

# Three-Dimensional Echocardiography-Derived Right Atrioventricular Coupling Index as a Predictor of Response to Balloon Pulmonary Angioplasty

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## Research Article

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**Additional Declarations:** No competing interests reported.



# Abstract

## Background

Balloon pulmonary angioplasty (BPA) improves hemodynamic status and clinical outcomes in patients with chronic thromboembolic pulmonary hypertension (CTEPH). However, reliable preprocedural predictors of treatment response remain lacking. The right atrioventricular coupling index (RACI) reflects the structural remodeling relationship between the right atrium and right ventricle. This study aimed to evaluate the efficacy of BPA in patients with CTEPH and to investigate the value of three-dimensional echocardiography-derived RACI in predicting treatment response.

## Methods

A total of 68 consecutive patients with CTEPH who underwent at least four BPA sessions at Beijing Chaoyang Hospital, Capital Medical University, between January 2017 and June 2023 were retrospectively enrolled. BPA responders were defined as patients who achieved a mean pulmonary arterial pressure (mPAP)  $\leq 30$  mmHg or a  $\geq 30\%$  reduction in pulmonary vascular resistance (PVR) after the final BPA session. Logistic regression analysis was performed to identify independent predictors of BPA response.

## Results

Following BPA, hemodynamic status improved significantly. mPAP decreased from  $50.96 \pm 10.15$  mmHg to  $33.72 \pm 10.18$  mmHg ( $P < 0.001$ ), PVR decreased from 892.00 (426.75) to 411.50 (279.00)  $\text{dyn} \cdot \text{s} \cdot \text{cm}^{-5}$  ( $P < 0.001$ ), and cardiac index increased from 2.18 (0.61) to 2.45 (0.62)  $\text{L}/\text{min}/\text{m}^2$  ( $P < 0.001$ ). In addition, RACI decreased significantly, whereas right ventricular ejection fraction (RVEF), 6-minute walk distance (6MWD), and World Health Organization functional class (WHO-FC) improved significantly (all  $P < 0.001$ ). After adjustment for potential confounders, multivariable logistic regression analysis identified baseline RACI as the only independent predictor of BPA response. Receiver operating characteristic curve analysis demonstrated an optimal RACI cutoff value of 37% for predicting BPA responders.

## Conclusions

BPA effectively reduces pulmonary artery pressure, promotes reverse right heart remodeling, and improves exercise capacity in patients with CTEPH. The three-dimensional echocardiography-derived RACI is an independent predictor of treatment response to BPA and may provide a valuable reference for individualized therapeutic decision-making in patients with CTEPH.

**Clinical trial number:** not applicable.

## Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is a severe pulmonary vascular disease resulting from persistent organized thromboembolic obstruction and stenosis of the pulmonary arteries following acute pulmonary embolism, and it is characterized by elevated pulmonary arterial pressure, right ventricular pressure overload, and progressive right heart remodeling, ultimately leading to right heart failure<sup>[1, 2]</sup>. Balloon pulmonary angioplasty (BPA) has emerged as an important interventional treatment for patients with CTEPH who are ineligible for pulmonary endarterectomy (PEA)<sup>[1]</sup>. By mechanically dilating stenotic or occluded pulmonary arterial branches, BPA effectively reduces pulmonary vascular resistance and improves pulmonary hemodynamics<sup>[3–5]</sup>. With the widespread adoption of BPA and the accumulation of clinical experience worldwide, accurate preprocedural risk stratification has become increasingly important for optimizing patient selection. However, accumulating evidence indicates substantial heterogeneity in treatment response among patients undergoing BPA and suggests that, despite technically successful completion of multiple BPA sessions, the therapeutic benefit varies considerably across individuals<sup>[4–6]</sup>. Nevertheless, robust evidence identifying which patients are most likely to derive the greatest benefit from BPA remains limited.

Against this background, right heart structure and function have emerged as key determinants of clinical outcomes following BPA in patients with CTEPH<sup>[7, 8]</sup>. Chronic pressure overload leads to a progressive increase in right ventricular end-diastolic pressure, which in turn promotes right ventricular chamber dilatation and maladaptive remodeling<sup>[9, 10]</sup>. Under conditions of persistently increased right ventricular afterload, the right atrium undergoes adaptive remodeling to preserve right ventricular filling and maintain adequate cardiac output<sup>[11]</sup>. As the disease progresses, progressive right atrial enlargement is accompanied by functional deterioration, with previous studies demonstrating that impaired right atrial function is associated with reduced cardiac functional reserve during exercise and adverse clinical outcomes in patients with CTEPH<sup>[11, 12]</sup>.

More recently, the right atrioventricular coupling index (RACI), defined as the ratio of the right atrial minimum volume index (RAmini) to the right ventricular end-diastolic volume index (RVEDVi), has been introduced as a novel imaging marker of right atrioventricular structural coupling<sup>[13]</sup>. Compared with the assessment of right atrial or right ventricular structure alone, RACI provides an integrated measure of the relative remodeling of the right atrium and right ventricle. In recent years, RACI has been shown to be associated with adverse clinical outcomes across a variety of cardiovascular diseases<sup>[13–16]</sup>.

Three-dimensional echocardiography (3DE), which enables accurate quantification of right heart chamber volumes without relying on geometric assumptions, has been increasingly adopted for the assessment of patients with pulmonary hypertension owing to its noninvasive nature, wide availability, and relatively low cost<sup>[17, 18]</sup>. By allowing precise and simultaneous quantification of right atrial and right ventricular volumes in a single examination, 3DE provides a robust imaging platform for RACI calculation and facilitates its application in preprocedural risk stratification before BPA<sup>[14]</sup>.

Accordingly, the present study aimed to: (1) evaluate the effect of BPA on the right atrioventricular coupling index (RACI) in patients with CTEPH; and (2) investigate the prognostic value of preprocedural RACI for predicting clinical outcomes following BPA, and to determine its optimal cutoff value for identifying patients most likely to derive clinical benefit from BPA.

## Materials and methods

### Study design and population

This was a single-center retrospective cohort study approved by the Ethics Committee of Beijing Chaoyang Hospital Affiliated to Capital Medical University. Since this study is retrospective, the requirement for informed consent was waived. Consecutive patients with CTEPH who underwent BPA at hospital between January 2017 and June 2023 were retrospectively enrolled. The diagnosis of CTEPH was established according to the 2022 European Society of Cardiology/European Respiratory Society (ESC/ERS) Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension<sup>[1]</sup>. The inclusion criteria were as follows: (1) confirmed diagnosis of CTEPH; (2) completion of at least four BPA sessions; and (3) availability of both right heart catheterization (RHC) and echocardiographic examinations performed before BPA treatment and within 3–6 months after the final BPA session. The exclusion criteria were: (1) partial BPA treatment performed at another institution or a history of PEA; and (2) lack of complete follow-up hemodynamic assessment. Consistent with previous studies, patients were classified as responders if they achieved a mean pulmonary arterial pressure (mPAP)  $\leq 30$  mmHg or a  $\geq 30\%$  reduction in pulmonary vascular resistance (PVR) from baseline at 3–6 months after the final BPA session. All remaining patients were classified as non-responders<sup>[19, 20]</sup>.

### Echocardiographic study of the right heart

All conventional two-dimensional and Doppler echocardiographic examinations were performed by experienced sonographers with expertise in the diagnosis and management of pulmonary hypertension using a commercially available ultrasound system (EPIQ 7C, Philips Healthcare, MA, USA) equipped with an X5-1 matrix-array transducer. The operators were blinded to the patients' clinical information and right heart catheterization findings. Images of five consecutive cardiac cycles were acquired during sinus rhythm and digitally stored for offline analysis. Echocardiographic image acquisition and measurements were performed in accordance with the recommendations of the American Society of Echocardiography (ASE) and the 2022 ESC/ERS Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension<sup>[1, 21]</sup>.

