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LETTERS TO THE EDITOR

OCT Imaging for the Management of Pulmonary Hypertension

Significant progress has been made in intravascular imaging with optical coherence tomography (OCT), which has enabled us to precisely examine pulmonary artery (PA) morphology in pulmonary hypertension (PH) patients, as we recently demonstrated (1,2). In the present study, we aimed to examine with OCT whether PA remodeling precedes the development of PH and whether reverse remodeling of the PA could be induced in response to current treatments.

The ethical committees of Tohoku University Hospital approved the study protocol and all patients provided written informed consent. We prospectively enrolled 124 individuals who underwent both right heart catheterization and PA-OCT at our hospital from February 2009 to December 2012, including 79 PH patient (mean pulmonary artery pressure [PAP] \geq 25 mm Hg at rest), 10 borderline PH patients (mean PAP between 21 and 24 mm Hg), and 35 non-PH subjects (mean PAP \leq 20 mm Hg).

We performed OCT imaging of the PA by using the time domain M2 OCT system (LightLab Imaging Inc., Westford, Massachusetts). For morphometric assessment, we determined the PA wall thickness, the thickness-diameter ratio defined as the wall thickness divided by the outer diameter, and the wall-area ratio; with all of these 3 parameters averaged over 2 to 6 representative cross sections (mean \pm SD, 2.65 \pm 0.76 sections; diameter between 1 and 4 mm) at each OCT examination in each subject. The wall-area ratio was determined as follows: the wall area was calculated as the whole-vessel area encircled by the outside edge of the vessel subtracted from the luminal area. We defined the ratio of the wall area divided by the whole-vessel area as the wall-area ratio. All of these morphometric evaluations were performed on offline saved images by using LightLab Imaging M2 Office Review Workstation (LightLab Imaging Inc.). We defined reverse remodeling as improvement of >2 of the 3 morphometric PA parameters. Correlation tests were performed using Pearson's correlation, except in those involving the brain natriuretic peptide (BNP) level, for which Spearman's correlation was used.

Representative cross-sectional images of PA-OCT are shown in **Figure 1A**. The 3 morphometric

parameters (wall-area ratio, thickness-diameter ratio, and thickness) were all significantly increased in borderline PH and PH compared with non-PH subjects (**Figs. 1B to 1D**). As continuous variables, the 3 morphometric parameters were highly and significantly correlated with the mean PAP (**Figs. 1E to 1G**) and pulmonary vascular resistance (PVR) ($r^2 = 0.2238$, $p < 0.0001$; $r^2 = 0.1941$, $p < 0.0001$; $r^2 = 0.2575$, $p < 0.0001$, respectively) in all subjects (N = 124).

We also evaluated the correlation of the 3 morphometric parameters with established prognostic factors, including cardiac index ($r^2 = 0.0147$, $p < 0.05$; $r^2 = 0.0378$, $p < 0.05$; $r^2 = 0.0198$, $p = \text{NS}$, respectively), plasma BNP level ($\rho = 0.2970$, $p < 0.001$; $\rho = 0.2815$, $p < 0.005$; $\rho = 0.1233$, $p = \text{NS}$, respectively), and serum uric acid level ($r^2 = 0.0502$, $p < 0.05$; $r^2 = 0.0566$, $p < 0.01$; $r^2 = 0.0632$, $p < 0.01$, respectively) in all subjects (N = 124). In the 29 pulmonary arterial hypertension (PAH) patients who underwent the 6-min walk test, we evaluated its association with OCT-detected morphology ($r^2 = 0.1662$, $p < 0.05$; $r^2 = 0.1414$, $p < 0.05$; $r^2 < 0.0001$, $p = \text{NS}$, respectively). All the 4 prognostic factors were significantly correlated with wall-area ratio and thickness-diameter ratio, but not thickness.

Of the 79 PH patients, 14 with PAH underwent follow-up PA-OCT and catheterization after the treatments. They underwent right heart catheterization and OCT ≥ 2 times (2.43 \pm 0.73 times, 34 times in total, 20 serial changes analyzed). No correlation was observed between the serial changes in mean PAP or PVR and those in wall-area ratio, thickness-diameter ratio, or thickness, except a significant correlation between the serial change in PVR and that in thickness ($r^2 = 0.2462$, $p < 0.05$). Among the 14 patients, 8 presented with morphological improvement in ≥ 2 parameters on the second examination compared with the first, defined as reverse remodeling. Compared with the remaining 6 patients without reverse remodeling, those with reverse remodeling were characterized with significantly less prevalence of PAH associated with connective tissue diseases, increased serum uric acid level, and more patients prescribed spironolactone ($p < 0.05$ each).

To the best of our knowledge, this is the first report that OCT can demonstrate the development of PA remodeling in the very early stages in PH, when the mean PAP is between 21 and 24 mm Hg, defined as borderline PH in the current criteria, as well as the occurrence of reverse remodeling in response to the treatment in PH patients.

