

Smernice za obravnavo odraslih bolnikov s sepsom in septičnim šokom – Kaj je novega?



Dragoslav Leković, dr. med.

UKC Ljubljana, Kirurška klinika, KOAIT

Oddelek za intenzivno terapijo (OIT)

Ljubljana, 13.9.2022

Screening in začetna obravnava

- ▶ Proti uporabi qSOFA kot **edinega** presejalnega orodja za sepso/septični šok v primerjavi s SIRS, NEWS ali MEWS (*močno priporočilo*)

- ▶ qSOFA (2016):

FD ≥ 22

Motnja zavesti

SAT ≤ 100 mmHg

- ▶ qSOFA – relativno slaba specifičnost in senzitivnost
- ▶ SIRS – večja občutljivost za diagnozo sepse
- ▶ qSOFA boljša napovedna vrednost za znotrajbolnišnično umrljivost

Conclusions

The SIRS was significantly superior to the qSOFA for sepsis diagnosis, and the qSOFA was slightly better than the SIRS in predicting hospital mortality. The association of both criteria could provide a better model to initiate or escalate therapy in patients with sepsis.

Screening in začetna obravnava

- 30 mL/kg kristaloidne raztopine iv tekom prvih 3 ur
- **Spremenjena** stopnja priporočila: močno → šibko

- SSC (2004, 2008, 2012): EGDT
- PROMISE, PROCESS, ARISE → 30 mL/kg (2016)

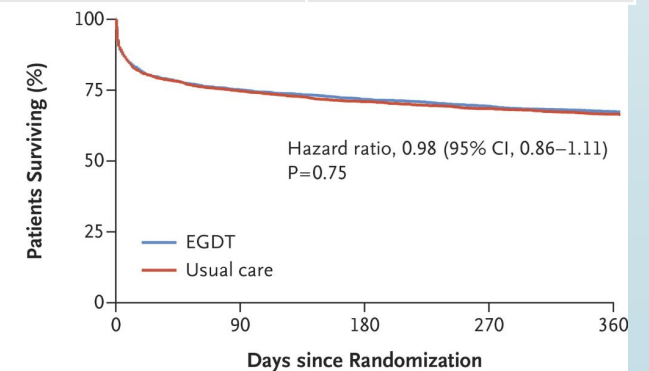
PRISM metaanaliza

	EGDT	Običajno
Mediana	27,5 mL/kg	27,7 mL/kg

CONCLUSIONS

In this meta-analysis of individual patient data, EGDT did not result in better outcomes than usual care and was associated with higher hospitalization costs across a broad range of patient and hospital characteristics. (Funded by the National Institute of General Medical Sciences and others; PRISM ClinicalTrials.gov number, [NCT02030158](#).)

PRISM Investigators, Rowan KM, Angus DC, Bailey M, Barnato AE, Bellomo R, Canter RR, Coats TJ, Delaney A, Gimbel E, Grieve RD, Harrison DA, Higgins AM, Howe B, Huang DT, Kellum JA, Mouncey PR, Music E, Peake SL, Pike F, Reade MC, Sadique MZ, Singer M, Yealy DM. Early, Goal-Directed Therapy for Septic Shock - A Patient-Level Meta-Analysis. *N Engl J Med*. 2017 Jun 8;376(23):2223-2234



No. at Risk	0	90	180	270	360
EGDT	1857	1391	1287	1209	1111
Usual care	1880	1395	1295	1206	1111

