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RESEARCH ARTICLE

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The beneficial effects of balloon pulmonary angioplasty for patients with chronic thromboembolic pulmonary hypertension are accompanied by increased body mass index and improved nutritional status

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Abstract

Although balloon pulmonary angioplasty (BPA) improves pulmonary hypertension and the prognosis of patients with chronic thromboembolic pulmonary hypertension (CTEPH), subsequent changes in body mass index (BMI), nutritional status, and appetite have not been fully investigated. This retrospective study aimed to clarify changes in BMI, nutritional status, and appetite after BPA. Fifty-two consecutive patients with CTEPH who underwent complete revascularization with BPA between July 2014 and July 2023 and were available for follow-up were evaluated. We compared the presence or absence of increased appetite, BMI change, and nutritional status before and after BPA treatment. BPA significantly improved the mean pulmonary artery pressure from 37.4 ± 8.7 mmHg to 18.7 ± 2.8 mmHg and the partial pressure of oxygen from 61.6 ± 9.3 mmHg to 82.8 ± 9.9 mmHg (both $p < 0.001$). Appetite was increased in 82.7% of the patients. BMI significantly increased from 23.9 ± 3.7 kg/m^2 to 24.9 ± 3.7 kg/m^2 ($p < 0.001$). As a nutritional indicator, the Geriatric Nutritional Risk Index increased from 105.3 ± 10.2 to 108.3 ± 8.3 ($p < 0.001$). The median Controlling Nutritional Status scores showed no significant change but the range was significantly improved from 0–9 to 0–3 ($p = 0.006$). In conclusion, patients with CTEPH show improved oxygenation and hemodynamics, increased BMI, and improved nutritional status following BPA. This sequence of changes may help improve patient prognosis.

KEYWORDS

appetite, body mass index, chronic thromboembolic pulmonary hypertension, nutritional status, oxygenation

Chronic thromboembolic pulmonary hypertension (CTEPH) is a condition in which the pulmonary arteries are narrowed or occluded by organized thrombi, resulting in pulmonary hypertension with impaired quality of life and poor prognosis.[1] Balloon pulmonary angioplasty (BPA) treatment in patients with CTEPH provides hemodynamic and prognostic improvement and benefits oxygenation and exercise capacity.[2,3] Although the effects of BPA on patients with CTEPH have been demonstrated, how the systemic status of patients changes and contributes to an improved prognosis has not been fully investigated.

Obese patients with left heart failure have a higher survival rate compared to nonobese patients.[4] Furthermore, obese patients assessed by body mass index (BMI) also have lower hospitalization rates.[4] This phenomenon is known as the obesity paradox.[5] Similar findings have been reported in patients with precapillary pulmonary hypertension, where obese patients have higher survival rates.

Furthermore, in heart failure, nutritional status is associated with prognosis,[6] and the assessment of nutritional status is recommended.[7] The Geriatric Nutritional Risk Index (GNRI), Prognostic Nutritional Index (PNI), and Controlling Nutritional Status (CONUT) score are widely used,[8–10] and studies in patients with heart failure confirmed correlations between these indexes and prognosis.[6–8,10–14] Recent studies have shown that some of these measures, as well as the degree of obesity, are associated with prognosis in pulmonary arterial hypertension and CTEPH.[15–21] However, the changes in the BMI and nutritional status of patients with CTEPH before and after BPA treatment have not been fully investigated.[22]

CTEPH-induced deterioration of pulmonary circulation causes hypoxia.[1] Several studies regarding the connection between hypoxia and appetite have been conducted, and appetite may be decreased in patients with CTEPH. Moreover, BPA treatment in patients with CTEPH improves oxygenation.[5] Therefore, it is unclear how changes in CTEPH-induced hypoxia before and after BPA treatment affect appetite in these patients. Changes in appetite may affect BMI and nutritional status. Therefore, the present study aimed to evaluate the changes in BMI, nutritional status, and appetite before and after BPA.

METHODS

Participants

We retrospectively enrolled 89 consecutive patients with CTEPH who underwent BPA with complete revascularization at the Saitama Cardiovascular and Respiratory Center between July 2014 and July 2023. These patients were diagnosed with CTEPH using echocardiography, chest computed tomography, pulmonary perfusion scintigraphy, right heart catheterization (RHC), and pulmonary angiography. Patients who underwent BPA after diagnosis, with the treatment selected based on the feasibility of pulmonary artery endarterectomy and the patient's willingness to undergo the procedure, were included. Pulmonary artery endarterectomy was considered only before BPA. Patients who underwent pulmonary artery endarterectomy were included in the registry. The following patients were excluded: those on dialysis ($N = 1$), those without lipid-related data ($N = 5$), those who received statins during the study period ($N = 10$), those with active cancer detected during the study period ($N = 5$), and those who did not undergo follow-up RHC within 1 year after the last BPA ($N = 16$).

