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ORIGINAL ARTICLE

Left ventricular strain–volume loops in bicuspid aortic valve disease: new insights in cardiomechanics

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Abstract

Aims By combining temporal changes in left ventricular (LV) global longitudinal strain (GLS) with LV volume, LV strain–volume loops can assess cardiac function across the cardiac cycle. This study compared LV strain–volume loops between bicuspid aortic valve (BAV) patients and controls, and investigated the loop's prognostic value for clinical events.

Methods and results From a prospective cohort of congenital heart disease patients, BAV patients were selected and compared with healthy volunteers, who were matched for age and sex at group level. GLS analysis from apical views was used to construct strain–volume loops. Associations with clinical events, i.e. a composite of all-cause mortality, heart failure, arrhythmias, and aortic valve replacement, were assessed by Cox regression. A total of 113 BAV patients were included (median age 32 years, 40% female). BAV patients demonstrated lower Sslope (0.21%/mL, [Q1–Q3: 0.17–0.28] vs. 0.27%/mL [0.24–0.34], $P < 0.001$) and ESslope (0.19%/mL [0.12–0.25] vs. 0.29%/mL [0.21–0.43], $P < 0.001$) compared with controls, but also greater uncoupling during early (0.48 ± 1.29 vs. 0.05 ± 1.21, $P = 0.04$) and late diastole (0.66 ± 1.02 vs. -0.07 ± 1.07, $P < 0.001$). Median follow-up duration was 9.9 [9.3–10.4] years. Peak aortic jet velocity (HR 1.22, $P = 0.03$), enlarged left atrium (HR 3.16, $P = 0.003$), E/e′ ratio (HR 1.17, $P = 0.002$), GLS (HR 1.16, $P = 0.008$), and ESslope (HR 0.66, $P = 0.04$) were associated with the occurrence of clinical events.

Conclusion Greater uncoupling and lower systolic and diastolic slopes were observed in BAV patients compared with healthy controls, suggesting presence of altered LV cardiomechanics. Moreover, lower ESslope was associated with clinical events, highlighting the strain–volume loop's potential as prognostic marker.

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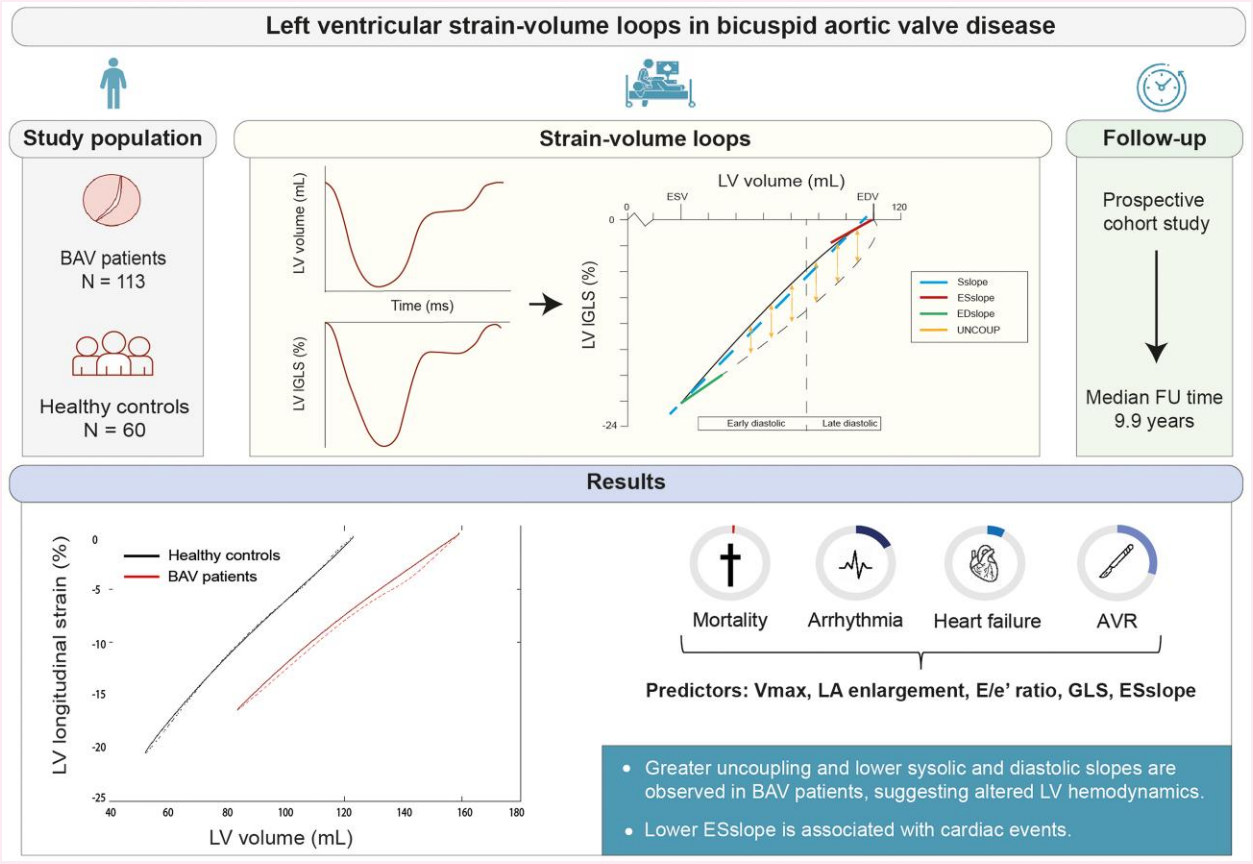
Graphical Abstract



