

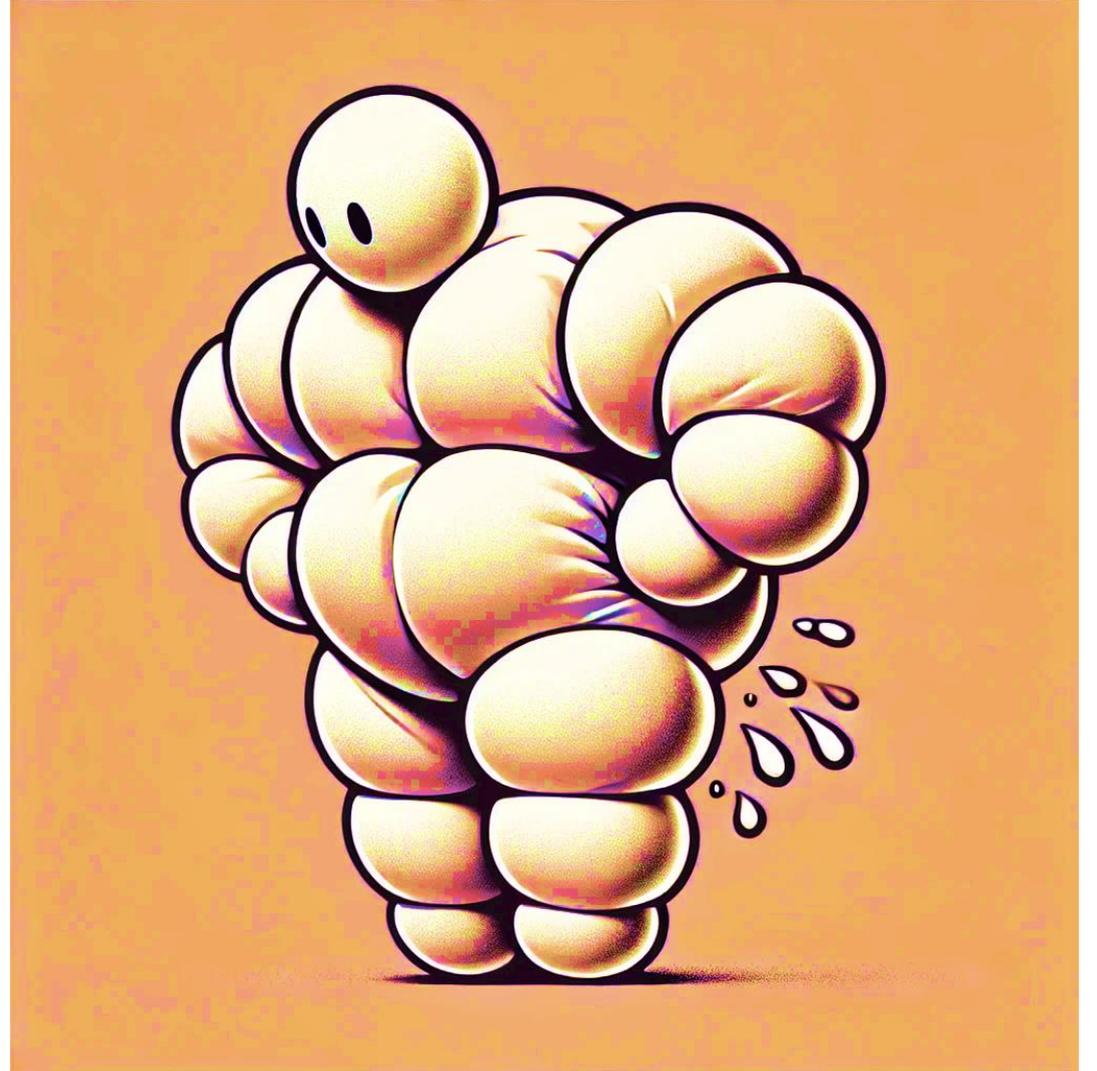
Current Fluid Controversies and Novel Therapies

Maintaining ICU Patients in a State of Dryness

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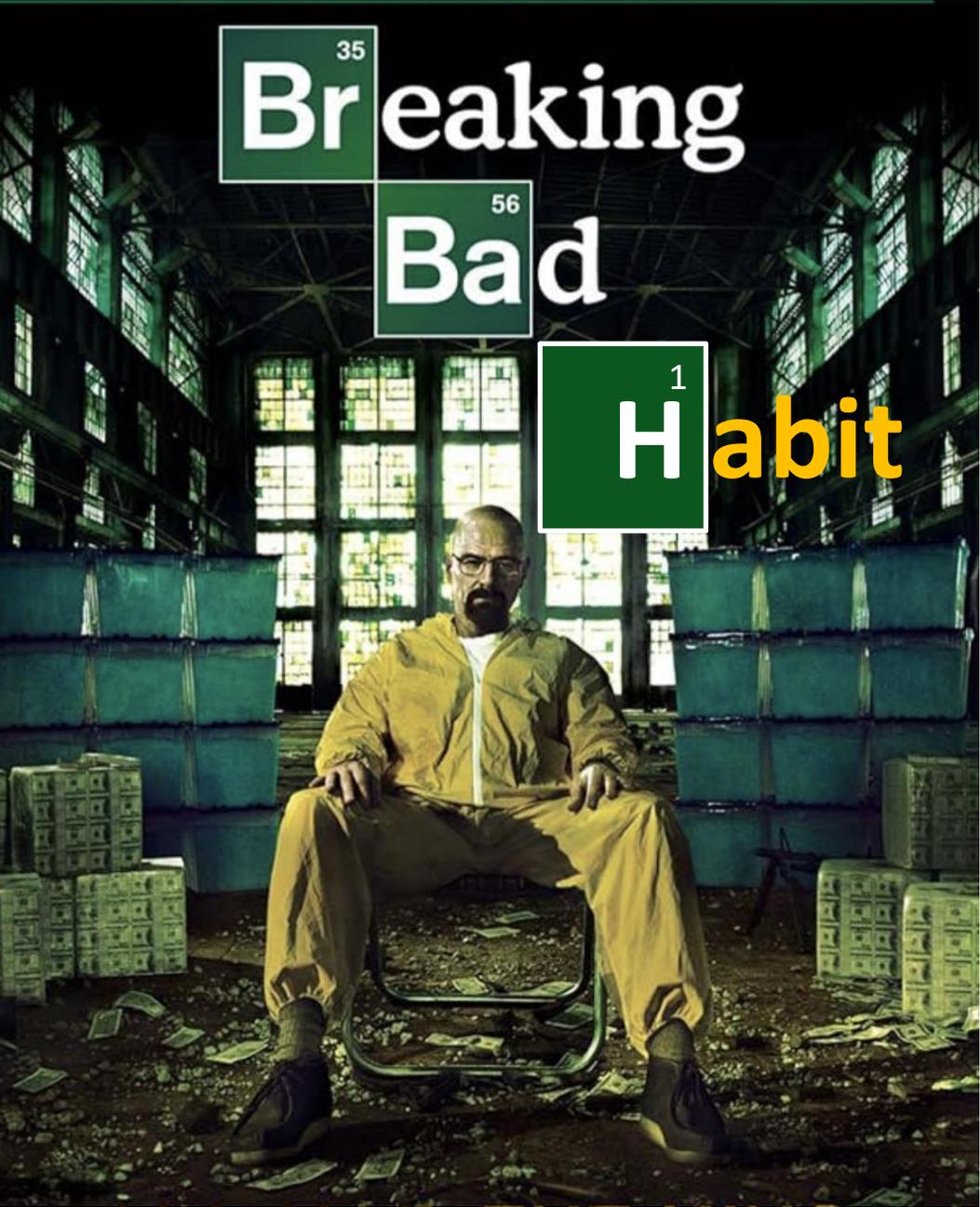
Disclosures

- I have nothing to disclose



fluid resuscitation
can have detrimental
effects.





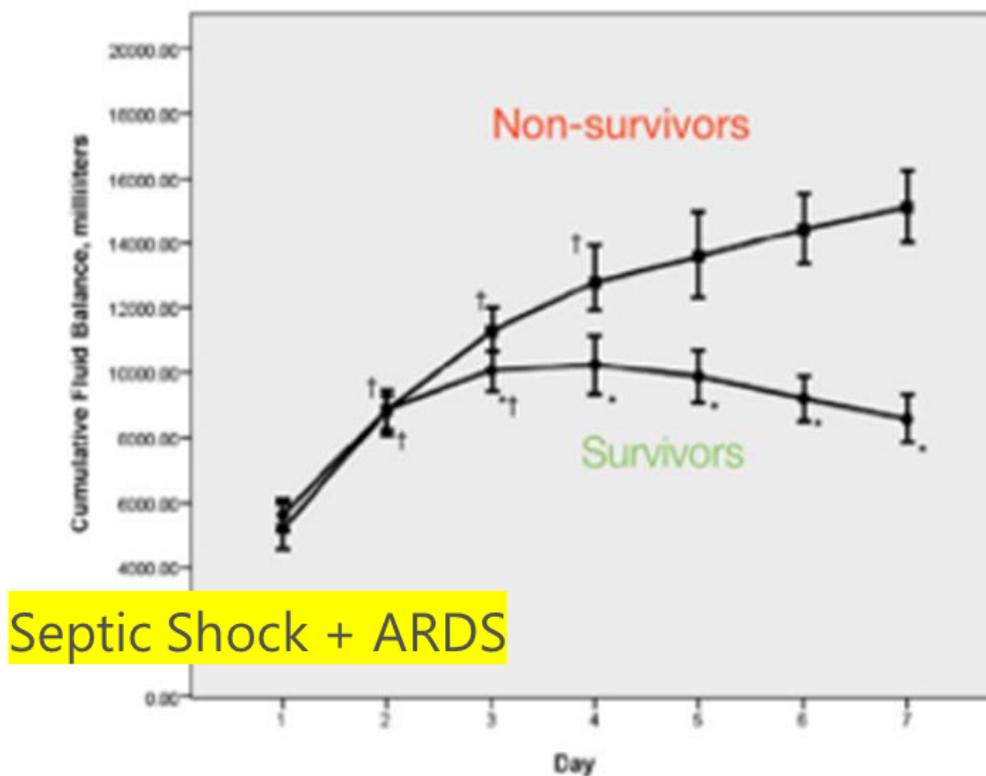
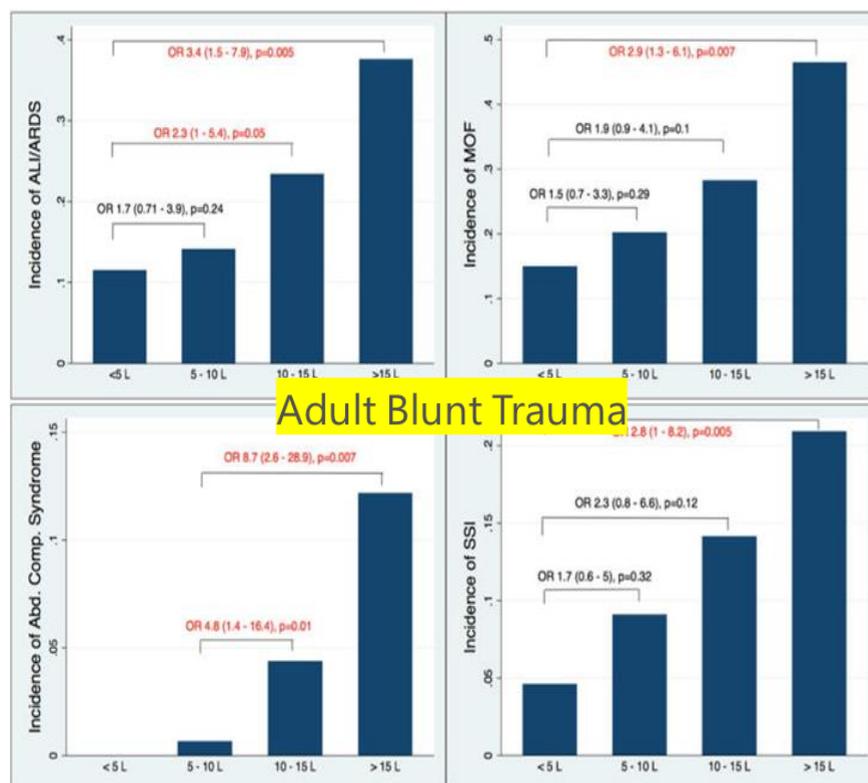
Definition

