TREATMENT OF HEART FAILURE FOR THE PRIMARY CARE PROVIDER

GET WITH THE GUIDELINES

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Disclosures

The speaker has no financial or other conflict of interests to report
Objectives

• Compare and contrast the American Heart Association (AHA)/American College of Cardiology (ACC) Heart Failure Stages and the New York Heart Association (NYHA) Heart Failure Classification systems.
• Describe physiologic targets for heart failure medication therapy
• Name three standard heart failure medications and their starting doses.
• Name the criteria for up-titration and down titration of ACE inhibitors
• Name the criteria for up-titration and down titration of beta blockers
• Name the indications for referral back to advanced heart failure cardiology team
• Describe the three advanced heart failure therapies
• Describe the criteria for advanced heart failure therapies
• Describe the role of Palliative Care in the treatment of heart failure
Marvel of the Cardiovascular System

By permission of Providence HVI
If I have heart failure, then I must be dying...
HF is a chronic condition that can usually be treated with medications
THE BURDEN OF HEART FAILURE

• 5-6 million Americans with HF and growing
• #1 admission/readmission
• 5-year mortality ~ 50%
• $244 per American Adult

Circulation 2014;129:e28-e292
What is HF?
Heart = pump
Heart failure = Inefficient pump
weak
(poor squeeze)
stiff
(poor filling)
Systolic HF
HFrEF

Diastolic HF
HFpEF
What causes HF?
Age
Smoking
Diabetes
High BP
High cholesterol

Retrieved from: https://commons.wikimedia.org/wiki/File:Endo_dysfunction_Athero.PNG#filelinks
by gandhiji40 heart attack anatomy
High Blood Pressure (Hypertension)
High Blood Pressure

High blood pressure is a sign that the heart and blood vessels are being overworked.

Untreated, the disease can lead to atherosclerosis and congestive heart failure.

Enlarged heart (heart failure)

Atherosclerosis
Main complications of persistent high blood pressure

**Brain:**
- Cerebrovascular accident (strokes)
- Hypertensive encephalopathy:
  - confusion
  - headache
  - convulsion

**Retina of eye:**
- Hypertensive retinopathy

**Heart:**
- Myocardial infarction (heart attack)
- Hypertensive cardiomyopathy:
  - heart failure

**Blood:**
- Elevated sugar levels

**Kidneys:**
- Hypertensive nephropathy:
  - chronic renal failure
Valve Disease
2013 ACCF/AHA Guideline for the Management of Heart Failure:

Executive Summary:

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines


Circulation, 128:1810-1852

doi: 10.1161/CIR.0b013e31829e8807
Guideline Title


https://www.guideline.gov/content.aspx?id=47343

Bibliographic Source:

EVALUATION

• History
• Physical Examination
• Initial Laboratory Testing
• Referral
What are the symptoms?
Shortness of breath

Dizziness

Fatigue

Swelling of legs

Cough

Rapid or irregular pulse

Sudden death

Difficulty lying flat
Classification of Heart Failure

ACC/AHA HEART FAILURE CLASSIFICATION

Risk factors  Asymptomatic  Symptomatic  Refractory
LV dysfn        HF        HF

NYHA FUNCTIONAL CLASS

I | II | IIIA | IIIB | IV
Lungs?
Kidneys?
Anemia?
Thyroid?
Heart?
Overweight?
Physical Examination

• Jugular Venous Distension
• Positive Hepato-Jugular Reflex
• S3 Gallop
• Lower Extremity Edema
• Ascites
## Best History/Physical Findings of Heart Failure

<table>
<thead>
<tr>
<th>Finding</th>
<th>Likelihood Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Past History</td>
<td>+ 5.8</td>
</tr>
<tr>
<td>JVD</td>
<td>+ 5.1</td>
</tr>
<tr>
<td>Rales</td>
<td>+ 2.8</td>
</tr>
<tr>
<td>PND</td>
<td>+2.6</td>
</tr>
<tr>
<td>LE Edema</td>
<td>+ 2.3</td>
</tr>
<tr>
<td>Orthopnea</td>
<td>+ 2.2</td>
</tr>
<tr>
<td>DOE</td>
<td>+ 2.1</td>
</tr>
<tr>
<td>S3</td>
<td>+1.1</td>
</tr>
</tbody>
</table>

