Facilitator Version

HEART FAILURE: DIAGNOSIS, CLASSIFICATION AND MANAGEMENT

Authors: Patrice Zigrossi, MD, and Angela Suen, MD
Internal Medicine Reviewer: Robert Metter, MD
Cardiology Reviewers: Miguel Pinilla Vera, MD and Hussein Abu Daya, MD

Educational Objectives:

1. Establish a differential diagnosis for new onset shortness of breath (SOB).
2. Understand the pathophysiology of heart failure (HF).
3. Recognize signs and symptoms of heart failure.
4. Describe the diagnostic approach to suspected heart failure.
5. Create a treatment plan for heart failure.

CASE ONE:
Mr. Lwanda is a 56-year old male cattle herder with a past medical history of untreated hypertension and chronic cough who presents to the clinic complaining of worsening shortness of breath. He reports that as a cattle herder he used to be able to walk many kilometers without issue. However, several months ago he developed difficulty breathing with walking. Now, he can only walk a half-kilometer before experiencing significant shortness of breath. He has no dyspnea at rest. He was seen in another clinic with similar symptoms one month ago and was told he had asthma. He could not afford to buy a salbutamol inhaler. He also reports soreness in his legs with swelling, as well as difficulty lying flat at night. While he does not have a nocturnal cough, he does report shortness of breath that often wakes him up from sleep at night and can be quite frightening.

On physical exam, his blood pressure measures 165/92 mmHg, respiratory rate is 12 breaths per minute, pulse is 72 heart beats per minute, temperature is 36.5 degrees Celsius and oxygen saturation of 92% on ambient air at rest. Pulmonary exam demonstrates bilateral crackles at posterior lung bases. Cardiac exam demonstrates a regular rate and rhythm, and normal S1 and S2 sounds with S3 gallop present. Estimated jugular venous pressure is approximately 14 cm H2O. His abdominal exam reveals palpation of the liver 2 finger-breadths below the costal margin of the ribs. His lower extremities are notable for palpable pedal pulses with 2+ pitting edema up to the knees bilaterally.

Questions:

1. What is your differential diagnosis for Mr. Lwanda's dyspnea? Which diagnoses are most likely given the provided history?

Encourage learners to name multiple etiologies across different organ systems before continuing to the next question. Highlight that a person can have more than one condition contributing to dyspnea.

The differential diagnosis for shortness of breath is quite extensive. It is helpful to separate it out by organ system. Table 1 provides a non-exhaustive list of conditions that cause dyspnea.

Table 1. Possible Etiologies of Dyspnea.[1,2]

Organ System/Physiology	Etiologies of Dyspnea
Cardiac	Heart failure/cardiomyopathy, valvular disease, myocardial infarction/coronary artery disease, arrhythmia, constrictive pericarditis, or intracardiac shunting
Pulmonary	Chronic obstructive pulmonary disease (COPD), asthma, pulmonary infection (e.g. community-acquired pneumonia, pneumocystis jirovecii pneumonia, or pulmonary tuberculosis), airway obstruction (e.g. compressive mass, vocal cord dysfunction, aspiration of foreign body, or anaphylaxis), pleural effusion, pneumothorax, pulmonary embolism, pulmonary hypertension, interstitial lung disease, or bronchiectasis
Hematologic	Anemia
Neuromuscular	Guillain-Barré syndrome, myasthenia gravis, or amyotrophic lateral sclerosis
Psychological	Anxiety
Other	Pregnancy, obesity, physical deconditioning, metabolic acidosis, thyroid disease, or alternative causes of volume overload, such as end-stage renal disease, chronic liver disease/cirrhosis, and hypoalbuminemia

In this case, heart failure (with systolic dysfunction or with preserved systolic function) should be at the top of the differential. Etiologies of heart failure include chronic hypertension, coronary artery disease-myocardial infarction, valvular disease (including rheumatic heart disease), arrhythmias, myocarditis, and long-term exposure to toxins, like alcohol or cocaine. Heart failure can also develop due to genetic diseases that specifically affect the myocardium, like hypertrophic or dilated cardiomyopathies. Infiltrative diseases such as amyloidosis are frequent causes of heart failure. Congenital heart disease is a growing problem as an etiology of heart failure since now more adults than children live with this disease. Conditions in which the right ventricle is primarily affected, like in pulmonary hypertension secondary to COPD, scleroderma, or idiopathic pulmonary arterial hypertension, can manifest with heart failure too. Furthermore, diseases in which high output heart failure may develop, like in endocrinopathies, or in the presence of arterio-venous fistulas, should be in the differential. Lastly, any cardiopulmonary pathology that affects cardiac hemodynamics or cardiac metabolism to the point of reaching the threshold for dyspnea can present with shortness of breath without the overt heart failure syndrome. These include, but are not limited to, cardiac ischemia, cardiac arrhythmias, hypertensive crisis, pulmonary embolism, diseases of the pericardium like constrictive pericarditis, cardiac tamponade, and pericardial effusion.

As aforementioned, the most likely diagnosis for Mr. Lwanda is heart failure (HF) exacerbation. Clues that should increase the clinical suspicion for HF include progressive SOB and orthopnea as well as key exam findings, which include an S3 gallop, elevated jugular venous pressure, hepatomegaly, and lower extremity edema. Other important diagnoses to rule out are asthma and COPD. Usually asthma and COPD present with other characteristic symptoms, such as dyspnea, dry or productive cough, wheezing,

and a prolonged expiratory phase. However, this patient exhibits signs of volume overload suggestive of heart failure. This patient also has a history of uncontrolled hypertension, which is a leading contributor to heart failure.

