VITEBSK STATE MEDICAL UNIVERSITY

CHAIR OF THE FACULTY THERAPY

**FACULTY THERAPY**

(Methodics work out for foreign students, studying the course of faculty therapy)

Part 1

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**CARDIOGENIC SHOCK**

Cardiogenic shock is characterized by a decreased pumping ability of the heart that causes a shocklike state with inadequate perfusion to the tissues. It most commonly occurs in association with, and as a direct result of, acute ischemic damage to the myocardium. Although shock is considered to be a clinical diagnosis, useful physiologic parameters include a systolic blood pressure less than 80 mm Hg, a cardiac index less than 1.8 L/min/m2, and a pulmonary capillary wedge pressure greater than 18 mm Hg.

**Frequency**

Cardiogenic shock occurs in approximately 5-10% of patients with AMI.

Mortality rates for medically treated patients with AMI and cardiogenic shock exceed 70%.

Outcomes significantly improve only when rapid revascularization can be achieved.

Rates vary depending on the procedure (eg, percutaneous transluminal coronary angioplasty, stent placement, thrombolytic therapy), but they have been reported to be as low as 30-50%.

**Causes**

The vast majority of cases of cardiogenic shock are due to acute myocardial ischemia.

Other related causes include the following:

Toxicity to drugs such as Adriamycin

Infectious and/or inflammatory processes (eg, acute myocarditis)

Pharmacologic agents (eg, beta-blockers, calcium-channel blockers)

Mechanical causes (eg, valvular dysfunction, tamponade, cardiomyopathy)

Risk factors for the development of cardiogenic shock include preexisting myocardial damage or disease (eg, diabetes, advanced age, previous AMI), AMI (eg, Q-wave, large, or anterior wall AMIs), and dysrhythmia.

**Pathophysiology**

 The most common initiating event in cardiogenic shock is acute myocardial infarction (AMI). Dead myocardium does not contract, and once more than 40% of the myocardium is involved, cardiogenic shock may result. On a mechanical level, a marked decrease in contractility reduces the ejection fraction and cardiac output. These lead to increased ventricular filling pressures, cardiac chamber dilatation, and ultimately univentricular or biventricular failure that results in systemic hypotension and/or pulmonary edema.

Cardiogenic shock occurs with a cascade of events and positive feedback loops. Hypoperfusion results in the release of endogenous substances including myocardial depressant factor, histamine, bradykinin, thromboxane, cytokines, leukotrienes, platelet-activating factor, and lactic acids. These substances further inhibit cardiac function, thereby increasing myocardial depression and worsening the shock state; this, in turn, increases the release of these substances. An extensive body of literature supports the existence of endogenously produced myocardial depressant factor. Myocardial depressant factor is a low-molecular-weight protein that is believed to be released from pancreatic lysosomes during shocklike states. Myocardial depressant factor causes direct myocardial depression by an unknown mechanism.

Similar events occur on a more macro level as well. Myocardial ischemia causes a decrease in contractile function, which leads to left ventricular dysfunction and decreased arterial pressure; these, in turn, exacerbate the myocardial ischemia. The end result is a vicious cycle that leads to severe cardiovascular decompensation.

**CLINICAL**

**History**

Most patients with cardiogenic shock have an AMI and, therefore, present with the constellation of symptoms of acute cardiac ischemia (eg, chest pain, shortness of breath, diaphoresis, nausea and vomiting). Patients experiencing cardiogenic shock also may present with pulmonary edema and presyncopal or syncopal symptoms.

**Physical**

 Physical examination often reveals that the patient is in the middle of an AMI. Patients are in frank distress, are profoundly diaphoretic, and have severe shortness of breath and chest pain.

Clinical assessment begins with attention to the ABCs and vital signs.

Although the patient may eventually require endotracheal intubation, the airway usually is patent initially.

Breathing may be labored, with audible coarse crackles or wheezing.

As in any shocklike state, circulation is markedly impaired.

Patients present with marked tachycardia, cool and clammy extremities, poor peripheral pulses, and varying degrees of end-organ dysfunction (eg, decreased mental function and urinary output).

Initial vital sign assessment should include BP measurements in both arms to evaluate possible thoracic aortic aneurysm or dissection. Vital signs should be regularly updated with continuous noninvasive physiologic monitoring.

Neck examination may reveal jugular venous distention, which may be prominent. This finding is evidence of right ventricular failure.

With increasing ventricular dysfunction, florid pulmonary edema and severe hypotension may develop.

