Pharmacotherapy for the Management of Heart Failure

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Presenter Disclosure Statement

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no commercial disclosures to report
Heart Failure: The Epidemic

- **5 MILLION** AMERICANS HAVE HEART FAILURE TODAY
  550,000 new onset cases diagnosed annually

- 2012 HEALTHCARE COST FOR HF - $35 BILLION

- RATE OF HOSPITALIZATION FOR HF HAS INCREASED BY 159% in last 10 years

- SYMPTOMATIC HEART FAILURE HAS A 1 YEAR MORTALITY OF 45%

- 2030 there will be a 46% increase in the number of chronically ill patients with heart failure

Common Causes of Heart Failure

- **#1 Ischemic Coronary Artery Disease/MI (70%)**
- **#2 Hypertension**
  - Lung disease
  - Diabetes
  - Anemia
  - Congenital Heart Disease
  - Smoking
  - ETOH Abuse
  - Obesity
- Idiopathic Cardiomyopathy
- Viral or Bacterial Cardiomyopathy (RHD)
- Pericarditis
- Endocarditis
- Dysrhythmias
- Thyroid Disease
- Pregnancy
- Septic Shock
- Valve Disease (especially aortic and mitral)
Aging and Heart Failure

• Age is the strongest predictor of HF
• Pathophysiological: arterial stiffening, myocardial fibrosis, HTN and CAD
• Comorbid disease presence.
• Most clinical trials exclude 70 & 80 year olds or include “healthy elderly patients”
• Pharmacotherapy often under dosed and under prescribed
• Aging changes of body absorption, distribution, metabolism and elimination of medications
Have We Made Progress in Managing Heart Failure?
### Historical Evolving Models of Heart Failure

<table>
<thead>
<tr>
<th>1940s</th>
<th>1960s</th>
<th>1970s</th>
<th>1990s–2015</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiorenal</strong>&lt;br&gt;digitalis and diuretic to perfuse kidneys</td>
<td><strong>Hemodynamic</strong>&lt;br&gt;Vasodilators or positive inotropes to relieve ventricular wall stress</td>
<td><strong>Neurohormonal</strong>&lt;br&gt;ACE inhibitors, beta-blockers, and other agents to block neurohormonal activation</td>
<td></td>
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</table>
Early Patient Identification of HF

• NO NATIONAL SCREENING PROGRAMS FOR EARLY DETECTION

• HOWEVER HF IS PREVENTIBLE THROUGH CONTROL OF VASCULAR RISK FACTORS INCLUDING HYPERTENSION.
CLASSIFICATION SYSTEMS FOR HEART FAILURE

AHA/ACC
NYHA
Ejection Fraction (EF) Based Classification
ACC/AHA 4 STAGES OF HEART FAILURE

• STAGE A – At high risk for the development of HF but have no apparent structural abnormality of the heart.
• STAGE B – Structural abnormality of the heart, but no symptoms of heart failure.
• STAGE C – Structural abnormality of the heart and current or previous symptoms of heart failure.
• STAGE D – End stage symptoms of heart failure that are refractory to standard treatment.
Functional Classification of Patients with Heart Disease (NY Heart Association)

• **Class I:** patients with cardiac disease but *without* resulting *limitations* in physical activity

• **Class II:** patients with heart disease who have *slight limitations* of physical activity

• **Class III:** patients with cardiac disease who have a *marked limitation* of physical activity

• **Class IV:** patients with cardiac disease who are *not able to carry out any physical activity without discomfort*
ACC/AHA versus NYHA CLASSIFICATION

- AHA/ACC classification identifies established risk factors and structural abnormalities that are necessary for the development of HF.
- ACC/AHA promotes PREVENTION of HF.
- Patients may go from A-D but can not go in reverse.
- NYHA based on *functional limitation*. Patients may move forward or backward with medical therapy.
- *... But rather a continuum*
HF Classification by Ejection Fraction (EF)  
2013 Guideline Update