BPA procedures

The BPA treatment strategy and perioperative management have been described previously.[5] We aimed at dilating as many lesions as possible in a single BPA session. The balloon size was adjusted based on reported efficacy, safety, and risk factors. To avoid vascular injury due to overexpansion, a balloon with a diameter smaller than that of the vessel was selected based on the mean pulmonary artery pressure (mPAP) before the BPA session.

Baseline parameters were assessed immediately before the first BPA session. RHC was performed immediately before and after each BPA session. Subsequent BPA sessions were performed at least 3 days after the previous BPA session and were based on the schedules of the operator and patients. The need for further BPA sessions was determined at the end of each BPA session based on the surgeon's subjective judgment of whether any residual lesions required treatment. In principle, all BPA sessions ended with complete revascularization. Follow-up RHC was performed approximately 1 year after the final BPA session.

Pulmonary hypertension medication

In principle, pulmonary vasodilators were used if the mPAP was >40 mmHg. If the patient did not meet this criterion but had already received pulmonary vasodilators at the referral hospital, pulmonary vasodilator treatment was continued, and BPA was started. Pulmonary vasodilators were actively discontinued based on the subjective judgment at the end of the BPA session that an mPAP of ≤25 mmHg or pulmonary vascular resistance (PVR) of ≤240 dyn s/cm^5 could be achieved without pulmonary vasodilators. In general, this decision was

guided by an mPAP ≤25 mmHg or PVR ≤ 240 dyn s/cm^5 during RHC at the end of the BPA session. However, even if these criteria were not strictly fulfilled, pulmonary vasodilators were actively discontinued if the BPA session was subjectively judged to be extremely successful.

Study design

In CTEPH patients with complete revascularization after BPA, data were extracted at baseline immediately before the first BPA session and at follow-up RHC 1 year after completion of the final BPA session. At follow-up, the patients were asked to indicate using a Yes or No response whether their appetite had increased since before the start of BPA therapy.

The primary endpoint was BMI. The secondary endpoints were nutritional status and the presence or absence of increased appetite. Nutritional status was assessed using the GNRI, PNI, and CONUT score. The GNRI[8] and PNI[9] were calculated as follows, with lower scores correlating with worse outcomes.

$$\text{GNRI} = 14.89 \times \text{serum albumin (g/dL)} + 41.7 \times [\text{BMI}(\text{kg/m}^2)/22].$$

$$\text{PNI} = 10 \times \text{serum albumin (g/dL)} + 0.005 \times \text{total lymphocyte count (per } \mu\text{L}).$$

The CONUT score was calculated from the sum of the scores assigned to several test results (Supporting Information S1: Table S1), with higher scores correlating with poorer results.[10]

In addition, hemodynamic data from RHC, blood gas analysis (arterial blood, venous blood in the pulmonary arteries), blood sampling data, assessment of exercise capacity based on the 6-min walk distance (6MWD), respiratory function by spirography, percentage of patients receiving pulmonary vasodilators, and the percentage of patients requiring oxygen therapy were analyzed for evaluating other therapeutic effects of BPA. RHC, blood gas analysis, and 6MWD test were performed without oxygen administration.

Statistical analysis

Data were analyzed for normality using the Shapiro–Wilk test. Continuous variables were expressed as mean ± standard deviation or median [interquartile range], and categorical variables were expressed as numbers (percentages). Data collected immediately before the first BPA session and at follow-up were compared using the Wilcoxon signed-rank or paired *t*-test. Categorical variables were compared between two groups using Pearson's χ^2 or Fisher's exact tests. Multivariate logistic analysis was performed to analyze the prespecifiers. The *p*-values <0.05 were considered statistically significant. All analyses were performed using SPSS Statistics version 25 (IBM Corp.).

RESULTS

Of the 89 patients with CTEPH who underwent BPA, 52 patients were selected (Figure 1). Their baseline characteristics are shown in Table 1. The median patient age was 68 (57–73) years and ranged from 30 years to 81 years; 29 (42.3%) patients had class III or IV World Health Organization (WHO) functional classification. All patients included in the analysis had a low partial pressure of oxygen (PaO_2), as indicated by arterial blood gas analysis. At the time of initial BPA, 24 patients (46.2%) were treated with pulmonary vasodilators. The mPAP was 37.4 ± 8.7 mmHg, the PNI ranged from 33 to 59, the GNRI from 79.3 to 127.1, and CONUT scores from 0 to 9. The median total number of BPA sessions was 4 (3–4).

Changes in hemodynamics, respiratory function, oxygenation capacity, exercise capacity, and laboratory data

Figure 2 shows hemodynamic RHC, respiratory function, arterial blood gas, and 6MWD data before the first BPA session and at follow-up after the final BPA session. Pulmonary circulatory pressure and PVR were significantly improved (both $p < 0.001$). At follow-up after the final BPA, mPAP was below 20 mmHg with 18.7 ± 2.8 mmHg, and PVR was 160 ± 65 dyn s/cm^5.