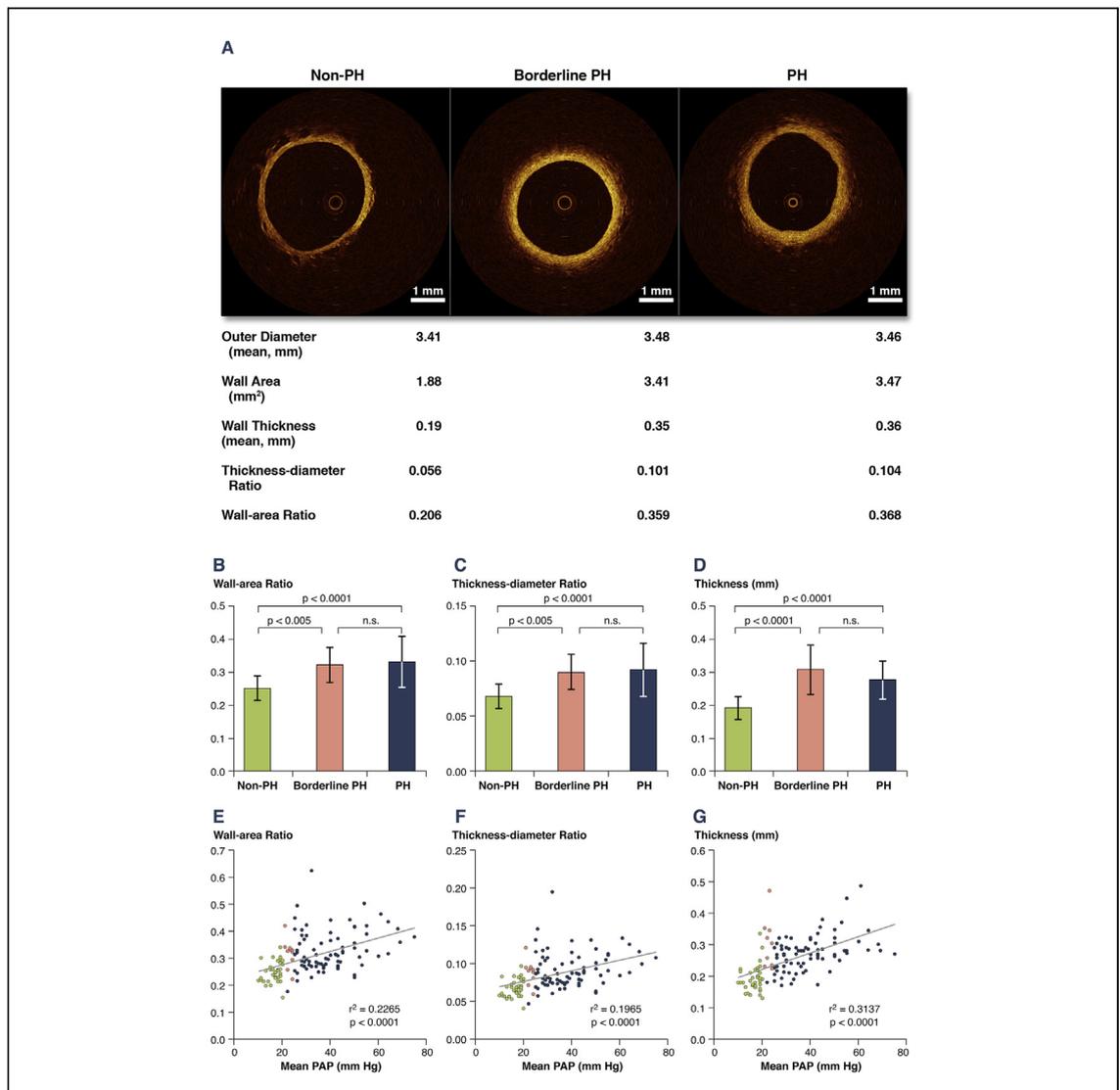


FIGURE 1 Representative Images and Assessment of Morphometric Parameters of the Pulmonary Artery by OCT

(A) Optical coherence tomography (OCT) images of the pulmonary artery obtained from a nonpulmonary hypertension (PH) subject, a borderline PH patient, and a PH patient. When assessed quantitatively, the wall-area ratio (B), thickness-diameter ratio (C), and thickness (D) were all significantly and equally increased in borderline PH ($n = 10$) and PH ($n = 79$) patients compared with non-PH subjects ($n = 35$). Wall-area ratio, thickness-diameter ratio, and thickness were significantly correlated with mean pulmonary arterial pressure (PAP) (E to G). Blue, pink, and green circles indicate PH, borderline PH, and non-PH subjects, respectively.

