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Fluid Management in Critical Care

Amir Kazory, MD, FASN, FACC
Professor of Medicine
Division of Nephrology, Hypertension, and Renal Transplantation
University of Florida

Outline

1- **Principles of Fluid Management in ICU**

2- **Strategies** (how much? When?)

3- **Outcome** (can we hurt the patients?)

4- **Impact on the Kidney** (the nephrologist in me!)

Illustrative Case

A 62-year-old woman with COVID-19 is admitted to the ICU with high-grade fever, multifocal opacities on chest x-ray, and respiratory failure requiring intubation. Despite an initial 2-L (30 mL/kg) bolus of crystalloid, the patient develops progressive hypotension.

The patient's mean arterial pressure (MAP) is 45 mm Hg, central venous pressure (CVP) is 11 mm Hg, and central venous oxygen saturation (ScVO2) is 89%. Arterial lactate level is 10.2 mmol/L, and urine output is 10 mL/h.

Adapted from: Griffin BR. Am J Kidney Dis 2020; 75: 435

Illustrative Case

Which of the following statements is correct regarding the next best step in management?

(a) The next best option is to initiate norepinephrine and perform a passive leg raise to assess whether she is likely to respond to additional fluids.

(b) The next best option is to initiate dopamine treatment.

(c) The next best option is to continue to administer IV fluids until CVP is ≥12 cm H2O.

(d) Because of the dangers associated with volume overload, the patient should not have been treated with a 30 mL/kg fluid bolus and should receive no further fluids.

(e) Because ScVO2 is >70%, oxygen delivery to her tissues is adequate and therefore no additional treatment is warranted.

Adapted from: Griffin BR. Am J Kidney Dis 2020; 75: 435

Treatment of Shock

4 phases

	0-6 hrs	6-36 hrs	36-48 hrs	>48 hrs
	Salvage	**Optimization**	**Stabilization**	**De-escalation**
Phase Focus	Obtain a minimal acceptable blood pressure	Provide adequate oxygen availability	Provide organ support	Wean from vasoactive agents
	Perform lifesaving measures	Optimize cardiac output, SvO_2, lactate	Minimize complications	Achieve a negative fluid balance

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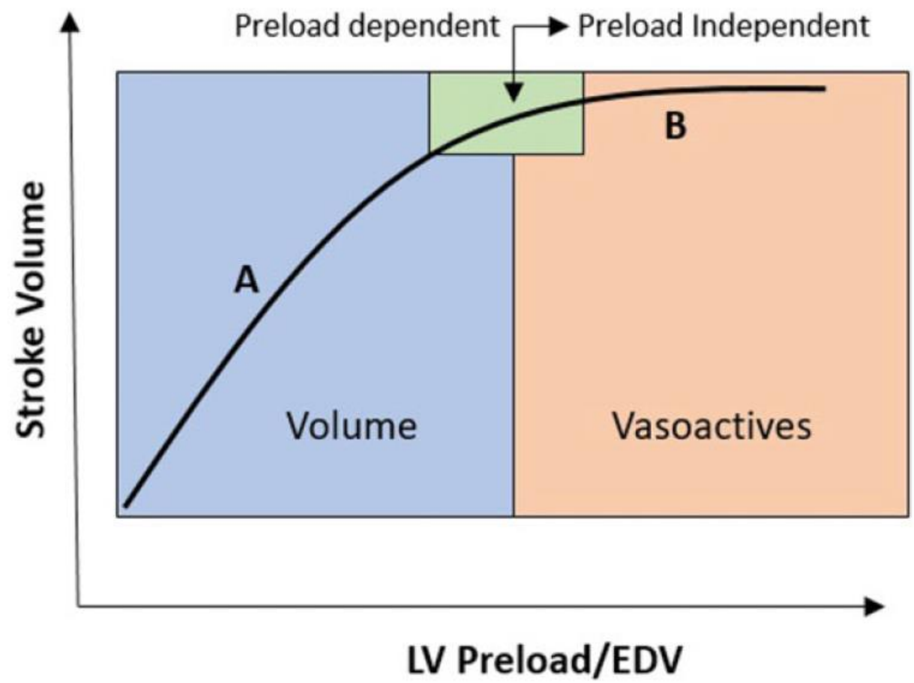
Vincent JL. N Engl J Med 2013;369:1726

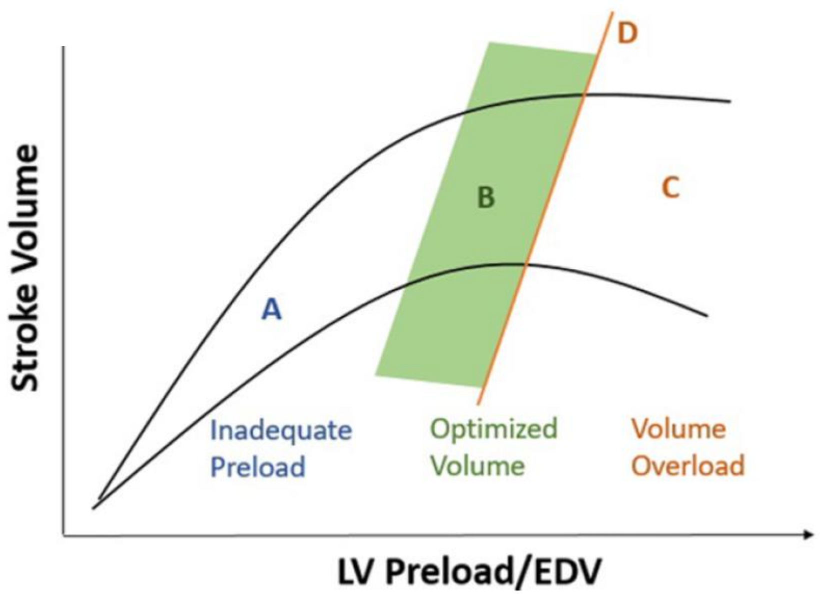
Volume Optimization: a Clinical Challenge

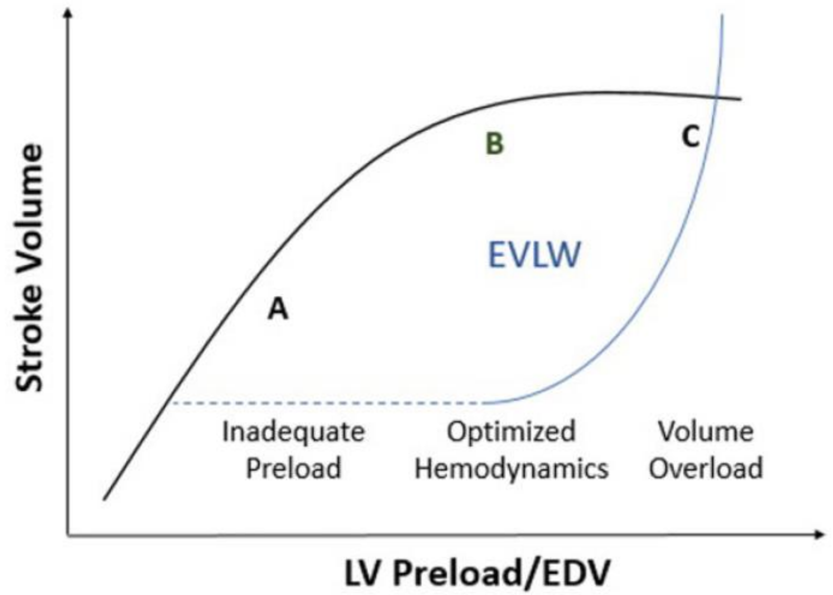


The transition point from volume resuscitation to vasopressor support in treatment for sustained hypotension

Jaffee W. J Intensive Care Med 2018; 33: 502

Volume Optimization: a Clinical Challenge





Optimized volume is achieved at different levels of stroke volume and end-diastolic volume (EDV) for each patient

