Comparison of the safety and efficacy of balloon pulmonary angioplasty in chronic thromboembolic pulmonary hypertension patients with surgically accessible and inaccessible lesions

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List of non-standard abbreviations

PEA, pulmonary endarterectomy

CTEPH, chronic thromboembolic pulmonary hypertension

BPA, balloon pulmonary angioplasty

WHO-Fc, World Health Organization functional class

SpO_2, percutaneous oxygen saturation

6MWD, 6-min walking distance

BNP, brain natriuretic peptide

RVAI, right ventricular area index

mPAP, mean pulmonary artery pressure

PVR, pulmonary vascular resistance

RHC, right heart catheterization

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Abstract

Background

Although pulmonary endarterectomy is the treatment of choice for chronic thromboembolic pulmonary hypertension, not all patients are eligible. While balloon pulmonary angioplasty is an alternative for such patients, its efficacy and safety may differ between patients with and without surgically accessible lesions.

Methods

This study involved 344 patients treated with balloon pulmonary angioplasty who were ineligible for pulmonary endarterectomy. Based on the angiographical lesion location, patients were divided into the surgically accessible (Group 1) and inaccessible (Group 2) groups, and percent changes in hemodynamics and clinical parameters before and after balloon pulmonary angioplasty were investigated. We also conducted survival analyses using Kaplan–Meier analysis.

Results

While no differences in baseline characteristics were identified between the groups, balloon pulmonary angioplasty significantly improved hemodynamics in both groups, without any difference regarding the incidence of complications. Meanwhile, the percent changes in the mean pulmonary arterial pressure, pulmonary vascular resistance, 6-min walk distance, right ventricular area index on echocardiography, and the achievement rate of World Health Organization functional class I after balloon pulmonary angioplasty were significantly lower in Group 1 than in Group 2. The cumulative survival rates at 1, 5, and 10 years after balloon pulmonary angioplasty were not significantly different between the two groups (Group 1: 92.5%, 86.1%, 84.3%; and Group 2: 96.5%, 92.9%, 90.1%, respectively).

Conclusions

The outcome of balloon pulmonary angioplasty in inoperable patients with surgically accessible proximal lesions was acceptable; however, further investigations are necessary to clarify the optimal treatment for such patients.

Introduction

Pulmonary endarterectomy (PEA) remains the preferred treatment for patients with chronic thromboembolic pulmonary hypertension (CTEPH),[1,2] offering the greatest symptomatic and prognostic improvement in those with surgically accessible proximal lesions. Excellent long-term results have been reported by some expert centers[3,4]; however, PEA is challenging and technically demanding. Hence, not all patients are eligible. While inability to undergo PEA is often attributed to the location of the lesion, patients with advanced age, comorbidities, or poor general condition are considered ineligible irrespective of lesion accessibility due to an unfavorable risk-benefit ratio for PEA.[5] Furthermore, some patients refuse to undergo PEA owing to its invasiveness.

Balloon pulmonary angioplasty (BPA) has emerged as an alternative treatment for patients considered ineligible for PEA.[6,7] With refinements and major improvements in the safety and efficacy of BPA,[8-12] the latest CTEPH guidelines recommend BPA for inoperable patients with CTEPH.[1,2] However, unlike PEA, BPA cannot directly resect large fibrotic thromboembolic material located on proximal lesions. As few studies have compared the efficacy and safety of BPA between patients with surgically accessible proximal and inaccessible distal lesions,[13,14] the therapeutic efficacy and safety of BPA may be affected by the location of the lesion.

We aimed to compare the efficacy and safety of BPA in the world's leading CTEPH referral center between patients with and without surgically accessible proximal lesions, including long-term survival.

