Tailored Volume Resuscitation in the Critically Ill is Achievable

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Objectives

- Describe the goal of resuscitation in shock.
- Recognize potential adverse outcomes of over resuscitation of the critically ill.
- Increase awareness of guided volume resuscitation strategies.
- Recognize applications and limitations of bioreactance derived hemodynamic monitoring..
- Recognize applications and limitations of pulse contour analysis derived hemodynamic monitoring.
- Describe potential benefits of volume targeted resuscitation to limit volume overload.

Clinical Case

- AR is a 72 yo 80 Kg female admitted from a SNF with a 1 day history of altered mental status and fevers. She is hypotensive on presentation with evidence of a UTI from an indwelling foley. She has a history of ischemic cardiomyopathy with an EF of 20% and chronic renal failure with crt of 2.4 She is given two 500mL boluses of fluid and abx in the ED and admitted to the ICU.
- First bolus resulted in 20% improvement in SV
- Second bolus resulted in 8% improvement in SV
- Post fluid vitals: T 39, BP 80/40, HR 95 (NSR), RR 28

Surviving Sepsis Campaign Guidelines

1. Severe Sepsis and Septic Shock are medical emergencies, and treatment and resuscitation should begin immediately. (BPS)
2. We recommend that, in the resuscitation from sepsis-induced hypoperfusion, at least 30 mL/Kg of IV crystalloid fluid be given within the first 3 hours
   - Strong recommendation, low quality of evidence

SSC. Crit Care Med. 2017; 45:486-552.

History of 30mL/Kg?

- Rivers—EGDT. NEJM 2001;345:1368-77.
  - Pre-randomization resuscitation
    - 20-30mL/Kg
- ProCESS. NEJM 2014; 370:1683-93.
  - Pre-randomization resuscitation
    - 20 mL/Kg
    - 2010 amendment→at least 1L
- ProMISe NEJM 2015; 372:1301-11
  - Pre-randomization resuscitation
    - At least 1L
- ARISE NEJM 2014;371:1495-506.
  - Pre-randomization resuscitation
    - At least 1L

30 ml/Kg seems to be standard practice…

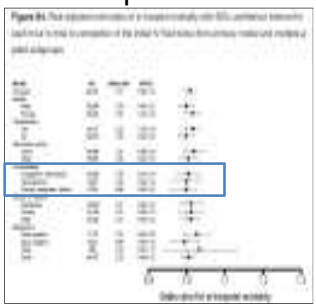
Trial	Time to randomization (hours)	Fluids received prior to randomization (mL)	Fluids Received prior to randomization (mL/kg)	Between 0 and 6 h after randomization (mL)
Rivers	0.8	NA	NA	3499 ± 2438
ProCESS	3.0	2083 ± 1405	28 ± 21	2279 ± 1881
ARISE	2.7	2591 ± 1331	34.7 ± 20.1	1713 ± 1401
PROMISE	2.5	1790 (1000, 2500)	24*	2022 ± 1271

The IMPRESS-SSC Study
An International Multi-Centre Prevalence Study of Sepsis

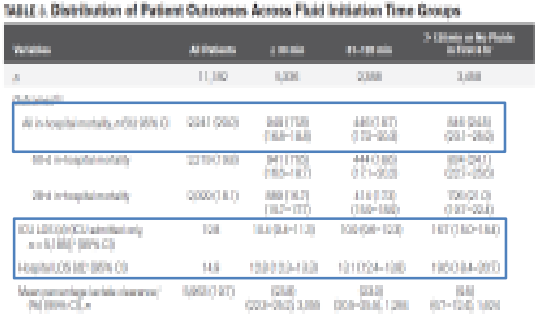
3 Hour Bundle Compliance	%
Measurement of Lactate	56
Obtain Blood Cultures Prior to Antibiotics	49
Administer Broad Spectrum Antibiotics	64
Administer 30 mL/kg crystalloid for hypotension or lactate ≥4mmol/L	57

