EVIDENCE OF AN EXCELLENT INTERNATIONAL COOPERATION IN THE MANAGEMENT OF CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

Dôkaz výbornej medzinárodnej spolupráce v liečbe chronickej tromboembolickej pľúcnej hypertenzie

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Abstract
Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare disease requiring centralized management in specialized centres. Balloon pulmonary angioplasty (BPA) is a treatment option for patients ineligible for pulmonary endarterectomy (PEA) or with residual pulmonary hypertension after PEA. Smaller countries collaborate with larger expert centres to ensure comprehensive care.
Methods: This retrospective study assessed international collaboration in CTEPH interventional treatment based on data from 43 BPA procedures performed on 13 patients.
Results: Significant improvements were observed between baseline and post-BPA parameters. WHO functional class improved from 23% to 77% in class I/II ($p = 0.019$), and the 6-minute walk distance increased by 191 meters ($p = 0.009$). Mean pulmonary artery pressure decreased by 27.9% ($p < 0.001$), and pulmonary vascular resistance was reduced by 35.3% ($p = 0.025$). Echocardiographic follow-ups demonstrated enhanced right ventricular function, alongside a reduction in the tricuspid regurgitation gradient by an average of 31 mmHg (40.2%; $p < 0.001$).
A total of 4 non-fatal complications (9.3% of procedures) were observed, with no fatal complications reported.
Conclusion: This study confirmed significant clinical and hemodynamic improvements following BPA, with outcomes comparable to those achieved in large expert centres. The rate of procedure-related complications was acceptable, highlighting the potential for successful international collaboration in CTEPH management *(Tab. 2, Fig. 2, Ref. 18). Text in PDF www.lekarsky.herba.sk.*
KEY WORDS: chronic tromboembolic pulmonary hypertension, pulmonary hypertension, balloon pulmonary angioplasty, expert centres, international cooperation.
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Abstrakt
Úvod: Chronická tromboembolická pľúcna hypertenzia (CTEPH) je zriedkavé ochorenie, ktoré si vyžaduje centralizovanú starostlivosť v špecializovaných centrách. Balóniková angioplastika pľúcnice (BPA) je liečebnou modalitou pre pacientov nevhodných na pľúcnu endarterektómiu (PEA) alebo s reziduálnou pľúcnou hypertenziou po PEA. Menšie krajiny nadväzujú spoluprácu s väčšími expertnými centrami, aby bola pre pacientov zabezpečená komplexná zdravotná starostlivosť.
Metódy: Retrospektívna štúdia hodnotila medzinárodnú spoluprácu v intervenčnej liečbe CTEPH na základe dát zo 43 BPA výkonov realizovaných u 13 pacientov.
Výsledky: Medzi východiskovými dátami a parametrami po BPA bolo zaznamenané významné zlepšenie vo viacerých parametroch. Funkčná trieda sa zlepšila do triedy WHO I/II z 23 na 77 % pacientov ($p = 0,019$) a vzdialenosť prejdená pri 6-minútovom teste chôdze sa zvýšila o 191 metrov ($p = 0,009$). Stredný tlak v pľúcnici sa znížil o 27,9 % ($p < 0,001$) a pľúcna cievna rezistencia poklesla o 35,3 % ($p = 0,025$). Echokardiografické sledovanie preukázalo zlepšenie funkcie pravej komory spolu so znížením regurgitačného gradientu na trikuspidálnej chlopni v priemere o 31 mmHg (40,2 %; $p < 0,001$).
Celkovo boli zaznamenané 4 nefatálne komplikácie (9,3 % výkonov) a žiadne fatálne komplikácie.
Záver: Táto štúdia potvrdila významné klinické a hemodynamické zlepšenie u pacientov po BPA s výsledkami porovnateľnými s veľkými expertnými centrami. Miera komplikácií súvisiacich s procedúrou bola prijateľná, čo poukazuje na potenciál úspešnej medzinárodnej spolupráce v multimodalitnom manažmente CTEPH *(tab. 2, obr. 2, lit. 18). Text v PDF www.lekarsky.herba.sk.*
KĽÚČOVÉ SLOVÁ: chronická tromboembolická pľúcna hypertenzia, pľúcna hypertenzia, balóniková angioplastika pľúcnice, pľúcna angioplastika, expertné centrá, medzinárodná spolupráca.
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Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is a pre-capillary pulmonary hypertension, classified as Group IV pulmonary hypertension according to the recent European Society of Cardiology/European Respiratory Society (ESC/ERS) guidelines, leading to right heart failure and premature death if left untreated. It is a chronic complication of acute pulmonary embolism caused by the formation of persistent thrombotic residues in the pulmonary vasculature, vascular remodelling, and endothelial dysfunction (1). Surgical pulmonary endarterectomy (PEA) is the standard treatment for 50–70% of CTEPH patients, offering the best outcomes for operable cases (2). However, some technically operable patients either cannot undergo surgery due to high risk or refusal and have a significantly worse prognosis compared to those after PEA. Approximately 25% of patients after PEA have residual pulmonary hypertension (PH), which is associated with persistent symptoms of CTEPH and a worse prognosis (3). In patients with developed peripheral vascular remodelling, pharmacological treatment with therapy for pulmonary arterial hypertension is successful. The currently approved drugs are riociguat, a soluble guanylate cyclase stimulator, and treprostinil, a subcutaneously administered prostaglandin analogue, though other pulmonary arterial hypertension (PAH) treatments are used off-label (4).

