Tekutiny v léčbě šokových stavů (SOSD, RACE)

Vladimír Šrámek

ARK, FNUSA

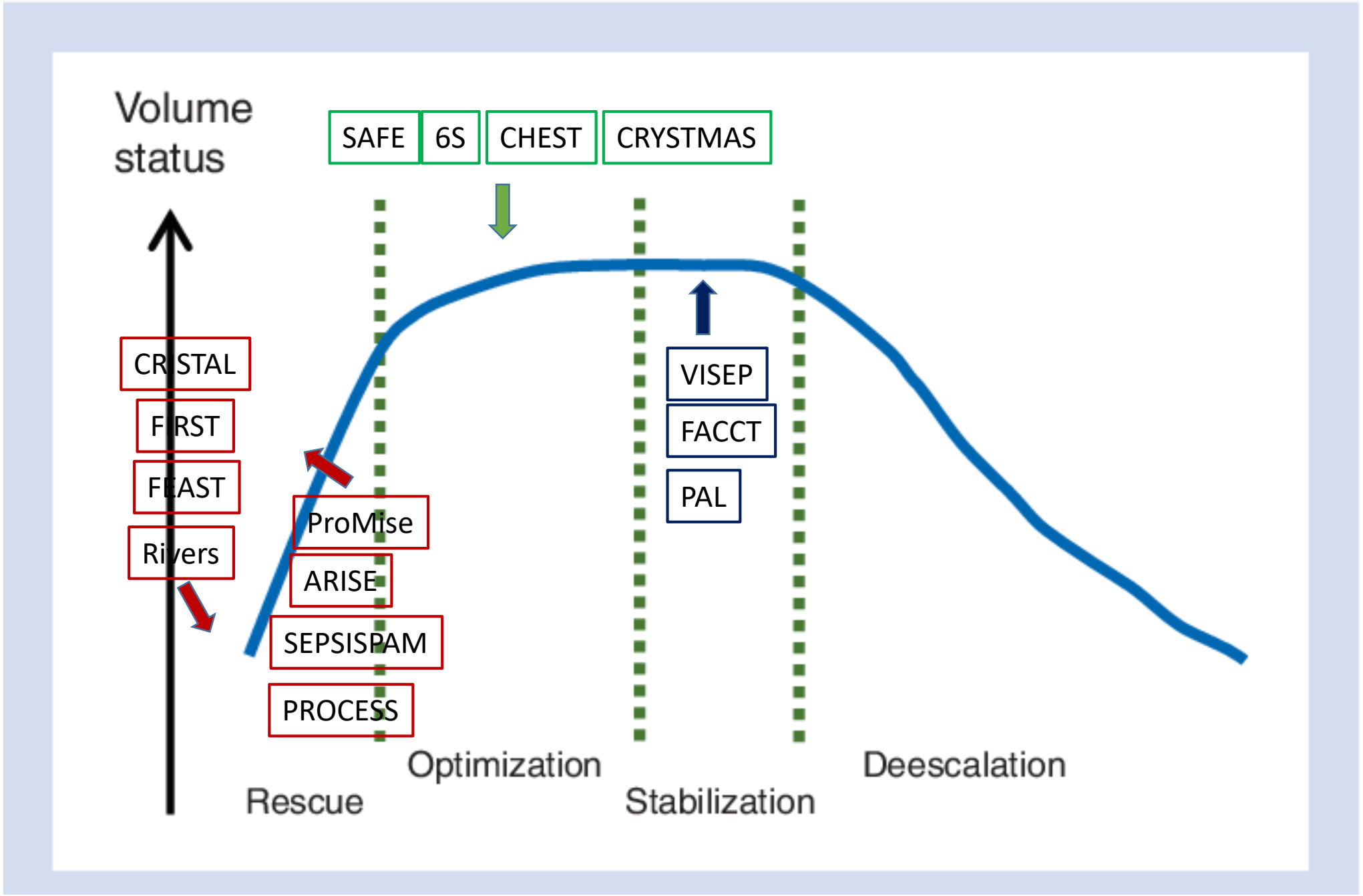
12. kongres ČSIM
Brno, 20.-22. červen 2018

nemám střet zájmů

struktura přednášky

- S alvage
- O ptimisation
- S tabilisation
- D e-escalation

- R esuscitation
- O ptimisation
- S tabilisation
- E limination


Volume status
SAFE
6S
CHEST
CRYSTMAS
CRISTAL
FIRST
FEAST
Rivers
ProMise
ARISE
SEPSISPAM
PROCESS
VISEP
FACCT
PAL
Rescue
Optimization
Stabilization
Deescalation
min
hrs
days
up to weeks

salvage

- Velikost bolusu
- Rychlost bolusu
- Podle čeho se orientuji
- Iniciální bolus nemusí být to pravé (reaguje jen 2/3 nemocných, nejnemocnější spíše ne, studie z Afriky, REFRESH studie)
- Early NA

bolus tekutiny

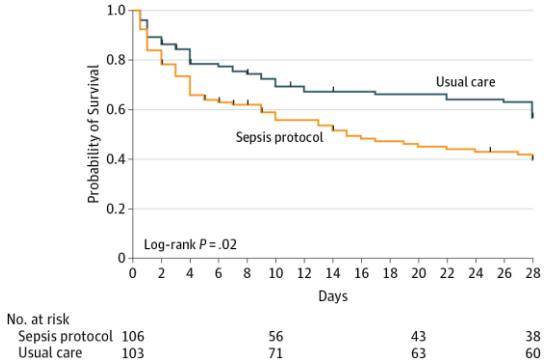
Maitland et al. BMC Medicine 2013, 11:68
http://www.biomedcentral.com/1741-7015/11/68

BMC Medicine

RESEARCH Open Access

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

Kathryn Maitland[1,2*], Elizabeth C George[3], Jennifer A Evans[4], Sarah Kiguli[5], Peter Olupot-Olupot[6], Samuel O Akech[2],



