Heart and Vessels (2019) 34:1491–1498
https://doi.org/10.1007/s00380-019-01372-7

ORIGINAL ARTICLE

Association of aortic root dilatation with left ventricular function in patients with postoperative ventricular septal defect

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Received: 5 December 2018 / Accepted: 1 March 2019 / Published online: 11 March 2019

Abstract

Proximal aortic enlargement is associated with an increased risk of heart failure and all-cause mortality. Recently, aortic root dilatation (ARD) was reported in postoperative patients with ventricular septal defects (VSDs). However, the impact of ARD on left ventricular (LV) function in postoperative VSD patients remains unclear. Thus, the aim of this study was to investigate the effect of ARD on LV function in patients with postoperative VSD. One hundred and thirty-five patients (> 15 years of age) with surgically repaired isolated ventricular defects and who underwent transthoracic echocardiography in our institution between 2009 and 2013 were identified. ARD was defined as an observed aortic root diameter/body surface area > 2.1 cm/m^2. The propensity score estimating the probability of having ARD adjusted for anatomical and clinical characteristics was calculated. Forty-four patients (32.6%) had ARD. In unadjusted analyses, right ventricular systolic pressure, Tei index, and E/e' were significantly ($p < 0.05$) higher in patients with ARD than in those without ARD (31.3 ± 7.5 vs. 35.4 ± 13.7 mmHg, 0.32 ± 0.10 vs. 0.44 ± 0.15, and 7.1 ± 1.7 vs. 9.5 ± 2.9, respectively). In the propensity score-adjusted analysis, significant differences in the Tei index and E/e' were confirmed between the two groups (Tei index difference: 0.11, 95% confidence interval 0.05–0.17; E/e' difference: 2.4, 95% confidence interval 1.3–3.5). However, there were no differences in the other echocardiographic measurements. The presence of ARD in patients with postoperative VSD was significantly associated with LV diastolic dysfunction. Thus, surgically repaired VSD patients require careful screening for aortic enlargement and LV function.

Keywords Ventricular septal defect · Aortic root dilatation · Left ventricular function · Echocardiogram

Introduction

The prognosis of patients with surgically repaired ventricular septal defect (VSD) is generally good, but not equivalent to that of the general population [1–4]. Aortic root dilatation (ARD) is associated with an increased risk of heart failure (HF) and all-cause mortality [5–7] and occurs in various congenital heart diseases [8–10]. Recent studies have reported a substantial prevalence of ARD in patients with postoperative VSD in Asian and European countries [11, 12]. Saito et al. reported ranges of 8.6–32.9% depending on the definition of ARD [11], while Gabriels et al. reported a prevalence of 15% [12]. To date, the impact of ARD on left ventricular (LV) function in patients with repaired VSD is largely unknown, despite the high frequency of VSD in congenital heart diseases. Therefore, we investigated the differences in LV function between postoperative VSD patients with or without ARD.

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Materials and methods

Patients and data collection

In this cross-sectional analysis of our case series, 135 patients with surgically repaired isolated VSD who were ≥ 15 years of age and who had undergone transthoracic echocardiography (TTE) in our institution between September 2009 and November 2013 were derived from an original data set of 152 patients [11]. Detailed sampling procedures and data collection were previously described [11]. In brief, the original data set excluded patients with (1) presence of another cardiac condition along with VSD, (2) multiple VSD, (3) concomitant aortic valve replacement or mitral valve replacement/plasty with surgical repair of VSD, and (4) insufficient operative and clinical data from 288 patients with surgically repaired VSD whose TTE was performed at our institution [11]. Of the original 152 patients, 17 were further excluded from the present study because of missing echocardiographic data. Analysis of LV function was not previously performed. This study was approved by the Tokyo Women's Medical University Ethics Committee.