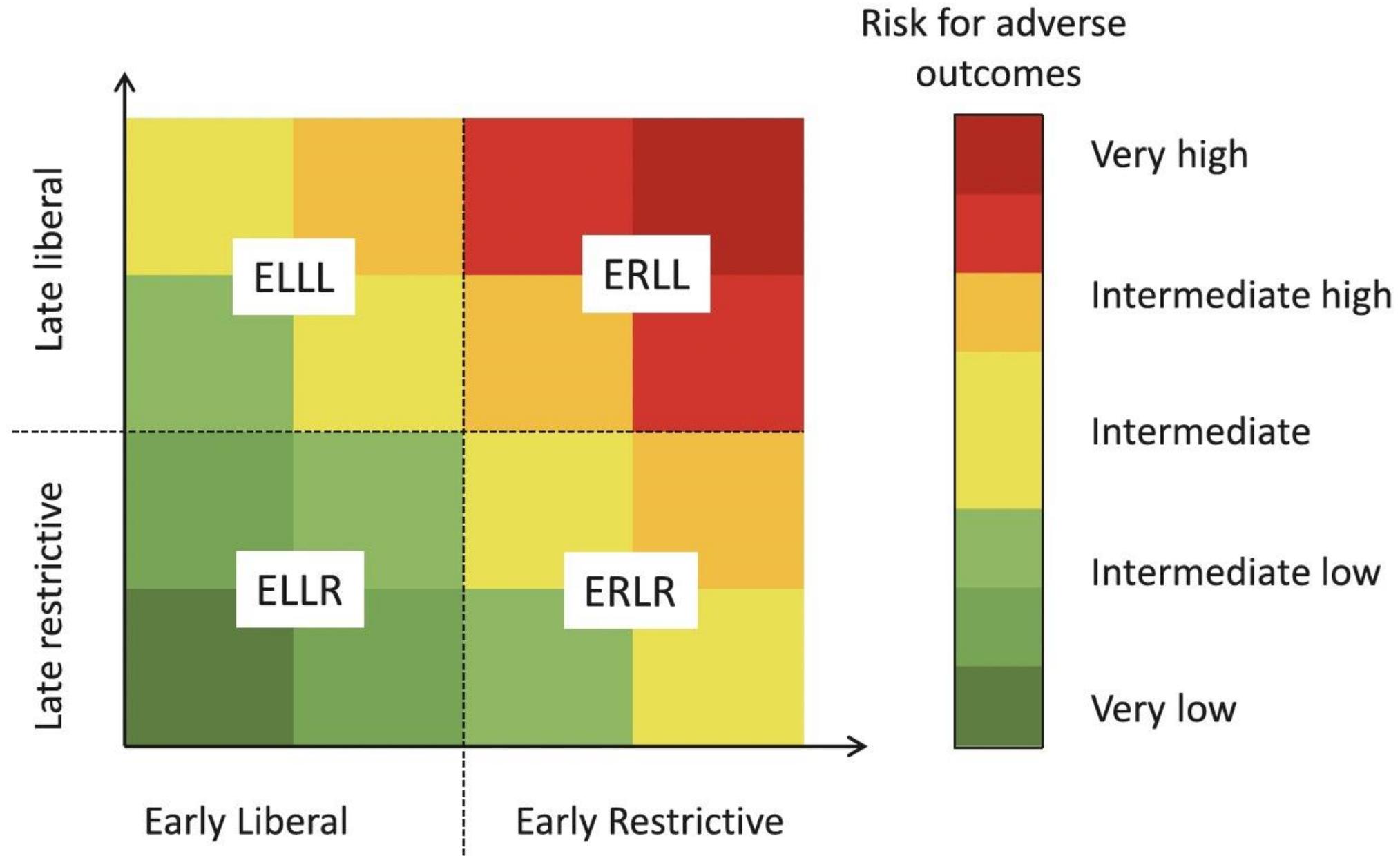
- **Fluid Overload:** Fluid intake > Output
> 10% increase in **weight** from baseline

$$\% \text{ Fluid overload} = ((\text{total fluid in} - \text{total fluid out}) / \text{admission body weight} \times 100)$$

- **Fluid Accumulation:** pathologic state of overhydration associated with clinical impact and worse outcomes which may vary depending on age, comorbidities and phase of illness.
- **Fluid Accumulation syndrome:** Fluid accumulation + negative impact on end-organ function.

Malbrain, et al. Intensive Care Med 48, 1781–1786 (2022).





Malbrain, et al. Intensive Care Med 48, 1781–1786 (2022).

Fluid Overload is associated with Increase Mortality

Fluid Overload and Mortality in Adult Critical Care Patients—A Systematic Review and Meta-Analysis of Observational Studies

Anna S. Messmer, MD¹; Carina Zingg¹; Martin Müller, MD^{1,3}; Joel Loic Gerber, MD¹; Joerg Christian Schefold, MD¹; Carmen Andrea Pfortmueller, MD¹

Messmer, A. et al. *CCM*. 2020;48(12):1862-70. PMID: 33009098

| | Relative Risk of Mortality: Adjusted (aRR) OR Unadjusted (uaRR) | 95% Confidence Intervals (# of trials) |
|------------------------------|--|---|
| FO at 3 days in ICU | aRR = 8.83 | 4.03-19.33 (n=1) |
| CFB at 3 days in ICU | aRR = 1.44 uaRR = 2.15 | 1.18-1.77 (n=4) 1.51-3.07 (n=6) |
| Peak FO at any time point | aRR = 2.79 | 1.55-5.00 (n=3) |
| Peak + CFB at any time point | aRR = 1.39 uaRR = 2.36 | 1.15-1.69 (n=5) 1.73-3.23 (n=7) |
| Per 1L increase in CFB | aRR = 1.19 | 1.11-1.28 (n=8) |
| FO in AKI | aRR = 1.99 | 1.34-2.98 (n=2) |
| FO in surgical patients | aRR = 6.17 | 4.81-7.97 (n=1) |
| CFB in sepsis | aRR = 1.66 | 1.39-1.98 (n=1) |
| CFB in AKI | aRR = 2.63 | 1.30-5.30 (n=1) |
| CFB in resp failure | aRR = 1.19 | 1.03-1.43 (n=1) |

A Positive Fluid Balance in the First Week Was Associated with Increased Long term Mortality

