Novel Angiographic Classification of Each Vascular Lesion in Chronic Thromboembolic Pulmonary Hypertension Based on Selective Angiogram and Results of Balloon Pulmonary Angioplasty

Takashi Kawakami, MD, PhD; Aiko Ogawa, MD, PhD; Katsumasa Miyaji, MD, PhD;
Hiroki Mizoguchi, MD, PhD; Hiroto Shimokawahara, MD, PhD; Takanori Naito, MD;
Takashi Oka, MD; Kei Yunoki, MD, PhD; Mitsuru Munemasa, MD, PhD;
Hiromi Matsubara, MD, PhD

Background—Balloon pulmonary angioplasty (BPA) is an alternative therapy for patients with chronic thromboembolic pulmonary hypertension who are ineligible for standard therapy, pulmonary endarterectomy. Although there are several classifications of vascular lesions, these classifications are based on the features of the specimen removed during pulmonary endarterectomy. Because organized thrombi are not removed during balloon pulmonary angioplasty, we attempted to establish a new classification of vascular lesions based on pulmonary angiographic images. We evaluated the success and complication rate of BPA in accordance with the location and morphology of thromboembolic lesions.

Methods and Results—We reviewed 500 consecutive procedures (1936 lesions) of BPA in 97 patients with chronic thromboembolic pulmonary hypertension and investigated the outcomes of BPA based on the lesion distribution and the angiographic characteristics of the thromboembolic lesions, as follows: type A, ring-like stenosis lesion; type B, web lesion; type C, subtotal lesion; type D, total occlusion lesion, and type E, tortuous lesion. The success rate was higher, and the complication rate was lower in ring-like stenosis and web lesions. The total occlusion lesions had the lowest success rate. Tortuous lesions were associated with a high complication rate and should be treated only by operators with extensive experience with BPA.

Conclusions—We modified the previous angiographic classification and established a new classification for each vascular lesion. We clarified that the outcome and complication rate of the BPA are highly dependent on the lesion characteristics. (*Circ Cardiovasc Interv*. 2016;9:e003318. DOI: 10.1161/CIRCINTERVENTIONS.115.003318.)

Key Words: angiography ■ angioplasty ■ arterial pressure ■ coronary artery disease ■ hypertension, pulmonary

Chronic thromboembolic pulmonary hypertension (CTEPH) is classified into group 4 as a cause of pulmonary hypertension according to the latest guideline for pulmonary hypertension.[1] It results from organized thrombi causing pulmonary artery stenosis/occlusion and leads to abnormal pulmonary blood flow distribution in lung perfusion scanning. Furthermore, it results in pulmonary hypertension, hypoxia, and right ventricular failure.[2] If left untreated, the 3-year survival rate for patients with a mean pulmonary arterial pressure of ≥30 mm Hg at the time of definitive diagnosis is poor.[3,4] Pulmonary endarterectomy (PEA) is the only curative treatment for selected CTEPH patients.[2] Although the mortality rate among the most experienced institutes is as low as 2.2%,[5] these excellent outcomes are not applicable worldwide, where it can be as high as 14.3%.[6–9] Moreover, the rate of inoperable CTEPH varies from 12.0% to 60.9%.[9]

Balloon pulmonary angioplasty (BPA) is an alternative therapy for CTEPH patients who are ineligible for PEA.[10,11] Recently, the efficacy of BPA in improving hemodynamics and exercise capacity has been established by case series reported by several groups, including our group.[12,13] There is a learning curve to safely and successfully perform BPA, as previously mentioned.[12] As our group has accumulated experience with BPA, we noted that some types of lesions were associated with better BPA success and a lower rate of complications when compared with other types of lesions. This is similar to the variance in outcomes and complications associated with specific types of lesions when performing percutaneous coronary intervention (PCI) for patients with coronary artery diseases. PCI is performed based on a classification of coronary angiogram. In PCI, a classification of lesion type based on the success rate of the procedure is widely used.[14] There are several classifications

WHAT IS KNOWN

- Recently, balloon pulmonary angioplasty (BPA) emerged as a new therapeutic option for patients with chronic thromboembolic pulmonary hypertension.
- Small observational clinical studies from different centers consistently show improvement in hemodynamics after BPA.
- There is limited information on the success and complication rate of BPA based on the type of pulmonary artery lesion defined by angiography.

WHAT THE STUDY ADDS

- We reclassified thromboembolic lesions of chronic thromboembolic pulmonary hypertension into 5 types based on the morphology of the vessels by modifying the widely used previous angiographic classification.
- This study demonstrates that the location and morphology of the thromboembolic lesion influence the outcome and complication rate of BPA.

of CTEPH lesions.[1,15] However, these classifications are based on the features of specimen removed from patients with CTEPH at the time of PEA. Because the organized thrombi are not removed during BPA and because we are able to evaluate lesions only by pulmonary angiographic images when performing BPA, we consider that it is necessary to establish a new classification for CTEPH lesions to help guide BPA. Therefore, we evaluated the success and complication rate of BPA according to the location and morphology of thromboembolic lesions based on a novel angiographic classification for BPA.

