Heart Failure

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DEFINITION

Heart failure (HF)

- is a progressive clinical syndrome caused by inability of the heart to pump sufficient blood to meet the body's metabolic needs.

- HF can result from any disorder that reduces ventricular filling (diastolic dysfunction) and/or myocardial contractility (systolic dysfunction).

TYPES

Types of heart failure:

- High Output HF
- Low Output HF

- *Left-sided HF*
- *Right-sided HF*
- *Biventricular HF*

TYPES

- *Diastolic dysfunction*
- *Systolic dysfunction*

- *Acute heart failure*
- *Chronic heart failure*

EPIDEMIOLOGY

- Incidence of HF is greater in men and in the elderly (age > 65 y)
- The incidence in black women is as high as that of white men

PATHOPHYSIOLOGY

Causes

- **Systolic dysfunction** (decreased contractility):

1. Reduced muscle mass (eg. MI)
2. Dilated cardiomyopathies
3. Ventricular hypertrophy

PATHOPHYSIOLOGY

- **Ventricular hypertrophy** can be caused by
  - Pressure overload
    - systemic or pulmonary hypertension
    - aortic or pulmonic valve stenosis
  - Volume overload
    - valvular regurgitation
    - high-output states

PATHOPHYSIOLOGY

- **Diastolic dysfunction** (restriction in ventricular filling):
  - Increased ventricular stiffness
    - Ventricular hypertrophy
    - Infiltrative myocardial diseases
      - endomyocardial
    - Myocardial ischemia and MI
  - Mitral or tricuspid valve stenosis
  - Pericardial disease
    - pericarditis , pericardial tamponade

PATHOPHYSIOLOGY

- The leading causes of HF are:
  - Coronary artery disease
  - Hypertension.
- As cardiac function decreases after myocardial injury, the heart relies on compensatory mechanisms

PATHOPHYSIOLOGY

Compensatory mechanisms:

1. Tachycardia and increased contractility through sympathetic nervous system activation
2. The Frank–Starling mechanism, whereby increased preload increases stroke volume
3. Vasoconstriction
4. Ventricular hypertrophy and remodeling.

PATHOPHYSIOLOGY

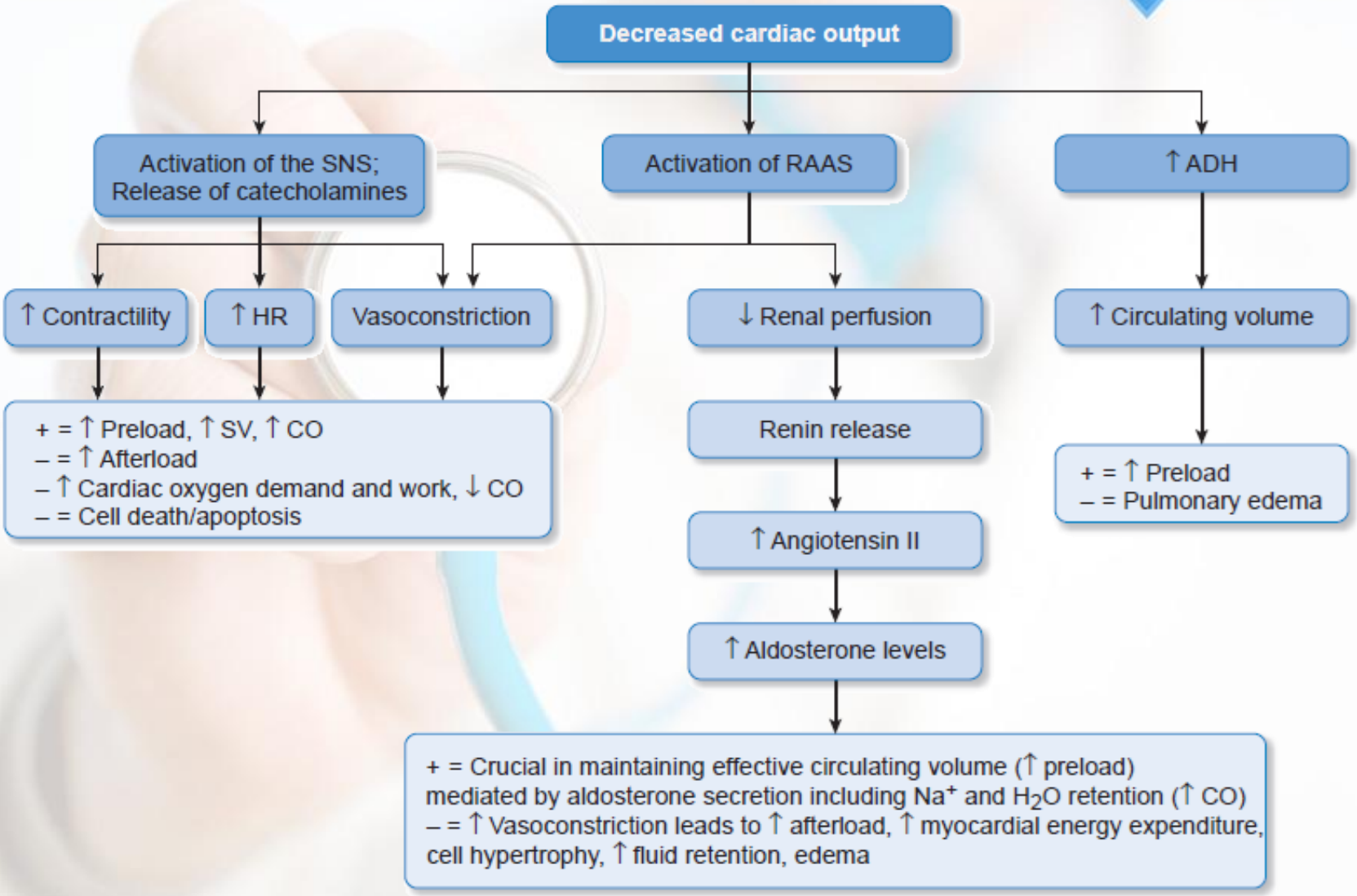
- Although these compensatory mechanisms initially maintain cardiac function, they are responsible for the symptoms of HF and contribute to disease progression.

