Importance of the topic.

- Latest updates in heart failure treatment
- How to make a diagnosis of the advanced heart failure, stage D cardiomyopathy?
- Permanent mechanical support.
- Introduction to transplantation.
- What is new on the Horizon?

Heart failure is a leading cause of hospitalization in the United States.

- In the past 40 years heart failure incidence is increasing
  - on one side because of the progressive ageing of the population, increasing risk of CAD such as obesity, more sedentary lifestyle, DM
  - and on the other side due to advances in medical and surgical therapies

Circulation 2000;110(14):e391-479
JAMA 2004
• Heart failure is costly.
• Heart failure expenses are driven mostly by hospitalizations (77% of total cost).

Bimodal Distribution of the Cost-Initial diagnosis and End of Life

• A major focus was placed on decreasing readmission rate to decrease cost of care
Trends in Heart Failure Hospitalization for Medicare Beneficiaries, 1998-2008

Chen et al. JAMA 2011; 306(15):1669

Trends in Heart Failure Mortality for Medicare Beneficiaries, 1998-2008

Chen et al. JAMA 2011; 306(15):1669

Annual number of deaths by cause, World, 2016

Data refers to the specific cause of death, which is distinguished from risk factors for death, such as air pollution, diet and other lifestyle factors. See source for further details on definitions of specific cause categories.
Age-standardized death rates and the observed and predicted number of cancer and heart disease deaths from 1969 through 2020

Forecasting the Impact of Heart Failure in United States

Heart Failure is Costly and Deadly
• Heart failure remains a chronic disease subject to time dependent deterioration.


Treatment Approaches
Entresto: Angiotensin Receptor Neprilysin Inhibition

Entresto

Angiotensin receptor blocker + Inhibition of neprilysin
PARADIGM-HF: Cardiovascular Death or Heart Failure Hospitalization (Primary Endpoint)

PARADIGM-HF: All-Cause Mortality
Among patients with heart failure with reduced EF who were hospitalized for acute decompensated heart failure, the initiation of sacubitril-valsartan therapy led to a greater reduction in the NT-proBNP concentration than enalapril therapy. (percent change, -46.7% vs. -25.3%; ratio of change with sacubitril-valsartan vs. enalapril, 0.71; 95% confidence interval [CI], 0.63 to 0.81; P<0.001)

Angiotensin–Neprilysin Inhibition in Acute Decompensated Heart Failure

Comparison of Sacubitril–Valsartan vs Enalapril on Effect on NT-proBNP in Patients Stabilized From an Acute Heart Failure Episode – PIONEER-HF
Entresto Summery
- HFrEF with EF < 40%
- NYHA class II, III, IV?
- Low enrolment of AA patients
- About 36 hours wash out period after d/c ACE-I
- Benefits from early initiation of Entresto therapy after heart failure related admission

Ivabradine
Slows HR independent of BB effect

Effect of Ivabradine on outcomes

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary composite endpoint (CV death or hospital admission for worsening HF)</td>
<td>0.82</td>
<td>(0.76;0.89)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>0.90</td>
<td>(0.86;1.02)</td>
<td>&lt;0.052</td>
</tr>
<tr>
<td>Death from heart failure</td>
<td>0.74</td>
<td>(0.58;0.96)</td>
<td>&lt;0.014</td>
</tr>
<tr>
<td>All-cause hospital admission</td>
<td>0.89</td>
<td>(0.82;0.96)</td>
<td>&lt;0.003</td>
</tr>
<tr>
<td>Any CV hospital admission</td>
<td>0.85</td>
<td>(0.78;0.92)</td>
<td>&lt;0.0002</td>
</tr>
<tr>
<td>CV death/hospital admission for HF or non-fatal MI</td>
<td>0.82</td>
<td>(0.74;0.89)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Patients in Ivabradine Trial (SHIFT)

- Class II- IV NYHA heart failure
- LV systolic dysfunction (EF ≤35%)
- Heart rate ≥70 bpm
- Sinus rhythm
- Documented hospital admission for worsening heart failure ≤12 months


Contraindications

- Acute decompensated heart failure
- Hypotension (BP less than 90/50)
- Sick sinus syndrome, sinoatrial block or third degree AV block, unless a functioning demand pacemaker is present
- Severe hepatic impairment

ACC/AHA Guidelines
Guideline-Directed Medical Therapy

Diuretics Recommendation

- Loop diuretics: Bumetanide, furosemide, and torsemide
- Consider starting alternative diuretics if there is a recurrent failure of lasix encountered
  - torsemide (Demadex) (5, 10, 20, 100mg)
  - bumetanide (0.5, 1, 2mg)

- Consider addition of sequential nephron blockade in resistant cases
  - Metolazone (oral 2.5-10 mg)
  - Chlorothiazide (oral or IV 250-1000 mg)
Aim for Target Doses

