CHAPTER 24

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Diagnosis and Management of Acute Heart Failure

CHAPTER OUTLINE

ABBREVIATIONS

ACC	American College of Cardiology
ACEi	Angiotensin converting enzyme inhibitor
ACS	Acute coronary syndromes
ADHF	Acute decompensated heart failure
AHA	American Heart Association
AR	Aortic regurgitation
ARB	Angiotensin II receptor blocker
ARNI	Angiotensin receptor-neprilysin inhibitor
BNP	B-type natriuretic peptide
BUN	Blood urea nitrogen
Ca	Calcium
cAMP	Cyclic adenosine monophosphate
CBC	Complete blood count
Cr	Creatinine
CRT	Cardiac resynchronization therapy
CVA	Cerebrovascular accident
CXR	Chest X-ray
HF	Heart failure
HFpEF	Heart failure with preserved ejection fraction
HFrEF	Heart failure with reduced ejection fraction
HFSA	Heart Failure Society of America
ICD	Implantable cardioverter defibrillator
JVP	Jugular venous pressure
K	Potassium
LFT	Liver function tests
LV	Left ventricle
LVEF	Left ventricle ejection fraction
MCS	Mechanical circulatory support
Mg	Magnesium
Na	Sodium
NSAIDs	Nonsteroidal anti-inflammatory drugs
NT-proBNP	N-terminal pro B-type natriuretic peptide
NYHA	New York Heart Association

PAD	Peripheral arterial disease
PCWP	Pulmonary capillary wedge pressure
PDE	Phosphodiesterase
PVC	Premature ventricular contractions
PVR	Pulmonary vascular resistance
RV	Right ventricle
SVR	Systemic vascular resistance
TIA	Transient ischemic attack
VAD	Ventricular assist device
VT	Ventricular tachycardia

EPIDEMIOLOGY [1]

- 670,000 people are diagnosed with HF annually in the US; about half of people who develop HF die within 5 years of diagnosis; more than 290,000 deaths are associated with HF
- HF costs the United States an estimated $30.7 billion each year
- HF is the most common reason for hospitalization in people over age 65
- Over one million hospitalizations occur annually due to acute HF
  - More than 70% of admissions are from worsening of chronic HF (i.e. acute on chronic HF)
    - In-hospital mortality is 4% and 1 year mortality is 20% [2]
    - 30-day readmission rate is high
      - Readmission rates of 26.9% for HF versus 19.1% for all comers [3]
- Based on acute HF registries (The Acute Decompensated Heart Failure National Registry [ADHERE] [2], Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure [OPTIMIZE-HF] [4], EuroHeart Failure Survey II [EHFS II] [5]), most who are admitted with HF are over age 70, have a prior history of admission for HF, and 40–52% have HFpEF

PATHOPHYSIOLOGY

A variety of mechanisms contribute to developing acute HF and they consist of an underlying substrate, a triggering mechanism, and perpetuating factors [6]. Regardless of the substrate, trigger, or perpetuating factor(s), a unifying theme in acute HF is the presence of volume overload/congestion.

A) **Substrate: myocardial structure and function**

- Normal myocardial substrate that has suffered an acute injury that could be completely reversible, partially reversible, or irreversible
  - Most common cause: myocardial ischemia/infarction
  - Inflammation (myocarditis, autoimmune)
  - Stress cardiomyopathy
- Abnormal underlying substrate
  - American College of Cardiology (ACC)/American Heart Association (AHA) Stage B HF with first symptomatic event
  - Those with chronic compensated HF who present with an acute decompensation event
    - Most common presentation

B) Triggering mechanisms

- Acute coronary syndromes (ACS)/ischemia
- Medication non-adherence, iatrogenic changes in medications, drug-drug interactions
- Dietary indiscretion
- Worsening renal dysfunction
  - Renal artery stenosis [7], so-called "Pickering Syndrome"
- Arrhythmias (atrial or ventricular)
  - Atrial fibrillation [8]
  - Premature ventricular contractions (PVC) [9]
  - Ventricular tachycardia (VT)
- Pulmonary embolism
- Infections
- Severe hypertension
- Iatrogenic volume administration (e.g. intravenous fluids or blood transfusion)
- Cardiotoxic agents
  - Antineoplastic agents
    - *Anthracyclines*
      - Doxorubicin
      - Daunorubicin
      - Epirubicin
      - Idarubicin
    - *Anthraquinolones*
      - Mitoxantrones
    - *Alkylating agents*
      - Busulfan
      - Cisplatin
      - Cyclophosphamide
      - Ifosfamide
    - *Antimetabolites*
      - 5-Fluorouracil
    - *Antimicrotubules*
      - Paclitaxel
      - Vinca alkaloids
        - Vi*ncristine*
        - *Vin*blastine
    - *Tyrosine-kinase inhibitors*
      - Bevacizumab
      - Imatinib
      - Lapatinib
      - Sunitinib
      - Sorafenib
      - Trastuzumab
    - *Hormone-modifying therapy*
      - Androgen-deprivation

- Aromatase inhibitors
- *Miscellaneous*
  - All-trans retinoic acid
  - Arsenic trioxide
  - Pentostatin
- Cocaine
- Alcohol
- Ephedra

