DOI: 10.1002/pul2.12312

REVIEW ARTICLE

Pulmonary Circulation Open Access | PVRI Pulmonary Vascular Research Institute | WILEY

Balloon pulmonary angioplasty in the current era of CTEPH treatment: How did we get here?

Jenny Z. Yang[1] | **David S. Poch**[1] | **Lawrence Ang**[2] | **Ehtisham Mahmud**[2] | **Nick H. Kim**[1]

[1]Department of Medicine, Division of Pulmonary, Critical Care, and Sleep Medicine, UC San Diego, La Jolla, California, USA

[2]Department of Medicine, Division of Cardiovascular Medicine, UC San Diego, La Jolla, California, USA

Correspondence
Jenny Z. Yang, Department of Medicine, Division of Pulmonary, Critical Care, and Sleep Medicine, UC San Diego, 9300 Campus Point Dr, MC 7381, La Jolla, CA 92037, USA.
Email: jey052@health.ucsd.edu

Funding information
None

Abstract

Chronic thromboembolic pulmonary hypertension (CTEPH) is caused by persistent organized thromboembolic obstruction of the pulmonary arteries from incompletely resolved pulmonary embolism. The treatment of choice is pulmonary thromboendarterectomy (PTE) surgery and all patients should be evaluated for operability candidacy. Despite advancements in PTE technique allowing more segmental–subsegmental surgeries, up to a third of patients with CTEPH may still be considered inoperable. Over the past decade, there have been increasing treatment options for these inoperable CTEPH patients. Balloon pulmonary angioplasty (BPA) is a percutaneous-based interventional treatment option for select CTEPH cases. Early BPA experiences were plagued by high complication rates, but further refinements in technique and equipment pioneered by Japan led to the worldwide spread and adoption of BPA. Multiple centers have shown that patients experience significant improvements in hemodynamics, quality of life, exercise capacity, and survival with BPA treatment. There remain many questions on best practices, but BPA has evolved into a pivotal cornerstone of CTEPH treatment.

KEYWORDS
balloon pulmonary angioplasty, BPA, chronic thromboembolic pulmonary disease, CTEPH, pulmonary vascular

INTRODUCTION

Chronic thromboembolic pulmonary hypertension (CTEPH) is a distinct form of pulmonary hypertension (PH) characterized by unresolved thromboembolic occlusions of the pulmonary arteries.[1,2] These chronic obstructions become organized and fibrotic, and, together with varying degrees of small vessel disease, can lead to progressive PH, right heart failure, and death. The clearance of the more proximal, mechanical, obstructive component of CTEPH is achieved with pulmonary thromboendarterectomy (PTE) surgery. In many patients, even those with severe PH, PTE surgery can lead to immediate and dramatic resolution of PH, leading to excellent long-term survival. Accordingly, PTE surgery remains the treatment of choice for operable CTEPH.

Despite advances in operative techniques allowing for more distal endarterectomies to be successfully performed,[3,4] up to a third of patients are still considered to be inoperable.[5–7] Multiple prior studies and registries have

shown that nonoperated subjects do poorly compared to those who receive surgery,[6,8] and this was true regardless of the reason why a patient was deemed inoperable. These inoperable patients previously had minimal therapeutic options. However, over the last 20 years, balloon pulmonary angioplasty (BPA) has emerged as a viable alternative, and it is now an established class I treatment option in select inoperable CTEPH cases with consensus BPA guidelines recently published.[9,10] In this manuscript, we review the history and evolution of BPA, as well as the landmark studies that have solidified BPA as an integral treatment modality for CTEPH, and how our understanding of the role of BPA in the treatment of CTEPH continues to evolve.

HISTORY

While initial attempts at PTE surgery date back to the 1950s, BPA only entered the scene in the 1980s. Balloon angioplasty was originally attempted in the treatment of nonatherosclerotic arterial stenoses and congenital valvular disease.[11,12] The first case report of balloon angioplasty of pulmonary arteries for chronic thromboembolism was published in 1988,[13] in which a 30-year-old man with "pulmonary hypertension after pulmonary embolism" was treated with balloon angioplasty. After three treatment sessions, his mean pulmonary artery pressure (mPAP) reduced from 46 to 35 mmHg. This became the first signal that BPA may be effective in the treatment of CTEPH.

Subsequently, the first major case series of BPA in CTEPH was out of Boston in 2001.[14] This series included 18 CTEPH patients, who underwent between 1 and 5 BPA sessions. Notably, there was a decrease in mPAP from 43 to 34 mmHg, and improvements in both New York Heart Association functional class (3.3–1.8) and 6-min walk distance (209–497 yards) over an average follow-up period of 36 months. However, these benefits came at the cost of high complication rates, including a mortality rate of 5.5%, pulmonary artery perforation in 5.5%, femoral artery pseudoaneurysm in 17%, and reperfusion pulmonary edema in 61% with mechanical ventilation required in 17%. With the high rates of complications noted in the series, BPA appeared abandoned in the United States for many years and did not gain popularity in the treatment of CTEPH patients until over a decade later.

RE-EMERGENCE AND SPREAD OF BPA

In 2012, three separate reports emerged from Japan on the efficacy of BPA in the treatment of CTEPH. These reports tallied a total of 109 patients and 318 BPA sessions, with a combined mortality rate of 1.8%.[15–17] Reperfusion edema was noted to occur in 103 out of the 318 sessions (32.4%), and mechanical ventilation was required in just five patients (4.6%), as compared to the 61% who developed reperfusion lung injury and 17% requiring mechanical ventilation reported by Feinstein et al. With the lower complication rates, there were still significant improvements in hemodynamics, functional class, exercise capacity, and N-terminal probrain natriuretic peptide. Importantly, it was observed that the improvements in hemodynamics were not seen immediately postprocedurally, but rather at subsequent follow-up, suggesting that there was ongoing beneficial vascular remodeling that occurred after balloon angioplasty.[16] Furthermore, the hemodynamic improvements were sustained over time.[17,18]

Following the individual single-center BPA successes in Japan, a multicenter BPA registry between seven Japanese centers was created.[18] This registry included 308 patients who were treated with BPA between 2004 and 2013. These 308 patients underwent a total of 1408 procedures, and significant improvements were observed in hemodynamics (mPAP 43.2–24.3 mmHg, pulmonary vascular resistance (PVR) 854–359 dynes s cm^{-5}, cardiac index 2.6–2.9 L/min/m^2), functional class (III–II) and exercise capacity via 6-min walk (318–401 m). Additionally, there were 196 patients who had follow-up hemodynamics at a mean of 1.2 years after completion of all BPA sessions. Pulmonary hemodynamics (mPAP, PVR), exercise capacity, and functional class continued to show ongoing improvements and with less use of PH-targeted therapies. Complications occurred in 36.3% of all procedures (511/1408). By this point, with feedback from PTE center experts visiting and witnessing Japanese BPA procedures, the previously reported complications termed reperfusion lung injury or reperfusion pulmonary edema from BPA were reclassified to pulmonary injury—acknowledging the injury stemming from BPA appeared different than the reperfusion lung injury described after PTE. The most common complications reported in this registry were pulmonary injury (17.8%) and hemoptysis (14%). Other vascular injuries including pulmonary artery perforation, pulmonary artery dissection, and pulmonary artery rupture occurred in 3.4% of all procedures. Mechanical ventilation was required in 5.5% and extracorporeal membrane oxygenation (ECMO) in 2.9%. The 30-day mortality was 2.6% and overall mortality was 3.9%. This pioneering work in Japan led to the worldwide surge in BPA interest and its eventual acceptance as a treatment option for CTEPH.

