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LETTERS TO THE EDITOR

OCT Assessment of Allograft Vasculopathy in Heart Transplant Recipients

Cardiac allograft vasculopathy (CAV) is the main cause of graft failure and death in heart transplant recipients surviving more than 1 year. The diagnosis of CAV is challenging because of cardiac denervation and the diffuse nature of the disease. Because of lack of early clinical symptoms, patients with CAV typically present late with silent myocardial infarction, loss of allograft function, or sudden death. Therefore, it is important to identify asymptomatic patients early during development of CAV. Coronary angiography remains the principal screening tool for CAV in most institutions. However, it is known that coronary angiography can underdiagnose or miss CAV (1,2).

In this study, we compared high-resolution (10 μm) optical coherence tomography (OCT) (time domain M3 system) with intravascular ultrasound (IVUS) to assess CAV in 7 long-term survivors (mean age 51 $\pm$ 12 years; follow-up 1.5 to 17.0 years after transplantation). This protocol was approved by the ethics committee of Harbin Medical University. All patients provided informed consent prior to participation.

The left anterior descending artery (LAD) was divided into 3 segments (proximal, mid, and distal) and was analyzed per segment by OCT and IVUS. Intimal hyperplasia (IH), defined by intimal thickness >100 μm was found in 14 of 21 (66.7%) segments by OCT, but only in 3 of 21 (14.3%) segments by IVUS ($p < 0.01$) (Fig. 1). Mean IH thickness and area were 180.8 μm and 1.4 mm^2, respectively, measured by OCT. Lipid-rich atherosclerotic plaques with thin fibrous caps were found only by OCT in 3 cases (Fig. 2).

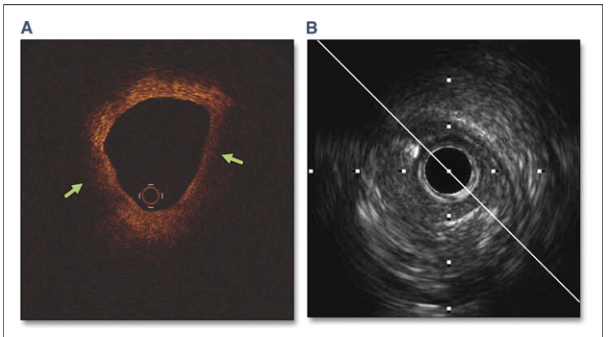

Figure 2. OCT and IVUS Images in a Patient 17 Years After Heart Transplantation

OCT **(A)** revealed a lipid-rich plaque with thin fibrous cap **(arrows)**, which is not obvious on IVUS **(B)**. Abbreviations as in Figure 1.

This study demonstrates that OCT, compared with IVUS, is more sensitive for early detection of CAV (3–5). IH thickness ≤150 μm accounted for 31.4% of all segments, which is under the resolution of IVUS and therefore can be diagnosed only with OCT. Moreover, OCT provides additional information on characteristics of IH such as lipid plaques and thin fibrous caps.

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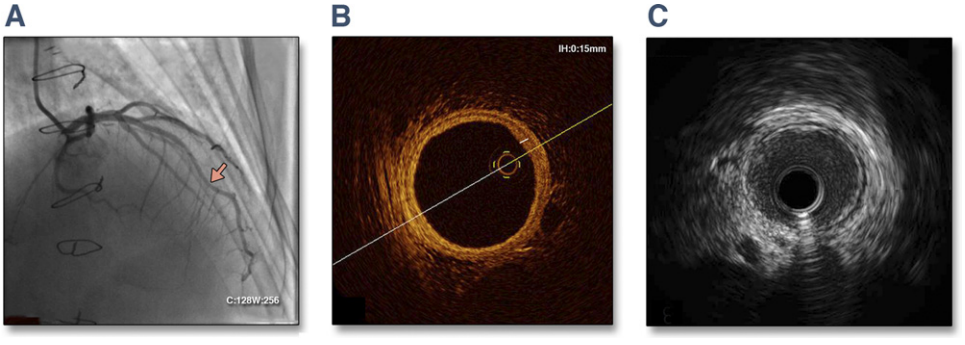

Figure 1. Coronary Angiogram, OCT, and IVUS Imaging in a Patient 8 Years After Heart Transplantation

(A) Quantitative coronary analysis showed 14% diameter stenosis in the mid–left anterior descending artery **(arrow)**. **(B)** Optical coherence tomography (OCT) revealed intimal hyperplasia (IH) with thickness of 150 μm. **(C)** Accurate measurement of IH was difficult with intravascular ultrasound (IVUS).

