Introduction

Heart failure (HF) was classically viewed as synonymous with left ventricular pump dysfunction, usually progressive, resulting in a common end-stage cardiac phenotype of dilation, thinned walls, and poor contractility **(Mann and Bristow, 2005).**

The prevalence of HF follows an exponential pattern, and it rises with age. Heart failure affects 6% to 10% of people over the age of 65 years. Although the relative incidence is lower in women than in men, women constitute at least half of the cases of HF because of their longer life expectancy. In the U.S., the treatment of HF has a direct cost of over $34 billion per year, most of which results from hospitalization **(Fang et al., 2008)**.

Heart failure may be caused by myocardial failure but may also occur in the presence of near-normal cardiac function under conditions of high demand. Heart failure always causes circulatory failure, but the converse is not necessarily the case, because various noncardiac conditions (eg, hypovolemic shock, septic shock) can produce circulatory failure in the presence of normal, modestly impaired, or even supranormal cardiac function. To maintain

the pumping function of the heart, compensatory mechanisms increase blood volume, cardiac filling pressure, heart rate, and cardiac muscle mass. However, despite these mechanisms, there is progressive decline in the ability of the heart to contract and relax, resulting in worsening heart failure **(O'Riordan, 2014)**.

Most patients admitted to the hospital with HF have a worsening of chronic HF, although 15% to 20% of HF hospitalizations represent new diagnoses of HF. Patients with a new diagnosis of HF are much more likely to present with pulmonary edema or cardiogenic shock, while decompensation of chronic HF usually presents with other signs of congestion and fluid retention, such as weight gain, exertional dyspnea, or orthopnea. These symptoms can begin days or weeks before presentation. A history of coronary artery disease (CAD) is present in 60% of patients, hypertension in 70%, diabetes in 40%, and renal impairment in 20% to 30%. At presentation, most HF patients are relatively normotensive. Patients admitted with HF having a relatively preserved LVEF tend to be older, female, and more likely to present with severe hypertension **(Fonarow et al., 2007)**.

Evidence-based treatment of heart failure includes Angiotensin-Converting Enzyme Inhibitors (ACE-I), Angiotensin II Receptor Blockers (ARB-II's), β-blockers,diuretics,aldosterone antagonists,and digitalis.They have shown their efficacy in improving the symptoms and natural history of heart failure independently of its cause. Diuretic therapy is certainly effective in improving symptoms in heart failure patients **(Flather et al., 2000)**.

Novel therapies for HF are promising as Angiotensin receptor-neprilysin inhibition with LCZ696, new aldosterone receptor blockers, serelaxin, ularitide, etc **(McMurray et al., 2013).**

Aim of the work

The aim of the study to discuss novel therapies of heart failure.

Anatomy and physiology of the heart

The heart is a midline, valvular, muscular pump that is cone-shaped and lies in the middle mediastinum of the thorax. The inferior (diaphragmatic) surface sits on the central tendon of the diaphragm, and the base faces posteriorly and lies immediately anterior to the esophagus and descending aorta. The base comprises mainly the left atrium, with a small amount of right atrium. The left surface (left ventricle) and right surface (right atrium) are each related laterally to a phrenic nerve and a lung. The segmental approach involves the sequential analysis of the three cardiac segments, atria, ventricles and great arteries, and knowledge of their connections **(Whitaker, 2010)**.

The atria:

The right atrium normally lies in the right hemithorax, and receives blood from the right-sided superior and inferior vena cava and, the coronary sinus. Identification of the right atrium as an anatomic structure in an abnormal heart is achieved by considering the visceroatrial situs, the great veins, and the atrial morphology. The right atrium normally receives the systemic venous return and flow from the

coronary sinus. Distinguishing morphologic features include the presence of the terminal sulcus and crest, and the rim of the oval fossa with the distinctive shape of the right atrial appendage, "a blunt triangle with a broad junction to the venous component of the atrium." The left atrium contains the flap-valve aspect of the fossa ovalis with the left atrial appendage that is narrower than the right-sided appendage.

(Anderson, 2010).

