Heart Failure: A contemporary and comprehensive approach and Novel Therapies

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Disclosures

- Nothing
- Nada
- Niente


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NO
FAILURE
ZONE

Heart Failure Definition

- 2013 Definition Yancy et al
- A complex clinical syndrome that results from any **structural or functional impairment** of ventricular **filling** or **ejection** of blood.
- A clinical diagnosis – no single diagnostic test because History/Physical/Testing together are used

Mortality Data

- Despite improvement in treatment, mortality rates in HF patients remain very high with 5 year survival just over 50 percent in all patients diagnosed with HF
- HF is mentioned in causation data in 1 in 9 deaths

- ARIC study – longitudinal data shows case fatality rates after hospitalization for HF were
- 10.4% at 30 days
- 22 percent at 1 year
- 42.3% at 5 years

Cost of Care

- 2013 data on cost for caring for patients with HF was approximately $30 Billion per year
- Predicted to rise each year due to population demographics
- Over 50% of this cost is In-Hospital Care

Hospital Admission Data

- HF is principal diagnosis in more than 1 million hospitalizations annally
- Cost of HF admission is > $27,000 per patient

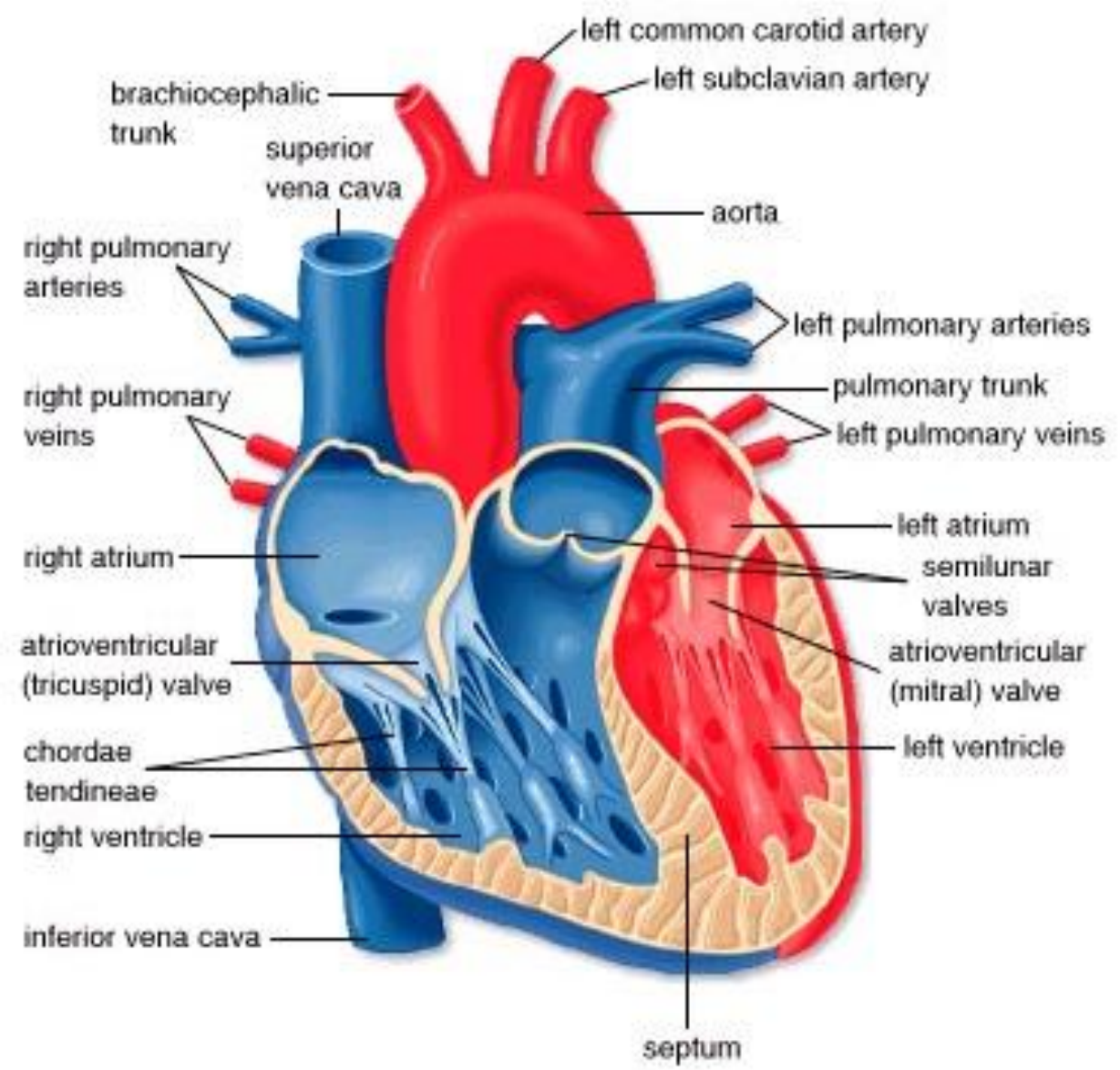
- Hospital 30 day readmission rates exceed 25% in 2013