- In the neurohormonal model of HF, an initiating event (eg, acute MI) → decreased cardiac output; the HF state then becomes a systemic disease whose progression is mediated largely by neurohormones and autocrine/paracrine factors.

PATHOPHYSIOLOGY

- These substances include:
  1. Angiotensin II
  2. Norepinephrine
  3. Aldosterone
  4. Natriuretic peptides
  5. Arginine vasopressin
  6. Endothelin peptides
  7. other circulating biomarkers (eg, C-reactive protein).

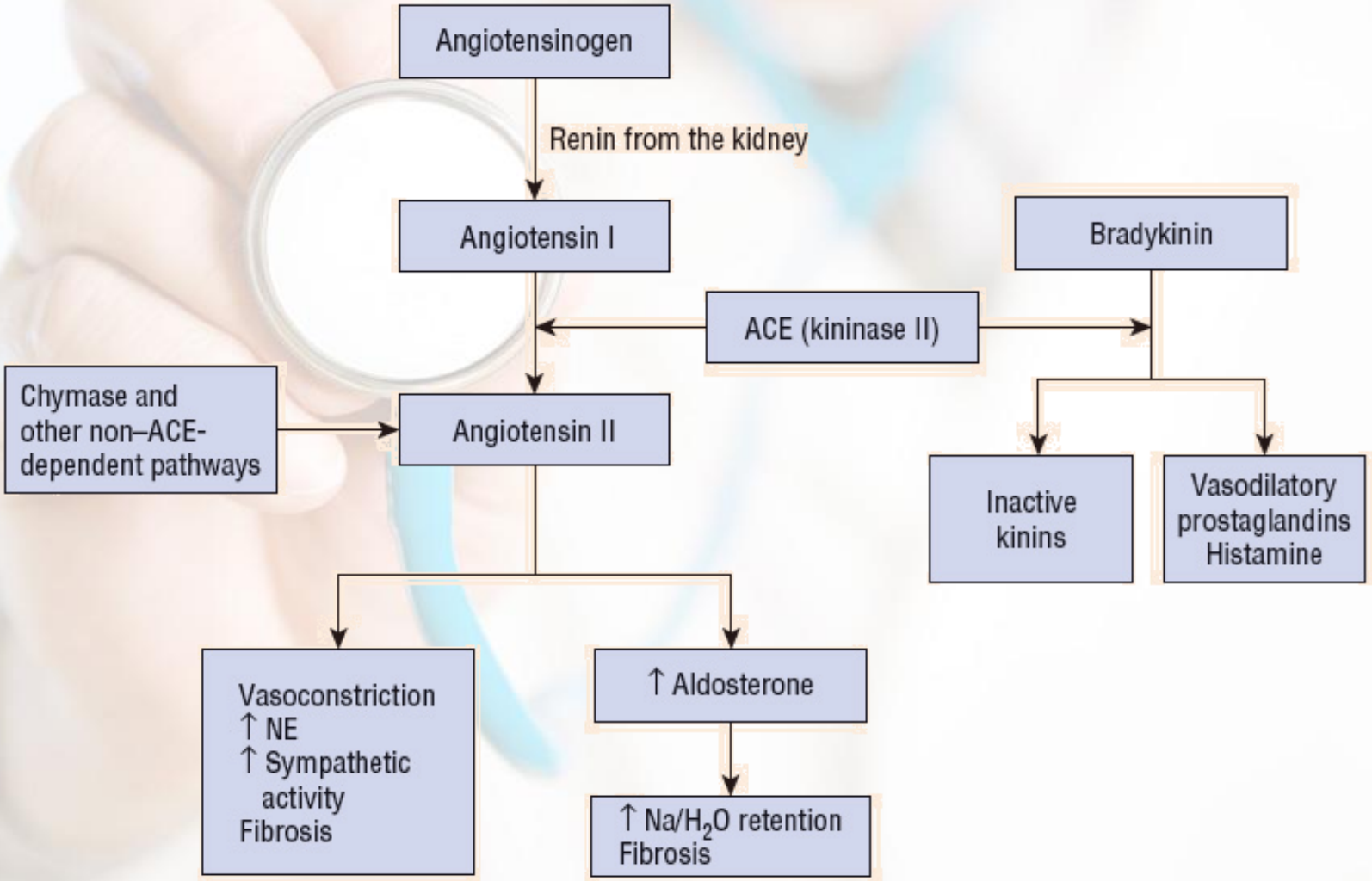
PATHOPHYSIOLOGY



Adaptive mechanisms in systolic heart failure.

+, beneficial results; –, negative (detrimental) effects; ADH, antidiuretic hormone; CO, cardiac output; HR, heart rate; H2O, water; Na+, sodium; RAAS, renin-angiotensin-aldosterone system; SNS, sympathetic nervous system; SV, stroke volume.

PATHOPHYSIOLOGY



PATHOPHYSIOLOGY

Common precipitating factors that may cause a previously compensated HF patient to decompensate include:

1. Myocardial ischemia and MI
2. Atrial fibrillation
3. Pulmonary infections
4. Nonadherence with diet or drug therapy
5. Inappropriate medication use.

PATHOPHYSIOLOGY

Drugs may precipitate or exacerbate HF because of :

- Their negative inotropic properties
- Cardiotoxic properties
- Sodium- and water-retaining properties.

