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## Evaluation of the relationship between ventricular end-diastolic pressure and echocardiographic measures of diastolic function in adults with a Fontan circulation☆

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### ABSTRACT

**Background:** Echocardiographic assessment of diastolic function in the setting of Fontan physiology is not well validated. We recently demonstrated that atrioventricular systolic to diastolic duration ratio (AVV S/D ratio) independently predicts mortality in Fontan-adults and that a value >1.1 was associated with poor prognosis.

**Purpose:** To correlate echocardiographic measures of diastolic function with direct measurement of ventricular end-diastolic pressure (VEDP).

**Methods:** A retrospective analysis was undertaken of Fontan-adults who had transthoracic echocardiography (TTE) within 12 months of direct measurement of VEDP during cardiac catheterisation.

**Results:** Fifteen Fontan adults (3 males, mean age  $29 \pm 9$  years) were evaluated. Thirteen patients had dominant morphologic left ventricle and 2 had morphologic right ventricle. Four had atriopulmonary connection and 11 had total cavopulmonary connection. Twelve patients were NYHA Class I/II and 3 were Class III. Time between TTE and cardiac catheter was  $46 \pm 113$  days; VEDP was  $8 \pm 5$  mmHg. Ten patients had preserved ventricular function, 3 had mild and 2 had moderate systolic impairment by subjective TTE assessment. AVV S/D ratio had the strongest correlation with VEDP ( $r = 0.8$ ,  $p = 0.001$ ). AVV S/D ratio  $\geq 1.1$  had 100% positive predictive value and 92% negative predictive value for detecting VEDP >10 mmHg. The only conventional echocardiographic measure of diastolic function that correlated with VEDP was pulmonary vein A wave - atrioventricular A wave duration difference ( $r = 0.8$ ,  $p = 0.02$ ).

**Conclusions:** TTE measures reflect VEDP in adults with a Fontan circulation. AVV S/D ratio is a simple parameter yet to enter standard practice that can be used to identify elevated VEDP.

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### 1. Introduction

Conventional echocardiographic measures of diastolic function are poorly validated in univentricular Fontan physiology although echocardiography is a central imaging modality for routine assessment in these patients [1]. Furthermore, raised diastolic pressure reduces cardiac filling and worsens systemic venous hypertension with important implications for long-term outcome [2]. We recently reported that

atrioventricular systolic to diastolic duration ratio (AVV S/D) was the strongest echocardiographic predictor of survival in a relatively large group of Fontan adults [3]. In this study we sought to investigate whether conventional echocardiographic measures of diastolic function and AVV S/D correlated with ventricular end-diastolic pressure (VEDP) measured invasively at cardiac catheterisation.

### 2. Methods

#### 2.1. Study design and patients

Adults with a Fontan circulation followed at our tertiary referral centres since January 2010 who had cardiac catheterisation and transthoracic echocardiography (TTE) within 12 months were screened for inclusion. Exclusion criteria were Kawashima repair, supra-ventricular arrhythmia during testing, pregnancy or paced ventricular rhythm. Clinical

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data were collected from hospital records. Echocardiographic analyses were blinded from clinical data. As this was a retrospective analysis of data collected for routine clinical care, individual informed consent was not required. The study was locally registered and approved for audit.