Auscultation of the chest may reveal varying degrees of congestive heart failure.

Careful cardiac examination may reveal mechanical causes of cardiogenic shock that are readily amenable to surgical intervention; without needed surgery, the mortality rate is dismal.

Causes amenable to surgery include papillary rupture, valvular dysfunction, myocardial wall or septal rupture, cardiac tamponade, and aortic aneurysm.

Loud murmurs may indicate a valvular dysfunction, whereas muffled heart tones with jugular venous distention and pulsus paradoxus may suggest tamponade.

**Lab Studies**

No one test is completely sensitive or specific for cardiogenic shock. Laboratory studies are directed at the potential underlying cause.

In most cases, the usual workup includes tests of all of the following, which usually are assessed in cases of suspected cardiac ischemia:

Cardiac enzymes (eg, creatine kinase, troponin, myoglobin)

CBC

Electrolytes

Coagulation profile (eg, prothrombin time, activated partial thromboplastin time)

An ABG test may be useful to evaluate acid-base balance, because acidosis can have a particularly deleterious effect on myocardial function.

**Imaging Studies**

* An ECG is helpful if it reveals an acute injury pattern consistent with an AMI. A normal ECG, however, does not rule out the possibility. ECGs are often most helpful when they can be compared with previous tracings.
* An echocardiogram obtained in the ED can be extremely useful.

It may be diagnostic and reveal akinetic or dyskinetic areas of ventricular wall motion.

It may reveal surgically correctable causes, such as valvular dysfunction and tamponade.

A portable chest radiograph is helpful because it gives an overall impression of the cardiac size, pulmonary vascularity, and coexistent pulmonary pathology, and it provides a rough estimate of mediastinal and aortic sizes in the event that an aortic etiology is being considered.

**Procedures**

Placement of a central line may facilitate volume resuscitation, provide vascular access for multiple infusions, and allow invasive monitoring of central venous pressure and pulmonary capillary wedge pressure. Although not necessary for the diagnosis of cardiogenic shock, invasive monitoring with a pulmonary artery catheter may be helpful in guiding fluid resuscitation in situations in which left ventricular preload is difficult to determine.

**TREATMENT**

Prehospital Care

Prehospital care is aimed at minimizing any further ischemia and shock.

All patients require intravenous access, high-flow oxygen administered by mask, and cardiac monitoring.

Further care is supportive and similar to that outlined below. Care depends on the provider's level of expertise and ability to perform certain maneuvers.

Emergency Department Care

ED care is aimed at making the diagnosis, preventing further ischemia, and treating the underlying cause. Treatment begins with assessment of the ABCs.

Once the ABCs are managed and while supportive measures are under way, an early focus of treatment should be reversing the underlying cause, means revascularization in most cases. The method varies according to locale and institution. If a catheterization laboratory is readily available, percutaneous transluminal coronary angioplasty with or without stent placement may be performed to achieve a better outcome. If no catheterization laboratory is available, the next best option is thrombolytic therapy, if no contraindications are present.

Supportive care and the prevention of further ischemia have various implications in these patients. They require oxygen, intravenous fluids, and close cardiac and hemodynamic monitoring. Providing high-flow oxygen, decreasing myocardial oxygen consumption, and increasing perfusion of the ischemic myocardium may reduce ischemia. Extreme heart rates should be avoided because they may increase myocardial oxygen consumption, increase infarct size, and further impair the pumping ability of the heart.

Pharmacologic interventions may be advisable, depending on the circumstance.

1. Nitrates and/or morphine are advised for the management of pain; however, they must be used with caution because these patients are in shock, and excessive use of either of these agents can produce profound hypotension.
2. Dopamine may provide vasopressor support. With higher doses, it has the disadvantage of increasing heart rate and myocardial oxygen consumption.
3. Dobutamine, inamrinone (formerly amrinone), or milrinone may provide inotropic support. In addition to their positive inotropic effects, inamrinone and milrinone have a beneficial vasodilator effect, which reduces preload and afterload.
4. Beta-blockers have been shown to be cardioprotective and should be used unless contraindicated (eg, heart rate <50 beats per minute or systolic BP <90 mm Hg).

The use of an intra-aortic balloon pump (IABP) is recommended for cardiogenic shock not quickly reversed with pharmacological therapy. It is also recommended as a stabilizing measure combined with thrombolytic therapy when angiography and revascularization are not readily available. Counterpulsation of the IABP reduces left ventricular afterload and improves coronary artery blood flow. Although this procedure is generally not performed in the ED, planning is essential, and early consultation with a cardiologist regarding this option is recommended. Although complications may occur in up to 30% of patients, extensive retrospective data support its use.