PATHOPHYSIOLOGY

Drugs That May Precipitate or Exacerbate Heart Failure

- **Negative inotropic effect**
  - Antiarrhythmics (e.g., disopyramide, flecainide, propafenone, and others)
  - β-Blockers (e.g., propranolol, metoprolol, atenolol, and others)
  - Calcium channel blockers (e.g., verapamil, diltiazem)
  - Terbinafine

- **Cardiotoxic**
  - Doxorubicin
  - Daunomycin
  - Cyclophosphamide
  - Trastuzumab
  - Imatinib
  - Ethanol
  - Amphetamines (e.g., cocaine, methamphetamine)

PATHOPHYSIOLOGY

- Sodium and water retention
  - Nonsteroidal antiinflammatory drugs
  - Cyclooxygenase-2 inhibitors
  - Rosiglitazone and pioglitazone
  - Glucocorticoids
  - Androgens and estrogens
  - Salicylates (high dose)
  - Sodium-containing drugs (e.g., carbenicillin disodium, ticarcillin disodium)
- Uncertain mechanism
  - Infliximab
  - Etanercept
  - Dronedarone

CLINICAL PRESENTATION

General

- Patient presentation may range from asymptomatic to cardiogenic shock

Symptoms

- Dyspnea, particularly on exertion
- Orthopnea
- Paroxysmal nocturnal dyspnea
- Exercise intolerance
- Tachypnea
- Cough
- Nocturia

CLINICAL PRESENTATION

- Hemoptysis
- Abdominal pain
- Anorexia
- Fatigue
- Nausea
- Bloating
- Poor appetite, early satiety
- Ascites
- Mental status changes
- Weight gain or loss

CLINICAL PRESENTATION

Signs

- Pulmonary rales
- Pulmonary edema
- Cool extremities
- Pleural effusion
- Tachycardia
- Narrow pulse pressure
- Cardiomegaly
- Peripheral edema
- Jugular venous distention
- Hepatojugular reflux
- Hepatomegaly
- Venous stasis changes
- Lateral displacement of apical impulse

DIAGNOSIS

- Consider diagnosis of HF in patients with characteristic signs and symptoms.
- A complete history and physical examination with appropriate laboratory testing are essential in evaluating patients with suspected HF.

DIAGNOSIS

Laboratory Tests

- Electrocardiogram may be normal or it could show numerous abnormalities including acute ST-T wave changes from myocardial ischemia, atrial fibrillation, bradycardia, left ventricular hypertrophy
- Serum creatinine: it may be increased due to hypoperfusion. Preexisting renal dysfunction can contribute to volume overload
- Complete blood count useful to determine if heart failure due to reduced oxygen-carrying capacity
- Chest x-ray: useful for detection of cardiac enlargement, pulmonary edema, and pleural effusions
- Echocardiogram: used to assess LV size, valve function, pericardial effusion, wall motion abnormalities, and ejection fraction
- Hyponatremia: serum sodium <130 mEq/L (<130 mmol/L) is associated with reduced survival and may indicate worsening volume overload and/or disease progression

