INTRODUCTION

Studies in heart failure (HF) generally focus on the functional assessment of the left ventricle. Conversely, the right ventricle has received far less attention in the evaluation of HF patients. Much of this neglect stems from the fact that the right ventricle has complex structural and physiological properties that pose challenges for the assessment of its morphology and function. However, adverse remodeling of the right ventricle is an important component of the HF syndrome. In particular, previous studies in HF cohorts of mixed etiology have suggested that right ventricular (RV) ejection fraction (RVEF), assessed by radionuclide or thermodilution techniques, may be a major determinant of exercise capacity and outcome. Consequently, there is growing interest regarding the clinical relevance of RV functional assessment in the HF population ***(Pennel, 2010).***

Dilated cardiomyopathy (DCM) is the second most common etiology of HF after coronary artery disease, and remains the leading indication for cardiac transplantation. Although the exact prevalence is poorly defined, RV systolic dysfunction (RVSD) has been reported in as many as 65% of DCM patients, suggesting that DCM is frequently a biventricular disease. The potential prognostic impact of RV impairment in DCM has been highlighted by 2 small studies that suggested that RVSD is an independent predictor of survival.

To date, the few studies evaluating RV systolic performance in DCM have used either thermodilution or contrast ventriculography to estimate RVEF. Such techniques are invasive with the result that their clinical application is limited. In contrast, echocardiography is a non-invasive, inexpensive and readily available method of right ventricular assessment ***(Pennel, 2010).***

AIM OF THE WORK

To review the alterations of cardiac right ventricular function associated with chronic heart failure.

To predict the prevalence of right ventricular systolic dysfunction in patients with dilated cardiomyopathy with EF ≤ 40%.

Chapter I

HEART FAILURE

Heart failure is a clinical syndrome characterized by systemic perfusion inadequate to meet the body's metabolic demands as a result of impaired cardiac pump function. This may be further subdivided into heart failure with systolic dysfunction as there is reduced cardiac contractility and heart failure with preserved left ventricular ejection fraction as there is impaired cardiac relaxation and abnormal ventricular filling.

The most common cause of heart failure is left ventricular (LV) systolic dysfunction (about 60% of patients). In this category, most cases are a result of end-stage coronary artery disease, either with a history of myocardial infarction or with a chronically underperfused myocardium. In many patients, both processes are present simultaneously. Other common causes of LV systolic dysfunction include idiopathic dilated cardiomyopathy, valvular heart disease, hypertensive heart disease, toxin-induced cardiomyopathies (e.g., doxorubicin, herceptin, alcohol), and congenital heart disease.

Right ventricular systolic dysfunction is usually a consequence of LV systolic dysfunction. It can also develop as a result of right ventricular infarction, pulmonary hypertension, chronic severe tricuspid regurgitation, or arrhythmogenic right ventricular dysplasia. A less-common cause of heart failure is

high-output failure caused by thyrotoxicosis, arteriovenous fistulae, Paget's disease, pregnancy, or severe chronic anemia.

Heart failure with preserved LV ejection fraction (impaired relaxation) usually is related to chronic hypertension or ischemic heart disease. Other causes include restrictive, infiltrative, and hypertrophic cardiomyopathies. Inadequate filling of the right ventricle can result from pericardial constriction or cardiac tamponade ***(La vecchia et al., 2001).***

Effect of LV systolic failure on RV systolic function:

Right ventricular dysfunction may develop in association with left ventricular dysfunction via multiple mechanisms: (1) left ventricular failure increases afterload by increasing pulmonary venous and ultimately pulmonary arterial pressure, partly as a protective mechanism against pulmonary edema (2) the same cardiomyopathic process may simultaneously affect the right ventricle; (3) myocardial ischemia may involve both ventricles; (4) left ventricular dysfunction may lead to decreased systolic driving pressure of right ventricular coronary perfusion, which may be a substantial determinant of right ventricular function

(5) ventricular interdependence due to septal dysfunction may occur; and (6) left ventricular dilation in a limited pericardial compartment may restrict right ventricular diastolic function. Conversely, right ventricular pressure overload,

as may occur with pulmonary hypertensive states, may compromise left ventricular function and lead to coincident evidence of left ventricular failure, such as pulmonary edema or effusion. Furthermore, when the right ventricle fails in the setting of left ventricular failure, it may be unable to maintain the flow volume required to maintain adequate left ventricular preload. Because of the multiple influences affecting right ventricular function due to left ventricular failure, right ventricular status may constitute a "common final pathway" in the progression of congestive heart failure and therefore may be a sensitive indicator of impending decompensation or poor prognosis.

