Spreading Knowledge – Improving Outcomes

Fluid Management in Septic Shock

Fluid Stewardship

4 Indications

- Resuscitation
- Maintenance
- Replacement
- Nutrition

4 Phases (ROSE model)

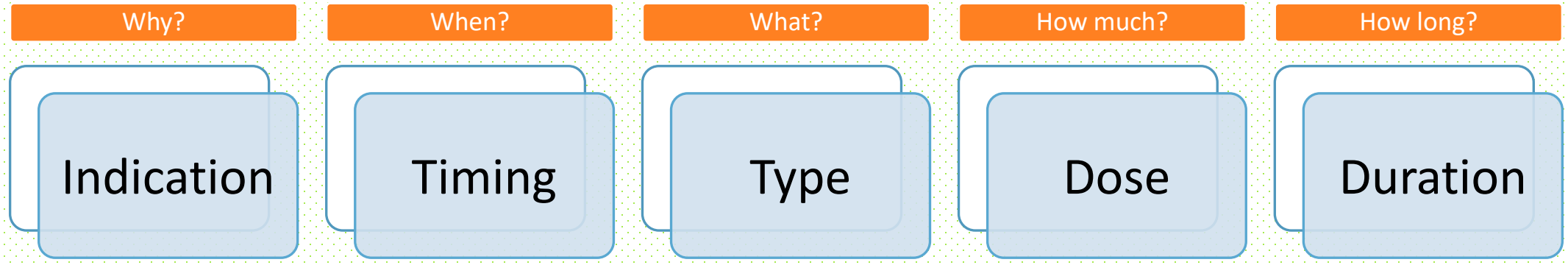
- Resuscitation
- Optimization
- Stabilization
- Evacuation

4 D's

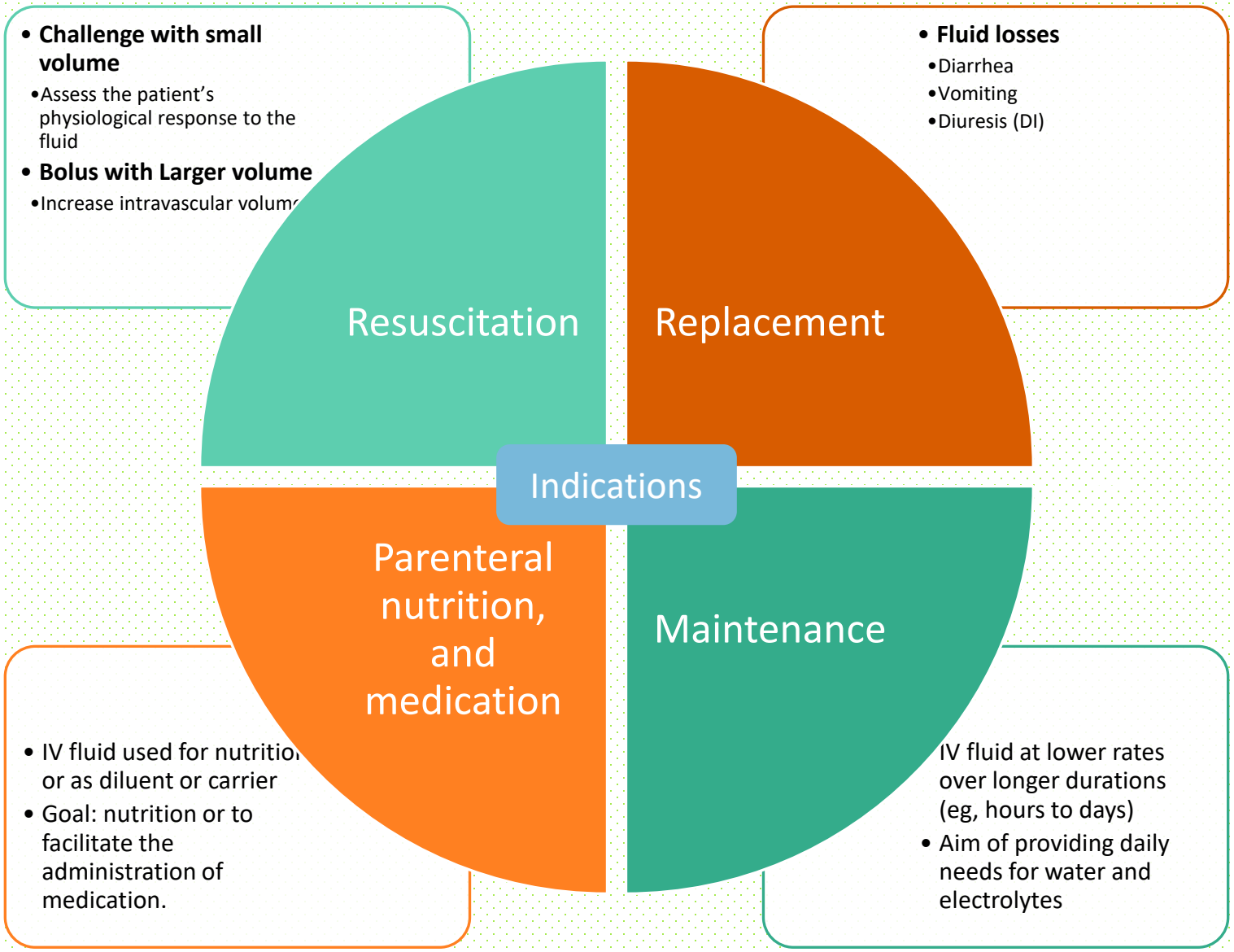
- Drug
- Dose
- Duration
- De-escalation

4 Questions

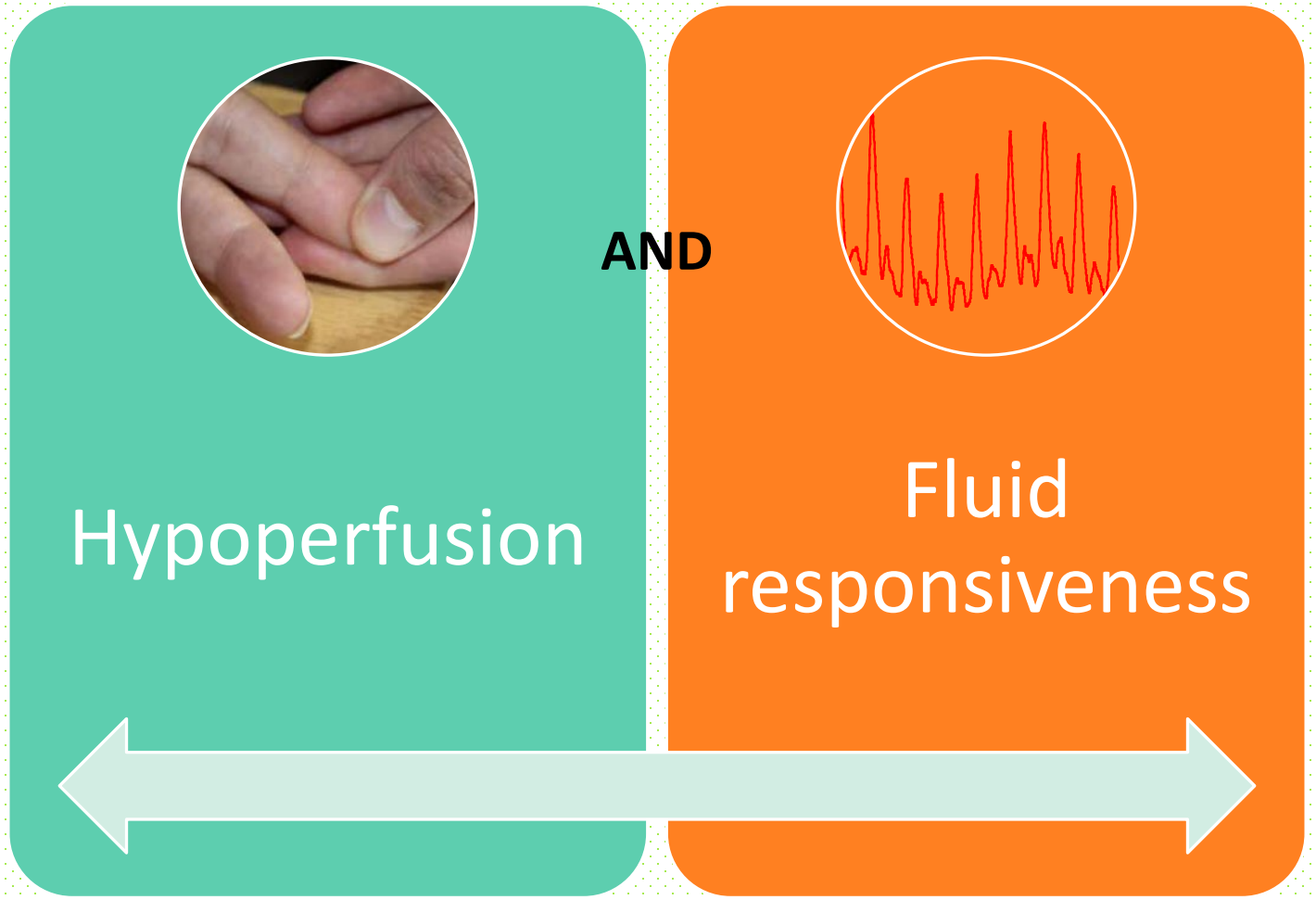
- When to start fluid therapy
- When to stop fluid therapy
- When to start fluid removal
- When to stop fluid removal


Why?
When?
What?
How much?
How long?
Indication
Timing
Type
Dose
Duration

Why?	When?	What?	How much?	How long?
Indication	Timing	Type	Dose	Duration



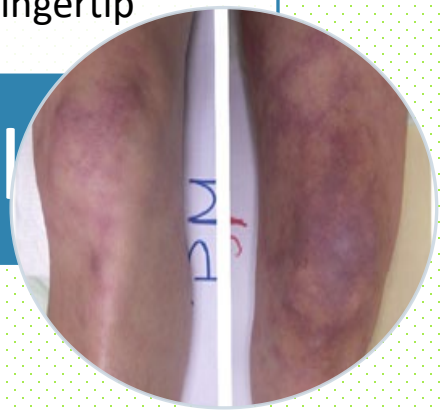
Zampieri FG, Bagshaw SM, Semler MW. Fluid Therapy for Critically Ill Adults With Sepsis: A Review. *JAMA.* 2023;329(22):1967–1980


AND
Hypoperfusion
Fluid responsiveness

Assessment of Peripheral Perfusion

Clinical

- Cold, pale, clammy, and mottled skin
- Prolonged capillary refill time
- Temperature gradients
  - Peripheral-to-ambient
  - Central-to-peripheral
  - Forearm-to-fingertip



Optical

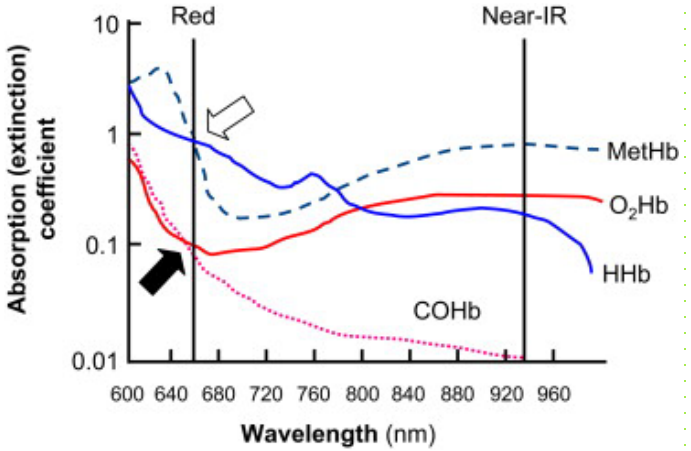
- Perfusion index
- Near-infrared spectroscopy
- Laser Doppler flowmetry
- Orthogonal polarization spectroscopy

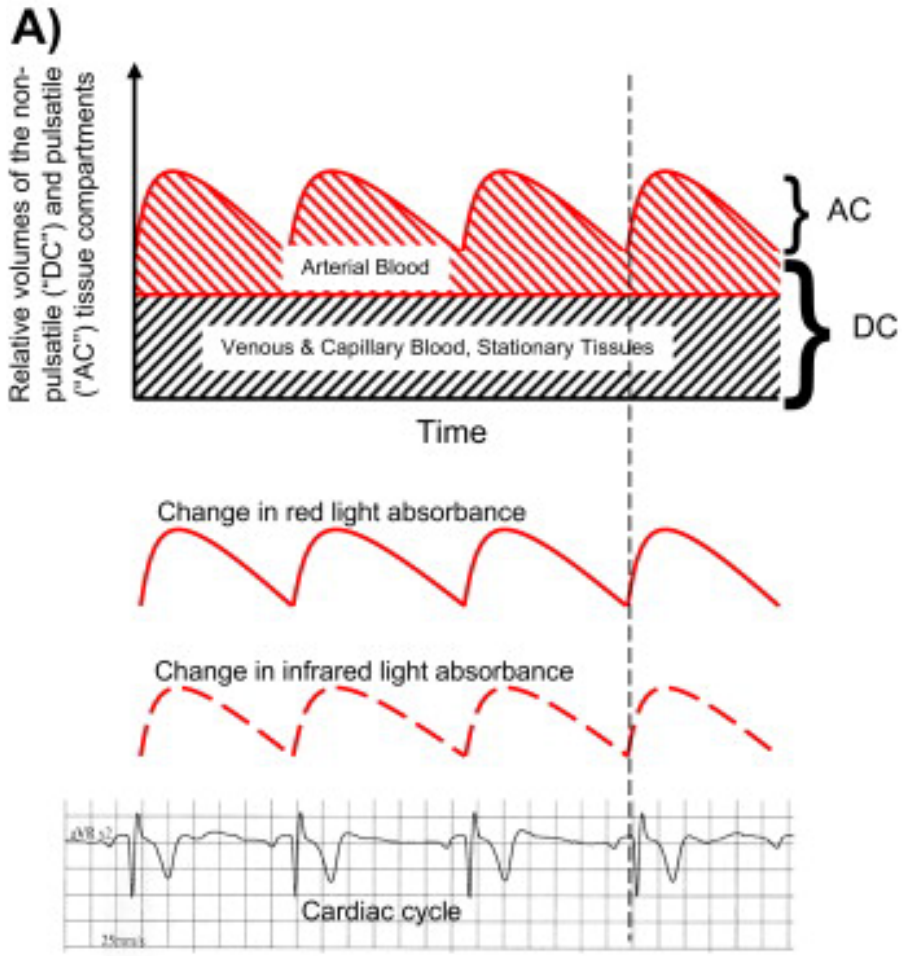
Others

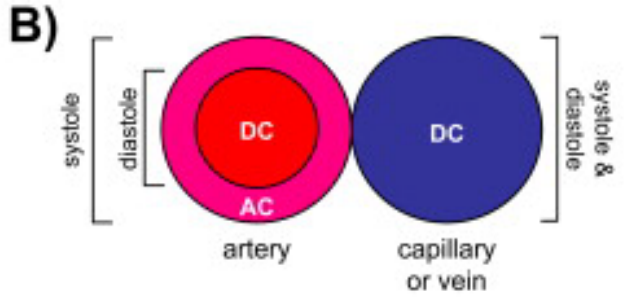
- Continuous noninvasive transcutaneous measurement of oxygen and carbon dioxide tensions.
- Sublingual capnometry

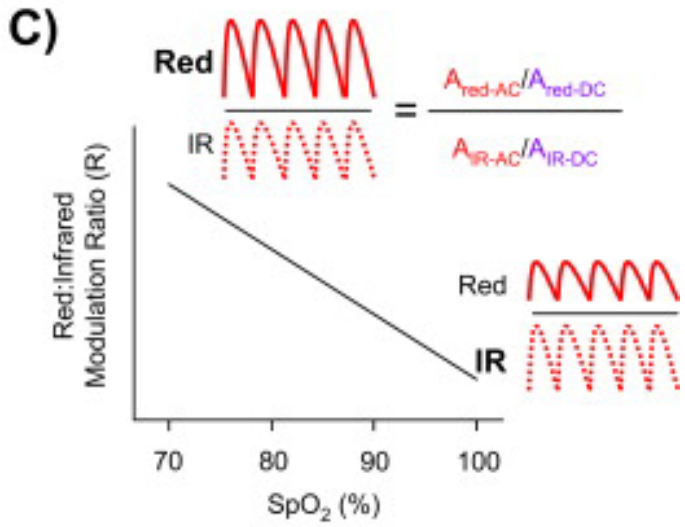
Light Absorbance by a Pulse Oximeter

Perfusion Index:
The ratio between the pulsatile and non-pulsatile component of the light reaching the pulse oximeter









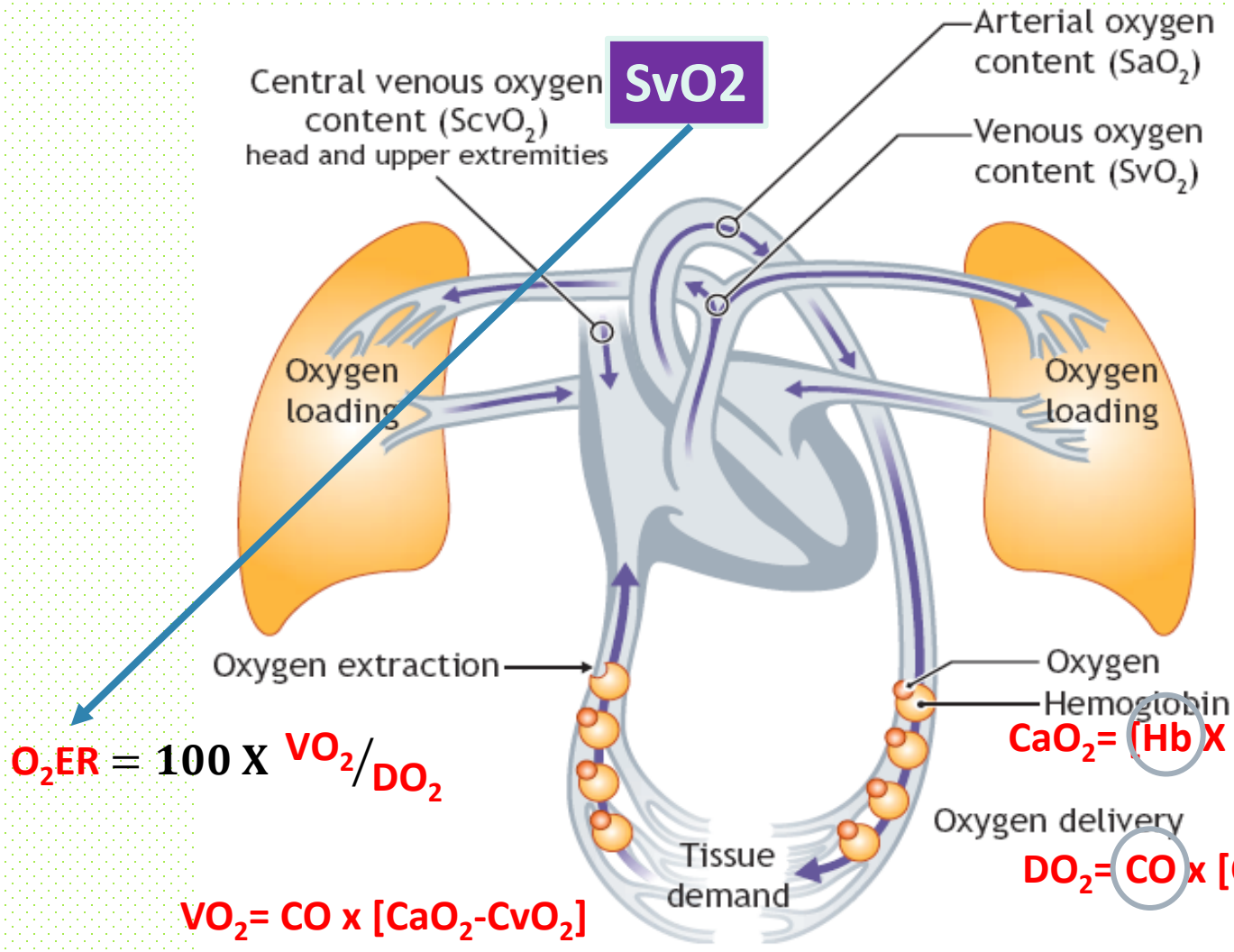
O_2Hb absorbs greater amounts of IR light and lower amounts of red light than does HHb

Perfusion Indicators

ScvO2	70%
Pv-aCO2 gap	<6 mmHg
Lactate (serial readings)	<2 mmol/L

These can be done if CVC and A-line are available.