## 2.2. Echocardiographic measurements

Our Methods have been described in detail previously [3]. In short, Two-dimensional and Doppler echocardiographic assessments were performed using Vivid 7 (General Electric Healthcare, Milwaukee, WI) and IE-33 ultrasound systems (Philips Medical Systems, Andover, MA) according to the recommendations of the American Society of Echocardiography [4–7]. A single cardiologist with expertise in echocardiography and congenital heart disease interpreted the echocardiographic data except for grading of overall ventricular systolic function that was agreed upon by 2 expert cardiologists to minimise potential confounders in analysis. Dominant ventricular morphology was classed as left ventricular, right ventricular or biventricular. Dominant atrioventricular (AV) valve pulsed-wave Doppler was performed in the best-aligned view with the sample volume placed at the tips of the valve leaflets. Early (E) and late (A) velocities and time intervals, E/A ratio and inflow duration were measured from the AV valve inflow profile. Pulmonary venous velocities and A wave duration were measured from the best-aligned pulmonary venous flow profile with the sample volume placed 0.5 to 1 cm into the vein. The myocardial systolic (S'), early diastolic (E') and late diastolic (A') velocities and isovolumic contraction time (ICT), isovolumic relaxation time (IRT) and systolic ejection time were obtained at the lateral dominant atrioventricular valve annulus only by placing a tissue Doppler sample volume at the basal part of the respective segment. No tissue Doppler or long-axis function parameters were analyzed for the ventricular septum because the majority of patients had a ventricular septal defect. Tei Index was calculated from tissue Doppler data as (ICT + IRT)/(systolic ejection time). Durations of systole and diastole were measured from the clearest continuous wave Doppler signal of dominant AV valve regurgitation. Effective systolic duration was measured from the onset to the end of AV valve regurgitation. Effective diastolic duration was measured from the end of AV valve regurgitation to the onset of the subsequent AV valve regurgitation signal. The systolic to diastolic duration ratio (AVV S/D) was then calculated (Fig. 1).

## 2.3. Cardiac catheterisation

Measurements were taken whilst patients were awake but fasting for at least 4 h prior to the procedure with maintenance intravenous fluids running during the procedure. VEDP was measured via a 6F fluid-filled pig-tail catheter connected to a pressure transducer that had been carefully zeroed at the patient's mid-thoracic level as per our standard practice. VEDP was taken as the point just prior to the rapid upstroke on the ventricular

pressure trace that corresponds to contraction and averaged over at least 1 respiratory cycle. A VEDP of 10 mmHg was considered pathological [8,9].

## 2.4. Cardiopulmonary exercise testing

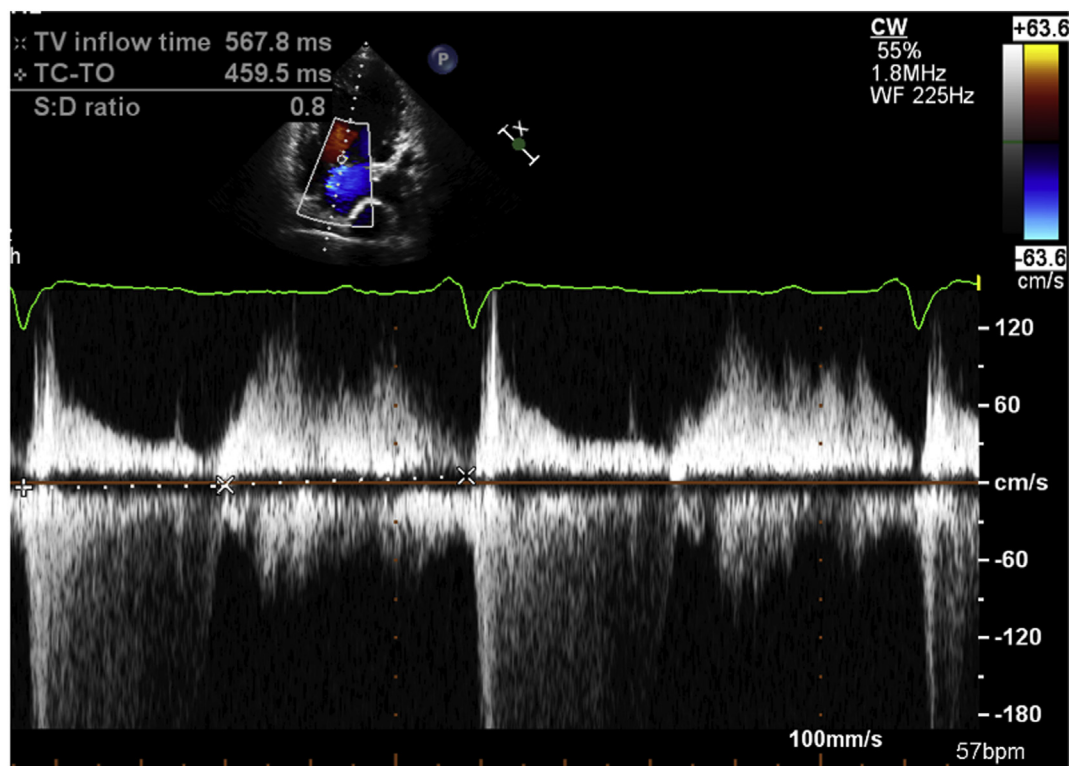
If maximal cardiopulmonary exercise testing had been performed within 12 months of echocardiography (RER > 1.1), a secondary analysis was undertaken to characterise the relationship between peak oxygen uptake and the most significant echocardiographic measure of VEDP. Symptom-limited maximal exercise tests were performed on an electronically braked ergometer cycle. Carbon dioxide elimination,  $\text{VO}_2$ , and minute ventilation were measured with a computerised breath-by-breath analyzer as described previously [10].

