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Original Article

Prevalence of Cardiac Dysfunction Among Adult Patients With Congenital Heart Disease: A Single-Center Investigation

Zahra Khajali[1], MD; Majid Maleki[1], MD; Ahmad Amin[1], MD; Sedigheh Saedi[1], MD; Maedeh Arabian[1], PhD; Mahmood Moosazadeh[2], PhD; Nasim Naderi[1], MD; Kambiz Mozzafari[1], MD; Hadi Khalaj[1], MS; Maryam Aliramezany[*1], MD

ABSTRACT

Background: In spite of achievements in the field of pediatric cardiology and surgical techniques, which have increased the chance of children with congenital heart diseases to reach adulthood, the inherent problems with the disease create a large number of complications for them in later life, including cardiac dysfunction. It is important to know the prevalence of cardiac dysfunction and its influential factor among adults with congenital heart diseases (CHDs); hence, the present study aimed to answer this question.

Methods: We measured the prevalence of cardiac dysfunction based on echocardiographic guidelines among ACHDS referred to Rajaie Cardiovascular, Medical, and Research Center between December 2017 and June 2018. Data analysis was performed using the χ^2 test and logistic regression through the SPSS software.

Results: Left and right ventricular dysfunction was 60.6% and 77.7%, respectively. Moreover, 58.7% of the patients were affected by both left and right ventricular dysfunction, while 20.9% had only one of the left or right ventricular dysfunction. Eighty-eight (20.4%) patients did not have dysfunction at the time of the study. The variables of moderately complex congenital heart disease, cyanosis, moderate pulmonary hypertension, the Eisenmenger syndrome, and the type of intervention were the predictors of left ventricular dysfunction.

Conclusions: The prevalence of cardiac dysfunction among our adult patients with CHDs was very high. Given that cardiac dysfunction starts at a young age in this group of patients in comparison with the general population, the quality of life of the former group is more seriously threatened. Our results identified factors that increased the likelihood of developing cardiac dysfunction. These factors should be considered when approaching patients with cardiac dysfunction. ***(Iranian Heart Journal 2019; 20(3): 12-19)***

KEYWORDS: Cardiac dysfunction, Heart failure, Adult congenital heart disease

[1] Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
[2] Health Science Research Center, Addiction Institute, Mazandaran University of Medical Sciences, Sari, Iran, IR Iran.

***Corresponding Author:** Maryam Aliramezany, MD; Rajaie Cardiovascular, Medical, and Research Center, Mellat Park, Vali-E-Asr Avenue, Tehran 1996911151 IR Iran.
Email: maliramezany@yahoo.com **Tel:** 09131961016

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Congenital heart diseases (CHDs) refer to all deformities of the heart that occur *in utero* and can exist at birth. [1] Early deaths occur in 2.3 per thousand infants usually as a consequence of severe hemodynamic lesions; thus, surgical or percutaneous approaches are considered prior to any irreversible complication in patients with CHDs. [2] Evidentially severe and moderately severe CHDs which require advanced cardiological care are found in 6 per thousand live births. [3] As a result of achievements in the field of pediatric cardiology, surgical techniques, and postoperative care, the number of adults with CHDs who are followed up in tertiary centers has increased progressively from 15% in the 1960s to more than 85% in the current era. [4] Nowadays, there are 1.2 million adult patients with CHDs in Europe and 1 million in North America. [5]

Based on the current evidence, the survival of infants suffering from CHDs has improved dramatically during recent decades as a consequence of surgical improvements for complex CHDs. Currently, adults with CHDs are living longer and the overall median age at death rose from 37 years in 2002 to over 57 years in 2007. [6] The mortality for patients with CHDs of great complexity has been changed considerably insofar as before 1995, the median age at death was 2 years compared with almost 25 years currently. [7]

