Heart Failure, What a Non-Heart Failure Specialist Needs to Know?

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Louis Horlick Chair in Medicine
Provincial Head, Medicine
Conflict of Interest

Nothing to report
What is heart failure?

• **Chronic Heart Failure (CHF):**
  – Heart failure is a complex syndrome in which abnormal heart function results in, or increases the subsequent risk of, clinical symptoms and signs of low cardiac output and/or pulmonary or systemic congestion.

• **Acute Heart Failure Syndrome (AHF):**
  – Gradual or rapid change in heart failure signs and symptoms resulting in the need for urgent therapy
Definition of HFrEF and HFpEF

HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction; LVEF: left ventricular ejection fraction

Steinberg et al. Circulation 2012;126:65–75
HF with Reduced and Preserved Ejection Fraction: HFrEF and HFpEF

Heart failure with reduced ejection fraction – EF ≤ 40%

Heart failure with preserved ejection fraction – EF > 50%

Systolic dysfunction

A condition of volume overload
1. Characterized by eccentric hypertrophy
2. Results in a globular heart with thinning of LV walls, decreased systolic function and enlarged LV volume

Diastolic dysfunction

A condition of pressure overload
1. Characterized by concentric hypertrophic growth
2. Results in a normal-sized LV cavity with thickened walls and preserved systolic function
HFpEF and HFrEF are associated with similarly high levels of mortality

- Survival rate among patients with a discharge diagnosis of HF in the USA was slightly higher among patients with HFpEF than those with HFrEF between 1987–2001.
  - respective mortality rates were 29% and 32% at 1 year and 65% and 68% at 5 years

- HFpEF is associated with significant morbidity and mortality, despite having a slightly higher survival rate compared with HFrEF.

HF: heart failure; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction; LVEF: left ventricular ejection fraction; USA: United States of America

Therapeutic Options are different for HFpEF and HFrEF

**Heart failure with reduced ejection fraction – EF ≤ 40%**

- Systolic dysfunction

**Heart failure with preserved ejection fraction – EF > 50%**

- Diastolic dysfunction

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### Chronic HFrEF chronic therapy
1. ACE/ARB
2. BB
3. MRA
4. ARNI, Ivabradine
5. ICD/CRT

### Chronic HFpEF Therapy
1. NO DEFINITIVE THERAPY
2. Treat underlying causes (e.g. HTN, DM, etc)
Objectives

• Burden of Heart Failure
• Heart Failure Pathophysiology
• Assessment of Patients with Heart Failure
• Optimal Management
• Future of Heart Failure Therapy
Objectives

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Heart Failure is the **Fastest Rising** Cardiovascular Condition in Canada

- **>750,000** people in Canada will have Heart Failure in 2030
- **50,000** New cases are diagnosed each year
- **1.4 million** hospital days per year
- The Estimated direct cost of heart Failure in Canada in 2012 was **$2.9 billion**

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1. Management of Heart Failure Patients in Ontario: Recommendations from Best Practice, April 2013, *Ross et al. Treating the right patient at the right time; Access to HF care, CJC 2006*
Heart Failure has high mortality

- 1-year mortality rate after diagnosis was 25% in Ontario in 2007\(^1\)
- 30-day mortality rate after HF hospitalization: 16%\(^1\)

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**Survival**

<table>
<thead>
<tr>
<th></th>
<th>WOMEN</th>
<th>MEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months of follow-up</td>
<td>0  6  12  18  24  30  36  42  48  54  60</td>
<td>0  6  12  18  24  30  36  42  48  54  60</td>
</tr>
</tbody>
</table>

**WOMEN**
- Breast
- MI
- Bowel
- Ovarian
- Heart Failure
- Lung

**MEN**
- MI
- Bladder
- Prostate
- Bowel
- Heart Failure
- Lung

---

5-year survival rate of Scottish patients following their first HF hospitalization in comparison with MI and 4 types of cancer\(^2\)