Once beyond point B and into C, improvement in cardiac output is lost, and extravascular lung water (EVLW) increases

Jaffee W. J Intensive Care Med 2018; 33: 502

Assessment of Volume Status

- Physical exam:
  - vital signs, perfusion, [POCUS]
- Lab studies:
  - lactate, BNP
- Diagnostic maneuvers:
  - passive straight-leg raise, IVF challenge
- Non-invasive monitoring:
  - lung U/S, IVC U/S, PPV, SVV, RBV/Hct
- Invasive monitoring:
  - CO, PCWP

There is no Consensus Approach

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Assessment of Volume Status

Method	Invasive or noninvasive	Static or dynamic	Assess fluid responsiveness	Comments
Historical findings	Noninvasive	Static	No	Of limited value with poor correlation with invasive pressure measurements
Physical exam	Noninvasive	Static and dynamic	Yes	Of limited value but serial examinations may detect changes in organ perfusion
Chest radiograph	Noninvasive	Static	No	Requires use of standardized measures of vascular pedicle width and cardiothoracic ratio. Serial chest X-ray may be helpful in determining effects of fluid therapy
Central venous pressure	Invasive	Static	No	Poor correlation with fluid responsiveness
Pulmonary capillary wedge pressure	Invasive	Static	No	Poor correlation with fluid responsiveness
Echocardiogram	Noninvasive	Static	No	Single measures of cardiac chamber volume hard to assess. Serial measures may be helpful
Stroke volume or pulse pressure variation	Invasive (pulse oximeter method in noninvasive)	Dynamic	Yes	Requires sedated, mechanically ventilated patient
Esophageal doppler	Invasive	Dynamic	Yes	Not useful for continuous measurements
Vena cava diameter	Noninvasive	Dynamic	Yes	Body habitus dependent
Passive leg raising	Noninvasive (bioreactance end-tidal CO_2) Invasive (FloTrac or PiCCO or LiDCO)	Dynamic	Yes	Unreliable with intra-abdominal hypertension
End-expiratory occlusion	Passive leg raising	Dynamic	Yes	Requires 15-s end-expiratory occlusion
Bioimpedance	Noninvasive	Static	No	Not able to assess intravascular volume

Key Concept: Fluid Responsiveness

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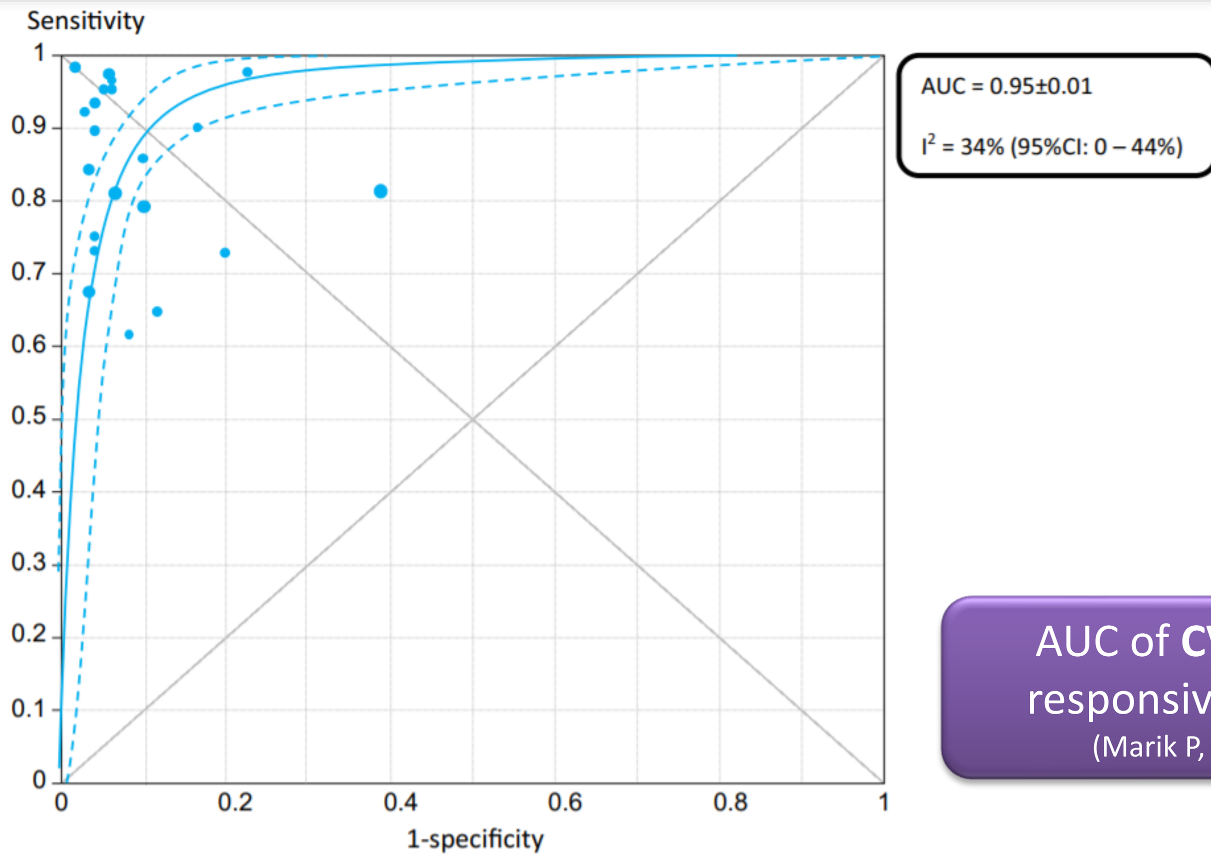
Kalantari K. Kidney Int 2013; 83: 1017

Passive Leg Raising



21 studies

991 patients

AUC of **CVP** for fluid responsiveness: **0.56**
(Marik P, Chest 2008)

PLR-induced changes in CO reliably predict the response of CO to volume expansion in adults with acute circulatory failure.