Evaluation of echocardiographic variables

A comprehensive TTE study that included M-mode, two-dimensional, continuous-wave, pulsed-wave, and color-flow Doppler echocardiography was performed according to the American Society of Echocardiography guidelines, as described previously [11, 13, 14]. All echocardiographic measurements were recorded by skilled echocardiography technicians and stored as digital video clips for offline analysis. Echocardiographic tracings were read by a single independent observer. To evaluate the reproducibility of echocardiographic tracings, measurements were taken again 6 months later. Aortic root diameter at the sinus of Valsalva was measured using the leading-edge-to-leading-edge approach in end-diastole. ARD was defined as the observed aortic root diameter/body surface area (BSA) > 2.1 cm/m^2, according to echocardiographic recommendations [15]. Left atrial end-systolic diameter was measured in the parasternal long-axis view. LV ejection fraction (EF) was calculated from LV end-diastolic and end-systolic volumes. LV mass was measured according to the American Society of Echocardiography guidelines [14].

The peak velocities of the early (E) and atrial (A) waves and the deceleration time of the E wave were measured using pulse Doppler imaging at the level of the mitral leaflet tips in the apical four-chamber view, and the E/A ratio was calculated [13]. Tissue Doppler early diastolic mitral annular velocity (e') was acquired at the septal mitral annulus, and the E/e' ratio was calculated as E wave divided by e' velocities [16]. The myocardial performance index (Tei index) was measured using Doppler echocardiography and was calculated as the sum of the isovolumic contraction time and the isovolumic relaxation time divided by the ejection time (Fig. 1). The normal range of the Tei index was proposed as < 0.40, which is used to assess systolic and diastolic LV function [17, 18]. Heart rate was obtained from the record of the TTE examination. Vivid E9 (GE Healthcare, Horten, Norway), Artida (Toshiba Medical Systems, Tokyo, Japan), SONOS 4500/5500 (Philips Healthcare, Bothell, WA, USA), or iE33 (Philips Healthcare) ultrasound machines were used for TTE examinations [11].

Covariates

Demographic, clinical, and anatomic characteristics were obtained from the patients' clinical and surgical records (Table 1) [11]. In this study, data on cardiometabolic comorbidities (Table 1) were confirmed at TTE examination. Hypertension was defined as any of the following: (1) diagnosis from the latest medical records in our hospital before

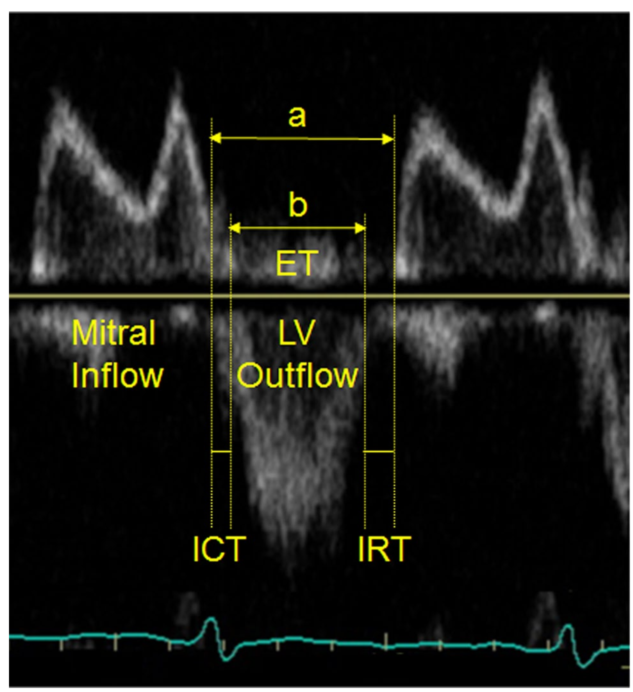

Fig. 1 Measurement of the Tei index. The Tei index was calculated as (isovolumetric contraction time [ICT] + isovolumetric relaxation time [IRT])/ejection time (ET); i.e., $(a-b)/b$, where a is the interval between cessation and onset of the mitral inflow, and b is the left ventricular ET

Table 1 Clinical characteristics of patients with surgically repaired ventricular septal defects (VSD) according to the two definitions of aortic root dilatation (ARD)

