DIASTOLIC HEART FAILURE
A Practical Clinical Approach

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Clinical Approach to Heart Failure
- ACE Inhibitors/ARBs
- β-Blockers
- Spironolactone
- Defibrillator
- CRT with Wide QRS
- Ivabradine

Increase in Heart Failure Patients with Preserved Ejection Fractions

Increase in Admissions of Heart Failure Patients with Preserved Ejection Fractions

Survival in Patients with Heart Failure

Changes in in Heart Failure Patient’s Survival
**Associations of Survival in Heart Failure With Gender**

- Normal EF-Female
- Normal EF-Male
- Low EF-Female
- Low EF-Male

**Clinical Characteristics in Patients with Heart Failure with Normal EF**

<table>
<thead>
<tr>
<th></th>
<th>PRESERVED</th>
<th>OPTIMIZED</th>
<th>ADJURED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>68</td>
<td>63</td>
<td>68</td>
</tr>
<tr>
<td>Gender</td>
<td>M</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>Ischemia (%)</td>
<td>38</td>
<td>20</td>
<td>38</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>66</td>
<td>16</td>
<td>66</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>21</td>
<td>13%</td>
<td>21%</td>
</tr>
<tr>
<td>COPD (%)</td>
<td>11%</td>
<td>11%</td>
<td>11%</td>
</tr>
<tr>
<td>Low EF-Male (%)</td>
<td>22%</td>
<td>23%</td>
<td>22%</td>
</tr>
<tr>
<td>Low EF-Female (%)</td>
<td>24%</td>
<td>25%</td>
<td>24%</td>
</tr>
<tr>
<td>Obesity</td>
<td>Physiological measures: BMI</td>
<td>BMI</td>
<td>BMI</td>
</tr>
</tbody>
</table>

**Features Associated with Heart Failure with Normal EF**

- **Hypertension**: 76-88%
- **Diabetes**: 27-45%
- **Obesity**: 28-50%

**Heart Failure with Normal EF**

More Common in Elderly


**WHAT IS DIASTOLIC HEART FAILURE?**

- Pulmonary Edema
- Normal Ejection Fraction

**Terminology**

- Diastolic Heart Failure
- Heart Failure with Preserved Ejection Fraction
- Heart Failure with Normal Ejection Fraction
Focus on Relaxation

Focus on Stiffness

Heart Failure With Normal Left Ventricular Ejection Fraction

Misha T. Madsen, MB; David M. Kapp, MD, PhD
Moorhouse, Australia

It is estimated that approximately 30% of the heart failure population has a normal left ventricular ejection fraction, a condition broadly referred to as heart failure with normal left ventricular ejection fraction (HFN). While these patients have been considered at cardiac risk, clinical trials have shown a marked improvement in outcomes, including a reduction in hospitalization rates and mortality, with the use of beta-blockers and angiotensin-converting enzyme inhibitors.

End-Diastolic Pressure Volume Relations

Compliant

Noncompliant (Stiff)

American Society of Echo Currently Advocates 2D Biplane Simpson's Rule for EF

Apical 4-Chamber View

Apical 2-Chamber View

Lano R et al. JASE 2007

Volume = Σ (¼ π D^2) h

EF = EDV-ESV/EDV

Lano R et al. JASE 2007

Quantiative Standard

Modified Simpson’s Rule

Improvements in EF by Echo

- Harmonic Imaging
- Digital Acquisition
- Echo Contrast Enhancement
- Continued Improvements in computer technology

Definity Contrast Bolus
**LOOK FOR EF! Hand-carried ultrasound**

**LOOK FOR EF!**
Pocketsize Ultrasound

**LOOK FOR EF!**
89 y.o woman with apical MI

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**HFNEF: A Diagnosis of Exclusion**

Shortness of Breath and LVEF > 50%

Cardiac Causes
- Coronary Disease
- Valvular Disease
- Hypertrophic Cardiomyopathy
- Restrictive Cardiomyopathy
- Intracardiac Shunt

Non-Cardiac Causes
- Pulmonary Disease
- Thyrotoxicosis
- Anemia
- Primary Pulmonary Hypertension
- Obesity
- Deconditioning
- Extracardiac Shunt

**Heart Failure with Normal EF**
Consensus Article: European Heart Journal 2007;28: 2539

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**CASE STUDY**

- 76 year old man, hypertensive smoker. Mostly sedentary, denies any exertional symptoms.
- Presents with “flash pulmonary edema” BP 185/90 mmHg.
- Rapidly resolves with 40 mg i.v. lasix.

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**79 y.o man with flash pulmonary edema**

Baseline

Peak Stress

Cardiac Cath: Severe 3 vessel CAD
CASE STUDY

- 67 year old woman, hx hypertension: β-blockers + HCTZ
- Presents with severe pulmonary edema
  BP 210/90 mmHg.
- Cardiac cath 6 mo. ago for atypical chest pain: “clean coronaries”

ECHO CASE # 2

Ejection Fraction = 63%

LEFT VENTRICULAR HYPERTROPHY

- In the Framingham Heart study, 45% of cardiovascular deaths were preceded by LVH.
- LVH is present in nearly 50% of all hypertensive patients.
- Next to age, LVH is the strongest predictor of cardiovascular disease.