DIAGNOSIS

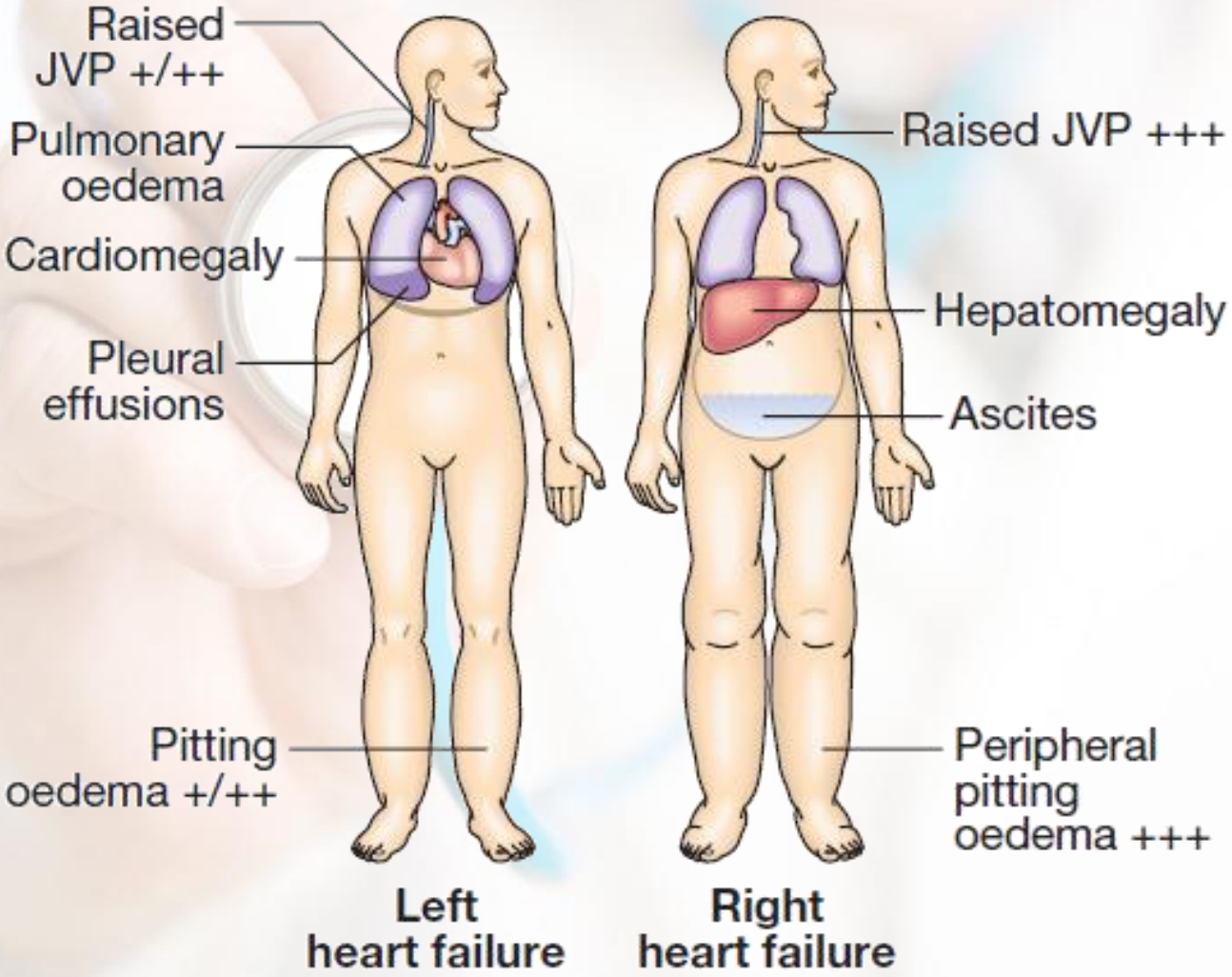


Fig. 18.24 Clinical features of left and right heart failure.
(JVP = jugular venous pressure)

TREATMENT OF CHRONIC HF

Goals of Treatment

1. Improve quality of life
2. Relieve or reduce symptoms
3. Prevent or minimize hospitalizations
4. Slow disease progression
5. Prolong survival.

TREATMENT OF CHRONIC HF

GENERAL APPROACH

- The first step is to determine the etiology or precipitating factors.
- Treatment of underlying disorders (eg, hyperthyroidism) may obviate the need for treating HF.

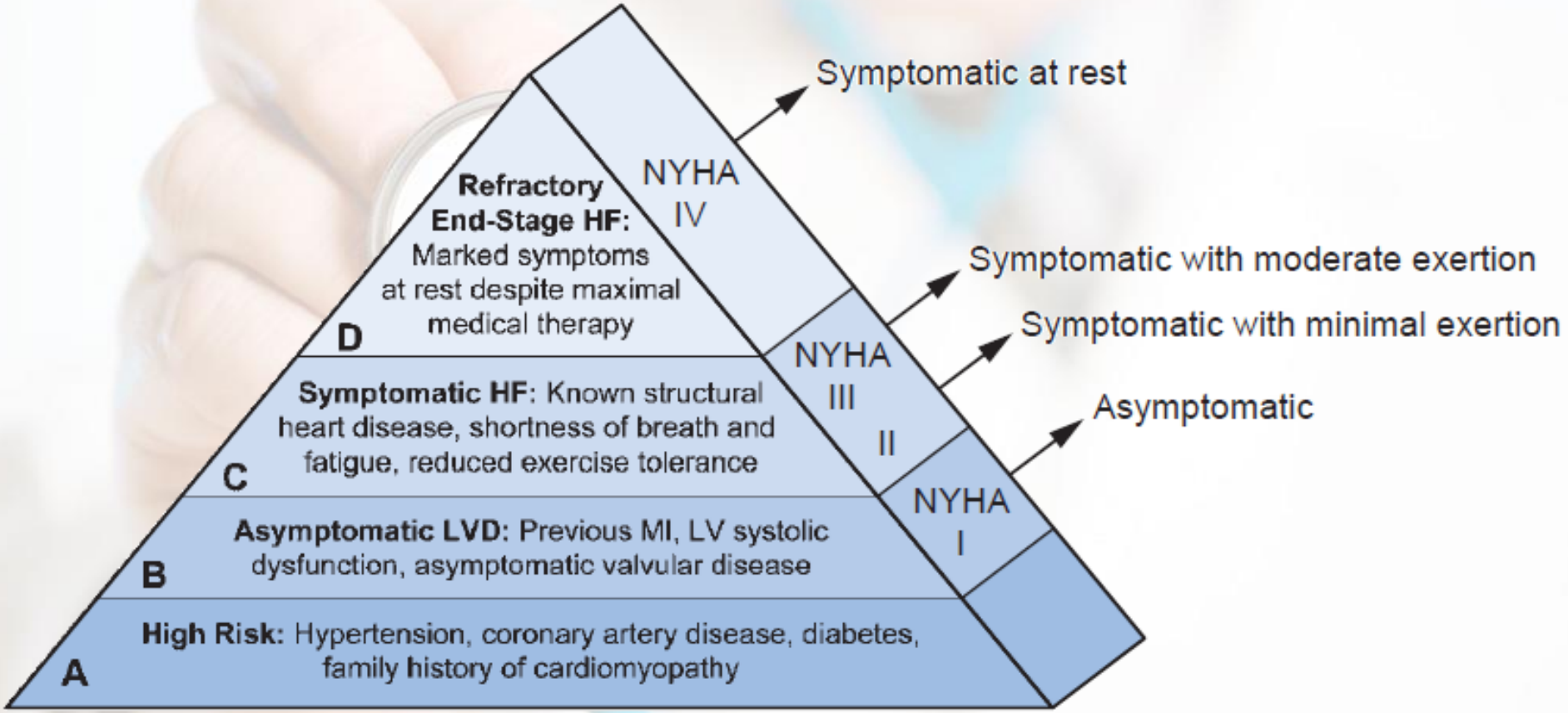
Nonpharmacologic interventions

1. Cardiac rehabilitation
2. Restriction of fluid intake (maximum 2 L/day from all sources) and dietary sodium (<2–3 g of sodium/day).

TREATMENT OF CHRONIC HF

The American College of Cardiology/American Heart Association (ACC/AHA) staging system provides a more comprehensive framework for evaluating, preventing, and treating HF.

