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Cardiogenic Shock in Pediatrics

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Introduction

- Cardiogenic shock: is an acute state of end-organ hypoperfusion following cardiac failure.

- Usually many children have good compensation, sometimes delay diagnosis leads to unfavorable outcome.

- Comprehensive approach in treatment is very important and proper management will prevent complication and mortality.
Definition

• The heart is unable to pump blood at a rate to satisfy body’s metabolic and growth demands.

• As shock progresses, it can lead to adverse responses such as on vascular system, inflammatory reactions, cellular and metabolic consequences, endocrine system, and ......
Cardiac Output Determinants

- Systemic O2 transport = CO X systemic O2 content
- CO = HR X SV
- SV depends to afterload, preload and contractility
Compensatory Mechanisms:

- Frank Starling Law
- ↑ Release of Catechol Amines
- Myocardial Hypertrophy & Dilatation
Fig. (1). Frank-Starling relationship of preload versus ventricular function (cardiac output). In the normal heart, increased preload produces improved ventricular function. In the failing heart, the curve is shifted downward and to the right. Inotropic therapy shifts the curve upward and to the left.
## Neurohormonal changes

<table>
<thead>
<tr>
<th>N/H changes</th>
<th>Favorable effect</th>
<th>Unfavor. effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ Sympathetic activity</td>
<td>↑ HR, ↑ contractility, vasoconst. → ↑ V return, ↑ filling</td>
<td>Arteriolar constriction → After load → ↑ workload → ↑ O₂ consumption</td>
</tr>
<tr>
<td>↑ Renin-Angiotensin – Aldosterone</td>
<td>Salt &amp; water retention → ↑ VR</td>
<td>Vasoconstriction → ↑ after load</td>
</tr>
<tr>
<td>↑ Vasopressin</td>
<td>Same effect</td>
<td>Same effect</td>
</tr>
<tr>
<td>↑ interleukins &amp; TNFα</td>
<td>May have roles in myocyte hypertrophy</td>
<td>Apoptosis</td>
</tr>
<tr>
<td>↑ Endothelin</td>
<td>Vasoconstriction → ↑ VR</td>
<td>↑ After load</td>
</tr>
</tbody>
</table>
Cellular changes

- Changes in Ca\(^{+2}\) handling.
- Changes in adrenergic receptors:
  - Slight ↑ in \(\alpha_1\) receptors
  - \(\beta_1\) receptors desensitization → followed by down regulation
- Changes in contractile proteins
- Program cell death (Apoptosis)
- Increase amount of fibrous tissue
Epidemiology

• Shock occurs in approximately 2% of all hospitalized infants, children, and adults in developed countries, and mortality rate varies substantially depending on etiology and clinical circumstances.
• Cardiogenic shock represents 5–13% of diagnosed cases of shock in pediatric emergencies.

• Mortality rate is similar to that observed in adults.

• Generally, mortality rates in cardiogenic shock remains as high as 35–50%.
Etiology

• Cardiogenic shock can be caused by various etiologies that also varies between ages.
Table 1. Causes of cardiogenic shock due to age-related (Chiwane et al., 2018).

