10 věcí, kterých bych se měl při léčbě sepse vyvarovat

Beneš Jan

Klinika anesteziologie, resuscitace a intenzivní medicíny,
Fakultní nemocnice a Lékařská Fakulta v Plzni Univerzity Karlovy v Praze

1. NE-LÉČIT SEPSI

1991/2 - První defince SEPSE (infekce + 2 kritéria SIRS)

Table 1. Diagnostic Criteria for Sepsis, Severe Sepsis, and Septic Shock.*

Sepsis (documented or suspected infection plus ≥1 of the following)†

General variables

- Fever (core temperature, >38.3°C)
- Hypothermia (core temperature, <36°C)
- Elevated heart rate (>90 beats per min or >2 SD above the upper limit of the normal range for age)

INFEKT + SIRS (≥2)

- T >38 C or <36 C
- P >90/min
- DF >20/min nebo PaCO2 <32 mmHg
- Leu >12 nebo >10%tyčí

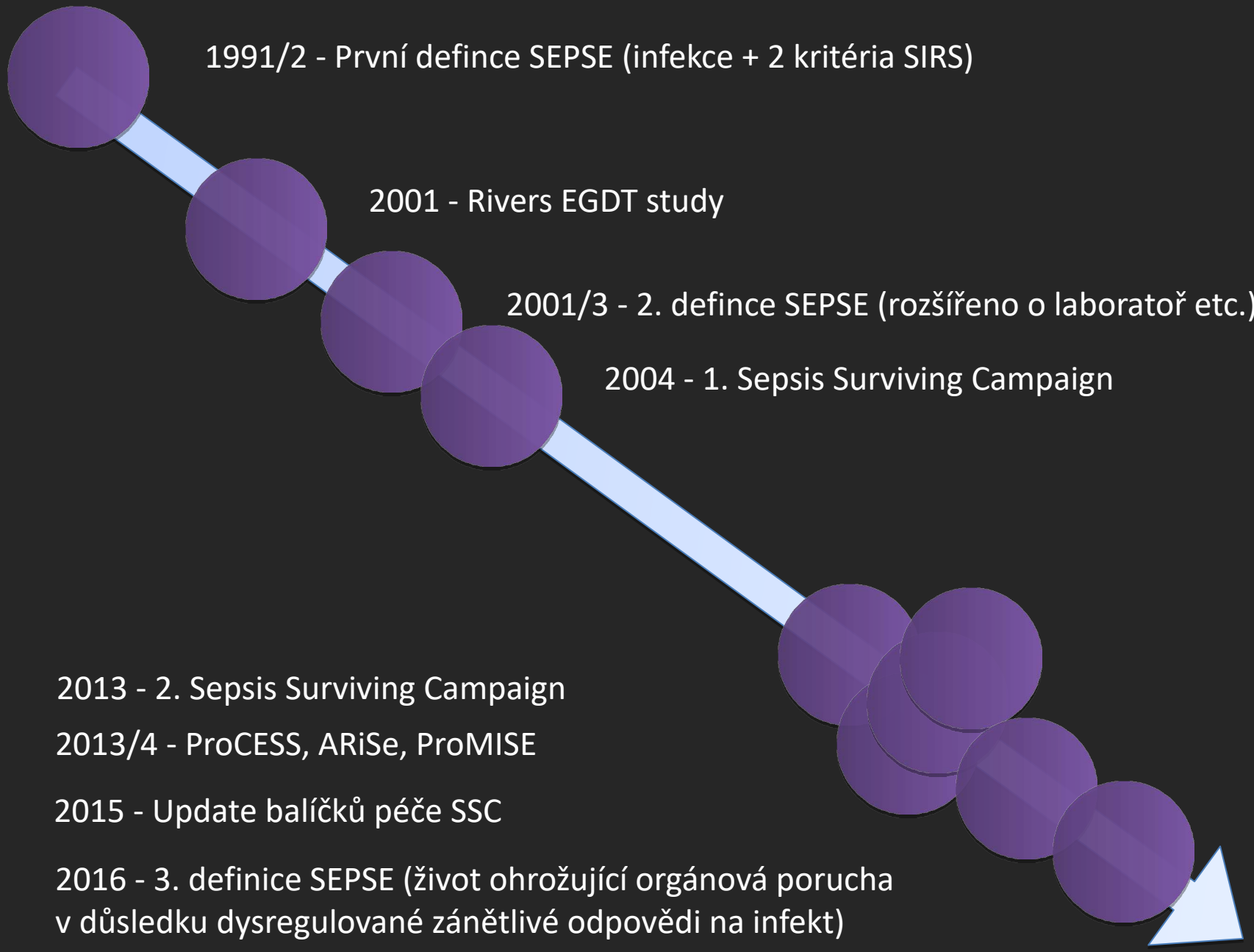
- Arterial hypoxemia (ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen, <300)
- Acute oliguria (urine output, <0.5 ml/kg/hr or 45 ml/hr for at least 2 hr)
- Increase in creatinine level of >0.5 mg/dl (>44 μmol/liter)
- Coagulation abnormalities (international normalized ratio, >1.5; or activated partial-thromboplastin time, >60 sec)
- Paralytic ileus (absence of bowel sounds)
- Thrombocytopenia (platelet count, <100,000/mm^3)
- Hyperbilirubinemia (plasma total bilirubin, >4 mg/dl [68 μmol/liter])

