

Angioscopic Evaluation During Balloon Pulmonary Angioplasty in Chronic Thromboembolic Pulmonary Hypertension



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Background

Chronic thromboembolic pulmonary hypertension (CTEPH) is a progressive disorder with a poor prognosis. Recently, balloon pulmonary angioplasty (BPA) has been reported to be an effective treatment for inoperable patients with CTEPH. However, this catheter-based treatment has potentially life-threatening vascular complications. To improve the efficacy and safety of BPA, we assessed the morphological evaluation of organised thrombus and the vascular injury by BPA procedure.

Methods

In this study, we assessed the morphology of organised thrombi and the vascular injury observed by angiography during BPA in 28 lesions from nine CTEPH patients.

Results

Angioscopy visualised various forms of organised thrombi such as 'Mesh', 'Slit', 'Flap' and 'Mass' and allowed for a detailed evaluation of organised thrombus that was difficult to do by conventional contrast angiography. In addition, after balloon dilation for BPA, angiography revealed a haemorrhage due to a vessel wall injury caused by wiring and/or ballooning.

Conclusions

Assessment of organised thrombus and vascular injury by angiography might contribute to improving the treatment of the patients with CTEPH.

Keywords

Chronic thromboembolic pulmonary hypertension • Angioscopy • Balloon pulmonary angioplasty

Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is defined as the elevation of the pulmonary arterial pressure and pulmonary vascular resistance, caused by persistent unresolved pulmonary vascular obstruction. Patients with surgically accessible obstructions can undergo pulmonary endarterectomy, which is a potentially curative treatment with improvement of functional outcome and a

high survival rate [1–4]. Recently, balloon pulmonary angioplasty (BPA) was reported to improve the haemodynamics, exercise capacity, and symptoms of patients with inoperable CTEPH [5–8]. Despite a lack of long-term data, BPA has spread worldwide as an alternative intervention for inoperable CTEPH. However, this catheter-based treatment has potentially life-threatening vascular complications. To improve the efficacy and safety of BPA, accurate assessment of thrombotic lesions and vascular injury related to BPA

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procedure are required. In this study, we assessed the morphological evaluation of organised thrombus and the vascular injury observed by angioscopy during BPA.

Methods

We performed a non-obstructive angioscopy to directly observe lesion morphology and vascular injury during BPA. To obtain the angioscopic images, a 4-Fr probing catheter was advanced to the distal segment of the pulmonary artery under the guidance of a 0.014 inch guidewire supported with a 2.6-Fr micro-catheter. An imaging fibre (VISI-BLE, FiberTech Co., Ltd., Tokyo, Japan) was inserted into the probing catheter and advanced to the tip. To remove the blood from the visual field during image acquisition, low-molecular-weight dextran was infused from both of the 4-Fr probing catheter and the 6-Fr guiding catheter [9]. Subsequently, BPA was performed using the guide of intravascular ultrasonography (IVUS) to decide the correct balloon size.

We evaluated the morphological features of an organised thrombus and the vascular injury in nine patients with CTEPH (28 lesions) who underwent blood flow-maintaining angioscopy during BPA. Our institutional review board approved this study.

Results

Angioscopy could directly visualise the organised thrombus that was difficult to observe by angiography. Angioscopy revealed various types of organised thrombi (Figure 1). Red-coloured mural thrombi were observed even on anticoagulant therapy. The most frequently observed type was the 'mesh' organised white thrombus. The 'slit' thrombi had similar morphology to 'mesh' lesions. Angioscopy clearly visualised these filamentous thrombi, although pulmonary angiography and IVUS sometimes failed to detect 'slit' lesions due to their small size. 'flap' thrombi almost completely occupied the vessel lumen and blocked blood flow. Angioscopy revealed that this type of lesion was formed by a membrane of an organised thrombus that only occupied a small volume. 'Mesh', 'slit', and 'flap' thrombi appear to be good indications for balloon angioplasty because these thrombi can be easily compressed against the vessel wall by balloon dilation due to their small size. We also detected 'mass'-like thrombi that formed a solid mass. Since these lesions seem to be composed of a massive organised thrombus, balloon dilation alone is less likely to be effective.