Notably, it was observed that the Japanese CTEPH population was uniquely different compared to that of Europe and the United States (Table 1). The Japanese

TABLE 1 Comparison of BPA population demographics and outcomes reported in Japan, Europe, and UCSD.

	No. of pts, *n*	No. of proc., *n*	Age (years)	Female, *n* (%)	Post-PTE, *n* (%)	History of VTE, *n* (%)	Splenectomy, *n* (%)	PH therapies, *n* (%)	Baseline 6MWD (m)	Baseline FC I/II/III/IV (%)	Base mPAP (mmHg)	Base PVR (dynes s cm^{-5})	Improvement in mPAP [mmHg (%)]	Improvement in PVR [dynes s cm^{-5} (%)]	Complications per proc. (per pt.) (%)	Mortality, *n* (%)
Japan 2017[18]	308	1408	61.5 ± 12.5	246 (80%)	14 (4.5%)	DVT: 107 (34.7%); PE: 47 (15.3%)	2 (0.6%)	222 (72%)	318 ± 122	0/19/66/15%	43.2 ± 11.0	854 ± 451	−18.9 (44%)	−494.2 (58%)	36.3% (n/a of patients)	12 (3.9%); 8 (2.6%) within 30 days
Germany 2017[19]	56	266	65 (55–74)	34 (61%)	7 (13%)	32 (57%)	NA	33 (59%)	358 ± 108	0/15/70/15%	40 ± 12	591 ± 286	−7 (18%)	−151 (26%)	9.4% (32% of patients)	1 (1.8%)
France 2018[20]	184 (154)[a]	1006	63 ± 14	90 (49%)	15 (8.2%)	135 (73%)	18 (9.8%)	114 (62%)	397 ± 117	1/35/59/5%	44.1 ± 9.8	610 ± 255	−12.3 (26%)	−275 (43%)	11.2% (46% of patients)	7 (3.8%)
UCSD 2022[21]	153	643	60 (22–91)	86 (56%)	32 (21%)	138 (90%)	29 (19%)	120 (78%)	408 ± 144	3/20/72/7%	37.0 ± 10.9[b]	399 ± 221[b]	−5.6 (15%)	−94 (24%)	10.4% (33% of patients)	0

Abbreviations: BPA, balloon pulmonary angioplasty; DVT, deep vein thrombosis; FC, functional class; mPAP, mean pulmonary artery pressure; no. number; PE, pulmonary embolism; PH, pulmonary hypertension; pts, patients; proc., procedures; PTE, pulmonary thromboendarterectomy; PVR, pulmonary vascular resistance; USCD, University of California San Diego; VTE, venous thromboembolism; 6MWD, 6-min-walk distance.

[a]One hundred and eighty-four patients analyzed for safety, and 154 patients analyzed for efficacy because 30 patients did not have final right heart catheterization after BPA.

[b]Ninety-seven patients who completed BPA treatment and had at least three BPA sessions included for hemodynamics analysis.

cohort was 80% female, with a history of deep venous thrombosis in only 35% and pulmonary embolism in 15%.[18] This is in contrast to the European and US CTEPH registries in which history of deep vein thrombosis was present in 56.1% and 46.3%, respectively, and history of PE was present in 74.8% and 87.9%, respectively.[5,6] Therefore, while BPA spread worldwide, there were still concerns regarding reproducibility outside of Japan given potential differences in CTEPH population and advanced technical experience. However, eventually, BPA reports from select BPA centers in Europe noted comparable outcomes. A German series of 56 patients undergoing BPA showed improvements in hemodynamics (mPAP 40–33 mmHg, PVR 591–440 dynes s cm^{-5}, cardiac output [CO] 4.4–4.6 L/min), functional class, and 6-min walk distance (358–391 m).[19] Complications occurred in 9.4% of all procedures (which was 32% of patients), with the most common complication observed being vascular injury (term interchanged with BPA-associated pulmonary or lung injury) from wire perforation. Mortality rate was 1.8% (one patient), which occurred due to fatal pulmonary bleeding from vascular injury.

Similar findings were observed in France.[20] In 184 consecutive patients who underwent 1006 BPA sessions, there were significant improvements in hemodynamics (mPAP 44–32 mmHg, CO 4.9–5.6 L/min, PVR 604–329 dynes s cm^{-5}), functional class, and exercise capacity (396–441 m) at a median follow-up of 6.1 months. BPA-related complications occurred in 11.2% of all procedures (46% of all patients). Similarly, lung injury was the most common complication observed and approximately 20% required support with noninvasive or invasive mechanical ventilation. Overall mortality rate at follow-up was 3.8%; the periprocedural mortality was 2.2%, all from severe lung injury. Notably, the authors highlighted the importance of technical experience by stratifying their cohort of patients into two groups based on chronological order of BPA, an initial period and a recent period. The latter group of patients in the "recent period" had even better improvements in hemodynamics, suggesting that providers became more efficient and effective at treating target lesions with experience. Importantly, there were also less complications in the more recent period, going from a rate of 15.8%–7.7%, as operator experience increased.

University of California San Diego (UCSD) is recognized as the pioneering center for PTE and remains one of the busiest centers in the world for the evaluation and treatment of CTEPH. After training in Japan, UCSD started its BPA program in March 2015 and now offers BPA routinely as part of multimodality therapy for CTEPH. The addition of the BPA program did not result in diminished PTE surgeries but rather allowed more comprehensive treatment options for all CTEPH patients.[22] Given the subjectivity of CTEPH operability assessment, and being the most experienced surgical center for CTEPH, UCSD witnessed a unique BPA population compared to perhaps centers with limited surgical experience (Figure 1). Approximately 45% of our BPA patients have risk factors associated with distal disease, such as splenectomy, indwelling venous catheters, pacemakers, upper extremity clot, and several others. Additionally, over 25% of our BPA patients have had prior PTE surgery. Despite the differences in population, our complication rates are fairly similar at about 10% per procedure with the most common being hemoptysis/vascular injury; there has been no procedure-related mortality. While reductions in PVR (399 − 304 dynes s cm^{-5}, $p < 0.01$) and mPAP (37– 31 mmHg, $p < 0.001$) are more modest in our cohort compared to some others, this may be associated with the unique patient population undergoing BPA (Table 1). Patients at UCSD with suspected segmental–subsegmental CTEPH and severe hemodynamics are preferentially triaged to PTE surgery following a multidisciplinary review. If these patients are deemed inoperable, PH-targeted medical therapy is usually initiated in an attempt to improve pulmonary hemodynamics before proceeding with BPA.[23]

BPA TECHNIQUE

The current BPA technique is well documented,[10,17,24] but briefly, vascular access is obtained via the femoral or internal jugular vein. A right heart catheterization is performed to obtain baseline hemodynamics to assess PH severity, and subsequently, a 6F 90-cm sheath is placed into the target pulmonary artery through a series of wire and catheter exchanges. After the 90-cm sheath is in place, anticoagulation is administered, usually intravenous unfractionated heparin to achieve a target activated clotting time (ACT) of 200–250 s. A 6F 110-cm Judkins right or multipurpose guide catheter is advanced into the lung region of interest. Selective pulmonary angiography is performed to identify target lesions. Subsequently, an atraumatic, low-tip load 0.014-in. guidewire is used to cross the target lesions and 2.0–4.0 mm (depending on the severity of PH and caliber of the target vessel) semi- or noncompliant balloons are advanced over the wire. Serial balloon inflations are performed in the diseased segments of interest. This process is repeated in other vessels until the procedure is completed, typically limited by contrast, radiation, or number of treated segments.