TREATMENT OF CHRONIC HF



Staging and New York Heart Association (NYHA) classification of heart failure.

TREATMENT OF CHRONIC HF

ACC/AHA stage A:

- These are patients at high risk for developing heart failure.
- The emphasis is on identifying and modifying risk factors to prevent development of structural heart disease and subsequent HF.
- Strategies include smoking cessation and control of hypertension, diabetes mellitus, and dyslipidemia.
- Although treatment must be individualized, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) are recommended for HF prevention in patients with multiple vascular risk factors.

TREATMENT OF CHRONIC HF

ACC/AHA stage B:

- In these patients with structural heart disease but no HF signs or symptoms, treatment is targeted at minimizing additional injury and preventing or slowing the remodeling process.
- In addition to treatment measures outlined for stage A, patients with a previous MI should receive both ACE inhibitors (or ARBs in patients intolerant of ACE inhibitors) and β-blockers regardless of the ejection fraction.
- Patients with reduced ejection fractions should also receive both agents, regardless of whether they have had an MI.

TREATMENT OF CHRONIC HF

ACC/AHA stage C:

- These patients have structural heart disease and previous or current HF symptoms.
- Most should receive the treatments for stages A and B, as well as initiation and titration of a diuretic (if clinical evidence of fluid retention), ACE inhibitor, and β-blocker (if not already receiving a β-blocker for previous MI, left ventricular [LV] dysfunction, or other indication).
- If diuresis is initiated, and symptoms improve once the patient is euvolemic, long-term monitoring can begin.

TREATMENT OF CHRONIC HF

- If symptoms do not improve, an aldosterone receptor antagonist, ARB (in ACE inhibitor–intolerant patients), digoxin, and/or hydralazine/isosorbide dinitrate (ISDN) may be useful with carefully screened patients.

- Other general measures include moderate sodium restriction, daily weight measurement, immunization against influenza and pneumococcus, modest physical activity, and avoidance of medications that can exacerbate HF.

TREATMENT OF CHRONIC HF

ACC/AHA stage D:

- These are patients with refractory HF (ie, symptoms at rest despite maximal medical therapy).
- They should be considered for specialized therapies, including
  - mechanical circulatory support
  - continuous IV positive inotropic therapy
  - cardiac transplantation, or
  - hospice care (when no additional treatments are appropriate).

Diuretics

- Compensatory mechanisms in HF stimulate excessive sodium and water retention, often leading to systemic and pulmonary congestion.
- Consequently, diuretic therapy (in addition to sodium restriction) is recommended for all patients with clinical evidence of fluid retention.
- However, because they do not alter disease progression or prolong survival, they are not mandatory for patients without fluid retention.

Diuretics

Thiazide diuretics (eg, hydrochlorothiazide)

- are relatively weak and are used alone infrequently in HF.
- However, thiazides or the thiazide-like diuretic metolazone can be used in combination with a loop diuretic to promote very effective diuresis.
- Thiazides may be preferred over loop diuretics in patients with only mild fluid retention and elevated blood pressure (BP) because of their more persistent antihypertensive effects.

Diuretics

Loop diuretics (furosemide, bumetanide, and torsemide)

- are usually necessary to restore and maintain euvolemia in HF.
- In addition to acting in the thick ascending limb of the loop of Henle, they induce a prostaglandin-mediated increase in renal blood flow that contributes to their natriuretic effect.
- Unlike thiazides, loop diuretics maintain their effectiveness in the presence of impaired renal function, although higher doses may be necessary.

Diuretics

	Furosemide	Bumetanide	Torsemide
Usual daily dose (oral)	20–160 mg/day	0.5–4 mg/day	10–80 mg/day
Ceiling dose[a]			
Normal renal function	80–160 mg	1–2 mg	20–40 mg
CL_{cr} 20–50 mL/min	160 mg	2 mg	40 mg
CL_{cr} <20 mL/min	400 mg	8–10 mg	100 mg
Bioavailability	10%–100% Average: 50%	80%–90%	80%–100%
Affected by food	Yes	Yes	No
Half-life	0.3–3.4 h	0.3–1.5 h	3–4 h

CL_{cr}, creatinine clearance.
[a]Ceiling dose: single dose above which additional response is unlikely to be observed

Loop Diuretic Use in Heart Failure

ACEI

Angiotensin Converting Enzyme Inhibitors

- decrease angiotensin II and aldosterone, attenuating many of their deleterious effects, including reducing ventricular remodeling, myocardial fibrosis, myocyte apoptosis, cardiac hypertrophy, norepinephrine release, vasoconstriction, and sodium and water retention.
- Clinical trials have produced unequivocal evidence that ACE inhibitors improve symptoms, slow disease progression, and decrease mortality in patients with HF and reduced LVEF (stage C).
- These patients should receive ACE inhibitors unless contraindications are present.
- ACE inhibitors should also be used to prevent the development of HF in at-risk patients (ie, stages A and B).

ACEI

Generic Name	Brand Name	Initial Dose	Target Dosing–Survival Benefit[a]	Prodrug	Elimination[b]
Captopril	Capoten	6.25 mg three times daily	50 mg three times daily	No	Renal
Enalapril	Vasotec	2.5–5 mg twice daily	10 mg twice daily	Yes	Renal
Lisinopril	Zestril, Prinivil	2.5–5 mg daily	20–40 mg daily[c]	No	Renal
Quinapril	Accupril	5 mg twice daily	20–40 mg twice daily[d]	Yes	Renal
Ramipril	Altace	1.25–2.5 mg twice daily	5 mg twice daily	Yes	Renal
Fosinopril	Monopril	5–10 mg daily	40 mg daily[d]	Yes	Renal/hepatic
Trandolapril	Mavik	0.5–1 mg daily	4 mg daily	Yes	Renal/hepatic
Perindopril	Aceon	2 mg daily	8–16 mg daily	Yes	Renal/hepatic

[a]Target doses associated with survival benefits in clinical trials.
[b]Primary route of elimination.
[c]Note that in the ATLAS trial (Circulation 1999;100:2312–2318), no significant difference in mortality was found between low-dose (~5 mg/day) and high-dose (~35 mg/day) lisinopril therapy.
[d]Effects on mortality have not been evaluated.

