Harmful Effects of Fluids in Sepsis

Amir A. Nassiri, M.D, D.I.U

SBUMS

Tabriz, 2019

Conflict of Interest

Conflict of Interest

Fluid therapy in sepsis

What is Sepsis ?

Sepsis is a “complete derangement” of the “immune system”.

- ***Sepsis is is a life-threatening organ dysfunction***

Septic Shock

- Sepsis + fluid unresponsive hypotension

requiring vasopressors to maintain MAP > 65 mmHg & serum lactate level > 2 mmol/L after adequate fluid resuscitation.

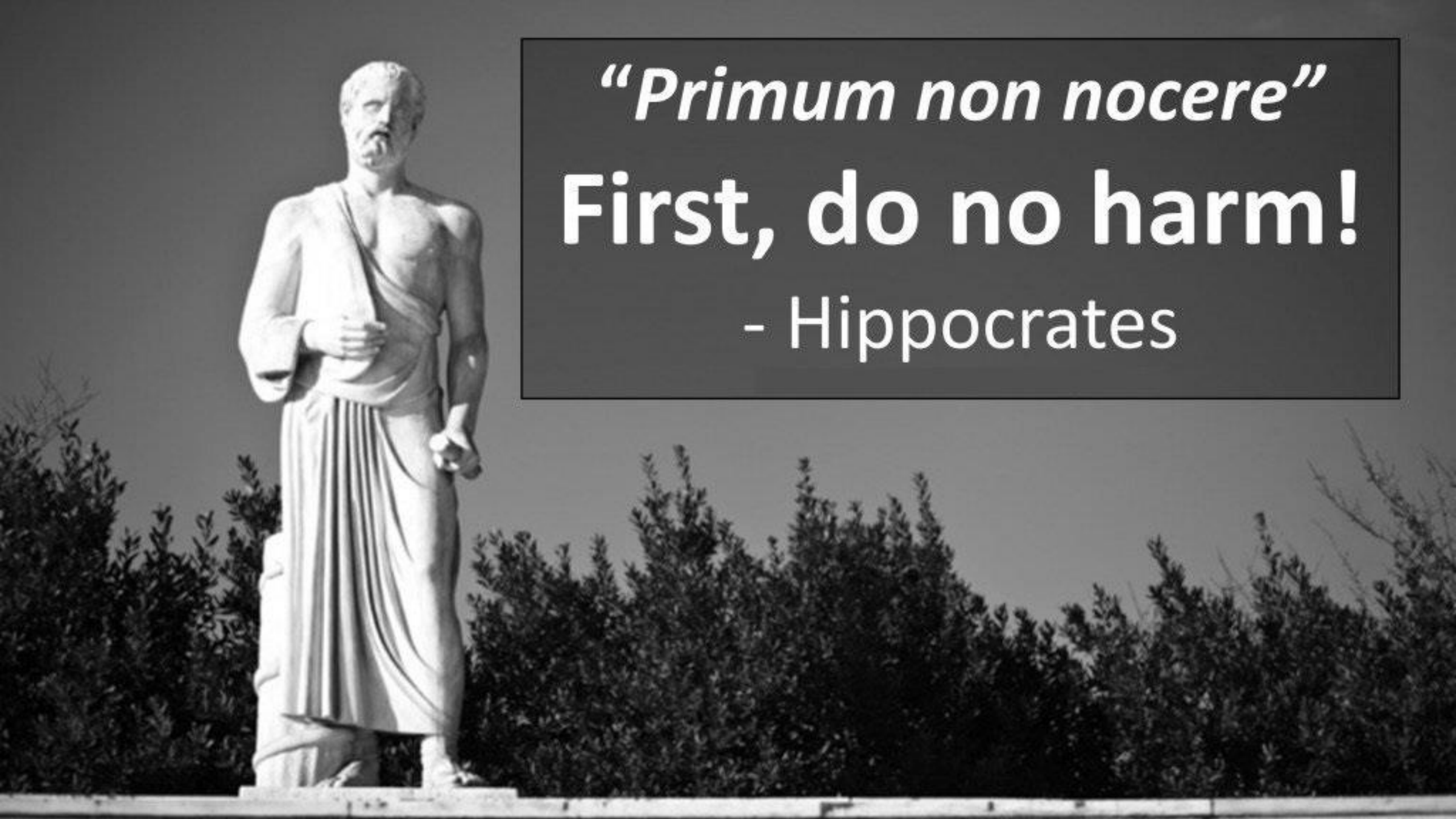

Infection
Dysregulated
Immune Response
Organ Damage


SEPSIS
KILLS

Sepsis Management
“the right strategy”

- We have to do something

- Sometimes there is no need to do anything !


"Primum non nocere"
First, do no harm!
- Hippocrates

Sepsis Management
"what we think we do"

- 1- Source control (Abx & possibly by endotoxin removal)
- 2- Modulate inflammation (immunomodulation & Cytk removal)
- 3- Support organ function (to get the pt alive)


… in practice !

to correct IV depletion & to increase COP & perfusion pressure

Based on Guidelines…

- Fluid therapy is one of the first-line intervention in pts with sepsis & evidence of hypo-perfusion

Intensive Care Med (2017) 43:304–377
DOI 10.1007/s00134-017-4683-6

CONFERENCE REPORTS AND EXPERT PANEL

CrossMark

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

A fixed recipes for all pts !

A. INITIAL RESUSCITATION

1. **Sepsis and septic shock are medical emergencies, and we recommend that treatment and resuscitation 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 h (strong recommendation, low quality of evidence).**
3. **We recommend that, following initial fluid resuscitation, additional fluids be guided by frequent reassessment of hemodynamic status (BPS).**

ORIGINAL

Fluid administration in severe sepsis and septic shock, patterns and outcomes: an analysis of a large national database

Paul E. Marik[1*], Walter T. Linde-Zwirble[2], Edward A. Bittner[3], Jennifer Sahatjian[4] and Douglas Hansell[3,4]

The administration of more than 5 L of fluid during the first ICU day is associated with a significantly increased risk of death and significantly higher hospital costs.

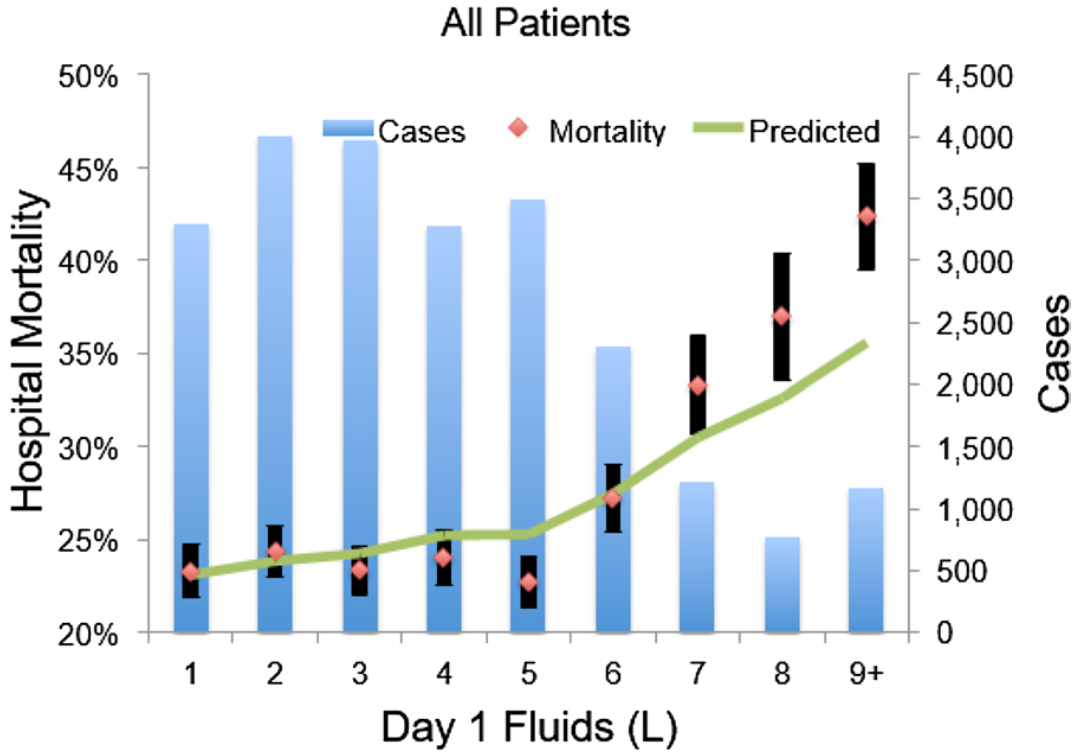
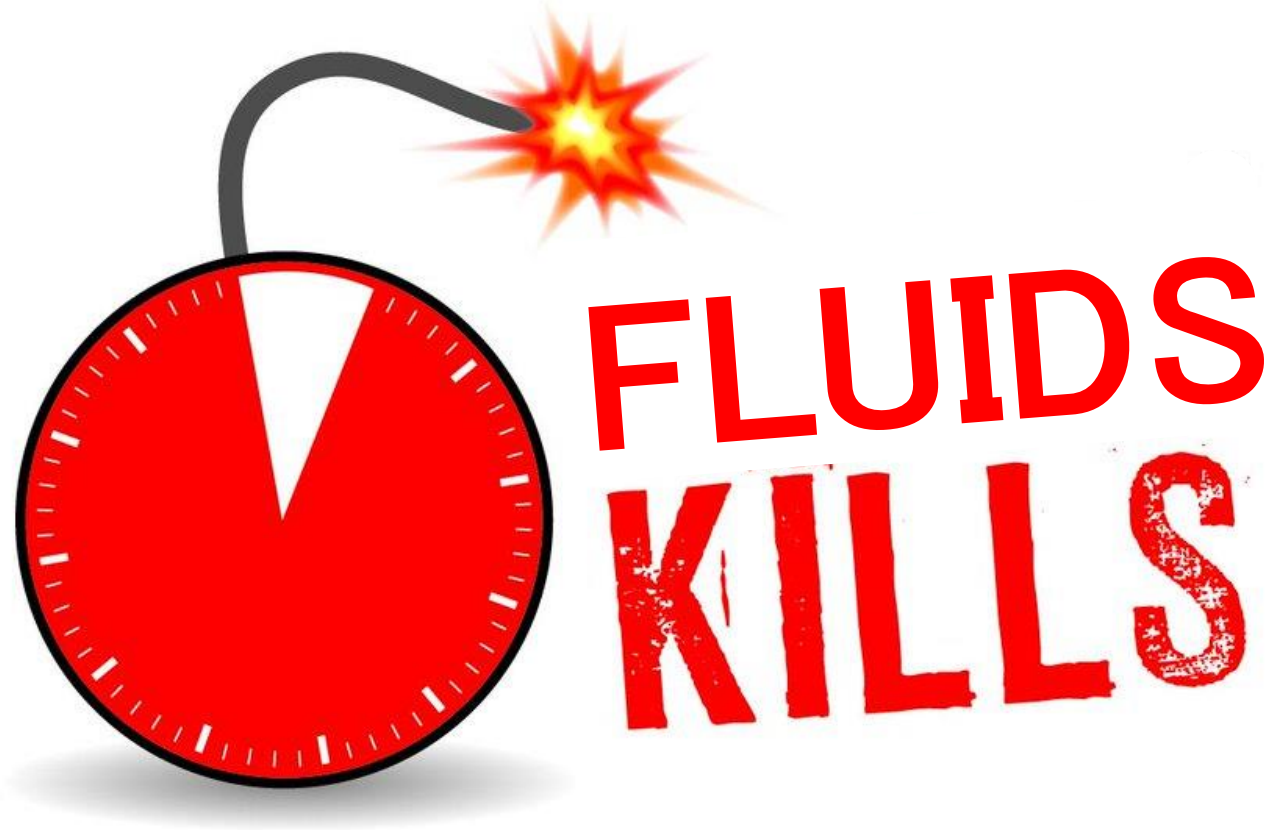


Fig. 2 Actual and expected hospital mortality, by day 1 fluid groups


FLUIDS
KILLS

Guidelines…

- provide an attractive approach >>> patient management
- not always used exclusively >>> what we must do !
- first >>> what not to do !

Strict adherence to guidelines

Am I going to kill my septic pt?

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CONFERENCE REPORTS AND EXPERT PANEL

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

As soon as "evidence of tissue hypoperfusion"

F. FLUID THERAPY

1. **We recommend that a fluid challenge technique be applied where fluid administration is continued as long as hemodynamic factors continue to improve (BPS).**

Rationale The use of IV fluids in the resuscitation of patients is a cornerstone of modern therapy. Despite this, there is little available evidence from RCTs to support its practice; this is an area in which research is urgently

SSC 2016

- “… a fluid challenge of 500-1000 mL of crystalloids (or 300-500 mL of colloids) over 30 min [grade E]…”

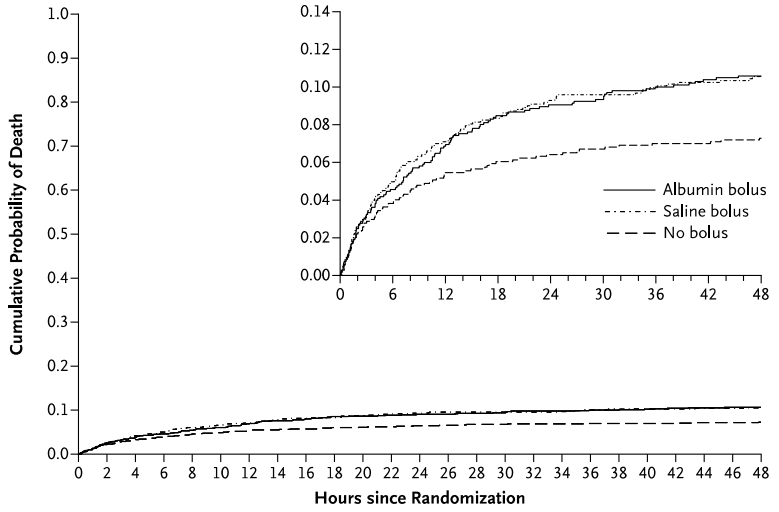
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 30, 2011 VOL. 364 NO. 26

Mortality after Fluid Bolus in African Children with Severe Infection

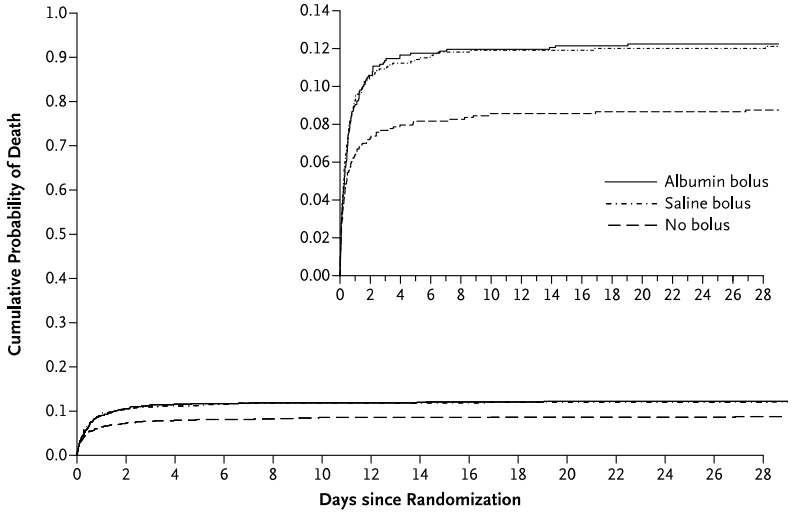
Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*

A Mortality at 48 Hours



	Hr 1			Hr 2			Hr 3			Hr 4			Hr 5–8			Hr 9–24			Hr 24–48		
	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus
No. at Risk	1050	1047	1044	1037	1033	1030	1024	1018	1021	1016	1010	1015	1010	1001	1011	992	980	996	954	945	975
Died	13	12	14	13	15	9	8	7	6	6	9	4	17	20	14	38	34	20	16	13	9
%	1.2	1.1	1.3	1.3	1.5	0.9	0.8	0.7	0.6	0.6	0.9	0.4	1.7	2.0	1.4	3.8	3.5	2.0	1.7	1.4	0.9

B Mortality at 4 Weeks



	Day 1			Day 2			Day 3–7			Day 8–14			Day 15–21			Day 21–28		
	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus
No. at Risk	1050	1047	1044	954	945	975	914	917	947	901	909	940	899	902	933	897	901	934
Died	95	97	67	16	13	9	11	7	7	2	6	2	2	1	4	2	1	1
%	9.0	9.3	6.4	1.7	1.4	0.9	1.2	0.8	0.7	0.2	0.7	0.2	0.2	0.1	0.4	0.2	0.1	0.2

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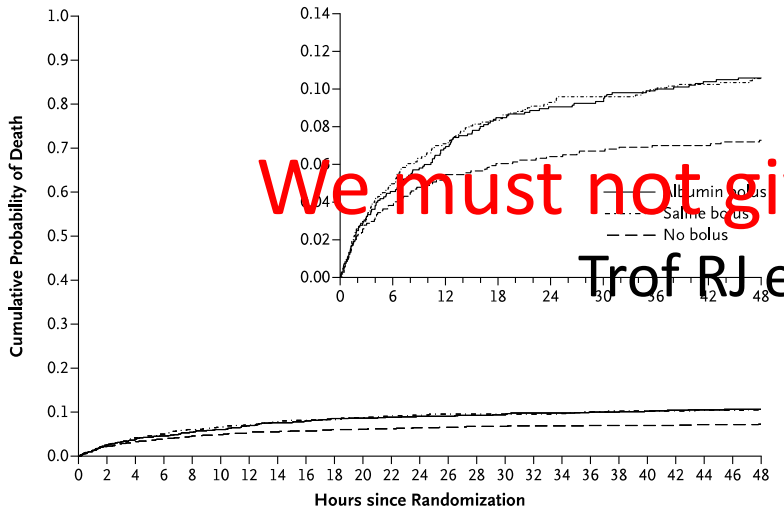

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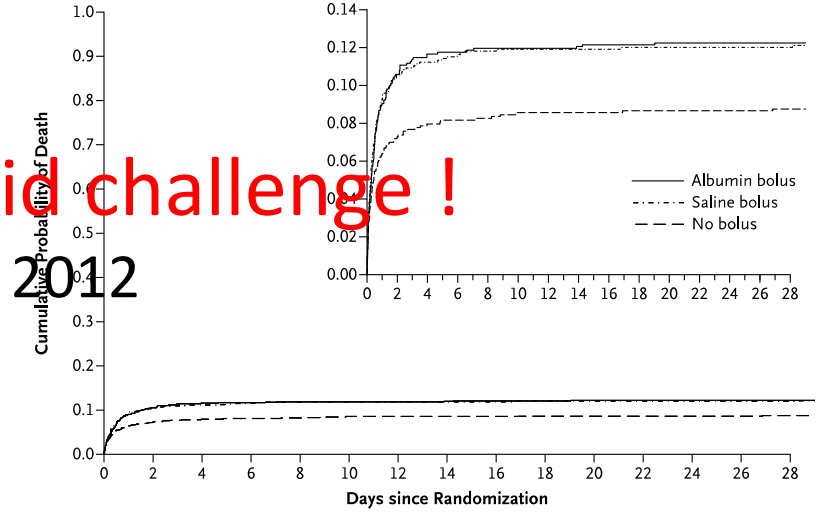

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We must not give a fluid challenge !