Keywords bicuspid aortic valve • echocardiography • prognosis • strain–volume loop

Introduction

Bicuspid aortic valve (BAV) is one of the most common congenital heart defects with a prevalence of 0.5–2% in the general population.[1–3] BAV patients may remain asymptomatic for decades, but gradual development of valve stenosis and regurgitation can lead to arrhythmias, heart failure, and sudden cardiac death at a relatively young age. In addition, the progression of aortic dilatation may warrant aortic surgery. The prevalent nature of these complications at a young adult age implies an important health problem, resulting in hospitalization and (re-)interventions.[4,5] Unfortunately, BAV disease and its cardiac hemodynamics remain poorly understood.

Current guidelines mostly focus on the aortic valve itself and left ventricular ejection fraction (LVEF) to assess progression of disease and need for intervention in asymptomatic patients.[6] However, LVEF remains normal for a long period, while signs of structural left ventricular (LV) remodelling can be present well before LVEF declines.[7] Global longitudinal strain (GLS) by speckle tracking echocardiography is a more sensitive marker for LV dysfunction and is a well-established prognostic factor in a variety of cardiovascular diseases.[8–11] Nonetheless, GLS is significantly influenced by loading conditions.[12] Consequently, GLS may not be perceived reliable in patients in whom increased pre- and/or afterload is causally linked to LV dysfunction, as in aortic valve disease. This highlights the need for imaging modalities that provide better insight into cardiomechanics, which subsequently may relate to future clinical events.

Recent work has introduced the combination of LV GLS with simultaneously measured LV volume across the cardiac cycle, leading to a strain–volume loop that may provide additional insight into cardiac function.[13,14] This study aimed to (i) compare characteristics of LV strain–volume loops between BAV patients with age- and sex-matched healthy controls and (ii) investigate the prognostic value of strain–volume loops with 10-year prospective clinical follow-up. We hypothesized that, as functional (strain) and structural (volume) information of the LV is combined, strain–volume loops will provide additional information on cardiomechanics in BAV patients. Moreover, we hypothesized that strain–volume loop parameters are impaired in BAV patients compared with controls.

Methods

Study population and design

BAV patients were selected from a prospective cohort of patients with a congenital heart disease who visited the outpatient clinic of our tertiary center between 2011 and 2013 (BioCon study). All included patients within the BioCon study underwent clinical examination, electrocardiogram and

transthoracic echocardiography at baseline. The study protocol has been described in more detail previously.[15] Data of all BAV patients were extracted, excluding patients with concomitant supravalvular aortic stenosis and patients in whom strain measurements were not feasible in all three apical views. Moreover, patients with severe aortic regurgitation (AR) were excluded, to mainly assess the effect of pressure overload on the LV. Data of BAV patients were compared with selected data from healthy volunteers included between 2014 and 2015[16] and matched for age and sex on a group level. The study complied with the principles of the Declaration of Helsinki and was approved by the local medical ethical committee. Written informed consent was provided by all participants.

Image acquisition

All echocardiographic examinations were performed by two dedicated sonographers. Two-dimensional greyscale harmonic images were obtained in the left lateral decubitus position using an iE33 or EPIC7 ultrasound system (Philips Medical Systems, Best, The Netherlands) equipped with a transthoracic broadband X5-1 matrix transducer. Chamber quantification was performed according to the guidelines from the European Association of Cardiovascular Imaging.[17] Peak aortic jet velocity was measured in apical three-chamber view with spectral Doppler.

Speckle tracking analysis

Speckle tracking analysis was performed with dedicated software (TomTec, 2D Cardiac Performance Analysis; Image Arena version 4.6) by two researchers. All measurements were performed blinded for clinical characteristics and outcome. Cardiac cycles were defined based on R-waves. LV endocardial strain analysis was performed in the apical two-, three-, and four-chamber (A2CH, A3CH, and A4CH) views. The width of the segments was set to line up with the endocardial border and tracked on a frame-by-frame basis. When tracking was considered suboptimal, borders were adjusted manually.