Resting arterial blood gas analysis showed a significant improvement in PaO_2 from 61.6 ± 9.3 mmHg to 82.8 ± 9.9 mmHg ($p < 0.001$), and the minimum oxygen saturation (SpO_2) during the 6MWD test also improved from 86 ± 6% to 92 ± 3% ($p < 0.001$). The 6MWD also significantly increased from 355 ± 126 m to 444 ± 104 m ($p < 0.001$). Thus, pulmonary hypertension and oxygenation capacity were sufficiently improved with successful BPA therapy.

Figure 3 shows the changes in laboratory data and mixed venous blood gas analysis data. Total cholesterol levels significantly increased from 188 ± 211 mg/dL to 309 ± 61 mg/dL ($p < 0.001$). The estimated glomerular filtration rates and creatinine levels, as well as the levels of brain natriuretic peptide and mixed venous blood

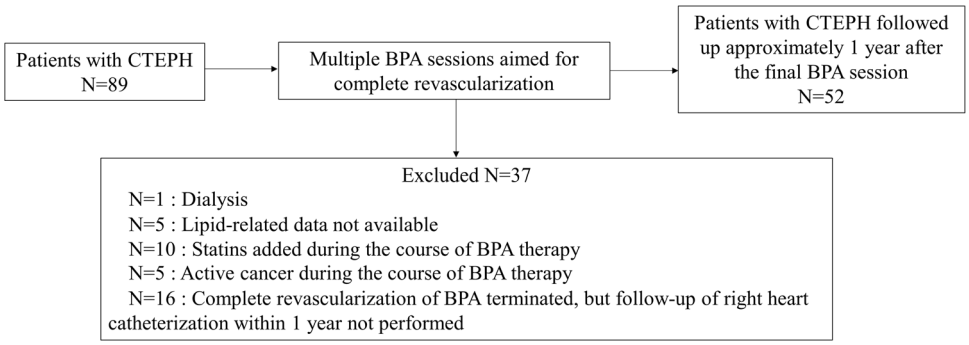

FIGURE 1 Flowchart of patient selection. From 89 patients with chronic thromboembolic pulmonary hypertension (CTEPH) who had undergone balloon pulmonary angioplasty (BPA), 52 patients were selected.

oxygen saturation (SvO_2) in venous blood gas analysis, improved significantly.

Changes in BMI, nutritional indexes, and appetite

Figure 4 shows the changes in BMI, nutritional indexes, and appetite before and at follow-up after the final BPA. BMI increased significantly from $23.9 \pm 3.7\,kg/m^2$ to $24.9 \pm 3.7\,kg/m^2$ ($p < 0.001$). The GNRI improved significantly from 105.3 ± 10.2 to 108.3 ± 8.3 ($p < 0.001$). The CONUT score did not change from 1 (0–2) to 1 (0–2) in median notation, but changed significantly in the statistical assessment ($p = 0.006$). And the range of CONUT score was improved from 0–9 to 0–3. The PNI improved from 48.0 ± 5.1 to 49.5 ± 3.9, but the difference was not significant ($p = 0.064$). Of the 52 patients with CTEPH, 43 (82.7%) reported an increase in appetite after BPA.

Factors affecting changes in BMI and nutritional indexes

Table 2 shows the comparison of the two groups based on the presence or absence of an increase in BMI. Age and sex were not significantly different between the two groups. Both the extent of changes in mPAP and PVR were also not significantly different. Significantly increased appetite was observed in the increased BMI group. The increased BMI group was also significantly less likely to have psychiatric disorders. In addition, the baseline PaO_2 values were higher in the increased BMI group. Multivariate analysis revealed that increased appetite was most strongly associated with increased BMI (Table 3).

Meanwhile, to determine the factors that influenced the improvement in GNRI and CONUT score, the patients were divided into two groups based on the presence of improvement (Supporting Information S2: Tables S2 and S3). The increased GNRI group showed higher mPAP and PVR at baseline, lower PaO_2 values, and greater improvement following BPA therapy. In addition, this group showed significantly greater increases in BMI, total cholesterol, cholinesterase, and serum albumin values. Given that BMI and serum albumin are directly included in the GNRI formula, multivariate logistic analysis excluding these two variables was performed. The results showed that increased cholinesterase levels after BPA and PVR at baseline were significantly correlated with increased GNRI (Table 4).

The group with decreased CONUT scores and improved nutritional status had significantly greater increases in total cholesterol, cholinesterase, serum albumin levels, and lymphocyte counts. Multivariate logistic analysis showed that the increases in total cholesterol and lymphocyte counts were significantly correlated (Table 4).

DISCUSSION

The current study found that in patients with CTEPH, BPA treatment aimed at complete revascularization improved pulmonary hypertension and oxygenation capacity and also increased BMI. The results suggested that increased appetite may have contributed to the increase in BMI. In addition, improvements in some nutritional indicators were also observed. This sequence of events may contribute to improvements in patient prognosis. To the best of our knowledge, this is the first study to demonstrate increased BMI and improved nutritional status following BPA therapy in patients with CTEPH.

TABLE 1 Patient characteristics at baseline.