ACE Inhibitors Routinely Used for Treatment of Heart Failure

β-Blockers

β-Blockers

- There is overwhelming clinical trial evidence that certain β-blockers slow disease progression, decrease hospitalizations, and reduce mortality in patients with systolic HF.
- The ACC/AHA guidelines recommend use of β-blockers in all stable patients with HF and a reduced LVEF in the absence of contraindications or a clear history of β-blocker intolerance.
- Patients should receive a β-blocker even if symptoms are mild or well controlled with ACE inhibitor and diuretic therapy.
- It is not essential that ACE inhibitor doses be optimized before a β-blocker is started because the addition of a β-blocker is likely to be of greater benefit than an increase in ACE inhibitor dose.

β-Blockers

- β-Blockers are also recommended for asymptomatic patients with a reduced LVEF (stage B) to decrease the risk of progression to HF.
- Initiate β-blockers in stable patients who have no or minimal evidence of fluid overload.
- Because of their negative inotropic effects, start β-blockers in very low doses with slow upward dose titration to avoid symptomatic worsening or acute decompensation.
- Titrate to target doses when possible to provide maximal survival benefits.

Drug Therapies to Consider for Select Patients

- Drug Therapies to Consider for Select Patients:

Angiotensin-II Receptor Blockers

- The angiotensin II receptor antagonists block the angiotensin II receptor subtype AT1, preventing the deleterious effects of angiotensin II, regardless of its origin.
- They do not appear to affect bradykinin and are not associated with the side effect of cough that sometimes results from ACE inhibitor–induced accumulation of bradykinin.
- Also, direct blockade of AT1 receptors allows unopposed stimulation of AT2 receptors, causing vasodilation and inhibition of ventricular remodeling.

Angiotensin-II Receptor Blockers

- Combination therapy with an ARB and ACE inhibitor offers a theoretical advantage over either agent alone through more complete blockade of the deleterious effects of angiotensin II.
- However, clinical trial results indicate that the addition of an ARB to optimal HF therapy (eg, ACE inhibitors, β-blockers, and diuretics) offers marginal benefits at best with increased risk of adverse effects.
- The addition of an ARB may be considered with patients who remain symptomatic despite receiving optimal conventional therapy.

EVALUATION OF THERAPEUTIC OUTCOMES

- Monitor BP to ensure that symptomatic hypotension does not develop as a result of drug therapy.
- Body weight is a sensitive marker of fluid loss or retention, and patients should weigh themselves daily and report changes to their healthcare provider so that adjustments can be made in diuretic doses.
- Symptoms may worsen initially on β-blocker therapy, and it may take weeks to months before patients notice symptomatic improvement.
- Routine monitoring of serum electrolytes and renal function is mandatory in patients with HF.

Aldosterone Antagonists

Aldosterone Antagonists

- Spironolactone and eplerenone block the mineralocorticoid receptor, the target site for aldosterone.
- In the kidney, aldosterone antagonists inhibit sodium reabsorption and potassium excretion.
- However, diuretic effects are minimal, suggesting that their therapeutic benefits result from other actions.
- Based on clinical trial results demonstrating reduced mortality, low-dose aldosterone antagonists may be appropriate for:

  (1) patients with mild to moderately severe systolic HF who are receiving standard therapy, &

  (2) those with LV dysfunction and either acute HF or diabetes early after MI.

Aldosterone Antagonists

- Aldosterone antagonists must be used cautiously and with careful monitoring of renal function and potassium concentration.
- They should be avoided in patients with renal impairment, recent worsening of renal function, high-normal potassium levels, or a history of severe hyperkalemia.
- Spironolactone also interacts with androgen and progesterone receptors, which may lead to gynecomastia, impotence, and menstrual irregularities in some patients.

Aldosterone Antagonists

- Initial doses should be low (spironolactone 12.5 mg/day; eplerenone 25 mg/day), especially in the elderly and those with diabetes or creatinine clearance less than 50 mL/min.
- A spironolactone dose of 25 mg/day was used in one major clinical trial.
- The eplerenone dose should be titrated to the target dose of 50 mg once daily, preferably within 4 weeks as tolerated by the patient.

Digoxin

Digoxin

- Although digoxin has positive inotropic effects, its benefits in HF are related to its neurohormonal effects.
- Digoxin does not improve survival in patients with HF but does provide symptomatic benefits.
- In patients with chronic systolic HF and supraventricular tachyarrhythmias such as atrial fibrillation, consider digoxin early in therapy to help control ventricular response rate.
- For patients in normal sinus rhythm, effects on symptom reduction and quality-of life improvement are evident in patients with mild to severe HF.

Digoxin

- Therefore, digoxin should be used together with standard HF therapies (ACE inhibitors, β-blockers, and diuretics) in patients with symptomatic HF to reduce hospitalizations.
- Adjust doses to achieve plasma digoxin concentration of 0.5 to 1 ng/mL (0.6–1.3 nmol/L).
- Most patients with normal renal function can achieve this level with a dose of 0.125 mg/day.
- Patients with decreased renal function, the elderly, or those receiving interacting drugs (eg, amiodarone) should receive 0.125 mg every other day.

