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Influence of Ventricular Ectopic Beats in Patients with Congenital Heart Disease

Liska J Hoppe[2], Franziska Markel[1*], Anna Michaelis[1], Michael Weidenbach[1], Ingo Daehnert[1], Frank-Thomas Riede[1], Roman A Gebauer[1], Christian Paech[1]

[1]Department for Pediatric Cardiology, University of Leipzig-Heart Center, Strümpellstr. 39, 04289 Leipzig, Germany

[2]Department for Cardiology, University of Leipzig, Liebigstrasse 20, 04103 Leipzig, Germany

***Corresponding Author:** Department for Pediatric Cardiology, University of Leipzig-Heart Center, Strümpellstr. 39, 04289 Leipzig, Germany; **E-mail:** Franziska.wagner@helios-gesundheit.de

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Abstract

Context: Isolated Premature Ventricular Contractions (PVCs) in children are generally regarded as benign. Although PVCs have been shown to correlate with impaired cardiac function in adults, this correlation remains controversial in children, especially in those with Congenital Heart Disease (CHD).

Objective: Evaluation of the influence of PVCs on systemic ventricular function in CHD-patients during long-term follow-up.

Settings and Design: The database of our pediatric cardiology department was analyzed retrospectively.

Participants: 97 Patients were eligible. Key inclusion criteria: CHD, age 0-21 years, initial systemic ventricular Ejection Fraction (EF)>0.35, follow-up of at least 30 months, and one Holter-ECG every year. Patients were classified into two groups correlative to a daily PVC burden at the time of inclusion (Group A >1% PVCs/24 hours, Group B<1% PVCs/24 hours). Furthermore, we defined a subgroup A1 presenting a persistent PVC burden of >1% from the time of inclusion to the last follow-up.

Results: 97 consecutive patients were included with a median follow-up of 84 months (range 33-196). Especially patients of subgroup A1 showed a clinically significant decrease in systemic ventricular ejection fraction (P=0.03), whereas group A and B showed a preserved EF. The negative correlation between EF and frequency of PVCs/24 h became stronger over time.

Conclusions: The current data suggest a detrimental influence of a constant PVC burden >1% on systemic ventricular function in patients with CHD during long-term follow-up.

Keywords

Congenital heart disease, Ventricular ectopic beats, Cardiac function, Genetic susceptibility

Introduction

Isolated Premature Ventricular Contractions (PVCs) in children are generally regarded as a benign phenomenon in the majority of affected individuals. Yet, current data in adult, as well as some pediatric patient collectives, implicate a correlation of the PVC-burden and an impairment of left ventricular function. As a consequence, these studies emphasize the need for revisiting this patient population that was formerly regarded as being healthy. Although PVCs have been shown to correlate with impairment of cardiac function in adults, the correlation of LV systolic function with PVCs in children remains controversial [1]. Nevertheless, data seem to support a negative effect of frequent PVCs and ventricular tachycardia on left ventricular function in pediatric patients without Congenital Heart Disease (CHD) [2]. Fortunately, severe PVC-induced cardiomyopathy appears to be rare in children, even in those with very frequent PVCs. Yet, mild LV systolic dysfunction is observed in approximately 15% and is most strongly associated with a shorter PVC coupling interval [3]. To date, there are only limited data on patients with congenital heart disease.

Although frequent PVCs seem to appear in up to 20% of otherwise healthy newborns, they are reported to decrease during childhood and adolescence to about 2-6% [4]. In contrast, up to 60% of patients with congenital heart disease show ventricular arrhythmias with frequent ventricular ectopy [5]. Baman et al. suggested a PVC burden of >24% as associated with PVC-induced cardiomyopathy in patients without congenital heart disease [6]. As patients with CHD are significantly more prone to ventricular dysfunction than healthy peers, the influence of PVCs on systemic ventricular function might be even more important in this patient collective.

This study aimed to evaluate the influence of PVCs on the systemic ventricular function of patients with congenital heart disease during long-term follow-up.

