Characterisation of aortic stenosis severity: a retrospective analysis of echocardiography reports in a clinical laboratory

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ABSTRACT
Objective To evaluate how common echocardiographic metrics of aortic stenosis (AS) influence the proportion of patients who may be categorised as having severe stenosis and therefore considered for valve replacement.

Methods Retrospective analysis was performed of all echocardiograms with aortic valve area (AVA) ≤1.2 cm² and peak jet velocity (Vmax) ≥3 m/s from 1 December 2014 through 30 October 2017 at a single academic medical centre. Echocardiographic indices collected include AVA, Vmax, left ventricular ejection fraction, stroke volume and annotated aortic stenosis severity.

Results Among 807 patients with AVA ≤1.2 cm² and Vmax ≥3 m/s (44.0% female, median age 74 years (IQR: 66–81)), 45.6% had Vmax ≥4 m/s, while 75.8% had AVA ≤1 cm². 40.0% of patients had concordant indices (Vmax ≥4 m/s and AVA ≤1 cm²), and 35.8% had discordant indices (Vmax <4 m/s and AVA ≤1 cm²) of severe AS. Compared with those with concordant indices, patients with discordant indices were more commonly female (54.0% vs 44.3%, p<0.05) and less commonly characterised as severe (42.6% vs 93.8%, p<0.001). Patients with paradoxical low-flow, low-gradient severe AS by echocardiography were disproportionately female (61.5% vs 41.8%, p<0.001), and their disease was characterised as severe only 49.5% of the time.

Conclusions Patients with discordant indices, who are disproportionately female, are commonly described in clinical echocardiography reports as having less than severe AS. Given the potential benefit of AVR in patients with AVA ≤1 cm² regardless of Vmax, this could have important clinical implications.

INTRODUCTION
Aortic stenosis (AS) accounts for approximately 15 000 deaths in North America each year, and the only effective treatment is surgical or transcatheter aortic valve replacement (AVR).1 Currently, AVR is recommended in patients with severe, symptomatic AS and in some cases in those with severe, asymptomatic AS.2 Determination of AS severity relies primarily on the haemodynamic indices of peak jet velocity (Vmax) or mean transvalvular gradient across the aortic valve, and secondarily on decreased aortic valve area (AVA).3 Commonly, patients are considered to have severe AS when they meet both the AVA criteria (≤1 cm²) and haemodynamic criteria (Vmax ≥4 m/s or mean gradient ≥40 mm Hg).3 However, the guidelines also indicate that patients with Vmax 3.0–3.9 m/s and AVA ≤1 cm² (‘discordant AS’) may have severe AS if certain criteria apply.2 A number of prior studies have demonstrated that such a discordance between these indices is common and suggested that patients with discordant AS would see a survival benefit
from AVR. Nonetheless, this discordance can yield uncertainty regarding the severity of AS, which influences clinical management.1–7

Herein, using echocardiographic data obtained in clinical practice, we evaluated how these indices of severe AS (Vmax ≥ 4 m/s and AVAi ≤ 0.6 cm²/m²) were analysed to include the spectrum of patients who would be classified as having severe AS when using the AVAi criteria instead of the Vmax criteria, and would particularly increase the proportion of female patients considered to have severe AS (44.9% vs 96.7%, p=0.02) and less likely to have their AS characterised as ‘severe’ on the clinical echocardiography report (42.6% vs 93.8%, p<0.001) (table 1). Based on the Vmax ≥ 1 m/s criterion, 45.6% of the cohort was classified as having severe AS (table 2). In contrast, based on the AVAi ≤ 0.6 cm² criterion, 75.8% was classified as having severe AS. This represents a relative 66.3% increase in the proportion of patients who would be classified as having severe AS when using the AVAi criteria instead of the Vmax criteria, and would particularly increase the proportion of female patients considered to have severe AS (44.9% vs 96.7%, p=0.02) and less likely to have their AS characterised as ‘severe’ on the clinical echocardiography report (42.6% vs 93.8%, p<0.001) (table 2). This difference persisted when expanding the ‘severe’ group to include those characterised as ‘moderate–severe’ (71.6% vs 98.8%, p<0.001). Replacing Vmax with mean gradient yields similar results with identical conclusions (online supplementary table 1, online supplementary figure 1). When AVAi ≤ 0.6 cm²/m² replaced AVAi ≤ 1 cm², patients with discordant indices were again less often characterised as ‘severe’ on the echocardiography report than those with concordant indices (32.2% vs 90.3%, p<0.001). Figure 1A shows data plotted by Vmax and AVAi, colour coded by the AS characterisation on the echocardiography report. The percentages reported as severe for each quadrant defined by an AVAi of 1.0 cm² and Vmax of 4 m/s are also shown. In figure 1B, data are plotted and colour coded by sex, and each quadrant shows the proportion of the population represented and the percentage female.

