Objectives

- Differentiate heart failure and COPD in the ambulatory setting
- Identify the appropriate treatment and management of heart failure and COPD in the ambulatory setting
Heart Failure

- 5.1 million people in the US have heart failure
- 1 in 9 deaths in 2009 included heart failure in contributing causes
- 50% of people who develop heart failure die within 5 years of diagnosis
- Heart failure costs the nation an estimated 32$ billion each year
  - Health care services
  - Medications
  - Missed work days

Heart Failure

- Clinical syndrome that can result from any structural or functional cardiac disorder that impairs ability of ventricle to fill with or eject blood
- Common characteristics
  - Dyspnea
  - Fatigue
  - Volume overload
    - Peripheral edema
    - Pulmonary rales

Heart Failure

- Risk Factors
  - Coronary Artery Disease
    - 60-70% patients with SHF
  - Hypertension
    - 1.4 times more likely to develop HF
  - Diabetes
  - Strong risk factor for HF in women
  - Valvular Heart Disease
    - 1.46 times more likely to develop HF
  - Smoking
  - Physical inactivity
  - Obesity
  - Lower socioeconomic status
Heart Failure

- Initial assessment includes
  - History and physical exam
  - Chest radiography
  - EKG
  - Laboratory assessment
  - ECHO
    - Can confirm diagnosis

Heart Failure

- Systolic Heart Failure
  - CO is decreased directly through reduced LV function
  - Reduced LVEF is predictor of mortality
- Diastolic Heart Failure
  - CO is compromised by poor ventricular compliance, impaired relaxation and worsened end-diastolic pressure
  - Lacks evidence based treatments
- No difference in survival between DHF and SHF that cannot be attributed to ejection fraction (EF)

Heart Failure

- Symptoms
  - Abdominal swelling
  - Dyspnea on exertion
  - Edema
  - Exercise intolerance
  - Fatigue
  - Orthopnea
  - Paroxysmal nocturnal dyspnea
  - Recent weight gain
Heart Failure

- Symptoms can occur with preserved or reduced EF
- NYHA is simplest and most widely used method to gauge symptom severity
  - Well established
  - Used at diagnosis and to monitor treatment response

NYHA Functional Classification of Heart Failure

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>No Limitations of physical activity</td>
</tr>
<tr>
<td>Class II</td>
<td>Mild limitation of physical activity</td>
</tr>
<tr>
<td>Class III</td>
<td>Heart failure symptoms with significant exertion; comfortable at rest</td>
</tr>
<tr>
<td>Class IV</td>
<td>Marked limitation of physical activity</td>
</tr>
<tr>
<td>Class V</td>
<td>Discomfort with any activity</td>
</tr>
</tbody>
</table>

Heart Failure

<table>
<thead>
<tr>
<th>Physical Exam Findings</th>
<th>Abdomen</th>
<th>Hepatojugular reflux, ascites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extremities</td>
<td>Cool, dependent edema</td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>Brady/tachycardia, laterally displaced point of maximal impulse, third heart sound (gallop or murmur)</td>
<td></td>
</tr>
<tr>
<td>Lungs</td>
<td>Laborated breathing, rales</td>
<td></td>
</tr>
<tr>
<td>Neck</td>
<td>Elevated jugular venous pressure</td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>Cyanosis, palor</td>
<td></td>
</tr>
</tbody>
</table>

2/11/2014
Heart Failure

### Laboratory Evaluation

<table>
<thead>
<tr>
<th>Initial tests</th>
<th>Other tests for alternative causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-type natriuretic peptide level</td>
<td>Arterial blood gases</td>
</tr>
<tr>
<td>Magnesium/Calcium level</td>
<td>Blood cultures (endocarditis)</td>
</tr>
<tr>
<td>CBC</td>
<td>Lipid profile</td>
</tr>
<tr>
<td>BMP (electrolytes)</td>
<td>HgA1c</td>
</tr>
<tr>
<td>LFTs</td>
<td>Troponin and CKMB</td>
</tr>
<tr>
<td>Scr</td>
<td>HIV (cardiomyopathy)</td>
</tr>
<tr>
<td>TSH</td>
<td>Lyme serology</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>Serum ferritin levels</td>
</tr>
</tbody>
</table>

### Framingham Diagnostic Criteria for Heart Failure

<table>
<thead>
<tr>
<th>Major Criteria</th>
<th>Minor Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute pulmonary edema</td>
<td>Ankle edema</td>
</tr>
<tr>
<td>Cardiomegaly</td>
<td>Dyspnea on exertion</td>
</tr>
<tr>
<td>Hepatopulmonary reflex</td>
<td>Hepatomegaly</td>
</tr>
<tr>
<td>Neck vein distention</td>
<td>Nocturnal cough</td>
</tr>
<tr>
<td>Paroxysmal nocturnal dyspnea or orthopnea</td>
<td>Pleural effusion</td>
</tr>
<tr>
<td>Rales</td>
<td>Tachycardia (&gt;120 bpm)</td>
</tr>
<tr>
<td>Third heart sound gallop</td>
<td></td>
</tr>
</tbody>
</table>

With chronic heart failure, the atria secrete increased amounts of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) in response to high atrial and ventricular filling pressures.

