Management of Heart Failure: State of the Art Update 2018

Alan S Maisel, MD, FACC
Professor of Medicine, University of California, SanDiego
Director, CCU and Heart Failure Program
San Diego VA Healthcare System
Disclosures

- Consulting – Abbott, Critical Diagnostics
- Speaking – Critical Diagnostics
Epidemiology and Pathophysiology of HF
Heart failure (HF) is a major public health problem resulting in substantial morbidity and mortality. There are 23 million people with HF worldwide, with 6–12 million office visits. Despite available effective treatments, a large number of eligible patients are not receiving optimal care.

### Population Group

<table>
<thead>
<tr>
<th>Population Group</th>
<th>Prevalence</th>
<th>Incidence</th>
<th>Mortality</th>
<th>Hospital Discharges</th>
<th>Cost¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Population</td>
<td>5,700,000</td>
<td>870,000</td>
<td>50% at 5 years</td>
<td>1,023,000</td>
<td>$30.7 billion</td>
</tr>
</tbody>
</table>

---

Risk factors for heart failure

- CAD
- Hypertension (LVH)
- Valvular heart disease
- Alcoholism
- Infection (viral)

- Diabetes
- Congenital heart defects
- Other:
  - Obesity
  - Age
  - Smoking
  - High or low hematocrit level
  - Obstructive sleep apnea

CAD = coronary artery disease; LVH = left ventricular hypertrophy.
Hospital discharges for HF


Discharges in Thousands

Years


Male Female

The short of breath pie
Heart Failure

Pneumothorax

Pneumomediastinum

Anxiety

Pulmonary Embolus

Empyema

Pneumonia

Mediastinitis

Panic Attack

Mondor’s Syndrome

Metabolic acidosis

Asthma

FB Aspiration

Chemical Exposure

Anemia

Anaphylaxis

IVDA Pulm Infarction

Cyanide poisoning

MetHgb

Tietze’s disease

DKA

COPD exacerbation

Breast Cancer

Subdiaphrag Abcess

Lung Cancer

Amniotic Fluid Embolus

Heart Failure
Diagnosis of HF

Differential Diagnosis

- Pulmonary infection
- Acute COPD / asthma exacerbation
- Acute coronary syndrome
- Pulmonary emboli
- Pneumothorax, pleural effusions
- Aortic dissection
- Renal failure
Congestion often does not translate in signs/symptoms

- Among pts. with severe heart failure and PCWP 33 mmHg, CI 1.8, LVEF 0.18 CXR: 27%
  - No congestion on x-ray: 41%
  - No rales: 84%
  - No edema: 80%
  - No JVP: 50%
When its very high it is often mistaken for carotid
 Docs tend to think if jvp is not elevated, it cant be heart failure
 Elevations only mean right sided- and might not explain sob
Chest X-Ray in HF

- Cephalization of vessels
- Bronchial cuffing
- Kerley B lines
- Hilar vasculature congestion
- Cardiomegaly
How sure are physicians in the ED about the diagnosis of HF?

Adapted with permission from McCullough PA et al. Circulation. 2002;106:416−422.
Objectives of biomarker testing in HF

Diagnosis

- To establish or refute a diagnosis
- To understand the underlying pathophysiologic processes

Risk Stratification/Screening

- To determine the presence or severity of disease
- To detect adverse consequences

Monitoring/Therapeutic Guidance

- To facilitate selection of an appropriate therapeutic intervention
- To guide or monitor responses to treatment

Many biomarkers may be risk factors themselves; therefore, may be potential targets of therapy

HF, heart failure.  
Breathing Not Properly STUDY

The New England Journal of Medicine

VOLUME 347  JULY 18, 2002  NUMBER 3

RAPID MEASUREMENT OF B-TYPE NATRIURETIC PEPTIDE IN THE EMERGENCY DIAGNOSIS OF HEART FAILURE

Alain S. Maisel, M.D., Pratima Keshrihomiya, M.D., Frederick M. Nowak, M.D., M.B.A., James McCord, M.D., Jandi E. Hollander, M.D., Philippe Duc, M.D., Torbjorn Olnd, M.D., Ph.D., Alan B. Storrow, M.D., William T. Abraham, M.D., Alan H.B. Wu, Ph.D., Paul Clopton, M.S., Philippe G. Steg, M.D., Arne Westheim, M.D., Ph.D., M.P.H., Catherine Wold Kozubik, M.D., Alberto Perez, M.D., Radima Kazanegra, M.D., Howard C. Herrmann, M.D., and Peter A. McCullough, M.D., M.P.H., for the Breathing Not Properly Multinational Study Investigators