RESULTS

Among 807 patients (44.0% female) who had a recorded AVAi ≤ 0.6 cm²/m², patients with discordant indices of severe AS (Vmax < 4 m/s and AVAi ≤ 1 cm²) made up 35.8% of the study cohort, and those with concordant indices of severe AS (Vmax ≥ 4 m/s and AVAi ≤ 1 cm²) comprised 40.0%. Compared with those with discordant indices, those with discordant indices were more likely to be female (54.0% vs 44.3%, p=0.02) and less likely to have their AS characterised as ‘severe’ on the clinical echocardiography report (42.6% vs 93.8%, p<0.001) (table 2). This difference persisted when expanding the ‘severe’ group to include those characterised as ‘moderate–severe’ (71.6% vs 98.8%, p<0.001). Replacing Vmax with mean gradient yields similar results with identical conclusions (online supplementary table 1, online supplementary figure 1). When AVAi ≤ 0.6 cm²/m² replaced AVAi ≤ 1 cm², patients with discordant indices were again less often characterised as ‘severe’ on the echocardiography report than those with concordant indices (32.2% vs 90.3%, p<0.001). Figure 1A shows data plotted by Vmax and AVAi, colour coded by the AS characterisation on the echocardiography report. The percentages reported as severe for each quadrant defined by an AVAi of 1.0 cm² and Vmax of 4 m/s are also shown. In figure 1B, data are plotted and colour coded by sex, and each quadrant shows the proportion of the population represented and the percentage female.

METHODS

Clinical transthoracic echocardiogram reports from 1 December 2014 to 30 October 2017 were retrospectively extracted from the Synthetic Derivative, a de-identified mirror of the electronic health record at Vanderbilt University Medical Center.10 Using previously described approaches that include regular expressions and natural language processing,11,12 these echocardiographic reports were generated in the course of clinical practice in the Vanderbilt University Medical Center echocardiography laboratory, where readers are instructed to follow society guidelines for characterisation of the severity of AS.2,3 For each patient, the report with the smallest AVAi represented and the percentage female.

Patient and public involvement

We did not directly include patient and public involvement in this study, but community representatives are involved in oversight of the database used in the study (the Synthetic Derivative) through the Vanderbilt Institute for Clinical and Translational Research.

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We further investigated these trends by comparing patients with discordant AS who were characterised as having either ‘severe’ or ‘non-severe’ disease (table 3).

There were no differences between the groups with respect to body size or LVOT dimension. Although all patients had an AVA and AVAi below the threshold for severe AS, those characterised as ‘severe’ on the echocardiography report had lower AVA and AVAi and a higher transvalvular gradient than those characterised as ‘non-severe’. To identify any subgroups that may be underdiagnosed, we divided patients with discordant AS into stages as defined by AHA/ACC recommendations (table 4).2 Among those with AVA ≤1.0 cm², AVAi ≤0.6 cm²/m² and Vmax < 4 m/s, patients with ejection fraction (EF) <50% (potentially stage D2 patients depending on the results of a dobutamine echocardiogram) comprised 7.3% of the total study cohort (20.8% of those with discordant indices) and were

