Approach to Shock

Is it Still All Clinical or Technology

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Shock

Shock is a state of

- Cellular energy failure resulting from
- An inability of tissue oxygen delivery to satisfy tissue oxygen demand.

Early, ‘‘compensated’’ phase

- Neuroendocrine compensatory mechanisms
  - Maintain appropriate perfusion to the vital organs (heart, brain, and adrenal glands)
- Selective vasoconstriction in nonvital organs
  - Allows maintenance of blood flow to vital organs.
- Normal systemic blood pressure but
  - Cold extremities, tachycardia, delayed CRT, oliguria

‘‘Uncompensated’’ phase

- The neuroendocrine compensatory mechanisms have failed
  - Hypotension
  - Decreased perfusion of vital organs, and
  - Worsening lactic acidosis
- If untreated, shock then progresses to its final phase and becomes “irreversible.”
  - Irreparable damage to tissues occurs and
  - No therapeutic intervention is effective in reversing the process.

Shock

- Tissues cannot be provided with adequate oxygen or nutrients.
- Circulatory failure or Derangement of perfusion.
  - Pump: Heart: Cardiac out
  - Flow of blood to the tissues: Blood Pressure / Systemic blood flow
  - Systemic vascular resistance (SVR)
  - Oxygen carrying capacity of blood : Hemoglobin and Oxygen content

How to identify Shock

Two of following Clinical Parameters:

- Feeble pulses
- Tachycardia
- Cold periphery (<34*C), CPTd
- CRT >3 sec
- Hypotension
- Decreased urine output
- Increased lactate levels

Utility of Clinical Signs

- Routinely used clinical signs
  - Limitation: low sensitivity during early periods of impaired perfusion
  - Are deranged only when the newborn has progressed to a state of uncompensated or irreversible shock
- Over the years we have been treating
  - Hypotension rather than impaired perfusion.
- Hypotension is a numerical or statistical value connoting
  - Blood pressure that is more than two SD from the mean.
  - This may or may not represent a pathological state of shock

Heart rate

- Tachycardia is the traditional indicator of cardiac compensation
- Cardiac output = Stroke volume × ***Heart rate***
- Stroke volume fixed in neonates
- Change in CO mainly depends upon HR
- Basal Heart rates are high in neonates (80 – 180/ min)

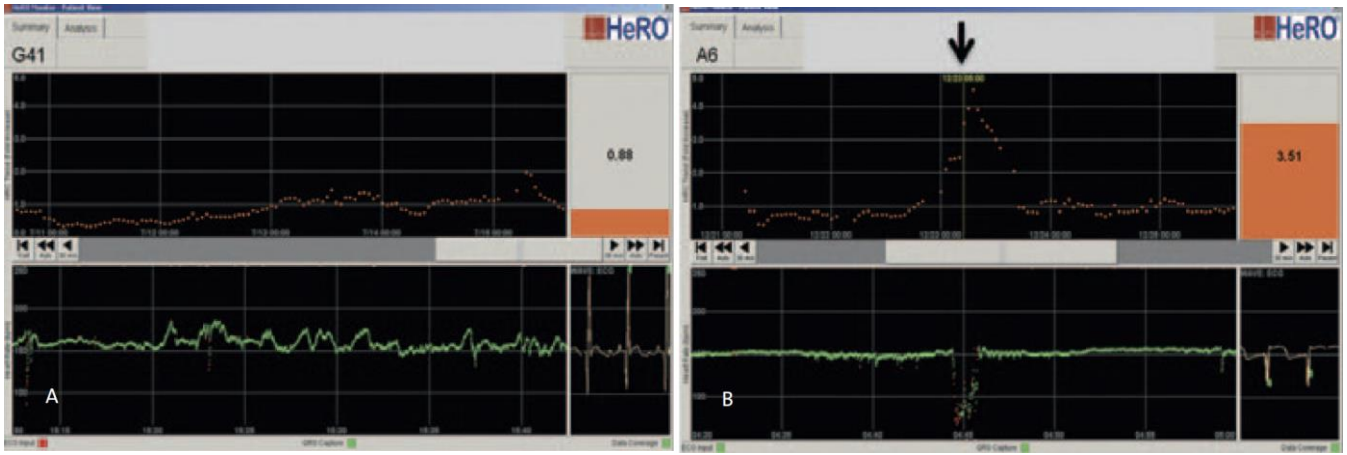
HR too high → diastolic coronary flow impeded → decrease in contractility

Heart rate

- In neonates especially preterms response attenuated:
  - Faster baseline heart rate
  - Immature myocardium
  - Immature autonomic nervous system
- Heart rate monitoring:
  - Usually by Monitors or Pulse oximeters
  - Trends over a period of time
- Heart rate variability

Heart Rate Variability

- HeRO (Heart rate Observation) monitoring
- Decreased heart rate variability in sick states
- Used heart rate characteristics (HRC) to develop HeRO Score



Blood Pressure & Hypotension

- Controversial, Different definitions
- <3rd , 5th or 10th centile as per normative data
  - Historically below this cut off neonates shown to be associated with brain injury
- Mean BP < 28 – 30 mmHg in VLBW
  - Loss of cerebral autoregulation
- Mean BP below numerical value of GA
  - Most widely used definition

Blood pressure

Measurement

- Continuous reading e.g. UA line: Gold standard
- Oscillometric method
  - Usually good agreement with invasive BP
  - Issues with technique, Cuff size
  - In a sick child multiple probes attached to limbs

