Practical Outpatient Management of Heart Failure in the Office

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Disclosure/Conflict of Interests

• Nothing to disclose.

Outline

- 1. Definition, Statistics, Epidemiology
- 2. Classification of HF
- 3. Risk Factors, Causes/Etiology
- 4. Diagnosis and Evaluation
- 5. Pathophysiology and Management

Definition of Heart Failure

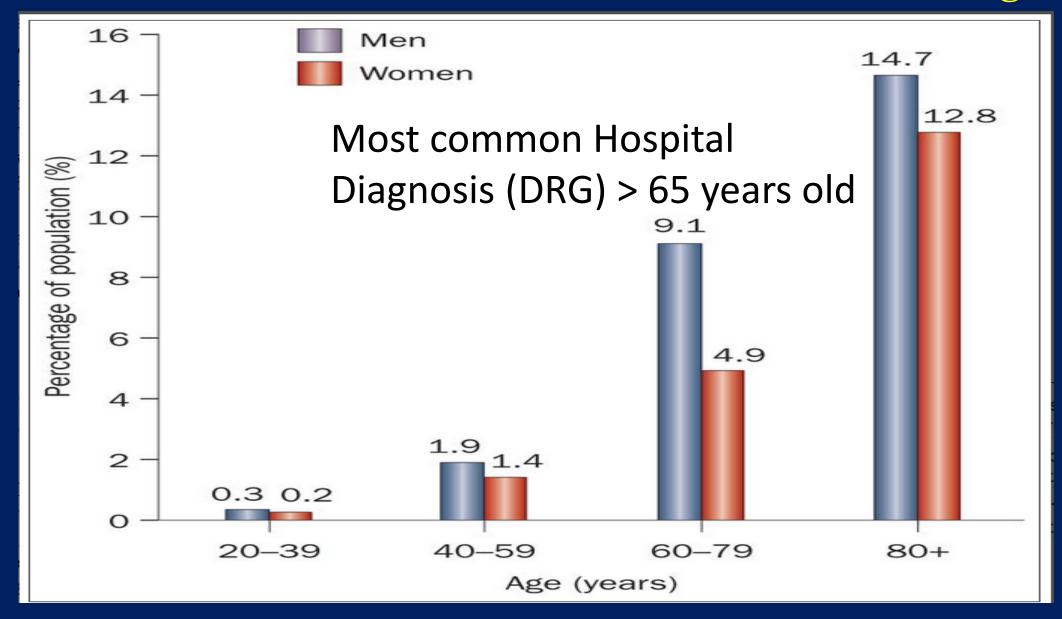
A clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood.

The heart is unable to maintain an adequate forward blood volume or Cardiac Output to meet the physiologic demands of the circulatory system.

Heart Failure Statistics and Epidemiology

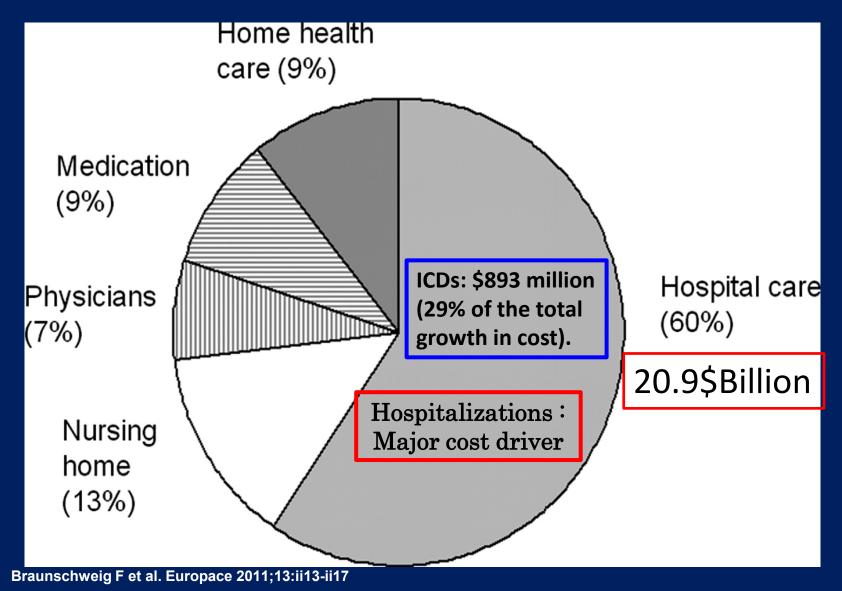
- Prevalence: 5.8 million in USA; 2.6% worldwide.
- ☐ Incidence : 650,000 (USA)
- ☐ Risk of mortality from diagnosis:
 - >20% at 1 year
 - >40% at 5 years
 - > Class III-IV: ≥ 50% 1year

Heart Failure Prevalence Increases with Age





Cost of Heart Failure Treatment in the USA Distribution of Direct Costs (\$ 39 Billion)



Classification of HF

Classification of HF

- 1*.Symptoms and Disease Progression
 - -NYHA Functional Class
 - -ACC/AHA Stage
- 2*. Ejection Fraction
 - -Reduced EF
 - -Preserved EF
- 3. Acute or Chronic
- 4. Cardiac Output (Low or High)
- 5. Left or Right Ventricular Failure

The fundamentals for diagnosis and classification of HF: Based in History-Symptoms* and Physical Exam

Principal manifestations:

1. Fatigue*: Due to low Stroke Volume/Cardiac output.

2. Dyspnea* due elevated ventricular filling pressure due to volume overload → pulmonary congestion.

1. Classification of Heart failure by Symptoms Functional Classification: New York Heart Association *

Designed in 1918 to quantify the degree of functional limitation imposed by HF

Class	Symptoms: Dyspnea or fatigue
I	No Symptoms with ordinary activity.
П	Symptoms with ordinary activity.
III	Symptoms with less than ordinary activity.
IV	Symptoms at rest.