Trof RJ et al, CCM 2012

Harms of Boluses therapy >>> not related to Fluid overload !

Maitland *et al. BMC Medicine* 2013, **11**:68
http://www.biomedcentral.com/1741-7015/11/68

BMC Medicine

RESEARCH Open Access

Exploring mechanisms of excess mortality with early fluid resuscitation: insights from the FEAST trial

- the **increase in mortality** did **not** appear to be related to **complications of fluid overload** but rather to **delayed cardiovascular collapse** causing **refractory shock**.

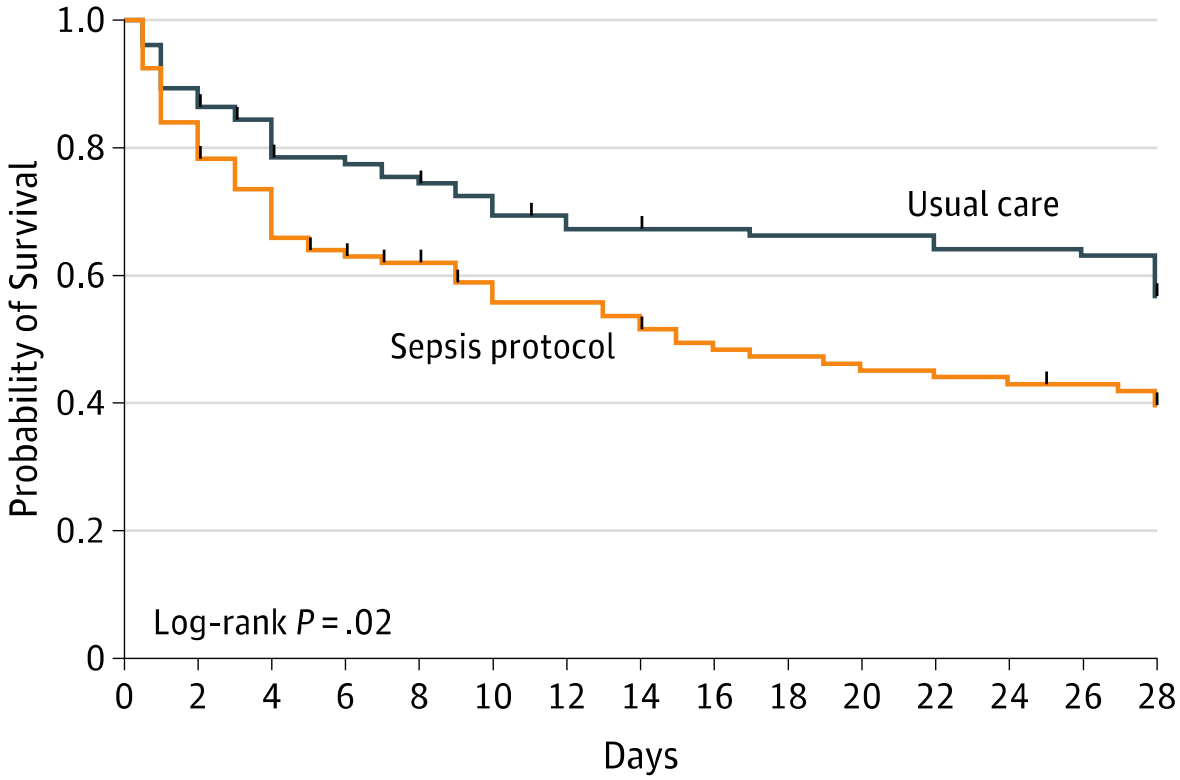
JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of an Early Resuscitation Protocol on In-hospital Mortality Among Adults With Sepsis and Hypotension
A Randomized Clinical Trial

Ben Andrews, MD; Matthew W. Semler, MD, MSc; Levy Muchemwa, MBChB; Paul Kelly, MD, FRCP; Shabir Lakhi, MBChB; Douglas C. Heimburger, MD, MS; Chileshe Mabula, MBChB; Mwango Bwalya, MBChB; Gordon R. Bernard, MD

The **sepsis protocol** resulted in greater intravenous fluid administration

The **sepsis protocol** caused **more** frequent **worsening of hypoxemia and tachypnea and higher rates of in-hospital and 28-day mortality**



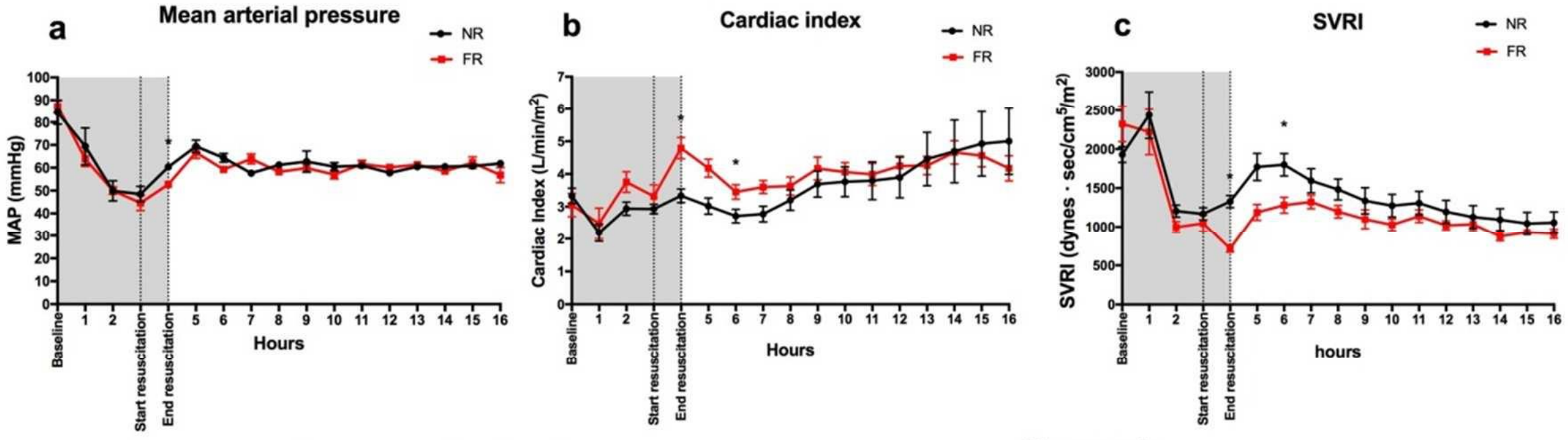
… and what is the mechanisms ?

Unintended consequences; fluid resuscitation worsens shock in an ovine model of endotoxemia

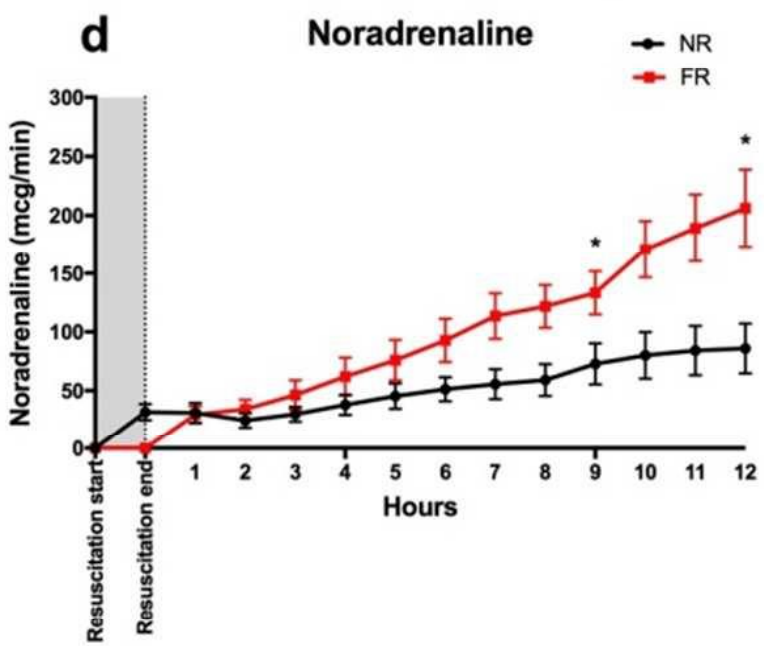
Liam Byrne[1,2,3*], Nchafatso G. Obonyo[#1], Sara D. Diab[1], Kimble R. Dunster[1,4], Margaret R. Passmore[1,5], Ai-Ching Boon[1,5], Louise See Hoe[1,5], Sanne Pedersen[1], Mohd Hashairi Fauzi[6], Leticia Pretti Pimenta[1], Frank Van Haren[2,3,7], Christopher M. Anstey[8], Louise Cullen[5,9], John-Paul Tung[1,10], Kiran Shekar[1,11], Kathryn Maitland[12], John F. Fraser[1,5,11].

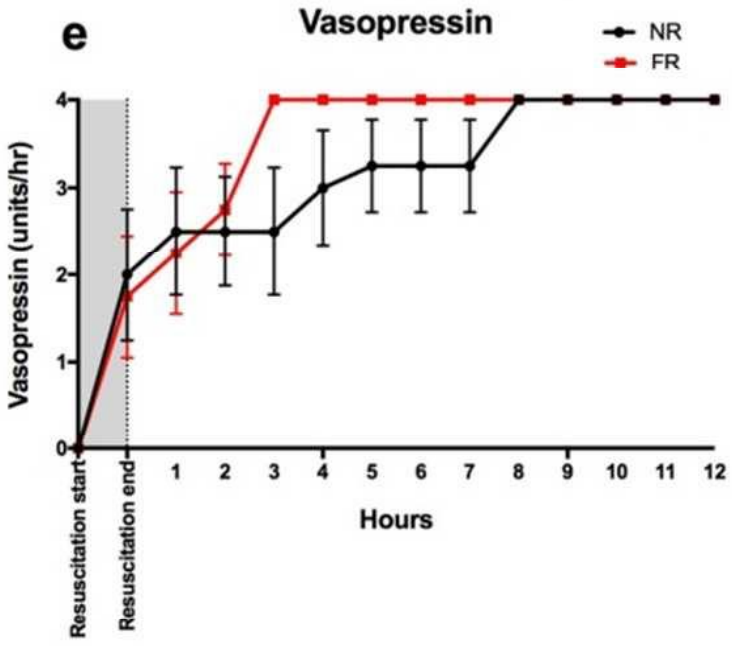
AJRCCM, June, 2018

Fluid Resuscitation-Induced Vasodilation

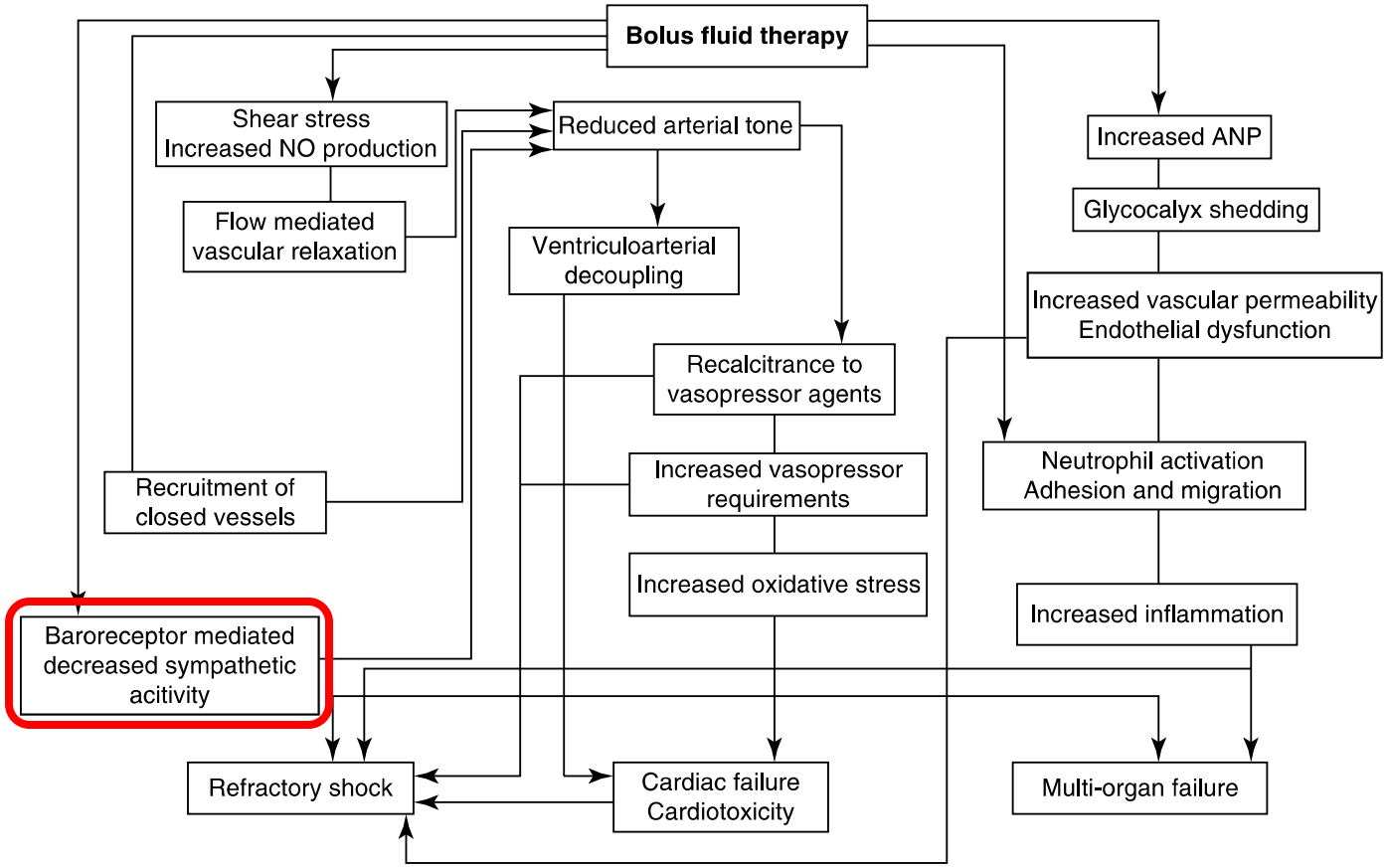


animals that received fluid resuscitation required significantly more norepinephrine to maintain the same MAP in the 12 h after resuscitation,





Cardiovascular dysfunction following bolus fluid therapy for sepsis-induced tissue hypoperfusion