• HF associated with a wide range of LV function and/or abnormalities
• EF an important measure so new terminology
• HF with Reduced EF (HFrEF)
  – HF clinical DX and EF ≤ 40% and clinical signs and symptoms of HF
• HF with Preserved EF (HFpEF) (50% HF population or greater have HFpEF)
  – Clinical signs and symptoms of HF, evidence of normal or preserved LVEF and evidence of abnormal LV diastolic dysfunction on echo or cardiac catheterization
• * Hypertension the most important cause of EFpEF (60-90% cases)

THE PHYSIOLOGY OF HEART FAILURE

Cardiac Reserve
Inotropy
Neurohormonal Compensation
Natriuretic Peptides
Cardiac Reserve

• Maximum percentage of increase in cardiac output that can be achieved above the normal resting level
  – Normally 300-400%

• Ability of the heart to increase output according to body needs depends on
  – Preload: ventricular filling
  – Afterload: resistance to ejection of blood from the heart
  – Cardiac contractility
  – Heart rate
Myocardial Contractility (*Inotropy*)

- Contractile elements of the heart muscle (*actin and myosin*) interact and shorten against a load.
- Contractility increases cardiac output *independent* of preload and afterload.
The HF Failure Cycle

• Endothelial dysfunction (in the cardiac, coronary and peripheral vasculature) key role in pump dysfunction → ventricular dilation

• Remodeling further impacts function UNLESS reversed by medication and therapeutic interventions

• HF begins with pathophysiological changes that continue to symptomatic decline due to ↓CO and pump failure
Compounding Comorbid Conditions

- Diabetes
- COPD
- CHD /Atrial fibrillation/Valvular heart disease
- Sleep apnea
- Reactive airway disease
- End Stage Renal Disease
- Rheumatic / Auto-immune disorders

To Review: Cardiac Failure

• Results in:
  – Decreased pumping ability
  – Decrease in cardiac reserve
  – Initiation of adaptive mechanisms
    • Maintain cardiac output
    • Contribute to heart failure
THE CASCADE OF NEUROHORMONAL AND CIRCULATORY COMPENSATORY MECHANISMS
Maintenance of Cardiac Reserve in Heart Failure

- Cardiac reserve
  - Maintained by compensatory/adaptive mechanisms
    - Frank-Starling mechanism
    - Neurohormonal influences
      - SNS
      - RAAS
      - Natriuretic peptides
      - Local vasoactive substances
    - Myocardial hypertrophy and remodeling

The Cycle of Heart Failure: Negative Feedback Loop Initiated by RAAS/SNS

- Myocardial injury to the heart (CAD, HTN, valvular disease)
- Initial fall in LV performance, ↑ wall stress
- Activation of RAAS and SNS
  - Fibrosis, apoptosis, hypertrophy, cellular/molecular alterations, myotoxicity
- Peripheral vasoconstriction, Hemodynamic alterations
- Heart failure symptoms
  - Fatigue
  - Altered activity
  - Chest congestion
  - Edema
  - Shortness of breath
- Remodeling and progressive worsening of LV function
- Morbidity and mortality
  - Arrhythmias
  - Pump failure
- CAD, coronary artery disease; HTN, hypertension; LV, left ventricular, RAS, renin-angiotensin system; SNS
The Role of Natriuretic Peptides

- NPs have powerful diuretic and smooth muscle effects
  - Natriuretic peptides: atrial natriuretic peptide (ANP) and b-type natriuretic peptide (BNP)
    - Released in response to increases in atrial volume/stretch and ventricular pressure (LVEND)/stretch
    - Promote venous and arterial vasodilation, reducing preload and afterload
    - Inhibit SNS, RAAS, endothelin, inflammatory cytokinens and vasopressin
    - Prolonged HF leads to a depletion of these factors
    - BNP used to guide HF therapy in euvolemic patients (2013 AHA/ACC Guidelines)
Myocardial Hypertrophy and Remodeling

• In HF inappropriate hypertrophy and remodeling occurs

• Alteration in the myocardium cells
  – myocytes
  – non myocytes: cardiac macrophages, fibroblasts, endothelial cells
    • Formation of collagen, fibrosis and stiffness

