

AER 2019



AER
ACTUALITÉS EN RÉANIMATION

25^{ème} AER : 19 & 20 novembre 2020

Gestion du bilan hydro-sodé du patient agressé

Pierre-Edouard Bollaert
pe.bollaert@chru-nancy.fr



Aucun conflit d'intérêts

L'équilibre hydro-sodé du malade de réanimation

- Fait l'objet depuis longtemps d'un intérêt marqué dans les premières 24 heures de séjour, notamment chez les patients instables (choc, SDRA, insuffisance rénale, inflammation, fuite capillaire) et amenant à prescrire du « remplissage vasculaire »
- Evolue souvent rapidement vers une balance hydrique parfois très positive dans la première semaine de séjour,
- Ne fait pas consensus sur le bien-fondé du retour à l'équilibre (dé-resuscitation), eu égard notamment à l'absence d'intérêt évident et aux risques putatifs: insuffisance circulatoire, création ou aggravation d'une insuffisance rénale, troubles hydro-électrolytiques,...

- Un bilan hydro-sodé excédentaire est associé de manière indépendante à un pronostic vital aggravé chez le patient agressé (notamment mais pas exclusivement au cours du choc septique et du SDRA)

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

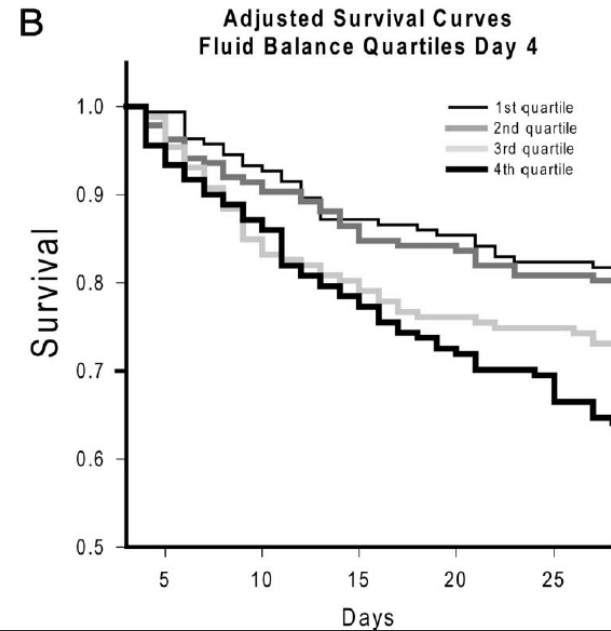
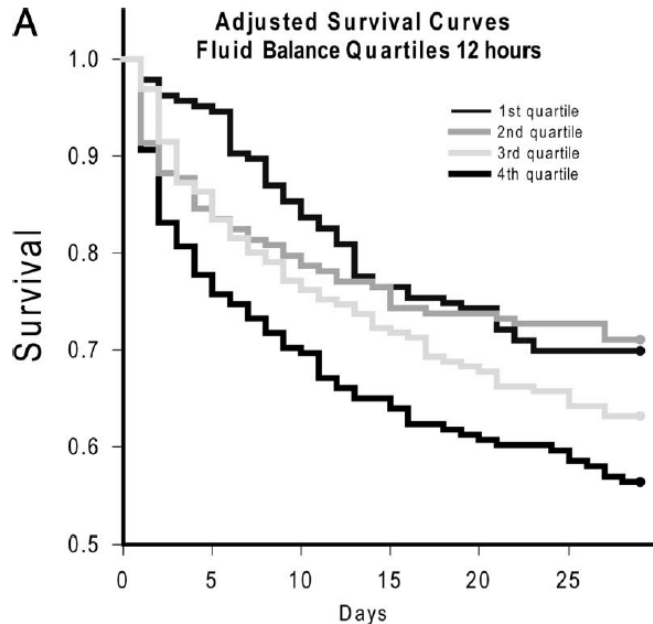


Table 1. Fluid intake, urine output, and net fluid balance at 12 hrs and cumu

	Quartile 1 (Dry)	Quartile 2	Quartile 3	Quartile 4 (Wet)
12 hrs				
Intake, mL	2900 (2050–3900)	4520 (3700–5450)	6110 (5330–7360)	10,100 (8430–12,100)
Output, mL	2200 (1100–3920)	1590 (960–2560)	1180 (600–2070)	1260 (600–2400)
Balance, mL	710 (–132–1480)	2880 (2510–3300)	4900 (4290–5530)	8150 (7110–10,100)
Day 4				
Intake, mL	16,100 (12,800–19,700)	18,500 (15,700–22,500)	22,800 (19,700–26,700)	30,600 (26,200–36,000)
Output, mL	14,600 (11,500–20,100)	11,000 (8,210–14,500)	9,960 (6,940–12,900)	8,350 (5,100–12,300)
Balance, mL	1560 (–723–3,210)	8,120 (6,210–9,090)	13,000 (11,800–14,700)	20,500 (17,700–24,500)

Volumes are expressed as median (25–75%).

Boyd JH, CCM, 2011

Prédiction de la mortalité du SDRA par le bilan hydrosodé (n=600)

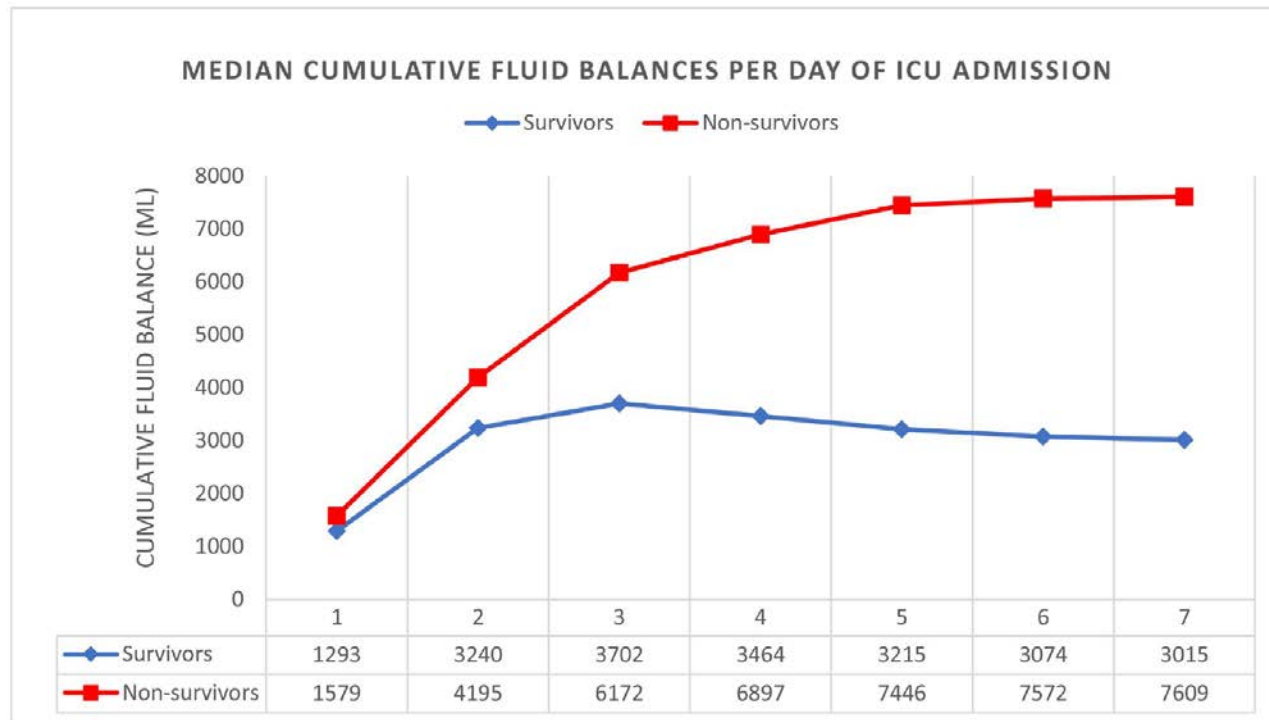
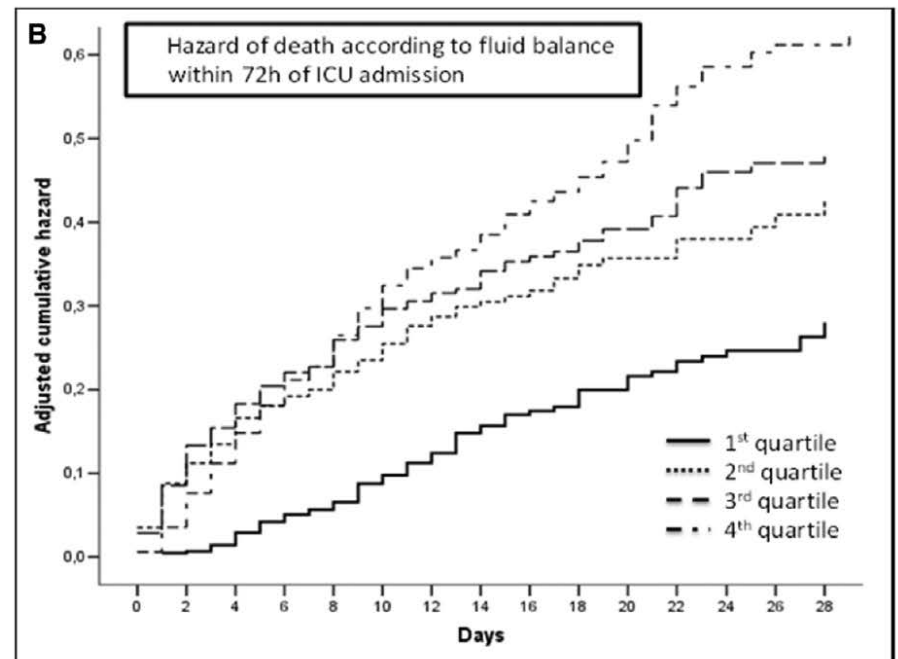
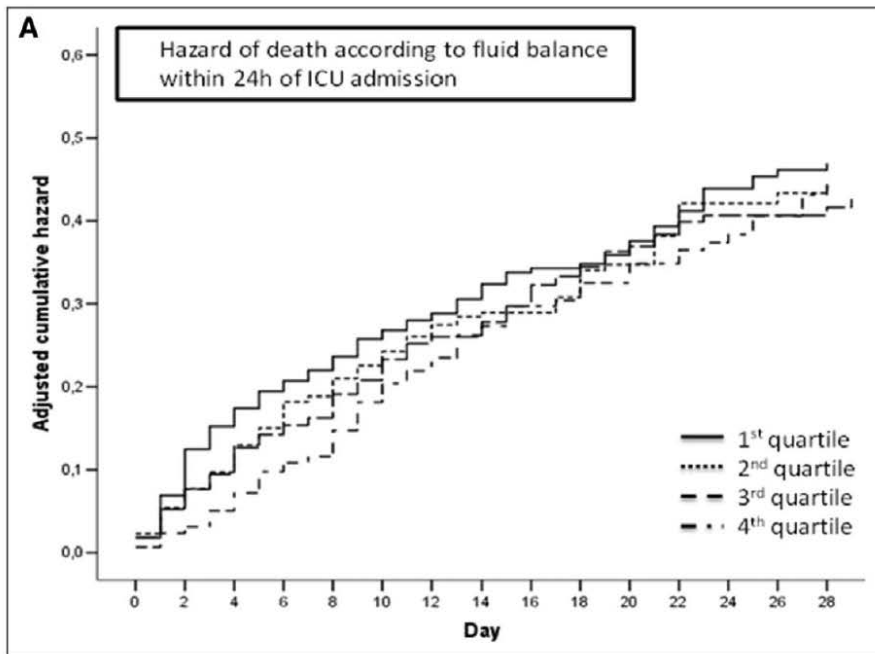