Usually is > 400 pg/mL in patients with dyspnea due to heart failure.
Heart Failure

- Differential diagnosis
  - Simple dependent edema
  - Pulmonary embolism
  - Exertional asthma
  - **Chronic obstructive pulmonary disease (COPD)**
  - Nephrotic syndrome
  - Cirrhosis
  - Anemia
  - Others

Heart Failure Treatment

- General principles
  - Correct systemic factors
    - Thyroid
    - Diabetes
    - Infection
  - Lifestyle modifications
  - Immunizations
  - Review drug therapy
    - Those that may contribute to HF
  - Treat the cause of heart disease
Heart Failure

Goal of pharmacotherapy is to improve symptoms, slow or reverse deterioration in myocardial function and reduce mortality
- Also decrease hospital readmissions
- Decrease direct and indirect costs to healthcare system

Pharmacotherapy
- Loop diuretics
- ACE inhibitors or ARBs
- Beta blockers
- Aldosterone antagonists
- Hydralazine plus nitrates
- Digoxin

Diuretics
- Congestive symptoms and pulmonary and peripheral edema are due to retention of sodium and water
  - Symptom control within hours to days with diuretic therapy
- Data is limited of diuretic efficacy
  - Meta analysis of few small trials show reduced mortality and reduced admission for worsening heart failure
- Goal of therapy
  - Eliminate clinical evidence of fluid retention while avoiding adverse events
Diuretics

- Furosemide
  - Most commonly used loop diuretic
  - 40 mg daily – starting dose
  - 1.0 kg/day weight loss is reasonable
  - In patients that do not respond, dose should be increased to find the effective dose
    - Opposed to increase frequency of previous dose
- Other diuretics
  - Bumetanide, Torsemide, Ethacrynic acid

ACE Inhibitors

- ACE inhibitors improve survival in patients with LVEF ≤ 40%
  - All patients with asymptomatic or symptomatic left ventricular dysfunction should be started on an ACE
- Start low and titrate dose every 1 to 2 weeks as tolerated
  - Check labs after 2 weeks of starting/changing doses
    - Plasma potassium and renal function
- Provides rapid hemodynamic benefit and will not exacerbate heart failure

ACE Inhibitors

- Lisinopril
  - Most common, most affordable
  - 5 mg daily – starting dose
  - 40 mg daily – target dose
  - Higher doses successful in trials
- Other ACE Inhibitors with HF data
  - Enalapril (BID dosing), Captopril (TID dosing)
- Most evidence does not support inhibitory effect of aspirin on outcome data for ACE inhibitors in HF patients
- ASA is still recommended for patients with CAD
**ARBs**

- The 2013 ACCF/AHA guidelines recommend an ARB in patients who cannot tolerate ACE inhibitors.
- ARBs are typically more expensive
- They should not be added to ACE inhibitor and beta blocker therapy

**Beta Blockers**

- Certain beta blockers improve overall and event-free survival in patients with NYHA class II to IV HF
  - Patients receiving beta blockers in trials were already receiving ACE inhibitor therapy
  - Survival is most likely additive
- Beta blockers with intrinsic sympathomimetic activity should be avoided (pindolol, acebutolol)
- Hemodynamic effects of beta blockers are delayed
  - Worsening cardiac function upon initiation of therapy
  - Long-term improvements are dose-dependent

**Beta Blockers**

- Relative contraindications
  - Heart rate < 60 bpm
  - Symptomatic hypotension
  - PR interval > 0.24 sec
  - Second or third degree AV block
  - History of asthma or reactive airways
  - PAD with resting limb ischemia
Beta Blockers

- Carvedilol, Metoprolol Succinate, Bisoprolol
  - All have been shown to reduce all-cause mortality and decrease hospitalization
  - Limited data comparing the drugs to each other
  - Patients with low blood pressure may not tolerate carvedilol due to vasodilatory properties
- Patients should be euvolemic prior to starting therapy
- Begin at low doses, double dose every 2 weeks until target dose is met or symptoms limit further increase
- Carvedilol – Target Dose 25-50 mg twice daily
- Metoprolol Succinate – Target Dose 200 mg daily
- Bisoprolol – Target Dose 5 to 10 mg daily