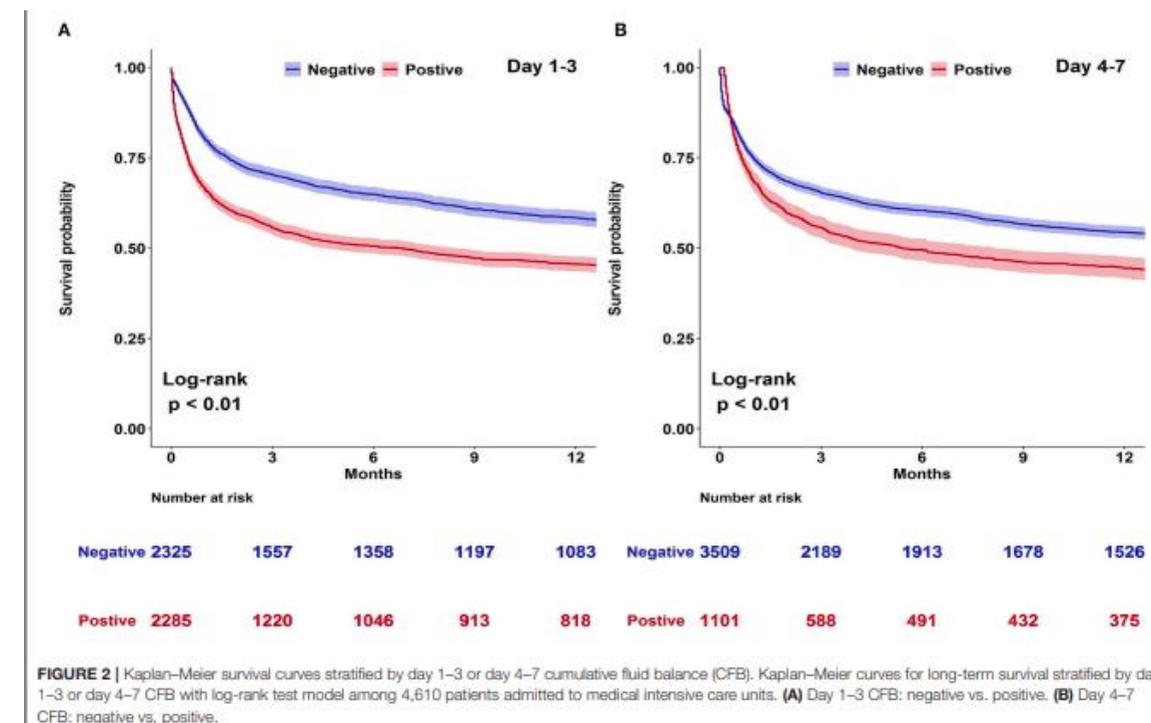
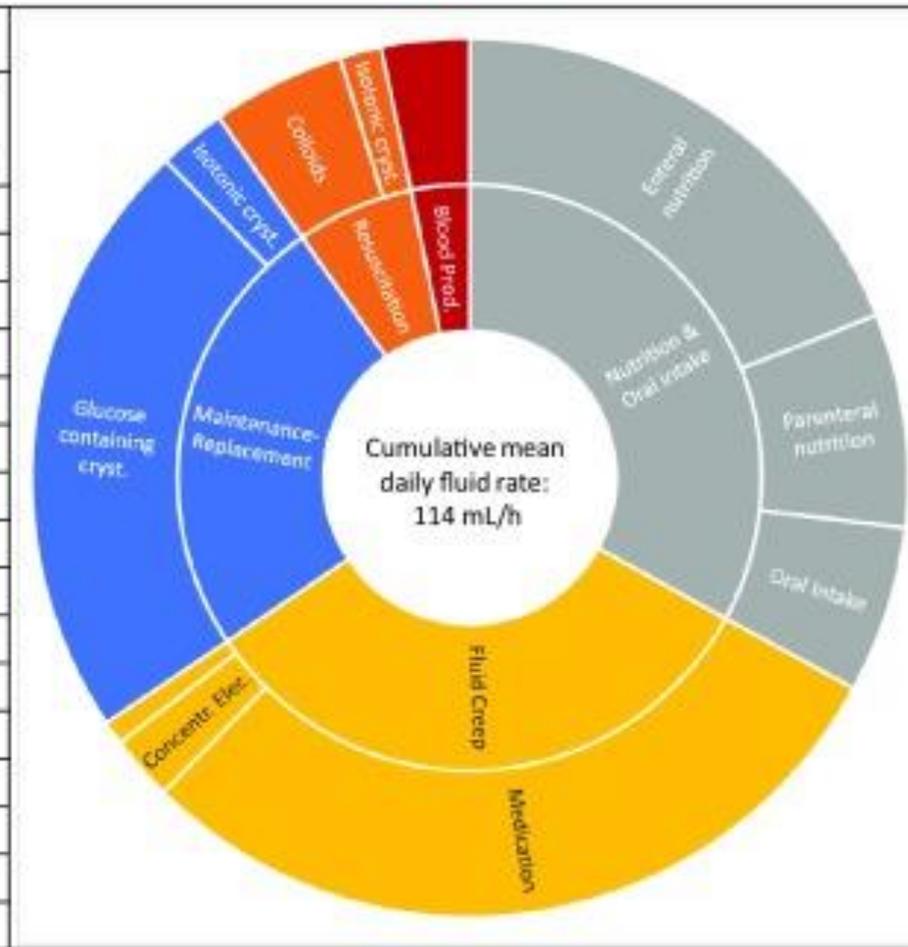


FIGURE 2 | Kaplan-Meier survival curves stratified by day 1–3 or day 4–7 cumulative fluid balance (CFB). Kaplan-Meier curves for long-term survival stratified by day 1–3 or day 4–7 CFB with log-rank test model among 4,610 patients admitted to medical intensive care units. **(A)** Day 1–3 CFB: negative vs. positive. **(B)** Day 4–7 CFB: negative vs. positive.

Fluid Overload

- **1970-2010: Swell to Get Well**

| Fluid Type | Volume | | | Sodium | Chloride |
|---|--------|--|---------------------------------------|------------------------------------|------------------------------------|
| | % | Mean daily fluid volume in mL \pm SD | Median daily fluid volume in mL (IQR) | Mean daily amount in mmol \pm SD | Mean daily amount in mmol \pm SD |
| Resuscitation fluids | 6.5% | 151 \pm 439 | 0 (0-100) | 21 \pm 63 | 17 \pm 49 |
| Isotonic crystalloids (rate >1L/6h) | 1.6% | 36 \pm 256 | 0 (0-0) | 5 \pm 36 | 4 \pm 28 |
| Colloids | 4.9% | 114 \pm 331 | 0 (0-98) | 16 \pm 48 | 13 \pm 37 |
| Blood products | 3.2% | 75 \pm 318 | 0 (0-0) | 11 \pm 48 | 7 \pm 29 |
| Maintenance and replacement fluids | 24.7% | 574 \pm 606 | 334 (150-894) | 68 \pm 78 | 79 \pm 78 |
| Glucose-containing crystalloids | 22.3% | 517 \pm 506 | 296 (150-812) | 59 \pm 65 | 73 \pm 70 |
| Isotonic crystalloids (rate \leq 1L/6h) | 2.5% | 57 \pm 273 | 0 (0-0) | 8 \pm 39 | 6 \pm 31 |
| Nutrition | 33.0% | 766 \pm 688 | 630 (0-1401) | | |
| Enteral nutrition | 19.0% | 441 \pm 593 | 0 (0-995) | 20 \pm 28 | 15 \pm 21 |
| Parenteral nutrition | 7.8% | 182 \pm 492 | 0 (0-0) | 0 \pm 0 ² | 0 \pm 0 ² |
| Oral fluid intake | 6.2% | 143 \pm 319 | 0 (0-150) | N/A | N/A |
| Fluid creep | 32.6% | 757 \pm 608 | 645 (308-1039) | | |
| Volume due to concentrated electrolytes | 2.4% | 56 \pm 62 | 42 (22-72) | 9 \pm 50 | 10 \pm 33 |
| Volume used to keep venous access open | 0.8% | 20 \pm 43 | 0 (0-28) | 3 \pm 7 | 3 \pm 8 |
| Intermittent and continuous medication | 29.3% | 681 \pm 580 | 565 (251-946) | N/A | N/A |
| Total amount | 100% | 2,322 \pm 1,315 | 2,296 (1,422-3,069) | 131 \pm 137 | 130 \pm 111 |



Conservative Vs. Liberal Fluid

The CLASSIC Trial

Conservative vs Liberal Approach to Fluid Therapy of Septic Shock in the Intensive Care

POINCARE-2

Fluid balance control in critically ill patients: results from POINCARE-2 stepped wedge cluster-randomized trial



Pierre-Edouard Bollaert¹, Alexandra Monnier², Francis Schneider³, Laurent Argaud⁴, Julio Badie⁵, Claire Charpentier⁶, Ferhat Meziani², Michel Bemer⁷, Jean-Pierre Quenot⁸, Marie Buzzi^{9,10*}, Hervé Outin¹¹, Cédric Bruel¹², Laurent Ziegler¹³, Sébastien Gibot¹, Jean-Marc Virion⁹, Camille Alleyrat⁹, Guillaume Louis¹⁴ and Nelly Agrinier^{9,10}

Abstract

Background In critically ill patients, positive fluid balance is associated with excessive mortality. The POINCARE-2 trial aimed to assess the effectiveness of a fluid balance control strategy on mortality in critically ill patients.

Methods POINCARE-2 was a stepped wedge cluster open-label randomized controlled trial. We recruited critically ill patients in twelve volunteering intensive care units from nine French hospitals. Eligible patients were ≥ 18 years old, under mechanical ventilation, admitted to one of the 12 recruiting units for > 48 and ≤ 72 h, and had an expected length of stay after inclusion > 24 h. Recruitment started on May 2016 and ended on May 2019. Of 10,272 patients screened, 1361 met the inclusion criteria and 1353 completed follow-up. The POINCARE-2 strategy consisted of a daily weight-driven restriction of fluid intake, diuretics administration, and ultrafiltration in case of renal replacement therapy between Day 2 and Day 14 after admission. The primary outcome was 60-day all-cause mortality. We considered intention-to-treat analyses in cluster-randomized analyses (CRA) and in randomized before-and-after analyses (RBAA).

Results A total of 433 (643) patients in the strategy group and 472 (718) in the control group were included in the CRA (RBAA). In the CRA, mean (SD) age was 63.7 (14.1) versus 65.7 (14.3) years, and mean (SD) weight at admission was 78.5 (20.0) versus 79.4 (23.5) kg. A total of 129 (160) patients died in the strategy (control) group. Sixty-day mortality did not differ between groups [30.5%, 95% confidence interval (CI) 26.2–34.8 vs. 33.9%, 95% CI 29.6–38.2, $p=0.26$]. Among safety outcomes, only hypernatremia was more frequent in the strategy group (5.3% vs. 2.3%, $p=0.01$). The RBAA led to similar results.

Conclusion The POINCARE-2 conservative strategy did not reduce mortality in critically ill patients. However, due to open-label and stepped wedge design, intention-to-treat analyses might not reflect actual exposure to this strategy, and further analyses might be required before completely discarding it.

Trial registration POINCARE-2 trial was registered at ClinicalTrials.gov (NCT02765009). Registered 29 April 2016.

Keywords Critical care, Water-electrolyte balance, Clinical trial, Complex intervention

Restriction of Intravenous Fluid in ICU Patients with Septic Shock

Meyhoff TS et al. DOI: 10.1056/NEJMoa2202707

CLINICAL PROBLEM

Intravenous fluids are recommended to improve circulation in patients with septic shock. However, higher fluid volumes have been associated with harms, including respiratory failure and death, in such patients. Whether restriction of intravenous fluids would benefit patients with septic shock is uncertain.