Jugular Venous Distension
Laboratory Analysis

Complete Blood Count
Urinalysis
Serum Electrolytes (including Magnesium and Calcium)
Renal Function (Creatinine and Blood Urea Nitrogen)
Lipid Profile (fasting)
Liver Function Tests (AST, ALT, Bilirubin)
Thyroid Stimulating Hormone
Blood Natriuretic Peptide (BNP)/ Pro BNP
ECG
Chest X-ray
Blood Natriuretic Peptide

Peptide secreted by atria and ventricles in response to stretching of muscle by fluid overload

Effects:
- Decrease systemic vascular resistance (decreased afterload)
- Increases urination of sodium and water by kidneys (decreased preload)

<table>
<thead>
<tr>
<th>BNP</th>
<th>NT-proBNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 100 pg/mL - HF unlikely</td>
<td>&lt; 300 ng/mL - HF unlikely</td>
</tr>
<tr>
<td>&gt;400 pg/mL - HF likely</td>
<td>Age &lt; 50 years, NT-proBNP &gt;450 pg/mL - HF likely</td>
</tr>
<tr>
<td>100-400 pg/mL – equivocal</td>
<td>Age 50-75 yrs, NT-proBNP&gt;900 pg/mL – HF likely</td>
</tr>
<tr>
<td></td>
<td>Age &gt;75 years, NT-proBNP &gt;1800 – HF likely</td>
</tr>
</tbody>
</table>

When/Who To Refer?

• New Onset
  • Identification and correct underlying cause

• When Medications Not Working Anymore
  • Down titration of medications
    • Hypotension
    • Worsening heart failure symptoms
No single test to diagnose HF in all cases
Amount of blood pumped out of the ventricle

Total amount of blood in ventricle

= Ejection Fraction (%)
# Definitions of Heart Failure Based on Ejection Fraction

<table>
<thead>
<tr>
<th>Category</th>
<th>EF Range</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Failure with reduced EF</td>
<td>EF &lt; 40%</td>
<td>Only category with proven interventions</td>
</tr>
<tr>
<td>(HFrEF)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart Failure with preserved EF</td>
<td>EF &gt; 50%</td>
<td>No efficacious therapies identified</td>
</tr>
<tr>
<td>(HFpEF)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HFpEF (Borderline)</td>
<td>EF 41-49%</td>
<td>Outcomes similar to HFpEF</td>
</tr>
<tr>
<td>HFpEF improved</td>
<td>EF &gt; 40%</td>
<td>Improved from lower EFs. This group needs more study.</td>
</tr>
</tbody>
</table>
Coronary Angiography
Further Diagnostic Testing

HIV Testing

Hemochromatosis
   Serum Transferrin Saturation, Ferritin

Rheumatologic Diseases
   ESR, ANA, CRP

Amyloidosis
   Biopsy or immunological testing

Family History of Idiopathic Cardiomyopathy (Possible Familial)
   Genetic Testing
   Screening of children and siblings
How is HF treated?
Treatment Depends on the Stage of Disease

• Life Style Changes
• Co-morbidity Control
• Medications
• Advanced Therapies
Risk Factors & Cardiovascular Disease

Diet, Smoking, Inactivity, Stress

Hypertension, Atherosclerosis, Thrombosis and Ischemia, Heart Attack, Congestive Heart Failure
Stage A Heart Failure

Risk Factors Without Structural Abnormalities

Hypertension control
- BP < 140/90 (without co-morbidities)
- BP < 130/80 (with diabetes, CAD, renal disease)