• Causing: cardiac dysynchrony
PHARMACOLOGICAL INTERVENTION FOR HEART FAILURE

Stage A
Stage B
Stage C
Stage D
Basic Principles of HF Pharmacotherapy

- Neurohormonal and RAAS axes serve as the treatment targets in HF
- Directed therapy to multiple targets
- Titration should be slow and controlled
- Euvolemic (stable fluid status) is imperative for medication tolerance
- Pharmacotherapy guidelines determined by HF Stage
Treatment: Stage A

• Pharmacotherapy directed towards treatment of chronic conditions.
  – Hypertension management
  – Dyslipidemia
  – Diabetes
  – Smoking cessation (lifestyle)
  – Obesity reduction (lifestyle)

Angiotensin-Converting Enzyme (ACE) Inhibitors
Angiotensin-II Receptor Blockers (ARBs)
Angiotensin-Converting Enzyme (ACE) Inhibitors
Angiotensin-II Receptor Blockers (ARBs)

• Critical drugs for hypertension management, HF, AMI and cardioprotection
  – Renoprotection, diabetic neuropathy, endothelial function benefits

• ACE act on the critical enzyme that generates angiotensin II

• ARBs act on the major angiotensin II receptor that responds to Angiotensin II stimulation

• Both well tolerated
Ace Inhibitors and Heart Failure

• Should be prescribed for *all* patients with HFrEF
• Can not be given if pregnant or planning pregnancy
• Caution with severe renal disease (creatinine > 3mg/dl)
• Discontinue with cough
ACE and Diabetes

- ACE lessen the development of diabetes in hypertensive pts.
- Improve endothelial dysfunction
  - Reduce plasminogen activator inhibitor (Pa₁)
  - Increase nitric oxide formation to reverse endothelial dysfunction
- Provide renal protection
  - Reduce proteinuria and protect against progressive glomerular sclerosis
ACE Inhibitors

• **Mechanism of Action**
  – Prevents conversion of angiotensin I to angiotensin II
  – Causes an increase in plasma renin activity & a decrease in aldosterone secretion
  – Potent vasoconstrictor

• **Adverse Effects**
  – Hyperkalemia
  – Deterioration in renal function in patients with bilateral renal artery stenosis
  – Cough
  – Orthostatic effects, hypotension
  – *Angioedema

• **Contraindications**
  – Bilateral renal artery stenosis
  – Pregnancy
# ACE Inhibitors

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosage</th>
</tr>
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<tbody>
<tr>
<td>Benazepril (Lotensin)</td>
<td>10-40 mg 1-2 times/day</td>
</tr>
<tr>
<td>Captopril (Capten)</td>
<td>25-100 mg twice daily</td>
</tr>
<tr>
<td>Enalapril (Vasotec)</td>
<td>2.5-40 mg 1-2 times/day</td>
</tr>
<tr>
<td>Fosinopril (Monopril)</td>
<td>10-40 mg/day</td>
</tr>
<tr>
<td>Lisinopril (Prinivil, Zestril)</td>
<td>10-40 mg/day</td>
</tr>
<tr>
<td>Moexipril (Univasc)</td>
<td>7.5-30 mg/day</td>
</tr>
<tr>
<td>Perindopril (Aceon)</td>
<td>4-8 mg 1-2 times/day</td>
</tr>
<tr>
<td>Quinapril (Accupril)</td>
<td>10-40 mg/day</td>
</tr>
<tr>
<td>Ramipril (Altace)</td>
<td>2.5-20 mg/day</td>
</tr>
<tr>
<td>Trandolapril (Mavik)</td>
<td>1-4 mg/day</td>
</tr>
</tbody>
</table>
Angiotensin II Antagonists (ARBs)

• **Mechanism of Action**
  – Direct antagonism of the angiotensin II receptors
  – Displaces angiotensin II from the AT1 receptor
  – Antagonizes AT1-induced vasoconstriction, aldosterone release, catecholamine release

• **Adverse Effects**
  – Hypotension, hyperkalemia
  – Less incidence of angioedema than ACEI
  – No cough
### Angiotensin II Antagonists