The RV is exposed to pressure overload by chronic pulmonary hypertension which is result from LV systolic dysfunction, An initial adaptive response of myocardial hypertrophy is followed by progressive contractile dysfunction. Chamber dilatation ensues to allow compensatory preload and maintain stroke volume despite reduced fractional shortening. As contractile weakening progresses, clinical evidence of decompensated right ventricular failure occurs, characterized by rising filling pressures, diastolic dysfunction, and diminishing cardiac output, which is compounded by tricuspid regurgitation due to annular dilatation and poor leaflet coaptation. The increased size and pressure overload of the right ventricle also produce diastolic dysfunction of the left ventricle then systolic dysfunction occur.

Chapter II

ANATOMY AND PHYSIOLOGY OF RIGHT VENTRICLE

Historical background

For over a thousand years, the world's view of the pulmonary circulation hewed to the teachings of Galen, who believed that blood was produced in the liver, then delivered by the right ventricle (RV) to the tissues and organs where it was consumed. In Galen's view, blood "seeped" into the left ventricle (LV) directly from the RV via invisible pores in the interventricular septum. While it may now seem self evident that this is impossible, Galen viewed blood movement as a low volume ebb and flow ***(Clifford, 2010).***

In the 13th century, Ibn al-Nafis of Syria rejected Galen's description and speculated that blood from the RV reached the LV via the lungs. While he deserves credit for the first accurate description of the pulmonary circulation, his works were lost and largely forgotten until quite recently, and it does not seem likely that they influenced the understanding of circulatory physiology in the western world ***(West and Ibn Alnafis, 2008).***

The first detailed description of the RV and pulmonary circulation to receive significant attention in the western world appeared near the beginning of the 16th century in the midest of a religious discourse by Michael Servetus of Spain. In this work

(for which Servetus was later burned at the stake, although presumably for the heretical nature of its religious content, rather than primarily because of his views on circulatory physiology), Servetus wrote: [The vital spirit] is generated in the lungs from a mixture of inspired air with elaborated, subtle blood which the right ventricle of the heart communicated to the left. However, this communication is made not through the middle wall of the heart, as is commonly believed, but by a very ingenious arrangement the subtle blood is urged forward by a long course through the lungs; it is elaborated by the lungs, becomes reddish-yellow and is poured from the pulmonary artery into the pulmonary vein ***(Cattermole, 1997).***

This model, based strictly on structural observations rather than on any experimental measurements, was a dramatic departure from Galen, but like Galen before him, Servetus assumed blood was continuously produced and consumed rather than re-circulated ***(Cattermole, 1997).***

Fifty years later, William Harvey would develop the first experimentally based model of the circulation. Despite not being the first to describe the pulmonary circulation, Harvey is considered the father of modern physiology because he was the first to perform detailed measurements and calculations that allowed him to deduce the existence of blood recirculation, and he demonstrated the pulmonary blood flow experimentally ***(Comtor et al., 1982).***

Over the next 400 years, the importance of the RV would be debated, with some investigators opining well into the 20th century that the RV served no purpose other than to provide capacitance to the pulmonary circulation ***(Kagan, 1952).*** In large part because of these early investigations, right heart failure was believed to be a problem mainly confined to idiopathic pulmonary hypertension and congenital heart disease, where it is a common cause of death. However, it is now known that pulmonary hypertension (PH) and right heart failure, far from being rare, complicate numerous other disease processes. RV failure is one of the most powerful predictors of mortality in left heart failure ***(Ghio and Tavazzil, 2005),*** right heart failure is the proximate cause of death in most of the 50 000 fatal cases of pulmonary embolism in the United States each year ***(Hirsh and hoak, 1996),*** and by some estimates, two to six in 1000 people with chronic lung disease will develop right heart failure, for several tens of thousands of new cases a year ***(Clifford and Greyson, 2010).***