Screening in začetna obravnava

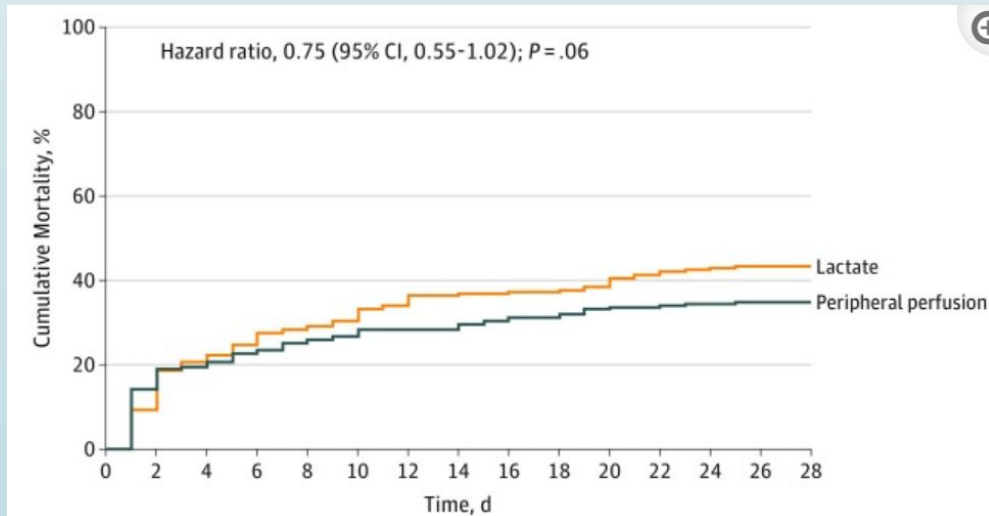
- **Ostaja** priporočilo o vodenju resuscitacije s pomočjo spremljanja koncentracije serumskega **laktata**
- **Novost** je (*šibko*) priporočilo o spremljanju **CRT** (kapilarnega povratka)

Hernández G, Ospina-Tascón GA, Damiani LP, Estenssoro E, Dubin A, Hurtado J et al. Effect of a Resuscitation Strategy Targeting Peripheral Perfusion Status vs Serum Lactate Levels on 28-Day Mortality Among Patients With Septic Shock: The ANDROMEDA-SHOCK Randomized Clinical Trial. JAMA. 2019 Feb 19;321(7):654-664

➤ ANDROMEDA-SHOCK RCT

(Effect of a Resuscitation Strategy Targeting Peripheral Perfusion Status vs Serum Lactate Levels on 28-Day Mortality Among Patients With Septic Shock):

34,9% vs 43,4% umrljivost
p=0,06



Kontrola okužbe

- SSC 2016: **Protimikrobno zdravilo iv** čimprej oz. **v eni uri** pri septičnem šoku IN sepsi brez šoka

- SSC 2021:
- 1. Pri **definitivni ali verjetni diagnozi sepse** priporočilo ostaja enako ne glede na prisotnost šoka (*močno*)
- 2. **Če je** Dg sepse možna IN je **prisoten šok** – priporočilo ostaja enako (*močno*)
- 3. Če je **Dg sepse možna in NI šoka**: sledi ocena verjetnosti neinfekcijski vs infekcijski vzroki obolenja in aplikacija protimikrobnega zdravila v roku **3 ur**, če ostaja sum, da gre za okužbo (*šibko*)

Tekočinsko zdravljenje

- SSC 2016: balansirani kristaloidi **ALI** fiziološka raztopina za tekočinsko resuscitacijo
- SSC 2021: priporočajo uporabo **balansiranih kristaloidov** namesto **FR** za tekočinsko resuscitacijo (*šibko*)

- Balanced Crystalloids versus Saline in Sepsis. A Secondary Analysis of the SMART Clinical Trial

Podskupina s sepso iz SMART RCT:

26,3% vs 31,2% umrljivost;
aOR 0,74 95%CI (0.59-0.93;
P = 0.01)

Pa vendar...

