A 41-year-old man was referred to our hospital for the treatment of chronic thromboembolic pulmonary hypertension (CTEPH). On admission, he was in World Health Organization functional class III. Right heart catheterization demonstrated that pulmonary arterial pressure (systolic/diastolic/mean) was 140/42/71 mm Hg, cardiac index was 1.6 L/min/m² and pulmonary vascular resistance was 1663 dyn · s·cm⁻⁵. The patient had severe pulmonary hypertension and was considered inoperable because of peripheral organized thrombi and coexisting seminoma; therefore, balloon pulmonary angioplasty (BPA) was performed. After BPA, pulmonary angiography showed improvement of pulmonary arterial flow (Figure 1A). Pulmonary arterial pressure was 108/42/67 mm Hg and cardiac index was 2.5 L/min/m² when he returned to the cardiac care unit after BPA. His condition temporarily improved; however, 2 hours later, it deteriorated because of reperfusion pulmonary injury and gastrointestinal bleeding. He required mechanical ventilation and percutaneous cardiopulmonary support. To improve hemodynamics, another session of BPA was tried 9 days later (Figures 2A and 3A) and pulmonary arterial pressure seemed to improve to 83/48/58 mm Hg. However, he died from right heart failure on day 26 after BPA despite intensive care.

Histological analysis of the autopsy specimens showed recanalized thrombi in the bilateral elastic pulmonary arteries (Figure 4). Diffuse pulmonary arterial medial and intimal thickening were also observed in muscular pulmonary arteries. These findings are consistent with CTEPH and the diagnosis was confirmed. The arterial media was dissected near the lamina elastica interna by BPA (Figures 1B, 2B, and 3B). The organized thrombi were forced to one side and the dissection formed pseudovascular spaces that configured new lumina, which were larger than the original channels. Newly formed intima was observed on the inner surface of these pseudovascular spaces (Figures 1B-c, 2B-b, and 3B-b, black arrowheads).

According to the guidelines for the diagnosis and treatment of pulmonary hypertension, pulmonary endarterectomy is a standard therapy for patients with CTEPH with proximal thrombi. However, not all patients can undergo this curative surgery because of the presence of thrombi in distal pulmonary arteries, difficulty of the operation, or comorbidities. We have reported that BPA could improve hemodynamics in inoperable patients with CTEPH. However, it is unknown how pulmonary arteries are changed by BPA and the mechanism by which hemodynamic improvement is achieved, although thrombi are not removed from the affected arteries. We have recently reported a case in which we were able to examine a pulmonary artery in a single lobe after BPA. A pathological examination of the dilated lesion showed that the vascular lumen was dilated by a small incision and compression of the thrombi without dissection. In contrast, the histology of the present case demonstrated that the lumina were diluted by the dissection at a plane in the media (Figures 1B, 2B, 3B, and 5). Dissection at this plane is exactly what expert surgeons do in pulmonary endarterectomy. Importantly, this dissection was not obvious and was not recognized by pulmonary angiography just after BPA (Figures 1A-b, 2A-b, and 3A-d).

There was also a lesion where vascular lumen was diluted by a small incision without dissection in the present case (Figure 3B-b, white arrow), which is similar to our previously reported case. There is a difference in the angiographic lesion types between the pulmonary arteries where dissection occurred and did not occur. Lesion types of each pulmonary artery in CTEPH are determined by abnormal angiographic patterns: pouching defects, webs or bands, intimal irregularities, abrupt vascular narrowing, and complete vascular obstruction. Although we do not know whether mechanism of dilating pulmonary artery differ depending on angiographic lesion type, at least, web lesions in the present case (Figures 1A, 2A, and 3A, black arrows) were dilated by dissection made by BPA and band lesion was dilated without dissection.

In BPA, complete removal of organized thrombi is impossible but the present case suggested that dissection and compression...
of the thrombi would help improve blood flow and ultimately reduce pulmonary arterial pressure and vascular resistance. This case also suggests that in performing BPA, we need to be aware that we might dissect the pulmonary arteries, as in pulmonary endarterectomy, and take care not to make a tear in the arteries, which could cause massive hemorrhage. Taking it into consideration, it would be better not to use a balloon with a large diameter compared with the lesion diameter. This case provides insight into the mechanisms responsible for improvement of hemodynamics and the risk of causing vascular injury in BPA.

**Disclosures**

Dr Matsubara received lecturer fees from GlaxoSmithKline, Actelion Pharmaceuticals Japan and Nippon Shinyaku. The other authors report no conflicts.