Anatomy of RV

Gross Anatomy

The right ventricle (RV) is the most anteriorly situated cardiac chamber and lies immediately behind the sternum. the RV may be divided into an inflow tract (beginning with the tricuspid annulus), an apical region, and an RV outflow tract (terminating in the pulmonic valve) figure 1. The RV free wall

constitutes the anterior border of the RV and consists of a relatively thin crescent of muscle, lying anterior to the LV and interventricular septum. The RV is normally less than 1-3 mm in thickness, in comparison with the 10 mm thick left ventricular free wall, and comprises roughly 1/6th of the total mass of the heart ***(Clifford and Greyson, 2010).***

Three prominent muscular bands are present in the RV: the parietal band, the septomarginal band, and the moderator band. The parietal band and the infundibular septum make up the crista supraventricularis. The septomarginal band extends inferiorly and becomes continuous with the moderator band, which attaches to the anterior papillary muscle. When abnormally formed or hypertrophied, the septomarginal band can divide the ventricle into 2 chambers (double chambered RV) ***(Ho et al., 2006).*** Another important characteristic of the RV is the presence of a ventriculo-infundibular fold that separates the tricuspid and pulmonary valves. In contrast, in the LV, the aortic and mitral valves are in fibrous continuity ***(Jiang, 1994).***

The shape of the RV is complex. In contrast to the ellipsoidal shape of the LV, the RV appears triangular when viewed from the side and crescent shaped when viewed in cross section. The shape of the RV is also influenced by the position of the interventricular septum. Under normal loading and electrical conditions, the septum is concave toward the LV in both systole and diastole ***(Jiang, 1994).***

Myofiber Architecture of the RV

The ventricles are composed of multiple layers of muscles that form a 3-dimensional (3D) network of fibers. As the RV wall is mainly composed of superficial and deep muscle layers. The fibers of the superficial layer are arranged more or less circumferentially in a direction that is parallel to the atrioventricular (AV) groove. These fibers turn obliquely toward the cardiac apex on the sternocostal aspect and continue into the superficial myofibers of the LV. The deep muscle fibers of the RV are longitudinally aligned base to apex ***(Farb, 1992).***

Spiral muscle bundles form a contiguous band-like structure functionally linking the RV and the LV, likely resulting in transmission of contractile force directly from the LV to the RV ***(Buckberg, 2006).*** Short axis cross sections through the heart from apex to base vary from a roughly triangular contour at the apex to a crescentic appearance at the base. This complex shape accounts for the difficulty in assessing RV size and function based on two dimensional imaging techniques ***(Ho, 2006).*** And also accounts for the dramatic changes in RV size and shape that occur with varying loading conditions.

Right ventricle coronary circulation

In humans, the RV is largely perfused from the right coronary artery. In the LV, myocardial perfusion occurs predominantly in diastole when intramyocardial tissue pressure falls below aortic root pressure. Under normal loading conditions, RV intramyocardial tissue pressure remains below aortic root pressure throughout the cardiac cycle, permitting continuous coronary flow, but in severe RV pressure overload the RV coronary perfusion pattern begins to approximate that of the LV ***(Clifford and greyson, 2010).***