Conventional right heart structural and functional parameters were recorded, including tricuspid annular plane systolic excursion (TAPSE), peak systolic velocity of the tricuspid annulus (S'), right ventricular index of myocardial performance (RIMP), right ventricular end-diastolic area (RVEDA), and right ventricular end-systolic area (RVESA). Pulmonary artery systolic pressure (PASP) was estimated from

the peak tricuspid regurgitation velocity (TRV) using the simplified Bernoulli equation. Right ventricular fractional area change (FAC) was calculated as follows:  $FAC = (RVEDA - RVESA) / RVEDA \times 100\%$ . All measurements were averaged over three consecutive cardiac cycles for statistical analysis.

## Three-dimensional echocardiography

Offline analysis was performed using TOMTEC software (Philips Healthcare). Measurements were obtained from a right ventricular-focused apical four-chamber view by an experienced investigator. The endocardial borders of the right ventricle or right atrium were manually traced. Right ventricular end-diastolic volume (RVEDV), right ventricular end-systolic volume (RVESV), right atrial maximum volume (RAmax), and right atrial minimum volume (RAmin) were measured. BSA-indexed right ventricular end-diastolic volume (RVEDVi), right ventricular end-systolic volume (RVESVi), right atrial maximum volume (RAmaxi), and right atrial minimum volume (RAmini) were calculated by dividing the corresponding chamber volumes by body surface area. Right ventricular ejection fraction (RVEF) was calculated as follows:  $RVEF = (RVEDV - RVESV) / RVEDV \times 100\%$ . The right atrioventricular coupling index (RACI) was defined as follows:  $RACI = RAmini / RVEDVi \times 100\%$ .

## Right heart catheterization

All patients underwent right heart catheterization before the first BPA session and within 3–6 months after the final BPA session. The procedure was performed using a Swan-Ganz catheter via the internal jugular or femoral vein. Hemodynamic parameters, including mPAP, PVR, central venous pressure (CVP), cardiac output (CO), and cardiac index (CI), were recorded. Cardiac index was calculated by indexing cardiac output to body surface area (BSA).

## Balloon pulmonary angioplasty

BPA was performed in a staged manner by experienced interventional radiologists. Following local anesthesia, femoral venous access was routinely established. Target lesions were identified based on pulmonary angiography findings, and an 8-French sheath was advanced to the target vessels over a guidewire. Stenotic or occluded pulmonary arterial branches were then serially dilated using appropriately sized balloon catheters. The total number of BPA sessions was determined according to improvements in hemodynamic status and the overall clinical assessment of each patient.

## Statistical analysis

Continuous variables are presented as mean  $\pm$  standard deviation (SD) or median and interquartile range based on the data distribution. Between-group comparisons were performed using the independent-samples t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. Categorical variables are presented as counts (percentages) and were compared

using the  $\chi^2$  test or Fisher's exact test. Univariable logistic regression analysis was performed to identify variables associated with BPA response, and variables with  $P < 0.05$  were subsequently entered into a multivariable logistic regression model to identify independent predictors of BPA response. Receiver operating characteristic (ROC) curve analysis was performed to evaluate discriminative performance, and the optimal cutoff value was determined using the Youden index. A two-sided  $P$  value  $< 0.05$  was considered statistically significant. Statistical analyses were performed using SPSS version 25.0 and GraphPad Prism version 10.0.

## Results

### Population cohort

A total of 68 patients with CTEPH who underwent at least four BPA sessions were included in this study. The median age was 60 years, and approximately 40% of the study population were male. Left ventricular systolic function was preserved in all patients, with a mean left ventricular ejection fraction (LVEF) of  $64.90 \pm 5.39\%$ . Based on the follow-up hemodynamic assessment performed within 3–6 months after the final BPA session, 53 patients (77.9%) were classified as responders, whereas 15 patients (22.1%) were classified as non-responders. The study flowchart is presented in Fig. 1, and the methodology for RACI measurement is illustrated in Fig. 2.

### Baseline characteristics of BPA responders and non-responders

Baseline characteristics of the study population are summarized in Table 1. There were no significant differences between the responder and non-responder groups with respect to demographic characteristics or BPA procedural characteristics (all  $P > 0.05$ ). Baseline mPAP ( $50.34 \pm 10.60$  mmHg vs.  $53.13 \pm 8.31$  mmHg,  $P = 0.350$ ) and PVR ( $871 [401.50]$  vs.  $956.10 \pm 358.53$ ,  $P = 0.631$ ) were also comparable between the two groups. However, the responder group exhibited better right ventricular function (including TAPSE and FAC) and clinical indicators (including 6-minute walk distance [6MWD] and N-terminal pro-B-type natriuretic peptide [NT-proBNP] level) than non-responders (all  $P < 0.05$ ). Three-dimensional echocardiographic analysis demonstrated that, compared with the non-responder group, the responder group had significantly lower RVEDVi, RVESVi, RAmassi and RAmassi (all  $P < 0.001$ ). In addition, RVEF was significantly higher in the responder group ( $36.79 \pm 5.31\%$  vs.  $32.50 \pm 2.15\%$ ,  $P < 0.001$ ), whereas the RACI was significantly lower ( $28.26 [8.55]\%$  vs.  $49.42 \pm 12.38\%$ ,  $P < 0.001$ ).

Table 1  
Baseline characteristics of all patients, BPA responders and non-responders

| Variables                                    | All patients (n = 68) | Responders (n = 53) | Non-responders (n = 15) | P-value |
|----------------------------------------------|-----------------------|---------------------|-------------------------|---------|
| Demographics                                 |                       |                     |                         |         |
| Age, years                                   | 60.00 (14.75)         | 59.00 (13.00)       | 56.00 (27.00)           | 0.428   |
| Male, n (%)                                  | 27 (39.71%)           | 22 (41.51%)         | 5 (33.33%)              | 0.568   |
| Clinical indicators                          |                       |                     |                         |         |
| 6MWD, m                                      | 368.00 (138.5)        | 405.00 (133.00)     | 291.27 ± 122.51         | 0.017   |
| WHO FC I/II/III/IV                           | 1/24/36/7             | 1/21/27/4           | 0/3/9/3                 | 0.071   |
| NT-proBNP, ng/L                              | 734.50 (1430.75)      | 587.00 (1156.50)    | 1234.00 (1282.00)       | 0.021   |
| BPA procedures                               |                       |                     |                         |         |
| Number of BPA sessions                       | 6.10 ± 1.64           | 6 (2)               | 6 (2)                   | 0.265   |
| Time Interval, days                          | 651.50 (959.75)       | 675.00 (975.50)     | 728.87 ± 480.22         | 0.492   |
| Two-dimensional echocardiographic parameters |                       |                     |                         |         |
| LVEF, %                                      | 64.90 ± 5.39          | 64.47 ± 5.26        | 66.40 ± 5.77            | 0.224   |
| PASP, mmHg                                   | 88.52 ± 23.20         | 86.74 ± 24.06       | 94.83 ± 19.28           | 0.236   |
| TAPSE, mm                                    | 14.61 ± 3.06          | 15.19 ± 3.13        | 12.87 ± 2.07            | 0.012   |
| S', cm/s                                     | 9.35 (2.59)           | 9.40 (2.96)         | 9.30 (2.10)             | 0.750   |
| RIMP                                         | 0.77 (0.25)           | 0.77 (0.30)         | 0.77 (0.08)             | 0.734   |
| FAC, %                                       | 29.19 ± 10.25         | 30.65 ± 10.42       | 24.05 ± 7.96            | 0.027   |