Clinical Investigation and Reports

B-Type Natriuretic Peptide and Clinical Judgment in Emergency Diagnosis of Heart Failure

Analysis From Breathing Not Properly (BNP) Multinational Study

Peter A. McCullough, M.D., MPH; Richard M. Nowak, MD, MBA; James McCord, MD; Judd E. Hollander, MD; Howard C. Herrman, MD; Philippe G. Steg, MD; Philippe Duc, M.D; Arne Westheim, MD, Ph.D.; Torbjorn Olmland, M.D, Ph.D; M.P.H; Catherine Wold Kozubik, M.D; Alan B. Storrow, M.D; William T. Abraham, M.D; Sumant Lamba, M.D; Alan H.B. Wu, Ph.D.; Alberto Perez, M.D; Paul Clopton, MS; Padma Krishnaswamy, M.D; Radima Kazanegra, M.D; Alan S. Maisel, M.D; for the BNP Multinational Study Investigators
Accuracy is 90%

Optimal cut-off point determined @ 100 pg/mL

<table>
<thead>
<tr>
<th>BNP 100 pg/mL “Test positive”</th>
<th>Final Diagnosis Heart Failure</th>
<th>673</th>
<th>Final Diagnosis NOT Heart Failure</th>
<th>227</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNP &lt;100 pg/mL “Test negative”</td>
<td>Sensitivity =90%</td>
<td>71</td>
<td>Specificity =73%</td>
<td>615</td>
</tr>
</tbody>
</table>
BNP levels adds to the physician’s ability

Clarification of diagnosis & BNP

Clinical Evaluation

Clinical Evaluation and BNP

BNP reduces clinical indecision by 74%

* $P < 0.0001$
NtproBNP cut-offs

1. $125 < 75 \text{ y.o. and } 450 > 75 \text{ y.o.}$
2. $450, 900, 1800$ based on age
3. $300$ to rule out
Caveats to NP testing

- Dry versus wet BNP
- Gray Zone
- Renal dysfunction
- Obesity
- Heart Failure with normal levels
• There appears to be a linear inverse relationship between BMI and NP levels

• Patients who are obese (BMI >35kg/m²) should have their NP doubled to use the standard cut-points.
The use of NPs for rule-out heart failure in symptomatic patients in primary care

Identifying the right patients for echocardiography

- Presenting at the GP with symptoms suggestive of heart failure
  - < cut-off value: “Rule out”
  - > cut-off value: Referral to specialist

Search for other explanation?
PATIENT WITH SUSPECTED HF
(non-acute onset)

ASSESSMENT OF HF PROBABILITY
1. Clinical history:
   - History of CAD (MI, revascularization)
   - History of arterial hypertension
   - Exposition to cardiotoxic drug/radiation
   - Use of diuretics
   - Orthopnoea / paroxysmal nocturnal dyspnoea
2. Physical examination:
   - Rales
   - Bilateral ankle oedema
   - Heart murmur
   - Jugular venous dilatation
   - Laterally displaced/broadened apical beat
3. ECG:
   - Any abnormality

Assessment of natriuretic peptides not routinely done in clinical practice

≥1 present
All absent

NATRIURETIC PEPTIDES
- NT-proBNP ≥125 pg/mL
- BNP ≥35 pg/mL
No
Yes

ECHOCARDIOGRAPHY
Normal

If HF confirmed (based on all available data):
determine aetiology and start appropriate treatment

HF unlikely: consider other diagnosis
NATRIURETIC PEPTIDES

- NT-proBNP $\geq 125$ pg/mL
- BNP $\geq 35$ pg/mL
Non-HF causes of high NP’s:

- Advanced age
- Renal dysfunction
- Acute coronary syndromes
- Pulmonary disease
  - E.g. ARDS, lung disease with right heart failure
- Pulmonary embolism
- High output states
  - E.g. sepsis, cirrhosis, hyperthyroidism
- Atrial fibrillation
- LV dysfunction
Guideline Recommended Medical Therapy for HF
# Types of Heart Failure