LV strain–volume loops

LV endocardial GLS and volume data were exported from TomTec software to text-files. Dedicated software developed in MATLAB (The MathWorks Inc., version 2019a, MA, USA) was used to combine strain and volume data from the text-files and generate strain–volume loops, without further interference of observers, as described elsewhere.[18] The script constructed all strain–volume loops within a minute, and parameters were automatically exported to a database. On both systolic and diastolic parts of the temporal GLS and volume curves, 300-point cubic spline interpolation was used. Moreover, markers for end-systole and end-diastole were based on the minimum and maximum values of the LV volume curve respectively. The following parameters were obtained within the strain–volume loops to assess systolic function:

(a) Linear slope of the strain–volume relation during systole (Sslope);
(b) Early linear slope during the first 5% of volume change during systole (ESslope); and
(c) End-systolic peak longitudinal strain (peak strain).

For the assessment of diastolic function, the following parameters were assessed:

(d) Early linear slope during the first 5% of volume change during diastole (EDslope);
(e) Late linear slope during the last 5% of volume change during diastole (LDslope); and
(f) The mean difference between systolic and diastolic strain for any given volume (UNCOUP).

Uncoupling was further divided into early uncoupling (UNCOUP ED), during the first two-thirds of volume increase in diastole, and late uncoupling (UNCOUP LD), during the last one-third of volume increase in diastole. (*Figure 1*) Individual strain–volume plots were manually assessed blinded for other study results, to evaluate the temporal strain and volume curves and detect incorrect interpolation. In case a drift in the temporal volume curve was seen, the concerning strain–volume parameters were excluded ($N = 4$).

Previous studies from our group described good intra-observer agreement for strain–volume loop parameters.[14,19] For the left ventricular measurements, intraclass correlation coefficient (ICC) for Sslope and ESslope were 0.945 and 0.950, respectively. For uncoupling ICC was 0.779 (UNCOUP ED) and 0.737 (UNCOUP LD).[14]

Clinical outcome

As different predictors are expected for events in patients with and without a native valve, occurrence of clinical events was assessed in a subgroup of patients without prior AVR. The primary endpoint was occurrence of clinical events and defined as a composite endpoint of all-cause mortality, supraventricular and ventricular arrhythmias (symptomatic and recorded, or requiring treatment), heart failure (requiring initiation or change in diuretics or hospital admission), and aortic valve replacement. When performed on clinical indication, Holter recordings were assessed for occurrence of arrhythmias. Premature ventricular and atrial complexes were not considered an arrhythmia. The Municipal Population Register was checked for survival status until 1 April 2022.

Statistical analysis

Distribution of continuous data was examined using histograms and Shapiro–Wilk test. When normally distributed, continuous variables were expressed as mean ± standard deviation and compared using a Student's *t*-test. Non-parametric variables were presented as median with quartiles [Q1–Q3] and compared using a Mann–Whitney *U* test. Categorical variables were presented as frequencies with percentages and compared using a χ^2 test. A one-way analysis of variance was used to assess differences between patients with varying degrees of AS in case of a normal distribution, and a Kruskal–Wallis test was used in case data was skewed. When the *P*-value of one-way analysis was <0.05, a *post hoc* analysis using Bonferroni correction was applied. Associations between clinical and echocardiographic variables and events were identified with a Cox proportional hazard model adjusted for age. A *P*-value of <0.05 was considered to be statistically significant. All statistical analyses were performed using SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp) or R (R Foundation for Statistical Computing, Vienna, Austria. Version 4.1.2).

Results

Patient characteristics

A total of 113 patients who met the inclusion criteria were identified (median age 32 years, 40% female). Sixty healthy controls matched for age and sex on a group level were included. *Table 1* displays the baseline characteristics. Severe AS was identified in 12 patients (11%). Thirty-three patients (29%) had a prior AVR, and 14 patients (12%) had prior Ross surgery. BAV patients had a significant lower GLS than healthy volunteers (−16.8% ± 2.9 vs. −20.5% ± 2.3, $P < 0.001$) whereas LVEF did not differ significantly (60%, [Q1–Q3: 56–63] vs. 61%, [Q1–Q3: 58–65], $P = 0.06$). Regarding diastolic LV function, E/e′ ratio was significantly higher in BAV patients (10.6 [Q1–Q3: 8.4–13.3] vs. 6.9 [Q1–Q3: 6.2–7.7]) and E/A ratio was significantly lower (1.5 [Q1–Q3: 1.2–2.0] vs. 1.9 [Q1–Q3: 1.4–2.2]). Signs of LV hypertrophy were present in 18 patients (18%).

