

CASE: 57 year old man with a history of hypertension presents to the Emergency Room with increasing shortness of breath and lower extremity edema for three weeks. The patient's activity level has decreased over the past three weeks due to shortness of breath. His medications include furosemide 20 mg qd, lisinopril 10 mg qd, and metoprolol 12.5 mg bid. His examination reveals BP 150/72 P98 T 37.2 RR 20, JVP elevated to 6cm, normal S1, S2, S4 present, bibasilar crackles, +2 non-pitting lower extremity edema. Labs notable for a creatinine 1.3, potassium 3.5, chest x-ray shows increased pulmonary vascularity bilaterally, ECG sinus HR 89 with non-specific t wave changes.

What is your differential diagnosis for shortness of breath? What in the history and physical examination suggest heart failure? How much furosemide would you initially give to the patient?

Systolic Heart Failure (HF)

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Definition: impaired ventricle ability to fill or eject blood secondary to structural or functional cardiac disorder. Diastolic heart failure is defined as heart failure in the presence of normal left ventricular systolic function and abnormal left ventricular filling and elevated pressures. Typically, diastolic heart failure treatment focuses on the treatment of underlying processes, such as hypertension or symptomatic heart disease. Diastolic heart failure will not be discussed further in this section.

Epidemiology¹

- Approximately 5 million people in the United States have heart failure
- 550,000 patients are diagnosed with heart failure for the first time each year
- 12 to 15 million medical office visits per year are due to heart failure
- 6.5 million hospital days are due to heart failure
- Primarily a condition of the elderly
- Approximately 80% of patients hospitalized with heart failure are greater than 65 years of age

Risk Factors: Hypertension, coronary artery disease (CAD), cardiomyopathy, valvular heart disease.

Classification of Heart Failure¹:

New York Heart Association (NYHA)

- Class I: patients with no limitation of activities; no symptoms from ordinary activities.
- Class II: patients with slight, mild limitation of activity; comfortable with rest or with mild exertion.
- Class III: patients with marked limitation of activity; comfortable only at rest.
- Class IV: patients who should be at complete rest, confined to bed or chair; any physical activity brings on discomfort and symptoms occur at rest

ACC Staging System

- Stage A Patients with CAD, hypertension, or diabetes mellitus who do not have impaired left ventricular function, hypertrophy, or chamber distortion.
- Stage B Patients with asymptomatic left ventricular hypertrophy or impaired left ventricular function.
- Stage C Patients with current or past symptoms of heart failure with underlying structural heart disease.
- Stage D Patients with refractory heart failure.

Note: NYHA is more clinical and more widely familiar/used, although ACC Staging may be helpful in detecting early HF. Stages A & B help to identify early patients at risk of developing heart failure. These patients do not clearly have heart failure.

Signs and Symptoms: non-specific and vary depending on the severity of heart failure.

Symptoms: dyspnea, fatigue, decreased exercise tolerance, orthopnea (the *absence* of orthopnea argues against the presence of left ventricular dysfunction), PND, cough

Signs: edema/anasarca, rales/crackles, tachycardia, hypertension or hypotension, elevated jugular venous pressure (if > 8 cm H₂O, specificity of 93-96% with + LR 9.0), possible S3 (presence indicates a depressed EF with LR 3.8 to 4.1 and elevated left atrial pressures with LR 5.7) or S4 (does not predict ejection fraction or left heart filling pressures).

NOTE: normal or elevated JVD does not predict a patient's ejection fraction.

Differential Diagnosis: Pneumonia, Chronic Obstructive Pulmonary Disease Exacerbation, Asthma, Interstitial lung disease, Pulmonary Embolus

Diagnosis:

Diagnosis should be based on history (i.e. non compliance with diet or medications, increasing weight gain, dyspnea, chest pain) and clinical examination **NOT** laboratory or radiologic tests. If unsure of the diagnosis, you should check B type natriuretic peptide (BNP)-(additional information below) and a chest x-ray (CXR), which will show increased pulmonary vascularity.

An echocardiogram may be helpful to determine abnormalities of the myocardium, heart valves, or pericardium, which can cause heart failure. Assessment of left ventricular function is a quality assurance measure at most hospitals.

Laboratory: Laboratory tests are helpful to determine a precipitating cause for heart failure, such as infection, myocardial ischemia, hyperglycemia.

Admission: STAT: electrolytes BUN, glucose, CBC, cardiac enzymes, BNP; UA to look for protein, infection; portable CXR if the patient is unable to tolerate a PA and lateral; ECG.

Next day: Chemistry panel, cardiac enzymes if concern for myocardial infarction.

If this is the first episode of HF, you may want to check glycohemoglobin, lipid panel, TSH as diabetes, hyperlipidemia, and hyper/hypothyroidism, respectively, may contribute to heart failure.