Fig 1. Median cumulative fluid balance in the first 7 days of ICU admission in survivors and non-survivors. Survival was based on 28-day mortality. Survivors are marked blue, non-survivors are marked red. On the Y-axis the cumulative fluid balance in mL is found. On the X-axis days of ICU admission with corresponding median cumulative fluid balances (mL) for survivors and non-survivors.

Van Mourik N, PLoS ONE, 2019

Higher Fluid Balance Increases the Risk of Death From Sepsis: Results From a Large International Audit*

Yasser Sakr, MD, PhD¹; Paolo Nahuel Rubatto Birri, MD¹; Katarzyna Kotfis, MD, PhD²; Rahul Nanchal, MD³; Bhagyesh Shah, MBBS, DA, IDCCM⁴; Stefan Kluge, MD⁵; Mary E. Schorr, MD⁶; John C. Marshall, MD⁷; Jean-Louis Vincent, MD, PhD, FCCM⁸; on behalf of the Intensive Care Nations Investigators



(*Crit Care Med* 2017; 45:386–394)

L'étude RADAR

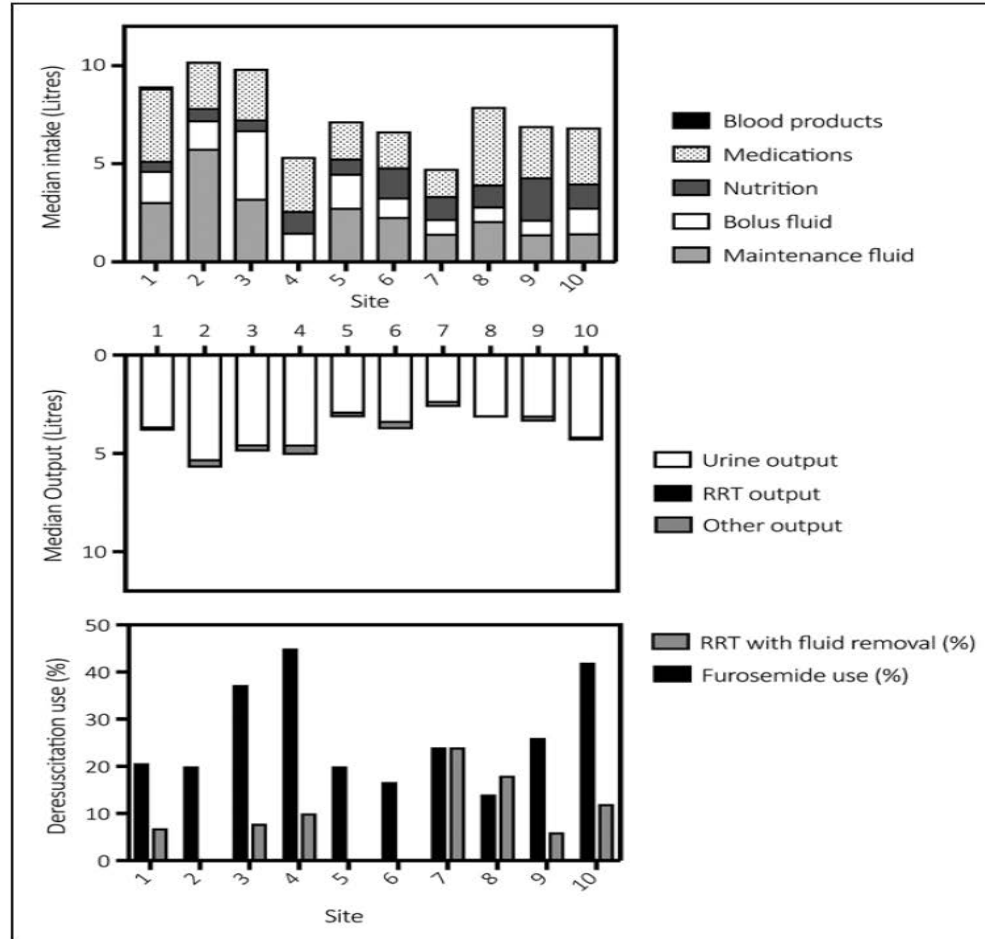


Figure 2. Median fluid input and output and use of deresuscitative measures for days 1–3 by study site. RRT = renal replacement therapy.

Silversides JA, et al, CCM 2018

Une semaine de bilan cumulatif hydro-sodé

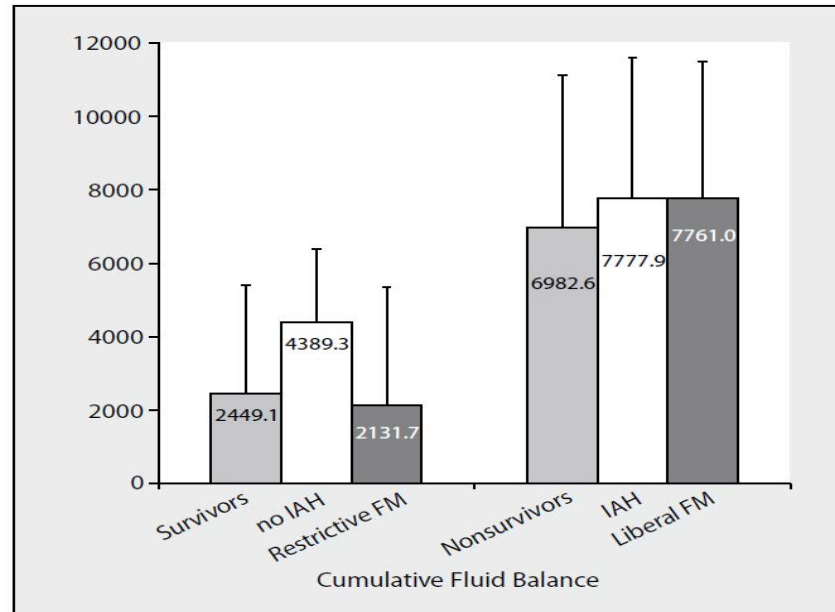


Figure 1. Bar graph showing mean cumulative fluid balance after one week of intensive care unit (ICU) stay. Light grey bars showing cumulative fluid balance in survivors (left) vs nonsurvivors (right), white bars show data in patients without intra-abdominal hypertension, IAH (left) vs IAH (right), and dark grey bars data in patients with restrictive fluid management (left) vs liberal fluid management (right)