RIVERS: 20-30ml/kg během 30 min

ProCESS: během studie změněno na 1000ml nebo více během 30 min

2L+2L (1+4hrs) vs < 2L/6hrs

ARISE: 1000 ml během 60 minut

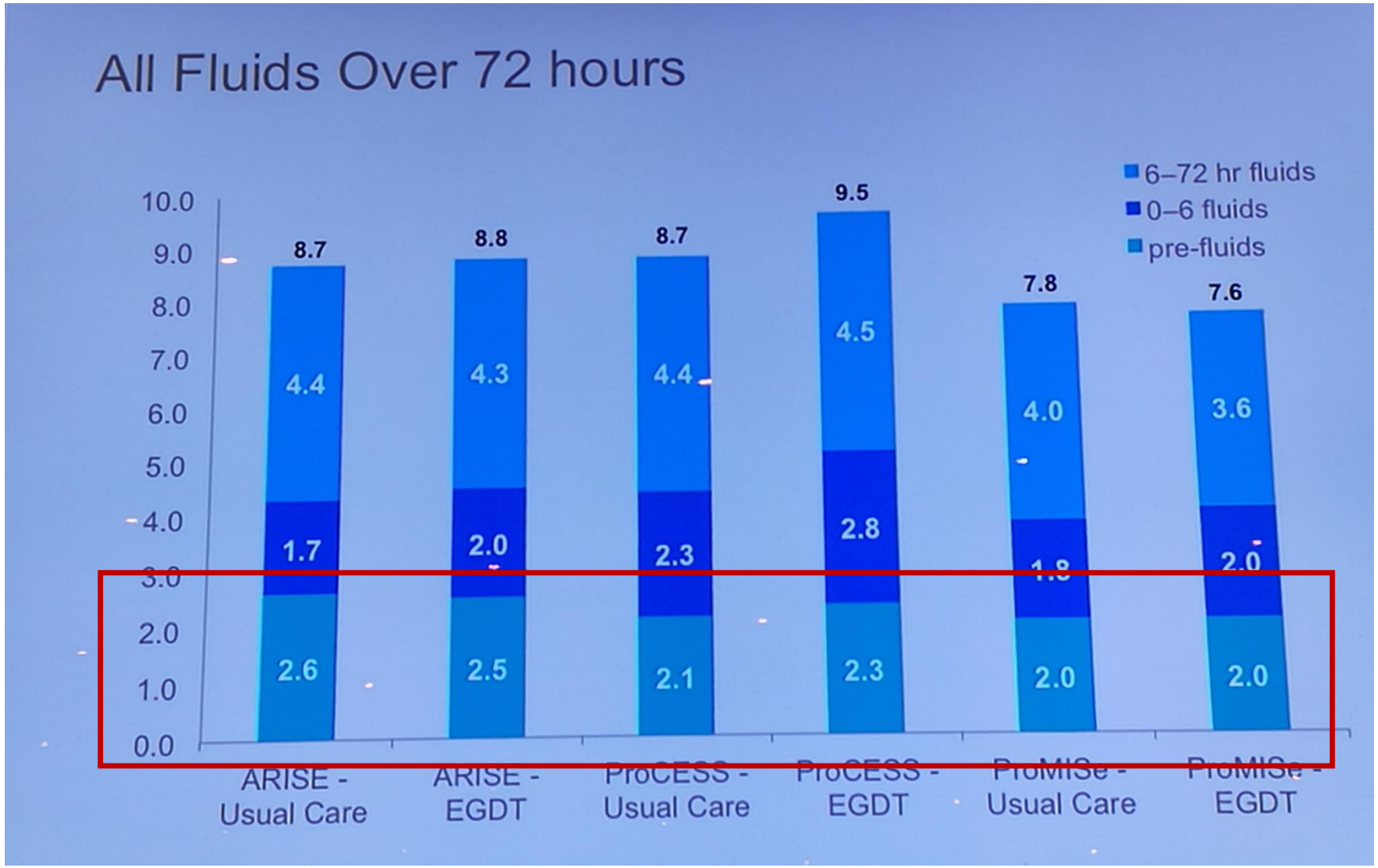
SSC guidelines 2016: 20-30ml/kg během 3 hodin

NOTE: JLV + DdB (NEJM 2013): fluid challenge: 300-500ml/20-30 min; sledovat HR, SAP, UO; pozor na vznik plicního edému (OI+CVP)

CAVE: studie FEAST (Maitland K, NEJM 2011); FIRST (Andrews B, JAMA 2017)

CAVE: 1 hr bundle SSC - **Key Recommendations -** The following should be **initiated** within 1 hour:

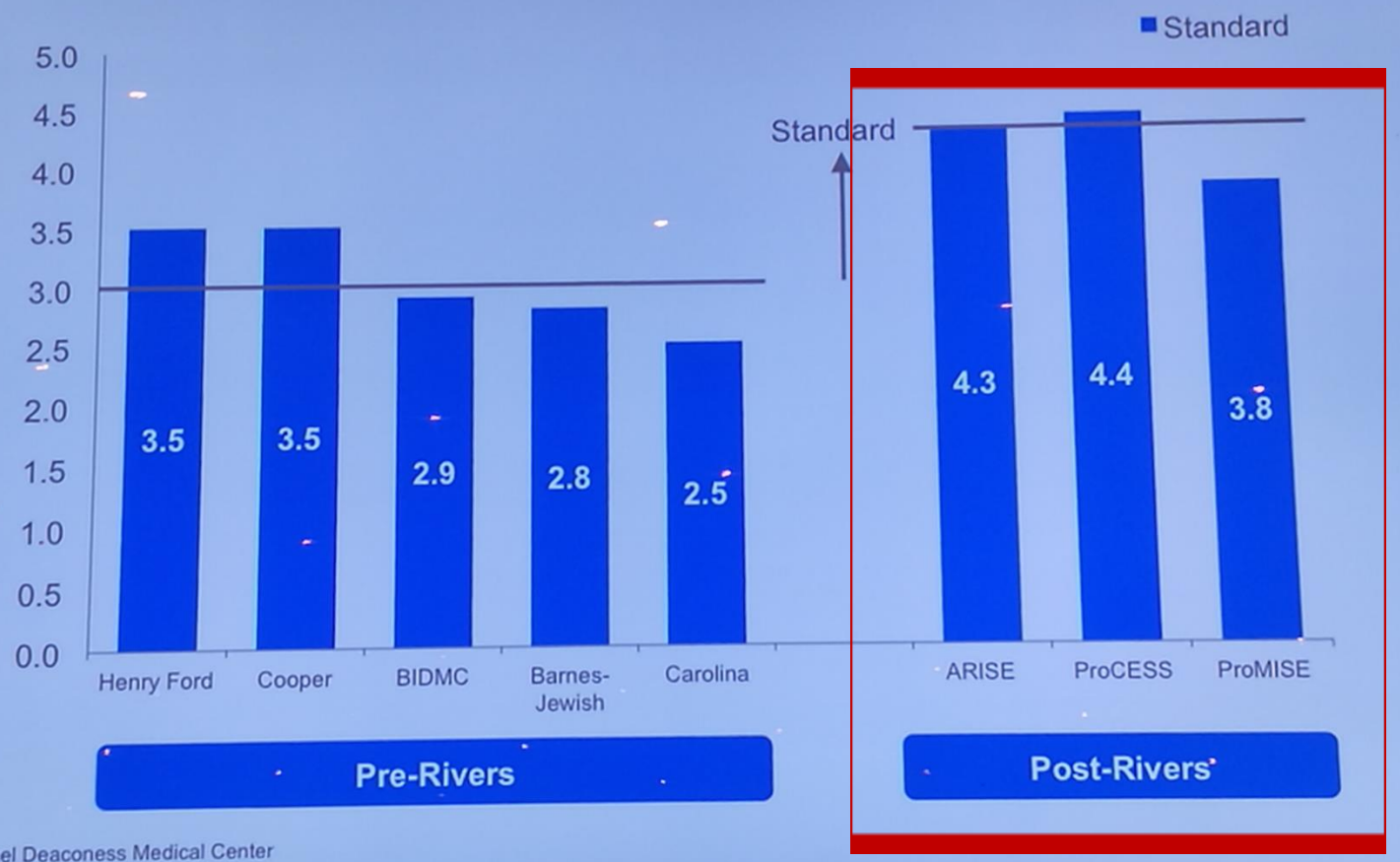
- Measure lactate and remeasure within 2–4 hours if level is >2 mmol/L. A normal lactate is one endpoint of resuscitation.
- Obtain at least two sets of blood cultures (aerobic and anaerobic) prior to administration of antibiotics. Do not withhold antibiotics pending blood cultures.
- Administer broad-spectrum intravenous antibiotics.
- **Initiate a bolus of 30 mL/kg of intravenous crystalloid. This bolus should be completed within 3 hours. Colloid is not recommended.**
- Use vasopressors to maintain mean arterial pressure (MAP) above 65 mm Hg during or after fluid resuscitation.


