Acute on Chronic Heart Failure with Reduced Ejection Fraction

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Disclosures

- No relevant commercial relationships to disclose.

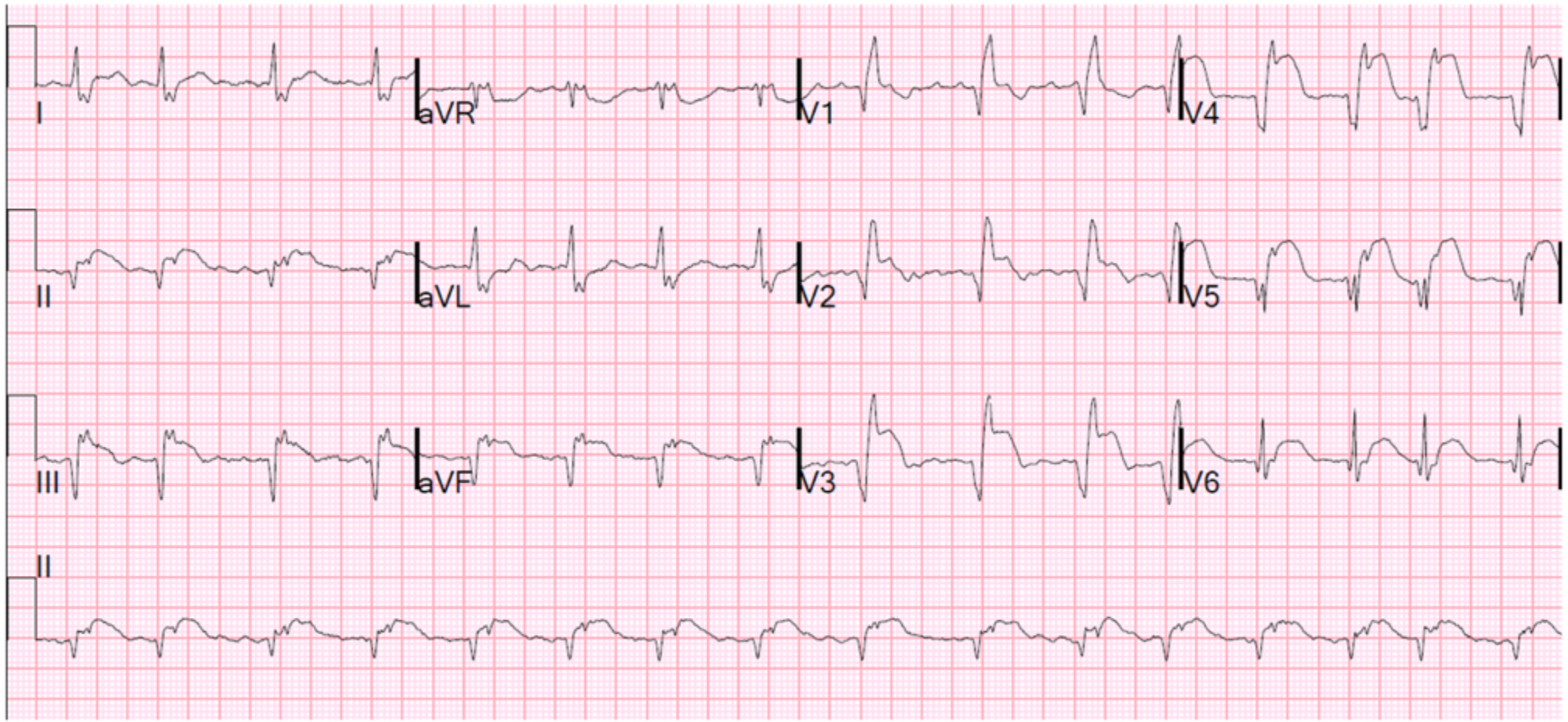
Learning Objectives

- At the conclusion of this session, participants should be able to:
- 1) Identify common medications used for managing heart failure
- 2) Identify the most common cause of acute and chronic heart failure in the United States
- 3) Understand how chronic heart failure is categorized based upon symptom presentation

Scenario

- RJ is a 48-year-old male who began to experience chest pain and shortness of breath while coaching his son's baseball team during a game. His chest pain started during the second inning. He continued to experience worsening symptoms throughout the game. At the end of the game, 2 hours later, he was diaphoretic and unable to walk to his vehicle. His co-parenting coach called EMS.

- Past medical history non-significant.
- Family history: Father deceased from MI at age 69.
- Social history: Works as a software engineer. Married. 3 kids.


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

Hospital Course

1

A Code STEMI was called as the patient approached the ER. He was given 162mg of ASA in route along with morphine and sublingual nitroglycerin.

2

He was brought to the CATH lab where interventional cardiologists successfully placed 2 stents: 1 to the left circumflex artery and one to the distal left anterior descending artery.