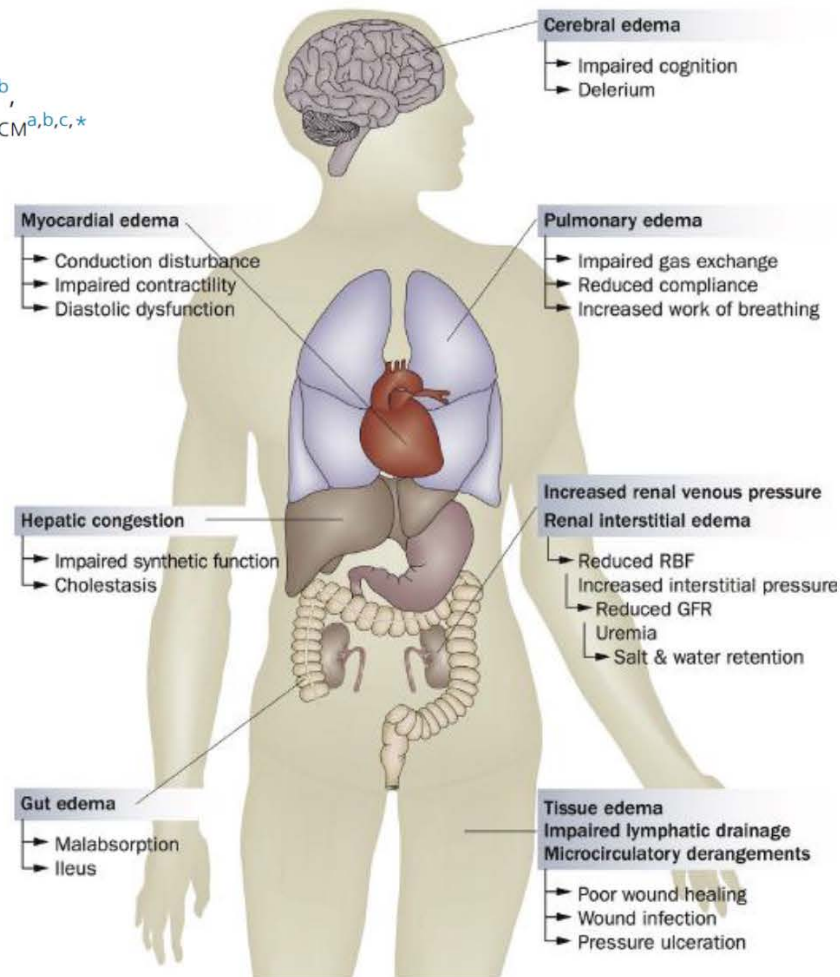
Malbrain MLNG et al, Anaesthesiol Intensive Ther 2014

Questions

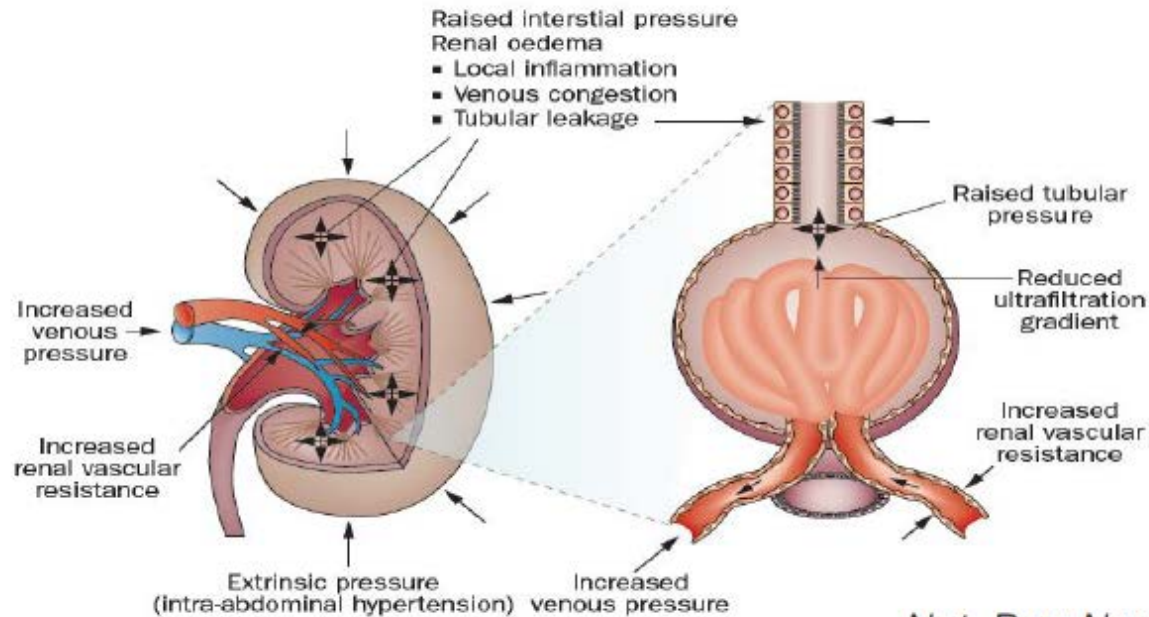
- L'association significative entre un bilan hydro-sodé fortement positif et la mortalité en fait un facteur de gravité mais on ne sait pas dans quelle mesure elle est une cible thérapeutique.
- La surcharge hydro-sodée est la conséquence de la pathologie initiale (hyperperméabilité endothéliale conduisant à un œdème interstitiel), mais dans quelle mesure peut-on (ou doit-on) la prévenir ou la réduire ?

Fluid Overload

Michael E. O'Connor, MBBS, BSc, MRCP, FRCA^{a,b},
John R. Prowle, MA, MB BChir, MSc, MD, FRCP, FFICM^{a,b,c,*}