Balloon pulmonary angioplasty (BPA) has emerged as an alternative for patients unsuitable for PEA, particularly for those with peripheral vascular lesions. BPA involves endovascular dilatation of pulmonary vessels over multiple sessions and is performed in specialized centres capable of managing possible complications. The use of BPA in a cohort of 18 inoperable CTEPH patients was first published in 2001 (5). Initially, BPA showed modest success with a high rate of complications. However, advancements, particularly from Japanese centres, significantly improved outcomes and reduced risks (6,7). Currently since 2015 BPA is well adopted in the CTEPH centres in Europe, incorporating techniques refined in Japan.

In Slovakia, the comprehensive management of patients with CTEPH is provided at the Department of Cardiology and Angiology of Slovak Medical University and the National Institute of Cardiovascular Disease with tradition over 25 years. Since 2017 the only one national expert center for CTEPH was officially established, given the policy that the management of CTEPH as a rare disease should be centralized. Our centre is from 2000 operating in close collaboration with high volume centres abroad – with the Centre for Pulmonary Hypertension at the General University Hospital in Prague, Czech Republic and with University Hospital Vienna in the past. BPA was incorporated into the therapeutic algorithm for CTEPH in Slovakia as a standard treatment modality in 2017.

Materials and methods

This retrospective observational study aimed to assess international collaboration in the interventional management of CTEPH at our national expert centre in conjunction with neighbouring foreign expert centres providing comprehensive multimodality treatment. These centres meet the ESC/ERS criteria for designated CTEPH expert centres performing BPA, defined as managing >30 patients per year or conducting >100 procedures annually (4). Due to the small population size and the rarity of this disease, the Slovak national CTEPH centre is unable to meet these criteria.

The analysis included data from 43 BPA procedures performed on 13 patients with CTEPH who underwent at least one BPA session. The study evaluated the efficacy and safety of BPA as a therapeutic intervention.

The diagnosis of CTEPH was based on clinical evaluation, hemodynamic parameters, and imaging studies in accordance with ESC/ERS guidelines (4). The management approach for CTEPH - whether surgery, pharmacotherapy, BPA, or a combination of these modalities - was determined by a multidisciplinary team comprising a PEA surgeon, a PH specialist, a cardioanesthesiologist, and an interventional cardiologist skilled in BPA. BPA was indicated for patients with inoperable CTEPH due to peripheral vascular involvement, persistent PH following PEA, or contraindications to surgery owing to significant comorbidities. Target lesion selection for BPA was guided by the angiographic classification system established by Kawakami et al., which includes ring stenosis, web lesions, subtotal lesions, total occlusions, and tortuous lesions (8).