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Hospital Readmission Rate

- In a study in **Ontario, Canada**, of 8543 newly discharged patients with HF, 67.3% of whom had reduced LVEF, 35,966 hospital readmissions occurred over the lifetime of the cohort\(^1\)
- Patients with HFrEF were more likely to experience an increased risk of early cardiovascular hospitalization, with an increase in hospitalizations for HF and coronary artery disease
- Adjusted hazard ratio (HR) for first CV hospitalization was 1.10 for HFrEF (95% CI 1.00-1.20; \(P = 0.045\))

### Hospital Readmission Rates per 100 Person-Years of Follow-up

<table>
<thead>
<tr>
<th>Hospitalization Type</th>
<th>Ischemic</th>
<th>Nonischemic</th>
<th>HFrEF</th>
<th>HFpEF</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV</td>
<td>96.7</td>
<td>62.1</td>
<td>83.8</td>
<td>72.9</td>
<td>84.4</td>
<td>80.9</td>
</tr>
<tr>
<td>HF</td>
<td>49.9</td>
<td>33.3</td>
<td>42.9</td>
<td>34.9</td>
<td>45.0</td>
<td>41.3</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>24.5</td>
<td>8.7</td>
<td>19.4</td>
<td>14.7</td>
<td>18.1</td>
<td>17.4</td>
</tr>
<tr>
<td>Other CV</td>
<td>29.9</td>
<td>23.0</td>
<td>28.9</td>
<td>28.1</td>
<td>27.8</td>
<td>26.5</td>
</tr>
<tr>
<td>Non-CV</td>
<td>154.0</td>
<td>137.0</td>
<td>137.3</td>
<td>132.2</td>
<td>149.9</td>
<td>146.0</td>
</tr>
</tbody>
</table>

For all comparisons, age and sex-adjusted \(P < 0.001\) for ischemic vs. nonischemic and HFrEF vs. HFpEF and age-adjusted \(P < 0.001\) for men vs. women.

CV = cardiovascular; HFrEF = heart failure reduced ejection fraction; LVEF = left ventricular ejection fraction; HFpEF = heart failure preserved ejection fraction

Prognosis Following Hospitalization for HF in Canada

- 50% of Patients will die within 2.5 years of their first hospitalization

Setoguchi S et al., 2007. Am Heart J, 154(2), 203-205
Causes of Heart Failure

- Coronary artery disease
- Volume overload
- Pressure overload
- Connective tissue diseases
- Primary cardiomyopathy
- Other diseases
- Drugs
- Infections
- Restrictive disease
- Inherited diseases
- Heavy metals
- Neurologic diseases
- Metabolic
Objectives

• Burden of Heart Failure
• Heart Failure Pathophysiology
• Assessment of Patients with Heart Failure
• Optimal Management
• Future of Heart Failure Therapy
Overactivation of the RAAS and SNS is detrimental in HFrEF and underpins the basis of therapy.

- The crucial importance of the RAAS is supported by the beneficial effects of ACEIs, ARBs and MRAs

- Benefits of β-blockers indicate that the SNS also plays a key role

**ACEI**: angiotensin-converting-enzyme inhibitor; **Ang**: angiotensin; **ARB**: angiotensin receptor blocker; **AT, R**: angiotensin II type 1 receptor; **MRA**: mineralocorticoid receptor antagonist; **NPs**: natriuretic peptides; **NPRs**: natriuretic peptide receptors; **RAAS**: renin-angiotensin-aldosterone system; **SNS**: sympathetic nervous system

Assessment of Patient with Heart Failure
Objectives

- Burden of Heart Failure
- Heart Failure Pathophysiology
- Assessment of Patients with Heart Failure
- Optimal Management
- Future of Heart Failure Therapy
Stage A: High Risk for developing Heart failure

Stage B: Asymptomatic LV dysfunction

Stage C: Past or current Symptoms of HF

Stage D: End-stage HF

NYHA Functional Class:
- Class I: symptoms at activity levels that would limit normal individuals
- Class II: symptoms of HF with ordinary exertion
- Class III: symptoms of HF with less than ordinary exertion
- Class IV: Symptoms of HF at rest
Landmark trials in patients with HFrEF