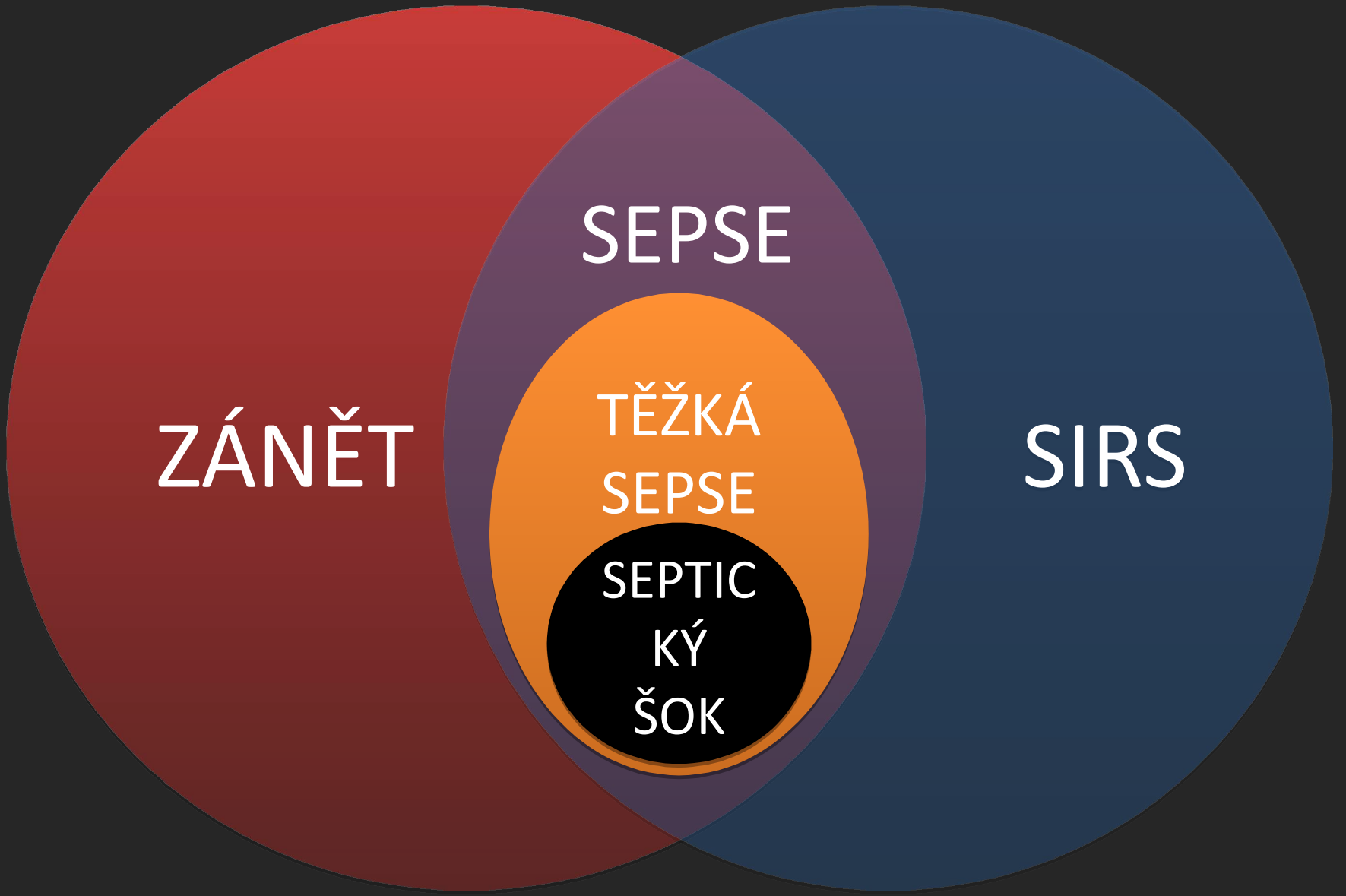
Tissue-perfusion variables

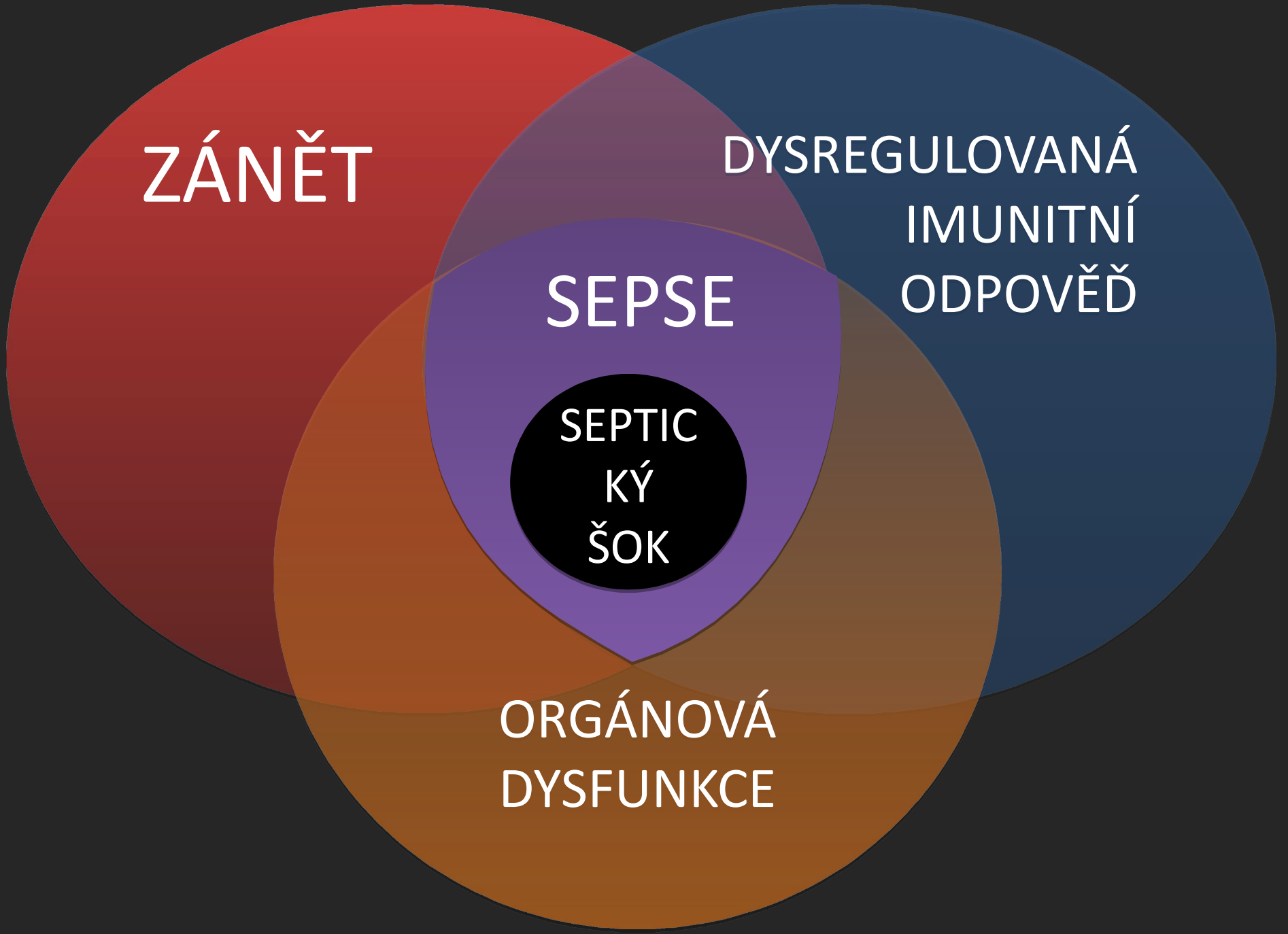
- Hyperlactatemia (lactate, >1 mmol/liter)
- Decreased capillary refill or mottling