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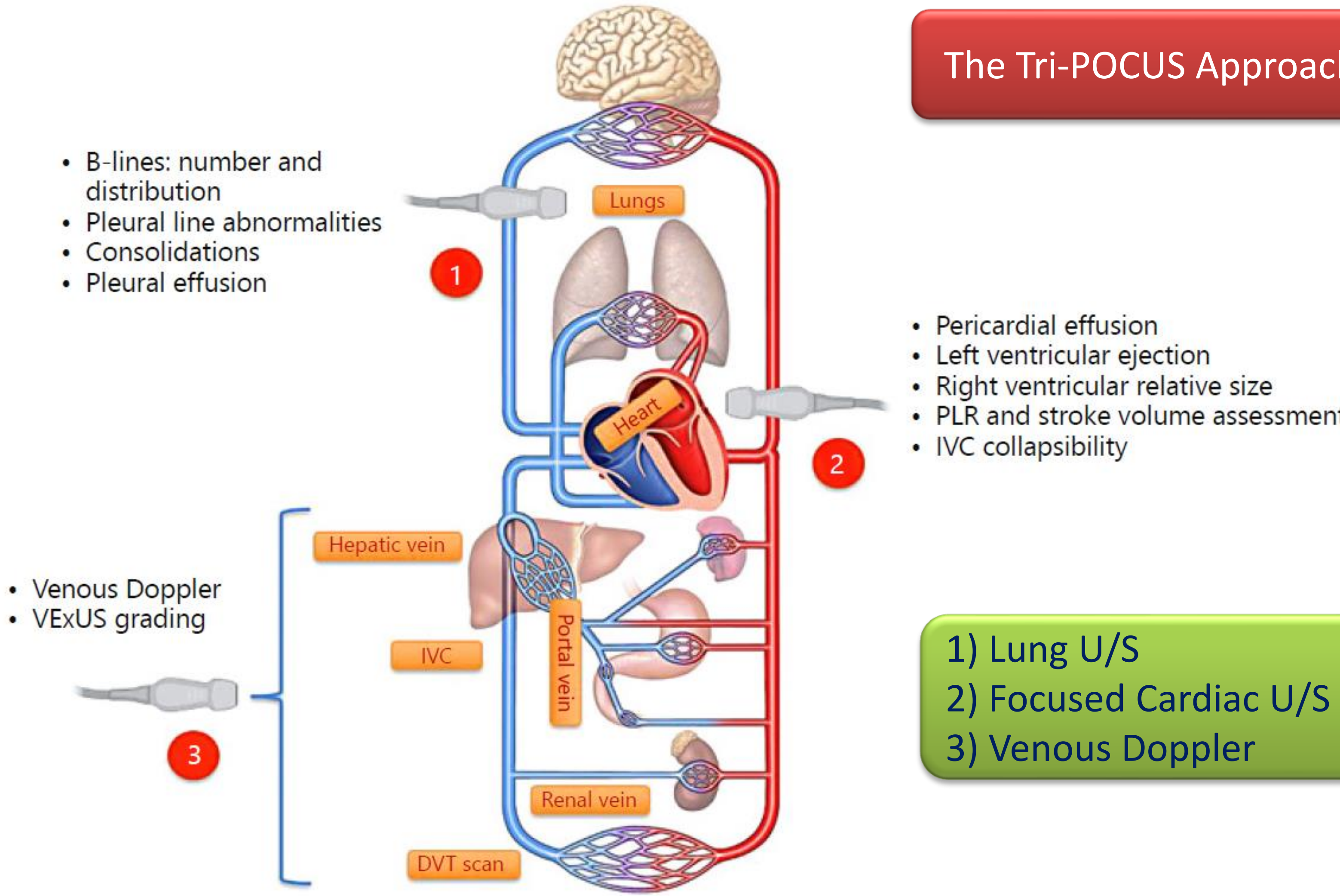
Monnet X. Intensive Care Med 2016;42:1935

Assessment of Volume Status



The Tri-POCUS Approach

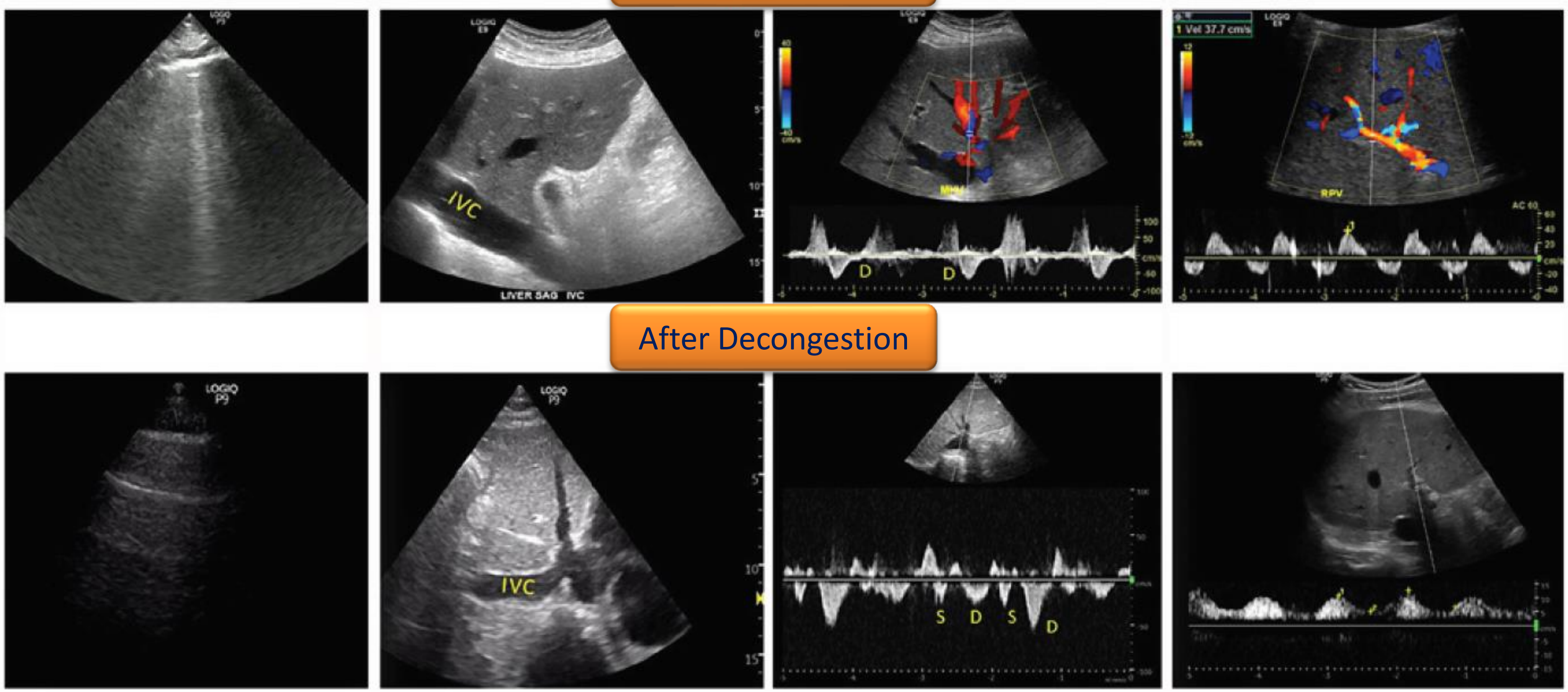
1) Lung U/S
2) Focused Cardiac U/S
3) Venous Doppler

Koratala A. Cardiorenal Med 2020

Assessment of Volume Status

The Tri-POCUS Approach

At Presentation



LUS
Right lateral zone is shown

IVC ultrasound

Heptic vein Doppler

Portal vein Doppler

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Koratala A. Cardiorenal Med 2020

Volume Management Strategies

NHLBI-ARDS Clinical Trials Network

FACT Trial

1000 patients

	Measured intravascular pressure (mm Hg)				MAP <60 mm Hg or a need for any vasopressor (except dopamine ≤5 µg/kg/min); consider correctable causes of shock first	MAP ≥60 mm Hg without vasopressors (except dopamine ≤5 µg/kg/min)			
	CVP		PAOP[G]			Average urinary output <0.5 ml/kg/hr		Average urinary output ≥0.5 ml/kg/hr	
	Conservative strategy	Liberal strategy	Conservative strategy	Liberal strategy		**Ineffective Circulation** Cardiac index <2.5 liters/min/m² or cold, mottled skin with capillary-refilling time >2 sec	**Effective Circulation** Cardiac index ≥2.5 liters/min/m² or absence of criteria for ineffective circulation	**Ineffective Circulation** Cardiac index <2.5 liters/min/m² or cold, mottled skin with capillary-refilling time >2 sec	**Effective Circulation** Cardiac index ≥2.5 liters/min/m² or absence of criteria for ineffective circulation
Range 1	>13	>18	>18	>24	1 Vasopressor[F] Fluid bolus[F]	3 KVO IV Dobutamine[A] Furosemide[B,1,2,4]	7 KVO IV Furosemide[B,1,2,4]	11 KVO IV Dobutamine[A] Furosemide[B,1,3,4]	15 KVO IV Furosemide[B,1,3,4]
Range 2	9–13	15–18	13–18	19–24		4 KVO IV Dobutamine[A]	8 KVO IV Furosemide[B,1,2,4]	12 KVO IV Dobutamine[A]	16 KVO IV Furosemide[B,1,3,4]
Range 3	4–8	10–14	8–12	14–18	2 Fluid bolus[F] Vasopressor[F]	5 Fluid bolus[C]	9 Fluid bolus[C]	13 Fluid bolus[C]	17 Liberal KVO IV; 18 Conservative Furosemide[B,1,3,4]
Range 4	<4	<10	<8	<14		6 Fluid bolus[C]	10 Fluid bolus[C]	14 Fluid bolus[C]	19 Liberal fluid bolus; 20 Conservative KVO IV