Values are expressed as mean ± SD, median (IQR), or frequency (percentage), as appropriate. 6MWD, 6-minute walk distance; WHO FC, World Health Organization functional class; NT-proBNP, N-terminal pro-B-type natriuretic peptide; BPA, balloon pulmonary angioplasty; LVEF, left ventricular ejection fraction; PASP, pulmonary artery systolic pressure; TAPSE, tricuspid annular plane systolic excursion; S', peak systolic velocity of the tricuspid annulus; RIMP, right ventricular index of myocardial performance; FAC, right ventricular fractional area change; RVEDVi, right ventricular end-diastolic volume index; RVESVi, right ventricular end-systolic volume index; RAmayi, right atrial maximum volume index; RAmayi, right atrial minimum volume index; RVEF, right ventricular ejection fraction; RACI, right atrioventricular coupling index; CVP, central venous pressure; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; CI, cardiac index.

| Variables                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | All patients (n = 68) | Responders (n = 53) | Non-responders (n = 15) | P-value |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|---------------------|-------------------------|---------|
| Three-dimensional echocardiographic parameters                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                       |                     |                         |         |
| RVEDVi, mL/m <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 66.97 (13.93)         | 64.06 (12.23)       | 78.72 ± 10.39           | < 0.001 |
| RVESVi, mL/m <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 41.83 (12.47)         | 39.75 (8.98)        | 53.11 ± 6.81            | < 0.001 |
| RAmaxi, mL/m <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 30.48 (14.56)         | 26.97 (9.55)        | 56.03 ± 17.00           | < 0.001 |
| RAmini, mL/m <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 20.77 (11.69)         | 18.38 (7.54)        | 39.39 ± 13.11           | < 0.001 |
| RVEF, %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 35.84 ± 5.11          | 36.79 ± 5.31        | 32.50 ± 2.15            | < 0.001 |
| RACI, %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 30.90 (12.91)         | 28.26 (8.55)        | 49.42 ± 12.38           | < 0.001 |
| Hemodynamics                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                       |                     |                         |         |
| CVP, mmHg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 7.88 ± 2.98           | 7.57 ± 2.80         | 9.00 ± 3.40             | 0.100   |
| mPAP, mmHg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 50.96 ± 10.15         | 50.34 ± 10.60       | 53.13 ± 8.31            | 0.350   |
| PVR, dyn·s·cm <sup>-5</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 892.00 (426.75)       | 871 (401.50)        | 956.10 ± 358.53         | 0.631   |
| CI, L/min/m <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 2.18 (0.61)           | 2.19 ± 0.40         | 2.21 ± 0.81             | 0.864   |
| Values are expressed as mean ± SD, median (IQR), or frequency (percentage), as appropriate. 6MWD, 6-minute walk distance; WHO FC, World Health Organization functional class; NT-proBNP, N-terminal pro-B-type natriuretic peptide; BPA, balloon pulmonary angioplasty; LVEF, left ventricular ejection fraction; PASP, pulmonary artery systolic pressure; TAPSE, tricuspid annular plane systolic excursion; S', peak systolic velocity of the tricuspid annulus; RIMP, right ventricular index of myocardial performance; FAC, right ventricular fractional area change; RVEDVi, right ventricular end-diastolic volume index; RVESVi, right ventricular end-systolic volume index; RAmassi, right atrial maximum volume index; RAmini, right atrial minimum volume index; RVEF, right ventricular ejection fraction; RACI, right atrioventricular coupling index; CVP, central venous pressure; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; CI, cardiac index. |                       |                     |                         |         |

## Changes after BPA

Changes in hemodynamic and echocardiographic parameters before and after BPA are summarized in Table 2. The mPAP showed a significant decrease after BPA (from 50.96 ± 10.15 mmHg to 33.72 ± 10.18 mmHg,  $P < 0.001$ ). The PVR decreased from 892.00 (426.75) dyn·s·cm<sup>-5</sup> to 411.50 (279.00) dyn·s·cm<sup>-5</sup> ( $P < 0.001$ ), and the CVP decreased from 7.88 ± 2.98 mmHg to 5.63 ± 2.68 mmHg ( $P < 0.001$ ). In contrast, the CI increased from 2.18 (0.61) to 2.45 (0.62) L/min/m<sup>2</sup> ( $P < 0.001$ ). A significant increase in 6MWD and a significant decrease in NT-proBNP levels were observed after BPA (all  $P < 0.001$ ). In addition, the distribution of World Health Organization functional class (WHO-FC) shifted toward lower functional classes after BPA ( $P < 0.001$ ). BPA resulted in a significant increase in TAPSE, S' and right ventricular FAC and a significant decrease in PASP, RIMP, RVEDVi, RVESVi, RAmassi, and RAmini (all  $P < 0.001$ ). The RVEF

increased from  $35.84 \pm 5.11\%$  to  $41.25 \pm 4.82\%$  ( $P < 0.001$ ), whereas the RACI decreased from 30.90 (12.91)% to 25.00 (12.12)% ( $P < 0.001$ ).

Table 2  
Comparison of pre-BPA and post-BPA parameters in all patients

| Variables                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Before BPA       | After BPA       | P-value |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|-----------------|---------|
| Clinical indicators                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                  |                 |         |
| 6MWD, m                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 368.00 (138.5)   | 447.00 (104.25) | < 0.001 |
| WHO FC I/II/III/IV                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 1/24/36/7        | 18/34/15/1      | < 0.001 |
| NT-proBNP, ng/L                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 734.50 (1430.75) | 117 (469.75)    | < 0.001 |
| Two-dimensional echocardiographic parameters                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                  |                 |         |
| LVEF, %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 64.90 ± 5.39     | 65.06 ± 4.41    | 0.848   |
| PASP, mmHg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 88.52 ± 23.20    | 62.82 ± 26.76   | < 0.001 |
| TAPSE, mm                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 14.61 ± 3.06     | 17.28 ± 3.54    | < 0.001 |
| S', cm/s                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 9.35 (2.59)      | 11.85 (3.95)    | < 0.001 |
| RIMP                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 0.77 (0.25)      | 0.62 (0.27)     | < 0.001 |
| FAC, %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 29.19 ± 10.25    | 37.83 ± 10.98   | < 0.001 |
| Three-dimensional echocardiographic parameters                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                  |                 |         |
| RVEDVi, mL/m <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 66.97 (13.93)    | 59.80 (13.52)   | < 0.001 |
| RVESVi, mL/m <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 41.83 (12.47)    | 34.66 (9.60)    | < 0.001 |
| RAmaxi, mL/m <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 30.48 (14.56)    | 19.33 (12.66)   | < 0.001 |
| RAmini, mL/m <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 20.77 (11.69)    | 14.86 (6.92)    | < 0.001 |
| RVEF, %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 35.84 ± 5.11     | 41.25 ± 4.82    | < 0.001 |
| RACI, %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 30.90 (12.91)    | 25.00 (12.12)   | < 0.001 |
| Hemodynamics                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                  |                 |         |
| CVP, mmHg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 7.88 ± 2.98      | 5.63 ± 2.68     | < 0.001 |
| Values are expressed as mean ± SD, median (IQR), or frequency (percentage), as appropriate. 6MWD, 6-minute walk distance; WHO FC, World Health Organization functional class; NT-proBNP, N-terminal pro-B-type natriuretic peptide; LVEF, left ventricular ejection fraction; PASP, pulmonary artery systolic pressure; TAPSE, tricuspid annular plane systolic excursion; S', peak systolic velocity of the tricuspid annulus; RIMP, right ventricular index of myocardial performance; FAC, right ventricular fractional area change; RVEDVi, right ventricular end-diastolic volume index; RVESVi, right ventricular end-systolic volume index; RAmassi, right atrial maximum volume index; RAmini, right atrial minimum volume index; RVEF, right ventricular ejection fraction; RACI, right atrioventricular coupling index; CVP, central venous pressure; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; CI, cardiac index. |                  |                 |         |