<table>
<thead>
<tr>
<th>ACE-I</th>
<th>BB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enalapril (Vasotec)</td>
<td>10 mg bid</td>
</tr>
<tr>
<td>Captopril (Capoten)</td>
<td>50 mg tid*</td>
</tr>
<tr>
<td>Ramipril (Altace)</td>
<td>5 mg bid</td>
</tr>
<tr>
<td>Lisinopril (Prinivil, Zestoril)</td>
<td>20 mg qd</td>
</tr>
<tr>
<td>Trandolapril (Mavik)</td>
<td>4 mg od</td>
</tr>
<tr>
<td>Quinapril (Accupril)</td>
<td>20-40 mg bid</td>
</tr>
<tr>
<td>Bisoprolol (Zebeta)</td>
<td>10 mg qd</td>
</tr>
<tr>
<td>Carvedilol (Coreg)</td>
<td>25-50 mg bid **</td>
</tr>
<tr>
<td>Metoprolol XL/CIR (Toprol XL)</td>
<td>200 mg qd</td>
</tr>
<tr>
<td>Metoprolol (Lopressor)</td>
<td>100 mg bid 1</td>
</tr>
<tr>
<td>Atenolol (Tenormin)</td>
<td>100 mg bid 1</td>
</tr>
</tbody>
</table>

*An effective dose, **Depends on weight
1 For mild to moderate hypertension

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CHF: Fluid and Electrolyte Imbalance

Initial Intravascular & Subsequent Extravascular Volume Expansions

- Initial 3 L retention with jugular venous distention
- Subsequent expansion of extravascular volume
- Progressive Na+ and H2O retention
- Edema at knees then thigh (10-20 L)
- Pitting edema at ankles (3 L)

---

Anasarca (30 L)

- 1000 mL/day = fixed movement of fluid from extra- to intravascular volume
- Oral intake = 1400 cc/day
- Urine output = 2400 cc/day
- Negative balance = -1000 cc/day (-1 kg BW)

---

Anasarca (30 L)

- Extravascular volume
- Intravascular volume
- J Kanub venous distention (3 L)
- Intravascular volume
- Kedneys
- 1000 mL/day = negative daily urine output
Water Restriction: Recommendation

Fluid restriction (1.5 to 2 L/d) is reasonable in stage D, especially in patients with hyponatremia, to reduce congestive symptoms. Class IIa (Level of Evidence: C)

- Recommendations for fluid restriction in HF are largely driven by clinical experience.
- Routine strict fluid restriction in all patients with HF regardless of symptoms or other considerations does not appear to result in significant benefit.
- Limiting fluid intake to around 2 L/d is usually adequate for most hospitalized patients.


Sodium Restriction

- For patients with stage C and D HF, currently there are insufficient data to endorse any specific level of sodium intake.
- Because sodium intake is typically high (>4 g/d) in the general population, clinicians should consider some degree (e.g., <3 g/d) of sodium restriction in patients with stage C and D HF for symptom improvement. Class IIa (Level of Evidence: C)
Exercise Training

- Exercise training (or regular physical activity) is recommended as safe and effective for patients with HF who are able to participate to improve functional status CLASS I, (Level of Evidence: A)
- Cardiac rehabilitation can be useful in clinically stable patients with HF to improve functional capacity, exercise duration, HRQOL, and mortality CLASS IIa, (Level of Evidence: B)

Cardiomems

- CHAMPION trial: Patients with NYHA class III heart failure, and a previous hospital admission for HF irrespective of LV EF were enrolled in 64 centers in the USA.
- During the entire follow-up (mean 15 months), the treatment group had a 37% reduction in heart-failure-related hospitalization compared with the control group (158 vs 254, HR 0.63, 95% CI 0.52–0.77; p<0.0001)
When should we intervene?
One of the challenges of treating heart failure is recognition of heart failure severity.

Predictors of Poor Outcome

- Poor functional status
  - Subjective: Inability to walk 1 block without dyspnea (NYHA class III-IV)
  - Objective: Poor performance at CPX, 6-MWT distance < 300 m (less in female and >75)

Objective Assessment.
Metabolic Exercise Testing.

