

Nature's right ventricle—limited by design

Lucas J. Witer, Koji Takeda, Hiroo Takayama

Columbia University Medical Center, New York-Presbyterian Hospital, New York, NY, USA

Correspondence to: Lucas J. Witer, MD. Columbia University Medical Center, New York-Presbyterian Hospital, New York, NY, USA. Email: ljw2157@cumc.columbia.edu.

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Right ventricular failure remains a vexing currently unreconcilable problem in modern cardiac surgery. The etiology is multifactorial, the prevalence significant, and the mortality risk substantial. Management paradigms of right ventricle (RV) failure have undergone historical changes as our experiences in advanced mechanical circulatory support have evolved (1-6). Our current treatment options, however, remain limited even as our understanding of the optimal management evolves.

In an interesting paradigm, Bowen and colleagues (7) sought to examine the cellular and molecular basis of right ventricular involution in their article, "Right ventricular involution: What can we learn from nature's model of compensated hypertrophy?" Within, they describe the structural and molecular features of the RV occurring in mice hearts transitioning from a high pressure (fetal) to a low-pressure (neonatal) system by characterizing the degree of right ventricular apoptosis at the transcriptome level. The authors suggest that the neonatal right ventricular phenotype prior to involution is nature's model of compensated sustainable right ventricular hypertrophy. Interestingly, the study demonstrates increased proapoptotic gene expression during this transition leaving the RV in an unoptimized design state destined for failure under certain pathophysiologic conditions.

The authors work is interesting, suggesting potential future therapeutic targets for research and drug development. How we can manipulate the adult heart to recreate a neonatal phenotype has not been investigated, however, the concept of using apoptosis inhibitors for a variety of other medical conditions is not a new one (8). Furthermore, prior studies have examined biomechanical compensatory mechanisms of the RV following the induction of apoptosis (9). In addition, there have been other transcriptome changes implicated in the development of cardiomyopathy (10).

The focus on identifying characteristics predisposing to right ventricular pathophysiology is particularly important in the post ventricular assist device patient population as most patients with advanced LV dysfunction also have some degree of RV dysfunction. On the contrary, whether there is an adult phenotype within this population maintaining a semi-protected RV (not dissimilar to the author's observations within Eisenmenger's) is difficult to observe directly. RV failure, however, still complicates 10–40% of left ventricular assist device implants (3-5). The importance of needing future therapeutic targets to support the failing right heart cannot be underscored as our current treatment options are severely limited and significantly impair quality of life. Novel therapies are needed.

Genetic sequencing techniques and our understanding of the role that the transcriptome plays on the future of cardiac failure continues to enhance our understanding of the consequences of nature's plan in cardiac development. Published works, such as these, serve to promote the basis for future research and drug development in our molecular understanding of modern heart failure and may promote ideas for future interventions in patients requiring chronic mechanical circulatory support.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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