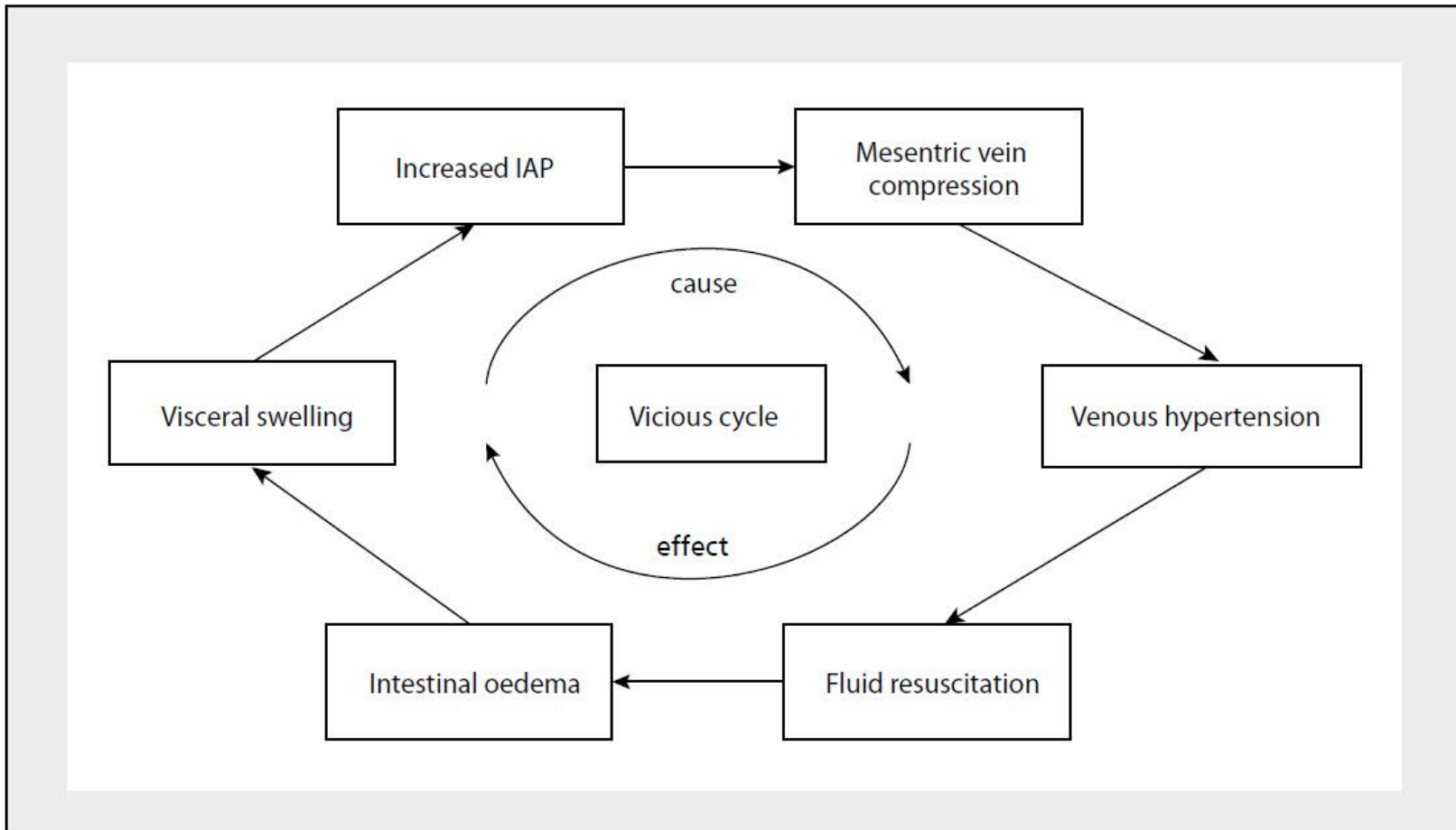
Le rein: un organe vulnérable



Nat. Rev. Nephrol. **10**, 37–47 (2014)

John R. Prowle, Christopher J. Kirwan and Rinaldo Bellomo

Surcharge hydro-sodée et pronostic: une vraie relation de causalité ?



Les facteurs contribuant à une balance hydro-sodée positive

	Early in Admission to Intensive Care	Later in Admission to Intensive Care
Excessive intake of fluid	Need for blood products Intravenous fluid resuscitation	Obligate daily fluid needs in terms of drug therapies and nutrition Intercurrent clinical events requiring fluid resuscitation
Inadequate fluid elimination	Acute or chronic kidney disease Acute hemodynamic instability Fluid losses from circulation to interstitial space	Ongoing renal impairment Cardiac and liver dysfunction Sequestration of fluid in the interstitium and body cavities

Michael E. O'Connor, MBBS, BSc, MRCP, FRCA^{a,b},

John R. Prowle, MA, MB BChir, MSc, MD, FRCP, FFICM^{a,b,c,*}

Crit Care Clin ■ (2015)

SPECIAL ARTICLES

Four phases of intravenous fluid therapy: a conceptual model[†]

E. A. Hoste^{1,2}, K. Maitland^{3,4}, C. S. Brudney⁵, R. Mehta⁶, J.-L. Vincent⁷, D. Yates⁸, J. A. Kellum⁹, M. G. Mythen¹⁰ and A. D. Shaw¹¹ for the ADQI XII Investigators Group

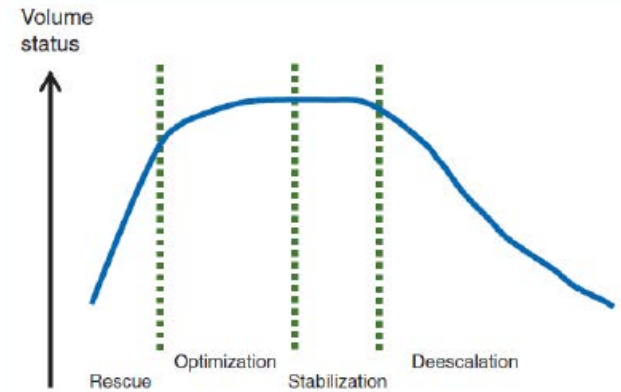


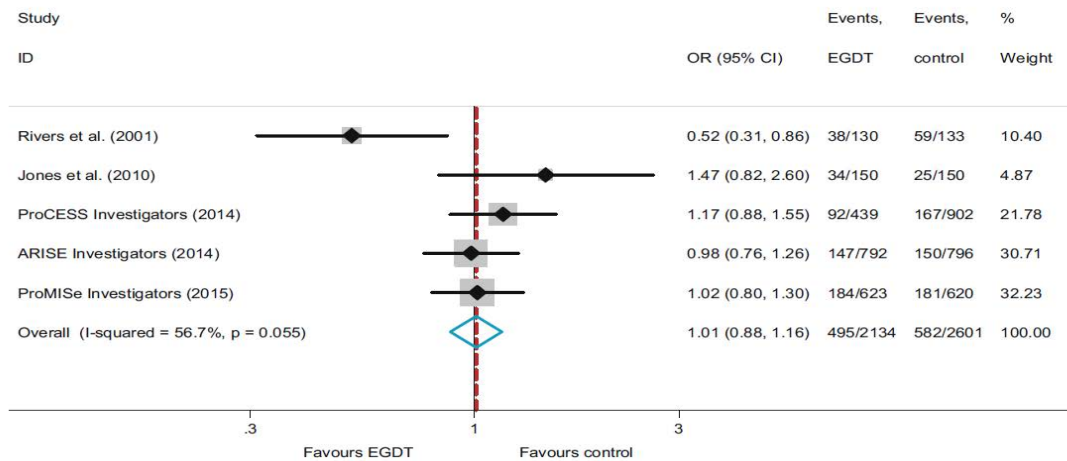
Fig 2 Patients' volume status at different stages of resuscitation. Reproduced with permission from ADQI (www.ADQI.org).

Table 1 Characteristics of different stages of resuscitation: 'Fit for purpose fluid therapy'. GDT, goal directed therapy; DKA, diabetic keto acidosis; NPO, nil per os; ATN, acute tubular necrosis; SSC, surviving sepsis campaign

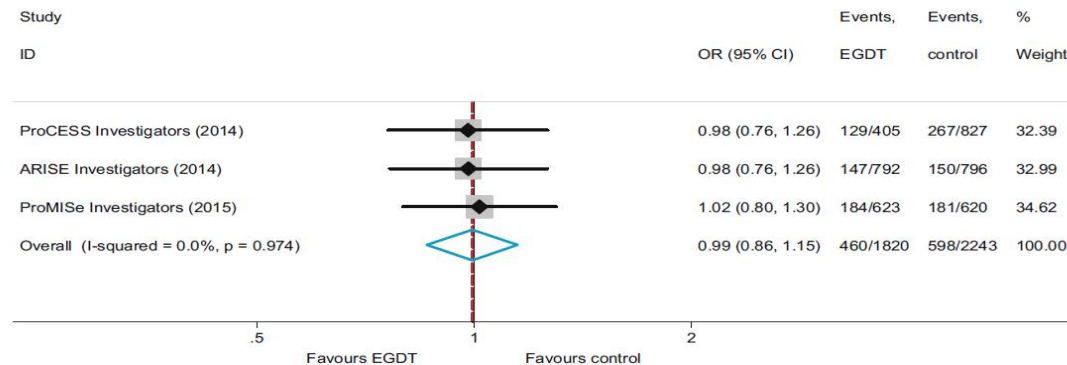
	Rescue	Optimization	Stabilization	De-escalation
Principles	Lifesaving	Organ rescue	Organ support	Organ recovery
Goals	Correct shock	Optimize and maintain tissue perfusion	Aim for zero or negative fluid balance	Mobilize fluid accumulated
Time (usual)	Minutes	Hours	Days	Days to weeks
Phenotype	Severe shock	Unstable	Stable	Recovering
Fluid therapy	Rapid boluses	Titrate fluid infusion conservative use of fluid challenges	Minimal maintenance infusion only if oral intake inadequate	Oral intake if possible Avoid unnecessary i.v. fluids
Typical clinical scenario	- Septic shock - Major trauma	- Intraoperative GDT - Burns - DKA	- NPO postoperative patient - 'Drip and suck' management of pancreatitis	- Patient on full enteral feed in recovery phase of critical illness - Recovering ATN
Amount	Guidelines, for example, SSC, pre-hospital resuscitation, trauma, burns, etc.			