$ScVO_2 = SaO2 - (VO2 / (CO \times Hb \times 1.34))$



$O_2ER = 100 \times VO_2/DO_2$

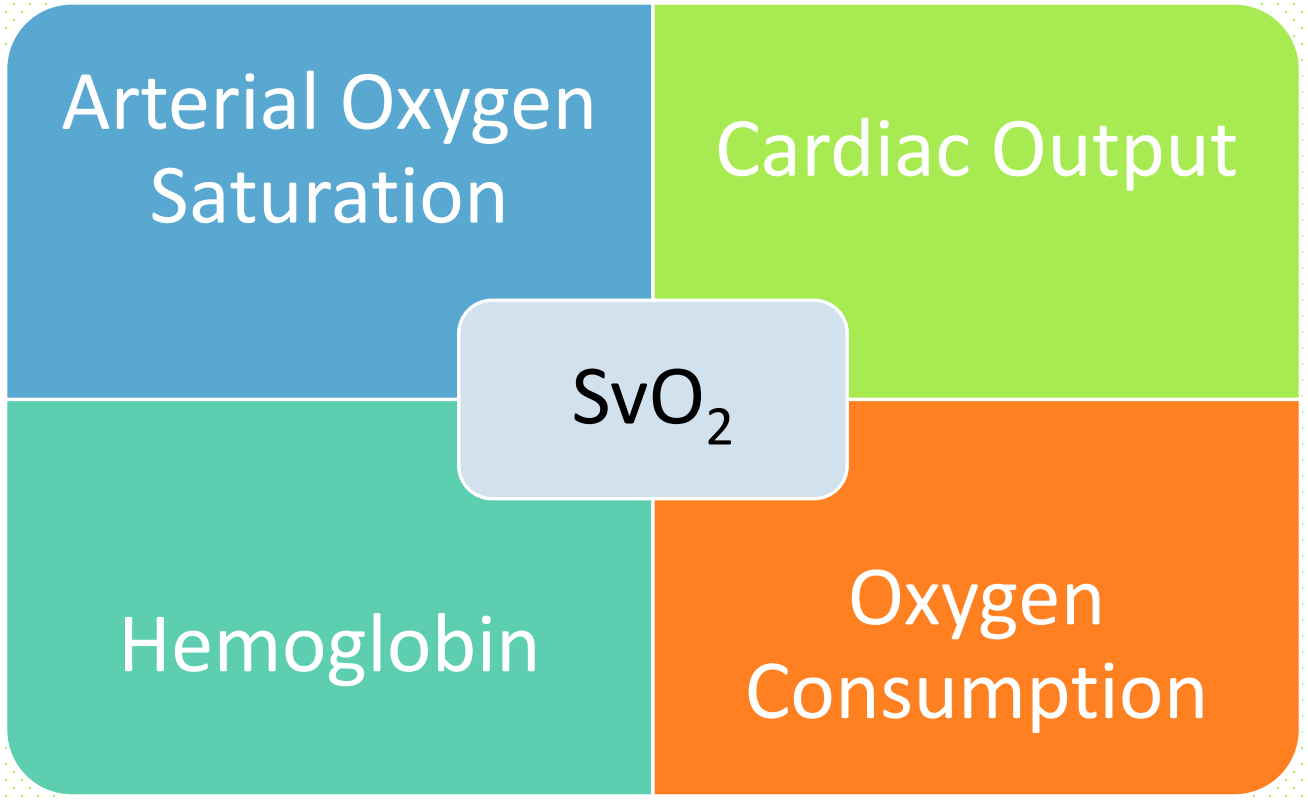
$VO_2 = CO \times [CaO_2 - CvO_2]$

$CaO_2 = [Hb \times 1.34 \times SaO_2] + 0.003 \times PaO_2$

Oxygen delivery

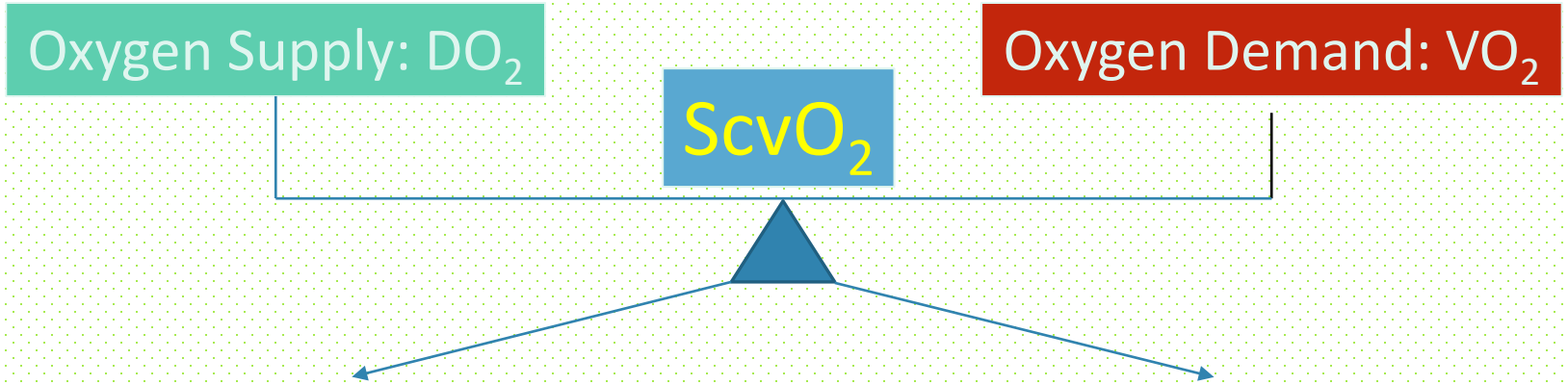
$DO_2 = CO \times [CaO_2]$

$SvO_2 = 1-O_2ER$



So if we kept Hb, saturations & VO2 constant then any change in CO will be reflected by change in the SvO2

Mixed Venous (and central venous) Saturation



Low	
↓DO_2	↑VO_2
Anemia	Pain
Bleeding	Agitation
Hypovolemia	Shivering
Hypoxia	Seizure
Low CO	Fever

High	
↑DO_2	↓VO_2
High Hg	Sedation
Hyperoxia	Analgesia
Fluids resuscitation	Hypothermia
Inotropes	Shunting:
	Poisons/sepsis.

Perfusion Indicators

ScvO2	70%
Pv-aCO2 gap	<6 mmHg
Lactate (serial readings)	<2 mmol/L

These can be done if CVC and A-line are available.

Modified Fick equation using CO2:

$$VCO_2 = CO \times (CvCO_2 - CaCO_2)$$

$$CO = VCO_2/CvCO_2 - CaCO_2$$

$$\mathbf{CvCO_2 - CaCO_2 = \frac{VCO_2}{CO}}$$

Advantages of CO2 v-a gap:

VCO2 is easier to obtain, from the fraction expired CO2.

Since CO2 is readily eliminated by the lung, an increase in P(v-a)CO2 above the normal threshold of 6 mmHg reflects intense CO2 stagnation in tissues either through local or global perfusion disorders.

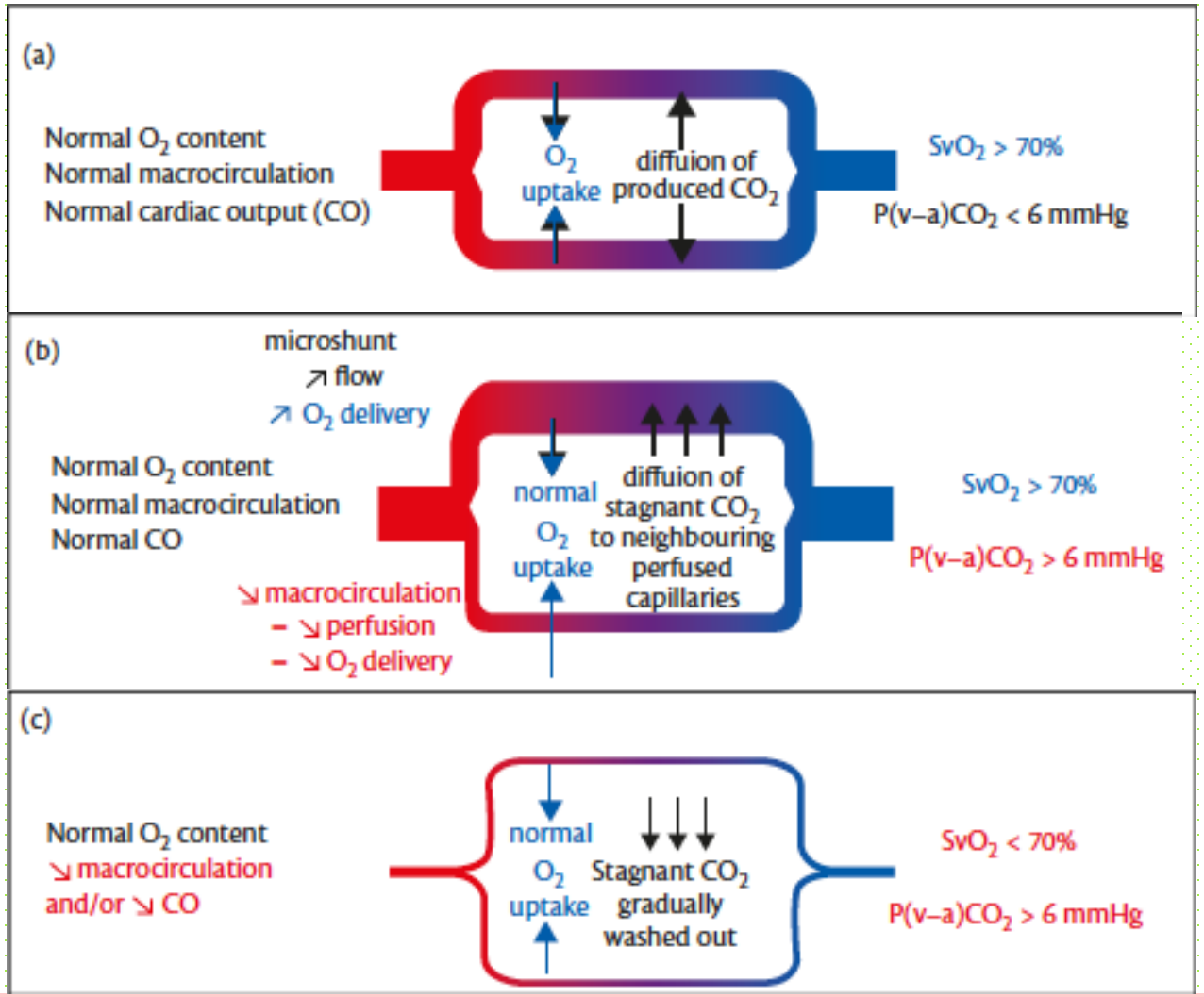
$$\Delta PCO_2 = K \times \frac{VCO_2}{Cardiac\ Output}$$

SVO2 and Pv-aCO2gap:

Normal

Poor Microcirculation
+ Micro Shunting

Low flow state: Poor local microcirculation &/or low CO.

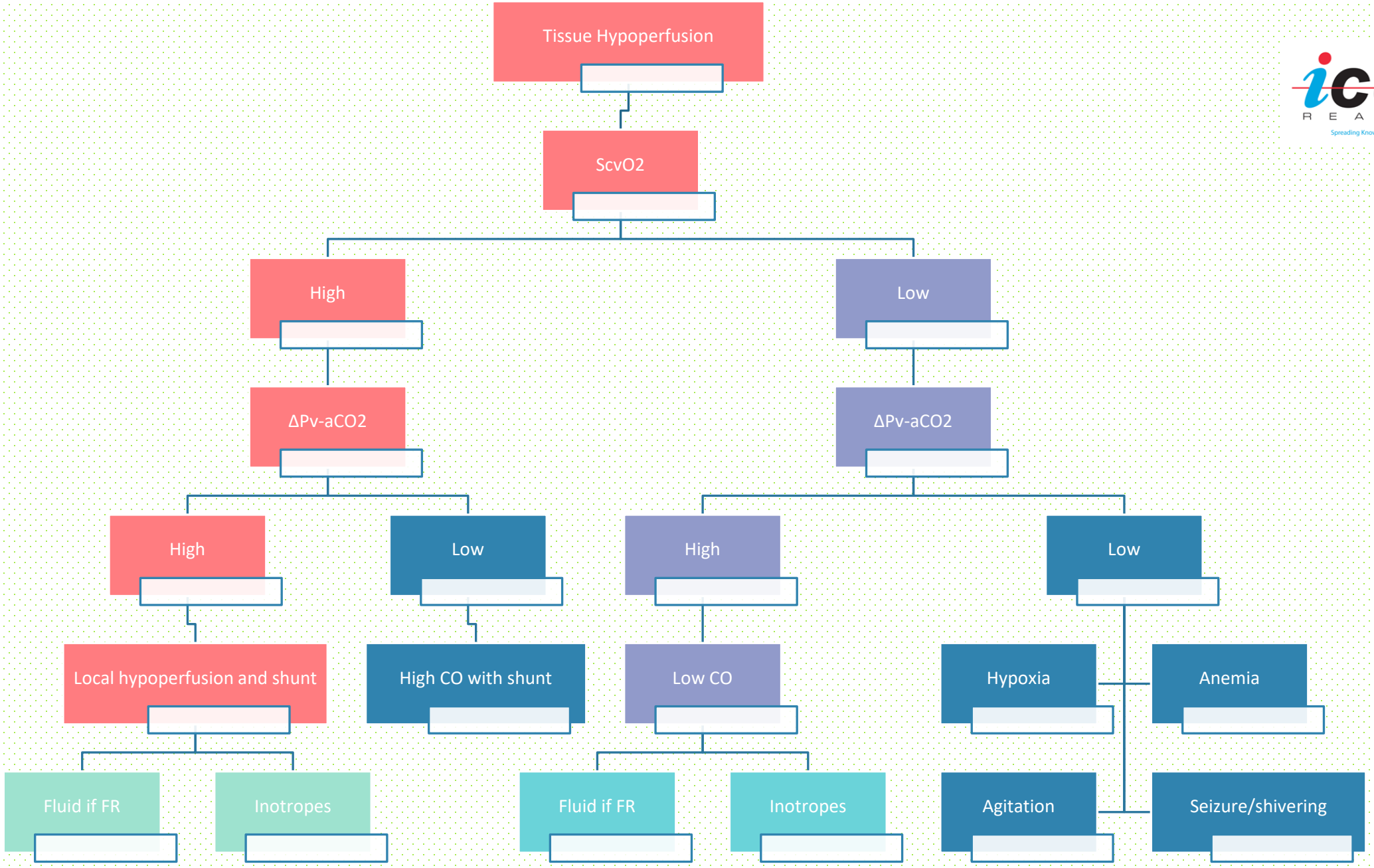


Oxford textbook of Critical care, 2nd Ed., 2016, pp640.

Please Mind the Gap

Vallet B, Pinsky MR, Cecconi M. Resuscitation of patients with septic shock: please “mind the gap”! Intensive Care Med. 2013 Sep;39(9):1653-5

Shock Type	Lactate	O2ER	ScvO2	CvaCO2Gap
Cardiogenic or Hypovolemic	High	High	Low	High
Anemic or Hypoxic	High	High	Low	Low
Distributive	High	Low	High	High
Cytopathic	High	Low	High	Low


Tissue Hypoperfusion
ScvO2
High
Low
ΔPv-aCO2
ΔPv-aCO2
High
Low
High
Low
Local hypoperfusion and shunt
High CO with shunt
Low CO
Hypoxia
Anemia
Fluid if FR
Inotropes
Fluid if FR
Inotropes
Agitation
Seizure/shivering

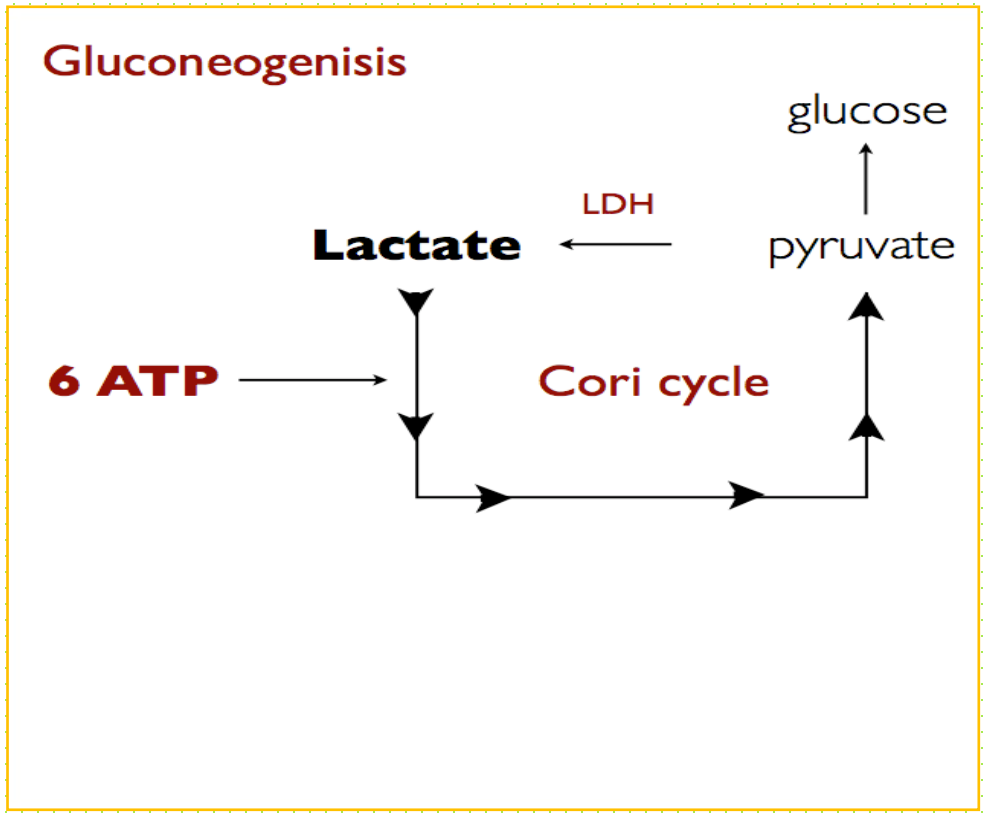
Perfusion Indicators

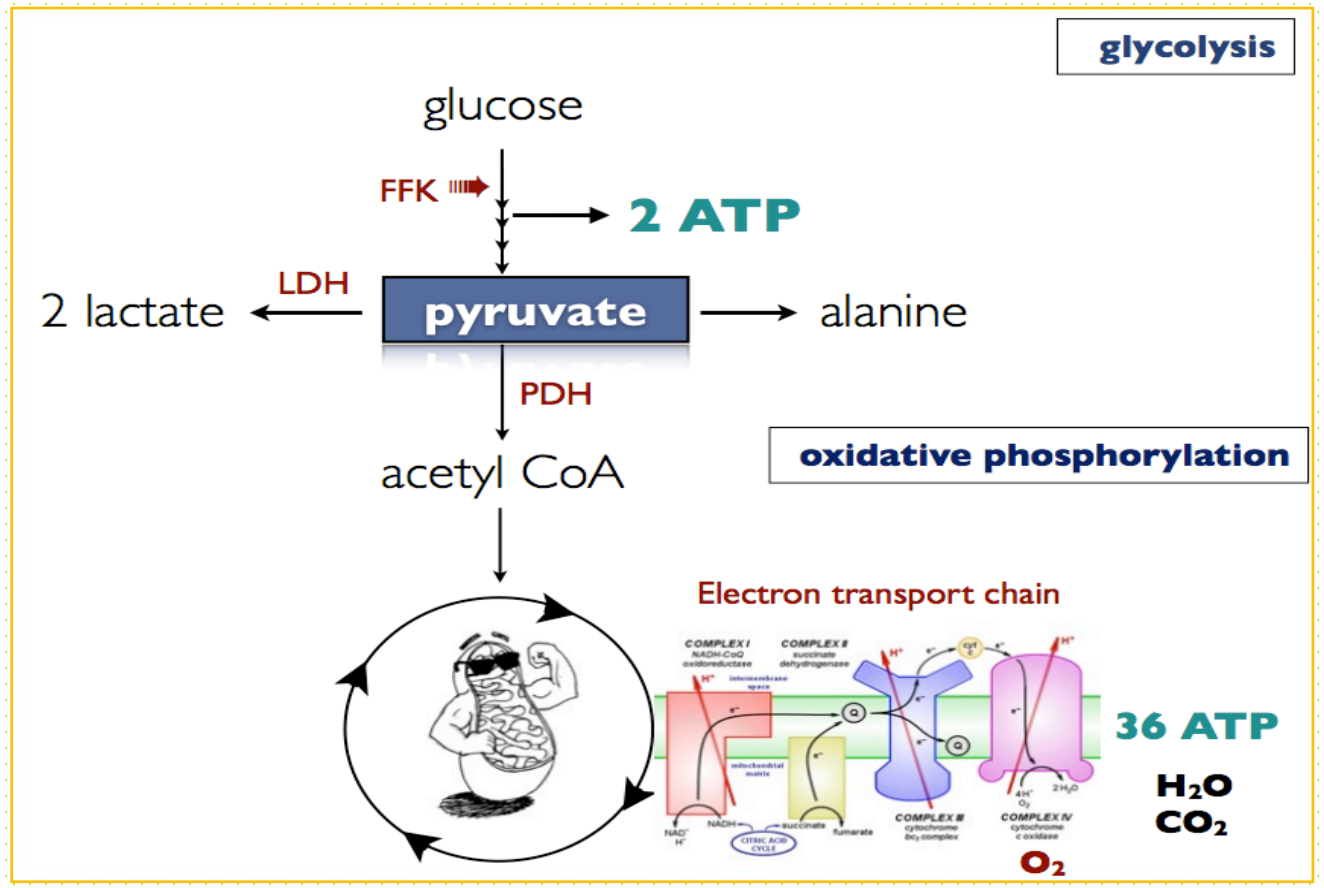
ScvO2	70%
Pv-aCO2 gap	<6 mmHg
Lactate (serial readings)	<2 mmol/L

These can be done if CVC and A-line are available.

Lactate metabolism..