Diabetes control

Decrease obesity to normal BMI

Stop smoking

Stop known cardio-toxic drugs/alcohol

Treat lipid disorders

Treat sleep apnea
Stage B Heart Failure

Structural Damage Without Signs or Symptoms

With or without MI and reduced EF:
- ACEs
- Beta Blockers
- Statins (MI or ACS)

With other structural abnormalities (ventricular hypertrophy)
- Blood Pressure Control to 130/80

Dietary control of salt

Cardiac Rehabilitation

Avoid CCB, NSAIDs
Salt leads to fluid retention
I don’t add salt to my food
<table>
<thead>
<tr>
<th>Amount Per Serving</th>
<th>% Daily Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories 230</td>
<td>100</td>
</tr>
<tr>
<td>Calories from Fat 100</td>
<td></td>
</tr>
<tr>
<td>Total Fat 11g</td>
<td>17%</td>
</tr>
<tr>
<td>Saturated Fat 2g</td>
<td>10%</td>
</tr>
<tr>
<td>Trans Fat 0g</td>
<td></td>
</tr>
<tr>
<td>Cholesterol 0mg</td>
<td>0%</td>
</tr>
<tr>
<td>Sodium 95mg</td>
<td>4%</td>
</tr>
<tr>
<td>Total Carbohydrate 32g</td>
<td>11%</td>
</tr>
<tr>
<td>Dietary Fiber 3g</td>
<td>12%</td>
</tr>
<tr>
<td>Sugars 18g</td>
<td></td>
</tr>
<tr>
<td>Protein 5g</td>
<td></td>
</tr>
<tr>
<td>Vitamin A 0%</td>
<td></td>
</tr>
<tr>
<td>Vitamin C 0%</td>
<td></td>
</tr>
<tr>
<td>Calcium 4%</td>
<td></td>
</tr>
<tr>
<td>Iron 10%</td>
<td></td>
</tr>
</tbody>
</table>

*Percent Daily Values are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs:

<table>
<thead>
<tr>
<th>Calories</th>
<th>2,000</th>
<th>2,500</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Fat</td>
<td>Less Than 65g</td>
<td>80g</td>
</tr>
<tr>
<td>Saturated Fat</td>
<td>Less Than 20g</td>
<td>25g</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Less Than 300mg</td>
<td>300 mg</td>
</tr>
<tr>
<td>Sodium</td>
<td>Less Than 2,400mg</td>
<td>2,400mg</td>
</tr>
<tr>
<td>Total Carbohydrate</td>
<td>300g</td>
<td>375g</td>
</tr>
<tr>
<td>Dietary Fiber</td>
<td>25g</td>
<td>30g</td>
</tr>
</tbody>
</table>

Calories per gram:
- Fat 9
- Carbohydrate 4
- Protein 4
2 L fluid
Stage C Heart Failure

Structural Damage With Symptoms

NYHA Class I- Symptoms with extraordinary activity

NYHA Class II- Symptoms with ordinary activity

NYHA Class IIIA- Symptoms with less than ordinary activity

NYHA Class IIIB- Recent symptoms at rest

NYHA Class IV- Symptoms at rest
Burden of Heart Failure In The United States

<table>
<thead>
<tr>
<th>Heart Failure Statistics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>35%</td>
</tr>
<tr>
<td>Class II</td>
<td>35%</td>
</tr>
<tr>
<td>Class III A</td>
<td>15%</td>
</tr>
<tr>
<td>Class III B</td>
<td>10%</td>
</tr>
<tr>
<td>Class IV</td>
<td>5%</td>
</tr>
</tbody>
</table>

6 million Heart Failure Patients

3 million Systolic Heart Failure

300, 000-500,000 Advanced Heart Failure

Circulation; 2011; 123, 1152-1158

Key: NP = natriuretic peptide; RAAS = renin-angiotensin-aldosterone-system
Stage C Heart Failure