A systematic review and meta-analysis of early goal-directed therapy for septic shock: the ARISE, ProCESS and ProMISe Investigators

A Primary mortality outcome of each study

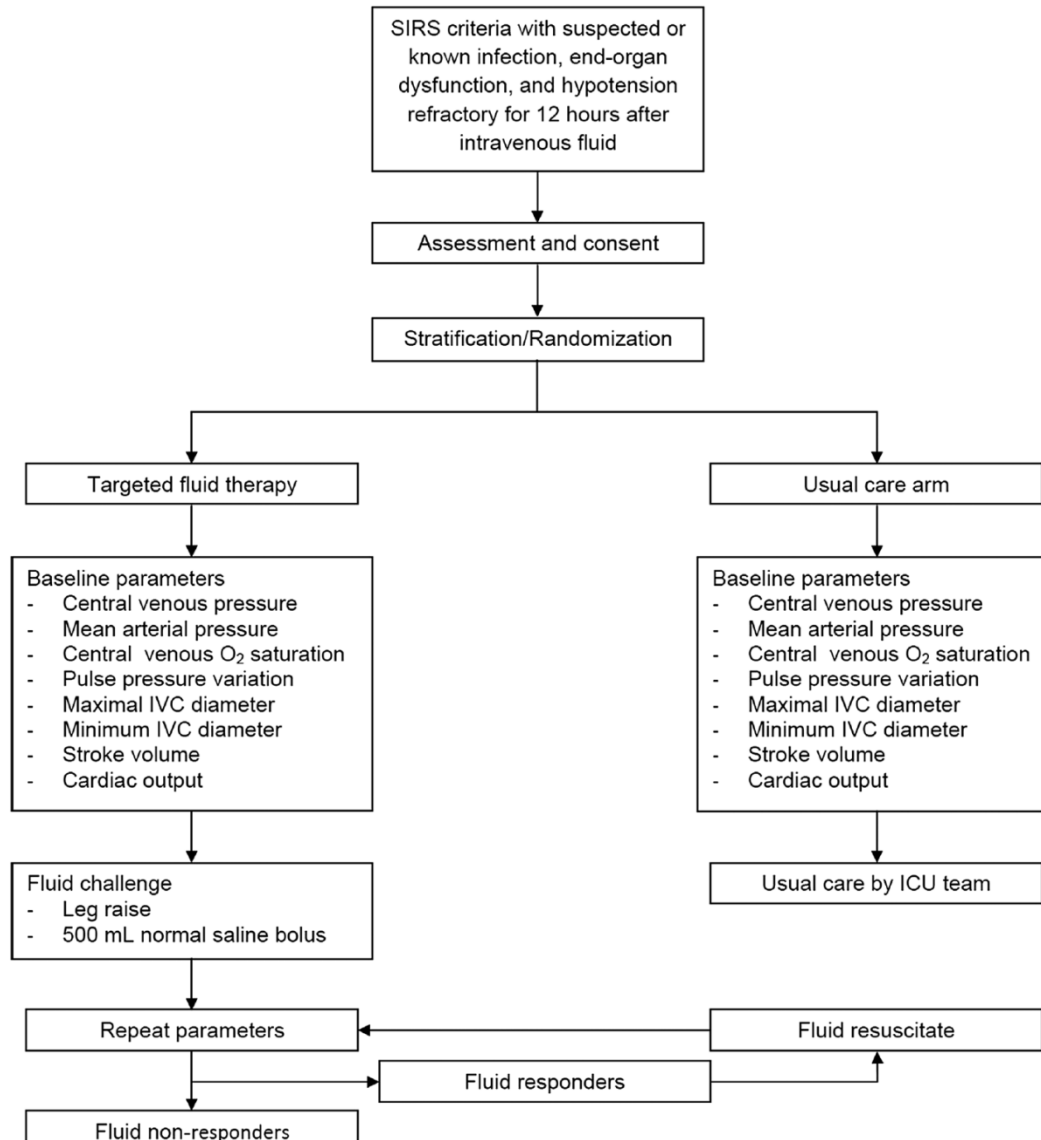


B 90-day mortality



Targeted Fluid Minimization Following Initial Resuscitation in Septic Shock

A Pilot Study Catherine Chen, MD; and Marin H. Kollef, MD CHEST 2015; 148(6):1462-1469



Targeted Fluid Minimization Following Initial Resuscitation in Septic Shock

A Pilot Study Catherine Chen, MD; and Marin H. Kollef, MD CHEST 2015; 148(6):1462-1469

TABLE 3] Primary Outcomes

Fluid	Control Arm		Intervention Arm		P Value
	No.	Volume	No.	Volume	
Study fluid, mL					
Day 3	38	4,110 (2,702 to 10,004)	36	4,417 (3,139 to 6,528)	.47
Day 5	31	8,690 (4,211 to 13,197)	31	6,244 (5,106 to 8,497)	.26
Nonstudy fluid, mL					
Day 3	38	1,854 (735 to 4,608)	36	1,664 (971 to 2,384)	.76
Day 5	31	2,660 (1,213 to 4,608)	31	2,920 (1,418 to 3,628)	.99
Net fluid output, mL					
Day 3	38	4,770 (2,021 to 6,479)	36	3,744 (2,354 to 6,163)	.77
Day 5	31	6,924 (3,351 to 11,968)	31	7,728 (3,146 to 1,0360)	.76
Net fluid balance, mL					
Day 3	38	3,124 (767 to 10,103)	36	1,952 (48 to 5,003)	.20
Day 5	31	3,616 (-1,513 to 9,746)	31	2,641 (-1,837 to 5,075)	.40

TABLE 4] Secondary Outcomes

Outcome	Control Arm (n = 41)	Intervention Arm (n = 41)	P Value
Renal replacement therapy	16 (39.0)	17 (41.5)	.82
Maximal vasopressor dose, $\mu\text{g}/\text{min}$	13 (7-25)	18 (9-35)	.15
Vasopressor days	4 (2-6)	4 (2-8)	.84
Vasopressor-free days	5 (0-16)	5.5 (0-10)	.84
Ventilator days	5 (3-9)	8 (3.25-15.25)	.30
Ventilator-free days	5.5 (0-16.75)	5.5 (0-12.25)	.05
In-hospital mortality	20 (48.8)	23 (56.1)	.51

Data are expressed as median (IQR) or No. (%). See Table 1 legend for expansion of abbreviation.

Effectiveness of treatment based on PiCCO parameters in critically ill patients with septic shock and/or acute respiratory distress syndrome: a randomized controlled trial

Intensive Care Med (2015) 41:444–451

Outcome variables	PiCCO group (<i>n</i> = 168)	Control group (<i>n</i> = 182)	<i>P</i> value
Primary outcome			
28-day mortality	83 (49.4)	90 (49.5)	0.993
Secondary outcomes			
Maximum SOFA	13 (10–15)	12 (9–14)	0.023
14-day mortality	68 (40.5)	75 (41.2)	0.889
Days on vasopressor	4 (2–6)	3 (2–6.5)	0.852
Days on MV	6 (3–12)	5.5 (3–12)	0.897
Days on CRRT	4 (3–7)	4.5 (3–7)	0.586
Length of stay in ICU	9 (5–13)	7.5 (4–15)	0.598
Days free of vasopressor in 14 days	10 (0–12)	9 (0–12)	0.562
Days free of MV in 14 days	1 (0–10)	4 (0–12)	0.127
Days free of CRRT in 14 days	11 (3–14)	14 (4–14)	0.0038
Days free of vasopressor in 28 days	14.5 (0–25)	19 (0–26)	0.676
Days free of MV in 28 days	3 (0–24)	6 (0–25)	0.168
Days free of CRRT in 28 days	15.5 (3–28)	21 (4–28)	0.048

Patients without use of MV, CRRT, or vasopressor were treated as missing variable, instead of zero

MV mechanical ventilation, *ICU* intensive care unit, *IQR* interquartile range, *CRRT* continuous renal replacement therapy

RESEARCH

Open Access

Preload dependence indices to titrate volume expansion during septic shock: a randomized controlled trial

Table 4 Study outcomes

	Control (n = 30)	Preload dependence (n = 30)	P
Time to shock resolution (days)	2.0 [1.2-3.1]	2.3 [1.4-5.6]	0.29
Ventilator-free days at day 28	8 [0-21]	14 [0-24]	0.35
Number of days with lactates above upper normal laboratory limit	1 [1-4]	2 [1-4]	0.14
Number of days with pulmonary edema (that is ELWI >10 ml.kg ⁻¹ PBW)	4 [1-5]	4 [1-6]	0.94
Number of days with organ system failure (that is SOFA ≥6)	4 [3-5]	4 [2-8]	0.61
ICU length of stay (days)	10 [7-20]	14 [6-28]	0.55
In survivors	14 [9-28]	22 [6-28]	0.89
In non-survivors	8 [5-11]	5 [3-17]	0.85
Mortality at day 28	14 (47%)	7 (23%)	0.10

Data are median [interquartile range] or number of patients (%). ELWI, extravascular lung water index; ICU, intensive care unit; PBW, predicted body weight; SOFA, Sequential Organ Failure Assessment score [21].