<table>
<thead>
<tr>
<th>Age</th>
<th>Causes of cardiogenic shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 of life</td>
<td>• Birth asphyxia</td>
</tr>
<tr>
<td></td>
<td>• Congenital heart disease (TAPVR with obstructions, TGA with IVS with restricted atrial septum, HLHS with restricted atrial septum)</td>
</tr>
<tr>
<td></td>
<td>• Sepsis</td>
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<tr>
<td></td>
<td>• Sepsis</td>
</tr>
<tr>
<td></td>
<td>• Fetal/neonatal myocarditis</td>
</tr>
<tr>
<td></td>
<td>• Hypocalcemia</td>
</tr>
<tr>
<td></td>
<td>• Hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>• Brady/tachyarrythmia</td>
</tr>
<tr>
<td>First week of life</td>
<td>• Ductal dependent systemic circulation (HLHS, critical aortic stenosis, interrupted aortic arch)</td>
</tr>
<tr>
<td></td>
<td>• Sepsis</td>
</tr>
<tr>
<td></td>
<td>• Congenital adrenal insufficiency and inborn errors of metabolism</td>
</tr>
<tr>
<td>2 – 6 weeks</td>
<td>• VSD</td>
</tr>
<tr>
<td></td>
<td>• Complete AV canal defects</td>
</tr>
<tr>
<td></td>
<td>• Aortopulmonary window</td>
</tr>
<tr>
<td></td>
<td>• Truncus arteriosus</td>
</tr>
<tr>
<td></td>
<td>• Unobstructed TAPVR</td>
</tr>
<tr>
<td></td>
<td>• Persistent PDA</td>
</tr>
<tr>
<td></td>
<td>• ALCAPA</td>
</tr>
<tr>
<td></td>
<td>• Coarctation of aorta</td>
</tr>
<tr>
<td></td>
<td>• Pompe’s disease</td>
</tr>
<tr>
<td></td>
<td>• Sepsis</td>
</tr>
<tr>
<td></td>
<td>• Myocarditis/cardioomyopathy</td>
</tr>
<tr>
<td>6 weeks to 1 year</td>
<td>• Coarctation of aorta</td>
</tr>
<tr>
<td></td>
<td>• Aortic stenosis</td>
</tr>
<tr>
<td></td>
<td>• Sepsis</td>
</tr>
<tr>
<td></td>
<td>• Kawasaki disease</td>
</tr>
<tr>
<td></td>
<td>• Dysfunction of repaired/palliated congenital heart disease</td>
</tr>
<tr>
<td></td>
<td>• Infective endocarditis</td>
</tr>
</tbody>
</table>
Older children and adolescents

- Arrythmias
- Acute rheumatic fever
- Infective endocarditis
- Acute aortic insufficiency
- Cardiomyopathy
- Drug ingestions: calcium channel and beta-blockers
- Hypertensive emergencies

- Dysfunction of repaired/palliated congenital heart disease (Fontan baffle obstruction, AV valve regurgitation, aortic arch obstruction)
Cardiogenic shock is potentially caused by:

- Severe cardiac dysfunction at before or after cardiac surgery,
- Septicemia,
- Severe burns,
- Anaphylaxis,
- Cardiomyopathy,
- Myocarditis,
- Myocardial infarction and
- Acute CNS disorders.
Generally, shock follows three distinct stages regardless of classification & underlying diseases:

1. Compensated shock,
2. Uncompensated shock,
3. Irreversible shock
In the first stage of compensation, a series of physiological changes occur to ensure that the core essential organs (brain, heart, lungs) are prioritized in terms of oxygenated blood supply:

1. Peripheral vessels constrict to minimize blood flow to extremities

2. HR increases the blood flow.

- During this stage, a child’s extremities may feel cold and clammy to the touch as a result of peripheral constriction.
- This vasoconstriction and poor perfusion can lead to prolonged capillary refill time (CRT).
• As opposed to adult, children can actually maintain an adequate BP through compensation as compensatory responses maintain homeostasis.
• Due to this, BP monitoring may not be helpful in recognizing shock in its early compensated form.
• Due to this, measuring HR may be more reliable to detect shock alongside with signs of peripheral constrictions such as cold and clammy extremities as well as prolonged CRT.
<table>
<thead>
<tr>
<th>Age</th>
<th>Heart rate (bpm)</th>
<th>Hypotensive SBP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 mo.</td>
<td>110 – 180</td>
<td>&lt;0</td>
</tr>
<tr>
<td>1 – 12 mo.</td>
<td>100 – 170</td>
<td>&lt;70</td>
</tr>
<tr>
<td>1 – 2 y.o.</td>
<td>85 – 150</td>
<td>&lt;70 + (2 x age in years)</td>
</tr>
<tr>
<td>3 – 5 y.o.</td>
<td>70 – 140</td>
<td>&lt;70 + (2 x age in years)</td>
</tr>
<tr>
<td>6 – 10 y.o.</td>
<td>60 - 110</td>
<td>&lt;70 + (2 x age in years)</td>
</tr>
<tr>
<td>&gt;10 y.o.</td>
<td>50 - 100</td>
<td>&lt;90</td>
</tr>
</tbody>
</table>
• Once peripheral vasoconstriction and increased cardiac effort failed to compensate, shock progresses into uncompensated state which leads to inadequate tissue perfusion.

• When tissues are deprived of oxygen, they have to shift their metabolism into anaerobic which can result in the increased lactic acid.

• This could lead to acidosis and can be used as a marker of hypoperfusion.
When hypoperfusion persists, it can lead to a reduction in blood flow and impairment of organ function.