This modern technique reflects refinements made by Japanese BPA experts. They established a few major modifications that allowed for lower complication rates while maintaining hemodynamic and functional

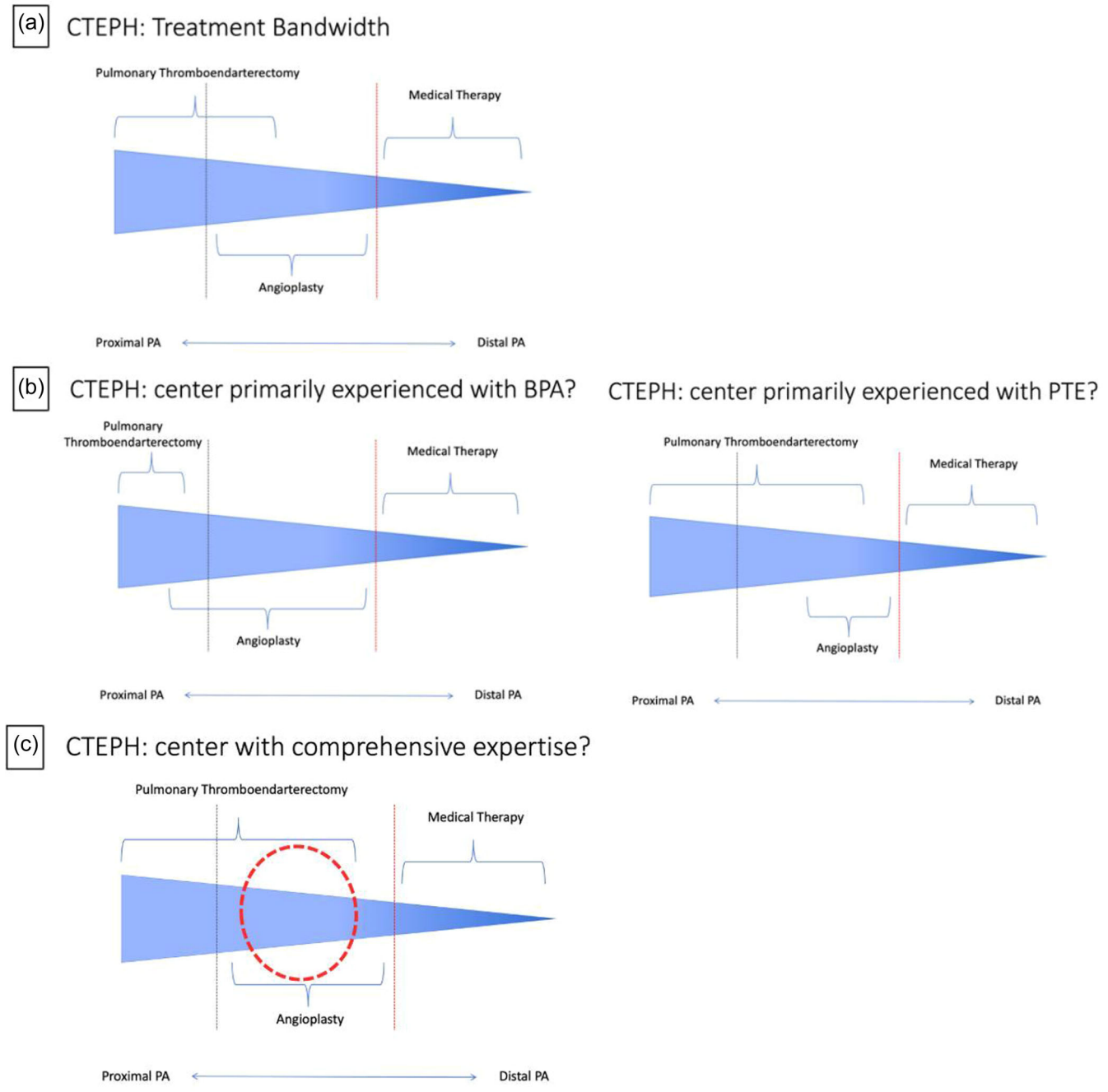

FIGURE 1 (a–c) Pulmonary thromboendarterectomy (PTE) surgery, balloon pulmonary angioplasty (BPA), and medical therapy are all essential components of chronic thromboembolic pulmonary hypertension (CTEPH) treatment. (a) Spectrum of CTEPH treatments available based on the location of disease within the pulmonary artery. Vertical black line represents separation of lobar and segmental pulmonary arteries. Vertical red line represents separation of subsegmental pulmonary arteries reachable by BPA and the microvascular territory beyond the reach of BPA. (b) Operability determination is subjective and the range of what is considered operable disease can differ at institutions based on operator experience. Left panel: More expansive range of diseases treated by BPA at a center primarily experienced with BPA. Right panel: More expansive range of disease treated by PTE at a center primarily experienced with PTE. (c) At a center with experience in both PTE and BPA, there is a group with overlap in treatment options. The dotted red oval represents the group with disease in the segmental and subsegmental pulmonary arteries, who may be treated with either intervention. This is a potential group for comparative outcomes between PTE and BPA, or a randomized interventional trial with long-term follow-up.

improvements. First, it was noted that BPA needed to be a staged procedure, with three to five segments of the lower lobes typically treated first.[18] The number of segments treated per session may also vary depending on severity of hemodynamics and early versus later BPA interventions. The majority of chronic thromboembolic disease is typically located in the lower lobes, so treating these areas early can often achieve greater improvements in hemodynamics and symptoms. The rationale for performing BPA interventions in a staged fashion was to reduce the rate of vascular injury. To further reduce complication rates, the wires and balloons were also amended. Utilizing advanced imaging modalities such as intravascular ultrasound (IVUS), cone beam computerized tomography (CT), or 320-slice electrocardiogram-gated CT pulmonary angiogram, the Japanese BPA specialists were able to facilitate identification of target lesions and appropriate balloon sizing. In general, they also employed 0.014-in. atraumatic wires as the workhorse wire for BPA. The balloons were semicompliant or noncompliant, and cutting balloons were avoided to prevent damaging the vasculature. This is in comparison to the initial case series by Feinstein et al. in which larger wires (0.035 in.) and balloons (up to 9.0 mm) were used. Most balloon sizes now range from 2.0 to 5.0 mm. Stents are not necessary for treating CTEPH with BPA. Advanced techniques including IVUS, optical coherence tomography, or pressure wire guidance may facilitate special situations but are not deemed necessary for routine BPA.