	All $N = 52$
Age, years	68 [57–73]
Height, cm	155.4 [149.7–163.1]
Body weight, kg	58.7 ± 11.9
BMI, kg/m^2	23.9 ± 3.7
Female sex, *n* (%)	37 (71.1)
WHO functional class II/III/IV, *n* (%)	32/24/5 (57.7/40.4/1.9)
Post-PEA, *n* (%)	0 (0)
Psychiatric disorder, *n* (%)	11 (21.2)
Hb, g/dL	13.3 ± 1.9
Lymphocyte count, /μL	1500 [1100–1825]
TP, g/dL	7.2 ± 0.5
Serum albumin, g/dL	4.0 ± 0.4
Cholinesterase, IU/L	283 ± 62
TC, mg/dL	188 ± 33
HbA1C, %	5.8 ± 0.6
BNP level, pg/dL	31.7 [17.9–145.3]
Cr, mg/dL	0.86 ± 0.31
eGFR, mL/min per 1.73 m^2	61.6 ± 16.8
GNRI	105.3 ± 10.2
PNI	48.0 ± 5.1
CONUT score	1.0 [0–2.0]
Respiratory function and exercise capacity	
VC, L	2.61 ± 0.86
%VC, %	82.3 ± 19.1
FEV1.0, L	1.94 ± 0.67
FEV1.0% Gaensler, %	77.4 [70.6–81.6]
PaO_2 with room air, mmHg	61.6 ± 9.3
Minimum SpO_2 during the 6MWD test, %	86 ± 6
6MWD, m	355 ± 126
Hemodynamics assessed with right heart catheterization	
Mean RAP, mmHg	5.0 ± 3.1
Systolic PAP, mmHg	65 ± 16.3
Diastolic PAP, mmHg	20.4 ± 6.4
Mean PAP, mmHg	37.4 ± 8.7
PAWP, mmHg	8.7 ± 2.9
Systolic NIBP, mmHg	131 ± 21
Diastolic NIBP, mmHg	77 ± 12
HR, bpm	72 ± 11
SvO_2 with room air, mmHg	60.5 ± 8.9
CO (thermodilution), L/min	5.12 ± 1.33
PVR (thermodilution), dyn s/cm^5	492 ± 259
Medication for PH, *n* (%)	24 (46.2)
ERA, *n* (%)	9 (17.3)
PDE5i, *n* (%)	5 (9.6)
Oral PGI2	5 (9.6)
sGC	16 (30.7)
Anticoagulants, *n* (%)	52 (100)
Oxygen therapy, *n* (%)	10 (19.2)

Note: Data are presented as the mean ± standard deviation, *n* (%), or median [interquartile range].

Abbreviations: 6MWD, 6-min walk distance; BMI, body mass index; BNP, brain natriuretic peptide; CO, cardiac output; CONUT, Controlling Nutritional Status; Cr, creatinine; eGFR, estimated glomerular filtration rate; ERA, endothelin receptor antagonist; FEV1.0, forced expiratory volume in 1 s; GNRI, Geriatric Nutritional Risk Index; HbA1C, glycated hemoglobin; Hb, hemoglobin; HR, heart rate; NIBP, noninvasive blood pressure; PaO_2, partial pressure of oxygen; PAP, pulmonary arterial pressure; PAWP, pulmonary arterial wedge pressure; PDE5i, phosphodiesterase-5 inhibitor; PEA, pulmonary endarterectomy; PGI2, prostaglandin I-2; PH, pulmonary hypertension; PNI, Prognostic Nutritional Index; PVR, pulmonary vascular resistance; RAP, right atrial pressure; sGC, soluble guanylate cyclase; SpO_2, oxygen saturation; SvO_2, mixed venous oxygen saturation; TC, total cholesterol; TP, total protein; VC, vital capacity; WHO, World Health Organization.

Association among BMI, appetite, hypoxia, and psychiatric disorders

The increase in BMI was not associated with baseline hemodynamics, but BMI was increased after BPA therapy in patients with CTEPH, regardless of severity of disease. This may be due to the influence of increased appetite.

Many studies found associations between appetite and hypoxia, with some reporting that exposure to hypoxia decreases appetite.[23,24] Hypoxia has been shown to affect various hormonal markers involved in the regulation of appetite, such as leptin, GLP-1, and ghrelin.[25] In the current study, appetite-related hormones were not measured. However, almost all patients showed improvement in hypoxia as assessed using resting arterial blood gases and minimum SpO_2 values during the 6MWD test. This improvement in hypoxia may have contributed to the increase in appetite. However, despite improvement in hypoxia, nine of the 52 patients had no improvement in appetite. Evaluation