Methods

Patient Selection

Ninety-seven consecutive patients with CTEPH who underwent BPA and who completed all procedures required to treat CTEPH between November 2004 and July 2012 at the National Hospital Organization Okayama Medical Center were enrolled in this study. BPA was performed after the approval of the Institutional Review Board, and written informed consent was obtained from each patient before the procedure. The present study was approved by the Institutional Review Board of the National Hospital Organization Okayama Medical Center.

A diagnosis of CTEPH was based on detailed medical history, a physical examination, chest radiography, chest computed tomography, transthoracic echocardiography, lung ventilation–perfusion scintigraphy, right heart catheterization, and angiographic demonstration of multiple stenoses and obstructions of the bilateral pulmonary arteries.[12] All patients presented ventilation–perfusion mismatch on lung scintigraphy. All patients had World Health Organization functional class III or IV disease despite medical treatment.

Selective Pulmonary Angiography and BPA

We performed BPA using the biplane angiographic system (Allura Xper FD10/10; Phillips Electronics, Amsterdam, the Netherlands). Briefly, we placed a 9F indwelling sheath in a central vein (eg, internal jugular, subclavian, or femoral vein). A 6F long sheath was introduced into the pulmonary main trunk via the 9F sheath using

a 0.035-inch wire. Selective pulmonary angiography (PAG) was performed before BPA to confirm the location and the detail of the thromboembolic lesions. This was done by manual injection of 4 to 6 mL of nonionized contrast medium through the 6F guiding catheter. A Mach1 peripheral MP (Boston Scientific, Natick, MA) catheter was generally used as a guiding catheter. In cases of difficulty in engaging (eg, arteries in the left lingular segment or right middle lobe), we used a Mach1 AL1 (Boston Scientific) catheter. The contrast medium was injected from segmental arteries. Selective PAG and BPA were conducted using 8-inch images.

We attempted BPA for all the recognized thromboembolic lesions by selective PAG, which caused delayed flow. The procedure used for BPA has been described previously.[12] After a 0.014-inch wire was crossed across the targeted lesions, we evaluated and measured the target vessel characteristics and diameter by PAG in all lesions. After determination of the vessel diameter, we dilated the vessel using balloon catheters of appropriate size (1.25–8 mm). The balloon was inflated by hand until the indentation disappeared or until the balloon had fully expanded (2–22 atm). All patients underwent right-sided heart catheterization at baseline and after the final procedure of BPA.

Evaluation of Thromboembolic Lesion Characteristics

Three cardiologists who were not aware of the results of BPA evaluated the location and the morphology of the lesions on selective PAG images. The location of the lesions were evaluated as follows: whether they are located at the bifurcation of the pulmonary artery branches, which lobe they are located in, and whether they are located proximal or distal to the subsegmental pulmonary arteries. We classified the lesion morphology based on the lesion opacity and the blood flow distal to the lesion on PAG.

Quantitative Vascular Analysis of Pulmonary Arteries

Quantitative vascular analysis (QVA) was analyzed using the CAAS Workstation 7.2.1 (Pie Medical Imaging, Maastricht, the Netherlands), referenced to the diameter of the guiding catheter. The proximal reference diameter (PRD), the distal reference diameter (DRD), the reference diameter (RD), the minimal lumen diameter, the percent diameter stenosis (%DS), and the lesion length of the treated lesion on selective PAG were determined and calculated by 4 cardiologists who were not aware of the results of BPA. Also, the size and the inflated pressure of the balloons in each lesion were compared.

Definition of Success and Complication of BPA

We determined the success of the BPA procedure according to the success rate in passing the guidewire across the lesion and delivering the balloon catheter to the lesion. We defined complications resulted from BPA procedure as balloon injury of the lesion, wire injury or perforation of the vessel, or dissection of vessels by PAG. When vascular complications caused massive alveolar hemorrhage, it was observed on PAG; however, PAG was unable to detect submassive alveolar hemorrhage. Therefore, computed tomography was performed after BPA to assess for hemorrhage.

Statistical Analysis

Descriptive data are expressed as the means±SD for continuous variables and as percentages for categorical variables. The difference in the success and complication rate among lesion types was examined using Fisher exact probability test with Bonferroni method. The difference in QVA among lesion types was analyzed using Kruskal–Wallis test. All analyses were performed with IBM SPSS 20 (IBM, Armonk, NY). Statistical significance was defined as $P<0.05$.

