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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)