## 2.5. Statistical analysis

Statistical analyses were performed using SPSS Version 21 (IBM, New York, United States). Data are reported as number (percentage) for categorical variables and mean  $\pm$  SD or median [25th, 75th percentile] for continuous variables, as appropriate. Data were tested for normality using the Shapiro-Wilk test. Pearson Product-Moment Correlation was used to assess for a correlation between echocardiographic measures and VEDP. Comparisons between groups were made using Student's *t*-test or Mann-Whitney *U* test as appropriate. A *p*-value < 0.05 was considered significant.

## 3. Results

In total, 15 patients were included; 3 were male (20%). Mean age was  $29 \pm 9$  years. Thirteen patients had dominant morphologic left ventricle and 2 had morphologic right ventricle. Four had atrioventricular connection (APC) and 7 had total cavopulmonary connection (TCPC) with intracardiac tunnel (2 were post adult APC to TCPC conversion) and 4 had extracardiac conduit. Twelve patients were NYHA Class I/II and 3 were Class III. Baseline characteristics are shown in Table 1. Time between TTE and cardiac catheter was  $46 \pm 113$  days. Mean VEDP was  $8 \pm 5$  mmHg. TTE results comparing the groups with VEDP above and below 10 mmHg are shown in Appendix Table 1. AVV S/D was higher ( $0.85 \pm 0.17$  in VEDP < 10 mmHg vs.  $1.33 \pm 0.32$ , *p* = 0.002) and aortic regurgitation was worse in the high VEDP group.



**Fig. 1.** Measurement of the atrioventricular systolic to diastolic duration ratio from the continuous wave Doppler signal. The atrioventricular systolic to diastolic duration ratio is calculated from the continuous wave Doppler signal of the dominant atrioventricular valve. S:D-systolic to diastolic duration, TC-TO-tricuspid valve closure to tricuspid valve opening, TV-tricuspid valve.

**Table 1**  
Baseline characteristics.

Patient characteristics	VEDP < 10mmHg (n = 11)	VEDP ≥ 10 mmHg (n = 4)	All (n = 15)	p value
Age (years)	28 ± 8	33 ± 11	29 ± 9	0.4
Sex	2 male	1 male	3 male	0.8
Dominant ventricular morphology	9 left 1 right	4 left 0 right	13 left 1 right	0.3
Cardiac anatomy	1 biventricular 6 tricuspid atresia 1 DILV 1 DILV 2 PA-IVS 1 DORV 1 VSD	2 tricuspid atresia 2 DILV	1 biventricular 8 tricuspid atresia 3 DILV 3 DILV 2 PA-IVS 1 DORV 1 VSD	
Fontan type	3 APC 5 TCPC (1 conv) 3 ECC (0 conv)	1 APC 2 TCPC (1 conv) 1 ECC (1 conv)	4 APC (27%) 7 TCPC (2 conv) (47%) 4 ECC (1 conv) (27%)	1.0
NYHA Class	1 NYHA I 8 NYHA II 2 NYHA III	0 NYHA I 3 NYHA II 1 NYHA III	1 NYHA I 11 NYHA II 3 NYHA III	0.6
History of arrhythmia	5	2	7 (47%)	0.9
Medications	4 beta blocker 3 antiarrhythmic 5 ACE inhibitor 7 diuretics 6 warfarin 5 antiplatelet agent 1 enoxaparin	2 beta blocker 0 antiarrhythmic 1 ACE inhibitor 2 diuretics 3 warfarin 1 antiplatelet agent 0 enoxaparin	6 beta blocker 3 antiarrhythmic 6 ACE inhibitor 9 diuretics 9 warfarin 6 antiplatelet agent 1 enoxaparin	0.9 0.3 0.5 0.2 0.5 0.7 0.6
Time between TTE and catheterisation (days)	22 ± 34	110 ± 219	57 ± 125	0.2
Ventricular end-diastolic pressure (mmHg)	6 ± 2	15 ± 4		<b>&lt;0.0001***</b>