Angioscopy performed after balloon dilatation revealed that the organised thrombus was disrupted and pushed against the vessel wall by balloon dilatation. This resulted in an enlargement of the lumen. However, we also found a haemorrhage due to balloon injury, guiding catheter injury, or dissection of the pulmonary artery (Figure 2A). After balloon dilation for BPA, angioscopy revealed a haemorrhage at the target lesion site due to a vessel wall injury.

Detection of vascular injury with a haemorrhage after BPA suggests that wiring and/or ballooning during this procedure can cause vessel wall damage or detach a strongly adherent organised thrombus. This presents the potential for bleeding complications such as parenchymal haemorrhage and haemoptysis.

Discussion

In this study, we demonstrated that various forms of organised thrombi in CTEPH can be observed by angioscopy which was difficult by angiography or IVUS in detail. Chronic thromboembolic pulmonary hypertension is a progressive disorder with a poor prognosis despite the recent progress of medical therapy such as soluble guanylate cyclase stimulators [10]. Balloon pulmonary angioplasty for inoperable CTEPH is now widely practiced, thus improvement in the safety of the BPA procedure is needed. Angioscopy might provide new insights into the detection of organised thrombus and the BPA procedure.

It was reported that the outcome and complication rates of BPA were dependent on the vascular lesion characteristics [11]. Cone-beam computed tomography (CT) can clearly depict thrombotic lesions and morphology of a thrombus in patients with CTEPH [12,13]. However, CT cannot evaluate the vascular complications during BPA. It is sometimes difficult to perform the detailed evaluation of organised thrombus and vascular injury only by conventional contrast angiography. Currently, several additional techniques such as IVUS and optical coherence tomography (OCT) are used to improve the management of BPA [14–16]. Although these imaging techniques are useful for the detection of thrombus as occupancy in the vessel, these devices are not enough to elucidate the vascular injury related to the BPA procedure.

Non-obstructive angioscopy is the only technique that directly and clearly visualises the vessel lumen and biological phenomena during BPA [9,17,18]. Pulmonary angiography only shows shadows of thrombus that appear as contrast defect. Assessment of the morphology of organised thrombi by angioscopy during BPA can accurately identify the thrombus, which is difficult in angiography and can assist to reduce unnecessary balloon dilatation to minimise vascular complications of BPA. Moreover, the detection of minor vascular injury by angioscopy during BPA might be able to avoid risk of further vessel damage due to additional balloon dilatation (Figure 2B).

We have some study limitations. First, the sample size is small and the association between the angioscopic observations and the efficacy of BPA was not evaluated. Second, the rate of bleeding due to vascular injury or the relationship between the vascular bleeding and reperfusion pulmonary injury are not well known. Further investigation is required to assess the utility of angioscopy for CTEPH.

In summary, we evaluated the morphological features of an organised thrombus and the procedural balloon injury by angioscopy in CTEPH patients undergoing BPA. Angioscopy