1. SOLVD-T\(^1\) (1991)
   2,569 patients
   *Key benefits of enalapril (ACEI) vs placebo:
   -16% \(\downarrow\) all-cause mortality

2. CIBIS-II\(^2\) (1999)
   2,647 patients
   *Key benefits of bisoprolol (BB) vs placebo:
   -34% \(\downarrow\) all-cause mortality

3. CHARM-Alternative\(^3\) (2003)
   2,028 patients
   *Key benefits of candesartan (ARB) vs placebo:
   -23% \(\downarrow\) CV mortality or HF hospitalization

   2,548 patients
   *Key benefits of candesartan (ARB) vs placebo:
   -15% \(\downarrow\) CV mortality or HF hospitalization

5. SHIFT\(^5\) (2010)
   6,558 patients
   *Key benefits of ivabradine (I inhibitor) vs placebo:
   -18% \(\downarrow\) CV mortality or HF hospitalization

6. PARADIGM-HF\(^7\) (2014)
   8,442 patients
   *Key benefits of LCZ696 (ARNI) vs enalapril:
   -20% \(\downarrow\) CV mortality or HF hospitalization

Percentages are relative risk reductions vs comparator


See notes for definitions of study names

SOLVD-Treatment: enalapril (ACEI) significantly reduced the risk of mortality in patients with HFrEF

<table>
<thead>
<tr>
<th>SOLVD-Treatment</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Enalapril 2.5–20 mg* QD vs placebo*</td>
</tr>
<tr>
<td>Number of patients</td>
<td>2,569</td>
</tr>
<tr>
<td>Average age (years)</td>
<td>61</td>
</tr>
<tr>
<td>Female (%)</td>
<td>19.7</td>
</tr>
<tr>
<td>LVEF</td>
<td>≤35% (NYHA I–IV)</td>
</tr>
<tr>
<td>Primary outcome</td>
<td>All-cause mortality</td>
</tr>
<tr>
<td>Mean follow-up (months)</td>
<td>41.4</td>
</tr>
</tbody>
</table>

* On top of standard therapy for HF.

CIBIS-II: bisoprolol (BB) significantly reduced all-cause mortality in patients with HFrEF


<table>
<thead>
<tr>
<th>CIBIS-II</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention</strong></td>
<td>Bisoprolol 1.25–10 mg* QD vs placebo*</td>
</tr>
<tr>
<td><strong>Number of patients</strong></td>
<td>2,647</td>
</tr>
<tr>
<td><strong>Average age (years)</strong></td>
<td>61</td>
</tr>
<tr>
<td><strong>Female (%)</strong></td>
<td>20</td>
</tr>
<tr>
<td><strong>LVEF</strong></td>
<td>≤35% (NYHA III–IV)</td>
</tr>
<tr>
<td><strong>Primary outcome</strong></td>
<td>All-cause mortality</td>
</tr>
<tr>
<td><strong>Mean follow-up (years)</strong></td>
<td>1.3</td>
</tr>
</tbody>
</table>

* On top of standard therapy with diuretics and ACEIs
ACEI: angiotensin-converting-enzyme inhibitor; BB: beta blocker; CIBIS: Cardiac Insufficiency Bisoprolol Study II; HFrEF: heart failure with reduced ejection fraction; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; QD: once daily
CHARM-Alternative: candesartan (ARB) significantly reduced CV mortality and morbidity in patients with HFrEF

<table>
<thead>
<tr>
<th>CHARM-Alternative</th>
<th>Candesartan 32 mg QD vs placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of patients</strong></td>
<td>2,028</td>
</tr>
<tr>
<td><strong>Average age (years)</strong></td>
<td>66.6</td>
</tr>
<tr>
<td><strong>Female (%)</strong></td>
<td>31.9</td>
</tr>
<tr>
<td><strong>LVEF</strong></td>
<td>≤40% (NYHA II–IV)</td>
</tr>
<tr>
<td><strong>Primary outcome</strong></td>
<td>Composite of CV mortality or CHF hospitalization</td>
</tr>
<tr>
<td><strong>Median follow-up (months)</strong></td>
<td>33.7</td>
</tr>
</tbody>
</table>