Wiedermann P. N Engl J Med 2006;354:2564
Heung M. ASN Roundtable June 2020

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Volume Management Strategies

NHLBI-ARDS Clinical Trials Network

Outcome	Conservative Strategy	Liberal Strategy	P Value
Death at 60 days (%)	25.5	28.4	0.30
Ventilator-free days from day 1 to day 28†	14.6±0.5	12.1±0.5	<0.001
ICU-free days†			
Days 1 to 7	0.9±0.1	0.6±0.1	<0.001
Days 1 to 28	13.4±0.4	11.2±0.4	<0.001
Renal failure	21.5±0.5	21.2±0.5	0.59
Dialysis to day 60			
Patients (%)	10	14	0.06
Days	11.0±1.7	10.9±1.4	0.96

FACT Trial

1000 patients

	Conservative	Liberal	p value
7-day net balance (mL)	**-136**	**6992**	<.001
Shock	2904	10,138	<.001
Non-shock	-1576	5287	<.001

Conservative strategy: improvement of lung function and shorter duration of MV and ICU w/o increasing non-pulmonary organ failures

Wiedermann P. N Engl J Med 2006;354:2564
Heung M. ASN Roundtable June 2020

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Volume Management Strategies

Recognition of AKI

AKI : Cr > 1.5-fold the BL, or ↑0.3 mg/dL

Post-hoc of FACT Trial

Initial Cr and volume status	Change in fluid balance	Subsequent Cr and volume status	AKI *before* Cr adjusted for fluid balance?	AKI *after* Cr adjusted for fluid balance?	
Cr = 1.0 mg/dL Volume of distribution: 45 L	*Even*	Cr = 1.2 mg/dL Volume of distribution: 45 L	NO	NO	A
Cr = 1.0 mg/dL Volume of distribution: 45 L	*+15L*	Cr = 1.2 mg/dL Volume of distribution: 60 L Cr corr = 60L/45L * 1.2 mg/dL = 1.6 mg/dL	NO	YES	B
Cr = 1.0 mg/dL Volume of distribution: 45 L	*-10L*	Cr = 1.5 mg/dL Volume of distribution: 35 L Cr corr = 35L/45L * 1.5 mg/dL = 1.2 mg/dL	YES	NO	C
Cr = 1.0 mg/dL Volume of distribution: 45 L	*+15L*	Cr = 1.5 mg/dL Volume of distribution: 60 L Cr corr = 60L/45L * 1.5 mg/dL = 2 mg/dL	YES	YES	D

Adjustment of Serum Creatinine for Fluid Balance; Impact on Ascertainment of AKI

Liu K. Crit Care Med 2011; 39: 2665

Volume Management Strategies

Recognition of AKI

Post-hoc of FACT Trial

Mortality

Table 3. Multivariable clinical model for death[a]

Variable	Odds Ratio	95% Confidence Interval	p
Age[b]	1.35	1.22–1.50	<.001
Male	1.11	0.80–1.54	.53
White race	0.57	0.41–0.80	.001
Fluid conservative strategy	0.96	0.69–1.33	.81
Pulmonary artery catheter	1.02	0.74–1.41	.90
Baseline vasopressor use	1.06	0.74–1.51	.76
Baseline creatinine[c]	0.98	0.81–1.17	.81
Acute lung injury secondary to infection	1.24	0.85–1.83	.27
Acute Physiology and Chronic Health Evaluation III score[d]	1.26	1.19–1.34	<.001
No AKI before adjustment; AKI after adjustment for fluid balance (group B referent to A)	2.09	1.19–3.67	.01
AKI before adjustment; no AKI after adjustment for fluid balance (group C referent to A)	1.17	0.45–3.02	.75
AKI before AND after adjustment for fluid balance (group D referent to A)	3.16	2.04–4.87	<.001

B

C

D

Increased mortality in patients without apparent AKI (AKI only after adjustment for fluid balance)

