Association Between Left Ventricular Apical-to-Basal Strain Ratio and Conduction Disorders after Aortic Valve Replacement

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Background: The aim of the study was to evaluate whether left ventricular apical-to-basal longitudinal strain differences, representing advanced basal interstitial fibrosis, are associated with conduction disorders after aortic valve replacement (AVR) in patients with severe aortic stenosis.

Methods: Patients with aortic stenosis undergoing AVR were included. The apical-to-basal strain ratio was calculated by dividing the average strain of the apical segments by the average strain of the basal segments. Values >1.9 were considered abnormal, as previously described. All patients were followed up for the occurrence of complete left or right bundle branch block or permanent pacemaker implantation within 2 years after AVR. Subgroup analysis was performed in patients undergoing transcatheter AVR.

Results: Two hundred seventy-four patients were included (median age of 74 years [interquartile range, 65, 80], 46.4% male). During a median follow-up of 12.2 months (interquartile range, 0.2, 24.3), 74 patients (27%) developed complete bundle branch block or were implanted with a permanent pacemaker. These patients more often had an abnormal apical-to-basal strain ratio. Cumulative event-free survival analysis showed worse outcome in patients with an abnormal apical-to-basal strain ratio (log rank $\chi^2 = 7.258$, $P = .007$). In multivariable Cox regression analysis, an abnormal apical-to-basal strain ratio was the only independent factor associated with the occurrence of complete bundle branch block or permanent pacemaker implantation after adjusting for other factors previously shown to be associated with conduction disorders after AVR. Subgroup analysis confirmed the independent association of an abnormal apical-to-basal strain ratio with conduction disorders after transcatheter AVR.

Conclusion: The apical-to-basal strain ratio is independently associated with conduction disorders after AVR and could guide risk stratification in patients potentially at risk for pacemaker implantation. (J Am Soc Echocardiogr 2023;■:■-■.)

Keywords: Aortic stenosis, Regional global longitudinal strain, Apical-to-basal strain differences, Conduction disorders

INTRODUCTION

Aortic stenosis (AS) is the most common valvular heart disease requiring valve replacement.[1] The use of transcatheter aortic valve replacement (TAVR) has increased over time. Conduction disorders are prevalent after surgical aortic valve replacement (SAVR), with an even higher incidence of pacemaker implantations after TAVR.[2-5] Various factors predictive of conduction disorders after TAVR have been identified, including electrocardiographic, periprocedural, and prosthesis characteristics.[6-14] However, specific echocardiographic markers associated with conduction disorders after aortic valve replacement (AVR) have not yet been identified. A thorough risk assessment before AVR is important to identify patients requiring more intensive or prolonged rhythm monitoring shortly after the intervention. Moreover, the need for pacemaker implantation could be anticipated before the intervention in high-risk patients. Since the conduction system is embedded in the basal part of the left ventricle (LV), regional LV global longitudinal strain (GLS) may be an interesting echocardiographic parameter identifying these high-risk patients. In patients with severe AS, longitudinal strain

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Abbreviations

AS = Aortic stenosis

AVA = Aortic valve area

AVR = Aortic valve replacement

ECG = Electrocardiogram

GLS = Global longitudinal strain

HR = Hazard ratio

IQR = Interquartile range

LV = Left ventricle, ventricular

LVEF = Left ventricular ejection fraction

SAVR = Surgical aortic valve replacement

TAVR = Transcatheter aortic valve replacement

is generally lower in the basal segments compared with the apical segments, leading to an apical-to-basal strain difference that may reflect the presence of more interstitial fibrosis in the basal part of the LV.[15,16] Accordingly, it may be that the conduction system is more affected by interstitial fibrosis in patients with a high apical-to-basal strain difference. Therefore, the aim of this study is to evaluate whether apical-to-basal strain differences are associated with conduction disorders in patients with severe AS undergoing AVR.

METHODS

Patient Selection and Clinical Covariables

Patients ≥18 years old with severe AS diagnosed at Leiden University Medical Center between May 1994 and October 2019 and with adequate image quality were selected. Severe AS was defined as an aortic valve area (AVA) ≤1 cm^2, a mean aortic valve gradient ≥40 mm Hg, or peak aortic valve velocity ≥4 cm/sec.[17] Patients with a left ventricular (LV) ejection fraction (LVEF) <50%, prior myocardial infarction, congenital heart defects, dynamic LV outflow tract obstruction, previous valve surgery, no AVR during follow-up, baseline QRS duration ≥120 ms, or implanted pacemaker were excluded (Figure 1). Clinical characteristics, including demographic data, cardiovascular risk factors, comorbidities, medication use and symptoms, laboratory results, and electrocardiogram (ECG) characteristics were retrospectively collected from the departmental electronic patient information system (EPD Vision). EuroSCORE I was calculated when the necessary information was available.[18]

Patient Outcomes

All patients were followed up for the occurrence of permanent pacemaker implantation or development of complete left bundle branch block (≥120 ms) or complete right bundle branch block (≥120 ms), documented on ECG after AVR within 2 years after AVR.[19] The ECGs were analyzed blinded from the echocardiograms. The ethics committee of the Leiden University Medical Center waived the need for written informed consent in view of the retrospective design of this study.