	Aortic diameter/BSA > 2.1 cm/m^2			Aortic observed diameter > predicted aortic diameter[a]		
	Without ARD (*n* = 91)	With ARD (*n* = 44)	*p* value	Without ARD (*n* = 105)	With ARD (*n* = 30)	*p* value
Male sex	47 (51.6)	20 (45.5)	0.50	54 (51.4)	13 (43.3)	0.43
BSA (cm/m^2)	1.63 (1.53, 1.76)	1.53 (1.44, 1.66)	< 0.001	1.60 (1.49, 1.74)	1.66 (1.49, 1.74)	0.54
BMI (kg/m^2)	21.8 (3.2)	21.1 (2.9)	0.20	20.4 (19.1, 23.3)	21.9 (19.6, 24.2)	0.10
Shunt duration (years)	5.1 (1.5, 12.9)	12.1 (5.9, 25.9)	< 0.001	5.6 (1.6, 14.1)	12.3 (6.0, 24.2)	0.01
Postoperative follow-up period (years)	17.3 (13.2, 22.4)	24.0 (15.0, 39.9)	0.002	18.3 (13.2, 24.2)	23.0 (14.7, 39.6)	0.06
Heart rate (bpm)	66 (12)	64 (12)	0.58	66 (12)	63 (12)	0.22
R/NCCP	36 (39.6)	17 (38.6)	0.92	39 (37.1)	14 (46.7)	0.35
Sub-aortic VSD, *n*	45 (49.5)	13 (29.5)	0.03	49 (46.7)	9 (30.0)	0.10
Greater than moderate AR, *n*	2 (2.2)	1 (2.3)	0.98	2 (1.9)	1 (3.3)	0.53
Transaortic surgical approach, *n*	50 (54.9)	16 (36.4)	0.04	53 (50.5)	13 (43.3)	0.49
VSD size, mm	11.0 (9.0, 15.0)	12.0 (10.0, 20.0)	0.18	11.0 (9.0, 15.0)	13.0 (10.0, 21.25)	0.03
Smoking, *n*	2 (2.2)	5 (11.4)	0.02	4 (3.8)	3 (10.0)	0.18
Hypertension, *n*	8 (8.8)	7 (15.9)	0.22	10 (9.5)	5 (16.7)	0.32
Diabetes mellitus, *n*	3 (3.3)	4 (9.1)	0.16	4 (3.8)	3 (10.0)	0.18
Dyslipidemia, *n*	5 (5.5)	3 (6.8)	0.76	6 (5.7)	2 (6.7)	0.85
Medication, *n*						
ACE-I or ARB	12 (13.2)	8 (18.2)	0.44	15 (14.3)	5 (16.7)	0.77
β-blocker	5 (5.5)	5 (11.4)	0.22	7 (6.7)	3 (10.0)	0.69

Data are expressed as mean (standard deviation), median (25th, 75th percentile), or number (%)

BSA body surface area, *BMI* body mass index, *R/NCCP* right or noncoronary cusp prolapse, *AR* aortic regurgitation, *ACE-I* angiotensin-converting enzyme inhibitor, *ARB* angiotensin II receptor blocker

[a]Predicted aortic diameter was calculated in every patient using the following formula: predicted aortic diameter adjusted by height = 1.519 + Age × 0.01 + Height × 0.01 − 0.247 × Sex + 0.215 × 1.96, with sex defined as: male = 1, female = 2

TTE examination, (2) use of antihypertensive drugs, or (3) measured systolic/diastolic blood pressure ≥ 140 mmHg and/or ≥ 90 mmHg, respectively [19]. Diabetes mellitus was defined as any of the following: (1) as for hypertension, (2) use of antidiabetic drugs, or (3) measured fasting blood glucose ≥ 126 mg/dl or HbA1c ≥ 6.5% [20]. Dyslipidemia was defined as any of the following: (1) as for hypertension, (2) use of lipid lowering drugs, or (3) measured LDL cholesterol ≥ 140 mg/dl [21].

