

Etiological Peculiarities in Pediatric Heart Failure

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ABSTRACT

Heart failure in children presents important characteristic features different from adult congestive failure, from a pathophysiological and mostly from an etiopathogenic point of view. Heart failure in children is, in most cases, a consequence of congenital structural cardiac abnormalities that remained unoperated, underwent a palliative operation or presented post-surgery complications, or of cardiomyopathy. Based on the nature of the clinical presentation, new onset heart failure can be differentiated from transient heart failure and chronic heart failure. Chronic heart failure may occur in children with biventricular circulation (systolic or diastolic dysfunction), in cardiac structural abnormalities with a right systemic ventricle and in the so-called univentricular heart. Acute heart failure can appear as acute heart failure at onset or as an aggravation of heart failure on the background of acute decompensated chronic heart failure.

Keywords: chronic, acute, causes, biventricular circulation, systemic right ventricle, univentricular circulation

INTRODUCTION

Heart failure (HF) is a complex clinical syndrome, with multiple etiologies, resulting from the incapacity of the heart to pump the blood amount required for the metabolic needs of the body, including adequate oxygen and nutrient intake (1). HF can evolve with systolic dysfunction, diastolic dysfunction or both.

SYSTOLIC VS. DIASTOLIC HF

The majority of the patients with HF have both systolic and diastolic dysfunction during exercise and/or at rest. Patients with diastolic HF have symptoms and/or signs of HF and preserved left ventricular ejection fraction (higher than 45-50%). The difference between the two types of HF is related to the fact that the main anomaly is the incapacity of the ventricle to contract normally and eject a sufficient

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1. Cardiac disorders with an intact myocardium (intact myocardial muscle fiber)
2. Cardiac disorders with an affected myocardium (damaged myocardial muscle fiber)
3. Pericarditis (cardiac tamponade – hypodiastolic cardiac failure, heart failure with diastolic dysfunction)
4. Intricate causes

TABLE 1. Etiological classification of HF in children.

blood amount (systolic failure) or the incapacity to relax and fill normally (diastolic failure). The main clinical manifestations of systolic HF are the consequence of low cardiac output, with the appearance of fatigue, a decrease in tolerance to exercise and other symptoms related to hypoperfusion, while clinical manifestations in diastolic failure are mainly due to an increase in the filling pressure. Diastolic HF can be caused by an increase in resistance to ventricular filling, as well as a decrease in the diastolic capacity of the ventricle (constrictive pericarditis, restrictive and hypertrophic cardiomyopathy), by an impairment of ventricular relaxation (hypertrophic cardiomyopathy).

HF has a significant incidence in the adult population and a low incidence in the pediatric population (2). The differences between adults and children are not only related to the incidence of HF. There are significant differences particularly in etiological circumstances (3). The most important causes of HF in adults are represented by: ischemic heart disease (40%), dilated cardiomyopathy (32%), valvular heart disease (12%), hypertension (11%), other causes such as myocarditis or arrhythmia (5%).

In the pediatric population, the causes of HF are very different, as it will be shown in what follows. HF is a major health problem in some countries. An annual incidence of 1.13 cardiomyopathies in 100.000 children was suggested by data of the American Pediatric Cardiomyopathy Registry (4), with mortality rate at 2 years from diagnosis is 13.6% in dilative cardiomyopathy forms (5). The great majority of statistical data refers to adults, because in children, the field of application of the problem is less well defined. Thus, it should be mentioned that there is no gold standard approach to the diagnosis of HF in children. Frequently, there is an ambiguity regarding the use of the term HF for children with structural congenital cardiac lesions (uncorrected by surgery) with left-to-right shunt with preserved systolic function, which is very different from HF associated with myocytic dysfunction. However, all

classifications include some congenital cardiac malformations in the etiology of pediatric HF (6, Table 1).

Depending on the onset age of the clinical picture of HF, certain etiological conditions are more frequent at certain ages.

In older children, HF is more frequently correlated with surgically uncorrected or palliatively corrected congenital cardiac malformations, rheumatic carditis, viral myocarditis, bacterial endocarditis. In the same age group, HF can be secondary in renal diseases with arterial hypertension, thyrotoxicosis, hemosiderosis, cardiomyopathy secondary to chemotherapy of neoplasms.