Transthoracic Echocardiography

All patients underwent transthoracic echocardiography at diagnosis. Echocardiographic data were digitally stored for offline analysis using commercially available software (EchoPAC vers. 113 and 203; GE Medical Systems). Echocardiographic examinations were retrospectively analyzed according to current guidelines, blinded from the ECG data.[17,20-23] From the parasternal long-axis view, LV dimensions were assessed and LV mass was calculated by the formula of Devereux.[20] From the apical 2- and 4-chamber views, LV end-diastolic and LV end-systolic volumes were measured and indexed for body surface area, calculated by the formula of Du Bois.[20] Left ventricular ejection fraction was calculated using Simpson's biplane method.[20] Left atrial volumes were assessed in the apical 4- and 2-chamber views, using the method of disks and indexed by body surface area.[20] Continuous-wave Doppler recordings were performed in the apical 3- or 5-chamber view to estimate peak aortic jet velocity, and mean aortic valve pressure gradients were calculated using the simplified Bernoulli equation.[17] Left ventricular outflow tract velocity-time integral was obtained from

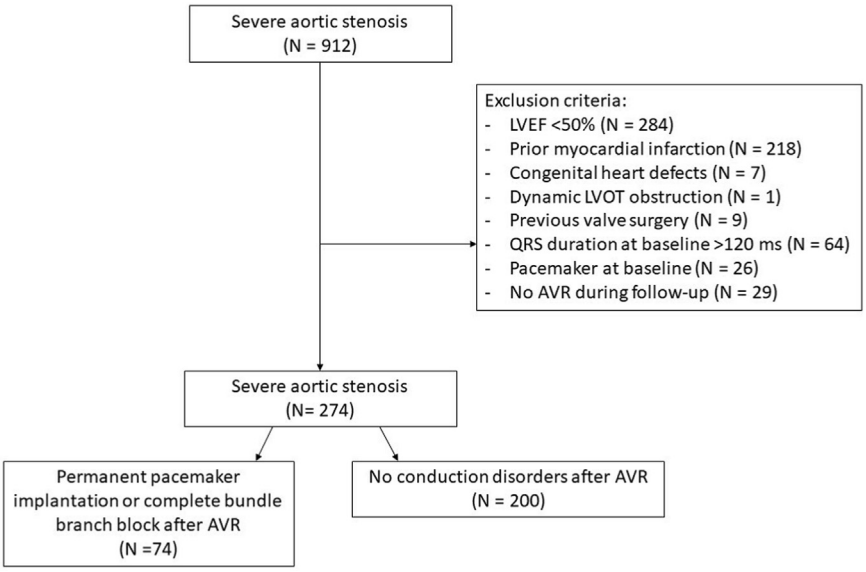


Figure 1 Patient selection. *AVB*, Atrioventricular block; *LBBB*, left bundle branch block; *LVOT*, LV outflow tract obstruction; *RBBB*, right bundle branch block.

HIGHLIGHTS

- AVR patients with conduction disorders have higher apical-to-basal strain ratios.
- Apical-to-basal strain ratio is associated with conduction disorders after AVR.
- Apical-to-basal strain ratio could guide pacemaker implantation necessity after AVR.

pulsed-wave Doppler recordings in the apical 3- or 5-chamber views.[17] Aortic valve area was calculated by the continuity equation using the LV outflow tract velocity-time integral, LV outflow tract diameter, and velocity-time integral of the aortic valve.[21] Severity of aortic regurgitation was graded according to a multiparametric approach.[23] The degree of aortic valve calcification was scored on the parasternal short-axis view according to Rosenhek *et al.*[24]: (1) no calcification, (2) mildly calcified (small isolated spots), (3) moderately calcificied (multiple larger spots), and (4) heavily calcified (extensive thickening and calcification of all cusps). Pulsed-wave Doppler recordings of the transmitral flow and tissue Doppler imaging of the mitral annulus were obtained from apical 4-chamber views. Peak early (E) velocity, late (A) diastolic velocity, and E/e′ ratio were assessed using these views.[22] Right ventricular systolic pressure was calculated with the Bernoulli equation from the peak velocity of the tricuspid regurgitant jet, summated with the right atrial pressure determined by the inspiratory collapse and diameter of the inferior vena cava.[20] M-mode imaging was used to assess tricuspid annular plane systolic excursion as an estimation of the right ventricular systolic function.[20]

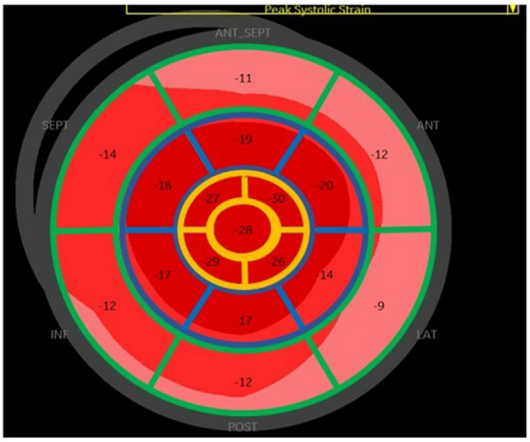
Left ventricular GLS was measured on the apical 4-, 2-, and 3-chamber views by two-dimensional speckle-tracking analysis.[20] The endocardial border was automatically traced and manually adjusted when needed. A bull's-eye plot was calculated, including 6 basal segments, 6 midventricular segments, and 5 apical segments (Figure 2). The basal longitudinal strain (GLS base) was defined as the average of the 6 basal segments. The midventricular longitudinal strain (GLS mid) was defined as the average of the 6 midventricular segments. The apical longitudinal strain (GLS apex) was defined as the average of the 5 apical segments. The apical-to-basal strain ratio was calculated as the average strain of the 5 apical segments divided by the average strain of the 6 basal segments. Apical-to-basal strain ratio was previously described in a healthy cohort age >55 years with an upper limit of the 99% CI for normal values of 1.9.[25] Relative apical sparing pattern was calculated as the average strain of the apical segments divided by the average strain of the basal and midventricular segments. The optimal cutoff value of 1 was previously determined.[26]

In patients with atrial fibrillation at the time of the echocardiogram, measurements were obtained on 3 consecutive cardiac cycles, when available.[20] The values of the different segments were then averaged to obtain values of LV GLS.