Statistical analysis

We compared echocardiographic measurements between patients with and without ARD using unadjusted and propensity score-adjusted models. Continuous variables are presented as mean ± standard deviation or median with interquartile range and were compared using the Student's *t* test or Mann–Whitney's test, as appropriate. Categorical variables are presented as a number (proportion) and compared using the Chi-square test or Fisher's exact test. Intraobserver repeatability was evaluated using the intraclass correlation coefficient with a 95% confidence interval. To account for possible confounding factors and given the study's limited sample size, we calculated the propensity score to estimate the probability of the presence of ARD for each patient. In our previous study [11], we reported that shunt duration, a longer postoperative follow-up period, the type of VSD (e.g., subarterial or nonsubarterial), and presence of preoperative right or noncoronary cusp prolapse were associated with the presence of ARD. Moreover, cardiovascular risk factors including the presence of hypertension, diabetes, and dyslipidemia, and sex were reported to be associated with ARD [22–24]. Greater than moderate aortic regurgitation, the surgical approach, size of VSD, BSA, body mass index, heart rate at TTE examination, and medication administered, including angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers and β-blockers [8], were also included in the calculation of the propensity score. Therefore, the propensity score was estimated using 17 covariates (Table 1). The relationship between the presence of ARD and each echocardiographic measurement was assessed by linear regression analysis in the unadjusted model and the propensity score-adjusted model. In the propensity score-adjusted model, each echocardiographic measurement was used as a dependent variable, while the presence of ARD (reference group was the absence of ARD) was used as the independent variable, and the calculated propensity score was simultaneously entered into this model as a covariate.

For sensitivity analysis, we used another definition of ARD, based on the predicted aortic diameter adjusted by height [25]. The predicted aortic diameter was calculated in every patient with the following formula: predicted aortic diameter adjusted by height = 1.519 + Age × 0.01 + Height × 0.01 − 0.247 × Sex + 0.215 × 1.96, with sex defined as male = 1 or female = 2 [26]. ARD using this criterion was defined as an observed aortic diameter > predicted aortic diameter adjusted by height [25]. The propensity score for the probability of the presence of height-adjusted ARD for each patient was recalculated using the same 17 covariates presented in Table 1. We set the statistical significance level at $p < 0.05$ for a two-sided test. All statistical analyses were performed using statistical software (IBM SPSS Statistics for Windows, v24.0; IBM Co., Armonk, NY, USA).

Results

Clinical characteristics

Of the 135 eligible patients, 44 (32.6%) had ARD (Table 1). A longer shunt duration and follow-up period from operation to TTE examination, low BSA, sub-aortic VSD, transaortic surgical approach, and higher prevalence of smoking were observed in postoperative VSD patients with ARD compared with those without ARD. There were no differences in the prevalence of male sex, comorbid preoperative right or non-coronary cusp prolapse, greater than moderate aortic regurgitation, cardiovascular risk factors, administered medication, body mass index, and VSD size between patients with and without ARD (Table 1).

Intraobserver repeatability of echocardiograms

The intraclass correlation coefficient was 0.99 for left atrial diameter, 0.97 for LV end-diastolic dimension, 0.97 for LV end-systolic dimension, 0.96 for LVEF, 0.86 for LV mass index, 0.99 for E/A ratio, 0.88 for deceleration time, 0.99 for right ventricular systolic pressure, 0.86 for Tei index, 0.93 for E/e', and 0.99 for aortic root diameter (Table 2).

Table 2 Intraobserver intraclass correlation coefficients (ICC) for echocardiographic measurements

	ICC	95% confidence interval (CI)
LAD, mm	0.99	0.978–0.989
LVDd, mm	0.97	0.952–0.975
LVDs, mm	0.97	0.957–0.978
EF, %	0.96	0.946–0.973
LVMI, g/BSA	0.86	0.806–0.901
E/A ratio	0.99	0.983–0.991
Deceleration time, ms	0.88	0.84–0.916
RVSP, mmHg	0.99	0.996–0.998
Tei index	0.86	0.779–0.912
E/e'	0.93	0.903–0.951
Aortic root diameters, mm	0.99	0.982–0.991

LAD left atrial diameter, *LVDd* left ventricular end-diastolic dimension, *LVDs*, left ventricular end-systolic dimension, *EF* ejection fraction (assessed by the Simpson method), *LVMI* left ventricular mass index, *E* early diastolic mitral inflow velocity, *A* late diastolic mitral inflow velocity, *RVSP*, right ventricular systolic pressure, *e'* early mitral annular velocity measured at the septal location