Some changes can be observed during this stage:

- Reduced urine output
- Increased respiratory effort
- Reduced consciousness
- Reduced blood pressure
• If the efforts to correct underlying diseases and restore an effective circulation fails, patient may fall into a state of irreversible shock.
• During this stage, tissues recovery is no longer possible and tissues continue to die.
• Despite continuous efforts to resuscitate and restore circulation, this stage is often irreversible and fatal.
Diagnosis

- It is based on a high clinical index of suspicion.
- Usually, a thorough history and physical examination, close attention to vital signs and response to therapies, and frequent clinical assessments will help make diagnosis.
- Pediatric patients will display a wide range of symptoms and signs in response to the interaction of cardiac, pulmonary, and GI systems as a result of the direct underlying diseases as well as compromised circulation.
<table>
<thead>
<tr>
<th>Symptom</th>
<th>Pathophysiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feeding difficulty</td>
<td>- Fatigue from low stroke volume</td>
</tr>
<tr>
<td></td>
<td>- Pulmonary congestion from increased left ventricular end-diastolic pressure</td>
</tr>
<tr>
<td>Failure to thrive</td>
<td>- Poor calorie intake from feeding difficulty</td>
</tr>
<tr>
<td></td>
<td>- Increased myocardial and respiratory muscle caloric demand</td>
</tr>
<tr>
<td>Irritability or lethargy</td>
<td>- Decreased oxygen delivery to the brain</td>
</tr>
<tr>
<td></td>
<td>- Myocardial ischemia</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>- Pulmonary congestion</td>
</tr>
<tr>
<td>Palpitations</td>
<td>- Tachycardia, bradycardia, or arrhythmias</td>
</tr>
<tr>
<td>Sweating</td>
<td>- Increased sympathetic activity</td>
</tr>
<tr>
<td>Abdominal pain and vomiting</td>
<td>- Congestive hepatomegaly</td>
</tr>
<tr>
<td></td>
<td>- Bowel ischemia</td>
</tr>
<tr>
<td>Sign</td>
<td>Pathophysiology</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Cold extremities, weak distal pulses, and prolonged CRT</td>
<td>Vasoconstriction</td>
</tr>
<tr>
<td>Disproportionate tachycardia</td>
<td>Sympathetic overactivity&lt;br&gt;- Rate-dependent cardiac output</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>Interstitial congestion due to lung tissue J receptor stimulation in response to increased pulmonary venous pressure</td>
</tr>
<tr>
<td>Narrow pulse pressure</td>
<td>Systemic vasoconstriction&lt;br&gt;- Decreased stroke volume</td>
</tr>
<tr>
<td>Crepitations</td>
<td>Alveolar edema due to increased pulmonary venous pressure</td>
</tr>
<tr>
<td>Dependent edema and hepatomegaly</td>
<td>Passive venous congestion due to elevated right atrial pressure</td>
</tr>
<tr>
<td>Gallop rhythm</td>
<td>S3: ventricular dilatation due to volume overload&lt;br&gt;- S4: ventricular hypertrophy due to pressure overload</td>
</tr>
</tbody>
</table>
Despite the different causes, cardiogenic shock and cardiac failure in children can be categorized in the same way as it does in adult according to presence or absence of two traits:

✓ Venous Congestion
✓ Hypoperfusion.

This is known as the warm, cold, wet, and dry concept, and is beneficial in choosing the right treatment later on.
Figure 1. Illustration of patient’s hemodynamic status in cardiogenic shock (Mendelson, 2018)
• Several studies can be used to determine the underlying causes of shock.

• Imaging studies are the mainstay to diagnose congenital abnormalities that may result in shock.
CXR, ECG

• CXR is often used as it is relatively cheap and widely available.
• Helps excluding other causes of shock and chest pain, assessing pulmonary vasculature and cardiomegaly.

• ECG is commonly performed to identify rhythm disturbance and structural diseases such as ALCAPA.
Ultrasound

• Ultrasound based studies is also a useful tool for it is relatively easy and quick to operate, and it has no radiation.

• Focused assessment with sonography for trauma (FAST) is used routinely in children and adults to identify hemoperitoneum, hemopericardium, and hemothorax, as well as pneumothorax in extended FAST (e-FAST)
Echo is often used to diagnose anatomic abnormalities, ascertain functional status, and to follow-up patient’s condition after therapy.

A parameter that can be assessed using echo is MPI.