Materials and methods

Patient selection

This single-center, retrospective observational study was approved by the Institutional Review Board of the National Hospital Organization Okayama Medical Center (approval number: H29-RINKEN-017). Our study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement reporting guidelines.[15] We included 344 patients with CTEPH who underwent BPA at our institution between November 2004 and January 2018. Patients deemed eligible for and

who underwent PEA were excluded. Written informed consent was obtained from each patient. The diagnosis of CTEPH was previously described.[8,9]

As indicated in Figure 1, patients were divided into the surgically accessible (Group 1: 81 patients, Figure 2A-a) and inaccessible (Group 2: 263 patients, Figure 2B-a) groups based on the location of the fibrotic thromboembolic material. Group 1 included patients deemed ineligible for PEA despite the presence of surgically accessible proximal lesions located at the main or lobal pulmonary arteries and proximal segmental pulmonary arteries; Group 2 included patients without proximal lesions. All patients were diagnosed as inoperable by a multidisciplinary CTEPH team comprising PEA surgeons, cardiologists experienced in the pharmacotherapy of pulmonary hypertension, interventionists experienced in BPA, and radiologists. The final judgment for PEA eligibility was made considering every aspect, including the risk of PEA defined by the presence of comorbidities, patients' age and frailty, severity of hemodynamic impairment, and patients' wishes.

Data collection

Data concerning medical history, medication, and comorbidities were obtained from medical records. World Health Organization functional class (WHO-Fc), percutaneous oxygen saturation (SpO_2) in room air, 6-min walk distance (6MWD), plasma brain natriuretic peptide (BNP) levels, echocardiographic parameters (right ventricular area index [RVAI], fractional area change, and tricuspid annular plane systolic excursion), hemodynamic parameters (mean pulmonary artery pressure [mPAP], pulmonary artery wedge pressure, right atrial pressure, cardiac output estimated by thermo-dilution method, and pulmonary vascular resistance [PVR]) were collected before and at 6 months after the final BPA.

Information regarding the angiographical lesion types and total number of BPA procedures, treated lesions per patient, procedures with hemosputum, severe BPA-related lung injuries requiring extracorporeal membrane oxygenation or mechanical ventilation, and procedural characteristics of BPA were also investigated. Additionally, long-term survival from the initial BPA procedure was evaluated. The primary outcome was all-cause death, determined using patients' medical records; the follow-up period ended in July 2021.

BPA procedure

BPA procedures and perioperative management were based on previous reports.[8,9,12] BPA was performed through either the right internal jugular or right femoral vein. After placing a 9-Fr indwelling sheath (ArrowFlex; Teleflex, Durham, NC), a 6-Fr guiding catheter (Mach 1 peripheral MP; Boston Scientific, Natick, MA) with a 6-Fr long introducer sheath (Bright Tip Sheath Introducer; Cordis/Johnson & Johnson, New Brunswick, NJ) was advanced into the pulmonary artery being treated. First, selective pulmonary angiography was performed to confirm the location and type of each lesion.[9] Then, a 0.014-inch guidewire (Agosal XS 0.8; Asahi Intec, Tokyo, Japan or Chevalier floppy; Cordis/Johnson & Johnson or Athlete B-pahm; Japan Lifeline, Tokyo, Japan) was passed through the lesion, and a balloon catheter of appropriate diameter (2–4 mm, IKAZUCHI PAD; Kaneka, Osaka, Japan or 5–7 mm, Bandicoot RX; St. Jude Medical, St. Paul, MN or Aviator Plus; Cordis/Johnson & Johnson or 8 mm, Sterling Monorail; Boston Scientific) was selected to dilate the lesion. The balloon size was selected based on angiographic findings and confirmed by intravascular ultrasound (Eagle Eye® Platinum Volcano, San Diego, CA) if necessary. We sequentially dilated the same lesion in stages via two separate BPA procedures: first, a balloon with a smaller diameter than that of the vessel was selected at the initial stage of BPA to reduce the risk of pulmonary vessel injury; then, the lesions were dilated again, if necessary, using the angiographically appropriate balloon size to optimize the lumen diameter.[12] The basic BPA procedure was similar in both groups.

Statistical analysis

Continuous variables are presented as means±standard deviation [SD], or medians with interquartile ranges, depending on the data distribution; categorical variables are presented as numbers and percentage (%). The Mann–Whitney U, Pearson's Chi-squared, or Fisher's exact test was used for comparison between groups for continuous and other categorical variables, as appropriate. Differences between variables measured before and after BPA were evaluated using the paired- t-test or Wilcoxon signed-rank test for each continuous variable. WHO-Fc was expressed as the number of patients in each class, and changes in WHO-Fc were evaluated using Fisher’s exact test. Percent

changes in each clinical parameter were compared between the two groups and evaluated using the Mann–Whitney U test; survival analyses were conducted using Kaplan–Meier analysis. The difference in the survival rate between the groups was compared using the log-rank test. All analyses were performed with IBM SPSS Statistics 20 (IBM, Armonk, NY); statistical significance was set at $p<0.05$.

