.0	−13.6 ± 4.8	<0.01*
Right ventricular diameter (long) (mm)	−2.1 ± 7.7	−4.5 ± 5.1	0.178
Mitral inflow velocity, E wave (cm/s)	13.4 ± 15.8	5.0 ± 30.2	0.216
Mitral inflow velocity, A wave (cm/s)	−1.2 ± 9.6	−1.9 ± 20.2	0.461
Tricuspid regurgitation pressure gradient (mm Hg)	−20.7 ± 33.8	−34.6 ± 23.8	0.115
Pulmonary regurgitation pressure gradient (mm Hg)	−9.2 ± 17.8	−5.3 ± 6.7	0.219
Estimated systolic pulmonary artery pressure (mm Hg)	−19.3 ± 39.3	−39.1 ± 28.0	0.073
Estimated diastolic pulmonary artery pressure (mm Hg)	−8.4 ± 9.7	−10.0 ± 11.8	0.359
Tricuspid annular plane systolic excursion (mm)	2.0 ± 4.1	1.8 ± 5.8	0.463
Peak systolic tricuspid annular velocity (cm/s)	2.1 ± 3.2	0.9 ± 2.2	0.129

* P value < 0.05.

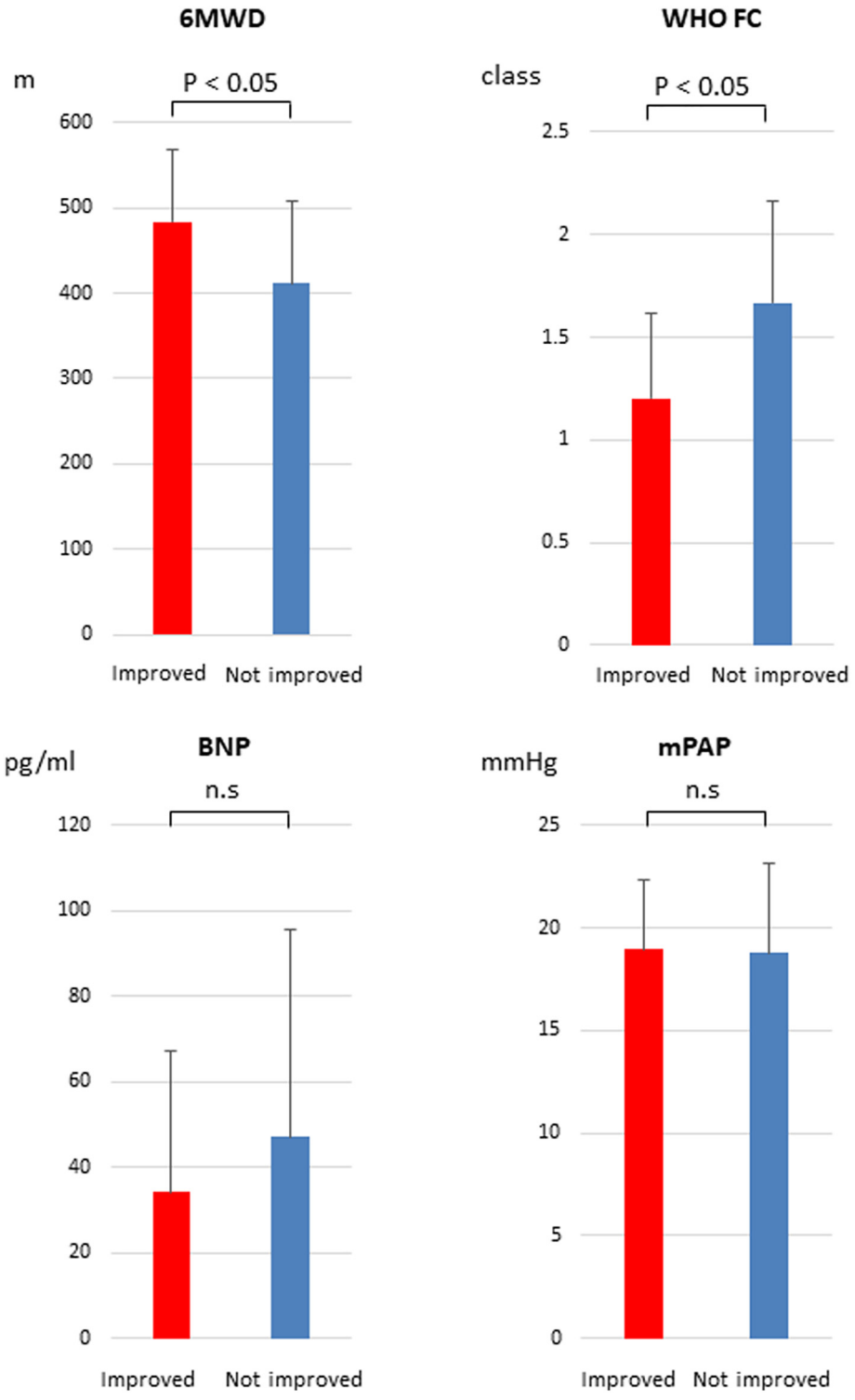


Fig. 4. The 6MWD and WHO FC at 6 months of follow-up significantly differ between the patients with and without an improvement in the R in V1 + S in V5. 6MWD = 6 minute walking distance, WHO FC = WHO functional class.

related to RVH. The correlation of the ECG parameters related to the hemodynamic findings was also elucidated. The predictive factors for the mPAP were the amplitude of the S and R waves in lead V6 and the P waves in lead II. In addition, the ΔS wave in leadI, ΔP amplitude in lead II, and ΔR in V1 + S in V5 were linked to the ΔmPAP. The improvement in the R in V1 + S in V5 implied a better functional status at 6 months of follow-up. The 12-lead ECG is an important examination tool for patients with CTEPH.

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Conflict of interest

The authors declare no conflict of interest associated with this article.

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