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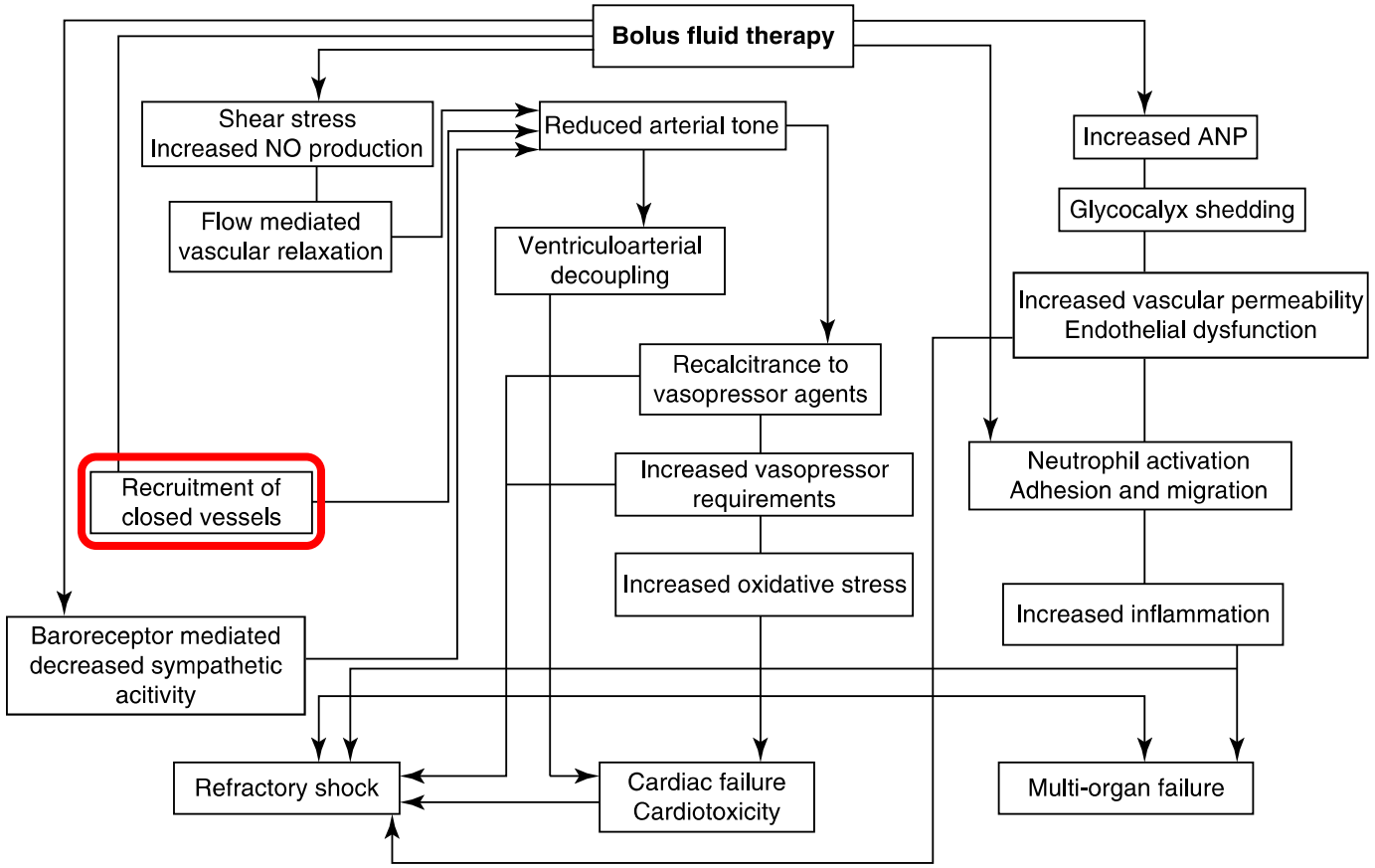

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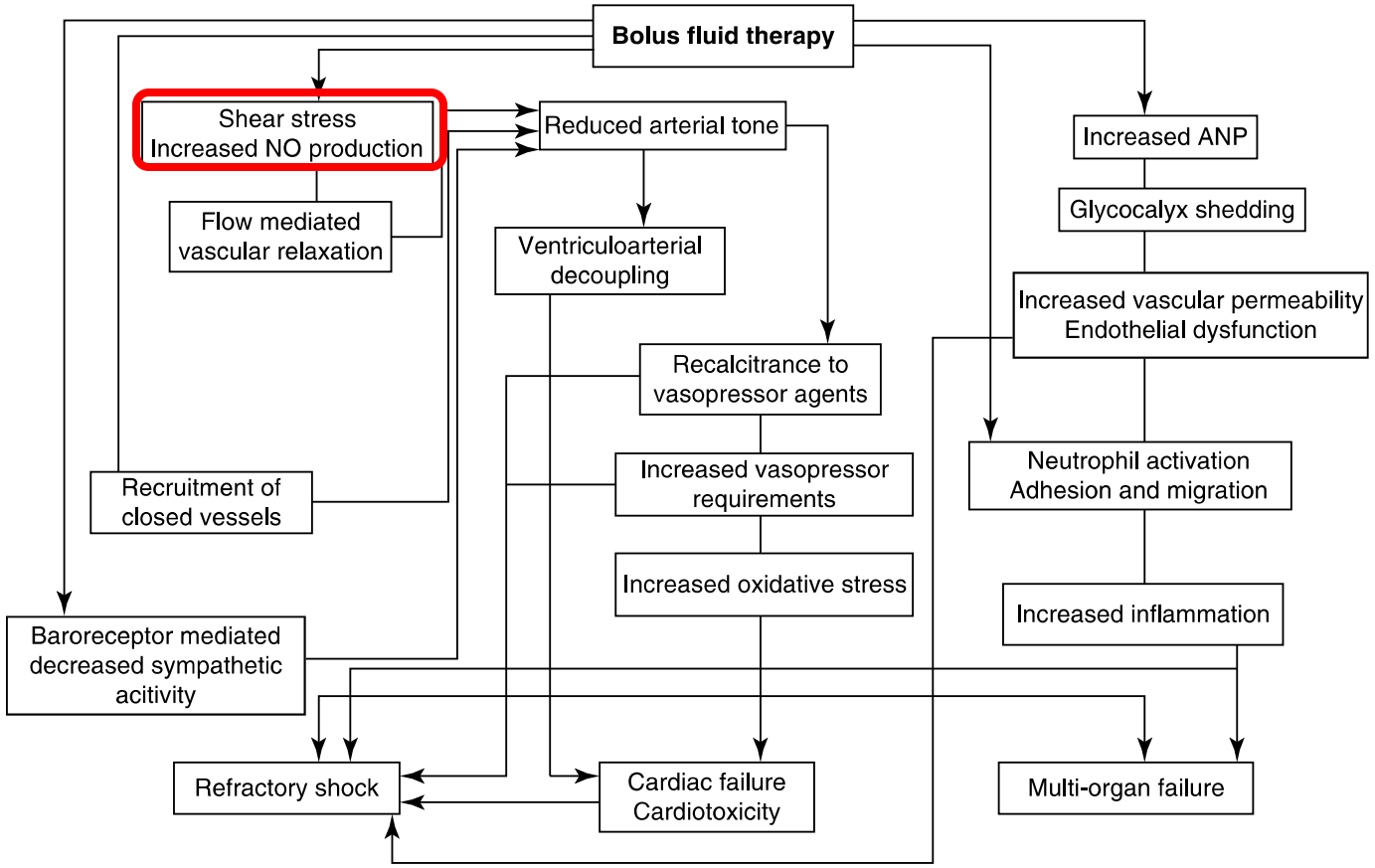
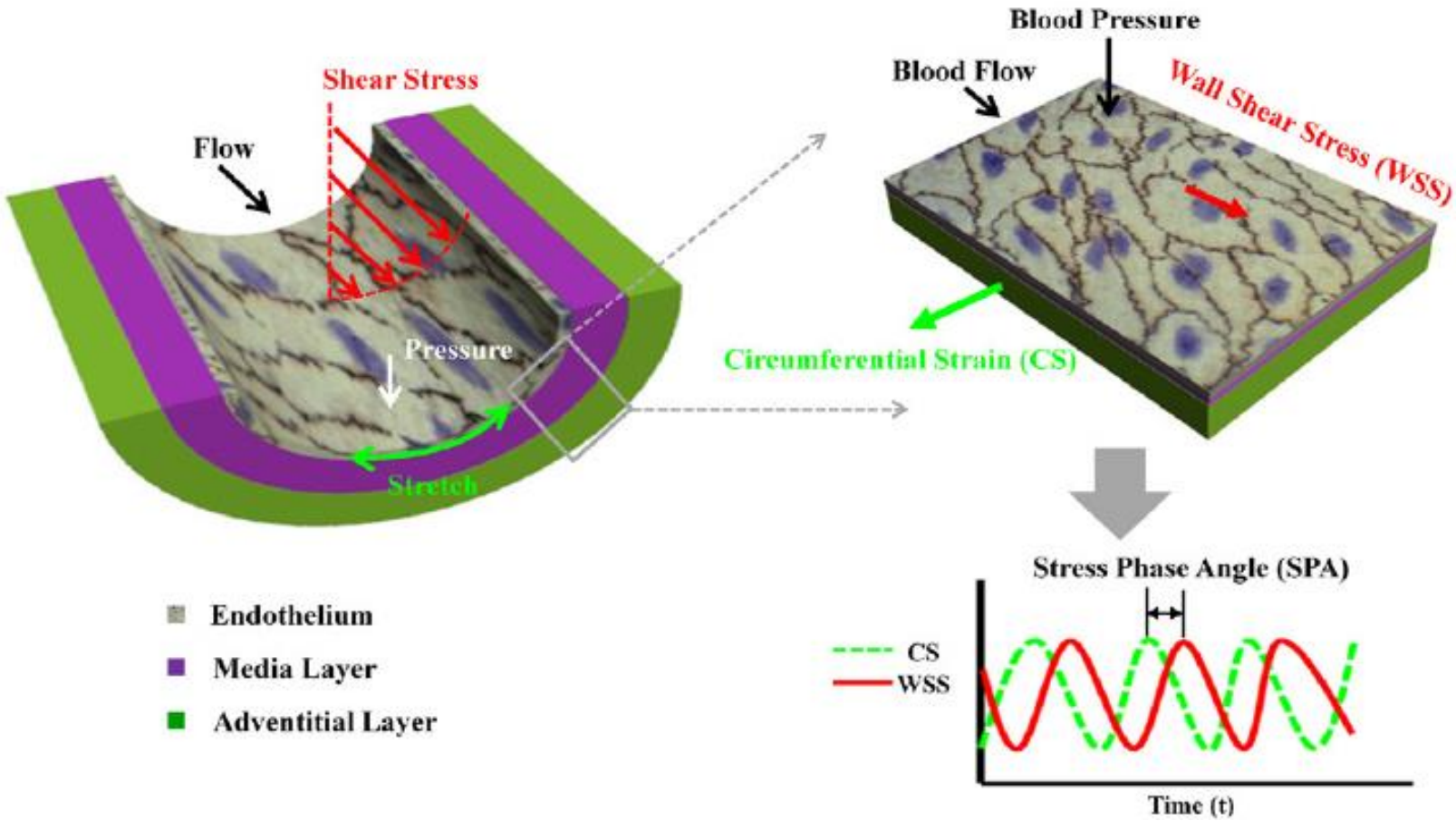


Increased blood flow/velocity >>> shear stress on the vessel wall >>> increased NO production & vessel dilation



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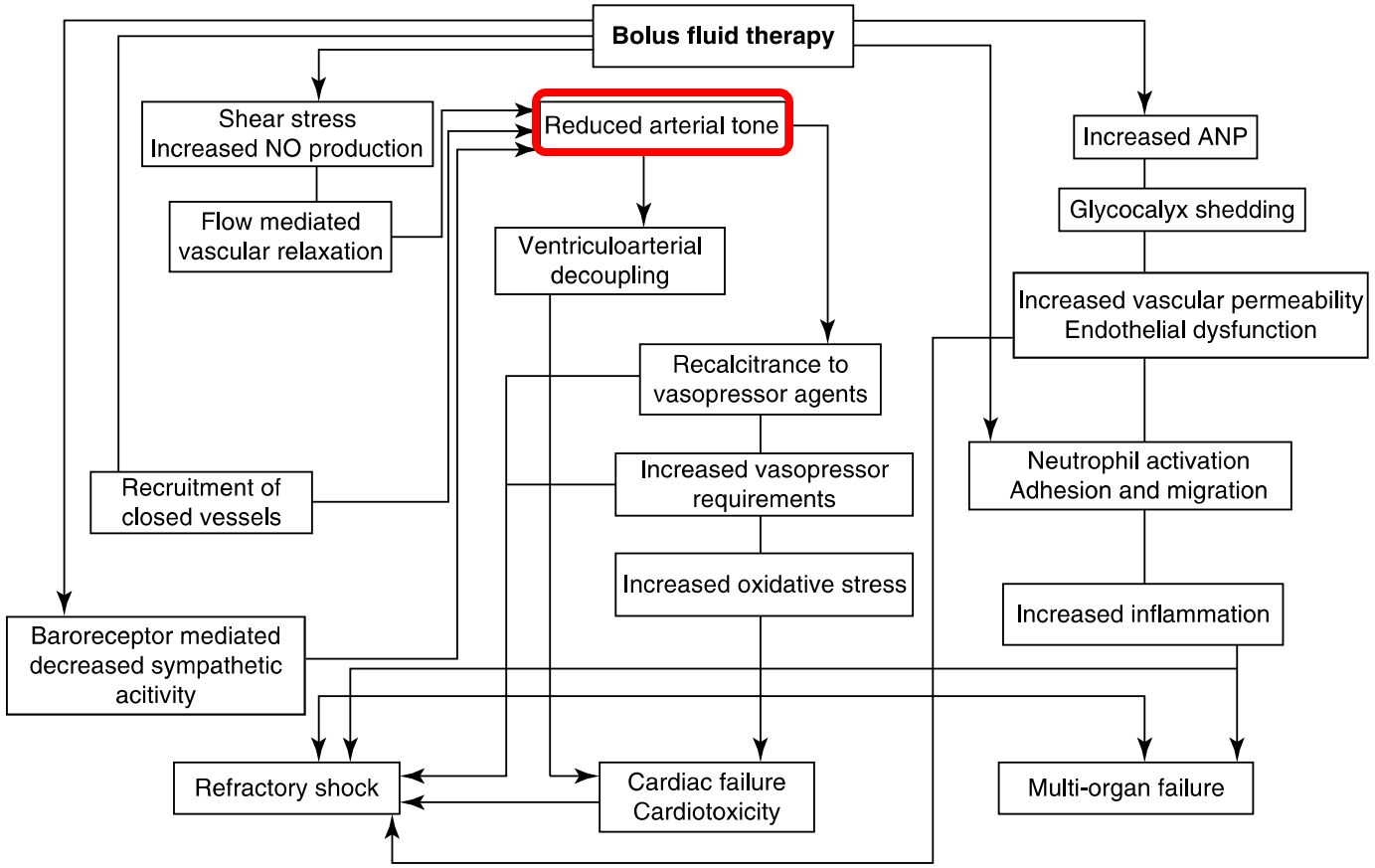