In the liver:





Courtesy: Prof. Jan Bakker

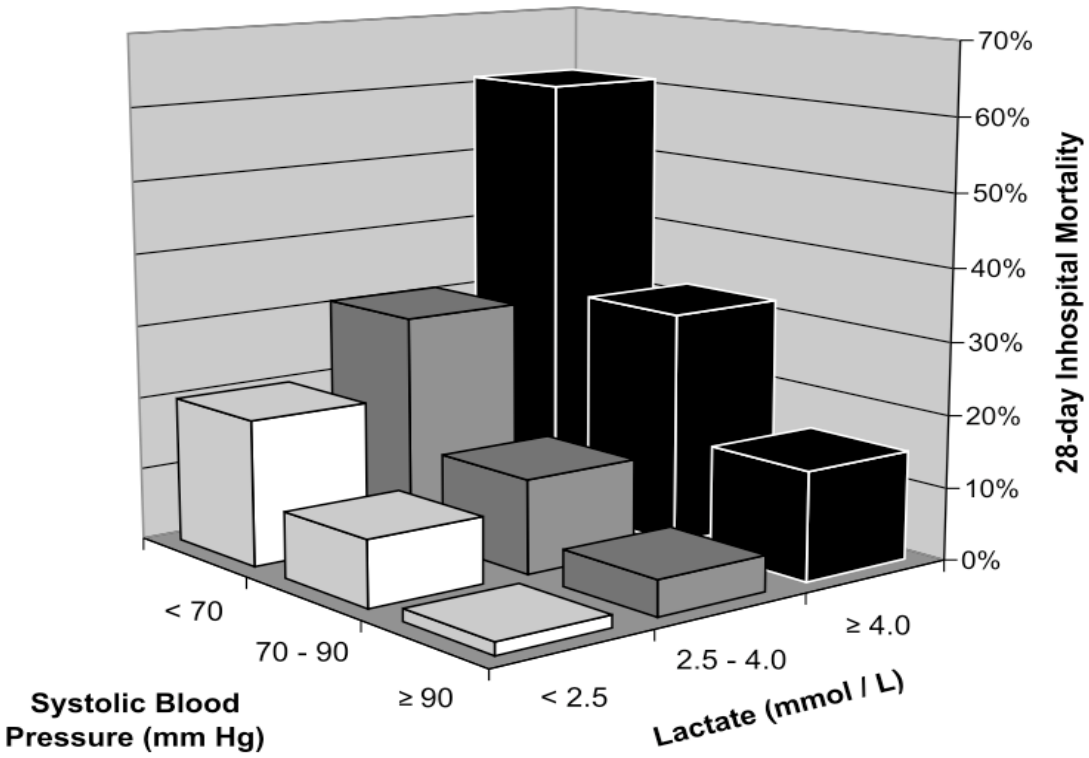
Intensive Care Med (2007) 33:1892–1899
DOI 10.1007/s00134-007-0680-5

ORIGINAL

Michael D. Howell
Michael Donnino
Peter Clardy
Daniel Talmor
Nathan I. Shapiro

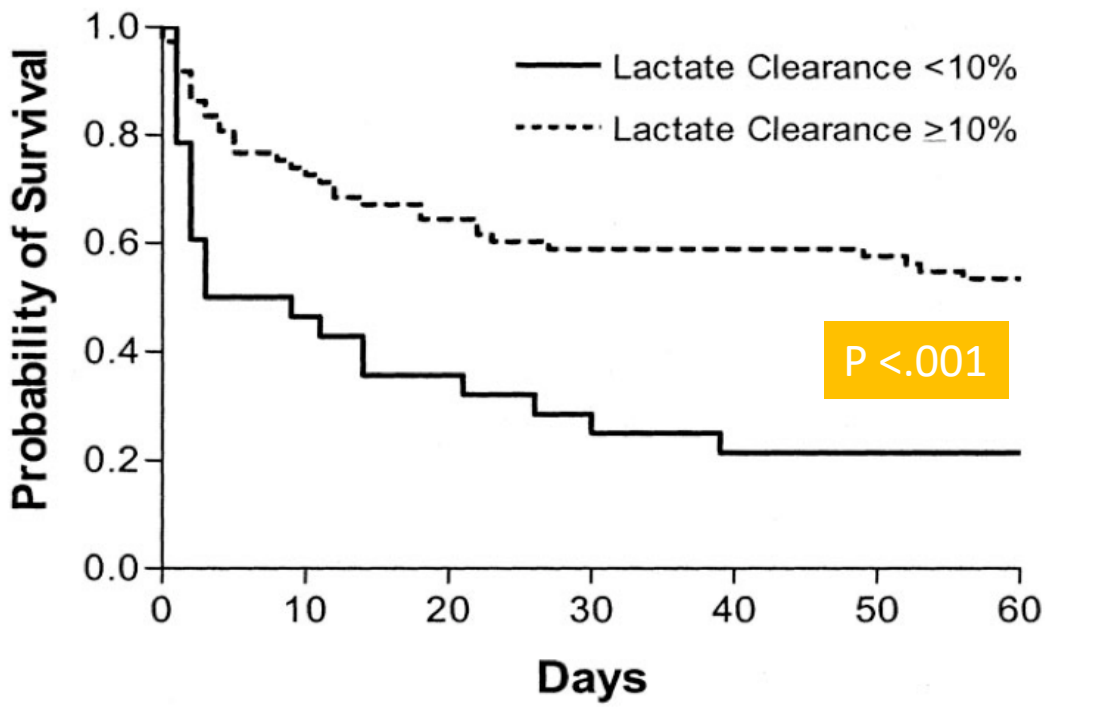
Occult hypoperfusion and mortality in patients with suspected infection

Lactate can help identifying OCCULT shock states



Early lactate clearance is associated with improved outcome in severe sepsis and septic shock*

H. Bryant Nguyen, MD, MS; Emanuel P. Rivers, MD, MPH; Bernhard P. Knoblich, MD; Gordon Jacobsen, MS; Alexandria Muzzin, BS; Julie A. Ressler, BS; Michael C. Tomlanovich, MD



Crit Care Med 2004 Vol. 32, No 8

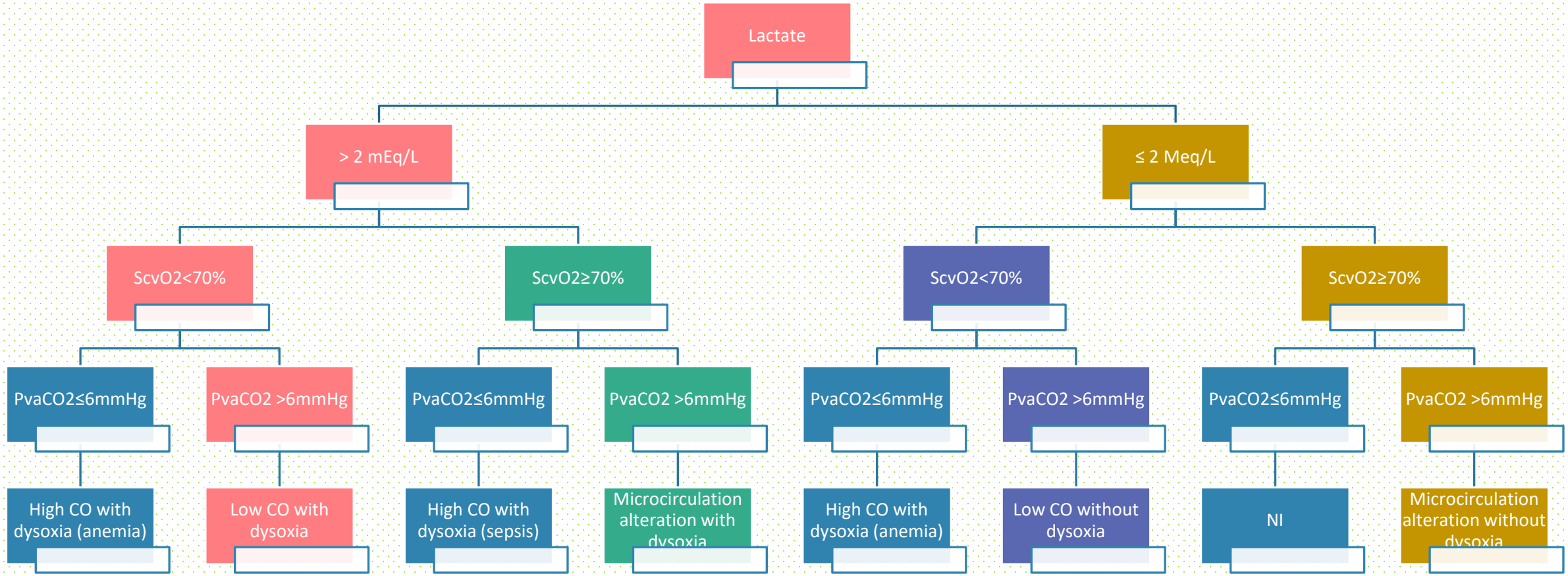
Causes of Hyperlactatemia

Type A

- **Loss of oxidative phosphorylation of pyruvate**:
  - **Global hypoxia:**
    - Shock (Septic, Hypovolemic, Cardiogenic)
    - CO poisoning
    - Severe Hypoxic respiratory failure
    - Severe anemia
  - **Local Ischemia**:
    - Ischemia
      - Limb
      - Gut

Type B

- **Glycolysis stimulation** (non oxidative pathway):
  - B2 agonist drugs, catecholamins, cocain
  - Malignancies: B-cell lymphoma
- **Impaired lactate clearance:**
  - Impaired Gluconeogenesis: Metformin & Ethanol intoxication.
  - Impaired Cori cycle: Hepatic failure
  - Renal failure
  - PDH inhibition: Thiamin deficiency
  - Mitochondrial toxicity: HAART drugs (NRTIs)



Scheeren et al, Understanding the carbon dioxide gaps; Current opinion in critical care 2018

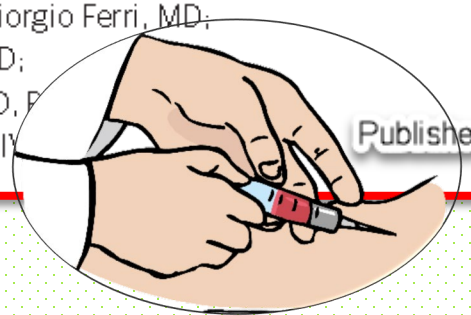
Resuscitation strategy in Septic shock: CRT vs Lactate

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of a Resuscitation Strategy Targeting Peripheral Perfusion Status vs Serum Lactate Levels on 28-Day Mortality Among Patients With Septic Shock

The ANDROMEDA-SHOCK Randomized Clinical Tri

Glenn Hernández, MD, PhD; Gustavo A. Ospina-Tascón, MD, PhD; Lucas Petri Damiani, MSc; Elisa Estenssoro, MD; Arnaldo Dubin, MD, PhD; Javier Hurtado, MD; Gilberto Friedman, MD, PhD; Ricardo Castro, MD, MPH; Leyla Alegría, RN, MSc; Jean-Louis Tebo PhD; Maurizio Cecconi, MD, FFICM; Giorgio Ferri, MD; Manuel Jibaja, MD; Ronald Pairuman nández, MD; Diego Barahona, MD; Vladimir Granda-Luna, MD, PhD; A valcanti, MD, PhD; Jan Bakker, MD, P ANDROMEDA-SHOCK Inves merica Intensive Care Network (LI



Published online February 17, 2019

JAMA Network™

QUESTION Does a resuscitation strategy targeting normalization of capillary refill time, compared with targeting serum lactate levels, reduce mortality in patients with septic shock?

CONCLUSION This randomized clinical trial of adults with septic shock found that use of a peripheral perfusion-targeted resuscitation strategy, compared with targeting serum lactate, did not significantly reduce mortality.

POPULATION

198 Men 226 Women

Adults in the ICU with septic shock

Mean age: 63 years

LOCATIONS

28 ICUs in 5 countries in South America

INTERVENTION

424 Patients randomized

212

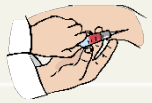
Peripheral perfusion group

Resuscitation protocol of normalizing capillary refill time (measured in seconds)

212

Lactate group

Resuscitation protocol of normalizing or decreasing lactate levels (>20% per 2 hours)



PRIMARY OUTCOME

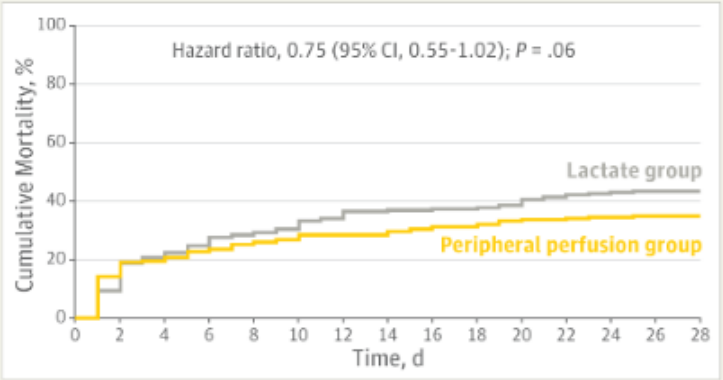
All-cause mortality at 28 days

FINDINGS

All-cause mortality at 28 days

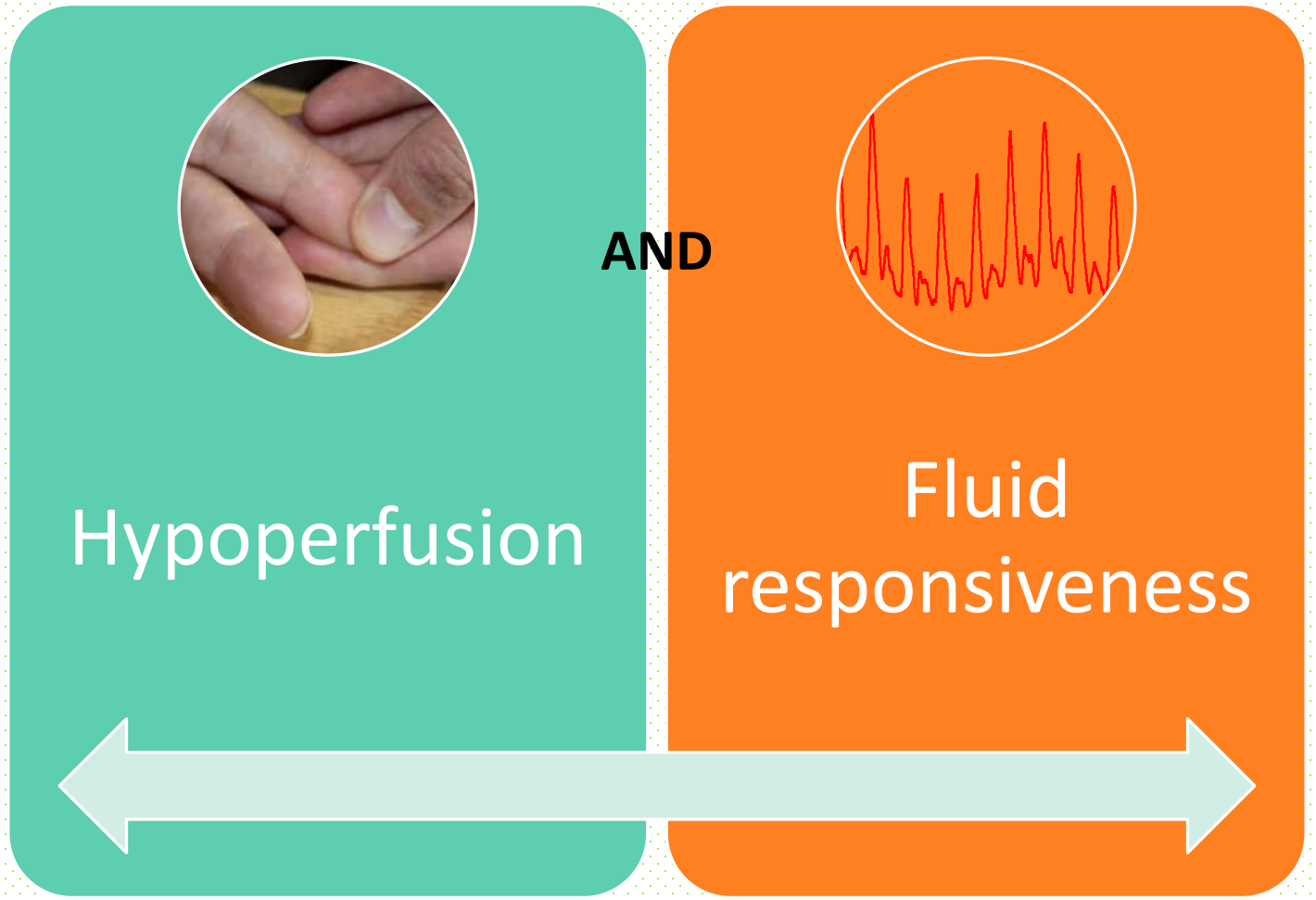
Peripheral perfusion group 34.9% (74 patients died)

Lactate group 43.4% (92 patients died)

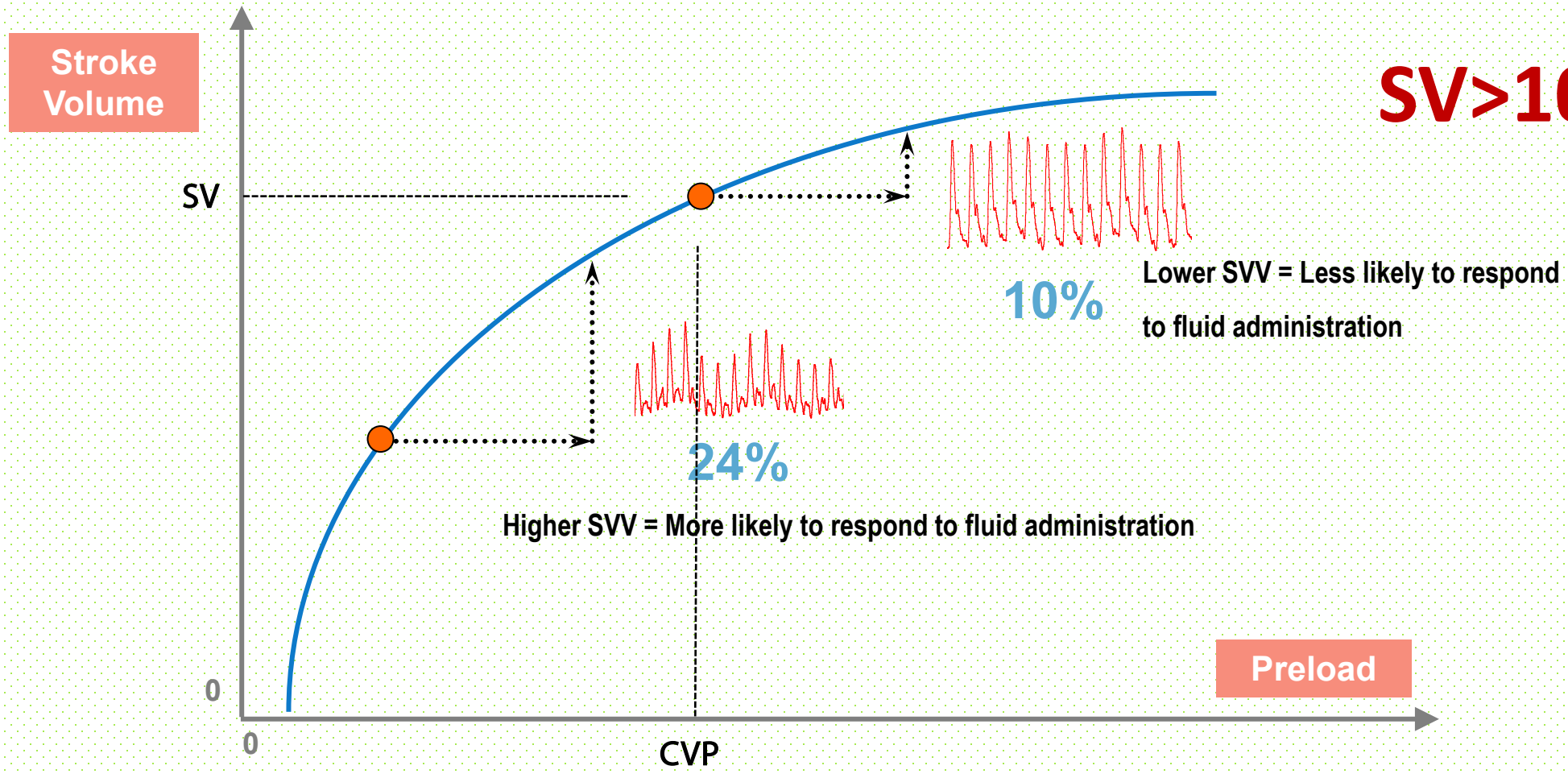


No significant risk difference between groups:

-8.5% (95% CI, -18.2% to 1.2%),

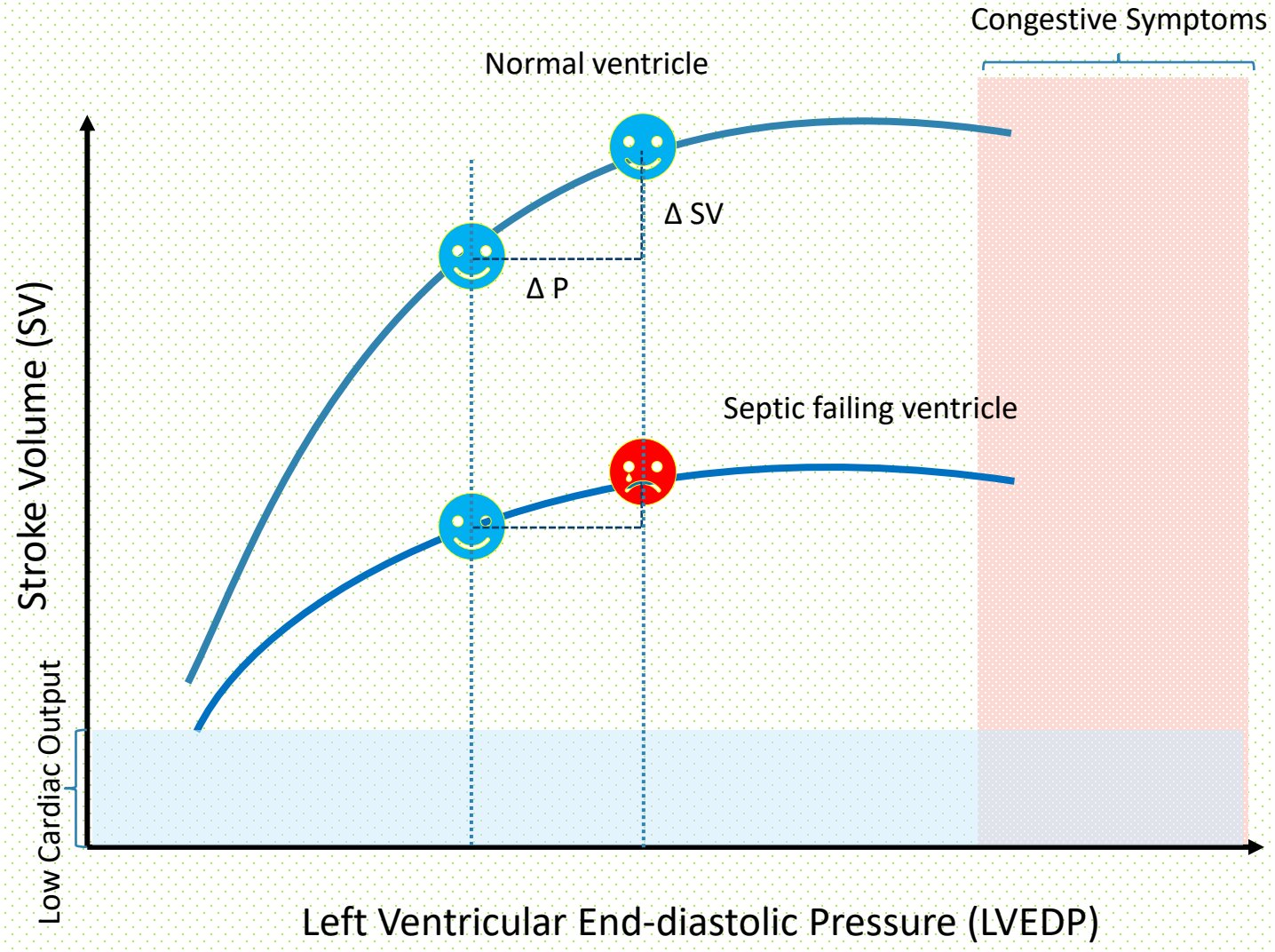

AND
Hypoperfusion
Fluid responsiveness

Frank Starling Curve

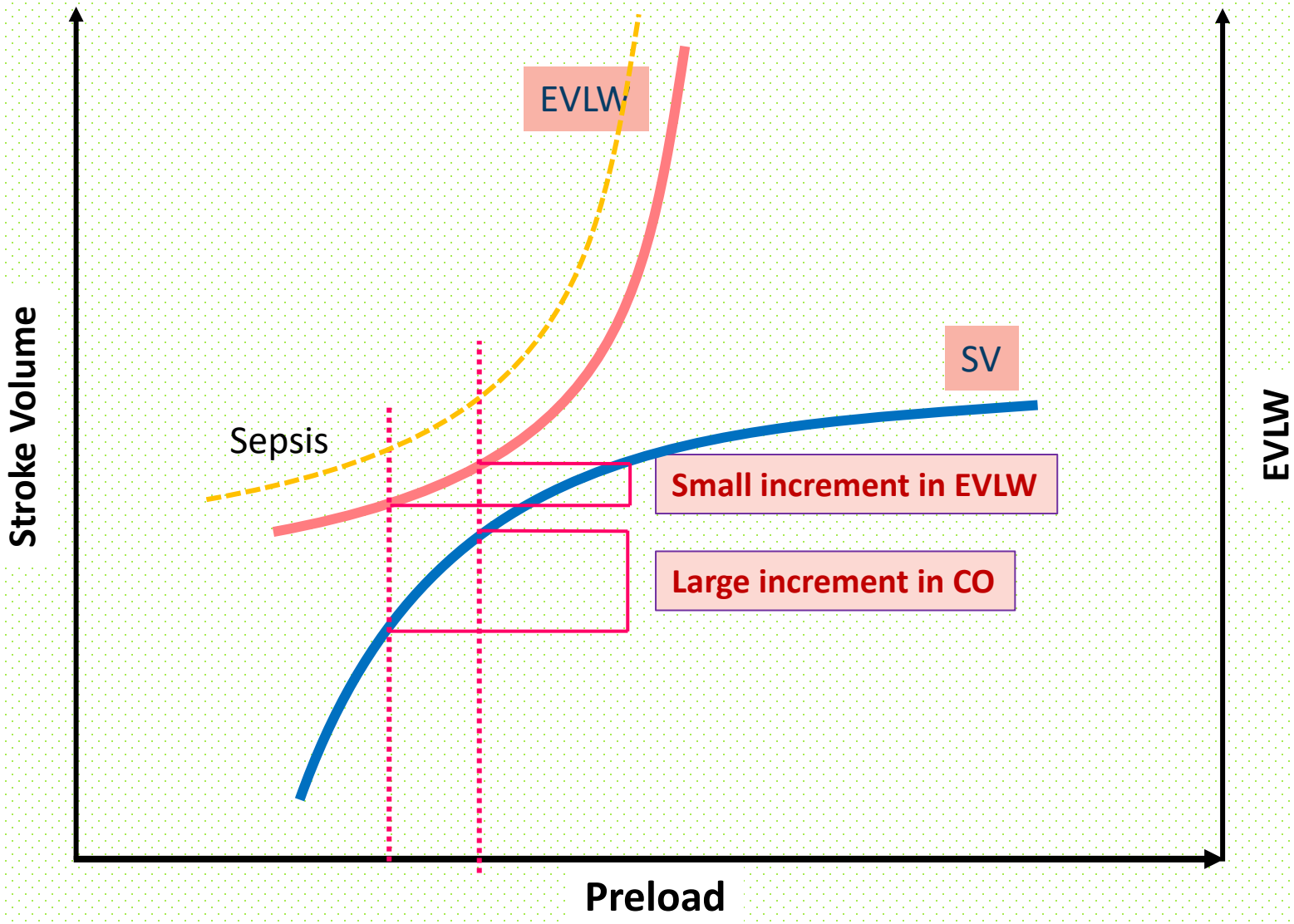


Rise in Stroke Volume by >10% has been widely accepted as an indicator of adequate response to fluid resuscitation.

