Original paper

Refined balloon pulmonary angioplasty in chronic thromboembolic pulmonary hypertension – reference center experience

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Abstract

Introduction: Chronic thromboembolic pulmonary hypertension (CTEPH), characterized by thromboembolic changes affecting the pulmonary bed, leads to ventricular function deterioration and premature death. The introduction of balloon pulmonary angioplasty (BPA) has significantly improved the prognosis of CTEPH patients.

Aim: The authors of this article decided to summarize the experience of the BPA program, conducted between 2014 and 2022, at the reference center.

Material and methods: Among 111 CTEPH patients, 55 were included in the analysis. A total of 226 sessions were performed, with a significant percentage of intravascular imaging and pressure catheter use.

Results: Mean pulmonary pressure decreased significantly from 42 (22–66) to 26.5 mm Hg (11–54) ($p < 0.05$). Pulmonary vascular resistance and natriuretic peptide concentration decreased from 6.67 (1.66–14) to 3.295 Wood units (1.09–11.11), respectively, and from 1934 (60–16963) to 296 (21–9901) ng/ml ($p < 0.05$). There was also an improvement in the functional class (WHO) from 2.85 ±0.61 to 2.15 ±0.62 and an increase in the 6-minute walking distance from 300 ±131 to 367 ±154 m ($p < 0.05$). There were no in-hospital deaths or within 30 days of the procedure. Arterial damage occurred during nine sessions ($n = 9/226$, 4%), while 0.9% ($n = 2/226$) were complicated by acute right ventricular failure. Post-reperfusion pulmonary edema (RPE 0 – none) was observed in almost 90% of the sessions, grade 1 to 3 RPE occurred in 10.2%, and grade 4 RPE was not noted.

Conclusions: BPA programs conducted in experienced centers are a safe and effective treatment option for inoperable CTEPH patients.

Key words: percutaneous, chronic thromboembolic pulmonary hypertension, balloon pulmonary angioplasty.

Summary

The introduction of balloon pulmonary angioplasty (BPA) has significantly improved the prognosis of inoperable chronic thromboembolic pulmonary hypertension (CTEPH) patients. 55 CTEPH patients were included in BPA program in or center. Mean pulmonary pressure reduced significantly from 42 (22–66) to 26.5 mm Hg (11–54) ($p < 0.05$). Similarly, pulmonary vascular resistance and natriuretic peptide concentration decreased from 6.67 (1.66–14) to 3.295 Wood units (1.09–11.11), respectively, and from 1934 (60–16963) to 296 (21–9901) ng/ml ($p < 0.05$). There was also an improvement in the World Health Organization functional class from 2.85 ±0.61 to 2.15 ±0.62 and an increase in the 6-minute walking distance from 300 ±131 to 367 ±154 m ($p < 0.05$). There were no in-hospital deaths or deaths within 30 days of the procedure and very small rate of periprocedural complications. BPA programs conducted in experienced centers are a safe and effective treatment option for CTEPH patients who are inoperable or at high risk of surgery-related complications.

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Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is characterized by chronic thromboembolic changes that involve the pulmonary arterial bed to varying degrees, leading to deterioration of proper ventricular function and premature death. Balloon pulmonary angioplasty (BPA) in patients with CTEPH is a dynamically developing form of therapy in the absence of indications for pulmonary endarterectomy (PEA). The essence of this procedure is the percutaneous insertion of a balloon catheter into the pulmonary artery and inflation of the fibrotic remnant of the thrombus, which improves perfusion, reduces vascular resistance and pressure in the vessel, and improves the prognosis. After the first reports from 1988 and initial unsatisfactory results, the method has been improved in recent decades and has consolidated its position in treating CTEPH patients [1–11].

Aim

The authors of this article decided to summarize their experience from the BPA program conducted since 2014 at a reference center.