Metabolic Acidosis / Lactic Acidosis

- Tissue hypoxia
  - Anaerobic metabolism at the cellular level- ↑ lactate
- Serum lactate concentration >2.8 mmol/l:
  - 100% sensitive & 60% specific for detecting a low flow state
- CRT of >4 s combined with serum lactate >4 mmol / L
  - Sensitivity- 50%, specificity - 97%, PPV- 80% & NPV - 88%

High serum lactates have been associated with increased mortality in ventilated neonates

Miletin et al Eur J Pediatr (2009) 168:809–813

Metabolic Acidosis / Lactic Acidosis

- Other reasons for metabolic or lactic acidosis – Sepsis
- Inotropes especially epinephrine and not nor-epinephrine may be associated with increase in serum lactate levels
- Blood lactate levels may rise subsequent to improvement in tissue perfusion

Miletin et al Eur J Pediatr (2009) 168:809–813

Check Lactate clearance

- Rather than using a singular lactate concentration
  - Serial measurements are more helpful to predict outcomes.

- In ventilated infants elevated lactate concentrations
  - which do not decrease over 24 h, are associated with high mortality

Deshpande SA, Platt MP. Association between blood lactate and acid-base status and mortality in ventilated babies. Arch Dis Child Fetal Neonatal Ed. 1997 Jan;76(1):F15-20.

Urine output

- Immature renal tubule in VLBW infants inefficient at concentrating urine
  - Unable to appropriately reduce urine flow in the face of high serum osmolality
- Accurate measurement of urine output not easy in neonates
- Despite shortcomings reasonable indicator of tissue perfusion
  - Indicator of tissue perfusion in recent past

Linshaw MA. Concentration of the urine. In: Polin RA, Fox WW, eds. Fetal and neonatal physiology

Once Shock is Diagnosed

First assessment:

- To assess intravascular volume status
  - History of blood or fluid loss
- Difficult especially in neonates
- Capillary leak states complicates assessment
- Often Fluid boluses are given to all neonates diagnosed with shock

Volume assessment: Echo

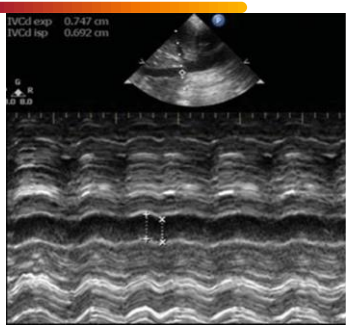
- Eye balling of ventricular volumes and filling
- Left ventricular end-diastolic area and volume.
- A dilated RA may indicate
    - volume overloading of the right side of the heart
- Bowing of intra-atrial septum toward the left atrium
    - may indicate elevated RA pressure and pulmonary hypertension.
- Triad of
    - “Kissing” small LV cavity, RV size, normal or small RA strongly associated with hypovolemia.

IVC assessment for Volume status

- A normally filled IVC
  - some pulsation with cardiac cycle & respiratory
- Ar
  -
- An over-filled IVC
  - will appear large, and minimally pulsatile.
- Caution is: ventilated infant: High MAP
  - IVC appear well-filled & underfilled cardiac chambers

When assessing preload status always examine the intracardiac filling.

Volume responsiveness to Fluid challenge



- A 10 – 15% increase in Stroke volume is taken as an indicator of Fluid responsiveness

EL-Nawawy et al. Role of inferior vena cava parameters as predictors of fluid responsiveness in pediatric septic shock: a prospective study. Journal of Child Science. 2021 Jan;11(01):e49-54.