Severe sepsis (sepsis plus organ dysfunction)

Septic shock (sepsis plus either hypotension [refractory to intravenous fluids] or hyperlactatemia)¶


1991/2 - První definice SEPSE (infekce + 2 kritéria SIRS)
2001 - Rivers EGDT study
2001/3 - 2. definice SEPSE (rozšířeno o laboratoř etc.)
2004 - 1. Sepsis Surviving Campaign
2013 - 2. Sepsis Surviving Campaign
2013/4 - ProCESS, ARiSe, ProMISE
2015 - Update balíčků péče SSC
2016 - 3. definice SEPSE (život ohrožující orgánová porucha v důsledku dysregulované zánětlivé odpovědi na infekt)


ZÁNĚT
SEPSE
TĚŽKÁ SEPSE
SEPTICKÝ ŠOK
SIRS


ZÁNĚT
DYSREGULOVANÁ IMUNITNÍ ODPOVĚĎ
SEPSE
SEPTICKÝ ŠOK
ORGÁNOVÁ DYSFUNKCE

qSOFA (2 kritéria) poukazuje na vysoké riziko rozvoje sepse a zvýšené mortality u nemocných mimo JIP

SEPSE je život ohrožující orgánová porucha (SOFA≥2) v důsledku infekcí vyvolané dysregulované zánětlivé odpovědi.

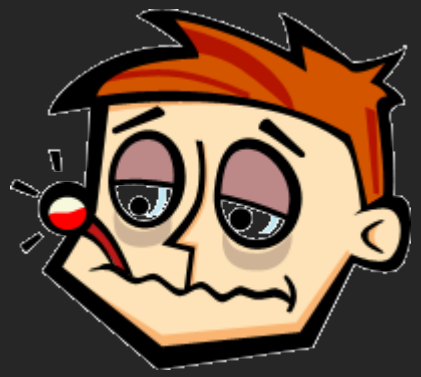
SEPTICKÝ ŠOK je definován přítomností oběhové nestability s nutností užití vazopressorů a poruchou buněčného metabolizmu (laktát >2 mmol/l)

qSOFA (2 kritéria)

Hypotenze (STK<100$_{mmHg}$)

Alterované vědomí

Tachypnea (DF>22$_{/min}$)

