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Breathless: Cardiac Output and Congestive Heart Failure Case Review

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Abstract: ***A moderately obese 63-year-old male presented with symptoms of extreme breathlessness that had been worsening since last three months. He also complained of peripheral edema, jugular vein distension, and a frothy and productive cough. The patient had tachypnoea with labored breathing and he had tachycardia with an irregular pulse. In the past history, the patient had history of a cardiac infarction and had undergone coronary artery bypass surgery. Based on the patient's medical history, physical exam, and test results, he was diagnosed to be suffering from congestive heart failure resulting in pulmonary and systemic edema. After initial treatment, the patient was prescribed a low sodium diet, diuretics, a positive inotropic agent (Digoxin), and an ACE inhibitor (Captopril) to reduce fluid overload and reduce the workload onthe heart. While these are effective methods for reducing the symptoms of congestive heart failure, it is an irreversible disease and researchers are searching for alternative forms of treatment. Our case review deals with the recent updates in the treatment protocols and prognostication of patients for better patient outcomes.***

Keywords: congestive cardiac failure, digoxin, Framingham classification, NYHA classification, RAAS, Ottawa heart failure risk score

1. Introduction

Congestive heart failure (CHF) is a chronic condition in which the heart cannot pump enough blood to the body. CHF affects almost 6 million Americans and nearly 700, 000 people are diagnosed with CHF annually (Lloyd-Jones, 2008). The most common causes of CHF are coronary artery disease, hypertension, and diabetes (CDC, 2010). These conditions may damage or weaken the heart to the point where it can no longer meet the normal demands of the body and eventually causes blood to back up into other organs, hence the "congestion" part of CHF (Mayo Clinic: Heart Failure, 2011). Jugular venous distension (JVD), the presence of distension in the neck veins, is indicative of increased blood pressure and increased central venous pressure (CVP), the blood pressure in the thoracic vena cava filling the right atrium of the heart. Therefore, JVD can reveal information about the pressure in the right atrium where blood is being returned to the heart from the systemic circulation. CVP is a strong determinant of right ventricular end diastolic volume and provides information about the right atrium and right ventricle. Typically, cases of elevated jugular venous pressure are indicative of right-sided congestive heart failure, a condition where the heart fails to keep blood moving sufficiently ([3] (Applefeld, 1990). Consequently, the amount of oxygen delivered to the tissues decreases, causing the kidneys to reabsorb water and salt from2 the blood, known as renal hypoperfusion. Renal hypoperfusion increases salt and water retention, thereby increasing fluid volume. This increases the workload of the heart, causing hypertrophy and increased heart rate in an attempt to provide the body with oxygen-rich blood ([4]. The veins swell with fluid as blood volume increases, altering the balance of pressures between fluids inside and outside the blood vessels. Fluids then seep into surrounding tissues, causing edema (Kay & Davis, 1999). Additionally, increased hydrostatic pressure on the vessels caused by hypotension can cause blood to leak through vessel membranes and eventually pool ([6] (Priollet, 2006). CHF may alter the homeostatic balance of the kidneys and could damage the endocrine system if left untreated (Kalra et al., 2001).

Pulmonary edema is a condition in which fluid backs up into the lungs from the left atrium. As a result, lung function is compromised due to improper oxygen exchange in the alveoli. A common symptom associated with pulmonary edema is shortness of breath attributable to the alveoli being saturated with fluid instead of oxygen ([5]. If left untreated, right ventricular failure is likely to occur due to increased pressure on the right ventricle. Increased pressure can even backup into the right atrium and eventually into the systemic circulation, resulting in peripheral edema, ascites, and swelling of the liver (Mayo Clinic: Pulmonary Edema, 2011).

2. Objectives

- Review the pathophysiology of congestive heart failure.
- Describe the diagnostic approach to patients presenting with clinical features of congestive heart failure.
- Outline the management of congestive heart failure.
- Explain the importance of collaboration and communication among the interprofessional team to educate the patients on the importance of medication compliance to improve outcomes for those with congestive heart failure.