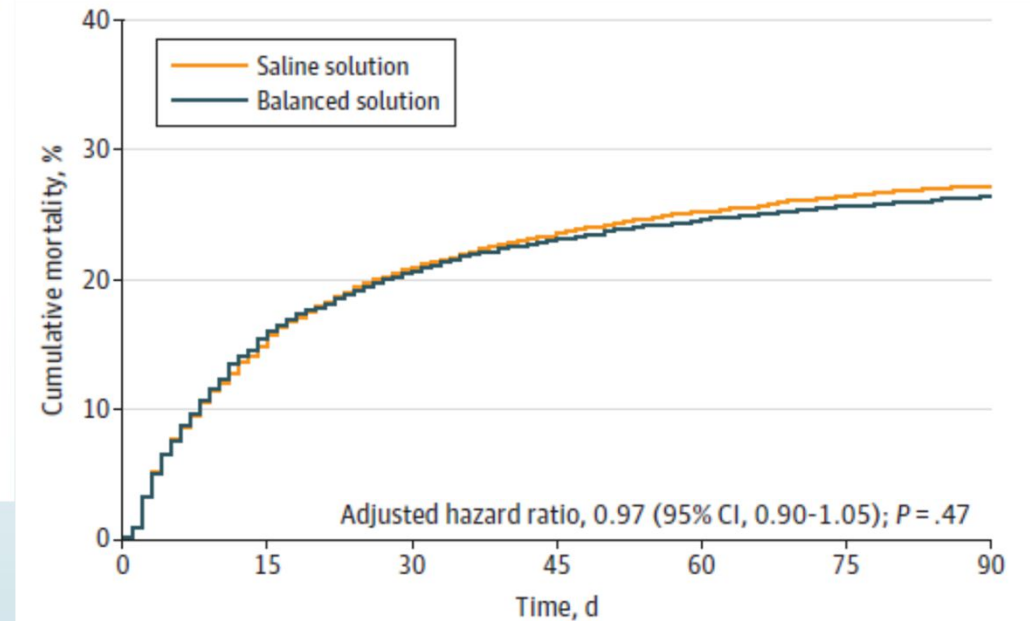
JAMA | Original Investigation

Effect of Intravenous Fluid Treatment With a Balanced Solution vs 0.9% Saline Solution on Mortality in Critically Ill Patients The BaSICS Randomized Clinical Trial

Fernando G. Zampieri, MD, PhD; Flávia R. Machado, MD, PhD; Rodrigo S. Biondi, MD; Flávio G. R. Freitas, MD, PhD; Viviane C. Veiga, MD, PhD; Rodrigo C. Figueiredo, MD; Wilson J. Lovato, MD; Cristina P. Amêndola, MD, PhD; Ary Serpa-Neto, MD, PhD; Jorge L. R. Paranhos, MD; Marco A. V. Guedes, MD, PhD; Eraldo A. Lúcio, MD, PhD; Lúcio C. Oliveira-Júnior, MD; Thiago C. Lisboa, MD, PhD; Fábio H. Lacerda, MD; Israel S. Maia, MD; Cintia M. C. Grion, MD, PhD; Murillo S. C. Assunção, MD, PhD; Airton L. O. Manoel, MD, PhD; João M. Silva-Junior, MD, PhD; Péricles Duarte, MD; Rafael M. Soares, PhD; Tamiris A. Miranda, MSc; Lucas M. de Lima, IT; Rodrigo M. Gurgel, Biomed Sci; Denise M. Paisani, PhD; Thiago D. Corrêa, MD, PhD; Luciano C. P. Azevedo, MD, PhD; John A. Kellum, MD; Lucas P. Damiani, MSc; Nilton Brandão da Silva, MD, PhD; Alexandre B. Cavalcanti, MD, PhD; for the BaSICS investigators and the BRICNet members

RESULTS Among 11 052 patients who were randomized, 10 520 (95.2%) were available for the analysis (mean age, 61.1 [SD, 17] years; 44.2% were women). There was no significant interaction between the 2 interventions (fluid type and infusion speed; $P = .98$). Planned surgical admissions represented 48.4% of all patients. Of all the patients, 60.6% had hypotension or vasopressor use and 44.3% required mechanical ventilation at enrollment. Patients in both groups received a median of 1.5 L of fluid during the first day after enrollment. By day 90, 1381 of 5230 patients (26.4%) assigned to a balanced solution died vs 1439 of 5290 patients (27.2%) assigned to saline solution (adjusted hazard ratio, 0.97 [95% CI, 0.90-1.05]; $P = .47$). There were no unexpected treatment-related severe adverse events in either group.