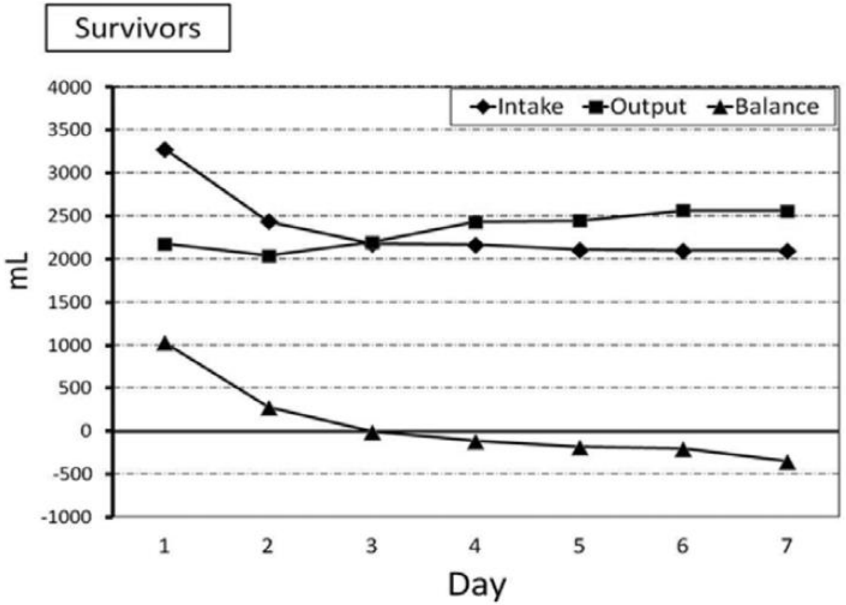
Liu K. Crit Care Med 2011; 39: 2665

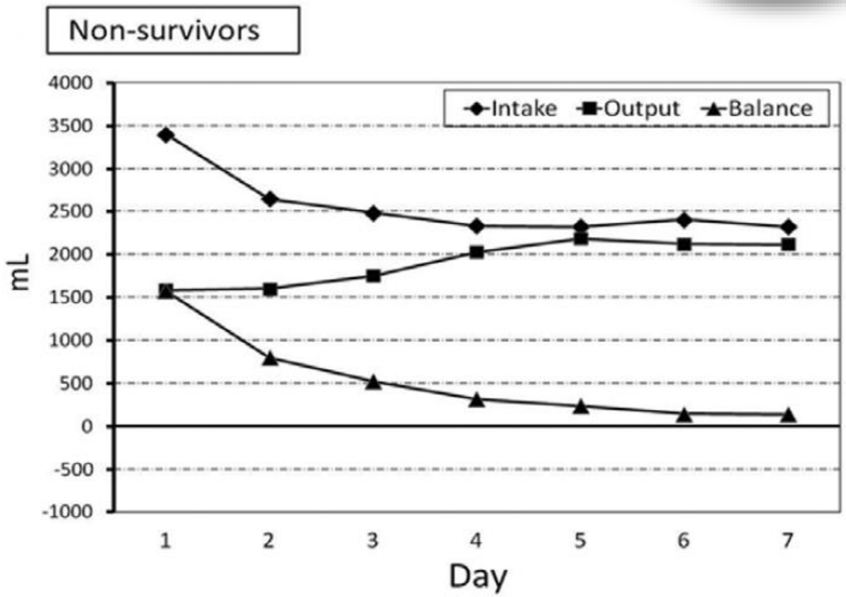
Fluid Balance and Mortality

28-day in-hospital death

Substudy of ICON

1,808 patients





Survivors: FB (-) at day 3; not in the Non-S

Difference in FB is due to Output, not Intake

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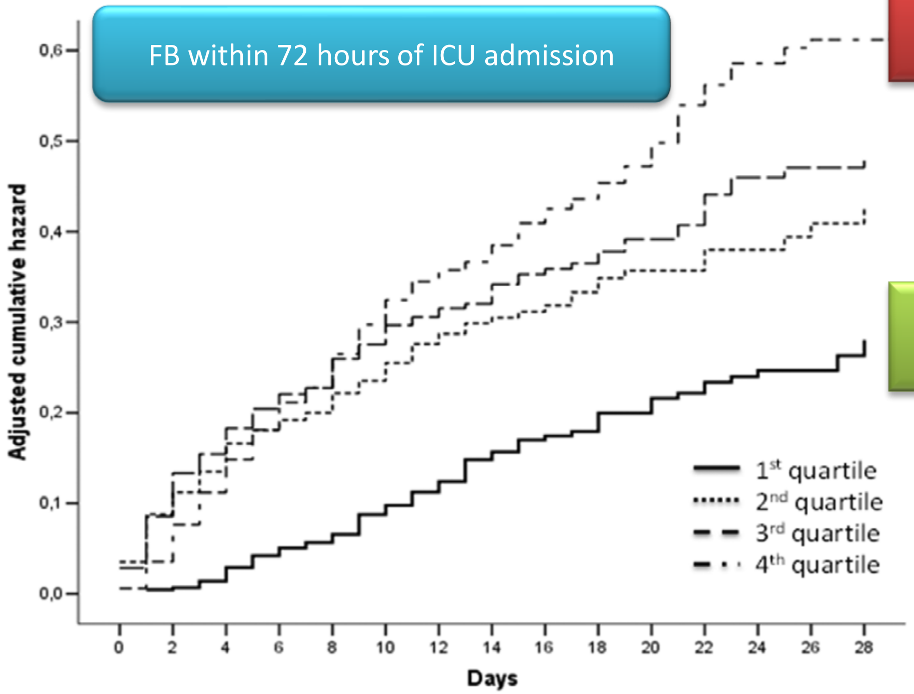
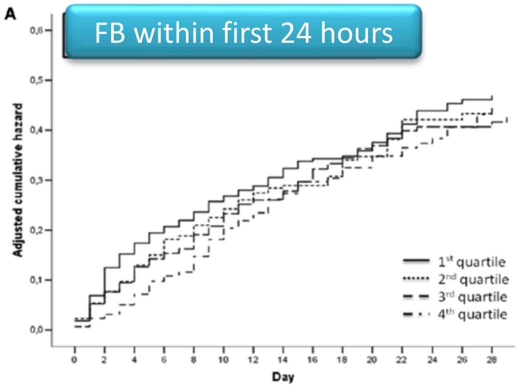
Sakr Y. Crit Care Med 2017; 45:386

Fluid Balance and Mortality

28-day in-hospital death

1,808 patients





Higher cumulative fluid balance at day 3 (but not in the first 24 hours); higher mortality

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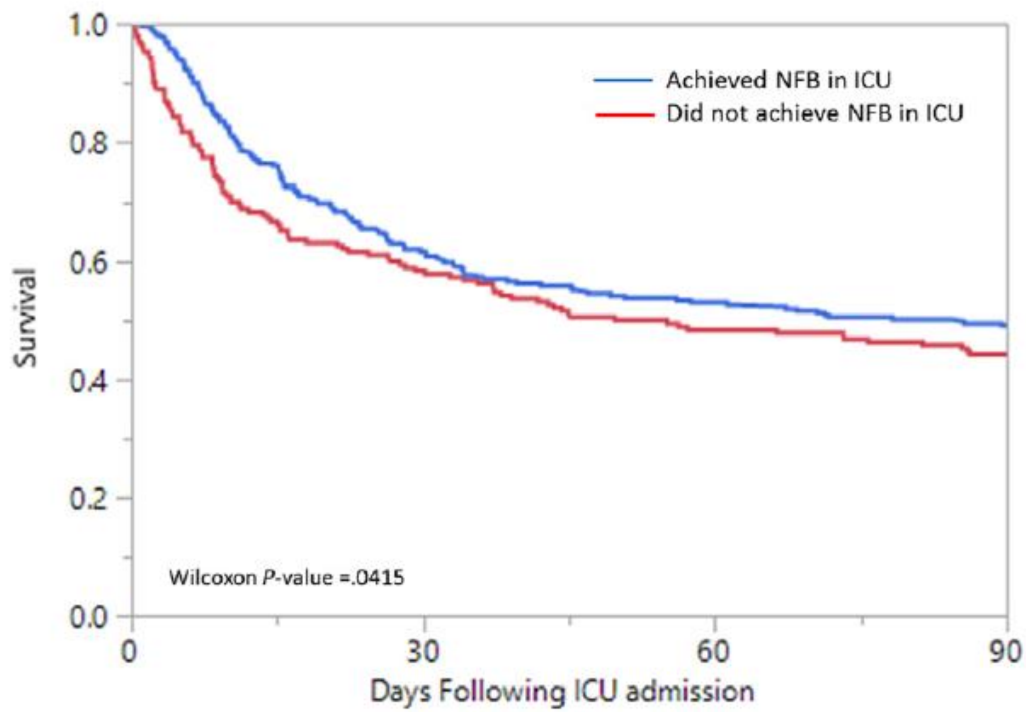
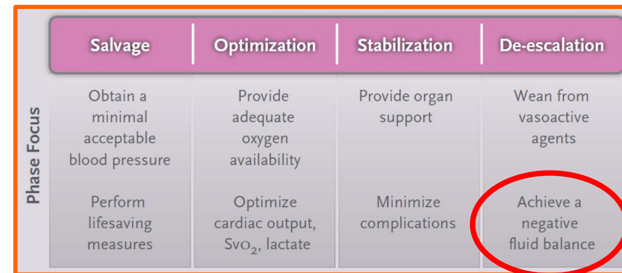
Sakr Y. Crit Care Med 2017; 45:386