ACE-angiotensin converting enzyme, APC-atriopulmonary connection, conv-conversion, DILV-double inlet left ventricle, DORV-double outlet right ventricle, ECC-extracardiac conduit, PA-IVS-pulmonary atresia with intact ventricular septum, NYHA-New York Heart Association, TCPC-total cavopulmonary connection, TTE-transsthoracic echocardiography, VEDP-ventricular end-diastolic pressure, VSD-ventricular septal defect.

Echocardiographic data and results of correlation analysis with VEDP are shown in Table 2. AVV S/D ratio had the strongest correlation with VEDP (0.8,  $p = 0.001$ ) in the group overall (Fig. 2). S/D ratio  $\geq 1.1$  had 100% positive predictive value and 92% negative predictive value for detecting VEDP > 10 mmHg. The only conventional echocardiographic measure of diastolic function (in the overall group) that correlated with VEDP was pulmonary vein A wave-atrioventricular A wave duration difference ( $R = 0.8$ ,  $p = 0.02$ ).

Post-hoc analysis to investigate the effect on heart rate and AVV S/D suggested that heart rate did not correlate significantly with AVV S/D ( $r = -0.3$ ,  $p = 0.3$ ) and correcting AVV S/D for heart rate

did not improve the correlation with VEDP ( $r = 0.7$ ,  $p = 0.008$  vs  $r = 0.8$ ,  $p = 0.001$  uncorrected for heart rate).

Six subjects had cardiopulmonary exercise testing during the study period. Percent predicted peak  $\text{VO}_2$  in those with AVV S/D ratio < 1.1 was  $67 \pm 8\%$  ( $n = 3$ , all had peak  $\text{VO}_2 > 55\%$  and VEDP  $\leq 7$  mmHg) vs.  $47 \pm 2\%$  in those AVV S/D > 1.1 ( $n = 3$ , all had peak  $\text{VO}_2 < 50\%$  and VEDP  $\geq 9$  mmHg),  $p = 0.01$ .

#### 4. Discussion

This study characterising important echocardiographic measures of diastolic function in adults with a Fontan circulation suggests that atrioventricular systolic to diastolic duration ratio is the most useful echocardiographic measure for identifying raised ventricular end-diastolic pressure and superior to conventional parameters of diastolic dysfunction.

Data validating the utility of conventional echocardiographic measures of diastolic function in the setting of a Fontan circulation are lacking although a non-invasive tool to easily identify patients with raised diastolic pressure would have important clinical utility in view of the negative implications high filling pressure has in this unique physiology. In a group of 32 children with a single ventricle circulation (28% post-Fontan), VEDP was found to correlate with E/E' (although the correlation coefficient was only 0.4), pulmonary vein atrial reversal duration ( $r = 0.8$ ) and E' ( $r = 0.5$ ) [9]. The authors did not report AVV S/D or time difference between pulmonary venous and AVV inflow A wave duration. In this current report we did not find a significant positive correlation between E/E', E' or pulmonary A wave reversal duration although interestingly we did find a significant correlation between VEDP and the pulmonary venous-AVV inflow A wave duration in our group of adults. In a group of children with single right ventricular physiology, only A velocity correlated with VEDP of the tissue and pulsed Doppler derived indices measured [11]. Invasive pressure-volume loop analysis to calculate the isovolumic relaxation time constant and the relationship with echocardiographic measures of diastolic function has also been assessed in a group of single-ventricle patients. The time constant correlated with