In infants and young children, HF occurs in congenital cardiac malformations with volume overload by shunt at the level of the great vessels (common arterial trunk, persistent arterial duct, aortopulmonary window), or by shunt at ventricular level (ventricular septal defect with massive left-to-right shunt, ventricular septal defect with transposition of the great arteries, ventricular septal defect with tricuspid atresia, atrioventricular duct) or shunt at atrial level (total anomalous pulmonary venous return). It is also found in myocardial anomalies such as fibroelastosis, metabolic cardiomyopathies, viral myocarditis, Kawasaki disease or it may be secondary in renal diseases with arterial hypertension, hemolytic-uremic syndrome, hypothyroidism, sepsis. HF with onset in the neonatal period involves myocardial dysfunction secondary to severe asphyxia at birth, sepsis, hypoglycemia. A number of severe congenital cardiopathies in the first days of life that are characterized by pressure overload such as aortic stenosis, aortic coarctation, hypoplastic left heart syndrome, or by volume overload through shunt at the level of the great vessels such as patent arterial duct, common arterial trunk, aortopulmonary window are other causes of HF in the newborn. Equally important in the etiology of HF during the neonatal period are cardiac malformations with significant shunt at ventricular level such as ventricular septal defect, single ventricle with pulmonary stenosis, atrioventricular duct, and arteriovenous fistulas. To the above, the following are added: extreme tachyarrhythmias such as supraventricular tachycardia, atrial flutter, atrial fibrillation or severe bradyarrhythmias such as congenital complete atrioventricular block and other atrioventricular blocks.

Sometimes, there are etiological circumstances for the onset of HF since intrauterine life. These are represented by severe anemia in hemolytic disease secondary to Rh sensitisation, or congenital cardiopathies with volume overload through atrioventricular valve regurgitation (atrioventricular duct), tricuspid regurgitation (severe Ebstein disease) or arteriovenous fistulas. Due to fetal circulation peculiarities, many disorders that overstrain the heart are relatively well tolerated in the fetal period. The time of onset of HF is frequently the key element in etiological diagnosis (Table 2).

Congenital cardiac malformations that decompensate during the neonatal period are duct-dependent, i.e. their hemodynamics worsens with the (physiological!) closure of the arterial duct.

According to the HF Guide published by the Working Group of the European Society of Cardiology in collaboration with the Heart Failure Association of European Society of Cardiology, a useful classification of HF in adults, based on the nature of the clinical presentation differentiates new onset HF from transient HF and chronic HF (7). Transient HF refers to symptomatic HF for a limited time period, although long-term treatment may be indicated. In children, chronic HF and acute HF are recognized.

CHRONIC HF in children can develop in disorders with biventricular circulation (with systolic or diastolic dysfunction), structural cardiac abnormalities in which the systemic ventricle is the right ventricle and univentricular heart.

1. Chronic HF in biventricular circulation may develop through myocyte dysfunction (e.g. in idiopathic cardiomyopathy) (8) or because of congenital cardiac abnormalities with volume or pressure overload. At present, these congenital cardiac malformations are usually – but not invariably – approached by surgery or in the catheterization laboratory.

Most of the patients with HF have evidence of both systolic and diastolic dysfunction during exercise and/or at rest. Diastolic dysfunction is a clinical HF syndrome with preserved systolic function, in which the alteration of diastole is the unique or primary cause of HF. Patients with diastolic HF have signs (9) and symptoms of HF and a left ventricular ejection fraction maintained at values higher than 45-50%.

There are no published estimates of the prevalence of diastolic dysfunction in the pediatric population. The conditions that cause diastolic dysfunction are varied and include pericardial and myocardial etiologies.

It should be mentioned that there is no gold standard approach for the diagnosis of HF in children. There is frequently an ambiguity regarding the use of the term HF for children with structural cardiac lesions (uncorrected by surgery), with left-to-right shunt (10), with preserved systolic function (11), whose expression is extremely different from HF associated with myocyte dysfunction.

2. Chronic HF in the case of systemic right ventricle

The morphological right ventricle may become the systemic ventricle when it is connected to the aorta, so it pumps the blood into the greater (systemic) circulation. There are two main groups of patients with biventricular circulation in which the right ventricle is the systemic ventricle: 1) patients with transposition of the great vessels with atrial switch surgery and 2) patients with congenitally corrected transposition of the great vessels (12).