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candesartan (Atacand)</td>
<td>8-32 mg/day</td>
</tr>
<tr>
<td>Eprosartan (Tevetan)</td>
<td>400-800 1-2 times/day</td>
</tr>
<tr>
<td>Irbesartan (Avapro)</td>
<td>150-300 mg/day</td>
</tr>
<tr>
<td>Losartan (Cozaar)</td>
<td>25-100 1-2 times/day</td>
</tr>
<tr>
<td>Olmesartan (Benicar)</td>
<td>20-40 mg/day</td>
</tr>
<tr>
<td>Telmisartan (Micardis)</td>
<td>20-80 mg/day</td>
</tr>
<tr>
<td>Valsartan (Diovan)</td>
<td>80-320 mg/day</td>
</tr>
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</table>
Beta Blockers
Beta Blockers

• Class of HF drugs that has the greatest impact upon mortality
• Recommended for **ALL** patients with current or prior symptoms of HFpEF
• FDA approved for HF: Bisoprolol (Zebeta), Carvedilol (Coreg) and Metoprolol (Lopressor or Toprol)
• Patients with and without MI and/or ACS history benefit
• Pts with COPD selective beta-1 receptor blockers are safe. Nonselective β-blockers should be avoided.
• Slow titration is imperative
β-Adrenergic Antagonists

• **Mechanism of Action**
  – Competitive inhibition of the effects of catecholamines at β-Adrenergic receptors
• Decreases heart rate & cardiac output
• Decrease plasma renin
• Cause release of vasodilatory prostaglandins, decrease plasma volume
• May have a CNS-mediated antihypertensive effect
Classes of β-Adrenergic Antagonists

• *Cardio-selective*
  – $\beta_1$ receptor blockade
• *Non-selective*
  – $\beta_1$ and $\beta_2$ receptor blockade
• *Intrinsic sympathomimetic activity*
  – Decrease vascular resistance & cardiac output less than other β-blockers
  – Possess greater agonist than antagonist effects at $\beta_2$ receptors
• *Combined α & β-blockers*
# Classes of β-Adrenergic Antagonists

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosage (mg/day)</th>
<th>Clinical Pearls</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardio-Selective</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metoprolol</td>
<td>50-100 (1-2/day)</td>
<td>Advantageous in treating HTN patients with asthma, diabetes, or peripheral vascular disease</td>
</tr>
<tr>
<td>Atenolol</td>
<td>25-100</td>
<td></td>
</tr>
<tr>
<td>Betaxolol</td>
<td>5-20</td>
<td></td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>2.5-10</td>
<td></td>
</tr>
<tr>
<td>Propranolol</td>
<td>40-160 (twice daily)</td>
<td>Caution with use in patients with asthma &amp; COPD/ Lipophilicity in brain storming</td>
</tr>
<tr>
<td>Carteolol</td>
<td>2.5-5</td>
<td></td>
</tr>
<tr>
<td>Nadolol</td>
<td>40-120</td>
<td></td>
</tr>
<tr>
<td><strong>Non-Selective</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pindolol</td>
<td>10-40 (twice daily)</td>
<td>Beneficial for patients with bradyarrhythmias or peripheral vascular disease</td>
</tr>
<tr>
<td>Penbutolol</td>
<td>10-40</td>
<td></td>
</tr>
<tr>
<td>Acebutolol</td>
<td>200-800 (twice daily)</td>
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</table>
Cardiovascular Effects of β-Blockade

- Inhibitory effects to the sinus node, AV node and myocardial contraction (*ionotropic effect*)
- Bradycardia --- *decreases* myocardial oxygen demand
  - Rx.– angina
  - Longer diastolic filling time ---from decreased HR – increased coronary perfusion – better myocardial perfusion
- Inhibition of the AV node --- Rx. Supraventricular tachycardia or Atrial fibrillation
Combination Anti-ischemic Therapy for Angina

- B-blockers often combined with nitrate vasodilators and calcium channel blockers in angina therapy.
- Mechanism of action different:
  - B-blockers decrease myocardial $O_2$ demand and improve myocardial blood flow via increase diastolic coronary blood flow
  - Nitrates dilate coronary arteries and coronary collaterals
  - CCBs – prevent exercise induced coronary constriction and reduce afterload
    - CCBs NOT recommended in the situation of HF
- **Hypotension
Noncardiac Indications for β-Blockade

• **Pre-operative** – perioperative MI and death decreased in vascular surgery pts. (high risk for coronary events) treated with βB.