All Fluids Over 72 hours
6–72 hr fluids
0–6 fluids
pre-fluids
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
8.7
8.8
8.7
9.5
7.8
7.6
4.4
4.3
4.4
4.5
4.0
3.6
1.7
2.0
2.3
2.8
1.8
2.0
2.6
2.5
2.1
2.3
2.0
2.0
ARISE - Usual Care
ARISE - EGDT
ProCESS - Usual Care
ProCESS - EGDT
ProMISe - Usual Care
ProMISe - EGDT

Fluids in Usual Care

Pre- and Post- Rivers

Pretreatment and 0-6 hrs



BIDMC, Beth Israel Deaconess Medical Center

1. Rivers E et al. N Engl J Med. 2001;345(19):1368-77; 2. Trzeciak et al. Chest. 2006;129(2):225-32; 3. Shapiro NI et al. Crit Care Med. 2006;34(4):1025-32; 4. Micek ST et al. Crit Care Med. 2006;34(11):2707-13; 5. Jones et al. Chest. 2007;132(2):425-32; 6. The ARISE Investigators and the ANZICS Clinical Trials Group. N Engl J Med. 2014;371:1496-1506; 7. The ProCESS Investigators. N Engl J Med. 2014;370:1683-1693; 8. Mouncey PR et al. Health Technol Assess. 2015;19(97):i-xxv, 1-150.

Predictors, Prevalence, and Outcomes of Early Crystalloid Responsiveness Among Initially Hypotensive Patients With Sepsis and Septic Shock*

Daniel E. Leisman, BS[1,2,3]; Martin E. Doerfler, MD[4,5]; Sandra M. Schneider, MD[1,6]; Kevin D. Masick, PhD[7]; Jason A. D'Amore, MD[1]; John K. D'Angelo, MD[1,2]

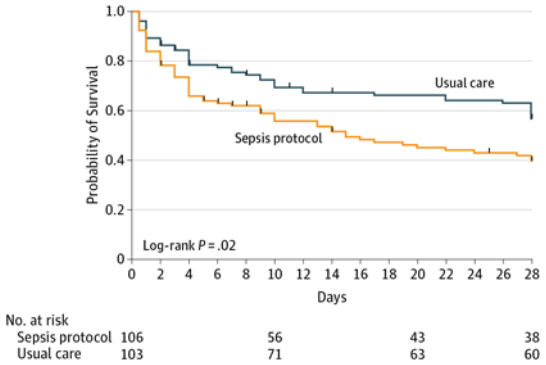
(*Crit Care Med* 2018; 46:189–198)

3700 nemocných se sepsí s septickým šokem (9 US nemocnic)
64% pozitivní odpověď na iniciální bolus tekutiny

Variables	AOR	95% CI		p
Predictive patient factors				
Congestive heart failure	1.43	1.20	1.72	< 0.001
Body temperature (vs > 38.3°C) (°C)				
36.0–38.3	1.06	0.91	1.25	0.44
< 36.0	1.37	1.10	1.69	0.005
Initial serum lactate (vs < 2.1 mmol/L) (mmol/L)				
2.1–3.9	1.08	0.92	1.27	0.36
≥ 4.0	1.28	1.08	1.52	0.005
Immunocompromise[a]	1.23	1.03	1.47	0.025
Coagulopathy[b]	1.23	1.03	1.48	0.024
Altered gas exchange[c]	1.33	1.12	1.57	0.001

tors) patients. Initiating fluids in greater than 2 hours also predicted refractoriness (odds ratio, 1.96; CI, 1.49–2.58). Mortality was 15% higher (CI, 10-18%) for refractory patients.

resuscitace hemodynamiky – jen tekutiny?



2L+2L (1+4hrs) vs < 2L/6hrs

The NEW ENGLAND JOURNAL of MEDICINE

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

Kathryn Maitland[1,2*], Elizabeth C George[3], Jennifer A Evans[4], Sarah Kiguli[5], Peter Olupot-Olupot[6], Samuel O Akech[2],

bolus 20-40 ml/kg vs nic

Katecholaminy – NA brzo

Hamzaoui *et al. Critical Care* 2010, **14**:R142
http://ccforum.com/content/14/4/R142

CRITICAL CARE

RESEARCH Open Access

Early administration of norepinephrine increases cardiac preload and cardiac output in septic patients with life-threatening hypotension

Olfa Hamzaoui, Jean-François Georger, Xavier Monnet, Hatem Ksouri, Julien Maizel, Christian Richard, Jean-Louis Teboul*

Effects of norepinephrine on mean systemic pressure and venous return in human septic shock

Romain Persichini, MD; Serena Silva, MD; Jean-Louis Teboul, MD, PhD; Mathieu Jozwiak, MD; Denis Chemla, MD, PhD; Christian Richard, MD; Xavier Monnet, MD, PhD

PETAL Network

(Prevention & Early Treatment of Acute Lung Injury)

- **CLOVERS: Crystalloid Liberal or Vasopressors Early Resuscitation in Sepsis**
- **Status:**
- Active
- **Period:**
- March 2018
- **NCT Identifier:**
- NCT03434028
- **Purpose**: The CLOVERS study compares two methods of increasing blood pressure in patients with dangerously low blood pressure due to a suspected infection. One method is the first provide intravenous fluids to the patient, and then use drugs such as adrenalin (called vasopressors); the other method is to use the drugs first, and then use fluids.
- **Trial summary**:
- Study design: this is a multi-center, prospective, phase 3 randomized non-blinded interventional trial of fluid treatment strategies in the first 24 hours for patients with sepsis-induced hypotension (dangerously low blood pressure from a suspected infection).
- Purpose: to determine the impact of a restrictive fluids strategy (vasopressors first followed by rescue fluids) as compared to a liberal fluid strategy (fluids first followed by rescue vasopressors) on 90-day in-hospital mortality in patients with sepsis-induced hypotension.
- Sample size: this trial will enroll up to 2,230 subjects from PETAL network emergency rooms.

