Post MI Congestive Heart Failure
Dr. Badri Paudel

HIS WALK IS HISTORY

“All the very essence of cardiovascular practice is the recognition of early heart failure”
- Sir Thomas Lewis 1933

ALL ROADS LEAD TO CCF

Heart Failure
- Final common pathway for many cardiovascular diseases whose natural history results in symptomatic or asymptomatic left ventricular dysfunction
- Prevalence: Asymptomatic - 4%. Symptomatic 2-3%, 10-20% in those aged>75yrs.
- Risk of death is 5-10% annually in patients with mild symptoms and increases to as high as 30-40% annually in patients with advanced disease.

Epidemiology
- Most common cause of hospitalization >65 years of age
- 1 per 1000 Indians
- Prevalence: 18.8 million (1.76% of total population)
- Incidence: 1.57 million cases per year (0.15% of total population)
- Mortality ~5-10% per year at early stages
- Up to 30-40% per year at advanced stages
Congestive Heart Failure

“The situation when the heart is incapable of maintaining a cardiac output adequate to accommodate metabolic requirements and the venous return”

- Eugene Braunwald

Definition

• AHA/ACC defines...
  A complex syndrome resulting from any structural or functional cardiac disorder that impairs the ability of the ventricles to fill with or eject blood.

• ESC defines...
  A Clinical symptoms/ signs secondary to abnormal ventricular function.
  A complex clinical syndrome in which the heart is incapable of maintaining a cardiac output adequate to accommodate metabolic requirements and the venous return.

The Donkey Analogy

Ventricular dysfunction limits a patient's ability to perform the routine activities of daily living...

Main causes

• Coronary artery disease - 70%
• Hypertension

• Valvular heart disease – 10%
• Cardiomyopathy – 10%
• Others – Drugs, Toxins, Nutritional, Infective, Infiltrative, Cor pulmonale, etc.

Risk Factors

➔ Coronary heart disease is the foremost
➔ CHD as a primary cause:-
  • SOLVD Trial (75% of the cases)
  • Hillingdon trial (36% of cases)
  • Framingham heart study (48% in men and 27% in women)

➔ Coronary artery disease and hypertension (either alone or in combination) account for cases > 90% in the Framingham study

NYHA Functional Classification of heart failure

• Class I: No limitation of physical activity
• Class II: Slight limitation of physical activity
• Class III: Marked limitation of physical activity
• Class IV: Unable to carry out physical activity without discomfort
EVOLUTION OF CLINICAL STAGES – ‘Heart Failure is a Continuum’

NORMAL
Asymptomatic LV Dysfunction
Compensated CHF
Decompensated CHF
Refractory CHF

Framingham Criteria for CHF

- Major criteria
  - PND
  - Neck vein distention
  - Rales
  - Radiographic cardiomegaly
  - Acute pulmonary edema
  - Pulmonary edema, visceral congestion or cardiomegaly at autopsy
  - Weight loss > 4.5 kg in 5 days in response to Rx of CHF

- Minor Criteria
  - Bilateral ankle edema
  - Nocturnal cough
  - Dyspnea on ordinary exertion
  - Hepatomegaly
  - Pleural effusion
  - ↓ in Vital capacity by 1/3rd from maximal value recorded
  - Tachycardia (>120/min)

TREATMENT OBJECTIVES

1. Survival
2. Morbidity
3. Exercise capacity
4. Quality of life
5. Neurohormonal changes
6. Progression of CHF
7. Symptoms

Pathophysiological Mechanisms

- Sympathetic over activity
- RAAS
- BNP
- Vasopressin
Adverse prognostic indicators
- Low systolic blood pressure
- Poor end organ perfusion
- Renal dysfunction
- Elevated catecholamines
- Raised BNP, Vasopressin
- Low serum sodium
- Widening QRS duration on ECG

Management
- Non Pharmacological:
- Pharmacological:
  - Diuretics, Digitalis
  - ACEi, ARBs
  - Beta Blockers
  - Aldosterone Antagonists
  - Vasodilators
  - others

PHARMACOLOGIC THERAPY
- Therapies that improve symptoms
  - Diuretics
  - Digoxin
  - Inotropes
- Therapies that improve survival
  - ACEI
  - Beta blockers
  - Aldosterone antagonists
  - ARB

PHARMACOLOGIC THERAPY (Cont’d)
- Investigational \ Emerging Drugs
  - Vasopeptide inhibitors
  - Cytokine antagonists
  - Endothelin antagonists
  - Vasopressin receptor antagonist
  - Adenosine antagonists
  - Metabolic modulators
  - Statins \ Omega3 fatty acids
  - If channel inhibitors
  - Cardiac myosin activators

TREATMENT IN VARIOUS STAGES

Conventional Treatments of ADHF
- Reduce fluid volume
- Decrease preload and/or afterload
- Augment contractility

McBride BF, White M. Pharmacotherapy. 2003;23:997-1020
**ACE Inhibitors in Heart failure**

- For many years, diuretics and digitalis were accepted as standard first-line therapy for HF.

