Srednji arterijski tlak pri bolnikih s sepso – kaj je dovolj?

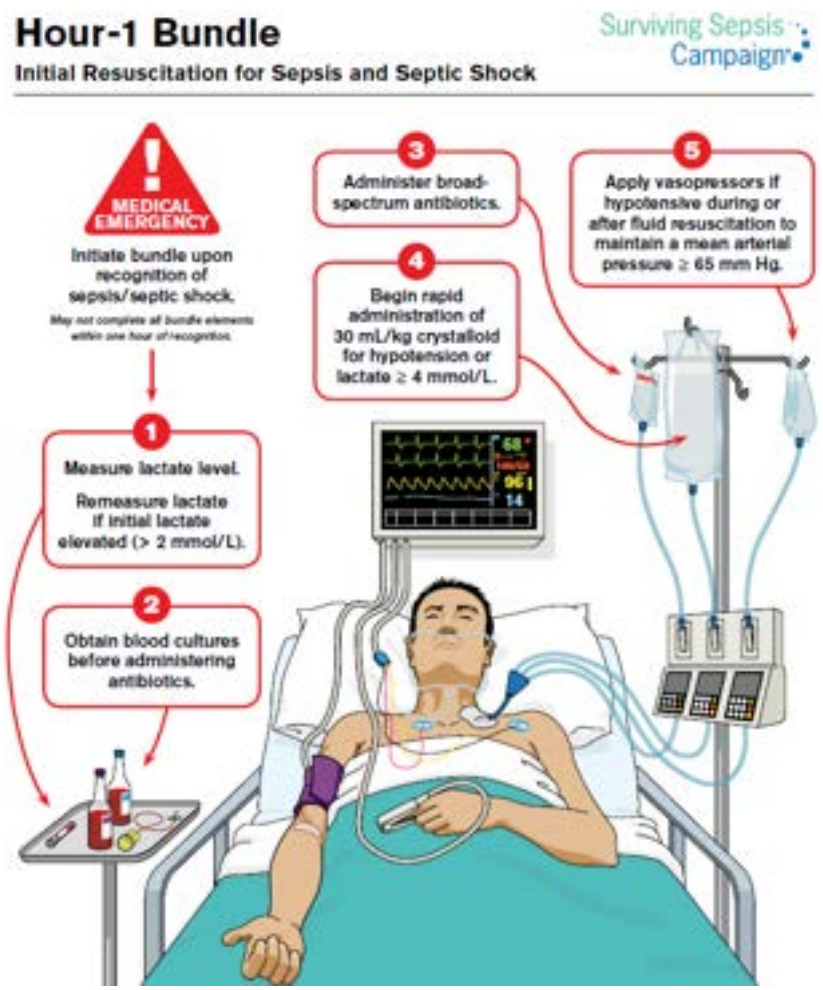
Dragoslav Leković, dr. med.
UKCL, Kirurška klinika, KOAIT, CIT

Ljubljana, 12.9.2024

Vprašanja:

- 1. Obstaja idealen tlak?
- 2. Kaj je dovolj?
- 3. Enak za vse bolnike?
- 4. Preživetje/dober izid zdravljenja odvisno (samo) od tlaka?
- 5. Na izid vpliva **način** zagotavljanja tlaka (tekočine, vazoaktivna zdravila)?
- 6. Res samo MAP?

Kaj pravi SSC?



Mean arterial pressure

Recommendation
9. For adults with septic shock on vasopressors, we **recommend** an initial target mean arterial pressure (MAP) of 65 mm Hg over higher MAP targets
Strong recommendation, moderate-quality evidence

Thank you for your attention!

Goodbye!

Zakaj MAP?

- Tlak, ki določa perfuzijo (=**PRETOK**)
- Pri oscilometričnem merjenju najbolj zanesljiv od vseh treh spremenljivk (SAP, **MAP**, DAP)
- Najbolj reproducibilen pri različnih tehnikah/mestih merjenja
- Septični, vazodilatirani pacienti imajo pogosto nizek DAP – normalen SAP lahko zavaja

SEPSISPAM

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 24, 2014 VOL. 370 NO. 17

High versus Low Blood-Pressure Target in Patients with Septic Shock

Pierre Asfar, M.D., Ph.D., Ferhat Meziani, M.D., Ph.D., Jean-François Hamel, M.D., Fabien Grelon, M.D., Bruno Megarbane, M.D., Ph.D., Nadia Anguel, M.D., Jean-Paul Mira, M.D., Ph.D., Pierre-François Dequin, M.D., Ph.D., s Weiss, M.D., Ph.D., François Legay, M.D., Yves Le Tulzo, M.D., Ph.D., t, M.D., Ph.D., Frédéric Gonzalez, M.D., Christophe Guitton, M.D., Ph.D., Marie Tonnelier, M.D., Pierre Guezennec, M.D., Thierry Van Der Linden, M.D., ., Ph.D., Eric Mariotte, M.D., Gaël Pradel, M.D., Olivier Lesieur, M.D., ien Hervé, M.D., Damien du Cheyron, M.D., Ph.D., Claude Guerin, M.D., Ph.D., ean-Louis Teboul, M.D., Ph.D., and Peter Radermacher, M.D., Ph.D., for the SEPSISPAM Investigators*

BACKGROUND

The Surviving Sepsis Campaign recommends targeting a mean arterial pressure of at least 65 mm Hg during initial resuscitation of patients with septic shock. However, whether this blood-pressure target is more or less effective than a higher target is unknown.

METHODS

In a multicenter, open-label trial, we randomly assigned 776 patients with septic shock to undergo resuscitation with a mean arterial pressure target of either 80 to 85 mm Hg (high-target group) or 65 to 70 mm Hg (low-target group). The primary end point was mortality at day 28.

SEPSISPAM

1. Ni razlike v umrljivosti
2. Pogosteje AF v skupini z višjo tarčno vrednostjo
3. Manj RRT med bolniki z AH v skupini z višjo tarčno vrednostjo

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RESULTS

At 28 days, there was no significant between-group difference in mortality, with deaths reported in 142 of 388 patients in the high-target group (36.6%) and 132 of 388 patients in the low-target group (34.0%) (hazard ratio in the high-target group, 1.07; 95% confidence interval [CI], 0.84 to 1.38; P=0.57). There was also no significant difference in mortality at 90 days, with 170 deaths (43.8%) and 164 deaths (42.3%), respectively (hazard ratio, 1.04; 95% CI, 0.83 to 1.30; P=0.74). The occurrence of serious adverse events did not differ significantly between the two groups (74 events [19.1%] and 69 events [17.8%], respectively; P=0.64). However, the incidence of newly diagnosed atrial fibrillation was higher in the high-target group than in the low-target group. Among patients with chronic hypertension, those in the high-target group required less renal-replacement therapy than did those in the low-target group, but such therapy was not associated with a difference in mortality.

CONCLUSIONS

Targeting a mean arterial pressure of 80 to 85 mm Hg, as compared with 65 to 70 mm Hg, in patients with septic shock undergoing resuscitation did not result in significant differences in mortality at either 28 or 90 days. (Funded by the French Ministry of Health; SEPSISPAM ClinicalTrials.gov number, NCT01149278.)