Patient characteristics included demographic data (age, sex), body mass index (BMI), body surface area (BSA), clinical profiles (comorbidities, CTEPH risk factors), and procedure-related details (number of vessels treated, complications such as haemoptysis, access site vascular complications, or life-threatening bleeding) (3). Pre- and post-procedure non-invasive assessments included The World health organisation/ New York Heart Association (WHO/NYHA) functional classification, six-minute walk distance (6MWD), and natriuretic peptide blood levels. Hemodynamic parameters were evaluated during right heart catheterization (RHC), including mean right atrial pressure (RAP), pulmonary artery pressures (systolic, diastolic, mean), pulmonary capillary wedge pressure (PCWP), and cardiac output (CO) measured using thermodilution or the Fick method. Cardiac index (CI) and pulmonary vascular resistance (PVR) were calculated. Echocardiographic assessment of right ventricular function included tricuspid annular plane systolic excursion (TAPSE), tissue Doppler imaging (TDI) of tricuspid annular velocity (S' wave), and fractional area change (FAC). Indicators of PH, such as tricuspid regurgitation gradient and right ventricular size (measured in end-diastole via the parasternal long axis view), were also monitored pre- and post-BPA.

Baseline data were obtained before the first BPA or at the time of CTEPH diagnosis. Hemodynamic follow-up data were derived from repeated catheterization performed >6 months after the final BPA. For patients without follow-up catheterization, parameters measured

immediately before the last BPA were used as endpoint data.

Statistical methods

Data were electronically recorded, verified, and processed using Microsoft Office Excel, followed by statistical analysis conducted with JASP software (version 0.14.1, JASP Team 2020, https://jasp-stats.org). Continuous variables are expressed as means with standard deviations, and categorical variables are reported as percentages. The normality of data distribution was assessed using the Shapiro-Wilk test. Comparisons of continuous variables were performed using the paired Student's t-test or the Wilcoxon signed-rank test, depending on data distribution. Categorical variables were compared using the Chi-square test or Fisher's exact test. A p-value of less than 0.05 was considered indicative of statistical significance.

BPA procedure

Warfarin therapy was discontinued 6 days before BPA, with low molecular weight heparin (LMWH) bridging when INR fell below 2. DOACs were discontinued 1 day prior without LMWH bridging. During BPA, oxygen was administered, and oxygen saturation, ECG, blood pressure, and heart rate were continuously monitored. All the procedures were performed by transfemoral approach. Hemodynamic parameters were measured with a Swan-Ganz catheter (B Braun Melsungen AG) inserted via a 7F sheath. For BPA, the sheath was replaced with a 6F sheath (Destination, Balt), and a guiding catheter (e.g., Multipurpose, Judkins, or Amplatz; Boston Scientific) was introduced, followed by the administration of 2500 IU unfractionated heparin. A guidewire (PT2 Moderate Support or Asahi Sion Blue) was used to navigate to the target pulmonary artery branch. Initial dilatation utilized balloons of 1.5–2.5 mm diameter (Abbott), with larger balloons (3-4 mm) for postdilation in later sessions. Each BPA session treated 2–8 branches using repeated inflations. Contrast agent use was limited to 300 mL, and total fluoroscopy time did not exceed 40 minutes (9).