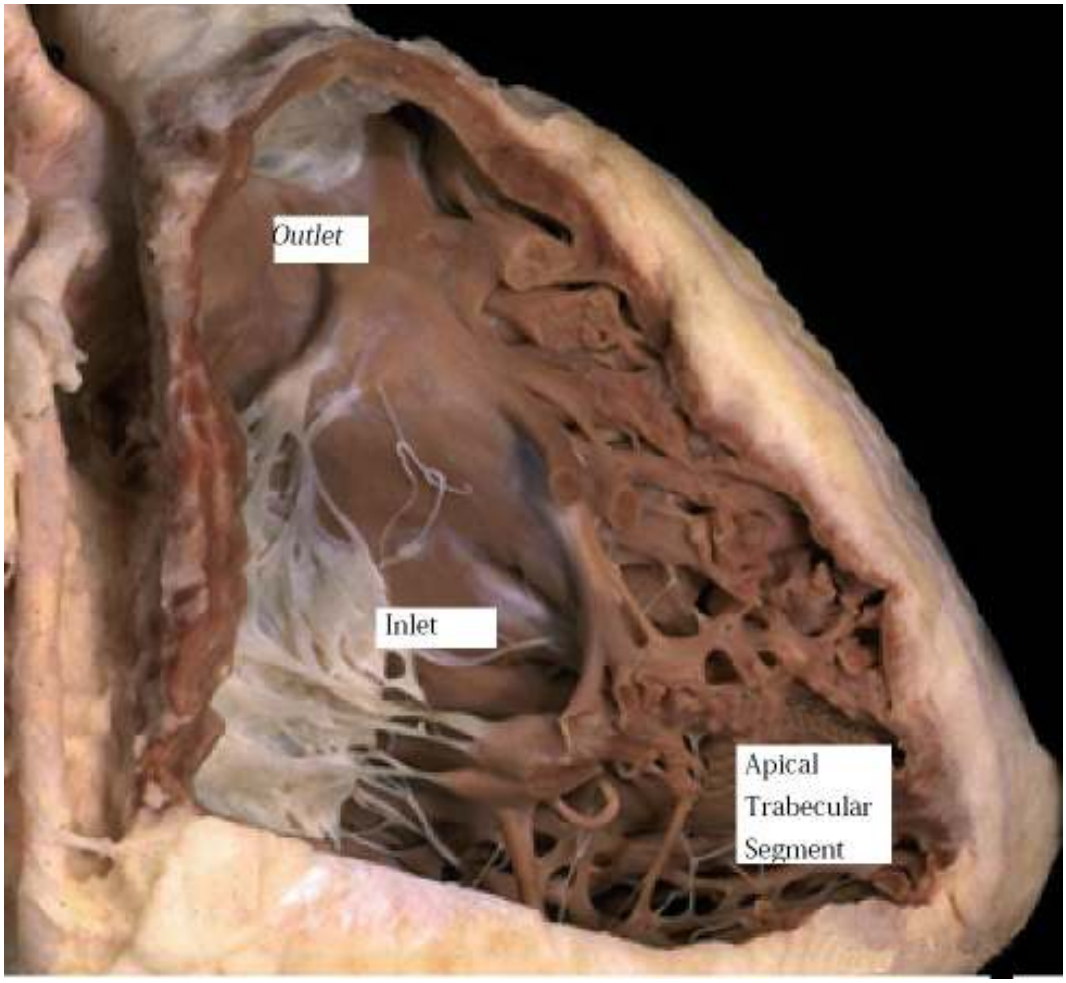

Figure (1): This window dissection shows the 3 components of a normal right ventricle ***(Rafael et al., 2010).***

Physiology and Hemodynamics of right ventricle

Normal right ventricle contraction

In the LV, development of ventricular pressure and ejection of blood is due to a concentric contraction of the LV free wall and septum, along with a twisting or "wringing" motion of the heart. In contrast, ejection of blood by the RV

proceeds with a sequential contraction beginning in the inflow tract, and moving in a wave toward the outflow tract. Normal ejection from the RV is a function of both a reduction in RV free wall surface area and a reduction in RV free wall septal distance ***(Sakuma et al., 2002),*** Figure 2 schematizes how the RV and the LV eject blood (neglecting any twisting motion of ventricular motion).

Since surface area of a cylinder is proportional to its radius, and volume is proportional to the square of the radius, ejection fraction in the LV is roughly proportional to the square of the change in endocardial surface area. In contrast, because of the greater surface area to volume ratio of the RV, a greater ejection fraction is produced by a smaller change in surface area than would be required in the LV. The bellows-like arrangement of the RV not only allows large changes in RV volume with small changes in RV free wall surface area, but also helps buffer respiratory changes in RV output without necessitating altered contractile function on a breath-to-breath basis ***(Santamore and Amoore, 1994).***

While the series configuration of the pulmonary and systemic circulation require average RV and LV stroke volume to be the same (in the absence of intracardiac shunts), RV end-diastolic volume is normally somewhat greater than LV end-diastolic volume, while ejection fraction is smaller. As afterload increases, RV end diastolic volume rises while ejection fraction falls ***(Clifford and Greyson, 2010).***