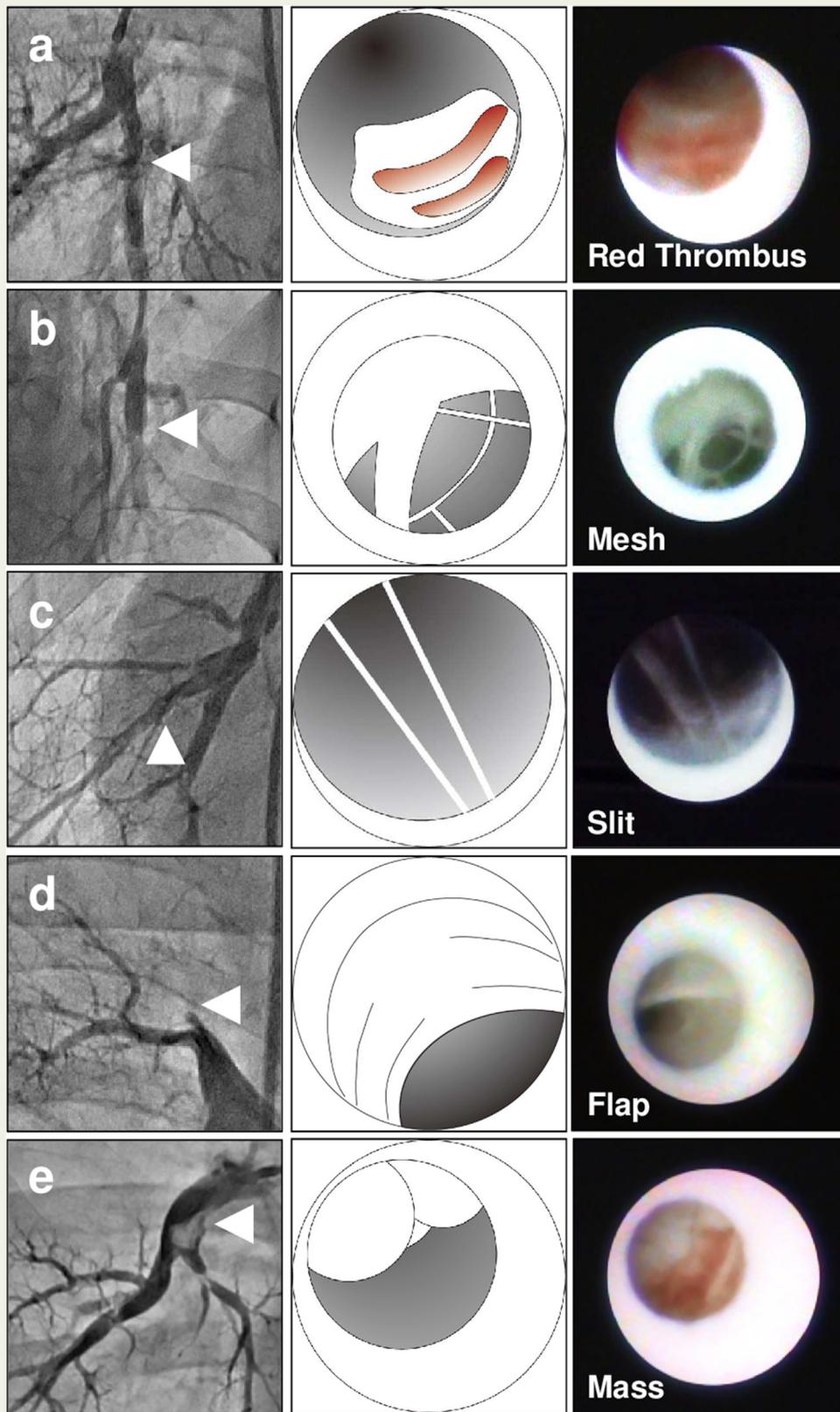


Figure 1 Various types of organised thrombi observed by angioscopy.

(a) Red thrombus; (b) Mesh thrombus; (c) Slit thrombus; (d) Flap thrombus; and (e) Mass-like thrombus. Left line: angiography, Middle line: scheme of organised thrombus, Right line: organised thrombi observed by angioscopy.