An angiographic classification system of chronic thromboembolic lesions treated by BPA was proposed with five categories depending on lesion morphology: (a) ring-like stenoses (bands); (b) web lesions; (c) subtotal lesions; (d) total occlusions; and (e) Tortuous lesions[25] (Figure 2). In the report, ring-like stenoses and webs were easier to treat with high success rates (100% and 98.7%, respectively) compared to total occlusions (52.2%) and tortuous lesions (63.6%).

COMPLICATIONS

The most common BPA-related complication is vascular injury, including wire-associated injury and less commonly pulmonary artery perforation and dissection.

In the early BPA experiences, most lung injury that occurred was thought to be related to reperfusion pulmonary edema as described after PTE surgery. This has been subsequently reclassified as vascular injury.[26] This was supported by post-BPA CT scans within 24 h after the procedure demonstrating focal infiltration only at the site of BPA-treated areas. The systematic use of post-BPA CT scans identified vascular injury in 76% of

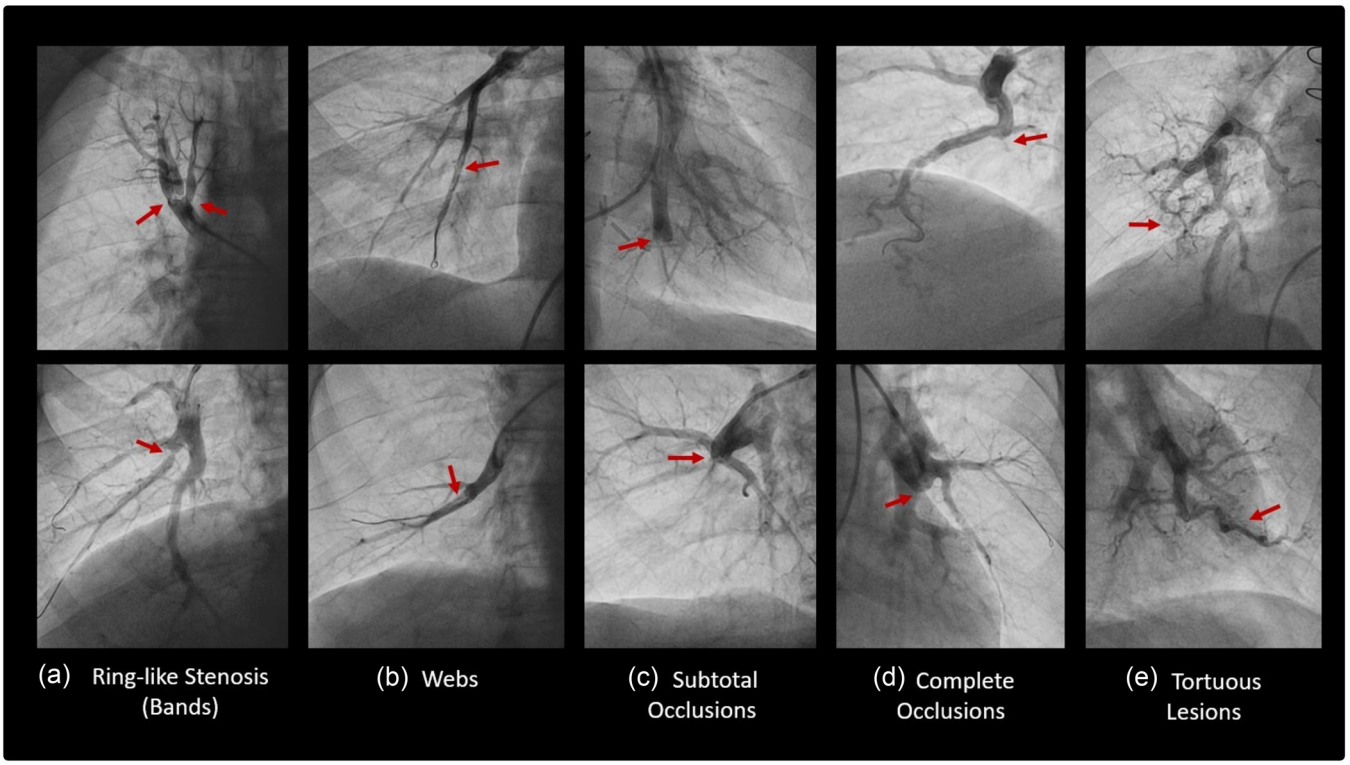

FIGURE 2 Examples of angiographic lesions that are potentially treatable by balloon pulmonary angioplasty.

patients (58/76) and 47% of procedures (138/297). However, there was angiographic evidence of BPA-related vascular injury in only 17% and clinical symptoms (hypoxia, hemoptysis) in 22%.[26] Therefore, routine post-BPA CT scans are likely unnecessary as a large majority of the vascular injury may be subclinical and does not warrant any intervention.

There are characteristics of both the patient and vascular lesion morphology that may be higher risk for the development of complications. Patients with longer duration of disease, increased BNP, worse 6-min walk distance, and more severely elevated mPAP and PVR were more likely to develop lung injury.[20,26,27] Kawakami et al. also noted complication rates varied with the lesion type. For ring-like stenoses and web lesions, complications occurred in less than 2.5% of all interventions (31/1483). This is in contrast to subtotal, total occlusion, and tortuous lesions in which complications occurred in 15.5% (53/342), 6% (4/67), and 43% (19/44), respectively. Lastly, similar to PTE, there is also a component of operator experience in achieving successful BPA and minimizing complications. When patients were stratified into cohorts of two groups based on chronological order of BPA (an initial group and a latter group), the complication rate per procedure during the initial period was 15.8% and decreased to 7.7% in the recent period.[20] Rates of vascular injury specifically were reduced from 13.3% to 5.9%, and severe complications requiring noninvasive positive pressure ventilation or invasive mechanical ventilation were also significantly reduced in the more recent period. There were also three patients who required ECMO post-BPA and all were during the initial period. In early Japan reports, rates of hemoptysis went from 67.5% during the initial 128 BPA sessions to 32.5% during the more recent 127 sessions; similarly, out of five cases of pulmonary artery perforations, four occurred during the early sessions.[17] There is an unavoidable learning curve to BPA, but as operator experience grows and BPA technique is further refined, the safety and efficiency of BPA increases.[28]

There are numerous, but mainly anecdotal options for management of BPA-related vascular injury. Most patients will respond to general supportive measures including anticoagulation reversal and oxygen supplementation.[29] Balloon occlusion proximal to the site of vascular injury can be considered to facilitate hemostasis while anticoagulation is being reversed. However, merely occluding flow from the proximal pulmonary artery branch may not be effective alone if the injury is to the collateral systemic vessels described in CTEPH—and hence the simultaneous need for anticoagulation reversal in cases of significant injury.[30] More aggressive, interventional options include gel foam embolization, coil embolization, or covered stent placement. For more severe cases of injury leading to respiratory decompensation, noninvasive or invasive mechanical ventilation support or even ECMO support may be necessary. With most vascular injury, and provided the patient can recover, PVR reduction can still be achieved despite such complications.[27]

MULTIMODALITY TREATMENT APPROACH

With a multitude of treatment options now available, a multidisciplinary team (MDT) consisting of cardiothoracic surgeons, PH specialists, BPA interventionalists, and chest radiologists specializing in CTEPH is key to determining the optimal treatment approach for patients.[2]

While PTE is the treatment of choice for all operable candidates, patients may have a seemingly asymmetric disease burden or disease thought to be too distal for endarterectomy. In these cases, there may be opportunity for treatment with alternative modalities. In select high-risk hemodynamic cases with unilateral operable and contralateral inoperable disease, combination hybrid PTE and BPA has been performed.[31] There are also reports of a stepwise approach to asymmetric disease. Both upfront unilateral BPA followed by subsequent PTE in the contralateral lung, as well as initial bilateral PTE followed by BPA and medical therapy for distal residual disease, have been reported.[21,32] Additionally, residual PH after PTE is common.[33] While re-do or second PTE surgery is possible in select cases at experienced centers,[34] these patients may also now be candidates for combination of medical therapy and BPA.