Strain–volume loops

An overview of the average strain–volume loop for healthy controls and BAV patients is displayed in *Figure 2*. In four BAV patients, uncoupling could not be reliably calculated due to variation in temporal LV volumes or error in interpolation and were therefore excluded. Differences in systolic parameters (Sslope, ESslope) were observed between BAV patients and healthy controls, with significant lower values in BAV patients (*Table 2*). Moreover EDslope was significantly lower in our BAV population compared with controls (0.21%/mL, [Q1–Q3: 0.11–0.32] vs. 0.30%/mL, [Q1–Q3: 0.15–0.46], $P = 0.005$), whereas

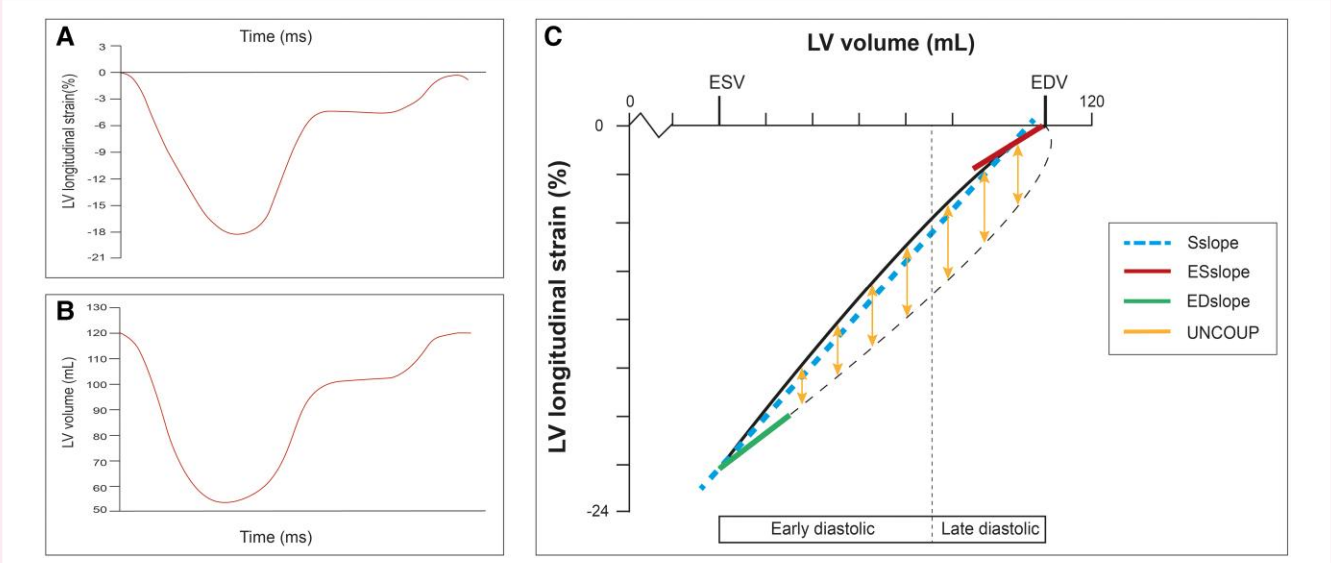


Figure 1 Average LV longitudinal strain (*A*) and LV volume (*B*) from A2CH, A3CH, A4CH views during one cardiac cycle. (*C*) Schematic overview of strain–volume loop characteristics. Black lines represent the strain–volume curve with the bold line representing systole and the dashed line representing diastole. UNCOUP is the mean difference between systolic and diastolic strain for the same volume, and can be divided in early diastolic (UNCOUP ED) and late diastolic (UNCOUP LD) based on the first two-thirds and last one-third of LV volume increase in diastole.

uncoupling was higher in BAV patients, both in early (0.48 ± 1.29 vs. 0.05 ± 1.21, $P = 0.04$) and late diastole (0.66 ± 1.02 vs. -0.07 ± 1.07, $P < 0.001$). Within the BAV population, significantly lower Sslope and ESslope were found in patients with moderate–severe stenosis compared with patients with no–mild stenosis. Moreover, significant differences were found in Sslope, ESslope, and UNCOUP between healthy controls and BAV patients with no or mild AS (*Figure 3*).

Clinical outcome

For our survival analysis, 33 patients with prior AVR were excluded. Characteristics of the patients with a native valve and prior AVR are described in Supplementary data online, *Table S1*. Follow-up data were complete for all patients. The median follow-up duration was 9.9 years [Q1–Q3: 9.3–10.4], during which 30 patients (38%) experienced a clinical event. One patient died during follow-up (1%), 13 patients experienced an arrhythmia (16%), 5 developed heart failure (6%), and 21 patients underwent aortic valve replacement (26%). An overview of the events can be found in Supplementary data online, *Table S2*. Event-free survival at 5 and 10 years was 81.0% and 62.5%, respectively. In multivariable Cox regression higher E/e′ ratio and presence of an enlarged left atrium (LA) were associated with clinical events (HR 1.17, 95% CI 1.06–1.29 and HR 3.16, 95% CI 1.37–7.29, respectively) when adjusted for age. Regarding the strain–volume loop characteristics, lower ESslope was significantly associated with event-free survival (HR 0.66, 95% CI 0.43–0.99). Moreover, decreased GLS (HR 1.16, 95% CI 1.04–1.29) and increased AV peak velocity (HR 1.22, 95% CI 1.02–1.46) increased the risk for clinical events (*Table 3*).

