Incremental value of left ventricular global longitudinal strain in moderate aortic stenosis and reduced left ventricular ejection fraction

Jan Stassen\textsuperscript{a,b}, Gurpreet K. Singh\textsuperscript{a}, Stephan M. Pio\textsuperscript{a}, Suren Chimed\textsuperscript{a}, Steele C. Butcher\textsuperscript{a}, Kensuke Hirawas\textsuperscript{a}, Nina Ajmone Marsan\textsuperscript{b}, Jeroen J. Bax\textsuperscript{a,b,\ast}

\textsuperscript{a} Department of Cardiology, Leiden University Medical Center, Leiden, the Netherlands
\textsuperscript{b} Department of Cardiology, Jessa Hospital, Hasselt, Belgium
\textsuperscript{c} Department of Cardiology, Turku University Hospital, Turku, Finland

\textbf{Abstract}

\textbf{Background:} Moderate aortic stenosis (AS) often coexists with left ventricular (LV) systolic dysfunction and may affect survival through afterload mismatch. Because outcomes are ultimately driven by the condition of the LV, accurate assessment of LV performance is crucial to improve risk stratification. This study investigated the prognostic value of LV global longitudinal strain (GLS) in patients with moderate AS and reduced LV systolic dysfunction.

\textbf{Methods:} Patients with moderate AS (aortic valve area \(1.0-1.5\text{ cm}^2\)) and reduced LV ejection fraction (EF) (<50\%) were included. LVGLS was evaluated with speckle-tracking echocardiography. Patients were divided into 2 groups according to an LVGLS value of 11\%, based on spline curve analysis. The primary endpoint was all-cause mortality.

\textbf{Results:} A total of 166 patients (mean age 73 \(\pm\) 11 years, 71\% male) were included. The cumulative 1- and 5-year mortality rates were higher in patients with LVGLS <11\% (25\% and 60\%) versus LVGLS \(\geq\)11\% (10\% and 27\%) \((p < 0.001)\). On multivariable analysis, LVGLS as a continuous variable (HR 0.753; 95\% CI 0.673-0.843; \(p < 0.001\)) and as a categorical variable (<11\%) (HR 3.028; 95\% CI 1.623-5.648; \(p < 0.001\)) were independently associated with outcomes, whereas LVEF was not. LVGLS provided additional prognostic information in patients with/without coronary artery disease and with mildly versus severely reduced LVEF. In addition, LVGLS had incremental prognostic value over established risk factors, including LVEF.

\textbf{Conclusion:} The combination of moderate AS and reduced LV systolic dysfunction is associated with a high mortality risk. LVGLS, but not LVEF, is independently associated with mortality and provides incremental prognostic value over established risk factors in patients with moderate AS and reduced LVEF.

\section{Introduction}

Aortic stenosis (AS) is the most common valvular heart disease, affecting 2-4\% of patients older than 65 years \cite{1}. Recent studies have demonstrated that moderate AS is not as benign as previously assumed, with reported outcomes almost as unfavorable as in severe AS \cite{2,3}. Moderate AS often coexists with left ventricular (LV) systolic dysfunction and patients with both moderate AS and reduced LV ejection fraction (EF) exhibit particularly poor outcomes \cite{4,5}. Indeed, moderate AS may further reduce LV systolic dysfunction through afterload mismatch, thereby compromising outcomes. An accurate assessment of LV systolic function therefore seems essential to better risk-stratify patients with moderate AS and reduced LVEF. In addition, although patients with moderate AS and reduced LVEF represent a heterogeneous population, previous papers have treated these patients as a homogeneous population and identification of variables that improve risk stratification in patients with moderate AS and reduced LVEF have not been evaluated. An improved risk stratification of these patients is important, especially...
with ongoing trials investigating the potential benefits of transcatheter aortic valve replacement (AVR) in patients with moderate AS and reduced LVEF [6]. Although LV systolic function is most commonly measured with LVEF, LV global longitudinal strain (GLS) has shown to be impaired at an earlier stage in patients with AS [7] and has shown incremental prognostic value over LVEF in patients with severe AS, as well as in patients with heart failure and reduced LVEF [8,9]. The prognostic value of LV GLS in patients with moderate AS and concomitant reduced LVEF, as well as its incremental prognostic value over LVEF, has not been previously investigated. Therefore, the aim of the current study was to evaluate the prognostic value of LV GLS in patients with moderate AS and reduced LVEF.