Since this condition is an important clinical and public health problem, which is associated with significant mortality, morbidity and healthcare expenditures, epidemiological studies on heart failure are ongoing. In sub-Saharan Africa (SSA), the most common causes of heart failure include hypertensive heart disease, cardiomyopathies, and rheumatic heart disease.[3,4,5] Other forms of HF, which are not unique to, but are common in SSA, include human immunodeficiency virus (HIV)-associated cardiomyopathy, tuberculous pericardial disease, endomyocardial fibrosis, cor pulmonale, and peripartum cardiomyopathy among other causes.[3,4,5]

2. What are some factors that contribute to heart failure?

Recall that the lungs and heart are intimately intertwined, and disease in one system can lead to disease in the other. Risk factors for developing heart failure include, but are not limited to, the following:[6]

- Lungs: Chronic obstructive pulmonary disease (COPD), sleep apnea, and pulmonary hypertension.
- Heart: Ischemic cardiomyopathy, valvular disease, including rheumatic heart disease, hypertension, pericarditis, congenital heart disease, viral cardiomyopathy, such as HIV-associated cardiomyopathy, Chagas cardiomyopathy, tachycardia-induced cardiomyopathy, Takotsubo or stress cardiomyopathy, peripartum cardiomyopathy, and toxic cardiomyopathy (secondary to chronic alcohol or cocaine use).
- Other: Vitamin B1 (thiamine) deficiency, obesity, diabetes mellitus, severe anemia, and thyroid disease.

3. What are common symptoms of a heart failure exacerbation?

Frequent symptoms of a heart failure exacerbation include:[2]

- Dyspnea on exertion (DOE): It is often helpful to quantify how far a patient can walk without dyspnea or shortness of breath and how this compares to baseline.
- Paroxysmal nocturnal dyspnea (PND) is a sensation of shortness of breath that awakens the patient, often after one or two hours of sleep, and is usually relieved in the upright position.
- Orthopnea is the sensation of breathlessness in the recumbent position, relieved by sitting or standing. It can be a subtle finding and while patients may not report shortness of breath at night, they may describe sleeping more comfortably on their side, with more pillows, or sitting up in a chair. Lying in the supine position increases blood return to the heart, leading to increased hydrostatic pressure of the pulmonary capillaries, increased interstitial edema, and reduced pulmonary compliance. It is a sign of advanced heart failure. Orthopnea and paroxysmal nocturnal dyspnea are key symptoms that are very helpful to differentiate heart failure from other causes of dyspnea.
- Lower extremity swelling or edema, although some patients will also report swelling of their abdomen and/or hands.
- Nonspecific symptoms, like fatigue and general malaise.

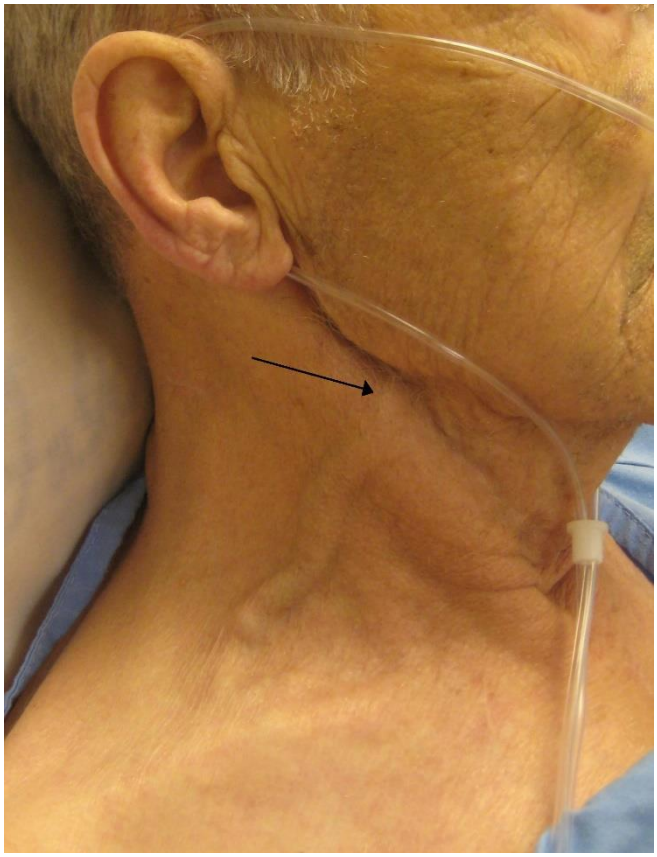
4. What are the characteristic physical exam findings of a heart failure exacerbation? Recall which physical exam findings Mr. Lwanda has.

The following are common physical exam findings of a heart failure exacerbation:

- Jugular venous pressure (JVP) elevation or jugular venous distention represents augmented cardiac filling pressures, which entail back up of fluid into the superior vena cava and from there to the jugular veins. This is one of the most common and significant findings of heart failure and one of the best indicators of a patient's volume status. In order to measure JVP, recline the patient in a semi-recumbent position with an elevation of the head to 30 to 45 degrees for the jugular venous pulsations to be visible between the angle of the mandible and the clavicle.[7,8] Turn the patient's head away and elevate the jaw, both slightly, to relax the sternocleidomastoid muscle, which lies anterior to each internal jugular vein.[7] Identify the venous pulsations and distinguish them from the carotid artery pulsations. The jugular pulse is not palpable; it can only be visualized and can easily be obliterated by light pressure of the fingers.[7,9] Shining a light tangentially to the skin is often helpful, casting shadows that improve the visibility of vein motion.[7,9] The JVP can be assessed on either the right or left. Identify JVP at the highest point of pulsation. Using rulers, measure the vertical distance between the sternal Angle of Louis (i.e. manubriosternal junction or the bony ridge adjacent to the second rib where the manubrium joins the body of the sternum) and the highest level of jugular vein pulsation. Extend a long centimeter ruler horizontally from the highest pulsation point and intersect at a right angle with another ruler placed vertically on the Angle of Louis.[7,9,10] Then add 5 centimeters to the measurement since the right atrium is 5 cm below the Angle of Louis and finally report JVP's units as centimeters of water (H2O), not mercury.[9,10] If the internal jugular vein is not detectable, examine the external jugular vein. The internal jugular vein is the preferred site of measurement. An elevated JVP is greater than 9 cm H2O.[10]