Subjects and Methods

Patient's collection

The patient database of our Department for pediatric cardiology was analyzed retrospectively to include patients that were treated between 1st January 1994 and 31st December 2017. Key inclusion criteria were: congenital heart disease, age 0-21 years at the time of inclusion, initial systemic ventricular Ejection Fraction (EF) of >0.35, follow-up of at least 30 months, at least one Holter-ECG every year, and not less than three Holter-ECGs in total. Key exclusion criteria were: EF2°, genetic disorders such as trisomy 21, CATCH22, Noonan, Goldenhaar and previous electrophysiology study with ablation of PVCs or a ventricular tachycardia. Demographic and echocardiographic data were obtained from all patients at the time of each Holter monitoring.

The patients within the diagnosis groups tetralogy of Fallot, transposition of the great arteries, and stenosis of the aortic valve all underwent a successful corrective heart surgery before enclosure in this study. The patients in the diagnosis groups DORV, univentricular, and others experienced the final stage of a palliative operation before being enrolled in this study (Table 1).

Ethical approval

All procedures performed involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Patient and public involvement

It was possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

ECG analysis

All available ECGs have been analyzed independently by two pediatric cardiologists. The PVC burden is presented as the ratio of total PVCs to the total number of ventricular (QRS) complexes per 24 hours in Holter-ECG. Patients were classified into two groups by the daily PVC burden at the time of inclusion (Group A>1% PVCs/24 hours, Group B<1% PVCs/24 hours). To obtain a relevant count of patients in every group, we chose the freely defined amount of 1% PVCs/24 hours as cut off. Furthermore, we defined a subgroup A1, which included patients with a lasting PVC burden >1% in every follow-up from the time of inclusion until the last follow-up.

Systemic ventricular function

Two-dimensional transthoracic echocardiography was performed in our in-house echocardiographic laboratory by three pediatric cardiologists specialized in echocardiography. Ventricular function of the systemic ventricle irrespective of left or right ventricular anatomy was calculated using the M-mode derived conventional teichholz formula (parasternal short and long-axis views) and the biplane Simpson method (apical 4-chamber and 2-chamber views) according to the recommendations of the American society of echocardiography [7]. Systemic ventricular function was defined as normal (EF>0.55), mildly impaired (EF 0.46-0.55), moderately impaired (EF 0.35-0.45) and severely impaired (EF<0.35).

For analysis, each patient`s initial EF was compared to his or her respective EF at the end of the follow-up period. This was done accordingly for all other parameters of cardiac function.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics Version 21. Descriptive statistics were used to summarize the data. Continuous variables are expressed as median (range) and categorical variables are given as the number of patients (percentage). Two-sample t-tests were used for comparison of continuous variables among the groups. Chi-square tests and exact Fisher tests were used for comparison of categorical variables. Change in EF and Systemic Ventricular End-Diastolic Diameter (SVEDD) over time was determined by Wilcoxon-Test. Two-tailed P<0.05 was considered statistically significant.

Results

Patient's characteristics

Patient's characteristics are displayed in Tables 1 and 2.

Demographic parameters			
Variable, n (%)	**Group A (n=20) (20.6%)**	**Group B (n=77) (79.4%)**	**P value**
Gender			0.46
female	10 (50%)	32 (40%)	
male	10 (50%)	46 (60%)	
Diagnosis group			
TGA[a]	3 (15%)	7 (9.1%)	0.43
TOF[b]/ DORV[c]	3 (15%)	22 (28.6%)	0.26
univentricular	6 (30%)	17 (22.1%)	0.56
Stenosis of aortic valve	1 (5%)	5 (6.5%)	1
other	7 (35%)	26 (33.8%)	1
Systemic ventricle			0.73
left	17 (85%)	67 (87%)	
right	3 (15%)	10 (13%)	
Age (years)	13 (5-20)	9 (0-21)	0.003
Weight (kg)	43 (14-76)	28 (5-82)	0.06
Antiarrhythmic medication	10 (50%)	22 (29%)	0.11
Systolic blood pressure (mmHg)	111 (96-151)	102 (78-151)	0.03
Diastolic blood pressure (mmHg)	56.5 (37-83)	57 (41-93)	0.87
Syncope	1 (5%)	3 (3.9%)	1
Exercise capacity			0.52
normal	14 (73.7%)	62 (81.6%)	
impaired	4 (21.1%)	14 (18.4%)	
Strongly impaired	1 (5.3%)	0 (0%)	
SCD[d], CPR[e], death	0 (0%)	0 (0%)	
Echocardiographic parameters			