Macdonald et al. Trials (2017) 18:399
DOI 10.1186/s13063-017-2137-7

Trials

STUDY PROTOCOL Open Access

REstricted Fluid REsuscitation in Sepsis-associated Hypotension (REFRESH): study protocol for a pilot randomised controlled trial

Stephen P. J. Macdonald[1,2,11*], David McD Taylor[3,4], Gerben Keijzers[5,6,7], Glenn Arendts[1,8,11], Daniel M. Fatovich[1,2,11], Frances B. Kinnear[9], Simon G. A. Brown[1,10,11], Rinaldo Bellomo[12,13], Sally Burrows[14], John F. Fraser[6,15,16], Edward Litton[1,7], Juan Carlos Ascencio-Lane[10], Matthew Anstey[18], David McCutcheon[1,11,19], Lisa Smart[1,11], Ioana Vlad[20], James Winearls[7,16,21] and Bradley Wibrow[18]

Abstract

Background: Guidelines recommend an initial intravenous (IV) fluid bolus of 30 ml/kg isotonic crystalloid for patients with sepsis and hypotension. However, there is a lack of evidence from clinical trials to support this. Accumulating observational data suggest harm associated with the injudicious use of fluids in sepsis. There is currently equipoise regarding liberal or restricted fluid-volume resuscitation as first-line treatment for sepsis-related hypotension. A randomised trial comparing these two approaches is, therefore, justified.

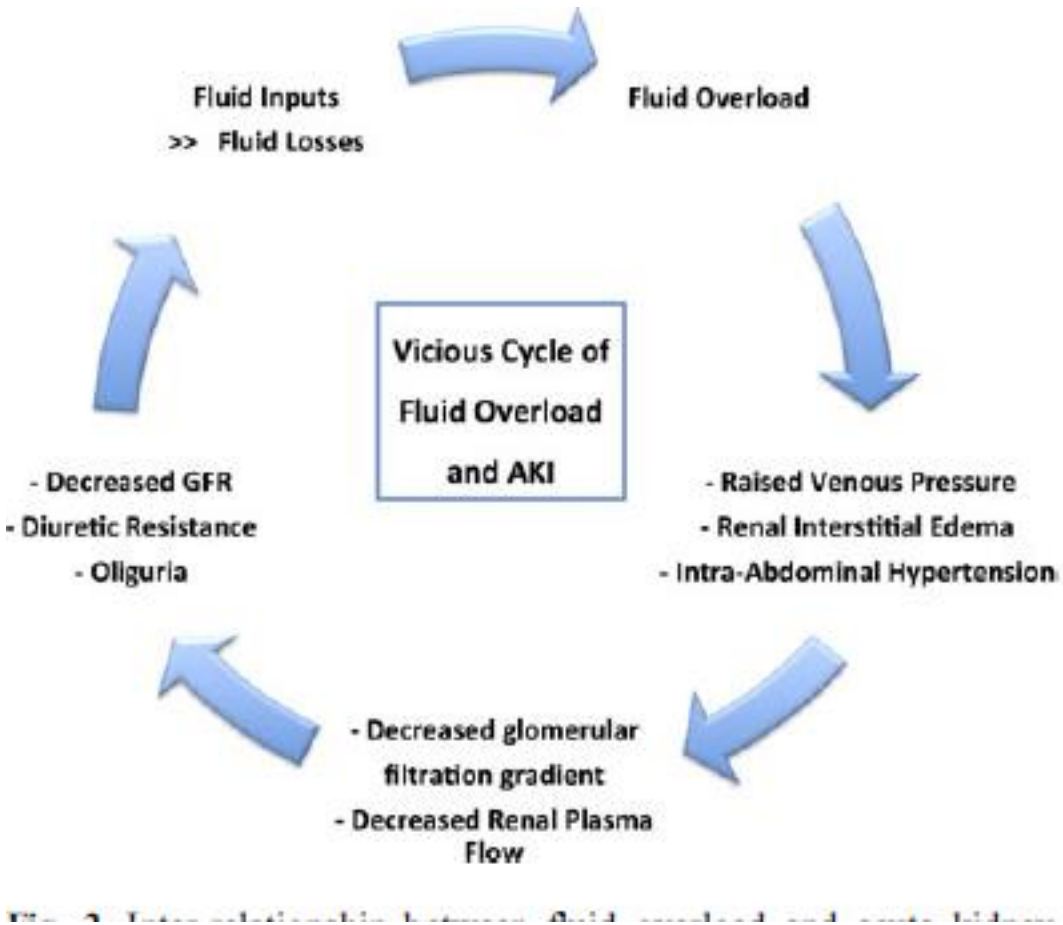
Methods/design: The REstricted Fluid REsuscitation in Sepsis-associated Hypotension trial (REFRESH) is a multicentre, open-label, randomised, phase II clinical feasibility trial. Participants will be patients presenting to the emergency departments of Australian metropolitan hospitals with suspected sepsis and a systolic blood pressure of < 100 mmHg, persisting after a 1000-ml fluid bolus with isotonic crystalloid. Partidpants will be randomised to either a second 1000-ml fluid bolus (standard care) or maintenance rate fluid only, with the early commencement of a vasopressor infusion to maintain a mean arterial pressure of >65 mmHg, if required (restricted fluid). All will receive further protocolised fluid boluses (500 ml or 250 ml, respectively), if required during the 6-h study period. The primary outcome measure is total volume administered in the first 6 h. Secondary outcomes include fluid volume at 24 h, organ support 'free days' to day 28, 90-day mortality, and a range of feasibility and process-of-care measures. Participants will also undergo serial measurement, over the first 24 h, of biomarkers of inflammation, endothelial cell activation and glycocalyx degradation for comparison between the groups.