3

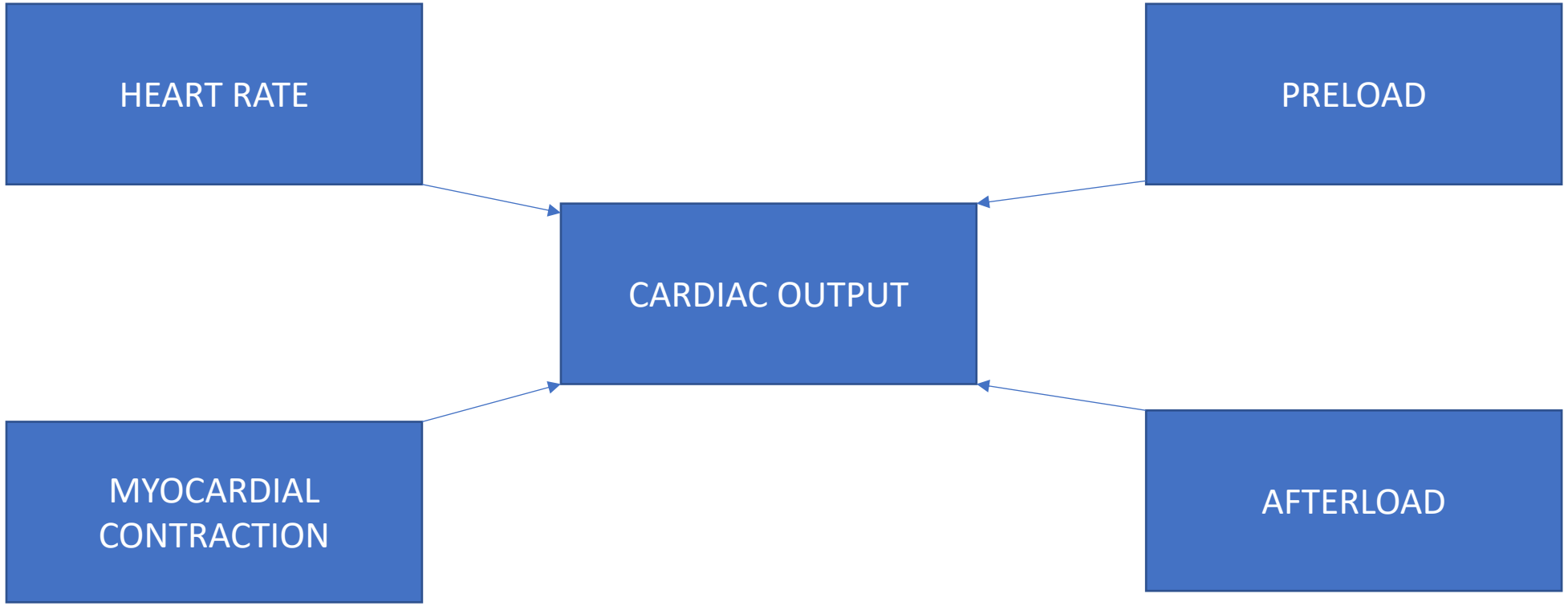
He was admitted to the intensive care unit for post stent management. He is intubated.

4

His EF is 15% with global hypokinesis. His cardiac index is 1.4. His BP is 85/44

Cardiogenic Shock

- Characterized by acute hypoperfusion and end organ dysfunction due to reduced cardiac output.



Main Cause of Cardiogenic Shock

- Most common cause is acute coronary syndrome accounting for 80% of all cases (Laslett, et al., 2012).
- In SHOCK trial and registry- 78.5% were attributed to LV failure.
  - 58.8% presented with anterior MI
  - 34.4% presented with inferior wall MI without anterior environment (Hochman, et al., 1999)