EF[f]	0.65 (0.4-0.9)	0.65 (0.41-0.9)	0.62
Systolic function			0.64
Normal	18 (90%)	70 (93.3%)	
Mildly impaired	0	4 (5.3%)	
Moderatly impaired	2 (10%)	1 (1.3%)	
SVEDD[g] (mm)	43 (33-50)	40 (24-62)	0.56
TR[h]			0.75
none	5 (33.3%)	17 (26.2%)	
1st degree	7 (46.7%)	33 (50.8%)	
2nd degree	3 (20%)	15 (23.1%)	
PR[i]			1
none	4 (33.3%)	18 (36.7%)	
1st degree	7 (58.3%)	13 (26.5%)	
2nd degree	1 (8.3%)	18 (36.7%)	
MR[j]			0.76
none	11 (73.3%)	31 (67.4%)	
1st degree	3 (20%)	11 (23.9%)	
2nd degree	1 (6.7%)	4 (8.7%)	
AR[k]			0.76
none	6 (46.2%)	26 (55.3%)	
1st degree	4 (30.8%)	17 (35.2%)	
2nd degree	3 (23.1%)	4 (8.5%)	
ECG parameters			
Frequency PVC[l]/24 h	3 (1.1-44.9)	0 (0-0.7)	0
Morphology types			
none	0	22 (38%)	
monomorphic	15 (79%)	24 (41%)	0.001
polymorphic	4 (21%)	12 (21%)	0.74
QRS duration in PVC (ms)	120 (100-160)	140 (100-160)	0.07
QRS duration in SR[m] (ms)	90 (60-160)	100 (50-160)	0.5
BBB[n] in SR			0.21
none	13 (65%)	33 (45.8%)	

LBBB[o]	1 (5%)	2 (2.8%)	
RBBB[p]	6 (30%)	37 (51.4%)	
Coupling interval (ms)	480 (320-640)	430 (200-720)	0.21
Absolute number of PVC	3356 (790-51521)	7 (0-1026)	0
Mean heart rate (bpm)	75 (56-110)	82 (45-124)	0.29
Z-Score heart rate	0 (-2 - 1)	0 (-2 - 2)	0.8
Associated arrhythmia	7 (35%)	34 (44%)	0.61
SVT[q]	0 (0-278)	0 (0-429)	0.82
Ventricular tachycardia	3 (15%)	2 (2.6%)	0.06
Abbreviations: a: TGA=Transposition of the Great Arteries; b:TOF=Tetralogy Of Fallot; c:DORV=Double Outlet Right Ventricle; d:SCD=Sudden Cardiac Death; e:CPR=Cardiopulmonary resuscitation; f:EF=Ejection Fraction; g:SVEDD=Systemic Ventricular End-Diastolic Diameter; h:TR=Tricuspid (valve) Regurgitation; i:PR=Pulmonal (valve) Regurgitation; j:MR=Mitral (valve) Regurgitation; k:AR=Aortic (valve) Regurgitation; l:PVC=Premature Ventricular Contraction; m:SR=Sinus Rhythm; n:BBB=Bundle Branch Block; o:LBBB=Left Bundle Branch Block; p:RBBB=Right Bundle Branch Block; q:SVT=Supraventricular tachycardia.			

Table 1: Baseline patient characteristic group A vs. B.