| Variables                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Before BPA      | After BPA       | P-value |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|-----------------|---------|
| mPAP, mmHg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 50.96 ± 10.15   | 33.72 ± 10.18   | < 0.001 |
| PVR, dyn·s·cm <sup>-5</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 892.00 (426.75) | 411.50 (279.00) | < 0.001 |
| CI, L/min/m <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 2.18 (0.61)     | 2.45 (0.62)     | < 0.001 |
| Values are expressed as mean ± SD, median (IQR), or frequency (percentage), as appropriate. 6MWD, 6-minute walk distance; WHO FC, World Health Organization functional class; NT-proBNP, N-terminal pro-B-type natriuretic peptide; LVEF, left ventricular ejection fraction; PASP, pulmonary artery systolic pressure; TAPSE, tricuspid annular plane systolic excursion; S', peak systolic velocity of the tricuspid annulus; RIMP, right ventricular index of myocardial performance; FAC, right ventricular fractional area change; RVEDVi, right ventricular end-diastolic volume index; RVESVi, right ventricular end-systolic volume index; RAmayi, right atrial maximum volume index; RAmayi, right atrial minimum volume index; RVEF, right ventricular ejection fraction; RACI, right atrioventricular coupling index; CVP, central venous pressure; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; CI, cardiac index. |                 |                 |         |

## Predictors of BPA outcomes

The results of the logistic regression analyses are presented in Table 3. Univariable logistic regression analysis demonstrated that 6MWD, TAPSE, right ventricular FAC, RVEDVi, RVESVi, RAmayi, RAmayi, RVEF, and RACI were all significantly associated with BPA response (all  $P < 0.05$ ). Variables with statistical significance in the univariable analysis were subsequently entered into the multivariable logistic regression analysis. Because RVEDVi, RVESVi, RAmayi, and RAmayi exhibited collinearity with RVEF and RACI, they were excluded from the multivariable model. Consequently, five variables were included in the final multivariable logistic regression model. Multivariable analysis demonstrated that RACI remained the only independent predictor of BPA response (OR = 0.841, 95% CI: 0.747–0.946,  $P = 0.004$ ).

Table 3  
Univariable and multivariable logistic regression analysis for BPA responders

| Univariable logistic regression |       |              |         | Multivariable logistic regression |             |         |
|---------------------------------|-------|--------------|---------|-----------------------------------|-------------|---------|
| Variable                        | OR    | 95% CI       | P-value | OR                                | 95% CI      | P-value |
| Age, years                      | 1.033 | 0.989–1.079  | 0.139   |                                   |             |         |
| Male, n (%)                     | 1.419 | 0.426–4.734  | 0.569   |                                   |             |         |
| 6MWD, m                         | 1.008 | 1.002–1.014  | 0.007   | 1.009                             | 1.000-1.018 | 0.056   |
| WHO FC III/IV                   | 0.352 | 0.089–1.398  | 0.138   |                                   |             |         |
| NT-proBNP, ng/L                 | 1.000 | 0.999-1.000  | 0.273   |                                   |             |         |
| Number of BPA sessions          | 1.210 | 0.829–1.766  | 0.323   |                                   |             |         |
| Time Interval, days             | 1.001 | 1.000-1.002  | 0.309   |                                   |             |         |
| LVEF, %                         | 0.932 | 0.833–1.044  | 0.223   |                                   |             |         |
| PASP, mmHg                      | 0.985 | 0.960–1.010  | 0.235   |                                   |             |         |
| TAPSE, mm                       | 1.339 | 1.055-1.700  | 0.016   | 1.000                             | 0.694–1.441 | 0.998   |
| S', cm/s                        | 1.019 | 0.782–1.327  | 0.889   |                                   |             |         |
| RIMP                            | 1.156 | 0.067–19.928 | 0.920   |                                   |             |         |
| FAC, %                          | 1.077 | 1.006–1.154  | 0.033   | 0.967                             | 0.854–1.095 | 0.597   |
| RVEDVi, mL/m <sup>2</sup>       | 0.875 | 0.813–0.941  | < 0.001 |                                   |             |         |
| RVESVi, mL/m <sup>2</sup>       | 0.845 | 0.771–0.926  | < 0.001 |                                   |             |         |
| RAmini, mL/m <sup>2</sup>       | 0.848 | 0.775–0.929  | < 0.001 |                                   |             |         |
| RAmaxi, mL/m <sup>2</sup>       | 0.893 | 0.842–0.948  | < 0.001 |                                   |             |         |
| RVEF, %                         | 1.230 | 1.057–1.430  | 0.007   | 1.145                             | 0.917–1.429 | 0.232   |

6MWD, 6-minute walk distance; WHO FC, World Health Organization functional class; NT-proBNP, N-terminal pro-B-type natriuretic peptide; BPA, balloon pulmonary angioplasty; LVEF, left ventricular ejection fraction; PASP, pulmonary artery systolic pressure; TAPSE, tricuspid annular plane systolic excursion; S', peak systolic velocity of the tricuspid annulus; RIMP, right ventricular index of myocardial performance; FAC, fractional area change; RVEDVi, right ventricular end-diastolic volume indexed to body surface area; RVESVi, right ventricular end-systolic volume indexed to body surface area; RAmini, minimal right atrial volume indexed to body surface area; RAmassi, maximal right atrial volume indexed to body surface area; RVEF, right ventricular ejection fraction; RACI, right atrioventricular coupling index; CVP, central venous pressure; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; CI, cardiac index.

| Univariable logistic regression                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |       |             |         | Multivariable logistic regression |             |       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|-------------|---------|-----------------------------------|-------------|-------|
| RACI, %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0.845 | 0.774–0.922 | < 0.001 | 0.841                             | 0.747–0.946 | 0.004 |
| CVP, mmHg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 0.845 | 0.689–1.035 | 0.104   |                                   |             |       |
| mPAP, mmHg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 0.973 | 0.919–1.030 | 0.346   |                                   |             |       |
| PVR dyn·s·cm <sup>-5</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 1.000 | 0.998–1.001 | 0.754   |                                   |             |       |
| CI, L/min/m <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0.887 | 0.231–3.412 | 0.861   |                                   |             |       |
| 6MWD, 6-minute walk distance; WHO FC, World Health Organization functional class; NT-proBNP, N-terminal pro-B-type natriuretic peptide; BPA, balloon pulmonary angioplasty; LVEF, left ventricular ejection fraction; PASP, pulmonary artery systolic pressure; TAPSE, tricuspid annular plane systolic excursion; S', peak systolic velocity of the tricuspid annulus; RIMP, right ventricular index of myocardial performance; FAC, fractional area change; RVEDVi, right ventricular end-diastolic volume indexed to body surface area; RVESVi, right ventricular end-systolic volume indexed to body surface area; RAmi, minimal right atrial volume indexed to body surface area; RAmxi, maximal right atrial volume indexed to body surface area; RVEF, right ventricular ejection fraction; RACI, right atrioventricular coupling index; CVP, central venous pressure; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; CI, cardiac index. |       |             |         |                                   |             |       |

The results of the ROC curve analysis are shown in Fig. 3. Variables that remained statistically significant in the multivariable logistic regression analysis were included in the ROC curve analysis. RACI demonstrated excellent discriminative performance for predicting BPA response, with an optimal cutoff value of 37% and an area under the curve (AUC) of 0.922 (95% CI: 0.858–0.986,  $P < 0.001$ ). Patients were subsequently stratified into the  $\text{RACI} \leq 37\%$  group and the  $\text{RACI} > 37\%$  group according to the optimal cutoff value (Fig. 4). At baseline, RACI differed significantly between the two groups ( $P < 0.001$ ), whereas mPAP, PVR, CI, and 6MWD were comparable between the groups (all  $P > 0.05$ ). Following BPA, patients with a baseline  $\text{RACI} \leq 37\%$  showed significant decreases in mPAP and PVR, together with significant increases in CI and 6MWD compared with baseline (all  $P < 0.05$ ). In contrast, among patients with a baseline  $\text{RACI} > 37\%$ , only mPAP and PVR decreased significantly after BPA, whereas neither CI nor 6MWD increased significantly.