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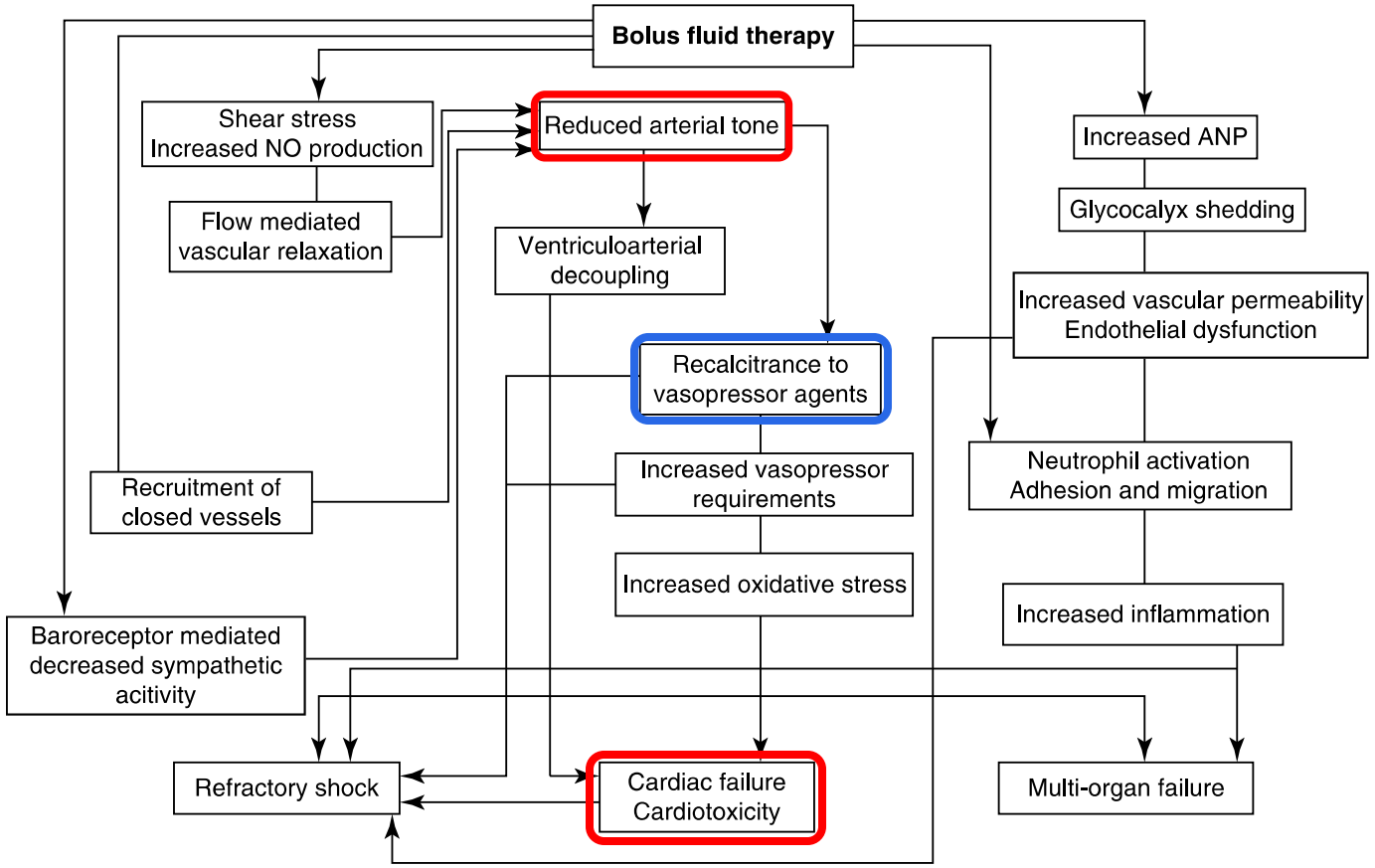
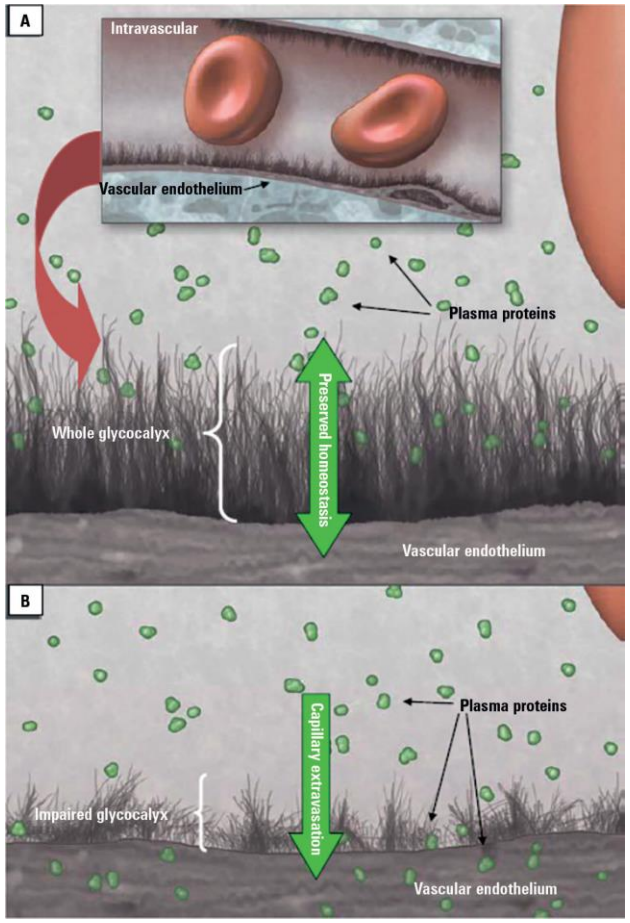
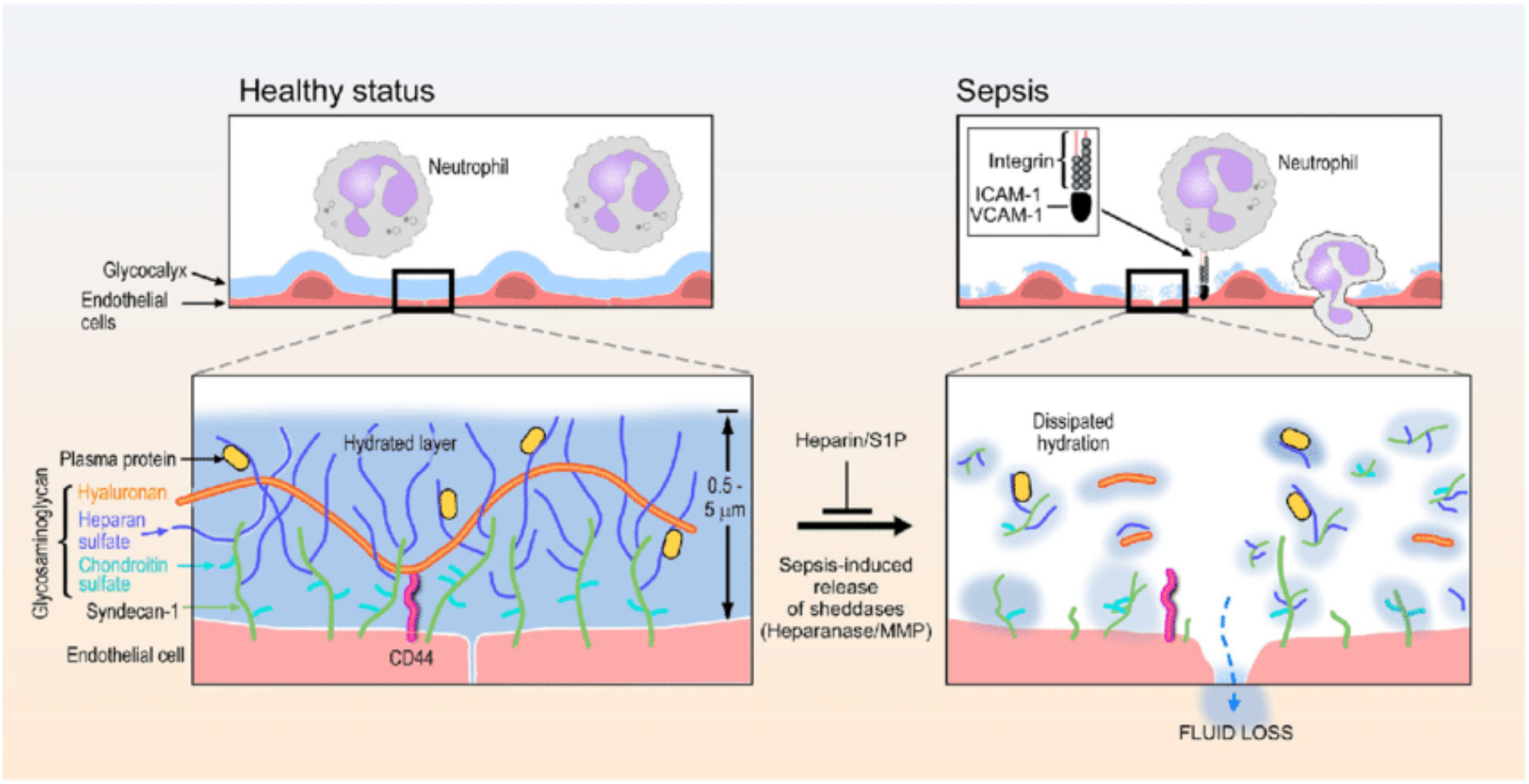


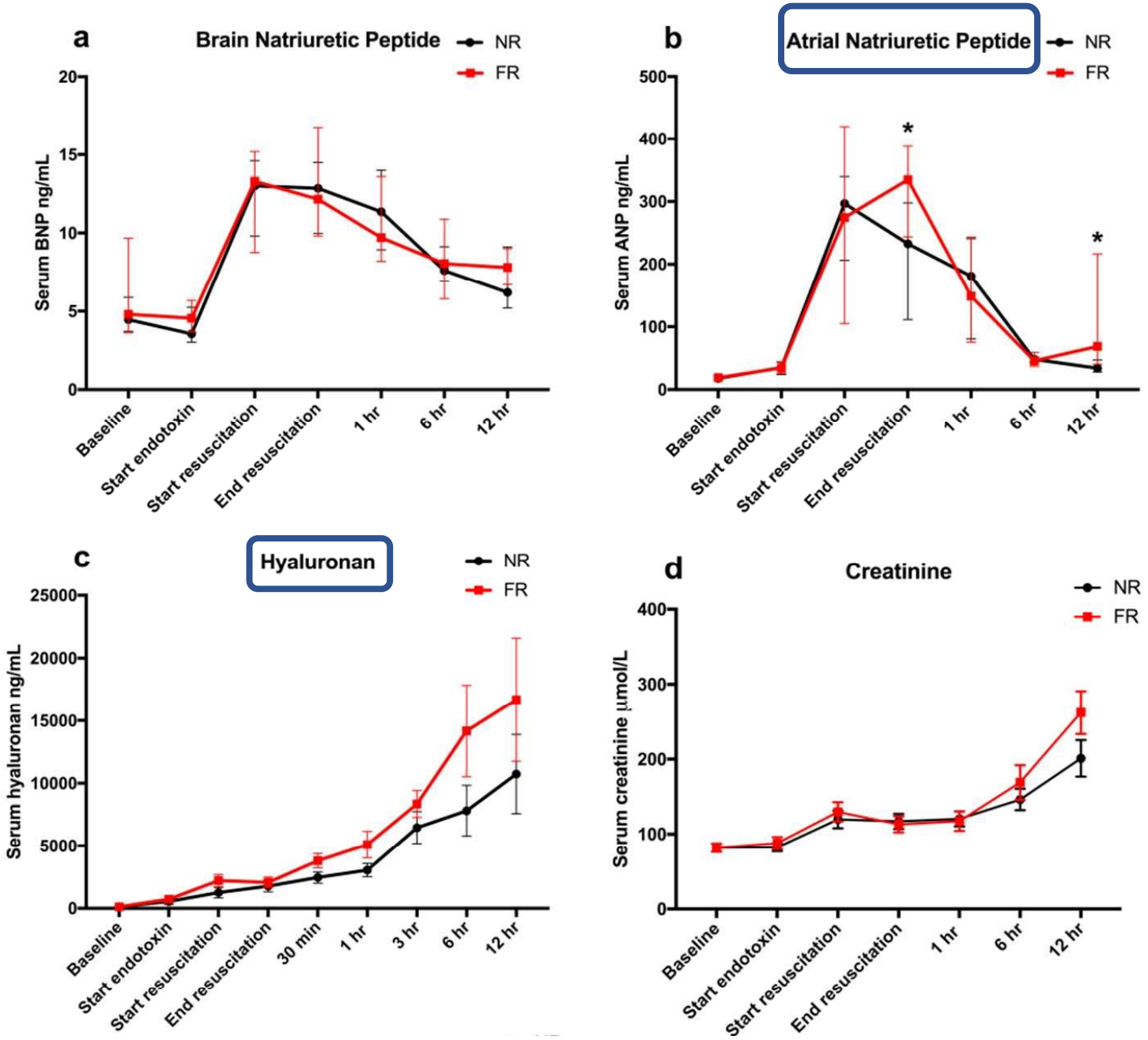
Glycocalyx

further damaged by the force of fluid boluses therapy



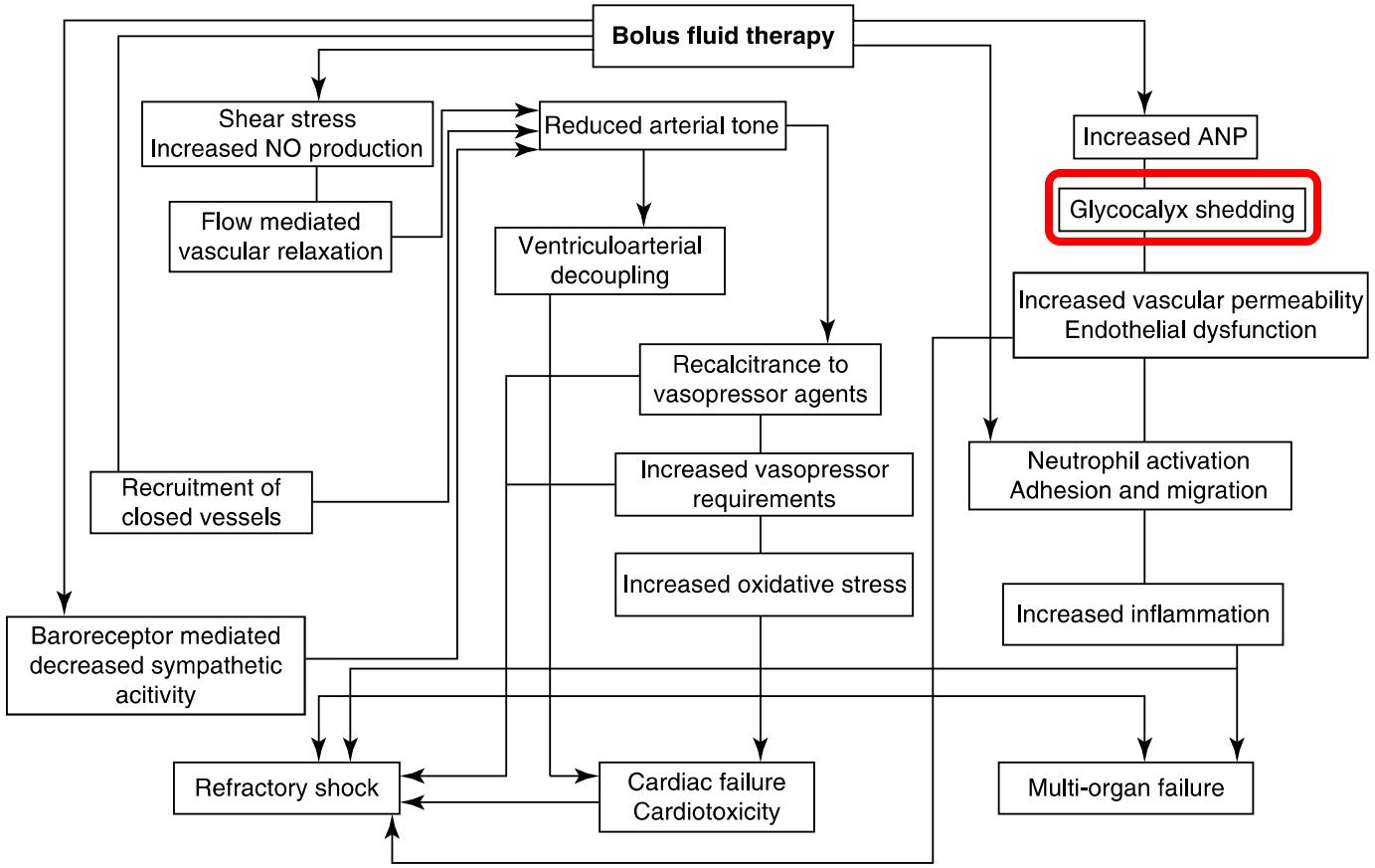


ACUTE hyper-volemia >>> ANP release >>> Glycox breakdown


a
Brain Natriuretic Peptide
NR
FR
Serum BNP ng/mL
20
15
10
5
0
Baseline
Start endotoxin
Start resuscitation
End resuscitation
1 hr
6 hr
12 hr
b
Atrial Natriuretic Peptide
NR
FR
Serum ANP ng/mL
500
400
300
200
100
0
*
*
Baseline
Start endotoxin
Start resuscitation
End resuscitation
1 hr
6 hr
12 hr
c
Hyaluronan
NR
FR
Serum hyaluronan ng/mL
25000
20000
15000
10000
5000
0
Baseline
Start endotoxin
Start resuscitation
End resuscitation
30 min
1 hr
3 hr
6 hr
12 hr
d
Creatinine
NR
FR
Serum creatinine µmol/L
400
300
200
100
0
Baseline
Start endotoxin
Start resuscitation
End resuscitation
1 hr
6 hr
12 hr


Don't be
FAST & FURIOUS
TAKEDOWN

Cardiovascular dysfunction following bolus fluid therapy for sepsis-induced tissue hypoperfusion



Fluids & dose-related pro-inflammatory properties

Clinical Investigations

Human neutrophil activation and increased adhesion by various resuscitation fluids