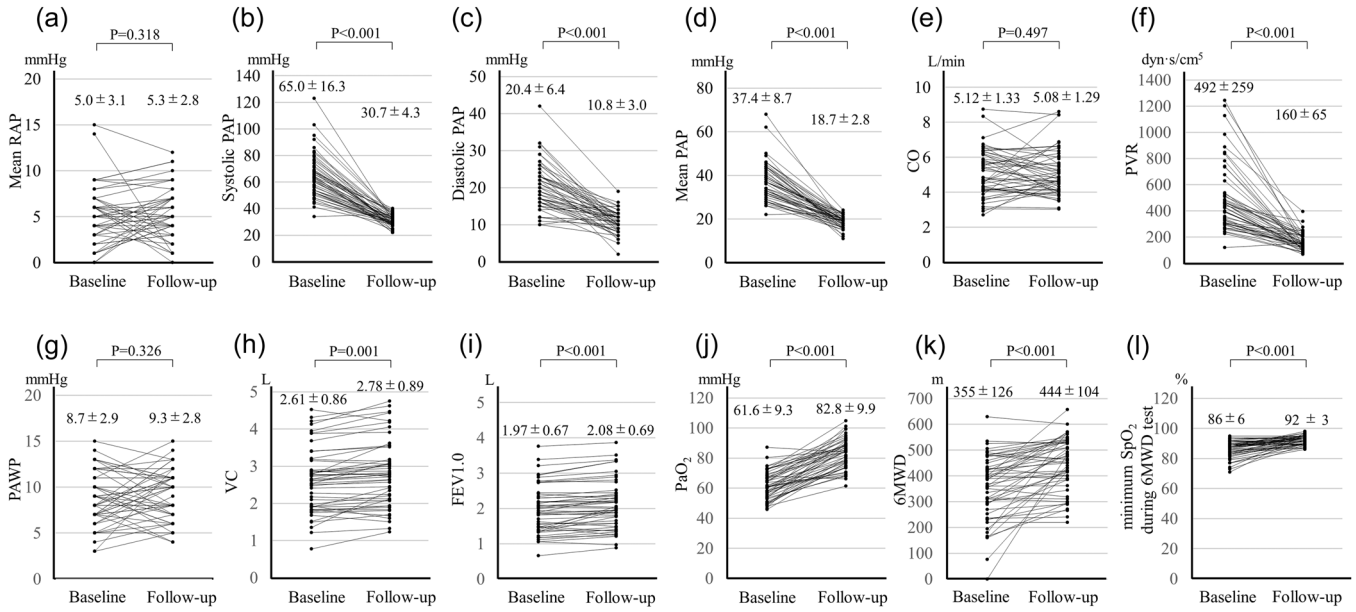

FIGURE 2 Changes in right heart catheterization parameters, respiratory function assessed by spirography, arterial blood gas analysis data, and 6-min walk distance. (a) Mean right arterial pressure (RAP). (b) Systolic pulmonary artery pressure (PAP). (c) Diastolic PAP. (d) Mean PAP. (e) Cardiac output (CO). (f) Pulmonary vascular resistance (PVR). (g) Pulmonary arterial wedge pressure (PAWP). (h) Vital capacity (VC). (i) Forced expiratory volume in 1 s (FEV1.0). (J) Partial pressure of oxygen (PaO_2). (k) 6-min walk distance (6MWD). (l) Minimum oxygen saturation (SpO_2) during the 6MWD test.