Discussion

The aim of this study was to compare LV strain–volume loops between patients with BAV and an age- and sex-matched control group, and investigate its prognostic value. First, we found significant differences in LV strain–volume loop characteristics, both related to systole and diastole, compared with healthy controls. Secondly, we found that lower early systolic slope was significantly associated with occurrence of clinical events during a 10-year follow-up period. Our observations provide better insight into alterations in cardiac dynamics in BAV patients and suggest potential prognostic value of LV strain–volume loop characteristics.

Systolic function

Strain–volume loops may provide additional insight into cardiac dynamics to better understand the impact of a variety of cardiac diseases.[18,20,21] Previous exploratory studies showed that LV strain–volume loops differ from healthy controls in the presence of severe AS and AR[14] and following AVR in AS patients.[22] However, patient numbers were low and data on the strain–volume loops in patients with congenital heart diseases was lacking. In our BAV population, a clear rightward shift in the strain–volume loops was observed compared with age- and sex-matched healthy controls, caused by larger end-diastolic and end-systolic volumes in BAV patients. The Sslope, representing the linear relation between LV longitudinal strain increase and LV volume decrease during systole, was lower in BAV patients. This seems, at least partly, explained by the lower peak strain that was observed for BAV patients. It is hypothesized that a lower peak strain may relate to LV hypertrophy in AS, that causes a diminished coronary blood flow reserve in the subendocardial layers,[23,24] eventually causing interstitial fibrosis that starts in the subendocardium and thereby affects the longitudinal myocardial fibres.[25–27] Despite the lower longitudinal strain, we found that LVEF was not significantly decreased in our BAV population. Possibly, an increase in circumferential strain compensated for the decrease in GLS and contributed to maintaining LVEF.[28,29] Interestingly, BAV patients also demonstrated a significantly lower ESslope, which represents the initial change in strain early in systole. This lower ESslope suggest that cardiac dynamics at the start of systole are altered, which may be related to the presence of an increased afterload or presence of LV remodelling. Impairment in both Sslope and ESslope was more profound in patients with a

Table 1 Baseline characteristics

	Controls (*N* = 60)	BAV patients (*N* = 113)	*P*-value
Baseline characteristics			
Age, years	33 (28–41)	32 (23–40)	0.21
Sex, female (%)	24 (40)	45 (40)	0.98
BSA, m^2	1.9 ± 0.19	1.9 ± 0.23	0.24
Heart rate, bpm	69 ± 12	71 ± 13	0.21
Systolic blood pressure, mmHg	126 (115–130)	125 (115–136)	0.85
Diastolic blood pressure, mmHg	78 (74–82)	79 (74–85)	0.62
NYHA ≥ 2, *n* (%)	0 (0)	4 (4)	0.14
Sinus rhythm, *n* (%)	60 (100)	107 (95)	0.07
Aortic coarctation, *n* (%)	0 (0)	40 (35)	<0.001
Coarctation repair		39 (35)	
Prior AV intervention, *n* (%)	0 (0)	57 (50)	<0.001
Balloon valvuloplasty		7 (6)	
Surgical valve repair		3 (3)	
AVR		33 (29)	
Ross procedure		14 (12)	
Echocardiographic parameters			
LVEF, %	61 (58–65)	60 (56–63)	0.06
LV GLS, %	−20.5 ± 2.3	−16.8 ± 2.9	<0.001
LV end-diastolic volume, mL	117 (100–136)	121 (97–150)	0.56
LV end-systolic volume, mL	44 (37–55)	51 (37–62)	0.14
E-wave, m/s	0.75 (0.62–0.86)	0.88 (0.74–1.05)	<0.001
A-wave, m/s	0.42 (0.33–0.51)	0.59 (0.46–0.69)	<0.001
Deceleration time, ms	183 ± 32	204 ± 48	0.002
E/A ratio	1.9 (1.4–2.2)	1.5 (1.2–2.0)	0.009
e′ wave, cm/s	10.9 ± 2.3	8.6 ± 2.5	<0.001
E/e′ ratio	6.9 (6.2–7.7)	10.6 (8.4–13.3)	<0.001
LA volume index > 34 mL/m^2, *n* (%)	11 (19)	22 (20)	0.92
LV mass index, g/m^2	—	88 (72–102)	
LV remodelling, (%)	—	35 (35)	
Concentric remodelling	—	17 (17)	
Concentric hypertrophy	—	6 (6)	
Eccentric hypertrophy	—	12 (12)	
Peak aortic jet velocity, m/s	—	2.3 (1.6–3.3)	
Peak aortic jet velocity > 4.0 m/s, *n* (%)	—	12 (11)	
Aortic regurgitation grade, *n* (%)			
None	—	38 (34)	
Mild	—	54 (48)	
Moderate	—	21 (19)	

AV, aortic valve; AVR, aortic valve replacement; BSA, body surface area; LA, left atrium; LVEF, left ventricular ejection fraction; LV GLS, left ventricular global longitudinal strain.

moderate–severe stenosis than patients with no–mild stenosis, suggesting a greater alteration in cardiomechanics alongside an increase in aortic valve peak velocity.