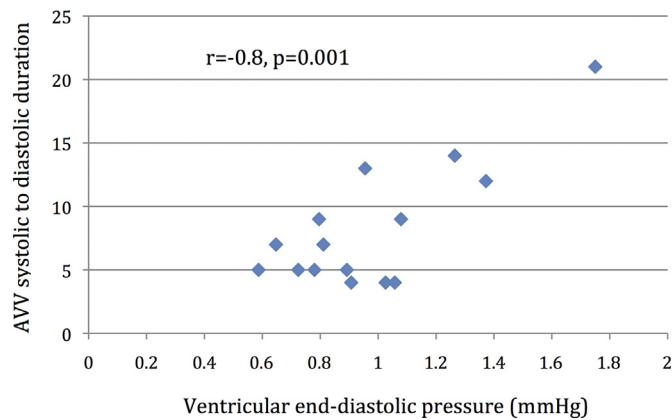
**Table 2**  
Echocardiographic correlation analysis with ventricular end-diastolic pressure (n = 15).

Echocardiographic measure	N or mean ± SD	r	p value
Ventricular systolic impairment (qualitative grade)	13 none/mild 2 mod/severe	0.3	0.3
FAC (%)	34 ± 4	-0.4	0.3
AVV S/D	1.0 ± 0.3	<b>0.8</b>	<b>0.001**</b>
E (cm/s)	65 ± 24	-0.2	0.4
E/A	1.4 ± 0.7	-0.1	0.8
Deceleration time (msec)	185 ± 69	0.5	0.09
E' (cm/s)	10 ± 4	0.1	0.9
E/E'	8 ± 4	-0.3	0.4
Pulm vein S/D	1.0 ± 0.6	0.3	0.4
Pulm vein A vel (cm/sec)	28 ± 16	0.3	0.9
Pulm vein A duration (msec)	120 ± 20	-0.4	0.3
AVV inflow A-pulm vein A (msec)	-17 ± 58	<b>0.8</b>	<b>0.02</b>
Isovolumic relaxation time (msec)	90 ± 30	-0.3	0.4
Tei Index	0.74 ± 0.12	-0.4	0.4
AVV regurgitation	12 none/mild, 3 mod/severe	0.3	0.2
Aortic regurgitation	13 none/mild, 2 mod/severe	<b>0.7</b>	<b>0.001**</b>

AVV-atrioventricular valve, FAC-fractional area change.

Bold data -  $p < 0.05$ .

\*\*  $p \leq 0.01$ .



**Fig. 2.** Correlation analysis of atrioventricular valve systolic to diastolic duration ratio and ventricular end-diastolic pressure. Of all the echocardiographic parameters assessed, atrioventricular valve systolic to diastolic duration ratio had the strongest correlation with ventricular end-diastolic pressure. AVV-atrioventricular valve.

E/A, lateral E/E' and isovolumic relaxation time [12]. The inconsistencies between these studies and our contrasting findings probably reflect highly heterogeneous single ventricle anatomy and differing loading conditions. Furthermore, our purely Fontan cohort, was markedly older. Altered cardiac position, rudimentary ventricles and ventricular septal defects complicate standard tissue Doppler measurements in many patients. It is unclear how to interpret disparate measures from both free walls and/or the septum. It is also possible that by adulthood an important impairment in relaxation has developed late after Fontan palliation. In our group, degree of aortic regurgitation correlated significantly with VEDP even though only 2 were mild and 2 were moderate, emphasising the importance of maintaining a competent aortic valve. Interestingly, we did not observe a similar relationship between AVV regurgitation and VEDP. It is possible that end-diastolic pressure rises later in the setting of AVV regurgitation but since only a small proportion of our cohort had moderate/severe regurgitation we were unable to explore this further.

AVV S/D reflects global ventricular function and can be measured simply and consistently, using continuous-wave Doppler assessment of the AV valve [13]. It reflects global cardiac function with pathological increase documented in both dilated and restrictive cardiomyopathy and hypoplastic left heart syndrome [13,14]. Only one study has investigated the relationship between catheter-derived haemodynamic data and AVV S/D ratio in the setting of single-ventricle hearts. The investigators studied a group of children at various stages of Norwood palliation for hypoplastic left heart syndrome but did not find any correlation between measures of VEDP or cardiac output and AVV S/D; [15] these children were at various stages of volume unloading and catheterisation

studies were performed under general anaesthesia in contrast to our cohort. Tissue Doppler-derived AVV S/D has been investigated in a paediatric population with hypoplastic left heart syndrome and found not to correlate with MRI-derived measures of cardiac systolic function [16]. It is possible that tissue Doppler derived indices that reflect motion in one wall are less useful due to dyssynchronous contraction compared with continuous-wave Doppler derived measurement but this has not been investigated.