Material and methods

Among 111 consecutive patients diagnosed with CTEPH under the care of our center, those who qualified for the BPA program from 2014 to 2022 were analyzed. The diagnosis of CTEPH was made according to the recommendations of the European Society of Cardiology (ESC) [9]. Based on clinical assessment, medical interviews, and imaging tests (computed tomography pulmonary angiography and ventilation-perfusion scintigraphy of the lungs), patients were referred for right heart catheterization (RHC) with simultaneous angiography of the pulmonary arteries. After confirming pulmonary hypertension and the presence of thromboembolic changes in the pulmonary arterial bed, patients were evaluated at an experienced cardiac surgery center. If they were not found eligible for PEA, they were included in the BPA program [7–9]. The treatments were performed using the protocol developed at the center. Our algorithm incorporated anatomical (angiography and intravascular ultrasound) and functional assessment of targeted lesions. This evaluation and baseline mean pulmonary arterial pressure (mPAP) allowed careful balloon catheter selection, with adequate reduction of the balloon diameter [7].

The safety and effectiveness of the treatments were substantially assessed, with the presence of comorbidities, World Health Organization functional class (WHO-FC), distance covered in the 6-minute walk test (6MWT), hemodynamic parameters, and natriuretic peptide concentration analyzed. The number of BPA sessions performed, the use of additional imaging methods and pressure catheters, the volume of contrast medium, and the dose of ionizing radiation were considered. The assessment of complications included periprocedural deaths, in-hospital deaths, and complications related to the BPA procedure itself. According to the ESC clinical consensus, procedural complications were divided into BPA-related (such as vascular injury or/and lung injury) and non-BPA-specific complications [8].

The goal of the therapy was to reduce the mPAP to normal values or below 30 mm Hg in cases with anatomically challenging lesions and clinical pictures. December 31, 2022, was assumed as the final reference point for the analyzed group. The local bioethics committee approved the implementation of the BPA program in the center (KB 163/2014), and all patients were informed about the risks and benefits of BPA and signed informed consent forms. Some patients were also treated with dedicated (targeted) pulmonary hypertension pharmacotherapy, according to the inclusion and reimbursement criteria of the National Health Fund.

Statistical analysis

Categorical variables are described as median with minimal and maximal value. For comparisons, variables with a normal distribution are given as means with standard deviation and analyzed using Student's *t*-test. The Mann-Whitney *U* test analyzed qualitative or non-normally distributed variables. Statistical analysis employed the Statistica program (TIBCO Software Inc., CA, USA), with statistical significance defined as $p < 0.05$.

Results

The BPA program included 55 patients, with the clinical characteristics of the study group shown in Table I. A total of 588 angioplasties were performed over 226 sessions, with a significant percentage using intravascular ultrasound (IVUS) (94%, $n = 213$), optical coherence

Table I. Clinical characteristics of analyzed group

Parameter	*n* (%) or mean ± SD
Number of patients	55 (100)
Age [years]	67.5 ±13.2
Female	27 (49)
Post APE	50 (90.9)
DVT	26 (47.3)
CAD	13 (23.6)
HT	40 (72.7)
CKD	19 (34.5)
DM	17 (30.9)
Thrombophilia	5 (9.09)
Post PEA	6 (10.9)
Riociguat	24 (43.6)

APE – acute pulmonary embolism, DVT – deep vein thrombosis, CAD – coronary artery disease, HT – hypertension, CKD – chronic kidney disease, DM – diabetes mellitus, PEA – pulmonary endarterectomy.

Table II. Procedural summary

Variable	*N* (%), median (range)
Sessions/dilated segmental arteries	226/588
Sessions per patient	3 (1–12)
Dilated segmental arteries per session	2.5 (1–7)
Contrast volume per session [ml]	230 (100–500)
Balloon size during procedure [mm]	2–8
Kerma [mGy]	542.5 (63–3483)
Access site jugular/femoral	181 (80.1)/45 (19.9)
IVUS/OCT during session	213 (94)/19 (8)
Pressure catheter/pulmonary pressure ratio assessment during session	158 (69)

IVUS – intravascular ultrasound, OCT – optical coherence tomography, Kerma – kinetic energy per unit mass, mGy – milligray.

tomography (OCT) (8%, *n* = 19), and a pressure catheter (69%, *n* = 158). The predominant vascular access was via the right internal jugular vein (Table II).