**Further Inpatient Care**

All patients require admission to an intensive care setting, which may involve emergent transfer to the cardiac catheterization suite, critical care transport to a tertiary care center, or internal transfer to the ICU.

**Complications**

Cardiopulmonary arrest

Dysrhythmia

Renal failure

Multisystem organ failure

Ventricular aneurysm

Thromboembolic sequelae

Stroke

Death

**Prognosis**

The prognosis is universally poor.

The mortality rate is more than 70% in patients treated medically. At best, the rate is 30-50% in those in whom surgical reperfusion is achieved.

**CARDIOGENIC PULMONARY EDEMA**

Pulmonary edema refers to extravasation of fluid from the pulmonary vasculature into the interstitium and alveoli of the lung. The formation of pulmonary edema may be caused by 4 major pathophysiologic mechanisms:

(1) increased capillary hydrostatic pressure,

(2) increased capillary permeability,

(3) decreased plasma oncotic pressure,

(4) lymphatic obstruction.

Cardiogenic pulmonary edema (CPE) is defined as development of pulmonary edema as a consequence of increased capillary hydrostatic pressure secondary to elevated pulmonary venous pressure. CPE reflects the accumulation of fluid with a low-protein content in the lung interstitium and alveoli, when left ventricular (LV) venous return exceeds LV output.

Increased hydrostatic pressure leading to pulmonary edema may result from many causes, including intravascular volume administration that is too excessive, pulmonary venous outflow obstruction (eg, mitral stenosis or left atrial myxoma), or LV failure secondary to systolic or diastolic dysfunction of the left ventricle. CPE leads to progressive deterioration of alveolar gas exchange and acute respiratory failure. Without prompt recognition and treatment, patients can deteriorate rapidly.

**Mortality/Morbidity**

Assigning a figure for in-hospital mortality is difficult because the causes and the severity vary considerably. In a high-acuity setting, in-hospital death may occur in up to 15-20% of cases.

Severe hypoxia may result in myocardial ischemia or infarction. Mechanical ventilation may be required if medical therapy is delayed or unsuccessful. Endotracheal intubation and mechanical ventilation also are associated with their own risks, including aspiration (during the process of intubation), mucosal trauma (more common with nasotracheal intubation than orotracheal intubation), and barotrauma.

**Causes**

* Acute exacerbation of chronic LV failure (systolic dysfunction): Chronic LV failure usually is the result of congestive heart failure (CHF) or a cardiomyopathy. Causes of acute exacerbations include the following:
* Acute myocardial infarction or ischemia
* Patient noncompliance with dietary restrictions (eg, dietary salt)
* Patient noncompliance with medications (eg, diuretics)
* Severe anemia
* Sepsis
* Thyrotoxicosis
* Myocarditis
* Myocardial toxins (eg, alcohol, chemotherapeutic agents such as Adriamycin)
* Nonischemic acute mitral regurgitation (ruptured chordae tendineae): This can cause acute severe systemic hypertension (diastolic dysfunction), resulting in CPE.
* Dysrhythmias: New-onset rapid atrial fibrillation and ventricular tachycardia can be responsible for the development of CPE.
* Acute left-sided valvular heart disorders: The most common valvular disorders contributing to CPE include aortic stenosis, acute aortic regurgitation, and acute mitral regurgitation secondary to papillary muscle dysfunction or ruptured chordae tendineae.
* Fluid overload in patients with renal failure: CPE can occur in patients with hemodialysis-dependent renal failure, often as the result of noncompliance with dietary restrictions or noncompliance with hemodialysis sessions.
* Acute myocardial infarction: A large myocardial infarction that produces infarction of at least 25% of the left ventricle can produce de novo CPE (Killip class III and IV).
* Other possible etiologies and contributing factors include the following:
* Mitral stenosis
* Peripartum cardiomyopathy
* Severe diastolic dysfunction
* Restrictive cardiomyopathy
* Constrictive pericarditis
* Pericardial tamponade
* Severe myocardial contusion

**Pathophysiology**

CPE is caused by elevated pulmonary capillary hydrostatic pressure leading to transudation of fluid into the pulmonary interstitium and alveoli. Increased left atrial pressure increases pulmonary venous pressure and pressure in the lung microvasculature, resulting in pulmonary edema.