- Medications
  - Corticosteroids
  - Negative inotropes (e.g. verapamil, diltiazem)
  - Nonsteroidal anti-inflammatory drugs (NSAIDs)
- RV apical pacing [10]
- Hyper/hypothyroidism
- Systemic inflammation, including infections such as influenza [11]
- Sleep apnea

C) **Perpetuating factors lead to chronic HF (see Chap. 25)**

CLASSIFICATION

Two major classification systems have been described for patients with HF [12]

A) New York Heart Association (NYHA) functional classification of HF symptoms (Table 24-1)
B) ACC/AHA staging system for HF (Table 24-2)

TABLE 24-1

NEW YORK HEART ASSOCIATION FUNCTIONAL CLASSIFICATION OF HEART FAILURE SYMPTOMS

Class I	No symptoms with ordinary activity
Class II	Slight limitation of physical activity; comfortable at rest, but **ordinary physical activity** results in fatigue, dyspnea or angina
Class III	Marked limitation of physical activity; comfortable at rest, **but less than ordinary physical activity** results in fatigue, dyspnea or angina
Class IV	Unable to carry out **any physical activity** without symptoms. Symptoms may be present at rest

TABLE 24-2

AMERICAN COLLEGE OF CARDIOLOGY/AMERICAN HEART ASSOCIATION STAGING SYSTEM FOR HEART FAILURE

Stage A	High risk for developing HF	Hypertension Coronary artery disease Diabetes mellitus Family history of cardiomyopathy
Stage B	Asymptomatic HF	Previous myocardial infarction Left ventricular systolic dysfunction Asymptomatic valvular disease
Stage C	Symptomatic HF	Known structural heart disease Shortness of breath and fatigue Reduced exercise tolerance
Stage D	Refractory end-stage HF	Marked symptoms at rest despite maximal medical therapy

HF heart failure

TABLE 24-3

ESTIMATION OF HEMODYNAMIC PROFILE BASED ON EXAM FINDINGS

Congestion
■ S3 and/or S4 gallop
■ Prominent P2
■ Elevated JVP (JVD >10 cm corresponds to PCWP >22 mmHg, with 80% accuracy)
■ Hepatojugular reflux
■ Hepatomegaly
■ Edema
■ Pulsatile liver
■ Ascites
■ Rales or wheezes
Low Cardiac Output
■ Narrow pulse pressure (usually less than 25 mmHg)
■ Cool extremities
■ Lethargy/altered mentation
■ Hypotension
■ Sinus tachycardia
■ Pulsus alternans

JVP jugular venous pressure, *JVD* jugular venous distention, *PCWP* pulmonary capillary wedge pressure

INITIAL ASSESSMENT

Presentation

a). Dyspnea on exertion

- Most **sensitive** symptom

b). Paroxysmal nocturnal dyspnea

- Most **specific** symptom [13]

c). Peripheral edema

- Relatively common (66%), but only present in those with right sided HF

d). Fatigue
e). Cough, particularly nocturnal
f). Chest discomfort

Physical Examination [14]

A rapid initial assessment should be performed to identify (Table 24-3):

- Presence of congestion
- Presence of low output/cardiogenic shock
- Presence of co-morbidities and precipitating factors
  - *Note: clinical evaluation is often inaccurate*

Diagnostic Evaluation (Table 24-4)

1. Chest X-ray (CXR)
   - Initial radiographs may not show evidence of pulmonary congestion [15]
   - >25% of patients with acute HF present without CXR findings [16]
   - CXR findings include:
     - Dilated upper lobe vessels
     - Interstitial edema

TABLE 24-4

POSSIBLE ETIOLOGIES OF ACUTE HEART FAILURE

Cardiac causes	■ Progression of underlying cardiomyopathy ■ New onset/acute cardiomyopathy – Postpartum cardiomyopathy – Myocarditis – Takotsubo cardiomyopathy ■ Ischemia ■ Arrhythmias ■ Pericardial – Constriction – Tamponade ■ Valvular dysfunction – Stenosis – Regurgitation
Pressure overload	■ Severe hypertension
Volume overload	■ Renal dysfunction ■ Sodium/volume load ■ Medication non-adherence
High output	■ Thyroid disease ■ Shunts – Intracardiac – Extracardiac (A-V fistula) ■ Anemia ■ Sepsis
Miscellaneous causes	■ Infection ■ Pulmonary embolism ■ New medications/substances – NSAIDs – Corticosteroids – Cardiotoxic agents

NSAIDs nonsteroidal anti-inflammatory drugs

- Enlarged pulmonary arteries
- Pleural effusions
- Alveolar edema
- Prominent superior vena cava
- Kerley B lines

2. Electrocardiogram
   - Assess for [17]
     - Acute myocardial ischemia/infarction
     - LV hypertrophy
     - Arrhythmias
       - Atrial fibrillation
         - Present in 31% of patients presenting with acute HF
       - Heart block
       - PVC
     - Pacemaker malfunction, particularly in those patients with cardiac resynchronization therapy (CRT) devices assess for adequate biventricular pacing
3. Laboratory tests
   - Electrolytes, including sodium (Na), calcium (Ca), potassium (K), and magnesium (Mg)