- More recently, however, large and well-designed clinical studies have shown consistently that ACE inhibitors improve survival and reduce morbidity in patients with LVSD, a condition that leads to chronic HF.

- A meta-analysis of 32 randomised controlled trials in which ACE inhibitors were compared with standard therapy or placebo in 7105 patients with symptomatic HF has shown statistically significant overall reductions with ACE inhibition in both total mortality and in a combined end-point of mortality or hospitalisation.

**AIRE – post MI**

AIRE Study demonstrated efficacy of Ramipril on mortality and morbidity in CHF post-MI NYHA class I-III patients

- 2006 patients enrolled in a double-blind, randomized, placebo-controlled study

- 27% reduction in the risk of death

- 23% decrease in progression to severe / resistant heart failure

**SAVE trial – post MI Captopril Trial**

- 26% RRR in Death

**TRACE trial – post MI Trandolapril**

- 27% RRR in Death or HF Hospitalisation

**ACEI MECHANISM OF ACTION**

- Angiotensinogen
- Kallikrein
- Bradykinin

**ACEIs and SURVIVAL**

- Placebo
- Enalapril

**SOLVD (Prevention)**

- n = 4228 No CHF symptoms EF < 35

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Summary

• In sum, both ACE inhibitors and ARB are considered appropriate first-line therapy for the treatment of patients with heart failure and LVSD barring a contraindication to therapy.

• Although there is some overlap in the contraindications to their use, existing data indicates significant differences in side effect profiles and tolerability between the two classes.

SENIORS: Primary and secondary outcomes

<table>
<thead>
<tr>
<th>Event-free survival (%)</th>
<th>Nebivolol</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality or CV hospital admission (primary outcome)</td>
<td>332 (31.1%)</td>
<td>375 (35.3%)</td>
</tr>
<tr>
<td>All-cause mortality (main secondary outcome)</td>
<td>169 (15.8%)</td>
<td>192 (18.1%)</td>
</tr>
</tbody>
</table>

Beta-Blockers in HF - New Paradigms

- Safe in mild, moderate and severe HF
- May initiate early rather than late
  - Start low, go slow
  - Initiate in the hospital when euvolemic and off inotropes
- If on a BB and decompensated CHF
  - Continue or reduce dosage
  - Rarely discontinue
- Long acting Metoprolol, Carvedilol, Bisoprolol, preferred

Major Trials of Beta Blockers in CHF

- MDC
- MERIT HF
- PRECISE
- MOCHA
- US Carvedilol heart study group
- ANZ trial Carvedilol
- CIBIS II
- CAPRICON
- COPERNICUS
- CARMEN
- COMET

Mechanism of action

- Density of β1 receptors
- Inhibit cardiotoxicity of catecholamines
- Neurohormonal activation
- HR
- Anti-ischemic
- Anti-hypertensive
- Anti-arrhythmic
- Anti-oxidant, Anti-proliferative
**β-Adrenergic Blockers - Dose (mg)**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisoprolol</td>
<td>1.25 / 24h</td>
<td>10 / 24h</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>3.125 / 12h</td>
<td>25 / 12h</td>
</tr>
<tr>
<td>Metoprolol tartrate</td>
<td>6.25 / 12h</td>
<td>75 / 12h</td>
</tr>
<tr>
<td>Metoprolol succinate</td>
<td>12.5-25 / 24h</td>
<td>200 / 24h</td>
</tr>
</tbody>
</table>

- Start Low, Increase Slowly
- Increase the dose every 2 - 4 weeks

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**Different Classes of Beta-Blockers and Specific Drugs**

<table>
<thead>
<tr>
<th>Class/Drug</th>
<th>Clinical Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol</td>
<td>Beta-blocker</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>Non-selective</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>Class/Drug</td>
</tr>
</tbody>
</table>