Cardinal Symptoms

- Dyspnea and Fatigue, limited exercise tolerance
- Fluid Retention – pulmonary, splanchnic or peripheral edema

Causation and Location

- Pericardium – e.g. pericarditis, pericardial effusion or tamponade
- Myocardium – cardiomyopathies, ischemic, viral, genetic myo or lipodystrophies, rate-related, toxic metabolic e.g. alcohol, drugs, chemotherapeutic agents
- Endocardium
- Valvular or papillary muscle disorders
- Great vessel abnormalities/anatomic disorders, e.g transposition, tetralogy, VSD
- Functional as a result of other organ dysfunction or failure.


left common carotid artery
left subclavian artery
brachiocephalic trunk
superior vena cava
aorta
right pulmonary arteries
left pulmonary arteries
pulmonary trunk
right pulmonary veins
left pulmonary veins
left atrium
right atrium
semilunar valves
atrioventricular (tricuspid) valve
atrioventricular (mitral) valve
chordae tendineae
left ventricle
right ventricle
inferior vena cava
septum

Most Common Causes of HF

- **HFrEF** – most commonly associated with **CAD**, though other major causes are well described

- **HFpEF** – most common cause is **HTN**, prevalence 60-89 percent in studies from HF registries

- It is well known that often patients who have HFpEF may have had at one time HFrEF and EF has improved from revascularization, rate control, rhythym control or correction of toxic metabolic causes, possible from new understandings of cardiac remodeling and inflammatory mediators involved in HF – Stay Tuned!!!!

Other mentionable cause DCM – Dilated Cardiomyopathy

- **Alcohol**, **Cocaine Methamphetamine** and other toxins
- **Viral CM** – common, Chagas disease (South America)
- **HIV** CM
- **Inflammation – RA**, **SLE**, Giant Cell myocarditis
- **Volume overload** – chronic conditions from anatomic considerations
- **Drug hypersensitivity** IgE mediated (biopsy may be helpful)
- **Rate-related** from tachyarrhythmias, including very frequent PVC's. Ablative therapies very helpful in these patients

Newer Descriptions of Heart Failure

- Useful because treatment and prognosis are different
- Replacement of the terms systolic and diastolic HF
- Reduced EF LVEF <= 40 percent
- HFrEF – approximately ½ of patients
- Preserved EF LVEF > 40 percent
- HFpEF – approximately ½ of patients

Classification of HF – 2 systems

- **Stages** – ACCF/AHA stages emphasize disease progression
- Progression of stages is associated with lower 5 year survival rates and increasing plasma naturetic peptide concentrations (47)
- **NYHA functional classification** – assesses symptom severity, subjective and may change over time
- Despite variability over time NYHA is an independent predictor of mortality (still useful for assessment for eligibility for services)