Results

Patients' Clinical Characteristics

Clinical characteristics of patients are shown in Table 1. Among 97 patients, 87 patients were ineligible for PEA because of the distribution of thrombi and surgical inaccessibility. PEA was not performed in remaining 10 patients for the following reasons. High age in 3 patients, severe right heart failure in 3 patients, patients' refusal in 3 patients, and residual pulmonary hypertension after PEA in 1 patient. The mean age was 61.7±12.3 years, with a range of 19 to 82 years at study entry. Our study included 72 women (74%) and 25 men (26%) with inoperable CTEPH. The duration between diagnosis and study entry was 32.7±36.8 months. The median Borg score was 4 (range, 0.5–7). Eighty-two patients (85%) were treated with one or more number of specific pulmonary vasodilators. The comorbidities were as follows: hypertension (24 patients), dyslipidemia (18 patients), thyroid function disorder (12 patients), diabetes mellitus (10 patients), coagulopathy (7 patients), and heart failure (5 patients).

Outcome and Complications of BPA

We performed 500 BPA procedures for 97 CTEPH patients during the study period. We repeated BPA procedures until a sufficient amount of stenoses were corrected. The average number of BPA procedures was 5.2±3.1 (median, 5) per person. The improvements in clinical and hemodynamic parameters in patients who underwent BPA are shown in Table 2. World Health Organization functional class, exercise tolerance, and plasma brain natriuretic peptide levels were significantly improved, as we had reported previously.[12] Hemodynamic parameters, including mean pulmonary artery pressure, which defines prognosis, significantly improved after BPA procedures. We succeeded in decreasing mean pulmonary arterial pressure by >20 mm Hg to an absolute pressure of <25 mm Hg.

In 500 procedures, hemoptysis occurred in 98 procedures (19.6%). Pulmonary injury after BPA, characterized by hypoxia and newly developed radiographic opacities after BPA, occurred in 130 procedures (26.0% of all procedures) in 65 patients. Fifty-five patients had mild pulmonary injury, and remaining 10 patients had severe pulmonary injury required the intubation in 10 procedures. Among these 10 procedures, percutaneous cardiopulmonary support was also required to maintain the patients' oxygenation in 7 procedures. Four patients died in hospital because of deterioration of right heart failure after BPA.

Classification of the Pulmonary Thromboembolic Lesions Based on PAG

The number of targeted lesions for BPA was 1936 during 500 procedures. We classified the lesion morphology based on the lesion opacity and the blood flow distal to the lesion on PAG as follows: type A, ring-like stenosis lesion; type B, web lesion; type C, subtotal lesion; type D, total occlusion lesion; and type E, tortuous lesion (Figure 1; Table 3). Type A–D lesions were located proximal to the subsegmental pulmonary artery, namely, the segmental and subsegmental arteries. Type E lesions were located distal to the subsegmental arteries. In addition, we evaluated the treated lesions by QVA.

Type A ring-like stenosis lesions are localized lesions with concentric stenosis of the vessel, as if a ring were put on the vessel (Figure 1A; Movie I in the Data Supplement). Organized ring-like thrombus forms these lesions.[16] The diameter distal to the lesion is similar to that proximal to the lesion, and the vessel distal to the lesion is opacified without delay.

In QVA, RD and DRD of ring-like stenosis was the largest in stenotic lesions (ring-like, web, and tortuous lesion; P<0.01). The difference between PRD and DRD is small. %DS was the largest, and lesion length was the shortest in stenotic lesions because of the localized lesions (P<0.01). The size and the inflated pressure of the balloons for BPA were 4.0 mm and 12 atm.

Type B web lesions are slit, hazy, or abrupt narrowing opacity of the vessel (Figures 1B and 2, Movie II in the Data Supplement). The opacity appears as if the organized thrombi forms a longitudinal defect of opacification (Figure 2A; Movie III in the Data Supplement), complex mesh (Figures 1B and 2B; Movie IV in the Data Supplement), or abrupt narrowing (Figure 2C; Movie V in the Data Supplement) within the vessel. The flow distal to the lesion is disturbed but reaches equal or more than half of the distance between the lesion and the pleura in the longest pulmonary artery distal to the lesion but images narrower than that in the proximal to the lesion.

PRD and minimal lumen diameter were similar to that of ring-like stenosis. DRD and RD were smaller than that of ring-like stenosis. %DS was smaller than that of ring-like stenosis. The size and the inflated pressure of the balloons were significantly smaller than those of ring-like stenosis (P<0.01).

Type C subtotal lesions are tapered and almost completely occluded but have subtle and slow blood flow distal to the obstruction, as if blood flow leaks from the occluded vessel (Figure 1C; Movie VI in the Data Supplement). The flow distal to the lesion reaches to less than half of the distance between lesion and the pleura in the longest pulmonary artery.