Figure 1 shows a person with congestive heart failure who presented with an exceedingly elevated JVP.[11] The arrow points to the external jugular vein. Note the vein resembles a rope as it courses diagonally in this patient who is sitting almost upright. The external jugular vein runs in an oblique direction over and across the sternocleidomastoid muscle. It is visible from the surface making it easy to locate. However, the internal jugular vein, which can also be visualized here, is the preferred site of measurement for JVP. The internal jugular vein runs between the two heads (sternal and clavicular) of the sternocleidomastoid muscle (SCM) and up in front of or anterior to the ear. The two heads of the SCM form the sides of a small, shallow triangle, with the clavicle making up the bottom edge. Impulses originating from the internal jugular vein are transmitted to the overlying skin in this area. The internal jugular vein is adjacent to the carotid artery, lying just lateral to it.

Figure 1. Elevated Jugular Venous Pressure.[11]



Credit: James Heilman, MD, CC BY-SA 4.0, Wikimedia Commons.

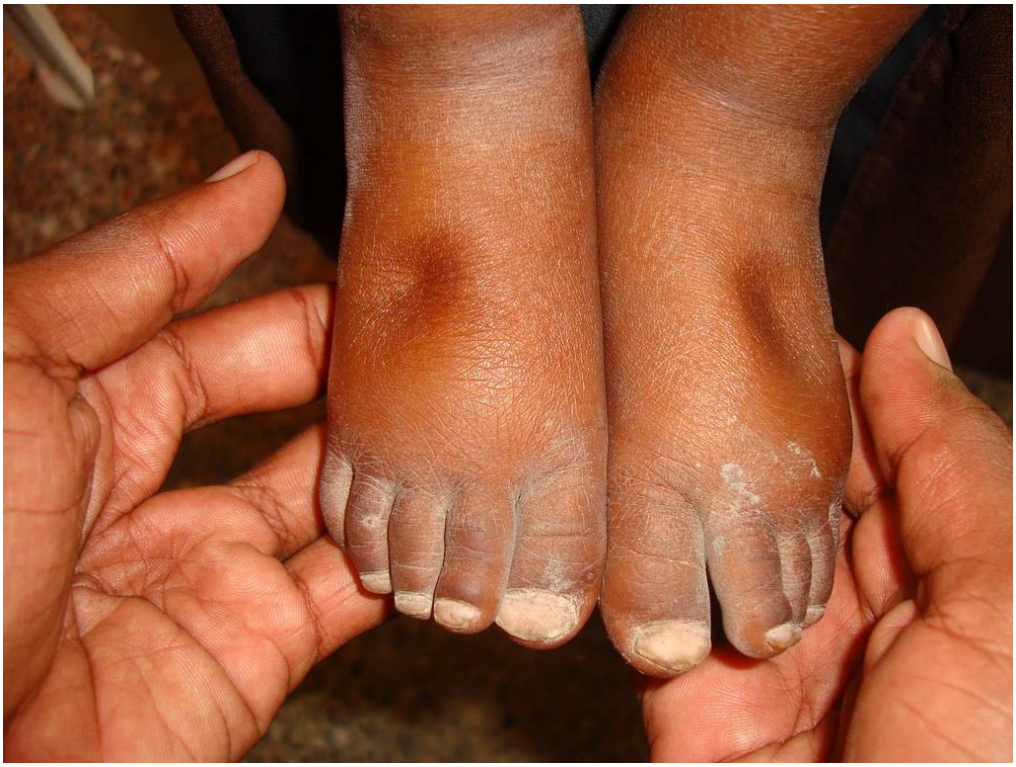
- Hepatojugular reflux (also known as the abdominojugular test) is a physical exam maneuver that increases venous return and pressure, thus facilitating analysis of the jugular venous pressure (JVP). First, recline the patient in a semi-recumbent position with an elevation of the head of the bed to 30 to 45 degrees.[8] Assess the hepatojugular reflux by applying firm, sustained pressure for 10 seconds over the upper right abdomen or the mid-epigastric region while the patient is breathing quietly. A transient elevation of JVP by 1 to 3 cm is considered normal.[8] Sustained elevation of JVP by more than 3 cm is considered a positive hepatojugular reflux.[8] With an abnormal test, the JVP will increase and stay elevated for at least 10 seconds after the examiner has removed the pressure from the patient's abdomen.

Instruct learners to demonstrate correct techniques for measuring jugular venous pressure and eliciting hepatojugular reflux. Make corrections where necessary.