Stages of Heart Failure

A	Presence of HF risk factors but no disease, no symptoms
B	Presence of structural disease but no symptoms
C	Presence of structural disease and symptoms have occurred
D	Presence of advanced heart disease with continued HF symptoms requiring aggressive medical therapy

NYHA Classification

I	No limiation on ordinary physical activity
II	Slight limitation on ordinary activity
III	Marked limitation of physical activity but comfortable at rest, less than ordinary activity causes fatigue, palpitations or dyspnea
IV	Unable to carry out any physical activity without discomfort, symptoms at rest

Peripartum Considerations

- Unknown Cause LV dysfunction typically in 3rd trimester
- 1:1300 to 1:4000 births (174)
- Risk factors:
  - Advanced Maternal Age
  - Multiparity
  - African Descent
  - Long term Tocolysis

Peripartum CM - continued

- Prognosis – directly related to recovery of LV function
- 30-50 percent of cases improve rapidly in 1st 6 months after presentation

- Cardiomegaly that persists more than 6 months has a poor prognosis with 50 percent mortality rate at 6 years
- Due to increased risk of VTE, anticoagulation is recommended

HF Initial Evaluation Guidelines

- Thorough H and P, including 3 generation history of HF, especially DCM
- Identify cardiac and non-cardiac disorders that might accelerate progression and treat

- Volume status assessed at EACH VISIT
  - Weight
  - Edema
  - Orthopnea
  - JVD

Diagnostic Tests Panel Recommendations Initial

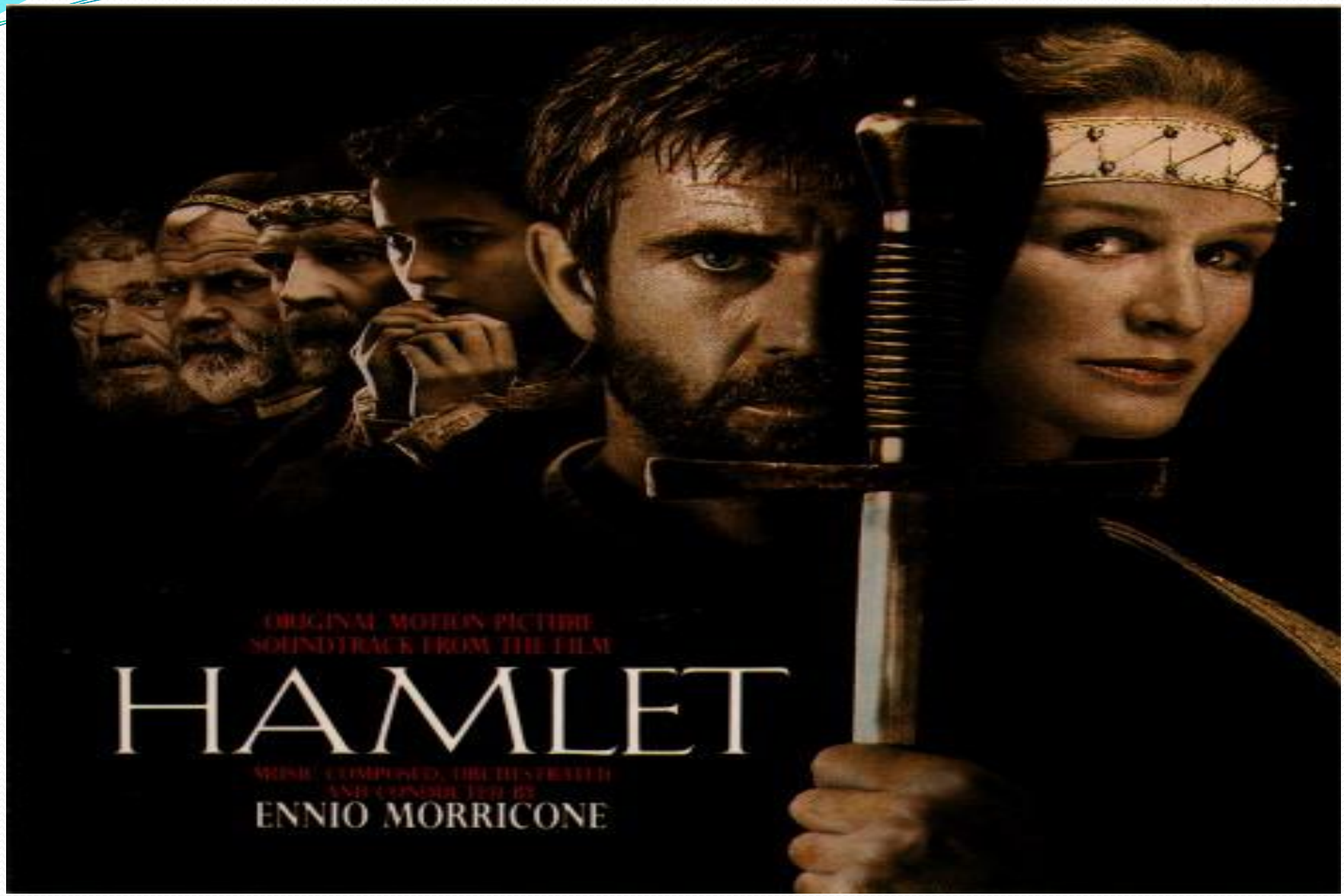
- CBC, serum electrolytes, including Ca and Mg
- UA or protein/cr ratio
- BUN and Cr
- Glucose
- Lipid Profile
- LFT's
- TSH