Mechanism of cardiogenic pulmonary edema

Pulmonary capillary blood and alveolar gas are separated by the alveolar-capillary membrane, which consists of 3 structurally different anatomical layers:

(1) the capillary endothelium;

(2) the interstitial space, which may contain connective tissue, fibroblasts, and macrophages;

(3) the alveolar epithelium. Exchange of fluid normally occurs between the vascular bed and the interstitium. Pulmonary edema occurs when the net flux of fluid from the vasculature into the interstitial space is increased. The Starling relationship determines fluid balance between the alveoli and vascular bed. Net flow of fluid across a membrane is determined by the following equation:

Q = K(Pcap - Pis) - l(Pcap - Pis)

Q is net fluid filtration.

K is a constant called the filtration coefficient.

Pcap is capillary hydrostatic pressure, which tends to force fluid out of the capillary.

Pis is hydrostatic pressure in the interstitial fluid, which tends to force fluid into the capillary.

l is the reflection coefficient, which indicates the effectiveness of the capillary wall in preventing protein filtration.

Pcap is the colloid osmotic pressure of plasma, which tends to pull fluid into the capillary.

Pis is the colloid osmotic pressure in the interstitial fluid, which pulls fluid out of the capillary.

The net filtration of fluid may increase with changes in different parameters of the Starling equation. CPE predominantly occurs secondary to either left atrial outflow impairment or LV dysfunction. In order for pulmonary edema to develop secondary to increased pulmonary capillary pressure, the pulmonary capillary pressure must rise to a level that is higher than the plasma colloid osmotic pressure. Normally, the pulmonary capillary pressure is 8-12 mm Hg and colloid osmotic pressure is 28 mm Hg. High pulmonary capillary wedge pressure (PCWP) may not always be evident in established CPE because the capillary pressure may have returned to normal at the time the measurement is performed.

Lymphatics

The lymphatics play a significant role in maintaining an adequate fluid balance in the lungs by removing solutes, colloid, and liquid from the interstitial space at a rate of approximately 10-20 mL/h. An acute rise in pulmonary arterial capillary pressure (ie, to >18 mm Hg) may result in increased filtration of fluid into the lung interstitium, but the lymphatic removal does not increase correspondingly. In contrast, in the presence of chronically elevated left atrial pressure, lymphatic removal can be as high as 200 mL/h, protecting the lungs from development of pulmonary edema.

**Stages**

The progression of fluid accumulation in CPE can be identified by 3 distinct physiological stages, as follows:

Stage I: Fluid and colloid shift into the lung interstitium from pulmonary capillaries, but an increase in lymphatic outflow efficiently removes the fluid.

Stage II: The continuing filtration of liquid and solutes overpowers the pumping capacity of the lymphatics. The fluid initially collects in the more compliant interstitial compartment, which generally surrounds bronchioles, arterioles, and venules in the dependent zones.

Stage III: As fluid filtration continues to increase and the filling of loose interstitial space occurs, fluid accumulation in the less compliant interstitial space takes place. The interstitial space can contain up to 500 mL of fluid; with further accumulations, the fluid crosses the alveolar epithelium in to the alveoli, leading to alveolar flooding.

Pathophysiological considerations

CPE usually occurs secondary to either left atrial outflow impairment or LV dysfunction. Left atrial outflow impairment may be acute or chronic in nature. Causes of chronic impairment include mitral stenosis or left atrial tumors. Increase in heart rate, which may occur secondary to atrial fibrillation or exertion, leads to pulmonary edema formation because of reduced LV filling. Acute mitral valve regurgitation secondary to papillary muscle dysfunction or ruptured chordae tendineae increases LV end-diastolic pressure and represents another cause of pulmonary edema.

The LV dysfunction can be systolic or diastolic LV dysfunction or both, LV volume overload, or LV outflow obstruction. The systolic dysfunction, a common cause of CPE, is defined as a decrease in myocardial contractility reducing cardiac output. The fall in cardiac output stimulates sympathetic activity and blood volume expansion through activation of the renin-angiotensin-aldosterone system.

The diastolic dysfunction signals a decrease in LV diastolic distensibility (compliance), requiring much higher diastolic pressure to achieve the similar stroke volume. Despite normal LV contractility, the reduced cardiac output in conjunction with excessive end-diastolic pressure generates hydrostatic pulmonary edema.

LV volume overload occurs in a variety of conditions, which may be cardiac or noncardiac in nature. Cardiac conditions are ventricular septal rupture and acute or chronic aortic insufficiency; the noncardiac condition is volume overload. These conditions cause elevation of LV end-diastolic pressure and left atrial pressure, leading to formation of pulmonary edema. LV outflow obstruction, such as aortic stenosis, produces increased end-diastolic filling pressure, increased left atrial pressure, and increased pulmonary capillary pressures.