| Table 1 | Cohort characteristics |
|---------|-----------------------|
| | All (807) | Female (355) | Male (452) | P value |
| Age, years | 73.7 (65.7 to 80.9) | 75.1 (67.0 to 82.5) | 72.9 (64.9 to 79.9) | 0.03 |
| BMI, kg/m² | 28.8 (25.3 to 33.8) | 29.3 (24.8 to 35.8) | 28.4 (25.6 to 32.6) | 0.04 |
| AVA, cm² | 0.86 (0.70 to 1.00) | 0.80 (0.65 to 0.94) | 0.90 (0.75 to 1.03) | <0.001 |
| AVAi, cm²/m² | 0.43 (0.36 to 0.51) | 0.44 (0.36 to 0.52) | 0.43 (0.36 to 0.50) | 0.09 |
| Vmax, m/s | 3.87 (3.41 to 4.38) | 3.80 (3.37 to 4.30) | 3.92 (3.45 to 4.41) | 0.02 |
| Mean gradient, mm Hg | 35.0 (26.7 to 45.3) | 33.0 (26.0 to 43.1) | 36.0 (27.5 to 46.0) | 0.01 |
| Peak gradient, mm Hg | 59.9 (46.7 to 76.9) | 57.8 (45.3 to 74.0) | 61.2 (47.7 to 78.3) | 0.03 |
| DI | 0.24 (0.20 to 0.29) | 0.26 (0.21 to 0.30) | 0.23 (0.20 to 0.28) | <0.001 |
| Ejection fraction, % | 55 (55 to 63) | 58 (55 to 63) | 55 (55 to 60) | <0.001 |
| SV, mL | 78.1 (64.6 to 90.4) | 73.1 (58.9 to 84.6) | 81.8 (70.2 to 94.1) | <0.001 |
| Indexed SV, mL/m² | 39.7 (32.9 to 46.3) | 39.9 (33.2 to 47.3) | 39.4 (32.8 to 45.6) | 0.22 |
| LVOT diameter, cm | 2.10 (2.00 to 2.29) | 2.00 (1.90 to 2.00) | 2.20 (2.10 to 2.30) | <0.001 |
| LVIDd, cm | 4.42 (3.90 to 4.90) | 4.10 (3.69 to 4.60) | 4.61 (4.22 to 5.09) | <0.001 |
| LVIDs, cm | 2.90 (2.50 to 3.46) | 2.66 (2.31 to 3.10) | 3.17 (2.76 to 3.62) | <0.001 |
| BSA, m² | 1.97 (1.77 to 2.15) | 1.78 (1.64 to 1.96) | 2.08 (1.93 to 2.23) | <0.001 |

Data presented as median (25th percentile, 75th percentile). 11 female and 16 male patients did not have reliable BMIs recorded, giving n=344 and 436 for this metric, respectively. 9 female and 5 male patients did not have LVID metrics, giving n=346 and 447, respectively.

AVA, aortic valve area; AVAi, indexed AVA; BMI, body mass index; BSA, body surface area; DI, dimensionless index; LVID, left ventricular internal dimension; LVIDd, LVID in diastole; LVIDs, LVID in systole; LVOT, left ventricular outflow tract; SV, stroke volume; Vmax, peak jet velocity.