<table>
<thead>
<tr>
<th>Classification</th>
<th>Ejection Fraction</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Heart Failure with Reduced Ejection</td>
<td>≤40%</td>
<td>Also referred to as systolic HF. Randomized clinical trials have mainly enrolled patients with HFrEF, and it is only in these patients that efficacious therapies have been demonstrated to date.</td>
</tr>
<tr>
<td>Fraction (HFrEF)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II. Heart Failure with Preserved Ejection</td>
<td>≥50%</td>
<td>Also referred to as diastolic HF. Several different criteria have been used to further define HFpEF. The diagnosis of HFpEF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. To date, efficacious therapies have not been identified.</td>
</tr>
<tr>
<td>Fraction (HFpEF)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. HFpEF, Borderline</td>
<td>41% to 49%</td>
<td>These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patients with HFpEF.</td>
</tr>
<tr>
<td>b. HFpEF, Improved</td>
<td>&gt;40%</td>
<td>It has been recognized that a subset of patients with HFpEF previously had HFrEF. These patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF. Further research is needed to better characterize these patients.</td>
</tr>
</tbody>
</table>

### Approach to the Classification of Heart Failure

<table>
<thead>
<tr>
<th>Stage</th>
<th>Patient Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>High risk for developing heart failure (HF)</td>
</tr>
<tr>
<td>B</td>
<td>Asymptomatic HF</td>
</tr>
<tr>
<td>C</td>
<td>Symptomatic HF</td>
</tr>
<tr>
<td>D</td>
<td>Refractory end-stage HF</td>
</tr>
</tbody>
</table>

**Stage A (At Risk)**
- High risk for developing heart failure (HF)
  - Hypertension
  - CAD
  - Diabetes mellitus
  - Family history of cardiomyopathy

**Stage B (At Risk)**
- Asymptomatic HF
  - Previous MI
  - LV systolic dysfunction
  - Asymptomatic valvular disease

**Stage C (Heart Failure)**
- Symptomatic HF
  - Known structural heart disease
  - Shortness of breath and fatigue
  - Reduced exercise tolerance

**Stage D (Heart Failure)**
- Refractory end-stage HF
  - Marked symptoms at rest despite maximal medical therapy (eg, those who are recurrently hospitalized or cannot be safely discharged from the hospital without specialized interventions)

---

### Classification of Heart Failure

<table>
<thead>
<tr>
<th>ACCF/AHA Stages of HF</th>
<th>NYHA Functional Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>A At high risk for HF but without structural heart disease or symptoms of HF.</td>
<td>None</td>
</tr>
<tr>
<td>B Structural heart disease but without signs or symptoms of HF.</td>
<td>I No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.</td>
</tr>
<tr>
<td>C Structural heart disease with prior or current symptoms of HF.</td>
<td>I No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.</td>
</tr>
<tr>
<td></td>
<td>II Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.</td>
</tr>
<tr>
<td></td>
<td>III Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF.</td>
</tr>
<tr>
<td>D Refractory HF requiring specialized interventions.</td>
<td>IV Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.</td>
</tr>
</tbody>
</table>
ACC/AHA HF Guidelines: Management of HFrEF (Stage C)

Life-Prolonging Medical Therapy

• ACE inhibitors or ARB (Class I, evidence A) in all patients without contraindications or intolerance.
• Evidence-based beta-blockers (Class I, evidence A) in all patients without contraindications or intolerance. This would include carvedilol (immediate or extended release), metoprolol succinate, or bisoprolol.
• Aldosterone antagonists (Class I, evidence A) in all patients with Class II–IV HF without contraindications or intolerance when close monitoring can be ensured.

ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker.
Pharmacologic Treatment for Stage C HFrEF

HFrEF Stage C
NYHA Class I–IV
Treatment:

Class I, LOE A
ACEI or ARB AND
Beta-blocker

For all volume overload, NYHA Class II–IV patients
Class I, LOE C
Loop Diuretics

For persistently symptomatic African Americans, NYHA Class III–IV
Class I, LOE A
Hydral-Nitrates

For NYHA Class II–IV patients. Provided estimated creatinine >30 mL/min and K+ <5.0 mEq/dL
Class I, LOE A
Aldosterone Antagonist

LOE = level of evidence.
Effect of ACE inhibitors on mortality and hospitalizations in patients with HF

32 Trials of ACEI in Heart Failure: ACEI (n=3870) vs. Placebo (n=3235)

- Total Mortality: OR 0.77 (0.67–0.88), p<0.001, -23%
- Death or Hospitalization: OR 0.65 (0.57–0.74), p<0.001, -35%
- CHF Hospitalization: OR 0.69 (0.58–0.83), p<0.001, -31%

OR = odds ratio.
ACEI/ARB in heart failure

• Indicated for all patients with asymptomatic LV dysfunction and for Class I to IV heart failure (contraindications: hyperkalemia, angioedema, pregnancy)

• Titrate to target doses (example enalapril 10 mg bid, lisinopril 20 qd, ramipril 10 mg qd, benazepril 40 qd, valsartan 160 mg bid, candesartan 32 mg qd)

• Monitor serum potassium and renal function. Advise checking chemistry panel 1–2 weeks after first dose

• Use of ACE inhibitor together with ARB reserved as a consideration only in patients not candidates for aldosterone antagonist

Endogenous vasoactive peptides
(natriuretic peptides, adrenomedullin, bradykinin, substance P, calcitonin gene-related peptide)

Neprilysin inhibition
Neurohormonal activation
Vascular tone
Cardiac fibrosis, hypertrophy
Sodium retention

Sacubitril/Valsartan: neprilysin angiotensin receptor inhibitor

Sacubitril/Valsartan = LCZ696.

Prospective comparison of ARNI with ACEI to determine impact on global mortality and morbidity in Heart Failure trial (PARADIGM-HF)

Specificially designed to replace current use of ACE inhibitors and angiotensin receptor blockers as the cornerstone of the treatment of heart failure.
PARADIGM-HF trial: design

Entry Criteria:
- NYHA Class II-IV HF, LVEF ≤40% → amended to ≤35%
- BNP ≥150 pg/mL (or NT-proBNP ≥ 600 pg/mL) or 1/3 lower if hospitalized for HF within 12 mos
- On a stable dose of ACEI or ARB equivalent to ≥10 mg of enalapril daily for ≥4 weeks
- Unless contraindicated, on stable dose of beta-blocker for ≥4 weeks
- SBP ≥95 mm Hg, eGFR ≥30 mL/min/1.73 m2 and serum K ≤5.4 mmol/L at randomization

Sac/Val = Sacubitril/Valsartan.
PARADIGM-HF: effect of Sac/Val vs. Enalapril on the primary endpoint and its components

<table>
<thead>
<tr>
<th></th>
<th>Sac/Val (n=4187)</th>
<th>Enalapril (n=4212)</th>
<th>Hazard Ratio (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary endpoint</td>
<td>914 (21.8%)</td>
<td>1117 (26.5%)</td>
<td>0.80 (0.73–0.87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>558 (13.3%)</td>
<td>693 (16.5%)</td>
<td>0.80 (0.71–0.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospitalization for heart failure</td>
<td>537 (12.8%)</td>
<td>658 (15.6%)</td>
<td>0.79 (0.71–0.89)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Sac/Val = Sacubitril/Valsartan.
Angiotensin neprilysin inhibition with Sac/Val doubles effect on CV death of current inhibitors of the RAS

Pharmacological treatment for stage C HF with reduced EF

Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>ARNI: B-R</td>
<td>In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.</td>
<td>NEW New clinical trial data necessitated this recommendation.</td>
</tr>
</tbody>
</table>
Pharmacological treatment for stage C HF with reduced EF

Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>III: Harm</td>
<td>B-R</td>
<td>ARNI should not be administered concomitantly with ACE inhibitors or within 36 hours of the last dose of an ACE inhibitor.</td>
<td>NEW Available evidence demonstrates a potential signal of harm for a concomitant use of ACE inhibitors and ARNI.</td>
</tr>
<tr>
<td>III: Harm</td>
<td>C-EO</td>
<td>ARNI should not be administered to patients with a history of angioedema.</td>
<td>NEW New clinical trial data.</td>
</tr>
</tbody>
</table>
Beta-Blockers differ in their long-term effects on mortality in HF