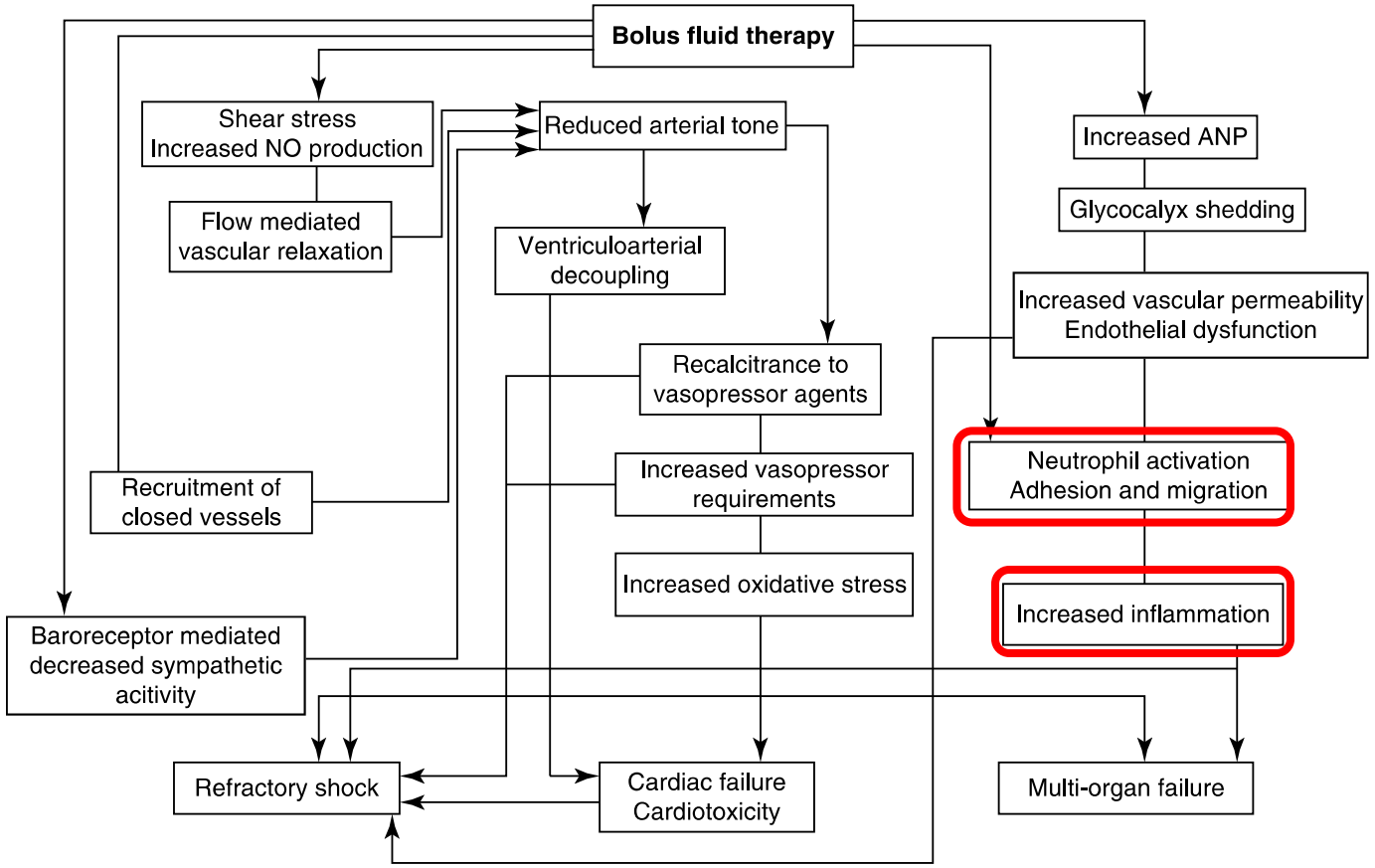
Peter Rhee, MD, MPH; Dennis Wang, MD; Paul Ruff, MD; Brenda Austin, BS; Solenn DeBraux, BS; Karen Wolcott, BS; David Burris, MD; Geoff Ling, MD, PhD; Leon Sun, MD, PhD

From the Department of Surgery, Uniformed Services University of the Health Sciences, Bethesda, MD.

This work was presented at the Society of Critical Care Medicine's 27th Educational and Scientific Symposium, San Antonio, TX, February 7, 1998.

isotonic fluid >>> genes implicated in leukocyte-endothelial interactions & capillary leakage

Cardiovascular dysfunction following bolus fluid therapy for sepsis-induced tissue hypoperfusion



However, despite early signs of cardiovascular improvement after bolus fluid therapy, cardiovascular dysfunction and outcomes in fact seem to worsen

On the other hand,…

- *there is no universally accepted definition of what bolus fluid therapy is, & how it should be administered*

what do you mean by saying "to give a bolus !"

Characteristics and expectations of fluid bolus therapy: a bi-national survey of acute care physicians

N. J. Glassford*, S. L. Jones†, J. Mårtensson‡, G. M. Eastwood§, M. Bailey**, A. M. Cross††, D. McD. Taylor‡‡, R. Bellomo§§

Summary

There is little consensus on the definition or optimal constituents of fluid bolus therapy (FBT), and there is uncertainty regarding its physiological effects. The aims of this study were to determine clinician-reported definitions of FBT and to explore the physiological responses clinicians expect from such FBT. In June and October 2014, intensive care and emergency physicians in Australia and New Zealand were asked to participate in an electronic questionnaire of the reported practice and expectations of FBT. Two hundred and fifty-one questionnaires were completed, 65.3% from intensivists. We identified the prototypical FBT given by intensivists is more than 250 ml of compound sodium lactate, saline or 4% albumin given in less than 30 minutes, while that given by emergency department physicians is a similar volume of saline delivered over a similar time frame. Intensive care and emergency physicians expected significantly different changes in mean arterial pressure (P=0.001) and heart rate (P=0.033) following FBT. Substantial variation was demonstrated in the magnitude of expected response within both specialties for each variable. Major variations exist in self-reported FBT practice, both within and between acute specialties, and wide variation can be demonstrated in the expected physiological responses to FBT. International explorations of practice and prospective quantification of the actual physiological response to FBT are warranted.

volume

	ICU specialists		ED physicians		*P*-value	
	n	%	n	%	Categorical comparison	Between specialties
CSL	*149*		*72*			
<250 ml	4	2.7%	4	5.6%	0.44	0.04
>250 ml	95	63.8%	34	47.2%	0.02	
>500 ml	44	29.5%	26	36.1%	0.36	
>1000 ml	6	4%	8	11.1%	0.07	
Plasma-Lyte	*135*		*39*			
<250 ml	5	3.7%	2	5.1%	0.65	<0.01
>250 ml	82	60.7%	13	33.3%	<0.01	
>500 ml	42	31.1%	18	46.2%	0.09	
>1000 ml	6	4.4%	6	15.4%	0.03	
0.9% saline	*146*		*81*			
<250 ml	4	2.7%	6	7.4%	0.17	<0.01
>250 ml	95	65.1%	36	44.4%	<0.01	
>500 ml	41	28.1%	28	34.6%	0.37	
>1000 ml	6	4.1%	11	13.6%	0.02	
Gelatin	*45*		*13*			
<250 ml	3	8.6%	2	15.4%	0.60	0.01
>250 ml	29	82.9%	6	46.2%	0.02	
>500 ml	3	8.6%	5	38.5%	0.03	
>1000 ml	0	0%	0	0%		
6% HES	*6*		*4*			
<250 ml	1	16.7%	1	25%		1
>250 ml	4	66.6%	2	50%		
>500 ml	1	16.7%	1	25%		
>1000 ml	0	0%	0	0%		
20% albumin	*55*		*11*			
<250 ml	53	96.36%	9	81.81%		0.13
>250 ml	2	3.64%	2	18.18%		
>500 ml	0	0%	0	0%		
>1000 ml	0	0%	0	0%		
4% albumin	*152*		*25*			
<250 ml	19	12.5%	4	16%	0.75	0.02
>250 ml	109	71.7%	11	44%	0.01	
>500 ml	22	14.5%	9	36%	0.02	
>1000 ml	2	1.3%	1	4%	0.37	

volume

	ICU specialists		ED physicians		*P*-value	
	n	%	n	%	Categorical comparison	Between specialties
CSL	*149*		*72*			
<250 ml	4	2.7%	4	5.6%	0.44	0.04
>250 ml	95	63.8%	34	47.2%	0.02	
>500 ml	44	29.5%	26	36.1%	0.36	
>1000 ml	6	4%	8	11.1%	0.07	
Plasma-Lyte	*135*		*39*			
<250 ml	5	3.7%	2	5.1%	0.65	<0.01
>250 ml	82	60.7%	13	33.3%	<0.01	
>500 ml	42	31.1%	18	46.2%	0.09	
>1000 ml	6	4.4%	6	15.4%	0.03	
0.9% saline	*146*		*81*			
<250 ml	4	2.7%	6	7.4%	0.17	<0.01
>250 ml	95	65.1%	36	44.4%	<0.01	
>500 ml	41	28.1%	28	34.6%	0.37	
>1000 ml	6	4.1%	11	13.6%	0.02	
Gelatin	*45*		*13*			
<250 ml	3	8.6%	2	15.4%	0.60	0.01
>250 ml	29	82.9%	6	46.2%	0.02	
>500 ml	3	8.6%	5	38.5%	0.03	
>1000 ml	0	0%	0	0%		
6% HES	*6*		*4*			
<250 ml	1	16.7%	1	25%		1
>250 ml	4	66.6%	2	50%		
>500 ml	1	16.7%	1	25%		
>1000 ml	0	0%	0	0%		
20% albumin	*55*		*11*			
<250 ml	53	96.36%	9	81.81%		0.13
>250 ml	2	3.64%	2	18.18%		
>500 ml	0	0%	0	0%		
>1000 ml	0	0%	0	0%		
4% albumin	*152*		*25*			
<250 ml	19	12.5%	4	16%	0.75	0.02
>250 ml	109	71.7%	11	44%	0.01	
>500 ml	22	14.5%	9	36%	0.02	
>1000 ml	2	1.3%	1	4%	0.37	

rate

	ICU		ED		*P*-value	
	n	%	n	%	Categorical comparison	Between specialties
CSL	145		72			
<10 minutes	72	49.7%	35	48.6%		0.97
<30 minutes	53	36.6%	30	41.7%		
<1 hour	19	13.1%	7	9.7%		
>1 hour	1	0.7%	0	0%		
Plasma-Lyte	*132*		*38*			
<10 minutes	65	49.2%	19	50%		0.98
<30 minutes	48	36.4%	15	39.5%		
<1 hour	17	12.9%	4	10.5%		
>1 hour	2	1.5%	0	0%		
0.9% saline	*142*		*80*			
<10 minutes	72	50.7%	40	50%		0.67
<30 minutes	49	34.5%	32	40%		
<1 hour	19	13.4%	8	10%		
>1 hour	2	1.4%	0	0%		
Gelatin	*35*		*13*			
<10 minutes	20	57.1%	5	38.5%		0.07
<30 minutes	10	28.6%	8	61.5%		
<1 hour	5	14.3%	0	0%		
>1 hour	0	0%	0	0%		
6% HES	*6*		*4*			
<10 minutes	6	100%	1	25%	0.03	0.03
<30 minutes	0	0%	3	75%	0.03	
<1 hour	0	0%	0	0%		
>1 hour	0	0%	0	0%		
20% albumin	*54*		*11*			
<10 minutes	15	27.8%	2	18.2%		0.67
<30 minutes	21	38.9%	6	54.6%		
<1 hour	12	22.2%	3	27.3%		
>1 hour	6	11.1%	0	0%		
4% albumin	*149*		*25*			
<10 minutes	68	45.6%	8	32%		0.51
<30 minutes	55	36.9%	13	52%		
<1 hour	24	16.1%	4	16%		
>1 hour	2	1.3%	0	0%		

volume	ICU specialists		ED physicians		*P*-value	
	n	%	n	%	Categorical comparison	Between specialties
CSL	*149*		*72*			
<250 ml	4	2.7%	4	5.6%	0.44	0.04
>250 ml	95	63.8%	34	47.2%	0.02	
>500 ml	44	29.5%	26	36.1%	0.36	
>1000 ml	6	4%	8	11.1%	0.07	
Plasma-Lyte	*135*		*39*			
<250 ml	5	3.7%	2	5.1%	0.65	<0.01
>250 ml	82	60.7%	13	33.3%	<0.01	
>500 ml	42	31.1%	18	46.2%	0.09	
>1000 ml	6	4.4%	6	15.4%	0.03	
0.9% saline	*146*		*81*			
<250 ml	4	2.7%	6	7.4%	0.17	<0.01
>250 ml	95	65.1%	36	44.4%	<0.01	
>500 ml	41	28.1%	28	34.6%	0.37	
>1000 ml	6	4.1%	11	13.6%	0.02	
Gelatin	*45*		*13*			
<250 ml	3	8.6%	2	15.4%	0.60	0.01
>250 ml	29	82.9%	6	46.2%	0.02	
>500 ml	3	8.6%	5	38.5%	0.03	
>1000 ml	0	0%	0	0%		
6% HES	*6*		*4*			
<250 ml	1	16.7%	1	25%		1
>250 ml	4	66.6%	2	50%		
>500 ml	1	16.7%	1	25%		
>1000 ml	0	0%	0	0%		
20% albumin	*55*		*11*			
<250 ml	53	96.36%	9	81.81%		0.13
>250 ml	2	3.64%	2	18.18%		
>500 ml	0	0%	0	0%		
>1000 ml	0	0%	0	0%		
4% albumin	*152*		*25*			
<250 ml	19	12.5%	4	16%	0.75	0.02
>250 ml	109	71.7%	11	44%	0.01	
>500 ml	22	14.5%	9	36%	0.02	
>1000 ml	2	1.3%	1	4%	0.37	

rate	ICU		ED		*P*-value	
	n	%	n	%	Categorical comparison	Between specialties
CSL	145		72			
<10 minutes	72	49.7%	35	48.6%		0.97
<30 minutes	53	36.6%	30	41.7%		
<1 hour	19	13.1%	7	9.7%		
>1 hour	1	0.7%	0	0%		
Plasma-Lyte	*132*		*38*			
<10 minutes	65	49.2%	19	50%		0.98
<30 minutes	48	36.4%	15	39.5%		
<1 hour	17	12.9%	4	10.5%		
>1 hour	2	1.5%	0	0%		
0.9% saline	*142*		*80*			
<10 minutes	72	50.7%	40	50%		0.67
<30 minutes	49	34.5%	32	40%		
<1 hour	19	13.4%	8	10%		
>1 hour	2	1.4%	0	0%		
Gelatin	*35*		*13*			
<10 minutes	20	57.1%	5	38.5%		0.07
<30 minutes	10	28.6%	8	61.5%		
<1 hour	5	14.3%	0	0%		
>1 hour	0	0%	0	0%		
6% HES	*6*		*4*			
<10 minutes	6	100%	1	25%	0.03	0.03
<30 minutes	0	0%	3	75%	0.03	
<1 hour	0	0%	0	0%		
>1 hour	0	0%	0	0%		
20% albumin	*54*		*11*			
<10 minutes	15	27.8%	2	18.2%		0.67
<30 minutes	21	38.9%	6	54.6%		
<1 hour	12	22.2%	3	27.3%		
>1 hour	6	11.1%	0	0%		
4% albumin	*149*		*25*			
<10 minutes	68	45.6%	8	32%		0.51
<30 minutes	55	36.9%	13	52%		
<1 hour	24	16.1%	4	16%		
>1 hour	2	1.3%	0	0%		

Min Hemodynamic Change for a +ve FB response	ICU specialists		ED physicians		*P*-value between specialties
	n	%	n	%	
Change in mean arterial pressure	*156*		*80*		
0–10 mmHg	106	68%	39	48.8%	<0.01
10–20 mmHg	50	32%	37	46.2%	
>20 mmHg	0	0%	4	5%	
Change in heart rate	156		80		
0–10/min	64	41%	20	25%	0.03
10–20/min	88	56.4%	56	70%	
>20/min	4	2.6%	4	5%	
Change in central venous pressure	*156*		*80*		
0–4 mmHg	110	70.5%	60	75%	0.63
4–8 mmHg	43	27.6%	18	22.5%	
>8 mmHg	3	1.9%	2	2.5%	
Change in urine output	*156*		*80*		
0–10 ml/h	33	21.2%	23	28.8%	0.21
10–20 ml/h	84	53.8%	44	55%	
>20 ml/h	39	25%	13	16.2%	
Change in central venous oxygen saturation	*156*		*80*		
0%–4%	56	35.9%	37	46.3%	0.14
4%–8%	88	56.4%	41	51.2%	
>8%	12	7.7%	2	2.5%	
Change in blood lactate concentration	*156*		*80*		
0–1 mmol/l	79	50.7%	39	48.8%	0.2
1–2 mmol/l	62	39.7%	38	47.5%	
>2.0 mmol/l	15	9.6%	3	3.7%	

Huge Variability between Physicians !

Bolus fluid therapy is a poorly defined intervention with considerable variability in preferred fluid choice, volume given and speed of delivery.