Statistical Analysis

Continuous variables are expressed as mean ± SD when normally distributed and as median and interquartile range (IQR) when not normally distributed. Categorical variables are presented as absolute numbers and percentages. Baseline clinical and echocardiographic variables were compared between patients with versus without the combined end point of complete bundle branch block and permanent pacemaker implantation within 2 years after AVR. The independent-sample Student *t* test was used to compare groups when the variables were normally distributed; the Mann-Whitney *U* test was used when the variables were not normally distributed. Categorical variables were compared using Pearson χ^2 test. Cumulative event-free survival analysis was performed for the overall population and censored at 2 years of follow-up, stratified by abnormal apical-to-basal strain ratio cutoff value, using the Kaplan-Meier method. The log-rank test was used to compare the groups. Consecutively, spline curve analysis was performed to investigate the hazard ratio (HR) changes for the combined end point across the range of apical-to-basal strain ratio values. The previously defined upper limit of normal was balanced against the cutoff value of apical-to-basal strain ratio associated with increased risk of the combined end point, using the fitted spline curve (i.e., in which the predicted HR was ≥1).

Univariable Cox proportional hazard regression analysis was performed with the apical-to-basal strain ratio and factors previously shown to be associated with conduction disorders and permanent



GLS parameter	Definition
GLS base	The average GLS of the 6 basal segments
GLS mid	The average GLS of the 6 midventricular segments
GLS apex	The average GLS of the 5 apical segments
Apical-to-basal strain ratio	GLS apex divided by GLS base
Relative apical sparing pattern	GLS apex divided by ((GLS mid + GLS base)/2)

Figure 2 Global longitudinal strain parameters.

Table 1 Baseline clinical characteristics

Variable	Overall population (*N* = 274)	Conduction disorders (*N* = 74)	No conduction disorders (*N* = 200)	*P* value
Demographic and clinical characteristics				
Age, years	74.0 (65.0, 80.0)	76.0 (71.0, 81.0)	71.5 (64.0, 79.0)	**.002**
Sex, male	127 (46.4)	33 (44.6)	94 (47.0)	.723
Body mass index, kg/m^2	26.1 (±3.9)	26.2 (±3.5)	26.1 (±4.0)	.887
Hypertension	201 (73.4)	54 (73.0)	147 (73.5)	.930
Hypercholesterolemia	161 (61.0)	47 (66.2)	114 (59.1)	.292
Diabetes mellitus	56 (20.4)	20 (27.0)	36 (18.0)	.100
Coronary artery disease	92 (33.6)	31 (41.9)	61 (30.5)	.076
Smoking history	103 (40.6)	26 (38.8)	77 (41.2)	.735
History of atrial fibrillation	40 (14.6)	18 (24.3)	22 (10.9)	**.006**
COPD	40 (14.6)	6 (8.1)	34 (17.0)	.064
Stroke	46 (16.8)	15 (20.3)	31 (15.5)	.348
NYHA class				**<.001**
I	107 (39.3)	20 (27.0)	87 (43.9)	
II	105 (38.6)	27 (36.5)	78 (39.4)	
III	51 (18.8)	25 (33.8)	26 (13.1)	
IV	9 (3.3)	2 (2.7)	7 (3.5)	
Angina	68 (24.9)	18 (24.3)	50 (25.1)	.892
Syncope	16 (5.9)	4 (5.4)	12 (6.0)	.845
EuroSCORE I	10.1 (6.6, 14.8)	11.0 (8.1, 17.5)	9.7 (6.2, 13.3)	**.017**
Medication				
Beta-blocker	141 (51.8)	43 (58.1)	98 (49.5)	.206
ACE-inhibitor/ARB	129 (47.1)	38 (51.4)	91 (45.5)	.389
MRA	7 (2.6)	2 (2.7)	5 (2.5)	.925
Aspirin	112 (40.9)	29 (39.2)	83 (41.5)	.730
Oral anticoagulation	49 (17.9)	20 (27.0)	29 (14.5)	**.016**
Statin	163 (59.5)	50 (67.6)	113 (56.5)	.098
Loop diuretic	91 (33.2)	32 (43.2)	59 (29.5)	**.032**
Calcium channel blocker	60 (21.9)	16 (21.6)	44 (22.0)	.946
Laboratory results				
eGFR MDRD, mL/min/1,73 m^2	69.8 (±20.7)	64.7 (±21.1)	71.7 (±20.2)	**.013**
Hemoglobin, g/dL	12.9 (±1.9)	12.6 (±1.8)	13.0 (±2.0)	.145
ECG characteristics				
Atrial fibrillation	18 (6.6)	10 (13.5)	8 (4.0)	**.005**
Heart rate, bpm	69.8 (±12.6)	71.8 (±13.8)	69.1 (±12.0)	.113
PR duration, ms	174.1 (±31.2)	182.3 (±38.7)	171.4 (±28.0)	**.017**
PR duration >200 ms	35 (13.9)	14 (22.6)	21 (11.1)	**.023**
QRS duration, ms	95.4 (±10.6)	95.6 (±13.2)	95.4 (±9.5)	.882
Left axis deviation	10 (3.6)	4 (5.4)	6 (3.0)	.346
AVR: TAVR	148 (54.0)	55 (74.3)	93 (46.5)	**<.001**

Data are shown as median (IQR), *n* (%), or mean (±SD). *ACE*, Angiotensin-converting enzyme; *ARB*, angiotensin II receptor blocker; *COPD*, chronic obstructive pulmonary disease; *eGFR MDRD*, estimated glomerular filtration rate by Modification of Diet in Renal Disease; *MRA*, mineralocorticoid receptor antagonist; *NYHA*, New York Heart Association.
Bold values indicate significant *P* values (<.05).