Diastolic function

During diastole, filling of the LV is associated with a concomitant decrease in longitudinal strain. In healthy individuals, this relationship between volume and strain during diastole follows a path that is largely similar to the relationship between both parameters during systole.[14] This 'coupling' between volume and strain during systole vs. diastole was also observed in our control group of healthy volunteers. In BAV patients however, we observed 'uncoupling' between the systolic and diastolic relation between strain and volume, with a relatively larger (i.e. more negative) strain during diastole than systole for any given volume. Early in diastole, untwisting of the LV is the driving force behind LV filling.[30] Presence of uncoupling in early diastole, further accompanied by a lower EDslope, may suggest altered untwisting of the LV in our patient group. In support of this hypothesis, altered untwisting has been described before in AS patients,[31–34] but further research to LV twist dynamics in BAV patients is necessary. Opposed to early diastole, LV compliance and atrial contraction are drivers for volume inflow in the

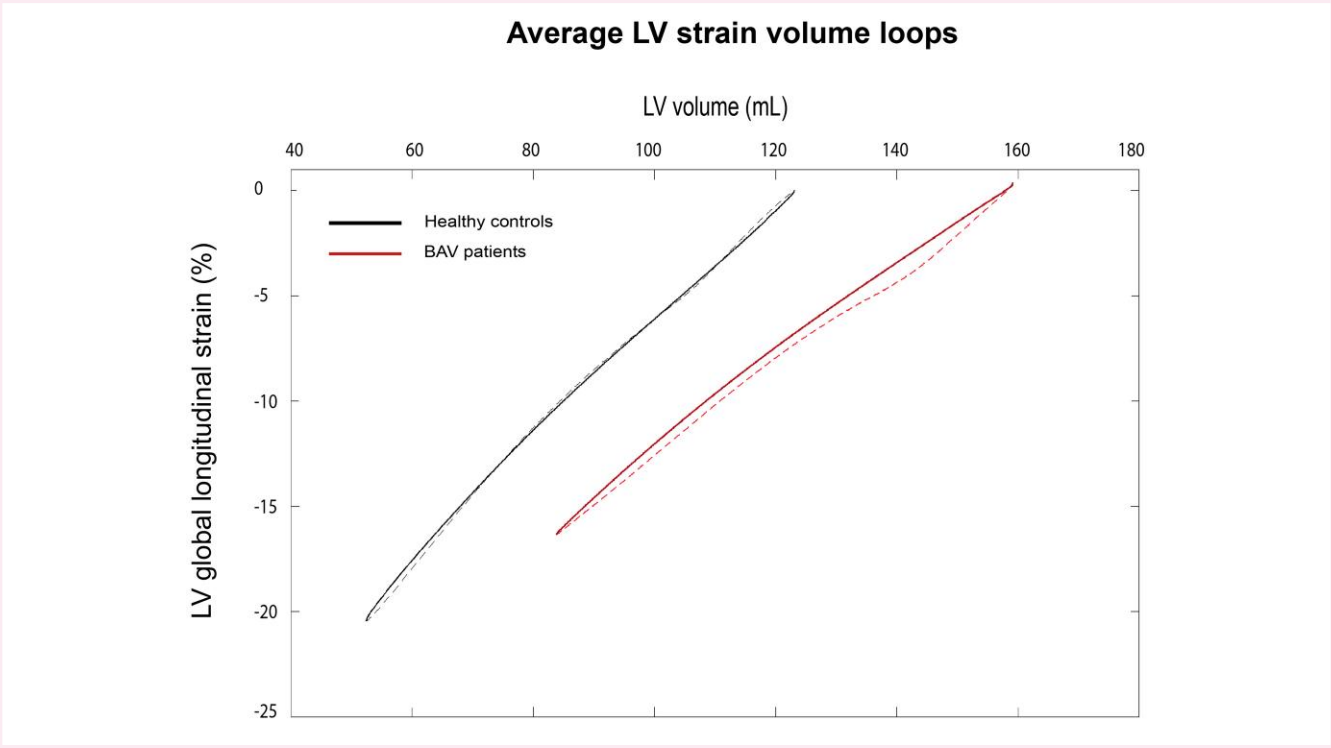


Figure 2 Average strain–volume loops for healthy controls and BAV patients. Bold lines represent systole, and dashed lines represent diastole.