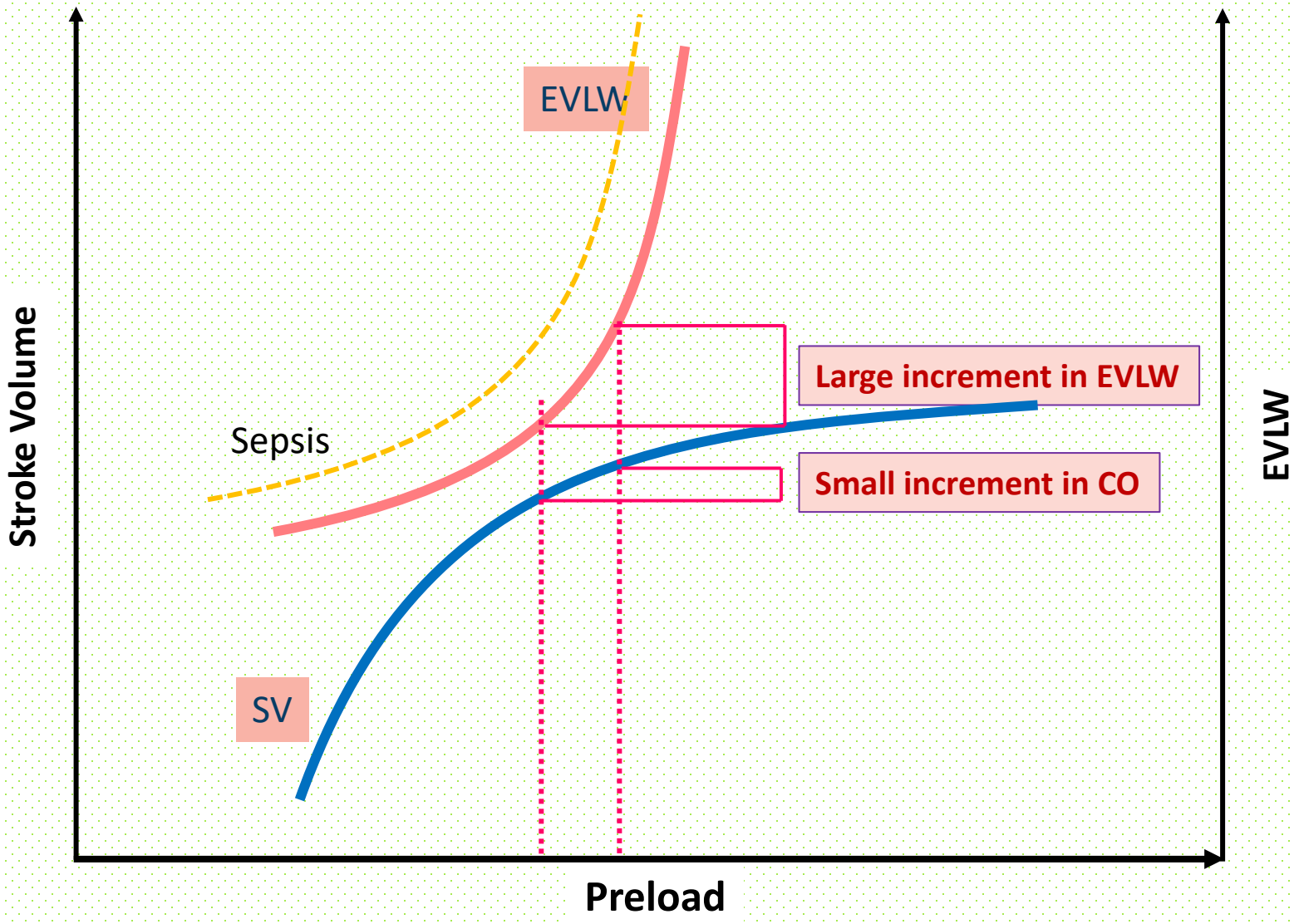
Beware!!


Congestive Symptoms
Normal ventricle
Δ SV
Δ P
Septic failing ventricle
Stroke Volume (SV)
Low Cardiac Output
Left Ventricular End-diastolic Pressure (LVEDP)

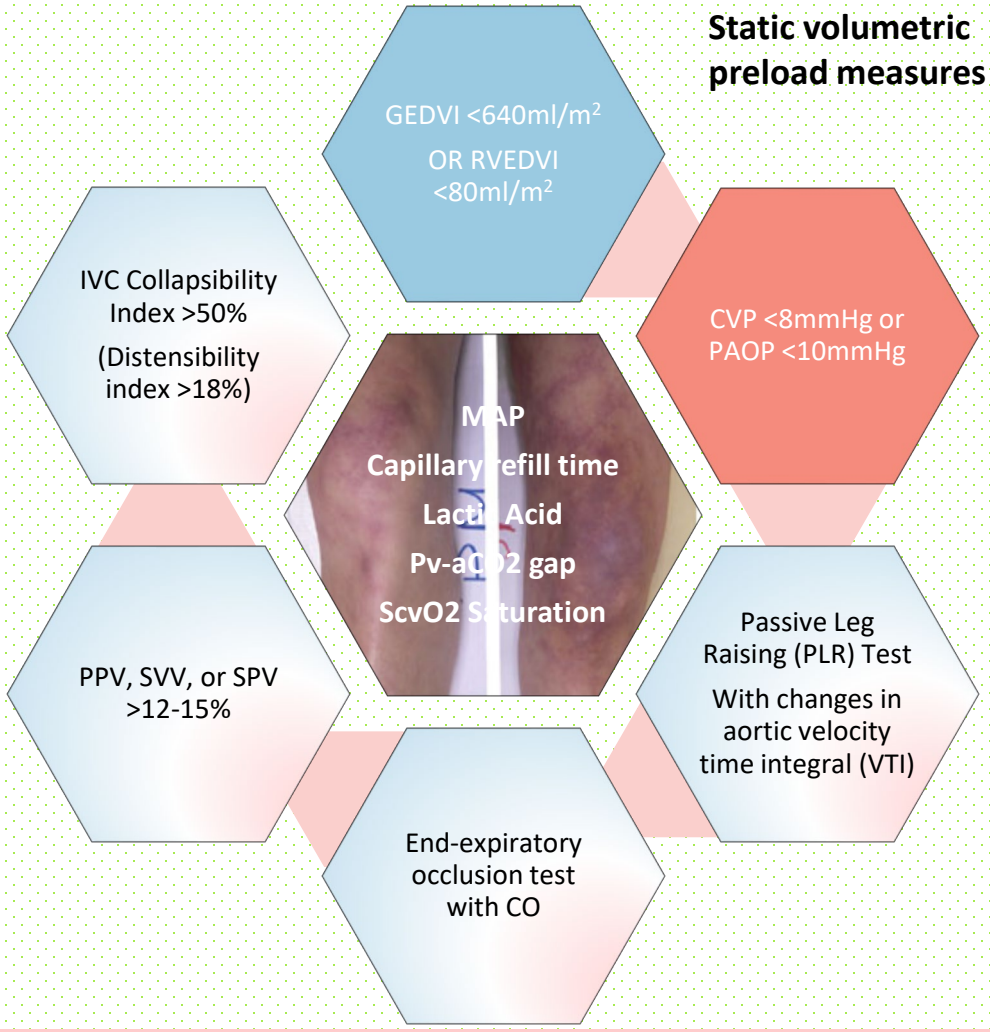
Frank-Starling & Marik-Phillips curves:



Frank-Starling & Marik-Phillips curves:



Consider Fluid Boluses



Static volumetric preload measures

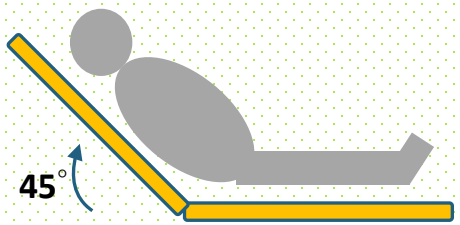
Static preload pressure measures

Passive Leg Raising Test

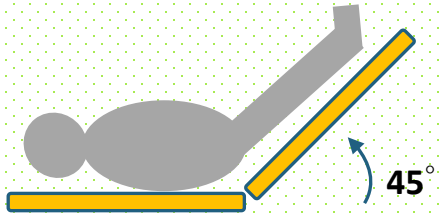
Raise the foot of the bed 30-45° whilst observing the effect for 60-90 seconds

Positive PLR if:

- Aortic Blood Flow increases by 10%. (AUC 0.96)
- SVV rises by 10%
- PPV rises by 10% (AUC 0.75)
- eTCO2 rises by 5%
- BP rise by 10%

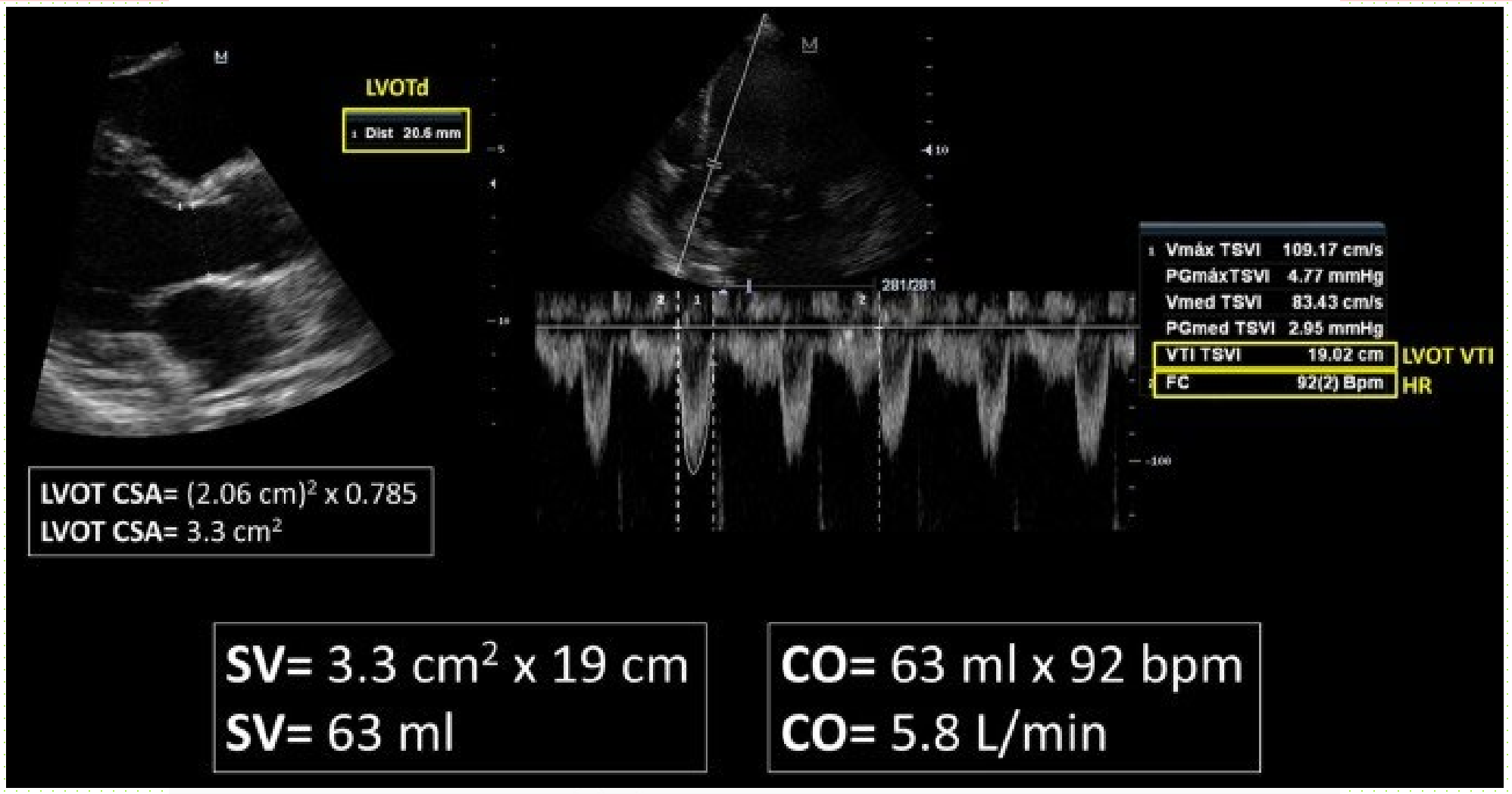


Semi-recumbent Position



Passive Leg Raising

Stroke Volume

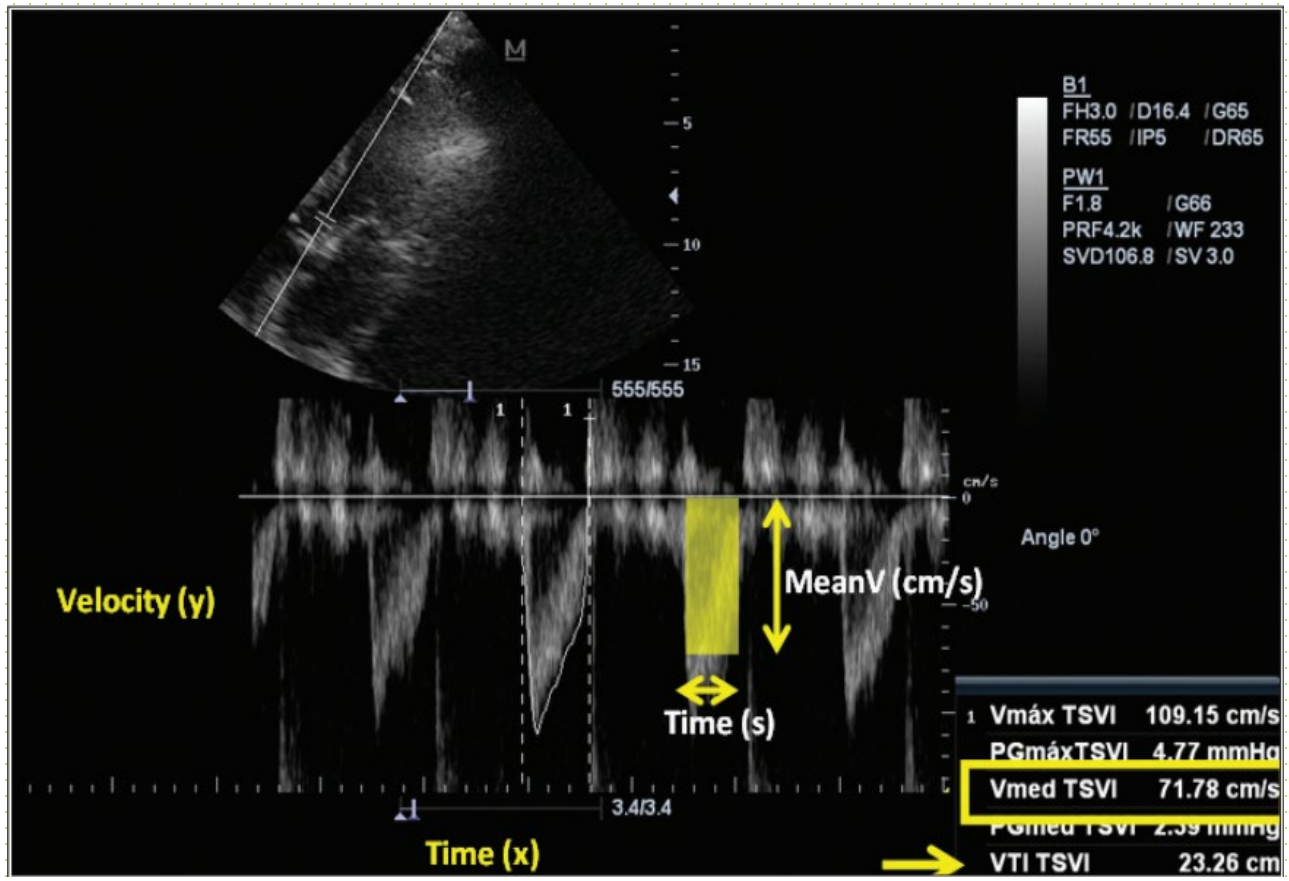


Blanco et al—Rapid Ultrasound in Shock Velocity-Time Integral, J Ultrasound Med 2015; 34:1691–1700

LVOT VTI:

The normal LVOT VTI is 18 to 22 cm.

A cutoff of **greater than 12% rise** in VTI after PLR discriminates patients with a preload reserve→ Fluid responders.



MV patient, VT 8ml/kg

Continuous CO monitoring e.g PiCCO/FloTrac

Expiratory hold for 15 seconds

+ve if CO increased by 5%.