pacemaker implantation after AVR. The predictive factors included in the analysis were age,[8] male sex,[9] coronary artery disease,[10] EuroSCORE I,[11] history of atrial fibrillation,[7] PR duration,[8] QRS duration,[4,6,7,12] left axis deviation,[9] severity of valve calcification,[9,27] bicuspid valve,[9] LV outflow tract <21 mm,[13] septal wall thickness,[9,11,14] LVEF,[8] self-expanding TAVR prosthesis,[8,10] TAVR access route,[8] and TAVR prosthesis size.[8,9] Variables with a *P* value <.100 were inserted in the multivariable model. Hazard ratios were

Table 2 Baseline echocardiographic characteristics

Variable	Overall population (*N* = 274)	Conduction disorders (*N* = 74)	No conduction disorders (*N* = 200)	*P* value
LV and left atrium				
Septal wall thickness, mm	13.6 (±3.7)	14.4 (±6.0)	13.2 (±2.3)	**.015**
Posterior wall thickness, mm	12.3 (±2.2)	12.7 (±2.6)	12.2 (±2.0)	.081
Relative wall thickness	0.6 (0.5, 0.7)	0.6 (0.5, 0.7)	0.5 (0.5, 0.7)	.123
LV mass index, g/m^2	113.6 (±31.8)	118.6 (±35.7)	111.8 (±30.2)	.118
LVEDV index, mL/m^2	44.8 (±12.8)	43.2 (±13.9)	45.4 (±12.4)	.215
LVESV index, mL/m^2	16.6 (±6.6)	15.5 (±7.1)	16.7 (±6.5)	.788
LVEF, %	63.4 (±7.5)	62.4 (±7.6)	63.8 (±7.5)	.182
Stroke volume index, mL/m^2	41.4 (±11.9)	38.4 (±12.9)	42.5 (±11.3)	**.010**
LV GLS, %	−17.1 (±3.4)	−16.9 (±3.4)	−17.2 (±3.4)	.443
GLS apex, %	−22.5 (±5.7)	−22.4 (±5.4)	−22.5 (±5.8)	.928
GLS mid, %	−15.8 (±3.6)	−15.7 (±3.3)	−15.9 (±3.7)	.675
GLS base, %	−12.0 (±3.9)	−11.5 (±3.7)	−12.2 (±3.9)	.158
AB ratio	1.8 (1.5, 2.2)	2.0 (1.6, 2.4)	1.8 (1.5, 2.1)	**.031**
AB ratio ≥ 2	104 (39.4)	37 (52.9)	67 (34.5)	**.007**
RASP	1.6 (1.4, 1.8)	1.7 (1.4, 1.9)	1.6 (1.3, 1.8)	.126
RASP > 1	252 (95.5)	68 (97.1)	184 (94.8)	.429
LAVI, mL/m^2	34.8 (25.0, 46.0)	39.1 (29.7, 52.4)	33.3 (24.3, 42.7)	**.003**
E/e'	15.3 (11.1, 22.3)	15.8 (12.0, 21.0)	14.8 (10.8, 21.0)	.185
Aortic valve				
LVOT < 21 mm	140 (51.1)	43 (30.7)	97 (48.5)	.158
Anatomy				**.015**
Bicuspid	33 (12.0)	2 (6.1)	31 (15.5)	
Tricuspid	215 (78.5)	64 (86.5)	151 (75.5)	
Moderate to severe calcification	223 (83.8)	67 (90.5)	156 (81.3)	.065
Mean gradient, mm Hg	43.2 (36.3, 53.5)	43.3 (32.6, 54.0)	43.2 (36.8, 53.3)	.521
Peak velocity, m/sec	4.2 (±0.7)	4.2 (±0.8)	4.2 (±0.7)	.549
AVA, cm^2	0.8 (±0.2)	0.8 (±0.2)	0.8 (±0.2)	.306
AVA index, cm^2/m^2	0.4 (±0.1)	0.4 (±0.1)	0.4 (±0.1)	.515
Moderate to severe AR	22 (12.6)	8 (16.3)	14 (11.2)	.360
Right ventricle				
PAPS, mm Hg	28.8 (±8.2)	28.6 (±9.0)	28.9 (±7.9)	.868
TAPSE, mm	21.9 (±3.9)	21.2 (±4.4)	22.2 (±3.7)	.058

Data are shown as median (IQR), *n* (%), or mean (±SD). *AB* ratio, Apical-to-basal strain ratio; *AR*, aortic regurgitation; *LAVI*, left atrial volume index; *LVEDV*, LV end-diastolic volume; *LVESV*, LV end-systolic volume; *LVOT*, LV outflow tract; *PAPS*, pulmonary artery pressure during systole; *RASP*, relative apical sparing pattern; *TAPSE*, tricuspid annular plane systolic excursion.
Bold values indicate significant *P* values (<.05).

presented with 95% CIs. Finally, a subgroup analysis was conducted in patients who underwent TAVR.

Twenty random echocardiographic examinations were selected for the evaluation of intra- and interobserver variability of the apical-to-basal strain ratio, using intraclass correlation coefficients. Excellent agreement was defined by an intraclass correlation coefficient >0.90, whereas good agreement was defined by a value between 0.75 and 0.90.

A 2-sided *P* value <.050 was considered statistically significant. All analysis were performed using SPSS Statistics for Windows, version 29 (IBM), and R software, version 4.2.1 (R foundation for Statistical Computing).