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*

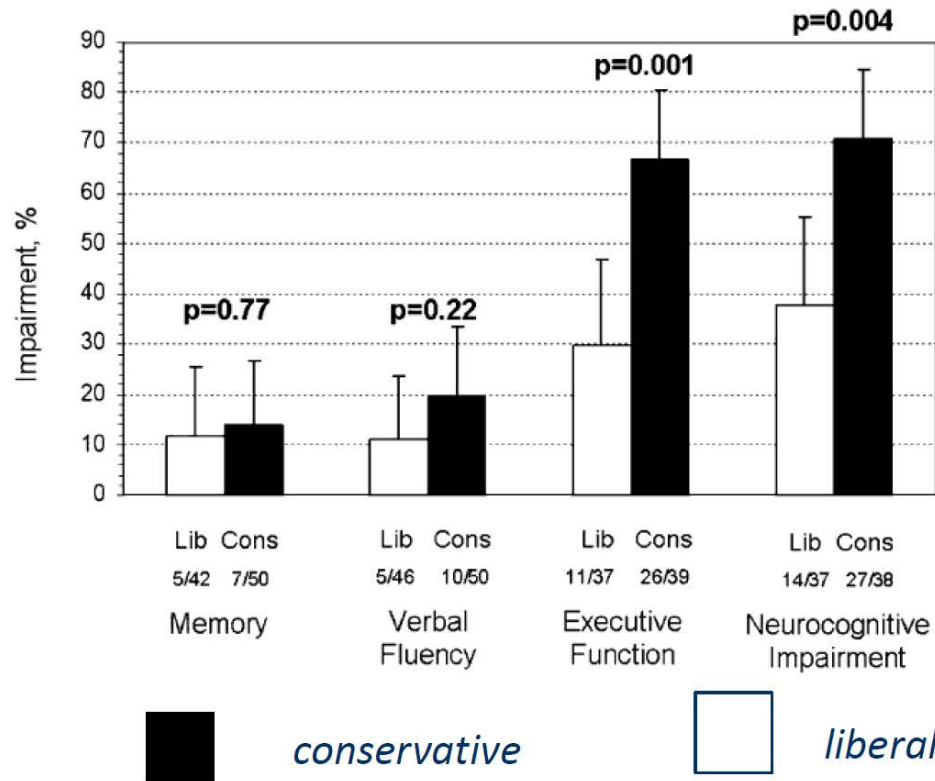
Table 3. Main Outcome Variables.*

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

The Adult Respiratory Distress Syndrome Cognitive Outcomes Study

Long-Term Neuropsychological Function in Survivors of Acute Lung Injury

Mark E. Mikkelsen^{1,2*}, Jason D. Christie^{1,2*}, Paul N. Lanken¹, Rosette C. Biester^{3,4}, B. Taylor Thompson⁵, Scarlett L. Bellamy², A. Russell Localio², Ejigayehu Demissie^{1,2}, Ramona O. Hopkins^{6,7}, and Derek C. Angus⁸

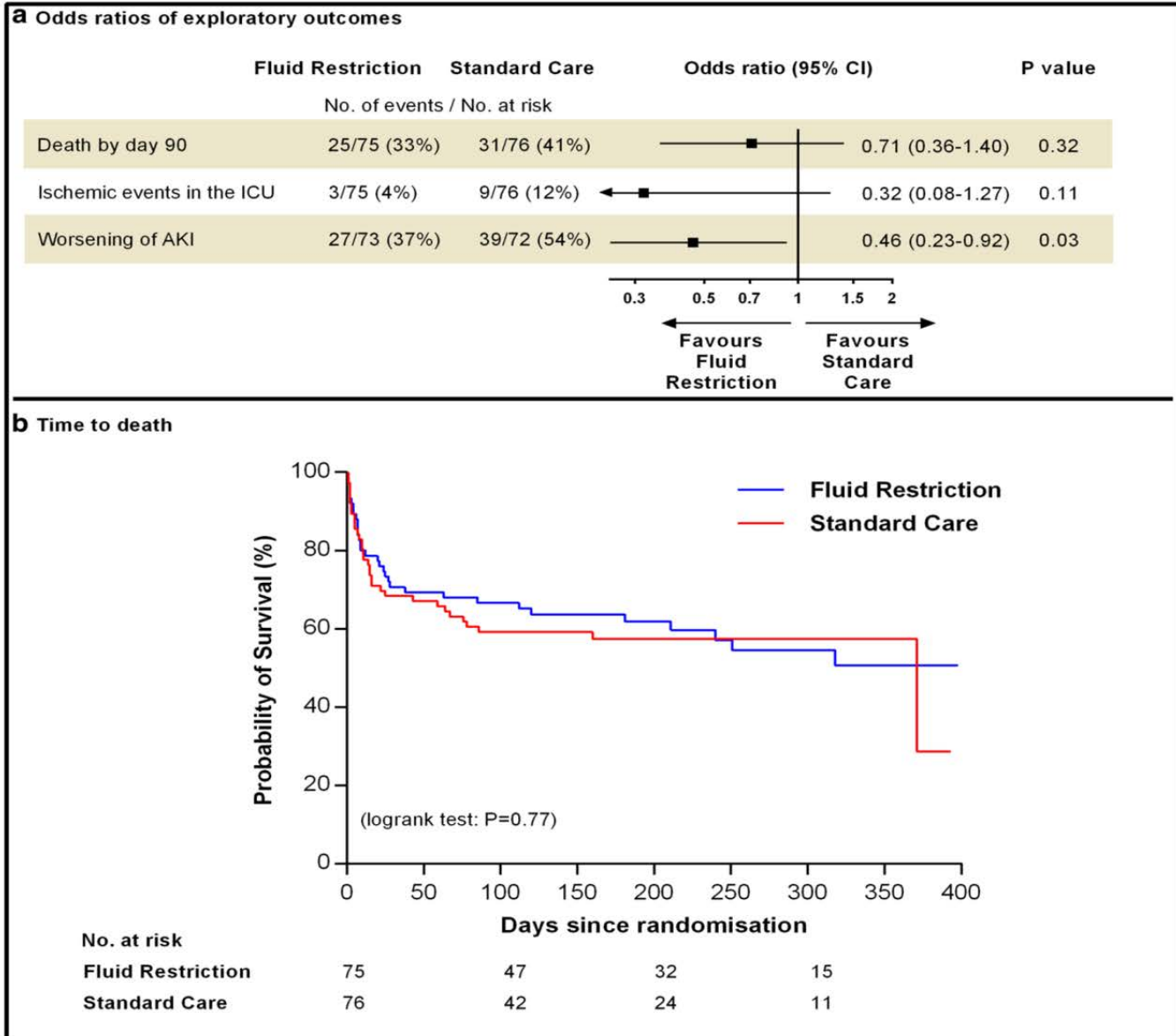


L'étude de faisabilité CLASSIC

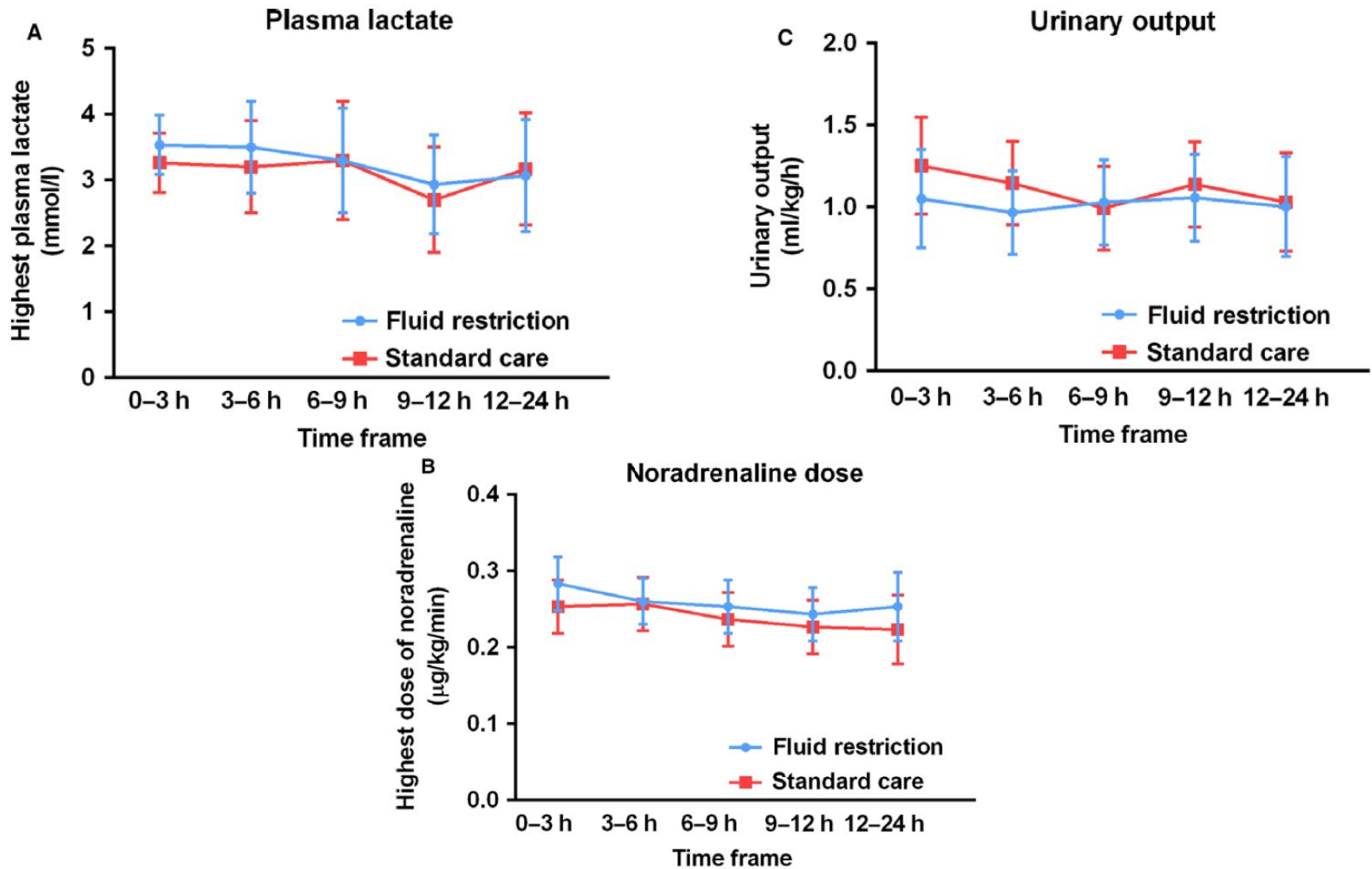
Table 2 Primary and secondary outcome measures