3. Case Presentation

A 63-year-old male arrived in the emergency room complaining of breathlessness for the past three days. He had a history of a myocardial infarction three years prior that was followed with a four-vessel coronary artery bypass, but had been asymptomatic since his surgery and had no complaints of chest pain. The patient noted shortness of

breath while carrying out average daily activities over the past three months, and also had difficulty sleeping flat on his back the last four nights before his admission to the ER. Two weeks prior to his ER visit, he was unable to complete his daily walk and noted swelling in his lower extremities. His chief complaint uponarrival was extreme shortness of breath without chest pain. The patient's vital signs were measured and blood samples tested; the results are summarized in the patient data table (Table 1).

Table 1: Patient Data

Data	Patient Value	Normal Value	Physiological Significance
Blood Pressure	108/52 mmHg	120/80 mmHg	Low – Hypotension (4)
Pulse	140 beats/min & irregular	60-100 beat/min	High - Tachycardia
Respiration Rate	30 breaths/min and labored	12 breaths/min	High – Shortness of breath
Na^+	130 mmol/l	135 - 147 mmol/l	Slightly low
K^+	3.8 mmol/l	3.5 – 5 mmol/l	Normal
$HCO3^-$	20 mmol/l	22 - 28 mmol/l	Low
BUN	18 mg/dl	8 - 23 mg/dl	Normal
Creatinine	1.0 mg/dl	0.8 - 1.3 mg/dl	Normal
pH	7.30	7.35 – 7.45	Low – slightly acidotic
PaO_2	55 mHg	80 – 100 mmHg	Low - Hypoxic
$PaCO_2$	28 mmHg	35-45 mmHg	Low

The patient is shown to be hypotensive with rapid heart rate and respiration rate. Blood tests show low sodium and carbonate ion levels, slightly acidic blood, and low oxygen and carbon dioxide partial pressures. Other indicators fall within the normal range. Physical examination revealed severe peripheral and pulmonary edema, as well as an enlarged and irregular heart. The evidence and physiological consequences are shown in Table 2.

Table 2: Patient Evidence Table

Evidence	Physiology	Physiological Consequence
Extreme SOB	Fluid buildup in lungs is increasing pressure	Increased pressure in lungs reduces oxygen exchange
Peripheral Edema	Backup of blood in lower extremities	Failure of ventricles to efficiently pump blood
JVD	Due to high pressure in the jugular vein caused by fluid backup	Right heart isn't functioning properly →causing fluid backup
Scattered ronchi & rales	Caused by fluid accumulation in lungs	Pulmonary edema due to insufficient blood pumping
Productive/ frothy cough	Caused by acute pulmonary edema	Pulmonary edema due to CHF
Systolic murmur & S3 gallop	S3 sound is the result of vibration of the ventricular walls caused by rapid ventricular filling	S3 sound indicative of left ventricular systolic dysfunction
Left bundle branch block & AFIB	Problems with conduction of electrical impulses	Improper electrical conduction leads to AFIB and irregular HR
Cardiomegaly	Heart is working harder to pump blood	Heart muscle enlarges as result of increased workload
Normal BUN/ Creatinine levels	Kidneys are still filtering properly	High BUN/Creatinine would indicate decreased renal function