Despite the improvements in the outcomes of repaired CHDs, it is still necessary to redo the intervention for late complications such as pacemaker installation to improve conduction disturbances, stenting to resolve stenosis, and defibrillation for ventricular arrhythmias. [8] On the other hand, in spite of remarkable successes in different interventions, many of them are not completely curative and patients often have recurrent and developed cardiac complications such as cardiac dysfunction. [9] Cardiac dysfunction was responsible for late deaths in a population study. It was also the main cause of deaths among patients with CHDs as it contributed to 26% of deaths in a national registry of more than 8000 adults with CHDs. [10-11] A previous study indicated that the mortality of adults with CHDs who exhibited heart failure symptoms was fivefold that of those who lacked heart failure symptoms. [12] Cardiac dysfunction is reported to affect adult patients with CHDs, but its prevalence and associating factors are not well described in the literature. We aimed to evaluate the prevalence of cardiac dysfunction among adult patients suffering from CHDs and to study its relating factors among patients referring to an Iranian adult CHD center.

METHODS

Data collection

The percentage of the individuals who have a specific disease at a certain time defines the prevalence of that disease. In this study, we measured the observed prevalence of cardiac dysfunction and pulmonary hypertension based on echocardiographic guidelines (Table 1 and Table 2) using a Philips EPIQ 7C device.

The study population consisted of all patients referred to the Adult CHD Clinic of Rajaie Cardiovascular, Medical, and Research Center between December 2017 and June 2018. All these patients were recruited in the study on a census basis. We classified the severity of CHDs to 3 groups of greatly complex, moderately complex, and simple according to the guidelines for the management of adults with CHDs by the American College of Cardiology (ACC)/American Heart Association (AHA). [9]

Data analysis

Data analysis was performed using descriptive and analytic statistics through the SPSS software, version 24. The variables were described in means, standard deviations, and percentages. The Mann–Whitney *U*-test was used to describe the mean age, and the χ^2 test was applied to compare the categorical

variables between the groups. To investigate the factors relating to heart failure, we adjusted the effects of the variables susceptible to be confounders using the logistic regression test. The predictive adequacy of the model was checked with the Nagelkerke R^2. The significance level was defined as a value lower than 0.05.

Table 1. Reference value and grading scale for the LVEF

LV function	LVEF%
Normal	≥55
Mildly reduced	45-55
Moderately reduced	30-44
Severely reduced	<30

LVEF, Left ventricular ejection fraction; LV, Left ventricle

Table 2. Classification of the pulmonary hypertension severity by echocardiography using RVSP

Severity of Pulmonary Hypertension	Estimated RVSP (mm Hg)
Normal	<35
Mild	35-45
Moderate	46-60
Severe Eisenmenger syndrome	>60

RVSP, Right ventricular systolic pressure

RESULTS

In the present study, 431 patients with CHDs were evaluated. The mean, standard deviation, and average of age were 29.68, 10.52, and 28 years, respectively. The majority of the patients were male (56.8%). The frequency of greatly complex, moderately complex, and simple CHDs was 16.2%, 53.4%, and 30.4%, respectively. Moreover, 45.9% of the patients were cyanotic, for 80.7% of whom intervention was performed. The frequency of left ventricular (LV) and right ventricular (RV) dysfunction was 60.6% and 77.7%, respectively.

Furthermore, 58.7% of the patients were affected by both LV and RV dysfunction, while 20.9% had only either LV or RV dysfunction and 88 (20.4%) patients did not have dysfunction at the time of the study.

The frequency of LV and RV dysfunction in terms of normal, mild, moderate, and severe as well as the degree of pulmonary hypertension, the type of intervention, and the presence of surgical residue is summarized in Table 3.

The mean and average age of the patients with and without LV dysfunction and RV dysfunction was 30.2, 28.9, 30.3, and 27.3; the differences were statistically significant (P = 0.021).

The prevalence of LV dysfunction was more likely to be lower in the female group (61.6% vs 59.1%; P = 0.600), but the prevalence of RV dysfunction in the female group was greater than that in the male group (76.7% vs 79%; P = 0.570). Additionally, the frequency of LV and RV dysfunction among the cyanotic patients was greater than that in the non-cyanotic patients (81.8% vs 42.5%; P < 0.001; 98% vs 60.5; P < 0.001, respectively).

The comparisons between LV and RV dysfunction are illustrated in Table 4.