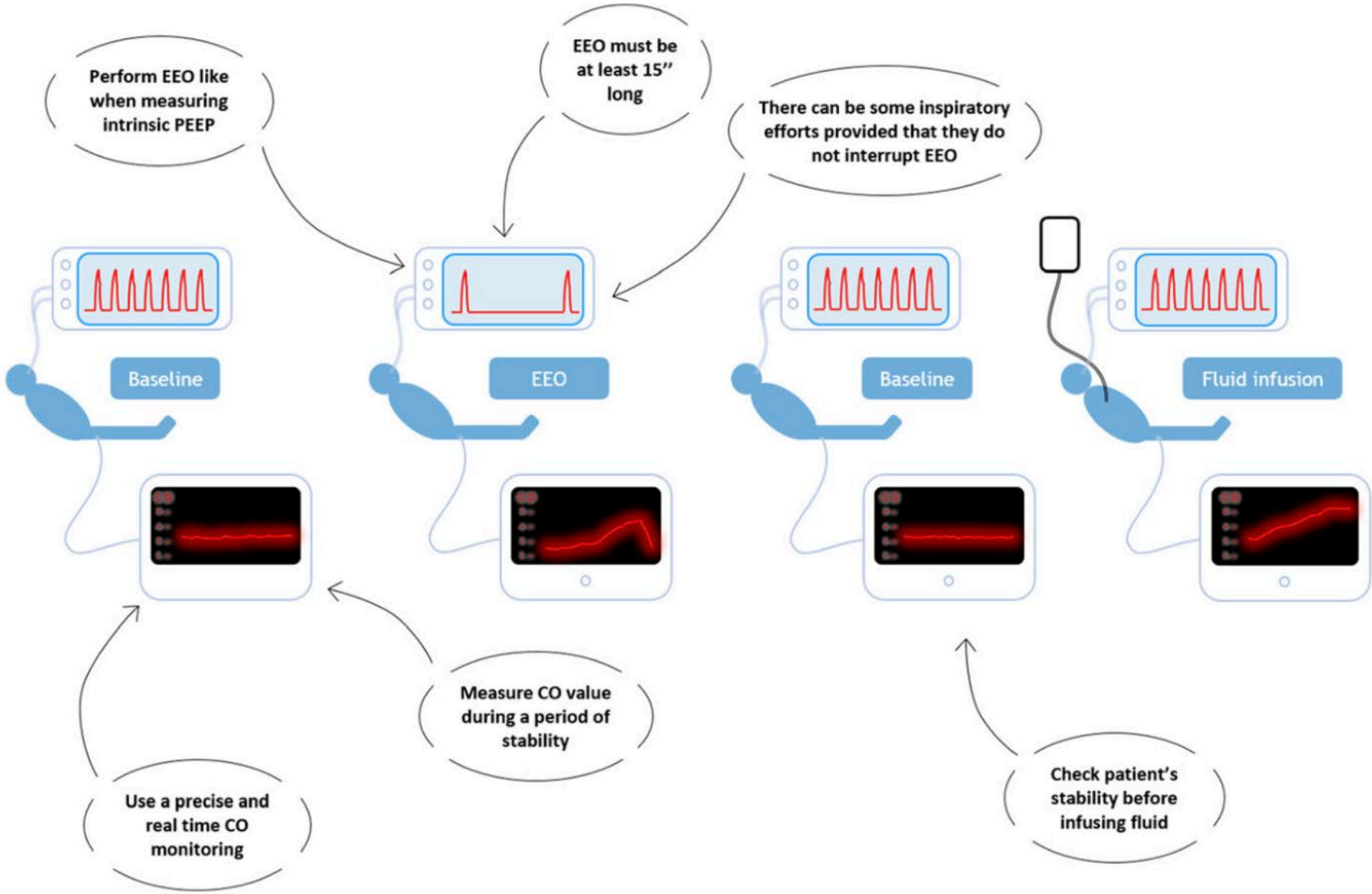


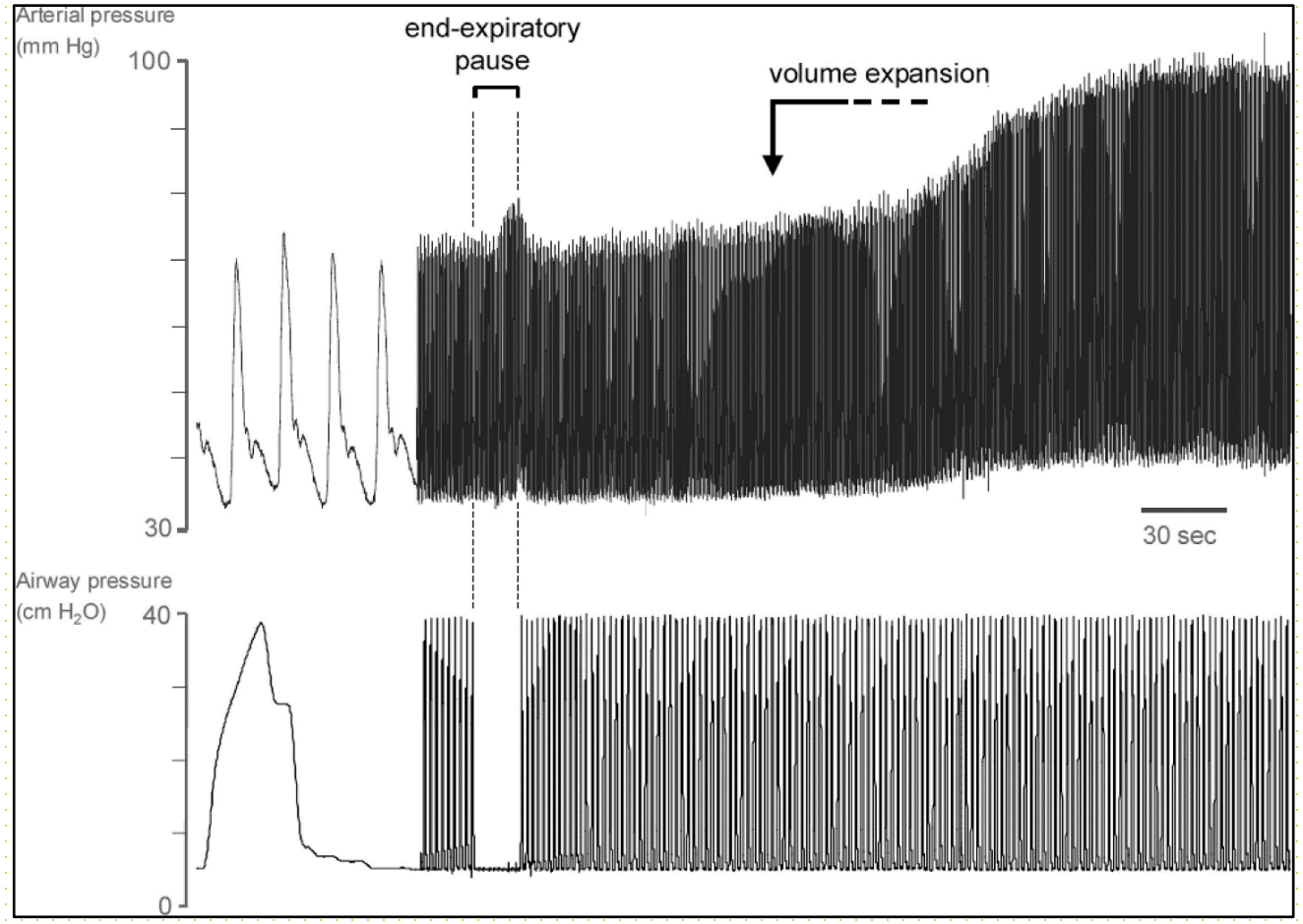
Fig. 1 Procedure to perform an end-expiratory occlusion test

End Expiratory Occlusion test:

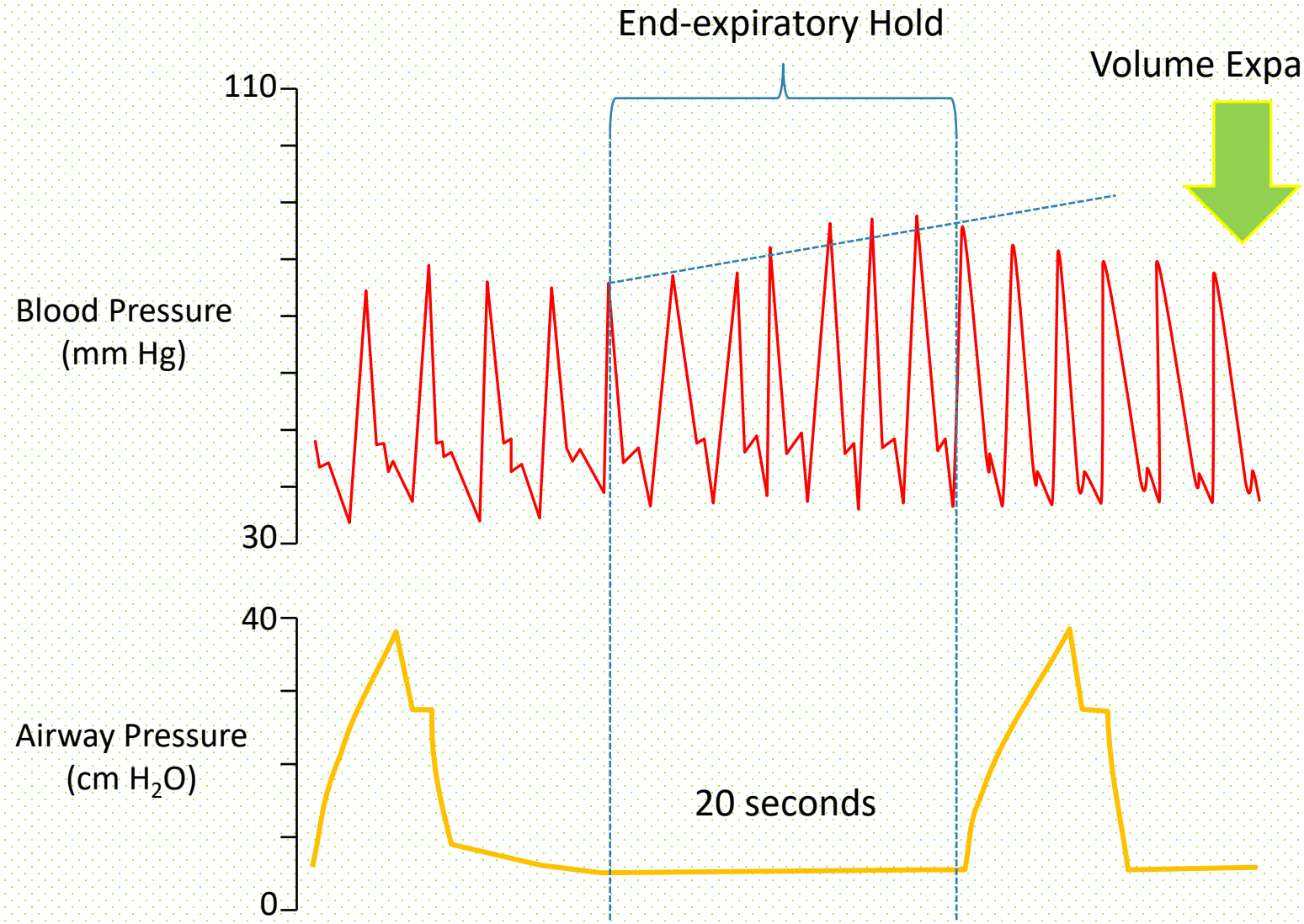
Pausing the vent at end expiration for 15 seconds leads to rise in the venous return →act like a fluid challenge.

5% increase in CO and BP predicts fluid responsiveness.

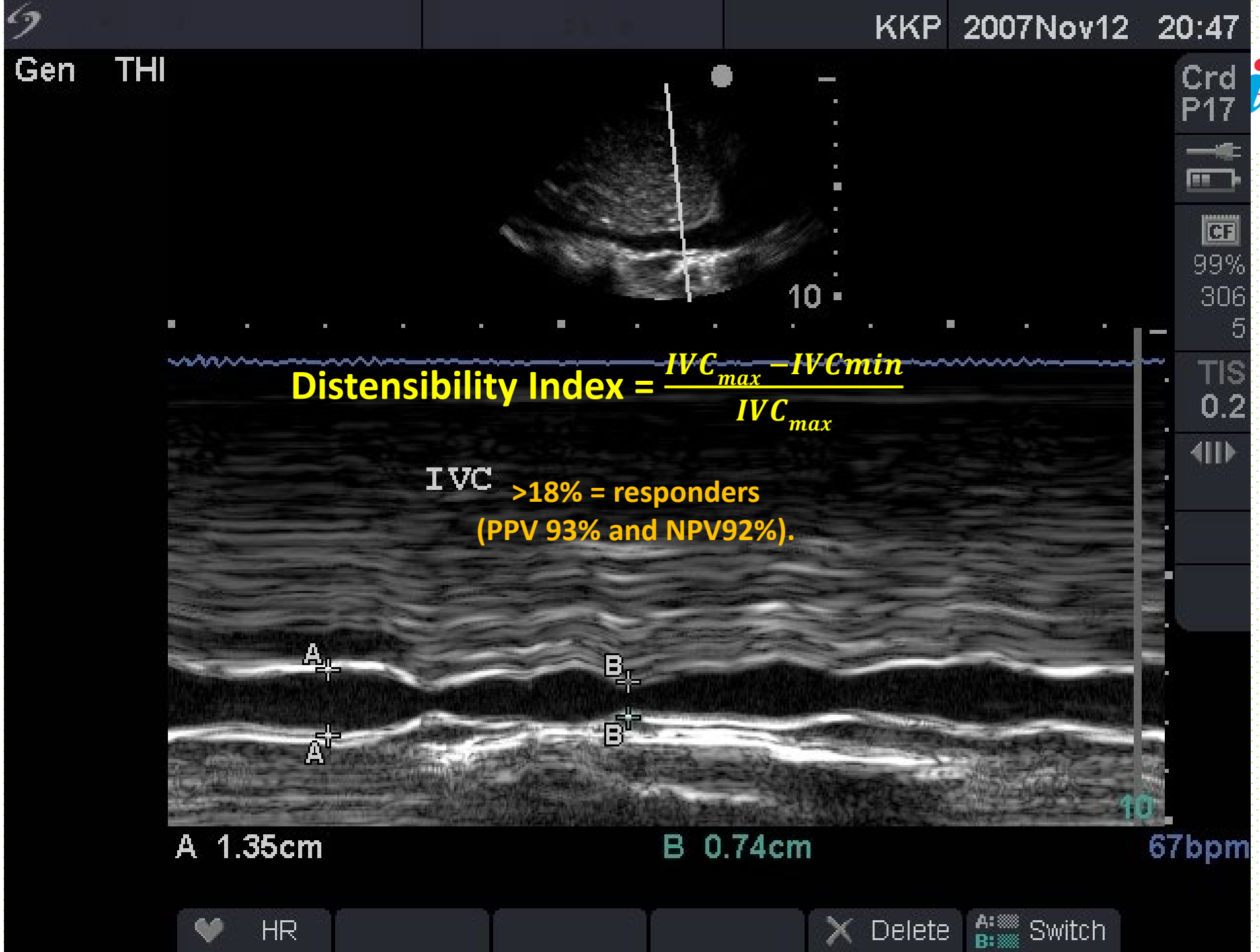
Can be used with arrhythmias and ARDS cases as well as occasional spontaneous breaths.



Monnet et al, Predicting volume responsiveness by using the EEO in MV ICU patients, CCM 2009 Vol 37, 951-956.

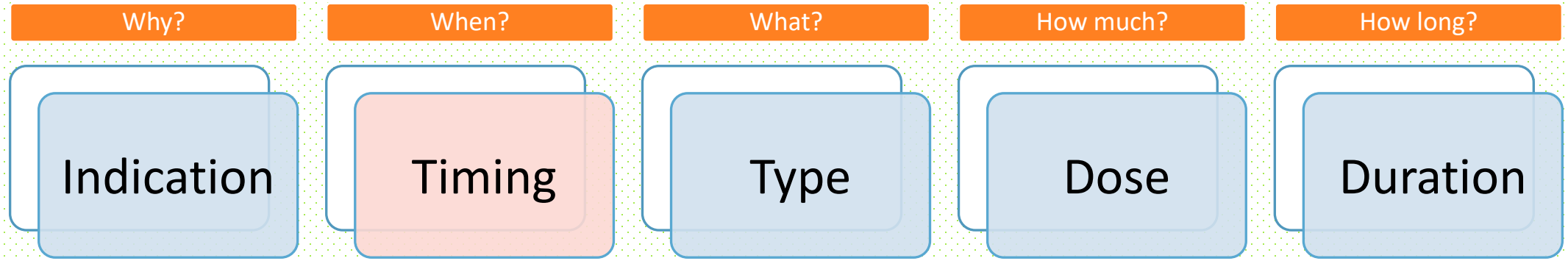

End-expiratory Hold
Volume Expansion
110
Blood Pressure
(mm Hg)
30
40
Airway Pressure
(cm H_2O)
0
20 seconds


543 SMF
Not Admitted
18 Nov 2022 16:02
ART Change Scale
Sinus Rhythm
HR bpm
150
50
87
Pulse bpm
87
PVC 0
1mV
Inspiration Expiration
ART
145
105
65
ART mmHg
Mean
110
60
106/51 (69)
Resp
10hm
RR rpm
13
Tcore °C
39.0
32.5
34.9
Pleth
SpO2 %
100
87
100
NBP mmHg Pulse 86
Sys.
160
90
Man
90/68 (76)
15:54
NBP
mmHg
12:30 145/85(102)
12:33 149/82(102)
13:00 141/90(106)
13:28 117/82(91)
13:30 105/91(97)
14:31 (-?-)
15:27 121/79(93)
15:54 90/68(76)
Clock
16:02
TimerA
15 min
No alarm recording available
Pause
Startf
NBP
Vitals
Profiles
Monitor
Print
Other
Zero
End
Main
Main


KKP 2007Nov12 20:47
Gen THI
Crd P17
CF
99%
306
5
TIS 0.2
10
Distensibility Index = $\frac{IVC_{max} - IVCmin}{IVC_{max}}$
IVC
>18% = responders
(PPV 93% and NPV92%).
A
B
A
B
10
A 1.35cm
B 0.74cm
67bpm
HR
Delete
A:
B:
Switch

Test		Threshold for FR	AUC	Comment
EEO test		5% in CI	0.97	MV
PPV		13%	0.94	MV, VT >8ml/kg &/or DD >20, No arrhythmias
dABF using ODM		>18%	0.93	MV, VT>8ml, No arrhythmias, Controlled ventilation
VTI		20%	0.86	MV
SPV		10mmHg	0.86	MV, Provided delta down >5mmHg
SVV		12%	0.84	MV, VT >8ml/kg, No arrhythmias
IVC	MV	15%	0.91	VT>8ml/kg, No PHTN or Hi IAP
	Spontaneous	50%	0.77	No PHTN or Hi IAP
CVP variation		>=1mmHg		Both MV & spontaneously breathing patients
Static tests CVP, PAOP, GEDVI)			0.55-0.64	

Note: the higher the threshold; the more certain the effect of Fluid bolus is.


Why?
When?
What?
How much?
How long?
Indication
Timing
Type
Dose
Duration

Hour-1 Bundle

Initial Resuscitation for Sepsis and Septic Shock

Surviving Sepsis Campaign

MEDICAL EMERGENCY

Initiate bundle upon recognition of sepsis/septic shock.

May not complete all bundle elements within one hour of recognition.

1 Measure lactate level.

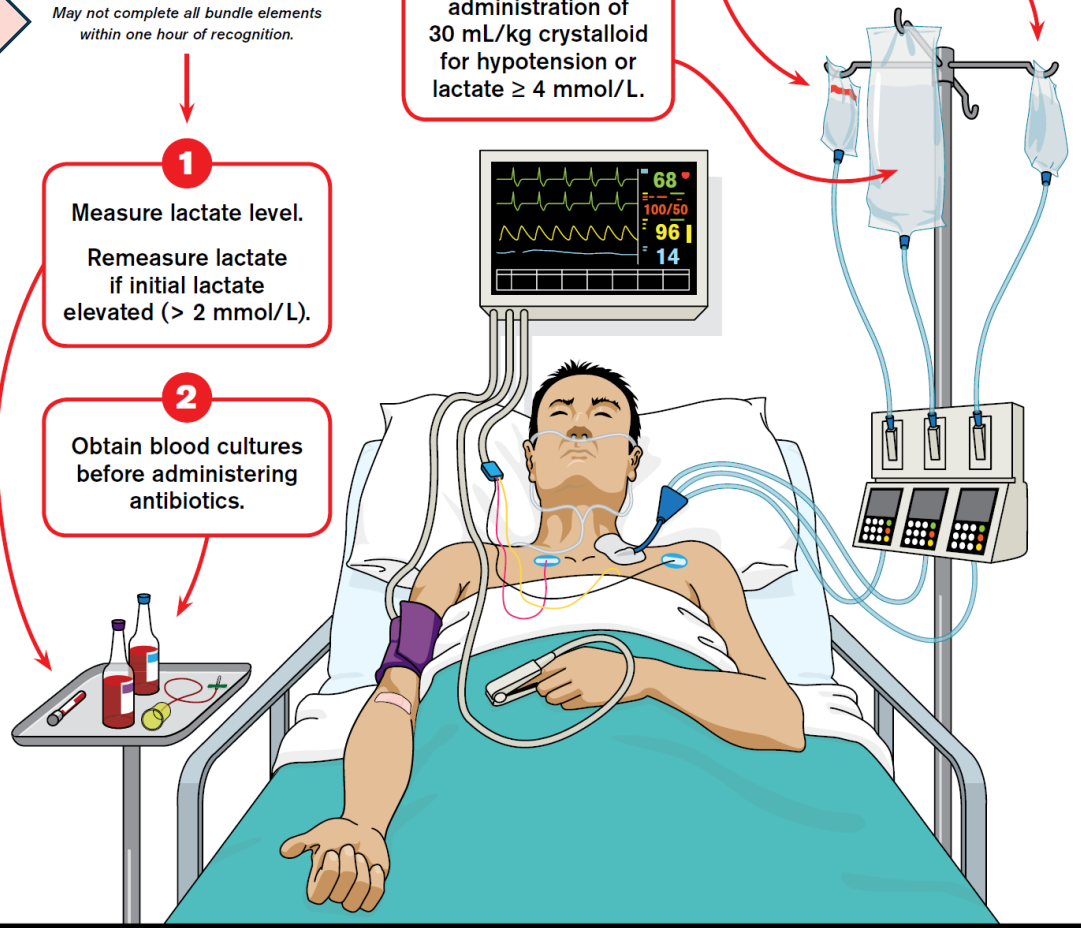
Remeasure lactate if initial lactate elevated (> 2 mmol/L).

2 Obtain blood cultures before administering antibiotics.

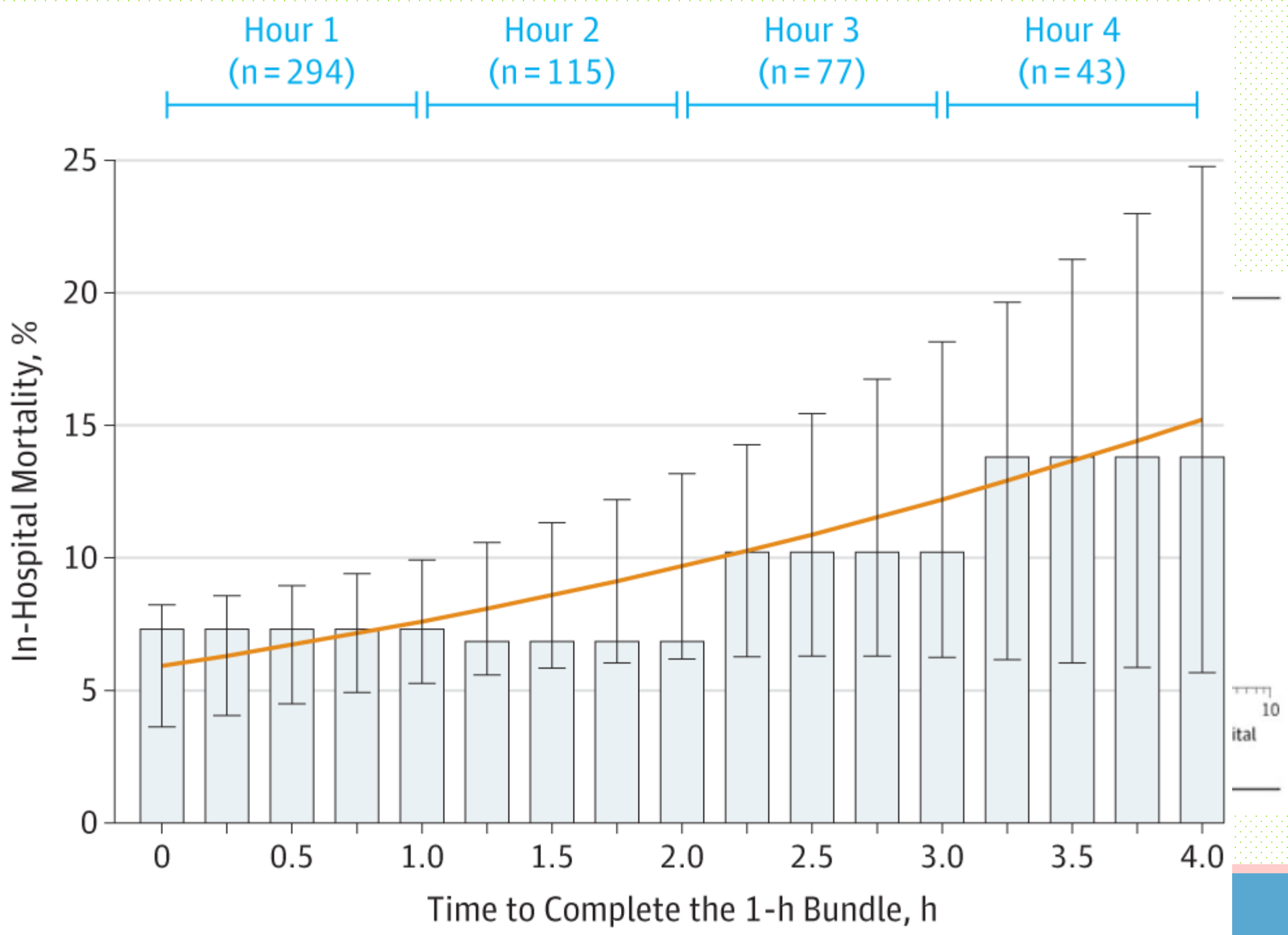
3 Administer broad-spectrum antibiotics.