PRD was similar to that of ring-like stenosis. Because the distal part of vessel was not completely visualized, other parameters of QVA were not obtainable. The size of the balloons for BPA procedures was similar to that of web lesion. The inflated pressure of the balloons was similar to that of ring-like stenosis.

Type D total occlusion lesions are concaved obstructions of segmental arteries (Figure 1D; Movie VII in the Data Supplement). The organized thrombi obstruct the vessel proximal to the segmental arteries. The distal vessel is not visible.

PRD was the largest in all targeted lesions (P<0.01). Because distal vessels were occluded, other parameters of QVA were not obtainable. The size and the inflated pressure of the balloons were similar to those of ring-like stenosis.

Type E tortuous lesions have no lesions proximal to the subsegmental arteries. There are web lesions with highly tortuous small vessels distal to subsegmental arteries, surrounded by cotton wool–like stains of capillary arteries (Figure 1E; Movie VIII in the Data Supplement).

In QVA of the tortuous lesions, PRD was the smallest in all lesions because of positioning distal to subsegmental arteries (P<0.01). %DS was the smallest in the stenotic lesions.

Table 1. Patients' Clinical Characteristics at Baseline

Total Number of Patients	97
Age, y	61.7±12.3
Male sex, n (%)	25 (25.8)
Duration between diagnosis and study entry, mo	32.7±36.8
Heart rate, bpm	73.6±12.9
Systolic blood pressure, mm Hg	111.8±15.9
Peripheral oxygen saturation, %	96.3±3.2
Borg score, median (range)	4 (0.5–7)
Serum creatinine level, mg/dL	0.9±0.9
Treatment	
Oral PGI$_2$, n (%)	49 (50.5)
Intravenous PGI$_2$, n (%)	9 (9.3)
ERA, n (%)	46 (47.4)
PDE5 inhibitor, n (%)	35 (36.1)
Number of PAH targeted drugs: 1, n (%)	35 (36.1)
Number of PAH targeted drugs: 2, n (%)	37 (38.1)
Number of PAH targeted drugs: 3, n (%)	10 (10.3)
Diuretics, n (%)	74 (76.3)
Warfarin, n (%)	97 (100)

Values other than Borg score are expressed as mean±SD. Borg score is presented as the median and the range. ERA indicates endothelin receptor antagonist; PAH, pulmonary arterial hypertension; PDE5, phosphodiesterase type 5; and PGI$_2$, prostacyclin.

Lesion length was similar to that of web lesion. The size of balloon was the smallest in all targeted lesions.

Number and Distribution of Each Lesion Type

The number of BPA-targeted lesions classified by our classification and the distribution of targeted vessels and lesion characteristics are shown in Table 3. Thromboembolic web-type lesions were observed more frequently than other types. Total occlusion and tortuous lesions were observed less frequently. Most thromboembolic lesions were located at the bifurcation of the pulmonary artery branches, except for tortuous lesions. The BPA-targeted vessels were distributed more dominantly in the right lobe (1197 lesions) than in the left lobe (739 lesions). Ring-like stenosis lesions were observed mostly in the right upper lobe. Web and subtotal lesions were distributed dominantly in the lower lobes. Numbers and types of thromboembolic lesions in each patient are shown in the Table I in the Data Supplement.

Success Rate and Complication Rate Among the Lesion Types

BPA procedure succeeded in 94.3% of all the targeted lesions. We compared the success and complication rate of BPA among different lesion types (Table 3). The success rate was dependent on the lesion type. In ring-like stenosis and web lesions, almost all BPA procedures were successful. On the contrary, the success rate in total occlusion and tortuous lesions was only 52.2% and 63.6%, respectively, which was significantly lower than that of the other lesion types.

Complications related to BPA include balloon injury, wire injury and perforation, and dissection of vessels (Figure 3). The complication rate was also dependent on the lesion type (Table 3). The compilation rate was 15.5% for subtotal lesions and <3% for ring-like stenosis and web lesions. The complication rate was the highest for tortuous lesion (>40%).

Discussion

In 1988, a special report was issued by the American College of Cardiology/American Heart Association Task Force on the Assessment of Diagnostic and Therapeutic Cardiovascular Procedures regarding PCI.[14] At that time, PCI was rapidly emerging as an alternative means of achieving myocardial revascularization. The subcommittee reviewed indications and developed guidelines for the use of PCI at that time and warned that there was some inappropriate broadening of the indications for PCI and overuse of PCI. They clearly described angiographic patterns, outlining the morphological characteristics of vessels and defining lesion-specific characteristics that greatly influenced the likelihood of a successful dilation. Furthermore, the subcommittee proposed a lesion-specific classification as a guide to estimate the likelihood of a successful procedure and the likelihood of developing abrupt vessel closure. That classification (types A–C) has been widely used for the evaluation coronary artery lesions for ≈30 years.