2. Methods

2.1. Patient population

Patients ≥18 years who presented between 2001 and 2019 with a first diagnosis of moderate AS in the presence of LV systolic dysfunction at the Leiden University Medical Center, Leiden, The Netherlands, were retrospectively identified. Moderate AS was defined as an aortic valve area between 1.0 and 1.5 cm² with a peak aortic jet velocity < 4 m/s and mean valve gradient < 40 mmHg [10]. Consequently, no patients with severe low-flow, low-gradient AS were included and the definition is in line with previous published articles on moderate AS [11,12]. LV systolic dysfunction was defined as LVEF <50% [13]. Patients with congenital heart disease, heart transplantation, supra- or subvalvular AS, dynamic LV outflow tract obstruction, infectious endocarditis, previous aortic valve surgery, a paced rhythm at the time of echocardiography or inadequate image quality for speckle tracking strain analysis (due to poor acoustic windows or insufficient data) were excluded. All patients underwent complete clinical and echocardiographic evaluation at the time of first diagnosis. Patient information was collected from the departmental cardiology information system and was retrospectively analyzed. Clinical data included demographic characteristics, cardiovascular risk factors, comorbidities and heart failure medication. Patients were divided into two groups according to LV GLS. An LV GLS value of 11% was chosen, based on spline curve analysis (Fig. 1). The study complies with the Declaration of Helsinki and was approved by the institutional review board. Due to the retrospective design of the study, the medical ethical committee waived the need for written informed consent.

2.2. Transthoracic echocardiography

Echocardiographic examinations were acquired by experienced echocardiographers using commercially available ultrasound systems (Vivid-7, E9 or E95, General Electric Vingmed, Horten, Norway). Images were digitally stored for offline analysis using commercially available software (EchoPac version 113 and 203; GE Medical Systems, Horten, Norway) and retrospectively analyzed according to current guidelines [14]. LV dimensions were assessed in the parasternal long-axis view and LV mass was calculated using the Devereux’s formula [14]. LV end-diastolic and end-systolic volumes were measured in the apical 2-chamber and 4-chamber views, and LVEF was calculated according to the Simpson’s biplane method [14]. Left atrial volumes were measured by the biplane method of disks [14]. Continuous wave Doppler recordings were obtained to estimate the peak aortic jet velocity from the apical 3- or 5-chamber views and the parasternal right view, if feasible [15]. Mean and peak transvalvular pressure gradients were calculated using the Bernoulli Eq. [15]. Aortic valve area was calculated using the continuity Eq. [15]. Pulsed wave-Doppler recordings of the transmitral flow were used to obtain peak early (E) and late (A) diastolic velocities [16]. Using tissue Doppler imaging of the mitral annulus on the apical 4-chamber view, the e’ was measured at both the lateral and septal side, and averaged to calculate the E/e’ ratio [16]. The right ventricular systolic pressure was calculated from the peak velocity of the tricuspid regurgitant jet, adding the right atrial pressure (determined by the inspiratory collapse and diameter of the inferior vena cava) [14,17]. Tricuspid annular plane systolic excursion was measured with the anatomical M-mode applied on the focused apical 4-chamber view of the right ventricle [17]. LV speckle tracking strain analysis was performed on the apical views (2-, 3-, and 4-chamber) at a frame rate > 40fps, using EchoPac (GE Medical Systems, Horten, Norway) [18]. The region of interest was automatically created and manually adjusted to the myocardial thickness. LV GLS was then calculated by averaging the peak longitudinal strain values of the 17 segments, excluding segments that could not be traced correctly [18]. The values of LV GLS are reported as positive values.
2.3. Clinical endpoints

All patients were followed-up for the primary endpoint of all-cause mortality. Data on mortality were obtained from the departmental cardiology information system (EPD-Vision, Leiden University Medical Center, Leiden, The Netherlands), which is linked to the governmental death registry database. Indications for aortic valve surgery were based on contemporary guidelines [10].