- Renal function (blood urea nitrogen [BUN], Creatinine [Cr])
- Liver function tests (LFT)
- Thyroid function tests
- Complete blood count (CBC)
- Natriuretic peptides
  - Two forms have been studied and are the gold standard HF biomarkers:
    - B-type natriuretic peptide (BNP) and its precursor N-terminal proBNP (NT-proBNP)
  - Can be used when the diagnosis of acute HF is uncertain and for prognostication [12]
    - In those with acute HF, marked elevation in BNP or NT-proBNP at presentation is prognostic for in-hospital death. A BNP or NT-proBNP after HF treatment provides incremental information regarding risk for post-discharge events
  - An elevated BNP or NT-proBNP is not sufficient to make a diagnosis of acute HF, as concentrations may be elevated in states other than acute HF, including chronic, compensated HF, acute myocardial infarction, valvular heart disease, and arrhythmias; non-cardiac causes include advanced age, sepsis, and renal failure
  - A low BNP or NT-proBNP has high negative predictive value to exclude HF
    - Falsely low BNP or NT-proBNP may be seen in obesity, HFpEF, or HF involving the RV more than the LV
- Troponins
  - As coronary ischemia is an important cause of de novo HF as well as decompensation of previously stable HF, troponin should always be measured in those presenting with acute HF
  - An elevated troponin may be seen in those with acute HF in the absence of coronary ischemia, however, so correlation with the entire clinical picture is advised
  - Elevated troponin in HF is associated with worse outcome, regardless of presence of acute MI

4. Echocardiography
   - Assess LV and RV Function
     1. Preserved or reduced
     2. Ventricular structure
     3. Size
     4. Wall thickness
   - Other structural abnormalities
     5. Valvular
     6. Pericardial
     7. Atrial size
5. Cardiac catheterization [12]
   - Routine use of invasive hemodynamic monitoring is not recommended in normotensive patients with acute HF
   - When ischemia may be contributing to HF, coronary arteriography is reasonable
   - Monitoring with a pulmonary artery catheter should be performed in patients with respiratory distress or impaired systemic perfusion when clinical assessment is inadequate
   - Invasive hemodynamic monitoring can be useful for carefully selected patients with acute HF with persistent symptoms and/or when hemodynamics are uncertain (for example, in a patient who is volume-overloaded by clinical exam but renal function continues to worsen with diuretic use)

6. Endomyocardial biopsy [12]
   - Should not be performed in the routine evaluation of patients with HF
   - Endomyocardial biopsy can be useful in patients presenting with HF when a specific diagnosis is suspected that would influence therapy (for example, in a patient presenting with incessant VT and hemodynamic collapse and a diagnosis of Giant Cell Myocarditis is suspected)

INDICATIONS FOR HOSPITALIZATION

A) According to the Heart Failure Society of America (HFSA) guidelines [12], hospitalization is recommended for patients with acute HF who present with the following clinical circumstances:
   - Hypotension
   - Worsening renal function
   - Altered mentation
   - Rest dyspnea
   - Tachypnea
   - Hypoxia
   - Hemodynamically significant arrhythmias
   - New onset rapid atrial fibrillation
   - ACS

B) Consideration of hospitalization should be made if:
   - Evidence of worsening pulmonary or systemic congestion (even in the absence of dyspnea or weight gain)
   - Marked electrolyte disturbances
   - Multiple implantable cardioverter defibrillator (ICD) firings
   - Co-morbid conditions
     - Pneumonia
     - Diabetic ketoacidosis
     - Pulmonary embolus
     - Transient ischemic attack (TIA)/cerebrovascular accident (CVA)

INITIAL MANAGEMENT OF ACUTE HF SYNDROMES

Goals

- Rapidly relieve symptoms of congestion
- Identify reversible causes, particularly ischemia
- Restore hemodynamics
- Ensure adequate oxygenation
- Prevent end organ damage
- Identify patients with low output states

Management Should Be Based on Hemodynamic Profile

- Rapid assessment and initiation of therapy can be made using the following 2 × 2 diagram demonstrating the various hemodynamic profiles of patients presenting with acute HF (Fig. 24-1) [18]