Recently, we are witnessing a worldwide expansion of the use of BPA for patients with CTEPH who are unsuitable for curative treatment of PEA.[12,17–19] Although the prevalence of CTEPH is much lower than that of coronary artery disease, the present situation with growing number of procedures of BPA might be similar to that at the time when the Task Force released the report on PCI for coronary artery diseases. As we perform more BPA procedures, we notify that differences in the morphology of the vessels in CTEPH influence the success and complication rate. Therefore, the goal of the present study

Table 2. Effect of BPA on Exercise Capacity and Hemodynamics

	Before BPA	After Final BPA	P Value
WHO functional class	3	2	<0.01
(I/II/III/IV)	(0/0/70/27)	(13/76/4/0)	
6MWD, m	276.3±123.2	359.3±91.9	<0.01
BNP, pg/mL	314.0±428.3	34.8±64.2	<0.01
sPAP, mm Hg	80.4±19.2	40.0±11.8	<0.01
dPAP, mm Hg	23.7±8.2	13.2±4.8	<0.01
mPAP, mm Hg	45.1±10.8	23.3±6.4	<0.01
RAP, mm Hg	8.1±4.4	2.2±2.5	<0.01
CI, L/min/m^2	2.2±0.7	3.1±0.6	<0.01
PVR, dyne·s/cm^5	960.6±457.8	314.5±150.4	<0.01

Values other than WHO functional class are expressed as mean±SD. WHO functional class is presented as the median and number of patients in each class. 6MWD indicates 6-min walk distance; BNP, B-type natriuretic peptide; BPA, balloon pulmonary angioplasty; CI, cardiac index; dPAP, diastolic pulmonary artery pressure; mPAP, mean pulmonary artery pressure; PVR, pulmonary vascular resistance; RAP, right pulmonary artery pressure; sPAP, systolic pulmonary artery pressure; and WHO, World Health Organization.
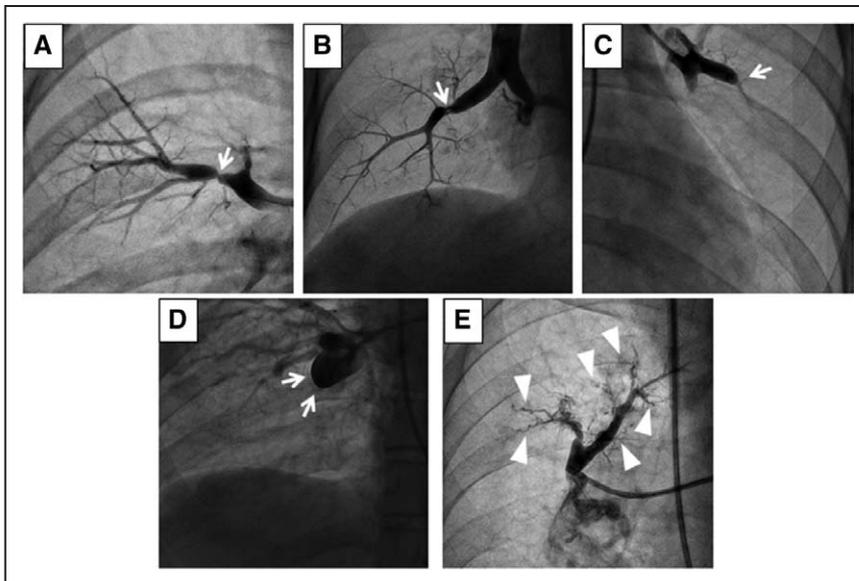
Figure 1. Angiographic classification of lesion morphology based on the lesion opacity and the blood flow distal to the lesion. **A**, Ring-like stenosis lesion. **B**, Web lesion. **C**, Subtotal lesion. **D**, Total occlusion lesion. **E**, Tortuous lesion. Type A–D lesions are located proximal to the subsegmental pulmonary artery, namely, the segmental and subsegmental arteries. Type E lesions are located distal to the subsegmental artery.

was to evaluate whether characteristics of specific lesions in patients with CTEPH affect the success and complication rate of BPA and establish the classification of CTEPH lesions useful in performing BPA as a guide to estimate the success and complication rate of BPA.

Several classifications of thromboembolic lesion in CTEPH have been proposed.[1,15,16] For example, CTEPH is classically divided into proximal type and distal type according to the location of the thromboembolic lesion.[1] Previously, proximal type disease was deemed accessible in PEA, whereas distal type was not accessible. This classification had been used widely because it is a simple method of determining whether PEA is indicated. However, the distinction can be unclear and can vary among individual centers and operators; as a result, this classification was not recommended in the previous guideline.[20] Instead, an operative classification of pulmonary thromboembolic lesions (types 1–4) based on their distribution in the excised tissue obtained during PEA has been widely used.[15] In this system, the outcomes of PEA are clearly dependent on the location and distribution of thromboembolic lesion. There is another classification of the local thromboembolic lesion that uses angiographic findings of CTEPH.[16] In that system, the thromboembolic lesions of lobar vessels in PAG of patients who underwent PEA were reviewed and classified into 5 types. The surgical findings were correlated with abnormal angiographic patterns. In this study, PAG was performed by a single injection of contrast medium into each main pulmonary artery with the catheter positioned in the main pulmonary arteries. Distal lesions in peripheral pulmonary arteries were not visualized clearly by this method.