Rhodes et al. Intensive Care Med. 2015 Sep;41(9):1620-8

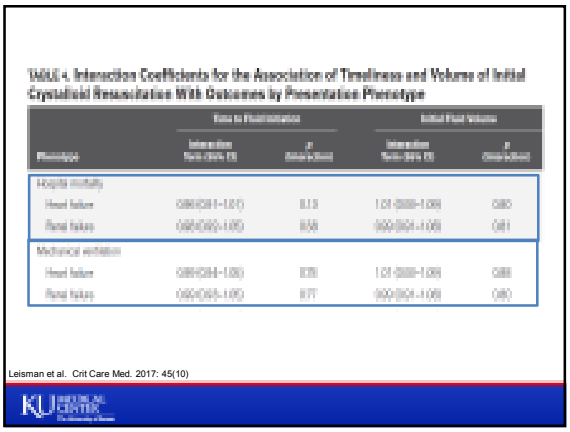
NYS Sepsis Initiative

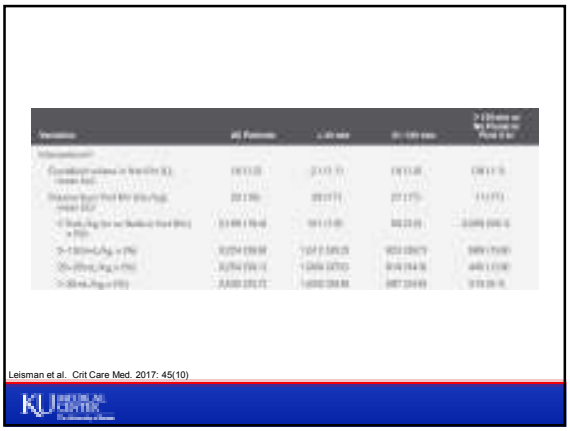


Seymour et al. N Engl J Med 2017;376:2235-44



Leisman et al. Crit Care Med. 2017: 45(10)





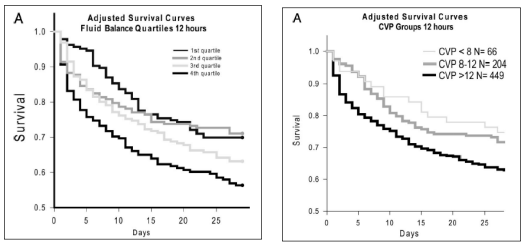
Goal of Resuscitation

- Achieve Adequate Perfusion Pressure
  - MAP > 65 mmHg
    - Volume Replacement
    - Vasopressors
    - Inotropic
- Improve Microcirculatory Flow
  - Rapidly treat underlying cause of shock
- Limit Tissue Edema

What's the Goal of Fluid Resuscitation?

- Improve Stroke Volume/Cardiac Output
- Fluid Responsiveness in Severe Sepsis/Septic Shock?
  - Approx 50%
    - Marik, et al. Ann Crit Care. 2011; 1:1
    - Marik, et al. Br J Anaesth. 2014; 112:620-22
    - Cavallaro et al. Inten Care Med. 2010; 36:1475-83
    - Latham et al. J Crit Care. 2017; 42:42-46

What are the Consequences?

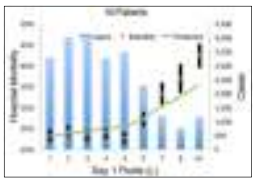


Boyd, J. Crit Care Med. 2011; 39:259-65.

What are the Consequences?

What is Too Much?

- Premiere Database
  - Severe/Septic Shock
  - 23,513 encounters
  - Day 1 ICU Fluid
  - Adjusted for Severity



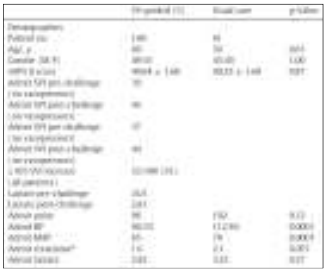
Marik, P et al. Int Care Med. 2017; 43:625-32.

Other Volume Sensitive Outcomes?

- Retrospective Chart Review
  - Medical ICU
  - Severe Sepsis/Septic Shock
  - April 2014-September 2014
    - Usual Care (91) vs SV Guided Resuscitation (100)
  - Hypothesis: Guided Resuscitation < Fluid

Latham HE, et al. Journal of Critical Care. 2017: 42;42-46.

Other Volume Sensitive Outcomes?



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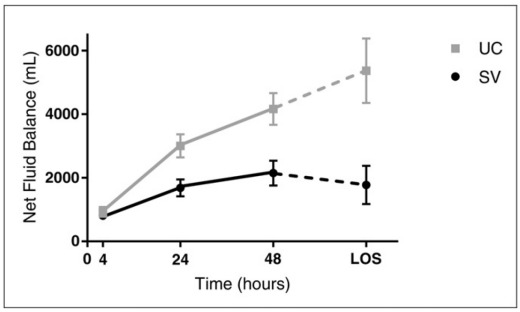
ICU Fluid Balance



Latham HE, et al. Journal of Critical Care. 2017: 42;42-46.