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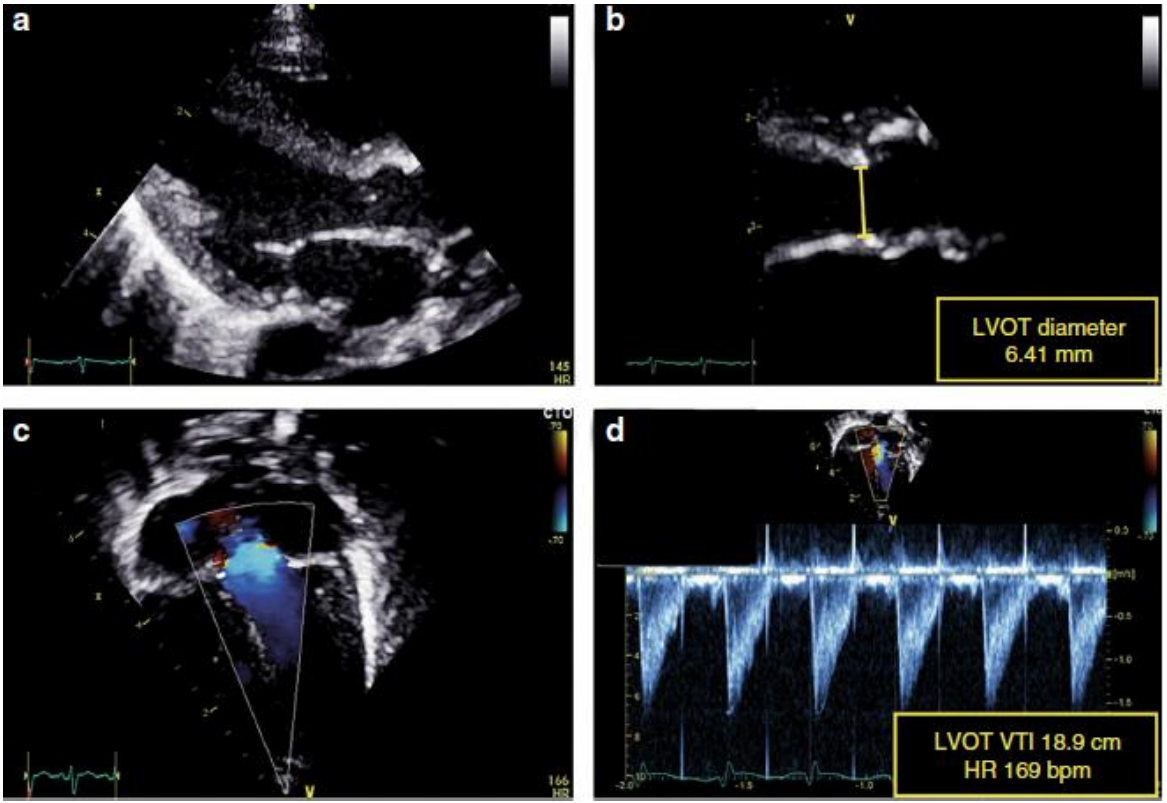
	AUC (95% CI)	*Z* (*p*-value)	Cutoff value[(YI)]	Sensitivity: (95% CI)	Specificity: (95% CI)	PPV (%): (95% CI)	NPV (%): (95% CI)
IVC min/BSA 1 h	0.88 (0.77–0.96)	7.89 (<0.0001*)	≤0.93 cm/m^2	70 (45.7–88.1)	100 (88.4–100)	100 (76.8–100)	83.3 (67.2–93.6)
IVC max/BSA 1 h#	0.68 (0.54–0.8)	2.2 (0.26)	–	–	–	–	–
IVCDI 1 h	0.87 (0.74–0.95)	6.55 (<0.0001*)	>12.32%	85 (62.1–96.8)	76.67 (57.2–90.1)	70.8 (48.9–87.4)	88.5 (69.8–97.6)
IVC min/BSA 6 h	0.86 (0.67–0.97)	4.67 (<0.0001*)	≤1.15 cm/m^2	92.86 (66.1–99.8)	72.7 (39–94)	81.2 (54.4–96)	88.9 (51.8–99.7)
IVC max/BSA 6 h#	0.59 (0.44–0.72)	1.01 (0.32)	–	–	–	–	–
IVCDI 6 h	0.86 (0.73–0.94)	4.72 (<0.0001*)	>15.86%	78.6 (49.2–95.2)	94.4 (81.3–99.3)	84.6 (585–95.6)	91.9 (80.6–96.9)
IVC min/BSA 24 h	0.77 (0.6–0.95)	1.98 (0.047*)	≤0.97 cm/m^2	75.4 (34.9–96.2)	83.33 (35.9–99.6)	85.7 (42.1–99.6)	71.4 (29.3–96.3)
IVC max/BSA 24 h#	0.55 (0.28–0.8)	0.31 (0.759)	–	–	–	–	–
IVCDI 24 h	1.00 (0.77–1.00)	NC (<0.0001*)	>22.57%	100 (63.1–100)	100 (54.1–100)	100 (63.1–100)	100 (54.1–100)

Echocradiographic Assessment in Shock



Reference values for blood flow measurements in mean (SD) ml/kg/min

	Postnatal age			
	3–9 h	24 h	Day 2	Days 7–14
RVO				
Preterm		260 (90)	270 (90)	430 (100)
Term		255 (60)		
LVO				
Preterm		240 (60)	260 (60)	400 (75)
Term		220 (60)		
SVC flow				
Preterm	60 (25)	80 (20)	90 (25)	90 (30)
Term	75 (25)	95 (30)	100 (30)	

RVO right ventricular output, *LVO* left ventricular output, *SVC* superior vena cava

Neonatal hemodynamic reference by electrical cardiometry *K-H Hsu et al*

Weight (g)	*CO (l min^{-1})*	*CI (l min^{-1} per m^2)*	*HR (beats min^{-1})*	*SV (ml)*	*Thoracic fluid content*	*Index of contractility*	*SVR (dyn·s cm^{-5})*
<1000	0.19 ± 0.03	2.32 ± 0.17	155 ± 6.8	1.26 ± 0.20	20.4 ± 4.9	79.2 ± 6.2	$15\,790 \pm 4117$
1000–1499	0.27 ± 0.04	2.41 ± 0.28	145 ± 12.9	1.90 ± 0.35	22.2 ± 3.9	84.1 ± 16.1	$12\,280 \pm 2865$
1500–1999	0.35 ± 0.05	2.58 ± 0.35	141 ± 12.1	2.54 ± 0.40	25.5 ± 4.3	83.7 ± 17.3	9198 ± 2159
2000–2499	0.41 ± 0.06	2.58 ± 0.31	137 ± 13.6	3.01 ± 0.46	26.3 ± 4.7	78.0 ± 13.8	8710 ± 1962
2500–2999	0.46 ± 0.08	2.56 ± 0.44	131 ± 14.0	3.58 ± 0.61	28.2 ± 5.7	73.1 ± 16.2	8530 ± 1978
3000–3499	0.51 ± 0.09	2.58 ± 0.40	131 ± 12.3	3.96 ± 0.67	28.1 ± 5.6	68.9 ± 15.6	8022 ± 2323
3500–3999	0.54 ± 0.08	2.51 ± 0.36	126 ± 11.4	4.34 ± 0.61	27.8 ± 4.9	67.3 ± 13.4	7280 ± 1917
$\geqslant 4000$	0.65 ± 0.11	2.76 ± 0.41	129 ± 9.8	5.10 ± 0.72	28.7 ± 5.4	70.5 ± 10.1	6575 ± 1385

Abbreviations: CI, cardiac index; CO, cardiac output; HR, heart rate; SV, stroke volume; SVR, systemic vascular resistance. Values are mean $\pm$ s.d.