Demographic parameters			
Variable, n (%)	**Subgroup A1 (n=7)**	**Group B (n=77)**	**P value**
Gender			0.44
female	4 (57.1%)	32 (40%)	
male	3 (42.9%)	46 (60%)	
Diagnosis group			
TGA[a]	2 (28.6%)	7 (9.1%)	0.16
TOF[b]/ DORV[c]	1 (14.3%)	22 (28.6%)	0.67
univentricular	1 (14.3%)	17 (22.1%)	1.00
Stenosis of aortic valve	0 (0%)	5 (6.5%)	1.00
other	3 (42.9%)	26 (33.8%)	0.69
Systemic ventricle			0.26
left	5 (71.4%)	67 (87%)	
right	2 (28.6%)	10 (13%)	
Age (years)	12 (8-20)	9 (0-21)	0.019
Weight (kg)	54 (33-70)	28 (5-82)	0.08

Antiarrhythmic medication	3 (42.9%)	22 (29%)	0.42
Systolic blood pressure (mmHg)	118.5 (100-149)	102 (78-151)	0.03
Diastolic blood pressure (mmHg)	67 (47-83)	57 (41-93)	0.22
Syncope	1 (14.3%)	3 (3.9%)	0.30
Exercise capacity			1.00
normal	5 (71.4%)	62 (81.6%)	
impaired	1 (14.3%)	14 (18.4%)	
Strongly impaired	0 (0%)	0 (0%)	
SCD[d], CPR[e], death	0 (0%)	0 (0%)	
Echocardiographic parameters			
EF[f]	0.66 (0.4-0.79)	0.65 (0.41-0.9)	0.93
Systolic function			0.43
Normal	6 (85.7%)	70 (93.3%)	
Mildly impaired	0 (0%)	4 (5.3%)	
Moderatly impaired	1 (14.3%)	1 (1.3%)	
SVEDD[g] (mm)	44 (33-49)	40 (24-62)	0.37
TR[h]			1.00
none	2 (28.6%)	17 (26.2%)	
1st degree	4 (57.1%)	33 (50.8%)	
2nd degree	1 (14.3%)	15 (23.1%)	
PR[i]			0.65
none	1 (14.3%)	18 (36.7%)	
1st degree	3 (42.9%)	13 (26.5%)	
2nd degree	1 (14.3%)	18 (36.7%)	
MR[i]			1.00
none	4 (57.1%)	31 (67.4%)	
1st degree	1 (14.3%)	11 (23.9%)	
2nd degree	0 (0%)	4 (8.7%)	
AR[k]			0.65
none	2 (28.6%)	26 (55.3%)	
1st degree	3 (42.9%)	17 (35.2%)	

2nd degree	0 (0%)	4 (8.5%)	
ECG parameters			
Frequency PVC[l]/24 h	1.6 (1.1-44.9)	0 (0-0.7)	0
Morphology types			
none	0 (0%)	22 (38%)	
monomorphic	4 (57.1%)	24 (41%)	
polymorphic	3 (42.9%)	12 (21%)	
QRS duration in PVC (ms)	140 (120-160)	140 (100-160)	0.40
QRS duration in SRm (ms)	80 (80-140)	100 (50-160)	0.18
BBB[n] in SR			0.06
none	6 (85.7%)	33 (45.8%)	
LBBB[o]	0 (0%)	2 (2.8%)	
RBBB[p]	1 (14.3%)	37 (51.4%)	
Coupling interval (ms)	450 (360-520)	430 (200-720)	0.82
Absolute number of PVC	2075 (790-51521)	7 (0-1026)	0.000
Mean heart rate (bpm)	79 (64-96)	82 (45-124)	0.57
Z-Score heart rate	-1 (-2-0)	0 (-2 - 2)	0.84
Associated arrhythmia	3 (42.9%)	34 (44%)	1.00
SVTq	0 (0-278)	0 (0-429)	0.39
Ventricular tachycardia	2 (28.6%)	2 (2.6%)	0.03

Abbreviations: a: TGA=Transposition of the Great Arteries; b:TOF=Tetralogy Of Fallot; c:DORV=Double Outlet Right Ventricle; d:SCD=Sudden Cardiac Death; e:CPR=Cardiopulmonary resuscitation; f:EF=Ejection Fraction; g:SVEDD=Systemic Ventricular End-Diastolic Diameter; h:TR=Tricuspid (valve) Regurgitation; i:PR=Pulmonal (valve) Regurgitation; j:MR=Mitral (valve) Regurgitation; k:AR=Aortic (valve) Regurgitation; l:PVC=Premature Ventricular Contraction; m:SR=Sinus Rhythm; n:BBB=Bundle Branch Block; o:LBBB=Left Bundle Branch Block; p:RBBB=Right Bundle Branch Block; q:SVT=Supraventricular tachycardia.