## Intra-observer and inter-observer agreement regarding RACI

Bland–Altman plots showed good intra-observer (bias:  $-0.35$ , 95% limits of agreement [LoA]  $-3.484$  to  $2.782$ ) and inter-observer (bias:  $-0.66$ , 95% LoA  $-5.620$  to  $4.292$ ) agreement for three-dimensional echocardiography-derived RACI measurements. Almost all data points were within the 95% LoA (Table 4, Fig. 5).

Table 4  
Intra-observer and inter-observer reproducibility

| Intra-observer analysis RACI                | Bias (SD)           | 95% Limits of Agreement |
|---------------------------------------------|---------------------|-------------------------|
|                                             | <b>-0.35(1.599)</b> | <b>-3.484 to 2.782</b>  |
| Inter-observer analysis RACI                | -0.66(2.529)        | -5.620 to 4.292         |
| RACI, right atrioventricular coupling index |                     |                         |

## Discussion

The principal findings of the present study are as follows: (1) BPA effectively improved hemodynamic status and reduced the right atrioventricular coupling index (RACI) in patients with CTEPH. (2) RACI played an important role in predicting treatment response to BPA, and a preprocedural  $\text{RACI} \leq 37\%$  was identified as an independent predictor of BPA response.

CTEPH is a potentially life-threatening yet treatable disease resulting from acute pulmonary embolism<sup>[22, 23]</sup>. Persistent organized thromboembolic lesions within the pulmonary arteries lead to progressive vascular stenosis or occlusion, resulting in increased pulmonary vascular resistance and right ventricular afterload, which subsequently drive progressive right ventricular remodeling and dysfunction<sup>[24, 25]</sup>. Chronic right ventricular pressure overload further affects the right atrium, resulting in progressive atrial enlargement and functional impairment<sup>[11]</sup>. Assessment of structural remodeling in a single cardiac chamber alone is insufficient to comprehensively characterize overall right heart remodeling and the structural coupling between the right atrium and right ventricle. The RACI, defined as the ratio of  $\text{RA}_{\text{mini}}$  to  $\text{RVEDVi}$ , provides a quantitative measure of the relative enlargement of the right atrium in relation to the right ventricle<sup>[14]</sup>. In the present study, compared with responders, non-responders exhibited a significantly greater  $\text{RA}_{\text{mini}}$  ( $39.39 \pm 13.11$  vs.  $18.38 [7.54]$  mL/m<sup>2</sup>) and a significantly higher RACI ( $49.42 \pm 12.38\%$  vs.  $28.26 [8.55]\%$ , respectively). Although the difference in  $\text{RVEDVi}$  between the two groups was statistically significant, the absolute difference was relatively modest ( $78.72 \pm 10.39$  vs.  $64.06 [12.23]$  mL/m<sup>2</sup>). These findings suggest that the increase in RACI is primarily driven by disproportionate right atrial enlargement, reflecting an imbalance in remodeling between the right atrium and right ventricle. This pattern may indicate more advanced global right heart remodeling and may represent an important pathological basis for a poor therapeutic response to BPA. Three-dimensional echocardiography enables accurate, noninvasive quantification of RA and RV volumes, allowing calculation of RACI. The ability of echocardiography to predict BPA response in patients with CTEPH may, to some extent, reduce the need for unnecessary invasive right heart catheterization.

## Efficacy of BPA

The 2022 ESC/ERS Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension recommend a multimodal treatment strategy for CTEPH, including pharmacological therapy, BPA, and PEA<sup>[1]</sup>. With

continued advances in interventional techniques, BPA has become an important therapeutic option for patients with CTEPH who are ineligible for PEA or have residual pulmonary hypertension following PEA<sup>[1, 26]</sup>. A multicenter study demonstrated that BPA significantly improves hemodynamic, functional, and biochemical parameters, which is consistent with our findings<sup>[4–6]</sup>. Our findings support the substantial clinical benefits of BPA in patients with CTEPH. Assessment of right heart remodeling remains challenging because of the complex anatomy of the right heart<sup>[17]</sup>. Nevertheless, echocardiography has been shown to provide a comprehensive assessment of right heart remodeling, including both structural and functional alterations, in patients with CTEPH undergoing BPA<sup>[27, 28]</sup>. Our results demonstrated that BPA significantly improved the three-dimensional echocardiography-derived RACI and further confirmed the significant reduction in PASP following BPA.

## **Baseline RACI predicts the outcomes of BPA**

The therapeutic goals for patients with CTEPH have not yet been clearly established, and current treatment response assessment still primarily relies on hemodynamic parameters<sup>[1]</sup>. In the present study, patients who achieved a mPAP  $\leq$  30 mmHg or a  $\geq$  30% reduction in PVR from baseline were classified as responders. At present, no widely accepted method is available for predicting treatment response to BPA<sup>[20]</sup>. Most experts consider right heart function to be the principal determinant of prognosis in patients with CTEPH<sup>[7, 8]</sup>. Consistently, univariable logistic regression analysis showed that functional markers, rather than hemodynamic parameters, exhibited the strongest associations with BPA outcomes. In the multivariable logistic regression analysis, baseline RACI remained significantly associated with BPA outcome. In our study, although baseline hemodynamic parameters were comparable between responders and non-responders, responders exhibited significantly lower baseline RACI values. These findings suggest that baseline RACI levels may influence BPA outcomes, and that a baseline RACI  $\leq$  37% can identify patients who are likely to respond to BPA.

Notably, after adjustment for multiple potential confounding factors, including 6MWD, TAPSE, right ventricular FAC and RVEF, baseline RACI remained the only independent predictor of BPA response (OR = 0.841, 95% CI: 0.747–0.946,  $P = 0.004$ ), whereas FAC and RVEF were no longer statistically significant. These findings suggest that the therapeutic response to BPA depends not only on right ventricular systolic function itself, but also on the extent of global right heart remodeling, particularly the adaptive remodeling of the right atrium in response to chronic pressure overload. An elevated RACI, reflecting more severe right atrioventricular uncoupling, may represent a more advanced and vulnerable right heart phenotype<sup>[29]</sup>. Consequently, even after successful mechanical relief of pulmonary vascular obstruction by BPA, the capacity for reverse remodeling may remain limited. This observation is consistent with previous studies on right heart remodeling phenotypes, which demonstrated that patients with more advanced right heart remodeling exhibit a lower likelihood of reverse remodeling and a less favorable therapeutic response. Furthermore, although 6MWD was significantly associated with BPA outcome in the univariable logistic regression analysis, it is not a highly objective measurement, which may explain

why the association was no longer significant after multivariable adjustment<sup>[30, 31]</sup>. Similarly, TAPSE also has inherent limitations, as it reflects only part of right ventricular systolic function<sup>[18]</sup>.

Although right heart catheterization has high diagnostic value for pulmonary hypertension, its invasive nature and high cost make it unsuitable for frequent use<sup>[1, 32]</sup>. Therefore, a convenient technique for routine monitoring and prognostic assessment of patients with CTEPH may facilitate clinical management. The present study demonstrated that three-dimensional echocardiography enables direct acquisition of right heart volumetric data without geometric assumptions, allowing accurate quantification of the morphologically complex right ventricle and right atrium<sup>[17, 33]</sup>. The derived RACI showed excellent reproducibility, providing methodological support for its application in clinical practice. The RACI derived from three-dimensional echocardiography has been used to assess prognosis in specific patient populations<sup>[14]</sup>. Therefore, it may also have potential value for predicting the hemodynamic response to BPA in patients with CTEPH. Although BPA has demonstrated favorable therapeutic efficacy in patients with CTEPH, there is currently no universally accepted consensus regarding the indications for BPA<sup>[26]</sup>. Our findings may help optimize the clinical selection of candidates for BPA by identifying patients with a baseline RACI  $\leq 37\%$  as those more likely to respond favorably to the procedure. However, we do not consider a baseline RACI  $> 37\%$  to be a contraindication to BPA. Rather, for these patients, individualized treatment strategies and closer follow-up should be considered after comprehensive clinical evaluation, including consideration of more aggressive therapeutic approaches, such as PEA, when appropriate.