HFrEF Stage C
NYHA Class I-IV
Treatment

ACE or ARB
&
Beta Blocker

Volume Overloaded
Class I-IV

Persistently Symptomatic
African Americans

Est. Creatinine clearance
>30 cc/min and K < 5 meq/dL

Loop Diuretics

Hydralazine
and Nitrates

Aldosterone Antagonist
# Diuretics

**Evidence of fluid overload**

<table>
<thead>
<tr>
<th>Drug (Examples)</th>
<th>Initial Daily Dose</th>
<th>Maximum Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Loop Diuretics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bumetanide</td>
<td>.5-1 mg QD or BID</td>
<td>10 mg</td>
</tr>
<tr>
<td>Furosemide</td>
<td>10-20 mg QD</td>
<td>600 mg</td>
</tr>
<tr>
<td>Torsemide</td>
<td>10-20 mg QD</td>
<td>200 mg</td>
</tr>
<tr>
<td><strong>Thiazide Diuretics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metolazone</td>
<td>2.5 mg QD</td>
<td>20 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May be given in concert with Loop Diuretics</td>
</tr>
<tr>
<td><strong>Potassium Sparing Diuretics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spirinolactone</td>
<td>12.5-25 mg QD</td>
<td>50 mg</td>
</tr>
</tbody>
</table>

Dose to Euvolemia if Possible
Careful Attention to Electrolytes/Renal Status
Beta Blockers

- Block the neuro-hormonal system.
- Encourages ventricular reverse remodeling
- Improves survival if started at time of discharge (Optimize Trial)
- Continue for life

<table>
<thead>
<tr>
<th>Commonly Used Beta Blockers</th>
<th>Starting Dose</th>
<th>Maximum Dose</th>
<th>Mean daily doses achieved in studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carvedilol</td>
<td>3.125 mg BID</td>
<td>50 mg BID</td>
<td>37 mg /d</td>
</tr>
<tr>
<td>Metropolol Succinate</td>
<td>12.5-25 mg QD</td>
<td>200 mg QD</td>
<td>159 mg/d</td>
</tr>
<tr>
<td>Extended Release</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**ACE Inhibitors**

- Blocks the Renin-Angiotensin-Aldosterone system
- Reduces afterload/ improves cardiac output
- Encourages ventricular reverse remodeling
- Improves survival (AIRE and TRACE Trials 90s)
- Continue for life

### Commonly Used ACE Inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Maximum Dose</th>
<th>Mean daily doses achieved in studies</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril</td>
<td>6.25 mg TID</td>
<td>50 mg TID</td>
<td>123 mg/d</td>
<td>Short ½ life. Useful when titrating up rapidly</td>
</tr>
<tr>
<td>Enalopril</td>
<td>2.5 mg BID</td>
<td>10-20 mg BID</td>
<td>16.6 mg/d</td>
<td></td>
</tr>
<tr>
<td>Lisinopril</td>
<td>2.5-5 mg QD</td>
<td>20-40 mg QD</td>
<td>35 mg/d</td>
<td></td>
</tr>
</tbody>
</table>

May be limited by renal insufficiency (accept 20-30% decrease in GFR)
May be limited by cough or hypotension
Angiotensin Receptor Blockers

• Recommended if Intolerant to ACE
  Elevated Creatinine > 30% baseline with ACE
  Elevated Potassium > 5 with ACE

• Should not be routinely added to ACE and beta blocker

• Can be considered if patient on ACE and beta blocker and intolerant to aldosterone antagonist

<table>
<thead>
<tr>
<th>Commonly Used ARBs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
</tr>
<tr>
<td>Candesartan</td>
</tr>
<tr>
<td>Losartan</td>
</tr>
<tr>
<td>Valsartan</td>
</tr>
</tbody>
</table>
Aldosterone Antagonists

• Recommended for HF patient with LVEF ≤ 35%
• Recommended for post-MI patient with LVEF ≤ 40%
  (with symptoms of HF or diabetes)

