Heart Failure 1: Pathophysiology, Etiology, and Disease Progression

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Cardiovascular Nursing Education Association

Heart Failure Guidelines

- McMurray et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. *Eur Heart J*. 2012;33:1787-847.
### Heart Failure Facts

- **5.1 million people in US have heart failure**
  - 650,000 new cases diagnosed each year
  - By 2030, >8 million people in the United States (1 in every 33) will have HF.

- **Mortality rate is 50% within 5 years of diagnosis**
  - SCD is 6-9 times higher in HF patients than in general population

- **Primary diagnosis in >1 million hospitalizations every year**

- **Total cost of HF care in the US in 2012 exceeded $40 billion**

- **Why?**
  - Aging population, improved survival after acute MI, and use of ICDs has contributed to increased number of HF patients
Heart
Arteries
Veins
Volume
Kidneys

Determinants of Cardiac Output

\[ CO = HR \times SV \]

Preload  Afterload  Contractility
Venous tone  Body Position  Intrathoracic pressure  Intrapericardial pressure
Blood Volume  Distribution of blood volume  Atrial Kick  LV Function

**PRELOAD**

Reducing preload in HF:
- **Diuretics**
- **Venous Dilators**: nitrates, ACEI, ARBs, aldosterone blockers, nesiritide

Sympathetic NS  Arteriolar Tone  Circulating vasodilator or vasoconstrictor mediators

**AFTERLOAD**

Reducing afterload in HF:
- **Arterial dilators**: nitroprusside, hydralazine, ACEI, ARBs

Aortic Pressure and Compliance  Aortic Stenosis HOCM
Increasing contractility in HF:
- **Positive inotropes**: dobutamine, milrinone, dopamine, digoxin
Heart Failure

- A complex clinical syndrome characterized by abnormal ventricular filling or ejection resulting in a low cardiac output state.
- As the syndrome progresses, a variety of compensatory mechanisms including hemodynamic, renal, neurohormonal and cellular process occur.
- These compensatory mechanisms contribute to the progression of the disease.

Heart Failure

- A complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood.
- Manifestations are:
  - Dyspnea and fatigue which limit exercise tolerance
  - Fluid retention leading to pulmonary and peripheral edema
Not “congestive” HF

▪ 80% of patients in end-stage LV failure do not have pulmonary congestion
▪ Patients admitted in pulmonary edema can be treated for volume overload and their symptoms of congestion can disappear, but the abnormalities in cardiac structure, hemodynamics, and neurohormonal activation persist despite the resolution of “congestive” symptoms.
▪ Heart failure progresses even in the absence of congestive symptoms

CHF = Chronic Heart Failure

Backward Failure

▪ Ventricular pressures rise
  • High LV pressure is transmitted backwards into lungs (LV backward failure)
  • High RV pressure is transmitted backwards into venous system (RV backward failure)
Forward Failure

- Ventricles fail to pump well in a forward direction
  - LV forwards failure results in peripheral hypoperfusion
  - RV forwards failure results in failure to adequately fill the LV

Systolic Dysfunction
HFrEF

- HFrEF is defined as the clinical diagnosis of HF and EF ≤40%
- Impaired LV contractility results in reduced ejection fraction (< 40%), increasing end-diastolic volume and pressure
- Ventricle is dilated, thin-walled, eccentrically hypertrophied

Only in these patients have effective therapies been demonstrated to date
• Eccentric Hypertrophy
  • Increase in chamber size without increase in muscle thickness (although muscle mass increases)
  • Due to volume overload
    • MI (↓CO results in fluid retention by kidneys)
    • Aortic or mitral regurgitation
    • Congenital defects
  • Results in systolic failure

• Patients with systolic dysfunction often have diastolic dysfunction too

Causes of Systolic Dysfunction

• CAD (2/3 of patients)
• MI
• Hypertension
• Tachyarrhythmias
• Valvular (aortic or mitral regurgitation)
• Myocarditis

• Toxins (ETOH, cocaine, chemo agents)
• Endocrine (hyperthyroidism, diabetes)
• Congenital
• Pregnancy
• Idiopathic
Diastolic Dysfunction
HFpEF

- HF with EF \( \geq 50\% \)
- Preserved or normal systolic function with impaired ability of the ventricle to relax and fill with blood (40-70% of HF patients)
- Results in increased filling pressures due to stiff, noncompliant ventricles
- Ventricle is thickened and concentrically hypertrophied