Riociguat was approved for inoperable or residual CTEPH in 2013. Therefore, both BPA and riociguat have been on the rise over the last decade, and questions emerged on how best to manage inoperable CTEPH patients with two viable options available. The recently published balloon pulmonary angioplasty versus riociguat in inoperable CTEPH (MR BPA): an open-label, randomised controlled trial and balloon pulmonary angioplasty versus riociguat for the treatment of inoperable CTEPH (RACE): a multicentre, phase 3, open-label, randomised control trial are two studies that have helped shed light on this question.[23,35] MR BPA was conducted in Japan, in which 61 patients with inoperable CTEPH were randomized to BPA or riociguat. At 12 months, those treated with BPA had an average reduction in mPAP of 16.3 mmHg while those treated with riociguat had a reduction of 7.0 mmHg. The greater improvement in mPAP with BPA came at the cost of more hemoptysis and pulmonary hemorrhage though compared to riociguat (44% vs. 4%).[35] Although this study

was a direct comparison between riociguat and BPA, the authors concluded that the two options are not mutually exclusive and could be considered complementary therapies for inoperable CTEPH patients. This concept was highlighted in the RACE trial, in which inoperable CTEPH patients were also randomized to BPA or riociguat, but with the option to cross-over with add-on riociguat after BPA or add-on BPA after riociguat at 26 weeks.[23] Similar to what was observed in MR BPA, patients treated with BPA had an initially larger reduction in PVR, but a higher rate of adverse events, most notably lung injury and hemoptysis. However, those who received riociguat initially then add-on BPA had significantly fewer BPA-related adverse events compared to those who received upfront BPA. The add-on BPA after riociguat group had improved functional status (FC II in 58% vs. 23%) and PVR (538 vs. 767 dynes) before the first BPA session compared to the group who received initial BPA. However, at the end of 52 weeks, both groups achieved similar reduction in PVR. This landmark trial highlights the importance of a multimodal treatment approach to inoperable CTEPH.

The complementary role of medical therapy with BPA continues to grow and evolve. Upfront combination therapy is the standard of care for PAH, but whether this approach is preferable to riociguat monotherapy for inoperable CTEPH before BPA is unclear. Riociguat is the only approved therapy in the United States for inoperable CTEPH, but subcutaneous treprostinil is approved in select European countries, selexipag is used in Japan, and macitentan had promising phase 2 results with an ongoing phase 3 study currently (MACiTEPH, ClinicalTrials.gov NCT04271475).[36–38] The IMPACT-CTEPH trial (ClinicalTrials.gov NCT04780932) will hopefully provide additional insight into the role of upfront combination medical therapy before BPA.

PATIENT SELECTION FOR BPA

Effective PH-targeted medical therapy and advances in BPA have resulted in improved outcomes for those patients with inoperable CTEPH.[39,40] Now that BPA has become an established treatment option and garnered a class I recommendation,[9] the dilemma has moved from debating if BPA is an appropriate treatment option to now choosing who are appropriate patients for BPA. There are no currently available precise guidelines or objective criteria on patient selection between BPA and PTE.

In the Japanese BPA registry of 308 patients, the most common indication for proceeding with BPA was surgically inaccessible lesions (76%).[18] This was followed by patient refusal of PTE surgery (13.6%), comorbidities leading to unfavorable risk/benefit ratio (5.8%), and post-PTE (4.5%). Similarly, at UCSD, the most common reason patients were chosen for BPA was also a surgically inaccessible disease (59%). Other reasons included post-PTE (21%), hemodynamic impairment or symptoms disproportionate to degree of visible disease (10%), comorbidities (7%), and patient refusal (3%).[21] Importantly, the definition of surgical accessibility is subjective and can change depending on institutional expertise.

MDT review is essential in this process as patients with operable disease should be offered PTE surgery as the treatment of choice.[1,9] At UCSD, seven patients who initially received prior BPAs at outside institutions were deemed to be surgical candidates following MDT evaluation. While PTE was safely performed in these patients, the cases were associated with longer than usual circulatory arrest times (reflection of technical difficulty) and longer lengths of stay. Whether the prior BPAs directly contributed to these observations is speculative. However, it highlights the importance of MDT and the challenges of patient selection for initial appropriate intervention.

There are also patients with CTEPD without PH who have been treated with BPA. The natural history of CTEPD without PH is unclear; there is no current data that these patients will progress to develop CTEPH and that discussion is beyond the scope of this review. While the treatment of patients with CTEPD without PH is not well-defined, there are patients with CTEPD without PH who have been successfully treated with BPA.[41,42]

TREATMENT GOALS

The optimal treatment endpoints for BPA remain unclear without consensus goals. Accordingly, the decision to end further BPA treatments is often individualized for each patient. The decision to stop often combines hemodynamic, radiographic, and clinical factors—all the while balancing with symptom burden and the risks/burden associated with additional treatments. In the Japanese registry, 249 out of 308 patients were deemed to be completed with all BPA sessions; the reason in the majority of patients (70.1%) was improvement in mPAP to less than 25 mmHg.[18] The other reasons for completion of BPA were: symptomatic improvement (6.8%), technical difficulty (1.6%), allergic reaction to contrast (0.3%), cerebral infarction (0.3%), and patient refusal (0.3%).

The International BPA registry (ClinicalTrials.gov NCT03245268) is a prospective, multicenter, long-term study that enrolled a total of 500 patients newly treated with BPA at expert centers from Japan, Europe, and the

United States. The registry aims to determine efficacy and safety, as well as evaluate patient selection criteria and treatment endpoints taking into account geographical, population, and practice differences. The results of the registry should be available soon and will hopefully provide further insight into the evolving field of BPA.

CONCLUSION

There have been remarkable advancements in the treatment of CTEPH over the last decade. In addition to successful segmental–subsegmental endarterectomies now being successfully performed at experienced centers, medical therapy and BPA have become well-established options for inoperable and residual disease. Although there is a wealth of data supporting the multiple benefits of BPA, there is an unavoidable learning curve and operator experience is essential in achieving these beneficial outcomes. The nuances of who should be selected for BPA, when BPA is deemed to be complete, and discrete treatment goals are individualized and require MDT discussion at each CTEPH center. There remain many unanswered questions on BPA, but what is clear is that it has become a pivotal cornerstone of CTEPH treatment. The field is evolving to a multimodal approach to CTEPH treatment where PTE, BPA, and medical therapy are all important components of the management strategy, and treatment should be at expert CTEPH centers where all three modalities can be performed to provide the optimal management for each individualized patient.