Lamontagne et al.: Higher versus lower blood pressure targets for vasopressor therapy in shock: a multicentre pilot randomized controlled trial, ICM 2016 (OVATION trial)

- **Methods**
- We randomly assigned critically ill patients who were presumed to suffer from vasodilatory shock regardless of admission diagnosis to a lower (60–65 mmHg) versus a higher (75–80 mmHg) MAP target. The primary objective was to measure the separation in MAP between groups. We also recorded days with protocol deviations, enrolment rate, cardiac arrhythmias and mortality for prespecified subgroups.
- **Results**
- A total of 118 patients were enrolled from 11 centres (2.3 patients/site/month of screening). The between-group separation in MAP was 9 mmHg (95 % CI 7–11). In the lower and higher MAP groups, we observed deviations on 12 versus 8 % of all days on vasopressors (p = 0.059). Risks of cardiac arrhythmias (20 versus 36 %, p = 0.07) and hospital mortality (30 versus 33 %, p = 0.84) were not different between lower and higher MAP arms. Among patients aged 75 years or older, a lower MAP target was associated with reduced hospital mortality (13 versus 60 %, p = 0.03) but not in younger patients.

65 TRIAL

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Reduced Exposure to Vasopressors on 90-Day Mortality in Older Critically Ill Patients With Vasodilatory Hypotension
A Randomized Clinical Trial

François Lamontagne, MD; Alvin Richards-Belle, BSc; Karen Thomas, MSc; David A. Harrison, PhD; M. Zia Sadique, PhD; Richard D. Grieve, PhD; Julie Camsooksai, BSc; Robert Darnell, BA; Anthony C. Gordon, MD; Doreen Henry, MSc; Nicholas Hudson, BA; Alexina J. Mason, PhD; Michelle Saull, BSc; Chris Whitman, BSc; J. Duncan Young, DM; Kathryn M. Rowan, PhD; Paul R. Mouncey, MSc; for the 65 trial investigators

INTERVENTIONS Patients were randomized 1:1 to vasopressors guided either by MAP target (60-65 mm Hg, permissive hypotension) (n = 1291) or according to usual care (at the discretion of treating clinicians) (n = 1307).

MAIN OUTCOME AND MEASURES The primary clinical outcome was all-cause mortality at 90 days.

	Permissive Hypotension n/N (%)	Usual Care n/N (%)	95% CI (p value)	OR (95% CI)
90 Day Mortality	500/1221 (41%)	542/1242 (43.8%)	-6.75 to 1.05 (p= 0.15)	0.89 (0.76 -1.04)
Adjusted 90-day mortality				0.82 (0.68 -0.98)
Chronic hypertension subgroup	214/560 (38.2%)	253/571 (44.3%)		0.67 (0.51-0.88)

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

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A Randomized Clinical Trial

François Lamontagne, MD; Alvin
M. Zia Sadique, PhD; Richard D. G
Doreen Henry, MSc; Nicholas Hu
J. Duncan Young, DM; Kathryn M

JAMA Network

QUESTION What is the effect on mortality at 90 days of reducing the exposure to vasopressors through permissive hypotension (mean arterial pressure target of 60-65 mm Hg) in ICU patients aged 65 years or older receiving vasopressors for vasodilatory hypotension?

CONCLUSION This randomized trial found that reducing the exposure to vasopressors through permissive hypotension did not significantly reduce mortality at 90 days. However, the CI around the point estimate for the primary outcome should be considered when interpreting the clinical importance of the study.

POPULATION

1388 Men
1067 Women

Patients aged ≥65 years with vasodilatory hypotension, as assessed by treating clinician

Mean age: 75 years

LOCATIONS

65 Adult ICUs in the UK

INTERVENTION

2463 Patients analyzed

1221
Permissive hypotension
Vasopressor use guided by mean arterial pressure, target of 60-65 mm Hg

1242
Usual care
Vasopressor use at discretion of treating clinicians

PRIMARY OUTCOME

All-cause mortality at 90 days

FINDINGS

All-cause mortality at 90 days

Permissive hypotension	Usual care
500 of 1221 patients	542 of 1242 patients

There was no statistically significant difference.

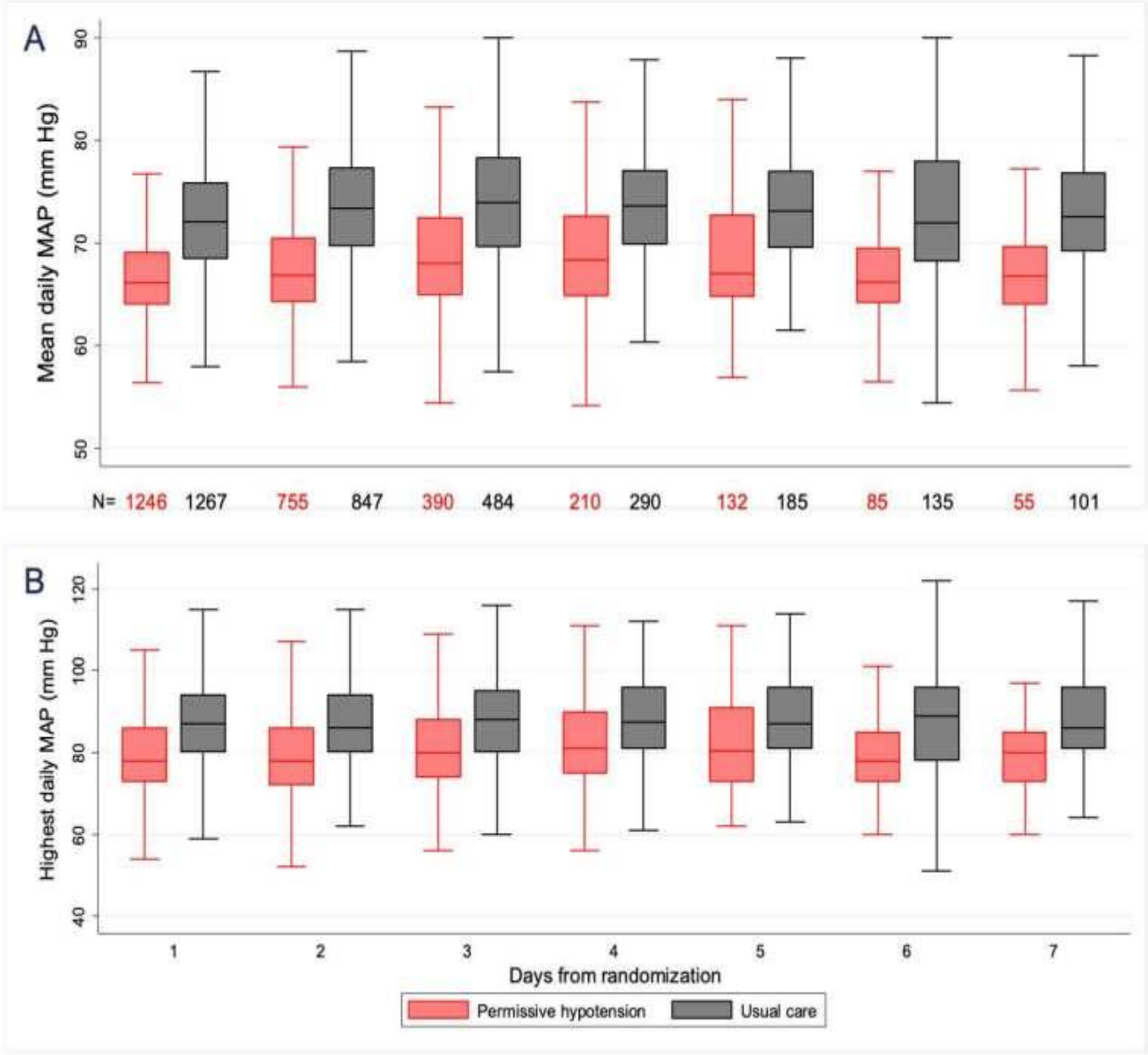
Absolute risk difference, −2.85%
(95% CI, −6.75% to 1.05%); $P = .15$

Lamontagne F, Richards-Belle A, Thomas K, et al; 65 Trial investigators. Effect of reduced exposure to vasopressors on 90-day mortality in older critically ill patients with vasodilatory hypotension: a randomized clinical trial [published online February 12, 2020]. *JAMA*. doi:10.1001/jama.2020.0930

65 TRIAL – CAVEAT

- Mean MAP 66.7 vs. 72.6

eFigure 10. MAP values days 1 to 7 post-randomization.