Table 2: Baseline Patient characteristic group B vs. subgroup A1.

Inclusion criteria were met by 128 patients with 22 excluded for 3° valve regurgitation, one patient for EF<0.35, and eight for a follow-up <30 months. The remaining 97 patients were included in the analysis. The median follow-up was 84 months (range 33-196). There were 77 patients in group B, 20 patients in group A of whom only 7 (35%) belonged to subgroup A1, i.e. patients with persistent PVC burden of more than 1%. Patients of group A were older (13 vs. 9 years, p=0.003), presented higher systolic blood pressure (111 vs. 102 mmHg, p=0.03), a higher

absolute number of PVCs (3356 in group A/ 2075 in subgroup A1 vs. 7 in group B, p=0.00) and respectively a higher frequency of PVCs/24 h (3% in group A/ 1.6% in subgroup A1 vs. 0% in group B, p=0.00) than those of group B. Ventricular tachycardia appeared more often in group A (15% vs. 2.6%, p=0.06) especially in subgroup A1 (28.6 vs. 2.6%, p=0.03) compared with group B. Also, patients in group A showed a tendency to a shorter QRS duration in PVC compared to group B (120 vs. 140 ms, p=0.07), although not statistically significant. We found no significant differences in baseline echocardiographic parameters in both groups at the time of inclusion.

50% of patients in group A received antiarrhythmic medication, 43% in subgroup A1 and 29% in group B.

Systemic ventricular function and systemic ventricular diameter

Table 3 shows the influence of PVCs on systemic ventricular function and systemic ventricular diameter in long-term follow-up. Presuming a deterioration of at least 5% causes a clinically relevant impairment of systemic ventricular function, only subgroup A1 showed a clinically and statistically significant decrease in EF at the last follow-up (EF initial 0.66 to EF follow-up 0.56, p=0.031). Patients in group B showed only a statistically but not clinically significant decrease from 0.67 in the beginning to 0.64 over time (p=0.034).

	EF[a] initial	EF[a] follow-up	P value	SVEDD[b] initial	SVEDD[b] follow-up	P value
Group A	0.66	0.62	0.3	42	46	0.003
Group B	0.67	0.64	0.034	40	48	0.000
Subgroup A 1	0.66	0.56	0.031	43	46	0.250
Abbreviation: a: EF=Ejection Fraction; b:SVEDD=Systemic Ventricular End-Diastolic Diameter						

Table 3: Development of EF and LVEDD from start to follow-up.

Influence of growth and aging on parameters of cardiac function

Data showed a significant positive correlation between SVEDD and age (correlation coefficient 0.481, P<0.001) and a significant increase of the SVEDD over time in both groups (Table 3). In the subgroup A1 the initial SVEDD of 43 mm did increase only slightly to a SVEDD of 46 mm in the last follow-up (p=0.25).

Influence of systemic ventricular anatomy on parameters of cardiac function

A negative correlation between EF and the presence of univentricular anatomy could be seen (correlation coefficient -0.233, p=0.023). Patients with univentricular anatomy were equally distributed between the groups. Yet, there was a difference in right or left systemic ventricular anatomy regarding initial EF and follow-up EF (Table 4). Patients with PVCs and right systemic ventricular anatomy had an overall slightly reduced initial EF that deteriorated further during follow-up.

	Right ventricular systemic ventricle		Left ventricular systemic ventricle	
	EF[a] initial	EF[a] follow-up	EF[a] initial	EF[a] follow-up
All patients	0.64	0.57	0.67	0.65
Group B	0.66	0.61	0.67	0.65
Group A	0.56	0.47	0.65	0.67
Group A 1	0.52	0.45	0.72	0.60
Abbreviation: a: EF=Ejection Fraction				

Table 4: Comparison of EF development with regard to systemic ventricular anatomy.