**References**


**Key Words**

angioplasty ▶ pathology ▶ pulmonary hypertension ▶ thrombosis

---

**Figure 1.** Representative images of pulmonary angiography and histology of pulmonary arteries of the upper lobe of the right lung. **A**, Angiographic images before (a) and after (b) BPA. A web lesion of the right pulmonary artery (arrow) was treated by BPA. Angiography after BPA showed a dilated vessel and increased flow in the distal arteries. Arrows indicate the areas where specimen for **B** was obtained. **B**, Histology of a pulmonary artery treated by BPA (arrow in **A**). This lesion was treated by BPA at the initial session and second session (26 and 17 days before death). (a) Hematoxylin–eosin stain, low magnification. A large lumen was formed in a pulmonary artery by BPA. Bar, 1 mm. (b) Elastic tissue stain revealed that the dissection occurred in the media. Bar, 1 mm. (c) Elastic tissue stain. High magnification of the dissection site (square in **B**-b). Dissection occurred in the middle of media (arrow). Intima was newly formed on the inner surface (arrowheads). One of recanalized lumina in organized thrombi was also seen on the right.

**Figure 2.** Representative images of pulmonary angiography and histology of pulmonary arteries of the lower lobe of the left lung. **A**, Angiographic images before (a) and after (b) BPA. After BPA, a web of the pulmonary artery (arrow) was successfully treated and increased flow is shown in the distal arteries. **B**, Histology of a pulmonary artery treated by BPA (arrow in **A**). This lesion was treated by BPA at the second session (17 days before death). (a) Hematoxylin–eosin stain. A large lumen in the middle and several small lumina are observed in the left. A large lumen is thought to be made by BPA. Bar, 200 μm. (b) Elastic tissue stain. Dissection occurred in the media near the lamina elastica interna (arrow). A pseudovascular space, made by BPA, was enlarged and compressed microchannels against the arterial wall. Newly formed intima (arrowheads) was observed on the inner surface of the dissection lumen. Bar, 200 μm.
Figure 3. Representative images of pulmonary angiography and histology of pulmonary arteries of the lower lobe of the right lung. A, Angiographic images before (a), during (b and c) and after (d) BPA. A web (b) and band (c) lesions of the right pulmonary arteries were treated by balloon pulmonary angioplasty (BPA). Angiography after BPA showed vessels were dilated at the site of angioplasty. Arrows indicate the areas where specimen for B was obtained. B, Histology of a pulmonary artery treated by BPA 17 days before death. (a) Elastic tissue stain, low magnification. A specimen was made at bifurcation by a horizontal sectional view. Bar, 1 mm. (b) High magnification of a square in B-a. In a pulmonary artery with web lesion treated by BPA (on the left), dissection occurred in the media under the lamina elastica interna (black arrows). Newly formed intima (arrowheads) was observed on the inner surface. A large pseudovascular space was made by BPA and pre-existing microchannels are compressed toward an adjacent artery. The pulmonary artery with band lesion (on the right) was treated by BPA. A small incision (white arrow) is observed. This artery was dilated not by dissection but by enlargement of a preexist lumen. Bar, 1 mm.

Figure 4. Representative images of pulmonary angiography and histology of pulmonary arteries of the upper lobe of the left lung. A, An angiographic image of pulmonary arteries where BPA was not performed. Complete obstruction (arrow) is shown in the distal artery. B, Histology of a pulmonary artery (arrow in A). Elastic tissue stain. The elastic pulmonary artery, where BPA was not performed, exhibits luminal stenosis and an organized thrombus with small recanalized channels. Bar, 200 μm.

Figure 5. Schematic diagram of proposed mechanism of balloon pulmonary angioplasty (BPA) dilating pulmonary occlusive lesions. Structure of pulmonary artery with organized thrombus (green) and recanalized channels (left) is thought to be changed by BPA (right). The lumen is opened wide by dissection in the medial wall and the organized thrombus is compressed to one side. Newly formed intima (blue) covers the inner surface of the dissected pulmonary artery.
Histological Changes of Pulmonary Arteries Treated by Balloon Pulmonary Angioplasty in a Patient With Chronic Thromboembolic Pulmonary Hypertension
Masashi Kitani, Aiko Ogawa, Toshihiro Sarashina, Ichiro Yamadori and Hiromi Matsubara

doi: 10.1161/CIRCINTERVENTIONS.114.001533
Circulation: Cardiovascular Interventions is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-7640. Online ISSN: 1941-7632

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circinterventions.ahajournals.org/content/7/6/857

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Interventions can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.
Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints
Subscriptions: Information about subscribing to Circulation: Cardiovascular Interventions is online at:
http://circinterventions.ahajournals.org//subscriptions/