Drug-coated balloon angioplasty for severe pulmonary vein stenosis resulting from cryoballoon ablation for atrial fibrillation

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Abstract: We performed a drug-coated balloon (DCB) angioplasty for severe pulmonary vein (PV) stenosis resulting from cryoballoon ablation for atrial fibrillation. Three and 14 months after the angioplasty, follow-up multidetector computed tomography did not show restenosis. Lesion regression was observed at 14-month follow-up. Two years after PV angioplasty with DCB, the patient was well without any symptoms. DCB angioplasty may become an alternative effective procedure for PV stenosis.

Learning objective: The usefulness and safety of DCB for severe pulmonary vein stenosis resulting from cryoballoon ablation for atrial fibrillation was observed at 14-month follow-up.

Introduction

Pulmonary vein (PV) stenosis is a known complication of PV isolation procedures for atrial fibrillation (AF). Frequent symptoms of PV stenosis include dyspnea, cough, chest pain, and hemoptysis. We often performed drug-coated balloon (DCB) angioplasty for stenosis of coronary artery and superficial femoral artery in daily practice. In the present report, we describe a case of DCB angioplasty for severe PV stenosis resulting from cryoballoon (CB, Artic Front Advance®, Medtronic Vascular, Santa Rosa, California) ablation for AF.

Case report

A 68-year-old male patient underwent second-generation CB ablation using a single 28-mm balloon for paroxysmal AF in our institution. CB application was performed once for each PV for 180 seconds. The balloon nadir temperature reached -55°C in the left superior pulmonary vein (LSPV), -41°C in the left inferior PV, -53°C in the right inferior PV, and -60°C in the right superior PV. The procedure was performed successfully without additional ablation.

After 9 months, multidetector computed tomography (MDCT) showed moderate stenosis in the LSPV (Fig. 1-A). Twelve months after the procedure, we performed an angioplasty for the LSPV, as MDCT showed that the stenosis of LSPV had progressed severely (Fig. 1-B) though the patient remained free from any symptoms attributable to PV stenosis. This procedure was approved by the Ethics Review Board at Tokushima University Hospital. The patient was pretreated with 75 mg clopidogrel. The initial angiography showed severe PV stenosis (Fig. 2-A1, 2). A 0.014-inch floppy guidewire with 4F multipurpose catheter was advanced through the orifice of the affected PV by the transseptal procedure after venous access. Gray scale and virtual histology intravascular ultrasound (VH-IVUS, Eagle Eye®, Volcano Corporation, Rancho Cordova, CA) showed the approximate vessel diameter (Fig. 2-C1) and fibrous and fibrofatty neointimal hyperplasia with little necrotic core and calcification in the stenotic lesion (Fig. 2-C2). Afterward, he was successfully treated with plain old balloon (Admiral extreme®: 7 × 20 mm, Medtronic Vascular, Santa Rosa, California) and DCB (Impact Admiral®: 7 × 40 mm, Medtronic Vascular, Santa Rosa, California, Fig. 2-A3). After the angioplasty, the stenotic lesion was dilated well (Fig. 2-A4, D) and the simultaneous pressure gradient of the distal site of the stenosis and left atrium decreased from 9 to 2 mmHg. Three (Fig. 3-A) and 14 (Fig. 3-B) months after the angioplasty, follow-up MDCT did not show restenosis, and lesion regression was also

observed at 14-month follow-up (Fig. 3-B). Two years after PV angioplasty with DCB, he was well without any symptoms, postoperative complications, and recurrent AF.

Discussion

The CB ablation system was introduced into clinical practice and the comparable efficacy of CB ablation to radiofrequency (RF) ablation was demonstrated. In RF ablation, PV stenosis results from thermal injury to the PVs that induces a progressive neointimal proliferation, proliferation of the elastic lamina, and myocardial fibrosis, resulting in endovascular contraction [1]. On the other hand, a previous study found that CB ablation had a lower risk of PV stenosis due to tissue shrinkage compared to RF ablation because of the preservation of the basic underlying tissue architecture with preserved endocardial contours and minimal cartilage formation after the ablation [1]. The prevalence of severe PV stenosis after CB ablation has been reported to be 1-4% [2,3].

Several predictors of the occurrence of severe PV stenosis after CB ablation were reported [2,3]. In the present study, horizontally connecting PV (the PV angle was 27°) and lower minimum freezing temperature (-55°C) were observed among those predictors.