**ARB**: angiotensin receptor blocker; **CHARM**: Candesartan in Heart failure Assessment of Reduction in Mortality and Morbidity; **CHF**: chronic heart failure; **CV**: cardiovascular; **HFrEF**: heart failure with reduced ejection fraction; **LVEF**: left ventricular ejection fraction; **NYHA**: New York Heart Association; **QD**: once daily

30% relative risk reduction

p<0.0001
EMPHASIS-HF: eplerenone (MRA) significantly reduced the risk of CV mortality and hospitalization in patients with HFrEF

<table>
<thead>
<tr>
<th>EMPHASIS-HF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
</tr>
<tr>
<td>Eplerenone 50 mg* QD vs placebo*</td>
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<tr>
<td>Number of patients</td>
</tr>
<tr>
<td>2,737</td>
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<tr>
<td>Average age (years)</td>
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<tr>
<td>68.7</td>
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<tr>
<td>Female (%)</td>
</tr>
<tr>
<td>22.3</td>
</tr>
<tr>
<td>LVEF</td>
</tr>
<tr>
<td>≤35% (NYHA II)</td>
</tr>
<tr>
<td>Primary outcome</td>
</tr>
<tr>
<td>Composite of CV mortality or HF hospitalization</td>
</tr>
<tr>
<td>Median follow-up (months)</td>
</tr>
<tr>
<td>21</td>
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</tbody>
</table>

* On top of standard therapy for HF

EMPHASIS-HF: Eplerenone in Mild Patients Hospitalization And Survival Study in Heart Failure; CV: cardiovascular; HF: heart failure; HFrEF: heart failure with reduced ejection fraction; LVEF: left ventricular ejection fraction; MRA: mineralocorticoid receptor antagonist; NYHA: New York Heart Association; QD: once daily.

A Comparison of Angiotensin Receptor-Neprilysin Inhibition (ARNI) With ACE Inhibition in the Long-Term Treatment of Chronic Heart Failure With a Reduced Ejection Fraction
Prospective comparison of ARNI with ACEI to determine impact on global mortality and morbidity in Heart Failure trial (PARADIGM-HF)

Aim of the PARADIGM-HF Trial

LCZ696 400 mg daily

Enalapril 20 mg daily

SPECIFICALLY DESIGNED TO REPLACE CURRENT USE OF ACE INHIBITORS AND ANGIOTENSIN RECEPTOR BLOCKERS AS THE CORNERSTONE OF THE TREATMENT OF HEART FAILURE
PARADIGM-HF: Entry Criteria

- NYHA class II-IV heart failure
- LV ejection fraction $\leq 40\% \rightarrow 35\%$
- BNP $\geq 150$ (or NT-proBNP $\geq 600$), but one-third lower if hospitalized for heart failure within 12 months
- Any use of ACE inhibitor or ARB, but able to tolerate stable dose equivalent to at least enalapril 10 mg daily for at least 4 weeks
- Guideline-recommended use of beta-blockers and mineralocorticoid receptor antagonists
- Systolic BP $\geq 95$ mm Hg, eGFR $\geq 30$ ml/min/1.73 m$^2$ and serum K $\leq 5.4$ mEq/L at randomization
PARADIGM-HF: Cardiovascular Death or Heart Failure Hospitalization (Primary Endpoint)

Kaplan-Meier Estimate of Cumulative Rates (%)

<table>
<thead>
<tr>
<th>Days After Randomization</th>
<th>Patients at Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LCZ696</td>
</tr>
<tr>
<td>0</td>
<td>4187</td>
</tr>
<tr>
<td>180</td>
<td>3922</td>
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<tr>
<td>360</td>
<td>3663</td>
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<td>540</td>
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<td>720</td>
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<tr>
<td>900</td>
<td>1544</td>
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<tr>
<td>1080</td>
<td>896</td>
</tr>
<tr>
<td>1260</td>
<td>249</td>
</tr>
</tbody>
</table>