Comparisons of echocardiographic variables with or without ARD

In the unadjusted model, a lower early diastolic mitral inflow velocity (E)/late diastolic mitral inflow velocity (A) ratio, and a higher right ventricular systolic pressure, Tei index, and e' measured at the septal location (E/e'), were observed in patients with ARD compared with those without ARD. However, there were no differences in left atrial diameter, LV diastolic and systolic diameter, LV EF, LV mass index, E/A ratio, deceleration time, and right ventricular systolic pressure between the groups (Table 3). In the propensity score-adjusted model, the significant differences in the Tei index and E/e' were confirmed (Table 4). Sensitivity analysis was performed using the definition of height-adjusted ARD. In the unadjusted model, there were significant differences in left atrial diameter, LV end-diastolic dimension, LV mass index, E/A ratio, Tei index, and E/e' between the two groups (Table 3). The propensity score-adjusted model also showed that Tei index and E/e' were significantly higher in patients with ARD than those without ARD in the sensitivity analysis (Table 4).

Discussion

A key finding of the present study was the presence of a higher Tei index and E/e', mainly reflecting LV diastolic dysfunction, in surgically repaired VSD patients with ARD compared with those without ARD. The survival of these patients during long-term observation was previously reported to be shorter than that of the general population [1, 4]. Our findings suggest a potential mechanism underlying this phenomenon.

Dilatation of the proximal aorta is frequently observed in adults with either unrepaired or repaired congenital heart disease [9, 11, 12]. It is increasingly recognized that dilation

Table 3 Comparison of echocardiographic measurements between patients with and without ARD according to the two definitions

	Aortic diameter/BSA > 2.1 cm/m^2			Aortic observed diameter > predicted aortic diameter[a]		
	Without ARD (*n* = 91)	With ARD (*n* = 44)	*p* value	Without ARD (*n* = 105)	With ARD (*n* = 30)	*p* value
LAD, mm	3.1 (0.5)	3.2 (0.7)	0.81	3.1 (0.6)	3.4 (0.7)	0.02
LVDd, mm	4.8 (0.5)	4.9 (0.5)	0.87	4.8 (0.5)	5.0 (0.4)	0.04
LVDs, mm	3.3 (0.5)	3.4 (0.5)	0.51	3.3 (0.5)	3.4 (0.4)	0.15
EF, %	59.5 (8.7)	57.7 (9.0)	0.26	59.0 (8.6)	58.5 (9.4)	0.75
LVMI, g/BSA	113.8 (32.3)	122.1 (33.2)	0.17	113.5 (31.2)	127.1 (35.8)	0.04
E/A ratio	2.1 (1.0)	1.6 (0.7)	0.003	2.1 (1)	1.6 (0.8)	0.02
Deceleration time, ms	187.4 (36.3)	190.2 (46.8)	0.71	187.8 (39)	190.2 (43.2)	0.77
RVSP, mmHg	31.3 (7.5)	35.4 (13.7)	0.03	32.3 (9.6)	34.3 (11.4)	0.33
Tei index	0.32 (0.10)	0.44 (0.15)	< 0.001	0.34 (0.11)	0.44 (0.16)	< 0.001
E/e’	7.1 (1.7)	9.5 (2.9)	< 0.001	7.5 (2)	9.2 (3.2)	0.001

Data are presented as mean (standard deviation)

[a]Predicted aortic diameter was calculated in every patient using the following formula: predicted aortic diameter adjusted by height = 1.519 + Age × 0.01 + Height × 0.01 − 0.247 × Sex + 0.215 × 1.96, with sex defined as: male = 1, female = 2

Table 4 Comparison of echocardiographic measurements between patients with and without ARD in the unadjusted and propensity score-adjusted model