• Creatinine should be < 2.5 mg/dl in men
  < 2.0 mg/dl in women

• Potassium should be < 5 meq/L

• Careful monitoring of creatinine and potassium levels
Other Medications

- Ivabradine (CORLANOR)
  - Novel Calcium Channel Blocker
  - Indicated for heart failure
    - EF >35%
    - HR > 70 BPM
    - Maximum doses of Beta Blockers

- Entresto (Sacubitril/Val
taran)
  - ARB and Neprilysin inhibitor
  - Cannot be given with ACE/ARB
  - Cannot be given if patient experienced angioedema with ACE/ARB.
Other Medication Management Questions

• Anticoagulation
  Not recommended unless patient in A FIB

• CCBs (except amlodipine), NSAID, and most anti-arrhythmics may be detrimental to patients with HF

• Blood Pressure control if ACE and beta blocker insufficient
Case Study #1

55 yo F hospitalized with 2 mo H/O abdominal bloating, dyspnea and recent orthopnea


Echocardiogram: Normal LV size. EF-15%

Normal coronaries

VT-NS, ACE inhibitor caused hypotension and discontinued
Case Study #1

Patient was sent back to PCP for co-management of HF.

Dyspneic walking 100 ft

Meds: coreg 3.125 mg BID, NSAID for arthritis, furosemide 40 mg QD

BP: 118/87, HR 86

JVP: 6 cm above clavicle, HJR +
S3 Gallop
Clear lungs
No edema
Case Study #1

JT

What physical exam finding is most useful in determining the patient’s volume status?

A. Edema
B. JVP
C. Crackles
D. S3 gallop
Case Study #1

What physical exam finding is most useful in determining the patient’s volume status?

A. Edema
B. JVP
C. Crackles
D. S3 gallop
Case Study #1

JT

Which of the following would you do next to decrease mortality?

A. Increase furosemide
B. Stop NSAID
C. Restart ACE-inhibitor
D. Stop carvedilol, start metoprolol tartarate
Case Study #1

JT

Which of the following would you do next to decrease mortality? (BP 118/67, HR: 86)

A. Increase furosemide
B. Stop NSAID
C. Restart ACE-inhibitor
D. Stop carvedilol, start metoprolol tartarate
Case Study #1

JT

Furosemide was increased to 40 mg BID and lisinopril 2.5 mg was started. Patient is down 8 pounds and feels much better.

Exam: BP 99/80, HR 79, JVP 3 cm above the clavicle, No S3

Labs are stable.
What would you do next?

A. Refer for heart transplant evaluation, unlikely to tolerate guideline directed medical therapy (GDMT)

B. Increase ACE-I

C. Increase carvedilol

D. Both B and C sequentially
What would you do next?

A. Refer for heart transplant evaluation, unlikely to tolerate guideline directed medical therapy (GDMT)

B. Increase ACE-I

C. Increase carvedilol

D. Both B and C sequentially
Medical Therapy for HFrEF

GDMT should be titrated to maximal tolerated doses (documented intolerances of BP, cough and renal function)

Beta-Blockers: carvedilol 50 mg BID, metoprolol succinate 200 mg QD

ACE-I: lisinopril 20-40 mg QD
20% develop cough
20-30% decrease in GFR expected
Sequence of ACE VS Beta Blocker Does Sequence Matter?

BRACE Study

- Randomized to either starting Beta Blocker or Ace First
- Groups followed for 18 months
- Both groups were 60% event free (hospitalization and death)

Low Dose ACE VS High Dose ACE
Dose Matters

Low Dose ACE (average 4.2 mg)
High Dose ACE (average 33.2 mg)

1 year Survival or lack of hospitalization
High ACE 55%
Low ACE 50%

4.5 year Survival or lack of hospitalization
High ACE 18%
Low ACE 10%

The highest side effect free dose best.

Practical Tips

In general, can alternate titrations of ACE/ARB and beta blocker; sequence is less important.

If CAD, arrhythmia, or advanced CKD, consider titrating beta blocker first.

Add aldosterone blocker once on ACE/ARB and beta blocker and still NYHA Class II-IV (if GFR>30 and K<5)
Practical Tips

Hypotensive?

