What is Heart Failure

- A complex clinical syndrome that can result from a structural or functional cardiac disorder that **impairs the ability of the ventricle to fill with or eject blood.**
Heart Failure in Simple Terms

• Heart failure is a condition in which the heart muscle becomes weakened and unable to pump enough blood or become stiff and unable to fill with blood.
• Congestive Heart Failure versus Heart Failure

Classification of Heart Failure

<table>
<thead>
<tr>
<th>Classification</th>
<th>Ejection Fraction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Failure with Reduced EF (HFrEF)</td>
<td>EF ≤ 40</td>
</tr>
<tr>
<td>Heart Failure with preserved EF (HFpEF)</td>
<td>EF ≥ 50</td>
</tr>
<tr>
<td>Heart Failure preserved borderline (HFpEF borderline)</td>
<td>EF 41 – 49</td>
</tr>
<tr>
<td>Heart Failure improved (HFpEF improved)</td>
<td>EF &gt; 40</td>
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Peripartum Cardiomyopathy (PCCM)

• Development of heart failure in the last month of pregnancy or up to 5 months after delivery
• Absence of determinable etiology of heart failure
• Absence of demonstrable heart disease before the last month of pregnancy
• Left ventricular (LV) systolic dysfunction demonstrated by echocardiography with LVEF <45%.
Peripartum Cardiomyopathy
The Impact

- Majority of cases occur within the first week postpartum.
- A national database analysis of 64 million hospital records included 1000 hospitals in 47 states reported 34,219 cases of postpartum cardiomyopathy (PPCM). Incidence of 1 in 978 births.
- The incidence is increasing:
  - 1990 and 2002 incidence of 2.3 – 4.5 per 10,000 live births
  - 2004 and 2011 incidence of 8.5 – 11.8 per 10,000 live births

Elkayam, 2011

<table>
<thead>
<tr>
<th>Year of Study</th>
<th>Sample Size</th>
<th>Ethnic Background</th>
<th>Period of Study</th>
<th>Incidence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1989-1994</td>
<td>67,349</td>
<td>African American 75%</td>
<td>24-90 (Mean)</td>
<td>1 in 1,400</td>
</tr>
<tr>
<td>1996-2001</td>
<td>69,071</td>
<td>African American 80%</td>
<td>18-99 (Mean)</td>
<td>1 in 1,540</td>
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<tr>
<td>2004-2011</td>
<td>70,272</td>
<td>African American 80%</td>
<td>18-99 (Mean)</td>
<td>1 in 1,540</td>
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Elkayam, 2011

Time of Diagnosis
Peripartum Cardiomyopathy

Elkayam, 2011
Associated Conditions

- Age ≥ 30
- Race considerably higher in African Americans
- Hypertension either chronic, pregnancy induced or preeclampsia
- Multifetal pregnancies
- Parity in the US first or second pregnancy > 50%

Symptoms of Heart Failure

- Fatigue
- Activity decrease, Abdominal Pain
- Cough; Chest Pain
- Edema
- Shortness of breath
  - Orthopnea – SOB lying flat
  - Paroxysmal Nocturnal Dyspnea
    - Severe SOB and coughing that occurs at night

Examination Findings

- Tachycardia
- Tachypnea
- Blood pressure may be elevated or reduced
- Do not tolerate lying flat on the exam table
- Increased Jugular Vein Distention
- Displaced Apical impulse
- Murmurs
- S3 heart sound
- Pulmonary rales
- Peripheral edema
Diagnosing Peripartum Cardiomyopathy

• Establishing the diagnosis relies upon a “high index of suspicion.”
• It can occur quickly, subtly or over several weeks.
• Early diagnosis is important in best efforts to ensure the best patient outcomes.

Diagnostic Tools

• Brain Natriuretic Peptide (BNP) - measures a protein hormone that is produced by the ventricles and is increased during heart failure. Normal value <100 is 98% accurate in ruling out HF.
• Electrocardiogram no specific pattern associated with PPCM, may see intraventricular conduction delays ex: left bundle branch block.
• Chest X-ray may demonstrate pulmonary edema, congestion, pleural effusion, and/or cardiomegaly.

Diagnostic Tools

• Echocardiogram “TTE” – the most important diagnostic tool for confirming or excluding Peripartum Cardiomyopathy.
• Recommended to be performed in every suspected case of Peripartum Cardiomyopathy.
Management of Peripartum Cardiomyopathy

- Heart failure during pregnancy poses a challenge due to the lack of evidence-based clinical data.
- During pregnancy, therapeutic interventions must consider the health of the mother and the fetus.
- Management includes: Medications, fluid and sodium restrictions.

During Pregnancy

- Cardiology Referral
- Medications contraindicated:
  - Angiotension Converting Enzyme Agents
  - Angiotension Receptor Blocker Agents
  - Aldosterone antagonist associated with antiandrogenic effects especially during 1st Tri.
  - Diuretics should only be used if pulmonary congestion exist due to can decrease fetal blood flow.