Enalapril (n=4212)
PARADIGM-HF: Cardiovascular Death or Heart Failure Hospitalization (Primary Endpoint)

Kaplan-Meier Estimate of Cumulative Rates (%)

Patients at Risk

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<tr>
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<th>LCZ696 (n=4187)</th>
<th>Enalapril (n=4212)</th>
</tr>
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<tbody>
<tr>
<td>Days After Randomization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days</td>
<td>0</td>
<td>1117</td>
</tr>
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<td></td>
<td>180</td>
<td>914</td>
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<td></td>
<td>540</td>
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<td>236</td>
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</tbody>
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PARADIGM-HF: Cardiovascular Death or Heart Failure Hospitalization (Primary Endpoint)

Kaplan-Meier Estimate of Cumulative Rates (%)

Days After Randomization

Patients at Risk

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<td>853</td>
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<td>1260</td>
<td>249</td>
<td>236</td>
</tr>
</tbody>
</table>

HR = 0.80 (0.73-0.87)
P = 0.0000002
Number needed to treat = 21
PARADIGM-HF: Cardiovascular Death

Kaplan-Meier Estimate of Cumulative Rates (%)

Days After Randomization

Enalapril (n=4212)

Patients at Risk

| LCZ696 | 4187 | 4056 | 3891 | 3282 | 2478 | 1716 | 1005 | 280
| Enalapril | 4212 | 4051 | 3860 | 3231 | 2410 | 1726 | 994  | 279

Days After Randomization

0 180 360 540 720 900 1080 1260

Kaplan-Meier Estimate of Cumulative Rates (%)

0 8 16 24 32
PARADIGM-HF: Cardiovascular Death

HR = 0.80 (0.71-0.89)  
P = 0.00004  
Number need to treat = 32

Kaplan-Meier Estimate of Cumulative Rates (%)

Days After Randomization

Patients at Risk

<table>
<thead>
<tr>
<th></th>
<th>LCZ696</th>
<th>Enalapril</th>
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<tbody>
<tr>
<td>Days</td>
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<tr>
<td></td>
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<td></td>
<td>1005</td>
<td>994</td>
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<tr>
<td>Patients</td>
<td>280</td>
<td>279</td>
</tr>
</tbody>
</table>

Enalapril (n=4212)

LCZ696 (n=4187)
PARADIGM-HF: Effect of LCZ696 vs Enalapril on Primary Endpoint and Its Components

<table>
<thead>
<tr>
<th></th>
<th>LCZ696 (n=4187)</th>
<th>Enalapril (n=4212)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary endpoint</strong></td>
<td>914 (21.8%)</td>
<td>1117 (26.5%)</td>
<td>0.80 (0.73-0.87)</td>
<td>0.0000002</td>
</tr>
<tr>
<td><strong>Cardiovascular death</strong></td>
<td>558 (13.3%)</td>
<td>693 (16.5%)</td>
<td>0.80 (0.71-0.89)</td>
<td>0.00004</td>
</tr>
<tr>
<td><strong>Hospitalization for heart failure</strong></td>
<td>537 (12.8%)</td>
<td>658 (15.6%)</td>
<td>0.79 (0.71-0.89)</td>
<td>0.00004</td>
</tr>
</tbody>
</table>
PARADIGM-HF: All-Cause Mortality

HR = 0.84 (0.76-0.93)  
P<0.0001

Kaplan-Meier Estimate of Cumulative Rates (%)

Days After Randomization

Patients at Risk

<table>
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</table>
Angiotensin Neprilysin Inhibition With LCZ696 Doubles Effect on Cardiovascular Death of Current Inhibitors of the Renin-Angiotensin System

Effect of ARB vs placebo derived from CHARM-Alternative trial
Effect of ACE inhibitor vs placebo derived from SOLVD-Treatment trial
Effect of LCZ696 vs ACE inhibitor derived from PARADIGM-HF trial
Ivabradine and outcomes in chronic heart failure (SHIFT):
Systolic Heart failure treatment with the If inhibitor ivabradine Trial
$I_f$ Current Inhibition with Ivabradine

Reduces spontaneous action potential frequency: the slope of diastolic depolarization in the sinus node cells is reduced, no impact on action potential threshold or shape

Use dependent: stronger rate-reducing effect when channels are open more frequently, i.e., at higher heart rates.