2. Classification and Evaluation of Heart failure by Stage: ACC/AHA Stages

ACC/AHA Stages of HF*	NYHA CLASS
Stage A: At Risk No structural abnormalities.	None
Stage B: Asymptomatic Structural abnormality.	
Stage C: Symptomatic Structural abnormality.	I, II, III, IV
Stage D: Symptomatic Structural abnormality.	IV

3. Classification of Heart Failure Ejection Fraction*

Classification	EF (%)	Description
HF with reduced Ejection Fraction (HFrEF)	< 40%	Referred to as Systolic HF.
HF with preserved Ejection Fraction (HFpEF)	>50 %	Referred to as Diastolic HF.
a. HFpEF, borderline	41-49%	HFmrREF (ESC) These patients are treated
b. HFrEF, with improved EF	>40 %	(GDMT) similar to patients with HFrEF.

4. Classification of Heart failure: High Output Heart Failure

- •Inappropriately high CO/CI: > 8 L/min or 4 L/min/m2
- •Causes/Mechanisms: \ Peripheral vascular resistance, A-V communication
 - -A-V fistulae and A-V malformations
 - -Anemia
 - -Hyperthyroidism
 - -Beriberi (thiamine)
 - –Paget's disease

Evaluation HF

1. Clinical Diagnosis*

> There is no single diagnostic test for HF.

The clinical diagnosis is based on history and physical examination: Framingham Criteria.

- Complementary Information:
 - Biomarkers of HF:BNP or NT-pro BNP.
 - •Imaging the Heart for LVEF Determination:
 - -Echocardiogram, Catheterization, MUGA, MRI

1. Framingham Criteria (1971) Today-On line Application*

Major criteria(:Symptoms/Signs* of congestion)

- Paroxysmal nocturnal dyspnea (PND)* or Orthopnea*
- Neck-vein distension (JVD*)
- Rales*
- Cardiomegaly*
- Acute pulmonary edema*
- S₃ gallop*
- Hepatojugular reflux*
- Bentopnea

Minor criteria:

- Ankle edema
- Night cough
- Dyspnea on exertion *
- Hepatomegaly
- Pleural effusion
- Tachycardia :rate of ≥120/min (Major or minor criterion)
- Weight loss ≥4-5 kg in 5 days in response to treatment
- Bentopnea

1. Framingham Criteria

Interpretation Heart Failure diagnosis requires:

- 1. At least 1 major and 2 minor criteria.
- 2. 2 major criteria.

Efficacy in HF Diagnosis: Sensitive but not specific.

1.Sensitivity: 97%

2. Specificity: 79%

3.Best for ruling out particularly HFrEF. ———— High Negative Predictive Value.

The absence of the Framingham criteria rules out the diagnosis of heart failure, particularly systolic heart failure. The presence of criteria do not necessarily confirm the diagnosis, which may need in additional information.

3. Initial Evaluation of HF- Investigate Etiology*: 1. Important Risk Factors for HF:

1. Hypertension: The single most important risk factor for HF.

2. Diabetes Mellitus: 2-3 times risk of heart failure.

3. Metabolic Syndrome.

4. Atherosclerosis: CAD

Causes of HF: Cardiac Structural Abnormalities

- ☐ Dilated Cardiomyopathies*:
 - -A large group of heterogeneous myocardial diseases.
- Note- In clinical practice and multicenter HF studies:
 - -Etiology of HF-Categorized into Ischemic or Nonischemic CMP.
 - -But the term "Nonischemic CMP" may include CMP due to any volume or pressure overload, not conventionally accepted as IDCM.

Idiopathic Dilated CMP*: Refers to Dilated Cardiomyopathy without ischemic heart disease/ CAD, pressure or volume overload, or other obvious etiology.

Initial Evaluation-Investigate Etiology:

History: Review of Systems and Family History*

Potential Clues/Information regarding Etiology:

Common Causes:

- 1*.CAD (MI, CABG, PCI, Angina)
- 2*.Hypertension
- 3*.ldiopathic Dilated CM (30% Familial CM)*(2members afflicted, 3 generation pedigree, Screening- Clinical and Genetic)
- -Valvular an Congenital Heart Disease
- -Tachycardia Induced CM: Hx. Palpitations Syncope.(SVT,VT, PM,>10% PVCs burden)
- -Alcohol*, Illicit Drugs (90 grs Eth-OH, 4-18% Asymptomatic cocaine users have ALVD)
- -Cancer-Chemotherapy/Radiation (Genetic damage)

Initial Evaluation of HF- Investigate Etiology:

2. History: Review of Systems-Continuation:

Less Common Causes:

- -Pericarditis and Myocarditis
- -HIV: (12% of asymptomatic HIV+ patients with asymptomatic LVD)
- -Post Partum Cardiomyopathy (HF during last trimester)
- -HCM
- -Amyloid (Low EKG voltage < 5mm , Thick LV, RV increased thickness, LAE)
- -Endocrine Diseases: DM, Thyroid Disease, Pheo., Acromegally
- -Collagen Disease: SLE, RA, Scleroderma.
- -Hemocrohrmatosis
- -Sarcoid