Table 5 indicates that the chance of LV dysfunction among the patients with moderately complex CHDs was 1.98 times that of the patients with simple CHDs (95% CI: 1.08 to 3.62) and in the cyanotic patients 3.16 times that of the non-cyanotic patients (95% CI: 1.78 to 5.59). In sum, the variables of moderately complex, cyanosis, moderate pulmonary hypertension, the Eisenmenger syndrome, and the type of intervention were the predictors of LV dysfunction. Additionally, according to the Nagelkerke test, the variables of age, gender, the type of CHD, interventions, pulmonary hypertension, the type of intervention, cyanosis, and having surgical residue predicted 34% of the LV dysfunction variations.

According to the logistic regression, the variables of age, the type of CHD, and low and moderate pulmonary hypertension were the predictors of RV dysfunction. The Nagelkerke test revealed that the variables of age, gender, the type of CHD, interventions, pulmonary hypertension, the type of intervention, cyanosis, and having surgical residue predicted 51% of the RV dysfunction variations.

Table 3. Characteristics of the study population

Variable		N	%
Gender	Male	245	56.8
	Female	186	43.2
Type of anomaly	Greatly complex	70	16.2
	Moderately complex	230	53.4
	Simple	131	30.4
cyanosis	Yes	198	45.9
	No	233	54.1
Intervention	Yes	348	80.7
	No	83	19.3
Left ventricular dysfunction	Mild	156	36.2
	Moderate	89	20.6
	Severe	16	3.7
	Normal	170	39.4
Right ventricular dysfunction	Mild	110	25.5
	Moderate	195	45.2
	Severe	30	7
	Normal	96	22.3
Pulmonary hypertension	Mild	49	11.4
	Moderate	18	4.2
	Severe	8	1.9
	Normal	322	74.7
	Eisenmenger syndrome	34	7.9
Type of intervention	Surgical cure	272	63.1
	Palliative surgery	43	10
	Intervention	32	7.4
	No	83	19.3
	Hybrid	1	0.2
Surgical residue	Yes	191	44.3
	No	157	36.4
	Not operated	83	19.3
Total		431	100

Table 4. Comparison of the clinical and demographic variables of the patients with cardiac dysfunction

Variable		N	Left Ventricular Dysfunction			Right Ventricular Dysfunction		
			Yes	No	*P* value	Yes	No	*P* value
Age (mean±SD)		431	30.2±9.9	28.9±11.3	0.021	30.3±10.3	27.3±10.8	0.002
Gender, n(%)	Male	245	151(61.6)	94(38.4)	0.600	188(76.7)	57(23.3)	0.570
	Female	186	110(59.1)	76(40.9)		147(79)	39(21)	
Type, n(%)	Greatly complex	70	59(84.3)	11(15.7)	<0.001	67(95.7)	3(4.3)	<0.001
	Moderately complex	230	156(67.8)	74(32.2)		201(87.4)	29(12.6)	
	Simple	131	46(35.1)	85(64.9)		67(51.1)	64(48.9)	
Cyanosis (%)	Yes	198	162(81.8)	36(18.2)	<0.001	194(98)	4(2)	<0.001
	No	233	99(42.5)	134(57.5)		141(60.5)	92(39.5)	
Intervention, n(%)	Yes	348	223(64.1)	125(35.9)	0.002	287(82.5)	61(17.5)	<0.001
	No	83	38(45.8)	45(54.2)		48(57.8)	35(42.2)	
Pulmonary hypertension, n(%)	Mild	49	28(57.1)	21(42.9)	<0.001	43(87.8)	6(12.2)	<0.001
	Moderate	18	15(83.3)	3(16.7)		17(94.4)	1(5.6)	
	Severe	8	6(75)	2(25)		8(100)	0	
	Normal	322	181(56.2)	141(43.8)		233(72.4)	89(27.6)	
	Eisenmenger syndrome	34	31(91.2)	3(8.8)		34(100)	0	
Type intervention, n(%)	Surgical cure	272	174(64)	98(36)	<0.001	227(83.5)	45(16.5)	<0.001
	Palliative surgery	43	39(90.7)	4(9.3)		40(93)	3(7)	
	Intervention	32	10(31.2)	22(68.8)		19(59.4)	13(40.6)	
	No	83	38(45.8)	45(54.2)		48(57.8)	35(42.2)	
	Hybrid	1	0	1(100)		1(100)	0	
Surgical residue, n(%)	Yes	191	129(67.5)	62(32.5)	0.003	169(88.5)	22(11.5)	<0.001
	No	157	94(59.9)	63(40.1)		118(75.2)	39(24.8)	
	Not operated	83	38(45.8)	45(54.2)		48(57.8)	35(42.2)	