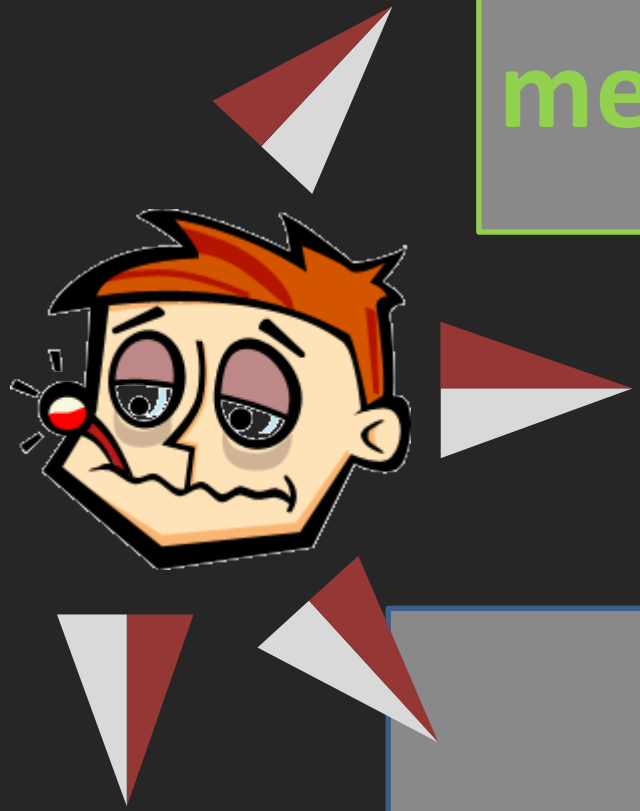


Patrání po INFEKTU jako zdroji obtíží nemocného a jeho kontrola

Pátrání po nové orgánové dysfunkci: SOFA≥2

Předání pacienta do adekvátní péče

22let slečna,
meningokoková sepse



80 letý CHOPN/ICHS pacient
s pneumokokovou pneumonií

60-letý diabetik
s flegmonou nohy

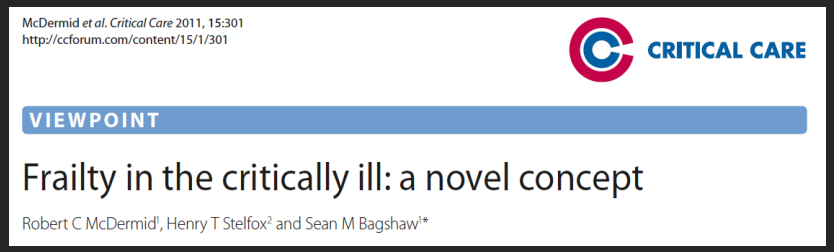
Neutropenická ALL s uroinfektem