Aldosterone Antagonists

- Randomized controlled trials have demonstrated the benefit of competition with aldosterone for mineralocorticoid receptor in prolonged survival for heart failure patients
- Guidelines recommend an aldosterone antagonist in patients with NYHA II to IV with LVEF ≤ 35% who have normal potassium
- Serum potassium and creatinine should be checked 1 – 2 weeks after starting therapy
  - Patients with renal dysfunction at high risk for hyperkalemia

Aldosterone Antagonists

- Spironolactone
  - Nonselective binding to androgen and progesterone receptors
  - Higher endocrine side effects (gynecomastia)
  - 25 – 50 mg daily
  - Less expensive than eplerenone
- Eplerenone
  - Greater specificity for mineralocorticoid receptor
  - Lower incidence (1% vs. 10% in clinical trials) of endocrine effects
  - 25 – 50 mg daily
Hydralazine plus Nitrates

- Clinical trials have proven this combination to provide symptomatic and mortality benefit in patients with HF due to systolic dysfunction
- Recommended for African Americans with NYHA III to IV with LVEF< 40 % despite optimal therapy with standard therapy
  - Strength of evidence is in African Americans
- May be useful in patients unable to tolerate ACE inhibitors or ARBs due to allergy or renal dysfunction

Hydralazine plus Nitrates

- Hydralazine – starting dose
  - 25 mg TID
- Isosorbide dinitrate – starting dose
  - 20 mg TID
- Titrate dose every 2 to 4 weeks
  - Avoid increasing dose if hypotension occurs
  - Hydralazine – Target Dose 75 mg TID
  - Isosorbide dinitrate – Target Dose 40 mg TID
  - Isosorbide mononitrate may be used
  - Improved compliance

Digoxin

- Given to control symptoms
  - Fatigue
  - Dyspnea
  - Exercise intolerance
  - Control rate in patients with AFIB
- No benefit in terms of overall mortality
  - Benefit in reduction in morbidity and hospitalizations for heart failure
- Dose based on renal function
  - Usually no more than 0.125 mg daily
  - Keep levels 0.5 and 0.8 ng/ml
Medication Reconciliation

- Important to recognize other medications in the profile that can contribute to new or worsening heart failure
  - NSAIDS
    - Can cause worsening of preexisting heart failure
  - Thiazolidinediones
    - Rosiglitazone (Avandia) and Pioglitazone (Actos)
    - Cause fluid retention that can exacerbate heart failure
  - Metformin
    - People with heart failure who take it are at increased risk of lactic acidosis

Patient Case

Chronic Obstructive Pulmonary Disease (COPD)
Chronic Obstructive Pulmonary Disease (COPD)

- Third leading cause of death in the US in 2011
- In the US, tobacco smoke is the key factor in the development and progression of COPD
- 2013 marks the tenth consecutive year in which women have exceeded men in the number of deaths attributable to COPD
- An estimated 715,000 hospital discharges were reported in 2010; a discharge rate of 23.2 per 100,000 population
  - Approximately 65% of discharges were in the 65 years and older population in 2010
- Exacerbations and comorbidities contribute to the overall severity in individual patients

Chronic Obstructive Pulmonary Disease (COPD)

- Chronic obstructive pulmonary disease (COPD) refers to a group of diseases that cause airflow blockage and breathing-related problems
  - Includes chronic bronchitis, emphysema and in some cases asthma
- Chronic bronchitis produces excess mucus that blocks your bronchial tubes
  - The lining of the airways may become irritated or inflamed, and the airway muscles may spasm
  - A cough with mucus that lasts 3 months for 2 years in a row may be chronic bronchitis
- Emphysema affects the air sacs in your lungs which cause them to become enlarged
  - As air sacs get bigger, the walls between the sacs are stretched thin and cannot spring back to their normal size
  - It then becomes difficult for fresh air with oxygen to enter the sacs and blood stream

Chronic Obstructive Pulmonary Disease (COPD)

- Risk factors
  - Genes
  - Exposure to particles
    - Tobacco smoke
    - Occupational dusts, organic and inorganic
    - Indoor air pollution from heating and cooking with biomass in poorly ventilated dwellings
    - Outdoor air pollution
  - Lung growth and development
  - Gender
  - Age
  - Respiratory infections
  - Socioeconomic status
  - Asthma/Bronchial hyperreactivity
  - Chronic Bronchitis
Chronic Obstructive Pulmonary Disease (COPD)