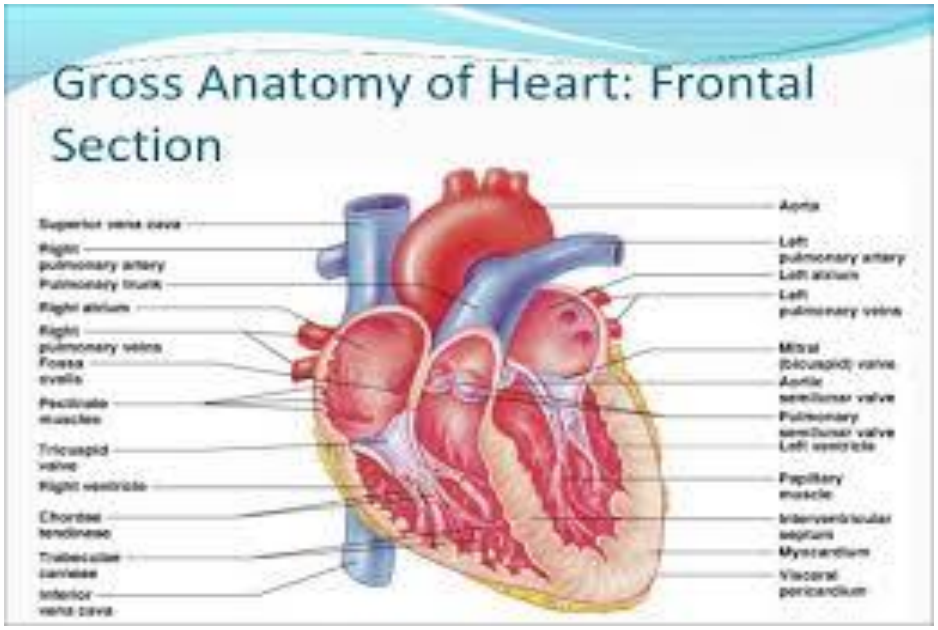
Ventricles and atrioventricular connections:

Right and left ventricles:

Ventricles are defined by their anatomic structure, not by their spatial relationships. Thus, the anatomic right ventricle is heavily trabeculated, while the anatomic left ventricle has a smoother lining with fine trabeculations. The right ventricle is a more triangular or pyramidal shape while the left ventricle is bullet ellipsoid shape. Depending on the ventricular loop during development, the right ventricle may be located spatially on the right or left side of the heart. When the ventricles are inverted, the anatomic left ventricle generally lies to the right and the anatomic right ventricle lies to the left **(Whitaker, 2010).**

Great vessel connections:

There may or may not be normal connections of the great vessels. When the great vessels are abnormally connected or related they are termed malposed. There are four types of malposition: transposition of the great arteries, double outlet right ventricle, double outlet left ventricle, and anatomically corrected malposition **(Figure 1) (Anderson, 2010)**.



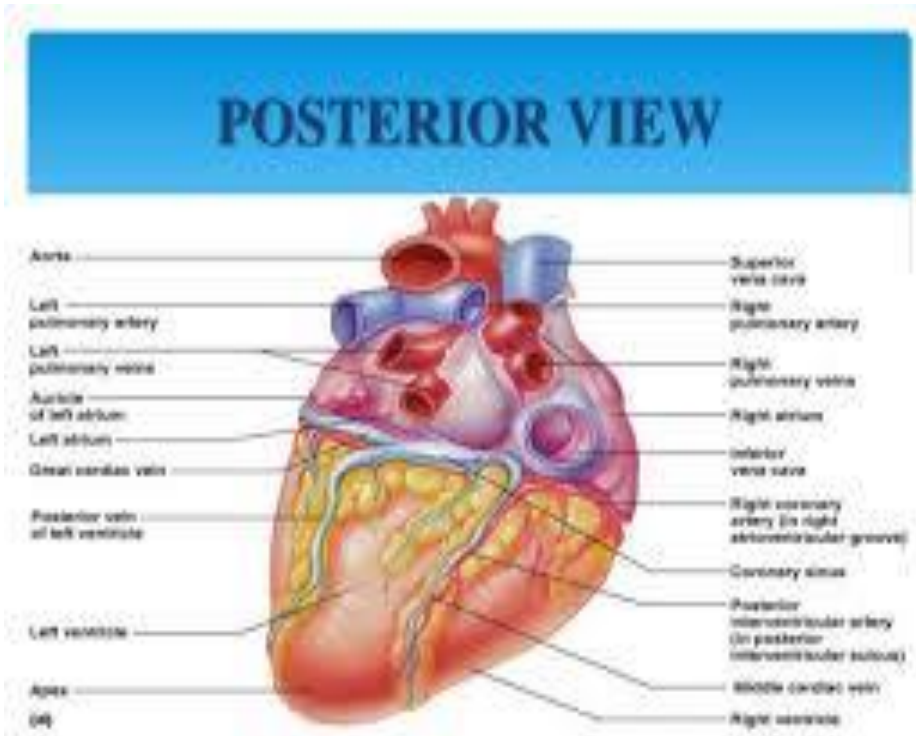


Figure (1): Anatomy of the heart **(Iaizzo, 2009)**

Blood supply of the heart:

The heart derives its arterial supply from the right and left coronary arteries **(Figure 2)**, which are the earliest branches of the aorta. The aortic root presents three natural dilatations termed the aortic sinuses (sinuses of Valsalva); one above each cusp of the aortic valve. Two of these sinuses (right and left aortic sinuses) give rise to the right and left coronary arteries respectively. Typically, the right coronary artery is of greater caliber than the left **(Cohn and Edmunds, 2003)**.