4 Begin rapid administration of 30 mL/kg crystalloid for hypotension or lactate ≥ 4 mmol/L.

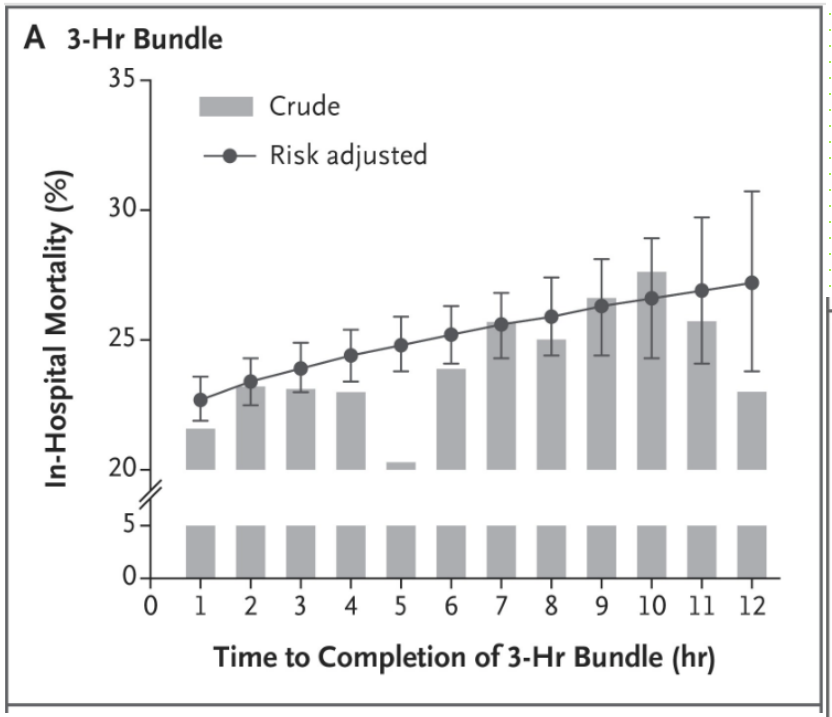
5 Apply vasopressors if hypotensive during or after fluid resuscitation to maintain a mean arterial pressure ≥ 65 mm Hg.



Bundle: SurvivingSepsis.org/Bundle Complete Guidelines: SurvivingSepsis.org/Guidelines

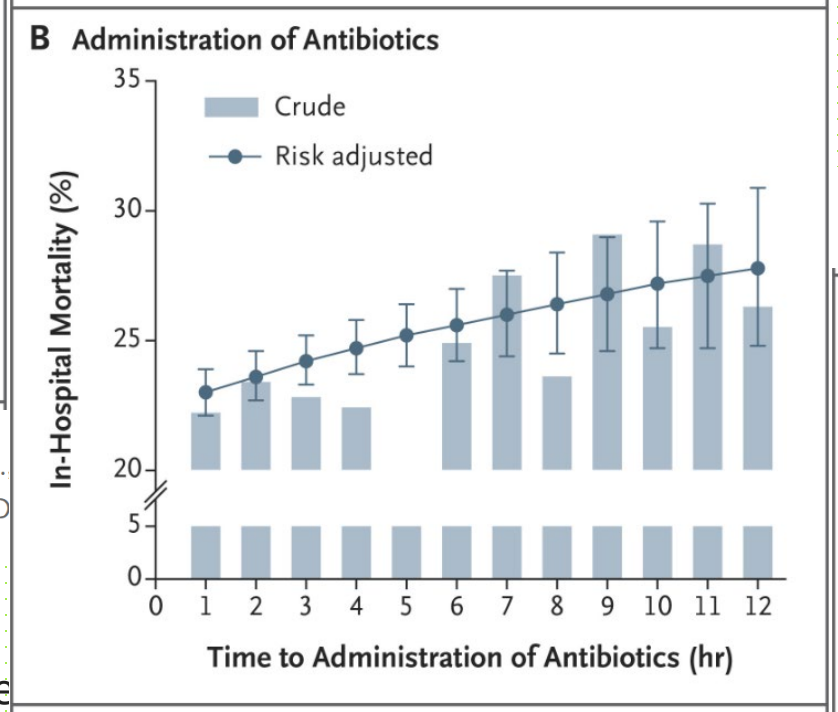

Hour 1
(n = 294)
Hour 2
(n = 115)
Hour 3
(n = 77)
Hour 4
(n = 43)
In-Hospital Mortality, %
25
20
15
10
5
0
0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
Time to Complete the 1-h Bundle, h

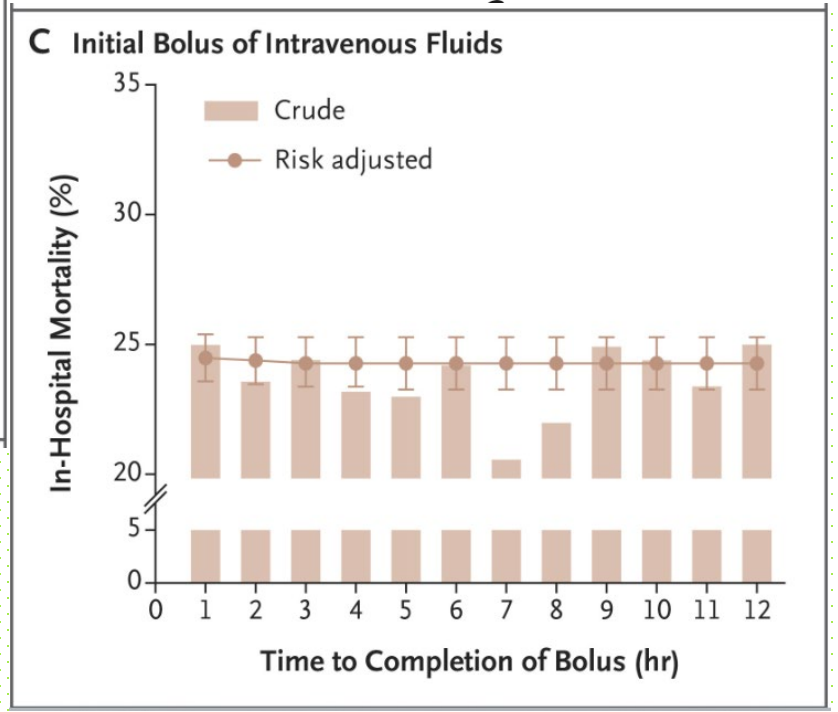
3-Hr Bundle: Blood cultures, broad-spectrum antibiotic agents, and lactate measurement



Christopher W. Seymour, M.D., Foster Gesten, M.D.
Lemeshow, Ph.D

NY State De





Time completion of initial fluid bolus was not associated with lower mortality (odds ratio, 1.01 per hour [95% CI, 0.99-1.02]; *P* = .21)

Fluid Management Phases: ROSE Model

Resuscitation

Early adequate fluid management (reverse hypoperfusion)

Administer initial fluid boluses (i.e. 30 ml/kg/1hour or a mini bolus 4ml/kg in 5-10 minutes)

Vasopressors if necessary

Assess responsiveness to fluid

Optimization

Establish perfusion and organ rescue

Fluid based on responsiveness and avoid fluid overload

Titrate vasopressors for specific hemodynamic targets

Aim for neutral balance

Stabilization

Maintain perfusion and organ support

Late conservative fluid management

Monitor for fluid overload and any organ dysfunction

Two consecutive negative balance within the 1st week after initial insult

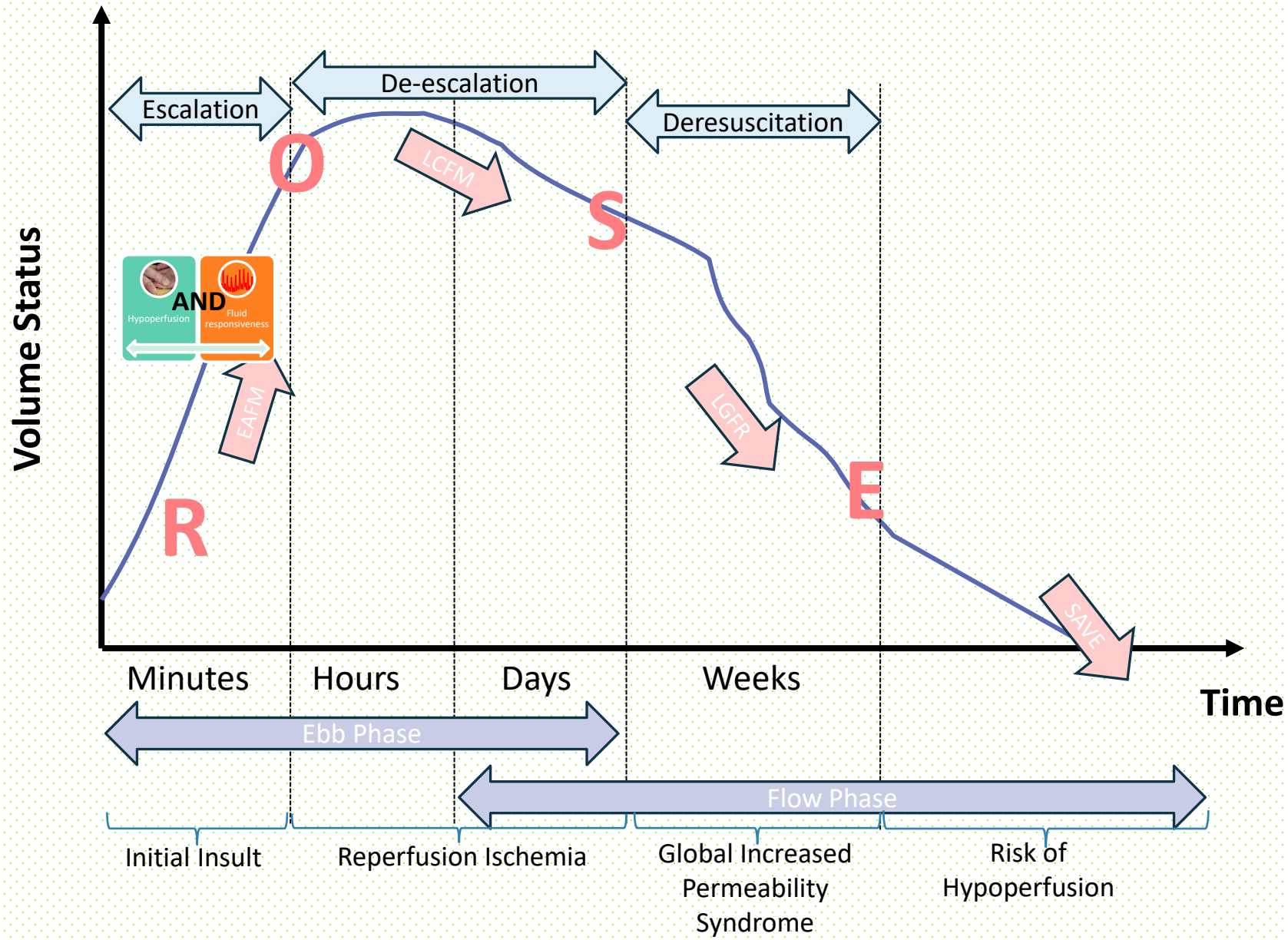
Evacuation

Organ recovery and removal of excess fluid

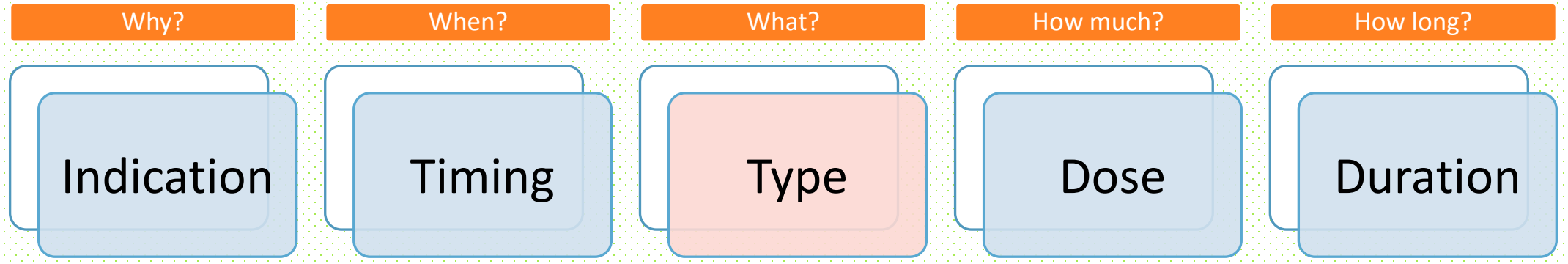
Resolving fluid overload

Active late goal directed fluid removal and negative FB with diuretics or kidney replacement therapy if indicated

Zampieri FG, Bagshaw SM, Semler MW. Fluid Therapy for Critically Ill Adults With Sepsis: A Review. *JAMA*. 2023;329(22):1967–1980

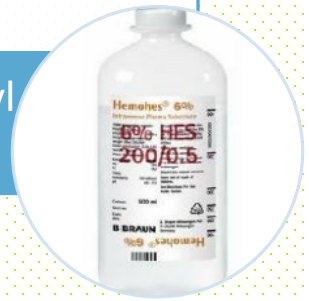


EAFM, early adequate fluid management - LCFM: late conservative fluid management – LGFR: late goal directed fluid removal


Why?
When?
What?
How much?
How long?
Indication
Timing
Type
Dose
Duration

- Increased rate of AKI/RRT
- Possible increased mortality

Hydroxyethyl starch (HES)



- Not preferred except if ↓Na, ↓Cl, liver failure or TBI
- Hyperchloremic acidosis,

Unbalanced: 0.9% NS

- Preferred except in liver failure, ↑Ca or TBI
- High probability of reduced mortality

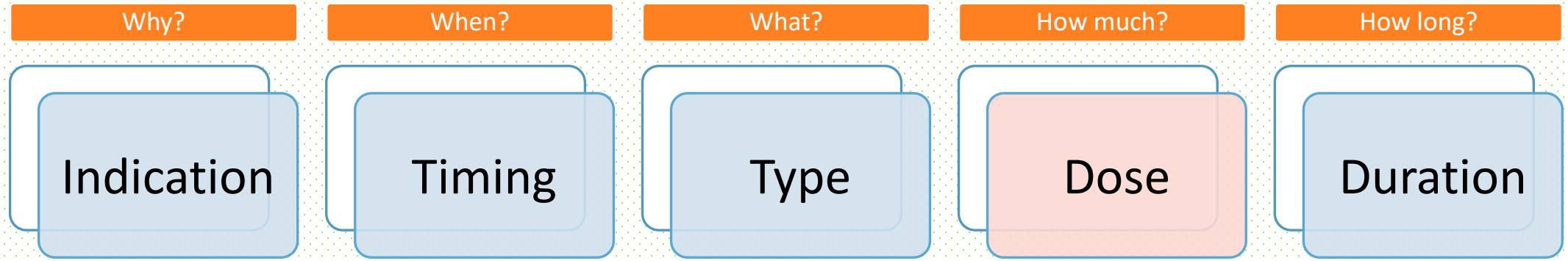
Balanced: Lactated Ring

- Avoid in TBI
- May benefit in Large volume resuscitation and severe septic shock

Albumin 5%

Balanced Fluid versus Saline in Critically-ill Patients

Evolving Evidence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Hour-1 Bundle

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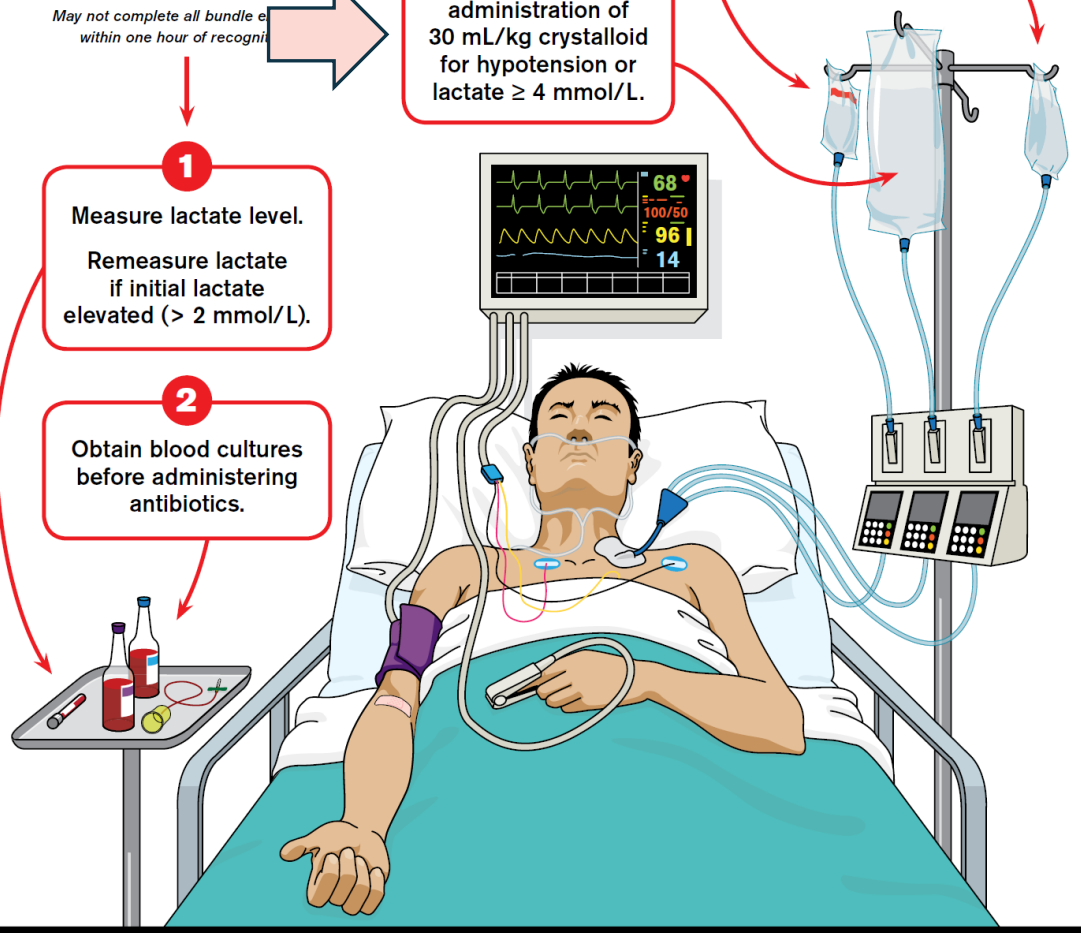


Bundle: SurvivingSepsis.org/Bundle Complete Guidelines: SurvivingSepsis.org/Guidelines

icu REACH

January 21, 2023

Sepsis-induced hypotensive patients after 1-3 liters of fluid resuscitation

60 Centers

THE CLOVERS TRIAL

Does restrictive fluid strategy used during the first 24 hours of resuscitation lead to lower 90-day mortality compared to liberal fluid strategy?

MULTICENTER - UNBLINDED - RANDOMIZED

1563 Patients

Pre-randomization fluid 1-3 L

Vasopressor-predominant Approach

Restrictive Strategy

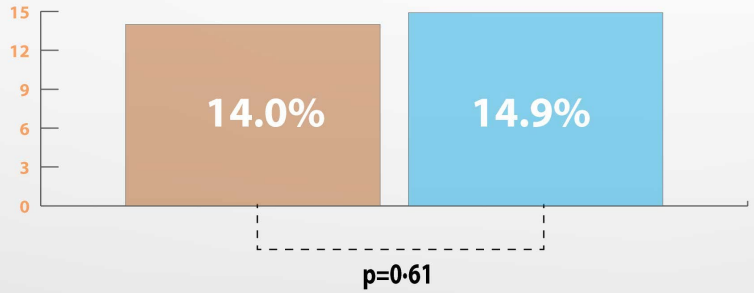
Vasopressors was used as the primary treatment for sepsis-induced hypotension with no fluid maintenance or boluses except rescue fluids for prespecified indications.

Median fluid over 6-hours (IQR): 500 (130-1097) mL.
Medan fluid over 24-hours (IQR): 1267 (555-2279) mL.
Vasopressor administration during first 24 hours: 59.0%.

Time to first vasopressor (hr): 1.8±3.4.
Duration of vasopressor use during first 24-hr period (hr): 9.6±10.0.

782 PATIENTS

90-day Mortality



Fluid-predominant Approach

Liberal Strategy

Recommended an initial 2000-ml intravenous infusion of isotonic crystalloid, followed by fluid boluses administered on the basis of clinical triggers (e.g., tachycardia) with “rescue vasopressors” permitted for prespecified indications.

Median fluid over 6-hours (IQR): 2300 (2000 to 3000) mL.
Medan fluid over 24-hours (IQR): 3400 (2500 to 4495) mL.
Vasopressor administration during first 24 hours: 37.2%.
Time to first vasopressor (hr): 3.2±4.7.
Duration of vasopressor use during first 24-hr period (hr): 5.4±8.6.

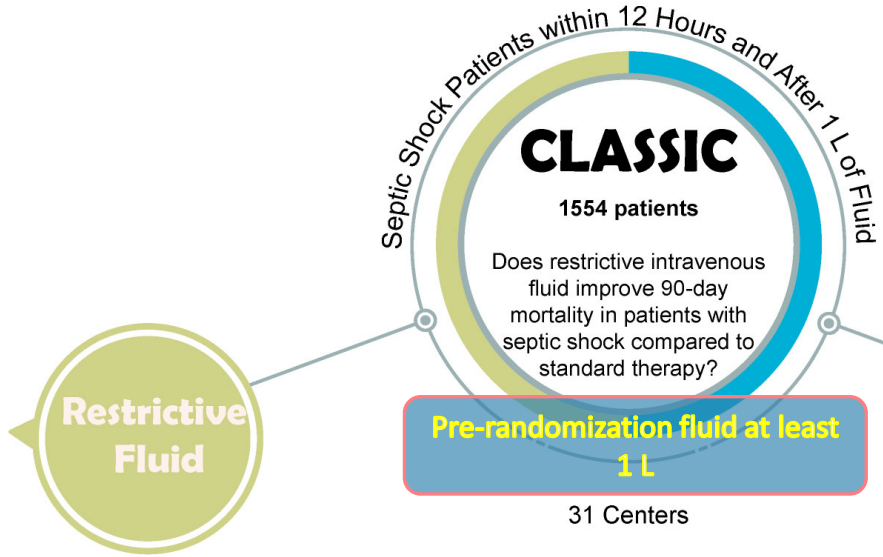
781 PATIENTS

Compared to a liberal fluid strategy, earlier vasopressor use in a restrictive fluid strategy did not result in any significant difference in mortality rate prior to discharge by day 90.