Results

Study population

Our cohort consisted of 13 patients (31% women, mean age 61.5 ± 14.4 years) out of 197 patients who were managed at that time at our centre and underwent at least one BPA session between November 2017 and January 2023. A total of 43 procedures (transfemoral approach) were performed, averaging 3.3 sessions per patient and 5.8 treated segments per session (range: 2–13). In 11 patients BPA session were finished due to angiographic and clinical results. At diagnosis, patients had a mean age of 56.7 ± 15.9 years. Multidisciplinary evaluation deemed 76.9% (10 patients) inoperable, while 2 had operable disease contraindicated by comorbidities, and 1 had residual PH after PEA. At diagnosis, 23.1% were in NYHA class II, 46.2% in class III, and 30.7% in class IV. Anticoagulation therapy for ≥3 months was used in all patients (76.9% warfarin, 23.1% direct oral anticoagulants-DOACs). Specific PH treatment with riociguat prior to BPA was taken by 7 patients (53.8%), 1 patient in combination with subcutaneous treprostinil. Diuretics were required in 69.2% due to clinical manifestation right heart failure, and 15.4% needed oxygen therapy for severe desaturation. Prior pulmonary embolism was noted in 76.9%, with 92.3% having at least one risk factor for CTEPH - most commonly non-0 blood type (83.3%), thyroid disease (58.3%), and recurrent venous thromboembolism (41.6%). Common comorbidities included arterial hypertension and chronic venous insufficiency (53.8%), arrhythmia (53.8%), and chronic obstructive pulmonary disease/asthma (53.8%), with 46.2% on bronchodilator therapy. Additional details are outlined in Table 1.

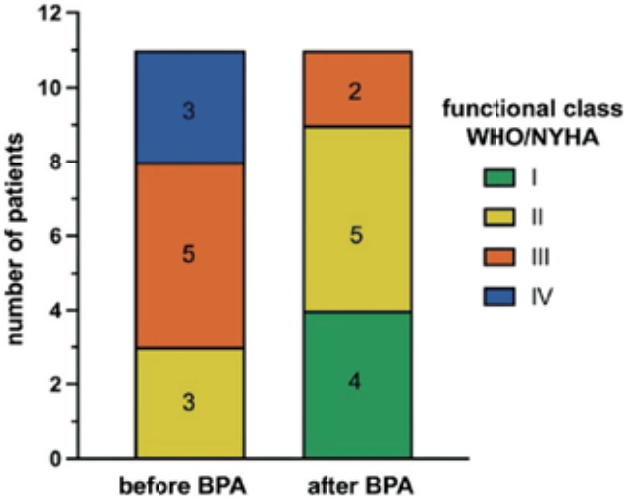
Table 1. Cohort characteristics.
Tabuľka 1. Charakteristika kohorty.

Parameter	Mean ± SD / n (%)
Age (years)	61,5 ± 14,4
Female	4 (31 %)
BMI (kg/m^2)	29,3 ± 4,5
BSA (m^2)	2,0 ± 0,2
Age at the time of diagnosis	56,7 ±15,9
Diseases duration (years)	4,9 ±2,9
NYHA I/II/III/IV	0/3/6/4
NTproBNP (ng/L)	3002,1 ± 3981,8
6MWD (m)	327,4 ± 185,4
Kreatinin (umol/L)	96,8 ± 45,0
Therapy	
VKA	10 (76,9 %)
DOAC	3 (23,1 %)
Diuretics	9 (69,2 %)
Bronchodilators	6 (46,2 %)
Riociguat	7 (53,8 %)
Treprostinil s.c.	1 (7,7 %)
Pulmonary embolism	
History of PE	10 (77 %)
Time from PE to diagnosis (months)	14,5 ± 15,9
CTEPH risk factors	12 (92,3 %)
Number of RF	2,6 ± 1,2
Hypothyroidism	7 (58,3 %)
Splenectomy	2 (16,6 %)
Blood type other than „0“	10 (83,3 %)
Thrombophilia	3 (25 %)
Recurrent venous thromboembolism	5 (41,6 %)
Comorbidities	
Arterial hypertension	9 (69,3 %)
Diabetes mellitus	2 (15,4 %)
Arrhythmia	7 (53,8 %)
COPD/Bronchial asthma	7 (53,8 %)

Parameter	Mean ± SD / n (%)
Chronic venous insufficiency	9 (69,3 %)
Obstructive sleep apnea	2 (15,4 %)
Hepatopathy	4 (30,8 %)
Hyperlipidemia	5 (38,5 %)
Stroke	2 (15,4 %)
Chronic kidney disease	6 (46,2 %)

6MWD -six-minute walking distance; BMI - body mass index; BPA – balloon pulmonary angioplasty; BSA – body surface area; COPD – chronic obstructive pulmonary disease; CTEPH – chronic thromboembolic pulmonary hypertension; DOAC - direct oral anticoagulants; NTproBNP - N-terminal pro B-type natriuretic peptide; NYHA – New York Heart Association; PE – pulmonary embolism; RF-risk factor; SD – standard deviation; VKA –vitamin K antagonist.