Initial Evaluation of HF: Basic Studies

4. Initial Evaluation of HF: Basic Studies

Diagnostic Evaluation Tests:

1.Electrocardiogram* (Class I)

-Rate, rhythm, QRS duration, ischemia

2.Chest radiography* (Class I):

-Cardiomegaly, pulmonary edema/congestion, other causes of dyspnea

4. Initial Evaluation of HF

Basic Routine Laboratory Tests (Class I):

- -CBC, UA
- -Renal Function and Electrolytes (Na, K, Mg)
- -Liver Function Tests
- -TSH, Lipids
- BNP* or NT-proBNP*

Initial Diagnostic Evaluation of HF Natriuretic Peptide Concentrations*

BNP

< 100 pg/mL - HF unlikely

>400 pg/mL - HF likely

100-400 pg/mL - Use clinical judgment

NT-proBNP: Age adjudgments

< 450 pg/mL - HF unlikely

Age < 50 years >450 pg/mL - HF likely

Age 50-75 years >900 pg/mL – HF likely

Age >75 years >1800 pg/mL – HF likely

Other factors may affect BNP levels

Lower levels:

In obese patients

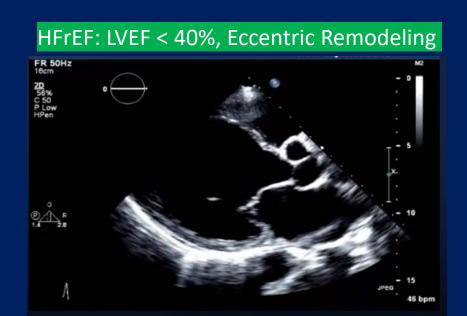
Higher levels:

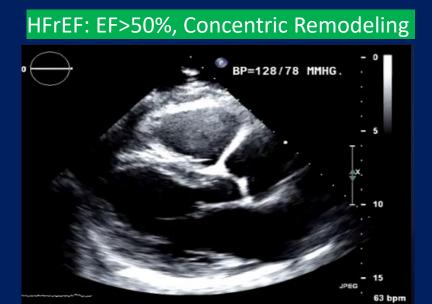
- Women
- Anemia
- Age: Older patients
- Concomitant pulmonary disease
 - -Chronic obstructive disease
 - Pulmonary hypertension
 - -Pulmonary embolus
- Renal dysfunction
- Atrial fibrillation.

Initial Diagnostic Evaluation of HF Transthoracic Echocardiogram (Class I)

Most Important initial Imaging modality* (Availability, and low cost)

- 1. Assessment of ventricular function to categorize HFrEF** or HFpEF*
- 2. Assessment of chambers size, wall thickness, wall motion, valve function.





Diagnostic Criteria: HFrEF and HFpEF

HFrEF** [Systolic HF]

- 1. Symptoms and Signs of HF
- 2. LVEF < 40%.
- 3. ↑BNP.

The prevalence of HF is evenly divided between HFrEF-(Systolic) and HFpEF- (Diastolic).

HFpEF* [Diastolic HF]

- 1. Symptoms and Signs of HF
- 2. LVEF>50%
- 3. Presence of diastolic dysfunction: Echo/Doppler.
- 4. ↑BNP*.

The Gold Standard to determine Diastolic Dysfunction is Cardiac Catheterization: -LVEDP= >12 mmHg or PCWP= >16mmHg

Evaluation of HF

Repeat assessment of ventricular function (LVEF):

- Repeat EF after a mayor change in clinical status or after optimizing medical Rx- typically 3-6 months (Class IIa)
- Implications for electrical device therapy AICD and or CTR
- •Routine repeat measurement of LV function assessment in the absence of clinical status change or treatment intervention should not be performed (Is not useful- Class III)

Initial Evaluation of HF Other Evaluation Laboratory Tests: Class IIa

- Screening for other diagnosis in selected patients:
- -Hemochromatosis (Iron studies)
- -HIV
- -Rheumatologic diseases (Autoimmune serology, Inflammatory markers)
 - -Amyloidosis (Protein Electrophoresis)
 - -Endocrine/Metabolic (Ex. Pheochromocytoma).

Initial Evaluation of HF Other Evaluation Tests: Class IIa

Cardiac MRI:

Iron Overload-Hemochromatosis, Sarcoidosis Myocarditis, Viability in CAD, Pericardial Disease.

- PET Scan: If concern of Sarcoidosis- Active disease.
- Cardiopulmonary Exercise Test:
 - 1. Determine cardiac versus non cardiac cause of symptoms.
 - 2. Quantify severity of physical limitation to consider advanced therapies (<14 ml O2/Kg/Min).
- Overnight oximetry: If OSA is suspected.

Initial Evaluation of HF Assessment for CAD

- Coronary angiography*:
 - Class I : If angina or known ischemia.
 - Class IIa: When ischemia may be contributing to HF.
 - •Ex: If atypical chest pain, known or suspected CAD
- ▼ Non Invasive Studies*: Stress Testing and/or imaging:
 - Class IIa: if known CAD but no angina.
 - Class IIb: To define likelihood of CAD.