SHIFT Primary Objective

To evaluate whether the $I_f$ inhibitor ivabradine improves cardiovascular outcomes in patients with:

1. Moderate to severe chronic heart failure
2. Left ventricular ejection fraction $\leq 35\%$
3. Heart rate $\geq 70$ bpm in sinus rhythm
4. Best recommended therapy
Figure 3: Kaplan-Meier cumulative event curves for (A) the primary composite endpoint of cardiovascular death or hospital admission for worsening heart failure, (B) hospital admission for worsening heart failure, and (C) cardiovascular death.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Ivabradine group</th>
<th>Placebo group</th>
<th>HR (95% CI)</th>
<th>Test for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 years (n=4031)</td>
<td>407 (20.6%)</td>
<td>527 (25.6%)</td>
<td>0.76 (0.67-0.87)</td>
<td>p=0.099</td>
</tr>
<tr>
<td>≥65 years (n=2474)</td>
<td>386 (30.5%)</td>
<td>410 (33.9%)</td>
<td>0.89 (0.77-1.02)</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (n=4970)</td>
<td>624 (25.4%)</td>
<td>725 (28.9%)</td>
<td>0.84 (0.76-0.94)</td>
<td>p=0.260</td>
</tr>
<tr>
<td>Female (n=1535)</td>
<td>169 (21.7%)</td>
<td>212 (28.0%)</td>
<td>0.74 (0.60-0.91)</td>
<td></td>
</tr>
<tr>
<td><strong>β blockers</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No β-blocker intake</td>
<td>101 (29.4%)</td>
<td>134 (39.3%)</td>
<td>0.68 (0.52-0.88)</td>
<td>p=0.103</td>
</tr>
<tr>
<td>at randomisation (n=685)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-blocker intake</td>
<td>692 (23.9%)</td>
<td>803 (27.5%)</td>
<td>0.85 (0.76-0.94)</td>
<td></td>
</tr>
<tr>
<td>at randomisation (n=5820)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cause of heart failure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-ischaemic (n=2087)</td>
<td>218 (21.3%)</td>
<td>296 (27.9%)</td>
<td>0.72 (0.60-0.85)</td>
<td>p=0.059</td>
</tr>
<tr>
<td>Ischaemic (n=4418)</td>
<td>575 (26.0%)</td>
<td>641 (29.1%)</td>
<td>0.87 (0.78-0.97)</td>
<td></td>
</tr>
<tr>
<td><strong>NYHA class</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA class II (n=3169)</td>
<td>300 (18.9%)</td>
<td>356 (22.5%)</td>
<td>0.81 (0.69-0.94)</td>
<td>p=0.793</td>
</tr>
<tr>
<td>NYHA class III or IV</td>
<td>493 (29.8%)</td>
<td>580 (34.5%)</td>
<td>0.83 (0.74-0.94)</td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No history of diabetes</td>
<td>525 (23.2%)</td>
<td>611 (27.1%)</td>
<td>0.83 (0.74-0.93)</td>
<td>p=0.861</td>
</tr>
<tr>
<td>(n=4526)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>History of diabetes</td>
<td>268 (27.5%)</td>
<td>326 (32.4%)</td>
<td>0.81 (0.69-0.95)</td>
<td></td>
</tr>
<tr>
<td>(n=1979)</td>
<td></td>
<td></td>
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<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No history of hypertension</td>
<td>274 (25.4%)</td>
<td>330 (29.7%)</td>
<td>0.81 (0.69-0.95)</td>
<td>p=0.779</td>
</tr>
<tr>
<td>(n=2191)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of hypertension</td>
<td>519 (24.0%)</td>
<td>607 (28.2%)</td>
<td>0.83 (0.74-0.93)</td>
<td></td>
</tr>
<tr>
<td>(n=4314)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Baseline heart rate</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>&lt;77 bpm (n=3144)</td>
<td>339 (21.4%)</td>
<td>356 (22.8%)</td>
<td>0.93 (0.80-1.08)</td>
<td>p=0.029</td>
</tr>
<tr>
<td>≥77 bpm (n=3357)</td>
<td>454 (27.4%)</td>
<td>581 (34.2%)</td>
<td>0.75 (0.67-0.85)</td>
<td></td>
</tr>
</tbody>
</table>
Patient with LVEF ≤ 40% and Symptoms