<table>
<thead>
<tr>
<th>Beta-Blocker</th>
<th>Long-Term Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisoprolol(^1)</td>
<td>Beneficial</td>
</tr>
<tr>
<td>Bucindolol(^2)</td>
<td>No effect</td>
</tr>
<tr>
<td>Carvedilol(^3)</td>
<td>Beneficial</td>
</tr>
<tr>
<td>Metoprolol tartrate(^6)</td>
<td>Not well studied</td>
</tr>
<tr>
<td>Metoprolol succinate(^7)</td>
<td>Beneficial</td>
</tr>
<tr>
<td>Nebivolol(^8)</td>
<td>No effect</td>
</tr>
<tr>
<td>Xamoterol(^9)</td>
<td>Harmful</td>
</tr>
</tbody>
</table>

Beta-Blocker therapy in heart failure

- Indicated for all patients with asymptomatic LVD dysfunction and for Class I to IV Heart Failure with LVEF ≤0.40.
- Contraindications: cardiogenic shock, severe reactive airway disease, 2/3rd-degree HB.
- Use of one the 3 evidence-based beta-blockers in HF: e.g., carvedilol, metoprolol succinate, bisoprolol.
- Start at very low HF doses and up-titrate to target doses at two-week intervals or highest dose short of target dose that is well tolerated.
- Monitor HR and BP.
Aldosterone antagonists in HF

RALES
(Severe HFrEF)
30% Risk reduction

EPHESUS
(Post-MI)
15% Risk reduction

EMPHASIS
(Mild HFrEF)
22% Risk reduction

Placebo
Spironolactone
Epleronone

Rate of Hyperkalemia after publication of RALES

Number of prescriptions of spironolactone in pts with HF on ACE-I

Number of admissions for hyperkalemia in pts with HF on ACE-I

Death due to hyperkalemia in pts with HF on ACE-I

Jurleenk DN et al NEJM. 2004;351:543
AHeFT: Trial Summary

1050 African Americans with Class III to IV HF, LVEF 24%, on ACEi, BB, AA

**All-Cause Mortality (%)**
- Placebo + Standard therapies: 6.2%
- Hyd/Nit + Standard therapies: 10.2%
- p=0.012

**First HF Hospitalization (%)**
- Placebo + Standard therapies: 16.4%
- Hyd/Nit + Standard therapies: 24.4%
- p<0.001

**Patient-Reported Functional Status**
- Placebo + Standard therapies: n=518
- Hyd/Nit + Standard therapies: n=532
- p<0.01

AHeFT = African-American Heart Failure Trial; BB = beta-blocker; AA = aldosterone antagonist.

Effect of Digoxin on mortality in heart failure: The Digitalis Investigation Group

DIG (Digitalis Investigation Group): 6,800 patients with LVEF <45% randomized to digoxin (n=3,403) or placebo (n=3,397) in addition to therapy with diuretics and ACEI followed for 37 months.

Ivabradine Mechanism of Action
Funny current? (1970)
The hyperpolarization-activated cyclic nucleotide-gated (HCN) channel responsible for the cardiac pacemaker $I_f$ current regulates heart rate.

HCN, hyperpolarization-activated cyclic nucleotide-gated; $K^+$, potassium; $N^+$, sodium; SA, sinoatrial.

Ivabradine blocks the HCN channel in the sinus node which reduces heart rate

Corlanor® (ivabradine) Prescribing Information, Amgen.
SHIFT Study Design

Randomized, double-blind, parallel-group study to assess the effect of ivabradine in addition to guidelines-based treatment in 6,558 patients with HF, conducted from October 2006 through March 2010.

14-day run-in

- Subjects ≥ 18 years
- In sinus rhythm and had a resting HR ≥ 70 bpm
- NYHA Class II, III, or IV and in stable condition for ≥ 4 weeks
- LVEF ≤ 35%
- Optimal stable Standard of Care (SOC) therapy, including maximally tolerated doses of beta-blockers
- Hospitalization for worsening HF within ≤ 12 months

Randomization

Ivabradine 5 mg twice daily for 2 weeks (n = 3,268)

Ivabradine 7.5/5.0/2.5 mg twice daily according to HR and tolerability

Placebo twice daily (n = 3,290)

Median follow-up duration: 22.9 months (interquartile range = 18 to 28 months)

HF, heart failure; HR, heart rate; LVEF, left ventricular ejection fraction.