There were no periprocedural deaths, in-hospital deaths, or deaths within 30 days of the procedure. Vascular injury (VI) occurred in nine (4%) sessions during the procedure. The percentage of sessions complicated by acute right ventricular failure requiring extracorporeal membrane oxygenation (ECMO) or the need for renal replacement therapy was < 1%. In just over 10% of the sessions, significant pulmonary complications (pulmonary injury [PI]) in the form of post-reperfusion pulmonary edema (RPE) were recorded. PI manifesting as significant hemoptysis, not requiring invasive ventilation, occurred in 2.65% of the sessions (Table III).

During the analyzed period (2014–2022), 32 patients from the program remained alive with completed treatment, and 19 patients died. Only 5 patients died due to right ventricle failure (Table IV). Data regarding median follow-up time and BPA procedures per year are presented in Table V. Compared to the initial assessment, the WHO-FC improved, and the distance covered in the 6MWT increased. A reduction in mPAP and pulmonary vascular resistance (PVR) was noted among the hemodynamic parameters, with an increase in the cardiac index

Table IV. Balloon pulmonary angioplasty program status: long-term follow-up period (2014–2022)

Parameter	*N* (%)
Alive	36 (65.5)
Death in follow-up period	19 (34)
Causes of death:	
COVID-19	5
Influenza	1
Stroke	1
Right ventricle failure	5
Cancer/leukemia	3
Accident/trauma	2
Sepsis/shock/multi-organ failure	2

Table III. Complications

Variable	*N* (%)
Periprocedural/in-hospital death	0
Death in 30 days	0
BPA-related complications:	
Vascular injury	9 (4)
BPA non-specific complications:	
ECMO/acute right ventricle failure	1/1 (0.9)
Hemodialysis	2 (0.9)
RPE:	
Grade 0 – none	203 (89.8)
Grade 1 present	7 (7.5)
Grade 2 NIV/NHFC	4 (1.8)
Grade 3 ventilation/ECMO	2 (0.9)
Grade 4 death	0
Prolonged hemoptysis	6 (2.65)

BPA – balloon pulmonary angioplasty, ECMO – extracorporeal membrane oxygenator, RPE – reperfusion pulmonary edema, NIV – noninvasive ventilation, NHFC – nasal high-flow cannula.

(CI). Moreover, a decrease in pro-B-type natriuretic peptide (pro-BNP) concentration was found (Table VI).

Discussion

The experiences and data presented are consistent with previously published reports [7, 11–17]. In our opinion, the lack of periprocedural and 30-day deaths is related to the systemic approach and implementation of the BPA program protocol adopted in a given center. The jugular vein access site provides instant mobility after the procedure and allows more effective handling of access site complications. Low complication rates may also be due to the widespread use of IVUS and the pressure catheter. IVUS allows careful selection and appropriate balloon size reduction, especially in patients with high mPAP values. Additional pressure gradient assessment

Table V. Additional data regarding follow-up, procedures per year

Parameter	*N* or median (range)
Follow-up [months]	65 (8–126)
Patients in BPA program with mPAP ≤ 20 mm Hg after treatment	12
Patients in BPA program with mPAP ≤ 30 mm Hg after treatment	26
BPA procedures per year:	
2014	6
2015	32
2016	39
2017	59
2018	36
2019	16
2020–2021 (COVID-19)	8 (5 + 3)
2022	30

Table VI. Hemodynamic and clinical efficacy

Selected hemodynamic and clinical parameters	Baseline	BPA (at end of analyzed period)	*P*-value
mPAP [mm Hg]	42 (22–66)	26.5 (11–54)	< 0.05
Pro-BNP [ng/ml]	1934 (60–16963)	296 (21–9901)	< 0.05
PVR [Wood units]	6.67 (1.66–14)	3.295 (1.09–11.11)	< 0.05
6MWT [m]	300 ±131	367 ±154	< 0.05
CI [l/min/m^2]	2.59 ±0.5	2.9 ±0.6	< 0.05
WHO-FC (mean)	2.85 ±0.61	2.15 ±0.62	< 0.05

mPAP – mean pulmonary artery pressure, Pro-BNP – pro-B-type natriuretic peptide, PVR – pulmonary vascular resistance, 6MWT – 6-minute walk test, CI – cardiac index, WHO-FC – World Health Organization functional class.

decreases aggressive (angiography based) dilatations and eventually results in no RPE or low rates. The potential cost of using additional tools seems to be lower than the costs of treating complications. These methods provide excellent support to BPA operators, with comparable X-ray exposure and contrast agent consumption to those reported in other BPA registries [7, 11–17].