This table lists evidence for the diagnosis of congestive heart failure. Physical examination revealed distended neck veins with visible cannon waves, jugular vein distension to 12 cm, and carotids without bruits. Auscultation of his chest revealed scattered rhonchi throughout and bilateral rales and he had a productive and frothy cough indicative of pulmonary edema. Palpation of the patient's abdomen revealed a palpable liver 3 cm below the right costal margin and auscultation of the heart revealed a grade 3/6 systolic murmur and an S3 gallop indicative of left ventricular dysfunction. There was also 4+ pitting edema of the lower extremities indicative of fluid overload. An electrocardiogram (ECG) revealed a left bundle branch block and atrial fibrillation with a ventricular rate of 140 BPM. Examination of his chest x-ray revealed cardiomegaly with diffuse pulmonary infiltrate, which was consistent with pulmonary edema. Each symptom has a physiological consequence that contributes to shortness of breath, edema, or increased workload for the heart. The patient's history, symptoms, and test results were consistent with CHF and an echocardiogram was ordered. Though there was not yet evidence of renal failure in the patient's labs, the kidneys may already have been attempting to regulate the sodium concentration in order to reach a homeostatic balance in this patient (Kalra et al., 2001). He was placed on a fluid restriction to 1.5L and a low sodium diet. The patient was prescribed diuretics (Lasix and Metolatzone), an inotropic agent (Digoxin) and an ACE inhibitor (Captropril) to treat the fluid overload and reduce the workload on his heart. He was also educated about following an appropriate diet.

4. Discussion & Conclusion

Classification of heart failure is based on symptoms and calculated left ventricular ejection fraction (LVEF). Heart failure due to left ventricular dysfunction is categorized into heart failure with reduced ejection fraction (HFrEF), heart failure with preserved ejection fraction (HFpEF), and heart failure with mid-range ejection fraction (HFmrEF). The latter may consist of mixed left ventricular dysfunction (a combination of systolic and diastolic heart failure). The definition of HFrEF has varied among different studies and guidelines but is generally defined as an ejection fraction (EF) of less than 40%. Heart failure with preserved ejection fraction (HFpEF) is generally defined as heart failure with an EF of greater than 50%. HFmrEF is defined as heart failure with an EF of 40% to 50%.1[8]

Framingham Diagnostic Criteria for Heart Failure
The commonly used Framingham Diagnostic Criteria for Heart Failure requires the presence of 2 major criteria or 1 major and 2 minor criteria to make the diagnosis of heart failure. This diagnostic tool is highly sensitive for the diagnosis of heart failure but has a relatively low specificity. The Framingham Diagnostic criteria are as follows: . [24]

Major Criteria
Acute pulmonary edema
Cardiomegaly
Hepatojugular reflex
Neck vein distention
Paroxysmal nocturnal dyspnea or orthopnea
Pulmonary rales

Third heart sound (S3 Gallop)
Weight loss of 4.5 kg or more in 5 days in response to treatment
Central venous pressure greater than 16 cm of water
Radiographic cardiomegaly.

Minor Criteria
Ankle edema
Dyspnea on exertion
Hepatomegaly
Nocturnal cough

Pleural effusion Tachycardia (heart rate greater than 120 beats per minute) A decrease in vital capacity by one third the maximal value recorded

New York Heart Association Functional Classification Based on symptoms, the patients can be classified using the New York Heart Association (NYHA) functional classification as follows: [[25]

Class I: Symptom onset with more than ordinary level of activity
Class II: Symptom onset with an ordinary level of activity
Class III: Symptom onset with minimal activity
Class IIIa: No dyspnea at rest
Class IIIb: Recent onset of dyspnea at rest
Class IV: Symptoms at rest

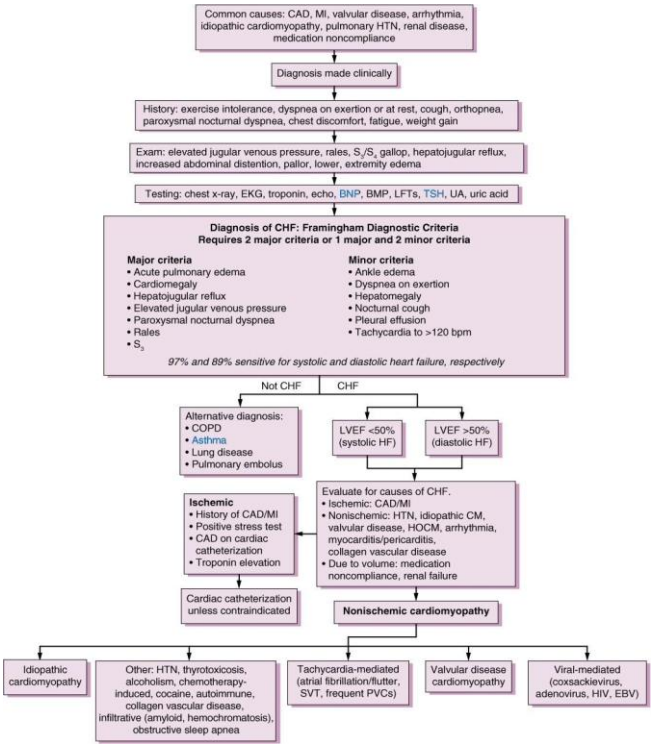
Pathophysiology
The adaptive mechanisms that may be adequate to maintain the overall contractile performance of the heart atrelatively normal levels become maladaptive when trying to sustain adequate cardiac performance.