Epidemiology of Acute Heart Failure

> 1 million people are admitted for AHF in the USA & Europe annually

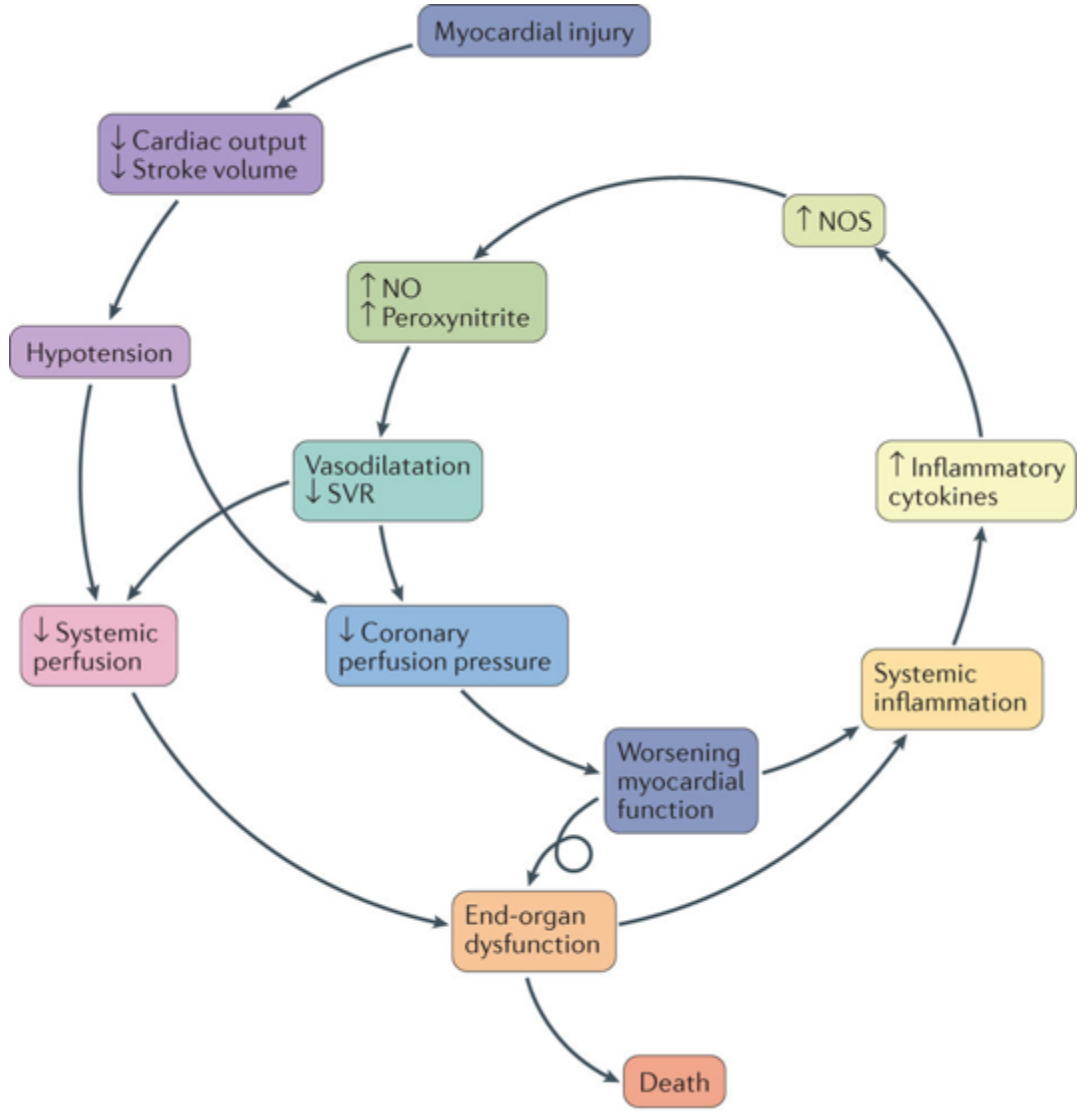
In contrast to improvement in the outcomes of patients with chronic heart failure over the past 3 decades, patients hospitalized for AHF continue to experience high morbidity.

1 year mortality is 30%. (Ambrosy, et al., 2014).

Cardiogenic shock accounts for less than 5% of AHF cases (Nieminen, et at., 2006)

Etiology of Cardio Shock

- Intrinsic
  - Myocardial injury*****
  - Tachycardia
  - Bradycardia
  - Valvular defect
- Extrinsic
  - Pericardial tamponade
  - Tension pneumothorax
  - Large pulmonary emblous



Nature Reviews | Cardiology

Therapeutic Goals for AHF

- Relieve Symptoms
- Reverse acute hemodynamic abnormalities
- Initiate treatments that will slow disease progress and improve long-term survival
- Apply treatment cost-effectively
- Prevent end-organ dysfunction

It’s more than the heart

LUNGS
Increased hydrostatic pressures

BRAIN
Cognitive impairment estimated at 54-75%

LIVER
Hepatic dysfunction is present in 20-30% of AHF

KIDNEYS
20-30% of AHF have renal involvement

INTESTINES
Contributes to the role of chronic inflammation and malnutrition

Harjola, et al., 2017

Ventricular Failure

- Systolic dysfunction (decreased contractility)
  - Ischemia/MI
  - Global hypoxemia
  - Valvular disease
  - Myocardial depressant drugs (eg, beta-blockers, calcium channel blockers, antiarrhythmics)
  - Myocardial contusion
  - Respiratory acidosis
  - Metabolic derangements (eg, acidosis, hypophosphatemia, hypocalcemia)
- Diastolic dysfunction/increased myocardial diastolic stiffness
  - Ischemia
  - Ventricular hypertrophy
  - Restrictive cardiomyopathy
  - Consequence of prolonged hypovolemic or septic shock
  - Ventricular interdependence
  - External compression by pericardial tamponade
- Greatly increased afterload
  - Aortic stenosis
  - Hypertrophic cardiomyopathy
  - Dynamic aortic outflow tract obstruction
  - Coarctation of the aorta
  - Malignant hypertension
- Valvular or structural abnormality
  - Mitral stenosis
  - Endocarditis
  - Mitral aortic regurgitation
  - Obstruction due to atrial myxoma or thrombus
  - Papillary muscle dysfunction or rupture
  - Ruptured septum or free wall arrhythmias
- Decreased contractility
  - RV infarction
  - Ischemia
  - Hypoxia
  - Acidosis

