Transvalvular Volume Flow Rate: A Useful Tool for Assessment of Aortic Valve Stenosis in Preserved Ejection Fraction Patients

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Aortic stenosis (AS) represents the most common primary cardiac valve disease and a remarkable source of excessive morbidity and mortality [1, 2]. The prevalence of AS consistently increases with age, averaging from 0.2% among individuals aged between 50 and 59 years to 9.8% among individuals in the 80- to 89-year age group [3]. The global prevalence and the clinical and epidemiologic significance of AS are expected to rise further over the next 50 years, alongside the projected ageing and increase of the world population [4].

Despite the frequency of the disease, several pitfalls remain in its diagnostic approach. The two basic parameters which define the need for treatment in patients with AS are severity of stenosis and symptomatology. The current European and American Guidelines characterize AS as severe when the mean transvalvular gradient is >40 mm Hg, the peak aortic jet velocity is >4.0 m/s, and the aortic valve area (AVA) is <1.0 cm², as calculated by Doppler echocardiography [1, 5, 6]. However, in clinical practice, there are frequently inconsistencies between the three aforementioned criteria. The category of patients with AVA <1.0 cm² and a mean transvalvular gradient <40 mm Hg in the presence of a preserved ejection fraction (EF) represent a special diagnostic conundrum. Apart from measurement errors that may lead to underestimation of AVA/gradients, these discrepancies may originate from the presence of small aortic annuli, small left ventricular (LV) chambers, or a high arterial afterload

[7, 8]. Importantly, gradients are highly dependent on transvalvular flow. For this reason, the current hemodynamic classification of AS in the clinical scenario of preserved EF takes into consideration the LV stroke volume index (SVi). Nonetheless, SVi represents a surrogate marker for flow rate (FR); the latter more reliably reflects transvalvular flow, which is the basic determinant of pressure gradients. An alternative approach, in which FR would substitute its surrogate (SVi), could theoretically improve the diagnostic accuracy and risk stratification in this patient subpopulation.

In this context, the article by Alexandru et al. [9] published in the last issue of *Cardiology* is of special interest. In their retrospective study, which initially included 11,440 transthoracic echocardiograms for AS assessment over a 13-year period, the authors analyzed 529 consecutive adult patients with sinus rhythm, AVA <1 cm², and EF $\geq 50\%$. Based on the cutoffs of 40 mm Hg for mean gradient (MG) and 200 mL/s for FR, patients were divided into low versus high gradient and low versus normal flow AS (4 groups in total). SVi <35 mL/m² was considered as low. Importantly, the authors demonstrated in highly adjusted models that FR correlated better to AVA compared with SVi ($r = 0.51$ vs. 0.41 , $p = 0.0002$). Furthermore, the authors reported that patients with normal FR and MG had the largest and patients with low FR and high MG the smallest AVAs. The cohort of patients was followed for 51 ± 29 (median 56) months. During this pe-

riod, aortic valve replacement was performed in approximately 6 out of 10 patients and was more frequent among patients with normal FR/high MG compared with patients with low FR. Over the follow-up period, 249 deaths were recorded, of which 73% occurred in medically treated patients. After adjustment for confounders, the low FR/low MG subgroup had the worse prognosis, demonstrating a 70% higher risk for all-cause death compared with the normal FR/high MG group. The same excess in risk for all-cause and cardiovascular mortality was reported among patients who underwent aortic valve replacement, but not in medically treated patients. Remarkably, aortic valve replacement provided a similar survival benefit irrespectively of the MG and FR group. However, the use of FR did not outperform SVi in predicting death in this patient cohort (AUC = 0.57 for FR vs. 0.58 for SVi, $p = 0.88$).

The study's findings may have significant implications for clinical practice and future research. This is the largest study to date that attempted to test the comparative performance of FR compared with SVi in the hemodynamic classification and prognostication of patients with severe isolated AS and preserved EF. Given that FR essentially determines transvalvular gradients, while AVA is relatively independent unless LV dysfunction is present, FR can enable more accurate interpretation of a given gradient/AVA, as, contrary to SVi, it is nondependent on the

ejection time [10]. FR can also be superior to SVi in patients with an increased body surface area, when the latter is underestimated [11]. In any case, one must not overlook the fact that FR correlated significantly better to AVA compared with SVi in this patient population. Although the present study did not corroborate the findings of previous ones which suggested that FR is superior to SVi in predicting outcomes of patients with AS [11, 12], one must keep in mind the inherent limitations pertaining to the retrospective design of the study.

The present study is thought-provoking and implies that FR may be superior to SVi in grading the severity of AS in patients with low MGs and preserved EF. However, the question of whether it is time to replace SVi with FR in patients with AS remains unanswered. Only large prospective studies (with predefined criteria for aortic valve replacement) will clarify if FR can outperform SVi in the prognostic stratification of patients with AS.

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