	Aortic diameter/BSA > 2.1 cm/m^2				Aortic observed diameter > predicted aortic diameter			
	Crude mean difference (95% CI)	*p* value	Adjusted mean difference* (95% CI)	Adjusted *p* value	Crude mean difference (95% CI)	*p* value	Adjusted mean difference[a] (95% CI)	Adjusted *p* value
LAD, mm	0.06 (− 0.16 to 0.27)	0.61	− 0.01 (− 0.28 to 0.31)	0.93	0.29 (0.05 to 0.53)	0.019	− 0.15 (− 0.14 to 0.43)	0.32
LVDd, mm	0.02 (− 0.16 to 0.21)	0.82	0.15 (− 0.10 to 0.40)	0.24	0.22 (0.16 to 0.43)	0.035	0.23 (− 0.02 to 0.47)	0.07
LVDs, mm	0.12 (− 0.06 to 0.29)	0.19	0.15 (− 0.09 to 0.39)	0.23	0.15 (− 0.05 to 0.34)	0.15	0.10 (− 0.14 to 0.33)	0.43
EF, %	− 1.8 (− 5.0 to 1.4)	0.26	− 0.6 (− 4.9 to 3.7)	0.79	−0.6 (− 4.2 to 3.0)	0.75	− 0.7 (− 3.6 to 5.1)	0.73
LVMI, g/BSA	8.3 (− 3.6 to 20.1)	0.17	6.5 (− 9.5 to 22.5)	0.42	13.6 (0.4 to 26.8)	0.044	14.5 (− 1.3 to 30.3)	0.07
E/A ratio	− 0.5 (− 0.8 to − 0.2)	0.003	− 0.1 (− 0.5 to 0.3)	0.62	− 0.5 (− 0.8 to − 0.1)	0.015	− 0.1 (− 0.5 to 0.3)	0.53
Deceleration time, ms	2.8 (− 11.7 to 17.3)	0.71	11.9 (− 7.7 to 31.4)	0.23	2.5 (− 13.9 to 18.9)	0.30	1.9 (− 17.7 to 21.5)	0.19
RVSP, mmHg	4.1 (0.5 to 7.7)	0.027	4.2 (− 0.7 to 9.1)	0.10	2.0 (− 2.1 to 6.1)	0.33	2.4 (− 2.6 to 7.4)	0.34
Tei index	0.12 (0.08 to 0.16)	< 0.001	0.11 (0.05 to 0.17)	< 0.001	0.10 (0.05 to 0.15)	< 0.001	0.08 (0.02 to 0.14)	0.01
E/e’	2.5 (1.7 to 3.3)	< 0.001	2.4 (1.3 to 3.5)	< 0.001	1.7 (0.7 to 2.7)	0.001	1.6 (0.4 to 2.8)	0.01

Data are presented as mean (standard deviation)

[a]Adjusted for propensity score

of the aorta influences the aorto-ventricular complex (termed ‘aortopathy’) [10, 27], which causes dysfunction of the systemic ventricle, as well as that of the aortic valve and the aortic vascular wall [9]. Indeed, in the present study, patients with surgically repaired VSD and ARD showed LV diastolic dysfunction. Moreover, Shiina et al. reported that aortopathy in adults with a repaired tetralogy of Fallot was associated with LV diastolic dysfunction [28]. Our data extend these findings into postoperative VSD patients.

We found that ARD was significantly associated with echocardiographic parameters related to LV function (i.e., Tei index and E/e’), predominantly reflecting diastolic dysfunction. There are several potential explanations for these findings. First, ARD was reported to be a marker of structural changes in the aortic wall (less elastin and more collagen) [29], which cause increasing arterial stiffness [27] and resulting LV diastolic dysfunction [30]. Thus, differences in LV function in the presence or absence of ARD may be explained, at least in part, as a consequence of aortic root remodeling [5, 8, 20]. Second, enlargement of the aortic root causes aortic root rotation [31], which affects basal LV motion, and thus the interaction between basal and apical LV motion (i.e., LV twisting motion or torsion). Although we did not examine LV twist using magnetic resonance imaging or speckle-tracking echocardiography in the present study, the reduction in LV untwisting likely contributes to diastolic dysfunction [32, 33]. Third, the anatomical effects of VSD may affect LV function. For example, Hoffman et al.

suggested that incoordination of the ascending spiral segment of the ventricular myocardial band, including the right ventricular side of the septum, is partially associated with LV diastolic dysfunction [34]. Thus, existing VSD may cause incoordination of the ventricular myocardial band of the septum. Overall, these potential factors, the combined or separate effects of LV torsion, and the incoordination of the ventricular band, likely change the isovolumetric time, causing an increase in the Tei index. Finally, all participants in this study received cardiac surgery. Matsuhisa et al. reported that a larger patch area located close to multiple ventricular septal defects was positively correlated with a higher Tei index [35]. Although we excluded patients with multiple ventricular septal defects [11], we have no data on patch size. Further, surgical closure with prosthetic materials was reported to affect postoperative global and regional LV function [35]. Thus, careful monitoring of the effects of ARD on LV function is required in postoperative VSD patients.