In PEA, the lesions are often removed en bloc, even if there are various lesions in many pulmonary arteries.[5] However, excised tissue is not obtained during BPA, and the balloon is dilated at single lesions in a sequential fashion in BPA. Therefore, the characteristics of each lesion must be considered to determine how it should be treated, which is similar to the method used when treating coronary artery lesions with PCI. Subsequently, the success and complication rate differ for each targeted vessel and should be assessed individually. Therefore,

a novel classification of each lesion based on angiographic thromboembolic findings should be developed for BPA.

We modified the previous angiographic classification and established a new classification as follows: ring-like stenosis lesion, web lesion, subtotal lesion, total occlusion lesion, and tortuous lesion. Various types of thromboembolic lesions were present in the pulmonary vasculature of each patient. Thromboembolic lesions were located more dominantly in the right lower lobe and at the bifurcation of branches. The mechanism of the lesion-specific distribution is unclear. Fluid dynamic effects with turbulent flow might be involved in the progression of the lesion. Further studies are needed to elucidate the mechanism of disease progression.

We also evaluated each target lesion of pulmonary arteries by QVA, as we do in coronary arteries (Table 3). %DS was 58% in ring-like stenosis and <50% in web and tortuous lesions. %DS could not be measured in subtotal and total occlusion lesions. %DS and minimal lumen diameter in hazy lesions and slit appearance of lesions of pulmonary arteries cannot be accurately measured by QVA. In performing BPA, it is better to evaluate severity of the lesions by the perfusion delay of the distal arteries in PAG rather than using QVA.

We further clarified that the outcome and the complication rate of the BPA are highly dependent on the lesion characteristics. Vascular complications occurred in >40% of the tortuous lesion in this study. Most of the complications were caused by the guidewire, including vessel perforation. When performing BPA for tortuous lesions, the tip of the guidewire should be advanced to small vessels, meaning that even subtle motion causes guidewire-induced injury, such as perforation of the vessel. The tip of the guidewire swings with the heartbeat and can often cause injury of the vessel, especially in small vessels. Therefore, careful procedures are required when performing BPA for tortuous lesion. Even with this careful effort, the success rate is low for such lesions. The success rate for BPA is the lowest for the total occlusion lesion. Total occlusion lesions are best treated with PEA, and patients who had total occlusion lesions are candidates for BPA only when they have comorbidities that make them unsuitable candidates for

Table 3. Numbers and Distribution of Pulmonary Thromboembolic Lesions

Lesion Type	A	B	C	D	E
Description of Lesion Type	Ring-Like Stenosis	Web	Subtotal	Total Occlusion	Tortuous
Number, n	248	1235	342	67	44
Bifurcation lesion, n (%)	248 (100)	1092 (88.4)	301 (88.0)	61 (91.0)	0 (0)
Distribution (upper/middle or lingular/lower)					
Right lung, n	103/7/46	215/172/367	64/42/118	6/16/24	5/3/9
Left lung, n	29/0/63	61/22/398	13/6/99	0/2/19	6/1/20
QVA					
PRD, mm	3.7 (1.3–9.5)	3.7 (0.3–9.3)	3.8 (0.7–12.9)	4.8* (0.8–17.1)	2.8† (1.5–6.4)
DRD, mm	3.5 (0.3–8.2)	2.3‡ (0.1–11.1)	…	…	2.0‡ (0.8–4.4)
RD, mm	3.9 (0.7–8.3)	3.1‡ (0.1–8.3)	…	…	2.4‡ (1.1–5.0)
MLD, mm	1.6 (0.2–5.6)	1.6 (0.1–6.5)	…	…	1.6 (0.2–4.6)
%DS, %	58 (16–91)	45‡ (2–95)	…	…	39‡ (1–99)
Lesion length, mm	4.6 (1.4–14.8)	12.8‡ (2.0–49.6)	…	…	12.8‡ (0.2–27.8)
Used balloon					
Size, mm	4.0 (1.5–8)	3.5‡ (1.5–8)	3.5‡ (1.25–7)	4.0 (1.5–8)	2.0† (1.5–4.5)
Inflated pressure, atm	12 (2–22)	8‡ (2–18)	10 (2–20)	12 (3–18)	10 (2–16)
Success, n (%)	248 (100)	1219 (98.7)	296§ (86.5)	35‖ (52.2)	28 (63.6)
Complication, n (%)	4 (1.6)	27 (2.2)	53* (15.5)	4 (6.0)	19 (43.2)
Type of complication					
Balloon injury, n	3	7	5	0	0
Wire injury/perforation, n	0	12	41	4	19
Dissection of vessels, n	1	8	7	0	0

Values are presented as the median and the range. DRD indicates distal reference diameter; %DS, percent diameter stenosis; MLD; minimal lumen diameter; PRD, proximal reference diameter; QVA, quantitative vascular analysis; and RD, reference diameter.

