Pathophysiology of right ventricular heart disease: the role of structure, apoptosis and inflammation
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“Every man's life lies within the present; for the past is spent and done with, and the future is uncertain.”

Marcus Aurelius
Knowledge of RV in health and disease has lagged behind that of LV. Less muscular, restricted to pumping blood through a single organ, and less frequently or obviously involved than LV in diseases of epidemic proportions such as myocardial ischemia, cardiomyopathy, or valvulopathy, the RV has generally been considered a simple spectator, a victim of pathological processes affecting the cardiovascular system. Accordingly, little attention has been devoted to how RV dysfunction may be best detected and measured, what specific molecular and cellular mechanisms contribute to maintenance or failure of normal RV function, how RV dysfunction evolves structurally and functionally, or what interventions might best preserve RV function. Nevertheless, the impairment of the RV in various disease states and its impact on the outcome of those diseases suggests that the RV is an important contributor and that further understanding of these issues is of fundamental importance. Data so far suggest that there are distinctions between the ventricles that need to be further evaluated and clarified to understand the differences, similarities, and interplay between the left and right ventricle. These issues can be addressed with chamber-specific studies in animal models that examine changes in gene expression, protein synthesis, histology, and geometry during initiation and progression of diseases, injury, and stress (exercise and disease).

Animal models are particularly useful in determining factors that initiate RV dysfunction. Models would also help to identify biomarkers and changes in gene expression and protein synthesis associated with RV failure. Valuable information can be obtained from animal models through side-by-side comparisons of changes in the left and right ventricles. Parameters on which to focus would include tissue analysis; gene and
protein expression; and markers of oxidative stress, apoptosis, inflammation, collagen deposition and cell growth. When possible, such analyses should compare samples of patients with RV disease with animal models of right heart failure and pulmonary hypertension. This would help to address the question whether data obtained from manipulated animals can be extrapolated to patients with RV diseases. Animal models will be a necessary component to determine whether RV failure is associated with myocyte apoptosis or cytokine expression. With the use of the monocrotaline-rat model, we proved that development of RV failure is associated with cardiomyocyte death, inflammation and collagen deposition. Furthermore, we demonstrated that inflammation and apoptosis are mechanisms that are activated early during RV disease progression, while fibrosis occurs at later stages. There has been great interest for \textit{in vivo} imaging of cellular remodelling. Non-invasive visualization of pathophysiological processes at the cellular level is a significant tool that helps translating findings in animals to the human setting. Disease progression and effects of novel treatments can be closely monitored with the use of $^{67}$Ga-scintigraphy and $^{99m}$Tc-ANX V scintigraphy. The development of new therapeutic strategies for RV failure should be promoted. These novel approaches may include cell-based or gene therapy, new drugs or combination of existing drugs. We strongly recommend, based on amongst others on the findings of the studies described in this thesis, to focus the development of new therapeutic strategies for RV failure on apoptosis inhibitors and anti-inflammatory therapies.