The optimal goal of therapy should be the normalization of mPAP, preferably confirmed by normal perfusion in lung scintigraphy. Considering comorbidities and technical and anatomical possibilities, the clinical picture modifies this goal. According to published data, the European population of CTEPH patients is older than the Japanese registries [16, 17]. Thus, in many cases, the effectiveness of BPA is defined by clinical improvement (WHO-FC and 6MWT). According to the authors, the satisfactory reduction of mPAP demonstrated in the study group is also due to the routine use of IVUS and a pressure catheter, which allow for more precise selection and adequate escalation of the size of balloon catheters during each BPA session.

The number of periprocedural complications in the study group does not differ from those found in European and American reports [10, 13, 14, 18–22], with the procedure methodology and many years of experience documented in Japanese publications significantly contributing to reducing the number of deaths [5, 16, 17, 23]. The available publications present various approaches to using additional endovascular techniques for BPA, but in the studied single-center group, this translated into treatment effectiveness and safety [11–17].

The main study limitation was its single-center nature and the small group of patients. Additionally, chest CT was not routinely performed after each BPA session and only in reported cases of significant, prolonged hemoptysis and/or decreased percutaneous oxygen saturation. In the light of published randomized studies comparing BPA to riociguat therapy that show the advantage of BPA in improving hemodynamic parameters in experienced centers, and due to the size of the group, the riociguat-treated subgroup was not analyzed in detail [24, 25]. The riociguat drug program has been available in our center since 2016, which resulted in a correspondingly smaller number of patients (n = 24). In our group the median mPAP in patients without riociguat was lower (21 mm Hg; 11–47) than on the medication (32 mm Hg; 17–54). Despite this statistically significant difference, riociguat is a useful option in patients with anatomical and technical challenges during BPA.

Conclusions

The BPA program conducted in experienced referral centers is a safe and effective therapeutic option for inoperable CTEPH patients. Using intravascular imaging methods and a pressure catheter during BPA procedures is a precious support for operators. The study group achieved statistically significant clinical and hemodynamic improvement, with a favorable periprocedural risk profile.

Conflict of interest

The authors declare no conflict of interest.

References

1. Voorburg JA, Cats VM, Buis B, et al. Balloon angioplasty in the treatment of pulmonary hypertension caused by pulmonary embolism. Chest 1988; 94: 1249-53.
2. Feinstein JA, Goldhaber SZ, Lock JE, et al. Balloon pulmonary angioplasty for treatment of chronic thromboembolic pulmonary hypertension. Circulation 2001; 103: 10-3.
3. Mizoguchi H, Ogawa A, Munemasa M, et al. Refined balloon pulmonary angioplasty for inoperable patients with chronic thromboembolic pulmonary hypertension. Circ Cardiovasc Interv 2012; 5: 748-55.
4. Kataoka M, Inami T, Hayashida K, et al. Percutaneous transluminal pulmonary angioplasty for the treatment of chronic thromboembolic pulmonary hypertension. Circ Cardiovasc Interv 2012; 5: 756-62.
5. Taniguchi Y, Miyagawa K, Nakayama K, et al. Balloon pulmonary angioplasty: an additional treatment option to improve the prognosis of patients with chronic thromboembolic pulmonary hypertension. Eurointervention 2014; 10: 518-25.
6. Andreassen AK, Ragnarsson A, Gude E, et al. Balloon pulmonary angioplasty in patients with inoperable chronic thromboembolic pulmonary hypertension. Heart 2013; 99: 1415-20.
7. Roik M, Wretowski D, Labyk A, et al. Refined balloon pulmonary angioplasty driven by combined assessment of intra-arterial anatomy and physiology--Multimodal approach to treated le-