ACUTE PULMONARY EDEMA ASSOCIATED WITH HYPERTENSION

- n = 38 with Acute Pulmonary Edema + Systolic BP > 160 mmHg
- Presenting Echo: BP 200 ± 26 mmHg
- Follow-up Echo: BP 139 ± 17 mmHg

Ghandi...Little et al, N Eng J Med 2001;334: 17-22

EJECTION FRACTION AND WALL MOTION WAS THE SAME ACUTELY AND AFTERWARD

END-SYSTOLIC PRESSURE-VOLUME RELATIONS

Ghandi...Little et al, N Eng J Med 2001;334: 17-22

Suga and Sugawa et al.
**END-SYSTOLIC PRESSURE-VOLUME RELATIONS**

Suga and Sugawa et al.

**VENTRICULAR-ARTERIAL COUPLING**

$E_a$

Suga and Sugawa et al.

**HEART FAILURE WITH NORMAL EJECTION FRACTION**

Increased Ees-Increased Arterial Stiffness

Kawaguchi...Kass et al. Circulation 2003;107:714-720

**JNC VII Blood Pressure Classification**

**Normal**

1. $< 130 < 85$
2. $< 120 < 80$
3. 130-139 85-89
4. 120-139 80-89
5. 140-159 90-99
6. 140-159 90-99

**Stage 1**

*“Prehypertension signals the need for increased education to reduce BP in order to prevent hypertension.”*

**LIFE: Blood Pressure Results**

Atenolol 145.4 mmHg

Losartan 144.1 mmHg

**LIFE: ECG-LVH Regression from Baseline**

Cornell Product

Sokolow-Lyon


n = 9,193

LVH and Hypertension
**LIFE: Primary Composite Endpoint**

Proportion of patients, with first event (%)

- **Intention-to-Treat**
  - n = 9,193

<table>
<thead>
<tr>
<th>Study Month</th>
<th>Losartan (n)</th>
<th>Atenolol (n)</th>
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<tbody>
<tr>
<td>6</td>
<td>4605</td>
<td>4624</td>
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<tr>
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<tr>
<td>66</td>
<td>3272</td>
<td>3271</td>
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</tbody>
</table>

Losartan: ○

Atenolol: ×

15% Reduction in Events

*p=0.009*

**MITRAL INFLOW VELOCITY TO ASSESS DIASTOLIC FUNCTION**

**FACTORS AFFECTING MITRAL INFLOW VELOCITY**

- LA Pressure
- LV relaxation (suction)
- Mitral Valve area
- LV compliance
- LV Volume

**DIASTOLE: ACTIVE RELAXATION**

Contraction

- LA volume
- LA contractility
- LA afterload
- LA compliance

Active Relaxation

- ATP Consumption

Early Diastole “E”

1. Healthy Heart has
   - LV Suction
   - High E Velocity
2. Myocardial Diseases
   - Low E Velocity
   - Ischemia
   - Infiltrative Amyloidosis
   - Hypertrophic Cardiomyopathy

**MITRAL ANNULAR VELOCITY**

**FAMILIAL HYPERTROPHIC CARDIOMYOPATHY**

LVH

No LVH

Sarcomere Mutation?

**Nagueh et al. Circulation 2001;104:128-130**

**MITRAL ANNULAR VELOCITY**

**FAMILIAL HYPERTROPHIC CARDIOMYOPATHY**

- Septal Velocity
  - Sa < 9 cm/sec
  - Ea < 10 cm/sec

**NORMAL**

- + Mutation
- No LVH
- LVH

**NORMAL**

- + Mutation
- No LVH
- LVH

n=30  n=13  n=30  n=30  n=13  n=30
Myocardial Diastolic Dysfunction

ASSESSMENT OF LV FILLING PRESSURE

Routine Doppler Mitral Inflow
Tissue Doppler Mitral Annulus

FUNDAMENTAL PROPERTY OF MYOCARDIAL FUNCTION

LV Filling and Active Relaxation are Coupled

PULSED-TISSUE DOPPLER ECHOCARDIOGRAPHY

Effects of an IVC Occlusion on Mitral Annular Velocities

Baseline JVCO IVC O IVC O
MITRAL ANNULAR VELOCITY IS DEPENDENT ON PRELOAD

- Normal Ventricular Function
- Acute Decreases in LV Filling
- Low range of filling pressures

How To Diagnose HFNEF

Symptoms &/or Signs of Heart Failure
EF > 50% & Normal LV Volume
Evidence of Diastolic Dysfunction
Echo-Doppler
Biomarkers
Invasive Hemodynamics