Initial Evaluation of HF Endomyocardial Biopsy

- Only useful in particular situations if results will influence therapy
- 1. Rapidly worsening ventricular dysfunction despite medical therapy.
 - •Giant cell myocarditis
- 2. Sarcoidosis
- 3.Infiltrative cardiomyopathies
 - Amyloidosis
 - Hemochromatosis

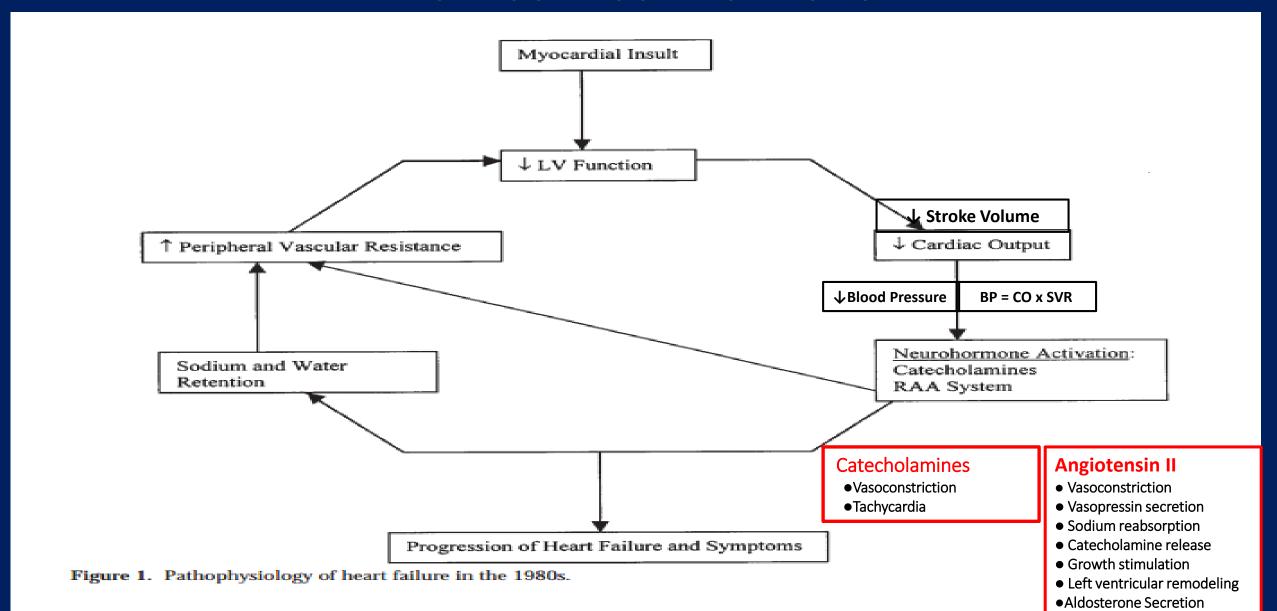
Diastolic Heart Failure

- ♥Usually not indicated in systolic heart failure:
 - •Should not be performed in the routine evaluation of systolic HF: Class III-Harm.