## Limitations

This study has several limitations. First, this was a single-center retrospective study with a relatively small sample size. Therefore, the optimal cutoff value of 37% requires further validation in large-scale, multicenter prospective cohorts. Second, the definition of BPA response in the present study was based on hemodynamic criteria and did not incorporate long-term clinical outcomes, such as all-cause mortality or hospitalization for heart failure. Future studies with longer follow-up are warranted to evaluate the prognostic value of RACI for long-term clinical outcomes. Finally, although multiple known confounding factors were adjusted for in the multivariable regression analysis, residual confounding due to unmeasured variables, such as specific pharmacological treatment regimens, cannot be excluded.

## Conclusion

BPA effectively reduces pulmonary artery pressure, promotes reverse right heart remodeling, and improves exercise capacity in patients with CTEPH. The three-dimensional echocardiography-derived RACI is an independent predictor of treatment response to BPA and may provide a useful reference for preprocedural patient selection and individualized therapeutic decision-making in patients with CTEPH.

## Abbreviations

ASE: American Society of Echocardiography

AUC: Area Under the Curve

BPA: Balloon Pulmonary Angioplasty

BSA: Body Surface Area

CI: Cardiac Index

CO: Cardiac Output

CTEPH: Chronic Thromboembolic Pulmonary Hypertension

CVP: Central Venous Pressure

ESC: European Society of Cardiology

ERS: European Respiratory Society

FAC: Fractional Area Change

LoA: Limits of Agreement

LVEF: Left Ventricular Ejection Fraction

mPAP: Mean Pulmonary Arterial Pressure

NT-proBNP: N-terminal Pro-B-type Natriuretic Peptide

PASP: Pulmonary Artery Systolic Pressure

PEA: Pulmonary Endarterectomy

PVR: Pulmonary Vascular Resistance

RA: Right Atrium

RACI: Right Atrioventricular Coupling Index

RAmax: Maximum Right Atrial Volume

RAmaxi: Maximum Right Atrial Volume Index

RAmin: Minimum Right Atrial Volume

RAmini: Minimum Right Atrial Volume Index

RHC: Right Heart Catheterization

RIMP: Right Ventricular Index of Myocardial Performance

ROC: Receiver Operating Characteristic

RV: Right Ventricle

RVEDA: Right Ventricular End-Diastolic Area

RVEDV: Right Ventricular End-Diastolic Volume

RVEDVi: Right Ventricular End-Diastolic Volume Index

RVEF: Right Ventricular Ejection Fraction

RVESA: Right Ventricular End-Systolic Area

RVESV: Right Ventricular End-Systolic Volume

RVESVi: Right Ventricular End-Systolic Volume Index

S': Peak Systolic Velocity of the Tricuspid Annulus

SD: Standard Deviation

TAPSE: Tricuspid Annular Plane Systolic Excursion

TRV: Tricuspid Regurgitation Velocity

WHO-FC: World Health Organization Functional Class

3DE: Three-Dimensional Echocardiography

6MWD: Six-Minute Walk Distance

## Declarations

### **Ethics approval and consent to participate**

This retrospective study was approved by the institutional ethics committee of Beijing Chaoyang hospital, and the requirement for informed consent was waived due to the use of anonymized patient data.

### **Consent for publication**

Not applicable.

## Availability of data and materials

All data generated or analysed during this study are included in this published article.

## Competing interests

The authors declare that they have no competing interests.

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## Authors' contributions

JYH and YDL contributed to conception and design of the study. QMX, XPD, JFW, JNG and SQY collected and organized the data. JYH performed the statistical analysis. JYH, YDL and YHY interpreted the results. JYH wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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## Figures

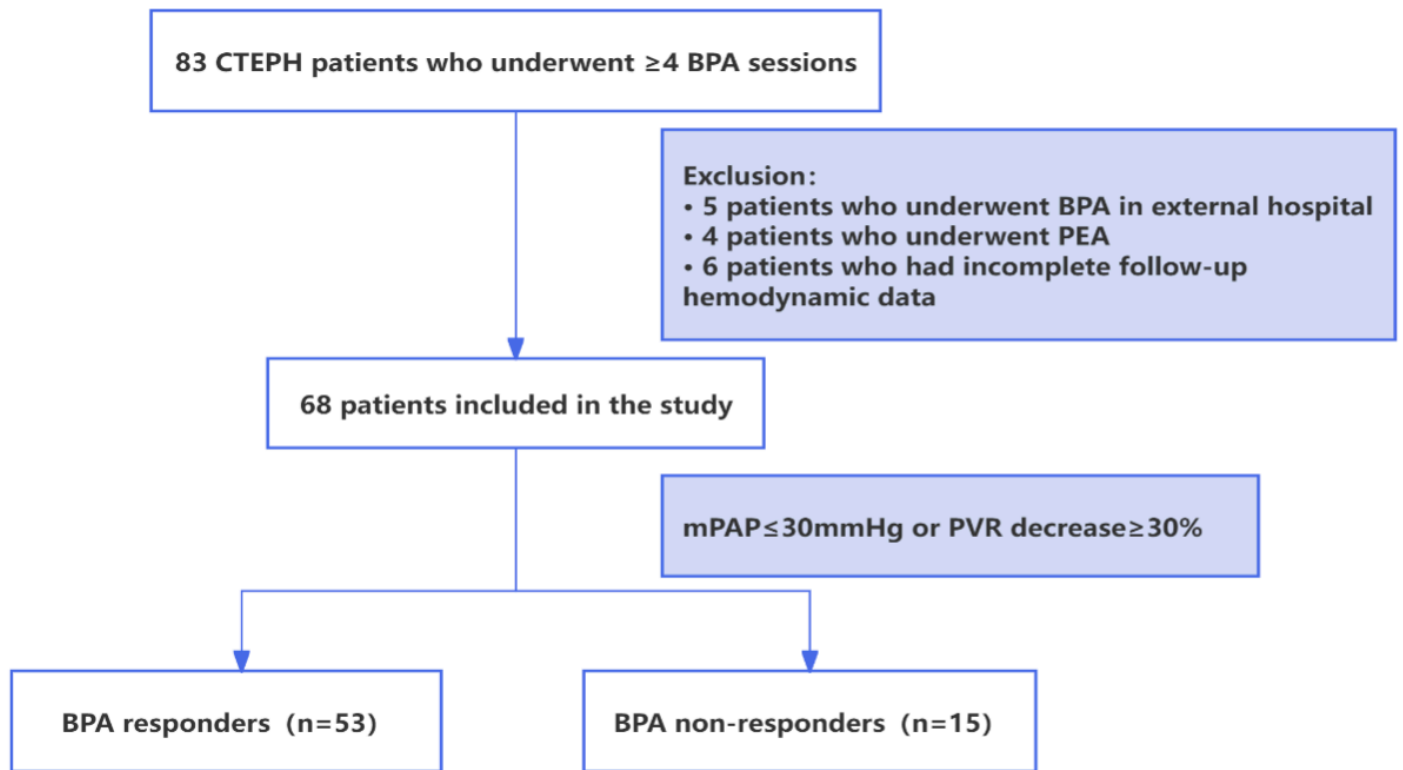


**Figure 1**

Study population selection. CTEPH, chronic thromboembolic pulmonary hypertension, BPA, balloon pulmonary angioplasty, PEA, pulmonary endarterectomy, mPAP, mean pulmonary arterial pressure, PVR, pulmonary vascular resistance