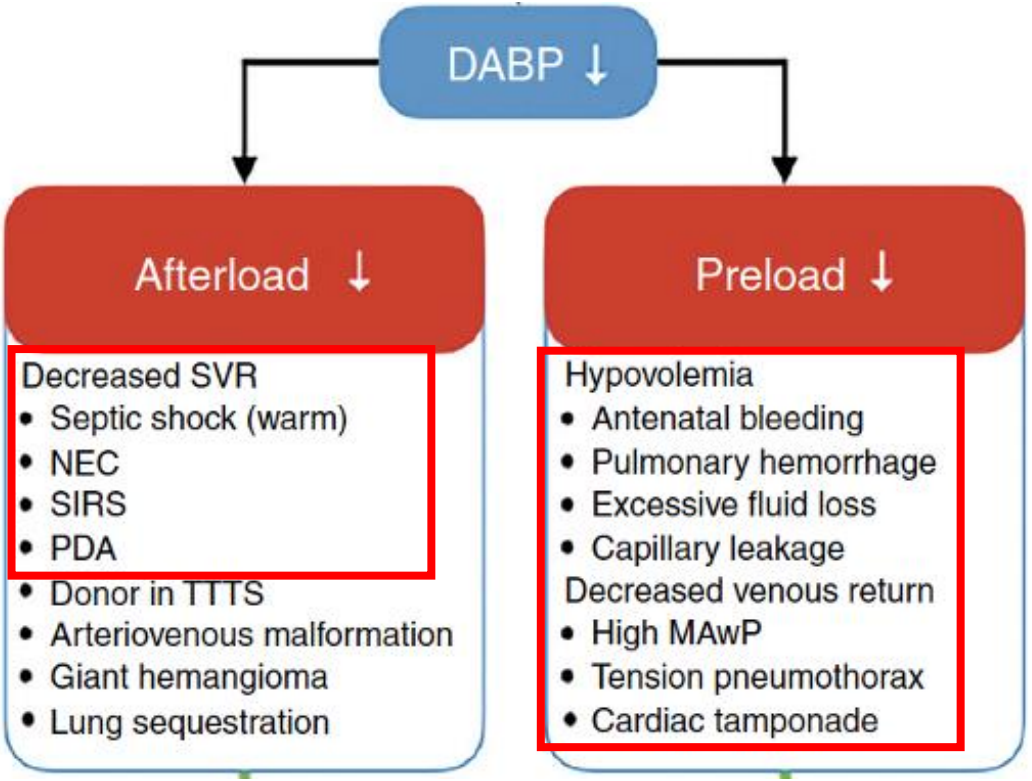
Traditional approach to management of Shock

- Intervention with volume followed by
- Dopamine
- Observation of the response in BP mean values
  - Intervene below a certain BP value
  - Titrate inotropic support to achieve certain BP values
- *In many situations this approach may result in a positive outcome for the infant*
  - It often fails to address the complexity of the underlying problem
  - In some circumstances may result in undue harm

Treatment of Shock

- Shall we treat low BP or take into account other parameters of tissue perfusion:
  - capillary refill time, urine output, heart rate, peripheral color, base excess, lactate concentration
  - Regional tissue oxygen saturations: NIRS
- What should be the target blood pressures

Choosing a Therapeutic Intervention



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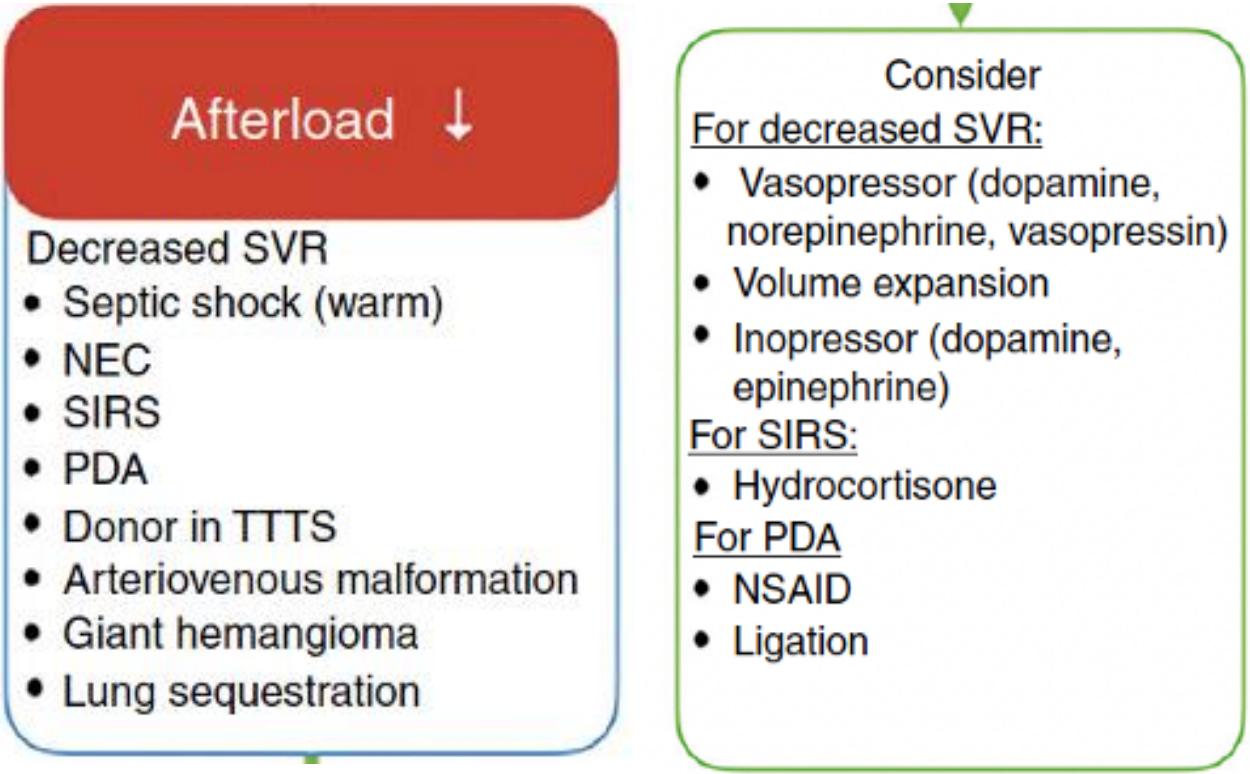