Nunes *et al. Annals of Intensive Care* 2014, **4**:25
http://www.annalsofintensivecare.com/content/4/1/25

Annals of Intensive Care
a SpringerOpen Journal

RESEARCH Open Access

Duration of hemodynamic effects of crystalloids in patients with circulatory shock after initial resuscitation

Thieme Souza Oliveira Nunes, Renata Teixeira Ladeira, Antônio Tonete Bafi, Luciano Cesar Pontes de Azevedo, Flavia Ribeiro Machado and Flávio Geraldo Rezende Freitas*

The duration of the volume effect was found to be short *cardiac output and blood pressure returning to baseline levels 60 min after the fluid bolus.*

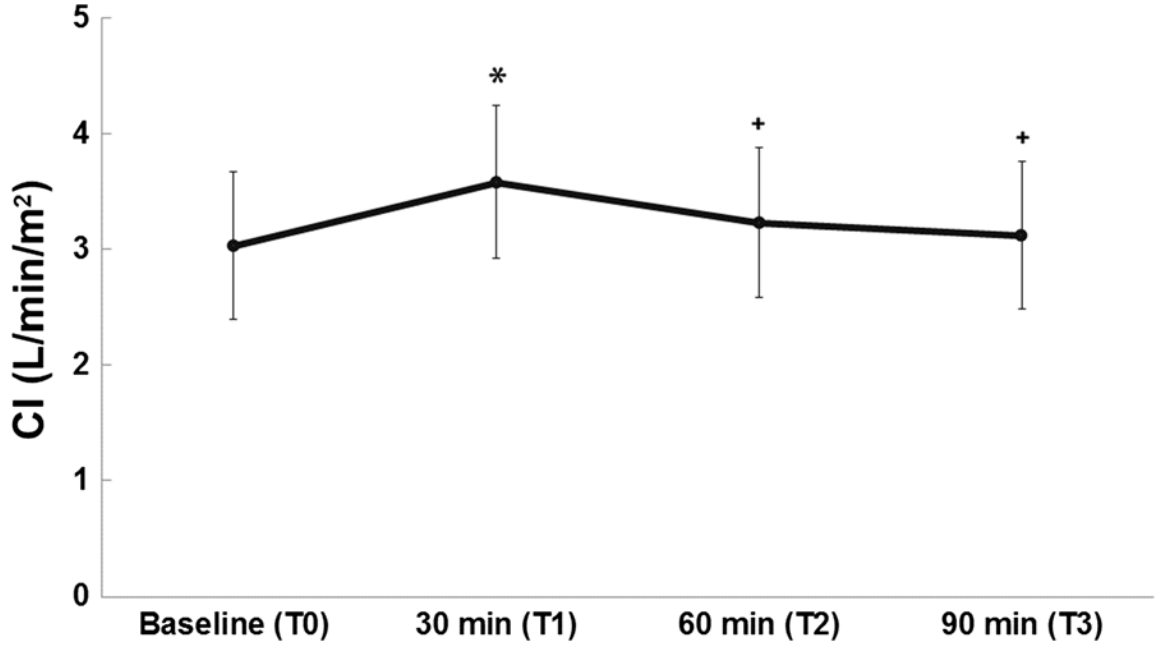
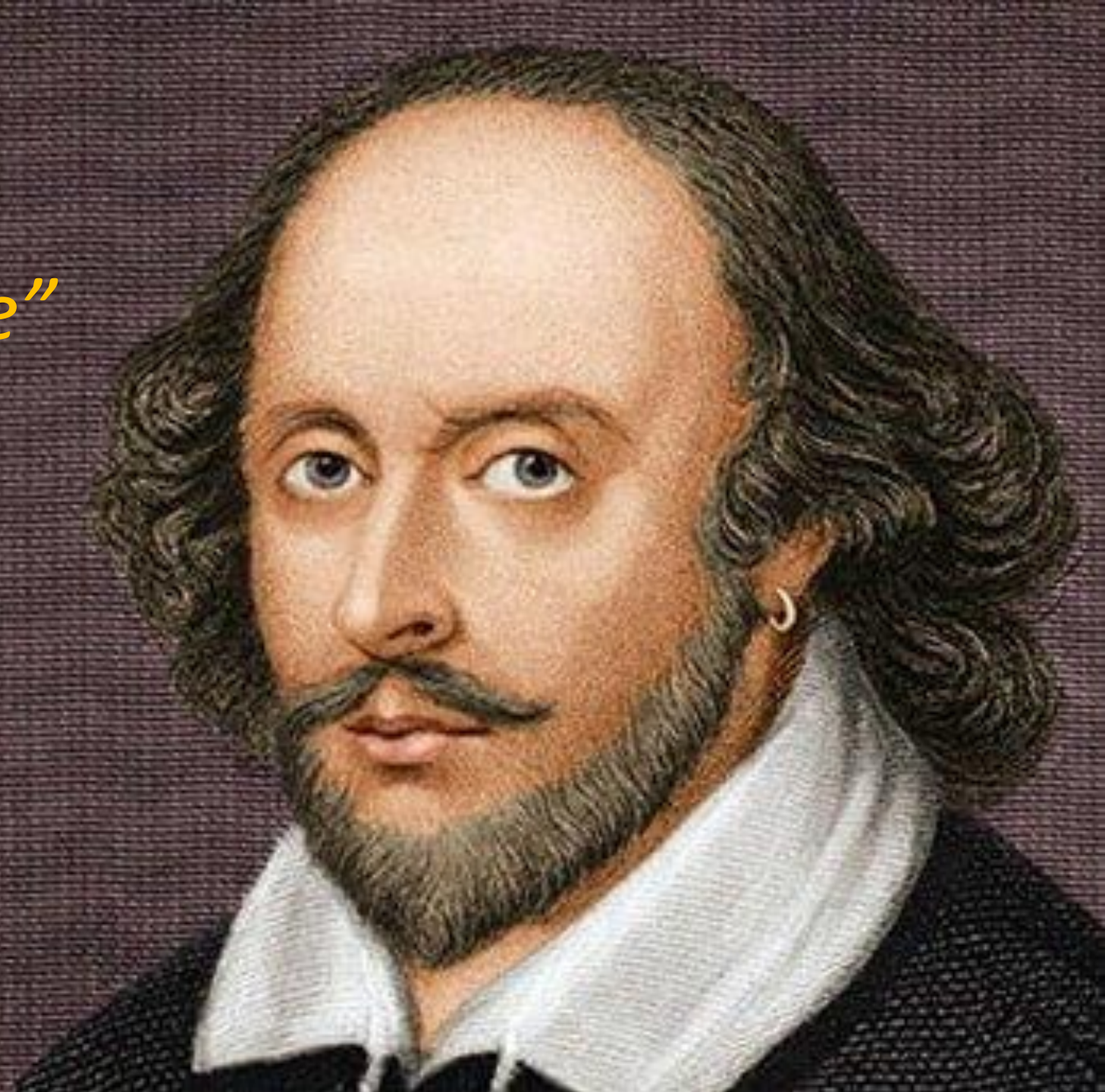


Figure 2 Cardiac index. CI, cardiac index. Baseline, 3.03 ± 0.64; T1, 3.58 ± 0.66; T2, 3.23 ± 0.65; T3, 3.12 ± 0.64. *$p < 0.05$ versus baseline, $^{+}p < 0.05$ versus T1.

FBT in sepsis

“to give or not to give”

That is the question

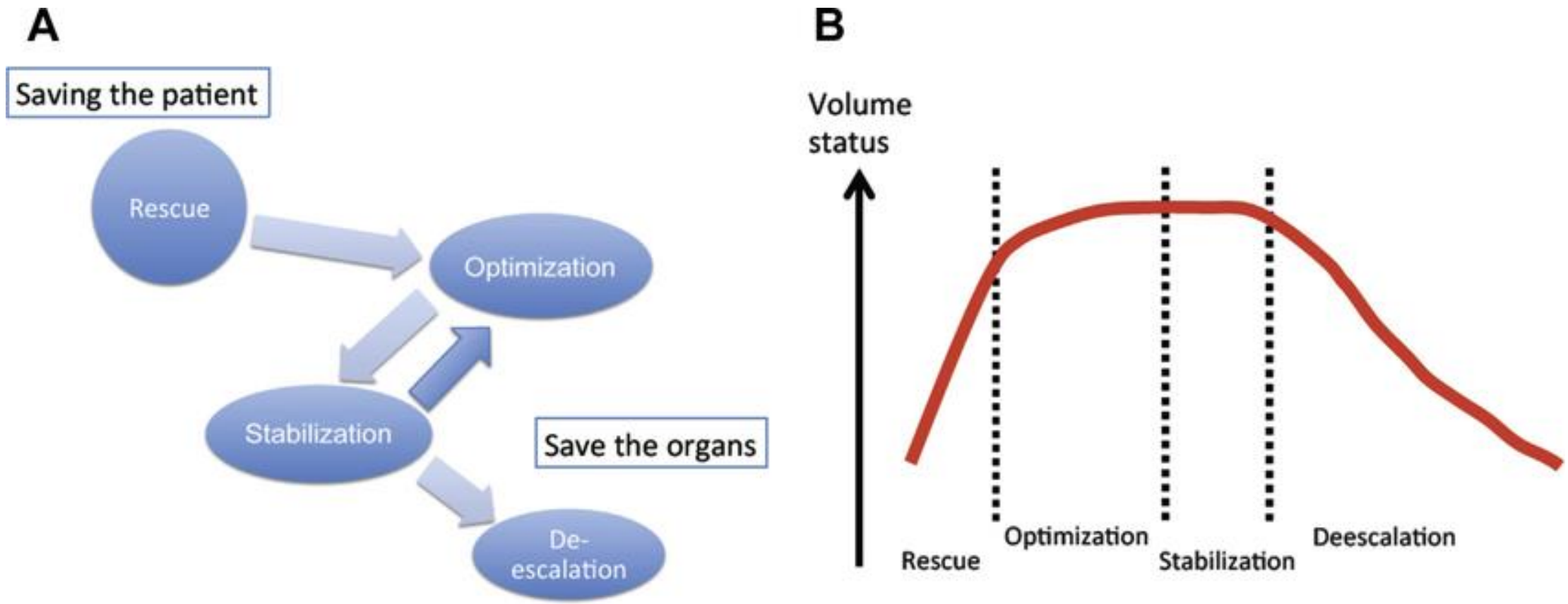


Harm Caused by Fluid Overload

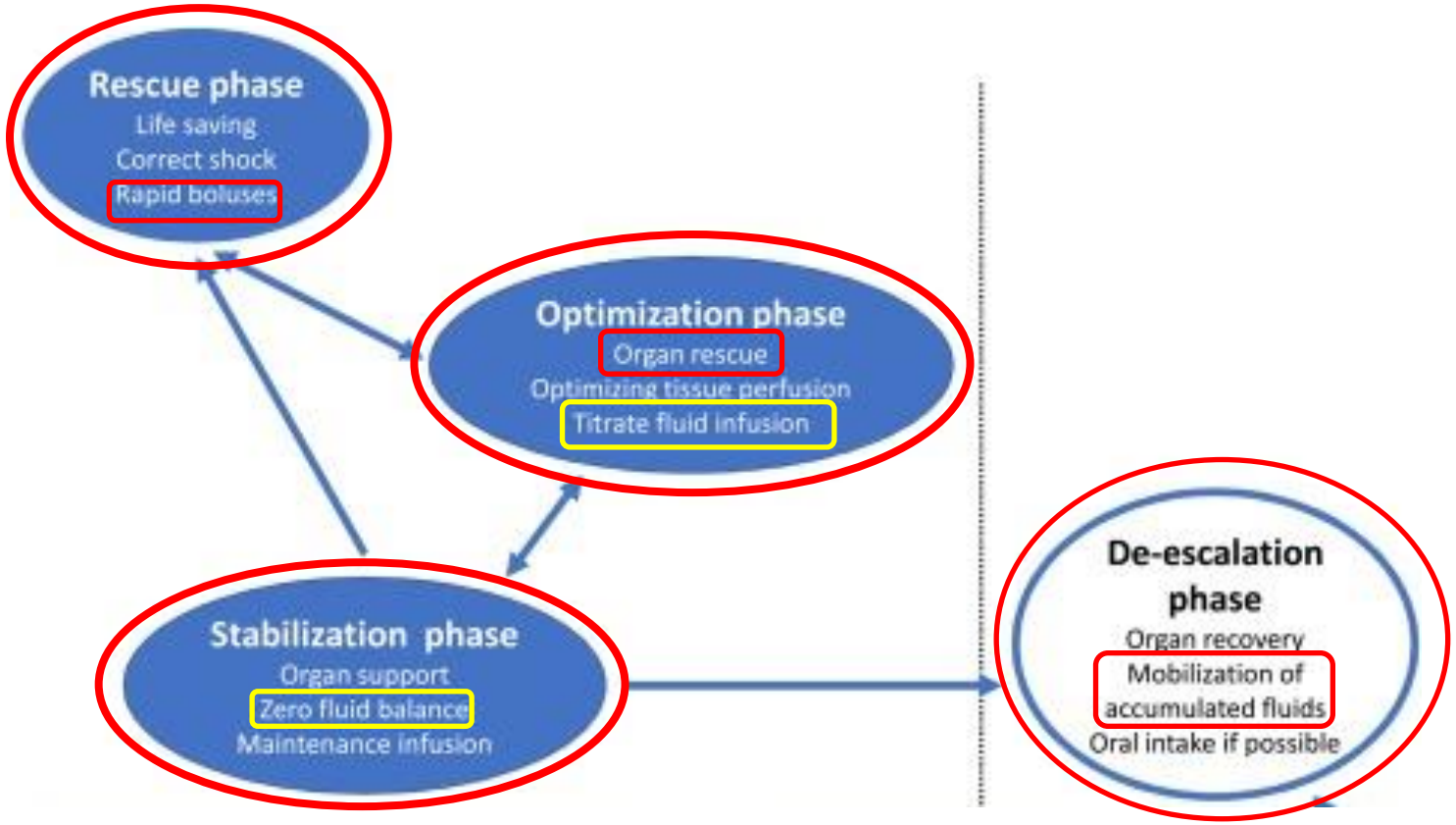
Fluid therapy in sepsis
is dynamic

The pt is not the same “all the way trough their medical care”

different strategies in different situation



The ROSE Concept



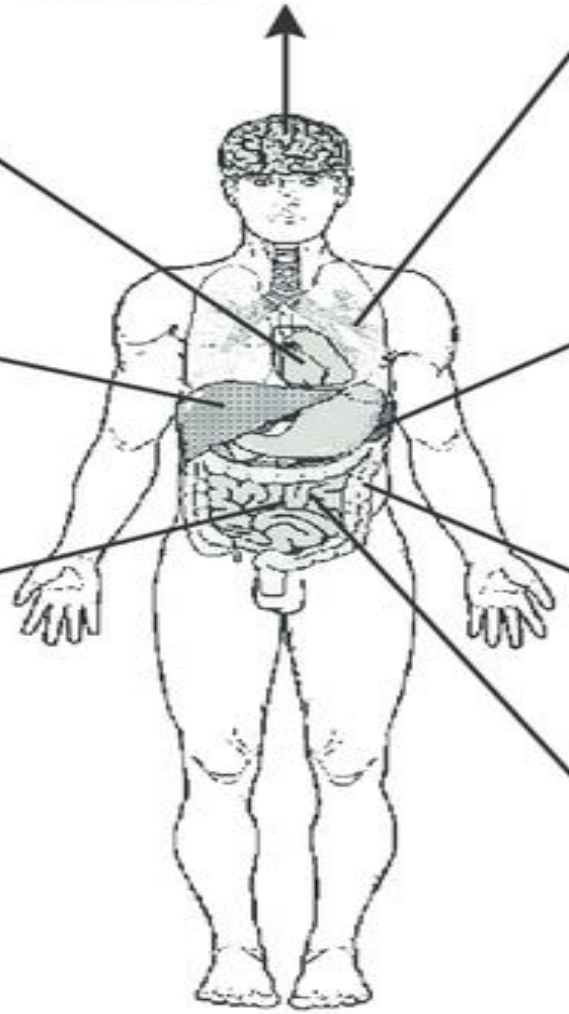
Too much water is not only bad for “Venice” but also for “Humans”

CARDIOVASCULAR SYSTEM*
Myocardial oedema ↑
Conduction disturbance
Impaired contractility
Diastolic dysfunction
CVP ↑ and PAOP ↑
Venous return ↓
SV ↓ and CO ↓
Myocardial depression
GEF ↓ GEDVI ↑
Pericardial effusion ↑
CARS ↑

CENTRAL NERVOUS SYSTEM
Cerebral oedema ↑
Impaired cognition ↑
Delirium ↑
Intracranial pressure ↑
Cerebral perfusion pressure ↓
Intra-ocular pressure ↑
ICH, ICS, OCS

RESPIRATORY SYSTEM
Pulmonary oedema ↑
Pleural effusion ↑
Altered pulmonary and
chest wall elastance (cfr IAP ↑)
Impaired gas exchange:
Hypercarbia ↑
PaO_2 ↓ and PaO_2/FiO_2 ↓
Extravascular lung water ↗
Lung volumes ↓ (cfr IAP ↑)
Prolonged ventilation ↑
Difficult weaning ↑
Work of breathing ↑

HEPATIC SYSTEM
Hepatic congestion ↑
Impaired synthetic function
Cholestasis ↑
Impaired Cytochrome P 450 activity
Hepatic compartment syndrome



RENAL SYSTEM
Renal interstitial oedema
Renal venous pressure ↑
Renal blood flow ↓
Interstitial pressure ↑
Glomerular filtration rate ↓
Uremia ↑
Renal vascular resistance ↑
Salt retention ↑
Water retention ↑
Renal compartment syndrome