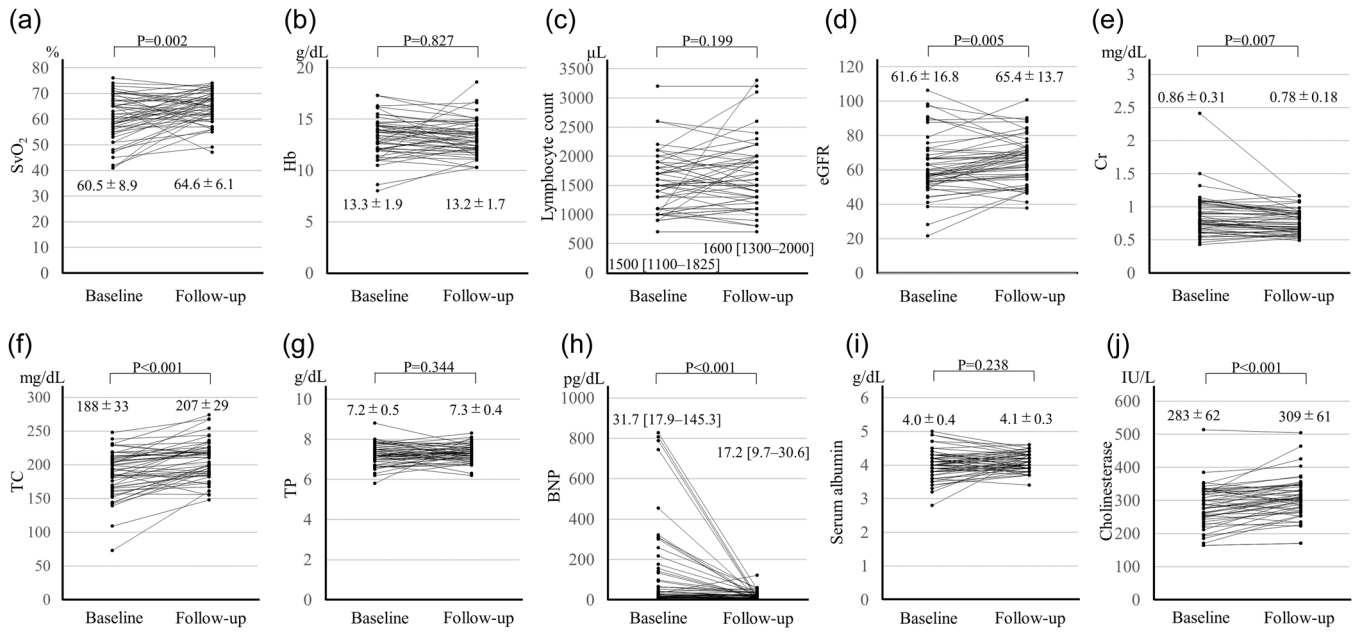

FIGURE 3 Changes in laboratory data and mixed venous blood gas analysis data. (a) Mixed venous oxygen saturation (SvO_2). (b) Hemoglobin (Hb) level. (c) Lymphocyte count. (d) Estimated glomerular filtration rate (eGFR). (e) Creatinine (Cr) level. (f) Total cholesterol (TC) level. (g) Total protein (TP) level. (h) Brain natriuretic peptide (BNP) level. (i) Serum albumin level. (j) Cholinesterase level.

of the characteristics of these nine patients revealed a significantly higher percentage of patients with psychiatric disorders (Supporting Information S3: Table S4).

Appetite is intricately regulated by neurohormonal mechanisms;[26,27] it is possible that neurotransmitter changes induced by the psychiatric illness itself or by medications for psychiatric diseases affect changes in BMI via appetite. CTEPH patients with a background of psychiatric disorders may differ in their profile from CTEPH patients without such diseases.

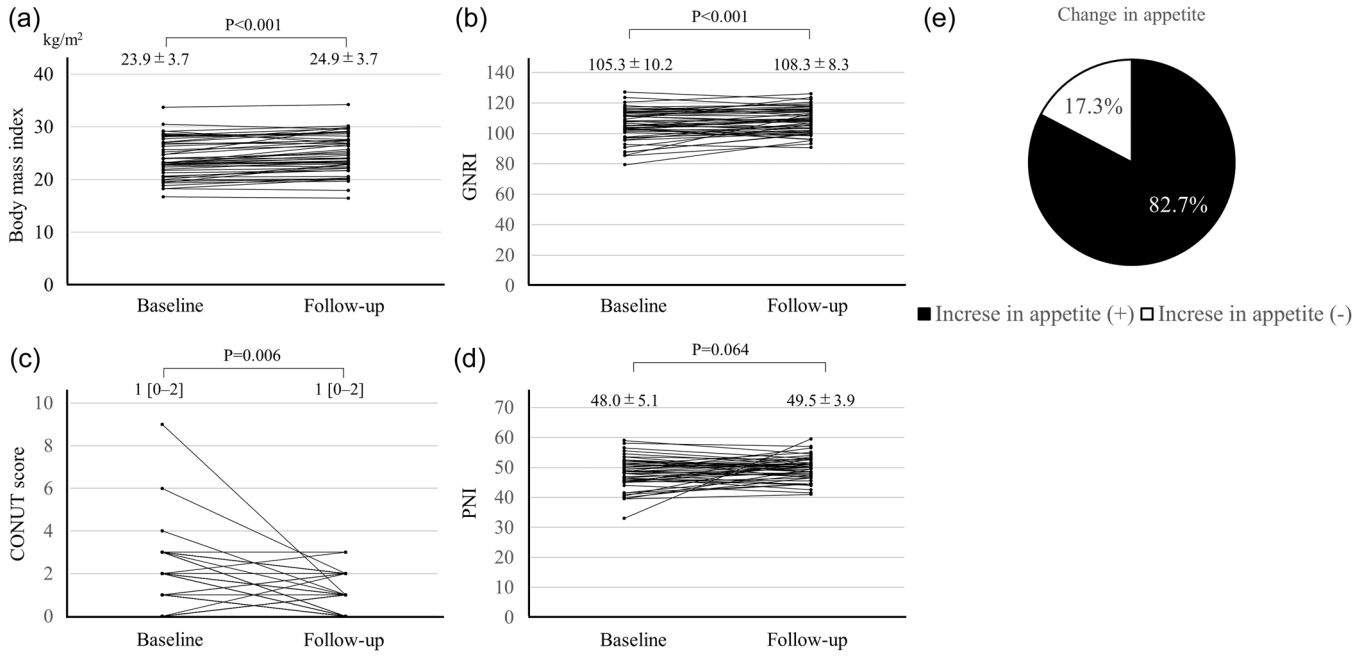

FIGURE 4 Changes in nutritional indexes, body mass index, and percentage of patients with increased appetite. (a) Body mass index. (b) Geriatric Nutritional Risk Index (GNRI). (c) Controlling Nutritional Status (CONUT) score. (d) Prognostic Nutritional Index (PNI). (e) Percentage of patients with increased appetite.