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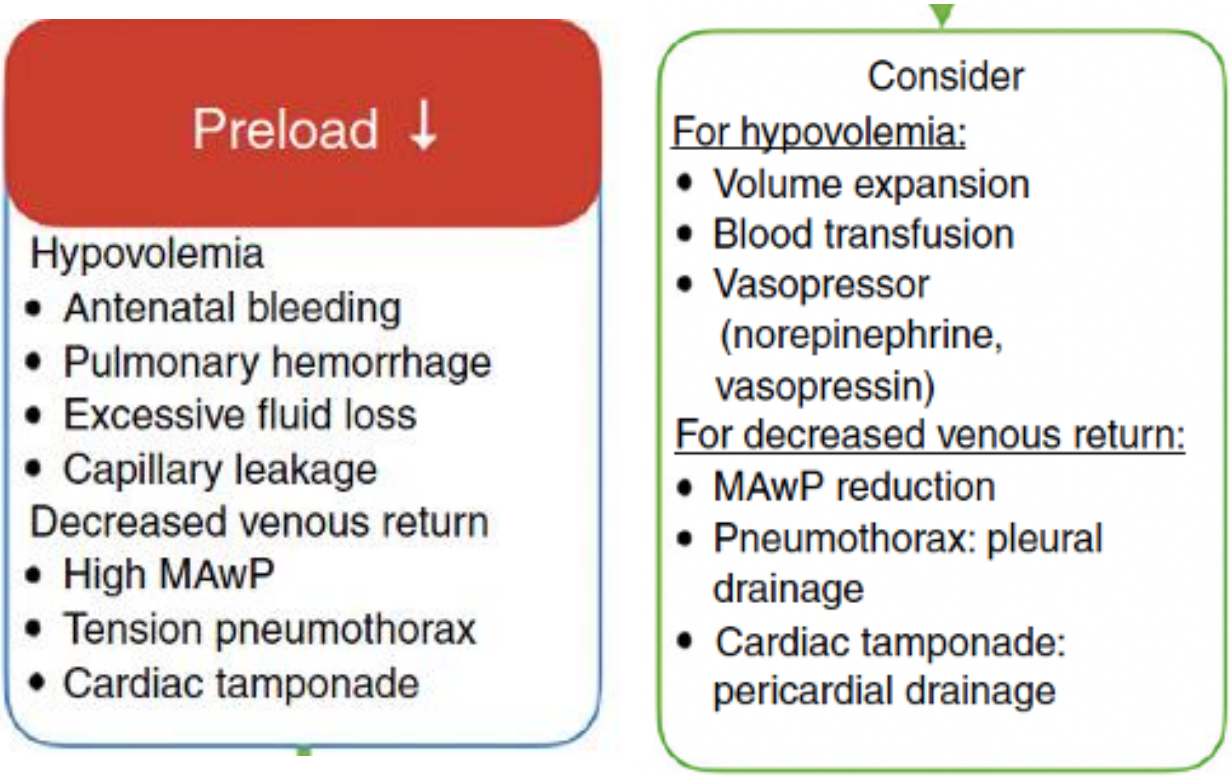