No effective therapies have been identified to date

Concentric Hypertrophy

- Increased ventricular wall thickness without dilation of chamber
- Due to pressure overload
  - Chronic HTN
  - Aortic stenosis
- Results in diastolic dysfunction

Usually older women with Hx of HTN
Causes of Diastolic Dysfunction

- Hypertension – most important cause
  - Present in 60 – 90% of patients with HFrEF
- CAD, obesity, diabetes, and AF are highly prevalent in patients with HFrEF
- Hypertrophic cardiomyopathy
- Infiltrative diseases
  - Sarcoidosis
  - Amyloidosis
- Aortic stenosis
Major Risk Factors for Developing HF

- **Hypertension** (2-3 fold increased risk)
  - Most important modifiable risk factor
  - Long-term treatment of both systolic and diastolic hypertension reduces the risk of HF by about 50%
- **Atherosclerotic disease** (coronary, cerebral, or peripheral)
  - MI (8-10 fold increased risk)
- **Diabetes** (2-5 fold increased risk, especially in women)
  - Markedly increases the likelihood of developing HF in patients without structural heart disease
  - Adversely affects the outcomes of patients with established HF
- **Metabolic syndrome**

Metabolic Syndrome (Insulin Resistance Syndrome)

- “The Deadly Quartet” (presence of any 3 of the following):
  - **Abdominal obesity**
    - Waist circumference in men > 40 inches and in women > 35 inches
  - **Hyperglycemia**
    - Fasting glucose ≥ 100 mg/dl
  - **Dyslipidemia**
    - Triglycerides ≥ 150 mg/dl
    - HDL < 40 mg/dl in men and < 50 mg/dl in women
  - **Hypertension**: BP > 130/85 mmHg
- >40% incidence in people over 40 in the US!

Appropriate treatment of hypertension, diabetes and dyslipidemia can significantly reduce the development of HF.
Other Contributors to HF

- Obesity - every 1 Kg/M$^2$ increase in BMI is associated with 5% increased risk of HF in men and 7% in women.
- Recent pregnancy – peripartum cardiomyopathy
- Tachycardia induced cardiomyopathy
- Takotsubo cardiomyopathy (stress induced)
- Family History – familial cardiomyopathy
- Drugs & Toxins – alcohol, cocaine, IV drugs, chemo, tobacco, NSAIDs, cobalt, anabolic steroids, many others
- Connective tissue & systemic disorders – lupus, scleroderma, sarcoidosis, amyloidosis
- Myocarditis – viral, bacterial, fungal, parasitic

NYHA Functional Classification in Patients With HF

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
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<tbody>
<tr>
<td>I</td>
<td>No limitation of physical activity. Ordinary physical activity does not cause symptoms*.</td>
</tr>
<tr>
<td>II</td>
<td>Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms.</td>
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</tbody>
</table>
| III    | IIIA: Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms.  
        | IIB: Marked limitation of physical activity. Comfortable at rest, but minimal exertion causes symptoms. Dyspnea with less than one block walking. |
| IV     | Unable to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency present at rest. If any physical activity is undertaken, discomfort is increased. |

* Symptoms = fatigue, palpitations, or dyspnea
### ACC/AHA Stages of Heart Failure

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>NYHA Class</th>
<th>Stage of HF</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>Patients at high risk for developing HF but have no structural disorder of the heart (HTN, atherosclerotic disease, diabetes, metabolic syndrome, obesity, family history of cardiomyopathy)</td>
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<tr>
<td>B</td>
<td>Patients with structural disorder of the heart but no symptoms of HF (History of MI, valve disease, LVH, low EF)</td>
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<tr>
<td>C</td>
<td>Patients with past or current symptoms of HF associated with structural heart disease (Known structural heart disease and signs and symptoms of HF)</td>
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<td>D</td>
<td>Patients with end-stage HF who require specialized treatment such as mechanical circulatory support, continuous inotropic infusions, cardiac transplant, hospice (Marked symptoms at rest despite maximal therapy, repeated hospitalizations for HF despite appropriate therapy)</td>
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### What NYHA class and Stage of HF?