DOI: 10.1056/NEJMoa2212663

Restriction of Intravenous Fluid in ICU Patients with Septic Shock

June 17, 2022



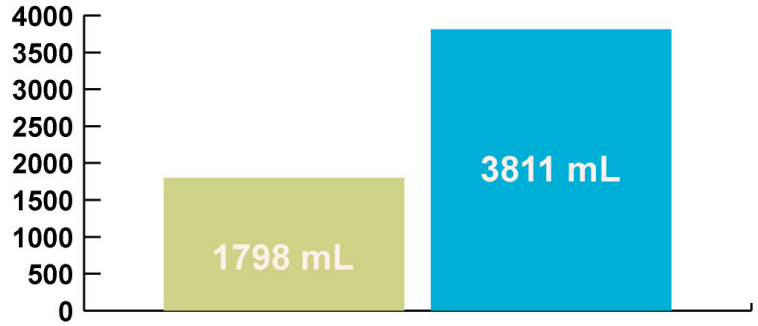
770 patients

Fluids were given for hypoperfusion state, fluid losses, dehydration, or daily intake of 1 L.

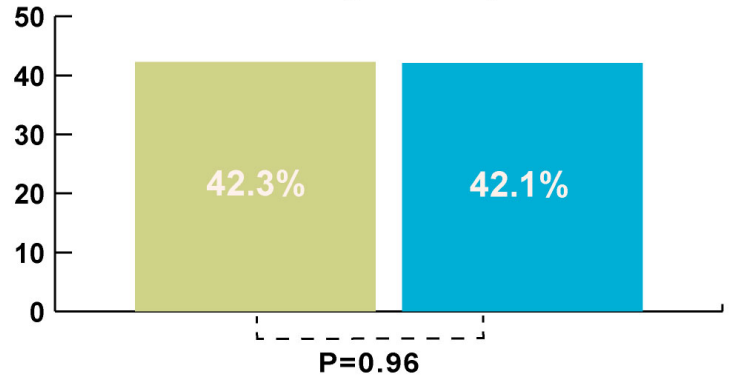
784 patients

Fluids were given as per surviving sepsis campaign, for observed losses or dehydration, or for maintenance as per local ICU protocols.

Median Fluid Volume in ICU



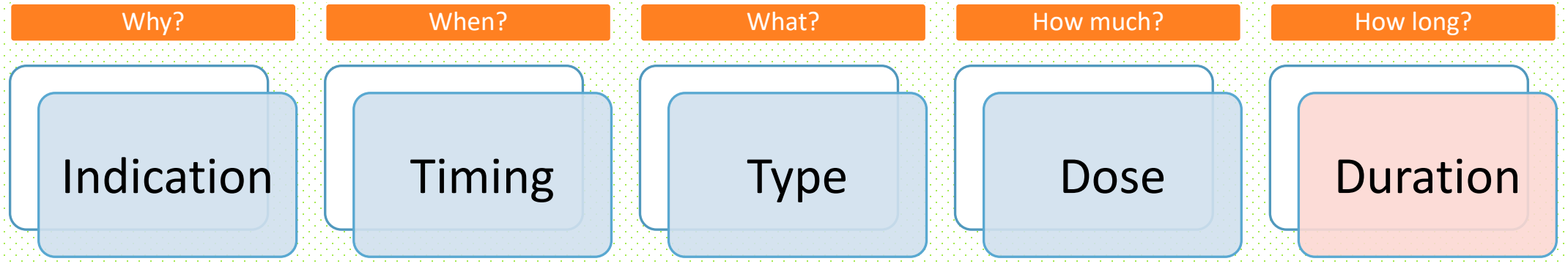
90-day Mortality

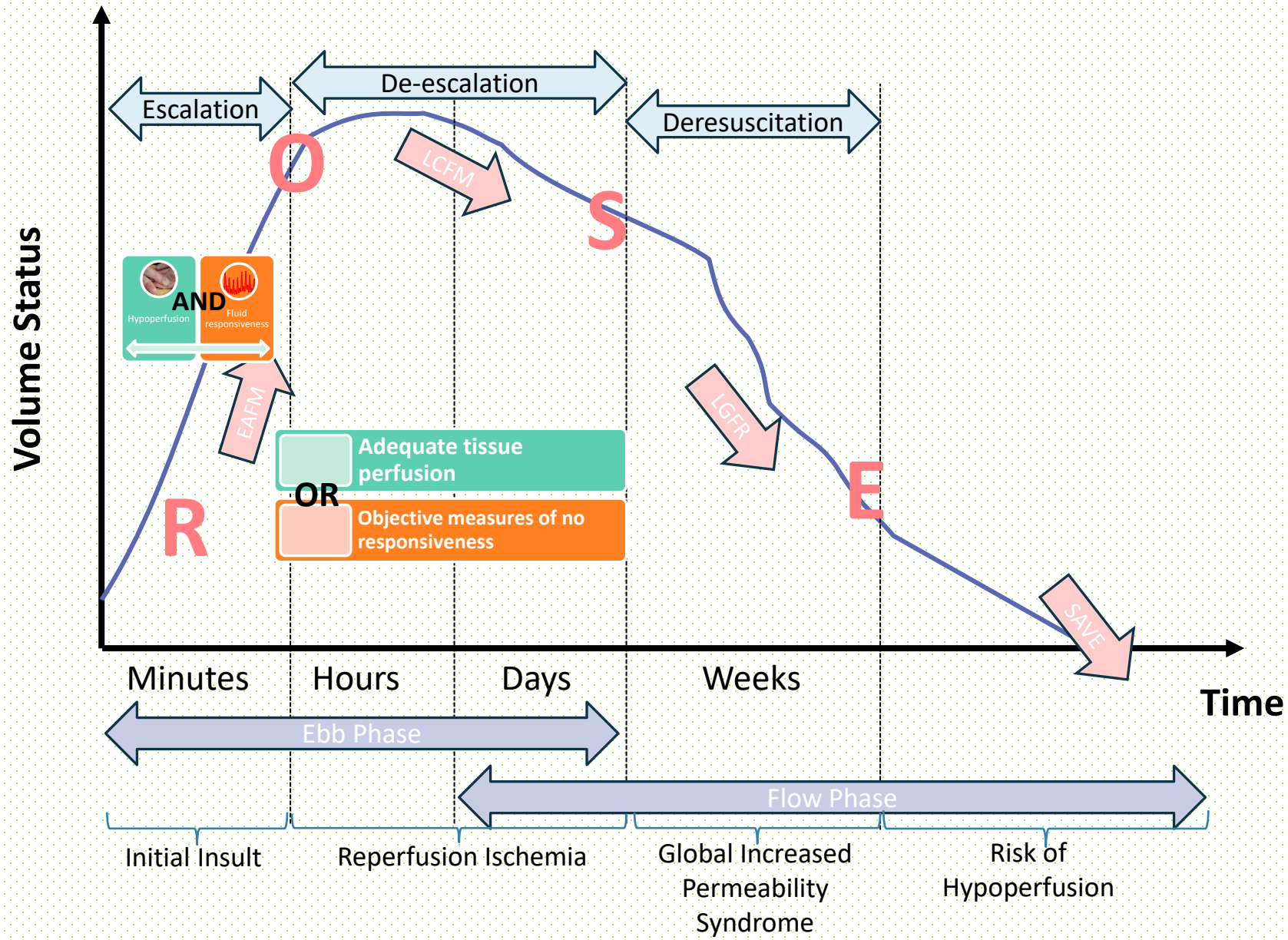


Absolute difference, 0.1; 95% CI, −4.7 to 4.9

CONCLUSION

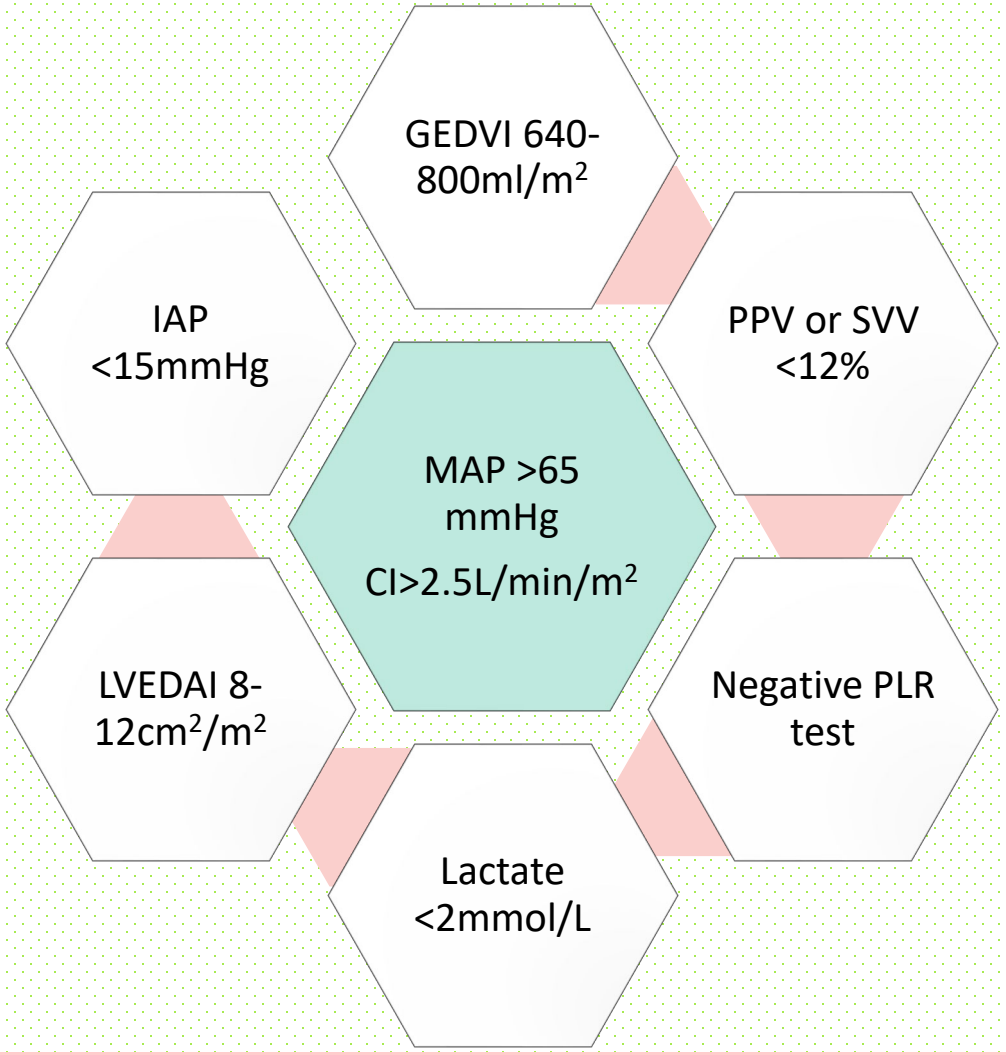
Restrictive fluid strategy did not reduce 90-day mortality in patients with septic shock compared to standard intravenous fluid therapy.


Why?
When?
What?
How much?
How long?
Indication
Timing
Type
Dose
Duration

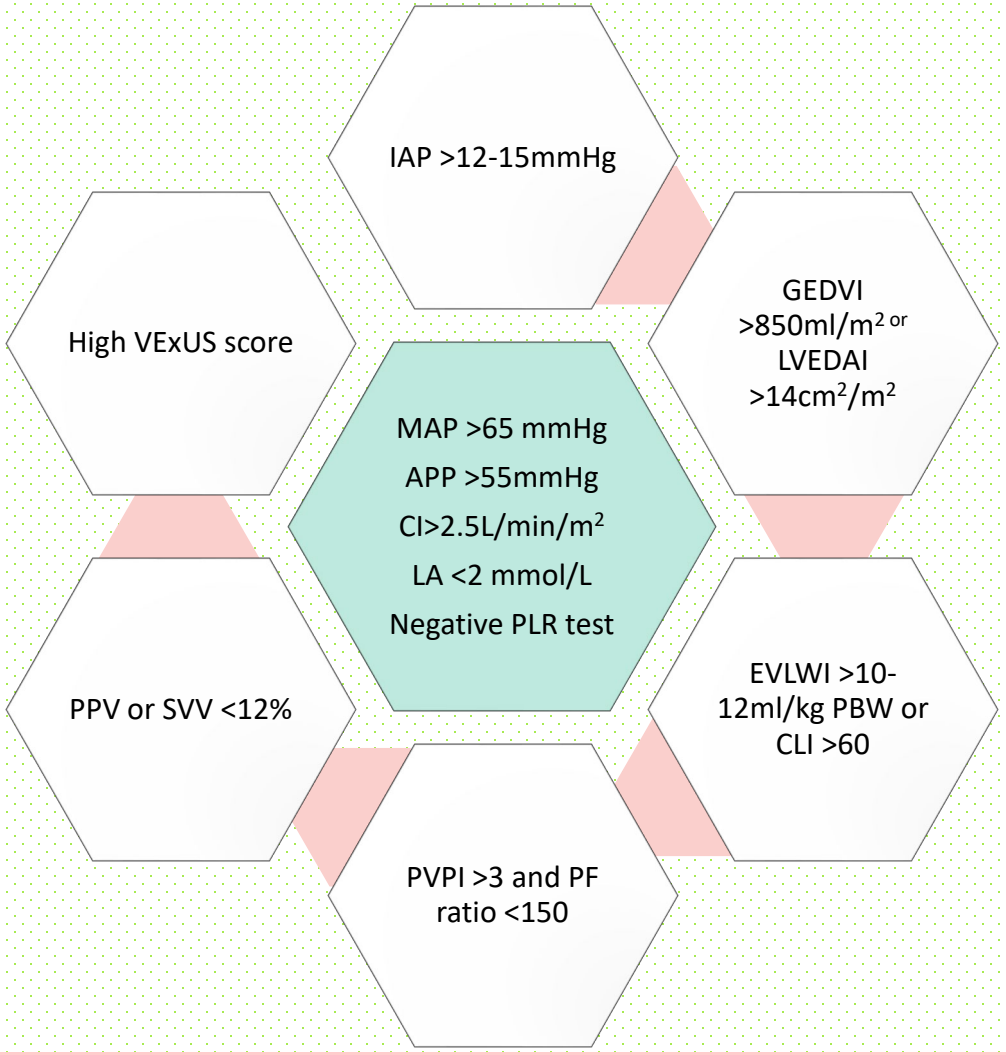


EAFM, early adequate fluid management - LCFM: late conservative fluid management – LGFR: late goal directed fluid removal

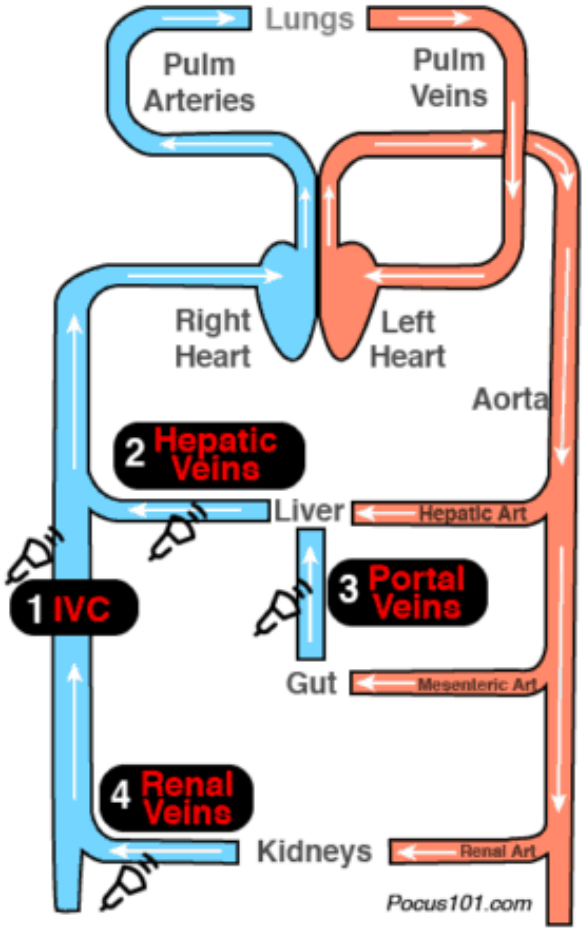
De-escalate!


GEDVI 640-800ml/m²
IAP <15mmHg
PPV or SVV <12%
MAP >65 mmHg
CI>2.5L/min/m²
LVEDAI 8-12cm²/m²
Negative PLR test
Lactate <2mmol/L

De-resuscitate!

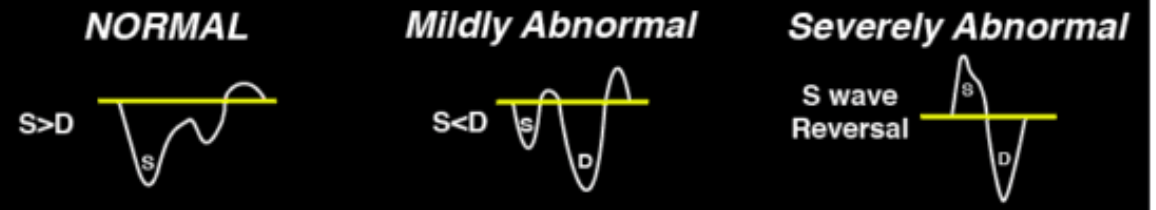


Venous Excess Ultrasound VExUS

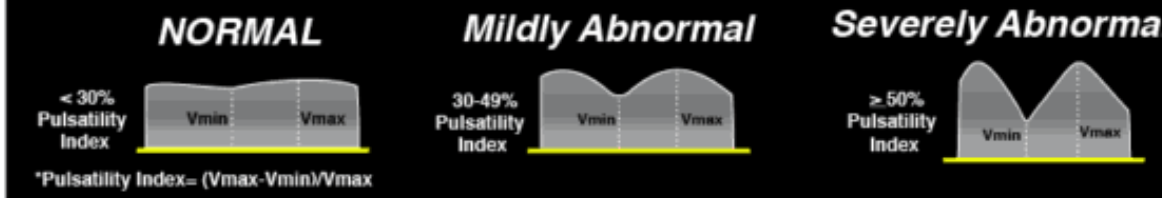


Step 1: IVC Diameter: If ≥2cm, proceed to step 2

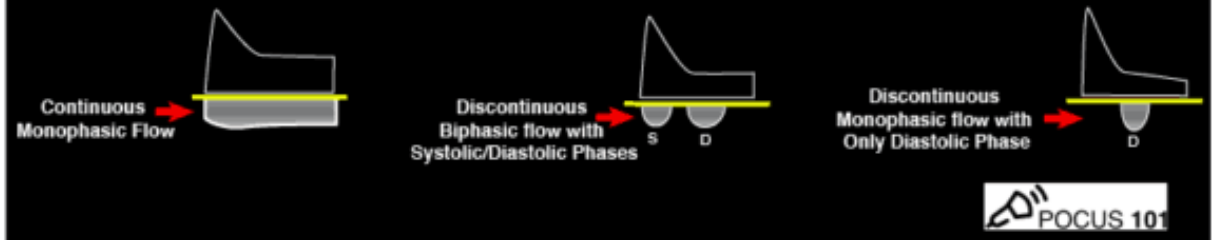
Step 2: Hepatic Vein Doppler



Step 3: Portal Vein Doppler



Step 4: Renal Vein Doppler



Interpretation

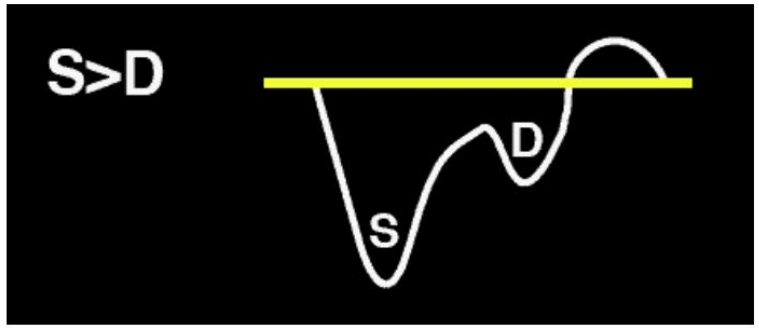
Grade 0
(no congestion)
IVC < 2cm

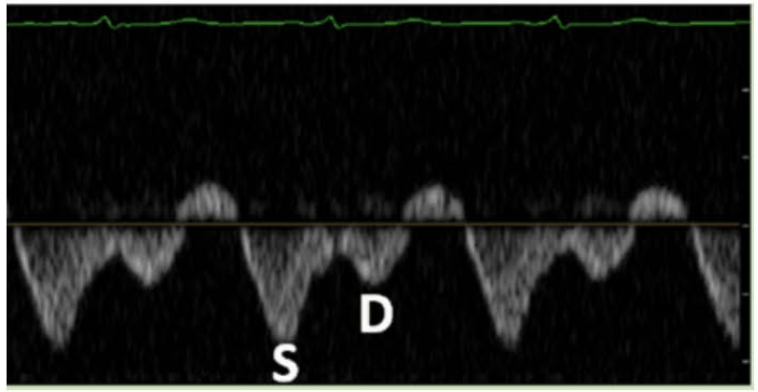
Grade 1
(Mild congestion)
IVC ≥2cm and any combo of Normal or Mildly Abnl Patterns

Grade 2
(Moderate congestion)
IVC ≥2cm and ONE Severely Abnl Pattern

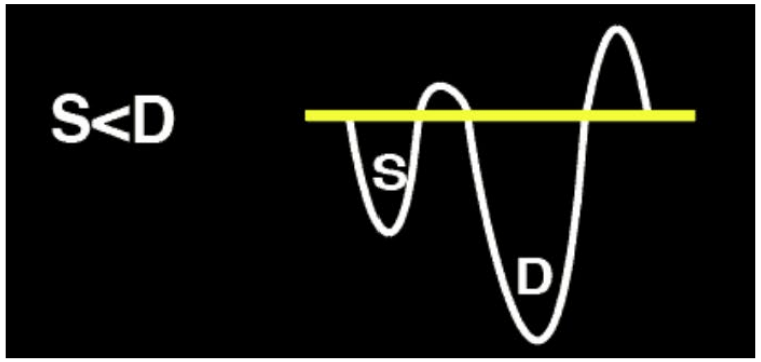
Grade 3
(Severe congestion)
IVC ≥2cm and ≥ 2 Severely Abnl Patterns