Kato and Pinsky *Ann. Intensive Care* (2015) 5:41
DOI 10.1186/s13613-015-0085-5

Annals of Intensive Care
a SpringerOpen Journal

REVIEW Open Access

Personalizing blood pressure management in septic shock

Ryotaro Kato and Michael R. Pinsky*

Abstract

This review examines the available evidence for targeting a specific mean arterial pressure (MAP) in sepsis resuscitation. The clinical data suggest that targeting an MAP of 65–70 mmHg in patients with septic shock who do not have chronic hypertension is a reasonable first approximation. Whereas in patients with chronic hypertension, targeting a higher MAP of 80–85 mmHg minimizes renal injury, but it comes with increased risk of arrhythmias. Importantly, MAP alone should not be used as a surrogate of organ perfusion pressure, especially under conditions in which intracranial, intra-abdominal or tissue pressures may be elevated. Organ-specific perfusion pressure targets include 50–70 mmHg for the brain based on trauma brain injury as a surrogate for sepsis, 65 mmHg for renal perfusion and >50 mmHg for hepato-splanchnic flow. Even at the same MAP, organs and regions within organs may have different perfusion pressure and pressure–flow relationships. Thus, once this initial MAP target is achieved, MAP should be titrated up or down based on the measures of organ function and tissue perfusion.

Keywords: Arterial blood pressure, Autoregulation, Critical closing pressure, Organ blood flow, Resuscitation, Sepsis, Septic shock, Vasopressor therapy

Intensive Care Med (2018) 44:1551–1552
https://doi.org/10.1007/s00134-018-5292-8

EDITORIAL

MAP of 65: target of the past?

Pierre Asfar[1*], Peter Radermacher[2] and Marlies Ostermann[3]

[6, 7]. In SEPSISPAM, patients were enrolled within 6 h of initiation of vasoactive drug treatment. In OVATION, patients were recruited up to 24 h after the diagnosis of septic shock. Target values were 80–85 vs. 65–70 and 75–80 vs. 60–65 mmHg for the high vs. low MAP in SEPSISPAM and OVATION, respectively. There was no significant survival difference between the treatment groups at day 28 in either trial. However, both trials were underpowered as the mortality rate in the control groups was lower than expected. In addition, patients assigned to the low MAP target groups achieved higher MAPs than planned according to the study protocol.

- MPP=MAP – CVP

Recent data suggest that mean perfusion pressure (MPP) may serve as a better surrogate marker of perfusion pressure than MAP. It is calculated as the difference between systemic mean arterial pressure (MAP) and CVP, i.e., MPP=MAP−CVP [10, 11]. Whether MPP is a better resuscitation target for patients with shock is unknown. It is also unclear whether different organ-specific perfusion targets are needed.

Pomen drugih tlačnih spremenljivk

Brez tlačne razlike NI pretoka

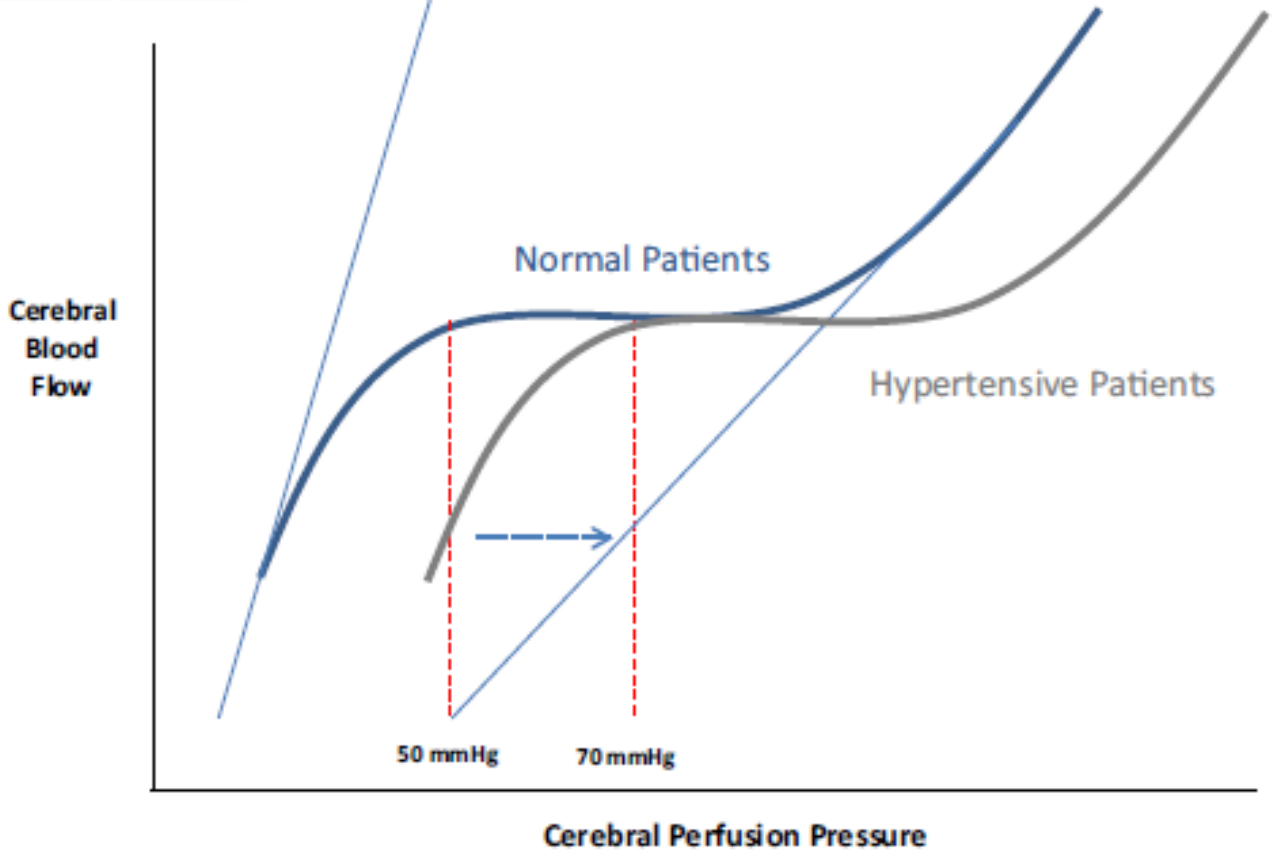
Table 1 Perfusion pressure for different organs