Figure 1. Functional class WHO/NYHA before and after BPA.
Obrázok 1. Funkčná trieda WHO/NYHA pred a po BPA.
BPA – balloon pulmonary angioplasty; NYHA – New York Heart Association; WHO – World Health Organisation.

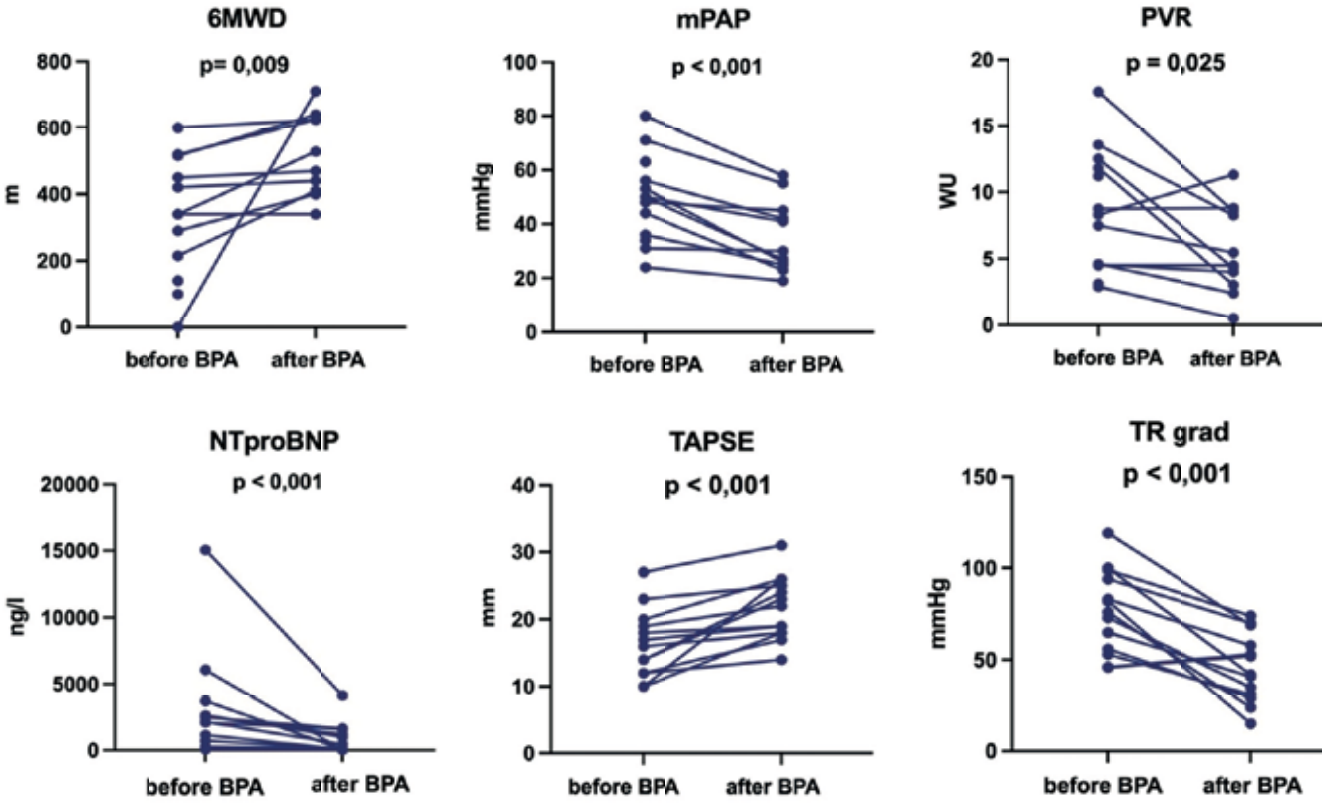


Effect of BPA on clinical and hemodynamic condition

Before the first BPA, 23.1%, 46.2%, and 30.7% of patients were classified as NYHA functional classes II, III, and IV, respectively. Post-BPA, 30.7%, 46.2%, and 23.1% were in classes I, II, and III, respectively ($p = 0.019$), there was no patient in class IV, with 92.3% showing at least one grade improvement (Figure 1).