- Initial assessment includes
  - History and physical exam
  - Chest radiography
  - Spirometry
    - Spirometry is required to make the diagnosis; the presence of a post-bronchodilator FEV₁/FVC < 0.70 confirms the presence of persistent airflow limitation and thus of COPD

Chronic Obstructive Pulmonary Disease (COPD)

- The characteristic symptoms of COPD are chronic and progressive dyspnea, cough, and sputum production that can be variable from day-to-day.
  - Dyspnea
  - Chronic cough
  - Chronic sputum production

Chronic Obstructive Pulmonary Disease (COPD)

- Assessment of symptoms
  - COPD Assessment Test (CAT): An 8-item measure of health status impairment in COPD
  - Breathlessness Measurement using the Modified British Medical Research Council (mMRC) Questionnaire: relates well to other measures of health status and predicts future mortality risk
  - Clinical COPD Questionnaire (CCQ): Self-administered developed to measure clinical control in patients with COPD
Classification of Severity of Airflow Limitation in COPD*

In patients with FEV₁/FVC < 0.70:

- GOLD 1: Mild  \( \text{FEV}_1 \geq 80\% \text{ predicted} \)
- GOLD 2: Moderate  \( 50\% < \text{FEV}_1 < 80\% \text{ predicted} \)
- GOLD 3: Severe  \( 30\% < \text{FEV}_1 < 50\% \text{ predicted} \)
- GOLD 4: Very Severe  \( \text{FEV}_1 < 30\% \text{ predicted} \)

*Based on Post-Bronchodilator FEV₁

Chronic Obstructive Pulmonary Disease (COPD)

<table>
<thead>
<tr>
<th>Physical Exam Findings</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Bronchitis</td>
<td>Emphysema</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>Barrel chest</td>
</tr>
<tr>
<td>Wheezing</td>
<td>Minimal wheezing</td>
</tr>
<tr>
<td>Weight gain</td>
<td>Accessory muscles used</td>
</tr>
<tr>
<td>Diminished breath sounds</td>
<td>Pursed lip breathing</td>
</tr>
<tr>
<td>Distant heart sounds</td>
<td>Cyanosis (slight or absent)</td>
</tr>
<tr>
<td>Breath sounds diminished</td>
<td></td>
</tr>
</tbody>
</table>

Laboratory Evaluation/Diagnostic Procedures

<table>
<thead>
<tr>
<th>Initial tests</th>
<th>Follow Up and Special Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABGs (hypercapnia, hypoxia)</td>
<td>Overnight oximetry</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>α1-antitrypsin screening</td>
</tr>
<tr>
<td>PFTs</td>
<td>Nocturnal oximetry</td>
</tr>
</tbody>
</table>
Chronic Obstructive Pulmonary Disease (COPD)

- Differential diagnosis
  - Asthma
  - Bronchiectasis
  - Lung cancer
  - Acute viral infection
  - Normal aging of the lungs
  - Chronic pulmonary embolism
  - Sleep apnea
  - Congestive heart failure (CHF)
  - Gastroesophageal reflux disease (GERD)

COPD Treatment

- General principles
  - Smoking cessation
  - Reduction of other risk factors
  - Vaccinations
  - Oxygen therapy
  - Pulmonary rehabilitation
Chronic Obstructive Pulmonary Disease (COPD)

- Goal of pharmacotherapy is to control symptoms, decrease exacerbations and improve patient function and quality of life
  - Also decrease hospital readmissions
  - Decrease direct and indirect costs to healthcare system

Pharmacotherapy

- Inhaled bronchodilators
  - Beta-agonists
  - Anticholinergics
  - Inhaled glucocorticoids
  - Theophylline
  - PDE4 Inhibitors
  - Additional therapies

Bronchodilators

- Mainstay for patients with COPD
  - Beta-agonists
  - Anticholinergics
  - Theophylline

- Long-term improvement in symptoms, exercise capacity and airflow limitation

- Available in short-acting and long-acting formulations

- Inhalation is the preferred method of medication delivery in COPD patients
  - Minimizes systemic effects
  - Maximizes direct effect of airways
Short-Acting Bronchodilators

- Beta agonists (albuterol, levalbuterol)
  - Generally prescribed on an as-needed basis
  - Scheduling does not improve outcomes
- Side effects (most do not occur at recommended doses)
  - Arrhythmias
  - Tremor
  - Reflex tachycardia
  - Hypokalemia