In order to better understand the situation, it should be said that in the case of the D- trans-

Age of onset of heart failure	Etiological circumstances
Fetus	Tricuspid regurgitation secondary to Ebstein disease Severe mitral insufficiency in the atrioventricular duct Severe anemia Paroxysmal supraventricular tachycardia Atrioventricular block
First day of life	Myocardial dysfunction secondary to asphyxia, hypoglycemia, sepsis. Tricuspid insufficiency determined by papillary muscle dysfunction secondary to hypoxia or Ebstein disease Arterial duct-dependent congenital cardiac malformations (see below)
First week of life	Arterial duct-dependent congenital malformations Persistent arterial duct in the premature newborn Adrenal insufficiency through genetic enzymatic deficiencies
After the 2 nd week of life	Congenital cardiac malformations that become symptomatic because of reduced pressure in the pulmonary artery: persistent arterial duct, ventricular septal defect – at 6-8 weeks.

TABLE 2. Etiology of HF in the newborn, depending on the age of onset.

position of the great arteries, if arterial switch (an anatomical correction consisting of the transposition of the aorta and pulmonary artery) has not been performed in the neonatal period, atrial switch is performed at a later stage. This is a physiological (not anatomical!) correction that consists of atrial reversal by directing systemic and pulmonary venous return so that the right atrium becomes the systemic atrium (taking over pulmonary venous return and channeling it through the tricuspid valve to the right ventricle and from there, to the aorta), and the left atrium becomes the atrium for pulmonary circulation (taking over systemic venous return from the venae cavae and channeling it through the mitral valve to the left ventricle and from there, to the pulmonary artery). Atrial switch can be followed by complications that may result in HF (rhythm and conduction disorders, obstruction of systemic or pulmonary venous return, right ventricular dysfunction).

The congenitally corrected transposition of the great arteries is a double atrioventricular and ventriculoatrial transposition resulting in a physiological correction of circulation. The clinical evolution of patients with congenitally corrected transposition of the great arteries is determined by the associated malformations (ventricular septal defect, pulmonary stenosis) or by the associated electrophysiological anomalies (atrioventricular block). HF develops with aging. The studies revealed that 25% of patients with congenitally corrected transposition of the great arteries without associated anomalies and 67% of patients with associated anomalies have HF at the age of 45 years (13).

The mechanism of right ventricular systemic dysfunction is controversial. Various theories include: a) suboptimal arrangement and mechanics of myocardial fibers in the right ventricle, b) adverse pattern and reduced heterogeneity of ventricular strain, c) tricuspid insufficiency, d) myocardial fibrosis secondary to prolonged hypoxemia during the waiting period for atrial switch.

3. Chronic HF in univentricular circulation

There are some etiological conditions that fall under the name of univentricular heart (14), which have in common the presence of a

single functional ventricle, of right or left morphology. The second ventricle (when present) is hypoplastic (15), making surgical biventricular correction impossible to perform. The single functional ventricle must support both the systemic and the pulmonary circulation (16).

Congenital cardiac malformations that are part of the univentricular heart fit into:

1. the ventricle has a univentricular atrioventricular connection (17), the two atrioventricular valves open into a dominant ventricle, usually of left morphology: double inlet left ventricle;

2. absence or severe stenosis of the right or left atrioventricular connection, almost constantly associated with severe hypoplasia of the corresponding ventricle: tricuspid atresia and pulmonary atresia with an intact septum (18); mitral valve atresia and hypoplastic left heart syndrome (19);

3. marked right or left ventricle hypoplasia, under the conditions of normal atrioventricular connections or abnormal atrioventricular or ventriculoarterial connections that prevent biventricular correction; common atrioventricular canal with unbalanced ventricles (20), complex forms of transposition of the great vessels and double outlet right ventricle (21).

ACUTE HF is defined as the appearance of HF manifestations or the rapid alteration of the signs and symptoms of chronic HF requiring emergency treatment (22). Consequently, it can appear as HF at onset or as an aggravation of HF on the background of acute decompensated chronic HF (23). The patient with acute HF will present with one of the following clinical categories: a) Aggravation or decompensation of chronic HF; b) Acute pulmonary edema; c) Cardiogenic shock; d) Hypertensive HF; h) Isolated right HF

In conclusion, pediatric HF has many characteristics that differentiates it from adult HF and in the first place, it has particular etiological circumstances correlated with the presence of congenital cardiac malformations. Etiological peculiarities also depend on the various stages of childhood.