| Table 2 | Aortic valve area and peak jet velocity as indices of severe aortic stenosis |
|---------|-----------------------|
| | Total | Vmax ≥4 | All | Vmax ≥4 | Vmax <4 |
| Total (% of cohort) | 807 | 364 (45.6%) | 612 (75.8%) | 323 (40.0%) | 289 (35.8%) |
| Male (% of male patients) | 452 | 214 (47.3%) | 313 (69.2%) | 180 (39.8%) | 133 (29.4%) |
| Female (% of female patients) | 355 | 150 (42.3%) | 299 (84.2%) | 143 (40.3%) | 156 (43.9%) |
| % Female | 44.0% | 41.2% | 48.9% | 44.3% | 54.0% |
| Severity | | | | | |
| None noted | 4 (0.5%) | 0 (0.0%) | 2 (0.3%) | 0 (0.0%) | 2 (0.7%) |
| Mild | 10 (1.2%) | 0 (0.0%) | 5 (0.8%) | 0 (0.0%) | 5 (1.7%) |
| Mild–moderate | 17 (2.1%) | 0 (0.0%) | 8 (1.3%) | 0 (0.0%) | 8 (2.8%) |
| Moderate | 181 (22.4%) | 10 (2.7%) | 71 (11.6%) | 4 (1.2%) | 67 (23.2%) |
| Moderate–severe | 140 (17.3%) | 28 (7.7%) | 100 (16.3%) | 16 (5.0%) | 84 (29.1%) |
| Severe | 455 (56.4%) | 326 (89.6%) | 426 (69.6%) | 303 (93.8%) | 123 (42.6%) |

Severity data presented as number (%). AVA, aortic valve area; Vmax, peak jet velocity.
infrequently female (27.1%), and patients with EF ≥50% comprised 27.8% of the study cohort (79.2% of those with discordant indices). Among this latter group, those with paradoxical low-flow, low-gradient AS (stroke volume index <35 mL/m², stage D3 by echocardiography) represented 11.3% of the study cohort (32.2% of those with discordant indices), were disproportionately female (61.5% vs 41.8%, p<0.001), and were characterised as having ‘severe’ AS only 49.5% of the time. Online supplementary figure 2 shows data plotted by Vmax and AVA, colour coded with ‘low-flow’ status by stroke volume index (≥35 mL/m² vs <35 mL/m²) in all patients. Left ventricular internal diameter was also assessed for characterisation of those with discordant AS, and within each sex there were no significant differences between those with non-severe, severe and discordant severe AS (online supplementary table 2).

![Figure 1](https://openheart.bmj.com/)

**Figure 1** The relationships of recorded severity and sex with AVA and peak jet velocity. (A) All patients in the cohort are plotted in both one and two dimensions by AVA and peak jet velocity, and colour-coded by clinician characterisation as severe (red) or non-severe (grey). The percentage of patients characterised as severe is annotated for each quadrant. (B) This same cohort is plotted coloured by female (red) and male (blue) sex. The percentage of the cohort in each quadrant, as well as the percentage of each quadrant that is comprised of female patients, is noted. AVA, aortic valve area.

### Table 3 Characteristics of patients with discordant aortic stenosis characterised as either severe or non-severe

|                      | Severe (123)      | Non-severe (160) | P value |
|----------------------|-------------------|------------------|---------|
| Age, years           | 76.4 (70.4 to 83.7) | 73.1 (63.5 to 80.1) | <0.001  |
| Sex, % male (n)      | 49.6% (61)        | 45.0% (72)       | 0.44    |
| BMI, kg/m²           | 27.8 (24.2 to 32.9) | 28.4 (24.9 to 33.8) | 0.66    |
| AVA, cm²             | 0.77 (0.63 to 0.86) | 0.90 (0.77 to 0.96) | <0.001  |
| AVAi, cm²/m²         | 0.40 (0.33 to 0.45) | 0.45 (0.40 to 0.51) | <0.001  |
| Vmax, m/s            | 3.58 (3.28 to 3.79) | 3.44 (3.24 to 3.63) | 0.004   |
| Mean gradient, mm Hg | 29.7 (25.5 to 33.1) | 27.0 (23.8 to 31.0) | <0.001  |
| Peak gradient, mm Hg | 51.8 (43.0 to 57.2) | 47.3 (42.0 to 52.8) | 0.003   |
| DI                   | 0.22 (0.19 to 0.26) | 0.26 (0.23 to 0.30) | <0.001  |
| Ejection fraction, % | 55 (38 to 60)      | 55 (55 to 61)     | <0.001  |
| SV, mL               | 61.1 (50.6 to 73.7) | 71.2 (60.2 to 80.0) | <0.001  |
| Indexed SV, mL/m²    | 32.5 (26.1 to 38.2) | 37.5 (30.7 to 42.8) | <0.001  |
| LVOT diameter, cm    | 2.02 (2.00 to 2.27) | 2.00 (2.00 to 2.20) | 0.20    |
| LVIDd, cm            | 4.59 (3.98 to 5.03) | 4.32 (3.93 to 4.80) | <0.001  |
| LVIDs, cm            | 3.17 (2.60 to 3.84) | 2.90 (2.50 to 3.30) | <0.001  |
| BSA, m²              | 1.93 (1.72 to 2.10) | 1.90 (1.73 to 2.06) | 0.72    |