Although previous studies reported that ARD was associated with LV hypertrophy [5, 20], we found no differences in the LV mass index between the study groups when ARD was defined as the observed aortic root diameter/BSA > 2.1 cm/m^2, according to echocardiographic recommendations. In this regard, the association of ARD with LV hypertrophy is inconsistent. For example, Milan et al. reported that compared with LV mass in hypertensive patients with a normal aortic dimension, a significant increase in LV mass was only detected in patients with both sinus of Valsalva and ascending aortic dilatation, but not with sinus of Valsalva dilatation alone [36]; it remains unclear why selective dilatation of Valsalva was not associated with LV hypertrophy. It is also important to consider differences between participants who had hypertension or congenital heart disease [36]. Indeed, secondary dilatation of the aorta is mainly at the root in patients with congenital heart diseases, while less involvement of the ascending aorta is usually seen after congenital cardiac surgery [9].

E/e’ values > 8 are noninvasive potential subclinical risk factors for the development of HF with preserved EF (≥ 50%) [32, 37], and Tei index values > 0.4 are moderate elevations above the normal upper range [17, 18]. In the present study, the mean values of the Tei index, E/e’, and EF in the ARD group were within these ranges [18, 32]. Moreover, ventricular–vascular remodeling causes disease progression over time [5], while Menting et al. reported that the cumulative incidence of HF at 40 years of age was 4% in patients with surgically repaired VSDs [1]. In the present study, the median postoperative follow-up period was approximately 25 years. Thus, reexamination of ARD and LV attributes at older ages may show larger differences between the groups. Additionally, the burden of exercise intolerance in patients after surgical closure of VSDs is a profound comorbidity for the development of symptomatic HF [2, 37]. By contrast, Kamimura et al. reported that a small proximal aortic diameter was associated with both higher all-cause mortality and cardiovascular mortality in Japanese patients with HF, although patients with congenital heart disease were excluded from that analysis [38]. Herein, we found a significant impact of ARD on LV function. Further studies are required to determine the impact of an increase in the Tei index and E/e’ values with ARD on the development of HF in patients with postoperative VSD.

Limitations

This study has several limitations. First, the results were based on a small sample from a Japanese single center, which may affect the prevalence of ARD [11, 12]. Second, the study has selection bias (i.e., only patients with a reason to attend our hospital and only surviving patients were included). Nevertheless, our results suggest that careful follow-up screening for ARD and LV function after discharge is required. Third, we were unable to address causal relationships between ARD and LV functions because of the cross-sectional study design. Further, it is possible that the observed differences in echocardiograms between patients with and without ARD may reflect the results of ventricular–vascular remodeling over time. In this regard, Nwabuo et al. reported that a larger change of increasing aortic root diameter over 20 years was associated with impaired E/e’ in women [20], while Lam et al. reported that ARD was associated with future development of HF in a longitudinal observational study [5]. Finally, unmeasured residual cofounders (e.g., arrhythmia, inflammatory makers, cytokines, and genetic factors) may have also affected our results [8, 39, 40].

Conclusions

The presence of ARD in patients with postoperative VSD was significantly associated with LV function, especially diastolic dysfunction. These findings suggest that ARD may be a marker for hemodynamic impairment in patients with postoperative VSD. A higher Tei index and E/e’ values with aortic root dilatation may be underlying mechanisms for the development of HF in these patients. The clinical impact of aortic root dilatation warrants further investigation.

Acknowledgements The authors thank Dr. Shinya Hatakeyama for assistance with data collection, Dr. Goki Matsumura for advice regarding the manuscript, and Edanz Group (http://www.edanzediting.com/ac) for editing a draft of this manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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