Co-founders for impairment of the EF

No correlation could be shown for EF and age (p=0.577), EF, and QRS in PVC (p=0.67), or EF and coupling interval (p=0.6). Importantly, although statistically non-significant, the negative correlation between EF and frequency of PVC/24 h (initial: correlation coefficient -0.041, p=0.697) became stronger over time (follow-up: correlation coefficient -0.104, p=0.312).

Discussion

This study evaluated the influence of PVCs on systemic ventricular function during long-term follow-up in patients with congenital heart disease. First, in 24 analyzed years, we found seven patients with known congenital heart defects and documented frequent PVCs persistent over several years of follow-up. In contrast to our expectation of higher vulnerability to PVCs in this patient population, it appears to be a rather uncommon phenomenon. Nevertheless, this study suggests that patients with congenital heart disease and constantly frequent PVCs seem to have a more marked deterioration of systemic ventricular function over time in comparison to those with low PVC burden.

This finding goes along with the findings by Bertels et al. [2], who reported an impairment of left ventricular function in otherwise healthy pediatric patients with a structurally normal heart and a PVC burden of >5%. When comparing data presented in the current study to studies in other pediatric collectives, it has to be kept in mind that most studies reporting a negative effect of PVCs on LV function are cross-sectional retrospective studies.

Detrimental factors other than the PVC burden remain unknown, as most of those patients were not examined for other factors like myocarditis, ARVC, or coronary artery disease. Sometimes patients underwent EP study with ablation of the ventricular ectopy, resulting in improvement of LV function; this makes the PVC very likely to represent a negative factor for LV function. In comparison, the data of this study add some information on the long-term effect of PVCs on the ventricular function in a collective of relatively healthy CHD patients and after exclusion of other detrimental factors like reoperation or reintervention. Statistical analysis did show that a constantly high (>1%) PVC burden might be a significant factor for the development of a systemic ventricular impairment in patients with CHD.

Noticeably, our patient collective presents a comparatively low number of PVCs per 24 hours. Only two patients offered a fraction of PVCs over 10% per day at the time of inclusion: one with 45% PVCs per 24 hours and the other with 12%. They belonged to subgroup A1 with decreased but persistent PVCs >1% in the follow-up. Both of them had a left ventricular systemic ventricle and presented a normal EF at the beginning and in the follow-up.

This underlines the assumption that the influence of a longer period of a PVC burden >1% might lead to PVC-induced dyssynchrony. This is especially supported by reports from experimental studies showing that dyssynchronous ventricular activation leads to mechanical dyssynchrony, as well as changes on the cellular level, even with a change of the genetic expression pattern in affected cells over time [8,9]. Additionally Agarwal et al. state that there are several pathways that can link premature ventricular complexes with a compromised heart function. This also includes the above mentioned dyssynchrony leading to adverse remodeling in ventricular dimensions and function. Changes of ventricular filling, contractility and baroreflex activity can result in an altered heart rate, blood pressure and stroke volume [10]. Despite some mechanisms outlined above, the causes of VPC-induced cardiomyopathy are still poorly understood [11].

When looking specifically at pediatric collectives, our data could not confirm the reported influence of the coupling interval or QRS duration of the PVCs. As the influence of coupling interval and PVC duration has been reported in several pediatric collectives [2,12] with relatively homogenous patients with a structurally normal heart, it might be speculated that similar effects could not be demonstrated in our collective due to the variety of underlying diseases.

As there are patients with biventricular, as well as single left or single right ventricular physiology included in this study, the same type of PVC morphology might be more detrimental in some patients than in others.