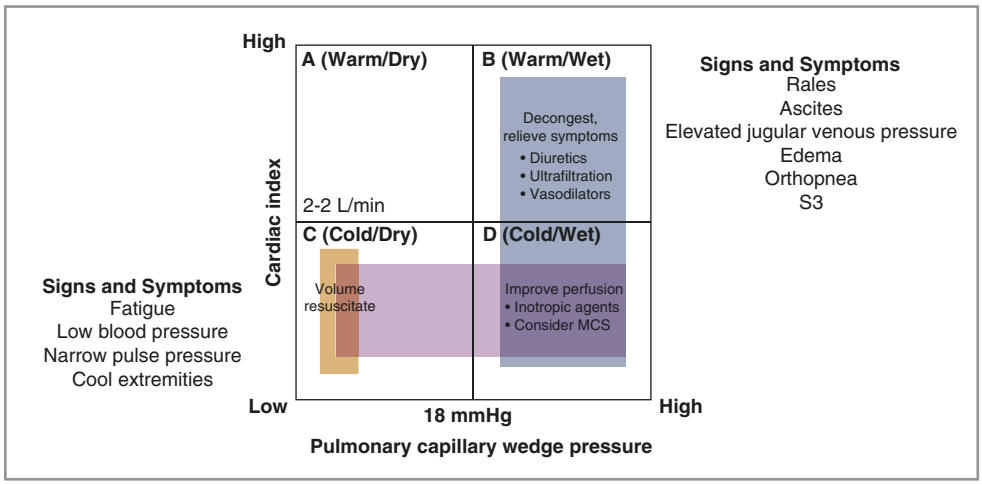

FIGURE 24-1

2 × 2 heart failure hemodynamic profiles. The diagram demonstrates the hemodynamic profiles, signs and symptoms and treatment approach of patients presenting with heart failure. Quadrant A represents the patient who is not congested and has adequate perfusion. Quadrant B represents the patient who is congested but has adequate perfusion. Quadrant C represents the patient who is congested and has poor perfusion. Quadrant D represents the patient who has a normal to low volume status and poor perfusion. Treatment approaches overlap in the low output profiles, as those patients who are congested and poorly perfused may need separate treatment approaches to both conditions. *MCS* mechanical circulatory support

After Admission

Practice guidelines recommend that the following parameters be monitored in patients hospitalized for acute HF [19]:

- Daily weight
- Daily measurement of fluid intake and output
- Vital signs (more than once daily, as indicated)
- Physical exams signs (at least daily)
  - Increased jugular venous pressure (JVP)
  - Hepatojugular reflux
  - Rales
  - Edema
  - Hepatomegaly
  - Liver tenderness
- Labs (at least daily)
  - Electrolytes
  - Renal function
- Symptom assessment (at least daily)
  - Fatigue
  - Dyspnea
  - Orthopnea
  - Paroxysmal nocturnal dyspnea or cough

Hemodynamic Monitoring (See Above)

- Studies, such as the evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness (ESCAPE) study, assessing the use of routine invasive monitoring such as pulmonary artery catheter have been essentially neutral [20]

- The routine use invasive hemodynamic monitoring is not recommended, but should be considered under the following circumstances:
  - In patients refractory to initial therapy
  - When volume status and cardiac filling pressures are unclear
  - When there is clinically significant hypotension, typically:
    - SBP <80 mmHg
    - Worsening renal function during therapy

Management of Congestion

Diuretics Are First Line Therapy in the Management of Patients with Congestion

- **Initial management consists of IV diuresis using loop diuretics** [21] **at intervals of twice to three times daily, and in some cases, continuous IV infusion**
  - Typically, **2–2.5×** home daily diuretic dose
    - For example, in a patient taking 80 mg oral furosemide daily, begin with 200 mg PO equivalent IV dosing—bumetanide 5 mg IV or furosemide 100 mg IV (1 mg of bumetanide = 20 mg of torsemide = 40 mg furosemide, roughly)
    - A response should occur within 30 min of administration
    - Diuretic dose should be escalated until desired effect occurs
    - Always watch out for electrolyte depletion (especially K and Mg) with aggressive diuresis
    - Furosemide
      - PO has an onset of 20–30 min, peak of 1–2 h and duration of 6–8 h (50% bioavailable)
      - IV has an onset of 5 min, peak of 30 min, and duration of 2 h (100% bioavailable)
  - Bolus versus continuous infusion administration of loop diuretics have similar outcomes [22]
  - Thiazide diuretics (e.g. chlorothiazide or metolazone) can be added when there is suboptimal response to loop diuretics, as they:
    - Block reabsorption of distal tubule Na
    - Antagonize renal adaptation to chronic loop diuretic treatment
    - Improve diuretic resistance with rebound Na retention
  - Caution should be exercised with aggressive diuresis, including sequential nephron blockade, as this may augment hypotensive effects of angiotensin converting enzyme inhibitors (ACEi)/angiotensin II receptor blockers (ARB)/angiotensin receptor-neprilysin-inhibitors (ARNI)

Ultrafiltration

- Consider use in patients who are refractory to IV diuretics [23]
- Uses a small extracorporeal circuit connected to the patient via peripheral or central venous access
- Patients with hypotension may not tolerate ultrafiltration
- The Ultrafiltration versus IV Diuretics for Patients Hospitalized for Acute Decompensated CHF (UNLOAD) trial [24] compared ultrafiltration to conventional diuretic therapy
  - At 48 h, compared to diuretics, ultrafiltration produced:
    - A greater reduction in weight
    - Greater fluid loss
    - Similar changes in serum creatinine

Non-invasive Positive Pressure Ventilation

- Can be considered in patients with pulmonary edema and severe dyspnea
- Improves dyspnea
- Probably has no impact on mortality or rate of intubation [25]

Vasodilator Therapy (Nitroglycerin, Nitroprusside, Nesiritide)

- Recommended for rapid symptom relief in those with pulmonary congestion or hypertension
- Use when symptoms persist despite aggressive diuretic and standard oral regimens
- Do not use if the patient has symptomatic hypotension

Nitroglycerin

- Provides venodilation, and thus reduces preload
- May reduce coronary ischemia
- At higher doses, provides reduction in systemic afterload
- Tachyphylaxis can occur
- Contraindicated in patients using phosphodiesterase (PDE)-5 inhibitors such as sildenafil