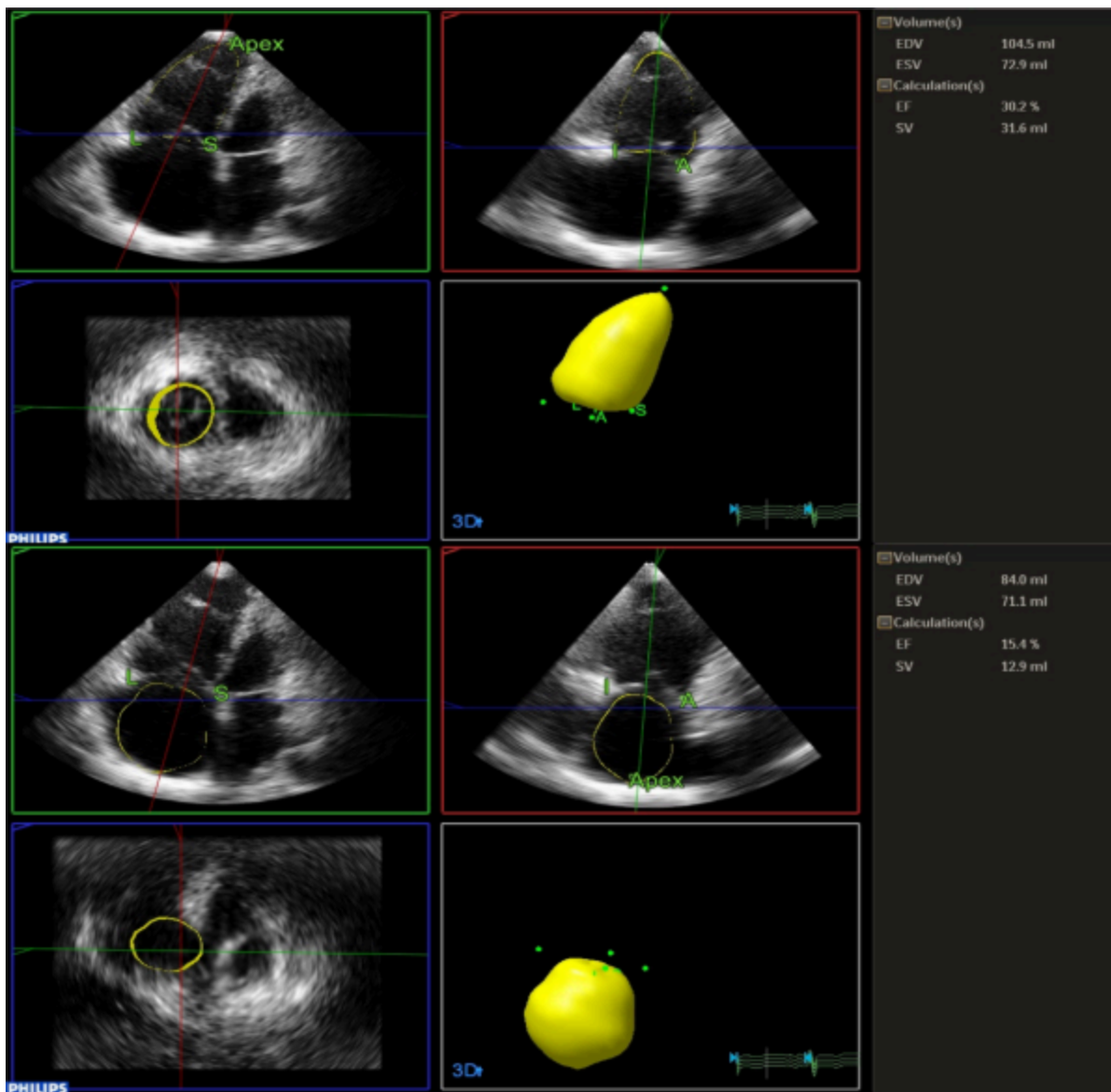


**Figure 2**

Three-dimensional echocardiography was employed to assess the right ventricular end-diastolic volume (RVEDV), the right ventricular end-systolic volume (RVESV), the right atrial maximum volume (RAmax) and the right atrial minimum volume (RAmin). The Right ventricular ejection fraction (RVEF) and right atrioventricular coupling index (RACI) measurement were based on these parameters.

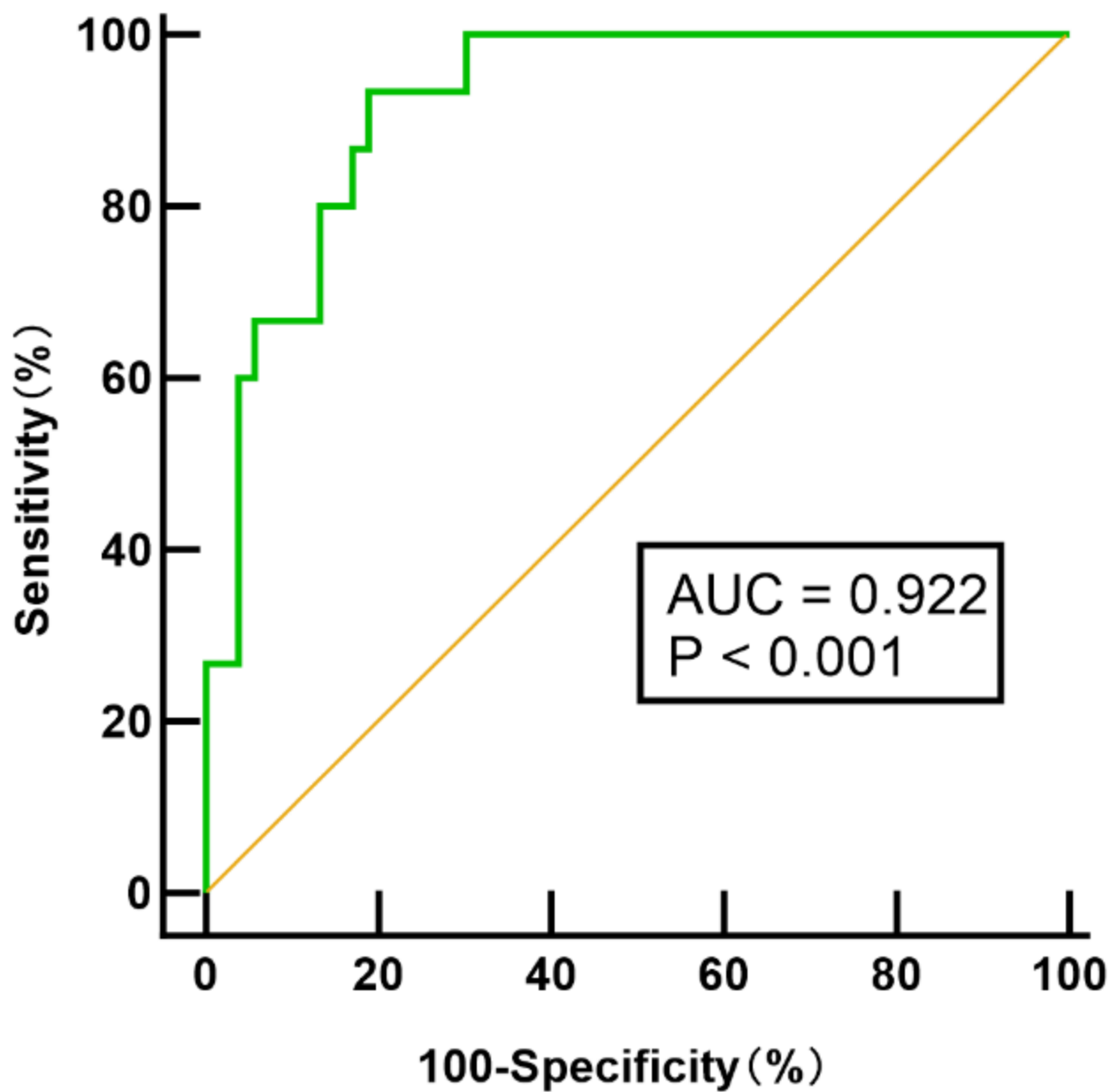


Figure 3

Receiver operating characteristic curve analysis demonstrating the ability of right atrioventricular coupling index (RACI) to predict BPA responders. AUC, area under the curve

