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The Pathology of Heart Failure

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Introduction

The topic I have chosen to research is heart failure. I have chosen this topic because I have treated many patients in the ICU with this condition, and find it an interesting pathology. Heart failure affects a significant portion of the patient population, and the rates are increasing. 5.1 million Americans ≥20 years of age have heart failure, projections show that by 2030, the prevalence of HF will increase 25% from 2013 estimates. At 40 years of age, the lifetime risk of developing HF for both men and women is 1 in 5. At 80 years of age, remaining lifetime risk for development of new HF remains at 20% for men and women, even in the face of a much shorter life expectancy. While patients are now living longer after initial diagnosis, about half of the patients diagnosed die within five years. Projections from the American Heart Association show in 15 years, the total cost of HF will increase almost 120% to $70 billion from the current estimated total cost of $32 billion.

Signs and Symptoms

The symptoms of heart failure can be divided into two categories; typical and less typical. Typical symptoms include shortness of breath, orthopnea, paroxysmal nocturnal dyspnea, decreased activity tolerance, fatigue/tiredness, and ankle swelling. Less typical symptoms include wheezing, nocturnal cough, weight gain(more than 2 kg in a week), weight loss(in advanced heart failure), loss of appetite, confusion more common in elderly), depression, palpitations, and syncope.

Signs of heart failure can also be divided into two categories; specific and less specific. Specific signs include elevated jugular pressure, hepato-jugular reflux, a third heart sound(gallop), laterally displaced apical impulse, and cardiac murmur. Less specific signs include sacral or scrotal edema, tachycardia, irregular pulse, tachypnea, hepatomegaly, ascites, and cachexia.

the echocardiogram and electrocardiogram (ECG) are the most useful tests in patients with suspected HF. A variety of ECG findings may occur for a patient in heart failure, and no sole specific abnormality is indicative of heart failure. However, less than 2% of patients with heart failure will have a normal ECG. This means that heart failure should at least be considered as a diagnosis in patients with any ECG abnormalities.

The specific ECG abnormality may be used to guide treatment of HF. The echocardiogram provides immediate information on chamber volumes, ventricular systolic and diastolic function, wall thickness, and valve function. The echocardiogram is central not only in the diagnosis of heart failure, but also in the identification of which specific type of heart failure. Findings and their corresponding abnormalities and implications can be seen in the table below

Measurement	Abnormality	Clinical implications
Parameters related to systolic function		
LV ejection fraction	Reduced (<50%)	LV global systolic dysfunction
LV fractional shortening	Reduced (<25%)	LV radial systolic dysfunction
LV regional function	Hypokinesis, akinesis, dyskinesis	Myocardial infarction/ischaemia Cardiomyopathy, myocarditis
LV end-diastolic size	Increased (diameter ≥60 mm, >32 mm/m², volume >97 mL/m²)	Volume overload HF likely
LV end-systolic size	Increased (diameter >45 mm/>25 mm/m², volume >43 mL/m²)	Volume overload HF likely
LV outflow tract velocity time integral	Reduced (<15 cm)	Reduced LV stroke volume
Parameters related to diastolic function		
LV diastolic dysfunction parameters	Abnormalities of the mitral inflow pattern, tissue velocities (e') or the E/e' ratio	Indicate LV diastolic dysfunction degree and suggest level of filling pressure
Left atrial volume index	Increased (volume >34 mL/m²)	Increased LV filling pressure (past or present) Mitral valve disease
LV mass index	Increased: >95 g/m² in women and >115 g/m² in men	Hypertension, aortic stenosis, hypertrophic cardiomyopathy
Parameters related to valvular function		
Valvular structure and function	Valvular stenosis or regurgitation (especially aortic stenosis and mitral regurgitation)	May be the cause of HF or a complicating factor or the result of HF (secondary mitral regurgitation) Assess dysfunction severity and haemodynamic consequences Consider surgery
Other parameters		
RV function (e.g.TAPSE)	Reduced (TAPSE <16 mm)	RV systolic dysfunction
Tricuspid regurgitation peak velocity	Increased (>3.4 m/s)	Increased RV systolic pressure
Systolic pulmonary artery pressure	Increased (>50 mmHg)	Pulmonary hypertension likely
Inferior vena cava	Dilated, with no respiratory collapse	Increased right atrial pressure RV dysfunction, volume overload Pulmonary hypertension possible
Pericardium	Effusion, haemopericardium, calcification	Consider tamponade, malignancy, systemic diseases, acute or chronic pericarditis, constrictive pericarditis

E/e' = ratio of the mitral inflow E wave to the tissue Doppler e' wave; HF= heart failure; LV = left ventricular; RV = right ventricular; TAPSE = tricuspid annular plane systolic excursion.

Underlying Pathology

Heart failure is a disease that results from the body compensating for a drop in cardiac output or blood pressure. Compensatory mechanisms help maintain cardiac output(increased contractility) and BP(vasoconstriction). However, these compensatory changes over months and years can eventually worsen cardiac function. Any phenomenon that can cause impaired cardiac output or low blood pressure can therefore be a cause of heart failure, some examples include cardiac structural abnormalities, MIs, HTN, diabetes, and respiratory diseases.