Nitroprusside

- Indicated when a marked reduction in afterload is desired
  - Hypertensive emergency
  - Severe mitral regurgitation
  - Severe aortic insufficiency
  - Acute ventricular septal rupture
  - Cardiogenic shock due to LV failure
- Potent vasodilation, equal venodilation, and arterial dilation
- Accumulation of the metabolites cyanide and thiocyanate may occur and in rare cases can be lethal; drug should only be administered for a limited period (24–48 h)
  - Thiocyanate is life-threatening when levels reach ~200 mg/L. Routine monitoring of plasma thiocyanate levels is recommended in patients with normal renal function when cumulative sodium nitroprusside doses exceed 7 mg/kg/day
- Use caution if renal or hepatic impairment
- May trigger reflex tachycardia
- Rebound vasoconstriction can occur upon discontinuation

Nesiritide

- Recombinant form of human BNP
- Reduces pulmonary capillary wedge pressure (PCWP), systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR)
- Increases cardiac output at higher doses
- Inconsistent effects on urine output, with some studies showing an increase and others with no effect [26]
- The Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF) trial [27] showed no difference in death or rehospitalization but more hypotension from nesiritide use

Support Hemodynamics

Inotropic Therapy (Table 24-5)

Vasodilating inotropes: milrinone, dobutamine
Vasopressor inotropes: dopamine, norepinephrine

- Consider use in patients who are non-responsive to or intolerant of vasodilators and diuretics
- No evidence that inotropic agents benefit patients without evidence of poor perfusion
- Short term therapy using inotropic agents has been associated with significantly higher in hospital mortality than vasodilator therapy [28, 29]

TABLE 24-5

COMPARISON OF VARIOUS VASODILATORS AND INOTROPIC AGENTS USED FOR ACUTE HEART FAILURE

MEDICATION (USUAL DOSE)	MECHANISM OF ACTION	PERIPHERAL VASODILATION	PERIPHERAL VASOCONSTRICTION	INOTROPY	CHRONOTROPY	PULMONARY VASODILATION	ARRHYTHMOGENIC
Nitroglycerin (5–10 μg/min, max 200 μg/min)	Stimulated cGMP production through activation of guanylyl cyclase	+	–	–	–	+	–
Nitroprusside (0.3–3 μg/kg/min, max 10 μ/kg/min)	Interacts with oxyhemoglobin, forming methemoglobin leading to cyanide ion and NO release	++	–	–	–	+	–
Nesiritide (0.01–0.03 μg/kg/min)	Recombinant BNP, binds to guanylate cyclase receptor, leading to increased cGMP	+	–	–	–	+	–
Milrinone (0.375–0.75 μg/kg/min)	Inhibits phosphodiesterase III	++	–	+	–	+	+
Dobutamine (2.0–20 μg/kg/min, max 40 μg/kg/min)	Stimulates β1 andβ2 receptors	+	–	+	+	–	+
Dopamine (2.0–20 μg/kg/min, max 50 μg/kg/min)	Dose dependent activation of D1, β1, and α1	–	+	+	+	–	+
Norepinephrine (0.01–3 μg/kg/min)	Potent α1 agonist, modest β1,β2 agonist	–	+	+	+	–	+
Epinephrine (0.01–0.10 μg/kg/min)	Stimulates β1,β2, and α1 receptors	–	+	+	+	–	+

cGMP cyclic guanosine monophosphate, *NO* nitric oxide, *BNP* B-type natriuretic peptide

- Should be reserved for patients with hemodynamic instability or evidence of poor cardiac output and end organ hypoperfusion ("wet and cold"):
  - Systemic hypotension
  - Renal dysfunction

Milrinone

- Inhibits PDE-3, preventing degradation of cyclic adenosine monophosphate (cAMP)
  - Increased cAMP leads to vasodilation
- Reduces RV and LV pre-load and afterload
- Potent pulmonary vasodilator
- Can cause marked hypotension
- Does not act via adrenergic receptors thus may be more desirable in patients on chronic beta blocker therapy
- Increased incidence of atrial and ventricular arrhythmias [30]
- Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbation of Chronic Heart Failure (OPTIME-CHF) in which hospitalized patients were randomized to a 48-h infusion of intravenous milrinone or placebo demonstrated that administration of milrinone was associated with:
  - A higher rate of early treatment failure
  - More sustained hypotension
  - New atrial arrhythmias
  - Had a higher composite rate of death or rehospitalization
  - Patients with an ischemic etiology that were treated with milrinone had a higher 60-day mortality

Dobutamine

- Synthetic catecholamine
- Nonselective beta-1 and beta-2 adrenergic receptor agonist
- Positive inotropy and chronotropy
- Decreases afterload
- Increases heart rate, stroke volume and cardiac output
- Dose-related increase in risk for atrial and ventricular arrhythmia

Dopamine

- Dose-dependent activation of D1, beta-1, and alpha-1 receptors
- Low dose (2 mcg/kg/min)—activates vascular D1 receptors (coronary/renal/mesenteric)
- Moderate dose (2–5 mcg/kg/min)—binds to beta-1 receptors in the heart leading to inotropy
- High doses (5–15 mcg/kg/min)—activates alpha-1 receptors
- Dose-related increase in risk for atrial and ventricular arrhythmia