- Crackles, rales or crepitations, especially at bilateral posterior bases, on pulmonary auscultation can be found in a heart failure exacerbation. This is due to fluid accumulation in the lungs secondary to increased hydrostatic pressure in the pulmonary vasculature.
- Pitting edema is a physical finding of heart failure that represents accumulation of fluid in the interstitial spaces. When point pressure with the finger is applied, a lasting indentation forms. Severity of pitting can correlate with severity of volume overload. Pitting edema in heart failure

usually starts around the feet and moves proximally. For the bedridden patient, gravity will preferentially move edema to the dependent regions of the legs, thighs, and back.[12]

Figure 2. Pitting Edema on Dorsum of Both Feet.[13]

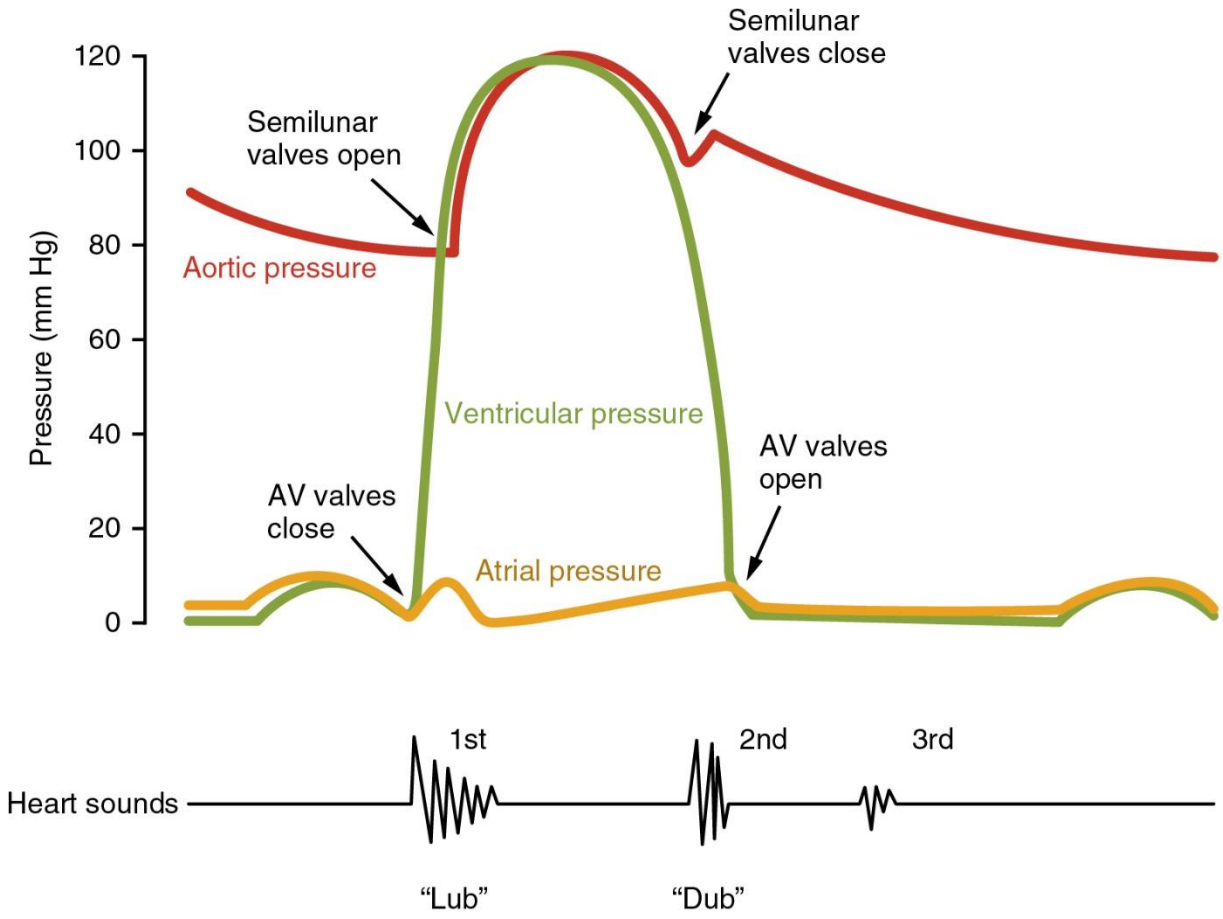


Credit: Geno Teofilo/Oxfam.

- The S3 heart sound is a physical finding that can be heard immediately after S2 on cardiac auscultation. It is a low-frequency, brief vibration occurring in early diastole at the end of the rapid diastolic filling period of the right or left ventricle. It represents a large volume of blood filling a dilated ventricle. S3 is best heard with the bell of the stethoscope over the cardiac apex with the patient in the left lateral decubitus position, lying on his or her left side.

As depicted by Figure 3, the first heart sound S1 represents closure of the atrioventricular or AV (i.e. mitral and tricuspid) valves as the ventricular pressures exceed atrial pressures at the beginning of ventricular contraction or systole. Clinically, S1 corresponds to the pulse. The second heart sound S2 represents closure of the semilunar (i.e. aortic and pulmonary) valves. S2 occurs at the end of systole and identifies the onset or beginning of ventricular diastole. S3 represents the most rapid filling of the ventricles in early diastole.

Figure 3. Heart Sounds and The Cardiac Cycle.[14]



Credit: "Heart Sounds and the Cardiac Cycle" by PhilSchatz. License: CC BY 4.0.