• **Thyrotoxicosis** – βB control tachycardia, palpitations, tremor, nervousness and reduces vascularity of thyroid gland

• **Anxiety states** – reduces tremor and tachycardia
  • *** propranolol FDA approved for this

• **Glaucoma** – open angle glaucoma
  • (timolol (Timoptic), carteolol, levobunolol, metipranolol)

• **Migraine** – to be used preventively.. Not acutely for migraine treatment
  • Propranolol (80-240mg daily)
Recent Clinical Trials Reporting on Beta Blockers and *HFrEF*

- **β-blockers and AF Trial in pts with HFrEF:**
  - Found patients with AF versus sinus rhythm + HF had no benefit from β-blocker therapy
- This differs from current guideline recommendations
- **β-blockers and 30 day readmissions in HFrEF pts**
  - Found elderly pts newly discharged on β-blockers DID NOT have an increased 30 day re-admission rate


Bhatia, V. et al. Beta-blocker use and 30 day all-cause readmission in Medicare beneficiaries with systolic heart failure. *American Journal of Medicine* 2015
Treatment: Stage B

• Even thought asymptomatic, initiate ACE inhibitors and β-blockers for patients with \textit{HFrEF} (regardless of MI history)

• Statin therapy for secondary prevention

• Initiation of diuretic – based antihypertensive therapy if BP not controlled


Diuretic Therapy in Heart Failure
Principles of Diuretic Therapy

• Aldosterone antagonists (spironolactone) should be considered as an additional agent.
• Eplerenone + enalapril has demonstrated a reduction in LV mass
• RALES (Randomized Aldactone Evaluation Study) elderly patients with HF had a 3-% reduction in mortality with the addition of spironolactone.
• Side effect of ↑ K+ especially in the elderly
Principles of Diuretic Therapy continued

• Loop diuretics may be needed as an adjunct in patients treated with neurohormonal blockade
• Loop diuretic often preferred in this case
• If discontinued important to educate on Na+ restriction
• ** Common mistake to “dry-out” patients too much with overzealous diuretic therapy
Diuretics That Alter Sodium & Water Balance

• Diuretics
  – Thiazides
  – Loop
  – Potassium-sparing
  – Aldosterone receptor blockers
Aldosterone Receptor Antagonist

- Recommended in for pts NYHA class II-IV and LVEF of 35% or less
- Creatine should be 2.5mg /dL or less men and 2.0mg/dL women
- Dosing: starting 12.5- 25 mg/qd up to 50mg/qd
- Risk of hyperkalemia correlates with high dose ACE
Aldosterone Receptor Blockers

• **Mechanism of Action**
  – Competes with aldosterone for receptor sites in the distal renal tubules, increasing sodium chloride & water excretion while conserving potassium & hydrogen ions

• **Adverse Effects**
  – Hyperkalemia, Hirsutism, gynecomastia & breast pain

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eplerenone (Inspira)</strong></td>
<td>50-100 mg/day</td>
</tr>
<tr>
<td><strong>Spironolactone (Aldactone)</strong></td>
<td>25-50 mg/day</td>
</tr>
</tbody>
</table>
Loop Diuretics

- **Mechanism of Action**
  - Inhibits reabsorption of sodium & chloride in the ascending loop of Henle & distal renal tubule & cause increased excretion of water, sodium, chloride, magnesium & calcium

- **Adverse Effects**
  - Hypokalemia, hyperuricemia, gout, Metabolic alkalosis, hypomagnesemia, hyponatremia, hyperglycemia

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
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<tbody>
<tr>
<td>Bumetanide (Bumex)</td>
<td>0.5-2 mg/day</td>
</tr>
<tr>
<td>Furosemide (Lasix)</td>
<td>20-80 mg/day</td>
</tr>
<tr>
<td>Torsemide (Demadex)</td>
<td>2.5-10 mg/day</td>
</tr>
</tbody>
</table>
Thiazide Diuretics