Ivabradine Titration

Starting dose

5 mg twice daily

Titration Period: D14 & D28
Follow-up Period: Every 4 months

< 50 bpm or patient experiencing signs or symptoms related to bradycardia
2.5 mg twice daily

50 to 60 bpm
5 mg twice daily

> 60 bpm
7.5 mg twice daily

Treatment was discontinued if heart rate remained below 50 bpm or symptoms of bradycardia persisted after dose reduction.

D, day.
Corlanor® (ivabradine) Prescribing Information, Amgen.
Difference in heart rate reduction between groups was early and sustained throughout study

Beta-blocker dose remained stable in 86% of the ivabradine group and 82% of the placebo group throughout the study.

Data on file, Amgen.
Time to first event of hospitalization for worsening HF or CV death

Hazard Ratio 0.82
95% CI (0.75–0.90)
ARR = 4.2%
\( P < 0.0001 \)

Placebo + SOC
(937 events)

Ivabradine + SOC
(793 events)

18% Relative Risk Reduction

The treatment effect reflected only a reduction in the risk of hospitalization for worsening HF; there was no favorable effect on the mortality component of the primary endpoint.

Primary Composite Endpoint: Time to CV Death or First Hospitalization for Worsening HF.

ARR, absolute risk reduction; CI, confidence interval; SOC, standard of care.

Corlanor® (ivabradine) Prescribing Information, Amgen.
Hospitalization for worsening HF at any time

Hazard Ratio 0.74
95% CI (0.66–0.83)
ARR = 4.7%
NNT = 21

26% Relative Risk Reduction

Placebo + SOC
(672 events)

Ivabradine + SOC
(514 events)

Pharmacological Treatment for Stage C HF with Reduced EF

Ivabradine

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HFrEF (LVEF ≤35%) who are receiving GDEM*, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest.</td>
<td>NEW New clinical trial data.</td>
</tr>
</tbody>
</table>
## Therapies approved for HF treatment over the past 4 decades

<table>
<thead>
<tr>
<th>HFrEF</th>
<th>HFpEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEIs and ARBs</td>
<td>None</td>
</tr>
<tr>
<td>Aldo receptor antagonists</td>
<td></td>
</tr>
<tr>
<td>Beta blockers</td>
<td></td>
</tr>
<tr>
<td>Hyd/ISDN</td>
<td></td>
</tr>
<tr>
<td>Ivabradine</td>
<td></td>
</tr>
<tr>
<td>ICDs</td>
<td></td>
</tr>
<tr>
<td>BiVs</td>
<td></td>
</tr>
<tr>
<td>LVADs</td>
<td></td>
</tr>
</tbody>
</table>
## Pharmacological Treatment for Stage C HF With Preserved EF

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B</td>
<td>Systolic and diastolic blood pressure should be controlled in patients with HFP EF in accordance with published clinical practice guidelines to prevent morbidity</td>
<td>2013 recommendation remains current.</td>
</tr>
<tr>
<td>I</td>
<td>C</td>
<td>Diuretics should be used for relief of symptoms due to volume overload in patients with HFP EF.</td>
<td>2013 recommendation remains current.</td>
</tr>
</tbody>
</table>
Pharmacological Treatment for Stage C HF With Preserved EF

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>C</td>
<td>Coronary revascularization is reasonable in patients with CAD in whom symptoms (angina) or demonstrable myocardial ischemia is judged to be having an adverse effect on symptomatic HFpEF despite GDMT.</td>
<td>2013 recommendation remains current.</td>
</tr>
<tr>
<td>IIa</td>
<td>C</td>
<td>Management of AF according to published clinical practice guidelines in patients with HFpEF is reasonable to improve symptomatic HF.</td>
<td>2013 recommendation remains current.</td>
</tr>
<tr>
<td>IIa</td>
<td>C</td>
<td>The use of beta-blocking agents, ACE inhibitors, and ARBs in patients with hypertension is reasonable to control blood pressure in patients with HFpEF.</td>
<td>2013 recommendation remains current.</td>
</tr>
</tbody>
</table>
Spironolactone in HFpEF: TOPCAT