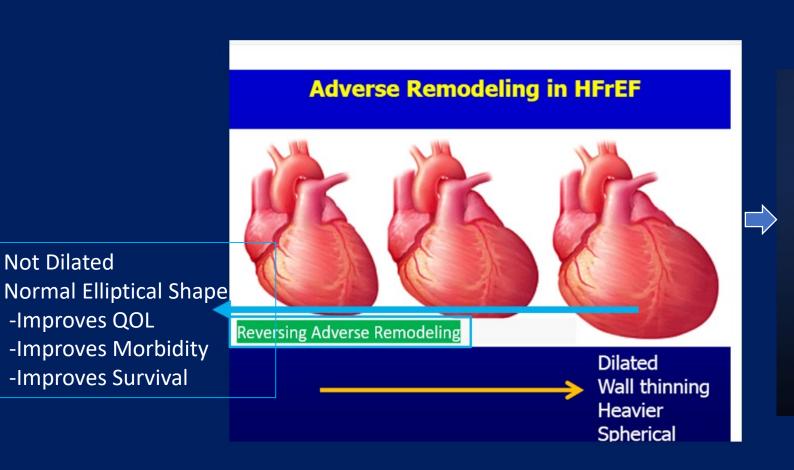
Pathophysiology

Heart Failure with reduced Ejection Fraction

Pathophysiology of Chronic Systolic Heart Failure Neuroendocrine Model

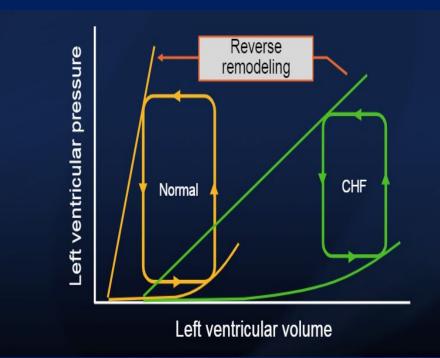


Goal of therapies in HF with Reduced Ejection fraction



Not Dilated

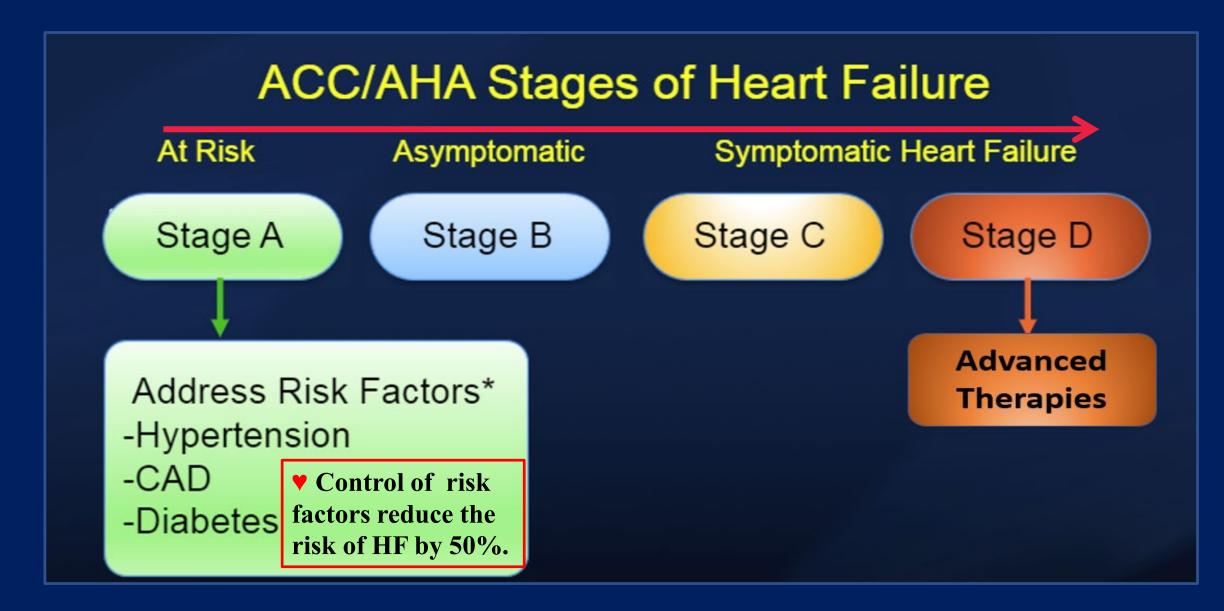
-Improves QOL

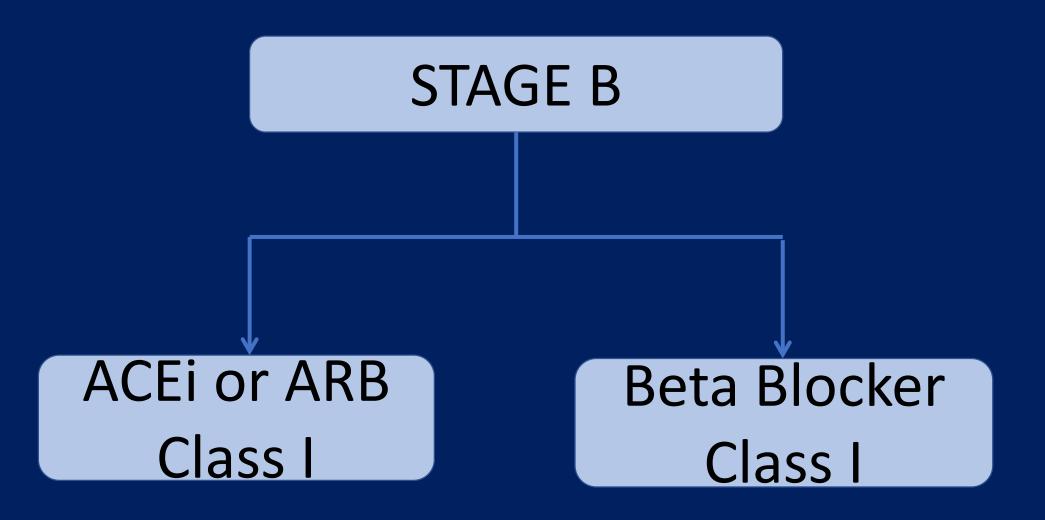


Management of HF

- Heart Failure with reduced Ejection Fraction*

 Well established Evidence based therapy
 Improved survival, QOL, and reversed remodeling
- 2. Heart Failure with preserved Ejection Fraction





Treatment of HF with Reduced Ejection Fraction Stage B: ACE or ARB (Class I)

Stage B



ACEi or ARB (Class I)

- 1.Class effect ,but preferred agents proved in clinical trials.
- 2.* Improves mortality: RRR=17%.
- 3.* Improves morbidity-hospitalizations: RRR=31%
- 4. Start with ACEi.
- 5. ARB when ACEi contraindicated.
- 6. Routine combination of ACEi/ARB is contraindicated (Class III)



ACE Inhibitors Used in Heart Failure

Generic Name	Trade Name	Initial Daily Dose	Target Dose	Mean Dose in Clinical Trials
Captopril	Capoten	6.25 mg tid	50 mg tid	128 mg
Enalapril*	Vasotec	2.5 mg bid	10 mg bid	17 mg
<u>Lisinopril*</u>	Zestril, Prinivil	2.5-5 mg qd	20 mg qd	35 mg
Fosinopril	Monopril	5-10 mg qd	80 mg qd	N/A
Quinapril	Accupril	5 mg bid	80 mg qd	N/A
Ramipril	Altace	1.25-2.5 mg qd	10 mg qd	N/A
Trandolapril	Mavik	1 mg qd	4 mg qd	N/A

Angiotensin Receptor Blockers Used in Clinical Trials

Generic Name	Trade Name	Initial Daily Dose	Target Dose	Mean Dose in Clinical Trials
Candesartan	Atacand	4-8 mg qd	32 mg qd	24 mg/day
Losartan	Cozaar	12.5-25 mg qd	150 mg qd	129 mg/day
Valsartan	Diovan	40 mg bid	160 mg bid	254 mg/day
Irbesartan	Avapro	75 mgs qd	300 mg qd	N/A

Treatment of HF with Reduced Ejection Fraction Stage B: Beta Blockers (Class I)

Stage B



Beta Blocker Class I

1.No Class effect.