MPI is a simple, reproducible, and noninvasive measure to assess systolic and diastolic function in comparison of ICT and IRT.
• MPI measures through the following equation:

\[ \text{MPI: } \frac{\text{ICT} + \text{IRT}}{\text{VET}} \]

• When systolic function worsens, ICT lengthens, the VET shortens, and subsequently the MPI increased.

• When diastolic function worsens, MPI will also increase but due to the lengthening of IRT.
Laboratory studies

Hematologic abnormalities include:

- Thrombocytopenia
- Prolonged PT & PTT
- Reduced serum fibrinogen level
- Elevation of fibrin split products
- Anemia
- Elevated neutrophil counts and increased immature forms (i.e., bands, myelocytes, promyelocytes), vacuolation of neutrophils, toxic granulations, and Döhle (with infection)
• Hyperglycemia or hypoglycemia may appear as a stress response.
• Electrolyte abnormalities such as hypocalcemia, hypoalbuminemia, and metabolic acidosis can also be present.
• Central venous pressure measurement can approximate RA pressure to assess preloading condition.
• SvO2 is considered as the balance between oxygen demand and delivery, and has been used as a determinant for tissue hypoxia.
Management and Treatment

- Needs a quick evaluation and stabilization without any delay.
- Initial treatment is focused on restoring enough oxygen delivery to peripheral tissue.
- All patient that come with cardiogenic shock should be placed and treated in PICU.
• Early goal directed therapy (EGDT) is focused in maintaining and restoring airway patency, oxygenation, ventilation, and circulation (perfusion, normal BP and HR based on age) on the first hour of shock onset.
• Oxygen should be administrated for any kind of shock despite the etiologies.
• Monitor and evaluate O2 Sat and give IV access immediately.
• Fluid resuscitation is needed immediately to correct hypovolemia and hypotension situation with precaution of pulmonary edema.
Therapeutic goals for management of pediatric shock should include the following points:

1. Normal mental status
2. Normal BP in accordance with age
3. Normal or threshold HR in accordance with age
4. Normal and equal both central and peripheral pulse
5. Warm extremities and capillary refill 2 sec. or less
6. Normal urine output (>1mL/kg/h)
7. Normal serum glucose levels
8. Normal serum calcium level
9. Decrease in lactate serum level
Cardiogenic Shock

Anamnesis

Symptom:
- Feeding difficulty
- Failure to thrive
- Irritability/lethargy
- Dyspnea
- Palpitation
- Sweating
- Abdominal pain and vomiting

Sign:
- Cold extremities
- Weak distal pulses
- Prolonged CRT
- Tachycardia
- Tachypnea
- Narrow pulse pressure
- Crepitation
- Edema
- Hepatomegaly
- Gallop rhythm

Clinical sign

Laboratory:
- Biochemical profile
- CBC
- Cardiac enzyme
- Arterial blood gases
- Lactate

Supporting diagnosis

Imaging:
- Echocardiography
- USG
- Chest radiographic
- Electrocardiography (ECG)

- High flow oxygen, high-concentration mask
- Non-invasive ventilation (and/or with pressure support)
- Endotracheal intubation, invasive mechanical ventilation
- Transfusion to reach hemoglobin $\geq 10$ g/dl

Ventilation management

preload (based on clinical condition)
- Fluid resuscitation 5-10 mL/kg with caution pulmonary edema
- Loop diuretic (Furosemide) IV, intramuscular: 0.5–2 mg/kg/dose every 6–24 h

preload and afterload management

afterload: mechanical ventilation

Drugs management

First line: Dobutamine 2-20 mcg/kg/min (Maximum 20 mcg/kg/min)

Alternative: Milrinone IV infusion: 0.25–0.75 $\mu$g/kg/min

Persistent shock?

Noradrenaline (start 0.01 mcg/kg/min) $\Rightarrow$ if SVR are low
Hypotension persist despite Dobutamine prescription $\Rightarrow$ Milrinone–Epinephrine
Hypotension persist $\Rightarrow$ Epinephrine

Persistent shock?

ECMO

Planning monitoring (Clinical & other modalities)
Optimizing preload using diuretics and fluid administration

- Fluid resuscitation should be given in any kind of shock: Isotonic crystalloid infusion for 20 mL/kg for 20 min. (IV/IO)
- But an exception given for children with cardiogenic shock.
- In neonates or children with cardiogenic shock, crystalloid fluid 5-10 mL/kg boluses can be administered.
For children suspected with RV dysfunction or hypertrophy need higher preload to correct contractility.