Ventricular Failure

- Greatly increased afterload
  - Pulmonary embolism
  - Pulmonary vascular disease (eg, pulmonary arterial hypertension, veno-occlusive disease)
  - Hypoxic pulmonary vasoconstriction
  - Peak end-expiratory pressure
  - High alveolar pressure
  - Acute respiratory distress syndrome
  - Pulmonary fibrosis
  - Sleep disordered breathing
  - Chronic obstructive pulmonary disease
- Arrhythmias
  - Atrial and ventricular arrhythmias (tachycardia-mediated cardiomyopathy)
  - Conduction abnormalities (eg, atrioventricular blocks, sinus bradycardia)

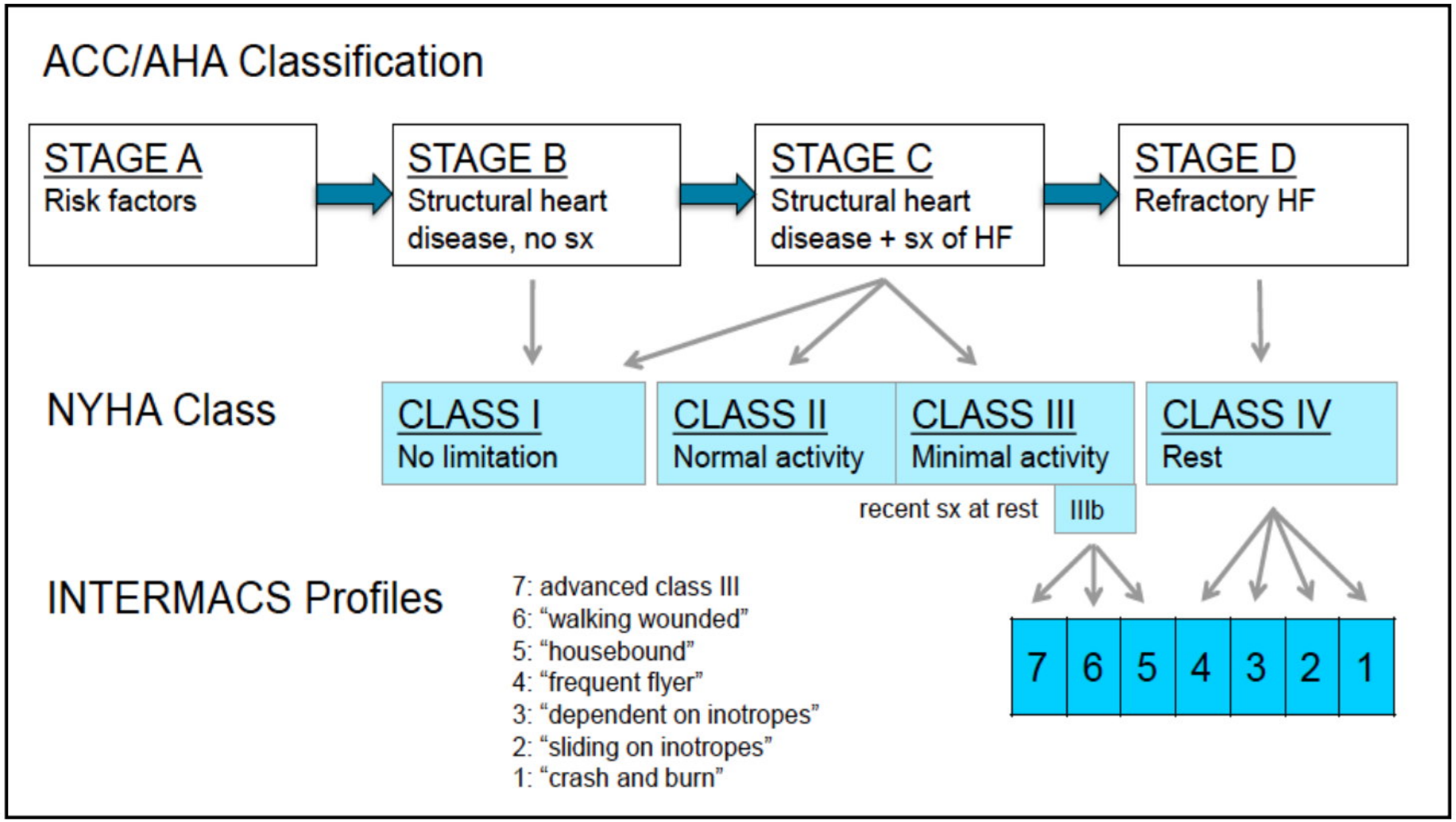
RJ Received 2 Stents: The Evidence

- In hospital mortality following PCI increased from 27.6% in 2005-2006 to 30.6% in 2011-2013 (Wayangankar, et al., 2016).
- CABG surgery has remained infrequently used despite the high prevalence of multi-vessel disease.
- A large study from 1998-2010 demonstrated that patients that underwent culprit only PCI had a significantly worse outcome ($p=0.008$) (Mylotte, et al., 2013).