RESULTS

Patient Population

Two hundred seventy-four patients with severe AS were included (Figure 1). The majority was excluded because of reduced LVEF (<50%) or prior myocardial infarction. Baseline clinical characteristics

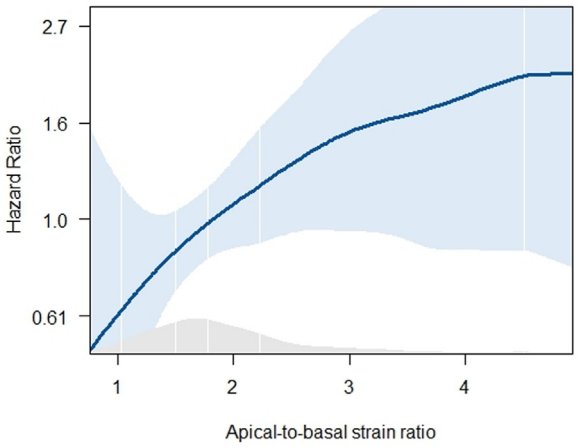


Figure 3 Spline curve analysis demonstrating the HR for developing conduction disturbances after AVR based on baseline apical-to-basal strain ratio (adapted). The curve shows the HR change for the development of conduction disorders with 95% CIs across a range of values of apical-to-basal strain ratio at the time of the index echocardiogram. The density plot below shows the distribution of the study population according to values of apical-to-basal strain ratio. A threshold of apical-to-basal strain ratio can be derived from this curve in which the predicted HR is ≥1.

are presented in Table 1. The median age of the population was 74 years (IQR, 65, 80), and 46.4% of the patients were male. During a median follow-up of 12.2 months (IQR, 0.2, 24.3), 74 (27%) patients experienced the combined end point. Eighteen (24%) patients needed permanent pacemaker implantation, 52 (70%) developed complete left bundle branch block, and 4 (5%) patients developed complete right bundle branch block. Patients with the combined end point were older (76.0 vs 71.5 years; $P = .002$), had worse kidney function (estimated glomerular filtration rate by Modification of Diet in Renal Disease 71.7 vs. 64.7; $P = .013$), and higher EuroSCORE I (11.0 vs 9.7; $P = .017$). Patients with the combined end point were more symptomatic according to New York Heart Association class and more often treated with loop diuretics compared with patients without conduction disorders. Patients with a permanent pacemaker implantation or bundle branch block more often had atrial fibrillation (24.3% vs 10.9%; $P = .006$) and consequently were more frequently treated with oral anticoagulants, but there was no difference in the use of beta-blockers and calcium channel blockers between the patient groups. All patients underwent AVR (including 126 [46%] SAVR and 148 [54%] TAVR); patients with a permanent pacemaker implantation or bundle branch block post-AVR were more often treated with TAVR. Electrocardiogram characteristics show a higher prevalence of first-degree atrioventricular block (PR duration >200 ms = 22.6% vs 11.1%; $P = .023$) in patients with the combined end point. The QRS duration at baseline was not different between patients with and without conduction disorders after AVR.

Table 2 shows the baseline echocardiographic characteristics. Of interest, patients with complete bundle branch block and permanent pacemaker implantation had more increased septal wall thickness and smaller indexed stroke volume. Patients with conduction disorders had higher indexed left atrial volume index, possibly related to the higher prevalence of atrial fibrillation in these patients. When comparing GLS measurements, there was no difference between LV GLS, GLS apex, GLS mid, or GLS base between groups. However, patients with conduction disorders after AVR more often had an apical-to-basal strain ratio above the upper limit of normal (i.e., 1.9; 37 [52.9%] vs 67 [34.5%] patients; $P = .007$), while an abnormal relative apical sparing pattern (>1) was not significantly different among groups.

Table 3 Univariable Cox regression analysis of variables for the association with the combined end point

Variable	HR (95% CI)	*P* value
Clinical variables		
Age, years	1.034 (1.012, 1.057)	**.003**
Sex, male	0.904 (0.572, 1.430)	.668
Coronary artery disease	1.520 (0.957, 2.413)	.076
History of atrial fibrillation	2.065 (1.214, 3.514)	**.008**
EuroSCORE I	1.036 (1.006, 1.066)	**.019**
ECG variables		
PR duration, ms	1.008 (1.002-1.015)	**.014**
PR duration >200 ms	1.986 (1.094, 3.607)	**.024**
QRS duration, ms	1.003 (0.981, 1.026)	.798
Left axis deviation	1.590 (0.580, 4.357)	.367
Echocardiographic variables		
Moderate to severe calcification	2.082 (0.955-4.538)	.065
Bicuspid valve	0.181 (0.044, 0.738)	**.017**
LV outflow tract <21 mm	1.383 (0.872, 2.196)	.169
Septal wall thickness, mm	1.051 (1.014, 1.088)	**.006**
LVEF	0.982 (0.951, 1.015)	.280
AB ratio >1.9	1.845 (1.153, 2.950)	**.011**

AB ratio, Apical-to-basal strain ratio.
Bold values indicate significant *P* values (<.05).

Association Between Apical-to-Basal Strain Ratio and Conduction Disorders After AVR

After dichotomizing the patient population using the cutoff value of 1.9, Kaplan-Meier survival analysis showed a higher incidence of pacemaker implantation and complete bundle branch block in patients with an apical-to-basal strain ratio >1.9 (log rank $\chi^2 = 7.258$, $P = .007$; Supplemental Figure 1). Based on spline curve analysis, increasing values of apical-to-basal strain ratio were associated with increased risk of conduction disorders after AVR (Figure 3). The previously defined upper limit of normal in healthy controls (1.9) corresponds with the cutoff value in which the predicted HR is ≥1.[26]

Univariable Cox regression analysis of variables for the association with the combined end point is presented in Table 3. Age, history of atrial fibrillation, EuroSCORE I, PR duration, first-degree atrioventricular block (PR duration >200 ms), bicuspid aortic valve, septal wall thickness, and an apical-to-basal strain ratio >1.9 were associated

Table 4 Multivariable Cox regression analysis of variables for conduction disorders after AVR (adapted)

Variable	HR (95% CI)	*P* value
Age, years	1.043 (0.999, 1.090)	.057
EuroSCORE I	1.002 (0.978, 1.068)	.337
History of atrial fibrillation	2.209 (0.981, 4.974)	.056
PR duration, ms	1.004 (0.997, 1.012)	.251
Moderate to severe calcification	3.099 (0.720, 13.329)	.129
Bicuspid valve	0.558 (0.125, 2.496)	.445
Septal wall thickness, mm	1.047 (0.992, 1.105)	.093
AB ratio >1.9	1.947 (1.025, 3.699)	**.042**

AB ratio, Apical-to-basal strain ratio.
Bold values indicate significant *P* values (<.05).

with the combined end point. The multivariable Cox regression analysis is presented in Table 4. Only an abnormal apical-to-basal strain ratio >1.9 was independently associated with the occurrence of complete left or right bundle branch block or the implantation of a permanent pacemaker.