Other Volume Sensitive Outcomes?

Secondary Outcomes

- Mortality: 21% vs 20%
- ICU LOS:
  - 6 vs 9 Days (p = 0.03)
- Mechanical Ventilation
  - 29% vs 57% (p = 0.001)
  - MV Days: 6.3 vs 6.7 (p = 0.76)

Secondary Outcomes

- Vasopressors
  - 48% vs 57% (p = 0.25)
  - Duration:
    - 32 vs 65 hrs (p = 0.001)
  - Hemodialysis
    - 6% vs 19% (p = 0.01)

Latham HE, et al. Journal of Critical Care. 2017; 42:42-46.

SV Guided Resuscitation

Outcome	Results	Confidence intervals	p-Value
Net fluid balance – 4 h	−160.91 mL	−727.16 to −5.340	0.053
Net fluid balance – 24 h	−1191.95 mL	−2150.96 to −632.95	<0.0001
Net fluid balance – 48 h	−1485.26 mL	−2496.60 to −473.92	0.004
Net fluid balance – ICU LOS	−2779.17 mL	−4686.48 to −871.86	0.005
In-hospital mortality	OR 0.58	0.23–1.47	0.25
ICU LOS – survivors	−2.55 days	−4.98 to −0.12	0.040
Mechanically ventilated	OR 0.34	0.15–0.80	0.01
Ventilator days	−2.15 days	−5.24–0.97	0.17
Vasopressor initiated	OR 0.57	0.26–1.24	0.15
Vasopressor duration	−27.94 h	−51.16 to −4.74	0.02
Acute dialysis initiated[2]	OR 1.11	0.08–15.74	0.94

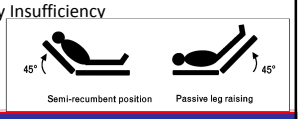
Latham HE, et al. Journal of Critical Care. 2017: 42;42-46.

Tailored Resuscitation

- Technology
  - Bioreactance
    - NICOM
    - Starling
  - Doppler Derived
    - Bedside US
    - USCOM
  - Pulse Contour Analysis
    - Flotrack/EV1000
    - LiDCO
    - PiCCO
- Challenge Technique
  - Volume Expansion
    - 500mL w/in 30 min
  - Passive Leg Raise (PLR)

Volume Responsiveness

- Passive Leg Raise
  - Reversible Volume Expansion
    - 250-350 mL
  - 3-5 Minutes in supine position
  - Caution
    - Labile Hemodynamics
    - Severe Ventilatory Insufficiency
    - At Risk Airway

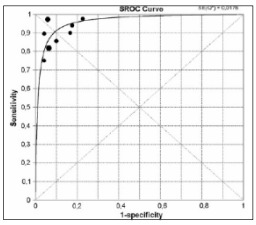


Passive Leg Raise

- Meta-Analysis
  - 9 Articles
  - 366 Pooled Interventions
  - ICU/Shock
- Mixed CI/SVI assessment
  - Doppler derived
  - Pulse contour analysis
- Mixed spontaneous ventilation
- Mixed Rhythms
- Results
  - PLR Accurately Predicts Volume Responsiveness
  - ΔSVI/CI > ΔPP
  - Unaffected
    - Technology used
    - Spontaneous Respiration
    - Arrhythmia

Cavallaro, F. Inten Care Med. 2010; 36:1475-83.

Passive Leg Raise

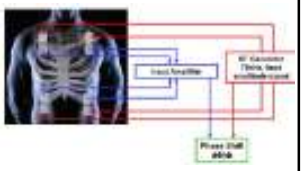


	Boluses	% Resp	AUC
	15		
	22	45	0.95
	71	52	0.96
	24	54	0.96
	24	54	
	34	50	0.89
	34	50	0.89
	102	46	0.89
	34	68	0.94
	30	67	0.96
	30	67	0.92
	34	41	0.94
Overall	366	52.9	0.95

Cavallaro, F. Inten Care Med. 2010; 36:1475-83.