Organs	Inflow pressure	Outflow pressure (whichever is higher)	Perfusion pressure
Brain	MAP	CVP or intracranial pressure (ICP)	MAP—CVP or ICP
Heart	Diastolic BP	CVP or intrathoracic pressure (ITP)	Diastolic BP—CVP or ITP
Kidney	MAP	CVP or intra-abdominal pressure (IAP)	MAP—CVP or IAP
Bowel	MAP	CVP or intra-abdominal pressure (IAP)	MAP—CVP or IAP

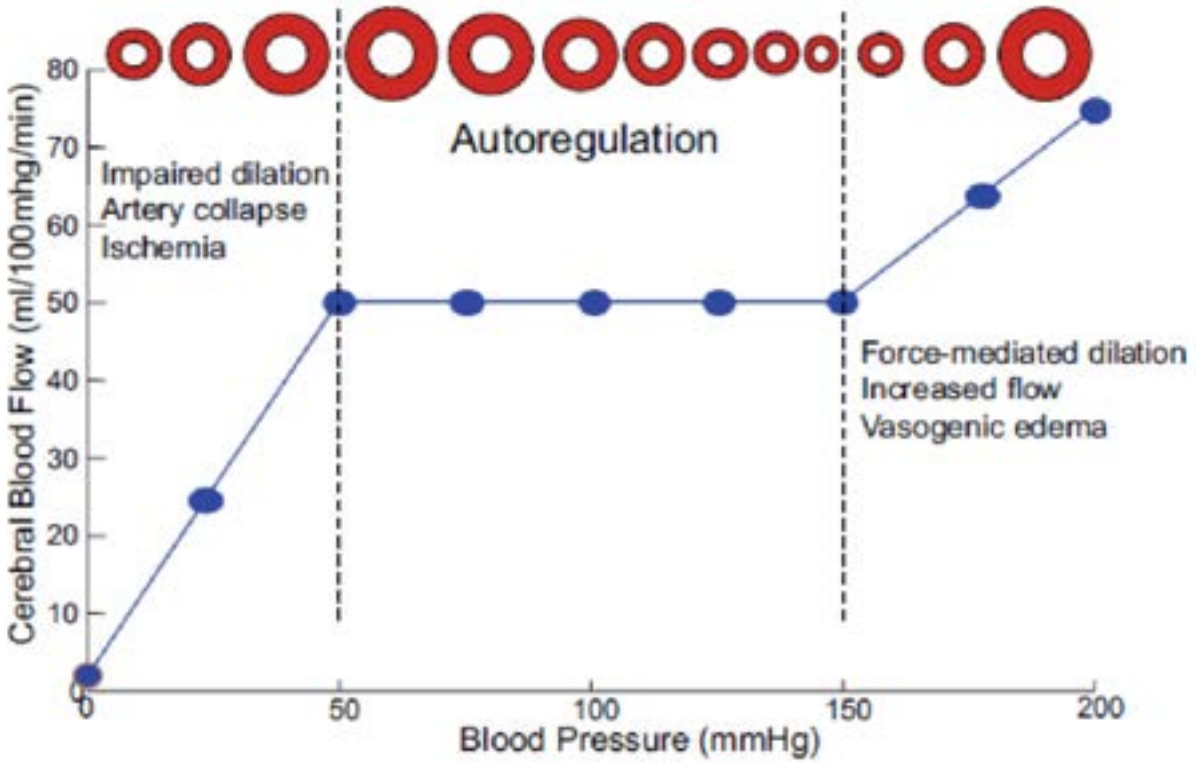
MAP mean arterial pressure, *BP* blood pressure, *CVP* central venous pressure

Perfuzija možganov

CPP=MAP – ICP (ali CVP)