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RV Volume Measurements by CMR

We want to compliment Clarke et al. (1) for their important work of thoroughly assessing the accuracy and reproducibility of right ventricular (RV) volume measurements by cardiac magnetic resonance in congenital heart disease. However, we think that 2 points warrant further comment.

First, Clarke et al. (1) considered a difference of 10 ml/m^2 of different measurement methods of RV stroke volume to be clinically significant. Taking into account that the mean RV stroke volume in their study was around 60 ml/m^2 with minimal values of around 20 ml/m^2, a difference of 10 ml/m^2 is fairly large. Translated into percentage values, this would amount to a 17% difference for the mean values and up to 50% for the smallest RV stroke volumes. Although clinical significance or relevance is a subjective measure, we think that 17% to 50% is too large. This problem could be addressed by comparing the percentage differences of the methods to each other.

Second, Clarke et al. (1) defined the first phase of each cine image as the end diastole. By doing this in patients with volume-loaded RV with wide QRS complexes, one will inadvertently underestimate the end-diastolic volume and stroke volume. This is because in patients with wide QRS complexes the computed trigger signal will be later than the upstroke of the QRS complex. Accordingly, the end diastole will not be found in the first phase of the cine image but in one of the last phases. Therefore, RV stroke volume is very likely to be significantly underestimated in this patient population as depicted in Figure 2 and Table 3 of Clarke et al. (1). Therefore, we suggest that the phase of the end diastole should be defined visually by the observer as the phase with the largest volume (2,3).

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REPLY

We thank Drs. Fratz and Stern for their interest in our recent publication (1) and for the opportunity to discuss their comments.

With respect to their first point regarding our definition of a clinically significant difference in right ventricular (RV) stroke volume, we agree that a value of 10 ml/m^2 is a relatively large difference given the observed stroke volumes of patients included in the study. However, it is important to keep in mind that the reported biases in RV stroke volumes are mean values calculated from the entire study population with RV stroke volumes that ranged from 17 ml/m^2 to 141 ml/m^2. Given that smaller biases in RV stroke volumes were generally observed among patients with smaller volumes (Fig. 2 from our paper [1]), a worst case scenario in which this mean bias is considered only among patients with the smallest RV stroke volumes substantially overestimates a potential difference when translated into a percentage value. This said, we agree that these results expressed as percentages provide a standardized scale to account for the magnitude of differences relative to RV stroke volumes. Therefore, we include the following results. The RV stroke volume mean bias for phase contrast imaging versus axial contours was 0% (95% confidence interval [CI]: −7% to 6%), and for phase contrast imaging versus short-axis contours, it was 2% (95% CI: −4% to 7%). The difference in mean biases was 2% (95% CI: −1% to 5%) ($p = 0.202$). Additionally, because the initial report includes absolute values of the biases and differences observed, readers can draw their own conclusions about whether these values are clinically meaningful with respect to mean RV volumes and ejection fractions.

With regard to the second comment regarding the phase of each cine image chosen as end-diastole, we agree that this is an important point and one we considered when planning this study. Defining the phase of end-diastole visually is likely to avoid underestimating end-diastolic measurements in some cases. Conversely, this may decrease reproducibility because it increases the number of variables defined by the reader. Therefore, this trade-off must be weighed by practitioners of cardiac magnetic resonance, particularly for patients who require repeated studies. The decision to define end-diastole as the first phase of each cine image is unlikely to affect conclusions regarding accuracy drawn in our report because differences in time between the computed trigger signal and the upstroke of the QRS complex should be consistent for each patient regardless of the imaging plane. Thus, any underestimation