2.4. Statistical analysis

Continuous data are presented as mean ± standard deviation when normally distributed and as median (interquartile range) when not normally distributed. Categorical data are presented as absolute numbers and percentages. Continuous variables were compared using the independent sample Student t-test when normally distributed whereas the Mann-Whitney U test was used to compare continuous variables that did not adhere to a normal distribution. Categorical variables were compared using the Pearson chi-square test. Changes in variables that did not adhere to a normal distribution. Categorical data are presented as absolute

| Table 1 | Baseline clinical characteristics and echocardiographic variables. |
|---------|---------------------------------------------------------------|
| Overall population | LV GLS < 11% | LV GLS ≥ 11% | p value |
| (n = 166) | (n = 89) | (n = 77) |
| Age, years | 73 (±11) | 73 (±10) | 73 (±12) | 0.990 |
| Male sex (%) | 118 (71%) | 67 (75%) | 51 (66%) | 0.200 |
| BMI, kg/m² | 27.5 (±4.6) | 27.4 (±4.5) | 27.6 (±4.6) | 0.824 |
| BSA, m² | 1.96 (±0.22) | 1.99 (±0.22) | 1.92 (±0.20) | 0.075 |
| Arterial hypertension (%) | 122 (74%) | 64 (72%) | 58 (76%) | 0.520 |
| Dyslipidemia (%) | 102 (62%) | 57 (64%) | 45 (59%) | 0.524 |
| DM (%) | 47 (29%) | 28 (32%) | 19 (25%) | 0.259 |
| Current smoker (%) | 19 (13%) | 9 (11%) | 10 (14%) | 0.539 |
| Obesity (%) | 43 (26%) | 21 (24%) | 22 (29%) | 0.460 |
| CAD (%) | 93 (56%) | 62 (70%) | 31 (40%) | <0.001 |
| Previous myocardial infarction (%) | 60 (36%) | 38 (43%) | 22 (29%) | 0.059 |
| Atrial fibrillation (%) | 61 (37%) | 39 (44%) | 22 (29%) | 0.042 |
| Previous stroke (%) | 30 (18%) | 15 (17%) | 15 (20%) | 0.661 |
| COPD (%) | 22 (13%) | 10 (11%) | 12 (16%) | 0.410 |
| NYHA class III-IV (%) | 39 (24%) | 23 (26%) | 16 (22%) | 0.503 |
| Angina (%) | 18 (11%) | 11 (13%) | 7 (9%) | 0.504 |
| Syncope (%) | 4 (3%) | 3 (5%) | 1 (1%) | 0.387 |
| Beta-blocker (%) | 98 (59%) | 54 (61%) | 44 (58%) | 0.717 |
| ACEi or ARB (%) | 100 (61%) | 56 (63%) | 44 (58%) | 0.510 |
| MRA (%) | 24 (15%) | 19 (22%) | 5 (7%) | 0.007 |
| Diuretic (%) | 89 (54%) | 58 (65%) | 31 (41%) | 0.002 |
| Statin (%) | 102 (62%) | 59 (66%) | 43 (57%) | 0.201 |
| Aspirin (%) | 68 (41%) | 41 (46%) | 27 (36%) | 0.170 |
| Oral anticoagulation (%) | 65 (39%) | 38 (43%) | 27 (36%) | 0.347 |
| eGFR, ml/min/1.73m² | 68 (±28) | 63 (±26) | 74 (±28) | 0.015 |
| Hemoglobin, g/dl | 13.0 (±1.9) | 12.9 (±1.8) | 13.2 (±2.0) | 0.295 |
| LV ESV, ml | 73 (52–100) | 91 (69–113) | 61 (42–76) | <0.001 |
| LV EDVi, ml/m² | 36 (29–51) | 45 (35–56) | 30 (21–40) | <0.001 |
| LV EDV, ml | 129 (95–163) | 144 (115–177) | 115 (82–141) | <0.001 |
| LV EDVi, ml/m² | 65 (50–81) | 72 (60–86) | 58 (41–72) | <0.001 |
| LVEF, % | 42 (35–47) | 38 (30–42) | 45 (42–48) | <0.001 |
| LV GLS, % | 11.0 (±3.5) | 8.3 (±1.8) | 14.1 (±2.0) | <0.001 |
| LVMI, g/m² | 128 (±38) | 138 (±38) | 116 (±34) | <0.001 |
| LAVI, ml/m² | 41 (33–52) | 45 (36–57) | 37 (29–46) | <0.001 |
| E/e’ | 15 (12–21) | 16 (12–24) | 15 (11–18) | 0.057 |
| Bicuspid valve, % | 17 (10%) | 6 (7%) | 11 (14%) | 0.110 |
| AVA, cm² | 1.23 (±0.13) | 1.25 (±0.14) | 1.22 (±0.12) | 0.155 |
| AVAi, cm²/m² | 0.64 (±0.09) | 0.64 (±0.10) | 0.64 (±0.08) | 0.923 |
| Peak aortic jet velocity, m/s | 2.8 (±0.55) | 2.7 (±0.55) | 2.9 (±0.55) | 0.100 |
| Aortic mean pressure gradient, mmHg | 20 (±8) | 19 (±8) | 21 (±9) | 0.195 |
| Stroke volume index, ml/m² | 38 (±10) | 36 (±10) | 41 (±9) | 0.004 |
| TAPSE, mm | 20 (±5) | 19 (±5) | 21 (±5) | 0.014 |
| PASP, mmHg | 33 (26–41) | 36 (27–48) | 31 (25–37) | 0.006 |