Once pulmonary edema begins to develop, a self-perpetuating cycle of events occurs within the cardiopulmonary system. The cycle begins when LV systolic dysfunction leads to decreased myocardial contractility and cardiac output, which results in activation of renin-angiotensin-aldosterone system and stimulation of catecholamine production. As a result, systemic vascular resistance increases and leads to increased myocardial wall tension and myocardial ischemia, worsening LV function, worsening cardiac output, and perpetuation of the cycle. The increase in myocardial wall tension also results in concurrent diastolic dysfunction, which causes an increase in pulmonary artery and pulmonary capillary pressures. When the pulmonary capillary hydrostatic pressure exceeds pulmonary interstitial pressure, transudation of fluid in the pulmonary interstitium and alveoli occurs. As this cycle progresses, pulmonary edema rapidly develops if the cycle is not aborted promptly with appropriate treatment.

**CLINICAL**

**History**

CPE presents with the most dramatic clinical features of left heart failure. Patients develop sudden onset of extreme breathlessness, anxiety, and feelings of drowning.

Clinical manifestations of acute CPE reflect evidence of hypoxia and increased sympathetic tone (increased catecholamine outflow).

Patients most commonly complain of shortness of breath and diaphoresis.

Patients in whom symptoms have been of more gradual onset (eg, 24 h) often will report dyspnea upon exertion, orthopnea, and paroxysmal nocturnal dyspnea.

Cough is another frequent complaint that may provide an early clue to worsened pulmonary edema in patients with chronic LV dysfunction. Pink frothy sputum may be present in patients with severe disease.

The presence of chest pain should alert the physician to the possibility of acute myocardial ischemia, infarction, or aortic dissection with acute aortic regurgitation as the precipitant of pulmonary edema.

**Physical**

The physical examination in patients with CPE is notable for tachypnea and tachycardia.

Patients may be sitting upright, may demonstrate air hunger, and may become agitated.

Central cyanosis generally is evident.

Patients usually appear very anxious and diaphoretic.

Hypertension often is present because of the hyperadrenergic state. Hypotension indicates severe LV systolic dysfunction and the possibility of cardiogenic shock.

Auscultation of the lungs usually reveals rales, but rhonchi or wheezes also may be present.

The cardiovascular examination usually is notable for S3 and jugular venous distension. Auscultation of murmurs can help in the diagnosis of acute valvular disorders presenting with pulmonary edema. Aortic stenosis is associated with a harsh crescendo-decrescendo systolic murmur heard best at the upper sternal border and radiating to the carotid arteries. In contrast, acute aortic regurgitation is associated with a short soft diastolic murmur. Acute mitral regurgitation produces a loud systolic murmur heard best at the apex or lower sternal border.

Another notable physical finding may be skin pallor or mottling, resulting from peripheral vasoconstriction and shunting of blood to the central circulation in patients with very poor LV function. Skin mottling at presentation has been identified as an independent predictor of increased in-hospital mortality.

Patients with concurrent right ventricular failure also may present with hepatomegaly, hepatojugular reflux, and peripheral edema.

Severe CPE may be associated with a change in mental status, which may be the result of hypoxia or hypercapnia.

CPE should be differentiated from pulmonary edema associated with injury to the alveolar-capillary membrane caused by diverse etiologies. Increased capillary permeability is observed in trauma, hemorrhagic shock, sepsis, respiratory infections, administration of various drugs, and ingestion of toxins such as heroin, cocaine, and toxic gases.

Several features may differentiate cardiogenic from noncardiogenic pulmonary edema (NCPE). In CPE, a history of an acute cardiac event usually is present. The physical examination shows a low-flow state, S3 gallop, elevated jugular venous distention, and crackles upon auscultation. Patients with NCPE have a warm periphery, a bounding pulse, and an absence of S3 gallop and jugular venous distention. Definite differentiation is made based on PCWP measurements. PCWP generally is higher than 18 mm Hg in CPE and lower than 18 mm Hg in NCPE, but superimposition of chronic pulmonary vascular disease can make this distinction more difficult.

**Lab Studies**

CBC count with differential helps assess for severe anemia and may suggest the presence of sepsis if a markedly elevated WBC count or bandemia is present.

Serum electrolytes

Patients with chronic CHF often use diuretics and, therefore, are predisposed to electrolyte abnormalities, especially hypokalemia and hypomagnesemia.