CLINICAL TRIAL

Design: An international, open-label, randomized trial evaluated the effects of intravenous fluid restriction on outcomes in adult patients with septic shock who were in the intensive care unit (ICU).

Intervention: 1554 patients who had already received at least 1 liter of intravenous fluids were randomly assigned, within 12 hours after shock onset, to receive either restrictive intravenous therapy (administered only in response to specifically defined clinical variables) or standard intravenous fluid therapy (without restrictions) until ICU discharge (maximum, 90 days). The primary outcome, death by day 90 after randomization, was assessed in 1545 patients.

RESULTS

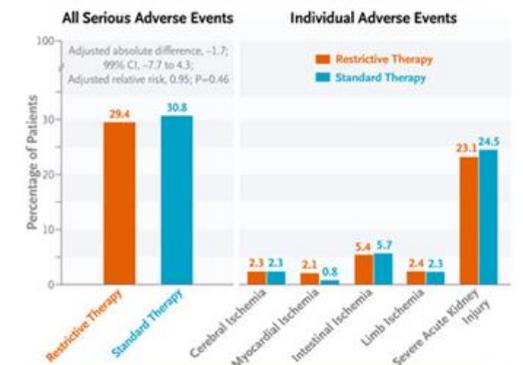
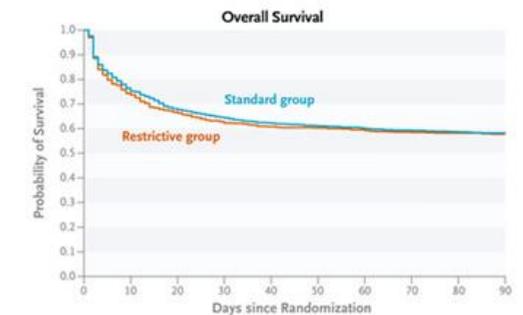
Efficacy: The median cumulative volume of intravenous fluids (excluding those given with medication or nutrition) was 1798 ml in the restrictive-fluid group and 3811 ml in the standard-fluid group. The percentage of patients who died by day 90 did not differ between the groups.

Safety: The percentage of patients with at least one serious adverse event was similar in the two groups.

LIMITATIONS AND REMAINING QUESTIONS

- Patients and personnel were aware of the group assignments.
- Protocol violations occurred, and most fluid was given outside the volumes specified by the protocol.
- Data on some co-interventions and hemodynamic factors were not collected.

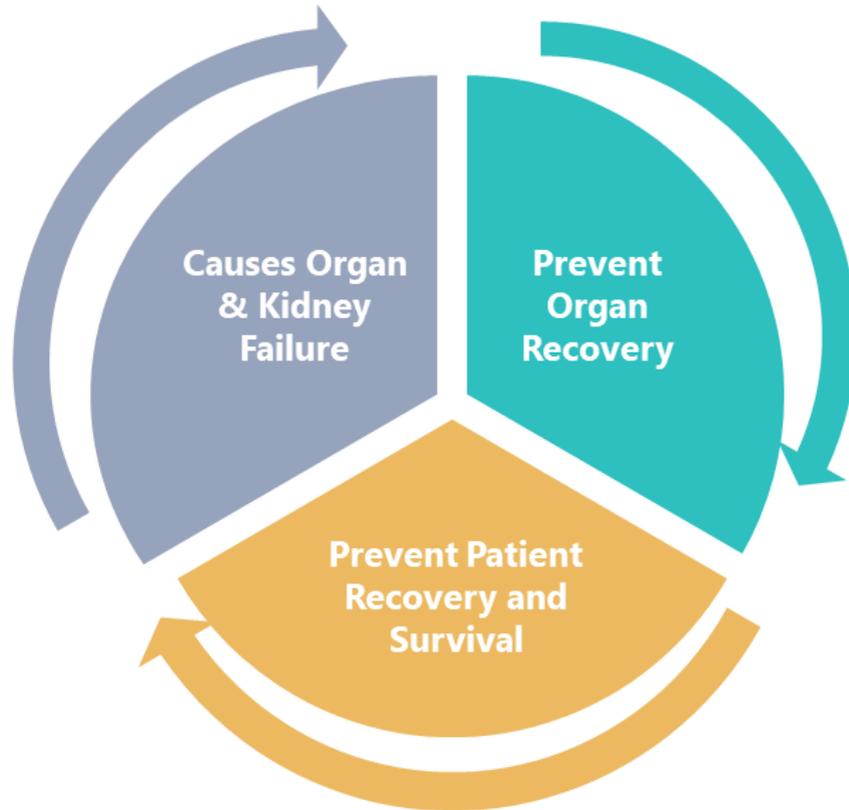
Links: Full Article | NEJM Quick Take | Editorial



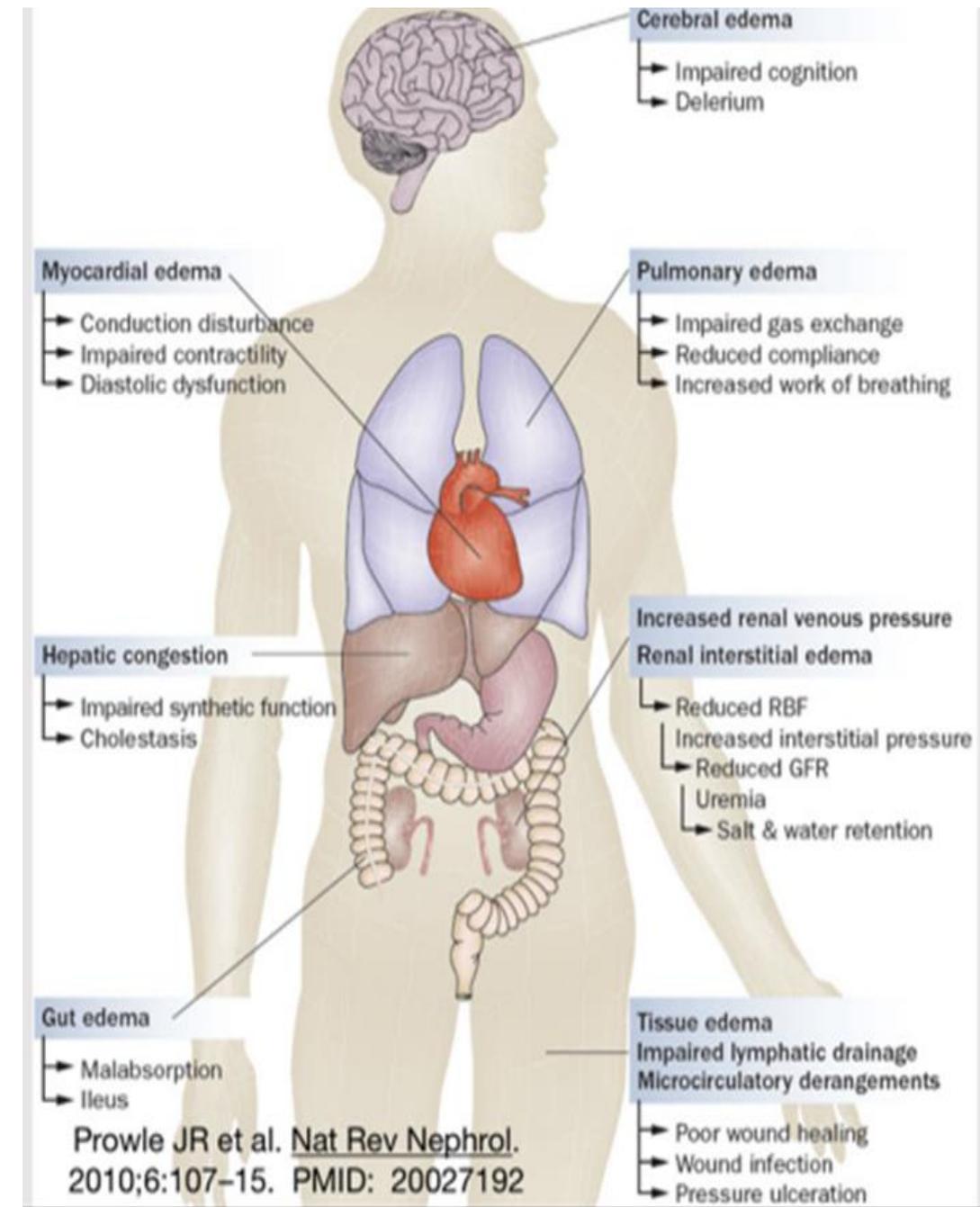
CONCLUSIONS

Among adult patients with septic shock who were in the ICU, intravenous fluid restriction did not result in fewer deaths at 90 days than standard intravenous fluid therapy.

Pathophysiology

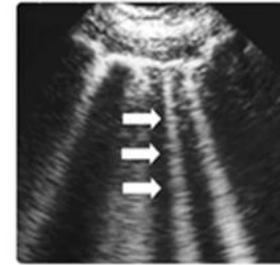


Effects of Venous Congestion & Fluid Overload



Measurement

- Change in daily body weight
- Urine output
- Daily Fluid Balance and cumulative fluid balance
- Point of Care Ultrasound: check Inferior vena cava collapsibility index, Lung ultrasound



Lung comet tail image. 'B lines' also known as comet-tail images are a marker of pulmonary edema. In the presence of extravascular lung water the reflection of the ultrasound beam on the sub-pleural interlobular septa thickened by edema creates comet-tail reverberation artifacts. The ultrasound appearance is of a vertical, discrete, hyperechoic image that arises from the pleural line and extends to the bottom of the screen moving synchronously with the respiration (white arrows)

- EVLWI: Extravascular Lung Water Index
- IAP: Intraabdominal pressure and APP abdominal Perfusion Pressure
- Capillary Leak Index: C reactive protein (mg/dl) over albumin (g/l) x 100
- Bio-electrical impedance analysis
- CXR: check for B lines, pleural effusions.