- AT
- VO2 max <12-14 ml/kg/min (<50% of age predicted)
- VE/VCO2 slope (> 34)
- Breathing reserve
Predictors of Poor Outcome

• >1 readmission in the last 6 month
• Low blood pressure
• Intolerance to ACE-I/ARB/BB or recent dose down titration
• Diuretic dose >1.5 mg/kg or need in dose increase


Mortality Based on the Diuretic and ACE-I Dose

- Diuretic High
  - Lasix >80 mg/d
  - Bumex >2 mg/day
- ACE-I High
  - Captopril >75 mg/d
  - Enalapril >10 mg/d
  - Lisinopril >10 mg/d

Neuberg et al. Am Heart J 2002; 144:31-8

Predictors of Poor Outcome

• High salt sensitivity
• Weight loss due to cachexia
• Hyponatremia
• Worsening of renal function
Predictors of Poor Outcome

- CRT nonresponders
- Need for inotropes use (inotropes - think LVAD/Tx)


Prognosis on Chronic Inotrope Infusion

Journal of Cardiac Failure Vol. 9 No. 3 2003
Gorodeski EZ et al. Circulation Heart failure, 2009

Recognition of low output Heart Failure

- “Phenotype” of heart failure seems to shift from congestion to low output due to improved diuretics, vasodilators.
- Fatigue, effort intolerance, lack of edema, decreased appetite, cachexia, end organ hypoperfusion, low blood pressure, inability to tolerate medications.
- Don’t disregard patients if they don’t look like they are in “heart failure”.

Journal of Cardiac Failure Vol. 9 No. 3 2003
Goal of early referral:
• Not to get to the crisis.
• Sicker patients have higher mortality.
• Prevention of end organ dysfunction.
• When patients are “too sick” they might not be candidates.
• Less critically ill patients have faster post-operative recovery.

Advanced Heart Failure Treatment Options
• Transplantation
• LVAD as BTT
• LVAD as DT
• TAH
• Palliation

Transplantation
• Once patient is accepted as a good candidate, he (she) is registered on the national waiting list (United Network for Organ Sharing-UNOS).
• A suitable heart donor is a young to middle-aged person who has been declared “brain dead” based on standard criteria, and whose heart has preserved function.
Donor hearts are provided to patients based on the donor's blood type and body weight, the recipient's severity of illness, and geographic location. These data are contained in the UNOS computer database.
LVAD Survival Compared To OMM Therapy

Ventricular Assist Devices

Park SJ. AHA Scientific Sessions, November 2010
Long-term LVADs

HeartMate III
Ultra-Compact, Fully Mag-Lev VAD
• Full magnetic levitation optimized for efficiency
  – Low power consumption - Longer battery runtime
  – Designed to generate a near physiologic pulse which may have meaningful clinical benefits
• Enhanced hemocompatibility / minimal thrombogenicity
  – Large blood path passages
  – Proven HeartMate textured blood contacting surfaces – potentially low/no anticoagulation therapy
  – Facilitates low speed operation without an increased risk of thrombus formation
• Less invasive implantation
  – Intro-thoracic placement
• Ultra-long life
  – Non-contacting FML rotor
  – Modular percutaneous lead (driveline)

HeartWare
What if the patient is not a good surgical candidate?

- He has advanced condition with severe end organ failure
- Active cancer
- Advanced age
- Severe PVD
- Psychiatric illness
Palliative care. Hospice.

Comparison of 1- and 5-year survival after hospitalization for heart failure

<table>
<thead>
<tr>
<th>Disease</th>
<th>1-Year</th>
<th>5-Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate cancer</td>
<td>99</td>
<td>99</td>
</tr>
<tr>
<td>Melanoma</td>
<td>98</td>
<td>66-92</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>76</td>
<td>89</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>82</td>
<td>62</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>76</td>
<td>45</td>
</tr>
<tr>
<td>Leukemia</td>
<td>63</td>
<td>51</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>42</td>
<td>16</td>
</tr>
</tbody>
</table>

Experience of Patients

- **Lung Cancer**
  - Clearer trajectory – able to plan for death
  - Initially feel well but told you are ill
  - Good understanding of diagnosis and prognosis
  - Care prioritized as “cancer” or “terminal”

- **Cardiac Failure**
  - Gradual decline, acute deterioration
  - Feel ill but told you are well
  - Little understanding of diagnosis and prognosis
  - Less priority as “chronic illness”

(Murray 2002)
Issues in Palliative Care

- Prognostication difficult
- Only 4% of patients dying of CHF get palliative care (40% in cancer pts) (Gibbs, 2002)
- Resuscitation is a difficult issue.
  DNR written on 5% (47% in Ca, 52% in AIDS)

- Turn off/disable ICD’s
  - No discussion about turning off ICD in 73% of pts prior to last hours of life (Goldstein, 2004)
  - 8% of patients receive shocks in the minutes before death (Goldstein, 2004)
“It is easier to die of Cancer than Heart or Renal Failure”

John Hinton, 1963

“People may forget what you said. People may forget what you did, but people never forget how you made them feel.”

- Maya Angelou, author and poet

Systolic HF: Multidisciplinary Care

- Primary Care Provider
- General Cardiologist
- Heart Failure Cardiologist
- Cardiac Surgeon
- EP Cardiologist
Thank You.