Results

Baseline patient characteristics

The baseline patient characteristics are summarized in Table 1; 344 patients (80 male and 264 female individuals; average age, 63.2±12.5 years) were enrolled. Most patients had severely compromised hemodynamics with a mean PAP >40 mmHg. Eighty-one patients were considered surgically accessible but inoperable due to patient refusal (n=41), advanced age (>80 years; n=7), comorbidities (n=19), poor general condition (n=8), and other reasons (n=6) (Group 1, Figure 2A-a); 263 patients were defined as inoperable owing to surgically inaccessible lesions (Group 2, Figure 2B-a). All patients in Groups 1 and 2 underwent BPA (Figure 2A-b and 2B-b); while there was no significant difference in baseline echocardiographic data, hemodynamics, SpO_2, 6MWD, or plasma BNP levels between the two groups, the number of patients with a history of acute pulmonary embolism was significantly higher in Group 1 than in Group 2 (37% vs. 26%; p=0.04). Sixty-five (80.2%) and 225 (85.6%) patients in Groups 1 and 2, respectively, underwent follow-up right heart catheterization (RHC) at least 6 months after the final BPA (Figure 1). The percentage of patients taking pulmonary vasodilators before and after BPA did not differ between the two groups. The mean follow-up durations (final BPA to follow-up RHC) for Groups 1 and 2 were 6.5±2.0 and 6.9±3.2 months, respectively.

Difference between procedural characteristics and complications in BPA

The angiographical lesion type of treated lesions, procedural characteristics of BPA, and frequency of complications are shown in Table 2. Group 1 had more total occlusions, while Group 2 had more ring-like stenoses. The number of procedures and treated lesions per patient, amount of contrast medium,

and radiation exposure time per procedure were similar in both groups. The maximum balloon size used in a series of BPA procedures was larger in Group 1 than in Group 2, while the incidence rate of complications during BPA was not different between the groups.

Change in clinical parameters before and after BPA

Figure 3 shows the changes in clinical parameters from baseline to follow-up. The mean PAP decreased from 38.2±10.8 to 21.4±4.6 mmHg ($p<0.001$), and from 42.4±11.4 to 21.5±4.7 mmHg ($p<0.001$) in Groups 1 and 2, respectively. PVR decreased after BPA in both groups (Group 1: from 8.0±4.2 to 3.4±1.4 wood units, $p<0.001$; Group 2: from 9.1±4.6 to 3.4±1.2 wood units, $p<0.001$). The 6MWD improved (Group 1: from 310±112 to 395±100 m, $p<0.001$: Group 2: from 306±113 to 405±110 m, $p<0.001$), and the RVAI on echocardiography decreased after BPA (Group 1: from 13.2±3.1 to 11.5±2.4 cm^2/m^2, $p<0.001$; Group 2: from 15.0±3.6 to 11.9±2.8 cm^2/m^2, $p<0.001$) in both groups.

Comparing improvements in clinical parameters after BPA between Groups 1 and 2

Figure 4 illustrates the percent changes in clinical parameters from baseline to follow-up in both groups. Percent changes in mPAP (-37.8% vs. -48.9%; p=0.005), PVR (-51.6% vs. -60.8%; p=0.006), 6MWD (+13.5% vs. +28.9%; p=0.017), and RVAI (-11.0% vs. -21.4%; p=0.044), were significantly lower in Group 1 than in Group 2 even with the same number of procedures.

Changes in WHO-Fc from baseline to follow-up are shown in Figure 4E. At baseline, WHO-Fc III or IV were predominant in both groups; however, most patients were categorized as WHO-Fc I or II at follow-up. The achievement rate of WHO-Fc I at follow-up was significantly lower in Group 1 than in Group 2 (14% vs. 30%; $p<0.05$).