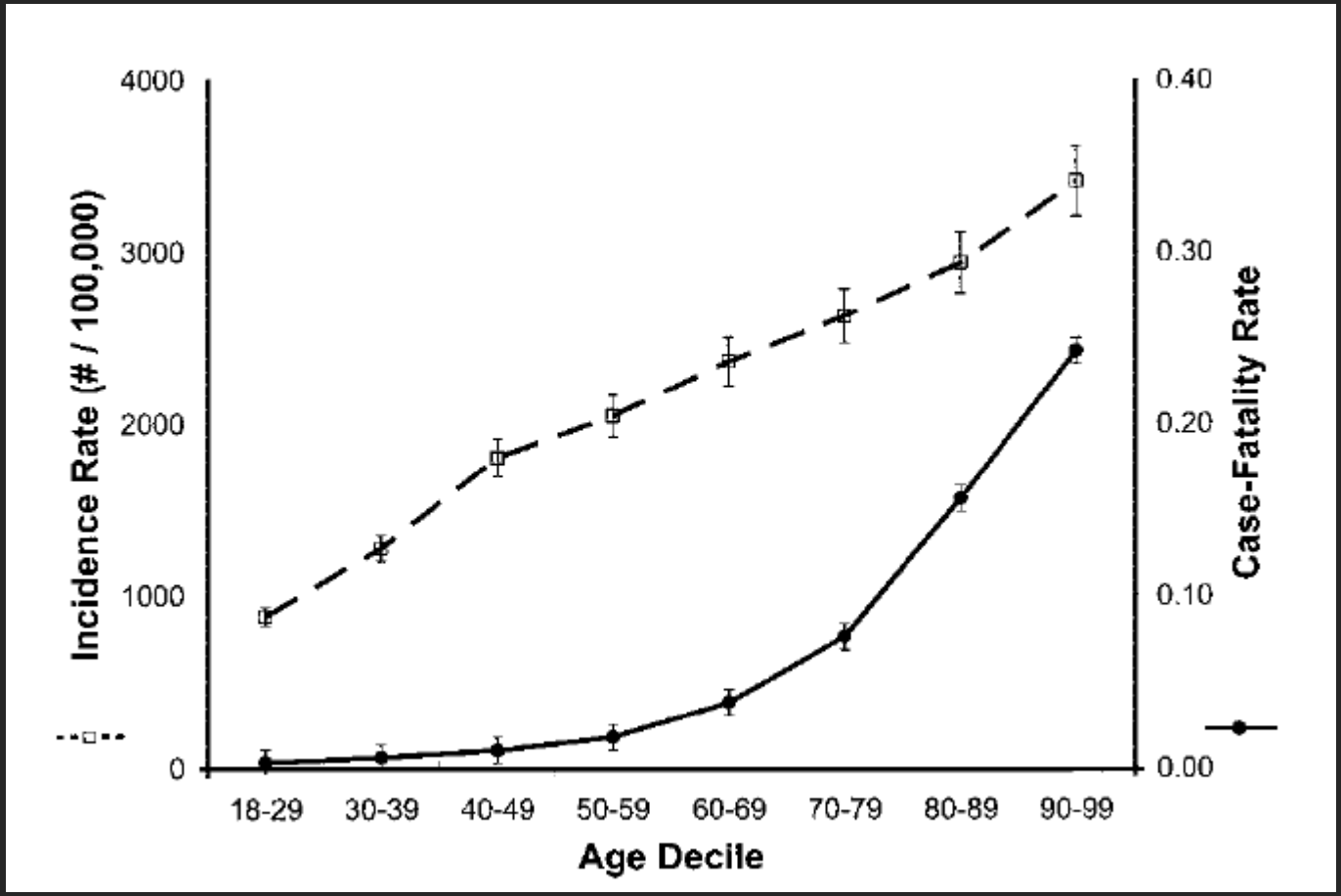
2. Nevzdávat to předčasně

80 letý CHOPN/ICHS pacient s pneumokokovou pneumonií

Genetické a imunitní vlivy
Komorbidity
Vstupní závažnost infektu
Věk nad 75let
Porucha vědomí

Křehkost





The effect of age on the development and outcome of adult sepsis*

Greg S. Martin, MD, MSc; David M. Mannino, MD; Marc Moss, MD **(Crit Care Med 2006; 34:15–21)**