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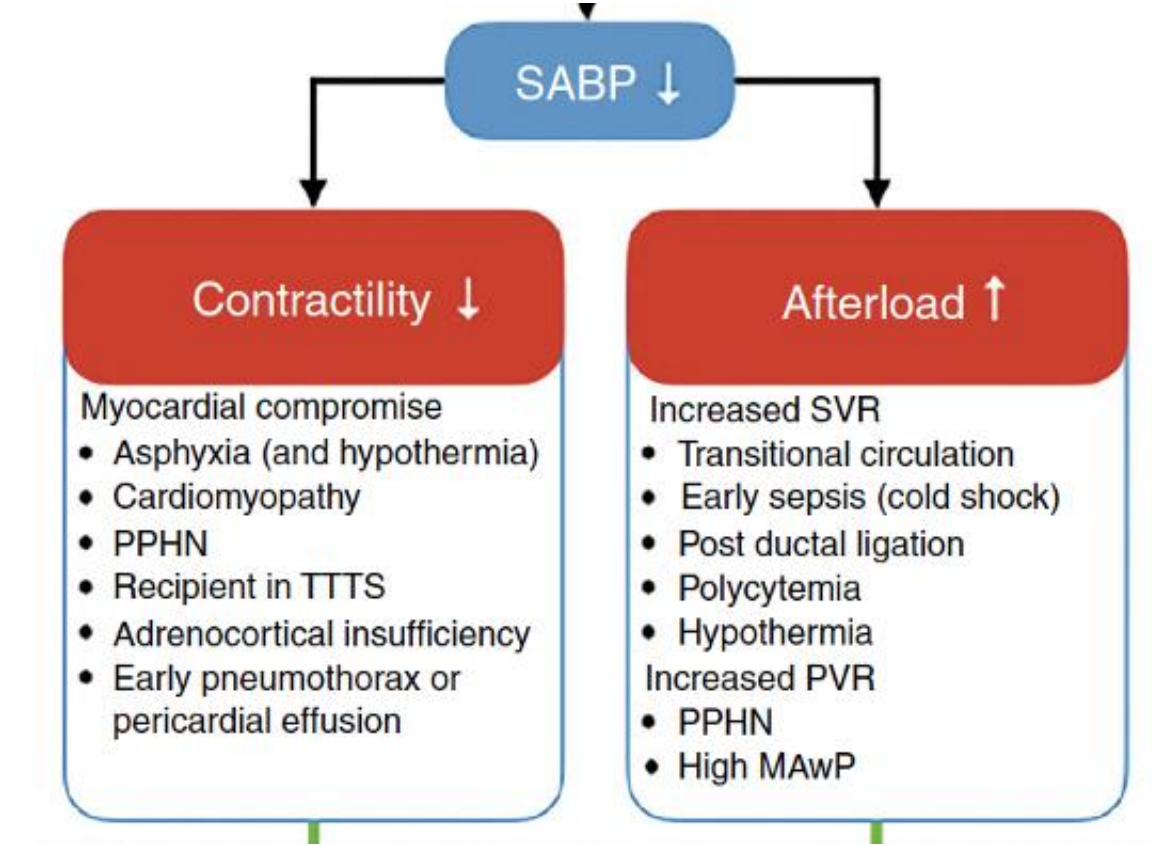

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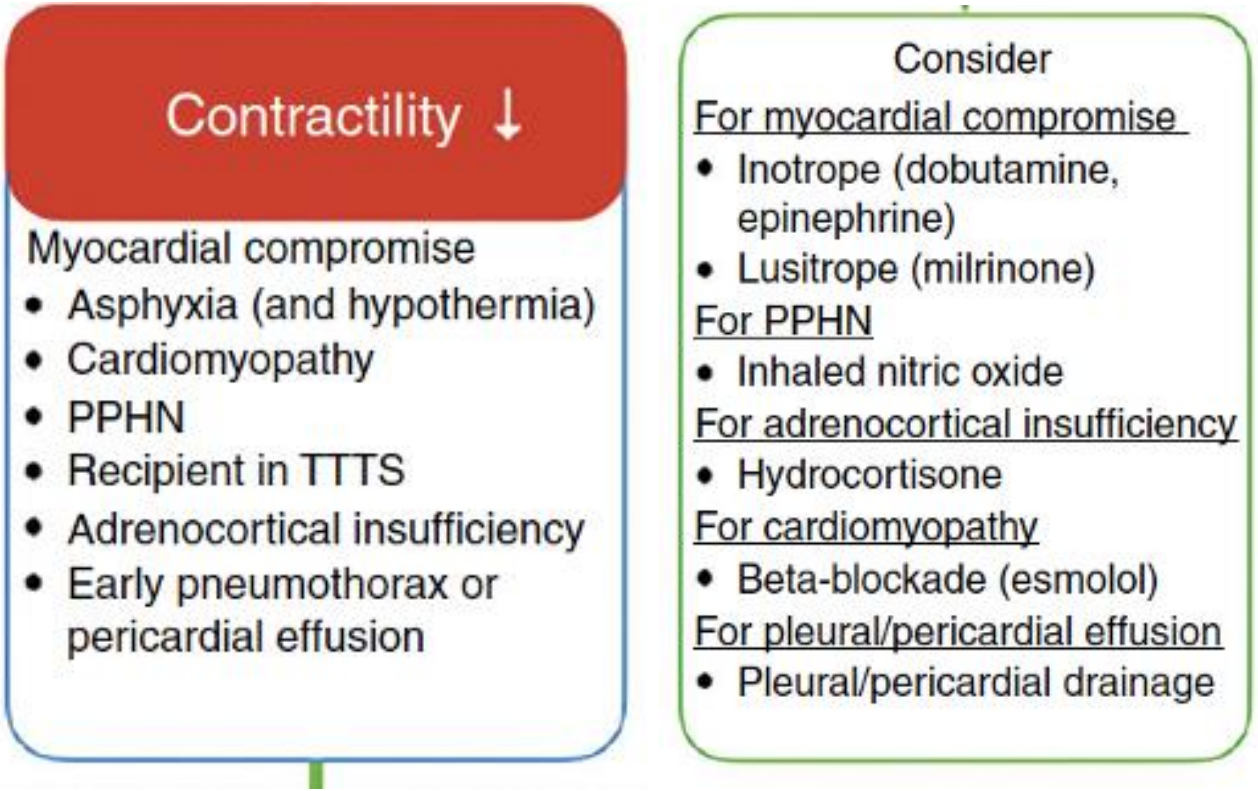