- Displaced point of maximal impulse occurs when the cardiac apex moves laterally due to heart enlargement. The maximal impulse follows the cardiac apex in heart failure and is also laterally displaced past the left midclavicular line.
- Ascites describes the accumulation of abdominal fluid. In severe heart failure, vascular congestion from the heart can increase orthostatic pressure in the portal veins. Water then moves from the vasculature into the abdominal compartment.
- Hepatomegaly or liver enlargement and often a liver edge that is firm to palpation result from volume overload in the setting of right ventricular dysfunction. Liver size is best measured as its cephalocaudal dimension along the right midclavicular line.[12] Percussion uncovers the upper border, and palpation and/or scratch-testing defines the lower border.[12]

5. How do we define heart failure?

Heart failure (HF) is a complex clinical syndrome in which the heart ventricles demonstrate impaired relaxation and blood filling (i.e. diastolic dysfunction) and/or inadequate ejection of blood (i.e. systolic dysfunction) to meet the body's demands.[6]

6. What is the difference between left and right sided heart failure? Explain in terms of pathophysiology, symptom presentation, and physical exam.

In left sided heart failure, there is impaired left ventricular contraction. This leads to back up of blood into the left atrium and pulmonary vasculature. Patients may present with symptoms of orthopnea, exertional dyspnea, paroxysmal nocturnal dyspnea, fatigue, and cough. Physical exam findings include crackles, rales, or crepitations on lung auscultation due to pulmonary vascular congestion as well as cyanosis (i.e. bluish discoloration) of the distal extremities. With severe left sided heart failure, blood may back up into the right side of the heart causing right sided heart failure.

In right sided heart failure, there is impaired contraction of the right ventricle. Therefore, blood backs up into the right atrium, superior and inferior venae cavae, and the systemic vasculature. Patients may complain of weight gain, loss of appetite, lower extremity edema, and ascites. Physical exam findings include elevated jugular venous pressure, dependent pitting edema, and hepatomegaly.

As blood flow from the heart is impaired, systemic vascular congestion leads to increases in hydrostatic pressure within the vessels. Water seeps out to the interstitial space and results in lower extremity edema. In the lungs, water can seep out of the pulmonary vasculature causing pulmonary edema and the presentation of crackles and cough.

Although differentiating left from right sided heart failure is very important in terms of diagnosis and management, this is not always easy based on the history and physical exam findings.

7. What diagnostic tests would you like to order for this patient?

If possible, the diagnostic testing should include:

- Cardiac ultrasound or transthoracic echocardiogram (TTE):
  - *Why is this important?* If possible, a 2-dimensional transthoracic echocardiogram (TTE) with Doppler flow studies should be performed during evaluation of patients with suspected HF to assess systolic and diastolic ventricular function, chamber sizes, wall thickness and motion, valvular function, and pericardial disease.[6] This test can identify abnormalities of myocardium, heart valves, and pericardium. Cardiologists can quantify myocardial function using TTE to determine the ejection fraction (EF). Ejection fraction gives a very good estimate of the status of ventricular contraction. Normal left ventricular ejection fraction (LVEF) ranges between 55 and 70%. The use of TTE in patients with suspected HF improves disease identification and provision of appropriate medical care.[6] While TTE requires a specialist, point-of-care cardiac ultrasound can be done quickly and relatively accurately.
- Chest radiograph or x-ray (CXR):
  - *Why is this important?* A chest x-ray is important for the evaluation of suspected HF because it assesses for cardiomegaly and pulmonary congestion and may reveal alternative causes, cardiopulmonary or otherwise, of the patient's symptoms.[6] In approximately 50% of patients with heart failure, cardiomegaly is visible on CXR, and evidence of specific chamber enlargement is helpful in detecting valvular heart disease.[2]
- Electrocardiography (ECG/EKG):
  - *Why is this important?* The electrocardiogram is a very helpful diagnostic test for patients with suspected cardiac disease. It helps to determine heart rhythm, heart rate, QRS complex morphology and duration, as well as to detect other relevant abnormalities. It can aid in defining

the etiology of heart failure. For instance, it can be helpful to detect the time course of myocardial infarction as a potential cause for heart failure. ECG can also show signs of left ventricular hypertrophy, which would raise suspicion for hypertensive cardiomyopathy as a potential cause of HF. Low precordial QRS voltages may be caused by pericardial effusion, infiltrative heart disease, COPD, hypothyroidism, or obesity.[2] ECG can also demonstrate certain arrhythmias, like atrial fibrillation with rapid ventricular response (AF with RVR), which can cause tachycardia-induced cardiomyopathy.

- B-type natriuretic peptide (BNP), N-terminal prohormone BNP (NT-proBNP) and cardiac troponin:
  - *Why are these important?* The neurohormone B-type natriuretic peptide (BNP) and its precursor N-terminal prohormone BNP (NT-proBNP) are secreted by cardiomyocytes in response to numerous triggers, most notably myocardial stretch from volume expansion and pressure overload. In patients with dyspnea, both of these biomarkers are increased by left ventricular dilatation, hypertrophy, systolic dysfunction, or diastolic dysfunction, but not by pulmonary dysfunction.[2,16] Thus, BNP and NT-proBNP levels can be used to distinguish between heart failure and pulmonary causes of dyspnea.[2,17] Measurement of BNP or NT-proBNP is useful to support clinical judgment for the diagnosis of acutely decompensated HF, especially in the setting of diagnostic uncertainty, and to establish prognosis or disease severity in HF.[6] Cardiac troponin level can also be elevated in heart failure with prognostic value.
- Screening for human immunodeficiency virus (HIV):
  - *Why is this important?* HIV is recognized as an important cause of dilated cardiomyopathy.[3,4]
- Thyroid-stimulating hormone (TSH):
  - *Why is this important?* Increased or decreased thyroid function can affect cardiac physiology and precipitate HF.
- Serum creatinine and blood urea nitrogen (BUN):
  - *Why are these important?* Increased BUN and creatinine levels usually indicate kidney disease and may change medical therapy. This testing evaluates for cardiorenal syndrome, a spectrum of disorders in which acute or chronic dysfunction of the heart or kidneys can induce acute or chronic dysfunction in the other organ.[15]
- Serum electrolytes (including calcium and magnesium, if available):
  - *Why are these important?* Electrolytes should be monitored when actively diuresing a patient who presents in a HF exacerbation.
- Complete blood count (CBC):
  - *Why is this important?* This test would evaluate for anemia or infection, which can precipitate or aggravate heart failure.
- Liver function tests:
  - *Why are these important?* HF can have negative effects on the liver due to hepatic vascular congestion.
- Fasting lipid profile:
  - *Why is this important?* Elevated total and low-density lipoprotein (LDL) cholesterol as well as low high-density lipoprotein (HDL) cholesterol are associated with increased cardiovascular risk.

