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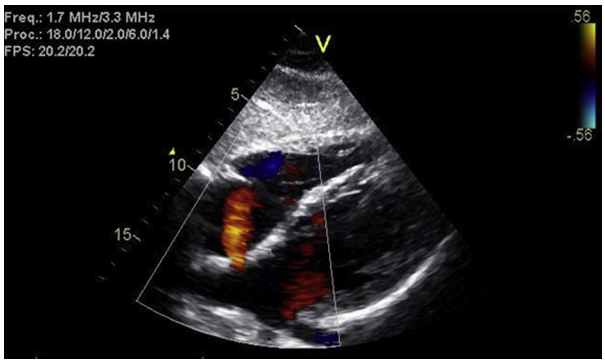

Figure 1 Color Doppler Echocardiogram in the Subcostal View at End Diastole

Echocardiogram in the subcostal view at end diastole showing left-to-right flow at 183 days post-procedure.

1 year, and did not report any adverse effects (4). Likewise, adverse effects attributable to iASD were not reported in the recently published prospective STOP-AF (Sustained Treatment Of Paroxysmal Atrial Fibrillation) trial; however, this was not a predefined endpoint and the study did not report post-procedure echocardiographic imaging (5). In our experience, 2 patients experienced symptoms or had documented hemodynamic significance in the course of follow-up. This suggests that we should be vigilant with regard to the effect of a larger transseptal sheath size and that further study is required to determine long-term sequelae and spontaneous closure rates over time.

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Letters to the Editor

Invasive Hemodynamic Assessment of "Paradoxical" Low-Flow Severe Aortic Stenosis

We read with interest the paper by Lauten et al. (1) discussing the invasive hemodynamic characteristics of low-gradient, severe aortic stenosis (AS) despite preserved ejection fraction. The authors' main finding was that low-gradient, severe AS despite preserved ejection fraction was not merely the result of a systematic bias in the echocardiographic calculation of the aortic valve area (AVA) as a result of measurement error and so forth, but was in fact a real entity as confirmed by invasively derived hemodynamic data using both the thermodilution and the oxygen consumption methods for stroke volume, cardiac output, and AVA calculation. This is an important study, but we would like to draw attention to the following limitations. First, criteria for inclusion in the study required an AVA <1 cm^2, a mean gradient $\leq$40 mm Hg, and an ejection fraction $\geq$50%. However, by not using the indexed AVA as an inclusion criterion, there remains the possibility that small body size could explain why at least some patients presented with guideline-discordant AVA and gradient patterns in both the echocardiography and invasive catheterization groups (2). Second, not all patients in the low-gradient group had a low stroke volume index (Table 3 in the article); therefore, these patients may have had a low gradient secondary to the inherent inconsistent grading related to discrepancy in guidelines criteria and not due to paradoxical low-flow, low-gradient, severe AS per se (2). Third, the calculated valvulo-arterial impedance (Zva) cannot be considered accurate given the fact that the systolic arterial pressure was not measured at the time of stroke volume calculation during echocardiography but instead "was taken from the closest recorded non-invasive measurement in the patient charts." In fact, a more accurate assessment of the Zva could have been derived invasively by dividing the left ventricular systolic pressure by the stroke volume index (3). Finally, the authors found that compared with patients with high-gradient severe AS, patients with "paradoxical" low-gradient, severe AS had higher energy loss index values, larger AVA values, similar Zva values, lower left ventricular mass index values, and lower mean gradient values. Taken together, these findings imply that patients with "paradoxical" low-gradient AS have a less severe form of AS compared with patients with high-gradient, severe AS. These findings therefore contradict two recent studies (4,5) that found that patients with "paradoxical" severe AS had

a similar or more severe form of AS compared with patients with high-gradient AS, based on AVA and Zva calculations.

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Reply

Invasive Hemodynamic Assessment of "Paradoxical" Low-Flow Severe Aortic Stenosis

We thank Dr. O'Sullivan and colleagues for their interest in our work and the opportunity to clarify the issues brought up in their letter concerning the study by Lauten and colleagues (1). They voice several concerns about our study. The first is the inclusion of patients with an aortic valve area $\leq$1 cm^2. Dr. O'Sullivan and colleagues suggest that indexing to body surface area would have put some of our patients in the moderate aortic stenosis (AS) category, thereby resolving the paradoxical association of low aortic valve area with a mean gradient <40 mm Hg; however, this is not the case. If indexed for body surface area, all patients with paradoxical AS had a valve area $\leq$0.6 cm^2/m^2 by echocardiography or catheterization, if using oximetry for cardiac output; when using cardiac output by thermodilution, aortic valve areas were slightly higher, and 3 of 58 patients with paradoxical AS had a valve area >0.6 cm^2/m^2. Thus, the effect of indexing on the classification is minimal.

The second concern refers to the fact that not all of our patients with "paradoxical" AS had a low stroke volume index (<35 ml/m^2). Five of 58 (9%) of our patients in this group had a stroke volume index $\geq$35 ml/m^2. However, stroke volume is rarely calculated routinely, whereas left ventricular ejection fraction is regularly determined. Thus, the designation as "paradoxical" AS stems from observing patients with an aortic valve area $\leq$1 cm^2 having low gradients despite normal ejection fraction (2). Further research revealed that these patients typically had low absolute stroke volumes (3), although their ejection fraction was preserved. The adjective "paradoxical" reflects the surprising finding of a normal ejection fraction associated with a low mean gradient in severe AS, because one generally assumes that a normal ejection fraction implies a normal stroke volume (there is nothing paradoxical about a low mean gradient being associated with a low stroke volume). Thus, we think that our inclusion criteria, which were not based on stroke volume (index), reflect typical clinical practice.

Third, they take issue with the fact that we calculated valvulo-arterial impedance noninvasively in the study, using echocardiography data together with the next available blood pressure reading in the patient charts. This noninvasive technique was the one used in our reference (3) and by others. Dr. O'Sullivan and colleagues are correct in pointing out that one could instead have calculated impedance from the invasive data, dividing left ventricular systolic pressure by stroke volume index. It should be clear, though, that this index is in any case just an approximation and not an exact calculation of arterial impedance (4).

Fourth, the authors of the letter point out that according to valve area and energy loss index, our patients with paradoxical AS had less severe AS than the comparison group of patients with high-gradient AS, although the stenosis was "severe" in all patients according to aortic valve area. This is entirely correct, as we stated in our "Discussion" section: "...overall there was a higher degree of obstruction, in accordance with lower valve areas, higher gradients, and lower energy loss index in this group [the high-gradient aortic stenosis group] than in the "paradoxical" aortic stenosis group." It is also worth remembering that the original clinical question was whether "paradoxical" AS is really severe at all. Further, the finding that the patients with paradoxical AS in our study had mildly less obstruction than high-gradient AS does not necessarily predict that the patients with paradoxical AS have a more benign variant of AS. Whether this is the case could be inferred only from a follow-up of patients with matched aortic valve areas but differing gradients despite preserved ejection fraction, which was not the goal of our study. Furthermore, prognosis of paradoxical AS might reflect other factors than pure valvular obstruction, for example, myocardial fibrosis. In any case, it seems possible that patients having what we and others have called "paradoxical AS" are not homogeneous and may include both patients with subtly decreased left ventricular function due to advanced valvular disease and patients transitioning from a moderate to a severe degree of conventionally defined AS, and that these two subgroups may have different natural histories.

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