*$P<0.05$ vs ring-like stenosis, web and subtotal lesions.

†$P<0.01$ vs ring-like stenosis, web, subtotal and total occlusion lesions.

‡$P<0.01$ vs ring-like stenosis.

§$P<0.01$ vs ring-like stenosis and web lesion.

‖$P<0.01$ vs ring-like stenosis, web and subtotal lesions.

PEA. Therefore, the incidence of total occlusion lesions in this study was low. The reason for the low complication rate is because the wire cannot pass the total occlusion lesion in many cases. The tortuous lesions are not good candidates for PEA but also not good targets for BPA because of the low success rate. It is better to treat such lesions with BPA, provided experienced operators are available.

The vascular complication rate is also higher for subtotal lesions than for ring-like stenosis and web lesions because the outline of the vessels distal to the lesion is ill defined in the context of a subtotal lesion. This makes handling of the guidewire difficult and causes worse outcomes for subtotal lesions. In ring-like and web lesions, the success rate is high and complication rate is low. Therefore, these lesion types can be universally treated with BPA.

We agree with the statement in the guidelines for PCI that because the technique of angioplasty is in evolution and the intermediate-term results are not yet fully elucidated, these recommendations are likely to change over the years. It is essential that physicians performing angioplasty and other
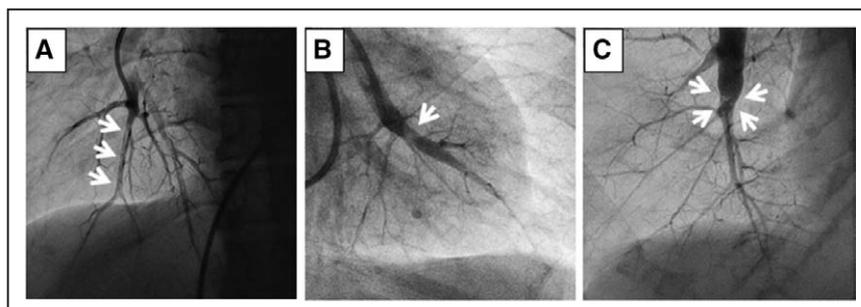