CASE ONE CONTINUED:
You have a high clinical suspicion for heart failure exacerbation. You order a transthoracic echocardiogram (TTE), which demonstrates enlarged left ventricle and impaired contraction with estimated left ventricular ejection fraction (LVEF) of 40%.

8. How would you describe the type and severity of heart failure in this patient? Under which New York Heart Association (NYHA) functional class would you categorize this patient?

As outlined in Table 2, there is a system named the New York Heart Association (NYHA) functional classification, which determines severity of heart failure based on the patient's symptoms and daily functioning. In Mr. Lwanda's case, based on his symptoms, he would have NYHA Class II to III heart failure.

Table 2. New York Heart Association (NYHA) Functional Classification of Heart Failure.[6,18]

Class	Patient Symptoms
I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitations (rapid/irregular heartbeat) and/or dyspnea (shortness of breath).
II	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitations and/or dyspnea.
III	Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitations and/or dyspnea.
IV	Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, symptoms increase.

Heart failure can also be defined based on left ventricular ejection fraction (LVEF) as follows:[19]

- HF with preserved ejection fraction (HFpEF): LVEF ≥50%
- HF with a mid-range ejection fraction (HFmEF): LVEF 41 to 49%
- HF with a reduced ejection fraction (HFrEF): LVEF ≤40%

The aforementioned ejection fraction terminology requires a transthoracic echocardiogram (TTE) and a well-trained sonographer as there is a wide range in user variability. Given an estimated left ventricular ejection fraction (LVEF) of 40%, Mr. Lwanda has heart failure with reduced ejection fraction (HFrEF).

9. What are some medications for heart failure? What are their therapeutic effects and adverse reactions?

The goal of therapy is to minimize myocardial damage and stress, as well as maximize cardiac functioning. Using symptoms to guide treatment is a reasonable way to treat heart failure. The following medications are utilized to manage heart failure:

- Diuretics: Loop diuretics (e.g. furosemide and torsemide) in oral or intravenous (IV) forms are the basis of early therapy directed towards patients with significant fluid overload or hypervolemia. The oral version of furosemide has approximately 50% bioavailability compared with IV furosemide; therefore, furosemide 40 mg by mouth is equivalent to 20 mg IV.[19] By generating water and sodium excretion, loop diuretics decrease cardiac filling pressures as well as peripheral and pulmonary edema.[19] Loop diuretics also have the potential to worsen renal function and produce electrolyte

disturbances, including hypokalemia (i.e. low blood potassium), hypomagnesemia (i.e. low blood magnesium), hypocalcemia (i.e. low blood calcium), and hyponatremia (i.e. low blood sodium). Therefore, serum creatinine and electrolytes must be monitored closely during diuresis. Patients may often require potassium and magnesium repletion. Diuretic doses should be adjusted accordingly to relieve symptoms and achieve euvolemia without inducing an excessively rapid reduction in intravascular volume, which could result in hypotension, kidney dysfunction, or both.[6] Patients' volume status, body weight, fluid intake, urine output, and vital signs should be monitored during diuresis. Since loop diuretics have a relatively short half-life, sodium reabsorption in the renal tubules will occur once the tubular concentration of the diuretic declines.[6] Therefore, dosing the diuretic multiple times per day (i.e. twice daily or three times per day dosing) or continuously will enhance diuretic effectiveness.[6] In patients with severe edema, oral loop diuretics might not be adequately absorbed in the gastrointestinal tract and might need to be transitioned to IV form.[19] When diuresis is inadequate to relieve symptoms, increasing the doses of the intravenous loop diuretic and/or adding a second diuretic, usually a thiazide (e.g. hydrochlorothiazide or chlorthalidone), can improve diuretic responsiveness.[6,19]

- Angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs): ACE inhibitors (e.g. captopril, enalapril and lisinopril) have been shown to prevent adverse cardiac remodeling and reduce mortality in patients with HFrEF.[6,19] ACE inhibitors should be prescribed to all patients with HFrEF unless they have a history of hereditary angioedema or angioedema related to previous ACE inhibitor exposure, or if they are pregnant or plan to become pregnant. Angioedema occurs in <1% of patients who take an ACE inhibitor, but it occurs more frequently in black individuals.[6] Cough occurs in 10 to 20% of patients receiving ACE inhibitors and does not require discontinuation of the agent unless it is bothersome to the patient.[19] ARBs (e.g. losartan, valsartan and candesartan) can be administered to patients who have a bothersome ACE inhibitor-induced cough. There have been case reports of patients who develop angioedema with ARB therapy after having experienced angioedema while receiving ACE inhibitor treatment, so caution is advised in these patients.[6,19] ACE inhibitors and ARBs tend to raise the serum potassium and creatinine levels. Treatment with ACE inhibitors or ARBs should be initiated at low doses, followed by gradual dose increments if lower doses have been well tolerated. Clinicians must prescribe ACE inhibitors or ARBs with caution if patients have very low blood pressures, elevated levels of serum potassium, or chronic kidney disease.[6]
- Beta-adrenergic receptor blockers or beta-blockers: Beta-blockers are used to slow down the heart rate to allow time for adequate filling and to prevent myocardial strain. Three beta-blockers have been shown to lessen HF symptoms, improve clinical status, and reduce disease progression as well as mortality in patients with HFrEF: bisoprolol, carvedilol and sustained-release metoprolol succinate.[6,19] Beta blockers should be prescribed to all patients with stable HFrEF unless they have a contraindication to their use.[6] Beta-blockers must not be initiated during an unstable HF exacerbation.[19] The starting dose of beta-blockers should be low and increased slowly.[6,19] Fluid retention might occur with initiation or uptitration of beta-blockers and might require changes in diuretic dosage. If concomitant reactive airways disease is present, clinicians should consider prescribing more selective beta-1 blockade (e.g. bisoprolol and metoprolol).[19] The bradycardia produced by beta-blockers is usually asymptomatic and thus requires no treatment. However, if this bradycardia is accompanied by presyncope or if second- or third-degree atrioventricular block occurs, clinicians should decrease the dose or discontinue the beta blocker.[6] Beta-blockers have a relatively weak effect on blood pressure. Nonetheless, the risk of hypotension may be minimized further by administering the beta-blocker and ACE inhibitor at different times during the day.[6]
- Aldosterone or mineralocorticoid receptor antagonists (MRAs): In patients with markedly reduced ejection fraction (i.e. LVEF ≤35%) or NYHA Class II to IV heart failure, MRAs (e.g. spironolactone and

eplerenone) have been shown to improve cardiac remodeling as well as reduce morbidity and all-cause and cardiovascular mortality. Unless contraindicated, clinicians should consider the addition of the MRAs for all patients with HFrEF who are already on ACE inhibitors (or ARBs) and beta-blockers. Although the evidence is not strong, these medications are often also used in patients with heart failure with preserved systolic function. To minimize the risk of life-threatening hyperkalemia, the initial serum creatinine should be <2.5 mg/dL in men or <2.0 mg/dL in women (or estimated glomerular filtration rate >30 mL/min/1.73 m^2), and serum potassium should be <5.0 mEq/L. [6] Careful monitoring of potassium, renal function, and diuretic dosing should be performed. Upon initiation of MRAs, potassium supplementation should be reduced or discontinued. For those with concerns of hyperkalemia or marginal renal function (estimated glomerular filtration rate 30 to 49 mL/min/1.73 m^2), an initial regimen of every-other-day dosing is advised.[6]

- Digoxin is not a first-line medication for heart failure but may benefit patients with HFrEF.[6] It works to slow down the heart rate and increase contractility, thereby increasing stroke volume and perfusion to the body. Unless contraindicated, clinicians may consider prescribing digoxin for patients with persistent symptoms of HFrEF despite the aforementioned guideline directed medical therapy.[6] Digoxin is renally cleared and has a narrow therapeutic window, which indicates that it is easy to under- or over-dose the medication. In patients receiving digoxin, serum potassium and creatinine should be measured with increases in digoxin or diuretic dose, or during a dehydrating illness, to reduce the risk of digoxin toxicity.[19] Patients with reduced kidney function, elderly patients, those with low body weight, and women are at increased risk of and might require closer monitoring for digoxin toxicity.[19] Signs of digoxin toxicity, including nausea, vomiting, anorexia, visual disturbances, confusion, and cardiac arrhythmias. The concomitant use of clarithromycin, erythromycin, amiodarone, itraconazole, verapamil, or quinidine can also increase serum digoxin concentrations and the likelihood of digoxin toxicity.[6] Low doses should be used initially if the patient is older than 70 years of age, has impaired renal function, or has a low lean body mass.[19] Finally, it is unclear whether the drug is safe to use in pregnancy (i.e. United States Food and Drug Administration Category C) as it crosses the placenta.

If available, this patient should be referred for a consultation to a cardiac specialist for acute management and follow-up.

10. What nonpharmacologic interventions and lifestyle modifications would you recommend to this patient?

- Daily weight monitoring: Patients should be advised to record their 'dry' or euvolemic weight and monitor their fluid status closely. They must weigh themselves every day and tell their healthcare providers if their weight increases one kilo or more in one day or more than 3 kilos over 2 to 3 days in order to adjust their diuretic dosing. For patients with severe HF, even mild shifts in fluid status can lead to marked symptoms and worsening of heart function.
- Dietary recommendations:
    - Sodium intake: Dietary sodium restriction is commonly recommended to patients with HF and is endorsed by many guidelines.[6] However, currently there is insufficient data to endorse any specific level of sodium intake.[6] Several studies suggest that lower dietary sodium intake is associated with better clinical outcomes, whereas other studies indicate that dietary sodium restriction can be deleterious.[19] Since sodium intake is typically high, over 4 grams per day, in the general population, and associated with hypertension and cardiovascular disease, some degree (e.g. less than 2 grams per day) of sodium restriction for patients with HF is reasonable for symptomatic improvement.[6]

- Fluid intake: Patients with HF often have an intense thirst, which can lead to excessive fluid intake and low serum sodium. Fluid intake should be limited, where possible, to about 2 liters a day for patients with fluid retention that is not easily controlled with diuretics.[19] During periods of hot weather, diarrhea, vomiting or fever, fluid intake may be increased, or the dose of diuretic reduced. Severe fluid restriction is not only difficult to maintain but could also have deleterious effects without additional benefits.[19]
- Alcohol intake: Alcohol can damage the myocardium and precipitate arrhythmias. Alcohol consumption should be limited for all patients with HF. If alcohol use is believed to be a causative factor of HF, it should be entirely avoided.[19]
- Weight management: All patients should be counseled on maintenance of optimal weight. Obesity increases the workload on the heart, especially during physical activity, and patients should be counseled on weight loss strategies. Conversely, improvement of the nutritional status in wasted, undernourished, or patients with alcohol use disorder is also important.