Triple Therapy ACEi (or ARB if ACEi intolerant), BB, MRA
Titrate to target doses or maximum tolerated evidence-based dose

REASSESS SYMPTOMS

NYHA I
Continue triple therapy

NYHA II–IV: SR, HR ≥ 70 bpm
ADD Ivabradine and SWITCH ACEi or ARB to ARNI* for eligible patients

NYHA II–IV: SR with HR < 70 bpm or AF or pacemaker
SWITCH ACEi or ARB to ARNI* for eligible patients

REASSESS SYMPTOMS AND LVEF

NYHA I or LVEF > 35%
Continue present management

NYHA I–III and LVEF ≤ 35%
Refer to ICD/CRT algorithm

NYHA IV
Consider:
- Hydralazine/nitrates
- Referral for advanced HF therapy (mechanical circulatory support/transplant)
- Palliative Care referral

Reassess every 1–3 years or with clinical status change

Consider LVEF reassessment every 1–5 years

Reassess as needed according to clinical status
ADHF
Suspect Acute Heart Failure

**INITIAL WORKUP**
- History, Physical, ECG, Chest x-ray, Biomarkers (electrolytes, Cr, CBC, +/−troponin, +/- BNP)

**Unlikely to be AHF**
- Consider other diagnosis

**Uncertain**
- Test BNP / NT-proBNP
  - BNP < 100 pg/ml
  - NT-proBNP < 300 pg/ml
  - Consider use of AHF Score
  - BNP 100-400 pg/ml
  - NT-proBNP 300-900 pg/ml (age 50-75)
  - NT-proBNP 300-1800 pg/ml (age >75)
  - Likely to be AHF
  - Treat
  - BNP > 400 pg/ml
  - NT-proBNP > 900 pg/ml (age 50-75)
  - NT-proBNP > 1800 pg/ml (age >75)
  - Likely to be AHF
  - Treat
**ADHF**

**Target O₂ Sats ≥ 92%**

**CONSIDER:**
- Oxygen ↑ FiO₂
- CPAP / BiPAP
- Mechanical intubation

**Volume overload**

**REVIEW:**
- IV furosemide 20–80 mg bolus OR IV furosemide infusion 5–20 mg/hour

**Review SBP / MAP**

**SBP < 90 mm Hg / MAP < 60 mm Hg**

*Consider:*
- Dopamine or other vasopressor
- Dobutamine

**SBP = 90–100 mm Hg / MAP = 60–65 mm Hg**

*Consider:*
If low cardiac output suspected by clinical exam and confirmed with PA catheter, add dobutamine or milrinone

**SBP > 100 mm Hg / MAP > 65 mm Hg**

*Consider:*
If not adequately responsive to IV diuretics, consider adding nitroglycerin IV / SL, nitroprusside IV
Quick Assessment of AHF

![Quick Assessment of AHF Diagram]

- Dry & Warm
- Wet & Warm
- Dry & Cold
- Wet & Cold

**PERFUSION**

**CONGESTION**
Treatment Algorithm for Acute HF

AHF diagnosed, treatment initiated based on symptoms and signs

Volume overload

Mild volume overload
- IV diuretics
- IV furosemide bolus
  - serum creatinine <200 µmol/L 40 mg
  - serum creatinine >200 µmol/L 80 mg