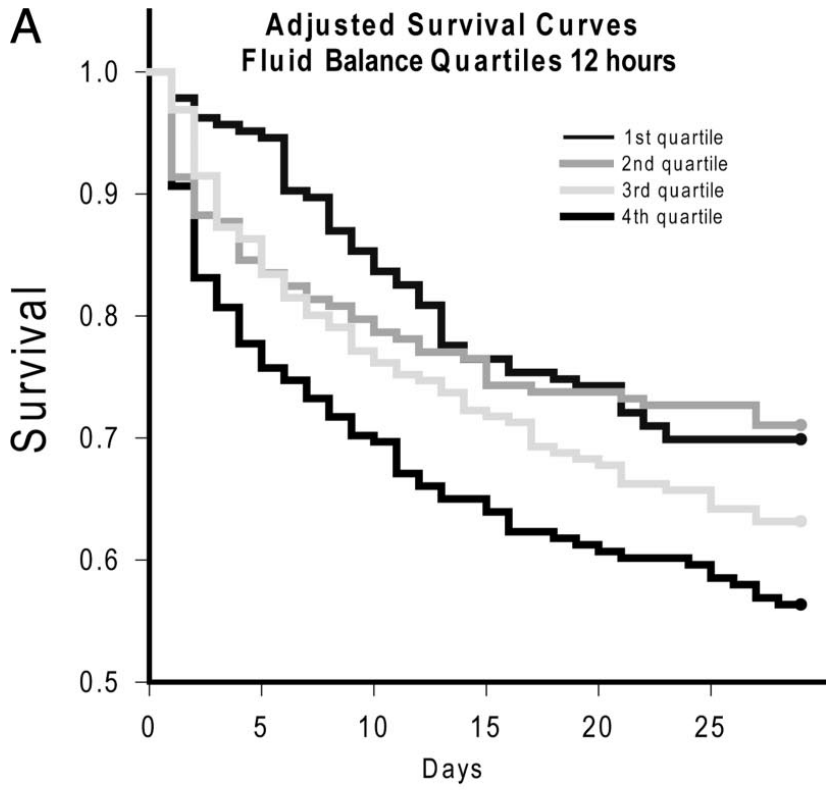
GASTRO-INTESTINAL SYSTEM
Ascites formation ↑
Gut oedema ↑
Malabsorption ↑
Ileus ↑
Abdominal perfusion pressure ↓
Bowel contractility ↓
IAP ↑ and APP (=MAP-IAP) ↓
IAH and ACS ↑
Successful enteral feeding ↓
Intestinal permeability ↑
Bacterial translocation ↑
Splanchnic microcirculatory flow ↓
ICG-PDR ↓, pHi ↓

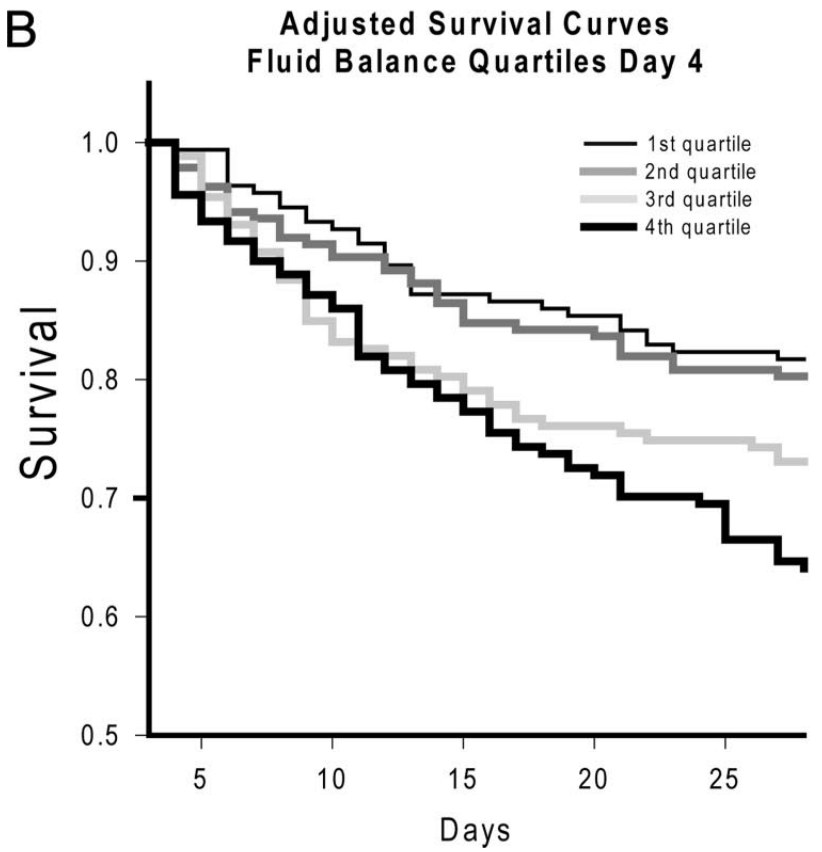
ABDOMINAL WALL
Tissue oedema ↑
Impaired lymphatic drainage ↑
Microcirculatory derangements ↑
Poor wound healing ↑
Wound infection ↑
Pressure ulcers ↑
Skin oedema ↑
Abdominal compliance ↓

ENDOCRINE SYSTEM
Release pro-inflammatory cytokines ↑
(IL-1b, TNF-α, IL-6)

Fluid resuscitation in septic shock: A positive fluid balance and elevated central venous pressure are associated with increased mortality*

John H. Boyd, MD, FRCP(C); Jason Forbes, MD; Taka-aki Nakada, MD, PhD; Keith R. Walley, MD, FRCP(C); James A. Russell, MD, FRCP(C)





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Fluid Resuscitation in Septic Shock: The Effect of Increasing Fluid Balance on Mortality

Farid Sadaka, MD[1], Mayrol Juarez, MD[1], Soophia Naydenov, MD[1], and Jacklyn O'Brien, RN[1]

Abstract

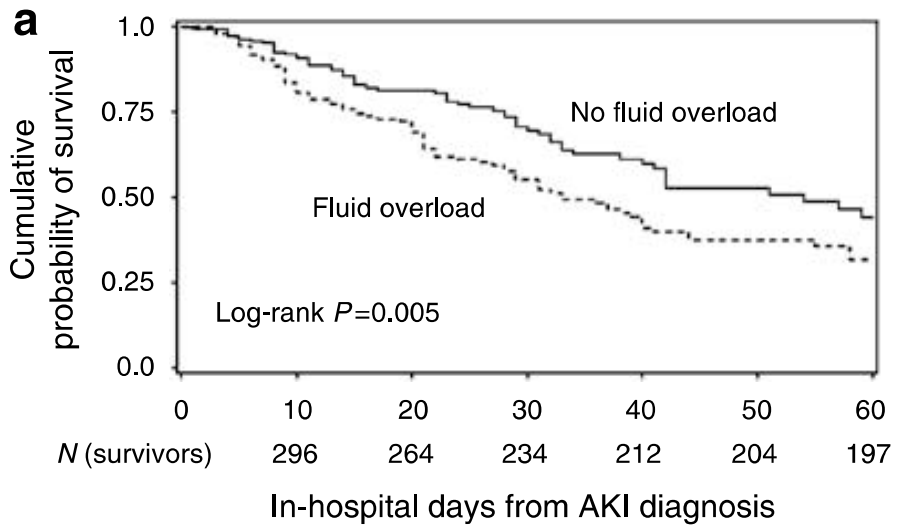
Purpose: To determine whether progressively increasing fluid balance after initial fluid resuscitation for septic shock is associated with increased mortality. **Methods:** A retrospective review of the use of intravenous fluids in patients with septic shock in a large university affiliated hospital with 56 medical–surgical intensive care unit beds. We analyzed the data of 350 patients with septic shock who were managed according to the Surviving Sepsis Campaign guidelines. Based on net fluid balance at 24 hours, we examined the results of increase in positive fluid balance on the risk of in-hospital mortality. Patients were divided into 4 groups based on the amount of fluid balance by 24 hours, based on 6-L aliquots. **Results:** At 24 hours, the average fluid balance was +6.5 L. After correcting for age and sequential organ failure assessment score, a more positive fluid balance at 24 hours significantly increased the risk of in-hospital mortality. Using Cox proportional hazard analysis, excess 12-, 18-, and 24-L positive fluid balance had higher risk of mortality than those patients with a neutral to positive 6-L fluid balance (reference group). Adjusted hazard ratios, 1.519 (95% confidence interval [CI], 1.353-1.685), 1.740 (95% CI, 1.467-2.013), and 1.620 (95% CI, 1.197-2.043), respectively, $P < .05$. **Conclusion**: In patients with septic shock resuscitated according to current guidelines, a more positive fluid balance at 24 hours is associated with an increase in the risk of mortality. Optimal survival occurred at neutral fluid balance and up to 6-L positive fluid balance at 24 hours after the development of septic shock.

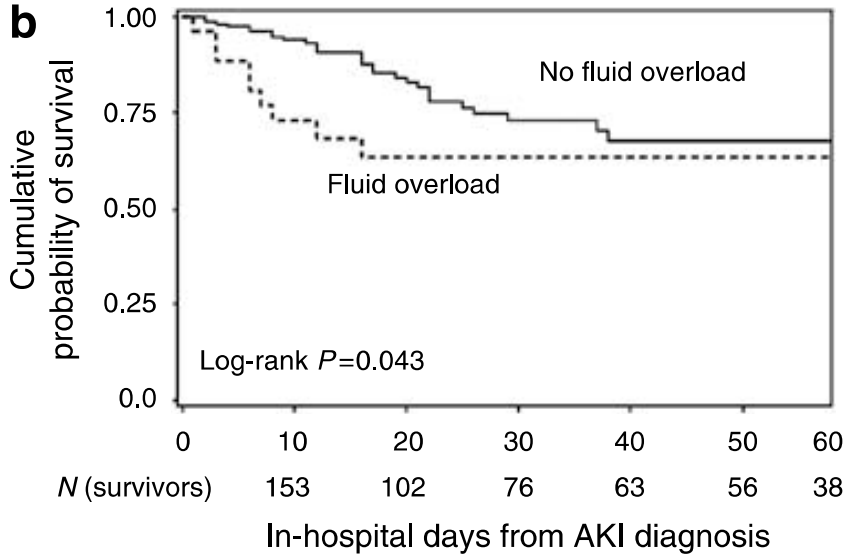
original article

http://www.kidney-international.org

Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury

Josée Bouchard[1], Sharon B. Soroko[1], Glenn M. Chertow[2], Jonathan Himmelfarb[3], T. Alp Ikizler[4], Emil P. Paganini[5] and Ravindra L. Mehta[1], Program to Improve Care in Acute Renal Disease (PICARD) Study Group

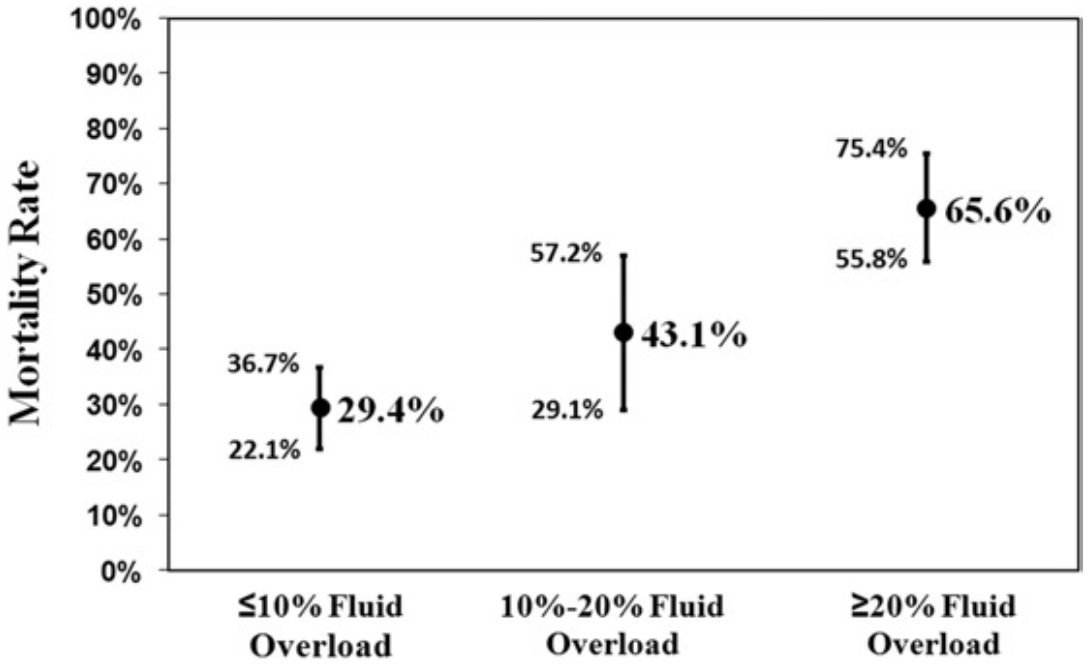




percent by percent

Fluid Overload and Mortality in Children Receiving Continuous Renal Replacement Therapy: The Prospective Pediatric Continuous Renal Replacement Therapy Registry

Scott M. Sutherland, MD,[1] Michael Zappitelli, MD, MSc,[2] Steven R. Alexander, MD,[1] Annabelle N. Chua, MD,[3] Patrick D. Brophy, MD,[4] Timothy E. Bunchman, MD,[5] Richard Hackbarth, MD,[5] Michael J.G. Somers, MD,[6] Michelle Baum, MD,[6] Jordan M. Symons, MD,[7] Francisco X. Flores, MD,[8] Mark Benfield, MD,[9] David Askenazi, MD,[9] Deepa Chand, MD,[10] James D. Fortenberry, MD,[11] John D. Mahan, MD,[12] Kevin McBryde, MD,[13] Douglas Blowey, MD,[14] and Stuart L. Goldstein, MD[3]



When resuscitating a septic pt:
A conservative fluid strategy may improve patient outcomes

The FACCT trial

The NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

Table 3. Main Outcome Variables.*

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
Organ-failure–free days†‡			
Days 1 to 7			
Cardiovascular failure	3.9±0.1	4.2±0.1	0.04
CNS failure	3.4±0.2	2.9±0.2	0.02
Renal failure	5.5±0.1	5.6±0.1	0.45
Hepatic failure	5.7±0.1	5.5±0.1	0.12
Coagulation abnormalities	5.6±0.1	5.4±0.1	0.23
Days 1 to 28			
Cardiovascular failure	19.0±0.5	19.1±0.4	0.85
CNS failure	18.8±0.5	17.2±0.5	0.03
Renal failure	21.5±0.5	21.2±0.5	0.59
Hepatic failure	22.0±0.4	21.2±0.5	0.18
Coagulation abnormalities	22.0±0.4	21.5±0.4	0.37
Dialysis to day 60			
Patients (%)	10	14	0.06
Days	11.0±1.7	10.9±1.4	0.96

SEVEN-DAY PROFILE PUBLICATION

Restricting volumes of resuscitation fluid in adults with septic shock after initial management: the CLASSIC randomised, parallel-group, multicentre feasibility trial

Peter B. Hjortrup[1], Nicolai Haase[1], Helle Bundgaard[2], Simon L. Thomsen[3], Robert Winding[4], Ville Pettilä[5], Anne Aaen[6], David Lodahl[7], Rasmus E. Berthelsen[8], Henrik Christensen[9], Martin B. Madsen[1], Per Winkel[10], Jørn Wetterslev[10], Anders Perner[1,11*], The CLASSIC Trial Group, The Scandinavian Critical Care Trials Group