B-type natriuretic peptide (BNP)

It should be used in an unclear diagnosis of HF or if the diagnosis is unknown. BNP has a negative predictive value of at least 96%, so HF can be ruled out if patients have a BNP in the normal range (this is variable depending on previous CHF or co morbid conditions but typically < 100 pg/ml)⁹. Typically, BNP in patients with HF will be in the 1000 pg/ml range⁹. BNP is lower in obese patients. BNP is more elevated in renal failure whether HF is present or not^{8,9}.

Management:

Vitals/Nursing/Diet:

- Obtain an admission weight, daily I/Os (a urinary catheter can be placed for more accurate monitoring), daily weights, as well as ask the patient about their dry weight or typical weight. These baseline values will aid in monitoring the patient's progress in the hospital and at home.
- The patient should be placed on a 2 gram sodium, low fat, low cholesterol diet.

Medications:

Diuretics(furosemide,torseamide)

- If a patient warrants admission to the hospital for HF, intravenous diuretics should be used. As the patient improves, a transition to oral diuretics can be made. Note that oral furosemide is twice the intravenous dose.
- **Furosemide** dosage is variable depending on patient's previous usage of furosemide (and/or presence of renal insufficiency) and symptoms; this may range from 20 mg-200 mg IV. Typical doses start at 20-40 mg IV. Patients previously taking furosemide may have a tolerance and require higher dosages than naïve patients¹. Aggressive diuresis should be achieved within the first 12 hours of admission. The goal is to achieve normalization of ventricular filling pressure, which is best measured by central venous pressure²⁸. However, typically clinical examination of euvolemia (improved peripheral and pulmonary edema) is used. Note: gut edema may inhibit the effectiveness of both oral and intravenous furosemide, although intravenous furosemide is more potent than oral. Therefore, higher doses may be needed.
- Some studies show that continuous infusion of loop diuretics (furosemide) may be safer and cause less resistance than bolus loop diuretics. More studies needed to validate this. Start with furosemide bolus 40 mg and then a 10 mg infusion rate, titrating to desired urine output.
- Alternative diuretics can be used if the patient is allergic to furosemide (sulfa containing medications) or does not respond to furosemide. Alternatives include bumetanide 1 mg(4-8 mg max single dose), torsemide 10 mg(100-200 mg max single dose), chlorothiazide 500 mg(1000 mg max single dose)¹. Metolazone 5-20 mg can be given one half hour before furosemide is administered for diuretic resistant patients. Torsemide is two times as potent as furosemide with a 90% oral bioavailability.
- NO strict guidelines of how often to check potassium levels while on diuretics, although it is reasonable to check potassium levels at least daily for the first few days of a new diuretic dose.

Aldosterone Receptor Antagonist(Spirolactone)

- Patients with a moderate to severe heart failure, low ejection fraction < 40%, creatinine < 2.5 and potassium < 5.0 have improved survival with the addition of **spironolactone** 25-50 mg po daily¹².

Vasodilators

- Limit use to severe heart failure patients
- Atrial natriuretic peptide is a vasodilator which lower systemic blood pressure, inhibits renin and endothelin secretion².
- **IV nitroglycerin** or **nesiritide** can be used in severe HF cases. If patients are refractory to vasodilators or nesiritide, a continuous infusion of **dobutamine** or **milrinone** can be tried (would limit use to patients in cardiogenic shock)¹. The use of dobutamine and milrinone has been shown to increase mortality when used in severe heart failure.
- Some studies have shown that nesiritide may increase mortality in acutely decompensated congestive heart failure³, although mortality was not the primary end point.
- ICU monitoring may be needed and is institution dependent.

Angiotension Converting Enzyme Inhibitors (ACE inhibitors)

- ACE inhibitors have been shown to improve mortality and slow the progression of HF by vasodilation and blood pressure effects, as well as remodeling. ACE inhibitors should be given to all patients with HF due to LV systolic dysfunction with reduced LVEF (< 40%)^{1, 15, 16}.
- It is recommended that ACE inhibitors be started first, then a beta blocker; ACE inhibitors do not exacerbate heart failure symptoms.
- Starting dose of enalapril 2.5-5 mg bid and titrate to 20 mg bid¹⁵. Note other ACE inhibitors, such as lisinopril 5 mg daily titrated to 40 mg daily, can be used as well.
- If it is unclear whether a patient will tolerate an ACE inhibitor hemodynamically, short acting captopril 12.5 mg tid.

- All patients with heart failure should be discharged on an ACE inhibitor or ARB for quality assurance.

NOTE: A chemistry panel should be checked upon initiation of an ACE inhibitor within two weeks after discharge.