Nutritional indexe change in healthy nutritional status

Overall, PNI did not improve significantly, whereas the GNRI and CONUT scores were significantly improved. PNI is essentially a prognostic indicator in patients with cancer and thus may not have been an appropriate measure.[9] The GNRI includes BMI and serum albumin, and the CONUT score includes serum albumin, lymphocyte counts, and total cholesterol. Of these parameters, serum albumin and lymphocyte counts remained unchanged after BPA, whereas total cholesterol and body weight significantly changed. Thus, the improvement in nutritional status can mainly be attributed to an increase in total cholesterol levels and body weight.

This study evaluated CTEPH patients with a relatively moderate baseline mPAP of 37.4 ± 8.7 mmHg. Furthermore, the study was conducted in a group of patients with a baseline BMI of 23.9 ± 3.7 and GNRI of 105.3 ± 10.2 (GNRI > 92 is considered to be no nutritional risk[11]), which is a good nutritional status assessment. However, the study also found a significant improvement in GNRI, with a mean value of 108.3 ± 8.3 after BPA, despite good nutritional status at baseline. This finding may suggest that BPA in patients with CTEPH may lead to overnutrition and obesity.

Meanwhile, GNRI was improved in patients with more severe CTEPH. Therefore, BPA treatment may improve GNRI in patients with severe CTEPH and poor nutritional status. Further studies are needed to determine whether nutritional status improves in CTEPH patients with poor nutritional status before and after BPA.

In this study, 10 patients were excluded from the analysis because their cholesterol levels increased during repeated BPA sessions, and they were treated with statins before follow-up (Figure 1). The nutritional status with respect to lipids may have changed more significantly if these patients had not received statins and had not been excluded. In patients with CTEPH who improved following BPA, there may be concerns about the effects of hypercholesterolemia on atherosclerotic disease.

The clinical significance of this study is that BPA therapy in patients with CTEPH, regardless of severity, increased BMI and altered nutritional status, primarily total cholesterol levels. It was also suggested that increased appetite may be involved in the increased BMI. Depending on health status, obesity and hypercholesterolemia may be a concern during improvement with BPA therapy in CTEPH patients.

Limitations

This study has several limitations. First, selection bias may be present because a considerable number of patients were excluded. Those who received statins during the study period and were excluded from the analysis were excluded because statins were added early in the process of repeating

TABLE 2 Comparison of patient characteristics according to the presence or absence of an increase in BMI.

	No increase in BMI $N = 10$	Increase in BMI $N = 42$	p value
Age, years	67 [56 to 71]	68 [57 to 74]	0.754
Female sex, *n* (%)	8 (80.0)	29 (69.0)	0.396
Increase in appetite, *n* (%)	2 (10)	41 (97.6)	**<0.001**
Psychiatric disorder, *n* (%)	5 (60.0)	5 (11.9)	**0.003**
PaO_2 with room air at baseline, mmHg	56.4 ± 6.7	62.8 ± 9.5	**0.049**
Mean PAP at baseline, mmHg	38.2 ± 10.2	37.2 ± 8.3	0.74
PVR at baseline (thermodilution), dyn s/cm^5	515 ± 240	486 ± 262	0.755
Amount of improvement			
BMI increase, kg/m^2	−1.3 ± 1.5	3.2 ± 2.8	**<0.001**
TC increase, mg/dL	13.5 ± 40.0	20.2 ± 21.9	0.561
Cholinesterase increase, IU/L	20.5 ± 42.5	27 ± 37.2	0.231
Serum albumin increase, g/dL	0.2 ± 0.4	0.05 ± 0.4	0.634
Lymphocyte count increase, μL	150 [0 to 200]	100 [−200 to 375]	0.889
eGFR increase, mL/min per 1.73 m^2	−0.9 ± 11.9	4.9 ± 10.5	0.133
PNI increase	2.5 ± 4.3	1.2 ± 5.6	0.484
GNRI increase	2.2 ± 6.0	3.0 ± 6.9	0.679
CONUT score decrease	0 [−1 to 1]	0 [0 to 1]	0.423
VC increase, L	0.05 ± 0.31	0.27 ± 0.49	0.193
FEV1.0 increase, L	0.04 ± 0.15	0.17 ± 0.25	0.119
PaO_2 increase with room air, mmHg	24.1 ± 11.5	22.1 ± 13.7	0.670
SvO_2 increase with room air, mmHg	6.0 ± 8.9	5.1 ± 13.0	0.834
6MWD increase, m	145 ± 105	76 ± 112	0.080
Increase in minimum SpO_2 during the 6MWD test, %	5.0 ± 4.1	8.2 ± 14.1	0.485
Mean RAP decrease, mmHg	0.4 ± 2.9	−0.7 ± 3.8	0.437
Systolic PAP decrease, mmHg	33.8 ± 15.8	34.5 ± 16.2	0.907
Diastolic PAP decrease, mmHg	11.7 ± 7.1	9.1 ± 6.4	0.273
Mean PAP decrease, mmHg	19.6 ± 8.7	18.5 ± 9.0	0.715
PVR decrease (thermodilution), dyn s/cm^5	330 ± 191	333 ± 261	0.981
PH medication at follow-up			
Any PH medication, *n* (%)	1 (10)	1 (2.4)	0.351
ERA	0	0	—
PDE5i	0	0	—
Oral PGI2	0	0	—
sGC	1 (10)	1 (2.4)	0.325
Oxygen therapy	0	1 (2.4)	0.767