Values are presented as mean ± SD, median (IQR) or n (%). ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; AVA = aortic valve area; AVAi = aortic valve area index; BMI = body mass index; BSA = body surface area; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; EDV = end-diastolic volume; EDVi = end-diastolic volume index; EF = ejection fraction; eGFR = estimated glomerular filtration rate; ESV = end-systolic volume; ESVi = end-systolic volume index; GLS = global longitudinal strain; LAVI = left atrium volume index; LV = left ventricular; MI = mass index; MRA = mineralocorticoid receptor antagonist, NYHA = New York Heart Association; PASP = pulmonary artery systolic pressure; TAPSE = tricuspid annular plane systolic excursion. Obesity was defined as BMI ≥ 30 kg/m².

3. Results

3.1. Patient characteristics

A total of 166 patients (mean age 73 ± 11 years, 71% male) were included. Baseline clinical and echocardiographic characteristics of the overall population are shown in Table 1. A history of coronary artery disease was seen in 93 (56%) patients, of whom 60 (36%) had a previous myocardial infarction. Atrial fibrillation was present in 61 (37%) patients. Patients with an LV GLS <11% were more likely to have coronary artery disease and atrial fibrillation, had more impaired renal function, and received more diuretics and mineralocorticoid receptor antagonists, compared to patients with an LV GLS ≥11%.

Mean aortic valve area was 1.23 ± 0.13 cm², mean pressure gradient 20 ± 8 mmHg and peak aortic jet velocity 2.8 m/s. The median LVEF was 42 (35–47%), mean LV GLS 11.0 ± 3.5% and mean stroke volume index 38 ± 10 ml/m². Patients with an LV GLS <11% had higher LV and left atrial volumes, higher LV mass index, lower LVEF and stroke volume index, more impaired right ventricular systolic dysfunction and higher pulmonary artery pressures. Aortic valve area and pressure gradients were not different between both groups.

3.2. Prognostic value of left ventricular global longitudinal strain

During a median follow-up of 34 (18–67) months, 73 (44%) patients
died. The cumulative 1-, 3- and 5-year survival rates were 82%, 68% and 55%, respectively. Sixty-eight (41%) patients underwent AVR at follow-up (transcatheter AVR: 31 (19%); surgical AVR: 37 (22%)). The clinical and echocardiographic characteristics of the patients who underwent AVR are shown in Table S1. Survival rates were significantly lower in patients with LV GLS <11% when compared to patients with LV GLS ≥11% (p < 0.001) (Fig. 2). Survival rates were 75% at 1 year, 55% at 3 years and 40% at 5 years among patients with LV GLS <11%, whereas survival rates were 90% at 1 year, 84% at 3 years and 73% at 5 years among patients with LV GLS ≥11%. The Kaplan-Meier curves according to LV GLS in patients with versus without coronary artery disease are shown in Fig. S1, whereas the Kaplan-Meier curves according to LV GLS in patients with mildly reduced (41–49%) versus reduced LVEF (<40%) are shown in Fig. S2. Both figures show the incremental value of LV GLS to identify high risk patients.