Data presented as median (25th percentile, 75th percentile) except where otherwise noted. 7 severe and 4 non-severe patients did not have reliable BMIs recorded, giving n=116 and 156 for this metric, respectively. 3 severe and 2 non-severe patients did not have LVID metrics, giving n=120 and 158, respectively.

AVA, aortic valve area; AVAi, indexed AVA; BMI, body mass index; BSA, body surface area; DI, dimensionless index; LVID, left ventricular internal dimension; LVIDd, LVID in diastole; LVIDs, LVID in systole; LVOT, left ventricle outflow tract; SV, stroke volume; Vmax, peak jet velocity.
DISCUSSION

Using data from clinical echocardiography reports of patients with AVA ≤1.2 cm² and V_max ≥3 m/s, we found that shifting from a specific definition of severe AS (V_max ≥4 m/s) to a sensitive definition (AVA ≤1 cm²) resulted in a 66% relative increase in the number of patients with potentially severe AS, with a 97% relative increase in female patients. This observed increase is similar to previously reported data, but it also provides quantitative insight into how this move would affect female patients in particular. Furthermore, while patients with concordant indices of AS severity by echocardiography are usually characterised as having severe AS (94% of the time in our study), discordant indices are common (observed almost as commonly as concordant indices among those with AVA ≤1 cm²), disproportionately observed in female patients, and yield a characterisation of ‘severe’ AS as a minority of the time (43%).

To our knowledge, this is the first study to demonstrate how echocardiographic data are integrated by an echocardiographer when reporting the overall AS severity in a clinical report. This has important implications, as those who receive and read an echocardiography report (particularly if they do not have expertise in valve disease or reading raw echocardiography images) may not be inclined to refer a patient with anything less than ‘severe AS’ for AVR consideration. In this sense, the summary statement of AS severity on the clinical echocardiography report is consequential. Multiple recent studies, although retrospective and non-randomised, report a survival advantage from AVR for those with AVA ≤1 cm² regardless of V_max≤1.2 cm², disproportionately observed in female patients.15 Between these, calcification was seen to

Table 4

| Severity grading | All | EF <50 | All | SVI <35 | SVI ≥35 |
|------------------|-----|--------|-----|--------|--------|
| None             | 1 (0.4%) | 0 (0.0%) | 1 (0.4%) | 1 (1.1%) | 0 (0.0%) |
| Mild             | 5 (1.8%) | 0 (0.0%) | 5 (2.2%) | 3 (3.2%) | 2 (1.5%) |
| Mild–moderate    | 8 (2.8%) | 0 (0.0%) | 8 (3.6%) | 4 (4.4%) | 4 (3.0%) |
| Moderate         | 65 (23.0%) | 10 (16.9%) | 55 (24.6%) | 21 (23.1%) | 34 (25.6%) |
| Moderate–severe  | 81 (28.6%) | 11 (18.6%) | 70 (31.3%) | 17 (18.7%) | 53 (39.8%) |
| Severe           | 123 (43.5%) | 38 (64.4%) | 85 (37.9%) | 45 (49.5%) | 40 (30.1%) |

Severity data reported as number (%).

AVA, aortic valve area; AVAi, indexed AVA; EF, ejection fraction; SVi, indexed stroke volume; V_max, peak jet velocity.
be associated with higher gradients. Female patients also tend to have a lower stroke volume than male patients, which is associated with lower transvalvular gradients.