AUTHOR CONTRIBUTIONS

All authors have reviewed, contributed, and approved this manuscript. All statements in this manuscript are true to our knowledge. Jenny Z. Yang accepts responsibility for the overall integrity of the manuscript.

ACKNOWLEDGMENTS

The authors have nothing to report.

CONFLICTS OF INTEREST STATEMENT

Jenny Z. Yang has served on the advisory board for Janssen. Nick H. Kim has served as a consultant for Bayer, Janssen, Merck, Pulnovo, Polarean, and United Therapeutics; speaker for Bayer and Janssen; and received research support from Altavant Sciences, Gossamer Bio, and International CTEPH Association. The remaining authors declare no conflict of interest.

ETHICS STATEMENT

Not applicable.

ORCID

Jenny Z. Yang http://orcid.org/0000-0002-4844-8715
David S. Poch http://orcid.org/0000-0002-7669-3662

TWITTER

Jenny Z. Yang @JennyYangMD
Nick H. Kim @nickhsk_phdoc

REFERENCES

1. Delcroix M, Torbicki A, Gopalan D, Sitbon O, Klok FA, Lang I, Jenkins D, Kim NH, Humbert M, Jais X, Vonk Noordegraaf A, Pepke-Zaba J, Brénot P, Dorfmuller P, Fadel E, Ghofrani HA, Hoeper MM, Jansa P, Madani M, Matsubara H, Ogo T, Grünig E, D'Armini A, Galie N, Meyer B, Corkery P, Meszaros G, Mayer E, Simonneau G. ERS statement on chronic thromboembolic pulmonary hypertension. Eur Respir J. 2021;57(6):2002828. https://doi.org/10.1183/13993003.02828-2020
2. Kim NH, Delcroix M, Jais X, Madani MM, Matsubara H, Mayer E, Ogo T, Tapson VF, Ghofrani HA, Jenkins DP. Chronic thromboembolic pulmonary hypertension. Eur Respir J. 2019;53(1):1801915. https://doi.org/10.1183/13993003.01915-2018
3. Madani MM. Pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension: state-of-the-art 2020. Pulm Circ. 2021;11(2):1–6. https://doi.org/10.1177/20458940211007372
4. Fernandes TM, Kim NH, Kerr KM, Auger WR, Fedullo PF, Poch DS, Yang J, Papamatheakis DG, Alotaibi M, Bautista MA, Pretorius VG, Madani MM. Distal vessel pulmonary thromboendarterectomy: results from a single institution. J Heart Lung Transplant. 2023;42:1112–9. https://doi.org/10.1016/J.HEALUN.2023.02.1500
5. Pepke-Zaba J, Delcroix M, Lang I, Mayer E, Jansa P, Ambroz D, Treacy C, D'Armini AM, Morsolini M, Snijder R, Bresser P, Torbicki A, Kristensen B, Lewczuk J, Simkova I, Barberà JA, de Perrot M, Hoeper MM, Gaine S, Speich R, Gomez-Sanchez MA, Kovacs G, Hamid AM, Jaïs X, Simonneau G. Chronic thromboembolic pulmonary hypertension (CTEPH): results from an international prospective registry. Circulation. 2011;124(18):1973–81. https://doi.org/10.1161/CIRCULATIONAHA.110.015008
6. Kerr KM, Elliott CG, Chin K, Benza RL, Channick RN, Davis RD, He F, LaCroix A, Madani MM, McLaughlin VV, Park M, Robbins IM, Tapson VF, Terry JR, Test VJ, Jain S, Auger WR. Results from the United States Chronic Thromboembolic Pulmonary Hypertension Registry: enrollment characteristics and 1-year follow-up. Chest. 2021;160(5):1822–31. https://doi.org/10.1016/j.chest.2021.05.052
7. Guth S, D'Armini AM, Delcroix M, Nakayama K, Fadel E, Hoole SP, Jenkins DP, Kiely DG, Kim NH, Lang IM, Madani MM, Matsubara H, Ogawa A, Ota-Arakaki JS, Quarck R, Sadushi-Kolici R, Simonneau G, Wiedenroth CB, Yildizeli B, Mayer E, Pepke-Zaba J. Current strategies for managing chronic thromboembolic pulmonary hypertension: results of the worldwide prospective CTEPH registry. ERJ Open Res. 2021;7(3):00850-2020. https://doi.org/10.1183/23120541.00850-2020