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**Results from COMET**

- Carvedilol improves vascular outcomes
- Carvedilol provides better protection against vascular events
- Carvedilol significantly reduces the occurrence of all MIs by 29%
- Carvedilol reduces hospitalization for unstable angina by 17%

**As compared to metoprolol...**

- Carvedilol reduces the risk of any MI, any unstable angina or any stroke by 19%
- The effect of v on the combined end point of MI or stroke was significant (HR 0.75) and the effect on fatal MI or fatal stroke was highly significant (HR 0.46)

**Reduces Mortality, Improves Survival**

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**Concluding Remarks**

- Administering carvedilol in addition to conventional therapy reduces mortality and attenuates myocardial re-modelling in patients with left ventricular dysfunction following acute MI

- Moreover, mortality has been significantly lower with carvedilol than with metoprolol in patients with mild to severe CHF, suggesting that carvedilol may be the preferred β-blocker

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**Diuretics in HF**

- Diuretics produce symptomatic benefits more rapidly than any other drugs for heart failure.

- They can relieve peripheral oedema within hours or days, whereas the clinical effects of digitalis, ACE inhibitors, or β-blockers may require weeks or months to become apparent.

(Hall 1995; Packer 1993)

Diuretics for heart failure (Review) 2
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CHF & Loop diuretics

- Overall incidence and prevalence increasing
- Aging of population
- Advances in MI management
- Most common cause of hospitalization in age group >65 years (US)
- Edema commonly associated with CHF
- Loop diuretics -- the preferred diuretics
- Indicated for symptomatic treatment of CHF
- Recommended by all guidelines (ESC, ACC, AHA)

Torsemide or Frusemide

- Efficacy of Torsemide Vs Furosemide in CHF
- Fewer deaths in Torsemide group (2.2% Vs 4.5% in the Furosemide group)
- Fewer episodes of hypokalemia but similar NYHA class improvement with Torsemide
- Torsemide, which has a more predictable bioavailability may be safer than Furosemide.

Pharmacological advantages of torsemide over frusemide (Summary)

- More potent diuresis and natriuresis
- Reduced kaliuresis
- Longer duration of action
- Greater secretion of prostacyclin
- More complete and predictable bioavailability
- Alternative metabolic pathways
CHAPTER 17: Myocardial ischemia

NITRATES: HEMODYNAMIC EFFECTS

1. Venous vasodilatation
   - Preload
   - Pulmonary congestion
   - Ventricular size
   - Vent. Wall stress
   - MVO2

2. Coronary vasodilatation
   - Myocardial perfusion

3. Arterial vasodilatation
   - Afterload
   - Cardiac output
   - Blood pressure

DIGOXIN: EFFECT ON CHF PROGRESSION

Digoxin Investigational Group (DIG) Study

Role of Aldosterone in CHF

Aldosterone and Aldosterone Antagonists

Placebo (273) —
Prazosin (183) —
Hz + ISDN (186) —

PROBABILITY OF DEATH

VOLUME

N Engl J Med 1993;329:1

N Engl J Med 1986;314:1547

RADIANCE

% WORSENING OF CHF

Placebo n=93
DIGOXIN Withdrawal

p = 0.001

Role of Parasympathetic Activity: Death
Endothelial Dysfunction
Stimulate Fibrosis
Hypertrophy
Na & Water Retention
Increase Preload
Reduction of Sympathetic Activity

Aldosterone

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Increase Preload
Reduction of Sympathetic Activity
Need of Aldosterone Antagonist

- Aldosterone Antagonist
- Reduce Sympathetic Activity: Reduce Arrhythmia
- Increase Na & Water Excretion: Reduce Preload
- Reduce Myocardial Collagen Turnover: Retains Mg & K levels
- Reduce Sympathetic Activity: Reduce Endothelial Dysfunction
- Increase of Parasympathetic Activity: Improve Endothelial Dysfunction

Randomized Aldactone Evaluation Study (RALES)

- Aldosterone Antagonist
- Spironolactone*
- Placebo

Remodeling and Survival Benefits by Drug Class

- Established Rx
  - ACE-I: Benefit
  - ARB: Benefit (+ACEI better)
  - Aldo-B: Benefit
  - Beta-B: Benefit

- Newer Therapies
  - Vasop-I: Benefit (ACEI-neutral)
  - ET-I-B: No Benefit
  - TNFα-B: No Benefit
  - Dopamine: Adverse