For this patient fluid challenge can give more advantage, slowly administer small dose of aliquots 5 mL/kg.

Reassess frequently to evaluate any signs of volume overload (hepatomegaly, S3 gallop, or rales/crackles), increased JVP, and poor perfusion.
• Meanwhile in children with LV dysfunction, diuretic can be administered to decrease preload.
• Diuretics works by decreasing plasma volume and peripheral edema causing decreased CO, and BP with increasing PVR as compensation mechanism.
• Diuretic mainly used to treat systemic and pulmonary vascular congestion.
• Diuretic agent is classified into four subgroups:
A. Loop diuretics

- Most common used loop diuretic is **furosemide**. Furosemide can be used to treat high preload in cardiogenic shock.
- Furosemide work by increasing the excretion of water by inhibiting reabsorption of sodium and chloride in the ascending loop of Henle and distal renal tubule.
- Furosemide is preferred among another diuretic (Bumetanide and Ethacrynic acid) because its rapid onset of action and long duration for almost 3 hours.
- Furosemide can be given as a bolus or infusion.
- Adverse effect of this medication includes hypokalemia, metabolic alkalosis, hypocalcemia, hyponatremia, and hyperuricemia.
B. Potassium-sparing diuretics

- **Spironolactone** (aldosterone receptor antagonist) is the most common potassium sparing diuretic used.
- Spironolactone use is limited because its nature as weak diuretic and it’s not preferred to be used as a single medication.
- Spironolactone can be used to treat edema in pediatric with CHF caused by excessive aldosterone produced.
- Spironolactone competes with aldosterone for receptor sites in distal renal tubules, making water excreted while potassium and hydrogen ions retained.
- Potassium-sparing diuretic is usually given orally few days after the patient has been stabilized.
C. Thiazide diuretics

- Thiazide can be differentiated into two classifications, hydrochlorothiazide and chlorothiazide.
- Compared to furosemide, thiazide agents have slower effect.
- Thiazide commonly prescribed for children with CHF.
- Hydrochlorothiazide inhibits sodium reabsorption in distal tubules. Sodium reabsorption causes increased sodium, water, potassium and hydrogen ions excretion.
D. Thiazide-like diuretics

- Commonly used thiazide-like diuretics is metolazone.
- Other agent of thiazide-like diuretics are indapamide and chlorthalidone.
- Metolazone mechanism is similar to thiazide diuretic by inhibiting sodium resorption at cortical diluting site and proximal convoluted tubule.
Improving Myocardial Contractility

- Vasoactive agent should be given to patient with persistent shock after administration of initial fluid resuscitation.
- Specific inotropic administration based on hemodynamics, cardiac output, systemic vascular resistance.
- Inotropic drug includes catecholamines, phosphodiesterase inhibitor (PDE Inhibitor), and calcium sensitizers.
E. Pure Vasopressor (pure vasoconstrictor)

1. Phenylephrine

- Stimulates in alpha-1 agonist receptor which causes vasoconstriction in peripheral artery helping the raise of BP.
- Vasoconstriction effect may cause bradycardia reflex though this condition is rarely found in pediatric patient.
- Most important indication is low SVR in CHD patient (TOF, HCM, etc.).
- Also in patient with partial obstruction in systemic to pulmonary shunt or pulmonary shunt in single V. patient with PS to improve oxygenation.
- Phenylephrine dosage in pediatric patients: Bolus 0.5-5 mcg/kg or higher and Infusion 0.02-0.3 mcg/kg/min.
• Phenylephrine induces cardiac output and cause angina exacerbation, heart failure, and pulmonary hypertension.

• Side effect can be found in phenylephrine administration including vasoconstriction of peripheral vascular that can be severe and disturb blood flow in vital organ, nausea, vomiting, headache, and nervousness.

• Precaution is needed in administrating phenylephrine because there’s high risk of extravasation into skin and subcutis which can result ischemia, even necrosis and tissue lost.

• Absolute contraindication in phenylephrine is patient with hypersensitivity to the agent.
2. Vasopressin (ADH exogen)

- Can be used after hemodynamic stable and commonly given in patient with vasodilatory shock.
- In pediatrics with septic shock, vasopressin could be administered after agent like norepinephrine given before.
- Vasopressin exerts intense vasoconstriction and antidiuretic effects.
- Vasopressin is indicated in pediatric patient with diabetes insipidus, polyuria, CPR, diagnostic procedure, and vasodilatory shock.
• In excessive alpha-adrenergic blockade, vasopressin is proved to be useful in treating low SVR.