Diagnostic Testing - additional

- One time screen for HIV, Hereditary Hemochromatosis considered reasonable
- Diagnostic tests if indicated by other symptoms or clinical suspicion include RA, SLE, amyloidosis (fat aspirate) Sarcoidosis, pheochromocytoma – these should be reserved for patients with reasonable clinical index of suspicion

Biomarkers

- **BNP** or N-terminal pro-BNP **NT proBNP** may be used in either Hospital, Emergent or Ambulatory setting
- Helpful at distinguishing HF from other causes of dyspnea in the setting of clinical uncertainty(A)
- Caution – The **presence of elevated BNP does NOT necessarily exclude other diagnoses**. Elevated BNP in setting of PE is an ominous indicator.
- Troponin or other markers myocardial injury measurement in Emergent or Hospital setting may also be helpful for risk stratification (A)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AND CONDUCTED BY
ENNIO MORRICONE

To BNP or Not to BNP – That is the question: Guiding therapy

- BNP or NT-proBNP therapy is controversial, results not widely reproducible, however, meta-analysis of RCT's suggestive that BNP guided therapy may reduce all cause mortality in chronic CHF vs usual care.

- BNP tends to decrease over time – often not days, but weeks, and varies substantially individually and with the presence or absence of other disease states

- No best practice has yet been identified, remains controversial
- Failure to lower BNP over time has been associated with higher mortality rates and higher rates of rehospitalization

New Onset HF Diagnostics

- CXR – assess pulmonary vasculature, cardiomegaly
- 2D echo – assess structure, function and valve function, pericardium
- EKG
- Laboratory Studies
- Non-invasive imaging to detect reversible myocardial ischemia with consideration for revascularization and viability assessment
- Cardiac MRI may be considered if Echo is inadequate or when considering other causes

Echo in Chronic Management

- There are exceptions such as patients with CM due to PE, Peripartum CM, viral CM or other treatable reversible causes of HF

- Generally, serial echocardiography in patients with no change in clinical status or treatment interventions should not be performed (such as annual Echo for all patients with HF) (B), Class III no benefit.