Our data seem to support a detrimental effect of PVCs on systemic ventricular function in some individuals. The current study could only identify a lasting PVC burden of >1% over time as a detrimental factor. This study could not identify other single factors like coupling interval, or PVC duration as crucial factors in the genesis of ventricular impairment. Following reports of the genesis of pacing-induced cardiomyopathy, the authors assume that there is rather an individual tendency to the development of mechanical dyssynchrony [13-15]. Similar to this phenomenon, only patients with an individual genetically determined tendency will develop manifest mechanical dyssynchrony as a result of the PVC-caused electrical dyssynchrony. In contrast, in most patients without this individual tendency, PVCs will result only in electrical dyssynchrony; yet, no cellular changes and therefore no lasting mechanical dyssynchrony will develop.

As shown in the presented data, it seems to matter if the systemic ventricle is an anatomically right or left ventricle. This corroborates various studies describing a higher incidence of ventricular dysfunction in patients with systemic right ventricle irrespective of PVCs [16-19]. Therefore, even if LVEF is worsening with the increased and prolonged appearance of PVCs, as has been seen in our small collective, in light of the fact that patients with systemic RV seem to start from an overall poorer EF, PVCs may represent an additional risk factor in these patients.

As shown in Table 3, there is a significant increase in Systemic Ventricular End-Diastolic Diameter (SVEDD) in groups A and B. We interpret this to be caused by the normal aging and growth of children in the long-term follow-up. Interestingly, the increase of subgroup A1 is not statistically significant. In comparison to group A, the individual patients of subgroup A1 are older (8-20 years vs. 5-20 years) and heavier (54 kg vs. 43 kg), thus more grown-up and with a lower potential for further growth during follow-up. Furthermore, the fraction of univentricular hearts is higher in group A (30% vs. 14.3% in A1).

After all, the authors have to mention that calculating systemic ventricular function by two-dimensional transthoracic echocardiography contains the risk of inaccuracies and errors. Especially if it is used for right ventricular function or univentricular anatomy. Nevertheless, the method is still a common clinical practice and is regarded as suitable enough for routine follow-up. Although, to date, there are more sophisticated methods like three-dimensional echocardiography, several authors, like Nascimento et al., stated that even visual estimation of ventricular function in two-dimensional echocardiography applies to most patients with congenital heart disease and yields results that correlate well with those determined from three-dimensional echocardiography [20].

Finally, as the presented data are retrospective in a heterogeneous population, the reported findings do not allow a generalization to other collectives. Further studies, especially prospective data, are needed to further illuminate this topic.

Conclusion

The current data suggest the detrimental influence of a constant PVC burden >1% on systemic ventricular function in patients with CHD during long-term follow-up. Nevertheless, the individual susceptibility of each patient might be a relevant issue.

Strengths and Limitations of this Study

- The current data suggest a detrimental influence of a constant PVC burden >1% on systemic ventricular function in patients with CHD during long-term follow-up
- The individual, genetically determined susceptibility of each patient might be relevant
- Patients with right systemic ventricular anatomy presented a poorer EF and a more pronounced deterioration during follow-up
- Due to the small number of patients further studies have to be done

Limitations

As a consequence of the retrospective nature of this study, there are some limitations such as incomplete data in medical records. Echocardiography is the common technique to calculate systemic ventricular ejection fraction. Yet, the method is limited by several especially interobserver variability as well as difficulties to correctly evaluate systemic right ventricular function. Although MRI enables a more precise calculation, the method was only used in a few patients. The heterogeneous patient collective with various congenital heart defects and small sample sizes provide the possibility for overlooking other defining variables or risk factors not mentioned in the current study.

Ethical Approval Information

All procedures performed in human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments.

Conflict of Interests

None declared.

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Data Sharing Statement

The authors confirm that the data supporting the findings of this study are available within the article.

References

1. Guerrier K, Anderson JB, Czosek RJ, Mays AW, Statile C, et al. Usefulness of ventricular premature complexes in asymptomatic patients ≤ 21 years as predictors of poor left ventricular function. Am J Cardiol. 115(5): 652-5 (2015).

2. Bertels RA, Harteveld LM, Filippini LH, Clur SA, Blom NA. Left ventricular dysfunction is associated with frequent premature ventricular complexes and asymptomatic ventricular tachycardia in children. Europace. 19(4): 617-621 (2017).