Subgroup Analysis in Patients Undergoing TAVR

One hundred forty-eight patients underwent TAVR. During a median follow-up of 4.5 (0.0, 12.9) months, 55 (37%) patients reached the combined end point. Fourteen (25%) patients were implanted with a permanent pacemaker, 38 (69%) patients developed complete left bundle branch block, and 3 (1%) patients developed complete right bundle branch block. Baseline characteristics are presented in Supplemental Table 1. Consistent with the findings in the complete patient population, patients with complete bundle branch block or implantation of a permanent pacemaker more often had atrial fibrillation and consequently were more frequently treated with oral anticoagulants. These patients also had worse kidney function. The TAVR specific variables are presented in Table 5. The types of prosthesis were categorized as early generation balloon expandable (Edwards Sapien [*N* = 17], Edwards Sapien XT [*N* = 28]), early generation self-expanding (Medtronic CoreValve [*N* = 10]), new generation balloon expandable (Edwards Sapien 3 [*N* = 62], Edwards Sapien 3 Ultra [*N* = 1]), and new generation self-expanding (Medtronic CoreValve Evolut R [*N* = 29]). Surprisingly, there was no difference in the procedural approach, type, or size of prosthesis in the patients with and without conduction disorders after TAVR. Echocardiographic characteristics in patients who underwent TAVR are presented in Supplemental Table 2. Of note, patients with conduction disorders after TAVR had lower indexed stroke volume and more often had an abnormal apical-to-basal strain ratio >1.9 (30 [57.7%] vs 30 [34.1%]; *P* = .006). Kaplan-Meier survival analysis, after dichotomizing the patients according to an abnormal apical-to-basal strain ratio, showed that patients undergoing TAVR with an apical-to-basal strain ratio >1.9 were more likely to develop complete bundle branch block or permanent pacemaker implantation after intervention (log rank χ^2 = 6.407; *P* = .011; Supplemental Figure 2). Univariable Cox regression analysis of variables for the association with the combined end point is presented in Supplemental Table 3. History of atrial fibrillation and an abnormal apical-to-basal strain ratio >0.9 were associated with the combined end point. Multivariable Cox regression analysis is presented in Supplemental Table 4. History of atrial fibrillation (HR = 2.182 [1.191, 3.995]; *P* = .012), septal wall thickness (HR = 1.045 [1.001, 1.091]; *P* = .046), and an abnormal apical-to-basal strain ratio >1.9 (HR, 1.899 [1.899, 3.356]; *P* = .027) remained independently associated with the occurrence of complete left or right bundle branch block or permanent pacemaker implantation after TAVR.

Reproducibility

The intraclass correlation coefficient for the intraobserver variability of the apical-to-basal strain ratio was 0.965 (95% CI, 0.919, 0.986; *P* < .001), indicating excellent agreement. The intraclass correlation coefficient for the interobserver variability of the apical-to-basal strain ratio was 0.894 (95% CI, 0.763, 0.955, *P* < .001), indicating good agreement.

DISCUSSION

The main findings of this study, which includes patients with severe AS undergoing SAVR or TAVR, can be summarized as follows: (1)

Table 5 TAVR specific variables (adapted)

TAVR specific variable	Overall population (*N* = 148)	Conduction disorders (*N* = 55)	No conduction disorders (*N* = 93)	*P* value
Transfemoral approach	111 (74.0)	42 (80.8)	69 (70.4)	.169
Type of prosthesis				.182
Early generation, balloon expandable	45 (30.4)	12 (21.8)	33 (35.5)	
Early generation, self-expanding	10 (6.8)	6 (10.9)	4 (4.3)	
New generation, balloon expandable	63 (42.6)	24 (43.6)	39 (41.9)	
New generation, self-expanding	30 (20.3)	13 (23.6)	17 (18.3)	
Size, mm				.477
23	38 (25.3)	16 (30.9)	22 (22.4)	
26	71 (47.3)	24 (46.2)	47 (48.0)	
29	41 (27.3)	12 (23.1)	29 (29.6)	

Data are presented as n (%).

patients with complete bundle branch block or pacemaker implantation after AVR have a higher apical-to-basal strain ratio, (2) an abnormal apical-to-basal strain ratio is independently associated with the occurrence of complete bundle branch block or the necessity of permanent pacemaker implantation; (3) a subgroup analysis in patients undergoing TAVR confirms the independent association of an abnormal apical-to-basal strain ratio with the occurrence of complete bundle branch block or pacemaker implantation after TAVR.