sions in patients with non-operable distal chronic thromboembolic pulmonary hypertension--Technique, safety and efficacy of 50 consecutive angioplasties. Int J Cardiol 2016; 203: 228-35.
8. Lang IM, Andreassen AK, Andersen A, et al. Balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension: a clinical consensus statement of the ESC working group on pulmonary circulation and right ventricular function. Eur Heart J 2023; 44: 2659-71.
9. Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Respir J 2023; 61: 2200879.
10. Sepúlveda P, Hameau R, Backhouse C, et al. Mid-term follow-up of balloon pulmonary angioplasty for inoperable chronic thromboembolic pulmonary hypertension: an experience in Latin America. Catheter Cardiovasc Interv 2021; 97: E748-57.
11. Darocha S, Roik M, Kopeć G, et al. Balloon pulmonary angioplasty in chronic thromboembolic pulmonary hypertension: a multicentre registry. Eurointervention 2022; 17: 1104-11.
12. Wiedenroth CB, Liebetrau C, Breithecker A, et al. Combined pulmonary endarterectomy and balloon pulmonary angioplasty in patients with chronic thromboembolic pulmonary hypertension. J Heart Lung Transplant 2016; 35: 591-6.
13. Araszkiewicz A, Darocha S, Pietrasik A, et al. Balloon pulmonary angioplasty for the treatment of residual or recurrent pulmonary hypertension after pulmonary endarterectomy. Int J Cardiol 2019; 278: 232-7.
14. Olsson KM, Wiedenroth CB, Kamp JC, et al. Balloon pulmonary angioplasty for inoperable patients with chronic thromboembolic pulmonary hypertension: the initial German experience. Eur Respir J 2017; 49: 1602409.
15. Brenot P, Jais X, Taniguchi Y, et al. French experience of balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension. Eur Respir J 2019; 53: 1802095.
16. Ogawa A, Satoh T, Fukuda T, et al. Balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension: results of a multicenter registry. Circ Cardiovasc Qual Outcomes 2017; 10: e004029.
17. Chausheva S, Naito A, Ogawa A, et al. Chronic thromboembolic pulmonary hypertension in Austria and Japan. J Thorac Cardiovasc Surg 2019; 158: 604-14e2.
18. Lang IM, Matsubara H. Balloon pulmonary angioplasty for the treatment of chronic thromboembolic pulmonary hypertension: is Europe behind? Eur Respir J 2019; 53: 1900843.
19. Roik M, Wretowski D, Kostrubiec M, et al. High prevalence of severe coronary artery disease in elderly patients with non-operable chronic thromboembolic pulmonary hypertension referred for balloon pulmonary angioplasty. Adv Interv Cardiol 2016; 12: 355-9.
20. Roik M, Wretowski D, Labyk A, et al. Refined balloon pulmonary angioplasty-a therapeutic option in very elderly patients with chronic thromboembolic pulmonary hypertension. J Interv Cardiol 2017; 30: 249-55.
21. Łabyk A, Wretowski D, Potępa M, et al. Refined balloon pulmonary angioplasty as the first-line therapy of complex thromboembolic lesions in patients with chronic thromboembolic pulmonary hypertension. Pol Arch Intern Med 2020; 130: 805-6.
22. Bashir R, Noory A, Oliveros E, et al. Refined balloon pulmonary angioplasty in chronic thromboembolic pulmonary hypertension: initial results of U.S. Regional Program. JACC Adv 2023; 2: 100291.
23. Poch DS, Mahmud E, Patel M, et al. Patient selection for balloon pulmonary angioplasty: six-year results from a high volume PTE surgical center. Pulm Circ 2022; 12: e12148.
24. Kawakami T, Matsubara H, Shinke T, et al. Balloon pulmonary angioplasty versus riociguat in inoperable chronic thromboembolic pulmonary hypertension (MR BPA): an open-label, randomised controlled trial. Lancet Respir Med 2022; 10: 949-60.
25. Jaïs X, Brenot P, Bouvaist H, et al. Balloon pulmonary angioplasty versus riociguat for the treatment of inoperable chronic thromboembolic pulmonary hypertension (RACE): a multicentre, phase 3, open-label, randomised controlled trial and ancillary follow-up study. Lancet Respir Med 2022; 10: 961-71.