Sympathetic Nervous System – The Neurohumoral Response

The hypothalamus begins the response to suboptimal cardiac output or BP. It begins the process by signaling for the adrenal glands to release epinephrine (EPI), and for noradrenergic neurons to release norepinephrine(NE). EPI and NE target adrenergic receptors, with the beta 1, beta 2, and alpha 1 receptors having the greatest affect on cardiac performance.

Alpha affects

Alpha1-ARs heavily populate major arteries (including the aorta, pulmonary arteries, mesenteric vessels, and coronary arteries) and activation of these receptors is a major contributor to the regulation of blood flow because they trigger vasoconstriction, resulting in increased cardiac output.

Beta affects

Activation of beta1- and beta2-ARs is the most powerful physiologic mechanism to acutely increase cardiac performance. Beta 1-ARs activate Gs proteins whereas beta 2-ARs use both Gs and Gi proteins. Gs signaling acts as a "receptor-accelerator," and Gi signaling as a "receptor-brake". Gs signaling stimulates the effector enzyme, adenyl cyclase, resulting in dissociation of adenosine triphosphate (ATP) into the second messenger(cAMP), which in turn binds to cAMP-dependent protein kinase A. Targets of protein kinase A-induced phosphorylations in the AR signaling pathway are:

1) the L-type calcium channels and ryanodine receptors, causing an increase in calcium entry into the cell.
2) the hyperpolarization-activated cyclic nucleotide-gated channels, which generate the hyperpolarization-activated cation inward current, stimulating pacemaker cells of the heart to increase the heart rate.
3) phospholamban, a modulator of the sarcoplasmic reticulum associated ATP-dependent calcium pump, which increases calcium reuptake by the sarcoplasmic reticulum, accelerating cardiac relaxation.
4) troponin I and myosin binding protein-C, which reduce myofilament sensitivity to calcium, accelerating the relaxation of myofilaments.
5) phospholemman, a subunit of Na+/K+-ATPase, relieving its inhibitory influence and resulting in the stimulation of the sodium pump.

These affects combine to increase heart rate and contractility.

Renin-Angiotensin-Aldosterone System

The RAAS plays an important role in increasing vascular volume and vascular resistance. RAAS is activated by beta 1, low BP, or low sodium in the kidneys. When renin is released into the blood, it acts upon a circulating substrate, angiotensinogen, that undergoes proteolytic cleavage to form angiotensin I. Vascular endothelium, particularly in the lungs, has angiotensin converting enzyme (ACE), that cleaves off two amino acids to form the octapeptide, angiotensin II (AII), although many other tissues in the body (heart, brain, vascular) also can form AII. Angiotensin II has the following affects:

-Arterial constriction, thereby increasing systemic vascular resistance and arterial pressure

-Stimulates sodium transport (reabsorption) in renal tubules, increasing sodium and water retention

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-Acts on the adrenal cortex to release aldosterone, which in turn acts on the kidneys to increase sodium and fluid retention

-Stimulates the release of vasopressin (antidiuretic hormone, ADH) from the posterior pituitary, which increases fluid retention by the kidneys

-Stimulates thirst

-Facilitates norepinephrine release from sympathetic nerve endings and inhibits norepinephrine re-uptake by nerve endings, thereby enhancing sympathetic adrenergic function

Remodeling

Once the above phenomenon have taken place, the remodeling process results, which is what puts a patient into heart failure. Although an exact picture of all the pathways and cells involved in remodeling is still unclear, the following scenario has been proposed at a molecular level. As myocytes stretch, local norepinephrine activity and angiotensin and endothelin release are increased. These changes stimulate expression of altered proteins and myocyte hypertrophy. The end result is further deterioration in cardiac performance and increased neurohormonal activation. In addition, increased activation of aldosterone and cytokines may also stimulate collagen synthesis, thus leading to fibrosis and remodeling of the extracellular matrix. The heart becomes enlarged to the point that it does not pump blood effectively, and signs and symptoms of heart failure begin.

Right Sided vs. Left Sided Failure

While much of the molecular process is the same for right heart failure as it is for left heart failure, the affects are different. Instead of fluid backing up into the lungs as it does with left sided failure, fluid backs up into the venous system, causing swelling in the periphery, typically in the lower extremities.