In the initial stages of congestive heart failure, cardiac physiology attempts to adapt via several compensatory mechanisms to maintain cardiac output and meet the systemic demands. These include the Frank-Starling mechanism, changes in myocyte regeneration, myocardial hypertrophy, and myocardial hypercontractility. With increased wall stress, the myocardium attempts to compensate via eccentric remodeling, which further worsens the loading conditions and wall stress. [26]

A decrease in cardiac output stimulates the neuroendocrine system with a release of epinephrine, norepinephrine, endothelin-1 (ET-1), and vasopressin. They cause vasoconstriction leading to increased after load. There is an increase in cyclic adenosine monophosphate (cAMP), which causes an increase in cytosolic calcium in the myocytes. This increases myocardial contractility and further prevents myocardial relaxation. An increase in after load and myocardial contractility with impaired myocardial relaxation leads to increased myocardial oxygen demand. This paradoxical need for increased cardiac output to meet myocardial demand eventually leads to myocardial cell death and apoptosis. As apoptosis continues, a decrease in cardiac output with increased demand leads to a perpetuating cycle of increased neurohumoral stimulation and maladaptive hemodynamic and myocardial responses. [26]

A decrease in cardiac output also stimulates the renin-angiotensin-aldosterone system (RAAS), leading to increased salt and water retention, along with increased vasoconstriction. These further fuels the maladaptive mechanisms in the heart and cause progressive heart failure. In addition to this, the RAAS system releases angiotensin II, which has been shown to increase myocardial cellular hypertrophy and interstitial fibrosis. This maladaptive function of angiotensin II has been shown to increase myocardial remodeling. [25]

In HFpEF, there is a decrease in myocardial relaxation and an increase in the stiffness of the ventricle due to an increase inventricular after load. This perpetuates a similar maladaptive hemodynamic compensation and leads to progressive heart failure.



In our case, the patient had atrial fibrillation and rapid heart rate so, his stroke volume (SV) would beexpected to be lower than normal. A rapid heart rate reduces the time available for blood to fill the ventricles and with less blood in the ventricles after diastole, or end-diastolic volume (EDV), there simply is not enough volume for the heart to pump out. As cardiac output (CO) and SV are directly related, CO can also be expected to be reduced, even with the rapid heart rate trying to compensate ([4]. Systolic volume would increase due to the fact that blood is not being pumped out and there is more blood remaining in the ventricle after systole (Widmaier et al., 2011). If end systolic volume is increased, then the blood moving into the ventricle before systole will result in an increase in EDV. Thus, an extremely low ejection fraction is expected because of the combination of a low SV and high EDV ([1]. When the heart is contracting poorly, excess blood remains in the ventricles that is unable to be pumped out. The pooling of blood in the left ventricle is consistent with the S3 gallop noted in the patient's physical examination and is commonly a sign of CHF. In the case of this patient, failing ventricles have caused the backup of blood into the systemic and pulmonary circuits, and its effect has become so severe as to induce pulmonary and peripheral edema. The patient's cardiomegaly is most likely due to his previous MI, though the excess blood may also responsible as increased volume in the left ventricle leads to stretching (Hastings, 2004). When the ventricle is overstretched, fewer actin and myosin

filaments in the heart muscle cells are able to overlap. Together, the actin and myosin cross-bridges determine the force with which a muscle can contract (Cooper, 2000). Thus, the patient's overstretched left ventricle has led to fewer actin and myosin overlaps, a significantly weaker muscle, and reduced contractility ([2]. Due to these explained problems, other possible illnesses can result as explained in Table 3.