Comparison of long-term survival rates of Groups 1 and 2

Thirty-five (10.2%) patients died during the observation period (median: 6.7 years, interquartile range: 4.6–8.6 years). Five patients in Group 1 and four in Group 2 died within 30 days of the final BPA due to multiple organ failure (n=3), septic shock (n=3), right heart failure (n=1), sudden death

(n=1), and cerebral hemorrhage (n=1). Eight patients in Group 1 and 18 in Group 2 died during the observation period because of cancer (n=6), pneumonia (n=4), multiple organ failure (n=3), suicide (n=3), senility (n=2), right heart failure (n=1), acute myocardial infarction (n=1), complication of cardiac surgery (n=1), suffocation (n=1), traffic accident (n=1), sudden death (n=1), cerebral hemorrhage (n=1), and unknown cause (n=1). No significant difference in the cumulative survival rate between the two groups was noted (p=0.10, log-rank test, Figure 5). The cumulative survival rates at 1, 5, and 10 years were 92.5%, 86.1%, and 84.3% in Group 1, and 96.5%, 92.9%, and 90.1% in Group 2, respectively.

Discussion

We compared the efficacy and safety of BPA between inoperable patients with and without surgically accessible proximal lesions, observing that percent changes in the mPAP, PVR, 6MWD, RVAI, and achievement rate of WHO-Fc I after BPA were lower in the surgically accessible than in the inaccessible group even with the same number of procedures and treated lesions per patient. To our knowledge, this is the first study to demonstrate differences in the efficiency of improvements in hemodynamics, exercise capacity, echocardiographic parameters, and symptoms after BPA, depending on lesion location. However, BPA significantly improved hemodynamics, exercise capacity, and symptoms to similar levels in both groups, with no difference in the frequency of complications. The cumulative survival rates after BPA did not differ between the two groups. Thus, BPA was acceptable even in patients with surgically accessible proximal lesions who were ineligible for PEA.

PEA is the standard treatment for CTEPH[1,2]; however, it is challenging and technically demanding. Although lesions may be surgically accessible and suitable for PEA, some patients are ineligible. PEA is an invasive procedure performed under intermittent total circulatory arrest with deep hypothermia[16,17]; thus, patients with advanced age, comorbidities, or poor general condition are considered ineligible.[5] Additionally, some eligible patients refuse to undergo the procedure. Previously, 8.7% of patients with surgically accessible proximal lesions refused to undergo PEA[18]; here, 41/81 (51%) patients with proximal lesions refused PEA. The high percentage of Japanese

patients who refused PEA is similar to the latest registry data, revealing that 77.8% of technically operable Japanese patients with CTEPH refused PEA, compared to their counterparts in Europe (3.7%), America, and other countries (2.5%).[19] We speculated that this may be related to the small number of PEA expert centers (conducting >50 PEAs per year) in Japan,[5,20] and Japanese patients' preference for less-invasive treatment.

The location of lesions suitable for PEA highly depends on the surgeon's skill. Generally, PEA is suitable for proximal lesions in the main, lobal, and segmental pulmonary arteries[16,17,21]; BPA primarily targets distal lesions in the segmental and subsegmental vasculature, down to small pulmonary arteries 2–5 mm in diameter.[22] There is no global consensus on whether segmental pulmonary arteries are suitable for BPA or PEA; in our study, surgically inaccessible lesions were defined as fibrotic thromboembolic material limited to distal segmental or subsegmental pulmonary arteries. Among all patients, 263 (76.5%) were considered surgically inaccessible. The latest registry data showed that 167/820 (20.3%) Caucasian/white and 63/142 (44.3%) Asian patients were diagnosed as technically inoperable.[19] Why a higher percentage of Asian patients—especially Japanese patients—were considered technically inoperable remains unclear. Regarding phenotypic differences of CTEPH between the racial and ethnic groups, female predominance and a low prevalence of acute pulmonary embolism in Japanese patients with CTEPH have been reported.[19,23] Further studies are necessary to clarify these details.