CONCLUSION AND RELEVANCE Among critically ill patients requiring fluid challenges, use of a balanced solution compared with 0.9% saline solution did not significantly reduce 90-day mortality. The findings do not support the use of this balanced solution.



► V podskupini septičnih bolnikov:

46,7% vs 49% umrljivost


aOR 0,93 (95% CI 0,82 – 1,06)

Vazopresorji

- ▶ **NOVO:**
(Šibko) priporočilo, da **pričnemo z vazopresorji na periferni iv kanal** z namenom korekcije MAP raje kot, da odlašamo do vzpostavitve centralnega dostopa (CVK)
- ▶ Safety of peripheral administration of vasopressor medications: A systematic review
- ▶ Zapleti so redki
- ▶ Vseeno: čim krajši čas (do 6 ur), bolj proksimalne vene


Vazopresorji

Vasoactive Agent Management


 Use norepinephrine as first-line vasopressor

For patients with septic shock on vasopressors


 Target a MAP of 65 mm Hg

 Consider invasive monitoring of arterial blood pressure


If central access is not yet available

 Consider initiating vasopressors peripherally*

If MAP is inadequate despite low-to-moderate dose norepinephrine

 Consider adding vasopressin

If cardiac dysfunction with persistent hypoperfusion is present despite adequate volume status and blood pressure

 Consider adding dobutamine or switching to epinephrine

Strong recommendations are displayed in green, and weak recommendations are displayed in yellow.

**When using vasopressors peripherally, they should be administered only for a short period of time and in a vein proximal to the antecubital fossa.*

Ventilacija

► Za odrasle s hipoksemično ARI povzročeno s sepso priporočajo uporabo **HFNC** raje kot NIV (šibko)

- High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure (FLORALI)

zmanjšana 90-dnevna umrljivost v HFNC skupini (p=0.006)

- The effect of high-flow nasal cannula in reducing the mortality and the rate of endotracheal intubation when used before mechanical ventilation compared with conventional oxygen therapy and noninvasive positive pressure ventilation. A systematic review and meta-analysis

zmanjšana potreba po intubaciji in MV ter umrljivost v ICU

Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, Prat G, Boulain T, Morawiec E, Cottureau A, Devaquet J, Nseir S, Razazi K, Mira JP, Argaud L, Chakarian JC, Ricard JD, Wittebole X, Chevalier S, Herbland A, Fartoukh M, Constantin JM, Tonnelier JM, Pierrot M, Mathonnet A, Béduneau G, Delétage-Métreau C, Richard JC, Brochard L, Robert R; FLORALI Study Group; REVA Network. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med.* 2015 Jun 4;372(23):2185-96

Ni YN, Luo J, Yu H, Liu D, Liang BM, Liang ZA. The effect of high-flow nasal cannula in reducing the mortality and the rate of endotracheal intubation when used before mechanical ventilation compared with conventional oxygen therapy and noninvasive positive pressure ventilation. A systematic review and meta-analysis. *Am J Emerg Med.* 2018 Feb;36(2):226-233

Ventilacija

- ▶ NOVO: pri odraslih bolnikih z **ARDS povzročnim s sepso priporočajo** uporabo **vv ECMO**, ko odpove konvencionalna MV (v izkušenih centrih)- *šibko priporočilo*

- ▶ Venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: a systematic review and meta-analysis

34% vs 47% umrljivost

RR 0.73 [95% CI 0.58-0.92];

p=0.008;