Mechanical Circulatory Support

In patients who have a persistent low output state ("cold") despite medical management, immediate consideration should be made for initiation of mechanical circulatory support

- Conditions in which MCS is generally accepted:
  - Fulminant myocarditis with cardiogenic shock
  - Acute hemodynamic compromise

    - Cardiopulmonary arrest
    - Cardiogenic shock
  - High risk percutaneous coronary interventions
  - In patients who are waiting for heart transplantation

The devices below specifically address acute needs and are for short term support only, and can be used for days to weeks. Long term devices can be used in patients waiting for transplant and are discussed in Chapter 25. A variety of devices are available, the ones most commonly used in clinical practice will be discussed here

Intraaortic Balloon Counterpulsation

- Most well studied
  - Data are mixed regarding effectiveness in those with cardiogenic shock after acute MI
- Increases coronary blood flow, decreases myocardial demand and increases oxygen supply, increases cardiac output
- Contraindications:
  - Aortic dissection
  - Severe aortic regurgitation (AR)
  - Severe peripheral arterial disease (PAD) (occlusive aortoiliac disease)

Percutaneous Ventricular Assist Devices (VAD)

- Impella
  - Uses a miniature impeller pump that is placed across the aortic valve into the LV; draws blood out of the ventricle and ejects blood through the ascending aorta
  - Can pump 2.5 or 5.0 L/min depending on size of pump used
  - Requires systemic anticoagulation
  - Can be used to vent the LV in patients on extracorporeal membrane oxygenation (ECMO) support
  - Contraindications—mechanical aortic valve, moderate-severe aortic valve disease, LV thrombus, moderate-severe peripheral arterial disease
- Tandem heart [31]
  - Left atrial-to-femoral artery bypass system using:
    - Transseptal cannula
    - Arterial cannula
    - Centrifugal blood pump
  - Provides flow rates up to 4.0 L/min
  - Requires systemic anticoagulation
  - Contraindications—ventricular septal defect, RV failure, left atrial thrombus, aortic insufficiency, aortic dissection, moderate-severe peripheral arterial disease
- ECMO [32]
  - Provides total circulatory support
  - Uses a centrifugal pump and membrane oxygenator
  - Can be placed percutaneously
  - Supports both the left and right ventricle
  - Requires systemic anticoagulation
  - Two types: venoarterial and venovenous
    - Only venoarterial ECMO provides hemodynamic support
    - Both venoarterial and venovenous provide respiratory support

– Contraindications—age >75 years, irreversible pulmonary or cardiac disease, metastatic malignancy, significant brain injury, end-stage renal/liver/lung disease, contraindication to anticoagulation

Complications of Mechanical Circulatory Support

- Infection
- Thrombosis
- Thrombocytopenia
- Hemolysis
- Bleeding
- CVA

MAINTENANCE THERAPY FOR HF

Once the acute episode has been initially managed, focus should shift toward education of the patient and initiation of medications that will promote neurohormonal blockade and prolonged survival (see Chap. 25)

Major society guidelines recommend the following agents for patients who have HF with reduced systolic function [12]:

A. Beta blocker therapy [33–35]

- Approved agents for HFrEF: bisoprolol, carvedilol, and metoprolol succinate (XL)
- For those taking beta blockers on admission, in absence of cardiogenic shock (i.e. the typical "wet/warm" presentation): continue without dose adjustment until decongested
- For those not taking beta blockers on admission: avoid initiation during acute congestion but then initiate low dose prior to discharge
- For both established or de novo HF: avoid use of beta blockers in those with shock (i.e. "cold") presentations
- Slowly uptitrate as an outpatient

B. ARNI [12]

- No data on inpatient initiation but should be considered in all patients with an LVEF <40% and NYHA II–III symptoms on an outpatient basis; should replace ACEi/ARB in outpatient setting

C. ACEi [36–38]

- Should be initiated prior to discharge in all patients with LV systolic dysfunction and slowly uptitrated
- Aggressive titration prior to stabilization of low output states can lead to decompensation
- Contraindications—pregnancy, previous angioedema, previous hypersensitivity, bilateral renal artery stenosis, hyperkalemia (K >5.5)

D. ARB [39]

- Administer to those patients intolerant to ACEi
- Similar contraindications to ACEi

E. Aldosterone antagonists [40]

- In patients already receiving ACEi/ARB/ARNI with symptomatic HF (NYHA class II–VI)
- Use with caution in those with significant renal dysfunction (serum creatinine ≤2.5 mg/dL in men and ≤2.0 mg/dL) or a history of hyperkalemia
- Initiation during acute decompensation of HF is relatively poorly studied

F. Hydralazine + Isosorbide dinitrate

- Certain populations [41]
  - Consider if intolerant to ACEi/ARB/ARNI
  - Significant increased survival in self-described African Americans in the Veterans Administration Cooperative Vasodilator—Heart Failure Trial (V-HeFT) trial
  - Initiation during acute decompensation of HF is relatively poorly studied, but probably safe

G. ICD [42, 43]

- Consider in patients with LVEF ≤35% (ischemic or non-ischemic) and persistent NYHA class II–III HF despite maximum tolerable medical therapy
- For de novo acute HF, ICD implantation should be deferred for up to 90 days to allow for initiation and titration of GDMT and promote recovery of LV function