Exercise capacity improved significantly after BPA, with a 6MWD increase of +191.3 m ($p = 0.009$, Figure 2), and NT-proBNP levels reduced by 72.9% ($p < 0.001$,

Figure 2. Selected clinical, hemodynamic, and echocardiographic parameters before and after BPA.
Obrázok 2. Vybrané klinické, hemodynamické a echokardiografické parametre pred a po BPA.



6MWD – six-minute walking distance; BPA – balloon pulmonary angioplasty; mPAP – mean pulmonary artery pressure; NTproBNP - N-terminal pro B-type natriuretic peptide; PVR –pulmonary vascular resistance; TAPSE - tricuspid annular plane systolic excursion; TR -tricuspid regurgitation; WU – Wood units.

Figure 2). Hemodynamic follow-up >6 months after BPA or immediately before the last session showed marked improvements, with mean pulmonary artery pressure (mPAP) decreased by 27.9% ($p < 0.001$, Figure 2) and pulmonary vascular resistance decreased by 35.3% ($p = 0.025$, Figure 2). No significant changes in CO or CI were observed.

After BPA, echocardiography confirmed enhanced right ventricular systolic function with significant improvements in both longitudinal (TAPSE: $p < 0,001$, TDIS: $p = 0,002$) and global (FAC: $p < 0,001$) parameters, as well as regression of right ventricle size, by a mean of 5.3 mm ($p=0,002$) in the end-diastolic diameter in parasternal long axis (Figure 2). A significant reduction in estimated systolic pulmonary pressure (sPAP) by mean 36,5mmHg ($p < 0,001$, Table 2) corelates with invasively measured gradients during RHC.

BPA safety

No fatal complications were reported during 43 BPA sessions, overall, 4 complications (9.3%) occurred in patients during the procedures. Haemoptysis without desaturation occurred in one patient during two sessions and was managed conservatively with temporary anticoagulation adjustment. One patient developed a large hematoma at the catheterization site requiring surgical evacuation, and another experienced a cutaneous allergic reaction managed with antihistamines after the fourth session. No cases of post-contrast nephropathy were observed, despite 46.2% of patients having chronic kidney disease. By the study endpoint (January 31, 2023), no deaths were reported, with a mean post-BPA follow-up of 16.1 month (± 16.4 months).

Discussion

This study presents the first comprehensive assessment of BPA in the treatment of CTEPH in Slovakia. Our findings corroborate its efficacy and safety, aligning with international data, while also offering insights into challenges unique to our healthcare setting.

The efficacy of BPA observed in our cohort aligns closely with data from other European centres and international registries. Improvement in WHO/NYHA functional class was significant, with 77% of patients in class III or IV at baseline and only 23% remaining in these categories after the final BPA session. These results compare favourably with data from France and the Czech Republic, where similar reductions in NYHA class were reported (9,10). Additionally, our cohort demonstrated an exceptional increase in six-minute walking distance (6 MWD), with an average improvement of 191.3 meters. This surpasses the gains reported

Table 2. Selected parameters before and after balloon pulmonary angioplasty.
Tabuľka 2. Vybrané parametre pred a po balónovej pľúcnej angioplastike.