Fluid Over Load
Fluid Accumulation
Prevention

Fluid Stewardship: 4 D's

Right Drug

Right Dose

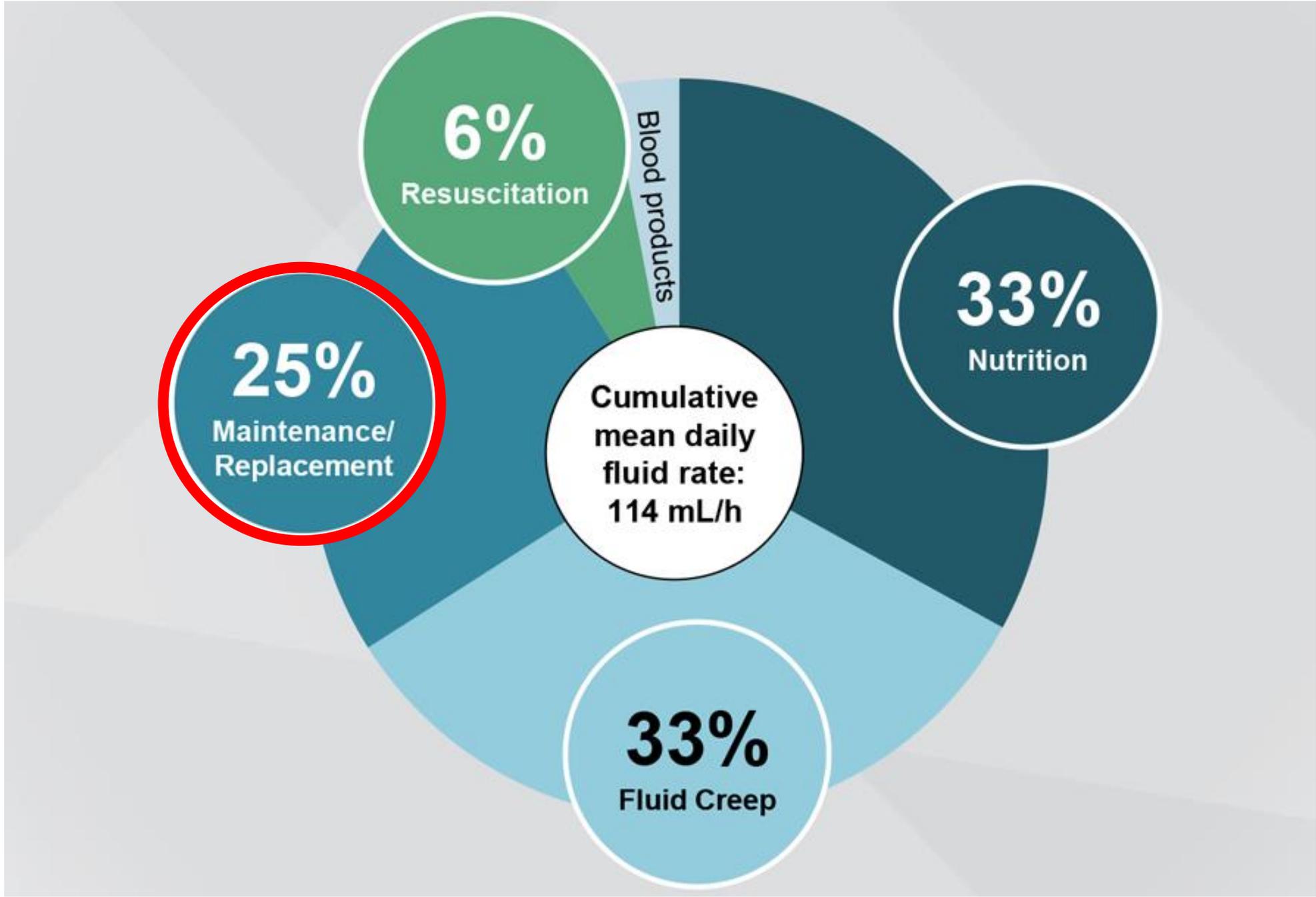
Right Duration

De-escalation

Maintenance fluids

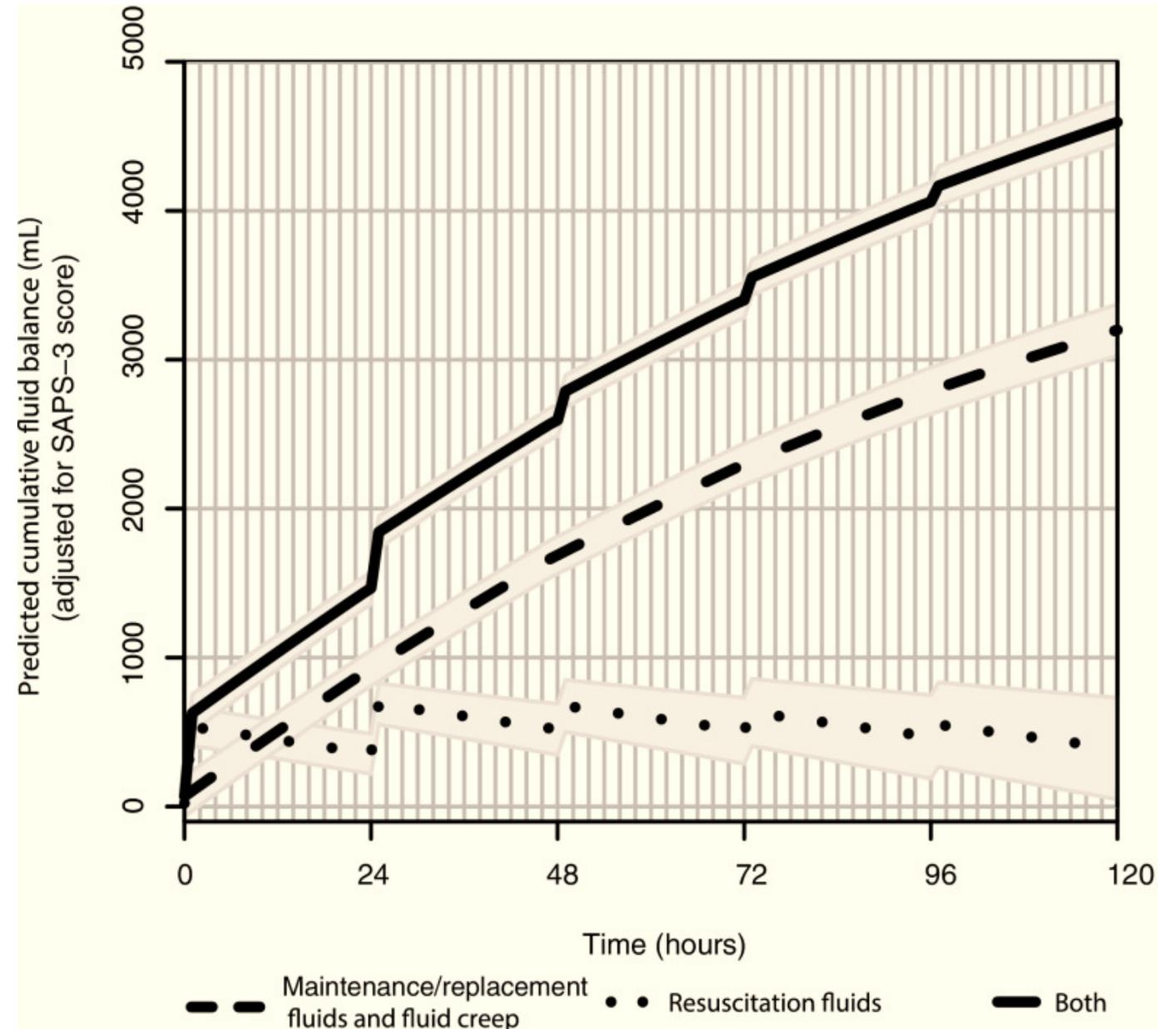
- **Few data on maintenance fluids in critically ill adults**
- **Postoperative period:**
May be losses should be replenished with colloids and free water given in smaller amounts
- **Maintenance probably unnecessary in critically ill patient**





Maintenance fluids

Van Regenmortel N, Verbrugghe W, Roelant E, Van den Wyngaert T, Jorens PG. Maintenance fluid therapy and fluid creep impose more significant fluid, sodium, and chloride burdens than resuscitation fluids in critically ill patients: a retrospective study in a tertiary mixed ICU population. *Intensive Care Med.* 2018 Apr;44(4):409-417.