Fluid Balance and Mortality

90-day mortality

633 patients





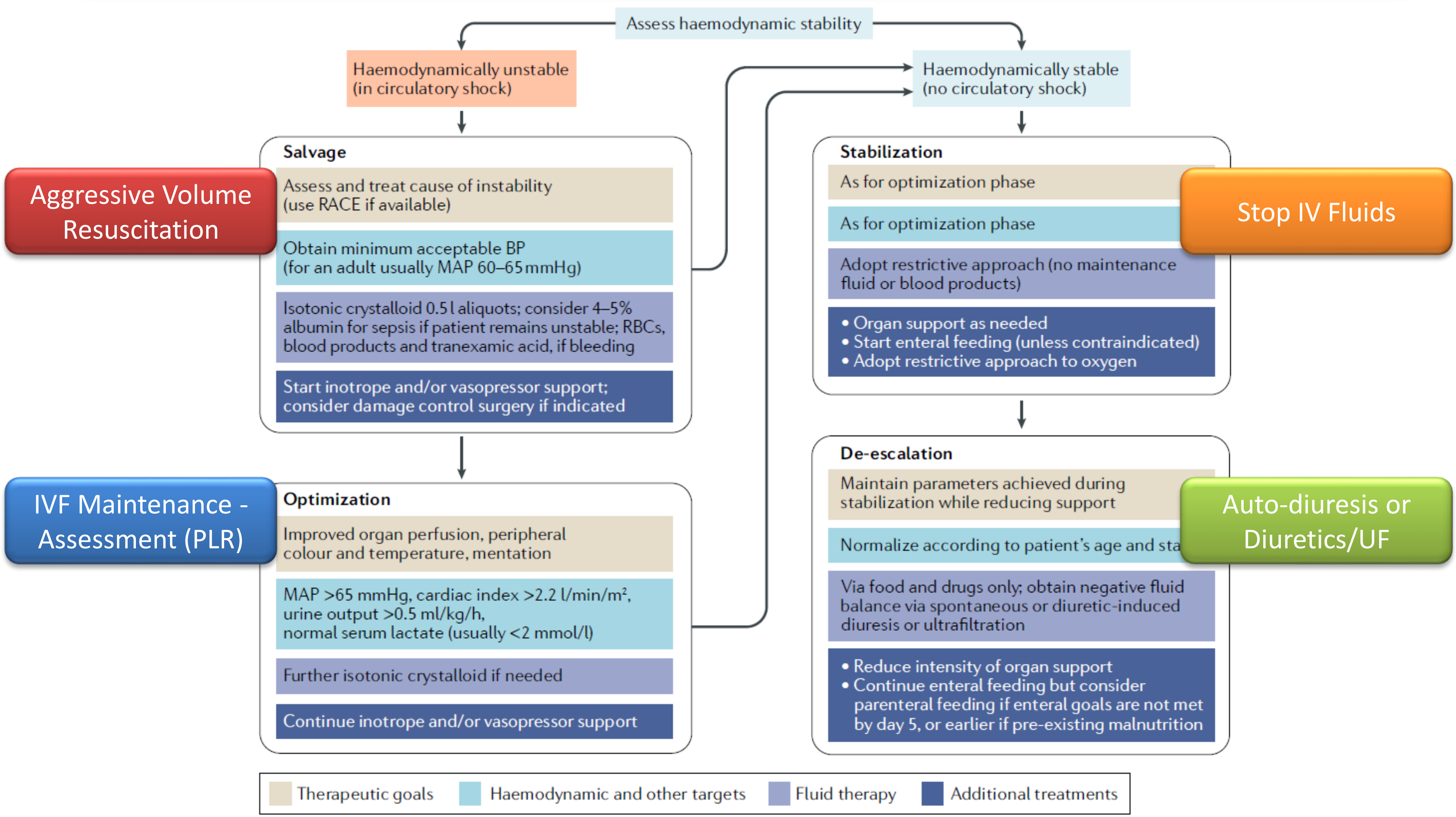
Phase Focus	Salvage	Optimization	Stabilization	De-escalation
	Obtain a minimal acceptable blood pressure	Provide adequate oxygen availability	Provide organ support	Wean from vasoactive agents
	Perform lifesaving measures	Optimize cardiac output, SvO_2, lactate	Minimize complications	Achieve a negative fluid balance

Higher mortality rate if no Negative Fluid Balance in the ICU despite lower illness severity scores

Dhondup T. J Crit Care 2020;55:16

Fluid Management in Shock

4 phases



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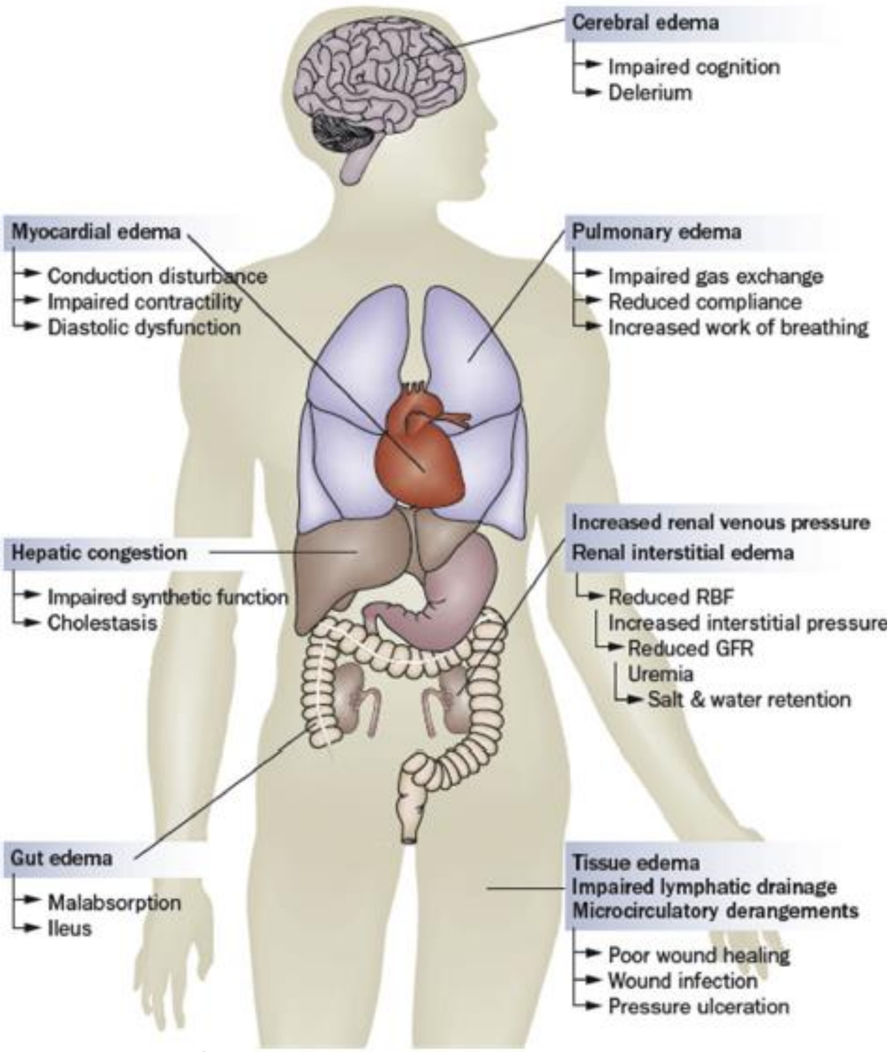
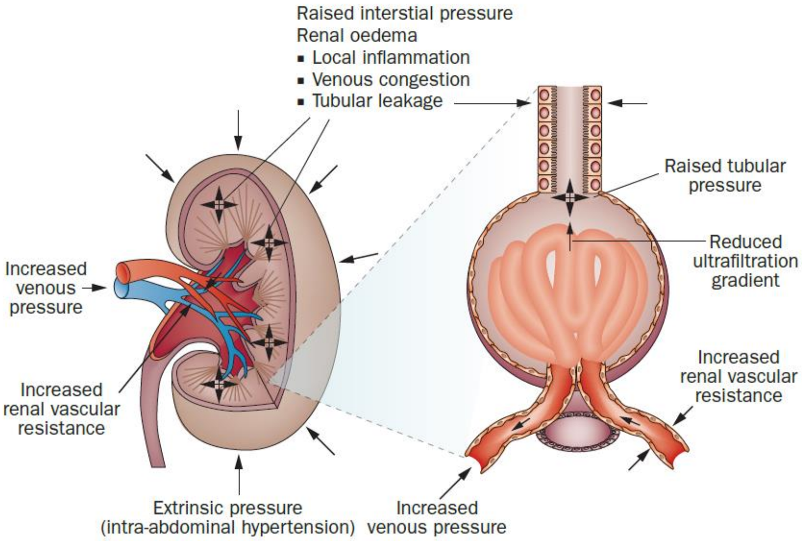
Finfer S. Nature Rev 2018;14:541