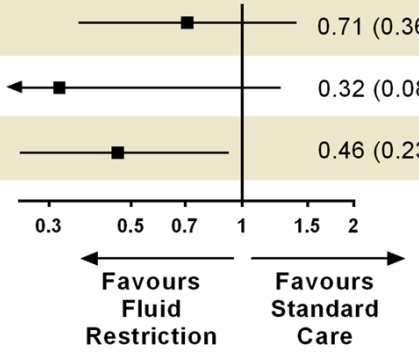
restricting, resuscitation fluid

vs

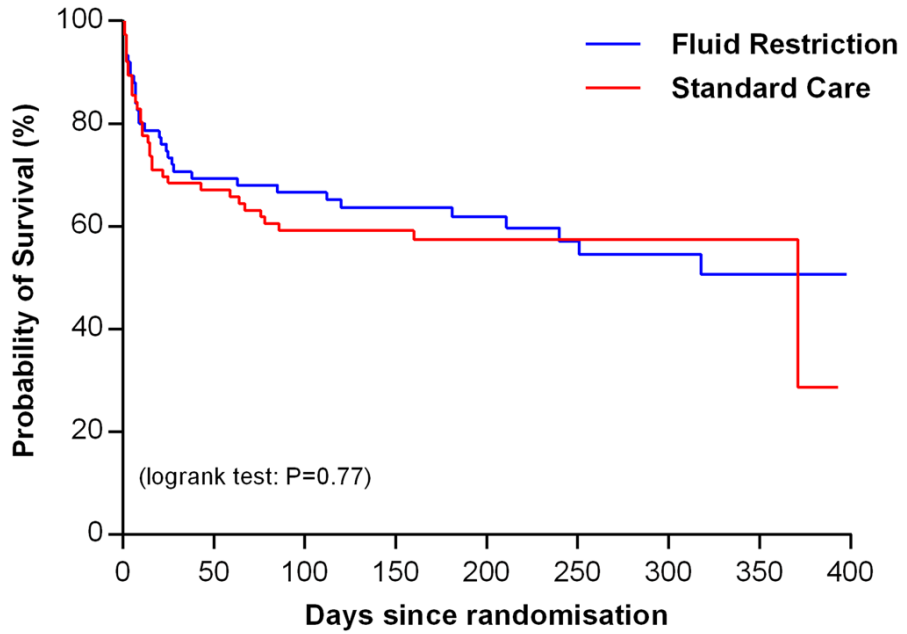
a standard care protocol in adult

a Odds ratios of exploratory outcomes

	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

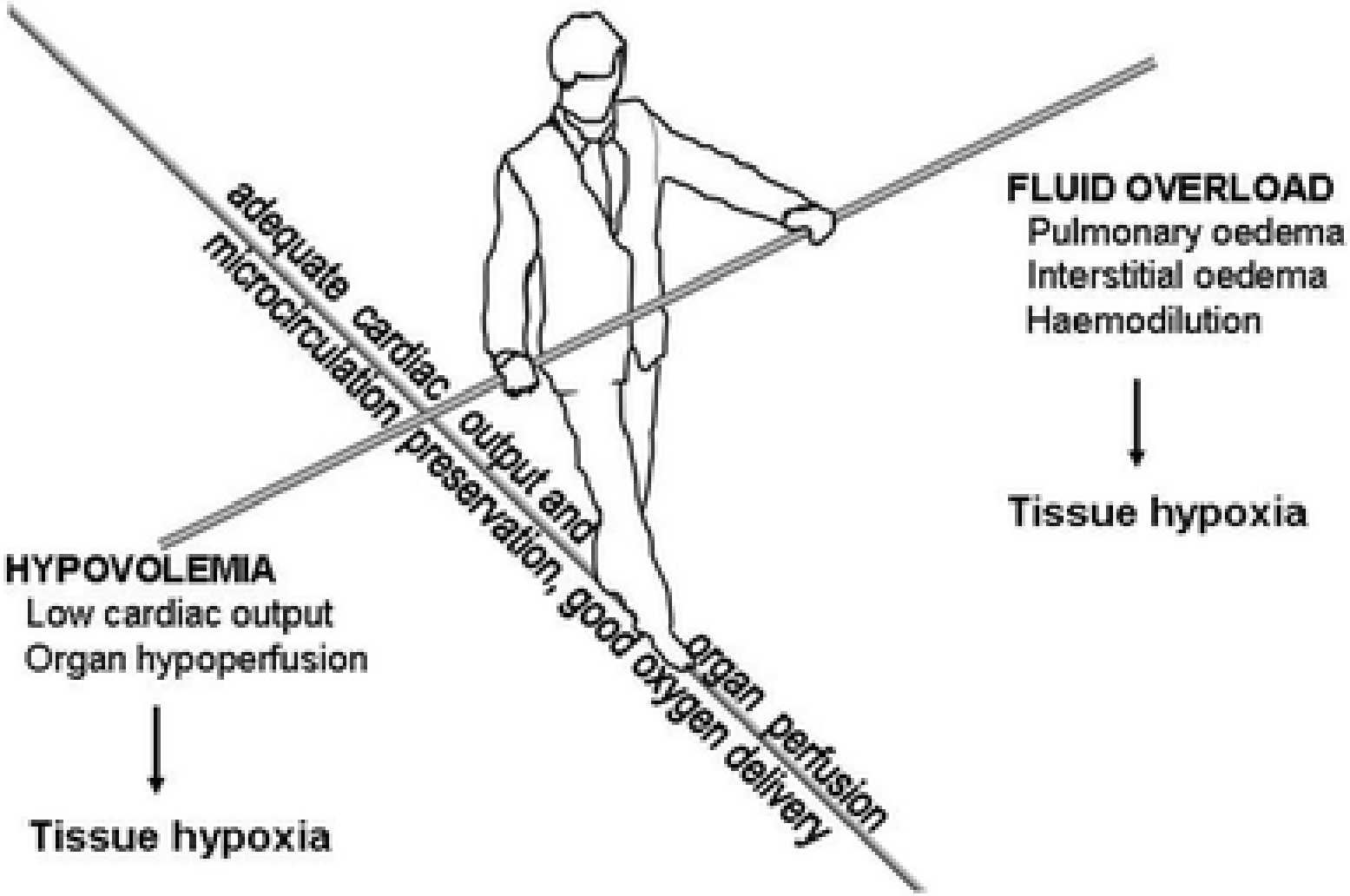


b Time to death

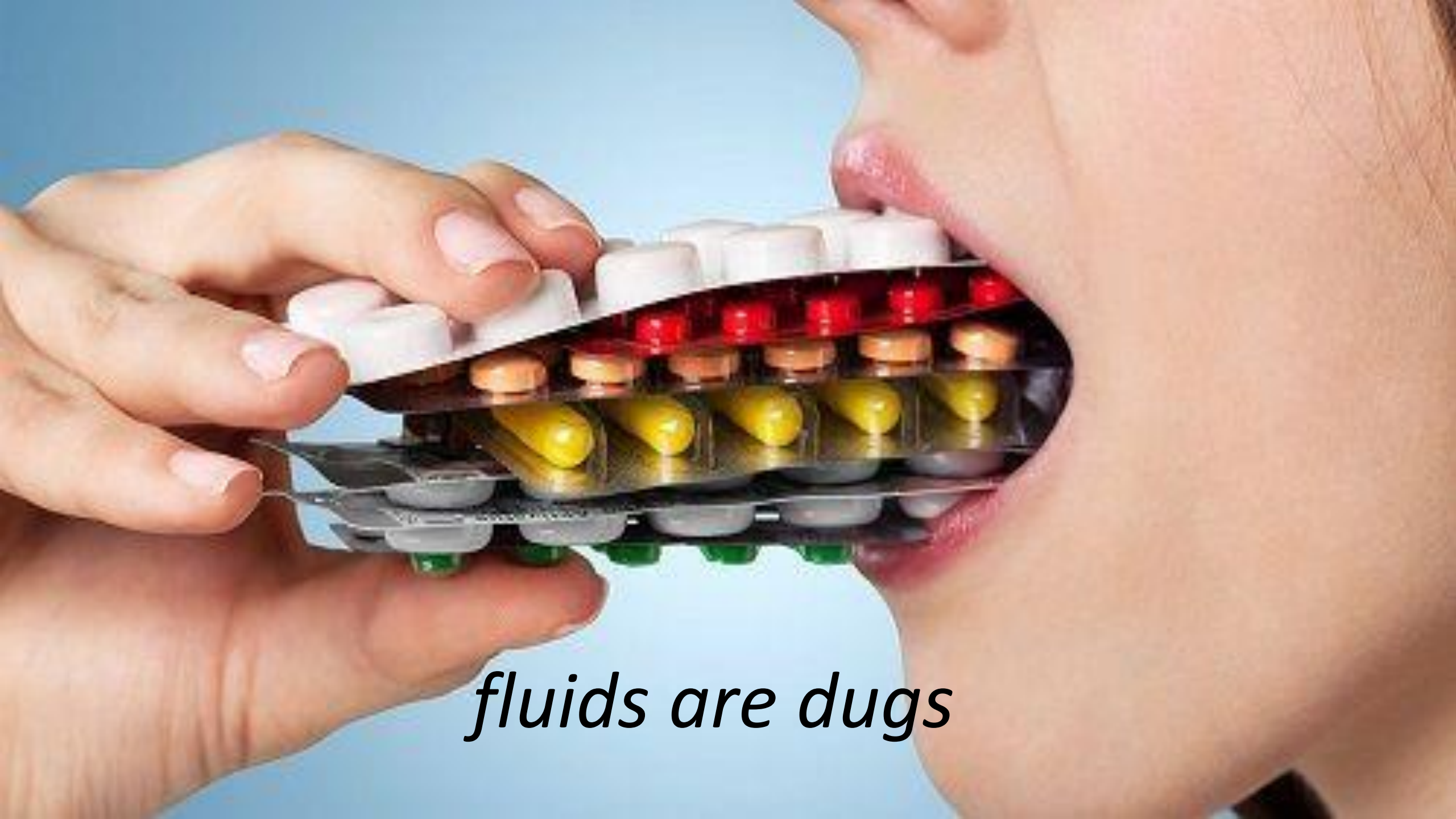


No. at risk				
Fluid Restriction	75	47	32	15
Standard Care	76	42	24	11

Optimizing fluid therapy



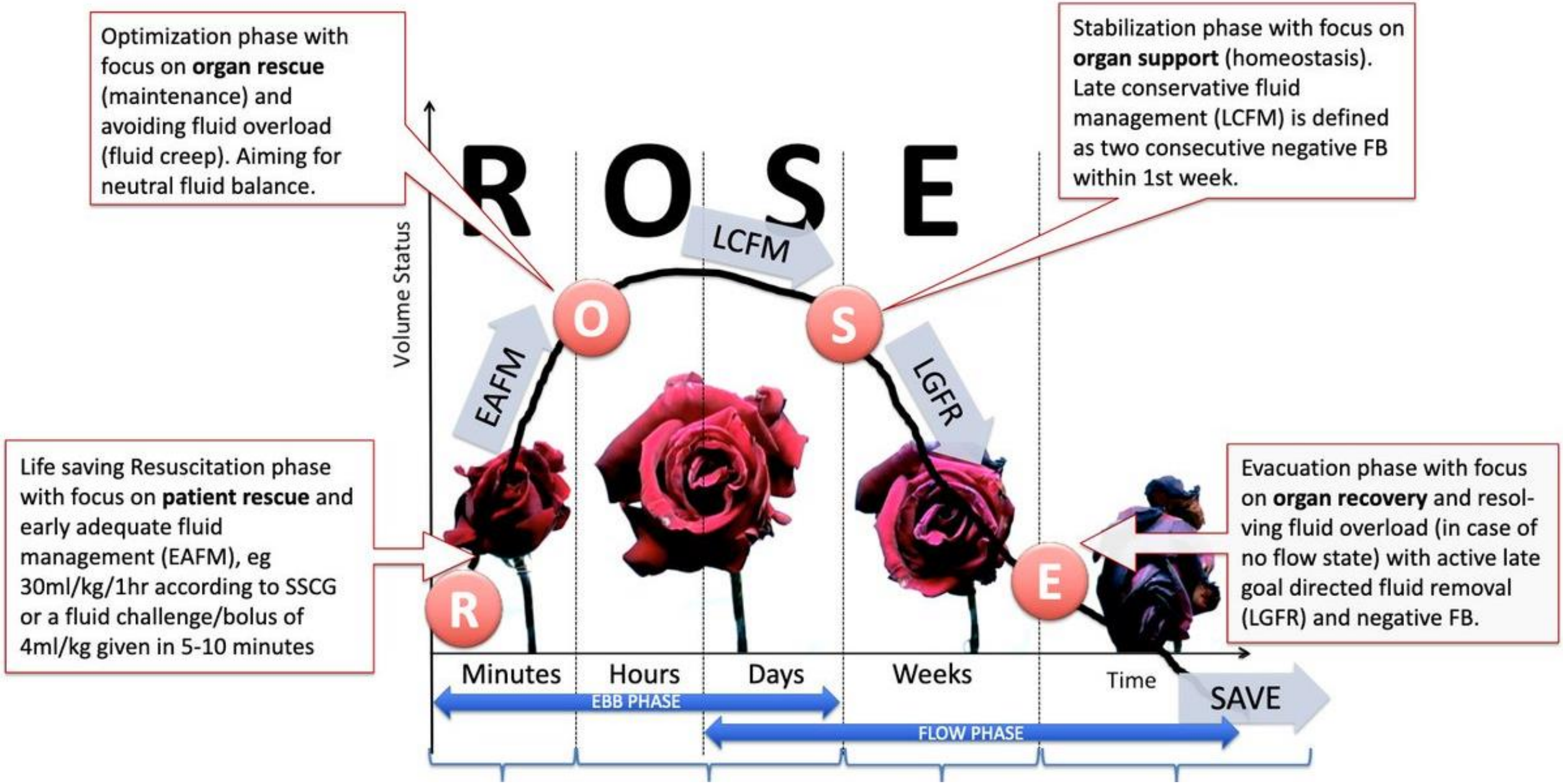
To wrap it up


fluids are dugs

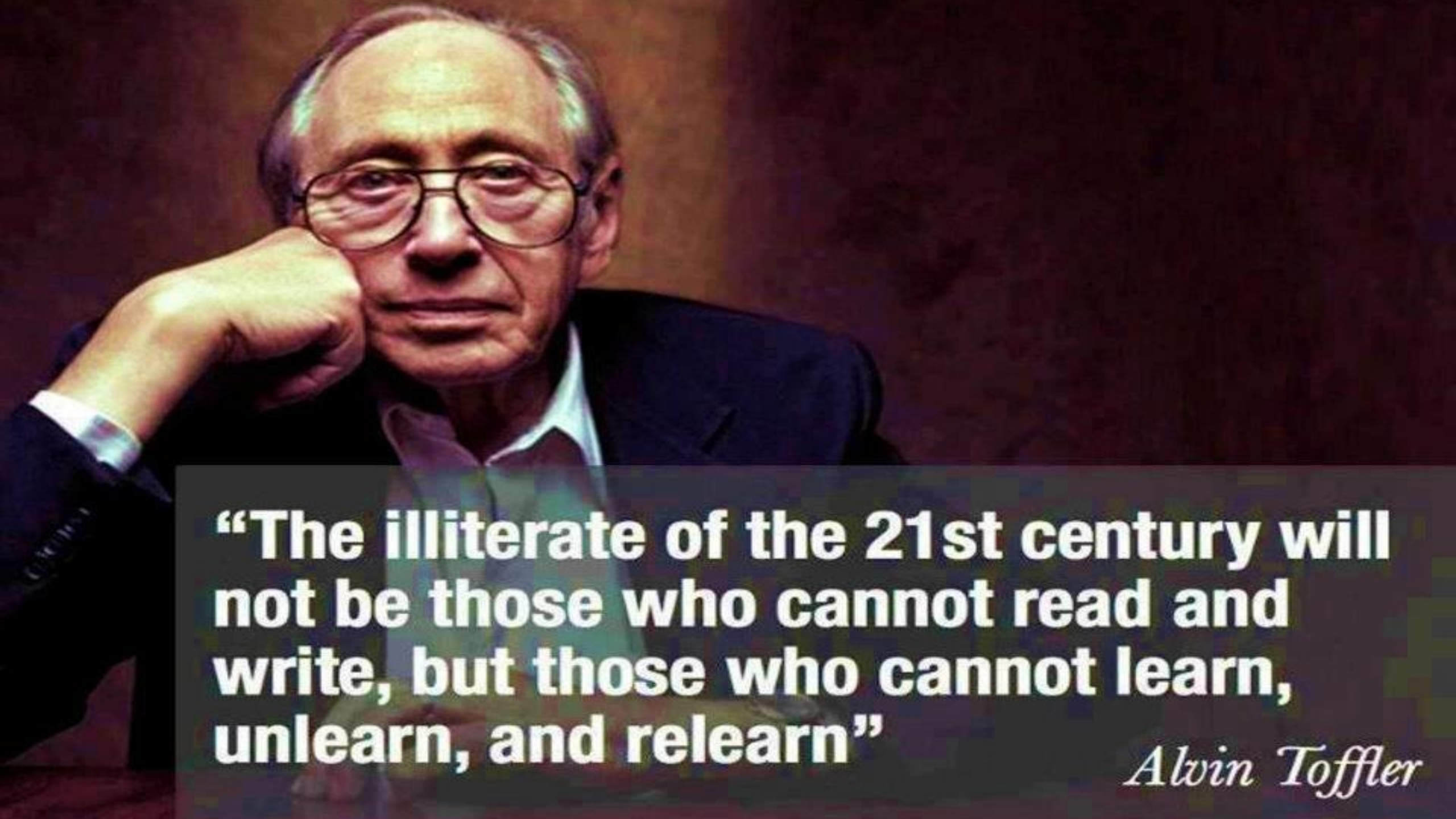
Cause harm: AKI

Save lives

Kill


Optimization phase with focus on **organ rescue** (maintenance) and avoiding fluid overload (fluid creep). Aiming for neutral fluid balance.
Stabilization phase with focus on **organ support** (homeostasis). Late conservative fluid management (LCFM) is defined as two consecutive negative FB within 1st week.
ROSE
LCFM
EAFM
LGFR
O
S
R
E
Volume Status
Life saving Resuscitation phase with focus on **patient rescue** and early adequate fluid management (EAFM), eg 30ml/kg/1hr according to SSCG or a fluid challenge/bolus of 4ml/kg given in 5-10 minutes
Evacuation phase with focus on **organ recovery** and resolving fluid overload (in case of no flow state) with active late goal directed fluid removal (LGFR) and negative FB.
Minutes
Hours
Days
Weeks
Time
EBB PHASE
FLOW PHASE
SAVE

Avoid Futile Over-resuscitation


"The illiterate of the 21st century will not be those who cannot read and write, but those who cannot learn, unlearn, and relearn"
Alvin Toffler

MERCI

Yashasin Azerbayejan