Invasive Management

- Coronary Angiography and LV venticulography is indicated in patients with HF and Angina and may be useful in patients with HF and LV dysfunction without angina, but only in patients who are candidates for revascularization

Treatment of Comorbid Conditions

- Hypertension and Lipid Disorders should be controlled in accordance with contemporary guidelines (A) evidence
- Other known risk factors, DM, obesity tobacco use, other cardiotoxic agents such as excess alcohol should be controlled or avoided (A)
- Treatment of sleep disorders is indicated (A)

Preventing HF by controlling Hypertension – Special Considerations

- Because HTN is most common controllable risk factor for the development of either HFrEF or HFpEF,
- NNT over 2 years is 52 diuretic based therapy for HTN in primary prevention of HF
- Elderly patients age > 65 with ECG evidence of prior MI, Qwaves, LBBB, prior diagnosis of STEMI, 80 percent absolute risk reduction NNT 1.25 for incident HF with aggressive BP control (<130/80 as treatment goal) (94)

HTN Primary Prevent- continued

- Data for nondihydropyridine-CCB's and alpha blockers are unclear in their ability to prevent HF
- Chlorthalidone and other diuretic therapies have been demonstrated to prevent HF consistently across studies.
- In appropriate populations ACE/ARB and diuretic therapies may be used 1st line, with dihydropyridine CCB (amlodipine, felodipine) also as a consideration

HTN Preventing HF considerations

- Beta Blockers are controversial in prevention (not treatment) of HF
- Are safe to use in pregnancy
- Are helpful in migraine patients
- Are mandated in patient with CAD unless contraindicated
- Have undesired side effects of
  - Fatigue
  - Depression
  - Nightmares and sleeplessness
  - ED
  - Consider metoprolol and carvedilol which are indicated in treatment of HF when using a B-blocker (COMET trial)

Management of HFrEF

- Patients with HF should receive specific education for self care (B)
- Home monitoring of weight, symptoms and BP especially with outpatient supervision has been shown to decrease hospitalizations (VA study and widely adopted practice)
- Sodium restriction (most studies are in white patients and data from these studies cannot be extrapolated to non-white patients (ACC statement 2013).
- Sodium restriction remains controversial, there are conflicting data and may be stage dependent. Na restriction appears to be appropriate in stage A and B HF but may not be in stage C and D HF.

Management of HFrEF – Stage B

- **ACE Inhibitors or ARB**
- All patients with **HFrEF** should receive ACE or ARB therapy unless contraindicated (A)
- All patients with **recent or remote history of MI or ACS** and **reduced EF** unless contraindicated should receive **ACE inhibitors**, ARB's are second line in case of ACE intolerance (A)
- All hypertensive patients with reduced EF with or without history of ACS or MI with or without symptomatic HF should receive ACE-I or ARB's (A)

Management of HFrEF

- **Beta Blockers - use evidence based drugs in all patients with HFrEF with or without history of CAD/MI/ACS**
  - **Metoprolol Succinate (sustained release) not tartrate**
  - **Carvedilol**
  - **Bisoprolol**

Superiority of one vs another is controversial COMET trial Carvedilol v Metoprolol showed equivalence

Another trial showed Carvedilol 31 percent ARR long term adverse event reduction NNT = approx 3.

Mangement of HFrEF

- Nondihydropyridine CCB's negative iontropic properties in established structure Heart Disease (low EF) **SHOULD BE AVOIDED**

- Even in patients without HF, use caution when using 2 negative ionotropic agents together. Combining Nondihydropyridine CCB's with B-blockers has been associated with symptomatic bradycardia, syncope, and even high-degree or complete heart block