E/E' > 15
E' < 8 cm/s

E/E' 8-15
E' < 8 cm/s

HFNEF

DECREASED LV ROTATION IN HEART FAILURE: NORMAL EF

The Pathophysiology of Heart Failure With Normal Ejection Fraction
Exercise Echocardiography Reveals Complex Abnormalities of Both Systolic and Diastolic Ventricular Function Involving Tension, Uartricity, and Longitudinal Motion
Ye Ting Tan, MBBS, Grace Wee, MBBS, MD, * Endal Loo, MBBS, MD, * Grant Hirstle, MBChB, PhD, Francisco Lopez, MD, * Jason Parch, MBBS, PhD, * Michael Freeman, MBChB, John E. Sarns, MBChB
Birmingham and Solihull Trust, United Kingdom

Conclusions
In HFNEF there are widespread abnormalities of both systolic and diastolic function that become more apparent on exercise. HFNEF is not an isolated disorder of diastole; J Am Coll Cardiol 2009;54:36–46

Summary Comparisons

Maeder et al. JACC 2008
HFNEF has Blunted Increases in LV Function with Exercise

\( n = 27 \) Normal Controls, \( n = 56 \) HFNEF,

![Graph showing Longitudinal Strain and Radial Strain](Tan...Sanderson et al. J Am Coll Cardiol 2009;54:36–46)

Proposed Pathophysiology HFNEF

- **Arterial Stiffness**
- **Diabetes & LVH**
- **Myocardial Infections**

- **LV Rotation Delayed unloading**
- **Strain**
- **Echocardiographic evidence for LV dysfunction**

![Diagram showing proposed pathophysiology](Tan...Sanderson et al. JACC 2009;54:36–46)

Is There Any Specific Agent to Treat HFNEF?

**Drugs Being Studied**

- **Angiotensin-receptor blockers**
- **Aliskiren (angiotensin II receptor antagonist)**
- **Aldosterone antagonist**
- **Spironolactone**
- **Eplerenone**
- **Hydrochlorothiazide**
- **Diltiazem**
- **Beta-blockers**

Maeder et al. JACC 2009

Effects of Intensive Blood Pressure Lowering

- **Hypertension**

- **American Heart Association**

- **Learn and Live**

- **Effects of Intensive Verapamil-XL Controlled Blood Pressure Lowering on Cardiovascular Events in Patients with Hypertension and Coronary Artery Disease**


![Image showing effects of intensive blood pressure lowering](Solomon, S. D. et al. Hypertension 2010;55:241-248)

Effects of Intensive Blood Pressure Lowering

- **Assessment of Eligibility**

- **Excluded (n = 375)**

- **Diasstolic Function (n = 440)**

- **Uncontrolled Analysis (n = 98)**

- **Discontinued Prior to Final Assessment (n = 16)**

- **Discontinued Prior to Final Assessment (n = 16)**

- **Diasstolic Function Assessment (n = 16)**

- **Diasstolic Function Response**

Hypertension


Diasstolic Function Assessed by Mitral Annulus

- **Frequency Shift (kHz)**

Effects of Intensive BP Control on Mitral Annular Diastolic Relaxation Velocity

Systolic BP Achieved


Prognosis of Heart Failure With Normal EF

JAMA®

Systolic Blood Pressure at Admission, Clinical Characteristics, and Outcomes in Patients Hospitalized With Acute Heart Failure

Minas Gheorghiade; William T. Abraham; Nancy M. Albert; et al. JAMA 2006;296(18):2217

- OPTIMIZE-HF Study
- 259 Sites in the US
- 48,612 patients Presenting with Heart Failure

In-Hospital Mortality: Heart Failure by Admission Systolic Blood Pressure

Normal EF vs. Low EF n = 41,276

Systolic BP mmHg

< 120 120-130 140-161 > 161

In Hospital Mortality %

p<0.001

Gheorghiade et al. JAMA 2006;296(18):2217

Post-Discharge Mortality: Heart Failure by Admission Systolic Blood Pressure

Normal EF vs. Low EF n = 41,276

Systolic BP mmHg

< 120 120-130 140-161 > 161

Post Discharge Mortality % (60-90 days)

p<0.001

Gheorghiade et al. JAMA 2006;296(18):2217

FEATURES ASSOCIATED WITH HEART FAILURE WITH NORMAL EF

Hypertension 76-88%

Important Risk Factors for MI and Stroke

Diabetes 27-45%

Obesity 28-50%

Gheorghiade et al. JAMA 2006;296(18):2217
1. Heart Failure with Normal EF has Increasing Prevalence and Similar Survival as Heart Failure with Depressed EF.
2. Important to Exclude Significant CAD & Others
3. Assess for LVH. Arterial Stiffness Plays a Role.
4. Agents Associated with LVH Regression
   1. ACE Inhibitors
   2. Angiotensin Receptor Blockers
5. Pathophysiology Appears to be Complex
   New Echo Tools – Strain and Twist Help Define
6. Tight Control of Hypertension is Important.