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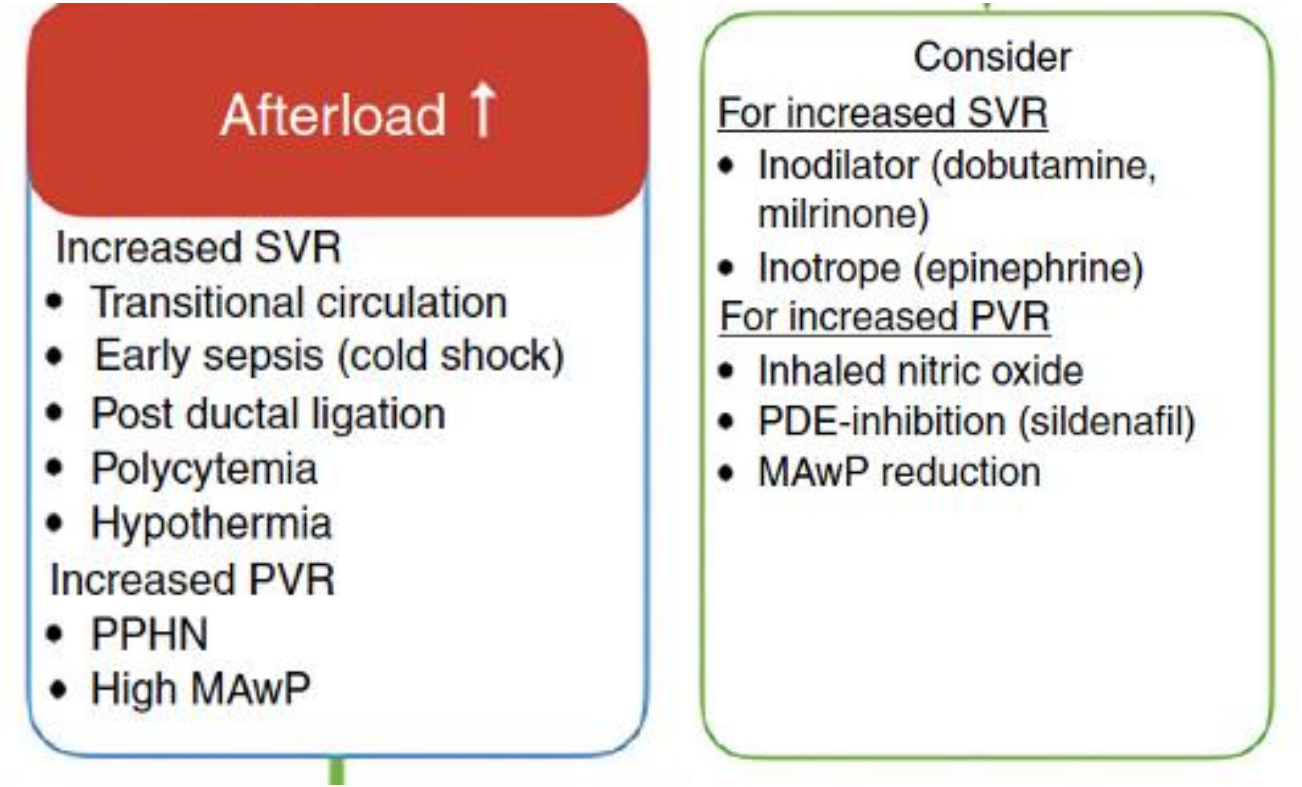

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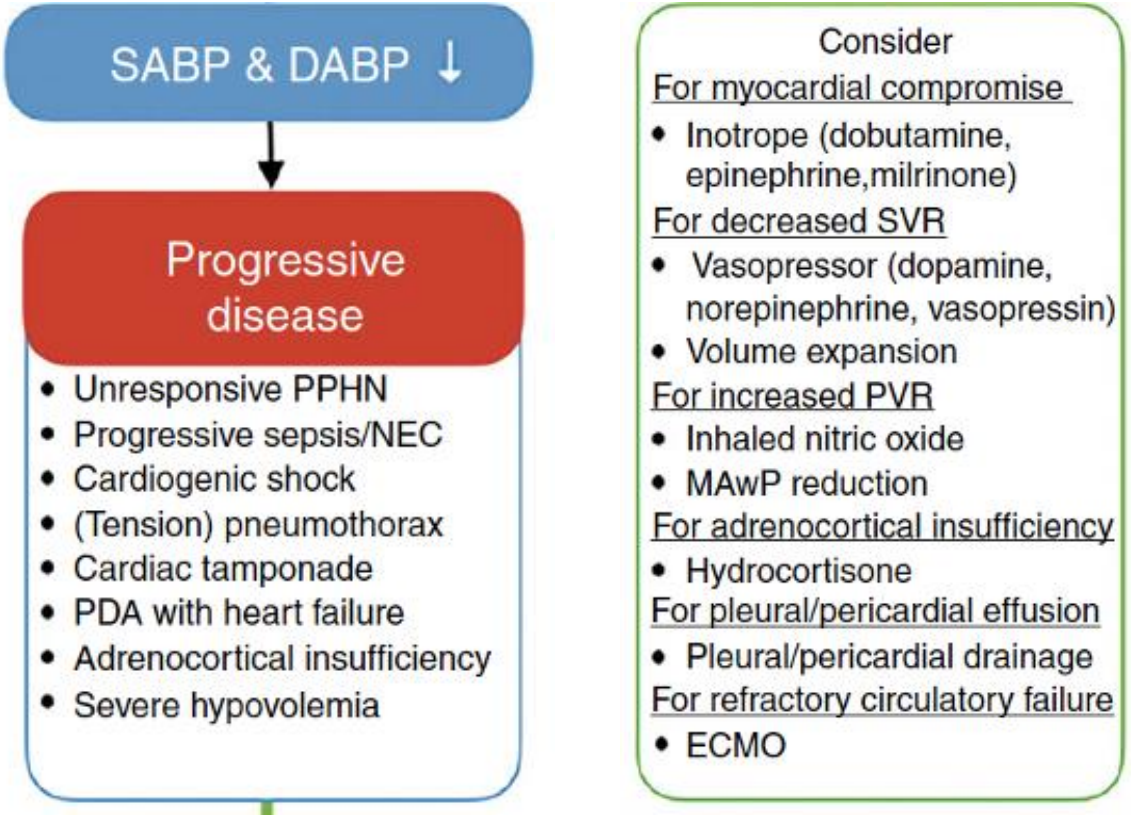