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Delayed Disruption of a Bioresorbable Vascular Scaffold

A 59-year-old man underwent percutaneous coronary intervention for a focal lesion at the ostium of the left circumflex artery (LCX) with a 3.5 × 12.0 mm everolimus-eluting Absorb bioresorbable vascular

scaffold (BVS) (Abbott Vascular, Santa Clara, California). This was followed by post-dilation with a 3.5-mm double-layered OPN NC (SIS Medical AG, Winterthur, Switzerland), which allowed super high-pressure dilation (presumed balloon diameter: 3.85 mm at 30 atm) (Figs. 1A and 1B). Post-procedural optical coherence tomography (OCT) showed excellent results without evidence of scaffold disruption (Figs. 1a to 1h). At 6 months, the patient underwent repeat coronary angiography due to recurrence of exertional angina. This showed severe focal restenosis of the BVS at LCX ostium (Figs. 1C and 1D). The OCT revealed significant neointimal hyperplasia within a disrupted (Figs. 1b' to 1e')

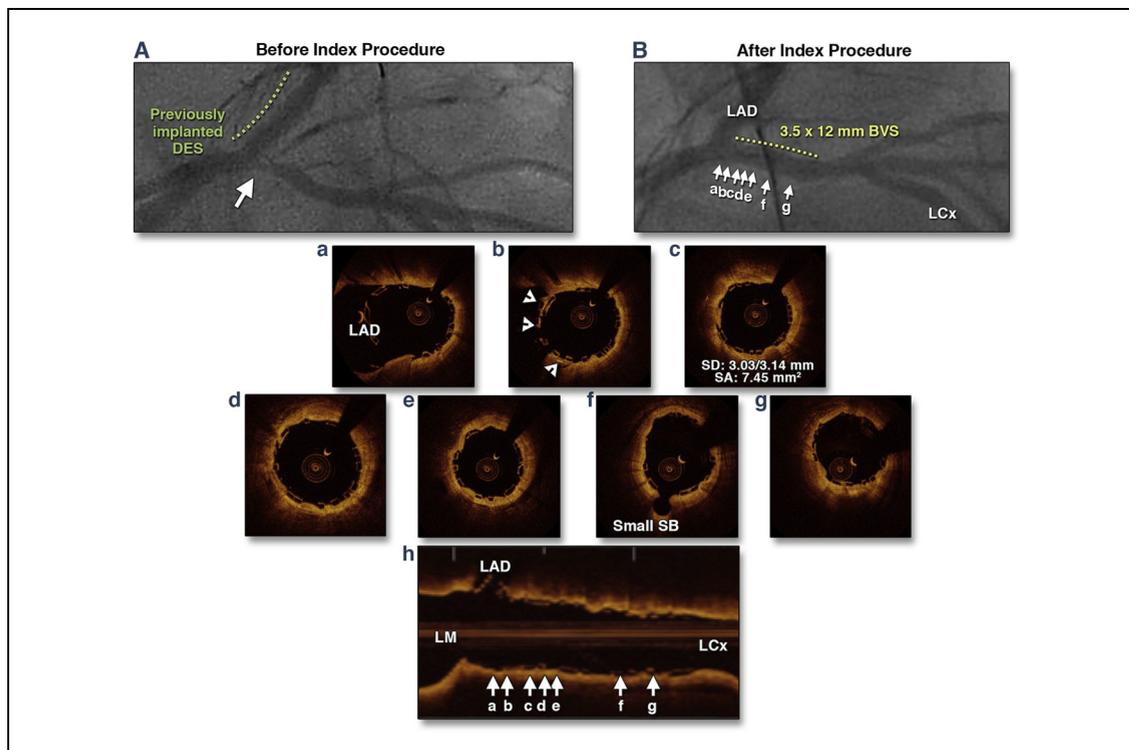


FIGURE 1 Comparison of Angiographic and OCT Images After Index Procedure and at 6-Month Follow-Up

(A) Pre-procedural angiogram demonstrating a focal lesion at left circumflex artery (LCX) ostium (arrow) and a patent drug-eluting stent (DES) previously implanted in the ostial left anterior descending artery (LAD). (B) Post-procedural angiogram showing an excellent result after implantation of a 3.5 × 12.0 mm bioresorbable vascular scaffold (BVS) with satisfactory lesion preparation, followed by post-dilation with a 3.5-mm noncompliant balloon. (C) The 6-month follow-up angiogram showing a focal severe BVS restenosis at LCX ostium. (D) The 6-month follow-up angiogram after gentle pre-dilation with a 2.0-mm balloon performed to allow adequate contrast flush through the tight stenosis, in order to obtain optical coherence tomography (OCT) images. (a) Adequate BVS expansion and good positioning with minimal protrusion of the proximal BVS edge into left main artery (LM). (b) Small neo-carina created with BVS and old DES struts (arrowheads). (c) Scaffold diameter (SD) and scaffold area (SA) were 3.03/3.14 mm and 7.45 mm², respectively. (d to g) Adequate BVS expansion without evident disruption. (h) OCT longitudinal view showing good positioning and adequate expansion of the BVS. (a') Elliptical deformation of the BVS. (b') Overlapping BVS struts suggesting disruption (arrow). (c') Recoil of the BVS. SD and SA were 2.26/2.71 mm and 5.01 mm², respectively. (d') Complete BVS disruption resulting in overlapping struts (arrow) as well as segmental absence of BVS struts (arrowheads). (e') Overlapping BVS struts suggesting disruption (arrow). (f' and g') Acceptable lumen and scaffold areas without evidence of BVS disruption, at a distance >8 mm from the LCX ostium. (h') OCT longitudinal view, showing a focal restenosis at LCX ostium. SB = side branch. *Continued on the next page.*