Table 2 Strain–volume loop characteristics in BAV patients and healthy controls

	Controls ($N = 60$)	BAV patients ($N = 113$)	*P*-value
Sslope, %/mL	0.27 (0.24–0.34)	0.21 (0.17–0.28)	<0.001
ESslope, %/mL	0.29 (0.21–0.43)	0.19 (0.12–0.25)	<0.001
EDslope, %/mL	0.30 (0.16–0.46)	0.21 (0.11–0.32)	0.004
LDslope, %/mL	0.23 (0.14–0.32)	0.24 (0.17–0.36)	0.30
UNCOUP, %	0.01 ± 1.08	0.54 ± 1.13	0.004
UNCOUP ED, %	0.05 ± 1.21	0.48 ± 1.29	0.04
UNCOUP LD, %	−0.07 ± 1.07	0.66 ± 1.02	<0.001

ES, early systolic; ED, early diastolic; LD, late diastolic; S, systolic; UNCOUP, uncoupling.

late diastolic phase. We hypothesized that the presence of late diastolic uncoupling reflects a decrease in compliance of the LV, suggesting an increased LV stiffness. Taken together, the presence of early and late diastolic uncoupling and the decrease in EDslope seem to reflect early stages of remodelling in BAV patients.

Prognostic factors

In support of previous work, E/e′ ratio and LA volume were associated with clinical events across a 10-year follow-up period.[35,36] However, these previous studies focused on valve intervention and mortality as endpoint and did not take occurrence of arrhythmias or heart failure into account. Our finding that E/e′ ratio and enlarged LA can also be of prognostic value for these important clinical events, underlines the importance to not only monitor systolic LV function in BAV patients, but also focus on diastolic LV function. Moreover, lower ESslope showed to be of prognostic value for event-free survival. A decrease in ESslope suggests altered LV cardiomechanics right after aortic valve opening, which can be an indicator of LV remodelling.

Limitations

There are a few limitations to our study that should be considered. First, in our study population volume and pressure overload both influence the LV. This makes it more difficult to identify which processes cause the alterations in LV cardiomechanics. However, a study population in which both AR and AS are present is representative for the general BAV population. To limit the influence of volume overload, patients