We found that percent changes in mPAP, PVR, 6MWD, RVAI after BPA, and the achievement rate of WHO-Fc I after BPA, were lower in the surgically accessible than in the inaccessible group, despite using a larger maximum balloon size in the same number of BPA procedures. BPA improves hemodynamics in patients with surgically accessible and inaccessible lesions.[13,14] Szymon et al.[14] reported that improvements in mPAP and PVR after BPA did not differ between the two groups. However, only 16 inoperable patients with surgically accessible lesions were included in that study, and improvements in mPAP and PVR after BPA were significantly lesser than in our study. In contrast, the absolute values in mPAP, PVR, and RVAI after BPA were similar in patients with surgically accessible and inaccessible lesions. The therapeutic efficacy of BPA appears to be sufficient even in patients with surgically accessible lesions in terms of normalization of resting

hemodynamics. However, there are no data or consensus on the final therapeutic goals of BPA[2]; normalization of resting hemodynamics alone may be insufficient to improve the quality of life of patients with CTEPH. Therefore, the differences in the improvement of 6MWD and the achievement rate of WHO-Fc I after BPA between the two groups should not be ignored. The exercise stress tests would be necessary to confirm the equivalence in the therapeutic outcome of BPA between the two groups.

It remains unclear why the therapeutic efficiency of BPA varies with the location of the lesion. Based on intravascular ultrasound before and after BPA, we previously reported that lumen enlargement mainly occurs because of overall expansion of the pulmonary artery through the fibrotic thromboembolic material.[10] Recoil of the lesion may more easily occur in proximal lesions rich in fibrotic thromboembolic material than in distal lesions. Furthermore, the maximum balloon size for large proximal pulmonary arteries was limited (up to 10 mm). If larger balloons were available, hemodynamic and symptomatic improvements in patients with proximal lesions may have been greater; however, few bigger balloons are currently commercially available. Additionally, the development of larger balloons may not be the only solution to this problem. It may be necessary to consider other devices to remove thromboembolic material or avoid recoiling of the lesion after BPA, such as debulking devices or stent implantation.[24] In our case, without such devices, it is more difficult to obtain an optimal lumen size for proximal than distal lesions.

Regarding the angiographical lesion types in this study, the distribution of ring-like stenoses and total occlusions was lower and higher, respectively, in Group 1 than in Group 2. A previous report revealed that the number of successfully recanalized occlusions had an impact on change in hemodynamics after BPA.[25] Given the difference in the BPA success rate between total occlusions and ring-like stenoses,[9] the different distribution of each lesion type in this study may have affected the difference in hemodynamic and symptomatic improvements after BPA between the two groups.

We did not directly compare the therapeutic outcomes of BPA and PEA for patients with surgically accessible proximal lesions; thus, few data are available to directly compare the outcomes of PEA and BPA in patients with surgically accessible lesions. D'Armini et al.[20] previously demonstrated improvements in hemodynamics and exercise capacity at 1 year after PEA for patients with CTEPH

with proximal lesions; the percent changes for mPAP, PVR, and 6MWD were 47.7% (from 44±10 to 23±7 mmHg), 72.3% (from 876±392 to 243±115 dyne.s.cm^{-5}), and 40.4% (from 277±118 to 389±118 m), respectively, while those in our study were 37.8%, 51.6%, and 13.5%, respectively. The therapeutic efficacy of BPA for proximal lesions appears to be inferior to that of PEA. However, it is challenging to directly compare these two studies as we could only compare the mean percent changes of each parameter. Additionally, the definition of proximal lesions and patients' characteristics were different in each study. A randomized trial comparing the efficacy and safety of PEA and BPA for proximal lesions is necessary to clarify the optimal treatment option for patients with CTEPH with proximal lesions.

The current CTEPH treatment algorithm includes a multidisciplinary approach, combining PEA, BPA, and medical therapies to target the mixed anatomical lesions: proximal, distal, and microvasculopathy.[2] While there are overlapping indications for each therapy, the outcomes of each treatment are not necessarily equivalent. This study demonstrated that patients with surgically accessible lesions who were ineligible for or refused PEA could be treated with BPA. Given the differences in percent changes in hemodynamics, exercise capacity, and symptoms after BPA depending on the location of the lesion, it would be ideal to treat surgically accessible lesions with PEA if the patients can undergo PEA; particularly, patients who refuse PEA should be persuaded.