Figure 2. Examples of web lesion. The opacity shows as if the organized thrombi form a longitudinal defect (**A**), complex mesh (**B**), or abrupt narrowing (**C**) within the vessel.
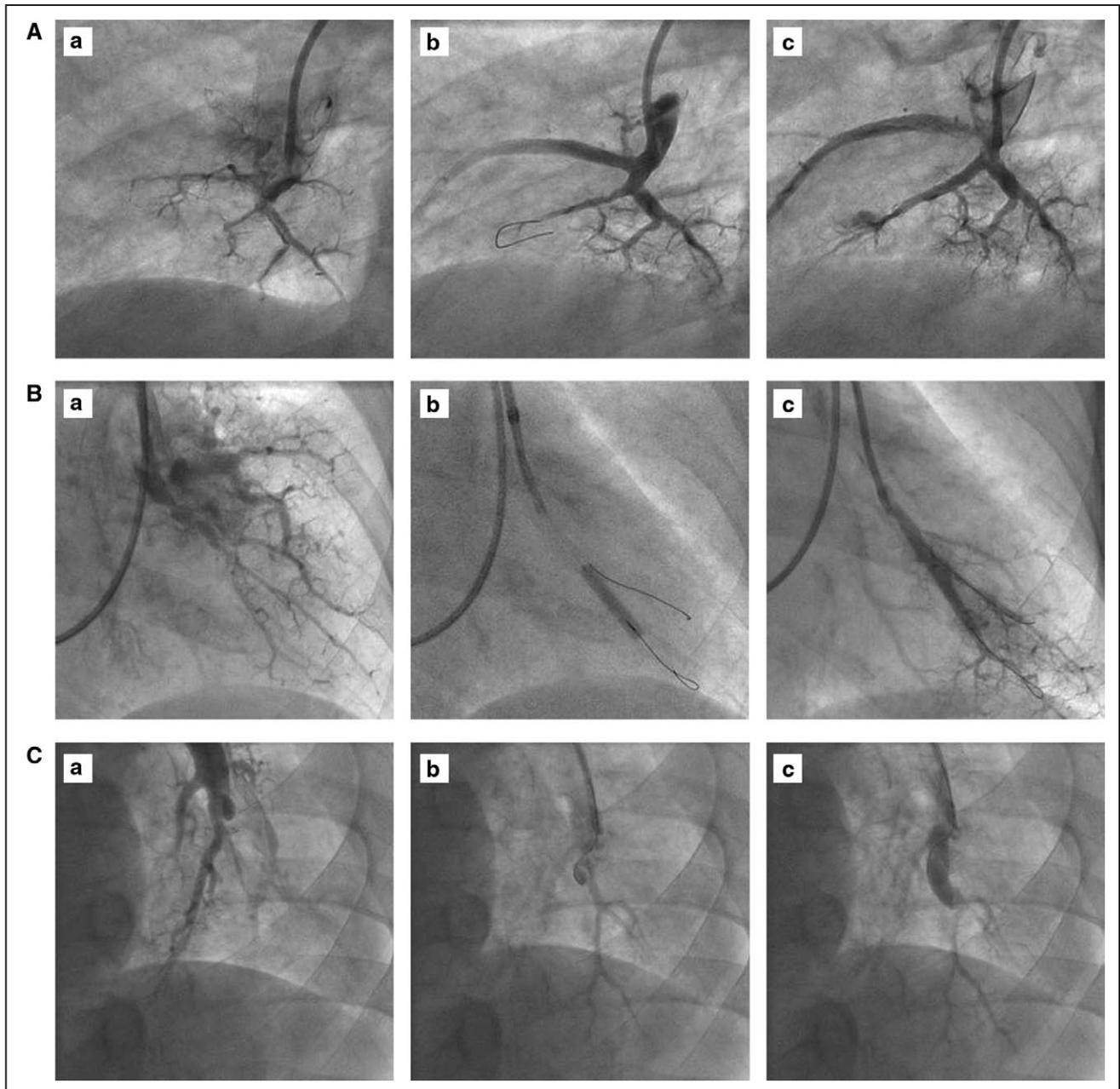
Figure 3. Representative angiographic images of complications of balloon pulmonary angioplasty (BPA). All the "a" parts show angiographic images before BPA. All the "b" parts show images during BPA when the complication occurs. All the "c" parts show images after the complication occurs. **A**, Wire injury and extravasation of contrast medium. At a subtotal lesion, the wire extends to the distal artery and injury occurs at the tip of the wire. **B**, Balloon injury. A web lesion, after inflation of the balloon, contrast medium pools, and stains. **C**, Dissection of vessels. At a subtotal lesion, after crossing the wire, dissection occurs, and the contrast medium stays at the site of dissection.

related procedures are adequately trained.[14] We need to understand the outcomes of severe complications (such as dissection or perforation of pulmonary arteries) and how to manage these complications when performing BPA for CTEPH.[21,22]

In conclusion, we reclassified thromboembolic lesions of CTEPH into 5 types by modifying the widely used previous angiographic classification and demonstrated that the outcome and complication rate of BPA are closely related to the location and morphology of the thromboembolic lesion. This novel classification might be helpful in developing strategies to perform BPA in patients with CTEPH who are unsuitable

for PEA. Further investigation within a multicenter prospective study is needed to evaluate the use of our classification.

Limitations

There are some limitations to this study. First, this study was conducted retrospectively at a single center with a limited number of patients. The reasonability of our classification should be confirmed within a multicenter prospective study. Second, data about the number and distribution of lesions may be biased. At the beginning, it was difficult to select arteries in the right middle lobe or the left lingual lobe. The number of

arteries accessed and success rate may improve after a learning curve.

Disclosures

Dr Ogawa received lecture fees from Bayer Yakuhin, Ltd, Pfizer Japan, Inc, Nippon Shinyaku, Co, Ltd, Actelion Pharmaceuticals Japan, Ltd, and GlaxoSmithKline K.K. Dr Miyaji received lecturer fees from Pfizer Japan, Inc, Actelion Pharmaceuticals Japan, Ltd, and GlaxoSmithKline K.K. Dr Matsubara received lecture fees from Bayer Yakuhin, Ltd, Pfizer Japan, Inc, Nippon Shinyaku, Co, Ltd, Actelion Pharmaceuticals Japan, Ltd, GlaxoSmithKline K.K., and Kaneka Medix Corporation. The other authors report no conflicts.

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Novel Angiographic Classification of Each Vascular Lesion in Chronic Thromboembolic Pulmonary Hypertension Based on Selective Angiogram and Results of Balloon Pulmonary Angioplasty

Takashi Kawakami, Aiko Ogawa, Katsumasa Miyaji, Hiroki Mizoguchi, Hiroto Shimokawahara, Takanori Naito, Takashi Oka, Kei Yunoki, Mitsuru Munemasa and Hiromi Matsubara

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