perceived that invasive hemodynamic values obtained by catheterization data in such patients may yield more concordant hemodynamic values (2). On the contrary, one recent study reported that even 53% of patients with normal-flow, normal ejection fraction have discrepant invasive hemodynamic indices of AS severity, viz. severe AS by valve area (<1 cm^2) and low transvalvular gradients (<40 mm Hg) (3). These results suggest that the internal inconsistencies in the proposed AS severity criteria by current guidelines indeed play a major role in the observed discrepancy of hemodynamic parameters in patients with AS (2,3). Carabello (4) has previously demonstrated the potential mismatch of the cutoff values proposed by current guidelines. For instance, a cardiac output of 6 l/min, systolic ejection period of 0.33 s, and heart rate of 80 beats/min, a mean gradient of 26 mm Hg actually yields to an AVA of 1.0 cm^2, whereas a mean gradient >40 corresponds with an AVA of 0.8 cm^2. Similarly, one striking finding from the prior studies is that the majority of discrepant indices are substantially prevalent when the calculated AVA is between 0.8 and 1.0 cm^2, whereas they appear more frequently consistent when the valve area is <0.8 cm^2. Moreover, mitral regurgitation is common in elderly AS patients, either as a consequence of left ventricular pressure overload or due to concomitant mitral valve disease (2). In AS patients with concomitant moderate to severe mitral regurgitation, mitral regurgitation may play a confounding role in the causation of a low effective transaortic flow and low transaortic gradient. Thus, accounting the presence of mitral regurgitation in the general clinical assessment may explain the discordance among the observed parameters of AS severity. The AS severity by valve area assessment usually remains unaffected in this setting, as the valve area calculation still remains accurate in this setting (2).

Nevertheless, more data from future randomized controlled investigations are needed to strengthen our understanding about the prognostic long-term outcomes of normal-flow low-gradient AS patients. Secondly, the future guidelines should account for such patients, and indeed, a consideration to revise the definition of severe AS should be made to resolve the discrepancy of hemodynamic parameters in a large proportion of AS patients. Lastly and most importantly, it is high time to realize that such an AS patient population with discrepant hemodynamics truly exists, and their treatment strategy should deserve the same priority as other subtypes. Low-pressure gradient per se as a lone parameter should not affect our treatment referral strategy for the management of such patients!

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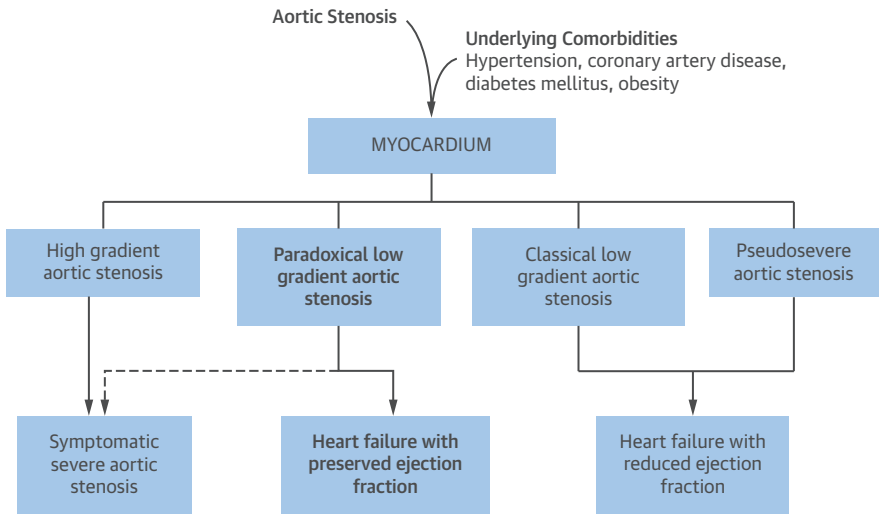
Paradoxical Low-Gradient Aortic Stenosis

The HFpEF of Aortic Stenosis

The flow and gradient patterns in aortic stenosis reflect the complex interaction of the valve and underlying comorbidities on the myocardium (**Figure 1**). In the presence of symptoms, we believe patients with paradoxical low-gradient (PLG) aortic stenosis have a syndrome akin to heart failure with preserved ejection fraction (HFpEF). As demonstrated by Dayan et al. (1), PLG aortic stenosis predominates in older patients, and has a higher prevalence of coronary artery disease, diabetes, and hypertension, as well as a tendency to female predisposition, all characteristics of HFpEF. Altered ventricular-arterial interaction is a key pathophysiological element of both entities (2). The increased afterload predisposes patients (particularly in women) to concentric myocardial remodeling and contractile dysfunction, thus explaining the lower gradients in PLG aortic stenosis and abnormal ventricular filling in HFpEF.

There is evidence that the prognosis in both PLG aortic stenosis and HFpEF is largely driven by comorbidities. PLG aortic stenosis has features intermediate of those observed in concordant nonsevere and severe disease (3), challenging the notion that it is an advanced stage of severe aortic stenosis. Moreover, the majority of patients with PLG progressed in severity, with nearly one-half progressing to

FIGURE 1 The Complex Interaction Between Aortic Stenosis and Underlying Medical Conditions on the Myocardium



high-gradient severe aortic stenosis (4). Therefore, it is unlikely that the adverse cardiovascular prognosis associated with PLG aortic stenosis is solely driven by the degree of aortic stenosis but more likely associated with the underlying comorbidities. Similarly, in HFpEF, a high percentage of adverse outcomes are related to noncardiovascular comorbidities (5).

Dayan et al. (1) have demonstrated lower mortality in patients with PLG who had aortic valve replacement, regardless of flow status. This is encouraging. However, there was moderate-to-substantial heterogeneity of the pooled observational studies, and the benefits of surgery may not be generalizable. Although this meta-analysis has set the stage for future randomized controlled studies, careful patient selection will be crucial to examine the effects of aortic valve replacement in patients with PLG, the HFpEF of aortic stenosis.

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REPLY: Inconsistency of Hemodynamic Data in Low-Gradient Severe Aortic Stenosis

Paradoxical Low-Gradient Aortic Stenosis
The HFpEF of Aortic Stenosis

We thank Dr. Chin and colleagues and Dr. Chhabra for their interest in our study and for their insightful comments. We agree with Dr. Chin and colleagues that paradoxical low-flow, low-gradient (PLF-LG) aortic stenosis (AS) shares several common pathophysiological and clinical features with the heart failure/preserved left ventricular ejection fraction (LVEF) entity and that the worse outcomes of patients with PLF-LG is, at least in part, due to comorbidities and not only to AS. However, patients with heart failure and preserved LVEF may actually be more vulnerable to the increased LV afterload due to hypertension and/or AS and so, in these patients, even moderate AS may actually be detrimental. Furthermore, other factors, including concomitant mitral regurgitation or stenosis, atrial fibrillation, and so on, may also cause a low-flow state in a patient with preserved LVEF.