Patients with chronic renal failure are at high risk for hyperkalemia, especially when noncompliant with hemodialysis sessions.

BUN and creatinine determinations help assess the presence of renal failure and anticipated response to diuretics.

**Imaging Studies**

* ECG may suggest an acute tachydysrhythmia or bradydysrhythmia as the cause of CPE.

ECG may suggest acute myocardial ischemia or infarction as the cause of CPE.

ECG is helpful when an acute valvular abnormality or LV systolic dysfunction is the suspected cause of CPE.

* Chest x-ray films

Chest x-ray (CXR) films are very helpful in distinguishing CPE from other pulmonary causes of severe dyspnea.

Classic CXR findings demonstrate cardiomegaly (in patients with underlying CHF) and alveolar edema with pleural effusions and bilateral infiltrates in a butterfly pattern. The other signs are loss of sharp definition of pulmonary vasculature, haziness of hilar shadows, and thickening of interlobular septa (Kerley B lines).

Utility in patients with abrupt onset is somewhat limited because a delay of as long as 12 hours is possible from the onset of dyspnea due to acute CPE to the development of classic x-ray film abnormalities.

**Other Tests**

* Arterial blood gases

This study is more accurate than pulse oximetry for measuring oxygen saturation.

It helps assess the presence of hypercapnia, a potential early marker for impending respiratory failure. Hypoxemia and hypocapnia occur in stage 1 and 2 of pulmonary edema due to ventilation-perfusion mismatch. In stage 3 of CPE, right-to-left intrapulmonary shunt develops secondary to alveolar flooding and further contributes to hypoxemia. In more severe cases, hypercapnia and respiratory acidosis usually are observed.

The decision to initiate mechanical ventilation is a clinical decision and rarely is based on arterial blood gas testing results.

* Pulse oximetry

Pulse oximetry is highly accurate at assessing the presence of hypoxia and, therefore, the severity of CPE.

It is useful for monitoring the patient's response to supplemental oxygen and other therapies.

Electrocardiogram

The presence of left atrial enlargement and LV hypertrophy is sensitive (although nonspecific) for chronic LV dysfunction.

* Procedures

Right heart catheterization

PCWP can be measured by using a pulmonary arterial catheter (Swan-Ganz catheter), and this helps differentiate CPE from NCPE. NCPE occurs secondary to injury to the alveolar-capillary membrane rather than to alteration in Starling forces. A PCWP exceeding 18 mm Hg in a patient not known to have chronically elevated left atrial pressure is indicative of CPE. In patients with chronic pulmonary capillary hypertension, capillary wedge pressures exceeding 30 mm Hg are required to overcome the pumping capacity of the lymphatics and produce pulmonary edema.

Large V waves sometimes may be observed in the PCWP tracing with acute mitral regurgitation because large volumes of blood regurgitate into a poorly compliant left atrium. This raises pulmonary venous pressure and causes acute pulmonary edema. The pulmonary artery waveform appears falsely elevated because of the large V wave reflected back from the left atrium through the compliant pulmonary vasculature. The Y descent of the waveform is quite rapid as the overdistended left atrium quickly empties.

Cardiogenic shock is the result of a severe depression in myocardial function. Cardiogenic shock is characterized by a systolic blood pressure less than 80 mm Hg, a cardiac index less than 1.8 L/min/m2, and a PCWP greater than 18 mm Hg. This form of shock can occur from a direct insult to the myocardium (large acute myocardial infarction, severe cardiomyopathy) or from a mechanical problem that overwhelms the functional capacity of the myocardium (acute severe mitral regurgitation, acute ventricular septal defect).

**TREATMENT**

Medical Care

Medical therapy of CPE focuses on 2 main goals:

1. reduction of pulmonary venous return (preload reduction)
2. reduction of systemic vascular resistance (afterload reduction). Preload reduction results in decreased pulmonary capillary hydrostatic pressure and reduction of fluid transudation into the pulmonary interstitium and alveoli. Afterload reduction results in increased cardiac output and improved renal perfusion, which allows for diuresis in the patient with fluid overload.

Patients with severe LV dysfunction and patients with acute valvular disorders may present with hypotension. These patients may not tolerate medications to reduce their preload and afterload. Therefore, a third goal in this subset of patients is to provide inotropic support to maintain adequate blood pressure.

Patients who remain hypoxic despite supplemental oxygen and patients who demonstrate severe respiratory distress require ventilatory support in addition to maximal medical therapy.