• Adverse effect that can occur in high doses include: hypertension and bradycardia due to severe vasospasm, limb ischemia due to vasoconstriction, necrosis due to extravasation, hyponatremia in prolong infusion, and hypersensitivity in susceptible patient.
F. Inoconstrictors
(Vasoconstrictor & Inotropic activity)

1. Epinephrine

- Effects in all adrenergic receptors (alpha-1, alpha-2, beta1, beta-2).
- The most potent alpha-adrenergic agonist. With lower dose infusion (<0.1-0.2 mcg/kg/min) affect predominantly in beta adrenoceptor (“pure inotropic” dose).
- Vasoconstrictor trait will increase with increasing dosage.
Epinephrine is indicated in patient with urgency CPR and rhythm disturbances, bronchospasm, anaphylaxis shock.

Epinephrine cause dilatation of smooth muscles in bronchi and iris dilatation, increasing blood glucose due to glycogenolysis, myocardial ischemia, tachyarrhythmia, and lactic acidosis.

Perfusion of hepatic and splanchnic will decrease and it can induce high hepatic metabolic workload, hypermetabolism, oxygen impairment, glycolysis, and insulin suppression which can lead to lactic acidosis and hyperglycemia condition.
2. Dopamine

• Induce chronotropic and inotropic effects on myocardium which can induce HR and myocardial contractility.

• Alpha- and beta-adrenergic receptors of Dopamine are weaker compared to Epi and NorEpi.

• Dopamine effect needs 5 min of time to start the effect, on the other side it takes only less than 10 min for systemic effect disappeared.
• Dopamine is indicated in patient with shock, acute renal failure, hepatorenal syndrome, CPR, and heart failure.

• Dopamine effect can be classified based on the dosage:
A) Low-dose dopamine (0.5-2 mcg/kg/min)

• Induce vasodilation effect.

Clinical presentation of low-dose dopamine:
• Increased GFR,
• Increased renal blood flow,
• Increased renal excretion of sodium,
• Increased urine flow.
B) Medium-dose dopamine (2-10 mcg/kg/min)

- Stimulates beta-1 receptor (beta-2 receptor is not stimulated by this dose).
- Clinical presentation of medium-dose dopamine includes increase myocardial contractility, increase SA node, increase impulse conduction, increase systolic pressure (diastolic is not affected much).
C) High-dose dopamine (10-20 mcg/kg/min)

- Mainly affects alpha receptor.
- Clinical result of high-dose dopamine administration include vasoconstriction, elevated blood pressure, renal and mesenteric vessel could be affected by increasing the dosage.
D) Very high dopamine dose (>20 mcg/kg/min)

• Could lead to ischemia.
• Limb circulation will be compromised and lead to ischemia condition.
• Prescription of very high dose of dopamine will give the same side effects as norepinephrine.
• Stopping Dopamine administration need to be decreased gradually while maintaining blood volume with IV fluid to prevent hypotension.

• Side effect that commonly occur with administration of Dopamine include tachycardia, angina, palpitation, vasoconstriction, hypotension, dyspnea, nausea and vomiting, and headache
3. Norepinephrine

Similar to epinephrine, stimulates beta-1 and alpha adrenergic receptors, causing increase in myocardial contractility, HR, and systemic vasoconstriction.

Even though norepinephrine is a potent alpha-1 receptor, it gives not significant effect on beta-2 receptors (which responsible for vasodilation).

It also can cause increase in systemic vascular retention and BP with low dose.
• Cardiac output will be decreased or maintained, and HR will decrease due to vagal reflex.
• Prolong infusion will induce hyperglycemia higher than epinephrine.
• Norepinephrine is indicated in patient with unresponsive to other vasopressor agent with need of very potent vasoconstrictor such as, shock (unresponsive to dopamine or dobutamine in neonates with septic shock), anaphylactic shock, myocardial infarction, severe hypotension, and pericardial tamponade.
• NorEpi is given IV infusion 0.02-0.2 mcg/kg/min, and it is recommended to use smallest dose and in shortest time.