Angiotension II Receptor Blockers (ARB)

- Patients with HF and low EF, intolerant of ACE inhibitors should be tried on an ARB (Candesartan, valsartan)¹⁹. Starting dose of candesartan 4 mg daily and valsartan 40 mg bid with goals of candesartan 32 mg daily and valsartan 160 mg bid.
- Valsartan is as effective as captopril in improving mortality in patients with left ventricular dysfunction in acute myocardial infarction²¹.

Beta Blockers (particularly carvediol^{17,22,23}, metoprolol²⁰, bisoprolol¹³)

- Acute HF activates the sympathetic nervous system which can have adverse effects on the heart remodeling^{17, 18, 20}. Beta blockers inhibit the sympathetic system. Beta blockers particularly help with reducing LV end diastolic and end systolic function. Some have been shown to improve morbidity and mortality.
- Avoid starting **beta blockers** in acute HF and patients not euvolemic, which might worsen HF symptoms and in patients who require intravenous therapy for HF. However, beta blockers should be initiated upon discharge if possible. Beta blockers should be continued in patients already on beta blockers at the time of admission.
- Starting dose of metoprolol CR/XL 12.5-25 mg daily and titrate every 2 weeks to a dose of 200 mg daily if tolerated.
- Starting dose of carvediol 3.125 mg bid and titrate to 25 mg bid.
- Starting dose of bisoprolol 1.25 mg daily and titrate to 10 mg daily.
- Goal BP 100/60 and HR 55-60.

Combination Beta Blockers and ACE inhibitors

- Most of the heart failure trials treating patients with beta blockers were also on ACE inhibitors. The combination has been shown to improve LV function and survival than either alone²⁶.

Combination ACE inhibitors and ARBs

- The CHARM Added Trial showed a benefit with combination therapy²⁴
- The Val-HeFT Trial which preceded the CHARM-Added showed an increase in complications in patients taking both an ACE inhibitor plus beta blockers and ARB²⁵.
- The addition of an ARB should be considered in patients still symptomatic on maximal treatment with an ACE inhibitor, beta blocker, and spironolactone. Potassium levels need to be monitored closely if the patient is on combinations of ACE inhibitors, spironolactone, and ARBs.

Digoxin

- Digoxin has been found to improve symptoms of HF and decrease hospitalization rates but has not been found to reduce mortality. Digoxin can be considered in patients already on optimal therapy on ACE inhibitors and beta blockers¹⁴.
- Low dose digoxin should be initiated, because the therapeutic window is narrow (0.6-1). Digoxin levels should be drawn 12-24 hours after the initial dose. Digoxin levels should be obtained 5-7 days after dosing changes.

Other Management Considerations:

- If patients present with a myocardial infarction leading to HF, you may need to use morphine sulfate 2-4 mg IV as needed for symptom relief, angiotension converting enzymes, nitrates and aspirin.
- Patients with heart failure are at risk for abnormal heart rhythms, which may lead to sudden cardiac arrest. Because of this risk, automatic implantable cardioverter-defibrillators have been placed in patients with heart failure¹¹.
- In heart failure patients, there is a delay in the contraction of the right ventricle and left ventricle. Biventricular pacing (cardiac resynchronization therapy) has been used to attempt to resynchronize the heart and improve quality of life in moderate to severe heart failure patients (ejection fraction of 35% or less) with a prolonged QRS interval (greater than 130 msec or more)¹⁰.
- Ventricular Assist Devices bridge a heart failure patient to cardiac transplant¹¹.
- Cardiac Transplant as a last option for severe heart failure patients.

Prevention:

1. Adhere to 2 gm sodium diet
2. Routine weights and alert an MD if deviations
3. Medication compliance
4. Medication counseling(adherence, rationale, side effects)
5. Avoid NSAIDs which can lead to an exacerbation
6. Smoking cessation
7. Annual influenza vaccination

Pearls:

- If unclear of the diagnosis based on physical examination, chest x-ray, EKG, check a BNP.
- Don't forget to determine the cause for their heart failure, and treat the underlying cause appropriately.
- Patients with heart failure should be on ACE inhibitors and beta blockers at maximal doses if there are no contraindications, titrated to goal BP 100/60 and HR 55-60.
- Counsel patients regarding diet and awareness of dry weight.

Case Follow Up

The patient had an admission BNP of 3000. Cardiac enzymes were negative for ischemia. An Echocardiogram showed concentric left ventricular hypertrophy. Diastolic filling parameters suggest a relaxation abnormality. Initially, the patient's home dose of furosemide was doubled; he was given furosemide 40 mg IV in the ER. Four hours after furosemide, the patient's urine output was 250 cc. A repeat dose of furosemide 80 mg IV was given with good urine output. The patient was maintained on furosemide 80 mg IV daily until he was clinically stable. The patient was discharged on oral furosemide 40 mg daily, metoprolol 25 mg bid, lisinopril 20 mg qd. His medications should be titrated to a goal blood pressure of 100/60 and HR 55-60. His BNP was down to 500ish pg/ml on discharge.

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