Table 5. Related factors with LV dysfunction and RV dysfunction, multivariate logistic regression

Variable (ref.)		LV Dysfunction			RV Dysfunction		
		OR	95% CI	*P* value	OR	95% CI	*P* value
Age		1.02	1.00-1.04	0.054	1.04	1.01-1.07	0.003
Gender (female)		1.18	0.74-1.87	0.492	0.87	0.48-1.58	0.639
Type (simple)	Greatly complex	1.88	0.63-5.61	0.259	2.49	0.55-11.30	0.236
	Moderately complex	1.98	1.08-3.62	0.027	2.05	1.05-4.03	0.037
Cyanosis (No)		3.16	1.78-5.59	<0.001	16.20	5.15-50.96	<0.001
Intervention (No)		1.48	0.49-4.45	0.481	2.81	0.96-8.24	0.059
PH (Normal)	Mild	1.20	0.59-2.41	0.615	3.09	1.12-8.49	0.029
	Moderate	8.26	2.07-32.99	0.003	14.62	1.53-139.52	0.020
	Severe	2.00	0.36-11.19	0.431	Not estimated	-	-
	Eisenmenger syndrome	9.79	2.21-43.42	0.003	Not estimated	-	-
Type of intervention (No)	Corrective surgery	3.06	1.23-7.61	0.016	1.80	0.73-4.47	0.202
	Palliative surgery	10.80	2.37-49.12	0.002	1.41	0.25-7.94	0.696
	Intervention	Omitted	-	-	Omitted	-	-
Surgical residue	Yes	0.72	0.42-1.21	0.212	1.44	0.72-2.91	0.300
	No	Omitted	-	-	Omitted	-	-

LV, Left ventricle; RV, Right ventricle; PH, Pulmonary hypertension

DISCUSSION

During the past 3 decades, remarkable advancements in pediatric cardiology have allowed infants with CHDs to survive to adulthood; nevertheless, epidemiological evidence is still limited. The prevalence of adult CHDs depends on multiple factors such as the incidence of CHD at live birth, accessibility, affordability, and the quality of the CHD program as well as the timing of its implementation. [8] An important problem associated with the expanding population of adult patients with CHDs is cardiac dysfunction, although there is no clear understanding about its prevalence either among children or among adults with CHDs. Some studies have reported a 5% prevalence rate of cardiac dysfunction among children with CHDs and between 10% and 20% among patients after the Fontan surgery. [13, 14] Both RV and LV dysfunction can cause cardiac dysfunction and heart failure symptoms in adult patients with CHDs; in addition, further complications are provoked because, in some conditions, the morphologic LV or RV can function as the systemic ventricle. [15] There are many factors that can influence cardiac dysfunction such as corrective or palliative surgical interventions at childhood. The type (corrective/ palliative), length, and techniques (to reduce intraoperative myocardial ischemia) of operations performed at the early life influence the time and severity of later life cardiac dysfunction. [16]

In our study, the analysis of data showed that the prevalence of LV and RV dysfunction was 60.6% and 77.7%, respectively. Moreover, 58.7% of the patients had both LV and RV dysfunction and 20.9% had LV or RV dysfunction. The figure was higher among the cyanotic patients than among their non-cyanotic counterparts (81.8% vs 42.5%; $P < 0.001$; 98% vs 60.5; $P < 0.001$, respectively).