- Used as initial therapy, either alone or in combination for BP control with ACE inhibitors, ARBs, β-blockers, CCBs
- **Mechanism of Action**
  - Inhibits sodium reabsorption in the distal tubules causing increased excretion of sodium & water, potassium and hydrogen ions
- **Adverse Effects**
  - Potassium depletion, Magnesium depletion, hyponatremia, hyperglycemia, Increase serum lipid concentrations, Precipitate gout

<table>
<thead>
<tr>
<th>Name</th>
<th>Dosage Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorothiazide (Diuril)</td>
<td>125-500 mg/day</td>
</tr>
<tr>
<td>Chlorthalidone (generic)</td>
<td>12.5-25 mg/day</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>12.5-50 mg/day</td>
</tr>
<tr>
<td>Indapamide (Lozol)</td>
<td>1.25-2.5 mg/day</td>
</tr>
<tr>
<td>Metolazone (Zaroxolyn)</td>
<td>2.5-5 mg/day</td>
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</table>

ARB: Angiotensin receptor blocker; CCB: Calcium channel blocker
Potassium-Sparing Diuretics

• **Mechanism of Action**
  – Interferes with potassium/sodium exchange in the distal tubule, cortical collecting tubule, and collecting duct by inhibiting sodium, potassium-ATPase; decreases calcium excretion; increases magnesium loss

• **Adverse Effects**
  – Hyperkalemia, hyponatremia, gynecomastia, hyperchloremic metabolic acidosis

<table>
<thead>
<tr>
<th>Amiloride (Midamor)</th>
<th>5-10 mg/day</th>
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</thead>
<tbody>
<tr>
<td>Triamterene (Dyrenium)</td>
<td>50-100 mg/day</td>
</tr>
</tbody>
</table>
**DIURETIC Therapy and HF**

- **Cortex**
  - Thiazides
  - Inhibit active exchange of Cl-Na in the cortical diluting segment of the *ascending loop of Henle*

- **Medulla**
  - K sparing
  - Inhibit reabsorption of Na in the *distal convoluted and collecting tubule*
  - Loop diuretics
  - Inhibit exchange of Cl-Na-K in the thick segment of the *ascending loop of Henle*
Treatment: Stage C

• Therapeutic goal to control symptoms and improve QOL, reduce hospital admissions and mortality

• Basic medications of stage A & B: ACE/ARB, Statin, β-blocker, and perhaps diuretic therapy

• Additional of Digoxin MAY be beneficial

• Additional of hydralazine + isosorbide dinitrate (African Americans) or nitrates with HFrEF

• Potential device therapy: implantable cardioverter–defibrillator (ICDs) and Cardiac resynchronization therapy (CRTs)


Digoxin

• Cardiac glycoside with a MILD positive inotropic effect
• Improves HF symptoms, reduces hospitalization BUT does not improve survival
• Easily toxic in the elderly
• May be prescribed for pts with AF + HF however β-blockers more effective for controlling ventricular response

Hydralazine and Isosorbide Dinitrate

- Direct arteriole vasodilation with a decreased systemic resistance in combination with a long acting nitrate
- Recommended in African Americans with HFrEF and NYHA class III – IV receiving optimal ACE and β-blocker therapy

- Side effects can be orthostatic hypotension and flushing
  - Dosing: fixed 37.5 mg hydralazine/20 mg isosorbide 3x daily
  - Dosing: separate: Hydralazine 25-50mg
    3-4x qd/isosorbide 20 -30 mg 3-4x daily
Nitrate therapy

- Short acting sublingual nitroglycerin for acute or prophylactic use
  - venous and arterial dilators that decrease myocardial oxygen demand
- Long acting
  - oral: Isosorbide and Imdur
  - cutaneous nitroglycerin (paste and patch)
Treatment: Stage D

• Symptoms can be refractory
• Basic medications of stage A, B & C: ACE/ARB, Statin, β-blocker, diuretic therapy and nitrates
• Possible addition of chronic inotrope therapy
• Device therapy: implantable cardioverter–defibrillator (ICDs), Cardiac resynchronization therapy (CRTs) possible LVAD
• Palliative and hospice care and end of life goals


IV Inotropic Agents

• Dopamine
• Dobutamine
• Milrinone
• May be continuous or intermittent
• Short term or long term or serve as a “bridge therapy” to transplantation or device therapy (LVAD)
Stages in the development of HF and recommended therapy by stage.