The uni- and multivariable Cox regression analyses are shown in Table 2. On univariable analysis, LV GLS as a continuous variable (HR GLS 0.753; 95% CI 0.673–0.843; p < 0.001) and as a categorical variable (HR 2.871; 95% CI 1.733–4.756; p < 0.001) were both significantly associated with outcomes. On univariable analysis, LVEF as a continuous variable was also significantly associated with outcomes (HR 0.972; 95% CI 0.946–0.998; p = 0.034) (Table S1). On multivariable analysis, both LV GLS as a continuous variable (HR 0.753; 95% CI 0.673–0.843; p < 0.001) as well as a categorical variable (HR 3.028; 95% CI 1.623–5.648; p < 0.001) remained independently associated with outcomes, after adjusting for age, sex, coronary artery disease, atrial fibrillation, LVEF and AVR as a time dependent covariable. In a sensitivity analysis, these findings were confirmed using a second, third and fourth multivariable model (Table 2). In contrast, LVEF was not independently associated with outcomes on any of these multivariable models (Table S2). The hazard ratio for each covariable is provided in Table S3. Fig. 1 also demonstrates that there was a more or less linear relationship between LV GLS and the HR of mortality, whereas no clear relationship was shown between LVEF and the HR of mortality.

Linear regression analysis was performed to identify variables that were associated with LV GLS. According to this analysis, coronary artery disease (β -0.276; 95% CI -2.952 to -0.889; p < 0.001), atrial fibrillation (β -0.156; 95% CI -2.210 to -0.027; p = 0.045), estimated glomerular filtration rate (β 0.207; 95% CI 0.006 to 0.407; p = 0.011), peak aortic jet velocity (β 0.159; 95% CI 0.037 to 0.1944; p = 0.042) and aortic mean pressure gradient (β 0.125; 95% CI 0.007 to 0.045; p = 0.031) were significantly associated with LV GLS. On multivariable analysis however, only CAD remained independently associated with LV GLS (β -0.210; 95% CI -2.677 to -0.325; p = 0.013) (Table S4).

3.3. Incremental prognostic value of LV GLS

To determine the incremental prognostic value of LV GLS in addition to currently used clinical and echocardiographic parameters, a likelihood ratio test was performed. The addition of LVEF to the baseline model showed no significant increase in the chi-square value (p = 0.321). In contrast, the addition of LV GLS to the baseline model and LVEF showed a significant increase in the chi-square value (chi-square difference 12.8, p < 0.001), demonstrating the incremental prognostic value of LV GLS over LVEF in patients with moderate AS and reduced LVEF (Fig. S3).

4. Discussion

The main findings of the current study, which included patients with moderate AS and reduced LVEF, can be summarized as follows: 1) the combination of moderate AS and reduced LVEF is associated with very high mortality rates; 2) LV GLS is independently associated with survival; and 3) LV GLS has incremental prognostic value over LVEF.

4.1. Outcomes of patients with moderate AS and reduced LVEF

Recent observational studies have shown that moderate AS is associated with an increased risk of adverse events [2,3]. In particular, patients with moderate AS and reduced LVEF seem to have very poor outcomes [4,5]. In 305 patients with moderate AS (aortic valve area 1.0–1.5 cm²) and LV systolic dysfunction (LVEF <50%), van Gils and colleagues showed that the rate of all-cause death or heart failure hospitalization was 48% and the mortality rate 36%, at 4 years follow-up.
5. Conclusion

In patients with moderate AS and reduced LVEF, LV GLS is independently associated with all-cause mortality and provides incremental prognostic value over established risk factors, whereas this was not the case for LVEF.