The majority of the patients in our study had moderately complex CHDs, which is in accordance with previous studies inasmuch as most of CHD survivors suffer from moderate problems such as ventricular and atrial septal defects. [17] Nonetheless, a large number of patients have more severe CHDs, including conotruncal defects and atrioventricular septal defects (30%) and more complex defects such as single ventricle defects. [18] Our results indicated that the chance of having LV and RV dysfunction was greater among the patients with moderately complex and greatly complex CHDs than the other types of CHDs. In this

regard, a previous study showed that although all adult patients with CHDs did not typically report heart failure symptoms, the prevalence of heart failure was 22.2%, 32.3%, and 40% among the patients after the Mustard repair for the transposition of the great arteries (TGAs), congenitally corrected transposition of the great arteries (ccTGA), and the Fontan palliation, respectively. [19] Another study showed that the chance of cardiac dysfunction in CHD lesions like the tetralogy of Fallot (TOF) and the TGA could be as high as 80% at the age of 50, while this figure was about 20–30% for isolated valvular diseases or defects that ended in left-to-right shunts. [20] Furthermore, the Dutch Registry of ACHDs, which followed up patients for more than 20 years, suggested that the prevalence of cardiac dysfunction differed by the patients' main CHD. [21] In another study, patients with single ventricle defects, the TOF, and the TGA after the atrial switch procedure were at the highest risk of heart failure, and patients with shunt lesions, coarctation of the aorta (CoA), and regurgitant valvular diseases were at a lower relative risk. [13] Similarly, our results showed that the prevalence of LV and RV dysfunction was higher among the patients who had already undergone intervention (either invasive or noninvasive), and the chance of LV dysfunction was significantly higher among those who had palliative surgery than among the ones who had corrective surgery (about 3 times) or who had no intervention (10.84 times). This can be explained by the fact that those who had palliative surgery might already have suffered from more severe and more complex anomalies, placing them at higher risks of cardiac dysfunction. Furthermore, although surgical intervention is the main treatment for most CHDs with the aim to repair the anatomical abnormalities at the earliest possible age, this is not the ultimate solution because all congenital anomalies are not suitable for surgical repair like single ventricular hearts and many cases of complex pulmonary atresia. For these conditions, palliative surgery is the only options. In addition, as much as it appears that the surgical repair of CHDs restores the usual architecture, some cardiac or extracardiac abnormalities may persist. [17]

The mean age of the patients who had LV and RV dysfunction in our study was 30.2 and 30.3 years, respectively, which is similar to what was reported in previous studies. In a previous study, cardiac dysfunction was the main problem among adult patients suffering from CHDs, with about a 25% incidence rate of cardiac dysfunction at the age of 30 years. [13] These patients were also older than those with no cardiac dysfunction (30.2 vs 28.9 y for LV dysfunction and 30.3 vs 27.3 y for RV dysfunction). Likewise, Norozi et al [13] reported that their patients with cardiac dysfunction were significantly older (30.8 ± 0.9 y vs 24.8 ±0.5 y). This might demonstrate that the development of cardiac dysfunction is age dependent. Additionally, the earlier onset of cardiac dysfunction among adult patients with CHDs relative to the general population calls for more precise attention to this group of patients with a view to achieving timely diagnoses.

CONCLUSIONS

The prevalence of cardiac dysfunction among our adult patients with CHDs was very high, with the condition starting at a young age by comparison with the general population. This can be translated into a considerable quality-adjusted life-year loss in the population, which in turn imposes subsequent costs to the health system. Despite all the improvements in the field of pediatric cardiology, surgical techniques, and noninvasive interventions, cardiac abnormalities still render patients prone to several complications including cardiac dysfunction. This study identified some factors that increased the chance of the development of cardiac dysfunction. These factors should be taken into account when approaching patients with cardiac dysfunction.

Limitations

The current study has some limitations. First, we could not analyze cardiac dysfunction separately for each CHD subgroup due to the relatively small sample size of the subgroups. Secondly, although our center is the only center for adult CHDs in Iran, some patients are referred to general clinics or even to pediatric cardiology centers, which might have caused the under or overestimation of the real numbers.

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