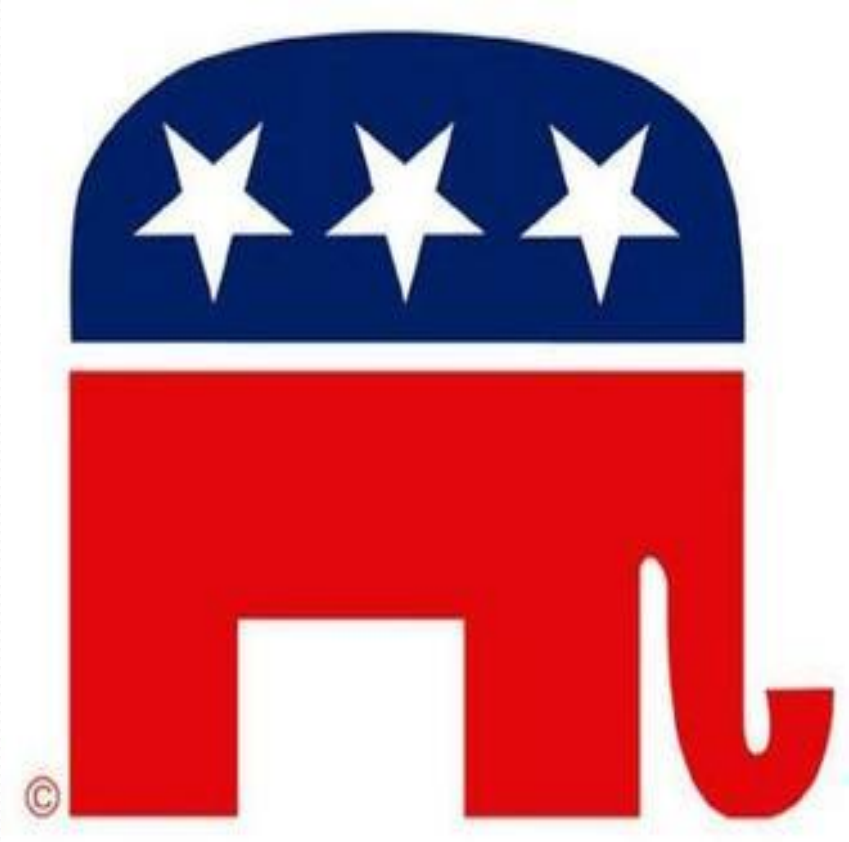
Management of HFrEF

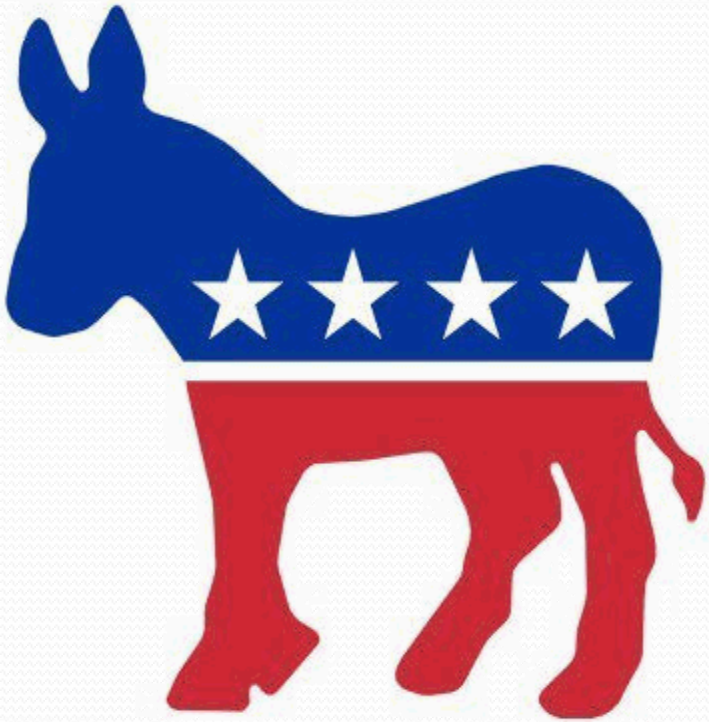
- **Aldosterone Antagonists – UNDERUSED!**
  - Recommended in NYHA II-IV patients with LVEF 35% or less (A) unless:
    - Cr 2.5 or less in men, Cr 2.0 or less in women GFR 30
    - Serum K < 5.0
    - Renal function and electrolytes should be careful monitored, 2-3 days, 7 days, monthly for 3 months, then q3 months.
    - Also recommended in all post MI patients who develop HF symptoms with EF less than 40 percent or with DM unless contraindicated and monitor as above (B)