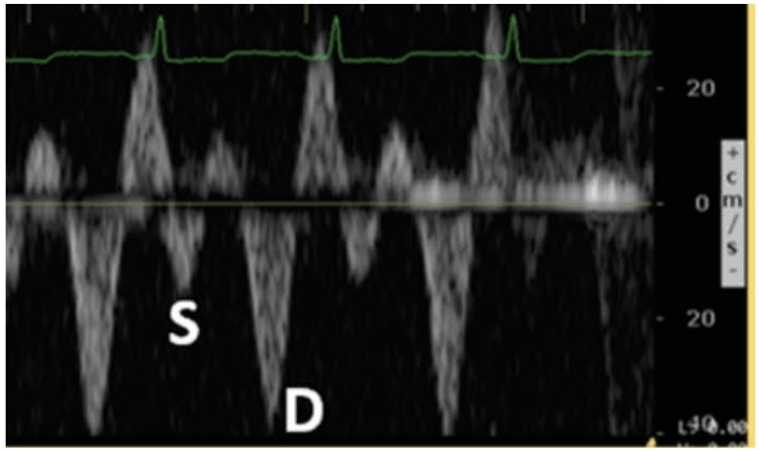
Normal Hepatic Vein Doppler: S>D



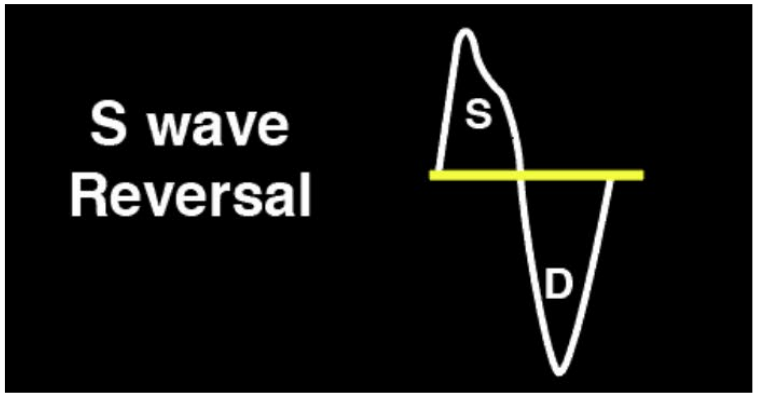


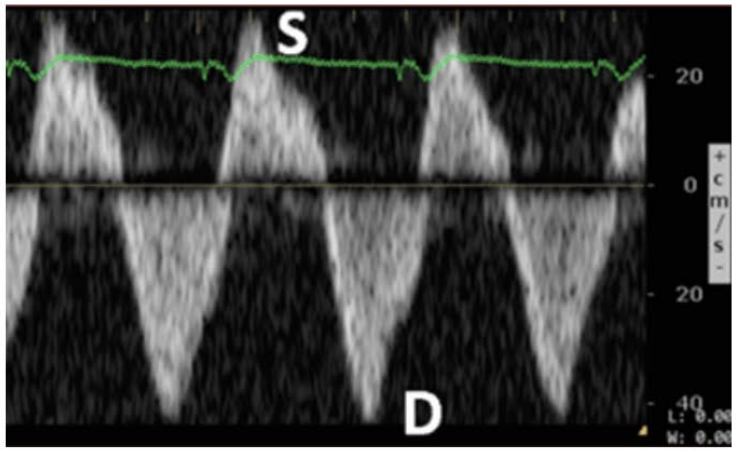
Mild Hepatic Vein Abnormality: S<D



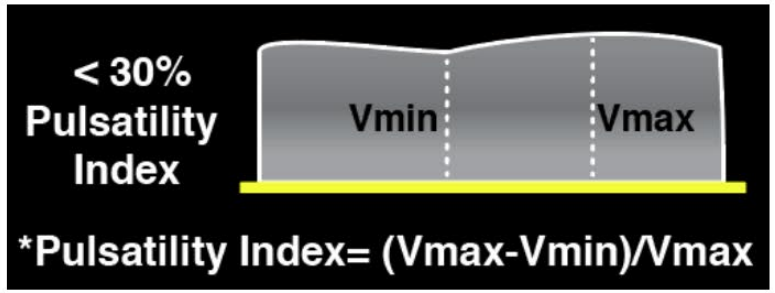


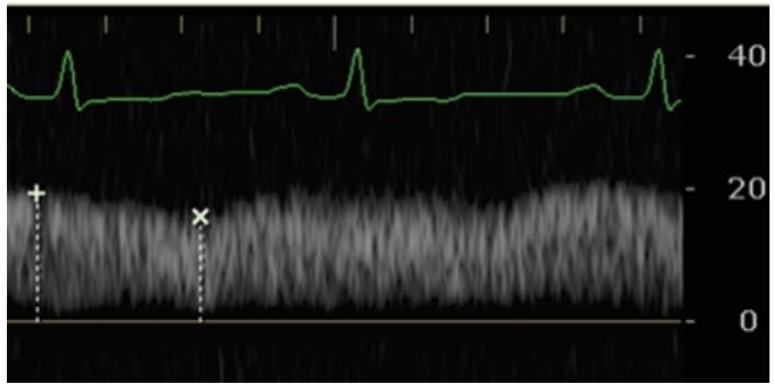
Severe Hepatic Vein Abnormality: S Reversal



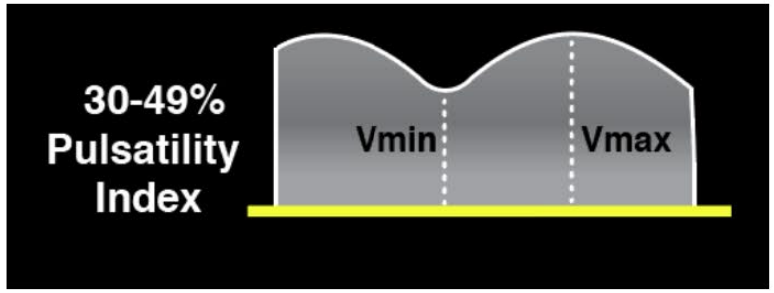


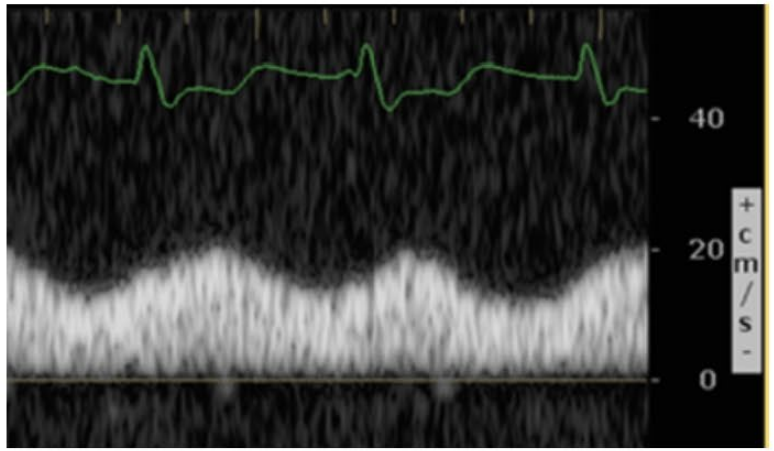
Normal Portal Vein Doppler





Mild Portal Vein Abnormality





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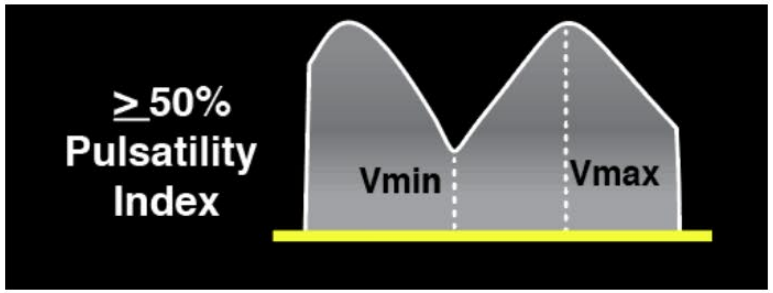
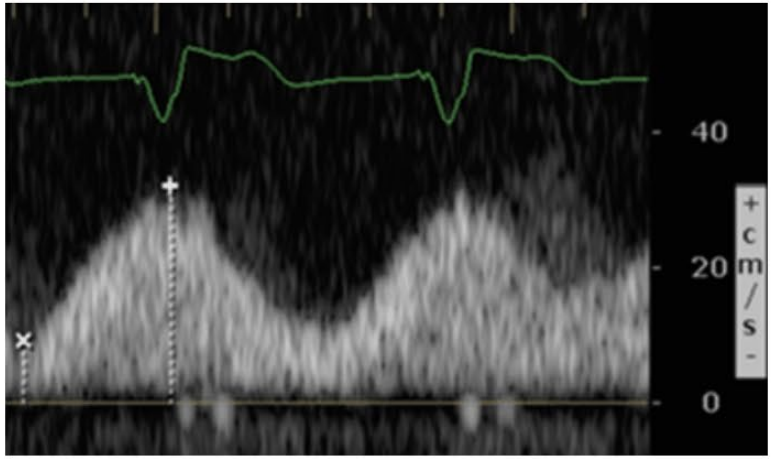
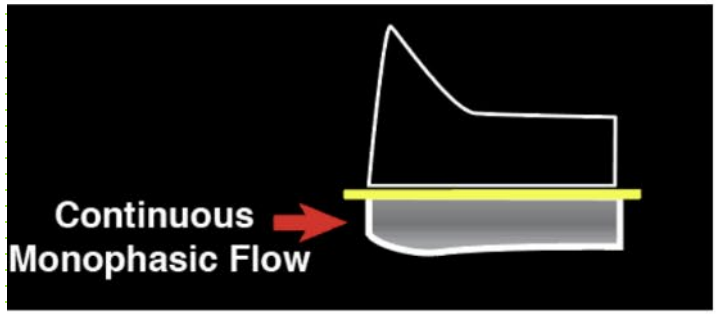
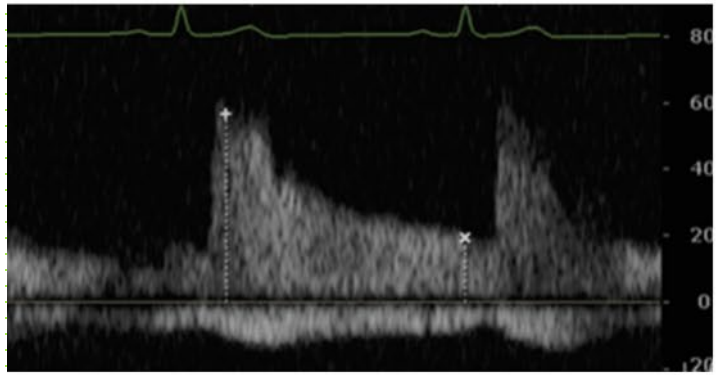


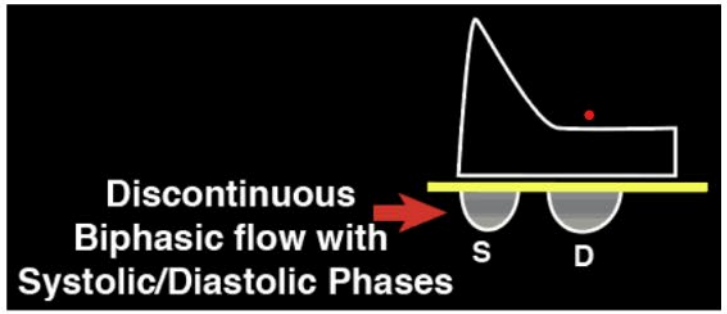


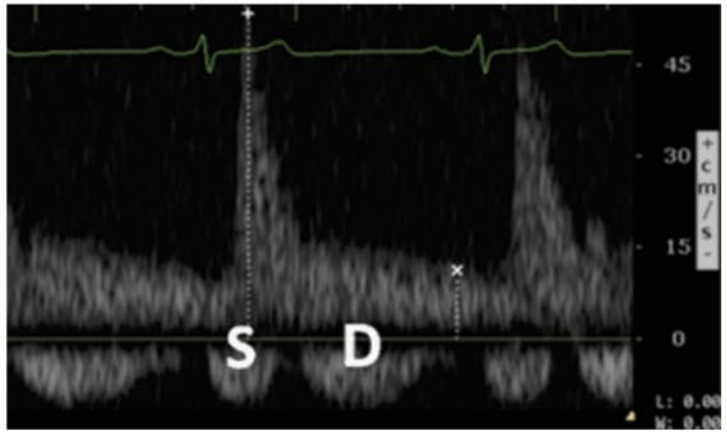
Normal Intrarenal Vein Doppler



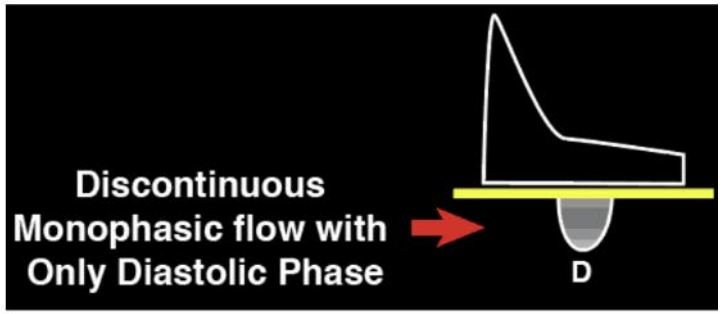


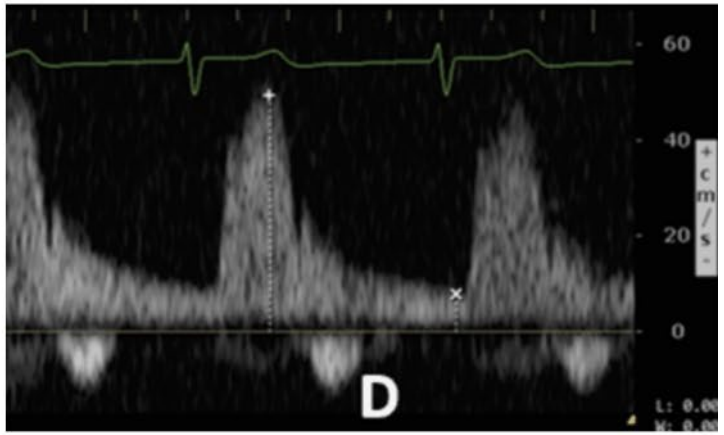
Mild Intrarenal Vein Abnormality

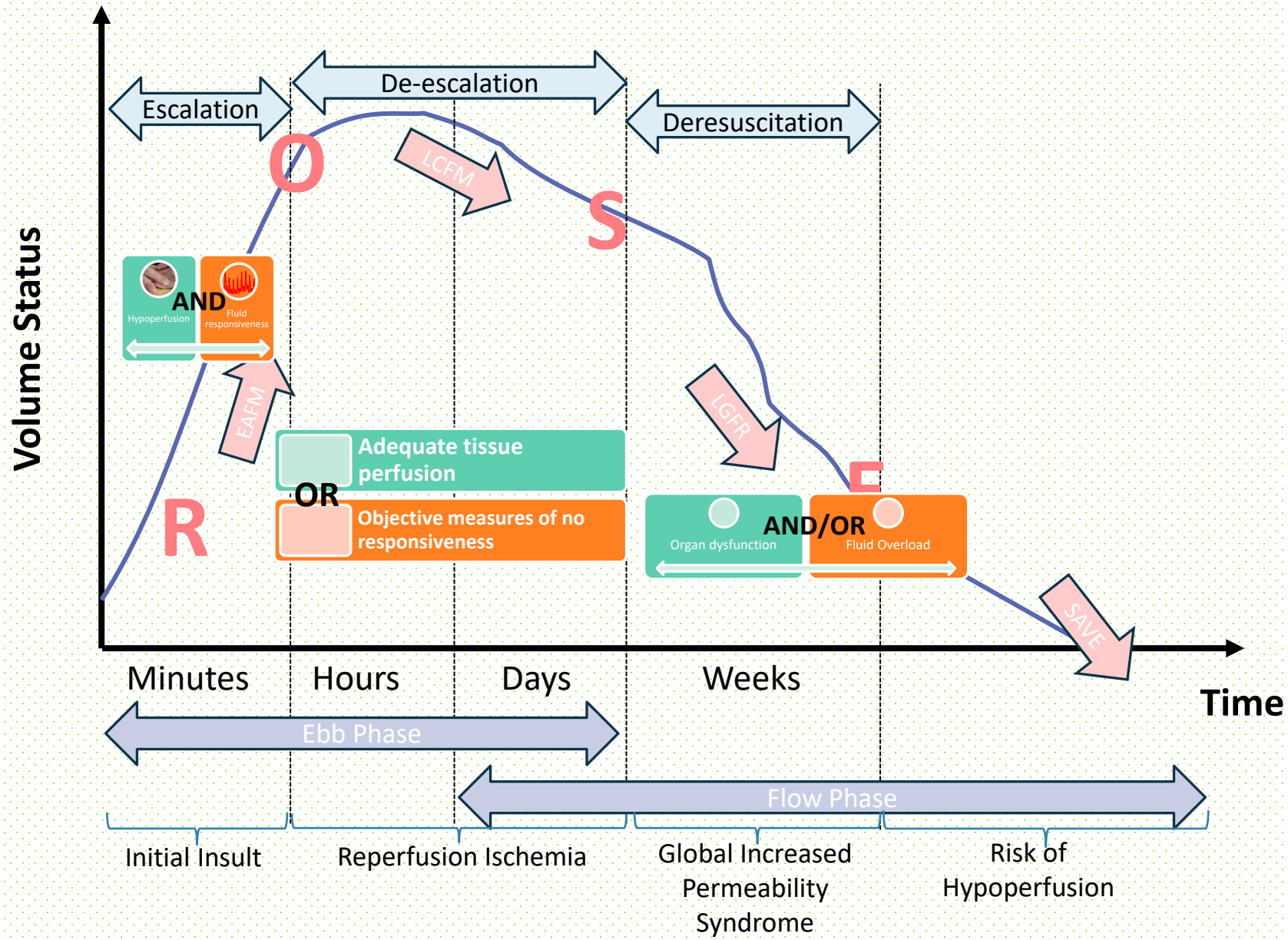




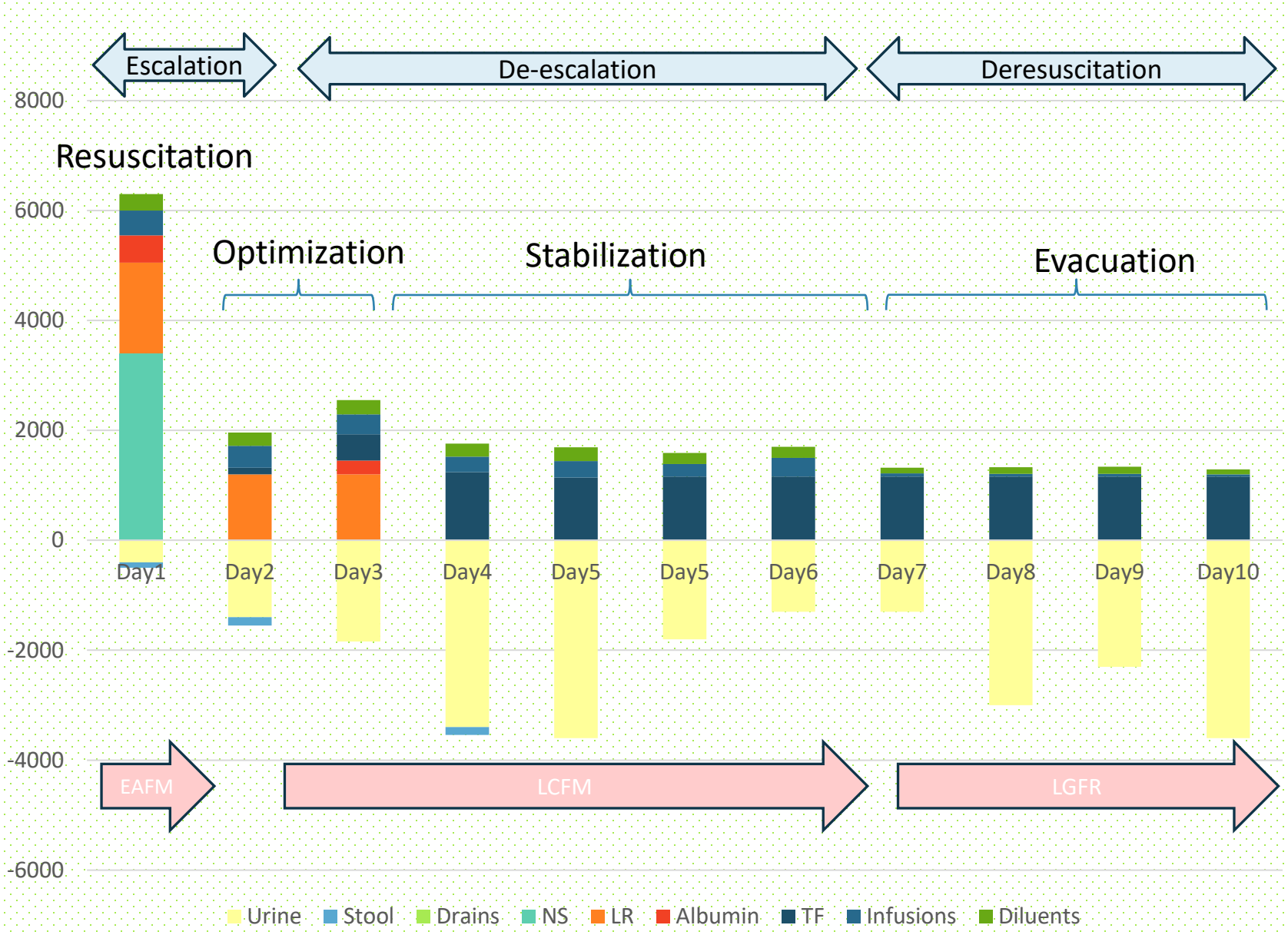
Severe Intrarenal Vein Abnormality







EAFM, early adequate fluid management - LCFM: late conservative fluid management – LGFR: late goal directed fluid removal


Escalation
De-escalation
Deresuscitation
8000
Resuscitation
6000
Optimization
Stabilization
Evacuation
4000
2000
0
Day1
Day2
Day3
Day4
Day5
Day5
Day6
Day7
Day8
Day9
Day10
-2000
-4000
EAFM
LCFM
LGFR
-6000
Urine
Stool
Drains
NS
LR
Albumin
TF
Infusions
Diluents

Why?

Indication

Resuscitation

Replacement

Maintenance

Nutrition

When?

Timing

1-hour bundle

Perfusion and fluid responsiveness status

What?

Type

LR

NS

Albumin

How much?

Dose

30 mL/kg?

EAFM

LCFM

LGFR

Perfusion and fluid responsiveness status

How long?

Duration

Avoid fluid overload

Measure to monitor fluid status

Thank you

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