Management of PPCM After Delivery

- After delivery standard therapy including the following are recommended:
  - Beta Blockers started at low doses
  - ACE inhibitors and if intolerant ARB therapy
  - Diuretics
  - Mineralocorticoid receptor antagonists
Angiotensin-Converting Enzyme Inhibitors

Inhibit the Angiotensin-converting enzyme (ACE), an important component to renin-angiotensin system which causes vasoconstriction, and increases afterload.

- Neurohormonal modification
- Decrease blood pressure
- Vasodilation
- Improvement in LVEF
- Decrease mortality
- Reduce kidney disease in Diabetes

- Side effects: angioedema, dry cough, hyperkalemia, hypotension, reduction in glomerular filtration rate, inflammation related pain

- Contraindications: Previous angioedema, anaphylaxis, renal stenosis, severe renal disease

- Lower doses may be necessary in patients with creatinine clearance of < 30mL/minute.

- Contraindicated in pregnancy.

- First Evidence was seen in 1987 in the CONSENSUS study 40% mortality reduction with severe HF treated with enalapril.

<table>
<thead>
<tr>
<th>ACE Inhibitors</th>
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<tbody>
<tr>
<td>Lisinopril (Prinivil, Zestril)</td>
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<tr>
<td>Ramipril (Altace)</td>
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<tr>
<td>Captopril (Capoten)</td>
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<tr>
<td>Enalapril (Vasotec)</td>
</tr>
<tr>
<td>Benazepril (Lotensin)</td>
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</tbody>
</table>

*Which ACE inhibitor?* Have been studied and demonstrated reduction in mortality.

- Captopril
- Enalapril
- Trandolapril
- Lisinopril
- Ramipril

*What dose?*

- The NETWORK and ATLAS studies have tried to answer this question.
- NETWORK no significant difference in outcomes patient treated with high and low dose enalapril.
- ATLAS N=1614 demonstrated a reduction in the combined endpoint of death and total hospitalization in the group treated with 32.5 – 35mg Lisinopril versus 2.5-5mg/day.
- High dose specifically the dose used in the mortality trial as the target dose unless the patient is intolerant to higher dose.

Angiotensin II Receptor Blocker

- ARBs block the action of Angiotensin II by preventing angiotensin II from binding to angiotensin II receptors.
- Do not inhibit the breakdown of bradykinin or other kinins.
- Vasodilation
- Reduces secretion of vasopressin
- Reduces production and secretion of aldosterone.
- Reduces blood pressure

- Side effects: headache, dizziness, hypotension, nausea, muscle cramps, myalgia, nasal congestion, weight gain, hypokalemia, hyperkalemia.

- Contraindicated in pregnancy.

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<tr>
<td>Atacand (candesartan)</td>
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<tr>
<td>Avapro (irbesartan)</td>
</tr>
<tr>
<td>Benicar (olmesartan)</td>
</tr>
<tr>
<td>Cozaar (losartan)</td>
</tr>
<tr>
<td>Diovan (valsartan)</td>
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<tr>
<td>Micardis (telmisartan)</td>
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<tr>
<td>Teveten (eprosartan)</td>
</tr>
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</table>

*Which ARB?* Atacand (candesartan) or Losartan

*What dose?*
- Losartan 50mg daily
- Valsartan 160mg twice daily

When using ARB therapy: Must follow algorithm for ACE inhibitors, Hypotension, Hypokalemia, weight gain, nausea, muscle cramps, myalgia, nasal congestion, weight gain, ARB intolerance, headache, hypokalemia, hypertension.
The Elite study sought to establish the tolerability of the ARB, losartan, compared with captopril, in a group of older patients with heart failure. It was not powered as a mortality study, but had the unexpected finding that there was a reduction in mortality in the losartan group.

However, the ELITE II enrolled a total of 3152 patients aged 60 years or more with an ejection fraction of 40% or less were randomized to losartan (50mg once daily) or captopril (50mg three times daily).

At follow-up of 555 days, there was no significant difference in all-cause mortality (11.7 vs 10.4% annual mortality) between the two treatment groups. Captopril appeared to produce better results. However, significantly fewer patients in the losartan group discontinued study treatment because of adverse effects (9.7 vs 14.7%, P<0.001), including cough (0.3 vs 2.7%).

The evidence has shown that ARB therapy is not superior to ACE inhibitor therapy for heart failure (HF) but should be prescribed if intolerant to ACE therapy.

• improved symptoms and exercise tolerance
• CHARM trial impact on mortality was not statistically significant
• Elite demonstrated an increase in mortality when co-prescribed beta blocker.