Short-Acting Bronchodilators

- Anticholinergics (ipratropium)
  - Improves lung function and symptoms
  - As-needed and regularly scheduled dosing regimens have not been compared with ipratropium
- Albuterol vs. Ipratropium
  - Both medications improve lung function to similar degree
  - Side effects are unique to each medication
- Combivent Respimat®
  - Combivent MDI no longer available after Dec. 31, 2013
  - Dosing: 1 puff by mouth 4 times daily (max 6 per day)
Long-Acting Bronchodilators

- Beta agonists (salmeterol, formoterol, arformoterol, indacaterol, and vilanterol)
  - All beta 2 selective
  - TORCH trial proved benefit
  - Decreased exacerbation rates
  - Improved lung function
  - Improved health-related quality of life
- Vilanterol is a new once-daily LABA
  - Rapid onset of action (10 minutes)
  - Developed for use with umecclidinium or fluticasone furoate
  - Not available for use as monotherapy

Long-Acting Bronchodilators

- Anticholinergics (tiotropium, aclidinium, umecclidinium, and glycopyrronium)
  - Tiotropium is the most studied
  - Improves lung function
  - Decreases dynamic hyperinflation
  - Decreased dyspnea and exacerbations
  - May slow decline in FEV₁
  - Spiriva® Respimat®
    - Concerns about increased CV risk
    - TIOSPIR trial reveal no safety issues
    - Not yet approved in US
  - Umecclidinium is a once-daily LAMA
    - Similar to tiotropium
    - Developed for combination with vilanterol for once-daily combination inhaler

Long-Acting Bronchodilators

- Combination therapy
  - Patients with GOLD II-IV may benefit from the addition of a second long-acting bronchodilator from a second class
  - Only slightly better quality of life and post-bronchodilator FEV₁
  - No difference in secondary end points
  - Anoro® Ellipta®
    - Umecclidinium-vilanterol dry powder inhaler
    - Once daily use, approved in the US
    - No data available for reduction in exacerbations
    - Minimal data available comparing to existing agents
Inhaled Glucocorticoids

- Aimed to decrease systemic inflammation that is often associated with COPD
- May decrease this inflammation
- Modestly decrease exacerbations
- Slow progression of respiratory symptoms
- Have little impact on mortality and lung function

- In COPD, must be part of a combined regimen
  - Should not be used as sole therapy in COPD

Bronchodilators plus Inhaled Glucocorticoids

- Typically used in patients with GOLD III-IV with:
  - Significant symptoms
  - Frequent exacerbations despite optimal therapy with bronchodilators

- If signs of inflammation or more of an asthmatic component of the disease is present sooner, then you may start it earlier

- Combination therapy significantly improves outcomes compared to any agent alone and compared to long-acting anticholinergics
  - TORCH
  - INSPIRE

Bronchodilators plus Inhaled Glucocorticoids

- Breo® Ellipta®
  - Once daily dry powder inhaler
  - Approved for use in the US
  - Contains fluticasone furoate and vilanterol
  - Multicenter, 24 week trial
  - Modest improvements in symptoms
  - Statistically significant increase in trough FEV₁
  - Sustained improvement in lung function
  - Increased rate of pneumonia
Triple Inhaler Therapy
- Reserved for severe COPD, GOLD IV
- Mixed data regarding improvements in mortality and reductions in hospitalizations and exacerbations
  - Most show trends towards better outcomes, however data is not consistent across the board

Theophylline
- Modest oral bronchodilator
- Typically used as last line therapy
- Standard released and extended release versions available on the market
- Can be toxic
  - Metabolized by the liver
  - Narrow therapeutic drug
    - Serum levels 8-12 mcg/ml for COPD

PDE 4 Inhibitors
- Roflumilast
  - Oral PDE 4 inhibitor
  - Decrease inflammation and promotes smooth muscle relaxation in the airway
  - Approved in US
    - Benefits are modest
  - $$$
Additional Therapies
- Systemic glucocorticoids
  - Significant adverse effects
  - Lowest dose possible, shortest time possible
- Mucoactive agents
  - Little evidence that thinning or increasing clearance of secretions provides any benefit
- Chronic antibiotic therapy
  - Not indicated for a majority of patients
    - Macrolide antibiotics have anti-inflammatory properties
    - Conflicting data on decreased exacerbations
    - Side effects

Additional Therapies
- Smoking cessation
  - Motivational interviewing
  - Nicotine replacement therapy
  - Chantix
  - Bupropion
  - Counseling
- Vaccinations
  - Pneumovax
  - Influenza

Patient Case
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- 2010 Heart Failure Society of America guidelines
- GOLD Guidelines