H. CRT [44]

- Consider in patients with LVEF ≤35% (ischemic or non-ischemic) and persistent NYHA class III or ambulatory class IV HF despite maximum tolerable medical therapy and a QRS duration ≥120 ms
- For de novo acute HF, CRT should be deferred to allow for initiation and titration of GDMT and promote recovery of LV function

QUESTIONS

1. A 28-year-old previously healthy gentleman is brought to the emergency department by his wife after she noticed mild confusion, weakness, fatigue, and dyspnea. She also notes that he has had a persistent nocturnal cough for the past 7 days. Approximately 10 days prior, he developed fevers, chills and myalgias; this was accompanied by a nonproductive cough and mild dyspnea. His fevers and myalgias resolved spontaneously, but she has noted a progressive decline in his energy level since. They have a 4-year-old son, and he has had difficulty keeping up with him on the playground. He has no prior medical history, and does not take any medications or dietary supplements. On exam, he is obtunded. VS: Afebrile. BP 78/60 mmHg, HR 118. Pulse oximetry 93% on RA. Height: 69 inches, weight: 165 pounds. Extremities are cool. There is no lower extremity edema. Heart sounds are regular with an audible S1 and S2. There is an S3 gallop noted. There is a faint holosystolic murmur at the LV apex which does not radiate. His neck veins are distended to 15 cm of water. Laboratory studies reveal a normal CBC, normal TSH, BUN 35 mg/dL, Creatinine 1.95 mg/dL, AST 1235 U, ALT 1412 U, Lactic acid 7.6, TnI 0.53 ng/mL (normal <0.03), NT-proBNP 23,055 pg/mL. ECG: Sinus tachycardia. CXR shows a mildly enlarged cardiac silhouette and dilated upper lobe vessels.

   Initial management of the patient includes all the following EXCEPT:
   A. Oxygen therapy via nasal cannula
   B. IV enalaprilat
   C. IV dobutamine
   D. Consideration of placement of a PA line
   E. Loop diuretics

   Answer: B. The patient has clinical evidence of hemodynamic instability, including, hypotension, sinus tachycardia, change in mental status, lactic acidosis and evidence of end organ dysfunction. Initial management should be aimed at restoration of hemodynamics and relief of symptoms. Initiation of an ACEi during profound shock could lead to worsening hemodynamics, and preferred agents would be those named at improving inotropy.

2. Regarding the patient in question 1, you choose to empirically start dopamine, but despite escalating doses, the patient remains cool, systolic blood pressure remains below 80 mm Hg, and the patient becomes anuric. He developed acute respiratory distress with worsening confusion, and is intubated. A pulmonary artery catheter is emergently placed, and demonstrates the following hemodynamics: RA 18 mmHg, PA 35/20 mmHg MPAP 25 mmHg, PCWP 20 mmHg, mixed venous oxygen saturation 34%, cardiac output 2.1 L/min. A bedside echocardiogram is performed and shows severe biventricular function, with an LVEF of 8%.

   What would be the next best option for this patient to support his hemodynamics?
   A. IV Nitroglycerin
   B. Ultrafiltration
   C. Placement of an intra-aortic balloon pump
   D. Placement of ECMO
   E. Nesiritide

   Answer: D. This patient has profound cardiogenic shock. It is unlikely that pharmacologic agents will be enough to support his hemodynamics. An intra-aortic balloon pump would provide some support to the left heart, but he has severe right ventricular

failure as well, evidenced by his high right atrial pressure and high PCWP; they are essential equivalent. Vasodilators are contraindicated due to hypotension. ECMO provides total circulatory support and is the appropriate choice in patients who have evidence of severe right ventricular failure or who have significant hypoxia related to their LV failure. Ultrafiltration can be considered after the patient is placed on ECMO.

3. Is an endomyocardial biopsy reasonable in this setting?
   A. Yes
   B. No

   Answer: A. Endomyocardial biopsy is indicated in patients who present with acute onset of heart failure symptoms of less than 2 weeks' duration and hemodynamic compromise. It is an ACC/AHA class IB indication [12].

4. Which of the following is the most likely diagnosis in this patient:
   A. Acute myocardial infarction
   B. Pulmonary embolism
   C. Chronic active myocarditis
   D. Fulminant myocarditis
   E. Hypovolemic shock

   Answer: D. This patient has fulminant myocarditis, which is characterized by acute onset of illness and profound cardiogenic shock. If a patient with fulminant myocarditis is recognized early on and aggressive treatment is administered, more than 90% of patients will develop a full recovery [45], with minimal long-term sequela. Fulminant myocarditis, when recognized and treated early as an excellent prognosis. In contrast to patients with acute myocarditis, who usually present with a less profound symptoms, and may go on to develop chronic, stable congestive HF, and can sometimes progressed to end-stage cardiomyopathy requiring cardiac transplantation. The differential diagnosis of the patients who presents with new onset, acute HF with cardiogenic shock include acute myocardial infarction, necrotizing eosinophilic myocarditis, giant cell myocarditis, peripartum cardiomyopathy, and sarcoidosis. Patients with fulminant myocarditis typically present with a flulike prodrome 2–4 weeks prior and frequently present with NYHA class IV symptoms and physical exam findings consistent with cardiogenic shock and hemodynamic compromise. This contrasts with those who have acute, non-fulminant myocarditis, who typically present with milder symptoms. With aggressive management, most patients with fulminant myocarditis will experience complete recovery of their ventricular function within several weeks after onset of symptoms [46].