• In giving norepinephrine, some precautions should be aware of including prolong administration (as it could induce cardiac output decrease, edema, hemorrhage, necrosis of organs due to severe shock or due to shock itself), severe vasoconstriction, increase myocardial oxygen consumption and the work of heart, arrhythmias, dizziness, tremor, and headache.
G. Inodilator (vasodilator and inotropic activity)

1. Milrinone
   - Works by inhibiting PDE3 which leads accumulation of cAMP.
   - It can stimulate and increase cardiac output.
   - cAMP has vasodilator effect causes dilatation of smooth peripheral vessel causing BP decreased.
Milrinone mechanism:
A) Exerting relaxation in arterial blood vessel smooth muscle
B) Inducing myocardial contractility (positive inotropic effect),
C) Improving Frank-starling curve in perioperative patient with low cardiac output (positive inotropic effect)
D) Increasing in systolic function, and diastolic relaxation.
• Milrinone is indicated in perioperative patient with low cardiac output (with systolic and/or diastolic dysfunction), heart failure (including cardiogenic shock), and PH.
• Loading dose administration 25-75 mcg/kg for patient with CPB (often given bolus during CPB), and IV administration should be indicated in patient CPB for 10-60 min.
• BP should be controlled.
• Maintenance dose administration 0.25-0.75 mcg/kg/min IV, maintenance dose can be given instead of loading dose because loading dose cause initial hypotension.
• **Milrinone** is contraindicated in patients with hypersensitivity, obstructive valve lesion, decreased AV node impulse delay causing increased ventricular responses, diuretic patients (induce abnormalities in renal perfusion and electrolyte balance), and decreased ventricular filling (severe hypotension).

• Adverse effect of milrinone is commonly arterial hypotension, compared to dobutamine, milrinone induce less tachycardia with more vasodilation, arrhythmias, thrombocytopenia, myocardial ischemia, but Milrinone does not increase myocardial oxygen demand.
2. Dobutamine

Stronger beta effects (dominant in beta-1 receptor) than alpha effects. Causes

- Systemic vasodilation and increase inotropic state.
- Reduction in systemic vascular resistance with increase in HR & BP.
- Reduction in SVR (compared with epinephrine or dopamine) through direct vasodilation and decrease in sympathetic vascular tone.
- This mechanism will increase C.O without changing MAP
Dobutamine *is indicated in:*
- Cardiac decompensation,
- Acute heart failure,
- Cardiogenic shock,
- Distributive shock,
- CHF.
• Prescription can be given through infusion 2-20 mcg/kg/min IV/IO and titrated until giving effect.
• Administration more than 20 mcg/kg/min induce tachycardia, ventricular ectopy, and exacerbation of myocardial ischemia.
• Infusion must be tapered in 48-72 hour since administration given.
• Adverse effect of dobutamine includes ectopic heartbeats, BP and HR elevation, hypotension, arrhythmia with hypokalemia risk, and increase of myocardial demand.
3. Levosimendan

- Causes cardiomyocyte more sensitive to ion intracellular calcium leading to rise of contractility.
- Inotropic effect in Levosimendan induces peripheral vasodilation by opening ATP-sensitive potassium channel in blood vessel.
- Unessential to have renal and hepatic dose adjustment.
- No effect on arrythmia.
- Loading dose of levosimendan 16-12 mcg/kg IV over 10 min. continued by IV 0.05 mcg/kg/min, effect will start in 5 min. until 10-30 min. and effects will stay in one to two hour, infusion should be given more than 24 hours.
Side effect include:

• Headache with or without hypotension due to vasodilatory effect of the drug,
• Risk for arrhythmia is not found,
• No renal or hepatic dose adjustment needed,
• No myocardial oxygen demand.
• Not enough mortality data found for pediatric patient
H. Pure vasodilators
(arterial dilators and/or venodilator)

Important to be used in patients with:
• Cardiogenic shock secondary to L-R shunt,
• Low cardiac output after operation,
• Severe A-V valve regurgitation,
• Dilated cardiomyopathy.
• Pure vasodilators have no inotropic activity, for example nitroglycerin, hydralazine, alprostadil, sodium nitroprusside, phentolamine mesylate
1. **Nitroglycerin**

- Induces relaxation of vascular smooth muscle by stimulating intracellular cGMP production.
- Improves cardiac index, decrease pulmonary and systemic blood pressure.
2. Hydralazine

- One of antihypertensive drug that lowers blood pressure with vasodilating effect in peripheral.
- Vasodilating effect of hydralazine occurs calcium flow blockade in vascular smooth muscle.
Electrolyte balance management

Evaluate any abnormalities in electrolyte balance because it can affect the myocardial function:

- Potassium
- Calcium
- Magnesium
Afterload management

- Reducing afterload by using vasodilator or positive pressure ventilation (PPV) is the only intervention that can improve stroke volume without increasing EDP.
- PPV helps reducing afterload greatly for LV.
Selective vasodilator infusion (sodium nitroprusside, esmolol, and nicardipine) can be prescribed.