- 2. Improves cardiovascular mortality: RRR=34*.
- 3.Improves morbidity-hospitalizations: RRR=41%
- 4. Aproved Agents:
 - Carvedilol*(Capricorn Trial)
 - Metoprolol Succinate
 - Bisoprolol



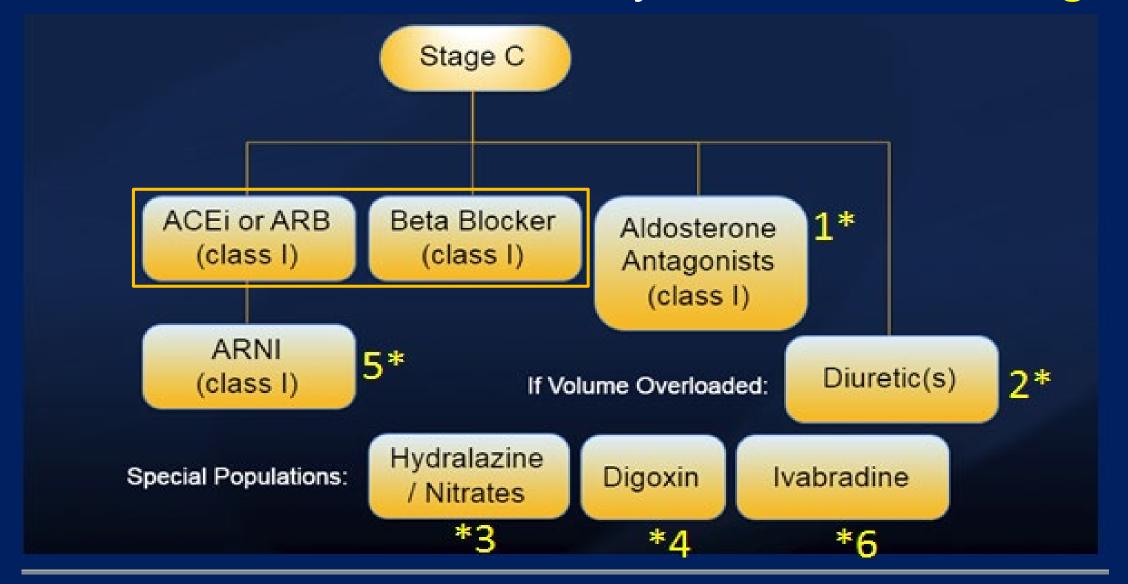
Beta Blockers Used in Clinical Trials

Generic Name	Trade Name	Initial Daily Dose	Target Dose	Mean Dose in Clinical Trials
Carvedilol*	Coreg	3.125 mg bid	25 mg bid	37 mg/day
Carvedilol	Coreg CR	10 mg qd	80 mg qd	N/A
Metoprolol* succinate	Toprol XL	12.5-25 mg qd	200 mg qd	159 mg/day
Bisoprolol*	Zebeta	1.25 mg qd	10 mg	8.6 mg

Treatment of HF with Reduced Ejection Fraction Carvedilol vs. Metoprolol Succinate

Characteristics	Carvedilol	Metoprolol Succinate
Dosing (Mgs)	3.125→6.25→12.5→25 -Low dose response (6.25 Mgs) -Goal: 25 Mgs BID	25→50→100→200 Once daily dose Goal: 200 Mgs
Blood Pressure Effect	Greater BP actions Use in setting of concomitant hypertension Preferred agent when BP is not a limitation.	Less BP ↓ action May facilitate up titration of other medications
Specific Populations	DM: Less insulin resistance	BA/COPD: Less bronchospasm

Bisoprolol: Similar to Metoprolol Succinate



Routine combination of ACEi + ARB + Aldosterone antagonist is contraindicated (Class III)

1. Aldosterone Antagonists

- 1. NYHA Class II-IV and LVEF < 40%. (Rec. Class I).
- 2. Follow potassium(K) closely:
 - Do not initiate if > 5 Meq/L.
 - Recheck in 3 days, each week x4 w, each month x3 months.
 - •Avoid if Creatinine > 2.5 in men and 2.0 in women.
- 3. Start with spironolactone.
- 4. Change to eplerenone if gynecomastia with spironolactone.

Treatment of HF with Reduced Ejection Fraction Stage C 2. Loop Diuretics for congestion

Agent	Initial Dose	Maximal Dose	Bioavailability	Action Duration
Furosemide	20-40 Mgs QD or BID	600 Mgs	10-100%	4- 6 Hours
Bumetanide	0.5-1 Mgs QD or BID	10 Mgs	80-100%	6-8 hours
Torsemide	10-20 Mgs QD	200 Mgs	80-100%	12-16 Hours
Ethacrynic Acid	25-50 Mgs QD or BID	200 Mgs	90-100%	6 Hours

Consider Torsemide or Bumetanide in Right Sided HF due to better bioavailability. Ethacrynic Acid: 1. Caution with sulfa allergy. 2. Very expensive (Particularly IV.)