We previously reported that AVV S/D is an independent predictor of survival in Fontan adults and that a ratio >1.1 is an especially poor prognostic marker [3]. In this current investigation, peak exercise capacity was also much poorer in those with AVV S/D > 1.1 (47% vs. 67%). Our findings suggest that raised ventricular end-diastolic pressure probably, at least in part, underlies these findings and that AVV S/D ≥ 1.1 is a strong predictor of VEDP ≥ 10 mmHg.

## 5. Limitations

We were limited by a small sample size that would have affected our power to detect less important relationships between echocardiographic measures and VEDP and prevented ROC analysis of AVV S/D for detection of VEDP. Cardiac catheterisation, whilst not performed under general anaesthesia, was performed in a fasted state, unlike echocardiography and thus loading conditions may have differed. Echocardiography was not performed simultaneously with cardiac catheterisation or exercise testing which may have confounded our results however the highly significant relationship with AVV S/D are supported by our previously reported outcome data and suggest these findings have important clinical implications. Due to the sample size and heterogeneity of the univentricular population we were not adequately powered to investigate whether there are differences between Fontan subgroups such as dominant right ventricle or those with single vs. two atrioventricular valves.

## 6. Conclusions

Transthoracic echocardiographic measures reflect VEDP in adults with a Fontan circulation. AVV S/D duration ratio is a simple parameter, not currently assessed in standard practice, that can be used to identify elevated VEDP in the setting of complex Fontan hearts.

## Acknowledgements

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## Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

## Appendix A

### Appendix Table 1

Echocardiographic data.

Echocardiographic measure	VEDP < 10mmHG (n = 11)	VEDP ≥ 10 mmHg (n = 4)	All (n = 15)	p value
Ventricular systolic impairment (qualitative grade)	9 none/mild 2 mod/severe	4 none/mild 0 mod/severe	13 none/mild 2 mod/severe	0.4
FAC (%)	35 ± 4	34 ± 3	34 ± 4	0.7
AVV S/D	0.9 ± 0.2	1.3 ± 0.3	1.0 ± 0.3	<b>0.002*</b>
E (cm/s)	69 ± 19	56 ± 36	765 ± 24	0.4
E/A	1.5 ± 0.7	1.2 ± 0.9	1.4 ± 0.7	0.5
Deceleration time (msec)	168 ± 42	226 ± 110	185 ± 767	0.2
E' (cm/sec)	9 ± 5	9 ± 3	10 ± 4	0.9
E/E'	9 ± 5	7 ± 5	8 ± 4	0.3
Pulm vein S/D	0.7 ± 0.2	1.3 ± 0.8	1.0 ± 0.6	0.2
Pulm vein A vel (cm/sec)	33 ± 21	23 ± 3	28 ± 16	0.4
Pulm vein A duration (msec)	130 ± 20	113 ± 26	120 ± 20	0.3

Appendix Table 1 (continued)

Echocardiographic measure	VEDP < 10mmHg (n = 11)	VEDP ≥ 10 mmHg (n = 4)	All (n = 15)	p value
AVV inflow A-pulm vein A (msec)	−24 ± 36	11 ± 66	−7 ± 54	0.2
Isovolumic relaxation time (msec)	90 ± 30	92 ± 30	90 ± 30	1.0
Tei Index	0.75 ± 0.14	0.72 ± 0.08	0.74 ± 0.12	0.8
AVV regurgitation	10 none/mild 1 mod/severe	2 none/mild 2 mod/severe	12 none/mild 3 mod/severe	0.5
Aortic regurgitation	11 none/mild 0 mod/severe	2 none/mild 2 mod/severe	13 none/mild 2 mod/severe	<b>0.002*</b>

AVV-atrioventricular valve, FAC-fractional area change.