5. A 65-year-old woman with a 4-year history of dilated cardiomyopathy, LVEF of 20–25%, presents with a progressive weight gain of approximately 18 pounds, worsening dyspnea on exertion and progressive lower extremity edema. She now has dyspnea after walking several steps. She has no other medical history. She adheres to a sodium restricted diet and drinks no more than 2 L of fluids per day. She has not missed any medications, and records when medications are taken. She does her own cooking and avoids processed foods. Denies fevers or chills. Current medications are lisinopril 5 mg daily, carvedilol 12.5 mg PO BID, furosemide 80 mg PO BID and spironolactone 25 mg PO Daily. VS: Afebrile, BP 128/65 mmHg, HR 98, Pox 95% on RA. CXR demonstrates mild pulmonary edema. ECG shows atrial fibrillation with a ventricular rate of 92 beats per min, her QRS duration is 102 ms. She has no history of atrial fibrillation.

   What is the most likely cause of her acute decompensation?
   A. Atrioventricular dyssynchrony
   B. Intraventricular dyssynchrony
   C. Dietary indiscretion
   D. Pneumonia
   E. Medication noncompliance

   Answer: A. Patients with LV systolic dysfunction and chronic HF often do not tolerate the atrioventricular dyssynchrony that occurs when atrial fibrillation develops, and worsening of HF symptoms occur. Management should be aimed at decongestion followed by restoration of sinus rhythm.

6. Which of the following statements regarding IV milrinone is false:
   A. It is a more potent pulmonary vasodilator than dobutamine
   B. It has been shown to decrease morbidity and length of hospital stay
   C. It prevents the breakdown of cAMP
   D. It has arrhythmogenic potential
   E. It increases myocardial oxygen consumption

   Answer: B. The OPTIME-CHF trial showed that treatment with milrinone was associated with a (non-significant) higher number of deaths, and no difference in length of hospital stay compared to placebo.

7. A 59-year-old gentleman presents for evaluation of progressive dyspnea, orthopnea, and lower extremity edema. He has a history of hypertension and complete heart block and had a dual chamber pacemaker placed approximately 1 year ago. He denies anginal symptoms. Exam reveals an S3 gallop, III/VI holosystolic murmur at the apex, distended neck veins and 2+ bilateral lower extremity edema. His ECG demonstrates 100% VVI pacing at 60 beats per min. A stress test was previously ordered by his primary care physician which revealed no evidence for ischemia, however, his LVEF was 28%. Current medications are aspirin and lisinopril.

   After he is treated with furosemide and decongested, which of the following medications should be started next?
   A. Digoxin
   B. Verapamil
   C. Bisoprolol
   D. Isosorbide mononitrate
   E. Hydralazine

   Answer: C. Initiation of beta blocker therapy in patients with HFrEF is a class IA recommendation per the ACC/AHA guidelines, and should be initiated once the patient is no longer acutely decompensated. Bisoprolol has been studied in the HFrEF population. Digoxin [47] does not confer a survival advantage and should be reserved for patients who are on optimal HF therapy and who have persistent NHYA class III, or in patients with atrial fibrillation in need of more optimal rate control. Verapamil should not be used in patients with HFrEF; its negative inotropic effects could lead to acute decompensation. Isosorbide mononitrate and hydralazine have been shown to be effective in certain populations (i.e. African Americans), but these agents would not be the appropriate choice as first line therapy.

8. A 56-year-old woman with a history of hypertension and PAD is brought to the emergency department by paramedics after awakening with acute dyspnea. Upon arrival, she is tachypneic and

hypoxic, and is emergently intubated. VS upon arrival: BP 230/118 mmHg, HR 97, Pox 84% on 2 L nasal cannula, respiratory rate 28. Exam reveals elevated JVP, regular rhythm and an S4 gallop. Lungs have diffuse crackles. Before intubation, she reported no dietary indiscretions. A 2-D echocardiogram done 6 months prior showed normal LV function with LV hypertrophy, normal RV function and no valvular abnormalities. Labs: Na 135 mmol, K 4.1 mg/dL, BUN 35 mg/dL, Cr 2.75 mg/dL. CBC, troponin and LFT's are normal. CXR shows diffuse alveolar infiltrated and peribronchial cuffing. ECG shows normal sinus rhythm with LV hypertrophy and no ischemic changes or evidence of prior infarction.

As part of her evaluation, which of the following tests should be ordered to identify the etiology of her decompensation?

A. Coronary angiogram
B. Renal duplex Doppler ultrasound
C. V/Q Scan
D. Cardiac MRI
E. Bronchoscopy

Answer: B. This patient has renal artery stenosis and renovascular hypertension. She likely has diastolic dysfunction in the setting of longstanding hypertension. She developed flash pulmonary edema which is more common in patients with bilateral renal artery stenosis than unilateral stenosis [48].

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