Discussion: This is the first randomised trial examining fluid volume for initial resuscitation in septic shock in an industrialised country. A pragmatic, open-label design will establish the feasibility of undertaking a large, international, multicentre trial with sufficient power to assess clinical outcomes. The embedded biomarker study aims to provide mechanistic plausibility for a larger trial by defining the effects of fluid volume on markers of systemic inflammation and the vascular endothelium.

(Continued on next page)

optimisation

- tekutiny kontrolovaně
- CAVE fluid overload



Legrand *et al. Critical Care* 2013, **17**:R278
http://ccforum.com/content/17/6/R278

CRITICAL CARE

RESEARCH Open Access

Association between systemic hemodynamics and septic acute kidney injury in critically ill patients: a retrospective observational study

Matthieu Legrand[1,2*], Claire Dupuis[1], Christelle Simon[1], Etienne Gayat[1,3], Joaquim Mateo[1], Anne-Claire Lukaszewicz[1,2,4] and Didier Payen[1,2,4]

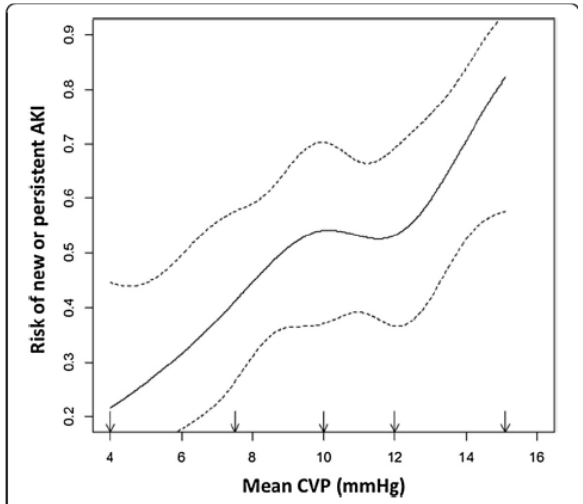


Figure 2 Statistical model of nonparametric logistic regression showing the relationship between mean central venous pressure during the first 24 hours after admission and the probability of new or persistent acute kidney injury. Note the plateau for the incidence of acute kidney injury (AKI) when the lower limit of central venous pressure (CVP) was between 8 and 12 mmHg. Over this limit, the rise in CVP was associated with a sharp increase in new or persistent AKI incidence.

Research

Open Access

Renal haemodynamic, microcirculatory, metabolic and histopathological responses to peritonitis-induced septic shock in pigs

Jiri Chvojka[1], Roman Sykora[1], Ales Krouzecky[1], Jaroslav Radej[1], Veronika Varnerova[1], Thomas Karvunidis[1], Ondrej Hes[2], Ivan Novak[1], Peter Radermacher[3] and Martin Matejovic[1]

Key messages

- The results of this experimental study argue against the concept of renal vasoconstriction in early sepsis-induced kidney dysfunction.
- Despite maintained renal perfusion significant renal cortex microvascular and metabolic stress developed very early in the course of AKI.
- Kidney oxygen extraction capabilities remained well-maintained during progressive hyperdynamic sepsis.
- Only subtle histological changes without signs of ATN occurred after 22 hours of peritonitis-induced septic shock.
- Renal venous congestion might be a hidden and clinically unrecognised factor contributing to the development of septic kidney dysfunction.

stabilisation

- méně tekutin (žádné tekutiny)
- hypotonické tekutiny

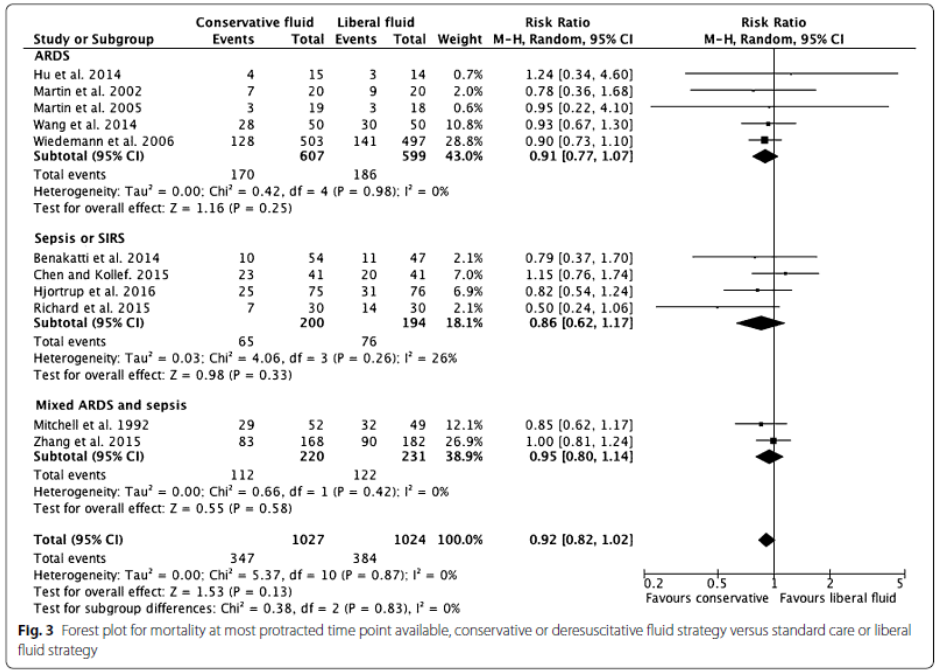


Fig. 3 Forest plot for mortality at most protracted time point available, conservative or deresuscitative fluid strategy versus standard care or liberal fluid strategy

MORTALITY

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

SYSTEMATIC REVIEW

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

Jonathan A. Silversides[1,2*], Emmet Major[2], Andrew J. Ferguson[3], Emma E. Mann[2], Daniel F. McAuley[1,4], John C. Marshall[5,6], Bronagh Blackwood[1] and Eddy Fan[5]