Dodatne terapije - kortikosteroidi

- ▶ SSC 2016: **proti uporabi iv hidrokortizona** pri zdravljenju septičnega šoka, **če tekočinska resuscitacija in vazopresor vzpostavijo** hemodinamsko stabilnost
- ▶ SSC 2021: pri bolnikih s septičnim šokom in **vztrajajočo potrebo po vazopresorju svetujejo** iv kortikosteroide (*šibko*)

Dodatne terapije - kortikosteroidi

- **Low-dose corticosteroids for adult patients with septic shock: a systematic review with meta-analysis and trial sequential analysis**

Brez vpliva na umrljivost, skrajšano trajanje šoka (za 1,52 d), MV (1,38 d) in čas hospitalizacije v EIT (0,75 d) – vsi $p < 0,05$

Rygård SL, Butler E, Granholm A, Møller MH, Cohen J, Finfer S, Perner A, Myburgh J, Venkatesh B, Delaney A. Low-dose corticosteroids for adult patients with septic shock: a systematic review with meta-analysis and trial sequential analysis. *Intensive Care Med.* 2018 Jul;44(7):1003-1016

- **Association of Corticosteroid Treatment With Outcomes in Adult Patients With Sepsis: A Systematic Review and Meta-analysis**

37 RCT (N=9564)

Zmanjšana 28-dnevna umrljivost (RR, 0.90; 95% CI, 0.82-0.98), umrljivost v EIT (RR, 0.85; 95% CI, 0.77-0.94) in hospitalna umrljivost (RR, 0.88; 95% CI, 0.79-0.99)

Fang F, Zhang Y, Tang J, Lunsford LD, Li T, Tang R, He J, Xu P, Faramand A, Xu J, You C. Association of Corticosteroid Treatment With Outcomes in Adult Patients With Sepsis: A Systematic Review and Meta-analysis. *JAMA Intern Med.* 2019 Feb 1;179(2):213-223

Dodatne terapije – adsorpcijske tehnike (blood purification)

- SSC 2016: brez priporočil
- SSC 2021: **proti** uporabi perfuzije s polimiksinom B (*šibko*)

- **Effect of Targeted Polymyxin B Hemoperfusion on 28-Day Mortality in Patients With Septic Shock and Elevated Endotoxin Level: The EUPHRATES Randomized Clinical Trial**

Summary of the Primary End Point of 28-Day Mortality for All Participants and for Patients With MODS of More Than 9

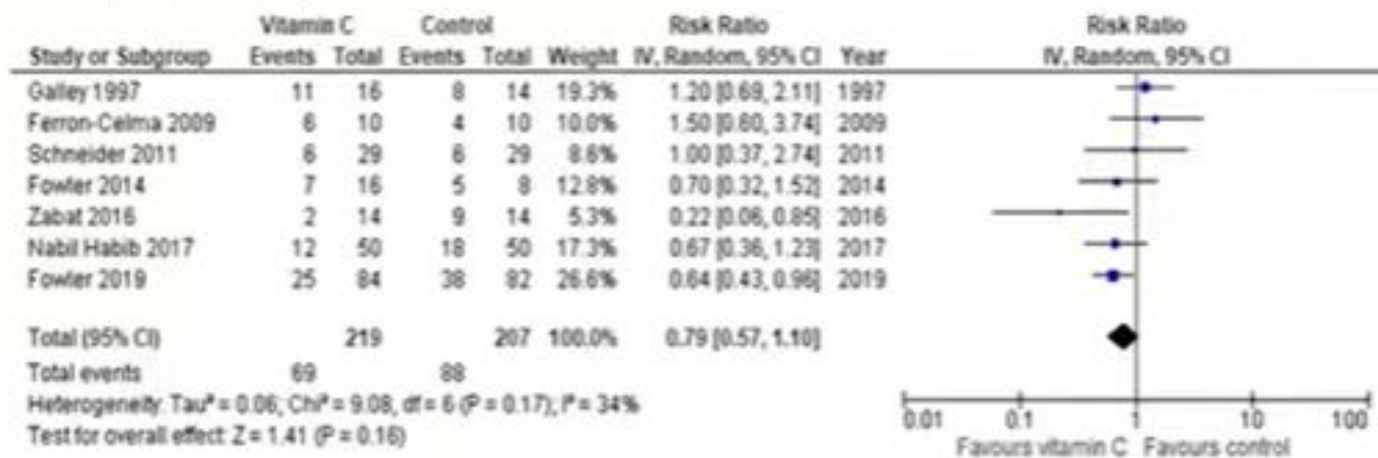
	No./Total (%)		(95% CI)		P
	Polymyxin-B Hemoperfusion	Sham	Risk Difference	Risk Ratio	Value ^a
All Participants	84/223 (37.7)	78/226 (34.5)	3.15 (-5.73 to 12.04)	1.09 (0.85 to 1.39)	.49
>9 MODS ^b	65/146 (44.5)	65/148 (43.9)	0.60 (-10.75 to 11.97)	1.01 (0.78 to 1.31)	.92