Apical-to-Basal Strain Difference in AS

Apical-to-basal strain differences are best known in the setting of cardiac amyloidosis. Phelan *et al.*[28] described the relative apical sparing pattern as a diagnostic marker for cardiac amyloidosis. However, the pathophysiology of this gradient is poorly understood. Phelan *et al.* hypothesized that less amyloid deposition in the apex could explain the relative apical sparing pattern. but a recent histopathological study could only find a gradient in amyloid deposition in 2 out of 8 patients with relative apical sparing pattern by echocardiography. Furthermore, apical-to-basal strain differences were also found in patients with hypertrophic cardiomyopathy and AS.[26,29-31] Various studies highlighted reduced longitudinal strain in the basal parts of the LV in patients with AS.[15,32,33] These studies suggested that reduced basal strain may relate to a difference in wall stress in the basal parts versus the apical parts of the LV. The apical parts contract earlier than the basal parts, and the progressive rise in intraventricular pressure combined with the increased afterload in patients with AS imposes increased wall stress at the basal versus the apical parts of the LV. This increased wall stress may result in more extensive interstitial fibrosis in the basal parts of the LV. Biopsies obtained from patients with AS revealed that patients with more extensive fibrosis had more reduced GLS.[34] As such, an apical-to-basal strain difference most likely reflects the presence of more fibrosis in the LV base versus the LV apex. Recently, Abecasis *et al.*[35] performed a study with cardiac magnetic resonance imaging in patients with severe AS undergoing AVR. In 23 of 150 patients, relative apical sparing pattern was observed by echocardiography without suspicion of amyloidosis on the cardiac magnetic resonance images or by histological analysis of myocardial biopsies. Furthermore, the authors noted that the relative apical sparing pattern was mostly reversible after AVR, suggesting a reversible mechanism, which is related to the increased afterload in severe AS, underlying the regional functional impairment.[35]

Apical-to-Basal Strain Differences and Outcome

Previous studies in patients with AS showed an association between diminished basal longitudinal strain and reduced exercise tolerance or development of symptoms.[15,32] Moreover, reduced basal LV strain was associated with an increased need for future AVR.[33] To evaluate the difference between apical and basal LV strain, other studies calculated ratios to quantify the strain difference. The apical-to-basal strain ratio was measured in a large cohort of patients undergoing TAVR, and a ratio above 4 was associated with lower survival, more symptoms, and higher N-terminal pro b-type natriuretic peptide levels.[29] Two smaller studies demonstrated that a higher apical-to-basal strain difference was associated with increased all-cause and cardiovascular mortality[30] and with a combined end point of sudden cardiac death and heart failure hospitalization.[31] Moreover, Ferreira *et al.*[30] reported a trend toward a higher prevalence of bundle branch block and pacemaker implantation in patients with a higher apical-to-basal strain difference undergoing TAVR. In the current study, an abnormal apical-to-basal strain ratio was independently associated with the need for permanent pacemaker implantation or the occurrence of complete bundle branch block after AVR.

Clinical Implications

The identification of patients at high risk for conduction disorders after AVR remains important, particularly with the early patient discharge after TAVR.[36,37]

Since all patients with AS undergo routine transthoracic echocardiography preoperatively, the calculation of the apical-to-basal strain ratio could help to risk stratify the patients for the potential development of conduction disorders after AVR. An early identification of these patients should prompt a more intensive and prolonged rhythm monitoring after AVR. In addition, patients at high risk for conduction disorders may benefit from preventative insertion of a temporary pacemaker lead, and a permanent pacemaker implantation could be anticipated.

Study Limitations

The current study had various limitations. The data were obtained in a single-center study and need external validation. Moreover, no systematic screening for ATTR cardiac amyloidosis was performed in these patients since this was not part of routine clinical practice when these patients were planned for intervention.

CONCLUSION

An abnormal apical-to-basal strain ratio is independently associated with the need for permanent pacemaker implantation or development of complete left bundle or right bundle branch block in patients with severe AS undergoing AVR. Implementing this echocardiographic marker in clinical practice could guide risk stratification in patients considered for AVR, who may need prolonged rhythm monitoring or pacemaker implantation after the intervention.

CONFLICTS OF INTEREST

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REVIEW STATEMENT

Given her role as *JASE* Associate Editor, Nina Ajmone Marsan, MD, PhD, had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Philippe Pibarot, DVM, PhD.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.echo.2023.09.008.

