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Heart Failure in Children with Congenital Heart Disease

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Abstract: Background: In the contemporary Western world, heart failure (HF) is one of the leading causes of hospitalization and death, the cause of heart failure in children may be pressure overload or volume overload or both. The most common cause of heart failure in infancy is CHD. Despite the fact that HF therapy has improved prognosis and quality of life, death is still relatively high. Neurohormonal inhibition of an overactive neurohormonal axis is the medical therapy approach. In terms of hospitalization, mortality, and the course of the disease, no one sign has been able to predict or track HF. As the molecular signatures of CHD and HF are being characterized with the use of available technology, it is increasingly appreciated that at least some disease pathways are shared. Determining the molecular basis of HF in CHD will play a crucial role in developing treatment strategies for this growing population. It is necessary to develop new techniques for prognosis, therapeutic monitoring, and diagnosis.

Conclusion: The most common cause of heart failure in infancy is congenital heart disease.

Keywords: Heart Failure, Congenital Heart Disease.

Introduction:

It is increasingly recognized that the biggest threat to the health of the world's population is cardiovascular disease (CVD). 17.8 million deaths (95% CI 17.5–18.0 million) are anticipated, CVDs are responsible for the greatest number of non-communicable disease-related deaths.

The etiology of HF in children plays a key role in the clinical course and outcome. The two most common causes of pediatric HF are CHD and cardiomyopathies. There is an inherent problem in classifying HF based on clinical presentation of CHD when described primarily in physiological terms. For example, outflow tract obstruction (pressure overload) or pulmonary over-circulation (volume overload) may be confusing because ventricular dysfunction may be associated with poor contractility (systolic dysfunction) or poor relaxation (diastolic dysfunction), with or without the clinical presence of HF. There is an overlapping relationship of HF, CHD, and cardiomyopathy **[1]**.

Of note, patients with CHD and HF, especially with single ventricle physiology, make up a significant proportion of the heart transplantation population, over 50% in infants **[2]**.

The clinical picture of HF is directly related to age. The symptoms of HF depend upon whether there is congestion due to chronic right HF or hypo-perfusion due to acute left HF. Signs and symptoms of chronic right HF include elevated jugular venous pressure, pleural effusion, ascites, pedal edema, abdominal discomfort, and hepatomegaly. Signs and symptoms of acute left HF include dyspnea, orthopnea, rales on auscultation due to pulmonary edema, dizziness, fatigability, nausea, vomiting, abdominal pain, and feeding intolerance. When right HF is acute it can present with hypo-perfusion, tachycardia and hypotension. Similarly, when left HF is chronic it can present with signs and symptoms of chronic congestion. Right HF associated with left HF and is a predictor of increased morbidity and mortality **[3]**.

Routes to Heart Failure in CHD Patients:

The progression to HF in patients with CHD involves proven and hypothesized mechanisms, which we classify into three routes (Figure 1).

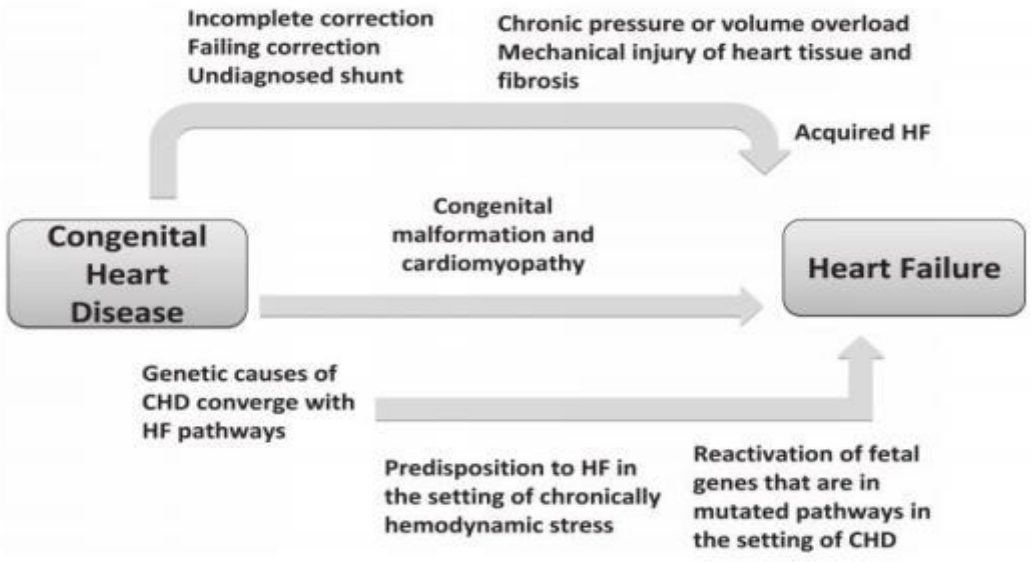

Figure (1): Schematic of the hypothesized mechanisms linking congenital heart disease with heart failure. We propose three putative routes which lead to HF in ACHD: rare monogenic entities that cause both CHD and HF (middle arrow), severe CHD lesions in which acquired modynamic effects of CHD or surgery result in HF (top arrow), and most commonly a combined effect of complex genetics in overlapping pathways and acquired stressors caused by the lesion (bottom arrow) **[5].**

The first route is purely acquired and mechanical with no genetic element. This includes incomplete or palliative correction of a lesion leading to a chronic state of hemodynamic stress and subsequent heart failure. The probability of heart failure in CHD lesions such as tetralogy of Fallot (TOF), and transposition of the great arteries (TGA) can be as high as 80% at 50 years of age, while it is around 20–30% for isolated valvular disease or defects that result in left-to-right shunt. Additional myocardial insults can complicate surgery, including injury to the myocardium, coronary arteries, and conduction system. Post-surgical conduction disease may require permanent ventricular pacing, which can lead to progressive contractile dysfunction.