Fast forward 4 years….

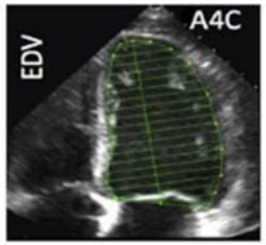
- RJ has moved to your local area and is on your docket for a first time visit. He set-up the appointment 3-months ago and arrives today with the main complaint of fatigue. He has noticed a significant reduction in his ability to "do anything." He gets short of breath when he tries to climb the stairs in his home. He is reluctant to walk the family dog because it's too exhausting. Your review of PMH is significant for the MI and stent placement 4 years ago. He has not seen a provider in over 2 years.
- He is only taking an Aspirin daily. No other medications.

Congestive Heart Failure Classification

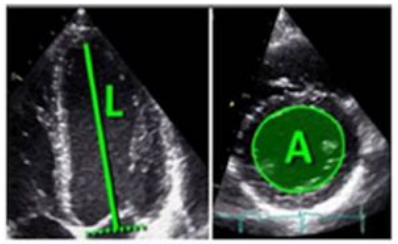


Role of echocardiography in the evaluation of heart failure patients

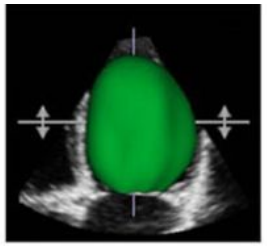
Phenotyping and prognostic assessment

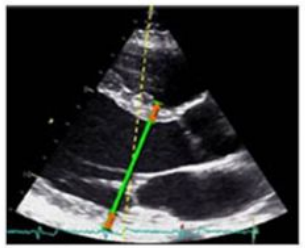


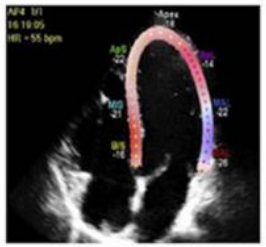
LV volumes and EF



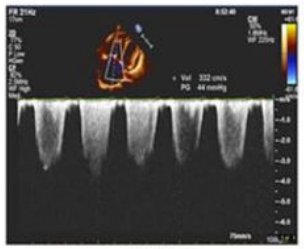
LV mass

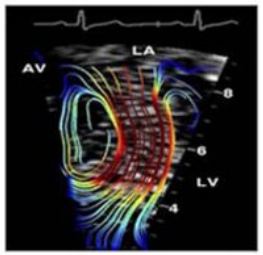

3D LV volumes and EF


LV wall thickness, volumes

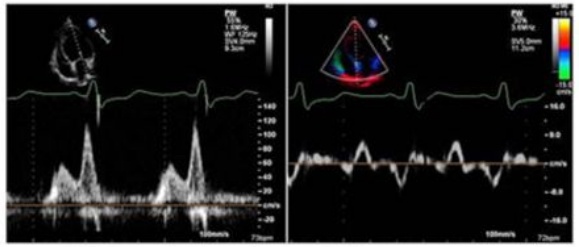

LV myocardial deformation

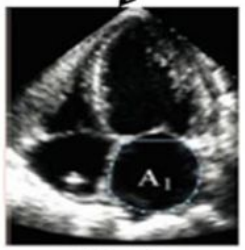
Additional markers of prognosis


PASP

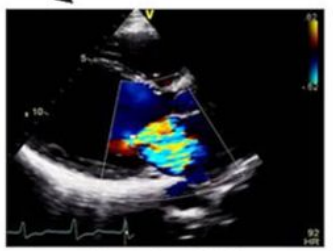


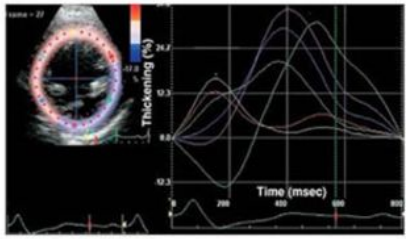
Intracardiac flow mapping


LV diastolic function and filling pressures



LA volume

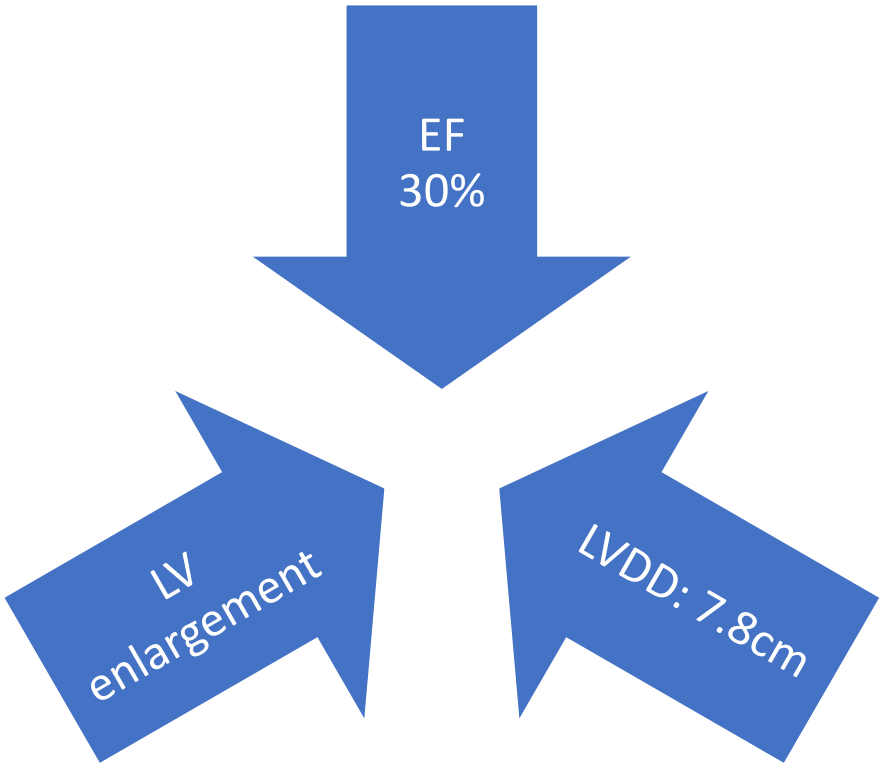

Functional MR



LV dyssynchrony

Making Decisions

ECHO Results



Current Vitals/Symptoms

- BP: 167/77
- HR 111 sinus
- SAT: 93% on RA
- Creatinine 0.95
- BNP 1900
- Na 133
- Short of breath with exertion but not at rest
- Sleeps upright in bed

Classifying RJ

- Stage C, Class III heart failure

Other Diseases To Consider

- Smoking
- Diabetes
- Central vs Sleep Apnea
- Obesity

ACEi vs ARB vs ARNI

- Angiotensin Converting Enzyme Inhibitor
  - Lisinopril, Enalapril
- Angiotensin II Reduction Blocker
  - Losartan
- Angiotensin Receptor Neprilysin Inhibitor
  - Entresto (Sacubitril/valsartan)

ACEi

- ACE inhibitors have been shown in large RCTs to reduce morbidity and mortality in patients with HFrEF with mild, moderate, or severe symptoms of HF, with or without coronary artery disease.
- Data suggest that there are no differences among available ACE inhibitors in their effects on symptoms or survival.