Disclosures

The department of Cardiology of the Leiden University Medical Centre received unrestricted research grants from Abbott Vascular, Bayer, Biotronik, Bioventrix, Boston Scientific, Edwards Lifesciences, GE Healthcare and Medtronic. Jan Stassen received funding from the European Society of Cardiology (ESC Training Grant App000064741). Stephan M. Pio received funding from the European Society of Cardiology (ESC Training Grant T-2018-17405). Steele C. Butcher received funding from the European Society of Cardiology (ESC Research Grant App000080404). Jeroen J Bax received speaker fees from Abbott Vascular. Nina Ajmone Marsan received speaker fees from Abbott Vascular and GE Healthcare. The remaining authors have nothing to disclose.

Data availability statement

Data are available upon reasonable request.

Author statement

Jan Stassen: conceptualization, acquisition, analysis, interpretation of data, writing - original draft; visualization; Gurpreet K Singh:
acquisition, interpretation of data; writing – review and editing; Stephan M Pio: acquisition, interpretation of data; writing – review and editing; Suren Chimed: acquisition, interpretation of data; writing – review and editing; Steele C Butcher: acquisition, interpretation of data; writing – review and editing; Kensuke Hirasawa: acquisition, interpretation of data; writing – review and editing; Nina Ajmone Marsan: conceptualization, writing – review and editing, supervision; Jeroen J Bax: conceptualization, writing – review and editing, supervision.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2022.11.035.