Medications of Harm for HF

• Concomitant administration of an ACE and ARB and/or ACE + ARB + Beta Blocker worsen survival and they should **NOT** be given together

• Dihydropyridine/Nondihydropyridine calcium channel blockers and alpha blockers generally ineffective in HF

• Aldosterone receptor antagonist in pts with creatine more than 2.5mg/dL in men or 2.0mg/dL in women or GFR <30mL/min/1.73 m2 or K+ > 5.0

• NSAIDs have ↑mortality and morbidity with HF
Complimentary Therapies and Heart Failure

• Vitamin D
• CoQ 10
• Omega 3 Fish oils
• Hormone therapies (growth, thyroid and/or testosterone)
• VITAL trial: Current 5 year trial (26,000) treated with Vit. D3 and/or 1g of omega-3 fatty acids to see if they reduce HD, stroke and cancer in healthy individuals (completed 2017)

O’Riordan, M. Coenzyme Q10 supplementation reduces HF admissions and improves survival. http://the heart.org/article1545585

ATRIAL FIBRILLATION AND HEART FAILURE

Precipitating Factors
Rate Control
Rhythm Control
Atrial Fibrillation and Heart Failure

• AF and HF the epidemics of the 21\textsuperscript{st} century
• AF is a strong independent risk factor for HF and HF decompensation
• AF predicts a worse NYHA classification
• AF rate control essential
  – Rate control versus rhythm control controversy
• Prevention of thromboembolism critical
  – Higher incidence due to ↓EF, LVH
Atrial Fibrillation and Heart Failure

• Consider precipitating factors:
  – Hemodynamic stress
    • Fluid overload
    • Excess sodium consumption
  – Noncardiovascular respiratory causes
    • Pneumonia
    • COPD exacerbation
    • PE
  – Neurological causes
    • Subarachnoid hemorrhage
    • Stroke
  – Hyperthyroid and diabetes
  – Anemia
  – Alcohol consumption
Treatment of Atrial Fibrillation

• Rate control pharmacology
  – βBlockers
  – Nondihydropyridine calcium channel blockers
  – Digoxin
  – Amioderone

• Rhythm control pharmacology
  – Flecainide
  – Propafenone
  – Amioderone
  – Sotalol
Treatment of Atrial Fibrillation continued

- Anticoagulation therapy
- Catheter ablation
  - Evidence-Based Care of the Patient with Atrial Fibrillation: A Call to Action for Nurses and Advanced Practice Nurses.

http://www.empr.com/atrial-fibrillation/section/4477/?publishDate=1&timestamp=635549246298585549
Novel Therapies for Heart Failure

- **Device therapy:**
  - MADIT-CRT trial (2014) compared with ICD alone, CRT-D reduced mortality among patients with HF

- **Pharmacologic therapy:**
  - PARADIGM (2014) angiotensin receptor and neprilysin inhibition with LCZ696 (a combination of sacubitril and valsartan) showed a decrease in cardiovascular mortality

  - PARADIGM-HF(2015) Angiotensin-neprilysin inhibitor LCZ696 compared to ACE Enalapril alone and Enalapril + LCZ696 in 8399 HF pts with HFrEF with the outcome of worsening HF and intensification of symptoms (hospitalization, medication titration required, BNP levels etc.) demonstrated significant **LESS** clinical worsening of symptoms, lower BNP and Troponin levels and increase QOL
Conclusion

• We have Made Progress in Managing Heart Failure
Conclusion

• We have reviewed the physiological alterations of heart failure now looking at the endothelial damage and remodeling concepts.

• We have responded with a multitude of pharmacological agents to combat and now support the physiological neurohormonal compensation occurring with heart failure.

• We have developed and continue to develop a “Chinese menu” of mechanical devices to “bridge” and also improve QOL and cardiovascular function ranging from ventricular assist devices to ICD/pacemaker combinations to CRT technology.
Bibliography

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