The PV stenosis progressed from 9 to 12 months after the procedure in this case. A previous report [4] stated that the PV stenosis after CB ablation did not progress if 7 months after the procedure had passed. However, the report did not include the patients with any moderate (50-70%) or severe (>70%) PV stenosis. In the present case, the PV stenosis in the stenotic lesion was almost severe (67%) at 9 months after CB ablation. We speculate that the PV stenosis with moderate or severe stenosis after CB ablation might progress even if 9 months after the procedure have passed.

DCB angioplasty is performed in Japan for stenosis of coronary artery and superficial femoral artery. This technology is used for short-term transfer and long-term retention of

paclitaxel into the arterial wall, leading to suppression of neointimal proliferation. Recently, usage of DCB in other organs is increasing. The usefulness of DCB for PV stenosis after repair of total anomalous pulmonary venous return with asplenia was reported [5]. In the present report, we used a DCB for PV stenosis resulting from CB ablation. The mechanism of PV stenosis after CB ablation may be related to freezing injury to the tissue that induces fibrosis, scarring, and progressive neointimal proliferation. In the present study, IVUS imaging with VH mainly showed fibrosis in the stenotic lesion of PV. Judging from the characteristics of the stenotic lesion, we performed DCB angioplasty.

Lesion regression was observed at 14-month follow-up. Previous studies reported that the neointimal volume of the coronary artery tended to decrease beyond the intervention, as assessed at follow-up [6], and paclitaxel caused apoptosis and necrosis of endothelial and smooth muscle cells [7]. Due to these local effects of paclitaxel, patency of the lesion persists and may even improve at convalescent phase such as its effect on the coronary artery.

Stenting significantly reduces the risk of subsequent PV restenosis in comparison with plain old balloon angioplasty; however, performing stent implantation for focal ostial lesion may result in stent disruption, stent embolization, or endothelial trauma to adjacent normal segments of vein [8]. In the present study, IVUS imaging with VH mainly showed fibrosis in the stenotic lesion. DCB is often used for the suppression of vessel wall fibrosis after balloon injury and neointimal hyperplasia [9]. Therefore, we selected stentless PV angioplasty with DCB as a first therapy for the focal ostial stenotic lesion. Two years after PV angioplasty with DCB, he was well without any complications and recurrent AF.

The frequent symptoms owing to PV stenosis include dyspnea, cough, chest pain, and hemoptysis. In the present report, the patient remained free from any symptoms in spite of severe stenosis of PV; however, PV angioplasty was thought to be necessary to avoid

severe symptoms associated with future progression to pulmonary vein occlusion.

The optimal DCB size for de novo PV stenosis after ablation therapy is unclear. A previous report [10] stated that if the PV is less than approximately 5 to 8 mm, long-term successful patency is low. For larger veins, even if there is a severe stenosis, long-term patency rates are improved. In their experience, balloon dilations with an 8- to 10-mm balloon were routinely performed and the use of a balloon >12 mm significantly increased the risk of dissection or rupture. In this case, we chose a Φ7.0 mm balloon and a Φ7.0 mm DCB. IVUS showed that the short axis diameter of the reference vessel was 7.7 mm and the long axis diameter was 8.5 mm. Therefore, we used the largest (7.0 mm diameter) and shortest (40 mm length) DCBs available in Japan to match the dimensions of the stenotic lesion in the PV ostium due to concerns about the occurrence of dissection. If the choice of DCB size variations had been possible, the DCB with a diameter of 8.0 mm and a length of 20 mm should have been selected at that time to enhance the efficacy and safety of the DCB. It is expected that larger and shorter DCB will be developed in future. DCB angioplasty without stenting may become an alternative effective procedure for PV stenosis resulting from ablation therapy.

Conflict of interest

The authors declare no conflict of interest in association with the present study.

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Figure legends

Fig. 1

Multidetector computed tomography images. A: Nine months after the ablation. B: Twelve months after the ablation. White arrows indicate the stenotic lesion.

Fig. 2

A1: Angiography in left atrium. Pulmonary vein was not observed owing to severe stenosis of the orifice. A2: Angiography with multipurpose catheter in the distal site of the stenosis. A3: DCB angioplasty in the stenotic lesion. A4: Final angiography. White arrows indicate the stenotic lesion. DCB, drug-coated balloon

B: Multidetector computed tomography images just before the angioplasty. White arrows indicate the stenotic lesion.