Since these insults often occur in the first years of life, the effects of altered hemodynamics or tissue injury accumulate over years, resulting in early development of HF**[4]**.

Although the increased prevalence of HF in ACHD is primarily viewed as a result of a volume or pressure overload, whereby the starting point is an abnormal heart, an independent genetic component is also present **[1]**.

The second route a purely genetic component that causes both cardiac malformation and a cardiomyopathy that result in HF, unrelated to hemodynamic stress. Many of the pathways involved in cardiac development in utero are also involved in myocardial structure and stability. Therefore, it is not surprising that certain molecular perturbations can cause both a cardiac defect at birth, and a cardiomyopathy that can present later in life, often in childhood. Noonan Syndrome (NS) is the second most frequent syndromic form of CHD and can cause both CHD and cardiomyopathy. Similarly, another example of congenital cardiomyopathy is left ventricular non-compaction (LVNC), a heterogeneous disorder that often results in HF. LVNC has been associated with CHD including atrial and ventricular septal defects, Ebstein anomaly and outflow tract lesions, and is caused by genes such as MYH7 and the transcription factor NKX2-5 among others **[6]**.

The true prevalence of HF is thought to be higher as not all HF events in CHD patients resulted in hospital admission. Low prevalence CHD lesions such as TGA and TOF that result in HF via markedly abnormal hemodynamics do not solely account for the epidemic of HF in CHD. Moreover, gene mutations that cause both cardiomyopathy and CHD are extremely rare. Therefore, it is unlikely that these two routes alone explain the high incidence of HF in CHD. This suggests additional mechanisms through which CHD patients can develop HF **[5]**.

The third route, which is a combination of congenital genetic risk and acquired hemodynamic stressors. There is significant overlap in the molecular pathways that result in CHD during development and those that are responsible for the integrity of the postnatal myocardium. This overlap suggests that molecular perturbations that result in abnormal cardiac development can increase the risk for heart failure in adulthood, especially in the presence of chronically perturbed hemodynamics. Heart failure also involves the reactivation of many fetal genes. One can expect the reactivation of a mutated pathway to exacerbate the progression to HF in the setting of CHD. With the current era of high throughput DNA, RNA, protein and metabolic analysis this hypothesis can be studied using a systems biology approach to investigate the development of HF in CHD patients, particularly those with mild phenotypes whose progression to HF might not be justified by the degree of volume or pressure overload caused by the lesion **[5]**.

Age is the sole determinant of the clinical presentation of pediatric heart failure. Infants and early children with HF typically appear with cyanosis, tachypnea, sinus tachycardia, diaphoresis, and difficulties feeding (from prolonged feeding time intake to frank intolerance). Adolescence and older kids could suffer The main symptoms include tachypnea, fatigue, shortness of breath, and exercise intolerance. There may also be leg pitting edema, oliguria, and abdominal pain **[7].**

Based on systolic function, heart failure can be categorized as either heart failure with preserved ejection fraction (HFpEF) or heart failure with reduced ejection fraction (HFrEF). HFpEF is the term used when the left ventricular ejection fraction (LVEF) exceeds 50%. when LVEF is less than 40%, it is called HFrEF. Patients with an LVEF between 40 and 49% are considered to be in a "gray area," also known as HF with mid-range EF (HFmrEF). . A diastolic dysfunction without a significant ejection fraction alteration is the hallmark of this form of heart failure .Notably, HFpEF is more difficult to diagnose than HFrEF since it typically does not have a dilated left ventricle, necessitating further testing and serum biomarker analysis. Notably, HFpEF is more difficult to diagnose than HFrEF since it typically does not have a dilated left ventricle, necessitating further testing and serum biomarker analysis **[8].**

The renin-angiotensin-aldosterone pathway and adrenergic receptors are the main targets of modern heart failure treatment due to a well-established understanding of the neurohormonal systems in particular. These include beta-blockers, angiotensin-converting enzyme inhibitors, and angiotensin-II receptor antagonists. It has not been widely recognized that HF patients have an overactive vasopressin system **[9].**

The improper activation of the vasopressin system is thought to be the cause of the severe water retention and volume overload experienced by patients with HF. Furthermore, it is thought that a non-osmotic mechanism controls the release of AVP through angiotensin II, pain, intracardiac pressures, intraarterial pressures, and adrenergic central nerve stimuli **[10].** “End-stage HF” is the final common pathway of all forms of heart disease and may lead to therapies such as orthotopic heart, lung, or heart-lung transplantation. It is important to distinguish “right HF” and “left HF” as the clinical management is different. There are also other nomenclatures, and HF may be described as “compensated HF” or “decompensated HF” depending upon whether end-organ perfusion is maintained. Heart failure can also be described as “systolic HF” with reduced ejection fraction, HF with preserved systolic function, which is synonymous with “diastolic HF”, and combined systolic and diastolic HF. The term “high output HF” is often used to describe cardiac or extra-cardiovascular conditions leading to volume overload and congestion. In general, a commonly accepted definition of HF has been challenging **[2]**.

Conclusion: congenital heart disease is considered most common cause of heart failure in children.

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