Table 2: Differential Diagnosis

Differential Diagnosis		
Illness	**Symptoms**	**Reasoning for Rejection**
Constrictive pericarditis	**Dyspnea**, fatigue, **edema of legs and ankles, swollen abdomen**, weakness, **Kussmaul's sign**, may have distant heart sounds	Not rejected as of yet, need echocardiogram
Cardiac tamponade	Anxiety, **excruciating chest pain**, dyspnea, fainting, cyanosis, swelling of abdomen, palpitations, rapid breathing, Kussmaul's sign	Chest pain is prominent symptom- absent
Restrictive Cardiomyopathy	Dry **cough**, **dyspnea**, fatigue, loss of appetite, swelling of abdomen, edema of feet, uneven or rapid pulse, Kussmaul's sign	Similar symptoms but often caused by diseases in other parts of body – absent
Congestive Heart Failure	Frothy or dry, hacking **cough**, wheezing **breathing**, fatigue, faintness, loss of appetite, **arrhythmia**, **dyspnea**, swollen **abdomen**, **edema**, **S3 gallop**, **rales**, **JVD**, **hepatomegaly**	Key symptoms are present in patient
Pericardial Effusion	**Chest pain**, fever, fatigue, muscle aches, **dyspnea**, **palpitations**, light headed	Chest pain is prominent symptom- absent

The symptoms bolded are what either support or reject the differential diagnoses. The prominent symptom of cardiac tamponade and pericardial effusion is chest pain and since the patient lacks this symptom, these illnesses can be rejected. Restrictive cardiomyopathy presents similar symptoms in patients, however this illness is usually acquired from another disease or inherited genetically and there is no family history present. Constrictive pericarditis exhibits similar symptoms and could be further assessed by the echocardiogram. Congestive heart failure is already present in the patient.

The goal of treatment of CHF patients is to manage symptoms, improve exercise tolerance, prolong life, and, when possible, correct the underlying cause. The medications prescribed aim to increase preload and reduce after load. Increasing preload increases stroke volume by providing more blood for the ventricles to pump with each contraction. Fluid reduction and vasodilation reduce after load to reduce the resistance the heart must overcome for circulation ([7].

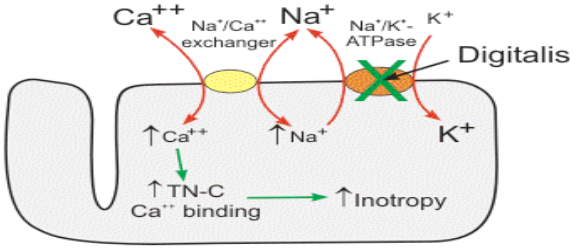


Figure 1

Digoxin is a positive inotropic agent used to regulate the heart by inhibiting Na + /K +ATPase pumps. Digoxin disrupts the normal ion concentration gradients to increase intracellularCa 2+ concentration and increase contractility and ejection fraction. Digoxin also increases parasympathetic innervation of the heart to increase the refractory period, thereby reducing heart rate, and allow the ventricles more time to fill ([8] (Klabunde, 2010). The digoxin mechanism is further delineated in Figure 1. shows the Action of the Na+/K+ ATPase membrane protein and Digoxin. The normal K+/Na+ ATPase pump exchanges three sodium ions for two potassium ions. There is also a sodium-calcium exchange pump that exchanges intracellular sodium for extracellular calcium. In the diseased state of CHF, the sodium-potassium ATPase pump in the myocardial cell pumps sodium out and allows potassium in. Less sodium inside means less calcium for helping with the muscle fiber contraction, and the result is a weakened heart-beat. Digoxin, also known as Digitalis, inhibits the sodium-potassium transport system and increases intracellular sodium levels. This increases the activity of the sodium-calcium pump thereby increasing the calcium in the myocardial cell and increasing inotropy. The patient was given the angiotensin converting enzyme (ACE) inhibitor, Captopril, which leads to decreased production of angiotensin II, relaxed blood vessels, reduced blood pressure, decreased mechanical strain on the heart, as well as decreased retention 4 of water to diminish edema ([9] (Figure 2) (Harrison-Bernard, 2009). The angiotensin converting enzyme (ACE) inhibitor, Captopril, acts to remove the action of Angiotensin II at the third level of this flow chart. The benefits of the drug are reduced blood volume and reduced mean arterial pressure, which can relieve edema and reduce the effort the heart must go through to pump blood effectively.