**Preload reduction**

* Nitroglycerin

Nitroglycerine (NTG) is the most effective, predictable, and rapid-acting medication available for preload reduction.

Multiple studies comparing NTG to furosemide or morphine sulfate have demonstrated greater efficacy and safety and a faster onset of action for NTG.

Use of sublingual NTG is associated with preload reduction within 5 minutes and some afterload reduction.

Topical NTG may be as effective as sublingual NTG in most patients with CPE but should be avoided in patients with severe LV failure because of poor skin perfusion (manifesting as skin pallor or mottling) and resultant poor absorption.

Intravenous NTG at higher dosages provides rapid and titratable preload and afterload reduction and has been demonstrated to be an excellent single-agent therapy for patients with severe CPE.

* Loop diuretics

Loop diuretics have been considered the cornerstone of CPE treatment for many years. Furosemide is used most commonly.

Loop diuretics are presumed to decrease preload through 2 mechanisms — diuresis and direct vasoactivity (venodilation).

In most patients, diuresis does not occur for at least 20-90 minutes; therefore, the effect is delayed.

Many patients with CPE are not actually fluid overloaded; continued diuretic use in these patients after resolution of acute symptoms may be associated with adverse outcomes, including electrolyte derangements and hypotension.

The presumption that these medications have a direct vasoactive (venodilating) effect has been questioned, with some studies actually demonstrating initially adverse hemodynamic consequences (eg, elevations of PCWP, LV filling pressure, heart rate, systemic vascular resistance) after administration of intravenous furosemide.

Premedication with medications that decrease preload (eg, NTG) and afterload (eg, angiotensin-converting enzyme [ACE] inhibitors) before the administration of loop diuretics can prevent potential adverse hemodynamic changes.

* Morphine sulfate

Morphine sulfate use in CPE for preload reduction has been commonplace for many years.

Good evidence supporting a beneficial hemodynamic effect is lacking.

Some studies suggest that morphine sulfate may contribute to a decrease in cardiac output and may be associated with a greater need for intensive care unit (ICU) admission and endotracheal intubation.

Adverse effects (eg, nausea/vomiting, local or systemic allergic reactions, respiratory depression) may outweigh any potential benefit, especially given the availability of much more effective medications for preload reduction (eg, NTG).

Any beneficial hemodynamic effect probably is due to anxiolysis, with a resulting decrease in catecholamine production and decrease in systemic vascular resistance. However, the authors prefer and advocate the use of low-dose benzodiazepines (eg, 0.5 mg doses of IV lorazepam) in patients who are extremely anxious because this practice is associated with less chance of respiratory depression in patients who have responded to initial therapy.

**Afterload reduction**

* Angiotensin-converting enzyme inhibitors

Although generally considered the cornerstone for treating chronic CHF, recent studies have demonstrated excellent results for treatment of acute decompensated CHF and CPE.

Studies demonstrate that the use of ACE inhibitors in CPE is associated with reduced admission rates to ICUs and decreased endotracheal intubation rates.

Hemodynamic effects of ACE inhibitors include reduced afterload, improved stroke volume and cardiac output, and slight reduction in preload.

When administered by either intravenous (enalapril 1.25 mg) or sublingual (captopril 25 mg) routes, hemodynamic and subjective improvements are noted within 10 minutes; improvements occur much more slowly with the oral route.

* Nitroprusside

Nitroprusside results in simultaneous preload and afterload reduction through direct smooth-muscle relaxation, although it has a greater effect on afterload.

Afterload reduction is associated with increased cardiac output.

Potency and rapidity of onset and offset of effect make this an ideal medication for patients who are critically ill.

It may induce precipitous falls in blood pressure; intraarterial blood pressure monitoring often is recommended.

Nitroprusside generally should be avoided in the setting of acute myocardial infarction. Its use has been associated with shunting of blood away from ischemic myocardium toward healthy myocardium (ie, coronary steal syndrome), potentiating ischemia.

If nitroprusside is used, convert patients to oral or alternative intravenous vasodilator therapy as soon as possible because prolonged use is associated with thiocyanate toxicity.

* Inotropic support

Dobutamine (catecholamine agent)

Dobutamine mainly serves as a beta1-receptor agonist, although it has some beta2-receptor and minimal alpha-receptor activity.

Intravenous dobutamine induces significant positive inotropic effects with mild chronotropic effects. It also induces mild peripheral vasodilation (decrease in afterload).

The combination effect of increased inotropy with decreased afterload results in a significant increase in cardiac output.