8. Quadery SR, Swift AJ, Billings CG, Thompson AAR, Elliot CA, Hurdman J, Charalampopoulos A, Sabroe I, Armstrong IJ, Hamilton N, Sephton P, Garrad S, Pepke-Zaba J, Jenkins DP, Screaton N, Rothman AM, Lawrie A, Cleveland T, Thomas S, Rajaram S, Hill C, Davies C, Johns CS, Wild JM, Condliffe R, Kiely DG. The impact of patient choice on survival in chronic thromboembolic pulmonary hypertension. Eur Respir J. 2018;52(3):1800589. https://doi.org/10.1183/13993003.00589-2018
9. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, Carlsen J, Coats AJS, Escribano-Subias P, Ferrari P, Ferreira DS, Ghofrani HA, Giannakoulas G, Kiely DG, Mayer E, Meszaros G, Nagavci B, Olsson KM, Pepke-Zaba J, Quint JK, Rådegran G, Simonneau G, Sitbon O, Tonia T, Toshner M, Vachiery JL, Vonk Noordegraaf A, Delcroix M, Rosenkranz S. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Respir J. 2022;61:2200879. https://doi.org/10.1183/13993003.00879-2022
10. Lang IM, Andreassen AK, Andersen A, Bouvaist H, Coghlan G, Escribano-Subias P, Jansa P, Kopec G, Kurzyna M, Matsubara H, Meyer BC, Palazzini M, Post MC, Pruszczyk P, Räber L, Roik M, Rosenkranz S, Wiedenroth CB, Redlin-Werle C, Brenot P. 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(29):2659–71. https://doi.org/10.1093/EURHEARTJ/EHAD413
11. Martin EC, Diamond NG, Casarella WJ. Percutaneous transluminal angioplasty in non-atherosclerotic disease. Radiology. 1980;135(1):27–33. https://doi.org/10.1148/RADIOLOGY.135.1.6127750
12. Rao PS. Transcatheter treatment of pulmonary stenosis and coarctation of the aorta: experience with percutaneous balloon dilatation. Heart. 1986;56(3):250–8. https://doi.org/10.1136/hrt.56.3.250
13. Voorburg JAI, Cats VM, Buis B, Bruschke AVG. Balloon angioplasty in the treatment of pulmonary hypertension caused by pulmonary embolism. Chest. 1988;94(6):1249–53. https://doi.org/10.1378/CHEST.94.6.1249
14. Feinstein JA, Goldhaber SZ, Lock JE, Ferndandes SM, Landzberg MJ. Balloon pulmonary angioplasty for treatment of chronic thromboembolic pulmonary hypertension. Circulation. 2001;103(1):10–3. https://doi.org/10.1161/01.CIR.103.1.10
15. Sugimura K, Fukumoto Y, Satoh K, Nochioka K, Miura Y, Aoki T, Tatebe S, Miyamichi-Yamamoto S, Shimokawa H. Percutaneous transluminal pulmonary angioplasty markedly improves pulmonary hemodynamics and long-term prognosis in patients with chronic thromboembolic pulmonary hypertension. Circ J. 2012;76(2):485–8. https://doi.org/10.1253/circj.CJ-11-1217
16. Kataoka M, Inami T, Hayashida K, Shimura N, Ishiguro H, Abe T, Tamura Y, Ando M, Fukuda K, Yoshino H, Satoh T. Percutaneous transluminal pulmonary angioplasty for the treatment of chronic thromboembolic pulmonary hypertension. Circ Cardiovasc Interv. 2012;5(6):756–62. https://doi.org/10.1161/CIRCINTERVENTIONS.112.971390
17. Mizoguchi H, Ogawa A, Munemasa M, Mikouchi H, Ito H, Matsubara H. Refined balloon pulmonary angioplasty for inoperable patients with chronic thromboembolic pulmonary hypertension. Circ Cardiovasc Interv. 2012;5(6):748–55. https://doi.org/10.1161/CIRCINTERVENTIONS.112.971077
18. Ogawa A, Satoh T, Fukuda T, Sugimura K, Fukumoto Y, Emoto N, Yamada N, Yao A, Ando M, Ogino H, Tanabe N, Tsujino I, Hanaoka M, Minatoya K, Ito H, Matsubara H. Balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension results of a multicenter registry. Circ Cardiovasc Qual Outcomes. 2017;10(11):e004029. https://doi.org/10.1161/CIRCOUTCOMES.117.004029
19. Olsson KM, Wiedenroth CB, Kamp JC, Breithecker A, Fuge J, Krombach GA, Haas M, Hamm C, Kramm T, Guth S, Ghofrani HA, Hinrichs JB, Cebotari S, Meyer K, Hoeper MM, Mayer E, Liebetrau C, Meyer BC. Balloon pulmonary angioplasty for inoperable patients with chronic thromboembolic pulmonary hypertension: the initial German experience. Eur Respir J. 2017;49(6):1602409. https://doi.org/10.1183/13993003.02409-2016
20. Brenot P, Jaïs X, Taniguchi Y, Garcia Alonso C, Gerardin B, Mussot S, Mercier O, Fabre D, Parent F, Jevnikar M, Montani D, Savale L, Sitbon O, Fadel E, Humbert M, Simonneau G. French experience of balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension. Eur Respir J. 2019;53(5):1802095. https://doi.org/10.1183/13993003.02095-2018
21. Poch DS, Mahmud E, Patel M, Papamatheakis D, Fernandes T, Kerr K, Yang J, Pretorius V, Madani MM, Kim NH. Patient selection for balloon pulmonary angioplasty: six-year results from a high volume PTE surgical center. Pulm Circ. 2022;12(4):e12148. https://doi.org/10.1002/PUL2.12148
22. Bautista A, Kasahara A, Fernandes TM, Hsiao A, Kerr KM, Kligerman SJ, Madani MM, Mahmud E, Papamatheakis DG, Patel M, Poch DS, Pretorius V, Yang J, Drcar T, Stinson M, Fedullo PF, Kim NH. Evolution towards multimodal treatment of chronic thromboembolic pulmonary hypertension: single high-volume united states center experience. Am J Respir Crit Care Med. 2021;203:A1632. https://doi.org/10.1164/ajrccm-conference.2021.203.1_meetingabstracts.a1632
23. Jaïs X, Brenot P, Bouvaist H, Jevnikar M, Canuet M, Chabanne C, Chaouat A, Cottin V, De Groote P, Favrolt N, Horeau-Langlard D, Magro P, Savale L, Prévot G, Renard S, Sitbon O, Parent F, Trésorier R, Tromeur C, Piedvache C, Grimaldi L, Fadel E, Montani D, Humbert M, Simonneau G. 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(0):961–71. https://doi.org/10.1016/S2213-2600(22)00214-4
24. Mahmud E, Behnamfar O, Ang L, Patel MP, Poch D, Kim NH. Balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension. Interv Cardiol Clin. 2018;7(1):103–17. https://doi.org/10.1016/j.iccl.2017.09.003
25. Kawakami T, Ogawa A, Miyaji K, Mizoguchi H, Shimokawahara H, Naito T, Oka T, Yunoki K, Munemasa M, Matsubara H. Novel angiographic classification of each vascular lesion in chronic thromboembolic pulmonary hypertension based on selective angiogram and results of balloon pulmonary

angioplasty. Circ Cardiovasc Interv. 2016;9(10):e003318. https://doi.org/10.1161/CIRCINTERVENTIONS.115.003318