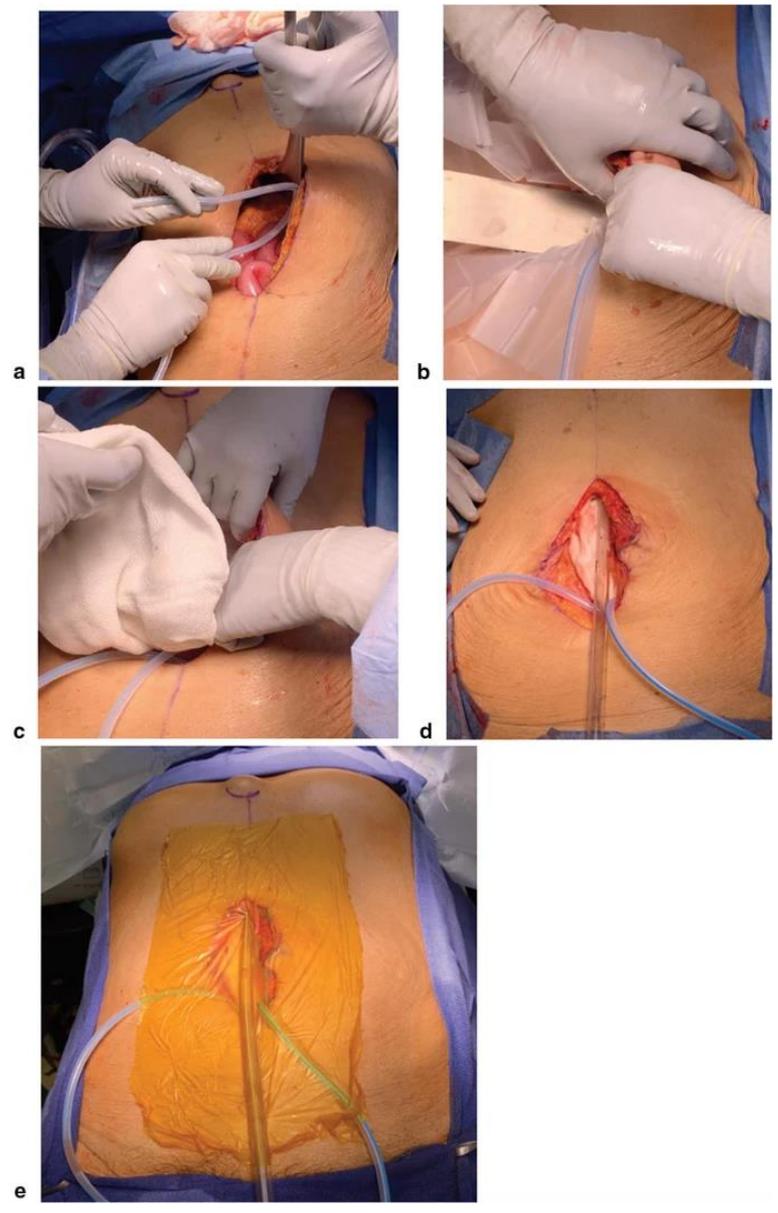
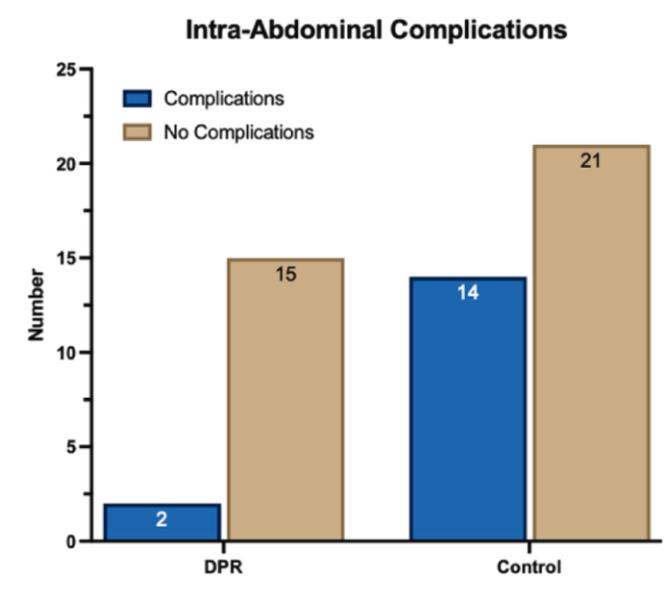
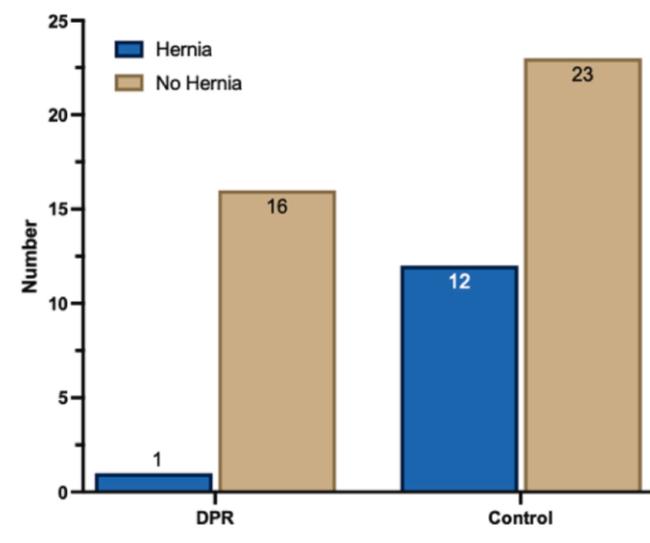
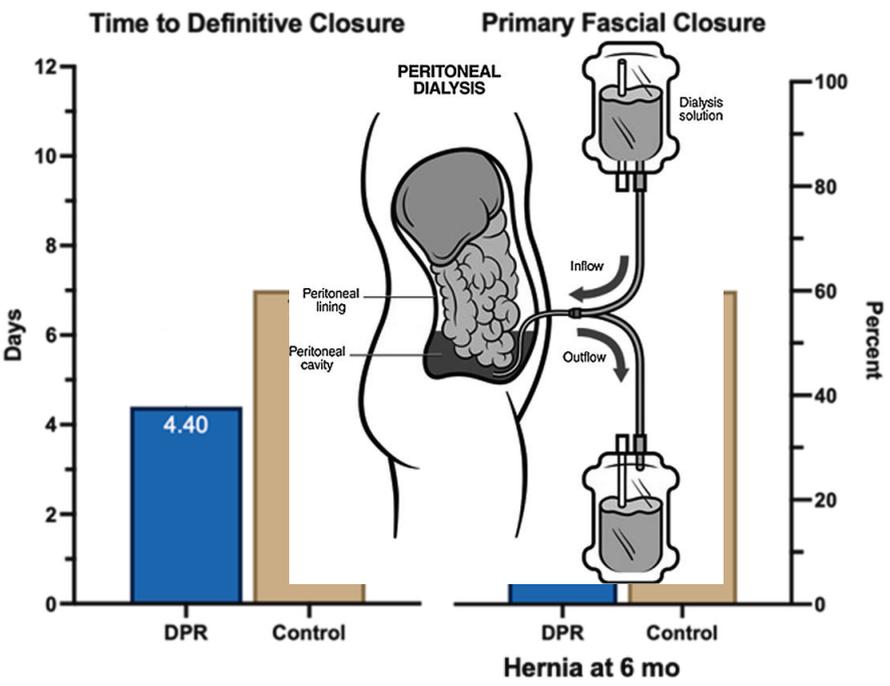
Permissive Oliguria

- Almost all major surgeries are performed under physiological antidiuretic state. Reflex vasoconstriction, mediated neuroendocrine response, trauma, blood loss, insensitve fluid loss. Urine output criterion is not applicable in the operating room.

Mendes RS, Suassuna J. Perioperative oliguria: adequate physiological response or risk for acute kidney injury? J Bras Nefrol. 2021 Jan-Mar;43(1):1-2. doi: 10.1590/2175-8239-JBN-2020-E001.

- Is 0.3 ml/kg/hour output the new 0.5?

Direct Peritoneal Resuscitation



Kim W, Tesoriero R, Stein D. W J Surg 44, 2982-2984.

Hypertonic Saline Solution in Resuscitation

- Immediate intravascular volume expansion via delivery of small volume of fluid
- 7.5% HTS – Tachycardia, 50% lower volume compared to LRS

Han, Juan; Ren, Hui-Qin; Zhao, Qing-Bo; Wu, You-Liang; Qiao, Zhuo-Yi. Comparison of 3% and 7.5% Hypertonic Saline in Resuscitation After Traumatic Hypovolemic Shock. Shock 43(3):p 244-249, March 2015. | DOI: 10.1097/SHK.0000000000000303

| | n (%) | | |
|-----------------------|--------------------|----------------------|-----------------|
| | 3% HSS (n = 82) | 7.5% HSS (n = 80) | LRS (n = 84) |
| Tachycardia | 5 (6.1) | 22 (27.5)* | 4 (4.8) |
| Coagulopathy | 0 | 2 (2.5) | 9 (10.7)* |
| Acute renal failure | 0 | 0 | 5 (6.0)* |
| Pulmonary edema | 0 | 0 | 4 (4.8)* |
| Anaphylaxis | 0 | 0 | 0 |
| Heart failure | 1 (1.2) | 1 (1.3) | 2 (2.4) |
| Transient hypotension | 0 | 4 (5.0)* | 0 |
| ARDS | 1 (1.2) | 1 (1.3) | 3 (3.6) |
| MODS | 2 (2.4) | 1 (1.3) | 3 (3.6) |
| Total | 9 (10.9) | 31 (38.8) | 30 (35.7) |

*Significant difference between groups ($P < 0.05$).

Hypertonic Saline Solution following Emergent Laparotomy & Temporary Abdominal Closure

| Outcomes | All patients n = 189 | HTS n = 36 | No HTS n = 153 | p |
|--------------------------------------|-------------------------|------------------|-------------------|--------|
| Primary fascial closure ^a | 151 (80%) | 33 (92%) | 118 (77%) | 0.063 |
| Days to fascial closure | 1.6 [1.1-2.8] | 1.5 [1.1-2.1] | 1.7 [1.1-3.3] | 0.202 |
| Peak sodium ^b (mEq/L) | 149 [145-153] | 150 [147-155] | 149 [145-152] | 0.093 |
| Peak chloride ^b (mEq/L) | 114 [109-117] | 115 [111-118] | 113 [109-117] | 0.134 |
| Peak creatinine ^b (mg/dL) | 1.4 [1.0-2.4] | 1.3 [1.0-1.8] | 1.5 [1.0-2.5] | 0.189 |
| Fascial dehiscence | 9 (5%) | 1 (3%) | 8 (5%) | >0.999 |
| Intra-abdominal abscess | 24 (13%) | 6 (17%) | 18 (12%) | 0.413 |
| Dialysis during admission | 26 (14%) | 4 (11%) | 22 (14%) | 0.790 |
| Discharged on dialysis | 22 (12%) | 3 (8%) | 19 (12%) | 0.772 |
| Hospital length of stay (days) | 18.8 [11.5-30.7] | 19.1 [13.1-31.4] | 18.8 [11.1-30.7] | 0.834 |
| ICU length of stay (days) | 10.0 [4.0-18.0] | 11.0 [4.0-18.0] | 10.0 [4.0-19.0] | 0.988 |
| ICU-free days | 7.2 [3.7-14.5] | 8.7 [3.6-16.3] | 7.2 [3.7-14.1] | 0.651 |
| Ventilator days | 7.0 [3.0-14.0] | 6.0 [3.0-10.5] | 7.0 [3.0-16.0] | 0.240 |
| Discharge disposition | | | | |
| Home | 69 (37%) | 16 (44%) | 53 (35%) | 0.336 |
| Subacute nursing facility | 27 (14%) | 6 (17%) | 21 (14%) | 0.605 |
| Long term care facility | 26 (14%) | 5 (14%) | 21 (14%) | >0.999 |
| Inpatient rehabilitation | 12 (6%) | 1 (3%) | 11 (7%) | 0.468 |
| Another hospital | 11 (6%) | 4 (11%) | 7 (5%) | 0.226 |
| Hospice | 11 (6%) | 0 (0%) | 11 (7%) | 0.128 |
| Inpatient mortality | 33 (17%) | 4 (11%) | 29 (19%) | 0.335 |