This study has some limitations; first, it was retrospectively conducted at a single center with a limited number of patients. Second, some patients with surgically accessible proximal lesions in one lung and inaccessible distal lesions in the other were considered to have surgically accessible lesions; thus, some patients with surgically accessible proximal lesions could also have surgically inaccessible distal lesions. Third, this study did not directly compare the therapeutic outcomes of BPA and PEA in patients with surgically accessible proximal lesions. Fourth, the number of all-cause deaths may be insufficient to compare mortality between the groups. Fifth, the number of patients with surgically accessible lesions may have increased if they were evaluated at global PEA expert centers, which have experienced a greater number of PEA; therefore, data generalizability is limited. Sixth, only resting hemodynamic parameters were evaluated. Exercise stress test was not available.

In conclusion, patients with CTEPH with surgically accessible proximal lesions who are ineligible for PEA could be safely and effectively treated with BPA. However, improvement efficiency of hemodynamics and the achievement rate of WHO-Fc I were lower in patients with surgically accessible proximal lesions. While BPA is a promising therapeutic option for surgically accessible proximal lesions, further investigations are necessary to clarify the optimal treatment for such patients.

Author contributions

Drs. Shimokawahara and Nishihara had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Shimokawahara.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Shimokawahara.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Drs. Shimokawahara and Nishihara.

Obtained funding: No sources of findings.

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Supervision: Shimokawahara and Matsubara.

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Figure Legends

Figure 1. Study flowchart of participants showing patient enrollment, allocation, and follow-up analysis

BPA, balloon pulmonary angioplasty; CTEPH, chronic thromboembolic pulmonary hypertension

Figure 2. Representative pulmonary angiogram before and after balloon pulmonary angioplasty

(A) Global pulmonary angiogram in a patient with surgically accessible proximal lesions (Group 1).

A-a: pulmonary angiogram before BPA

A-b: pulmonary angiogram after four BPA procedures

(B) Global pulmonary angiogram in a patient with surgically inaccessible distal lesions (Group 2).

B-a: pulmonary angiogram before BPA

B-b: pulmonary angiogram after four BPA procedures

BPA, balloon pulmonary angioplasty

Figure 3. Change in clinical parameters before and after balloon pulmonary angioplasty (BPA) in Groups 1 and 2

(A) The change in mPAP from baseline to follow-up. mPAP significantly decreased at follow-up in Groups 1 (indicated by the solid line with green circle) and 2 (indicated by the dotted line with blue triangle).

(B) The change in PVR from baseline to follow-up. PVR significantly decreased after BPA in both groups.

(C) The change in 6MWD from baseline to follow-up. The 6MWD significantly improved after BPA in both groups.

(D) The change in the RVAI from baseline to follow-up. The RVAI significantly improved after BPA in both groups.

*; $p<0.05$ compared with the value at baseline

BPA, balloon pulmonary angioplasty; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; 6MWD, 6-min walk distance; RVAI, right ventricular area index

Figure 4. Comparison of percent changes in clinical parameters after BPA in Groups 1 and 2

(A) Percent decrease in mPAP after BPA in Group 1 (indicated by the green squares) and 2 (indicated by the blue squares). The percent decrease in mPAP was significantly smaller in Group 1 than in Group 2.

(B) Percent decrease in PVR after BPA between the two groups. The percent decrease in PVR was significantly smaller in Group 1 than in Group 2.

(C) Percent increase in 6MWD after BPA between the two groups.

The percent increase in 6MWD in Group 1 was significantly lesser than that in Group 2.

(D) Percent decrease in RVAI after BPA between the two groups. The percent decrease in RVAI was significantly smaller in Group 1 than in Group 2.

(E) Change in WHO-Fc at baseline and at follow-up for Groups 1 and 2.

Patients predominantly distributed in WHO-Fc III and IV at baseline improved to WHO-Fc I and II in both groups at follow-up. The percentage of patients who achieved WHO-Fc I at follow-up was lower in Group 1 than in Group 2.

BPA, balloon pulmonary angioplasty; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; 6MWD, 6-min walk distance; RVAI, right ventricular area index; WHO-Fc, World Health Organization functional class

Figure 5. Survival curves for Groups 1 and 2

No significant differences in cumulative survival rates were identified between the two groups. The 1-, 5-, and 10-year cumulative survival rates were 92.5%, 86.1%, and 84.3% in Group 1, and 96.5%, 92.9%, and 90.1% in Group 2, respectively.

BPA, balloon pulmonary angioplasty