Treatment of HF with Reduced Ejection Fraction Stage C 2. Thiazide Diuretics

- I. Use in combination with loop diuretics.
- II. Watch/Caution for electrolytes disturbances:
 - 1. Hypokalemia.
 - Consider K supplement /or K sparing diuretic
 - 2. Hypomagnesemia.
 - 3. Hyponatremia.
- III. Azotemia.
- IV. Avoid daily dosing. (Ex. Start metolazone qod)

- 1. Verify compliance, assess for precipitants of fluid overload
- 2.Double→ Tipple loop diuretic dose.
- 3*.Change to an alternative loop diuretic
 - Torsemide
 - Bumetanide
- 4*.Add a thiazide diuretic (Metolazone)

3. Hydralazine/Nitrates Class I

- 1. For persistently symptomatic African-Americans.
 - Despite ACE/ARB and Beta Blocker therapy.
- 2. Class IIa for patients intolerant to ACE/ARB:
 - Due to renal dysfunction or hyperkalemia.

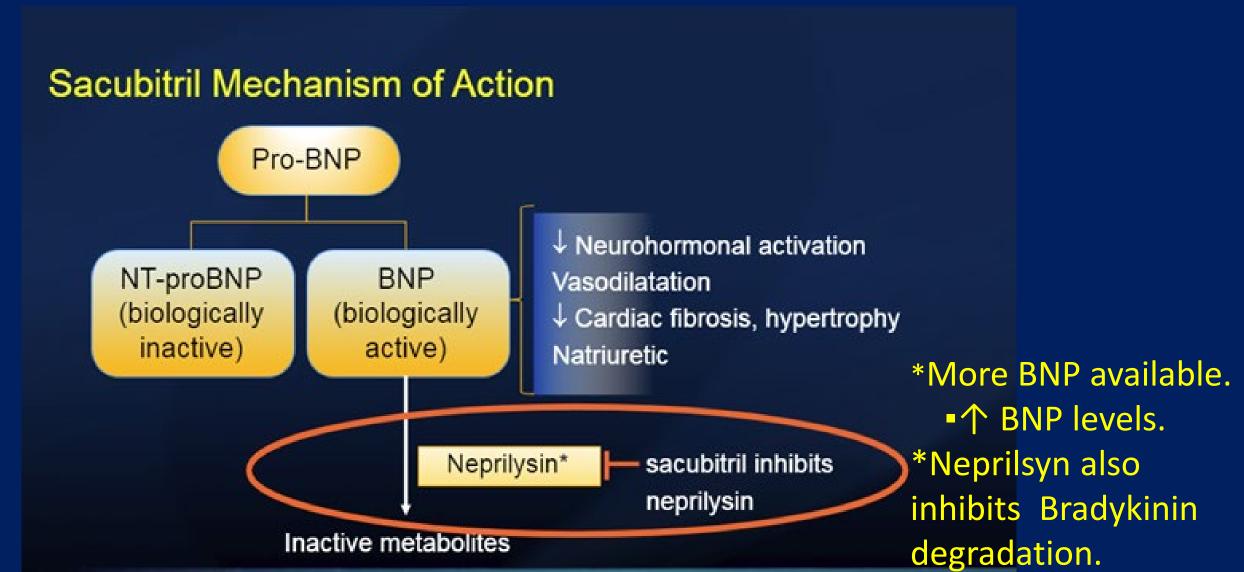
4. Digoxin Class Ila

- 1. Consider if LVEF < 40%.
 - Decreases HF hospitalizations, not mortality.
- 2. Consider in AF with suboptimal heart rate control despite or intolerant to beta blocker
- 3. Goal blood level 0.5- 0.9 ng/ml²

2016 and 2017 ACC/AHA HF Guideline Update

Sacubitril/Valsartan (ARNI)* : COR I

Ivabradine* : COR IIa



5

PARADIGM-HF*

- Sacubitril / valsartan versus enalapril
- LVEF < 40%; NYHA II-IV; tolerated ACEi

	LCZ696 (n=4187)	Enalapril (n=4212)	Hazard ratio (95% CI)	Р
Primary endpoint	914 (21.8%)	1117 (26.5%)	0.80 (0.73-0.87)	0.0000002
Cardiovascular death	558 (13.3%)	693 (16.5%)	0.80 (0.71-0.89)	0.00004
Hospitalization for heart failure	537 (12.8%)	658 (15.6%)	0.79 (0.71-0.89)	0.00004

Improved hospitalizations vs. ACEi: 20% RRR. Improves mortality vs. ACEi: 19% RRR.

5. Sacubitril/Valsartan

- Paradigm HF Trial: Published 2014
- FDA approved: 2015
- ACC/AHA HF Guidelines Update: 2016 and 2017
- Class I indication HFrEF NYHA Class II-IV:
 - 1) In patients previously tolerated ACEi or ARB: EF< 40%.
 - 2) Contraindicated in history of angioedema.
 - 3) Contraindicated concomitant ACEi or ARB.
 - 4) Hold ACEi or ARB for 48 hours before starting.
 - 5) *NT-pro BNP: Biomarker in patients using Sacubitril/Valsartan.