REFERENCES

1. Iung B, Delgado V, Rosenhek R, et al. Contemporary presentation and management of valvular heart disease: the EURObservational research programme valvular heart disease II survey. Circulation 2019;140:1156-69.
2. Dolci G, Vollema EM, van der Kley F, et al. One-year follow-up of conduction abnormalities after transcatheter aortic valve implantation with the SAPIEN 3 valve. Am J Cardiol 2019;124:1239-45.
3. Tzikas A, van Dalen BM, Van Mieghem NM, et al. Frequency of conduction abnormalities after transcatheter aortic valve implantation with the Medtronic-CoreValve and the effect on left ventricular ejection fraction. Am J Cardiol 2011;107:285-9.
4. Poels TT, Houthuizen P, Van Garsse LA, et al. Frequency and prognosis of new bundle branch block induced by surgical aortic valve replacement. Eur J Cardiothorac Surg 2015;47:e47-53.
5. Khounlaboud M, Flécher E, Fournet M, et al. Predictors and prognostic impact of new left bundle branch block after surgical aortic valve replacement. Arch Cardiovasc Dis 2017;110:667-75.
6. Urena M, Mok M, Serra V, et al. Predictive factors and long-term clinical consequences of persistent left bundle branch block following transcatheter aortic valve implantation with a balloon-expandable valve. J Am Coll Cardiol 2012;60:1743-52.
7. Husser O, Pellegrini C, Kessler T, et al. Predictors of permanent pacemaker implantations and new-onset conduction abnormalities with the SAPIEN 3 balloon-expandable transcatheter heart valve. JACC Cardiovasc Interv 2016;9:244-54.
8. Siontis GC, Jüni P, Pilgrim T, et al. Predictors of permanent pacemaker implantation in patients with severe aortic stenosis undergoing TAVR: a meta-analysis. J Am Coll Cardiol 2014;64:129-40.
9. Khawaja MZ, Rajani R, Cook A, et al. Permanent pacemaker insertion after CoreValve transcatheter aortic valve implantation: incidence and contributing factors (the UK CoreValve Collaborative). Circulation 2011;123:951-60.
10. Franzoni I, Latib A, Maisano F, et al. Comparison of incidence and predictors of left bundle branch block after transcatheter aortic valve implantation using the CoreValve versus the Edwards valve. Am J Cardiol 2013;112:554-9.
11. Saia F, Lemos PA, Bordoni B, et al. Transcatheter aortic valve implantation with a self-expanding nitinol bioprosthesis: prediction of the need for permanent pacemaker using simple baseline and procedural characteristics. Catheter Cardiovasc Interv 2012;79:712-9.
12. Boerlage-Van Dijk K, Kooiman KM, Yong ZY, et al. Predictors and permanency of cardiac conduction disorders and necessity of pacing after transcatheter aortic valve implantation. Pacing Clin Electrophysiol 2014;37:1520-9.
13. Baan J Jr., Yong ZY, Koch KT, et al. Factors associated with cardiac conduction disorders and permanent pacemaker implantation after percutaneous aortic valve implantation with the CoreValve prosthesis. Am Heart J 2010;159:497-503.
14. Jilaihawi H, Chin D, Vasa-Nicotera M, et al. Predictors for permanent pacemaker requirement after transcatheter aortic valve implantation with the CoreValve bioprosthesis. American heart journal 2009;157:860-6.
15. Lafitte S, Perlant M, Reant P, et al. Impact of impaired myocardial deformations on exercise tolerance and prognosis in patients with asymptomatic aortic stenosis. Eur J Echocardiogr 2009;10:414-9.
16. Ng AC, Delgado V, Bertini M, 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 2011;32:1542-50.
17. Baumgartner HC, Hung JC-C, Bermejo J, 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 2017;18:254-75.
18. Roques F, Nashef SA, Michel P, et al. Risk factors and outcome in European cardiac surgery: analysis of the EuroSCORE multinational database of 19030 patients. Eur J Cardiothorac Surg 1999;15:816-22. discussion 22-3.
19. Surawicz B, Childers R, Deal BJ, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part III: intraventricular conduction disturbances: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. J Am Coll Cardiol 2009;53:976-81.
20. Lang RM, Badano LP, Mor-Avi V, 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 2015;28:1-39.e14.
21. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS guidelines for the management of valvular heart disease: developed by the task force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2021;43:561-632.
22. Nagueh SF, Smiseth OA, Appleton CP, 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 2016;29:277-314.
23. Lancellotti P, Tribouilloy C, Hagendorff A, et al. Recommendations for the echocardiographic assessment of native valvular regurgitation: an executive summary from the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 2013;14:611-44.
24. Rosenhek R, Binder T, Porenta G, et al. Predictors of outcome in severe, asymptomatic aortic stenosis. The New England journal of medicine 2000;343:611-7.
25. Larsen AH, Clemmensen TS, Wiggers H, et al. Left ventricular myocardial contractile reserve during exercise stress in healthy adults: a two-dimensional speckle-tracking echocardiographic study. J Am Soc Echocardiogr 2018;31:1116-26.e1.
26. Phelan D, Collier P, Thavendiranathan P, et al. Relative apical sparing of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis. Heart (British Cardiac Society) 2012;98:1442-8.
27. Sharma E, McCauley B, Ghosalkar DS, et al. Aortic valve calcification as a predictor of post-transcatheter aortic valve replacement pacemaker dependence. Cardiol Res 2020;11:155-67.
28. De Gaspari M, Sinigiani G, De Michieli L, et al. Relative apical sparing in cardiac amyloidosis is not always explained by an amyloid gradient. Eur Heart J Cardiovasc Imaging 2023;24:1258-68.
29. Dahl Pedersen AL, Povlsen JA, Dybro A, et al. Prevalence and prognostic implications of increased apical-to-basal strain ratio in patients with aortic stenosis undergoing transcatheter aortic valve replacement. J Am Soc Echocardiogr 2020;33:1465-73.
30. Ferreira VV, Rosa SA, Pereira-da-Silva T, et al. Prevalence and prognostic impact of apical sparing contractility pattern in patients with aortic stenosis referred for transcatheter aortic valve implantation. Am J Cardiovasc Dis 2021;11:283-94.
31. Saito M, Imai M, Wake D, et al. Prognostic assessment of relative apical sparing pattern of longitudinal strain for severe aortic valve stenosis. Int J Cardiol Heart Vasc 2020;29:100551.

32. Attias D, Macron L, Dreyfus J, et al. Relationship between longitudinal strain and symptomatic status in aortic stenosis. J Am Soc Echocardiogr 2013;26:868-74.
33. Carstensen HG, Larsen LH, Hassager C, et al. Basal longitudinal strain predicts future aortic valve replacement in asymptomatic patients with aortic stenosis. Eur Heart J Cardiovasc Imaging 2016;17:283-92.
34. Puls M, Beuthner BE, Topci R, et al. Impact of myocardial fibrosis on left ventricular remodelling, recovery, and outcome after transcatheter aortic valve implantation in different haemodynamic subtypes of severe aortic stenosis. Eur Heart J 2020;41:1903-14.
35. Abecasis J, Lopes P, Santos RR, et al. Prevalence and significance of relative apical sparing in aortic stenosis: insights from an echo and cardiovascular magnetic resonance study of patients referred for surgical aortic valve replacement. Eur Heart J Cardiovasc Imaging 2023;24:1033-42.
36. Alkhalil A, Lamba H, Deo S, et al. Safety of shorter length of hospital stay for patients undergoing minimalist transcatheter aortic valve replacement. Catheter Cardiovasc Interv 2018;91:345-53.
37. Wood DA, Lauck SB, Cairns JA, et al. The Vancouver 3M (multidisciplinary, multimodality, but minimalist) clinical pathway facilitates safe next-day discharge home at low-, medium-, and high-volume transfemoral transcatheter aortic valve replacement centers: the 3M TAVR Study. JACC Cardiovasc Interv 2019;12:459-69.