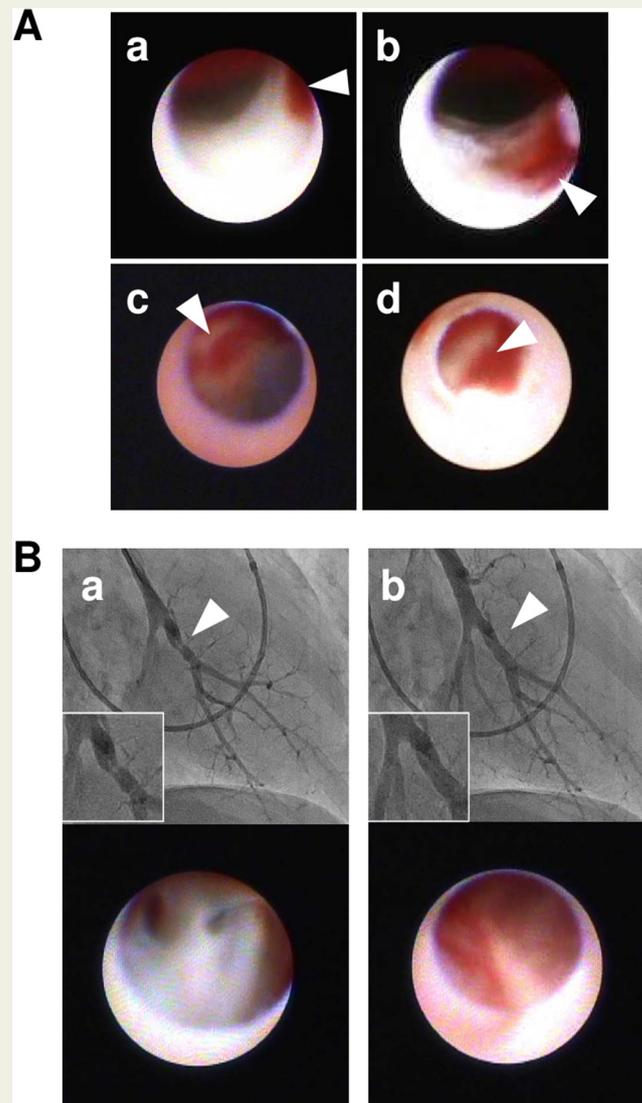


Figure 2 Vascular injury observed by angioscopy.

A: (a) Bleeding from a lesion without an organised thrombus; (b) Bleeding from the target lesion; (c) Guiding catheter injury; and (d) Dissection with bleeding.

B: Angiography and angioscopy before balloon pulmonary angioplasty (BPA) (a) and after BPA (b). Although angiography before BPA revealed organised thrombus as the translucent of contrast, angioscopy can detect the thrombus directly. After balloon dilation, we can see that, although slit-like translucent thrombus remains, blood flow is improved and no vascular complication is seen in contrast angiography. However, angioscopy can demonstrate the bleeding at the target lesion site due to a vessel wall injury.

directly revealed the morphology of various types of organised thrombus in detail that was difficult to evaluate by conventional pulmonary angiography. Angioscopy revealed a haemorrhage due to a balloon injury after BPA. Assessment of organised thrombus and vascular injury by angioscopy might contribute to improving the treatment of the patients with CTEPH.

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Disclosures

The authors declare no competing financial interests.

References

- [1] Freed DH, Thomson BM, Berman M, Tsui SS, Dunning J, Sheares KK, et al. Survival after pulmonary thromboendarterectomy: effect of residual pulmonary hypertension. *J Thorac Cardiovasc Surg* 2011;141:383–7.
- [2] Jamieson SW, Kapelanski DP, Sakakibara N, Manecke GR, Thistlethwaite PA, Kerr KM, et al. Pulmonary endarterectomy: experience and lessons learned in 1,500 cases. *Ann Thorac Surg* 2003;76:1457–62. discussion 62–4.