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<tr>
<td>Patient with Hx of HTN who is post MI 2 years ago, EF 30%. Hx of SOB &amp; fatigue when golfing 18 holes so can now play only 9 holes. Meds: diuretic, ACEI, beta blocker. Asymptomatic around the house and with usual activities but notices that he is tired and slightly SOB near the end of 9 holes of golf.</td>
<td>II</td>
<td>C</td>
</tr>
<tr>
<td>Patient who has HTN, diabetes, overweight. No history of MI, EF 55%. Meds: diuretic, Ca++ blocker, ACEI, oral hypoglycemic. Asymptomatic with all activities but is relatively sedentary.</td>
<td>I</td>
<td>A</td>
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<tr>
<td>Patient with Hx of MI, moderate renal failure, and diagnosed with HF for 3 years. Has been managed with diuretics, ACEI, beta blocker, aldosterone blocker, and has a biventricular pacemaker. EF 20% with this Rx. Has been progressively more SOB with even minimal activity and now is symptomatic at rest. Has been hospitalized with ADHF twice in the past 6 months.</td>
<td>IV</td>
<td>D</td>
</tr>
<tr>
<td>Patient with aortic valve disease, LVH, and diagnosed HF. EF 26%. Comfortable while watching TV or reading, gets SOB and fatigued when walking to bathroom and fixing dinner.</td>
<td>III</td>
<td>C</td>
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Pathophysiology of Heart Failure

**Physiologic Change**
- ↓ ability of LV to pump blood
- ↑ LVEDV & LVEDP
- ↑ Left atrial pressure

**Signs & Symptoms**
- Fatigue, chest pain (if coronary arteries underperfused)
- S3 and/or S4 gallop
- ↑ PWP
- Atrial arrhythmias (atrial fib)
Pathophysiology of Heart Failure

**Physiologic Change**
- ↑ pressure in pulmonary capillaries & pulmonary artery
- Leaking of fluid from pulmonary capillaries into lungs

**Signs & Symptoms**
- ↑ PA pressure & PAD
- Crackles, SOB, cough, orthopnea, wheezing, hypoxia

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**Pathophysiology of Heart Failure**

**Physiologic Change**
- ↑ right ventricular pressure
- ↑ right atrial pressure
- Backup of blood into systemic veins

**Signs & Symptoms**
- Sternal heave, RV $S_3$
- ↑ CVP, ↑ neck veins
- Peripheral edema, + abdominojugular test
Compensatory Mechanisms in HF: Neurohormonal Activation

- ↓ Contractility (MI, ischemia, cardiomyopathy)
- ↓ Stroke Volume

↑ SNS Activation
- ↑ heart rate
- ↑ contractility
- ↑ SVR (vasoconstriction)

↑ Renin-Angiotensin – Aldosterone System
- ↑ Blood Volume (Na⁺ & H₂O reabsorption)
- ↑ SVR (vasoconstriction)

↑ CO

Ventricular Remodeling

Pathologic myocardial hypertrophy or dilation in response to increased myocardial stress

- ↓ Contractility
- ↓ Stroke Volume

Activation of SNS & RAAS
- ↑ Ventricular Volume
- ↑ Ventricular Pressure
- ↑ Ventricular Wall Tension
Ventricular Remodeling

- Increased Wall Tension
  - Thin ventricular wall & chamber dilation
  - Decreased contractility
  - Increased MVO_2
  - Fibrous tissue deposits

Heart Failure

- Initiated by damage to heart
  - MI or other injury
  - Increased pressure or volume load
- Eccentric hypertrophy develops
  - Increase in chamber size and muscle mass (not muscle thickness)
- Fibrous tissue deposition in ventricle and changes in collagen characteristics
  - Contribute to reduced systolic function and increased stiffness of ventricle
- Continues after resolution of initiating event and progresses over time
Sympathetic Nervous System

**Alpha Receptors**
(Arteries & Veins)

- Vasoconstriction

**Beta Receptors**

- **Beta**
  - Beta$_1$
    - (Heart)
    - ↑ heart rate
    - ↑ contractility
    - ↑ automaticity
    - ↑ conduction velocity
    - ↑ Renin release
  - Beta$_2$
    - (Arteries, veins, Lungs)
    - Vasodilation
    - Bronchodilation

Role of Kidney in HF

- Efferent arteriole
- Juxtaglomerular cells
- Afferent arteriole
Renin-Angiotensin-Aldosterone System

↓ Renal blood flow (↓ BP, ↓ Na⁺, diuresis) 