For patient with severe AI or AV regurgitation, administration of antihypertensive drugs is able to decrease SVR making stroke volume improved.
• **Milrinone** reduces systemic and pulmonary afterload.

• Pulmonary vasodilator (inhaled NO and milrinone) can be administered for patient with RV dysfunction.

• Prostaglandin can be used to reduce afterload in children with COA.
• Afterload can be reduced using mechanical intervention which includes:
  • Intra-aortic balloon pump (IABP),
  • ECMO,
  • VAD,
  • Abdominal compression device.
- ECMO is the most common mechanical circulatory support which is used for pediatric patient.
- Venoatrial (VA) ECMO is the mode used in infant and children with myocardial dysfunction.
Three modes of ECMO cannulation used for pediatric patient include:

A. Transthoracic cannulation
B. Right internal jugular vein and right carotid artery percutaneously cannulation or through cervical incision
C. Femoral vein and femoral artery cannulation
• Cannulation depends on size of vessel, obstructed vessel, cardiac anatomy, surgeon preference.
• Peripheral cannulation through the carotid artery and internal jugular vein are commonly used for pediatric and infant patient as long as there’s no contraindication.
• ECMO help patient in recovery, transplant, and many mechanical assists to place device, or CPR.
• The main benefit using ECMO is that it can be rapidly deployed, and done in a child with closed chest, and provide cardiac support well.
Figure 4. ECMO (Extracorporeal membrane oxygenation) Mechanism pumping blood from circulation through artificial lung back into bloodstream (Cashen et al., 2018).
Atrioventricular (AV) synchronicity management

- By evaluating and correcting electrolyte concentration, arrhythmias can be prevented.
- In some cases where arrhythmia is commonly found such as acute myocarditis, cardiomyopathy, and coronary ischemia, the use of catecholaminergic inotropic agents should be avoided or use the lowest doses if it’s possible.
- Recommended treatment for arrhythmias is pharmacotherapy, pacing, cardioversion, or defibrillation.
Increasing arterial oxygen carrying capacity

- Increasing arterial oxygen carrying capacity improves not only systemic oxygen delivery but also myocardial oxygen delivery hence it can improve myocardial function.

- PPV could increase lung’s oxygenation by improving functional residual capacity.
• Administering packed RBC helps improving oxygen carrying capacity but transfusion is limited only to induce myocardial contractility or in severe blood loss.

• Side effect of transfusion include volume overload and increasing fluid viscosity which cause afterload increasing
Prognosis

• The **key to improve outcomes** and decrease mortality in pediatric patients with cardiogenic shock is **early identification, evaluation and treatment**.

• However, despite improvements in both medical and mechanical management, morbidity and mortality remain high as compared to other forms of pediatric shock.
• The current estimated mortality rate is as high as 5 to 10 percent, but increases up to fivefold in the presence of comorbidities such as acute kidney or liver failure and sepsis.

• Early myocardial support, both with medical or mechanical support, can improve end-organ function and perfusion, and thus reduce morbidity and mortality in this patient population.
• A study by Othman et al, in 2020 reviews patients’ data from National Inpatient Sample from 2002-2016.

• The study reveals that patients with cardiogenic shock that stemmed from cardiomyopathies had higher mortality than those that had CHD.

• The use of ECMO had a comparable rate between the two groups, while heart transplantation and the use of VAD were significantly higher in those with cardiomyopathies.
Left ventricular assist devices - LVAD
Thoratec pVAD
Major VAD Complications

- Bleeding
- Thrombosis
- Infection
  - sepsis is leading cause of death in long-term VAD support
- RV dysfunction/failure
- Suck down (low preload causes a nonpulsatile VAD to collapse the ventricle)
- Device failure/malfunction (highly variable by device type)
- Hemolysis (the VAD destroys blood cells)
Intra aortic balloon pumps - IABP
Heart

• Typically beats

3.000.000.000 times in person’s life time

• Any attempt by man to repair, augment, replace .... are only suboptimal till now and never performs like the one God created !!