- [3] Bonderman D, Skoro-Sajer N, Jakowitsch J, Adlbrecht C, Dunkler D, Taghavi S, et al. Predictors of outcome in chronic thromboembolic pulmonary hypertension. *Circulation* 2007;115:2153–8.
- [4] Condliffe R, Kiely DG, Gibbs JS, Corris PA, Peacock AJ, Jenkins DP, et al. Improved outcomes in medically and surgically treated chronic thromboembolic pulmonary hypertension. *Am J Respir Crit Care Med* 2008;177:1122–7.
- [5] 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;5:748–55.
- [6] Fukui S, Ogo T, Morita Y, Tsuji A, Tateishi E, Ozaki K, et al. Right ventricular reverse remodelling after balloon pulmonary angioplasty. *Eur Respir J* 2014;43:1394–402.
- [7] Andreassen AK, Ragnarsson A, Gude E, Geiran O, Andersen R. Balloon pulmonary angioplasty in patients with inoperable chronic thromboembolic pulmonary hypertension. *Heart* 2013;99:1415–20.
- [8] Taniguchi Y, Miyagawa K, Nakayama K, Kinutani H, Shinke T, Okada K, et al. Balloon pulmonary angioplasty: an additional treatment option to improve the prognosis of patients with chronic thromboembolic pulmonary hypertension. *EuroIntervention* 2014;10:518–25.
- [9] Komatsu S, Ohara T, Takahashi S, Takewa M, Minamiguchi H, Imai A, et al. Early detection of vulnerable atherosclerotic plaque for risk reduction of acute aortic rupture and thromboemboli and atheroemboli using non-obstructive angioscopy. *Circ J* 2015;79:742–50.
- [10] Ghofrani HA, D'Armini AM, Grimminger F, Hoeper MM, Jansa P, Kim NH, et al. Riociguat for the treatment of chronic thromboembolic pulmonary hypertension. *N Engl J Med* 2013;369:319–29.
- [11] Kawakami T, Ogawa A, Miyaji K, Mizoguchi H, Shimokawahara H, Naito T, et al. 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.
- [12] Fukuda T, Ogo T, Nakanishi N, Ueda J, Sanda Y, Morita Y, et al. Evaluation of organized thrombus in distal pulmonary arteries in patients with chronic thromboembolic pulmonary hypertension using cone-beam computed tomography. *Jpn J Radiol* 2016;34:423–31.
- [13] Ogo T, Fukuda T, Tsuji A, Fukui S, Ueda J, Sanda Y, et al. Efficacy and safety of balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension guided by cone-beam computed tomography and electrocardiogram-gated area detector computed tomography. *Eur J Radiol* 2017;89:270–6.
- [14] Sugimura K, Fukumoto Y, Miura Y, Nochioka K, Miura M, Tatebe S, et al. Three-dimensional-optical coherence tomography imaging of chronic thromboembolic pulmonary hypertension. *Eur Heart J* 2013;34:2121.
- [15] Ishiguro H, Kataoka M, Inami T, Shimura N, Yanagisawa R, Kawakami T, et al. Diversity of lesion morphology in CTEPH analyzed by OCT, Pressure wire, and angiography. *JACC Cardiovasc Imaging* 2016;9:324–5.
- [16] Ikeda N, Kubota S, Okazaki T, Hara H, Hiroi Y. Comparison of intravascular optical frequency domain imaging versus intravascular ultrasound during balloon pulmonary angioplasty in patients with chronic thromboembolic pulmonary hypertension. *Catheter Cardiovasc Interv* 2016;87: E268–74.
- [17] Nakanishi N, Nakamura T, Yamano T, Shiraishi H, Matoba S, Matsumuro A, et al. Angioscopic observation in chronic thromboembolic pulmonary hypertension before and after balloon pulmonary angioplasty. *J Cardiovasc Med (Hagerstown)* 2016;17(Suppl 2). e129–e31.
- [18] Chibana H, Tahara N, Itaya N, Sasaki M, Sasaki M, Nakayoshi T, et al. Optical frequency-domain imaging and pulmonary angioscopy in chronic thromboembolic pulmonary hypertension. *Eur Heart J* 2016;37:1296–304.