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REFERENCES

1. **Deedwania PC, Carbajal E** – Evidence-based therapy for heart failure. *Med Clin North Am* 2012;96:915-31.
2. **Clark BJ 3rd** – Treatment of heart failure in infants and children. *Heart Dis* 2000;2:354-61.
3. **Butnariu A, Samasca G** – Particular Aspects in Pediatric Congestive Heart Failure. *J Clin Exp Cardiol* 2012;3:1000e104.
4. **Wilkinson JD, Landy DC, Colan SD, et al.** – The pediatric cardiomyopathy registry and heart failure: key results from the first 15 years. *Heart Fail Clin* 2010;6:401-13.
5. **Svendsen A** – Heart failure: an overview of consensus guidelines and nursing implications. *Can J Cardiovasc Nurs* 2003;13:30-4.
6. **Menteer JD, Hogarty A, Chrisant MRK** – Heart Failure Chapter in *Requisites in Pediatrics: Cardiology*. Vetter VL, ed. Elsevier Science. (in Press);
7. **Tan LB, Williams SG, Tan DK, et al.** – So many definitions of heart failure: are they all universally valid? A critical appraisal. *Expert Rev Cardiovasc Ther* 2010;8:217-28.
8. **Cosper PF, Harvey PA, Leinwand LA** – Interferon- γ causes cardiac myocyte atrophy via selective degradation of myosin heavy chain in a model of chronic myocarditis. *Am J Pathol* 2012;181:2038-46.
9. **Weidemann F, Niemann M, Herrmann S, et al.** – Assessment of diastolic heart failure: Current role of echocardiography. *Herz* 2013;38:18-25.
10. **Soliman AT, Elawwa A, Khella A, et al.** – Linear growth in relation to the circulating concentration of insulin-like growth factor-I in young children with acyanotic congenital heart disease with left to right shunts before versus after surgical intervention. *Indian J Endocrinol Metab* 2012;16:791-5.
11. **Bu'Lock FA, Mott MG, Oakhill A, et al.** – Left ventricular diastolic function after anthracycline chemotherapy in childhood: relation with systolic function, symptoms, and pathophysiology. *Br Heart J* 1995;73:340-50.
12. **Chira M, Samasca G, Butnariu M** – Congenital Heart Defects: Early Surgical Correction and Heart Failure–Brief History. *J Biomol Res Ther* 2013;2:1000108.
13. **Graham TP Jr, Bernard YD, Mellen BG, et al.** – Long-term outcome in congenitally corrected transposition of the great arteries: a multi-institutional study. *J Am Coll Cardiol* 2000;36:255-61.
14. **Gupta P, McDonald R, Goyal S, et al.** – Extubation failure in infants with shunt-dependent pulmonary blood flow and univentricular physiology. *Cardiol Young* 2014;24:64-72.
15. **Connor JA, Thiagarajan R** – Hypoplastic left heart syndrome. *Orphanet J Rare Dis* 2007;2:23.
16. **Shiraishi Y, Sugai TK, Tanaka A, et al.** – Structural design of a newly developed pediatric circulatory assist device for Fontan circulation by using shape memory alloy fiber. *Conf Proc IEEE Eng Med Biol Soc* 2011;2011:8353-5.
17. **Cerillo AG, Murzi B, Giusti S, et al.** – Pulmonary artery banding and ventricular septal defect enlargement in patients with univentricular atrioventricular connection and the aorta originating from an incomplete ventricle. *Eur J Cardiothorac Surg* 2002;22:192-9.
18. **Odemis E, Ozyilmaz I, Guzeltas A, et al.** – Transcatheter management of neonates with pulmonary atresia with intact ventricular septum: a single center experience from Turkey. *Artif Organs* 2013;37:E56-E61.
19. **Park MV, Fedderly RT, Frommelt PC, et al.** – Leftward Displacement of Septum Primum in Hypoplastic Left Heart Syndrome. *Pediatr Cardiol* 2013;4:942-7.
20. **Cohen MS, Jacobs ML, Weinberg PM, et al.** – Morphometric analysis of unbalanced common atrioventricular canal using two-dimensional echocardiography. *J Am Coll Cardiol* 1996;28:1017-23.
21. **Ruzmetov M, Rodefeld MD, Turrentine MW, et al.** – Rational approach to surgical management of complex forms of double outlet right ventricle with modified Fontan operation. *Congenit Heart Dis* 2008;3:397-403.
22. **Pang PS, Jesse R, Collins SP, et al.** – Patients with acute heart failure in the emergency department: do they all need to be admitted? *J Card Fail* 2012;18:900-3.
23. **Lassus JP, Siirilä-Waris K, Nieminen MS, et al.** – Long-term survival after hospitalization for acute heart failure - Differences in prognosis of acutely decompensated chronic and new-onset acute heart failure. *Int J Cardiol* 2013;168:458-62.