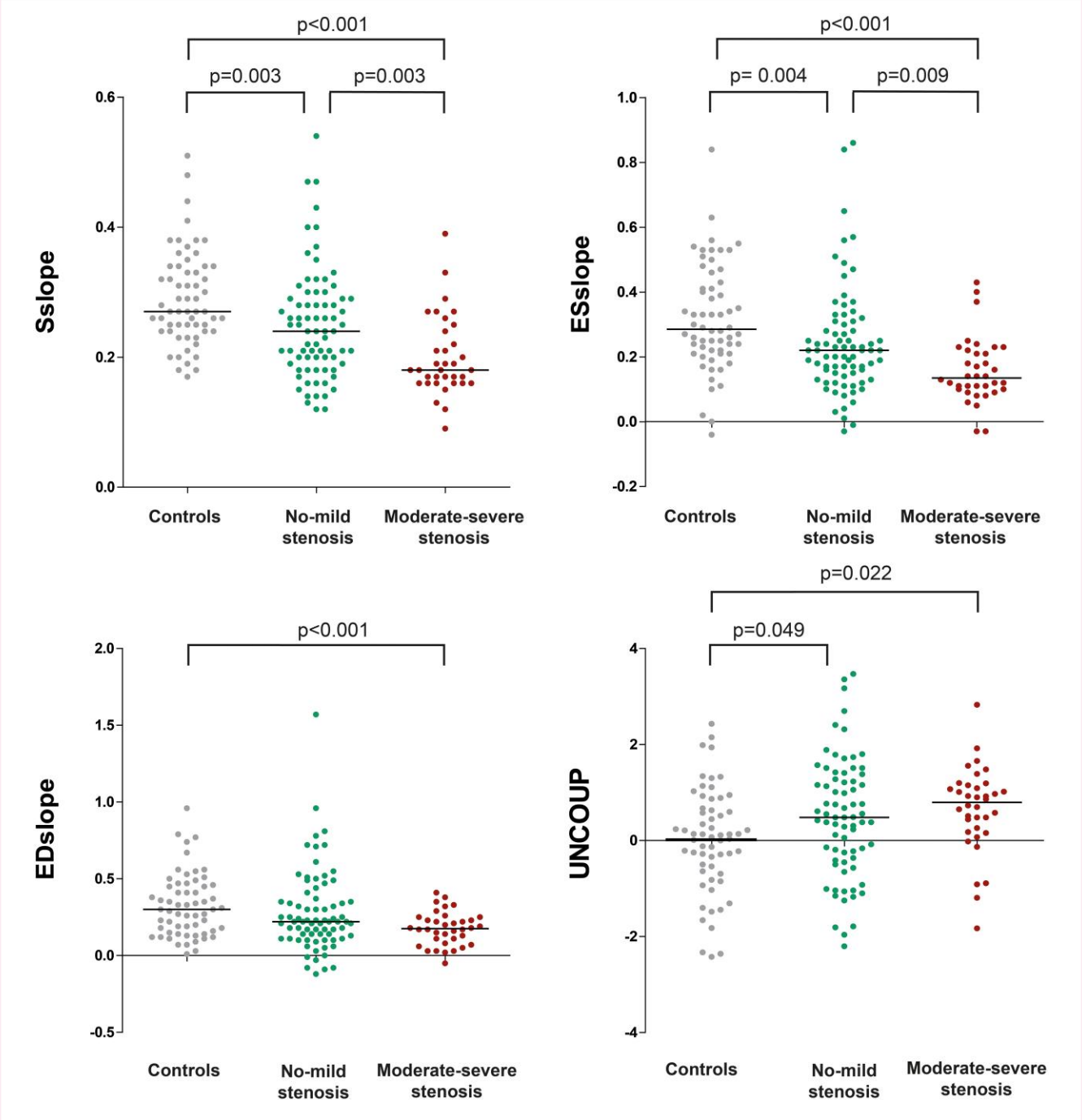


Figure 3 Distribution of strain–volume loop characteristics in healthy controls and BAV patients with no–mild stenosis or moderate–severe stenosis. The horizontal black line represents the median (Sslope, ESslope, EDslope) or mean (UNCOUP) value. Significant differences between groups are displayed with respective *P*-values.

with severe AR were excluded. Secondly, the BAV patients included in our study were recruited from a tertiary centre, with a relatively high rate of prior aortic valve interventions and comorbidities such as aortic coarctation. Therefore, caution should be taken when generalizing our findings to other BAV populations. Lastly, for our results regarding survival analysis, the low number of events must be taken into account. Our data suggest that strain–volume loop parameters may hold prognostic information, but these findings must be further investigated in larger cohorts of BAV patients to be able to assess the additive value beside the more common echocardiographic parameters.

Clinical implications

It is known that systolic and diastolic dysfunction can be present well before a decline in LVEF is visible.[7] With the strain–volume loops, data on cardiac contraction are combined with volume during the

Table 3 Cox regression analysis for event-free survival

	HR[a]	95% CI	*P*-value
Sex, female	0.96	0.46–1.98	0.91
AV peak velocity, per 0.5 m/s	1.22	1.02–1.46	0.03
LVEDV, per 5 mL	1.04	1.00–1.08	0.06
LVESV, per 5 mL	1.04	1.00–1.09	0.06
LVEF, %	0.99	0.94–1.04	0.62
GLS, %	1.16	1.04–1.29	0.008
LV mass index, per 10 g/m^2	1.13	0.98–1.30	0.09
LA volume index > 34 mL/m^2	3.16	1.37–7.29	0.003
E/e′ ratio	1.17	1.06–1.29	0.002
Sslope, per 0.1%/mL	0.58	0.33–1.02	0.06
ESslope, per 0.1%/mL	0.66	0.43–0.99	0.04
EDslope, per 0.1%/mL	0.85	0.66–1.11	0.24
LDslope, per 0.1%/mL	1.07	0.86–1.33	0.55
UNCOUP, %	1.22	0.83–1.80	0.32
UNCOUP ED, %	1.17	0.83–1.63	0.37
UNCOUP LD, %	1.39	0.91–2.13	0.13

AV, aortic valve; ES, early systolic; ED, early diastolic; GLS, global longitudinal strain; LA, left atrium; LD, late diastolic; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; S, systolic; UNCOUP, uncoupling.
[a]Adjusted for age.

entire cardiac cycle. This study suggests that strain–volume loops may provide additional insight into altered LV cardiomechanics in BAV patients in both systole and diastole. The non-invasive nature and limited time needed to construct strain–volume loops, supported by our observations, make the strain–volume loop potentially suitable and relatively easy to implement in clinical practice. Moreover, early systolic slope may also be an interesting new prognostic marker, but future studies are warranted to better understand the potential clinical value in BAV patients.

Conclusion

This study demonstrates significant differences between BAV patients and healthy controls for systolic and diastolic strain–volume loop parameters, supporting the hypothesis of altered cardiomechanics in BAV patients compared with healthy controls. Moreover, early change in the relation between strain and volume during systole (ESslope) was associated with the occurrence of clinical events during a 10-year follow-up period and can be an interesting new prognostic marker.

Supplementary data

Supplementary data are available at *European Heart Journal – Imaging Methods and Practice* online.

Conflict of interest: None declared.

Consent

The authors confirm that patient consent forms have been obtained for this article.

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Data availability

Data are available from the corresponding author on reasonable request.

Lead author biography

Annemien van den Bosch is a cardiologist at the Erasmus University Medical Center in Rotterdam, The Netherlands. Her clinical work and research involves adult congenital heart disease, echocardiography, and pulmonary hypertension. She is also involved in basic and translational research on new echocardiographic techniques. She has authored and co-authored over 100 scientific publications and mentored nine PhD students. She is member of the ESC working group on Adult Congenital Heart disease and member of the EACVI congenital echocardiographic exam committee.

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