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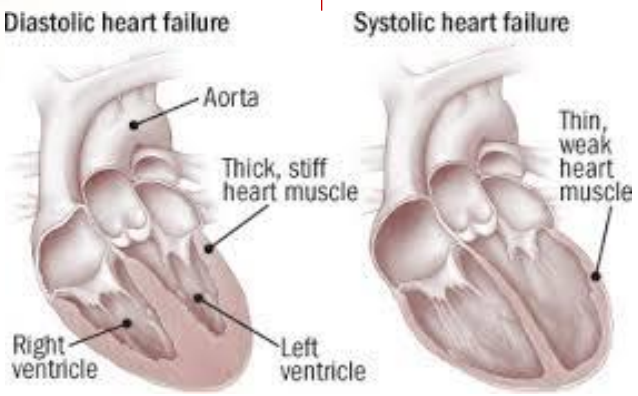
Systolic vs. Diastolic Failure

Once the diagnosis of heart failure has been made, the diagnosis may be classified as systolic or diastolic failure. This differentiation is primarily made using the left ventricular ejection fraction(LVEF), revealed by an echocardiogram. A reduced LVEF is indicative of systolic heart failure, while a normal result indicates the failure is diastolic. The neurohormonal process is similar for both types of failure, the difference originates from the remodeling process.

In systolic heart failure(SHF), the remodeling process has resulted in a larger left ventricle and larger left ventricular cavity, but the wall thickness is decreased or unchanged.

The heart wall does not have enough muscle mass to overcome the increased amount of blood in the ventricle, so a less than optimal amount of blood is ejected. In diastolic heart failure(DHF), the remodeling process has resulted in an increased wall thickness, but the size of the left ventricular cavity has not increased, or has decreased. The ventricular contraction ejects enough blood to result in a normal LVEF, but since the volume of blood in the ventricle before the contraction was lower than normal, ejecting a normal percentage of it is still inadequate.



Diastolic heart failure involves thickened heart muscle that reduces maximum filling volume of ventricles. Systolic heart failure features thin heart muscle that is too weak to eject the increased volume of blood filling the larger ventricles.

Nursing Implications

Individuals diagnosed with heart failure may be treated medically and with lifestyle modifications. To avoid fluid overload, salt intake should be restricted to 2-3g sodium diets. Fluid restriction is also recommended, and patients should weigh themselves frequently to monitor their status. Exercise should be encouraged. Medical management includes the use of diuretics to decrease fluid overload, nitrates to reduce vascular resistance, and beta blockers to suppress sympathetic stimulation of heart rate, contractility, and vasoconstriction. ACE inhibitors may be prescribed to interrupt the renin-angiotensin-aldosterone system's affects. Treatments of chronic heart failure do not cure the disease, but slow its progression and make symptoms more manageable. Patients in acute heart failure will need emergent intervention, including administration of nitrates and diuretics as appropriate with BP. Inotropic agents are generally not recommended unless the patient is in cardiogenic shock, because inotropic drugs increase the workload of the heart. If cardiac output is severely compromised, inotropic meds may be considered. Dobutamine is the inotrope of choice for increasing cardiac output, blood pressure, and peripheral circulation. In the patient with heart failure that has produced pulmonary edema, CPAP may be considered

Conclusions

Rates of heart failure are increasing. Understanding the pathology and progression of the disease can help healthcare providers assist patients in their management of heart failure. Patient education and adherence to treatment plans is very important in successfully managing the disease, and improving quality of life.

References

Wrigley, Benjamin J., Lip, Gregory Y.H., & Shantsila, Eduard. (2014). The role of monocytes and inflammation in the pathophysiology of heart failure. *European Journal of Heart Failure.* Volume 13, Issue 11, 1161-1171 DOI: 10.1093/eurjhf/hfr122

Haddad, F., Doyle, R., Murphy, D., Hunt, S. (2008). Right ventricular function in cardiovascular disease. *Contemporary Reviews in Cardiovascular Medicine.* 117: 1717-1731. doi: 10.1161/CIRCULATIONAHA.107.653584

Triposkiadis, F., Karayannis, G., Giamouzis, G., Skoularigis, J., Louridas, M., Butler, J. (2009). The sympathetic nervous system in heart failure. *Journal of the American College of Cardiology.* 54(19): 1747-1762. doi:10.1016/j.jacc.2009.05.015

Neiderer, S., Smith, N. (2009). The role of the Frank-Starling law in the transduction of cellular work to whole organ pump function: A computational modeling analysis. *Computational Biology.* DOI: 10.1371/journal.pcbi.1000371

McMurray, J. et al. (2012) ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *European Journal of Heart Failure.* 14(8), 803-869. DOI: 10.1093/eurjhf/hfs105

Go, A., Mozaffarian, D., Roger, D., et al. (2013). American heart association statistical update. *American Heart Association.* 127: e6-e245. DOI: 10.1161/CIR.0b013e31828124ad

Klabunde, R. (2011). Cardiovascular physiology concepts, 2nd edition. Chapter 6. ISBN 9781451113846

Levick, R., Michel, C. (2010). Microvascular fluid exchange and the revised Starling Principle. *Cardiovascular Research.* DOI: http://dx.doi.org/10.1093/cvr/cvq062 198-210

Chatterjee,K., Massie, B. (2007). Systolic and diastolic heart failure: similarities and differences. *Journal of Cardiac Failure.* Volume 13, No.7

Grady, K., Dracup, K., Kennedy, G., Moser, D., Piano, M., Stevenson, L., Young, J. (2000). Team management of patients with heart failure. *American Heart Association.* 102: 2443-2456. Doi: 10.1161/01.CIR.102.19.2443

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