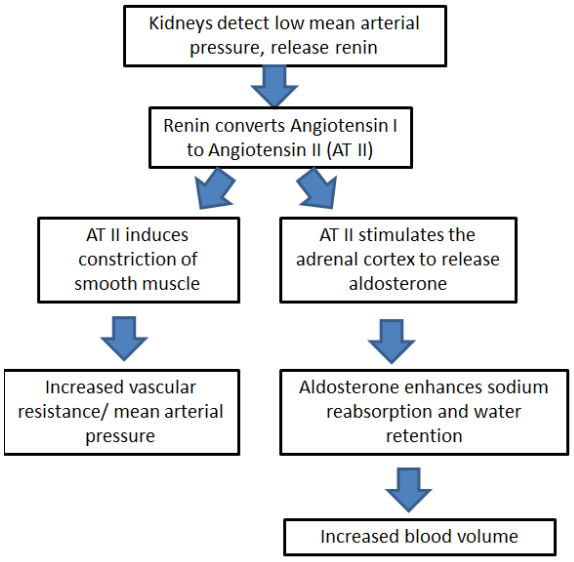


Figure 2

Diuretics are used to reducesodium reabsorption and increase water losses. Excess salt and water are eliminated from the body, thereby reducing blood volume and relieving edema ([10] (Brater, 2012).

Recent studies, however, have brought into question the use of diuretics in patients with CHF. Though they are vital for reducing fluid levels, diuretics can cause the kidneys to lose more sodium than water, leading to hyponatremia. Thus, researchers are experimenting with the vasopressin receptor antagonist, Lixivaptan, signalling the kidneys to excrete more water than salt and maintaining a more favorable electrolyte balance (Finley et al., 2008). As researchers gain a better understanding of the physiology behind CHF, they will continue to introduce new drugs like Lixivaptan, as more efficient means of treating the disease. Though many

of the physiological complications resulting from systolic heart failure are treatable with the drugs outlined above, the disease itself is irreversible. Thus, medical professionals continue to work on the development of viable treatment alternatives. One advancement is the regenerative treatment therapy Revascor, which is currently in its trial stages. The adult stem cell therapy is designed to rebuild heart muscle cells, while improving blood flow. The results of a phase II clinical trial showed decreased mortality, due to cardiac events, in patients suffering from CHF (Ilic, 2011). However, the results of a phase III clinical trial remain to be seen and the proliferation of any type of stem cell therapy could be decades away as they are subject to political and social debate. Thus, as it stands, the best way to avoid CHF is to have an active lifestyle, a healthy diet, and regular physical examinations.

Staging

ACC/AHA Heart Failure Stages [[19]
Stage A: Patients at high risk for HF but have no symptoms or structural heart disease
Stage B: Patients have structural heart disease but are asymptomatic
Stage C: Patients have structural heart disease plus symptoms
Stage D: Patients have refractory HF that requires modified interventions

Management Recommendations by ACC/AHA According to HF Stages [[19]

Stage A: Reduction of risk factors and aggressive treatment of comorbidities

Stage B: Aggressive risk factor reduction and treatment with an angiotensin-converting enzyme inhibitor/ angiotensin-receptor blocker (ACEI/ARB) and/or beta-blocker.