Outcome: CV Death, HF Hosp, or Resuscitated Cardiac Arrest

Class I recommendations for devices in patients with LV systolic dysfunction

<table>
<thead>
<tr>
<th>ICD</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior resuscitated cardiac arrest</td>
<td>Class I Level A</td>
</tr>
<tr>
<td>Ischaemic aetiology and &gt;40 days of MI</td>
<td>Class I Level A</td>
</tr>
<tr>
<td>Non-ischaemic aetiology</td>
<td>Class I Level B</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CRT</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA Class III/IV and QRS &gt;120 ms</td>
<td>Class I Level A</td>
</tr>
<tr>
<td>To improve symptoms/reduce hospitalization</td>
<td>Class I Level A</td>
</tr>
<tr>
<td>To reduce mortality</td>
<td>Class I Level A</td>
</tr>
</tbody>
</table>
Implantable Wireless Heart Sensor

No batteries or internal power source, sensor is powered by RF-energy provided by an external electronics module.

Coil and a pressure sensitive capacitor encased in a hermetically sealed silica capsule covered by silicone. The device has no leads or batteries. Two nitinol loops at the ends of the capsule serve as anchors in the pulmonary artery. The coil and capacitor form an electrical circuit that resonates at a specific frequency, and pressure applied to the sensor causes deflections of the pressure-sensitive surface. An external antenna provides power to the device, continuously measuring its resonant frequency, which is then converted to a pressure waveform. The interrogating device has an atmospheric barometer which automatically subtracts the ambient pressure from that measured from the implanted sensor.
Wireless pulmonary artery hemodynamic monitoring in chronic heart failure: CHAMPION

Wireless pulmonary artery hemodynamic monitoring in chronic heart failure: CHAMPION

HeartMate II LVAS

- A surgically implanted, rotary continuous-flow device in parallel with the native left ventricle
  - Left ventricle to ascending aorta
- Percutaneous driveline
- Electrically powered
  - Batteries & line power
- Fixed speed operating mode
- Home discharge
Destination VAD therapy trials

Figure 1. Survival Rates in Two Trials of Left Ventricular Assist Devices (LVADs) as Destination Therapy.

The curves labeled 2009 are those reported by Slaughter and colleagues in this issue of the Journal; those labeled 2001 were reported for the REMATCH trial.↑
Mechanical Circulatory Support (MCS)

Indications

• Failure to wean off CPB (post-cardiotomy syndrome)
• ESHD pt with inadequate organ perfusion despite optimal medical management (BT Tx)
• Acute myocarditis/post-partum CMY (BT Recovery)
• Acute, massive MI with shock
• Destination therapy (DT) for non-transplant candidates with end stage HD
• Incessant VT/cardiac arrest

CPB, cardiopulmonary bypass; ESHD, end-stage heart disease; BTT, bridge to transplant; CMY, cardiomyopathy; BTR, bridge to recovery; VT, ventricular tachycardia.
Final Takeaways

• The treatment of HF continues to evolve with new therapies and emerging new devices
• New treatment algorithms address the increasing complexity of HF therapy
• Application of GDMT for HFrEF markedly improves outcomes in clinical practice
• A specific intervention is now indicated for HFpEF, but mortality reducing therapies urgently needed
• Co-Morbidities matter; overzealous treatment may lead to harm
• PREVENTION of HF is essential
Improved Adherence to HF Guidelines Translates to Improved Clinical Outcomes in Real World Patients

- Each 10% improvement in guideline recommended composite care was associated with a 13% lower odds of 24-month mortality (adjusted OR 0.87; 95% CI, 0.84 to 0.90; \( P<0.0001 \))

ACC/AHA/HFSA Guideline Directed Therapy for Heart Failure Improves Outcomes

Fonarow GC et al J Am Heart Assoc 2012;1:16-26
Advances in the Treatment of HF

- Increased attention to prevention
- ACEI / β-blocker / aldosterone antagonist combination established as the “cornerstone” of therapy
- ARNI further reduce morbidity and mortality
- Evidence that β-blockers’ effects are not homogeneous
- Downgrade in recommendation for use of digoxin
- Integration of CRT and ICD device therapy into the standard therapeutic regimen
- Recognition that “special populations” of HF patients may benefit from or require different approaches
- New strategies to improve utilization of evidence based therapies