Combination use with intravenous NTG may be ideal for patients with myocardial infarction and CPE and mild hypotension in order to provide simultaneous preload reduction with increased cardiac output.

In general, avoid dobutamine in patients with moderate or severe hypotension (eg, systolic blood pressure <80 mm Hg) because of the peripheral vasodilation.

Dopamine (catecholamine agent)

Vascular and myocardial receptor effects are dose dependent.

Low dosages (0.5-5 mcg/kg/min) cause stimulation of dopaminergic receptors within the renal and splanchnic vascular beds, causing vasodilation and increased diuresis.

Moderate dosages (5-10 mcg/kg/min) cause stimulation of beta-receptors in the myocardium, resulting in increased cardiac contractility and heart rate.

High dosages (15-20 mcg/kg/min) cause stimulation of alpha-receptors, resulting in peripheral vasoconstriction (increased afterload), increased blood pressure, and no further improvement in cardiac output.

Moderate and high dosages are arrhythmogenic and also result in increased myocardial oxygen demand (potential for myocardial ischemia); therefore, only use these dosages in patients with CPE who cannot tolerate the use of dobutamine because of severe hypotension (eg, systolic blood pressure 60-80 mm Hg).

* Norepinephrine (catecholamine agent)

Norepinephrine primarily stimulates alpha-receptors, resulting in significant increases in afterload (and potential myocardial ischemia) and reduced cardiac output.

Use of norepinephrine generally is reserved for patients with profound hypotension (eg, systolic blood pressure <60 mm Hg). Once blood pressure is restored, add other medications to maintain cardiac output.

* Phosphodiesterase inhibitors

Phosphodiesterase inhibitors (PDIs) increase intracellular cyclic adenosine monophosphate, which results in a positive inotropic effect on the myocardium and peripheral vasodilation (decreased afterload) and a reduction in pulmonary vascular resistance (decreased preload).

PDIs, unlike the catecholamine inotropes, are not dependent on adrenoreceptor activity; therefore, patients are less likely to develop tolerance to these medications. Tolerance to catecholamine inotropes can develop rapidly through down-regulation of the adrenoreceptors.

PDIs are less likely than catecholamine inotropes to cause adverse effects that typically are associated with adrenoreceptor activity (eg, increased myocardial oxygen demand, myocardial ischemia).

The use of all known intravenous inotropic agents has been associated with an increased long-term mortality compared with placebo and thus should be reserved for heart failure patients with markedly depressed cardiac index and stroke volume.

* Ventilatory support

Noninvasive pressure support ventilation

Mechanical ventilation

**Surgical Care**

Intraaortic balloon pumping (IABP) was initially described by Kantrowitz in 1953, but IABP was first used clinically in 1969 in a patient with cardiogenic shock. Since the 1980s, IABP has been used increasingly in various clinical situations as a life-saving intervention to obtain hemodynamic stabilization prior to definite therapy.

**Further Inpatient Care**

When the patient has been stabilized initially, further inpatient care depends on the underlying cause of the episode of CPE.

Admit patients to a telemetry bed to monitor for acute dysrhythmias. Pay strict attention to the patient's fluid balance, monitoring fluid input and output closely. Maintain patients who are fluid-overloaded in negative fluid balance through the use of diuretics or hemodialysis (in patients with renal failure).

Check cardiac enzymes to evaluate for myocardial infarction. Stress testing also can be performed later during hospitalization to evaluate for reversible ischemia as the cause of pulmonary edema.

Consider ECG to evaluate for evidence of acute valvular dysfunction, wall motion abnormalities, and to assess the patient's ejection fraction. Patients with very poor ejection fractions or severe dilated cardiomyopathies often are placed on digoxin.

In general, begin patients on oral vasodilator therapy, most commonly ACE inhibitors. If the patient initially was treated with inotropic medications, wean the patient off as soon as the patient is stable in order to minimize adverse effects.

Patients in whom the cause of pulmonary edema was either dietary in nature or due to medication noncompliance need strict counseling and education to help prevent recurrence.

**Complications**

The major complication associated with CPE is respiratory fatigue and failure. Prompt diagnosis and treatment usually prevent this complication, but the physician must be prepared to provide assisted ventilation if the patient begins to show signs of respiratory fatigue (eg, lethargy, fatigue, diaphoresis, worsening anxiety).

**Prognosis**

In general, the inpatient mortality rate for patients with CPE is 15-20%.

CPE associated with acute myocardial infarction is associated with a mortality rate of at least 40%; the mortality rate approaches 80% if the patient also is hypotensive.