Endothelin Antagonists

- ENCOR – ENRASENTAN → Fared worse than placebo
- REACH – 1 → BOSENTAN → similar to placebo
- ENABLE 1 & 2 – BOSENTAN → Low dose not superior to placebo
- DARUSENTAN – ET<sub>α</sub> selective antagonist - Results awaited

Stages in the Evolution of HF-Treatment

- Treat risk factors: Avoid factors
  - ACE-I in selected patients
  - β blockers
  - Diuretics/Digoxin
  - Palliative therapy
  - Mechanical Assisted Devices
  - Heart Transplant

   A

   B

   C

   D
Despite Current Drug Therapies, Heart Failure Morbidity and Mortality Remain High

- 30% to 40% of patients are in NYHA class III or IV
- Re-hospitalization rates
  - 2% at 2 days
  - 20% at 1 month
  - 50% at 6 months
- 5-year mortality ranges from 15% to more than 50%
  - Asymptomatic LVD = 15%
  - Mild-moderate HF = 35%
  - Advanced HF = 50%

Table 1. Approaches in refractory heart failure

<table>
<thead>
<tr>
<th>Approach</th>
<th>Modalities</th>
</tr>
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<tbody>
<tr>
<td>Optimal Compressed Heart Function</td>
<td>Optimal medical therapy, Cardiac Resynchronization Therapy, ICD</td>
</tr>
<tr>
<td>Reverse remodeling</td>
<td>Drugs, CRT, surgical or interventional atrial septal repair / annuloplasty, access device</td>
</tr>
<tr>
<td>Regrettful Ablation</td>
<td>Stroke, AF, pulmonary hypertension, exacerbation of end-organ systems, use of device</td>
</tr>
<tr>
<td>Replace the Heart</td>
<td>Assist devices, destination therapy, Cardiac transplantation</td>
</tr>
<tr>
<td>Treatment of comorbidities</td>
<td>Acute decompensation, dyspnea, atrial arrhythmias, CHF</td>
</tr>
<tr>
<td>Treatment of Consequences</td>
<td>Pulmonary hypertension with diuretics, Volume overload with ultrafiltration, fibrillation, CCBs</td>
</tr>
<tr>
<td>Better delivery of care</td>
<td>Hospitalization, Intervention care, Improved patient care</td>
</tr>
</tbody>
</table>

2005 ACC/AHA Heart Failure Guideline: CRT in Stage C Heart Failure

- **Class I Indication:** Patients with LVEF ≤35%, sinus rhythm, and NYHA functional Class III or ambulatory Class IV symptoms despite recommended optimal medical therapy and who have cardiac dysynchrony, which is currently defined as a QRS >120 msec, should receive CRT, unless contraindicated

Level of Evidence: A

2005 ACC/AHA Heart Failure Guideline: ICDs in Heart Failure

- **Class I Indication:** ICD therapy is recommended for primary prevention of sudden cardiac death to reduce total mortality in patients with non-ischemic dilated cardiomyopathy or ischemic heart disease at least 40 days post-MI, a LVEF less than or equal to 35%, and NYHA functional class II or III symptoms while receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 year

Level of Evidence: A

Hunt SA, Abraham WT, Chin MH, et al., Circulation and JACC, 2005

Jessup M, Abraham WT, Casey DE, et al., Circulation and JACC 2009
ICDs Save Lives In Heart Failure

• Second Multicenter Automatic Defibrillator Implantation Trial (MADIT II) – 31% ↓
• Prophylactic Defibrillator Implantation in Patients with Nonischemic Dilated Cardiomyopathy (DEFINITE) trial – 30% ↓
• Sudden Cardiac Death-Heart Failure Trial (SCD-HeFT) – 23% ↓

Implantable Hemodynamic Monitors

- LV Pressure Sensor
- RV Pressure Sensors
- PA Pressure Sensors
- LA Pressure Sensor

CARDIAC TRANSPLANT

CONCLUSION

• MORBIDITY & MORTALITY REMAINS HIGH IN HEART FAILURE DEPITE CURRENT DRUG THERAPY.
• PHARMCO THERAPY-TREATMENT OF CHOICE- ALL STAGES OF CCF.
• CORONARY INTERVENTIONS IN REVASCULARABLE ANATOMY.
• DEVICES & SURGERY – HAS A ROLE IN REFRACTORY FAILURE.
• CARDIAC TRANSPLANT IS AN OPTION.

MY TIME IS UP
KINDLY WAKEUP

SMILE PLEASE
TORTURE IS OVER

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