The frequent characterisation of patients with discordant AS indices as having less than severe AS is likely due to two primary reasons. First, it is likely influenced by the explicit prioritisation in the guidelines of $V_{\text{max}}$ and transvalvular mean gradient over AVA in the assessment of AS severity. While updates in the guidelines have increasingly allowed for subgroups of patients to be classified as having severe AS despite a $V_{\text{max}} < 4$ m/s, the long-standing paradigm of prioritising $V_{\text{max}}$ over AVA leads to clinicians reluctant to classify a patient as having severe AS with $V_{\text{max}} < 4$ m/s. However, the rationale for prioritising $V_{\text{max}}$ over AVA in the diagnosis of severe AS is based on small studies that neither examine hard clinical events nor compare prompt AVR versus clinical surveillance at various $V_{\text{max}}$ or AVA thresholds. Second, in cases of discordant measurements, additional testing with nitroprusside, dobutamine, or aortic valve calcium scoring is increasingly performed to clarify whether AS is severe. Previous work has highlighted the need for such additional testing in discordant AS. Knowing this, echocardiographers may be reluctant to over-call ‘severe AS’ when they know these additional tests may help clarify the diagnosis. However, to readers of echocardiography reports who do not commonly care for patients with AS, the diagnosis of anything other than ‘severe AS’ on the echocardiography report may simply be interpreted as a signal to ‘continue watching’ that patient rather than to perform an adjunctive test to clarify the true severity of stenosis.

System-level changes may be warranted to address these challenges, which likely have adverse clinical consequences. So as not to potentially delay referral for valve replacement in patients with discordant indices of AS severity, if the echocardiographer is not going to characterise discordant AS indices (AVA <1 cm² and $V_{\text{max}} < 4$ m/s) as ‘severe’ on the clinical report, then it may be appropriate to include the following on the report: ‘possibly severe AS, but additional evaluation or testing is needed.’ This would enable the echocardiographer to not ‘over-call’ severe AS when they believe further testing is needed, but also help ensure that these patients with discordant indices are not passively watched but instead further evaluated and, as appropriate, referred for AVR in a timely manner. In addition, quality improvement efforts in echocardiography laboratories could reinforce that a $V_{\text{max}} \geq 4$ m/s is not required for the diagnosis of severe AS.

**Limitations**

In this cross-sectional study based solely on echocardiography data, we do not have information on clinical presentation, symptoms, referral to AVR or long-term outcomes. Furthermore, we do not have data from dobutamine echocardiograms or valve calcium scores from CT studies. Our focus was on relating the haemodynamic indices of AS obtained on an echocardiogram to how echocardiographers assimilate that information and report a summative characterisation of AS severity. Using the resting echocardiographic indices alone is consistent with the fact that most of the studies on the relationship between AS severity and outcomes simply rely on these resting echocardiographic haemodynamic indices (AVA, $V_{\text{max}}$) and not on adjunctive information from stress testing or valve calcium scores. Additionally, we did not assess for measurement error or attempt to validate sonographer measurements. Importantly, we are not commenting here on the underlying biology or pathology. Instead, we have evaluated the cardiologist’s qualitative read given these values. Finally, these data were collected from a single academic medical centre, which may not be representative of other echocardiography laboratories.

**Conclusions**

The proportion of patients and relative percentage of female patients potentially categorised as having severe AS is markedly influenced by the echocardiographic indices of severe AS used. Clinical echocardiography reports usually characterise discordant indices of AS severity, which are common and disproportionately observed in female patients, as less than severe, which could have adverse clinical consequences. When discordant indices of AS severity are encountered and characterisation of AS severity is uncertain, notation in the clinical echocardiography report of the need for additional evaluation or testing may minimise the number of patients who experience a delay in referral for AVR.

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**Contributors** Study conception and design: MAR, BRL and WDM. Acquisition and technical analysis of the data: MAR, EF and QSW. Data interpretation: MAR, HMG, BRL and WDM. Manuscript preparation: MAR, HMG, BRL and WDM.