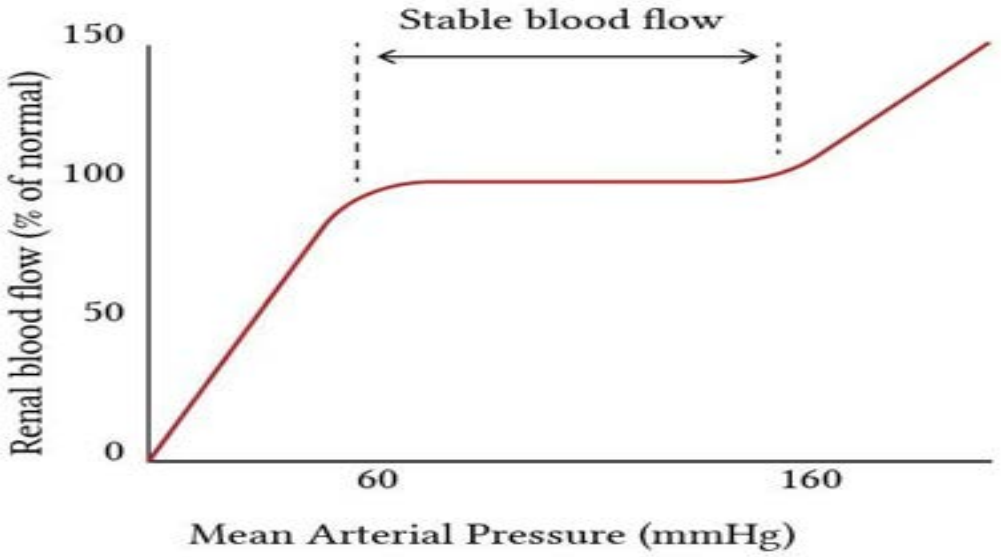
Vir: Kato et Pinsky, 2015



Vir: ukessays.com

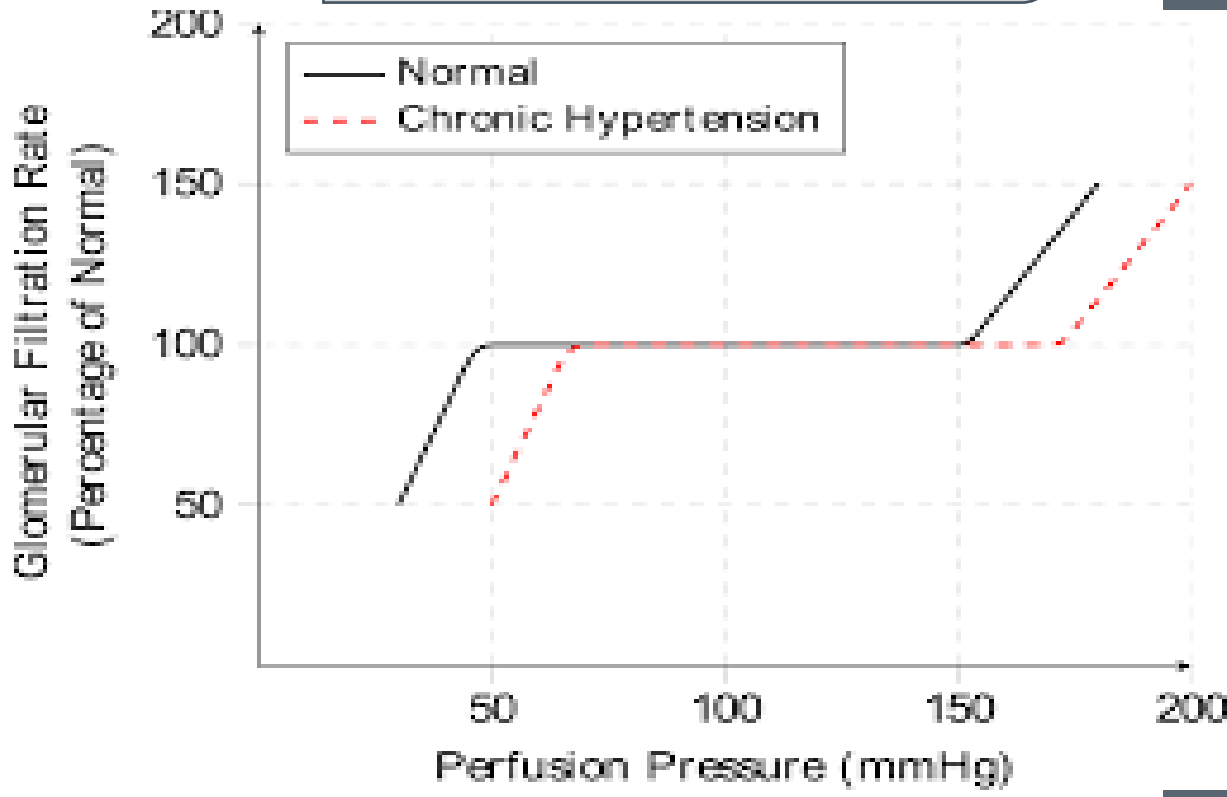
Perfuzija ledvic

RPP=MAP – CVP (ali IAP)



Vir: derangedphysiology.com

Pomen IAH oz. ACS

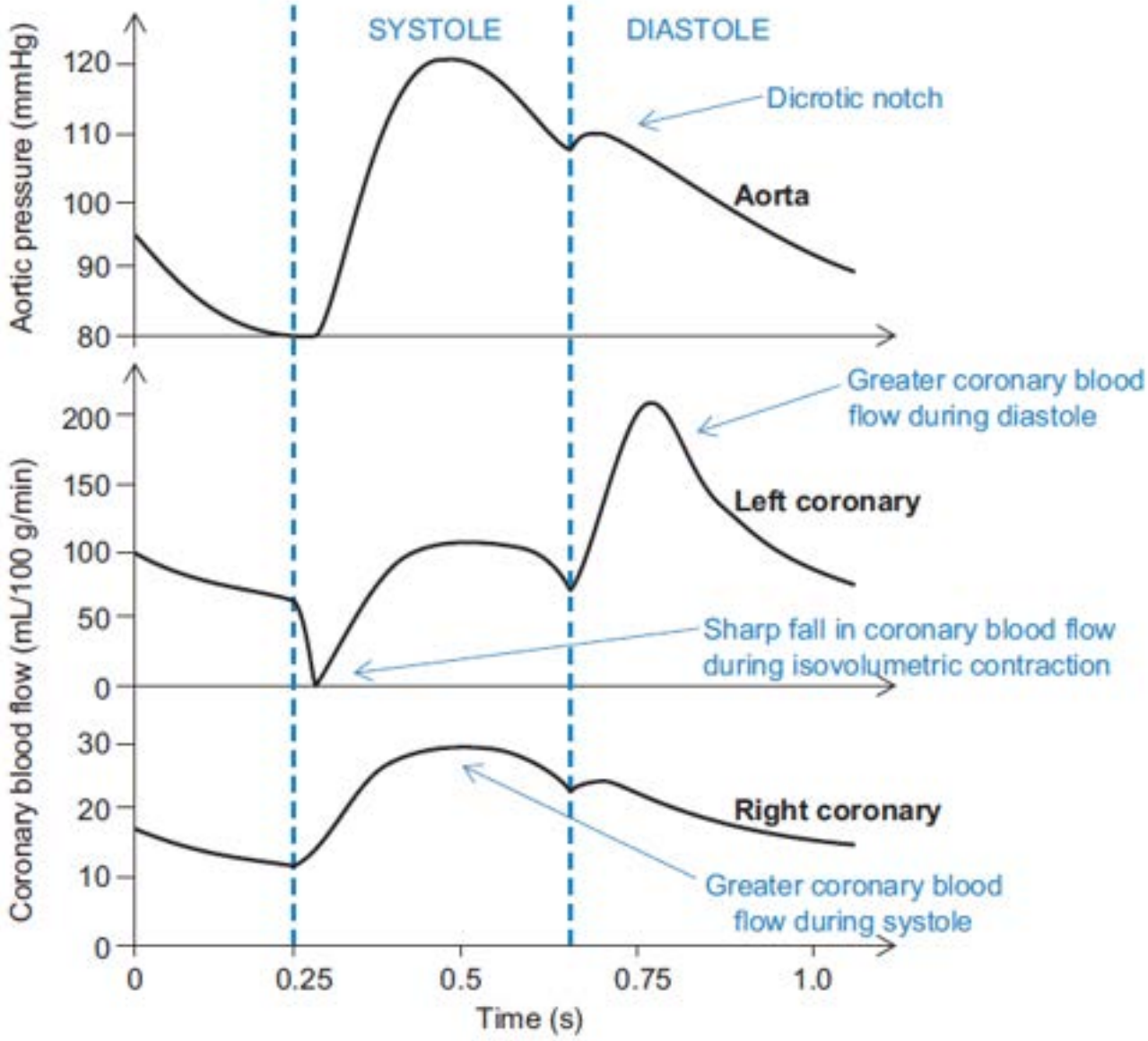


Vir: https://partone.litfl.com/

Koronarna perfuzija

CPP=Aort. DAP – LVEDP

Pomen DAP (ki ga SSC ne omenja)



Ospina-Tascón et al. Ann. Intensive Care (2020) 10:41
https://doi.org/10.1186/s13613-020-00658-8

Annals of Intensive Care

RESEARCH Open Access

Diastolic shock index and clinical outcomes in patients with septic shock

Gustavo A. Ospina-Tascón[1,2*], Jean-Louis Teboul[1,3,4], Glenn Hernandez[1,5], Ingrid Alvarez[1], Alvaro I. Sánchez-Ortiz[1], Luis E. Calderón-Tapia[1], Ramiro Manzano-Nunez[1], Edgardo Quiñones[1], Humberto J. Madriñan-Navia[1], Juan E. Ruiz[1], José L. Aldana[1] and Jan Bakker[1,5,6,7,8]

$$DSI = \frac{HR}{DAP}$$

- DSI pred uvedbo vazopresorja (N=337)
- DSI ob uvedbi vazopresorja (N=424)
- RR smrti

Background: Loss of vascular tone is a key pathophysiological feature of septic shock. Combination of gradual diastolic hypotension and tachycardia could reflect more serious vasodilatory conditions. We sought to evaluate the relationships between heart rate (HR) to diastolic arterial pressure (DAP) ratios and clinical outcomes during early phases of septic shock.

Methods: Diastolic shock index (DSI) was defined as the ratio between HR and DAP. DSI calculated just before starting vasopressors (Pre-VPs/DSI) in a preliminary cohort of 337 patients with septic shock (January 2015 to February 2017) and at vasopressor start (VPs/DSI) in 424 patients with septic shock included in a recent randomized controlled trial (ANDROMEDA-SHOCK; March 2017 to April 2018) was partitioned into five quantiles to estimate the relative risks (RR) of death with respect to the mean risk of each population (assumed to be 1). Matched HR and DAP subsamples were created to evaluate the effect of the individual components of the DSI on RRs. In addition, time-course of DSI and interaction between DSI and vasopressor dose (DSI*NE.dose) were compared between survivors and non-survivors from both populations, while ROC curves were used to identify variables predicting mortality. Finally, as exploratory observation, effect of early start of vasopressors was evaluated at each Pre-VPs/DSI quintile from the preliminary cohort.