Note: Data are presented as the mean ± standard deviation, *n* (%), or median [interquartile range]. Bold numbers highlight a significant difference at $p < 0.05$.

Abbreviations: 6MWD, 6-min walk distance; BMI, Body mass index; CONUT, Controlling Nutritional Status; eGFR, estimated glomerular filtration rate; ERA, endothelin receptor antagonist; FEV1.0, forced expiratory volume in 1 s; GNRI, Geriatric Nutritional Risk Index; PaO_2, partial pressure of oxygen; PAP, pulmonary arterial pressure; PDE5i, phosphodiesterase-5 inhibitor; PGI2, prostaglandin I-2; PH, pulmonary hypertension; PNI, Prognostic Nutritional Index; PVR, pulmonary vascular resistance; RAP, right atrial pressure; sGC, soluble guanylate cyclase; SpO_2, oxygen saturation; SvO_2, mixed venous oxygen saturation; TC, total cholesterol; VC, vital capacity.

TABLE 3 Statistical analysis of variables correlated with an increase in BMI.

	Odds ratio	95% CI	*p* value
Increase in appetite	160.0	12.9–1983.8	**<0.001**
PaO_2 with room air at baseline	—	—	0.121
Psychiatric disorder	—	—	0.464

Note: Bold numbers highlight a significant difference at $p < 0.05$.

Abbreviations: CI, confidence interval; PaO2, partial pressure of oxygen.

TABLE 4 Statistical analysis of variables correlated with nutritional status.

	Odds ratio	95% CI	*p* value
GNRI improvement (increase)			
Cholinesterase increase	1.037	1.011–1.065	**0.006**
PVR at baseline	1.007	1.001–1.013	**0.028**
Mean PAP at baseline	—	—	0.076
PaO_2 with room air at baseline	—	—	0.101
TC increase	—	—	0.072
Lymphocyte increase	—	—	0.588
CONUT score improvement (decrease)			
TC increase	1.055	1.012–1.100	**0.012**
Lymphocyte count increase	1.003	1.000–1.005	**0.02**
Serum albumin increase	10.039	0.884–114.041	0.063

Note: Bold numbers highlight a significant difference at $p < 0.05$.

Abbreviations: CONUT, Controlling Nutritional Status; GNRI, Geriatric Nutritional Risk Index; PaO_2, partial pressure of oxygen; PAP, pulmonary arterial pressure; PVR, pulmonary vascular resistance; TC, total cholesterol.

BPA and pulmonary hypertension had not yet sufficiently improved. Second, the assessment of appetite enhancement in this study was based on the patients' subjective responses to a questionnaire and not on objective scores. Therefore, objectivity is not ensured in the evaluation of appetite. Third, nutritional status was assessed based only on certain nutritional indexes, which may have biased the assessment. It is also unclear whether nutritional indices improve in CTEPH patients with severe nutritional disorders. Fourth, this study did not consider the unwanted effects of drugs, including those for pulmonary hypertension and psychiatric disorders. Thus, the possibility of drug-induced effects on appetite and nutritional status could not be ruled out. Fifth, some patients had untreated type D lesions, which were not evaluated. Therefore, this study is not an evaluation of patients with equally complete revascularization. Last, because the outcomes of BPA without complete revascularization have not been evaluated, this study only provided an evaluation of CTEPH patients under one BPA strategy.

In conclusion, CTEPH patients who achieved complete revascularization after BPA therapy had improved pulmonary hypertension, oxygenation capacity, and increased BMI regardless of disease severity. Increased appetite may have contributed to the increased BMI. In addition, improvements in nutritional status, primarily increased cholesterol levels, were observed. This sequence of changes may contribute to improved patient prognosis.

AUTHOR CONTRIBUTIONS

Shinya Fujii planned the study, analyzed the data, and wrote the manuscript. Shinya Nagayoshi performed BPA and interpreted the results. Takashi Miyamoto planned and reviewed this project. Kazuo Ogawa analyzed the data and interpreted the results. Michihiro Yoshimura interpreted the results and reviewed, revised, and approved the manuscript for submission.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

ETHICS STATEMENT

This study was approved by the Ethics Committee of the Saitama Cardiovascular and Respiratory Center (approval number 2023026) and was conducted in accordance with the Declaration of Helsinki. All study participants were provided with information regarding the opt-out option.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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