Nitrates and Hydralazine

Nitrates and Hydralazine

- Nitrates (eg, ISDN) and hydralazine have complementary hemodynamic actions.
- Nitrates are primarily venodilators, producing reductions in preload.
- Hydralazine is a direct arterial vasodilator that reduces systemic vascular resistance (SVR) and increases stroke volume and cardiac output.
- The combination of nitrates and hydralazine improves the composite endpoint of mortality, hospitalizations for HF, and quality of life in African Americans who receive standard therapy.

TREATMENT OF ADHF

TREATMENT OF ACUTE DECOMPENSATED HEART FAILURE

Goals of Treatment:

1. Relieve congestive symptoms
2. optimize volume status
3. Treat symptoms of low cardiac output
4. minimize risks of drug therapy so the patient can be discharged in a compensated state on oral drug therapy.

TREATMENT OF ADHF

GENERAL APPROACH

- Acute decompensated heart failure (ADHF) involves patients with new or worsening signs or symptoms (often resulting from volume overload and/or hypoperfusion) requiring additional medical care, such as emergency department visits and hospitalizations.
- Hospitalization is recommended or should be considered depending on patient presentation.
- Admission to an intensive care unit (ICU) may be required if the patient experiences hemodynamic instability requiring frequent monitoring, invasive hemodynamic monitoring, or rapid titration of IV medications with close monitoring.

TREATMENT OF ADHF

- Address and correct reversible or treatable causes of decompensation.
- Medications that may aggravate HF should be evaluated carefully and discontinued when possible.
- The first step in managing ADHF is to ascertain that optimal treatment with oral medications has been achieved.
- If fluid retention is evident, aggressive diuresis, often with IV diuretics, should be accomplished.
- Standard treatment should be optimized with an ACE inhibitor and β-blocker.

TREATMENT OF ADHF

- β-blockers should generally be continued during hospitalization unless recent dose initiation or up-titration was responsible for decompensation.
- In such cases, β-blocker therapy may be temporarily withheld or dose-reduced. Most patients may continue to receive digoxin at a low dose targeting a trough serum concentration of 0.5–1 ng/mL (0.6–1.3 nmol/L).
- Appropriate management of ADHF is aided by determination of whether the patient has signs and symptoms of fluid overload (“wet” HF) or low cardiac output (“dry” HF)

Dobutamine

Positive Inotropic Agents

Dobutamine

- Dobutamine is a β1- and β2-receptor agonist with some α1-agonist effects.
- The net vascular effect is usually vasodilation.
- It has a potent inotropic effect without producing a significant change in heart rate.
- Initial doses of 2.5 to 5 mcg/kg/min can be increased progressively to 20 mcg/kg/min on the basis of clinical and hemodynamic responses.
- Dobutamine increases cardiac index because of inotropic stimulation, arterial vasodilation, and a variable increase in heart rate.

Milrinone

Milrinone

- Milrinone inhibits phosphodiesterase III and produces positive inotropic and arterial and venous vasodilating effects (an inodilator).
- It has supplanted use of amrinone, which has a higher rate of thrombocytopenia.
- During IV administration, milrinone increases stroke volume (and cardiac output) with minimal change in heart rate.
- It also lowers pulmonary capillary wedge pressure (PCWP) by venodilation and is particularly useful in patients with a low cardiac index and elevated LV filling pressure.

Milrinone

- The most notable adverse events are arrhythmia, hypotension, and, rarely, thrombocytopenia.
- Measure platelet count before and during therapy.
- Routine use of milrinone (and perhaps other inotropes) should be discouraged because recent studies suggest a higher in-hospital mortality rate than with some other drugs.
- However, inotropes may be needed with certain patients, such as those with low cardiac output states with organ hypoperfusion and cardiogenic shock.
- Milrinone may be considered for patients receiving chronic β-blocker therapy because its positive inotropic effect does not involve stimulation of β-receptors.

Dopamine

Dopamine

- Dopamine should generally be avoided in ADHF, but its pharmacologic actions may be preferable to dobutamine or milrinone in patients with marked systemic hypotension or cardiogenic shock in the face of elevated ventricular filling pressures, where dopamine in doses greater than 5 mcg/kg/min may be necessary to raise central aortic pressure.
- Dopamine produces dose-dependent hemodynamic effects because of its relative affinity for α1-, β1-, β2-, and D1- (vascular dopaminergic) receptors.

Dopamine

- Positive inotropic effects mediated primarily by β1-receptors become more prominent with doses of 2 to 5 mcg/kg/min.
- At doses between 5 and 10 mcg/kg/min, chronotropic and α1-mediated vasoconstricting effects become more prominent.

Vasodilators

Vasodilators

- Arterial vasodilators reduce afterload and cause a reflex increase in cardiac output.
- Venodilators reduce preload by increasing venous capacitance, improving symptoms of pulmonary congestion in patients with high cardiac filling pressures.
- Mixed vasodilators act on both arterial resistance and venous capacitance vessels, reducing congestive symptoms while increasing cardiac output.

Nitroprusside

Nitroprusside

- Sodium nitroprusside is a mixed arteriovenous vasodilator that acts directly on vascular smooth muscle to increase cardiac index and decrease venous pressure.
- Despite its lack of direct inotropic activity, nitroprusside exerts hemodynamic effects that are qualitatively similar to those of dobutamine and milrinone.
- However, nitroprusside generally decreases PCWP, SVR, and BP more than those agents do.
- Hypotension is an important dose-limiting adverse effect of nitroprusside and other vasodilators.
- Therefore, nitroprusside is primarily used with patients who have a significantly elevated SVR and often requires invasive hemodynamic monitoring.