3. Abadir S, Blanchet C, Fournier A, et al. Characteristics of premature ventricular contractions in healthy children and their impact on left ventricular function. Heart Rhythm. 13(11): 2144-2148 (2016).

4. Beaufort-Krol GC, Dijkstra SS, Bink-Boelkens MT. Natural history of ventricular premature contractions in children with a structurally normal heart: does origin matter? Europace. 10(8): 998-1003 (2008).

5. Alexander ME, Berul CI. Ventricular arrhythmias: When to worry. Pediatr Cardiol. 21(6): 532-41 (2000).

6. Baman TS, Lange DC, Ilg KJ, Gupta SK, Liu TY, et al. Relationship between burden of premature ventricular complexes and left ventricular function. Heart Rhythm 7(7): 865-9 (2010).

7. Lopez L, Colan SD, Frommelt PC, Ensing GJ, Kendall K, et al. Recommendations for quantification methods during the performance of a pediatric echocardiogram: A report from the Pediatric Measurements Writing Group of the American Society of Echocardiography Pediatric and Congenital Heart Disease Council. J Am Soc Echocardiogr. 23(5): 465-95 (2010).

8. Barth AS, Aiba T, Halperin V, DiSilvestre D, Chakir K, et al. Cardiac resynchronization therapy corrects dyssynchrony-induced regional gene expression changes on a genomic level. Circ Cardiovasc Genet. 2(4): 371-8 (2009).

9. Spragg DD, Kass DA. Pathobiology of left ventricular dyssynchrony and resynchronization. Prog Cardiovasc Dis. 49(1): 26-41 (2006).

10. Agarwal SK, Simpson RJ, Rautaharju P, Alonso A, Shahar E, et al. Relationship of Ventricular Premature Complexes to Heart Failure (From the Atherosclerosis Risk in Communities [ARIC] Study). Am J Cardiol. 109(1): 105-109 (2012).

11. Sharma N, Cortez D, Jason R. Imundo. High burden of premature ventricular contractions in structurally normal hearts: To worry or not in pediatric patients? Ann Noninvasive Electrocardiol. 24(6): e12663 (2019).

12. Martin AP, Skinner JR. Ventricular extrasystoles and ventricular dysfunction: Too close for comfort? Heart Rhythm. 13(11): 2149-2150 (2016).

13. Kass DA. An epidemic of dyssynchrony: But what does it mean? J Am Coll Cardiol. 51(1): 12-7 (2008).

14. Helm RH, Leclercq C, Faris OP, Ozturk C, McVeigh E, et al. Cardiac dyssynchrony analysis using circumferential vs. longitudinal strain: Implications for assessing cardiac resynchronization. Circulation. 111(21): 2760-7 (2005).

15. Vardas PE, Auricchio A, Blanc JJ, et al. European Society of C and European Heart Rhythm A. Guidelines for cardiac pacing and cardiac resynchronization therapy: The Task Force for Cardiac Pacing and Cardiac Resynchronization Therapy of the European Society of Cardiology. Developed in collaboration with the European Heart Rhythm Association. Eur Heart J. 28: 2256-95 (2007).

16. Zaragoza-Macias E, Zaidi AN, Dendukuri N, et al. Medical therapy for systemic right ventricles: A systematic review (Part 1) for the 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. (2018).

17. Piran S, Veldtman G, Siu S, Webb GD, Liu PP. Heart failure and ventricular dysfunction in patients with single or systemic right ventricles. Circulation. 105(10): 1189-94 (2002).

18. Brida M, Diller GP, Gatzoulis MA. Systemic right ventricle in adults with congenital heart disease: Anatomic and phenotypic spectrum and current approach to management. Circulation. 137(5): 508-518 (2018).

19. Filippov AA, Del Nido PJ, Vasilyev NV. Management of systemic right ventricular failure in patients with congenitally corrected transposition of the great arteries. Circulation. 134(17): 1293-1302 (2016).

20. Nascimento R, Pereira D, Freitas A, et al. Comparison of left ventricular ejection fraction in congenital heart disease by visual vs. algorithmic determination. Am J Cardiol. 80(10): 1331-5 (1997).