Ivabradine Class IIa

- Inhibits the If current in the sinoatrial node, reduces heart rate
- SHIFT trial (published 2010): reduced HF admissions among EF
 35%, NYHA II-IV, sinus rhythm, HR > 70; no mortality benefit
- FDA approved in 2015
- Ila recommendations in the 2016 ACC / AHA HF guideline update
- Ensure goal beta blocker dose before starting

TIPS Treatment of HF with Reduced Ejection Fraction

- 1. Go slowly with doses:
 - Start lowest dose, and Increase (2x dose) every 2 weeks.
- 2. Tolerate "asymptomatic hypotension".
- 3. Diuretic requirements may decrease with positive remodeling.
- 4. Treat the patient not the creatinine.
- 5. Repeat TTE 3-6 months after medical optimization

Drugs to Avoid in HFrEF

- NSAIDs
- Calcium channel blockers (Except amlodipine- neutral in mortality)
- Most antiarrhythmic drugs (Except amiodarone and dofetilide)
- Thiazolidinedione (Glitazones: rosiglitazone, pioglitazone)

Lifestyle and Non-Medical Interventions

Sodium restriction: < 2 grams per day.</p>

Fluid restriction: < 2 liters per day.</p>

Exercise: 30 minutes, 5 days per week.

 Alcohol intake: Ideally abstinence, otherwise < 2 drinks per week.

Device Therapy HF-rEF (Systolic HF)

AICD: Class I Recommendation

- 1. NYHA Class II-III.
- 2. LVEF ≤ 35%.
- 3. Caveats:
 - Survival > 40 days post MI.
 - Survival expectancy > 1year
- 4. Decreases mortality.

CRT or AICD/CRTAICD: Class I Recommendation

- 1. NYHA Class II-IV.
- 2. LVEF ≤ 35%.
- 3. EKG
 - NSR.
 - QRS ≥ 150 Ms, with LBBB.
- 4. Decreases mortality, hospitalization, and reverse remodeling.

Therapeutic Interventions that Improve Mortality and morbidity and reverse Remodeling

Improve Mortality

ACE I

ARBs

ARNI

Aldosterone antagonists

Beta Blockers

CRT

AICD

Improve Mortality, Morbidity and Remodeling:

ACE I

ARBs

ARNI

Aldosterone antagonists

Beta Blockers

CRT

LVADs in Stage D

Digoxin and Ivabradine*: Only hospitalizations.

H F Preserved Ejection Fraction Diastolic Heart Failure

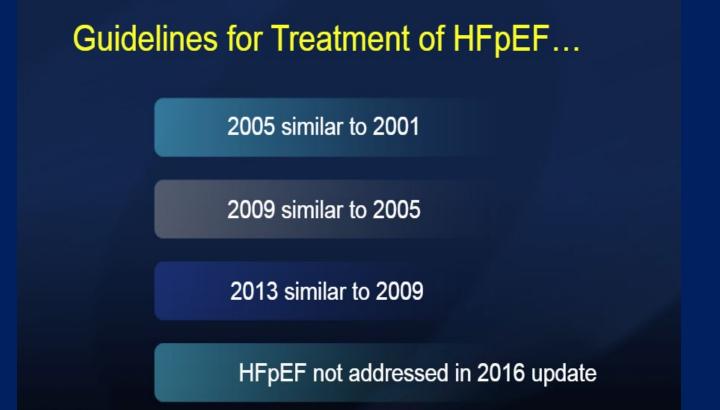
DIASTOLIC HEART FAILURE

Causes HFNEF with LV diastolic dysfunction

- 1. Hypertension
- 2. Infiltrative cardiomyopathy
 - -Amyloidosis
 - -Hemochromatosis
- 3. Hypertrophic cardiomyopathy
- 4. Restrictive cardiomyopathy
- 5. Diabetes
- 6. Obesity
- 7. Advanced age

Not well established evidence base therapeutic recommendations as in HFrEF.

Therapeutic recommendations: Generalizations.



COR	LOE	Recommendations	Comment
ı	В	Control of Systolic and diastolic blood pressure* in accordance with clinical practice guidelines.	Same 2013 Guidelines
T	С	Diuretics for relief volume overload.	Same 2013 Guidelines
lla	C	Coronary revascularization: with CAD in with symptoms (angina) or that demonstrable ischemia is having an adverse effect on HFpEF despite GDMT.	Same 2013 Guidelines

COR	LOE	Recommendations	Comment
lla	C	Hypertension: Beta-blocking agents, ACE inhibitors, and ARBs first line therapy. ARBs may reduce hospitalizations. Goal of blood pressure: < 130/80 mm Hg.	Same 2013 And new HTN Guideline
lla	С	Atrial Fibrillation: Management according to published guidelines . Goal: rhythm control.	Same 2013 HF, Guideline
IIb	B-R	Aldosterone receptor antagonists: Selected patients with EF >45%, elevated BNP levels or HF admission within 1 year, GFR >30 mL/min, Cr. <2.5 mg/dL, K <5.0 mEq/L), to decrease hospitalizations	NEW

Clinical Pearls:

- Focus on aggressive treatment of hypertension.
 - > Beta-blocking agents, ACE inhibitors, and ARBs preferred.
- Diuretics for volume overload.
- Goal in atrial fibrillation: Rhythm control.
- Exercise program.
- Consider aldosterone antagonist.

Thank You! hector.banchs3@upr.edu