Ospina-Tascón et al. Ann. Intensive Care (2020) 10:41
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Results: Risk of death progressively increased at gradual increments of Pre-VPs/DSI or VPs/DSI (One-way ANOVA, $p < 0.001$). Progressive DAP decrease or HR increase was associated with higher mortality risks only when DSI concomitantly increased. Areas under the ROC curve for Pre-VPs/DSI, SOFA and initial lactate were similar, while mean arterial pressure and systolic shock index showed poor performances to predict mortality. Time-course of DSI and DSI*NE. dose was significantly higher in non-survivors from both populations (repeated-measures ANOVA, $p < 0.001$). Very early start of vasopressors exhibited an apparent benefit at higher Pre-VPs/DSI quintile.

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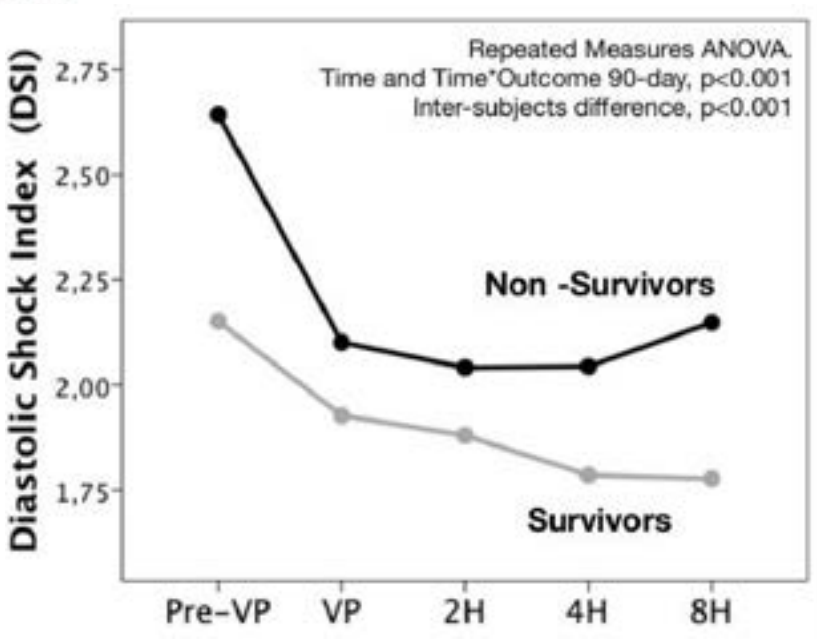
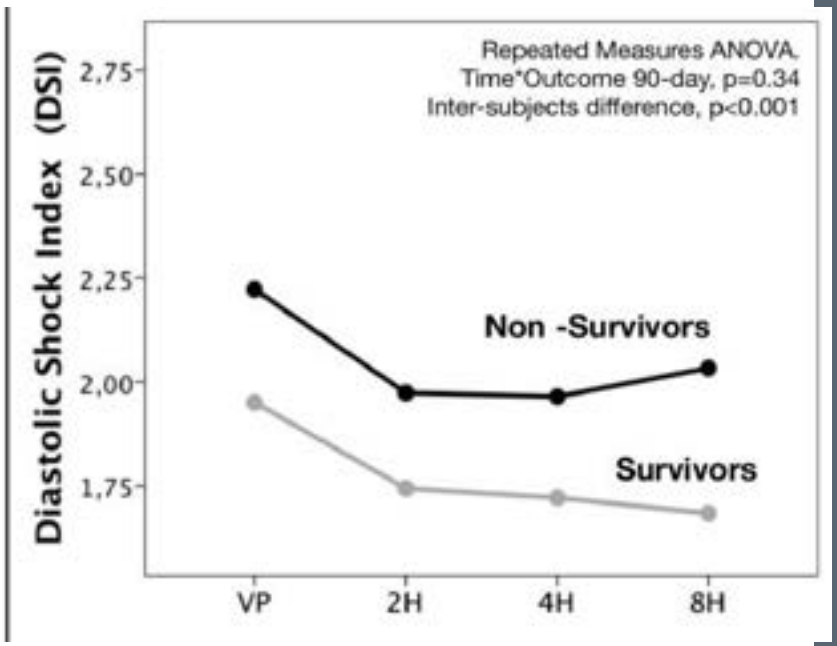
› Najbolj nevarna kombinacija: nizek DAP in visok HR





Conclusions: DSI at pre-vasopressor and vasopressor start points might represent a very early identifier of patients at high risk of death. Isolated DAP or HR values do not clearly identify such risk. Usefulness of DSI to trigger or to direct therapeutic interventions in early resuscitation of septic shock need to be addressed in future studies.

Tlak vs. pretok

$$Q = \frac{\Delta P}{R}$$

$$\mathbf{CO = \frac{MAP - CVP}{SVR}}$$

frontiers | Frontiers in Physiology

TYPE Systematic Review
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Optimal target blood pressure in critically ill adult patients with vasodilatory shock: A systematic review and meta-analysis

Hidero Yoshimoto[1,2], Satoshi Fukui[3], Koki Higashio[3], Akira Endo[4], Akira Takasu[1] and Kazuma Yamakawa[1]*

[1]Department of Emergency and Critical Care Medicine, Osaka Medical and Pharmaceutical University, Takatsuki, Osaka, Japan, [2]Department of Surgery, Osaka Medical and Pharmaceutical University, Takatsuki, Osaka, Japan, [3]Faculty of Medicine, Osaka Medical and Pharmaceutical University, Takatsuki, Osaka, Japan, [4]Trauma and Acute Critical Care Center, Tokyo Medical and Dental University Hospital, Bunkyo-ku, Tokyo, Japan

We performed a meta-analysis to evaluate the optimal MAP for patients with vasodilatory shock, which included three randomized controlled trials that recruited 3,357 patients. Between the lower (60–70 mmHg) and higher (>70 mmHg) MAP target groups, there was no significant difference in all-cause mortality (risk ratio [RR], 1.06; 95% confidence intervals [CI], 0.98–1.16) which was similar in patients with chronic hypertension (RR, 1.10; 95% CI, 0.98–1.24) and patients aged ≥65 years (RR, 1.10; 95% CI, 0.99–1.21). No significant difference in adverse events was observed between the different MAP groups (RR, 1.04; 95% CI, 0.87–1.24); however, supraventricular arrhythmia was significantly higher in the higher MAP group (RR, 1.73; 95% CI, 1.15–2.60). Renal replacement therapy was reduced in the higher MAP group of patients with chronic hypertension (RR, 0.83; 95% CI, 0.71–0.98). Though the higher MAP control did not improve the mortality rate, it may be beneficial in reducing renal replacement therapy in patients with chronic hypertension.