ICU stay

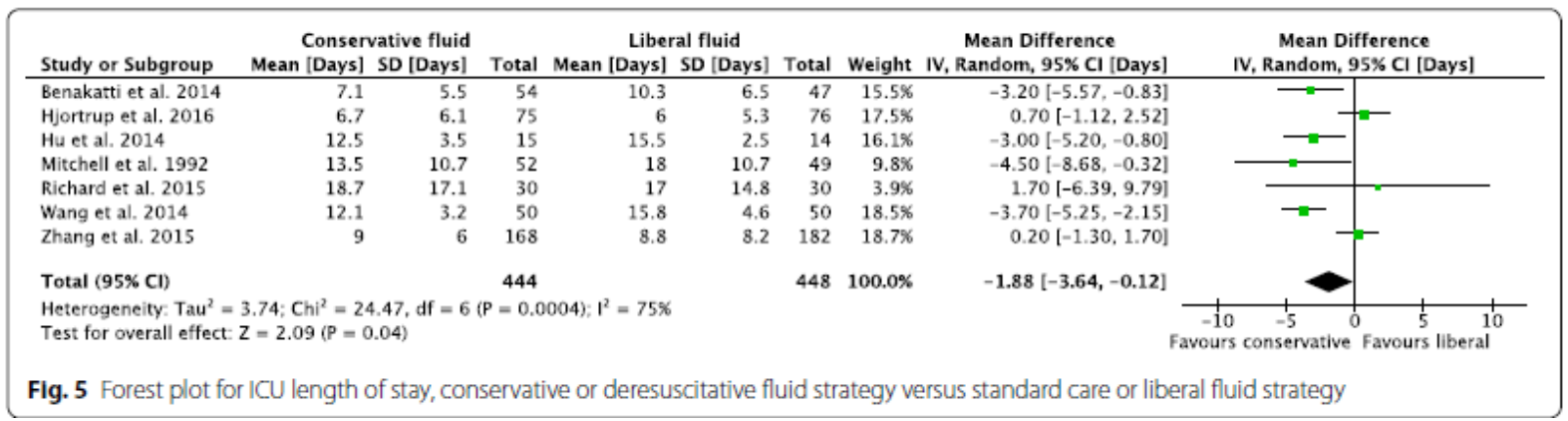


Fig. 5 Forest plot for ICU length of stay, conservative or deresuscitative fluid strategy versus standard care or liberal fluid strategy

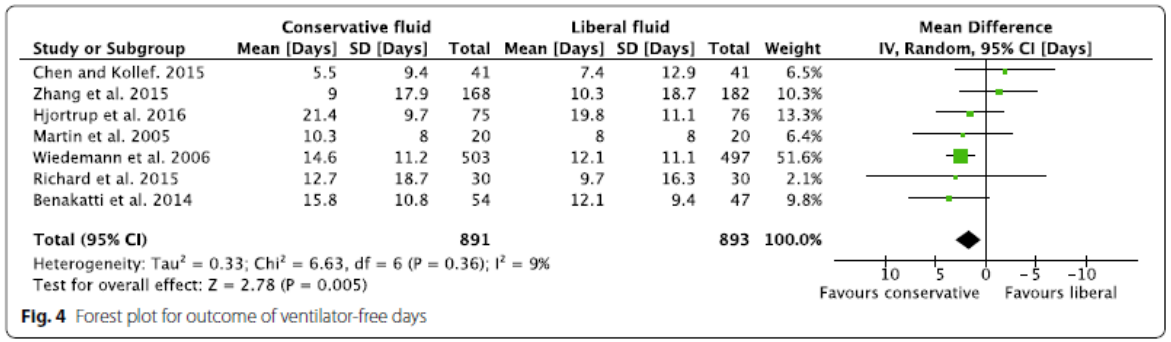


Fig. 4 Forest plot for outcome of ventilator-free days

Ventilator free days

Table 2 GRADE summary of evidence table for key outcomes

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Conservative or deresuscitative fluid strategy	Liberal fluid strategy or usual care	Relative (95 % CI)	Absolute (95 % CI)		
Mortality												
11	Randomised trials	Serious[a]	Not serious	Very serious[b]	Serious	None	337/973 (34.6 %)	373/977 (38.2 %)	RR 0.92 (0.82–1.03)	31 fewer per 1000 (from 11 more to 69 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
Ventilator-free days												
7	Randomised trials	Not serious	Not serious	Very serious[b]	Not serious	None	891	893	–	MD 1.82 days more (0.53 more to 3.1 more)	⨁⨁◯◯ LOW	IMPORTANT
ICU length of stay												
7	Randomised trials	Serious[c]	Serious[d]	Very serious[b]	Not serious	None	444	448	–	MD 1.88 days fewer (0.12 fewer to 3.64 fewer)	⨁◯◯◯ VERY LOW	IMPORTANT
RRT use												
3	Randomised trials	Not serious	Not serious	Very serious[b]	Serious[e]	None	83/619 (13.4 %)	100/614 (16.3 %)	RR 0.88 (0.64–1.22)	20 fewer per 1000 (from 36 more to 59 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
Post-ICU cognitive function (assessed with QLQ-C30 cognitive function domain; scale from 0 to 100, with higher scores denoting better cognitive function)												
1	Randomised trials	Very serious[f]	Not serious	Serious[g]	Serious[e]	None	50	50	–	MD 10.71 points higher (5.22 higher to 16.2 higher)	⨁◯◯◯ VERY LOW	CRITICAL


MihMoSa
ifa
RESEARCH
Hypotonic vs Isotonic Maintenance Fluids

BJA

British Journal of Anaesthesia, 118 (6): 892–900 (2017)

doi: 10.1093/bja/aex118
Advance Access Publication Date: 16 May 2017
Clinical Practice

Effect of isotonic *versus* hypotonic maintenance fluid therapy on urine output, fluid balance, and electrolyte homeostasis: a crossover study in fasting adult volunteers

N. Van Regenmortel[1,2,*], T. De Weerdt[3], A. H. Van Craenenbroeck[3], E. Roelant[4,5], W. Verbrugghe[1], K. Dams[1], M. L. N. G. Malbrain[2], T. Van den Wyngaert[6,7] and P. G. Jorens[1,7]

Methods. This crossover study consisted of two 48 h study periods, during which 12 fasting healthy adults were treated with a frequently prescribed solution (NaCl 0.9% in glucose 5% supplemented by 40 mmol litre^{-1} of potassium chloride) and a premixed hypotonic fluid (NaCl 0.32% in glucose 5% containing 26 mmol litre^{-1} of potassium) at a daily rate of 25 ml kg^{-1} of body weight. The primary end point was cumulative urine volume; fluid balance was thus calculated. We also explored the physiological mechanisms behind our findings and assessed electrolyte concentrations.

Results. After 48 h, 595 ml (95% CI: 454–735) less urine was voided with isotonic fluids than hypotonic fluids ($P<0.001$), or 803 ml (95% CI: 692–915) after excluding an outlier with 'exaggerated natriuresis of hypertension'. The isotonic treatment was characterized by a significant decrease in aldosterone ($P<0.001$). Sodium concentrations were higher in the isotonic arm ($P<0.001$), but all measurements remained within the normal range. Potassium concentrations did not differ between the two solutions ($P=0.45$). Chloride concentrations were higher with the isotonic treatment ($P<0.001$), even causing hyperchloraemia.