Hypertonic Saline Solution

| Study or Subgroup | Hypertonic | | Control | | Weight | Odds Ratio M-H, Random, 95% CI |
|---|------------|-------|---------|-------|--------|-----------------------------------|
| | Events | Total | Events | Total | | |
| 1. Hypertonic saline / dextran (HSD) | | | | | | |
| Bulger 2008 | 78 | 110 | 77 | 99 | 15.2% | 0.70 [0.37, 1.30] |
| Bulger 2011 | 164 | 220 | 279 | 376 | 25.2% | 1.02 [0.70, 1.49] |
| Holcroft 1989 | 20 | 29 | 12 | 31 | 6.9% | 3.52 [1.21, 10.24] |
| Morrison 2011 | 35 | 50 | 42 | 57 | 10.0% | 0.83 [0.36, 1.94] |
| Subtotal (95% CI) | | 409 | | 563 | 57.3% | 1.06 [0.64, 1.77] |

Total events

297

410

Heterogeneity: $\tau^2 = 0.14$; $\chi^2 = 6.79$, $df = 3$ ($P = 0.08$); $I^2 = 56\%$ 1 HSD

Test for overall effect: $Z = 0.24$ ($P = 0.81$)

2. Hypertonic saline (HS)

| | | | | | | |
|-------------------|-----|-----|-----|-----|-------|-------------------|
| Bulger 2011 | 187 | 256 | 279 | 376 | 26.3% | 0.94 [0.66, 1.35] |
| Younes 2002 | 74 | 101 | 71 | 111 | 16.5% | 1.54 [0.86, 2.78] |
| Subtotal (95% CI) | | 357 | | 487 | 42.7% | 1.14 [0.71, 1.83] |

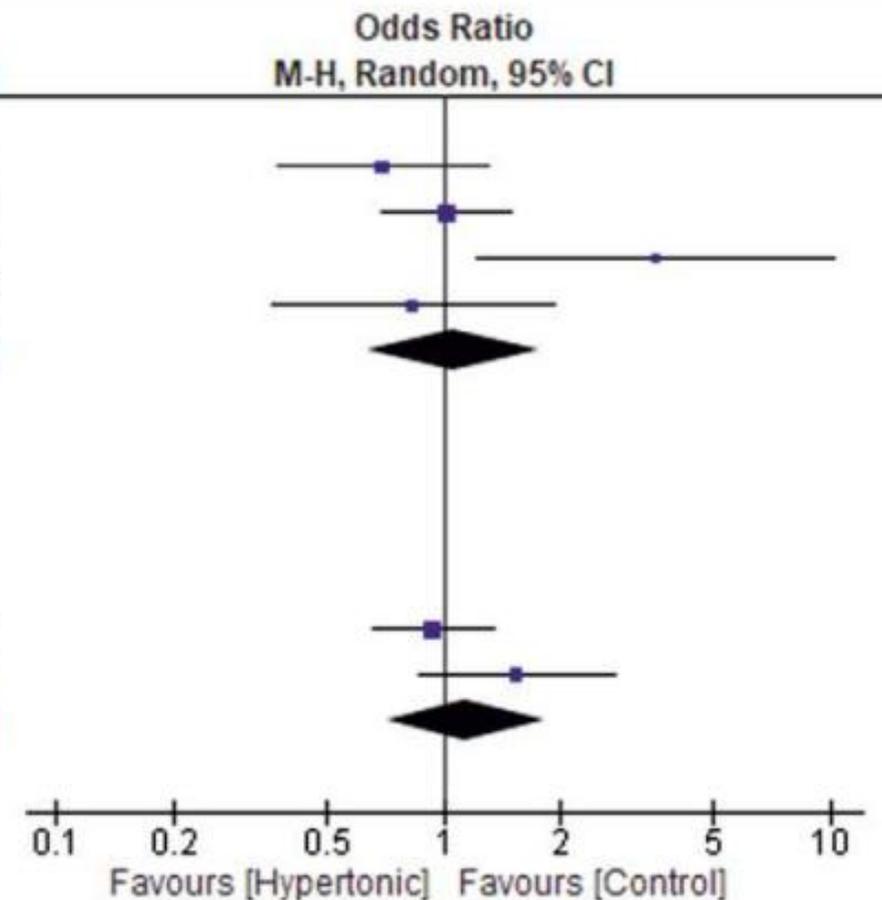
Total events

261

350

Heterogeneity: $\tau^2 = 0.06$; $\chi^2 = 1.98$, $df = 1$ ($P = 0.16$); $I^2 = 49\%$

Test for overall effect: $Z = 0.54$ ($P = 0.59$)



Hypertonic Saline Solution

García *et al.*
World Journal of Emergency Surgery (2023) 18:4
<https://doi.org/10.1186/s13017-023-00475-x>

World Journal of
Emergency Surgery

RESEARCH

Open Access

Hypertonic saline infusion does not improve the chance of primary fascial closure after damage control laparotomy: a randomized controlled trial



Alberto F. García^{1,2,3,4*}, Ramiro Manzano-Nunez^{5,6,7}, Diana Cristina Carrillo³, Julian Chica-Yanten³, María Paula Naranjo^{3,11}, Álvaro I. Sánchez^{1,3}, Jorge Humberto Mejía², Gustavo Adolfo Ospina-Tascón^{2,9}, Carlos A. Ordoñez^{1,2,4}, Juan Gabriel Bayona¹⁰ and Juan Carlos Puyana⁸

Abstract

Background Previous observational studies showed higher rates of abdominal wall closure with the use of hypertonic saline in trauma patients with abdominal injuries. However, no randomized controlled trials have been performed on this matter. This double-blind randomized clinical trial assessed the effect of 3% hypertonic saline (HS) solution on primary fascial closure and the timing of abdominal wall closure among patients who underwent damage control laparotomy for bleeding control.

Methods Double-blind randomized clinical trial. Patients with abdominal injuries requiring damage control laparotomy (DCL) were randomly allocated to receive a 72-h infusion (rate: 50 mL/h) of 3% HS or 0.9 N isotonic saline (NS) after the index DCL. The primary endpoint was the proportion of patients with abdominal wall closure in the first seven days after the index DCL.

Results The study was suspended in the first interim analysis because of futility. A total of 52 patients were included. Of these, 27 and 25 were randomly allocated to NS and HS, respectively. There were no significant differences in the rates of abdominal wall closure between groups (HS: 19 [79.2%] vs. NS: 17 [70.8%]; $p = 0.71$). In contrast, significantly higher hypernatremia rates were observed in the HS group (HS: 11 [44%] vs. NS: 1 [3.7%]; $p < 0.001$).

Conclusion This double-blind randomized clinical trial showed no benefit of HS solution in primary fascial closure rates. Patients randomized to HS had higher sodium concentrations after the first day and were more likely to present hypernatremia. We do not recommend using HS in patients undergoing damage control laparotomy.

Trial registration The trial protocol was registered in clinicaltrials.gov (identifier: NCT02542241).

Keywords Damage control surgery, Abdominal injuries, Hypertonic saline, Trauma and injuries

Fluid Over Load

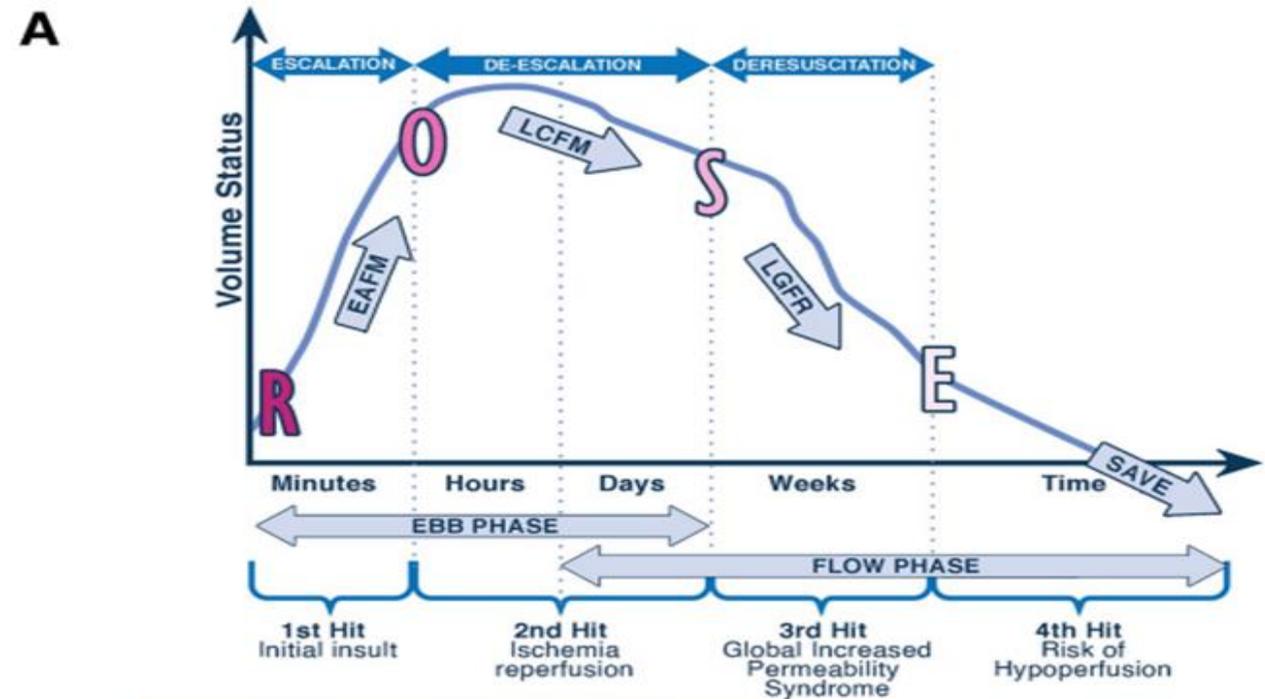
Treatment

#Deresuscitation

Active fluid removal in patient with fluid overload using drugs or UF.