Nitroprusside

- Nitroprusside is effective in the short-term management of severe HF in a variety of settings (eg, acute MI, valvular regurgitation, after coronary bypass surgery, decompensated chronic HF).
- Generally, it will not worsen, and may improve, the balance between myocardial oxygen demand and supply.
- However, an excessive decrease in systemic arterial pressure can decrease coronary perfusion and worsen ischemia.

Nitroglycerin

Nitroglycerin

- IV nitroglycerin decreases preload and PCWP because of functional venodilation and mild arterial vasodilation.
- It is often the preferred agent for preload reduction in ADHF, especially in patients with pulmonary congestion.
- In higher doses, nitroglycerin displays potent coronary vasodilating properties and beneficial effects on myocardial oxygen demand and supply, making it the vasodilator of choice for patients with severe HF and ischemic heart disease.

Nesiritide

Nesiritide

- is a recombinant product that is identical to endogenous BNP secreted by the ventricular myocardium in response to volume overload.
- Nesiritide mimics the vasodilatory and natriuretic actions of the endogenous peptide, resulting in venous and arterial vasodilation; increased cardiac output; natriuresis and diuresis; and decreased cardiac filling pressures, sympathetic nervous system activity, and renin–angiotensin–aldosterone system activity.

Nesiritide

- The role of nesiritide in pharmacotherapy of ADHF remains controversial.
- Compared with nitroglycerin or nitroprusside, it produces marginal improvement in clinical outcomes and is substantially more expensive.
- Concerns about potential negative effects on renal function and increased morality are also unsettled.

Vasopressin Receptor Antagonists

- The vasopressin receptor antagonists currently available affect one or two arginine vasopressin (AVP; antidiuretic hormone) receptors, V_{1A} or V_2.
- Stimulation of V1A receptors (located in vascular smooth muscle cells and myocardium) results in vasoconstriction, myocyte hypertrophy, coronary vasoconstriction, and positive inotropic effects.
- V_2 receptors are located in renal tubules, where they regulate water reabsorption.

Tolvaptan

Tolvaptan

- selectively binds to and inhibits the V2 receptor.
- It is an oral agent indicated for hypervolemic and euvolemic hyponatremia in patients with syndrome of inappropriate antidiuretic hormone (SIADH), cirrhosis, and HF.
- Tolvaptan is typically initiated at 15 mg orally daily and then titrated to 30 or 60 mg daily as needed to resolve hyponatremia.
- It is a substrate of cytochrome P450-3A4 and is contraindicated with potent inhibitors of this enzyme.
- The most common side effects are dry mouth, thirst, urinary frequency, constipation, and hyperglycemia.

Conivaptan

Conivaptan

- nonselectively inhibits both the V_{1A} and V_2 receptors.
- It is an IV agent indicated for hypervolemic and euvolemic hyponatremia due to a variety of causes; however, it is not indicated for hyponatremia associated with HF.

MECHANICAL CIRCULATORY SUPPORT

MECHANICAL CIRCULATORY SUPPORT

The intraaortic balloon pump (IABP)

- is typically employed in patients with advanced HF who do not respond adequately to drug therapy, such as those with intractable myocardial ischemia or patients in cardiogenic shock.
- IV vasodilators and inotropic agents are generally used in conjunction with the IABP to maximize hemodynamic and clinical benefits.
- Ventricular assist devices are surgically implanted and assist, or in some cases replace, the pumping functions of the right and/or left ventricles.

MECHANICAL CIRCULATORY SUPPORT

- They can be used in the short-term (days to several weeks) for temporary stabilization of patients awaiting an intervention to correct underlying cardiac dysfunction.
- They can also be used long term (several months to years) as a bridge to heart transplantation.

SURGICAL THERAPY

- Orthotopic cardiac transplantation is the best therapeutic option for patients with chronic irreversible New York Heart Association class IV HF, with a 10-year survival of ~50% in well-selected patients.

EVALUATION OF THERAPEUTIC OUTCOMES

CHRONIC HEART FAILURE

- Ask patients about the presence and severity of symptoms and how symptoms affect daily activities.
- Evaluate efficacy of diuretic treatment by disappearance of the signs and symptoms of excess fluid retention.
- Physical examination should focus on body weight, extent of jugular venous distention, presence of hepatojugular reflux, and presence and severity of pulmonary congestion (rales, dyspnea on exertion, orthopnea, and paroxysmal nocturnal dyspnea) and peripheral edema.
- Other outcomes are improvement in exercise tolerance and fatigue, decreased nocturia, and a decrease in heart rate.

EVALUATION OF THERAPEUTIC OUTCOMES

ACUTE DECOMPENSATED HEART FAILURE

- Initial stabilization requires adequate arterial oxygen saturation, cardiac index, and blood pressure.
- Functional end-organ perfusion may be assessed by mental status, renal function sufficient to prevent metabolic complications, hepatic function adequate to maintain synthetic and excretory functions, stable heart rate and rhythm, absence of ongoing myocardial ischemia or MI, skeletal muscle and skin blood flow sufficient to prevent ischemic injury, and normal arterial pH (7.34–7.47) and serum lactate concentration.
- These goals are most often achieved with a cardiac index greater than 2.2 L/min/m2, mean arterial BP greater than 60 mm Hg, and PCWP 15 mm Hg or greater.

EVALUATION OF THERAPEUTIC OUTCOMES

- Daily monitoring should include weight, strict fluid intake and output measurements, and HF signs/symptoms to assess the efficacy of drug therapy.
- Monitoring for electrolyte depletion, symptomatic hypotension, and renal dysfunction should be performed frequently.
- Vital signs should be assessed frequently throughout the day.
- Discharge from the ICU requires maintenance of the receding parameters in the absence of ongoing IV infusion therapy, mechanical circulatory support, or positive pressure ventilation.

Thank You