HIP Trial: Dempsey et al. Hypotension in Preterm Infants (HIP) randomised trial. Arch Dis Child Fetal Neonatal Ed. 2021 Jul;106(4):398-403.

- Infants: GA of <28 weeks at birth;
- An indwelling arterial line to monitor BP
- Cranial ultrasound scan: no significant IVH
- Low BP, defined as a mean BP of
  - 1 mm Hg or more below a mean BP value equivalent to the GA in completed weeks
  - Persisted over at least a 15 min period within the first 72 hours of birth

HIP Trial: Dempsey et al. Hypotension in Preterm Infants (HIP) randomised trial. Arch Dis Child Fetal Neonatal Ed. 2021 Jul;106(4):398-403.

- Intervention: saline bolus followed by Randomization to
  - by either a dopamine infusion (standard management)
- *The trial terminated early due to significant enrolment issues (7.7% of planned recruitment).*
- *58 infants were enrolled*
  - *18/29 (62%) achieved the primary outcome compared with 20/29 (69%) in the restrictive group (p=0.58).*

Conclusion

Though this study lacked power

Did not detect major differences in clinical outcomes between standard or restrictive approach to treatment.

HIP Trial

Signs of Poor perfusion and Additional therapy

- Mean BP was more than 5 mm Hg below threshold OR
- Infants had two or more of
  - Mean BP of 3 mm Hg less than the threshold value
  - Lactate greater than 4 mmol/L and
  - Prolonged capillary refill time (>4 s).
- Weaning of the study drug if:
  - BP was 5 mm Hg greater than threshold, then study drug was reduced by 5 mcg/kg/min
  - if >10 mm Hg, it was reduced by 10 mcg/ kg/min; and
  - if 15 mm Hg greater, the study drug was stopped.

Tissue Perfusion and NIRS

- Preterm brain injury is strongly associated with
  - abnormal cerebral perfusion and oxygenation
- Suboptimal cerebral oxygenation associated with poor neurodevelopmental outcome
- Low arterial blood pressure and periventricular white matter injury has been reported
- Systemic BP or arterial SpO_2:
  - not enough to guarantee proper cerebral perfusion or oxygenation
  - SpO_2 only reflects arterial oxygen saturation (SaO_2), and not real oxygen saturation in deep tissues.

NIRS: Near-infrared spectroscopy

- A noninvasive technique: continuously monitors regional oxygen saturation (rSO2)
- Predominantly measures rSO2 of venous blood
  - mixture of venous (75%), arterial (20%), capillary (5%)
- CrSO2 values between 60 and 80 percent
- The fractional tissue oxygen extraction (FTOE)
  - Amount of oxygen extracted from tissues (15-30%)
- A decrease in rSO2 indicates
  - decreased blood flow, resulting in decreased oxygen delivery or
  - increased oxygen extraction by the underlying tissue.

Bonestroo et al. Pediatrics 2011;128(6):e1502–10.

Effect of antihypotensive treatment on cerebral oxygenation of preterm infants without PDA.

- Compared neonates with BP below GA who were given volume vs inotropes
- Monitored $CrSO_2$ and Arterial blood pressures
- No difference in any clinically relevant outcomes
- These authors suggested that
  - Very preterm infants with hypotension, but without signs of a compromised $CrSO_2$
  - Might not require anti-hypotensive therapy.

Alderliesten T, et al. Hypotension in preterm neonates: low blood pressure alone does not affect neurodevelopmental outcome. J Pediatr 2014;164(5):986–91.

- Prospective observational study
- Preterm neonates less than 32 weeks without a PDA Treated for hypotension (dopamine ≥5 mg/kg/min)
- Matched to controls for gestation age, birth weight, sex
- Mean blood pressure < GA was not associated with
  - lower cerebral oxygenation or neuro Developmental outcome scores.
  - Regardless of the BP, CrSO2 value <50% associated with lower neurodevelopmental outcome scores.

Summary

- The diagnosis and management still remains clinical in most situations
- Technology has helped us understand physiology better
- Technology based decisions are now being increasingly used
- Work in progress
- Need for more accurate tools to measure real time hemodynamics
- Bed side application needs standardized protocols
- Use of Artificial Intelligence

Thank You