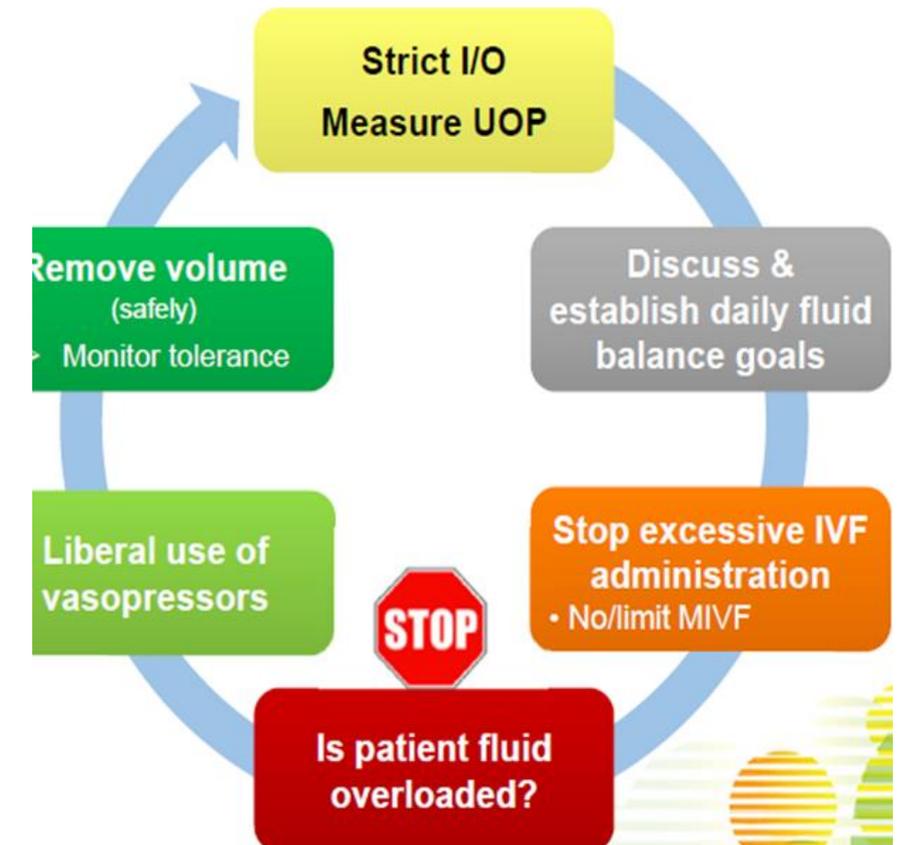
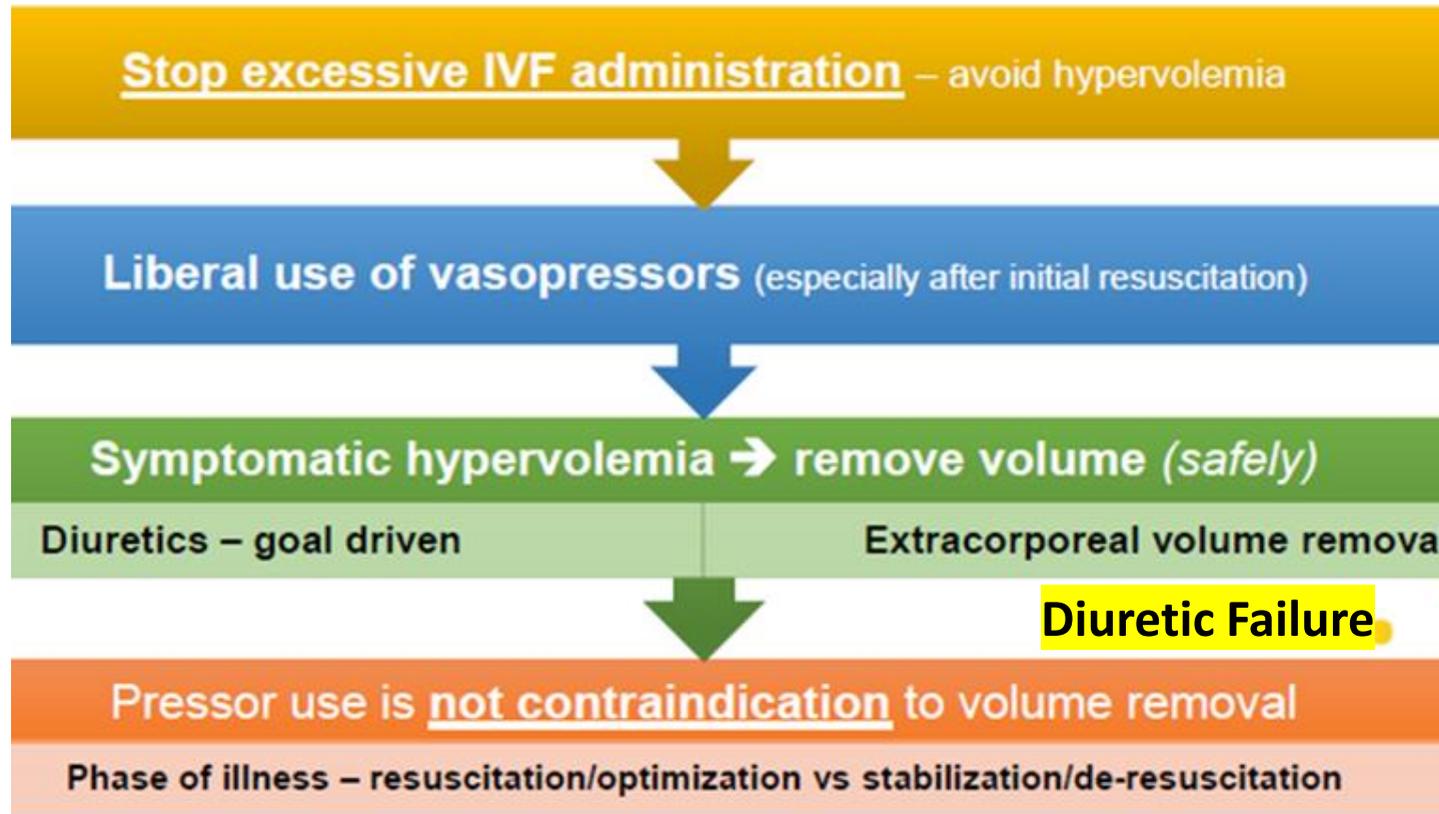
De-escalation

Reducing the amount of previously started fluid administration



| | | |
|----------|--|---|
| R | <p>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.</p> | <p>Triggers to start IV fluids: shock</p> <ul style="list-style-type: none"> • MAP < 65mmHg • GEDVI < 640ml/m² • (RVEDVI < 80ml/m²)# • (CVP < 8mmHg)* • (PAOP < 10mmHg)* • CI < 2,5L/min/m² • PPV or SVV > 12-15% • PLR test positive • Lactate > 3mmol/L (shock) • IVCCI > 50% |
| O | <p>Optimization phase with focus on organ rescue (maintenance) and avoiding fluid overload (fluid creep). Aiming for neutral fluid balance.</p> | <p>Triggers to stop IV fluids: unresponsiveness</p> <ul style="list-style-type: none"> • MAP/APP > 65/55mmHg • GEDVI 640-800ml/m² • CI > 2,5 L/min/m² • PPV or SVV < 12% • PLR test negative • Normal lactate < 2mmol/L • LVEDAI 8-12cm²/m² • IAP < 15mmHg |
| S | <p>Stabilization phase with focus on organ support (homeostasis). Late conservative fluid management (LCFM) is defined as two consecutive negative FB within 1st week after initial insult.</p> | <p>Triggers to start fluid removal: FAS/GIPS</p> <ul style="list-style-type: none"> • MAP/APP > 65/55mmHg • GEDVI > 850ml/m² • EVLWI > 10-12ml/kg PBW • PVPI > 3 and PF ratio < 150 • PPV or SVV < 12% • PLR test negative • LVEDAI > 14cm²/m², high VExUS score • IAP > 12-15mmHg • COP < 16-18mmHg; CLI > 60 • BIA: ECW/ICW > 1; V_E > 5% |
| E | <p>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.</p> | <p>Triggers to stop fluid removal: hypoperfusion</p> <ul style="list-style-type: none"> • MAP/APP < 55/45mmHg** • PPV or SVV > 15% • PLR test positive • Lactate > 2,5mmol/L • S_vO₂ < 70-75% • S_{cr}O₂ < 65-70% • ICG PDR < 14-16% |

Management of Fluid Overload



Conclusion

- **1970-2010: Swell to Get Well**
- **Present and Future: Pee to be Free of the ICU**
- Measure, measure and measure
- Fluid Stewardship
- Permissive oliguria
- Direct peritoneal resuscitation
- Hypertonic saline solution ?
- #Deresuscitation Protocol

CONFIDENCE TRIAL: completion by end December 2024

Blok et al. *Trials* (2023) 24:226
<https://doi.org/10.1186/s13063-023-07171-w>

Trials

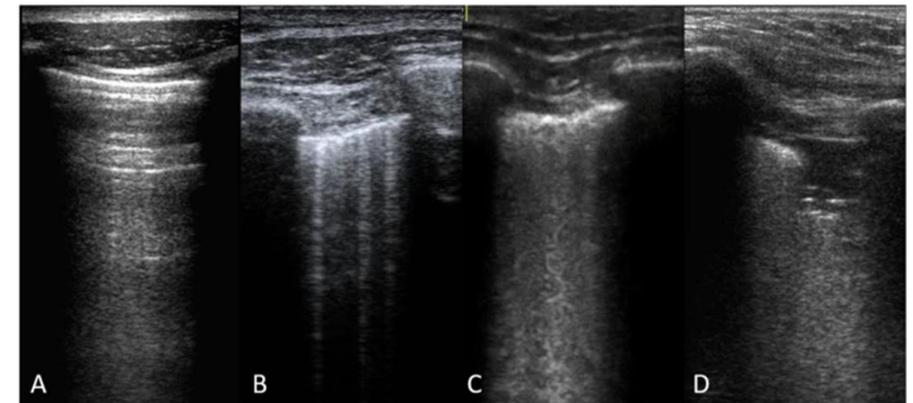
STUDY PROTOCOL

Open Access



Effect of lung ultrasound-guided fluid deresuscitation on duration of ventilation in intensive care unit patients (CONFIDENCE): protocol for a multicentre randomised controlled trial

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Thank You