Conclusions. Even at maintenance rate, isotonic solutions caused lower urine output, characterized by decreased aldosterone concentrations indicating (unintentional) volume expansion, than hypotonic solutions and were associated with hyperchloraemia. Despite their lower sodium and potassium content, hypotonic fluids were not associated with hyponatraemia or hypokalaemia.

Clinical trial registration. ClinicalTrials.gov (NCT02822898) and EudraCT (2016-001846-24).

Intensive Care Med (2018) 44:409–417
https://doi.org/10.1007/s00134-018-5147-3

ORIGINAL

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

Niels Van Regenmortel[1,2*], Walter Verbrugghe[1], Ella Roelant[3], Tim Van den Wyngaert[4,5] and Philippe G. Jorens[1,5]

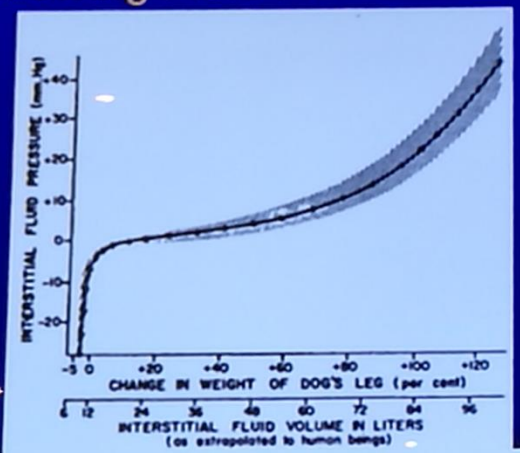
Conclusions: Inadvertent daily volume, sodium, and chloride loading should be avoided when prescribing maintenance fluids in view of the vast amounts of fluid creep. This is especially important when adopting an isotonic maintenance strategy.

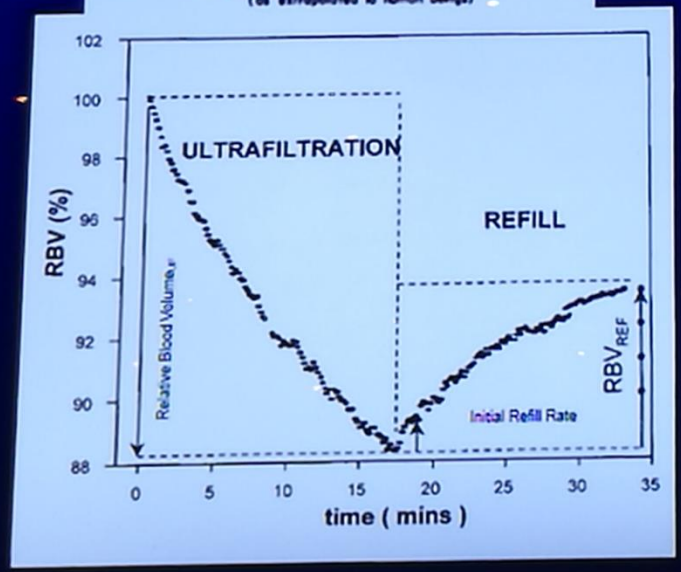
de-escalation

- omezení příjmu
- diuretika (+albumin)
- RRT – zvolit vhodné parametry

Transcapillary Refill

Following Fluid Removal





- ~ 5 mL/kg/hour
  - Average Capillary refill rate
- ≥ 10 mL/kg/hour
  - Coronary hypoperfusion
  - Myocardial stunning
  - Vascular risk
- > 13 mL/kg/hour
  - ↑ Risk of death

Kim E et al . Trans Am Soc Artif Intern Organs. 1970, 16:508–514
Jaeger JQ, Mehta RL. JASN. 1999, 10:2392–2403
Saran R et al. Kidney Int. 2006, 69:1222–1228
Movilli E et al. Nephrol Dial Transplant. 2007, 22:3547–3552
Selby NM et al. Clin J Am Soc Nephrol. 2006, 1:696–705
Mitra S et al Am J of Kid Dis, 40, 200
Drucker et a. Arch Surg 1981;116:1344-135

Monnet et al. Ann. Intensive Care (2016) 6:46
DOI 10.1186/s13613-016-0149-1

Annals of Intensive Care

RESEARCH Open Access

The passive leg raising test to guide fluid removal in critically ill patients

Xavier Monnet[1,2,4*], Flora Cipriani[1,2], Laurent Camous[1,2], Pierre Sentenac[1,2], Martin Dres[1,2], Evguenia Krastinova[2,3], Nadia Anguel[1,2], Christian Richard[1,2] and Jean-Louis Teboul[1,2]

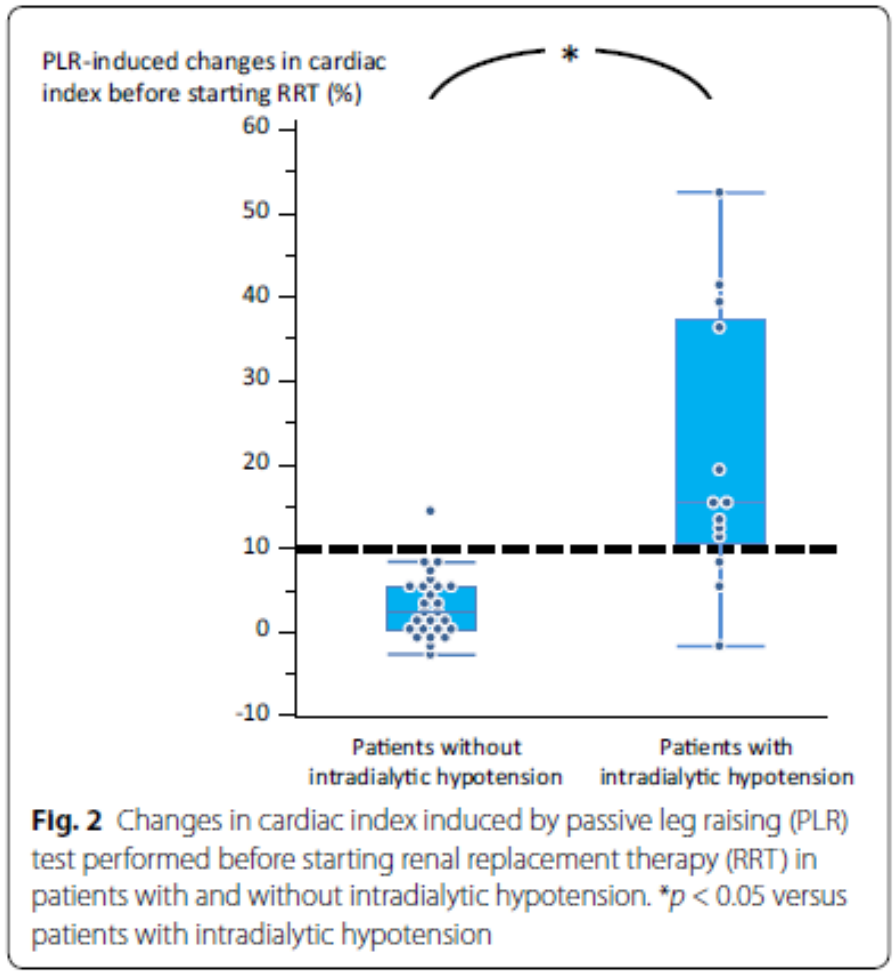


Fig. 2 Changes in cardiac index induced by passive leg raising (PLR) test performed before starting renal replacement therapy (RRT) in patients with and without intradialytic hypotension. *$p < 0.05$ versus patients with intradialytic hypotension