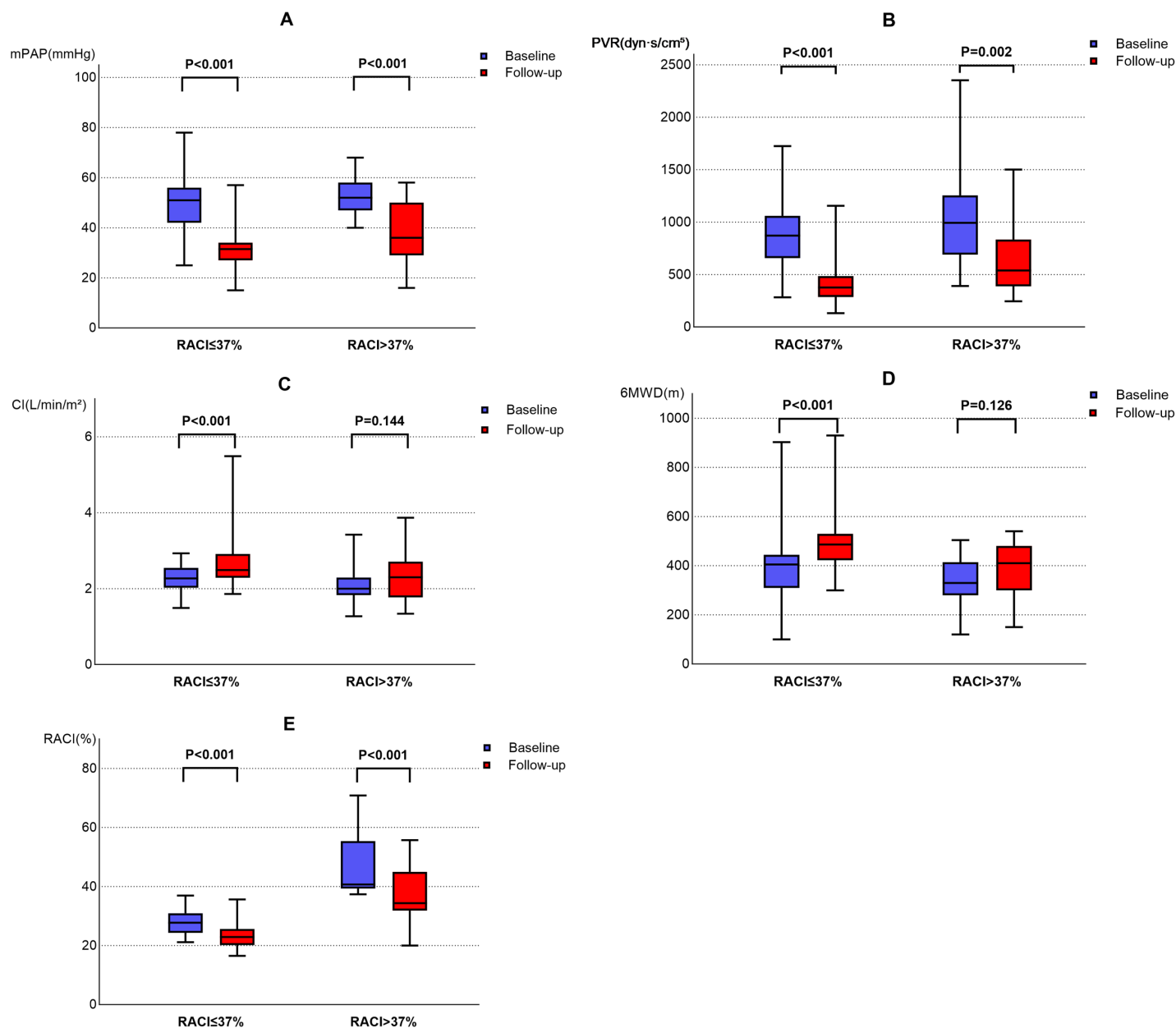


**Figure 4**

Hemodynamics, 6-minute walk distance (6MWD), cardiac index (CI) and right atrioventricular coupling index (RACI) at baseline and follow-up in CTEPH patients with RACI ≤37% and >37%: mPAP (A), PVR (B), CI (C), 6MWD (D), and RACI (E) at baseline and follow-up. At baseline, RACI ≤37 vs. RACI >37 (mPAP:  $50.20 \pm 11.37$  mmHg vs.  $52.43 \pm 7.17$  mmHg,  $p = 0.327$ ; PVR:  $888.96 \pm 302.55$  dyn·s·cm<sup>-5</sup> vs.  $1014.70 \pm 429.70$  dyn·s·cm<sup>-5</sup>,  $p = 0.166$ ; CI:  $2.25 \pm 0.37$  L/min/m<sup>2</sup> vs.  $2.09 \pm 0.52$  L/min/m<sup>2</sup>,  $p = 0.153$ ; 6MWD:  $381.82 \pm 123.78$  m vs.  $329.83 \pm 104.83$  m,  $p = 0.090$ ; RACI:  $27.93 \pm 4.35$  vs.  $47.85 \pm 10.91$ ,  $p < 0.001$ ). mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance.

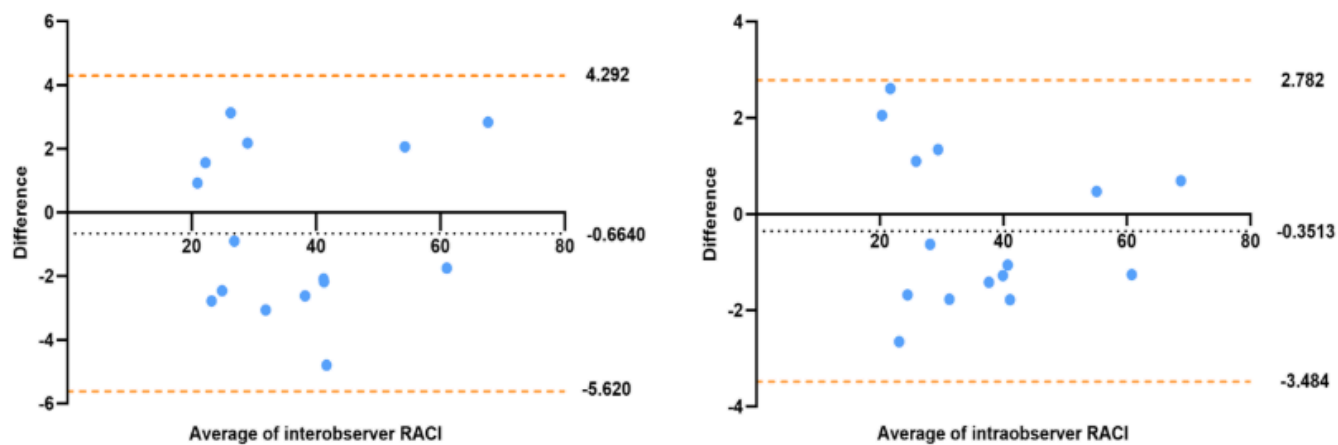


**Figure 5**

Bland-Altman plots for Intra-observer and Inter-observer agreement of right atrioventricular coupling index (RACI) findings. The horizontal dots represent the mean difference, and the yellow lines represent the mean difference  $\pm$  1.96 standard deviations...