Beta Blocker Therapy

- Beta adrenergic blocking agents block the effects of the hormone epinephrine (adrenaline) by blocking the receptor sites.
  - Beta 1 receptor located in the heart & kidneys
  - Beta 2 receptors located in the lungs, GI liver, uterus, vascular smooth muscle and skeletal muscle.
- Reduce heart rate
- Decrease in renin secretion
- Reduce heart oxygen demand
- Peripheral vasodilation
- Initial reduction in ejection fraction but with continued therapy results in improved ejection fraction.
- Reduce mortality in heart failure

Diuretic Therapy

- Diuretic therapy in heart failure with fluid retention is used to maintain euvoemia “dry weight” and prevent fluid volume overload
- Loop Diuretics are more commonly used:
  - Furosemide more intense and shorter diuresis than thiazide diuretics
  - Bumetanide
  - Torasemide – longer half life and in the TORIC trial was associated with lower HF mortality than Furosemide
Spironolactone and ACE therapy

- The RALES study demonstrated a survival benefit for patients with NYHA class III symptoms treated with aldosterone receptor antagonist Spironolactone and eplerenone (Inspra). “reduces the effect of aldosterone.”
- Reduces absorption of sodium and water
- Often used with other diuretics to correct or prevent potassium deficiency.
- Contraindicated Creatinine >2.5mg/DL or clearance <30mL/min, serum potassium >5.0

Reduces absorption of sodium and water

- Contraindicated Creatinine >2.5mg/DL or clearance <30mL/min, serum potassium >5.0

Measure potassium at baseline, 1 week, 1 month, and every 3 months.

Hydralazine

- Action: a direct-acting smooth muscle relaxant and acts as a vasodilator primarily in resistance arterioles. Results in smooth muscle relaxation and decrease peripheral vascular resistance. (decreased blood pressure and afterload)
- Action 15 minutes up to 6 hours.
- Can increase the heart rate and not recommended in the setting of Coronary Artery Disease resulting in chest pain—MI.
- Dosing: Start low and increase as tolerates maximum dose 100mg TID
- Side effects: Prolonged treatment can cause syndrome similar to Lupus d/c if occurs.
- Elevated heart rate, Headache, Dizziness, Palpitations

Isosorbide Dinitrate

- Vasodilator effect
- Dosing: start low and increase as tolerate.
- Side effects: Dizziness, orthostatic hypotension, can worsen chest pain due to neurohormonal activation
- BiDil 20mg/37.5mg (2-3 times daily)
New Medication Strategies

• Angiotensin Receptor Neprilysin Inhibitor
  - Sacubitril is an antihypertensive medication used in combination with valsartan.
  - Action: Inhibits the enzyme neprilysin which is responsible for the degradation of atrial and brain natriuretic peptide, by reducing blood volume. Neprilysin also degrades bradykinin which exhibits a potent vasodilatory action.
  - Entresto: significant reduction in all-cause mortality HFrEF

Entresto

• Indications: to reduce the risk of heart failure mortality and hospitalization in patients with chronic heart failure (NYHA class II-IV) and reduced ejection fraction.
• Administered with other HF medications in placed of ACE or ARB therapy.
• Side effects: angioedema, hypotension, hyperkalemia, impaired renal function, cough, dizziness, renal failure.
• Contraindications: pregnancy.

Other Treatments

• Anticoagulation due to increase incidence of thromboembolism associated not only with pregnancy by PPCM.
• Automatic Implantable Cardioverter-defibrillators
• LV Cardiac Assist device
• Cardiac Transplantation
Digoxin

- Actions slow cardiac conduction through AV node and increases force of myocardial contraction. May help to achieve a satisfactory ventricular rate in patients in atrial fibrillation and may improve exercise capacity in patients with symptomatic HFrEF.
- Did not demonstrate an effect on mortality, some impact on decrease hospitalization in patients with HFrEF.
- Used as a part of first line therapy in HFrEF in the setting of atrial fibrillation.
- Used as a second line drug after diuretics, ACEs, beta blockers for patient with HFrEF who are in normal sinus rhythm.
- Dose: 0.125mg daily

Recovery of LV Function

- 18% occurred with 1 week of diagnosis; 87% within 6 months of diagnosis
- Death was either due to Progression of HF or Sudden Cardiac Death
- Mortality was higher in women with baseline LVEF ≤ 25% and women with delayed diagnosis
A subsequent pregnancy carries a recurrence risk of PPCM of 30-50%. When the EF has not normalized a subsequent pregnancy should be discouraged.

Finally

- Breast feeding should be encouraged if possible, the rate of recovery of LV function was significantly higher in lactating women.
- ACE Trials: Benazepril, Captopril, and Enalapril have been tested in breastfeeding women and proved to be safe for babies.

Case Study:

- 36 YO AA female G4P3 at 33 weeks gestation presents for a routine appointment. She continues to emphasize this was unplanned, and this pregnancy is very different from prior pregnancies.
- PMH: Psoriasis; Preeclampsia with last pregnancy
- Complaints: Fatigue and shortness of breath
- Allergies: No Known Drug Allergies
- Medications:
  - Prenatal vitamins one tablet daily
- Vital signs: 140/98, 110, 24, 90%, 98.6
- Weight increased 9 pounds since last visit

What would you do in the management to this patient?