Accept BP < 100 and > 80

Separate ACE-I and beta blocker administration by two hours

Minimize diuretics. Keep hydrated

Stop/avoid nonessential medications (CCB, Alpha-blockers, etc.)
Case Study #1
Take Home Points

JVP is most specific exam/history indicator of volume status

Start Low/ Go Slow to maximum tolerated GDMT

Continue for life

Accept 20-30% decline in GFR with increases in ACE-I/ARB
Case Study #1

Conclusion:

Meds: carvedilol 25 mg BID, losartan 100 mg QD, spirinolactone 25 mg, furosemide 20 mg prn five pound weight gain

EF- 10% (2008), 45% (2011) → 60% (2014)

Continue medications for life
ICD- EF ≤ 35 % and NYHA II-III
Cardiac conduction system

- Sinus Node
- AV Node
- Right Atrium
- Left Atrium
- Right Bundle Branch
- Left Bundle Branch
- Right Ventricle
- Left Ventricle
EF ≤ 35%, LBBB, NYHA II - Ambulatory IV
Referral back to Heart Failure Program?

Increasing hypotension requiring down titration of GDMT

Increasing incidence of hospitalizations

- WARM
- WET
- HF
- AHF
- COLD
- DRY
Heart Failure with Preserved Ejection Fraction

- Limited GDMT to improve survival
- Control hypertension
  - ACE, Beta blockers
- Diuretics to control symptoms
- Revascularization if angina
- Control Atrial Fibrillation
- Cardiomems wireless PA pressure monitoring
  - Reduced recurrent hospitalizations
    - (Relative risk reduction of 50%)
Advanced Heart Failure
Decision Tree

Advanced Heart Failure
NYHA IIIB or IV
Maximum tolerated GDMT
Candidate for CRT-D

Cardio-Pulmonary
Exercise Test ≤ 14

Heart Transplantation
<68 y.o.
-Intact organ systems
-No cancer for 5 years
-Normal pulmonary pressures
-Intact Social Structure

Permanent LVAD
(Destination Therapy)
->68 y.o.
-Intact organ systems
-Life expectancy > 2 years
-Intact Social Structure

Palliative Care
Palliative IV Inotropes Hospice
Heart Transplantation

Adult Heart Transplants: Survival by era

- 1982-1991
- 1992-2001
- 2002-2005
- 2006-6/2011

Survival (%) vs Years
Heart Transplantation

Adult heart transplants performed per year

- North America
- Europe
- Other

Years: 1982 to 2010
Left Ventricular Assist Device

1. Blood enters the device from the ventricle.
2. A rotor inside the pump creates a continuous flow of blood.
3. The device pumps the blood into the aorta and then through the body.
Survival with LVADs has improved with technologic advancement and wider adoption.
Essential Member of Care Team
Required for Advanced Heart Failure Program by TJC
Aim of therapy is to alleviate symptoms

Chronic IV Inotrope Therapy
Increase strength/endurance for surgical therapy
Palliative to decrease symptoms
Survival on Long Term Inotropic Therapy

Figure 2. Kaplan-Meier survival curves for patients on dobutamine vs milrinone. Log rank $P=0.01$. 
Chronic Infusion Care Management

• Weekly central venous catheter dressing change
• Weekly or bi-weekly blood work
• Daily self monitoring/management
• Weekly calls to verify supplies, dose and delivery of medication
• Routine follow-up with HF management team and PCP
• Ongoing communication with infusion supplier, home care team, referring provider and PCP
References


References

Packer M; Poole-Wilson PA; Armstrong PW; Cleland JG; Horowitz JD; Massie BM; Ryden L; Thygesen K; Uretsky BF. (1999) Comparative effects of low and high doses of the angiotensin-converting enzyme inhibitor, lisinopril, on morbidity and mortality in chronic heart failure. ATLAS Study Group. *Circulation*. 100(23):2312-8.


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Questions?