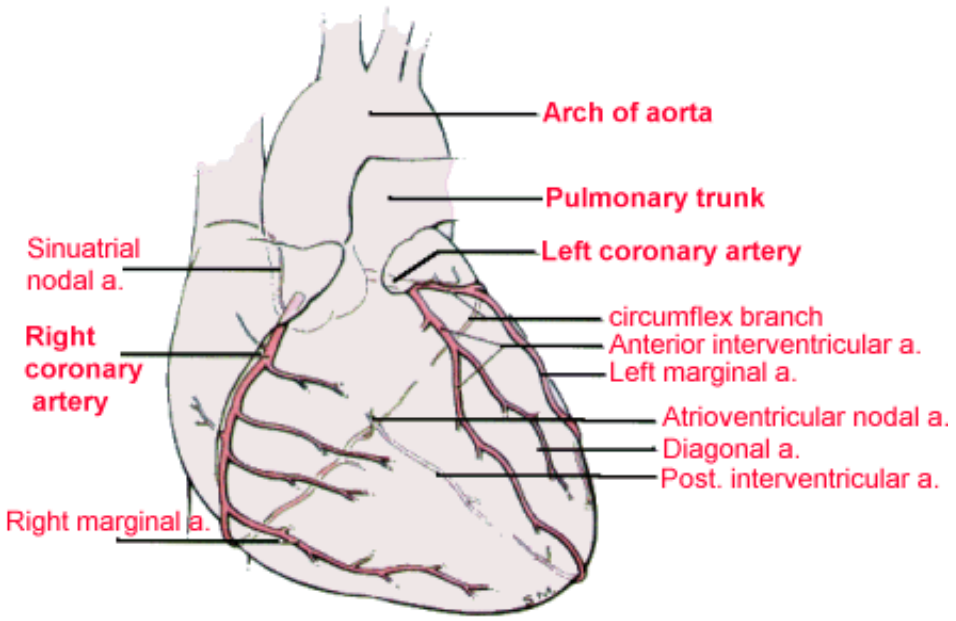


Figure (2): Blood supply of the heart **(Cohn and Edmunds, 2003)**

Right coronary artery:

From its origin, the right coronary artery runs between the right auricle (right atrial appendage) and infundibulum of the right ventricle, and then vertically downwards in the atrioventricular groove on the anterior aspect of the heart. On reaching the inferior heart border, it turns backwards to continue in the atrioventricular groove on the inferior (diaphragmatic) surface of the heart. While on the anterior aspect of the heart the right coronary artery gives:

- Multiple small branches to the right atrium.
- The sinoatrial nodal artery (in 55-60% of individuals).
- A branch to the infundibulum of the right ventricle (the right conus branch).
- Additional branches to the anterior aspect of the right ventricle including the right (acute) marginal artery which runs just above the inferior margin of the heart.
- The atrioventricular nodal artery (in 90% of individuals).
- The posterior interventricular artery (in 90% of individuals), which supplies the posterior one-third of the interventricular septum, the inferior surface of the right ventricle and a portion of the inferior surface of the left ventricle. The termination of the right coronary artery,

now much reduced in calibre, anastomoses (at the arteriolar level) with the termination of the circumflex branch of the left coronary artery in the posteroinferior part of the atrioventricular sulcus.

(Moffat, 1993)

Left coronary artery:

Arising from the left aortic sinus, the left coronary artery passes leftwards, between the left atrial appendage and pulmonary trunk, to enter the posterosuperior part of the atrioventricular sulcus. Within a few millimetres of its origin, the left coronary artery gives off (in about 40% of individuals) the sinoatrial nodal artery. Soon after, it gives off a fairly large branch, the anterior interventricular artery (which, in the nomenclature of cardiac physicians, surgeons and radiologists, is termed the left anterior descending artery), and continues in the atrioventricular groove as the circumflex artery. The anterior interventricular artery runs down the anterior interventricular groove towards the cardiac apex where it anastomoses (at the arteriolar level) with the termination of the posterior interventricular branch of the right coronary artery **(Lumely et al., 1995)**.

Venous drainage of the heart:

Most of the venous blood return from the heart enters the coronary sinus (a 2-3-cm long venous sac in the posterior part of the atrioventricular sulcus). The coronary sinus receives the following veins **(Figure 3):**

- Great cardiac vein (which initially accompanies the anterior interventricular artery and then the circumflex artery).
- Middle cardiac vein (which accompanies the posterior interventricular artery).
- Small cardiac vein (which accompanies the right marginal artery).
- Posterior vein of the left ventricle.
- Oblique vein of the left atrium.

