

EDITORIAL COMMENT

# Aortic Stenosis Grading and Outcome

## New Categories, New Therapeutic Challenges\*



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The current understanding of severe aortic stenosis (AS) has changed considerably. Transthoracic echocardiography is the cornerstone noninvasive technique to assess severity. Evaluation of AS severity should integrate the transvalvular flow, in the form of stroke volume index (SVi), to mean pressure gradient (MPG) and aortic valve area (AVA) measurement (1-3). As underpinned by Bavishi et al. (4) in this issue of *JACC*, the SVi has become a barometer in the interpretation of the relationship between MPG and AVA (5,6). Only a modest decrease of flow may, in fact, lead to an important reduction in MPG (square function of flow) and to

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misinterpretation of AS severity, which may potentially lead to inappropriate delay of aortic valve replacement (AVR) in symptomatic patients. SVi is an estimate of left ventricular (LV) pump function and is influenced by the LV contractility and geometry, and the global afterload (valvular + arterial). It suffers from imprecise means of estimation because the Doppler method through which it is assessed may be prone to measurement errors (underestimation of LV outflow tract diameter, misplacement of pulsed-wave Doppler sample in the outflow tract, underestimation of MPG by misalignment with flow direction or very eccentric jets) (7). Despite these limitations, SVi still proved to be an independent predictor of mortality in patients with severe AS (AVA <1.0 cm<sup>2</sup>) and preserved left ventricular ejection fraction (LVEF >50%) (8).

In these patients, 4 flow-gradient patterns have been described: normal flow/low gradient (NF/LG, i.e., SVi ≥35 ml/m<sup>2</sup> and MPG <40 mm Hg), normal flow/high gradient (NF/HG, i.e., SVi ≥35 ml/m<sup>2</sup> and MPG ≥40 mm Hg), low-flow/high gradient (LF/HG, i.e., SVi <35 ml/m<sup>2</sup> and MPG ≥40 mm Hg) and low-flow/low gradient (LF/LG, i.e., SVi <35 ml/m<sup>2</sup> and MPG <40 mm Hg). These patterns stand for different pathophysiologic forms of severe AS with different outcomes and management strategies (Figure 1) (7,9-15).

### IMPACT OF FLOW-GRADIENT PATTERN CLASSIFICATION ON OUTCOME AND TREATMENT

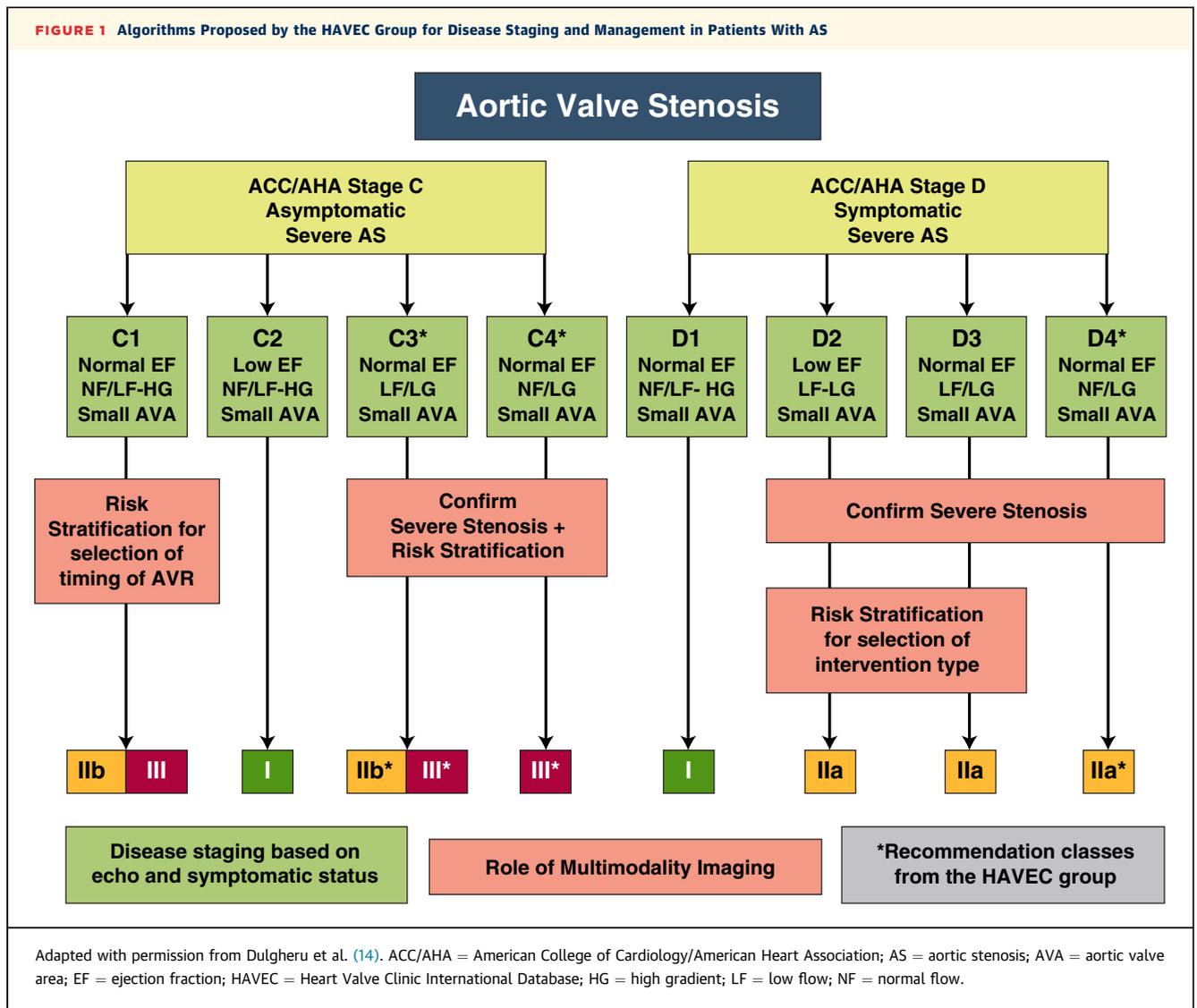
Our group was among the first to report that the clinical outcome of patients (normal exercise test) with an AVA <1.0 cm<sup>2</sup> varied significantly according to the flow-gradient relationships (7). When compared with other AS categories, patients with NF/LG had the best cardiac event-free survival. Conversely, both LF/LG and LF/HG AS were associated with a poorer outcome, whereas patients with NF/HG, the pattern without discordant MPG and AVA, displayed an intermediate prognosis.