C1: Gray-scale IVUS image of the stenotic lesion indicated that the short axis diameter of the reference vessel was 7.7 mm and the long axis diameter was 8.5 mm. White line

indicates outline of the vessel. White dotted line indicates outline of the lumen. C2: VH-IVUS image of the stenotic lesion. The image displays with 4 color codes: red for necrotic core, light green for fibrofatty tissue, dark green for fibrous tissue, and white for dense calcium.

D: Multidetector computed tomography images just after the angioplasty. White arrows indicate the stenotic lesion. IVUS, intravascular ultrasound; VH, virtual histology

Fig. 3

Multidetector computed tomography images. A: Three months after the angioplasty. B: Fourteen months after the angioplasty. White arrows indicate the stenotic lesion.

Fig. 1

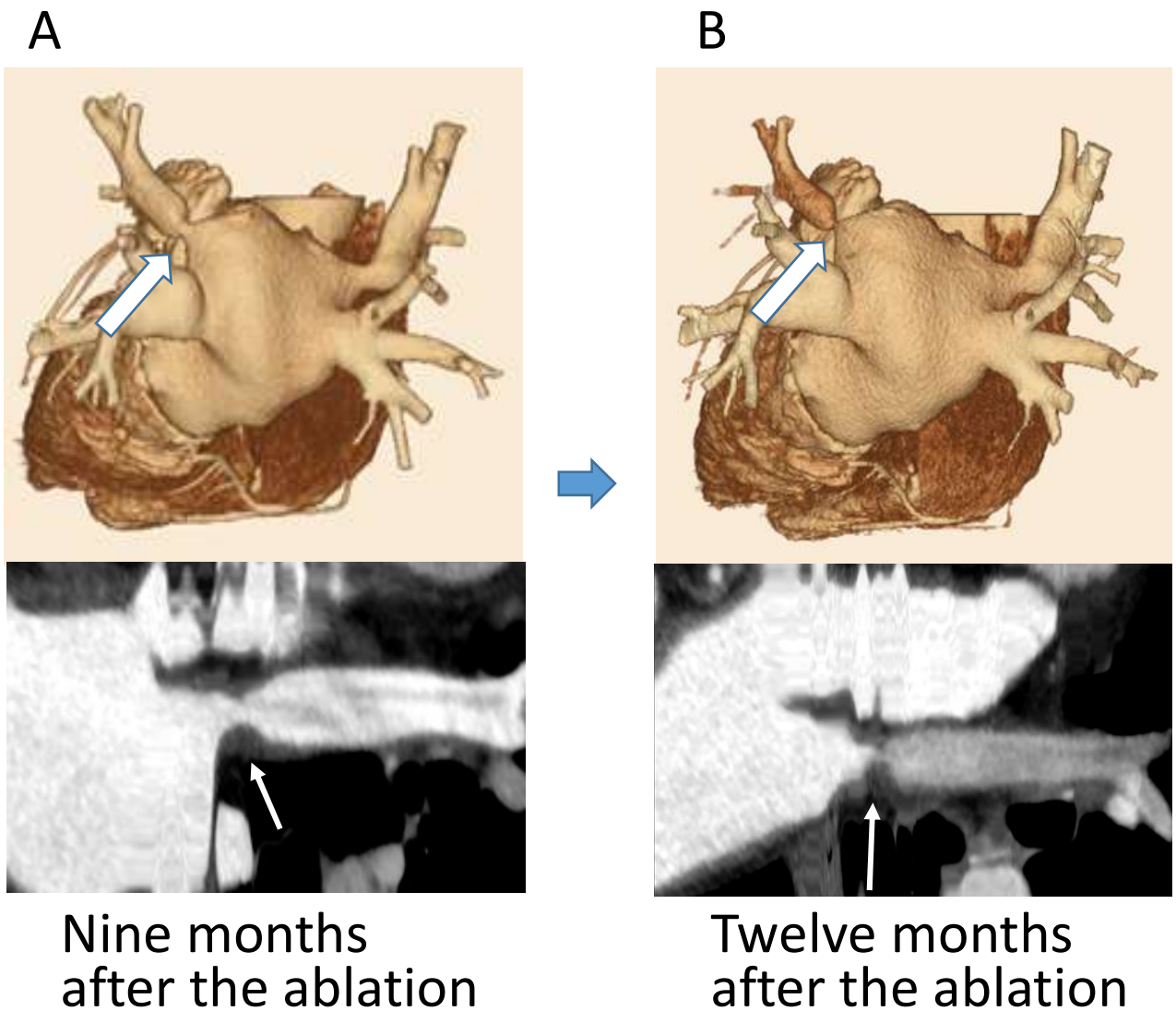

A
B
Nine months
after the ablation
Twelve months
after the ablation

Fig. 2

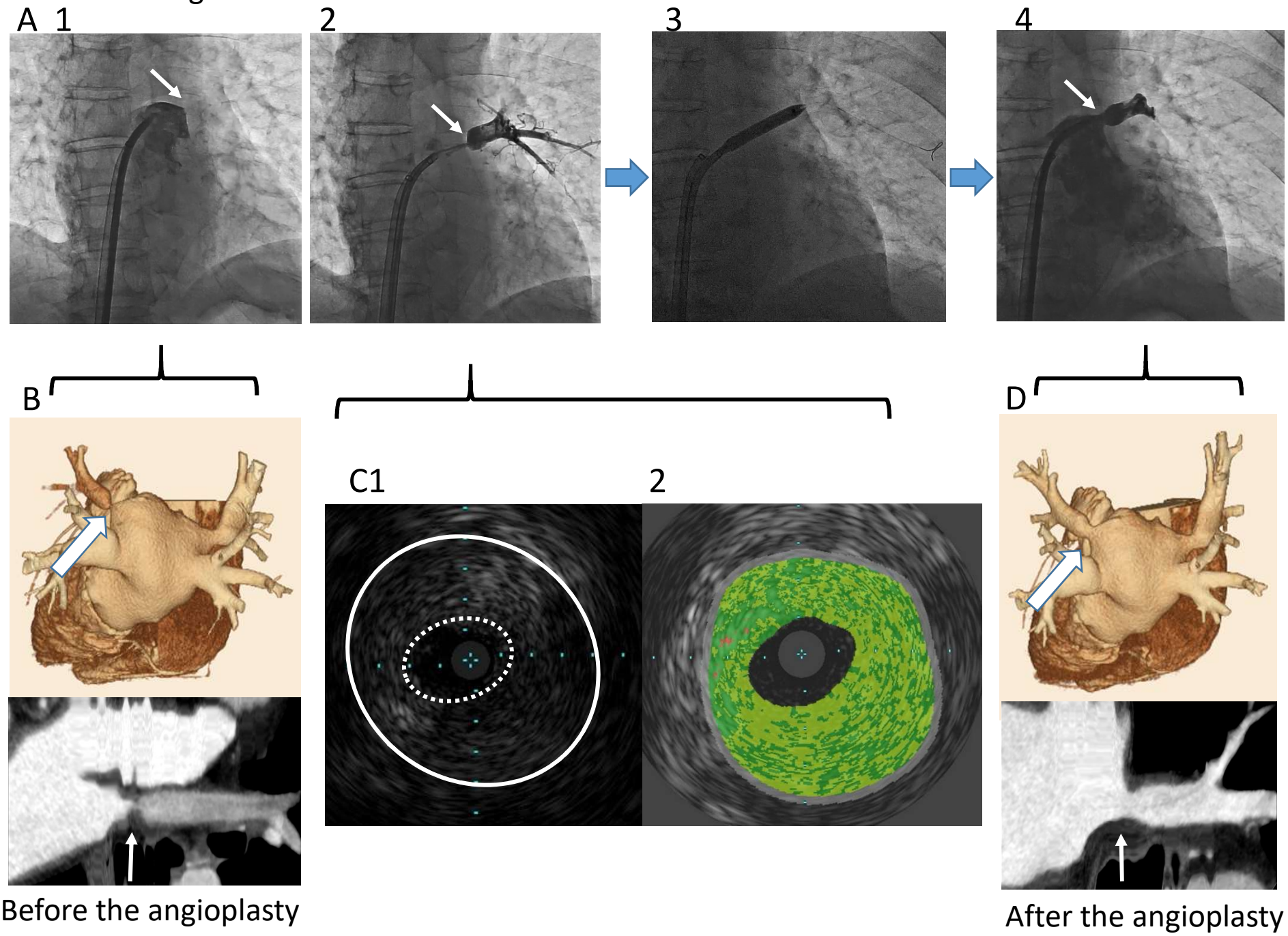
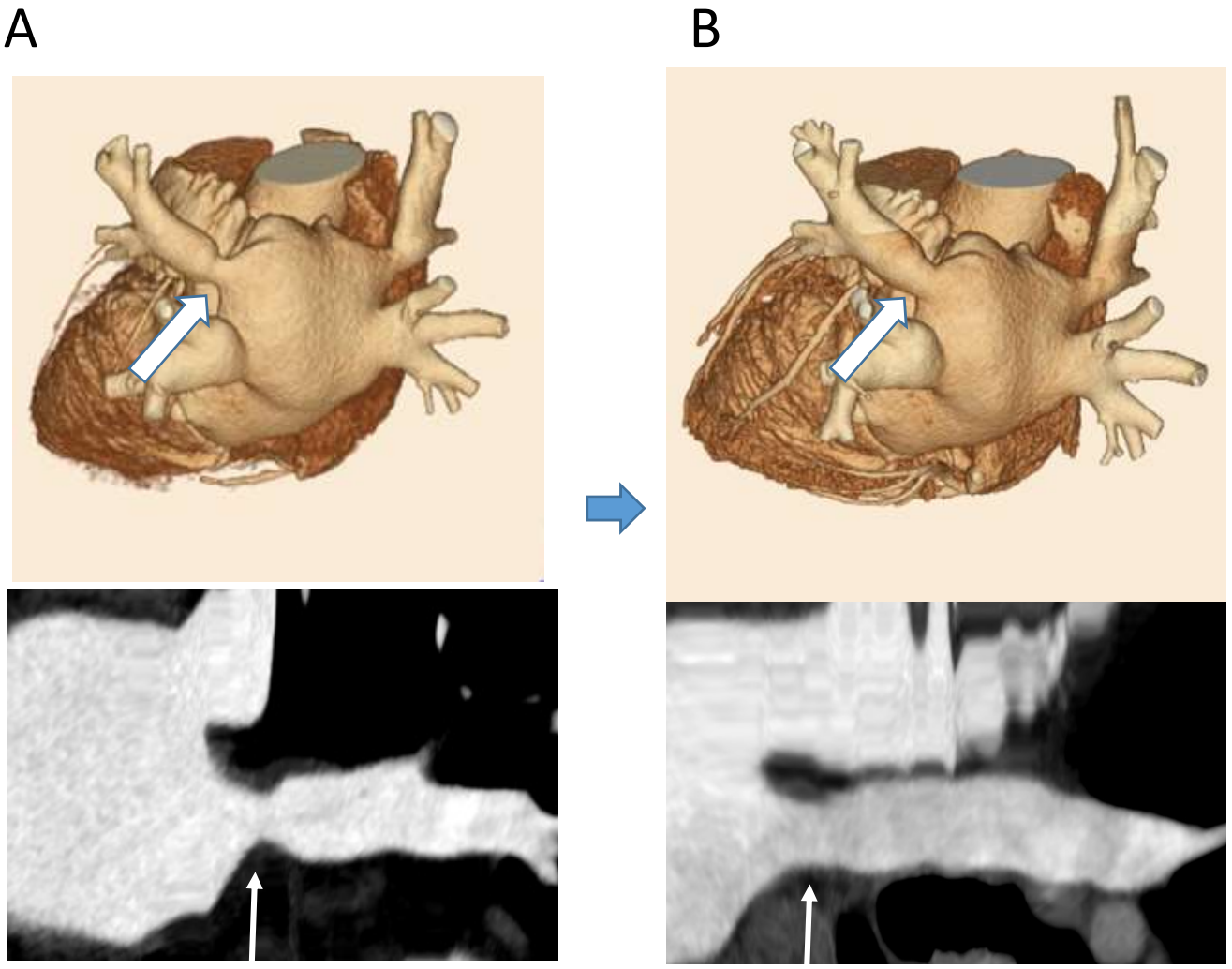


Fig. 3


A
B
Three months
after the angioplasty
Fourteen months
after the angioplasty