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

L'étude de faisabilité CLASSIC



Efficacité circulatoire comparée



Conservative fluid management or deresuscitation for patients with sepsis or acute respiratory distress syndrome following the resuscitation phase of critical illness: a systematic review and meta-analysis

Intensive Care Med (2017) 43:155–170
DOI 10.1007/s00134-016-4573-3

Jonathan A. Silversides^{1,2*}, Emmet Major², Andrew J. Ferguson³, Emma E. Mann², Daniel F. McAuley^{1,4}, John C. Marshall^{5,6}, Bronagh Blackwood¹ and Eddy Fan⁵

Mortalité

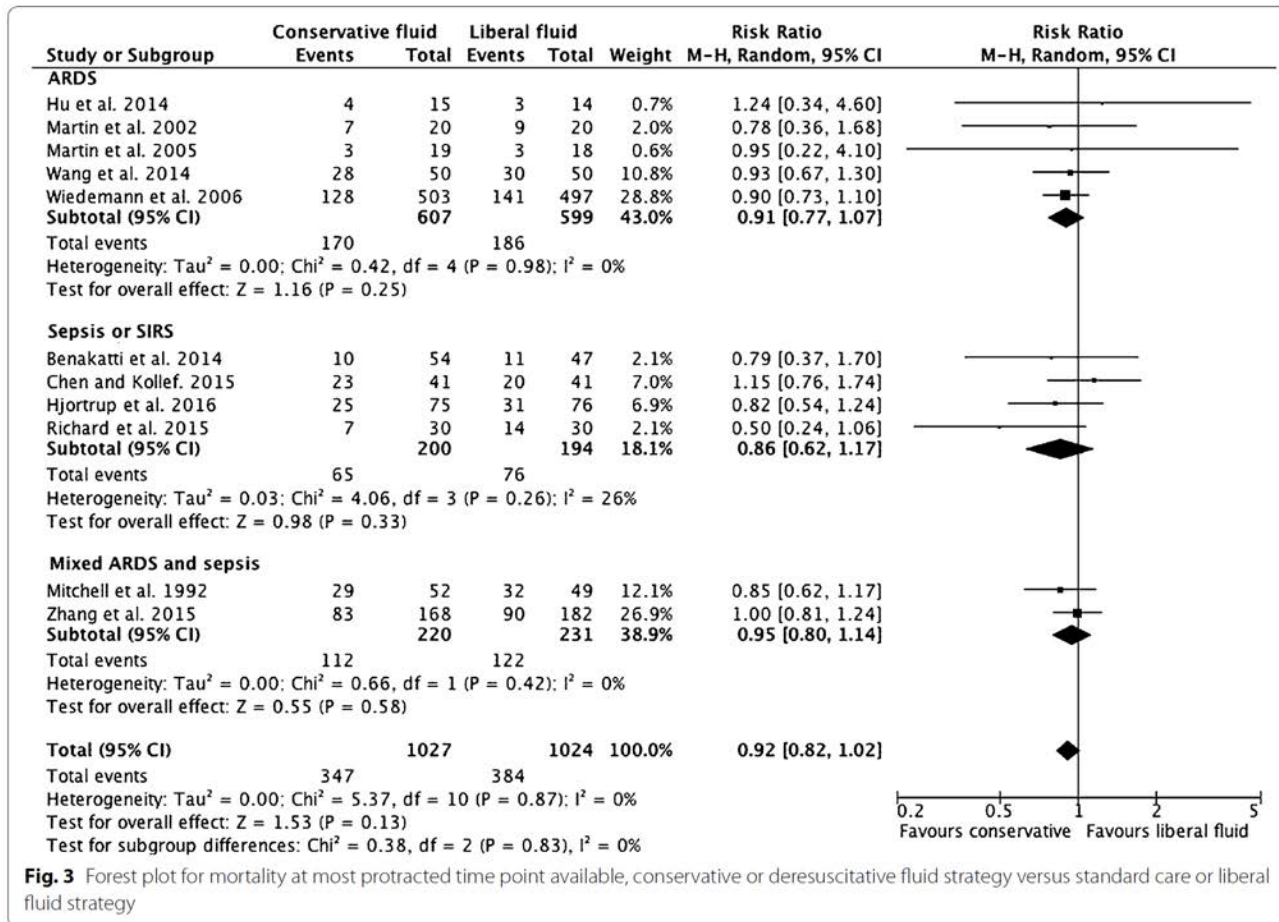


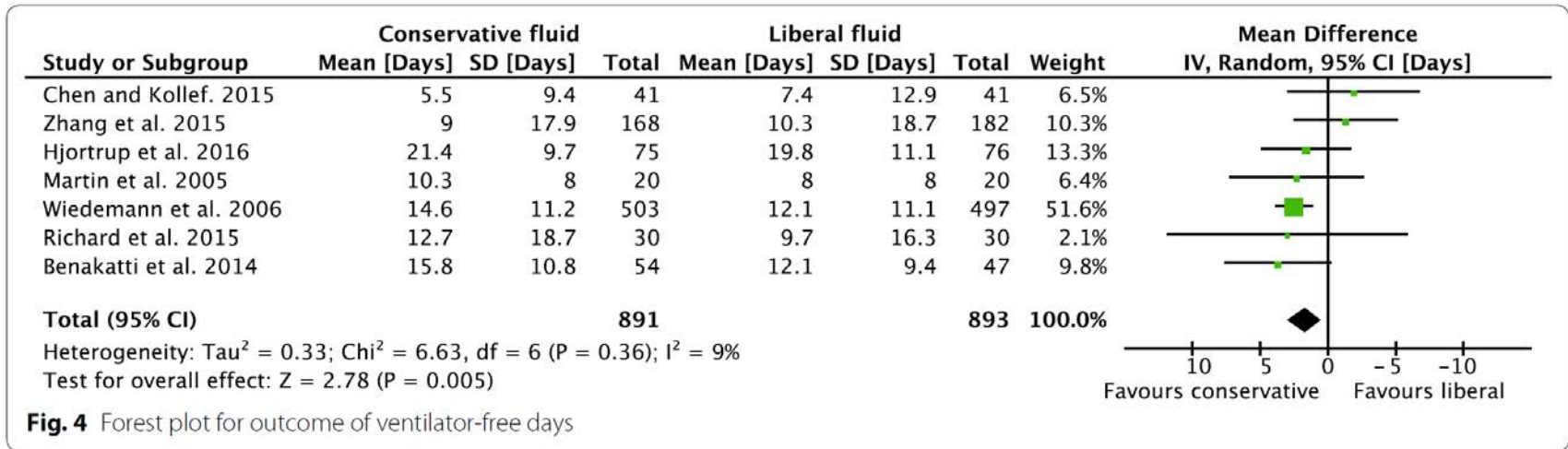
Fig. 3 Forest plot for mortality at most protracted time point available, conservative or deresuscitative fluid strategy versus standard care or liberal fluid strategy

Conservative fluid management or deresuscitation for patients with sepsis or acute respiratory distress syndrome following the resuscitation phase of critical illness: a systematic review and meta-analysis