Since our report, several other studies have confirmed these findings or raised controversies (7-12). Most of them agreed on the fact that the NF/LG pattern is likely associated with a better prognosis, with little benefit or none after AVR (7,8). Although these patients are believed to have a less severe degree of AS (inherent inconsistency contained in the guidelines about AS grading), no or minimal sub-endocardial dysfunction, and lower brain natriuretic peptide (BNP) level (7), a substantial proportion may nonetheless have severe AS as suggested by the increased aortic valve calcium score on cardiac multislice computed tomography (13), and the survival benefit after AVR (13). The NF/LG pattern is observed in one-third of AS patients and might be categorized as Heart Valve Clinic International Database (HAVEC) stages C4 (asymptomatic) and D4 (symptomatic)

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**FIGURE 1** Algorithms Proposed by the HAVEC Group for Disease Staging and Management in Patients With AS



according to the American College of Cardiology/American Heart Association (ACC/AHA) disease staging (14). Yet, the current guidelines do not provide any recommendation on the specific management of these patients (1,3).

LF/HG and NF/HG AS patterns raise less controversy and are encountered in up to 70% of patients. In these categories, AVR improves outcomes when patients are symptomatic according to the ACC/AHA guidelines and European Society of Cardiology guidelines Class I indication for AVR (1,3), whereas when asymptomatic, the management of these patients underlines the need for optimized risk stratification with multimodality imaging and biomarkers assessment (14). No separation between NF/HG and LF/HG AS patterns is made in the current guidelines (1,3). However, the outcome of LF/HG AS patients

tends to be worse both before and after AVR (5,7,15). So, these patients deserve closer follow-up and prompt referral for AVR when symptoms develop.

The LF/LG AS pattern raises the most controversy. Although little is known about its natural history, LF/LG AS with preserved LVEF seems to have a distinct pathophysiology characterized by severe LV concentric remodeling with smaller LV diastolic cavity size, depressed LV longitudinal systolic function, restrictive LV filling physiology, higher BNP levels, lower arterial compliance, and higher arterial and valvular load, altogether translating into a decreased SVi and a poorer outcome (7). Other causes of low transvalvular flow may be identified in patients with LF/LG: significant mitral regurgitation, atrial fibrillation, constrictive pericarditis, or severe pulmonary hypertension with right heart failure. These patients

may not exhibit the echocardiographic features of LF/LG AS, including a relative wall thickness  $>0.5$ , an end-diastolic volume index  $<55$  ml/m<sup>2</sup>, and a global longitudinal strain  $<16\%$ . Based on a worse prognosis and improved survival after AVR, it seems that among the 4 flow-gradient groups with small AVA and preserved LVEF, the LF/LG AS represents a more advanced stage of the disease (8,9,15). It remains uncertain what is the proportion of patients who evolve directly from moderate AS to LF-LG AS (i.e., those who never reach the HG stage) versus those who evolve from moderate AS to NF-HG, and then to LF-LG. In contrast, other reports suggest that LF/LG AS characterizes moderate AS and is merely an intermediate form to HG AS, with outcomes similar to moderate AS (10-12).

Bavishi et al. (4) further clarified the prognostic impact of the flow-gradient AS patterns. In their meta-analysis, the authors confirmed that the prognosis of patients in the LF/LG group is compromised in the absence of diagnosis and appropriate treatment. All of this emphasizes that the evaluation of AS should be comprehensive, and when conflicting results in AS grading exist, multimodality imaging assessment is required to confirm disease stage and guide therapeutic decision-making (14).

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