Parameter	before BPA (Mean ± SD)	after BPA (Mean ± SD)	p value
NTproBNP (ng/l)	**3002,1 ± 3981,8**	**814,9 ± 1171,4**	**< 0,001**
NYHA I/II/III/IV (%)	**0/23/46/31**	**31/46/23/0**	**0,019**
6MWD (m)	**327,4 ± 185,4**	**518,7 ± 124,8**	**0,009**
Borg class	**6,8 ± 2,9**	**4,6 ± 2,1**	**0,027**
SpO_2 (%)	**92,1 ± 3,2**	**95,1 ± 3,0**	**0,006**
Hemodynamic parameters			
mPAP (mmHg)	**49,2 ± 16,0**	**35,5 ± 13,3**	**< 0,001**
sPAP (mmHg)	**84,8 ± 33,9**	**61,5 ± 27,8**	**< 0,001**
RAP (mmHg)	**16,4 ± 7,8**	**9,5 ± 5,1**	**0,021**
PCWP (mmHg)	12,9 ± 2,7	10,5 ± 3,7	0,064
PVR (WU)	**8,5 ± 4,6**	**5,5 ± 3,3**	**0,025**
CO (L/min)	4,5 ± 0,9	4,9 ± 0,8	0,107
CI (L/min/m^2)	2,2 ± 0,3	2,5 ± 0,4	0,056
Echocardiographic parameters			
RVEDD (mm)	**40,3 ± 7,1**	**35,1 ± 4,9**	**0,002**
TAPSE (mm)	**16,3 ± 5,9**	**21,7 ± 4,7**	**< 0,001**
TDI vlna S (cm/s)	**9,6 ± 2,6**	**12,6 ± 2,4**	**0,002**
FAC (%)	**34,5 ± 8,9**	**43,8 ± 8,5**	**0,002**
sPAP (mmHg)	**89,8±24,9**	**53,3±20,6**	**< 0,001**
TR grad. (mmHg)	**76,3 ± 22,8**	**45,6 ± 18,8**	**< 0,001**
I VC (mm)	**23,2 ± 3,7**	**17,8 ± 2,7**	**0,001**

6MWD – six-minute walking distance; BPA – balloon pulmonary angioplasty; CI – cardiac index; CO – cardiac output; FAC - fractional area change; IVC – inferior vena cava; mPAP – mean pulmonary artery pressure; NTproBNP - N-terminal pro B-type natriuretic peptide; NYHA – New York Heart Association; PCWP – pulmonary capillary wedge pressure; PVR –pulmonary vascular resistance; SD – standard deviation; SpO2 - blood oxygen saturation; RAP – right atrial pressure; RVEDD – right ventricle enddiastolic diameter; TAPSE - tricuspid annular plane systolic excursion; TDI – tissue doppler imaging; TR -tricuspid regurgitation; WU – Wood units.

in the French (+45 m) and Czech (+54 m) cohorts (9,10). It is worth noting that two patients in our study initially recorded a 6MWD of 0 meters due to severe clinical limitations, including syncope with minimal exertion and continuous oxygen dependence, which may have influenced the substantial post-BPA improvement in 6MWD. These findings underscore BPA's ability to significantly improve exercise tolerance and quality of life, even in patients with advanced disease.

Hemodynamic parameters, particularly mPAP and PVR, are well-established prognostic markers in CTEPH. Reducing mPAP and PVR is critical for alleviating right ventricular afterload and improving right heart function, which are key determinants of survival (11). In our study, baseline mPAP was notably elevated at 49.2 ± 16.0 mmHg, reflecting a more compromised patient population compared to other published cohorts. This may be attributed to the prolonged disease duration in our cohort (mean 4.9 ± 2.9 years), which likely contributed to progressive vascular remodelling. Despite this challenging baseline, BPA achieved significant reductions in both mPAP (28%) and PVR (35%). These results are consistent with findings from the French cohort (26% reduction in mPAP and 43% in PVR) (12) and demonstrate comparable efficacy to outcomes reported in Japanese and European studies five per patient. In addition to hemodynamic improvements, BPA significantly reduced NT-proBNP levels, a biomarker of right ventricular strain, supporting its beneficial impact on right heart function. Echocardiographic parameters, including TAPSE and sPAP, also improved, further corroborating the positive effects of BPA on right ventricular performance.

