are expensive, potentially dangerous, and current guidelines recommend their use in IPAH, but not in PH-HFpEF, where they are harmful (2).

In HFpEF, there is preserved LV systolic function, but impaired diastolic function with abnormal LV relaxation and increased LV filling pressure. Sustained elevations of LV diastolic filling pressures will result in enlargement of the thin-walled left atrium, allowing LAV to be used as a marker of the severity and chronicity of diastolic dysfunction (4). Thenappan et al. (1) noted echocardiographic left atrial enlargement in 64% of their PH-HFpEF group and only 1% of IPAH patients (p<0.001).

We acknowledge that echocardiography will give a measure of LAV, but note the following limitations: 1) echocardiography underestimates CMR-derived LAV in both healthy subjects and patients with cardiovascular disease; and 2) CMR can be used when acoustic windows are poor (3). We have shown that a single, noninvasive, CMR-derived variable, LAV of <43 ml/m², will distinguish IPAH from PH-HFpEF, which is attractive for busy cardiovascular centers.

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Temporal Course of Vessel Healing and Neoatherosclerosis After DES Implantation

Recently, late drug-eluting stent (DES) failure has become a potential cause for concern following first-generation DES implantation. Although these phenomena may result from multiple etiologic factors, emerging evidence consistently suggests the importance of delayed arterial healing and neoatherosclerosis progression as major contributors. In vivo assessment of long-term vessel healing after sirolimus-eluting stent (SES) deployment is limited, and the incidence and process of in-stent atheroma formation remain unknown.

Although SES is no longer used in our clinical practice, many patients have already undergone SES implantation, and a clear understanding of the long-term status of vessel reaction after stenting is of clinical importance. Hence, this optical coherence tomography (OCT) examination focusing on features inside the SES was performed to elucidate neointimal changes during an extended period (5 years) by comparing mid-phase and late-phase OCT findings.

From the Kobe University Hospital OCT database, 87 patients underwent mid-phase (3 to 12 months) coronary angiography and OCT examination after SES (Cypher, Cordis Corp., Miami Lakes, Florida) implantation between October 2004 and January 2008. The patients with target lesion revascularization before late-phase follow-up were excluded from this study.

Quantitative OCT measurements were done as previously reported (1). Peri-strut low intensity area (PLIA) was defined as the LAV threshold represents the LAV threshold of 43 ml/m². PH = pulmonary hypertension; PH-HFpEF = pulmonary hypertension due to heart failure with preserved ejection fraction.

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![Figure 1. LAV Was Significantly Lower in IPAH Than in PH-HFpEF](http://dx.doi.org/10.1016/j.jcmg.2013.05.014)
The percentage of uncovered and malapposed struts decreased significantly from the mid- to late-phase follow-up.

The percentage of struts with PLIA, the frequencies of intrastent thrombus, and extra-stent lumen decreased significantly during the follow-up period. The incidence of AN was 3.1% (2 stents) at the mid-phase and 23.4% (15 stents) at the late-phase follow-up with significant increases \((p < 0.0001)\) (Fig. 1).

Recently, Kim et al. (3) reported the improvement of stent coverage and progression of in-stent neatherosclerosis from the observation of 9-month to 2-year serial OCT follow-up. The present study expanded those findings to 5 years with additional data that the frequencies of malapposed struts, PLIA, and intrastent thrombus decreased dramatically during follow-up.

Pathologic examination of human specimens suggests that so-called delayed arterial healing is associated with late stent thrombosis. Delayed arterial healing is characterized by the presence of exposed stent struts and fibrin or thrombus deposition with inflammatory cell infiltration, therefore several in vivo OCT findings, such as uncovered struts, malapposed struts, and PLIA, can function as surrogate markers of these phenomena. Among those, a recent OCT report showed a strong association between OCT-detected uncovered stent struts and late stent thrombosis (4). In the present study, the frequency of covered struts increased to 99.1%.

Nakazawa et al. (5) reported a high incidence of neoatherosclerosis in the neointima of DES compared with bare-metal stents based on pathology. The high frequency of the neoatherosclerosis of neointima has been reported in lesions with DES and late-phase bare-metal stents, which required repeat revascularization. Here, we expanded these findings by assessing the incidence of neoatherosclerotic changes within event-free SES. AN was observed at both mid- and late-phase examinations, but it was significantly increased at the late-phase follow-up.

An important limitation of the present study is the exclusion of patients with adverse events prior to late OCT follow-up. The present results thus apply to AN in SES not sufficiently severe to cause restenosis or stent thrombosis.

Although speculative, a variety of factors, such as the presence of traditional coronary risk factors, responsiveness to antiplatelet therapy, and shear stress distribution within the stent, can theoretically affect the development of AN. Our results may suggest a potential benign nature of late neoatherosclerosis, however, close observation of these cases should be continued because the natural course of

![Figure 1. Representative OCT Images and Analyzed Data](image-url)

(A) Representative optical coherence tomography (OCT) images. White arrows indicated covered strut (a), uncovered strut (b), malapposed strut (c), peri-strut low intensity area (d), extra-stent lumen (e), intrastent thrombus (f), and atherogenic neointima (g). (B) Representative case of atherogenic neointima formation (yellow arrows) at the late-phase. (C) Change in OCT parameters from the mid- to late-phase. Comparison of percentage of uncovered struts and malapposed struts between mid- and late-phase OCT examinations. (D) Change in OCT parameters from the mid- to late-phase. Comparison of the stent with extra-stent lumen, intrastent thrombus, atherogenic neointima, and strut with peri-strut low intensity area between mid- and late-phase OCT examinations.
neoatherosclerosis after detection remains unclear. A longer-term follow-up study with larger sample size will be warranted to further address the natural course and the clinical impact of AN.

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