Journal of Hepatology
Volume 79, Issue 2, August 2023, Pages 349-361

Research Article

A randomised-controlled trial (TARGET-C) of high *vs.* low target mean arterial pressure in patients with cirrhosis and septic shock

Rakhi Maiwall [1], Samba Siva Rao Pasupuleti [2,7], Ashini Kumar Hidam [3], Anupam Kumar [3], Harsh Vardhan Tevethia [1], Rajan Vijayaraghavan [1], Arpita Majumdar [1], Adarsh Prasher [3], Sherin Thomas [4], Rajendra Prasad Mathur [5], Guresh Kumar [6], Shiv Kumar Sarin [1]

High (80-85 mmHg) vs. Low (60-65 mmHg)

Highlights

- A higher target MAP strategy does not confer any survival benefit in patients with cirrhosis and septic shock.
- A higher target MAP strategy was associated with more frequent adverse events.
- This strategy was associated with decreased incidence of intradialytic hypotension, better tolerance of dialysis, and improved renal recovery.
- A higher target MAP strategy can be considered alongside careful monitoring for adverse events.

Sledi...

Revista Española de Anestesiología y Reanimación 71 (2024) 112–124

Revista Española de Anestesiología y Reanimación

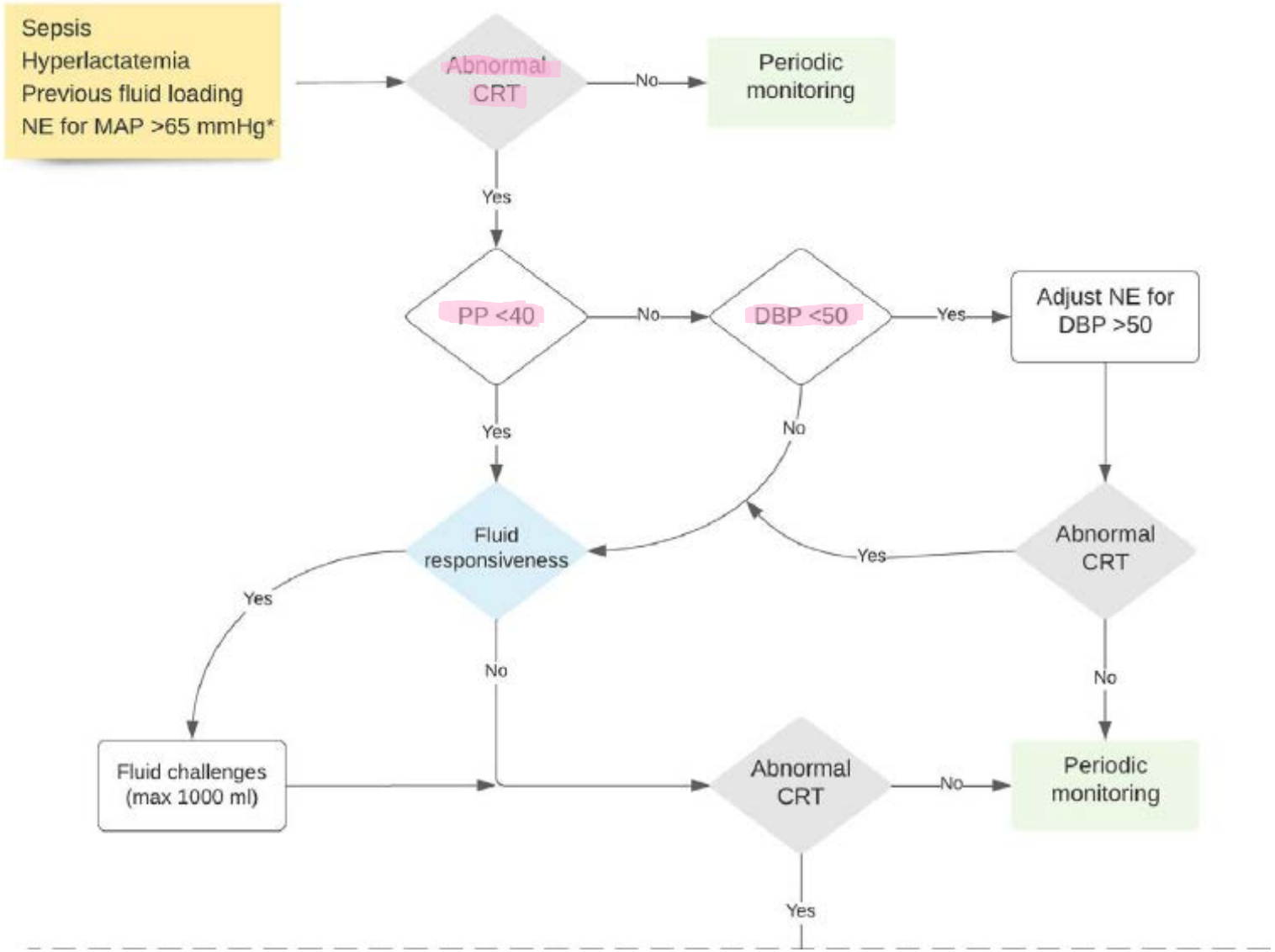
www.elsevier.es/redar

SPECIAL ARTICLE

Towards the personalization of septic shock resuscitation: the fundamentals of ANDROMEDA-SHOCK-2 trial

F. Ramasco[a,*], G. Aguilar[b], C. Aldecoa[c], J. Bakker[d,e,f,g], P. Carmona[h], D. Dominguez[i], M. Galiana[j], G. Hernández[d,e], E. Kattan[d,e], C. Olea[k], G. Ospina-Tascón[e,l,m], A. Pérez[n], K. Ramos[d,e], S. Ramos[o], G. Tamayo[p], G. Tuero[q], for the ANDROMEDA-SHOCK-2, Spanish Investigators, Sociedad Española de Anestesiología, Reanimación y Terapéutica del Dolor (SEDAR)[1]

Tier 1


Sepsis
Hyperlactatemia
Previous fluid loading
NE for MAP >65 mmHg*
Abnormal CRT
No
Periodic monitoring
Yes
PP <40
No
DBP <50
Yes
Adjust NE for DBP >50
Yes
No
Fluid responsiveness
Yes
Abnormal CRT
Yes
No
No
Fluid challenges (max 1000 ml)
Abnormal CRT
No
Periodic monitoring
Yes

Tier 2

* Vasopressor therapy should be continously titrated to mantain MAP >65 mmHg throughout the study period