- ACE inhibitors should be started at low doses and titrated upward to doses shown to reduce the risk of cardiovascular events in clinical trials. ACE inhibitors can produce angioedema and should be given with caution to patients with low systemic blood pressures, renal insufficiency, or elevated serum potassium (>5.0 mEq/L).

ARB

- ARBs have been shown to reduce mortality and HF hospitalizations in patients with HFrEF in large RCTs.
- Long-term therapy with ARBs in patients with HFrEF produces hemodynamic, neurohormonal, and clinical effects consistent with those expected after interference with the renin-angiotensin system.
- Unlike ACE inhibitors, ARBs do not inhibit kininase and are associated with a much lower incidence of cough and angioedema, although kininase inhibition by ACE inhibitors may produce beneficial vasodilatory effects

Case Study

- Xi is a 74 year-old-male with known heart failure following a MI 6 years ago and subsequent CABG x 3. He has been managed with Coreg 25 mg BID, Lisinopril 20 mg daily, Torsemide 40 mg daily and 80 mg of Atorvastatin daily.
- His weight is stable today.
- Labs today show no significant change with the exception of his creatinine. Over the past year his baseline creatinine was 1.1. It is now 1.4. His GFR has decreased from >60 to 59.

- Should a medication change be made?

AHA Recommendation

- Discontinuation of angiotensin-converting enzyme (ACE) inhibitor is recommended if patients experience ≥30% acute increase in serum creatinine after starting this therapy. However, the long-term effects of its continuation or discontinuation on major clinical outcomes after increases in serum creatinine are unclear.

  - Ohuma, et al. 2019.

What happens to people when the plasma creatinine goes up after starting an ACEi or ARB (RASi)?

CJASN
Clinical Journal of American Society of Nephrology

31,951

People started RASi with pre- and post-creatinines

Cr increase Reference: < 10%	Mortality	Heart Failure	ESKD	Heart Attack
	3.5 years follow-up. Multivariable Cox regression. Adjusted hazard ratios			
10-19%	**1.15**	**1.14**	**3.25**	1.05
20-29%	**1.22**	**1.23**	**2.65**	**1.32**
≥ 30%	**1.55**	**1.41**	**8.31**	1.29

Conclusions Among real-world monitored adults, increases in creatinine as small as 10% were associated with poorer mortality, as well as worse cardiac and kidney outcomes.