Volume Overload: Detrimental Effects





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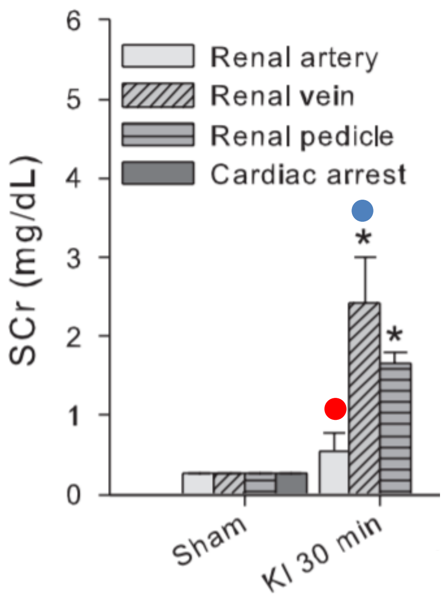
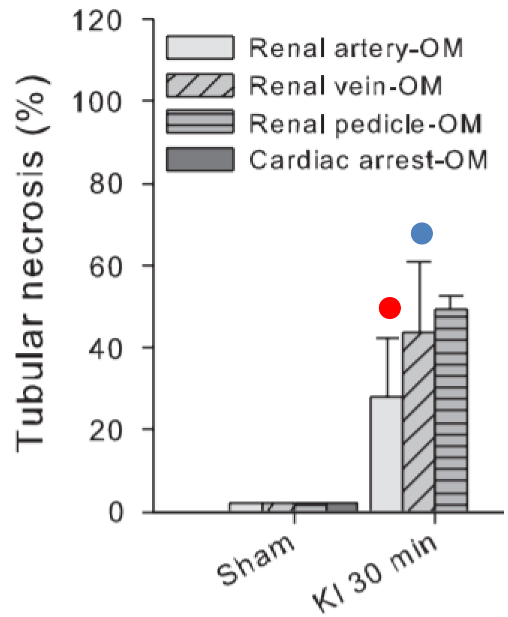
Prowle JR. Nat Rev Nephrol 2010;6:110

Volume Overload: Kidney in the Spotlight

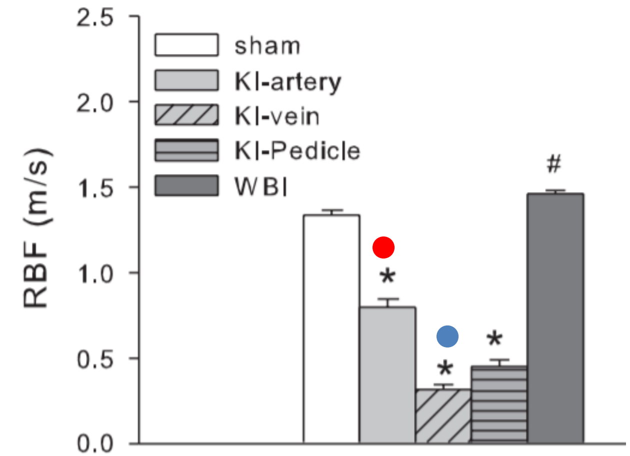
Murine Model



Function



Structure



Hemodynamics

Acute Renal Venous obstruction;
more detrimental than Arterial Occlusion

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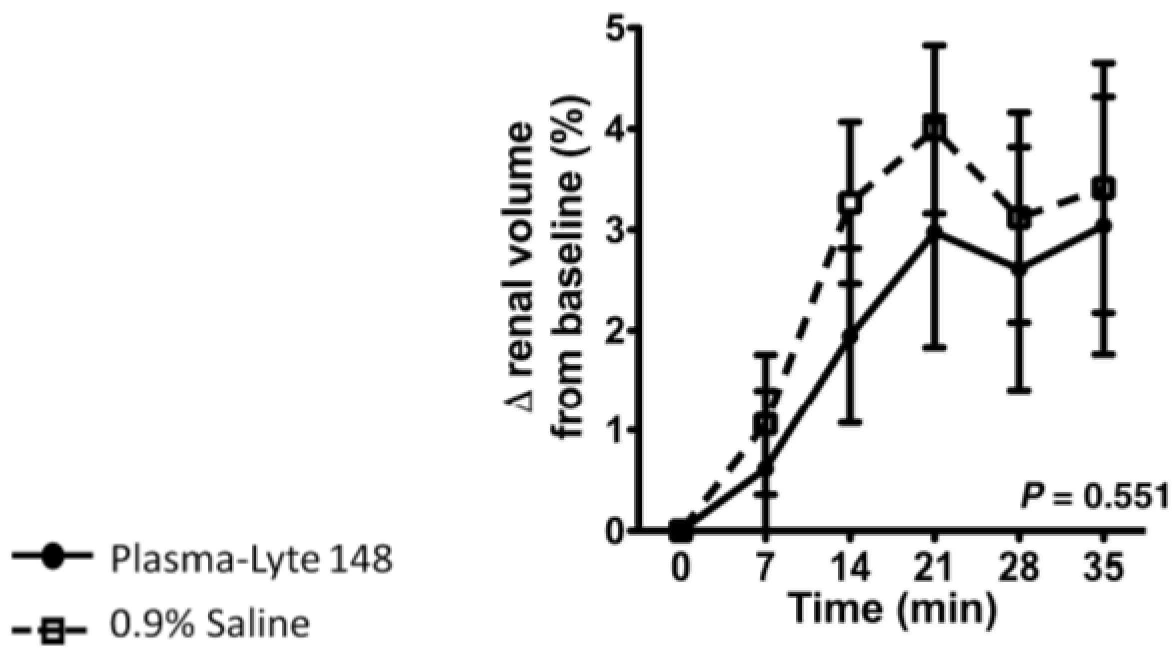
Li X. Am J Physiol Renal Physiol 2012; 302: F519

Volume Overload: Kidney in the Spotlight

Healthy Volunteers

12 adults



Infusion of 2 liters of IV fluid over 1 hour; increase in kidney volume by 3-4% (?edema)

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Chawdhury AH. Ann Surg 2012;256:18

Fluid Resuscitation Strategies and the Kidney

Conservative vs. Liberal Approach to fluid therapy of Septic Shock in Intensive Care (CLASSIC)

151 patients

Outcome	Fluid restriction group ($n = 75$)	Standard care group ($n = 76$)	Fluid restriction vs. standard care (95 % CI)[a]	*P* value
Co-primary outcome measures				
Volumes of resuscitation fluid (mL)				
First 5 days after randomisation	500 (0 to 2500) [1687]	2000 (1000 to 4100) [2928]	−1241 (−2043 to −439)	<0.001[b]
During ICU stay after randomisation	500 (0 to 3250) [1992]	2200 (1000 to 4750) [3399]	−1407 (−2358 to −456)	<0.001[b]
Secondary outcome measures				
Total fluid input (mL)[c]				
First 5 days after randomisation	12,411 (5518 to 17,035) [11,777]	13,687 (7163 to 17,082) [12,597]	−820 (−2968 to 1329)	0.45
During ICU stay after randomisation	18,291 (5518 to 34,045) [21,459]	16,970 (7163 to 29,889) [23,495]	−2036 (−10,920 to 6848)	0.65
Cumulated fluid balance (mL)				
First 5 days after randomisation	1752 (−1153 to 3758) [2141]	2680 (407 to 5114) [3289]	−1148 (−2531 to 235)	0.06[b]
During ICU stay after randomisation	1923 (−1964 to 5415) [2,032]	2014 (−168 to 4678) [2507]	−475 (−2254 to 1304)	0.60
Serious adverse reactions[d]				
Number of reactions per day during the ICU stay	0.14 (0 to 0.50) [0.37][e]	0.15 (0 to 0.52) [0.33][e]	NA	0.85[b]

Restrictive strategy (bolus by indication)
led to lower amount of administered fluid