- Tobacco use cessation: Smoking increases the risk of many cardiovascular, pulmonary, and other problems, including cancers, and must be avoided. Patients should be strongly advised about the hazards of smoking and counseled to quit.[6]
- Routine exercise: Early mobilization after a heart failure exacerbation is important. Regular physical activity appropriate for the condition of the patient should be encouraged. This has significant benefits, including improvements in exercise capacity, symptoms, and quality of life, in patients with HF.[19] Dynamic exercise activities, such as walking and swimming, should be continued at a pace that is comfortable for the patient.
- Vaccinations: Heart failure may predispose to and be exacerbated by pulmonary infection, which is a common cause of hospitalization. Therefore, influenza and pneumococcal vaccinations are recommended, if available.[19]

References:

1. Zoorob RJ, Campbell JS. Acute dyspnea in the office. *Am Fam Physician.* 2003;68(9):1803-1810.
2. Wahls SA. Causes and evaluation of chronic dyspnea. *Am Fam Physician.* 2012;86(2):173-182.
3. Damasceno A, Cotter G, Dzudie A, Sliwa K, Mayosi BM. Heart failure in sub-saharan Africa: time for action. *J Am Coll Cardiol.* 2007;50(17):1688-1693. doi:10.1016/j.jacc.2007.07.030
4. Bloomfield GS, Barasa FA, Doll JA, Velazquez EJ. Heart failure in sub-Saharan Africa. *Curr Cardiol Rev.* 2013;9(2):157-173. doi:10.2174/1573403x11309020008
5. Gallagher J, McDonald K, Ledwidge M, Watson CJ. Heart Failure in Sub-Saharan Africa. *Card Fail Rev.* 2018;4(1):21-24. doi:10.15420/cfr.2018:4:1
6. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation.* 2013;128(16):1810-1852. doi:10.1161/CIR.0b013e31829e8807
7. Chua Chiaco JM, Parikh NI, Fergusson DJ. The jugular venous pressure revisited. *Cleve Clin J Med.* 2013;80(10):638-644. doi:10.3949/ccjm.80a.13039
8. Vaidya Y, Bhatti H, Dhamoon AS. Hepatojugular Reflux. In: *StatPearls.* StatPearls Publishing; 2020. Accessed March 10, 2021. https://www.ncbi.nlm.nih.gov/books/NBK526097/
9. Bickley LS, Szilagyi PG, Bates B. *Bates' guide to physical examination and history-taking.* 11th ed. Wolters Kluwer/Lippincott Williams & Wilkins; 2013:361-365.
10. Conn RD, O'Keefe JH. Simplified evaluation of the jugular venous pressure: significance of inspiratory collapse of jugular veins. *Mo Med.* 2012;109(2):150-152.

11. Heilman J. Elevated Jugular Venous Pressure. Wikimedia Commons. 2017. Accessed May 28, 2021. https://commons.wikimedia.org/wiki/File:Elevated_JVP.JPG
12. Leier CV, Chatterjee K. The physical examination in heart failure--Part II. *Congest Heart Fail.* 2007;13(2):99-104. doi:10.1111/j.1527-5299.2007.06491.x
13. Teofilo G. Indication of Edema – Mother and Child Nutrition. The Mother and Child Health and Education Trust. September 2019. Accessed March 8, 2021. https://motherchildnutrition.org/early-malnutrition-detection/detection-referral-children-with-acute-malnutrition/screening-for-acute-malnutrition.html
14. Betts JG, Young KA, Wise JA, et al. Cardiac Cycle. In: *Anatomy and Physiology*. https://openstax.org/books/anatomy-and-physiology/pages/19-3-cardiac-cycle. Accessed August 18, 2021.
15. Rangaswami J, Bhalla V, Blair JEA, et al. Cardiorenal Syndrome: Classification, Pathophysiology, Diagnosis, and Treatment Strategies: A Scientific Statement From the American Heart Association. *Circulation.* 2019;139(16):e840-e878. doi:10.1161/CIR.0000000000000664
16. Mogelvang R, Goetze JP, Schnohr P, et al. Discriminating between cardiac and pulmonary dysfunction in the general population with dyspnea by plasma pro-B-type natriuretic peptide. *J Am Coll Cardiol.* 2007;50(17):1694-1701. doi:10.1016/j.jacc.2007.07.073
17. Wright SP, Doughty RN, Pearl A, et al. Plasma amino-terminal pro-brain natriuretic peptide and accuracy of heart-failure diagnosis in primary care: a randomized, controlled trial. *J Am Coll Cardiol.* 2003;42(10):1793-1800. doi:10.1016/j.jacc.2003.05.011
18. The Criteria Committee of the New York Heart Association. *Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels*. 9th ed. Little, Brown & Co; 1994:253-256.
19. Ezekowitz JA, O'Meara E, McDonald MA, et al. 2017 Comprehensive Update of the Canadian Cardiovascular Society Guidelines for the Management of Heart Failure. *Can J Cardiol.* 2017;33(11):1342-1433. doi:10.1016/j.cjca.2017.08.022