Moderate to severe volume overload
- IV diuretics
- IV furosemide bolus
- increased oxygen requirement
- CPAP and BiPAP requirement
- fatigue
- consider furosemide infusion
- add IV nitroglycerin starting at 5-10 µg/kg/min, titrate to clinical status, BP or PCWP, if available

Volume overload + low cardiac output

Mild to moderate low output
- SBP >90 mmHg
  - milrinone 0.275 µg/kg/min or
dobutamine
- SBP <90 mmHg
  - consider PA line
  - add vasodilator after BP stabilized
  - may also require vasopressors

Very low output
- add vasodilator after BP stabilized
HF Management

- Medications
- Multidisciplinary team
- Device therapy
- Risk factor modification
- Procedures
- Self-care
The Multidisciplinary team (MDT)

- Lifestyle management advice
- Ongoing patient education
- Pharmacological and/or non-pharmacological interventions
- Treatment goals
Self-Care Tips

- Understand patient and caregiver beliefs about HF and its self-care, their expectations and aspirations for daily life

- Patients’ home environments and routines to increase adherence patterns

- Plan ahead using a problem-solving approach that for supporting self-care when usual activities are altered

- Involve caregivers - key source of support
Self-Care Tips

- Personalize Signs and Symptoms- How do you know if you are starting to retain fluid?

- Expect a large variety of vague descriptions from patients/family caregivers.

- Highlight signs or symptoms that reflect HF decompensation.

- Help clarify signs and symptoms that are probably not related to HF.
“Teach back” technique

I want to make sure I explained this in a way you could understand...
Can you tell me...

So when you go home to your (family)... how are you going to explain...

➔ Sometimes the information is not clear to the patient, not 'clicking' with them, ensure they understand what it is you are explaining.
Medications

“Medications don’t work in patients who don’t take them”

- C. Everett Koop
Summary

• Heart Failure is very complex condition requires resources and team approach

• Right diagnosis is good start!

• Early intervention is the way to go

• Self-care is a skill and needs practice and learning over time.

• Teach back techniques help ensure understanding.

• Involvement of family member/caregiver is often necessary.

• Consider formal screening for underlying sleep disorders, depression or subtle cognitive impairment in patient who have ongoing challenges with self-care.
Clinical and biochemical predictors of acute heart failure, expressed with their respective odds ratios, 95% CI, β-coefficient, and the integer score derived from each predictor\textsuperscript{11}

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>β Coefficient</th>
<th>Integer score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated NT-proBNP*</td>
<td>44</td>
<td>21.0-91.0</td>
<td>3.8</td>
<td>4</td>
</tr>
<tr>
<td>Interstitial edema on chest x-ray</td>
<td>11</td>
<td>4.5-26.0</td>
<td>2.4</td>
<td>2</td>
</tr>
<tr>
<td>Orthopnea</td>
<td>9.6</td>
<td>4.0-23.0</td>
<td>2.26</td>
<td>2</td>
</tr>
<tr>
<td>Lack of fever</td>
<td>6.0</td>
<td>2.0-18.0</td>
<td>1.80</td>
<td>2</td>
</tr>
<tr>
<td>Current loop diuretic use</td>
<td>3.4</td>
<td>1.8-6.4</td>
<td>1.23</td>
<td>1</td>
</tr>
<tr>
<td>Age &gt; 75 y</td>
<td>2.7</td>
<td>1.4-5.2</td>
<td>1.0</td>
<td>1</td>
</tr>
<tr>
<td>Rales on lung exam</td>
<td>2.4</td>
<td>1.2-4.7</td>
<td>0.86</td>
<td>1</td>
</tr>
<tr>
<td>Lack of cough</td>
<td>2.3</td>
<td>1.2-4.3</td>
<td>0.81</td>
<td>1</td>
</tr>
</tbody>
</table>

A final possible score of 0 to 14 points is possible. Integeric Score: 0 to 5 low likelihood of heart failure; 6 to 8 intermediate likelihood of heart failure; 9 to 14 high likelihood of heart failure.

*Elevated NT-proBNP was defined as >450 pg/mL if age <50 years and >900 pg/mL if age >50 years.