The right ventricle under acute and chronic overload: early detection of right ventricular dysfunction
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Citation for published version (APA):
Tulevski, I. I. (2003). The right ventricle under acute and chronic overload: early detection of right ventricular dysfunction

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Outline of The Thesis
The topic of the right ventricle (RV) is increasingly prominent in the discussions of the optimal treatment of patients with chronic and acute RV overload. The rapid and widespread development of possible treatments of these patients has resurrected considerations of an old problem – when is the right ventricle unable to sustain increased pressure or volume overload? To answer this question, reliable, reproducible and quantitative parameters for RV function are required. The focus of this thesis is to relate already known and new quantitative parameters for RV function to patient's clinical status and explore their possible clinical implementation.

The first part and the chapter 1, introduction of the thesis describe quantitative methods for assessment of RV function under chronic pressure and volume overload in adult congenital heart disease. The long-term prognosis of these patients is unknown and mainly dependent on factors such as RV (dys)function, the occurrence of RV failure, and rhythm disorders. In these patients ventricular dysfunction often is first apparent during exercise, and loss of cardiac reserve could reasonably be expected before impairment of resting function.

In chapters 2,3, and 4 we will address the effect of dobutamine stress and its possible clinical implications in different groups of asymptomatic or minimally symptomatic patients with chronic RV pressure overload due to congenital heart disease.

The assessment of the differences in RV function between patients with isolated chronic pressure overload and patients with combined pressure and volume overload was the main issue in chapter 5. In this study we will also discuss the lack of accurate clinically applicable parameters for RV function and its negative effect on the appropriate stratification, and the decision-making as to the optimal timing for surgery in patients with valvular regurgitation. The problem of absence of quantitative parameters for RV function and follow-up also affects patients with congenitally corrected transposition of the great arteries ccTGA where the RV is supporting the systemic circulation. In the course of time, systemic ventricular dysfunction and failure may occur. The factors contributing to this problem are poorly understood, but it has been hypothesized that myocardial ischemia may contribute to RV dysfunction in these patients.

In chapter 6 we quantified regional wall motion and wall thickening (often used as markers for myocardial ischemia) as possible parameters for early detection of RV dysfunction in patients with ccTGA, and examined the correlation between regional myocardial function (wall motion and wall thickening) and global RV function (ejection fraction (EF)). Ventricular arrhythmia, beside ventricular failure, is another important cause of death in patients with a chronic pressure
overloaded RV due to congenital heart disease. Stratification of patients at risk of life threatening arrhythmias is therefore mandatory in clinical follow-up.

The clinical significance of electrocardiographic (ECG) parameters as non-invasive quantitative parameters for RV function in patients with chronic RV pressure overload due to congenital heart disease will be the focus of chapter 7. In this study we retrospectively examined the changes of ECG parameters over time and their correlation with other quantitative RV function parameters as for example end-diastolic volume, myocardial mass and brain natriuretic peptide (BNP). Another quantitative and relatively new parameters for ventricular function, the plasma neurohormones, have drawn our attention and were extensively examined in the setting of RV overload. Recent literature has shown that plasma concentrations of atrial natriuretic peptide (ANP) and BNP are elevated in patients with asymptomatic ventricular dysfunction and these parameters are highly accurate for the detection of ventricular failure.

In chapter 8 plasma levels of ANP and BNP were investigated in asymptomatic or minimally symptomatic patients under circumstances of chronic RV pressure overload. Plasma neurohormones were related to right ventricular EF determined by magnetic resonance (MR) imaging.

The second part of the thesis will focus on RV function under acute pressure overload and early determinants for dysfunction. RV function is of major prognostic significance in patients with acute pulmonary embolism (PE). Early diagnosis of RV dysfunction is difficult and once identified, patients with PE and RV dysfunction need close monitoring and appropriate therapy. The role of plasma neurohormones and their applicability in detection of RV dysfunction in patients with acute pulmonary embolism are discussed in chapter 9. In this study we examined the plasma BNP as possible parameter for assessment of RV function in patients with acute PE. In chapter 10 we emphasize the clinical importance of BNP as a supplementary tool for assessment of RV function and discrimination between patients with normal RV function, RV dysfunction and failure under circumstances of acute pressure overload.

In chapter 11 we will discuss the association of elevated BNP levels in patients with acute PE and their association with adverse outcomes during follow-up. In the recent literature, beside BNP, cardiac troponine T (cTnT) has been also proposed as a marker for RV function and adverse outcomes in patients with acute PE.

In chapter 12 we have combined these two independent prognostic factors to elucidate their complementary value as quantitative indicators for RV function in patients with acute PE. The
change patterns of BNP, and cTnT levels during the initial management of PE were the focus of this study.

**Chapter 13** is a case report showing very strong relation between increased BNP, ANP and RV function as determined by MRI in patients with chronic PE before and after surgical treatment. **Chapter 14** contains the conclusions of this thesis.