Stage C: Combination goal-directed therapy with ACEI/ ARBs or angiotensin receptor–neprilysin inhibitors ARNIs), beta-blockers, and loop diuretics for fluid retention. The most recent AHA/ACC update from 2017 added a class IIa recommendation for ivabradine in patients with stage C HF. [20]

Stage D: Goal-directed medical therapies indicated for stage C and consideration for heart transplantation. In patients with advanced disease and decreased life expectancy, palliative care discussions and advance directive planning should be considered.

Prognosis
According to the Centers for Disease Control and Prevention (CDC), in December 2015, the rate for heart failure related deaths decreased from 103.1 deaths per 100, 000 population in 2000 to 89.5 in 2009 but subsequently increased to 96.9 in 2014. They note that the trend correlates with a shift from coronary heart disease as the underlying cause of heart failure deaths to metabolic diseases and other noncardiac causes of HF such as obesity, diabetes, malignancies, chronic pulmonary diseases, and renal disease. The mortality rate following hospitalization for heart failure is estimated at around 10% at 30 days, 22% at 1 year, and 42% at 5 years. This can increase to greater than 50% for patients with NYHA class IV, stage D heart failure. [22]

OTTAWA HEART FAILURE RISK SCORE [[23]
The Ottawa Heart Failure Risk Score is a useful tool for prognosis determination in patients with HF who present to the emergency department with symptoms of HF. It determines the 14-day risk of mortality, hospital readmission, and acute coronary syndrome in patients who presented to the emergency department with symptoms of HF to help arrive at safe disposition planning. Patients with a score of 0 are considered low risk. A score of 1-2 is considered moderate risk, a score of 3-4 is considered high risk, and a score of 5 or higher is considered very high risk. The scoring criteria are as follows:

One point for each of the following-
- History of stroke or transient ischemic attack
- Oxygen saturation less than 90%
- Heart rate greater than 110 beats per minute on the 3-minute walk test
- Acute ischemic ECG changes
- An NT-proBNP level of greater than 5000 ng/L

Two points for each of the following-
- Prior history of mechanical ventilation for respiratory distress
- Heart rate greater than 110 beats/min on presentation
- Blood urea nitrogen (BUN) greater than 33.6 mg/dl (12 mmol/L)

Summary of Recommendations for Pharmacotherapy in HF by the 2013 ACC/AHA Guideline Update [[19] [20]

Class I Recommendations
1) Evidence-based specific beta-blockers (carvedilol, bisoprolol, and metoprolol succinate) with one of the following:
   - Angiotensin-converting enzyme inhibitors (ACEIs)
   - Angiotensin receptor blockers (ARBs)
   - Angiotensin receptor–neprilysin inhibitor (ARNI)
2) Chronic symptomatic HFrEF NYHA class II or III, replace an ACEI or ARB with an ARNI

Class IIa
Ivabradine for patients with symptomatic HF while on goal-directed medical therapy for chronic HFrEF withLVEF less than or equal to 35% and in sinus rhythm with a heart rate of at least 70 bpm at rest.

Class III
ARNI should not be given with or within 36 hours of the last dose of an ACEI or in patients with a history ofangioedema.
The Heart Failure Society of America (HFSA) Guidelines for Management of Acute Decompensated HF [21]

- Oral therapy should be continued in most patients with HFrEF and up titrated as needed.
- Continue angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) and beta blockers during treatment of acute exacerbations.

- Only consider withholding beta-blockers in patients hospitalized after a recent beta-blocker initiation.
- Loop diuretics remain the cornerstone of therapy. (Class I recommendation)
- Vasodilators (e. g., nitroprusside, nitroglycerin, or nesiritide) can be used as adjuvant therapies in patient with
  systolic blood pressure above 90 mmHg.
- Inotropic agents can be used short-term in patients with hypotension (SBP < 90 mmHg) and the patient is symptomatic from hypotension.

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