↓ Renin release 

Angiotensinogen → Angiotensin I (converting enzyme) → Angiotensin II

Vasoconstriction → Aldosterone release

↑ Na⁺ & H₂O retention

↑ BP & Organ perfusion

When there is decreased LV function and cardiac output:

- Kidneys think body is hypovolemic → Na⁺ & H₂O retention
- Baroreceptors think body is hypotensive → peripheral vasoconstriction, release of vasopressin (causes H₂O retention and hyponatremia)
- Endothelin – vasoconstrictor substance made in myocardium and vascular endothelium in response to neurohormones → negative inotrope, peripheral VC, contributes to remodeling
Compensatory Mechanisms in Heart Failure

• ↑ sympathetic NS activity
  – Results in tachycardia, ↑ contractility, ↑ SVR
• ↑ Renin-angiotensin-aldosterone activity
  – Results in Na⁺ and H₂O retention, ↑ SVR
• ↑ release of natriuretic peptides (ANP, BNP)
  – Attempt to counteract vasoconstriction with vasodilation, diuresis, and natriuresis

Natriuretic Peptides

▪ ANP synthesized in atria
  • Released in response to atrial stretch
  • Acute response to increased volume

▪ BNP synthesized in ventricles
  • Released in response to prolonged volume overload
  • Elevated in heart failure (also higher in women and people > 60 without HF)
  • Sensitive marker for severity of HF (↑ in proportion to NYHA class)
  • Help different HF from other causes of SOB
  • Causes arterial and venous dilation (preload and afterload reduction)
Natriuretic Peptides

- Cause smooth muscle relaxation
  - Arterial dilation = afterload reduction
  - Venous dilation = preload reduction
  - ↓MAP, ↓PAP, ↓PWP, ↓RAP
- Suppress renin and aldosterone release
- Act on kidney to cause diuresis and natriuresis
- Function to help maintain compensated state in heart failure

The Natriuretic Peptide System is Overwhelmed in Acute Decompensated Heart Failure

Vasoconstrictors
- Aldosterone
- Endothelin
- Epinephrine
- Vasopressin
- Angiotensin II

Vasodilators
- ANP
- BNP
- Nitric oxide
BNP Levels to Diagnose HF

BNP < 100 pg/ml  BNP 100-400 pg/ml  BNP > 400 pg/ml

Baseline LV dysfunction, underlying cor pulmonale, acute PE?

Yes  No

HF very unlikely (2%)  Possible exacerbation of HF (25%)  HF likely (75%)  HF very likely (95%)

Recommendations for Biomarkers in HF

<table>
<thead>
<tr>
<th>Biomarker, Application</th>
<th>Setting</th>
<th>COR</th>
<th>LOE</th>
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<tr>
<td>Natriuretic peptides (BNP or NT-proBNP)</td>
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<tr>
<td>Diagnosis or exclusion of HF</td>
<td>Ambulatory, Acute</td>
<td>I</td>
<td>A</td>
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<td>Prognosis or severity of HF</td>
<td>Ambulatory, Acute</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Achieve optimal dosing of GDMT in chronic HF</td>
<td>Ambulatory</td>
<td>IIa</td>
<td>B</td>
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<td>managed by specialized HF program</td>
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<tr>
<td>Guidance of acutely decompensated HF therapy</td>
<td>Acute</td>
<td>IIb</td>
<td>C</td>
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<tr>
<td>Biomarkers of myocardial injury (Troponins)</td>
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<td>Additive risk stratification</td>
<td>Acute, Ambulatory</td>
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<td>Biomarkers of myocardial fibrosis (Galectin-3)</td>
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<td>IIb</td>
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Assessment in Heart Failure

Evaluation for clinical manifestations of HF with a routine history and physical examination is recommended in patients with the following medical conditions or test findings that place patient at high risk for HF:

- Hypertension
- Diabetes
- Obesity
- CAD (after MI, PCI, CABG)
- Peripheral arterial disease or cerebrovascular disease
- Valvular heart disease
- History of exposure to cardiac toxins
- Family history of cardiomyopathy in a first degree relative (parent, sibling, child)
- Sleep-disordered breathing
- Abnormal ECG (LVH, LBBB, pathologic Q waves)
- Cardiomegaly on chest X-ray
Using Physical Assessment to Obtain Hemodynamic Data

Preload
- Neck Veins
  - JVD is indication of elevated RV preload
- Lung Sounds
  - Rales or crackles can indicate elevated LV preload