Bold -  $p < 0.05$ , bold \* -  $p$  less than or equal to 0.01, bold \*\*  $p$  less than or equal to 0.001, bold \*\*\*  $p$  less than or equal to 0.0001.

## References

- [1] C.A. Warnes, R.G. Williams, T.M. Bashore, et al., ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease). Developed in collaboration with the American Society of Echocardiography, Heart Rhythm Society, International Society for Adult Congenital Heart Disease, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons, *J. Am. Coll. Cardiol.* 52 (2008) e143–263.
- [2] M.G. Earing, F. Cetta, D.J. Driscoll, et al., Long-term results of the Fontan operation for double-inlet left ventricle, *Am. J. Cardiol.* 96 (2005) 291–298.
- [3] R. Cordina, K. von Klemperer, A. Kempny, et al., Echocardiographic predictors of mortality in adults with a Fontan circulation, *J. Am. Coll. Cardiol. Img.* 10 (2017) 212–213.
- [4] L.G. Rudski, W.W. Lai, J. Afilalo, et al., Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography, *J. Am. Soc. Echocardiogr.* 23 (2010) 685–713 (quiz 86–8).
- [5] R.M. Lang, L.P. Badano, V. Mor-Avi, et al., Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging, *J. Am. Soc. Echocardiogr.* 28 (2015) 1–39 (e14).
- [6] S.F. Nagueh, C.P. Appleton, T.C. Gillebert, et al., Recommendations for the evaluation of left ventricular diastolic function by echocardiography, *J. Am. Soc. Echocardiogr.* 22 (2009) 107–133.
- [7] W.A. Zoghbi, M. Enriquez-Sarano, E. Foster, et al., Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography, *J. Am. Soc. Echocardiogr.* 16 (2003) 777–802.
- [8] D.D. Mair, D.J. Hagler, F.J. Puga, H.V. Schaff, G.K. Danielson, Fontan operation in 176 patients with tricuspid atresia. Results and a proposed new index for patient selection, *Circulation* 82 (1990) IV164–9.
- [9] S.C. Menon, R. Gray, L.Y. Tani, Evaluation of ventricular filling pressures and ventricular function by Doppler echocardiography in patients with functional single ventricle: correlation with simultaneous cardiac catheterization, *J. Am. Soc. Echocardiogr.* 24 (2011) 1220–1225.
- [10] G.P. Diller, A. Giardini, K. Dimopoulos, et al., Predictors of morbidity and mortality in contemporary Fontan patients: results from a multicenter study including cardiopulmonary exercise testing in 321 patients, *Eur. Heart J.* 31 (2010) 3073–3083.
- [11] N. Husain, J. Gokhale, L. Nicholson, J.P. Cheatham, R.J. Holzer, C.L. Cua, Noninvasive estimation of ventricular filling pressures in patients with single right ventricles, *J. Am. Soc. Echocardiogr.* 26 (2013) 1330–1336.
- [12] S.M. Chowdhury, R.J. Butts, J. Buckley, et al., Comparison of pressure-volume loop and echocardiographic measures of diastolic function in patients with a single-ventricle physiology, *Pediatr. Cardiol.* 35 (2014) 998–1006.
- [13] M.K. Friedberg, N.H. Silverman, Cardiac ventricular diastolic and systolic duration in children with heart failure secondary to idiopathic dilated cardiomyopathy, *Am. J. Cardiol.* 97 (2006) 101–105.
- [14] M.K. Friedberg, N.H. Silverman, The systolic to diastolic duration ratio in children with heart failure secondary to restrictive cardiomyopathy, *J. Am. Soc. Echocardiogr.* 19 (2006) 1326–1331.
- [15] M.K. Friedberg, N.H. Silverman, The systolic to diastolic duration ratio in children with hypoplastic left heart syndrome: a novel Doppler index of right ventricular function, *J. Am. Soc. Echocardiogr.* 20 (2007) 749–755.
- [16] H.R. Bellsham-Revell, S.M. Tibby, A.J. Bell, et al., Tissue Doppler time intervals and derived indices in hypoplastic left heart syndrome, *Eur. Heart J. Cardiovasc. Imaging* 13 (2012) 400–407.