Bioreactance

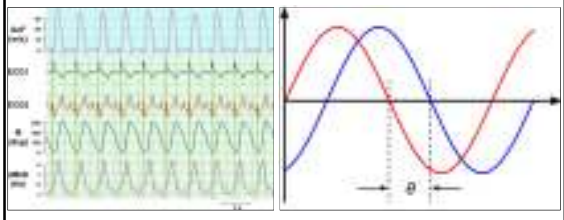
- Completely Non-Invasive
- 4 Electrodes on Chest
  - Assess change in current
- Spontaneous Breathing
- Mobile Patient
- Updates every minute



Keren H, et al. 2007. Am J Physiol Heart Circ Physiol; 293:H583-H589.

How it Works

- Ventricular outflow drives changes in Phase (Phase Shift) of radiofrequency waves as they cross the chest
- Measuring the Frequency (Phase Shift) enables exact calculation of flow



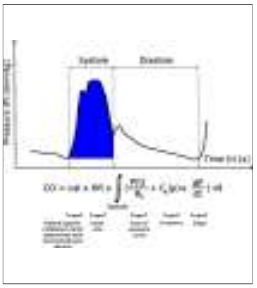
Keren H, et al. 2007. Am J Physiol Heart Circ Physiol; 293:H583-H589.

Bioreactance

- Tested in Various Settings
  - ER
  - ICU
  - Pregnancy
  - Pulmonary HTN
- Not Effected by External Electronics
- Applicable in Non-Physician Algorithms
- Limitations
  - Electrode Durability
  - Inaccurate
    - Severe AI
    - Thoracic Aneurysms
    - Balloon Pump
    - LVAD
    - ? Dense Infiltrates
    - Cautery

Pulse Contour Analysis

- Estimation of SV
  - Area under the curve
    - Systolic portion
  - Presumed constants
    - Vascular compliance
    - Aortic impedance
    - PVR
  - Pulse Regularity
    - Improves accuracy



Huber, et al. BMC Anesthesiology. 2015; 15:45.

Pulse Contour Analysis

- Advantages
  - Simple to use
  - Real time data
  - Utilize arterial line already in place
  - Continuous CO
  - Non-physician resuscitation protocols
- Disadvantages
  - Requires excellent waveforms
  - Re-calibration
  - SVV Limited to Optimal Parameters
    - Sinus Rhythm
    - Vt >8 mL/Kg
    - HR/RR > 3.6
    - No Spontaneous Resp

Doppler Derived Stroke Volume

- Bedside US with Doppler
  - Echocardiography
  - Peripheral artery Doppler
- Esophageal Doppler
- USCOM Device

Bedside Ultrasound

- Advantage of US in Shock
  - Assess Cause of Shock
    - Cardiac
    - Pulmonary
    - Septic
  - Assess Volume Responsiveness
  - Assess Therapeutic Result

Bedside Ultrasound

- Disadvantage of US in Shock
  - Competence of User
    - Training* in bedside ultrasound
    - Training* in doppler-based measurements
  - Inter/Intra-observer Variability
  - How Many Devices Are Needed
  - No Form of Continuous Measurement
    - Nursing can't monitor change in hemodynamics

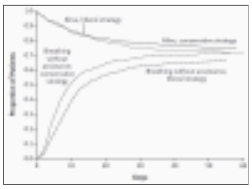
Is Fluid Limited Care Realistic?

- Single Center Targeted Fluid Management (TFM)
  - 82 Randomized Septic Shock Patients
  - Usual Care vs Targeted Fluid Therapy Followed by Conservative Fluid
  - Net Fluid Balance
    - Day 3: 3.1L vs 1.9 L
    - Day 5: 3.6L vs 2.6L
  - No Difference:
    - Mortality
    - RRT
    - Ventilator Days
    - Vasopressors

Chen C, Kollef M. CHEST. 2017; 148:1462-69.

Is Fluid Limited Care Realistic?

- FACTT Trial 2006
  - Multicenter ARDSnet Trial
  - Fluid Conservative vs Liberal
  - Sepsis Major Cause of ARDS



ARDSnet. NEJM. 2006; 354:2564-75.

Conclusion

- Guidelines Serve to Limit Care Variation
  - 30mL/Kg = Low Level of Evidence
- Mounting Evidence of Potential Harm From Excess Volume
  - Mortality
  - Secondary Outcomes
- Technology is Available for SV Guided Resuscitation
- Prospective RCT Are Needed to Further Assess the 30mL/Kg