Timely intervention also plays a crucial role in optimizing BPA outcomes. In our cohort, the average time from CTEPH diagnosis to the first BPA session was 31.5 ± 30.4 months, reflecting delays in establishing the BPA program and integrating it into routine care. Prolonged disease duration increases the risk of irreversible vascular remodelling, which may limit the therapeutic impact of BPA. Encouragingly, for patients diagnosed after 2017, the average time to BPA initiation decreased to 6.5 ± 2.0 months, suggesting improvements in referral pathways and procedural accessibility.

Safety is a critical consideration in evaluating BPA, given its invasive nature and potential for complications. Our study demonstrated a low complication rate of 9.3% across 43 BPA sessions, with no fatal events reported. Complications included two instances of haemoptysis in the same patient, a hematoma at the catheterization site requiring surgical intervention, and a cutaneous allergic reaction managed with antihistamines. These findings align with reported complication rates from other European centres, including 9,4% in the Germany (15) and 15.8% during the early phase of the French BPA program (12). Severe complications, such as pulmonary haemorrhage or pulmonary oedema, were rare, and our results compare favourably with Japanese registry data, which reported an overall complication rate of 36.3% (15,16). The absence of post-contrast nephropathy, even in patients with chronic kidney disease, further supports the safety of BPA in appropriately selected patients. Long-term survival following BPA could not be extensively analysed in our cohort due to the relatively short follow-up duration (mean 16.1 months). However, the absence of mortality during the study period is encouraging and aligns with international reports of high survival rates post-BPA. For example, the Japanese registry reported 1- and 2-year survival rates of 93% and 91%, respectively (16). Future studies with extended follow-up will be essential to assess the durability of BPA's benefits and its impact on long-term outcomes.

Despite its promising results, this study has several limitations. The small sample size reflects the preliminary nature of our BPA program and limits the generalizability of our findings. However, our cohort size is comparable to other early reports from countries with emerging BPA programs, such as Greece and South Korea (17,18). Additionally, the retrospective design and lack of a control group restrict our ability to draw definitive conclusions about BPA's comparative efficacy. Finally, long-term follow-up data are currently unavailable, although prospective monitoring is planned as the program matures.

Our study highlights the important role of BPA as a safe and effective treatment for CTEPH, particularly in patients ineligible for PEA. The observed improvements in functional capacity, hemodynamic, and right ventricular function underscore BPA's potential to significantly enhance quality of life and prognosis. Moreover, the successful implementation of a BPA program in our centre and so throughout our country demonstrates the feasibility of introducing this advanced technique in settings without an established program, provided that appropriate training and international collaboration are in place. Moving forward, efforts to streamline diagnosis, optimize patient selection, and expand access to BPA will be critical for improving outcomes and ensuring that all eligible patients benefit from this innovative therapy. Our findings contribute to the growing body of evidence supporting BPA and emphasize its value as a cornerstone of CTEPH management.

Conclusion

In conclusion, this study highlights the significant clinical and hemodynamic benefits of BPA in the management of CTEPH, especially in patients ineligible for PEA. Our results demonstrated marked improvements in functional status, exercise capacity, and right ventricular function, with a low complication rate, aligning with international data. Importantly, the study underscores the feasibility and success of implementing a BPA program in Slovakia through international collaboration with high volume expert centres in Prague and Vienna. This partnership has allowed patients in a smaller country, lacking a fully developed local CTEPH surgical and interventional program, logically due to small number of patients

with this rare disease as well as of procedures, access to multimodal, guideline-recommended treatment.

The outcomes illustrate how international cooperation can bridge healthcare gaps, ensuring equitable access to advanced therapies even in resource-limited settings. This approach not only addresses immediate clinical needs but also lays a foundation for building local expertise and enhancing the overall standard of care. Moving forward, optimizing patient selection, ensuring timely diagnosis, and expanding BPA accessibility will be crucial for improving outcomes. This study contributes to the growing body of evidence supporting BPA as a cornerstone of CTEPH management and offers a model for other regions seeking to establish comprehensive, multidisciplinary programs through international partnerships.*

*__Compliance with Ethics Requirements:__ Authors declare no conflict of interest regarding this article. The authors declare, that all the procedures of this research respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008 (5), as well as the national law.

Conflict of interest: The authors declare no conflict of interest.

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