Journal of the American College of Cardiology
© 2007 by the American College of Cardiology Foundation
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Vol. 49, No. 6, 2007
ISSN 0735-1097/07/$32.00
doi:10.1016/j.jacc.2006.07.073

Heart Failure

Ultrafiltration Versus Intravenous Diuretics for Patients Hospitalized for Acute Decompensated Heart Failure

Maria Rosa Costanzo, MD, FACC,* Maya E. Guglin, MD, FACC,†
Mitchell T. Saltzberg, MD, FACC,* Mariell L. Jessup, MD, FACC,‡ Bradley A. Bart, MD, FACC,§
John R. Teerlink, MD, FACC,‖ Brian E. Jaski, MD, FACC,¶ James C. Fang, MD, FACC,#
Erika D. Feller, MD, FACC,** Garrie J. Haas, MD, FACC,†† Allen S. Anderson, MD, FACC,‡‡
Michael P. Schollmeyer, DVM,§§ Paul A. Sobotka, MD, FACC,§§ for the UNLOAD Trial Investigators

and central venous catheters. The ultrafiltration procedure has been previously described (14). During the first 48 h after enrollment, hypervolemia was treated exclusively with ultrafiltration and intravenous diuretics were prohibited. The duration and rate (up to 500 ml/h) of fluid removal were decided by treating physicians. The ultrafiltration device consists of a 0.12-m^2 polysulphone filter with a blood flow adjustable between 10 and 40 ml/min and total extracorporeal blood volume of 33 ml (14).

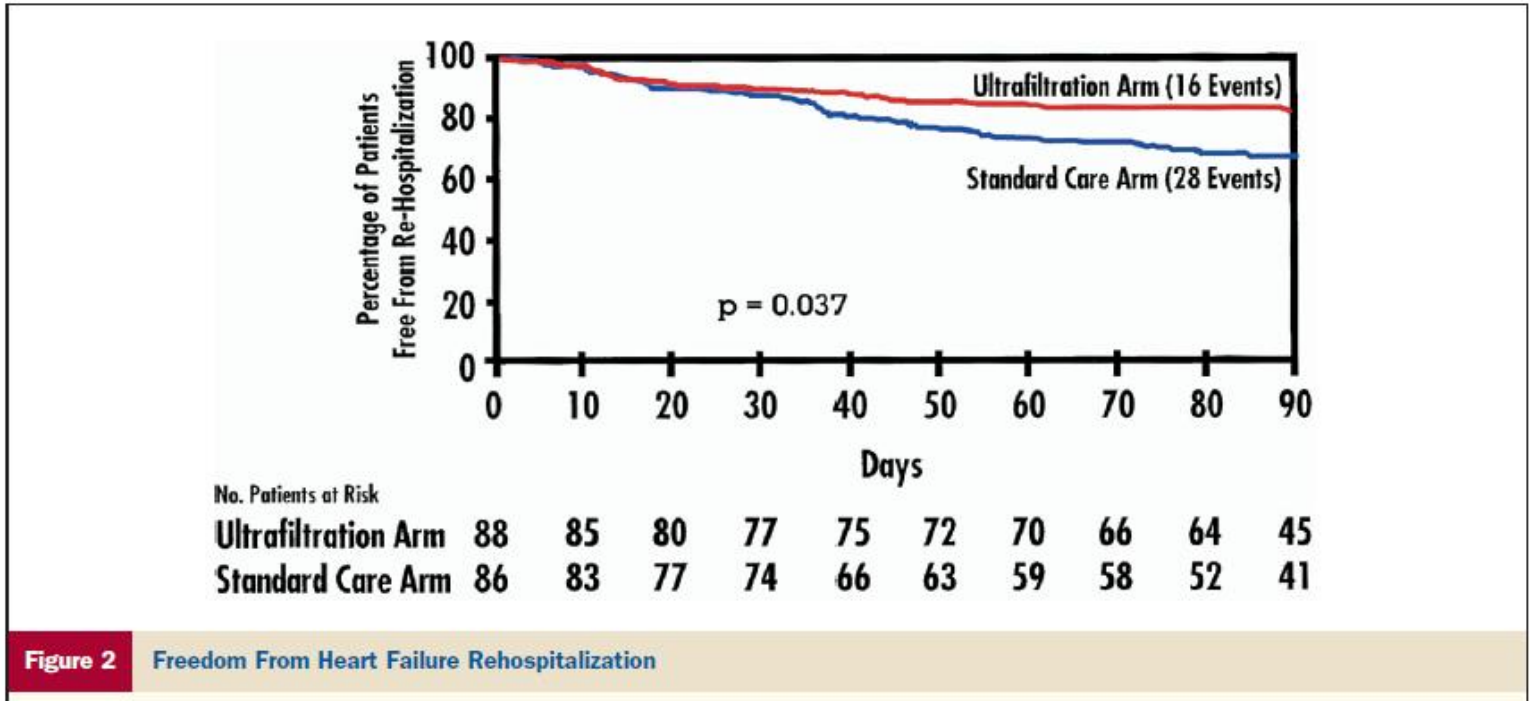

Figure 2 Freedom From Heart Failure Rehospitalization

Závěr

Tekutiny v resuscitaci SŠ ne příliš rychle (**NE** přetlakem)
1/3 nemocných nereaguje na úvodní bolus (ECHO)
Moderní metody dynamického preloadu (dVt)
NA v podstatě paralelně (koncept)
Balancované roztoky (hypotonické?)
CVP není úplně na nic (CAVE vysoký CVP)
NA dle „perfusion pressure“ i pro ledviny, splanchnicus?
Diuretika (albumin) v de-eskalační fázi, de-eskalace je +

7. SVATOMARTINSKÝ WORKSHOP

www.hemodynamika.cz

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- ČSIM akademie

8. – 9. listopadu 2018