Some of the venous blood is returned by the anterior cardiac veins, small venous channels which run on the anterior aspect of the right atrium and open directly into the latter. Finally, a negligible amount of venous blood is returned to the heart by the Thebesian veins, which drain into all four chambers of the heart **(Cohn and Edmunds, 2003)**.

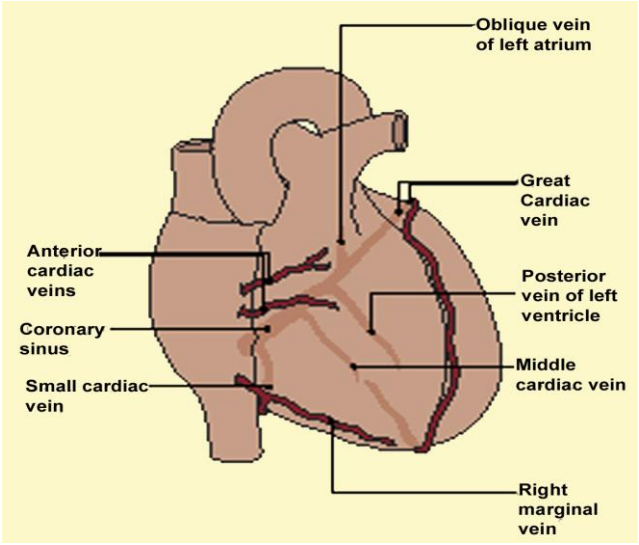


Figure (3): Venous drainage of the heart **(Cohn and Edmunds, 2003)**

Cardiac physiology :

Human heart is actually two pumps in one. The right side receives oxygen-poor blood from the various regions of the body and delivers it to the lungs. In the lungs, oxygen is absorbed in the blood. The left side of the heart receives oxygen-rich blood from the lungs and delivers it to the rest of the body ***(*Maton and Anthea, 1993).**

The contraction of the cardiac muscle tissue in the ventricles is called systole. When the ventricles contract, they force the blood from their chambers into the arteries leaving the heart. The left ventricle empties into the aorta and the right ventricle into the pulmonary artery. The increased

pressure due to contraction of the ventricle is called systolic pressure.

The relaxation of the cardiac muscle tissue in the ventricles is called diastole. When the ventricles relax, they make room to accept the blood from the atria. The decreased pressure due to relaxation of the ventricle is called diastolic pressure **(Guyton and Hall, 2006)**.

Electrical conduction system:

The heart is composed primarily of muscle tissue. A network of nerve fibers coordinates the contraction and relaxation of the cardiac muscle tissue to obtain an efficient wave-like pumping action of the heart.

The SinoAtrial Node (often called SA node or sinus node) serves as the natural pacemaker for the heart. Nestled in the upper area of the right atrium, it sends the electrical impulse that triggers each heart beat. The impulse spreads through the atria, prompting the cardiac muscle tissue to contract in a coordinated wave-like manner **(Cecie and Lisa, 2009)**.

The impulse that originates from the SA node strikes the AtrioVentricular node (or AV node) which is situated in the

lower portion of the right atrium. The AV node is in turn sends an impulse through the nerve network to ventricles initiating the same wave-like contraction of the ventricles. The electrical network serving the ventricles, leaves the AV node through the right and left bundle branches. These nerve fibers transmit the impulses that cause the cardiac muscle tissue to contract (**Figure 4):**

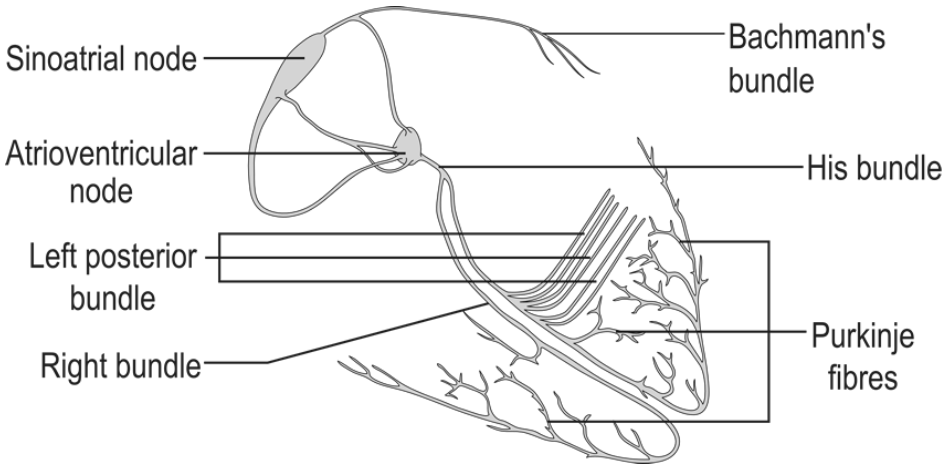


Figure (4): Electrical conduction nerve system of the heart.

(Cecie and Lisa, 2009)