** Perform succesive fluid challenges until CRT normalizes, FR becomes negative or safety limits are met

*** If patient already receiving dobutamine due to cardiac dysfunction treatment, skip this step

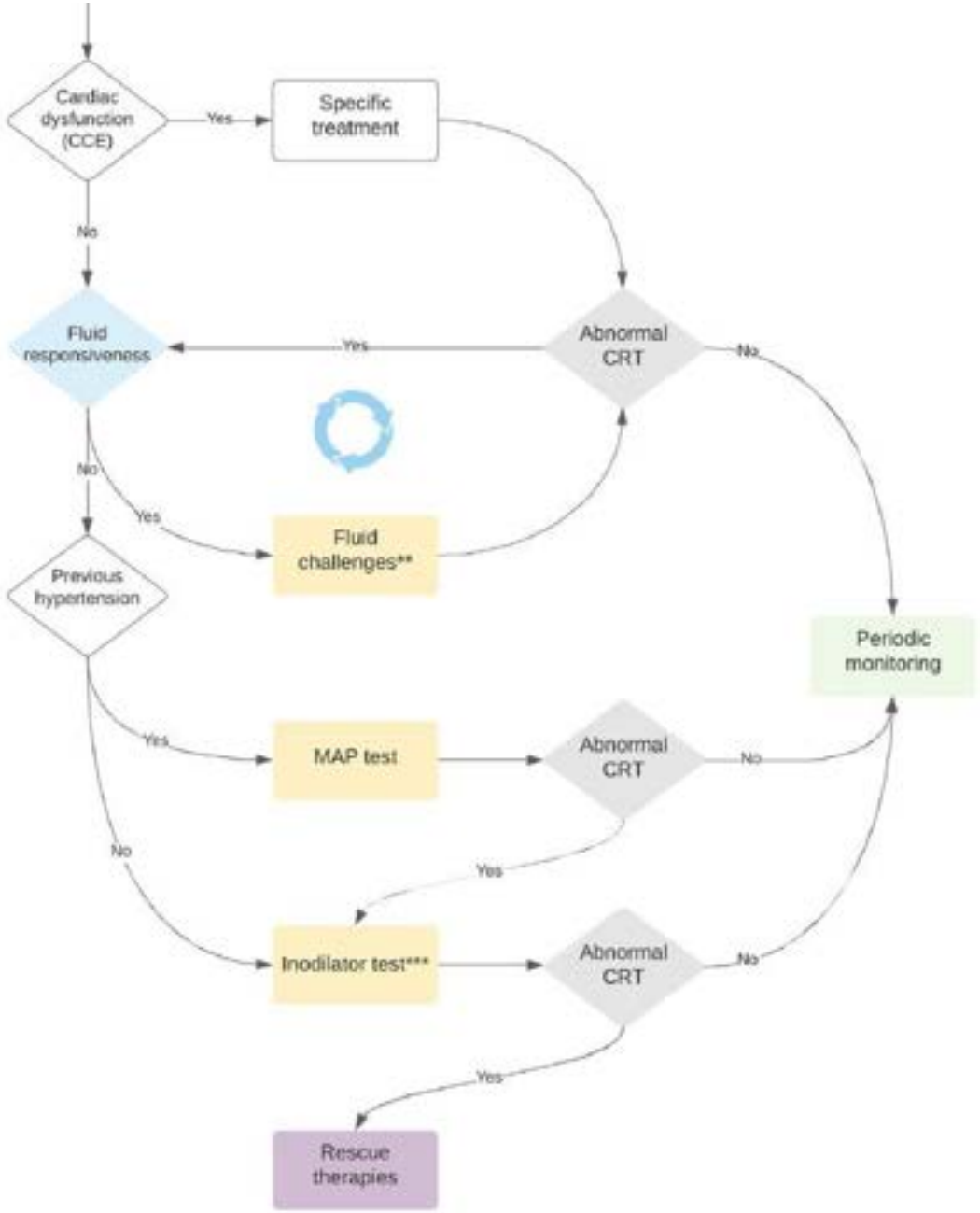


Figure 1 ANDROMEDA-SHOCK-2 study protocol.

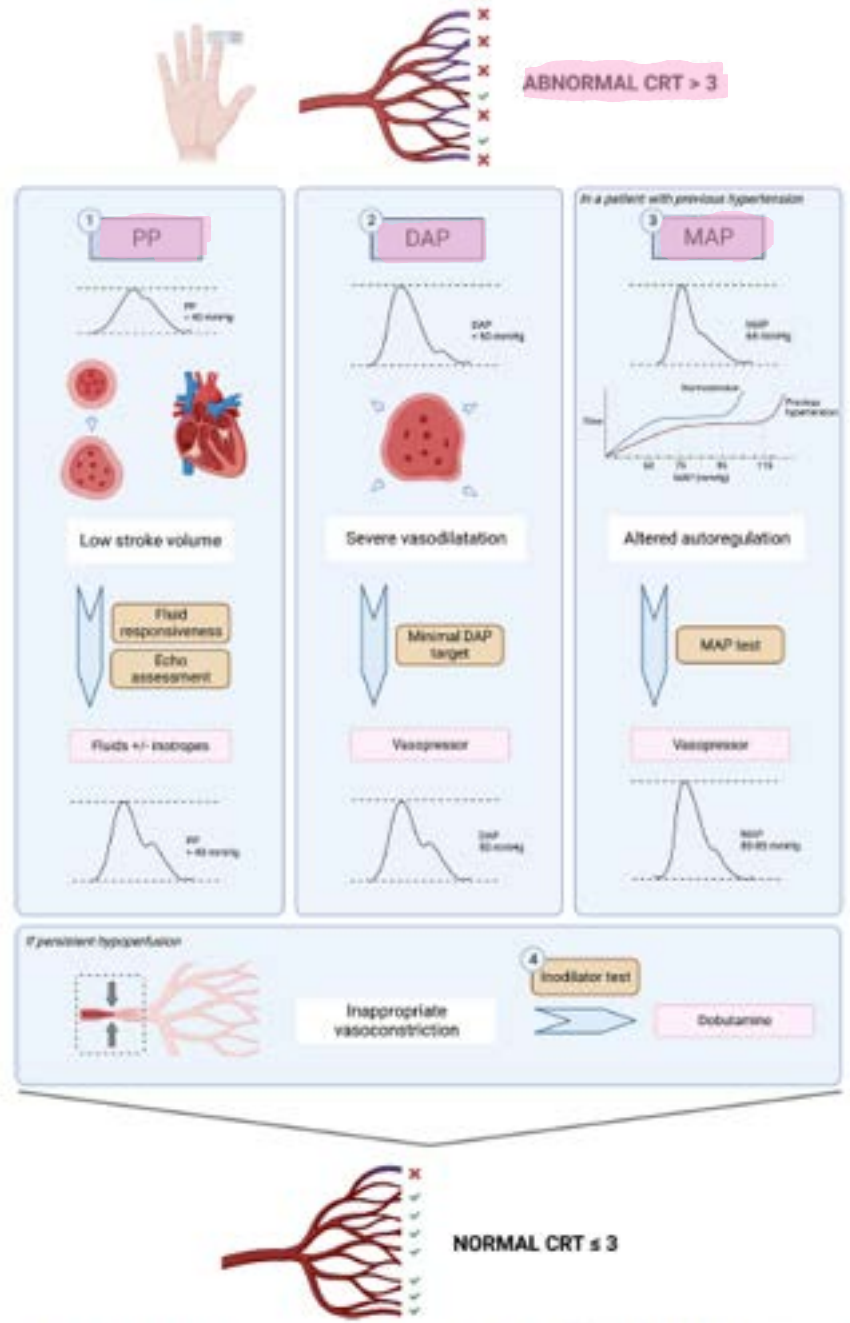


Figure 2 Key hemodynamic patterns and resuscitative interventions on the ANDROMEDA-SHOCK-2 trial. Created with BioRender.com.

Potekajo nove študije...

Parametri makrocirkulacije:

1. krvni tlak (MAP, DAP +/- PP?) + HR (+/- DSI?)
2. MVS (CO) ?

Parametri mikrocirkulacije:

1. laktat
2. Mottling score
3. **CRT**
4. Diureza
5. ScvO2?
6. $\Delta P_{v\text{-}a\ CO2}$?

Salomonska rešitev (po Ponciju)

› Zadosten tlak pri septičnem šoku je tlak, ki bo zagotovil preživetje bolnika in dober izid zdravljenja.

π

HVALA!