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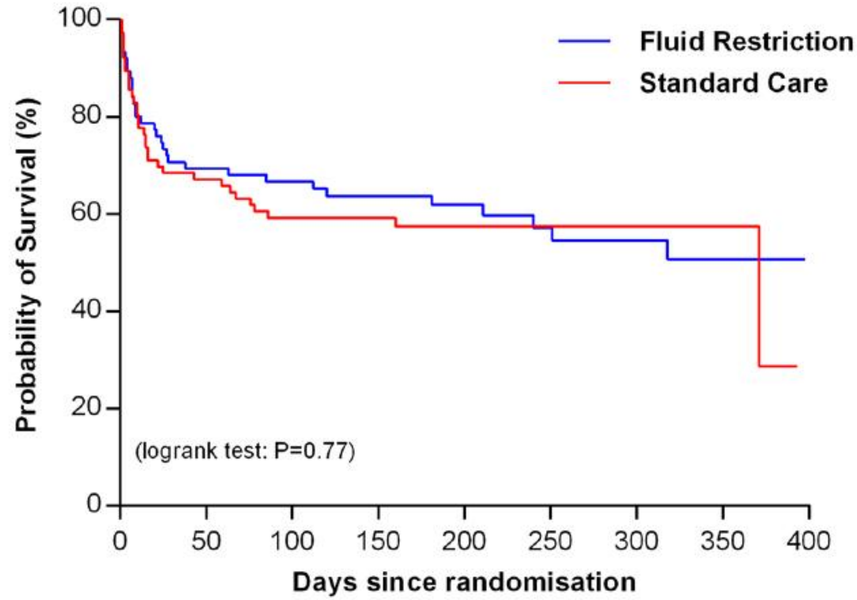
Hjortrup PB. Intensive Care Med 2016;42:1695

Fluid Resuscitation Strategies and the Kidney

Conservative vs. Liberal Approach to fluid therapy of Septic Shock in Intensive Care (CLASSIC)

151 patients



No. at risk				
Fluid Restriction	75	47	32	15
Standard Care	76	42	24	11

Similar mortality rate at latest follow up

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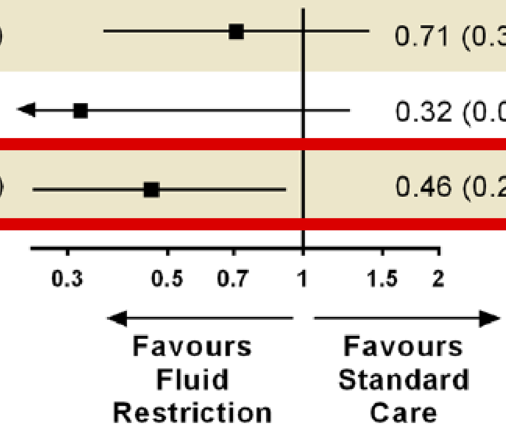
Hjortrup PB. Intensive Care Med 2016;42:1695

Fluid Resuscitation Strategies and the Kidney

Conservative vs. Liberal Approach to fluid therapy of Septic Shock in Intensive Care (CLASSIC)

151 patients

	Fluid Restriction	Standard Care	Odds ratio (95% CI)	P value
	No. of events / No. at risk			
Death by day 90	25/75 (33%)	31/76 (41%)	0.71 (0.36-1.40)	0.32
Ischemic events in the ICU	3/75 (4%)	9/76 (12%)	0.32 (0.08-1.27)	0.11
Worsening of AKI	27/73 (37%)	39/72 (54%)	0.46 (0.23-0.92)	0.03



Development of AKI, or worsening of AKI (KDIGO stage) after randomization; more often in standard care

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Hjortrup PB. Intensive Care Med 2016;42:1695

Fluid Balance and Kidney

Reference	Study type	Population	*n*	Average fluid balance in less-positive group	Average fluid balance in more-positive group	Renal function measure	Renal outcome with more-restrictive fluid balance strategy	Principal outcome with more-restrictive fluid balance strategy
ARDS Clinical Trials Network (2006)[88]	Multicenter RCT	ARDS	1,000	–136 ml on day 7	+6,992 ml on day 7	Need for RRT; change in creatinine	No difference	Shorter duration of ventilation and ICU stay
Martin *et al.* (2005)[86]	Single-center RCT	Mixed ALI	40	–5,480 ml on day 5	–1,490 ml on day 5	Change in creatinine	No difference	Improved oxygenation
Martin *et al.* (2002)[85]	Single-center RCT	ALI after trauma	37	–3,300 ml on day 5	+500 ml on day 5	Change in creatinine	No difference	Improved oxygenation
Mitchell *et al.* (1992)[127]	Single-center RCT	Mixed ICU needing PAC	102	+142 ml	+2,239 ml	Change in creatinine	Small rise in creatinine	Shorter duration of ventilation and ICU stay
Bouchard *et al.* (2009)[25]	Retrospective observational	Mixed ICU with AKI	542	<10% rise	>10% rise	Dialysis independence	Improved	Decrease in mortality
Payen *et al.* (2008)[6]	Retrospective observational	Mixed ICU with or without AKI	3,147	–1,000 ml	+3,000 ml	Renal SOFA score	Improved	Decrease in mortality in patients with AKI
Vidal *et al.* (2008)[72]	Prospective observational	Mixed ICU with elevated or normal IAP	83	+5,000 ml	+9,000 ml	Renal SOFA score	Improved	Normal IAP associated with less organ failure and shorter ICU stay
Adesanya *et al.* (2008)[128]	Retrospective observational	Surgical ICU	41	+5 kg	+8.3 kg	Change in creatinine	No difference	Shorter duration of ventilation and ICU stay
McArdle *et al.* (2007)[87]	Retrospective observational	Surgical ICU	100	+7,500 ml	+10,000 ml	Change in creatinine	No difference	Decrease in postoperative complications
Arlati *et al.* (2007)[99]	Prospective observational	Burns ICU	24	+7,500 ml	+12,000 ml	Urine output	No difference	Decrease in organ dysfunction score

*See Supplementary Information online for systematic search strategy. Abbreviations: AKI, acute kidney injury; ALI, acute lung injury; ARDS, acute respiratory distress syndrome; IAP, intra-abdominal pressure; ICU, intensive care unit; PAC, pulmonary artery catheter; RCT, randomized, controlled trial; RRT, renal replacement therapy; SOFA, sequential organ failure assessment.

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Prowle JR. Nat Rev Nephrol 2010; 6: 107

Fluid Management Guidelines

Fluid Stewardship

Surviving Sepsis Campaign

- Measurir
to assess f
- Using a c
administra
- Using cry
to colloids
- Balanced
over unba

World Health Organization

guide volume administration
beyond initial resuscitation.

International Fluid Academy

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Common Themes:

1- Conservative Fluid Administration

2- Use of Dynamic Indices of Volume Responsiveness

3- Early Use of Pressors

Malbrain M. ICU management and Practice 2020; 20: 6

Illustrative Case

A 62-year-old woman with COVID-19 is admitted to the ICU with high-grade fever, multifocal opacities on chest x-ray, and respiratory failure requiring intubation. Despite an initial 2-L (30 mL/kg) bolus of crystalloid, the patient develops progressive hypotension.

The patient's mean arterial pressure (MAP) is 45 mm Hg, central venous pressure (CVP) is 11 mm Hg, and central venous oxygen saturation (ScVO2) is 89%. Arterial lactate level is 10.2 mmol/L, and urine output is 10 mL/h.

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Adapted from: Griffin BR. Am J Kidney Dis 2020; 75: 435

Illustrative Case

Which of the following statements is correct regarding the next best step in management?

(a) The next best option is to initiate norepinephrine and perform a passive leg raise to assess whether she is likely to respond to additional fluids.

(b) The next best option is to initiate dopamine treatment.

(c) The next best option is to continue to administer IV fluids until CVP is ≥12 cm H2O.

(d) Because of the dangers associated with volume overload, the patient should not have been treated with a 30 mL/kg fluid bolus and should receive no further fluids.

(e) Because ScVO2 is >70%, oxygen delivery to her tissues is adequate and therefore no additional treatment is warranted.

Adapted from: Griffin BR. Am J Kidney Dis 2020; 75: 435

Take-Home Message

- There is no single tool for precise assessment of volume status; need for “combinational or dynamic” approaches

- Aggressive fluid administration is recommended at the initial phase of distributive shock (e.g. 30 ml/kg) followed by maintenance fluid only “if needed” (frequent assessment).

- A restrictive fluid strategy is recommended in the critically-ill, especially in those with rapidly expanding lung lesions (role of early de-escalation).


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