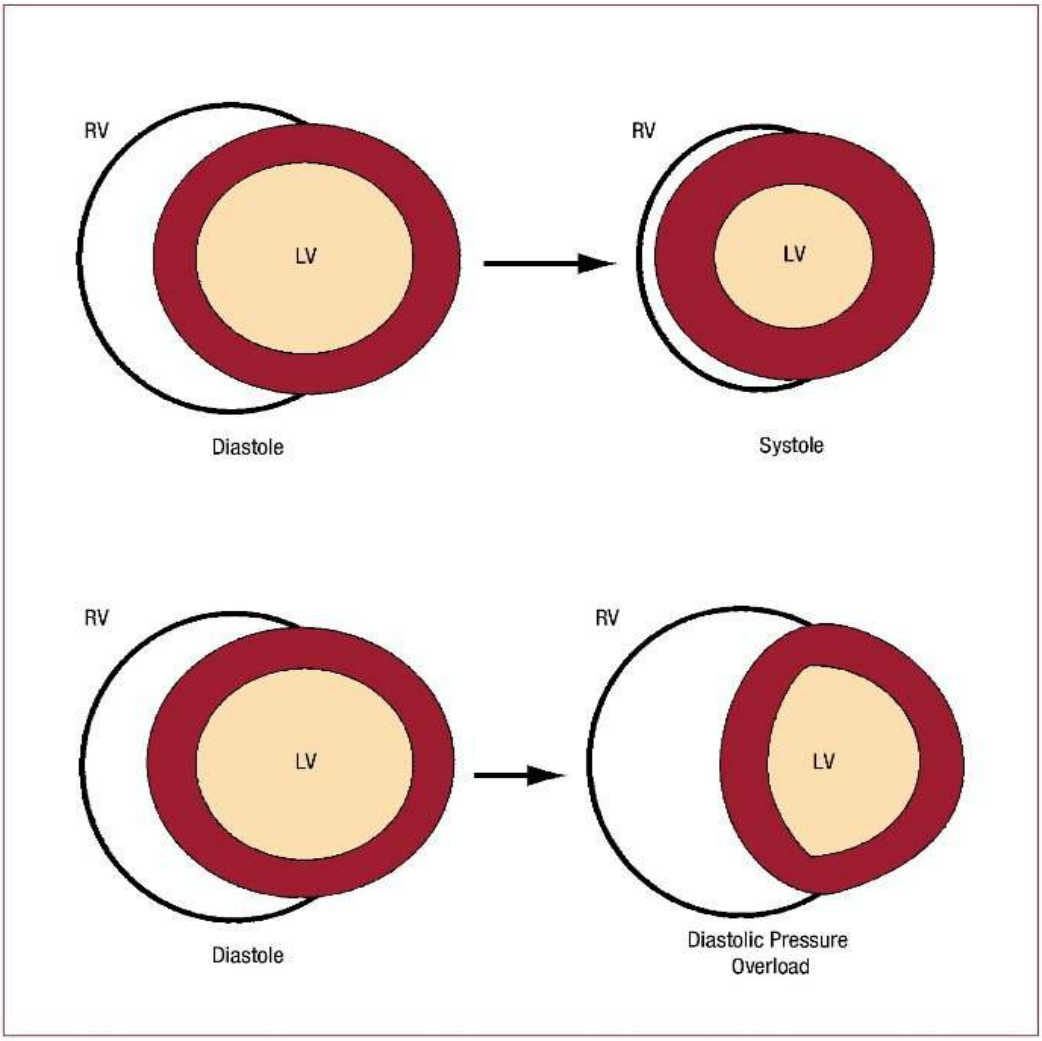

Figure (2): Illustration of shape changes in the heart during contraction. The circular cross section LV contracts by a uniform reduction in endocardial surface area, maintaining a nearly constant relationship between volume and surface area. The crescentic RV flattens in systole, leading to a large volume change with minimal change in RV free wall area. During severe pressure overload, the interventricular septum shifts, increasing RV diastolic volume with little increase in RV free wall surface area. Without an increase in surface area, the RV cannot recruit additional function via the Frank-Starling mechanism. At the same time, there is a reduction in LV end-diastolic volume and surface area, resulting in impaired LV pump function ***(Reproduced from Greyson CR. Crit Care Med. 2008; 36:S57-65. Copyright 2008, with permission from Lippincott, Williams & Wilkins)*** LV indicates left ventricle; RV, right ventricle.