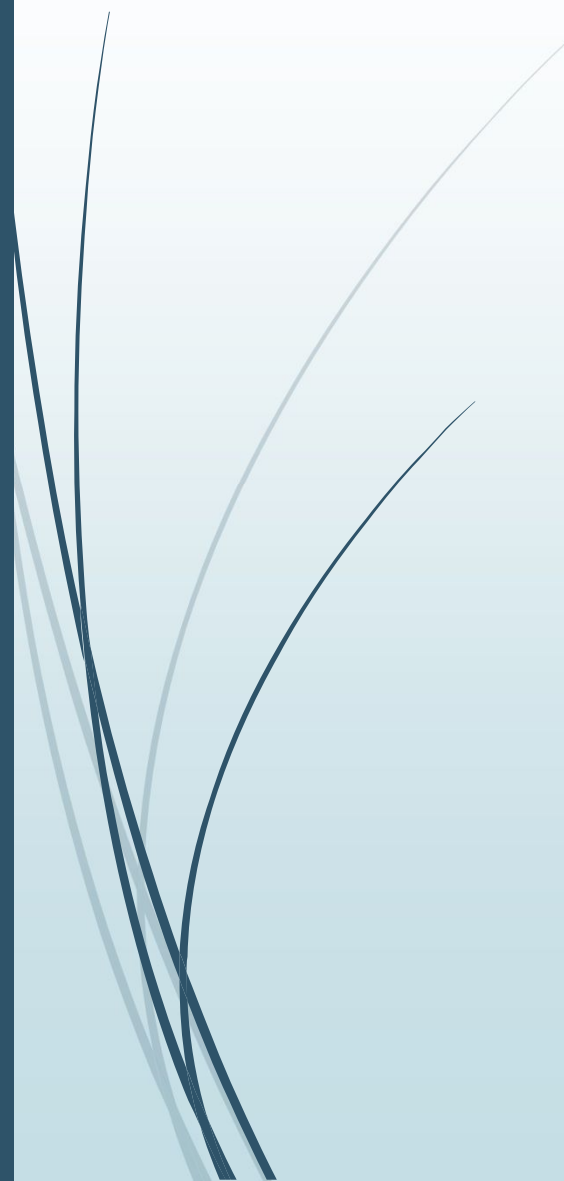
hemoperfuzija s polimiksinom B NI zmanjšala 28-dnevne umrljivosti

Dodatne terapije – Vitamin C

- Pri odraslih s sepsom/septičnim šokom **odsvetujejo** uporabo iv vitamina C
- 7 RCT (N=416): Uporaba vitamina C ni zmanjšala umrljivosti (RR, 0.79; 95% CI, 0.57 - 1.1)

Forest plot for mortality





HVALA