Edouard L. Fu, Marco Trevisan, et al. ***Association of Acute Increases in Plasma Creatinine following Renin-Angiotensin Blockade with Subsequent Outcomes.*** CJASN doi: https://doi.org/10.2215/CJN.03060319. **Visual Abstract by Joel Topf, MD, FACP**

ARNI

- Benefits of ACE inhibitors with regard to decreasing HF progression, hospitalizations, and mortality rate have been shown consistently for patients across the clinical spectrum, from asymptomatic to severely symptomatic HF.
- Evidence suggests benefits even in Stage 1 heart failure.

Clinical Pearls

- Although the use of an ARNI in lieu of an ACE inhibitor for HFrEF has been found to be superior, for those patients for whom ARNI is not appropriate, continued use of an ACE inhibitor for all classes of HFrEF remains strongly advised.
- Head-to-head comparisons of an ARB versus ARNI for HF do not exist.
- In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.
- Not for patients with a history of angioedema
- Allow about 2 days of washout from ACE before starting ARNI.

CENTRAL ILLUSTRATION: Evidence to Support the Use of Angiotensin-Converting Enzyme Inhibitor, Angiotensin Receptor Blocker, Mineralocorticoid Receptor Antagonist, and Angiotensin Receptor-Neprilysin Inhibitors in Coronary Artery Disease and Heart Failure

Atherosclerotic Coronary Disease – Increasing Risk

Heart Failure - Increasing Left Ventricular Ejection Fraction

	Stable Atherosclerotic Vascular Disease	High-Risk Post-Myocardial Infarction	Acute Post-Myocardial Infarction	Heart Failure With Reduced Ejection Fraction	Heart Failure With Midrange Ejection Fraction	Heart Failure With Preserved Ejection Fraction
Angiotensin-Converting Enzyme Inhibitor	+	+	+	+	?	-
Angiotensin Receptor Blockers	+	+	+	+	?	-
Mineralocorticoid Receptor Antagonists	?	+	+	+	?	(+)
Angiotensin Receptor-Neprilysin Inhibitors	?	To Be Determined	To Be Determined	+	To Be Determined	To Be Determined

Leong, D.P. et al. J Am Coll Cardiol. 2019;74(5):683-98.

Beta-Blockers

- Use of 1 of the 3 beta blockers proven to reduce mortality is recommended for all patients with current or prior symptoms of heart failure.
- Bisoprolol
- Carvedilol
- Sustained-release Metoprolol Succinate
- Titrate to effect
- Caution: fluid retention and worsening HF; fatigue; bradycardia or heart block; and hypotension can be seen with Beta-blockers

Ivabradine

- Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HFrEF (LVEF ≤35%) who are receiving (guideline-directed evaluation and management) GDEM , including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest.

- Diuretics should be prescribed to all patients who have evidence of, and to most patients with a prior history of, fluid retention.
- Diuretics should generally be combined with an ACE inhibitor, beta blocker, and aldosterone antagonist.
- Few patients with HF will be able to maintain target weight without the use of diuretics

To make them pee or not?

Table 1: Summary of Diuretic Drugs used in Heart Failure

Drug	Site of Action	Duration of Action	Common Starting Dosage	Maximum Dosage	Common Side Effects
Loop diuretics	Inhibition of Na-K-Cl co-transporter in the thick ascending loop of Henle				Hypokalaemia, hypomagnesaemia, hyperuricaemia, hypocalcaemia, hyponatraemia, otoxicity
Furosemide		7 h	20 to 40 mg once or twice	600 mg	
Bumetanide		4 to 6 h	0.5 to 1.0 mg once or twice	10 mg	
Torasemide		12 to 16 h	10 to 20 mg once	200 mg	
Ethacrynic acid		6 h	25–50 mg once or twice	200 mg	
Thiazide-like diuretics	Inhibition of Na-Cl transporter at distal nephron				Hypokalaemia, hypomagnesaemia, hypercalcaemia, hyponatraemia, hyperuricaemia
Chlorothiazide		6 to 12 h	250 to 500 mg	Once or twice	1,000 mg
Chlorthalidone		24 to 72 h	12.5 to 25 mg once	100 mg	
Indapamide		36 h	2.5 mg once	20 mg	
Potassium-sparing diuretics	Inhibition of mineralcarticoid receptor or its effectors at distal nephron				Hyperkalaemia
Amiloride		24 h	5 mg once	20 mg	
Triamterene		7 to 9 h	50 to 75 mg twice	200 mg	
Spironolactone		1 to 3 h	12.5 to 25.0 mg once	50 mg	Gynecomastia

Case Study

- Your 63 year old female patient Burnadette arrives to your clinic because she made an appointment due to increasing fatigue. She has known chronic heart failure secondary to non-ischemic cardiomyopathy. During her last visit, she was noted to have Stage B Class II heart failure.

- Notables on physical exam are +3 pitting edema in her LE bilaterally.
- Abdominal swelling

Important related information

- Her BP is 145/67, HR 88, SAT 92% on RA, RR 14, subjectively she reports fatigue and shortness of breath
- Her Na level is 128. Her baseline has been around 134.
- Her weight is up approximately 8 pounds.
- Her BNP normally around 400 is now 2500.

- What do you do as an outpatient provider in your clinic?
- Does she need to be admitted to the hospital ?

