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Editorial

What we should know about pediatric heart failure: children are not small adults

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Key message

- Pediatric heart failure (PHF) features high morbidity and mortality rates.
- Although adults and children can share a common diagnosis of heart failure, the underlying causes can differ significantly and require distinct therapeutic approaches.
- Treatments designed for adults are often applied to PHF despite the fundamental physiological and developmental differences between them.
- Child-specific data are vital for the development of tailored treatments to meet the unique needs of patients with PHF.

Pediatric heart failure (PHF) is a major medical condition with high morbidity and mortality rates. Determining its incidence is challenging because of the differences in its definition compared with heart failure (HF) in adults. Although the overall burden of PHF is lower than that of adult HF, PHF cases require greater resource utilization per patient and feature higher mortality rates than adults with HF.[1] Improvements in the surgical and medical care of patients with congenital heart disease (CHD) have decreased mortality rates and extended overall average life expectancy. Consequently, there has been an increase in the number of hospitalizations and burden associated with PHF.[2] Hence, understanding the mechanisms of, promptly diagnosing, and ensuring the effective treatment of PHF are crucial.

In a recent issue of *Clinical and Experimental Pediatrics*, Agrawal et al.[3] comprehensively summarized the diagnostic and therapeutic approaches to PHF that encompasses the current methods. The authors offer a thorough review of PHF, highlighting the point that "PHF is different from adult heart failure." They stressed the importance of conducting more research and putting in greater effort to understand the unique pathophysiology of PHF and create more tailored treatments for pediatric patients. As mentioned in this article, PHF has various etiologies, such as volume overload, pressure overload, cyanosis, primary myocardial disease of either or both ventricles, metabolic abnormalities, and genetic mutations. Unlike in adults, structural anomalies due to CHD accounts for the majority of pediatric cases.[4] This category mainly involves volume and pressure overload, with a significant proportion requiring surgical intervention. Therefore, establishing tailored treatment plans based on underlying causes is even more crucial in children than in adults.[5]

Similar to other pediatric diseases, PHF has a low prevalence and exhibits heterogeneous characteristics, making it challenging to provide standardized diagnostic methods and treatment guidelines. Therefore, when treating PHF, we typically extrapolate treatments from adult HF approaches owing to the limited availability of specific pediatric data. However, because PHF differs substantially from adult HF in etiology, pathophysiology, response to medications, and prognosis, it is unknown whether the approaches used to manage adult HF would yield equivalent effectiveness and safety for PHF.

Guideline-directed medical therapy for HF has led to better outcomes for adult patients. This approach is supported by the strong foundation of multiple well-designed phase 3 clinical trials, which have recommended guidelines for effective HF management. However, a more essential distinction in the treatment of HF between adult and pediatric patients is that only a small proportion of the drugs proven effective through evidence-based studies in adults with HF have received official authorization for use in children.[6] Drug pharmacokinetics and pharmacodynamics can vary according to age and developmental stage. However, owing to the lack of research in this area, the current practice involves adjusting adult dosages for pediatric use based on weight.[7] Thus, we must perform well-designed studies to

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establish whether the dosages of such medication will effectively control PHF or carry any side effects.

The latest guidelines issued by the United States and Canada offer recommendations for the treatment of acute PHF including diuretics, the cautious administration of inotropes to stabilize hemodynamics, and angiotensin-converting enzyme inhibitors; alternatively, that for chronic PHF includes angiotensin receptor blockers, β-blockers, and mineralocorticoid receptor antagonists.[4] However, most of the class I recommendations have an evidence level of C.[8] New drugs including sacubitril-valsartan and ivabradine, which have been proven effective in adult HF, lack study data in pediatric populations. However, the encouraging aspect is that, despite these challenges, well-designed studies related to PHF are gradually emerging, including PANORAMA-HF, whose results are expected to be available soon.[9]

Although it may take considerable time for such new drugs to become applicable to children with HF, efforts to reduce this temporal gap could involve rigorous trials and studies. To facilitate this, regulatory authorities and pharmaceutical companies must endorse these endeavors to enable research advances.

For end-stage PHF that is refractory to surgical and medical therapy, mechanical assist devices and heart transplantation may be the next treatment options. Significant progress has been made in the field of mechanical support technology for children, leading to an increased capacity to facilitate successful bridging to heart transplantation without negatively affecting outcomes after transplantation.[10] Although noteworthy hurdles persist, particularly for neonates and individuals with CHD, continuous advancements suggest that better support techniques are on the horizon.

Although heart transplantation is considered the gold standard for children with advanced HF, the number of suitable donors is limited, resulting in extended transplant list waiting times and higher mortality rates. Therefore, a novel approach is required to expand the donor pool.

As the burden of PHF increases, it becomes crucial to actively comprehend its pathophysiology from perspectives distinct from those of adults and establish optimal treatment strategies based on well-conducted trials with adequate power. These efforts will provide valuable advancements for patients with PHF.

See the article "Heart failure in children and adolescents: an update on diagnostic approaches and management" via https://doi.org/10.3345/cep.2023.00528.

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