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**Competing interests** BRL has received research grants from Edwards Lifesciences and Roche Diagnostics; served on scientific advisory boards for Roche Diagnostics and has been a consultant to Medtronic and Roche Diagnostics.

**Patient consent for publication** Not required.

**Ethics approval** Use of the Synthetic Derivative is classified as non-human research by Vanderbilt University’s Institutional Review Board (IRB), and approval was given for this study (IRB #180320).

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**Data availability statement** Deidentified data are available upon reasonable request by contacting david.merryman@vanderbilt.edu.

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REFERENCES

1. Lindman BR, Clavel M-A, Mathieu P, et al. Calcific aortic stenosis. Nat Rev Dis Primers 2016;2:1606.
2. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: Executive summary: a report of the American College of Cardiology/American heart association Task force on practice guidelines. Circulation 2014;129:2440–92.
3. Baumgartner H, Hung J, Bermejo J, et al. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. Eur J Echocardiogr 2009;10:1–25.
4. Berthelot-Richer M, Pibarot P, Capoulade R, et al. Discordant Grading of Aortic Stenosis Severity: Echocardiographic Predictors of Survival Benefit Associated With Aortic Valve Replacement. JACC Cardiovasc Imaging 2016;9:797–805.
5. Dayan V, Vignolo G, Magne J, et al. Outcome and impact of aortic valve replacement in patients with preserved LVEF and Low-Gradient aortic stenosis. J Am Coll Cardiol 2015;66:2594–603.
6. Hachicha Z, Dumesnil JG, Bogaty P, et al. Paradoxical low-flow, low-gradient severe aortic stenosis despite preserved ejection fraction is associated with higher afterload and reduced survival. Circulation 2007;115:2566–64.
7. Malouf J, Le Tourneau T, Pelilikka P, et al. Aortic valve stenosis in community medical practice: determinants of outcome and implications for aortic valve replacement. J Thorac Cardiovasc Surg 2012;144:1421–7.
8. Minners J, Allgeier M, Gohlike-Baervwolf C, et al. Inconsistencies of echocardiographic criteria for the grading of aortic valve stenosis. Eur Heart J 2008;29:1043–8.
9. Minners J, Allgeier M, Gohlike-Baervwolf C, et al. Inconsistent grading of aortic valve stenosis by current guidelines: haemodynamic studies in patients with apparently normal left ventricular function. Heart 2010;96:1463–9.
10. Roden DM, Pulley JM, Basford MA, et al. Development of a large-scale de-identified DNA Biobank to enable personalized medicine. Clin Pharmacol Ther 2008;84:362–9.
11. Mosley JD, Levinson RT, Brittain EL, et al. Clinical features associated with nascent left ventricular diastolic dysfunction in a population aged 40 to 55 years. Am J Cardiol 2018;121:1552–7.
12. Wells QS, Farber-Eger E, Crawford DC. Extraction of echocardiographic data from the electronic medical record is a rapid and efficient method for study of cardiac structure and function. J Clin Bioinforma 2014;4:12–11.
13. R Development Core Team. R: a language and environment for statistical computing, Vienna, Austria: R Foundation for Statistical Computing, 2018.
14. Fuchs C, Messcherbauer J, Rosenhek R, et al. Gender differences in clinical presentation and surgical outcome of aortic stenosis. Heart 2010;96:539–45.
15. Aggarwal SR, Clavel M-A, Messika-Zeitoun D, et al. Sex differences in aortic valve calcification measured by multidetector computed tomography in aortic stenosis. Circ Cardiovasc Imaging 2013;6:40–7.
16. Clavel M-A, Magne J, Pibarot P. Low-gradient aortic stenosis. Eur Heart J 2016;37:2645–57.
17. Bonow RO, Carabello BA, Chatterjee K, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease. Circulation 2006;114:e84–231.
18. Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease. Eur Heart J 2017;38:2739–91.