References

[1] B.A. Carabello, Evaluation and management of patients with aortic stenosis, Circulation 105 (2002) 1746–1750.
[2] G. Strange, S. Steward, D. Celeremajer, et al., Poor long-term survival in patients with moderate aortic stenosis, J. Am. Coll. Cardiol. 74 (2019) 1851–1863.
[3] J. Stassen, S. Butcher, K. Hirawat, et al., Moderate aortic stenosis: importance of symptoms and left ventricular ejection fraction, Eur. Heart J. Cardiovasc. Imaging 23 (6) (2022) 790–799.
[4] G. Jean, N.M. Van Mieghem, T. Gegenova, et al., Moderate aortic stenosis in patients with heart failure and reduced ejection fraction, J. Am. Coll. Cardiol. 77 (2021) 2796–2803.
[5] L. van Gils, M.A. Clavel, E.M. Vollema, et al., Prognostic implications of moderate aortic stenosis in patients with left ventricular systolic dysfunction, J. Am. Coll. Cardiol. 69 (2017) 2383–2392.
[6] E. Spitzer, N.M. Van Mieghem, P. Pibarot, et al., Rationale and design of the Transcatheter aortic valve replacement to UNload the left ventricle in patients with Advanced heart failure (TAVR UNLOAD) trial, Am. Heart J. 182 (2016) 80–86.
[7] A.C. Ng, V. Delgado, M. Bertini, et al., Alterations in multidirectional myocardial functions in patients with aortic stenosis and preserved ejection fraction: a two-dimensional speckle tracking analysis, Eur. Heart J. 32 (2011) 1542–1550.
[8] A.C.T. Ng, E.A. Prabhadi, M.L. Antoni, et al., Left ventricular global longitudinal strain is predictive of all-cause mortality independent of aortic stenosis severity and ejection fraction, Eur. Heart J. Cardiovasc. Imaging 19 (2018) 859–867.
[9] M. Sengeløv, P.G. Jørgensen, J.S. Jensen, et al., Global longitudinal strain is a superior predictor of all-cause mortality in heart failure with reduced ejection fraction, JACC Cardiovasc. Imaging 8 (2015) 1351−1359.
[10] A. Vahanian, F. Beyersdorf, F. Praz, et al., Recommendations for the management of valvular heart disease, Eur. Heart J. 43 (7) (2022) 561–632.
[11] G. Delesalle, Y. Bobot, D. Ruzinara, Q. Delpierre, S. Marcheaux, C. Tribouloy, Characteristics and prognosis of patients with moderate aortic stenosis and preserved left ventricular ejection fraction, J. Am. Heart Assoc. 8 (2019), e011036.
[12] S. Ito, W.R. Miranda, V.T. Nkomo, et al., Prognostic risk stratification of patients with moderate aortic stenosis, J. Am. Soc. Echocardiogr. 34 (2021) 248–256.
[13] T.A. McDonagh, M. Metra, M. Adamo, et al., 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure, Eur. Heart J. 42 (36) (2021) 3599–3726.
[14] R.M. Lang, L.P. Badano, V. Mor-Avi, et al., Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging, J. Am. Soc. Echocardiogr. 1 (2015) 1–39.
[15] H.C. Baumgartner, J.C.-C. Hung, J. Bermojo, et al., Recommendations on the echocardiographic assessment of aortic valve stenosis: a focused update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography, Eur. Heart J. Cardiovasc. Imaging 18 (2017) 254–275.
[16] S.F. Naghavi, O.A. Smieth, C.P. Appleton, et al., Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging, J. Am. Soc. Echocardiogr. 29 (2016) 277–314.
[17] L.G. Rudski, W.W. Lai, J. Alfilalo, et al., Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography, J. Am. Soc. Echocardiogr. 23 (2010) 685–713, quiz 786–8.
[18] K. Negishi, T. Negishi, K. Kurosawa, et al., Practical guidance in echocardiographic assessment of global longitudinal strain, JACC Cardiovasc. Imaging 8 (2015) 489–492.
[19] M. Briand, J.G. Dumensil, L. Kadem, et al., Reduced systemic arterial compliance impacts significantly on left ventricular afterload and function in aortic stenotic implications for diagnosis and treatment, J. Am. Coll. Cardiol. 46 (2005) 291–298.
[20] T. Stanton, R. Leano, T.H. Marwick, Prediction of all-cause mortality from global longitudinal speckle strain: comparison with ejection fraction and wall motion scoring, Circ. Cardiovasc. Imag. 2 (2009) 356–364.
[21] M. Cameli, S. Mondillo, F.M. Righini, et al., Left ventricular deformation and myocardial fibrosis in patients with advanced heart failure requiring transplantation, J. Card. Fail. 22 (2016) 901–907.
[22] S. Jin, J. Weber, H. Singh, K. Gligoric, J.J. Cao, The association of reduced left ventricular strains with increased extracellular volume and their collective impact on clinical outcomes, J. Cardiovasc. Magn. Reson. 23 (2021) 93.
[23] B.A. Carabello, Clinical practice. Aortic stenosis, N. Engl. J. Med. 346 (2002) 677–682.
[24] K. Rajappan, O.E. Rimoldi, D.P. Dutka, et al., Mechanisms of coronary microcirculatory dysfunction in patients with aortic stenosis and angiographically normal coronary arteries, Circulation 105 (2002) 470–476.
[25] S. Hein, E. Arnon, S. Kostin, et al., Progression from compensated hypertrophy to failure in the pressure-overloaded human heart: structural deterioration and compensatory mechanisms, Circulation 107 (2003) 984–991.
[26] F. Weidemann, S. Herrmann, S. Stork, et al., Impact of myocardial fibrosis in patients with symptomatic severe aortic stenosis, Circulation 120 (2009) 577–584.
[27] L.G. Rudski, W.W. Lai, J. Afilalo, et al., Guidelines for the echocardiographic assessment of aortic stenosis in patients with left ventricular systolic dysfunction, J. Am. Coll. Cardiol. 53 (2009) 39–58.
[28] J. Stassen, S.M. Pio, S.H. Ewe, et al., Left ventricular global longitudinal strain in patients with moderate aortic stenosis, J. Am. Soc. Echocardiogr. 35 (8) (2022) 791–800 (Online ahead of print).
[29] D. Mohy, J.G. Dumensil, N. Echahidi, et al., Impact of prosthesis patient mismatch on long-term survival after aortic valve replacement: influence of age, obesity, and left ventricular dysfunction, J. Am. Coll. Cardiol. 53 (2009) 39–47.
[30] Z. Samad, A.N. Vora, A. Dunnin, et al., Aortic valve surgery and survival in patients with moderate or severe aortic stenosis and left ventricular dysfunction, Eur. Heart J. 37 (2016) 2276–2286.