Aldosterone Antagonists

Landmark **RALES** trial showed 30 percent risk reduction all cause mortality in HF patients HFrEF EF< 35%, NNT 3.3 . Start at 12.5 to 25mg per day and increase to 50mg daily as tolerated

- Eplerinone has a bit broader indications and wider range of patients. Starting dose 25mg per day
- Avoid NSAIDS in patients using aldosterone antagonists
- Dosage adjustments in ACE or ARB should trigger a new cycle of monitoring
- Routine triple combination **ACE/ARB/Aldosterone** antagonist **should be avoided**





TINA – There Is No Alternative…Or Is There? Nitrates and Hydralazine

- The combination Hydralazine and Isosorbide dinitrate is recommended to reduce morbidity and mortality for African-American patients with NYHA Class III-IV, HFrEF receiving optimal doses of ACE/ARB and B-blocker therapy unless contraindicated (A)

- To reduce morbidity and mortality in patients with current or prior symptomatic HFrEF who cannot tolerate or have contraindication to ACE/ARB therapy Hydralazine and Isosorbide dinitrate can be used unless contraindicated (B)

Statins in HF

- Statins are not beneficial when prescribed solely for the diagnosis of HF, but should be prescribed for other indications for their use (A).

Digoxin Recommendations

- Digoxin may be used in patients for 1-3 months or in patients still with symptoms despite optimizing other treatments in HFrEF
- Avoid in patients with Heart Block.
- Use with caution with B-blockers and amiodarone
- Loading doses are not necessary

HFpEF Recommendations

- Systolic and Diastolic BP should be controlled in patients with HFpEF (B)
  - ACE/ARB – ARB may decrease Hospitalization
  - B-Blockers
- Loop Diuretics should be used for symptoms of volume overload (C)

- Blood pressure control remains the most important therapy in HFpEF

Device Therapies

- AICD may be considered for patients with DCM and Ischemic CAD, at least 40 days post MI with EF < 35% who have life expectancy of more than 1 year with NYHA II or III symptoms to reduce SCD.
- CRT – cardiac resynchronization (Biventricular Pacing) is indicated for patients who have LVEF of 35 percent or less and NYHA class II, III, or ambulatory IV and have sinus rhythm, LBBB with QRS duration of 150ms or greater (A) for III/IV and (B) for NYHA II, or may be considered for LBBB 126-149 ms (B)
- May be used in AF with other criteria


CAUTION
EPIC
FAILURE

Advanced Heart Failure Stage D

- Patients with truly refractory symptoms despite optimal medical therapy
- May include Cardiac cachexia, hyponatremia
- Severe limitations, dyspnea at rest
- Poor quality of life
- Identify and treat other causes of dyspnea
- Symptom, not EF dependent
- Repeated Hospitalizations, poor prognosis
- Appropriate for Hospice, not appropriate for device therapy, Younger patients < 65 without other life limiting disease may be eligible for transplantations.
- Fluid restriction is appropriate for these patients 1.5-2l/day

Novel Therapy and Targets

- ARB with Neprilysin Inhibitor (called ARNI)
  - Neprilysin degrades Naturetic Peptides, bradykinin, and other vasoactive peptides
  - Valsartan/sacubitril in RCT compared with enalapril in symptomatic patients with HFrER (Stage C or NYHA II-III) the ARNI reduced death or Hospitalization by 20 percent NNT 5 and is recommended in chronic symptomatic HFrER who tolerate an ACE-I to replace by ARNI to further reduce morbidity and mortality
  - Like ACE, ARB, ARNI may be associated with renal insufficiency, angioedema, and may have increased risk of hypotension over enalapril (ACE or ARB alone)

ARNI

- Intended to replace, not be used concomitantly with ACE inhibitor or other ARB.
- 3 doses – target dose is 97/103mg twice daily, if tolerated.
- ARNI is contraindicated in patients with angioedema these patients were excluded in the trial

Ivabradine

- Novel agent for further reduction in heart rate, inhibiting the I f current in the Sinoatrial node, thereby yielding HR reduction
- Intended to be used after maximizing dose of beta blocker, in addition to usual therapy
- Class II-III HFrEF patients with EF < 35% and resting HR > 70
- Reduction in Hospitalizations, mortality benefit not yet seen, therefore recommendation is for maximum tolerated dose of B-Blocker then addition of Ivabradine if HR > 70.