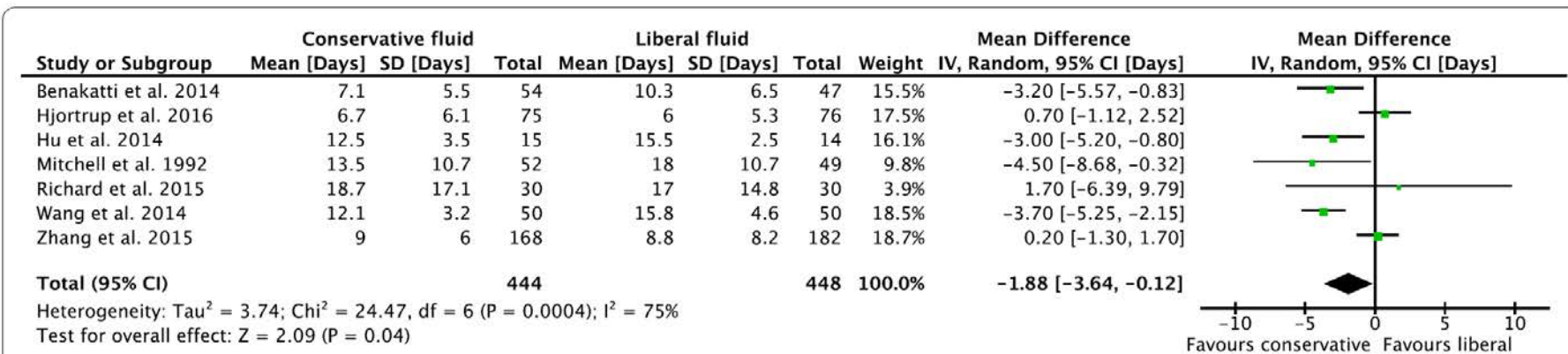
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Jonathan A. Silversides^{1,2*}, Emmet Major², Andrew J. Ferguson³, Emma E. Mann², Daniel F. McAuley^{1,4}, John C. Marshall^{5,6}, Bronagh Blackwood¹ and Eddy Fan⁵

Nombre de jours vivant sans ventilation mécanique



Durée de séjour en réanimation



Conservative fluid management or deresuscitation for patients with sepsis or acute respiratory distress syndrome following the resuscitation phase of critical illness: a systematic review and meta-analysis

Intensive Care Med (2017) 43:155–170

DOI 10.1007/s00134-016-4573-3

Jonathan A. Silversides^{1,2*}, Emmet Major², Andrew J. Ferguson³, Emma E. Mann², Daniel F. McAuley^{1,4}, John C. Marshall^{5,6}, Bronagh Blackwood¹ and Eddy Fan⁵

Divers autres critères de jugement:

- SOFA (3 études): NS
- Epuration extra-rénale: équivoque (3 études)
- Fonctions cognitives

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

A Randomized Clinical Trial

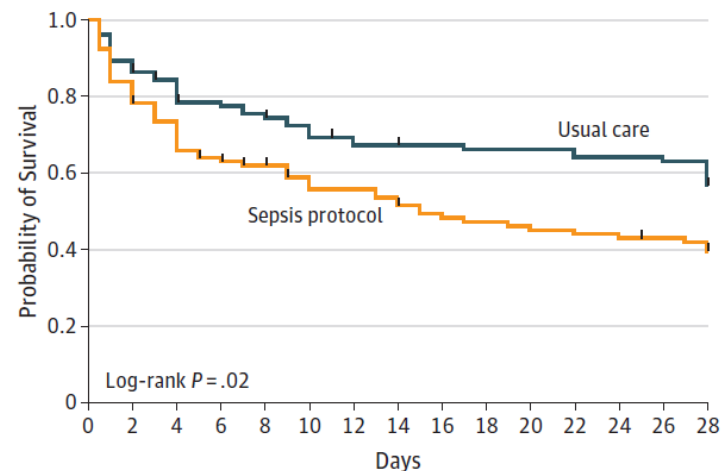
JAMA. 2017;318(13):1233-1240. doi:10.1001/jama.2017.10913

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

- Randomisation entre soins usuels et protocole de prise en charge précoce selon pression veineuse jugulaire, FR et SpO2
- Prévalence élevée de VIH et tuberculose
- Déroulement de l'étude en Zambie

6 premières heures: groupe protocole reçoit une médiane de 3,5l et le groupe contrôle reçoit une médiane de 2,0 l ($p > 0,001$) de cristalloïdes isotoniques

Figure 2. Kaplan-Meier Plot of the Probability of Survival Until Day 28 After Enrollment



No. at risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28
Sepsis protocol	106	98	90	82	74	66	58	50	42	34	26	18	10	2	0
Usual care	103	95	87	79	71	63	55	47	39	31	23	15	7	0	0

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

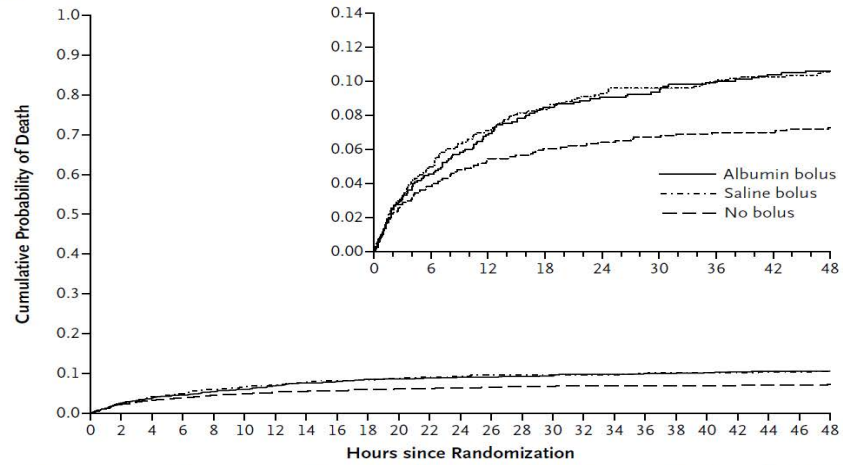
JUNE 30, 2011

VOL. 364 NO. 26

Mortality after Fluid Bolus in African Children with Severe Infection

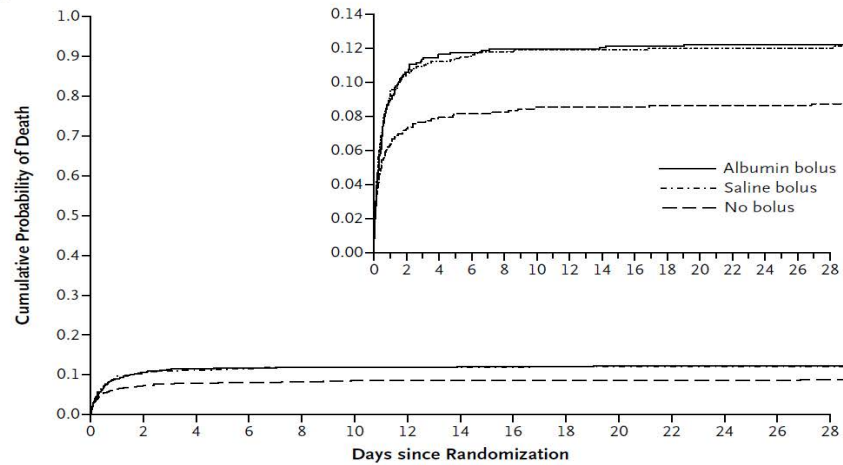
Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, 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

Conclusions

- Les données actuelles suggèrent que la surcharge hydro-sodée se construit précocément et ne régresse que difficilement à partir de J4-J7.
- On dispose de beaucoup d'études pilotes qui montrent des résultats assez variables en matière de correction de la surcharge hydro-sodée.
- Point important, les craintes d'effets secondaires (insuffisance circulatoire, hypotension, ischémie, dépendance marquée aux vasopresseurs, aggravation de l'insuffisance rénale) ne sont pas confirmées.

Grands essais cliniques en cours

	Patients	Protocole	Objectif principal	Lieu	Statut
CLOVERS	Choc septique	Vasopresseur d'abord vs fluides d'abord	Mortalité 90j 2320 patients	USA	Recrute
CLASSIC	Choc septique	Restriction de tous fluides IV vs soins usuels	Mortalité 90j 1554 patients	Europe	Recrute
ARISE FLUIDS	Choc septique	Vasopresseur d'abord vs fluides d'abord	Mortalité 90j 3000 patients	Australie et Nouvelle Zélande	Recrute
POINCARE	Ventilation mécanique > 48h	Restriction et élimination retardées des fluides excédentaires > 48h	Mortalité 60j 1450 patients	France	Recrutement terminé
GOAL	Choc septique	Mini fluid challenge vs SSC	Delta SOFA score 711 patients	France	Recrutement pas encore commencé