Perfusion (forwards flow)
- Skin Temperature
  - Warm and dry indicates adequate perfusion
  - Cold and moist indicates reduced perfusion
- Pulse Pressure
- Capillary Refill
- Urine Output
- Mentation

- Evaluating Neck Veins
  - Blood in jugular veins assumes level corresponding with right atrial pressure so estimates CVP
    - Right jugular vein reflects pressure best
    - Normal CVP = <9 cm H₂O (2-6 mmHg)
  - Position patient so internal jugular is visible (45 degrees)
    - Angle of Louis is 5 cm above right atrium
    - Place ruler vertically at Angle of Louis
    - Measure in cm how far above Angle of Louis the neck vein is visible
    - Add this measurement to 5 = estimated CVP
    - Normal JVD level is no more than 3 cm above the sternal angle
Neck veins are distended whenever CVP is high or something interferes with RV filling:
RV failure, cardiac tamponade, restrictive pericarditis, restrictive cardiomyopathy, tension pneumothorax

- **Abdominojugular reflux** – seen in RV failure
  - Press on upper right quadrant for 30-60 seconds while watching neck veins
  - Rise in neck veins of 1 cm or more = positive abdominojugular reflux

- **Kussmaul’s sign** (paradoxical elevation of jugular venous pressure during inspiration)
  - Normally the neck veins empty during inspiration as intrathoracic pressure drops and venous return to the heart increases
  - In “restrictive” disease (pericardial effusion, constrictive pericarditis, cardiomyopathy, diastolic HF) the heart cannot handle the increased venous return so neck veins elevate when venous return increases during inspiration
Evaluating Blood Pressure

- Systolic BP is affected by
  - LV stroke volume
  - Peak rate of LV ejection
  - Distensibility of blood vessel walls
- Diastolic BP is affected by peripheral vascular resistance (arteriolar tone)
  - A rise in DBP is the first BP change – due to compensatory vasoconstriction

Pulse Pressure

- Difference between systolic BP and diastolic BP
  - Normal = 40 mmHg (120/80 = 40 mmHg PP)
  - Influenced by stroke volume and arterial compliance (beat-to-beat change reflects SV)
- ↓ PP is an early sign of ↓ cardiac output
  - PP < 30 mmHg is sign of advanced heart failure
  - PP can be increased due to high stroke volume (↑preload, ↑contractility) or high compliance (vasodilation)
  - PP can be decreased due to low stroke volume (↓preload, ↓contractility) or low compliance (vasoconstriction)
Evaluation of pulse

- Pulsus alternans is diagnostic of LV failure
  - Alternating strong and weak pulse during regular rhythm
  - Can hear it with slow release of BP cuff - every other beat heard with strong pulse, eventually every beat heard

Assessing Volume Status

- Paroxysmal nocturnal dyspnea or orthopnea
- Dyspnea on exertion
- Daily weights
- Vital signs
- Assess for orthostatic BP and HR changes
- Rales, crackles
- S3 gallop
- Elevated jugular venous pressure
- Hepatic enlargement and tenderness
- Positive hepatojugular reflux
- Edema
- Ascites
Four major assessment findings suggest severity of the cardiac dysfunction:

- **Resting sinus tachycardia**
- **Narrow pulse pressure**
  - A decrease in cardiac output should be suspected when the pulse pressure is reduced below 30 mmHg.
- **Diaphoresis**
- **Peripheral vasoconstriction**
  - Cool, pale, and sometimes cyanotic extremities

Three major manifestations of volume overload in patients with HF:

- **Pulmonary congestion** (crackles, orthopnea, dyspnea)
- **Peripheral edema** (weight gain)
- **Elevated jugular venous pressure**

Careful physical examination with determination of vital signs and evaluation for these signs of HF:

| Elevated cardiac filling pressures and fluid overload | • Elevated jugular venous pressure  
<table>
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<td></td>
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<td>Cardiac enlargement</td>
<td>• Laterally displaced or prominent apical impulse</td>
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<td>Reduced cardiac output</td>
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<td></td>
<td>• Cool extremities</td>
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<td></td>
<td>• Tachycardia with pulsus alternans</td>
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<tr>
<td>Arrhythmia</td>
<td>• Irregular pulse suggestive of atrial fibrillation or frequent ectopy</td>
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</tbody>
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Sunrise at my house