Anticoagulation in HFrEF – Avoiding Fashion Faux Pas

- Anticoagulation is not recommended in non-pregnant patients with chronic HFrEF without Afib, a prior thromboembolic event, or evidence of cardioembolic source (B)

- Follow anticoagulation guidelines specific to the underlying disease, use CHADS2 score to assess patient risk for adverse event before initiating an anticoagulant therapy in AF (example HF, AF +1 = Anticoagulation)

- In patients without AF, Warfarin vs Aspirin vs Clopidigrel, there were no overall benefit of warfarin and there is increased risk of bleeding, therefore routine use of anticoagulant in HFrEF without AF, VTE, or cardioembolic event is not recommended

There's nothing fishy about FISH

- Omega -3 PUFA supplementation may be used as adjunctive therapy in patients with NYHA class II-IV symptoms in either HFrEF or HFpEF to reduce mortality and cardiovascular hospitalizations (B)
- Multiple studies in primary and secondary CAD studies show 10-20 percent ARR in fatal and non-fatal cardiovascular events (Primarily Italian studies) GISSI Prevenzione HF investigators also
- Dose 850-1g of DHA/EPA This may require more than 1 pill – count your mg of DHA/EPA.

Other Supplements

- No data to support routine supplementation with supplements other than omega-3
- CoQ10 studies are inconclusive, but may reduce symptoms – no consistent results across studies, do not appear to be harmful
- Not enough evidence as of 2013 to support other supplements, however, tart cherry, resveratrol show some promise at reducing inflammation associated with CAD – stay tuned.

Big Hair and Shoulder Pads – or, the I can't believe we used to do that. Out of fashion drugs in HF

- NSAIDS – inhibit renal prostaglandins which inhibit sodium reabsorption, therefore the use of NSAIDS promotes sodium reabsorption in the thick ascending loop of Henle and collecting tubule. Several studies show increased mortality for selective and non-selective NSAIDS
- CCB's (A) – even amlodipine shows no survival benefit
- TZD's – also by dysregulation of sodium absorption in the kidney

HF Summary

- ACE/ARB therapy is appropriate for Stage A and B HF, for either HFrEF or HFpEF. Identify your patients Stage and NYHA classification by symptoms and Echocardiogram. BNP may be useful.
- Replacing ACE/ARB with ARNI is appropriate and recommended for HFrEF, Stage C NYHA class II-III patients to further reduce hospitalizations and mortality
- Beta Blockers – evidence based, carvedilol, metoprolol, or bisoprolol should be used in all HF patients with CAD, NYHA class II or greater or Stage B or greater in either HFrEF or HFpEF
- Loop Diuretics should be used for symptoms of fluid overload in all patients with HF

HF Summary

- Aldosterone Antagonists should be used in NYHA Class II and III patients with HFrEF unless contraindicated eGFR > 30, serum K < 5.0. Monitor therapy 2-3 days after initiation, 7 days, then monthly for 3 months then q 3 months. Monitoring cycle begins again each time after adjusting ACE/ARB/ARNI
- Do not combine ACE/ARB/Aldosterone antagonists using all 3 drugs together as risk for hyperkalemia increases substantially
- Use statin drugs where appropriate and otherwise indicated
- Use aspirin in HF patients rather than anticoagulation except where anticoagulation would otherwise be indicated, strongly consider using Factor Xa inhibitors due to fewer drug drug interactions than warfarin
- Avoid NSAIDS in patients with HF
- Treat HTN aggressively in patients at risk for HF or who have HF
- Use of Omega-3 dosed at 1-2g/day of EPA/DHA is indicated in HF patients and in patients with CAD, other supplements have not been shown to have significant benefit in HF


THANK YOU!