BNP Levels

- **A normal level of NT-proBNP**, based on Cleveland Clinic's Reference Range is:
- Less than 125 pg/mL for patients aged 0-74 years
- Less than 450 pg/mL for patients aged 75-99 years
- **Possible Problem**
- Higher than 450 pg/mL for patients under age 50
- Higher than 900 pg/mL for patients age 50 and older

Managing Burnadette

- Increasing her diuretic for a short-term is okay. For example, if she is on 20 of Torsemide daily, go ahead and increase to 40 mg a day.
- Possibly give her IV Lasix in the office if you have the ability
- Increase her blood pressure control.
- Metolazone has a role sometimes in this situation.
- Base your next decision for further care based upon her response to the increase diuretic.

Aldosterone Receptor Antagonists:

- Aldosterone receptor antagonists (or mineralocorticoid receptor antagonists) are recommended in patients with NYHA class II–IV HF and who have LVEF of 35% or less, unless contraindicated, to reduce morbidity and mortality.
- Patients with NYHA class II HF should have a history of prior cardiovascular hospitalization or elevated plasma natriuretic peptide levels to be considered for aldosterone receptor antagonists.
- Creatinine should be 2.5 mg/dL or less in men or 2.0 mg/dL or less in women (or estimated glomerular filtration rate >30 mL/min/1.73 m^2), and potassium should be less than 5.0 mEq/L.

Hydralazine and Isosorbide Dinitrate

- The combination of hydralazine and isosorbide dinitrate is recommended for African Americans with HF*r*EF who remain symptomatic despite concomitant use of ACE inhibitors, beta blockers, and aldosterone antagonists.
- Whether this benefit is evident in non–African Americans with HF*r*EF remains to be investigated.

Digoxin?

- In a long-term trial that primarily enrolled patients with NYHA class II or III HF, treatment with digoxin for 2 to 5 years had no effect on mortality but modestly reduced the combined risk of death and hospitalization.

Anticoagulation

- Patients with chronic HF with permanent/persistent/paroxysmal AF and an additional risk factor for cardioembolic stroke (history of hypertension, diabetes mellitus, previous stroke or transient ischemic attack, or ≥75 years of age) should receive chronic anticoagulant therapy.
- Chronic anticoagulation is reasonable for patients with chronic HF who have permanent/persistent/paroxysmal AF but are without an additional risk factor for cardioembolic stroke
- Anticoagulation is not recommended in patients with chronic HF*r*EF without AF, a prior thromboembolic event, or a cardioembolic source

Other Meds

- Statins- no benefit in HF alone without other evidence of disease
- Omega-3: Minimal evidence, appears no harm
- Avoid Calcium Channel Blockers (Except Amlodapine)
- Avoid NSAIDs

Invasive Monitoring

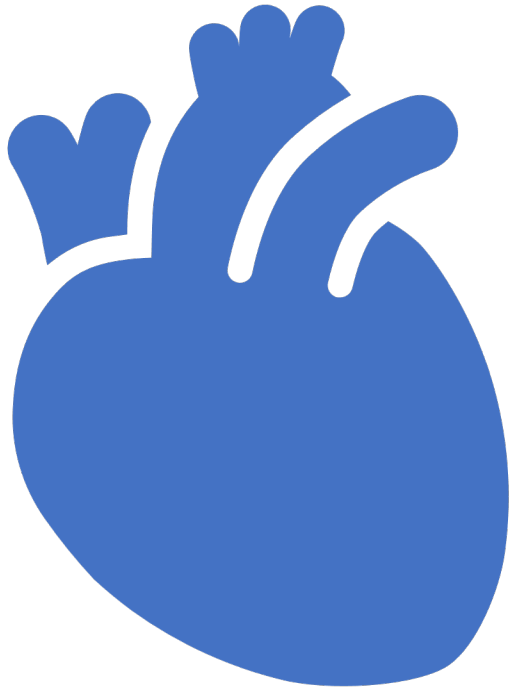
- Currently, no evidence supports the use of:
  - Cardiac Biopsy
  - Frequent Right Heart Catheterization
    - Potentially beneficial in select groups of patients

Referring to Electrophysiology

- To prevent sudden death, placement of an ICD is reasonable in patients with asymptomatic ischemic cardiomyopathy who are at least 40 days post-MI, have an LVEF of 30% or less, are on appropriate medical therapy, and have reasonable expectation of survival with a good functional status for more than 1 year.

Class IV, Stage D

- Left Ventricular Assist Device
  - Becoming more common as either a temporary device or bridge to transplant.
  - Anticoagulation
  - Same management as heart failure without the pump (in some aspects).



Take Home Points

- 1. Management of Heart Failure is largely based upon symptoms.
- 2. There are variations in symptoms that do not match % EF.
- 3. Close follow-up is generally needed in recently hospitalized patients
- 4. There is an art to titration of heart failure medications.

A special thanks to the American College of Cardiology and the European Society of Cardiology

Special Thanks

Questions?

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