26. Ejiri K, Ogawa A, Fujii S, Ito H, Matsubara H. Vascular injury is a major cause of lung injury after balloon pulmonary angioplasty in patients with chronic thromboembolic pulmonary hypertension. Circ Cardiovasc Interv. 2018;11(12):e005884. https://doi.org/10.1161/CIRCINTERVENTIONS.117.005884
27. Wiedenroth CB, Deissner H, Adameit MSD, Kriechbaum SD, Ghofrani HA, Breithecker A, Haas M, Roller F, Rolf A, Hamm CW, Mayer E, Guth S, Liebetrau C. Complications of balloon pulmonary angioplasty for inoperable chronic thromboembolic pulmonary hypertension: impact on the outcome. J Heart Lung Transplant. 2022;41(8):1086–94. https://doi.org/10.1016/j.healun.2022.05.002
28. Jain N, Sheikh MA, Bajaj D, Townsend W, Krasuski R, Secemsky E, Chatterjee S, Moles V, Agarwal PP, Haft J, Visovatti SH, Cascino TM, Rosenfield K, Nallamothu BK, Mclaughlin VV, Aggarwal V. Periprocedural complications with balloon pulmonary angioplasty. JACC Cardiovasc Interv. 2023;16(8):976–83. https://doi.org/10.1016/j.jcin.2023.01.361
29. Ejiri K, Ogawa A, Shimokawahara H, Matsubara H. Treatment of vascular injury during balloon pulmonary angioplasty in patients with chronic thromboembolic pulmonary hypertension. JACC Asia. 2022;2(7):831–42. https://doi.org/10.1016/J.JACASI.2022.08.011
30. Dorfmüller P, Günther S, Ghigna MR, Thomas de Montpréville V, Boulate D, Paul JF, Jaïs X, Decante B, Simonneau G, Dartevelle P, Humbert M, Fadel E, Mercier O. Microvascular disease in chronic thromboembolic pulmonary hypertension: a role for pulmonary veins and systemic vasculature. Eur Respir J. 2014;44(5):1275–88. https://doi.org/10.1183/09031936.00169113
31. Wiedenroth CB, Liebetrau C, Breithecker A, Guth S, Lautze HJF, Ortmann E, Arlt M, Krombach GA, Bandorski D, Hamm CW, Möllmann H, Mayer E. Combined pulmonary endarterectomy and balloon pulmonary angioplasty in patients with chronic thromboembolic pulmonary hypertension. J Heart Lung Transplant. 2016;35(5):591–6. https://doi.org/10.1016/j.healun.2015.10.030
32. Mercier O, Dubost C, Delaporte A, Genty T, Fabre D, Mitilian D, Girault A, Issard J, Astaneh A, Menager JB, Dauriat G, Mussot S, Jevnikar M, Jais X, Humbert M, Simonneau G, Dartevelle P, Ion I, Stephan F, Brenot P, Fadel E. Pulmonary thromboendarterectomy: The Marie Lannelongue Hospital experience. Ann Cardiothorac Surg. 2022;11(2):143–50. https://doi.org/10.21037/ACS-2021-PTE-20
33. Cannon JE, Su L, Kiely DG, Page K, Toshner M, Swietlik E, Treacy C, Ponnaberanam A, Condliffe R, Sheares K, Taboada D, Dunning J, Tsui S, Ng C, Gopalan D, Screaton N, Elliot C, Gibbs S, Howard L, Corris P, Lordan J, Johnson M, Peacock A, MacKenzie-Ross R, Schreiber B, Coghlan G, Dimopoulos K, Wort SJ, Gaine S, Moledina S, Jenkins DP, Pepke-Zaba J. Dynamic risk stratification of patient long-term outcome after pulmonary endarterectomy: results from the United Kingdom national cohort. Circulation. 2016;133(18):1761–71. https://doi.org/10.1161/CIRCULATIONAHA.115.019470
34. Astashchanka A, Kerr KM, Yang JZ, Bautista A, Papamatheakis DG, Poch DS, Kim NH, Pretorius VG, Madani MM, Fernandes TM. Repeat pulmonary thromboendarterectomy outcomes: A 15 year single center retrospective review. J Thorac Cardiovasc Surg. 2023;166(0):1512–9. https://doi.org/10.1016/j.jtcvs.2023.02.028
35. Kawakami T, Matsubara H, Shinke T, Abe K, Kohsaka S, Hosokawa K, Taniguchi Y, Shimokawahara H, Yamada Y, Kataoka M, Ogawa A, Murata M, Jinzaki M, Hirata K, Tsutsui H, Sato Y, Fukuda K. Balloon pulmonary angioplasty versus riociguat in inoperable chronic thromboembolic pulmonary hypertension (MR BPA): an open-label, randomised controlled trial. Lancet Respir Med. 2022;10(0):949–60. https://doi.org/10.1016/S2213-2600(22)00171-0
36. Sadushi-Kolici R, Jansa P, Kopec G, Torbicki A, Skoro-Sajer N, Campean IA, Halank M, Simkova I, Karlocai K, Steringer-Mascherbauer R, Samarzija M, Salobir B, Klepetko W, Lindner J, Lang IM. Subcutaneous treprostinil for the treatment of severe non-operable chronic thromboembolic pulmonary hypertension (CTREPH): a double-blind, phase 3, randomised controlled trial. Lancet Respir Med. 2019;7(3):239–48. https://doi.org/10.1016/S2213-2600(18)30367-9
37. Ogo T, Shimokawahara H, Kinoshita H, Sakao S, Abe K, Matoba S, Motoki H, Takama N, Ako J, Ikeda Y, Joho S, Maki H, Saeki T, Sugano T, Tsujino I, Yoshioka K, Shiota N, Tanaka S, Yamamoto C, Tanabe N, Tatsumi K. Selexipag for the treatment of chronic thromboembolic pulmonary hypertension. Eur Respir J. 2021;60(1):2101694. https://doi.org/10.1183/13993003.01694-2021
38. Ghofrani HA, Simonneau G, D'Armini AM, Fedullo P, Howard LS, Jaïs X, Jenkins DP, Jing ZC, Madani MM, Martin N, Mayer E, Papadakis K, Richard D, Kim NH, Lang I, Kähler C, Delcroix M, Bshouty Z, Varela PS, Jing ZC, Yang Y, Liu J, Zhang G, Zhang N, Mi Y, Zhu X, Jansa P, Jaïs X, Prévot G, Bouvaist H, Sanchez O, Grimminger F, Held M, Wilkens H, Rosenkranz S, Grünig E, Karlócai K, Temesvári A, Edes I, Aidietienė S, Miliauskas S, Zamudio TRP, Sanchez CJ, Noordegraaf AV, Lewczuk J, Podolec P, Kasprzak J, Mularek-Kubzdela T, Grzywna R, Dheda K, Moiseeva O, Chernyavskiy A, Shipulin V, Barbarash O, Martynyuk T, Kim HK, Park JB, Lee JS, Speich R, Ulrich S, Aubert JD, Phrommintikul A, Jaimchariyatam N, Sompradeekul S, Onen ZP, Okumus G, Solovey L, Gavrysyuk V, Howard L, Pepke-Zaba J, Condliffe R, McConnell J, Kerr K, Nguyen LH, Pham NV. Macitentan for the treatment of inoperable chronic thromboembolic pulmonary hypertension (MERIT-1): results from the multicentre, phase 2, randomised, double-blind, placebo-controlled study. Lancet Respir Med. 2017;5(10):785–94. https://doi.org/10.1016/S2213-2600(17)30305-3
39. Taniguchi Y, Jaïs X, Jevnikar M, Boucly A, Weatherald J, Brenot P, Planche O, Parent F, Savale L, Fadel E, Montani D, Humbert M, Sitbon O, Simonneau G. Predictors of survival in patients with not-operated chronic thromboembolic pulmonary hypertension. J Heart Lung Transplant. 2019;38(8):833–42. https://doi.org/10.1016/j.healun.2019.04.006
40. Wiedenroth CB, Rolf A, Steinhaus K, Adameit MSD, Kriechbaum SD, Haas M, Roller F, Hamm CW, Ghofrani HA, Mayer E, Breithecker A, Guth S, Liebetrau C. Riociguat and balloon pulmonary angioplasty improve

prognosis in patients with inoperable chronic thromboembolic pulmonary hypertension. J Heart Lung Transplant. 2023; 42(1):134–9. https://doi.org/10.1016/j.healun.2022.08.011

41. Wiedenroth CB, Olsson KM, Guth S, Breithecker A, Haas M, Kamp JC, Fuge J, Hinrichs JB, Roller F, Hamm CW, Mayer E, Ghofrani HA, Meyer BC, Liebetrau C. Balloon pulmonary angioplasty for inoperable patients with chronic thromboembolic disease. Pulm Circ. 2018;8(1):1–6. https://doi.org/10.1177/2045893217753122
42. Inami T, Kataoka M, Kikuchi H, Goda A, Satoh T. Balloon pulmonary angioplasty for symptomatic chronic thromboembolic disease without pulmonary hypertension at rest. Int J Cardiol. 2019;289:116–8. https://doi.org/10.1016/J.IJCARD.2019.04.080

How to cite this article: Yang JZ, Poch DS, Ang L, Mahmud E, Kim NH. Balloon pulmonary angioplasty in the current era of CTEPH treatment: how did we get here? Pulm Circ. 2023;13:e12312. https://doi.org/10.1002/pul2.12312