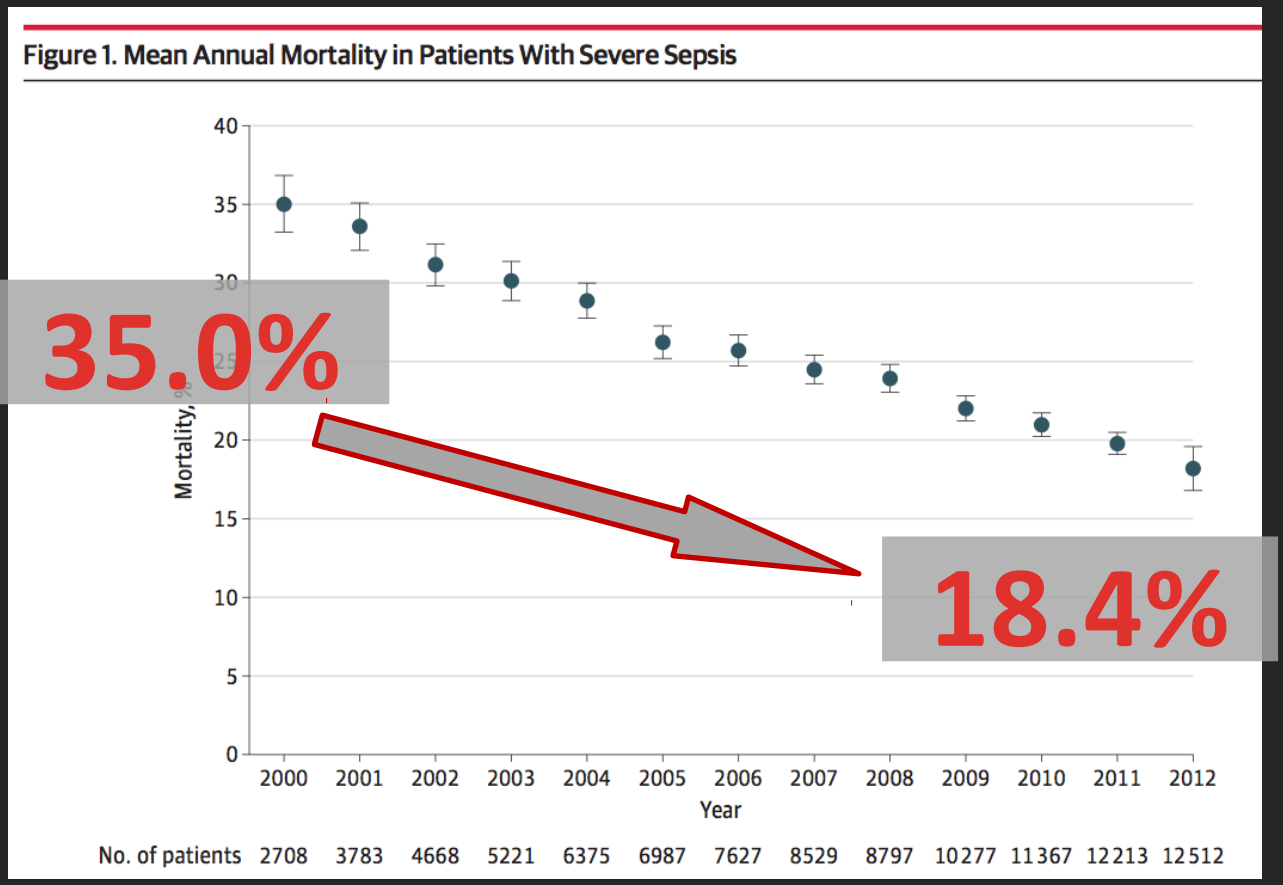
Mortality Related to Severe Sepsis and Septic Shock Among Critically Ill Patients in Australia and New Zealand, 2000-2012

Kirsi-Maija Kaukonen, MD, PhD, EDIC[1,2]; Michael Bailey, PhD[1]; Satoshi Suzuki, MD[3]; David Pilcher, FCICM[1,4,5]; Rinaldo Bellomo, MD, PhD[1,3]

[+] Author Affiliations

JAMA. 2014;311(13):1308-1316. doi:10.1001/jama.2014.2637.

Figure 1. Mean Annual Mortality in Patients With Severe Sepsis



Increased intensity of treatment and decreased mortality in elderly patients in an intensive care unit over a decade*

(Crit Care Med 2010; 38:59–64)

Nicolas Lerolle, MD, PhD; Ludovic Trinquart, MSc; Caroline Bornstain, MD; Jean-Marc Tadié, MD; Audrey Imbert, MD; Jean-Luc Diehl, MD; Jean-Yves Fagon, MD, PhD; Emmanuel Guérot, MD

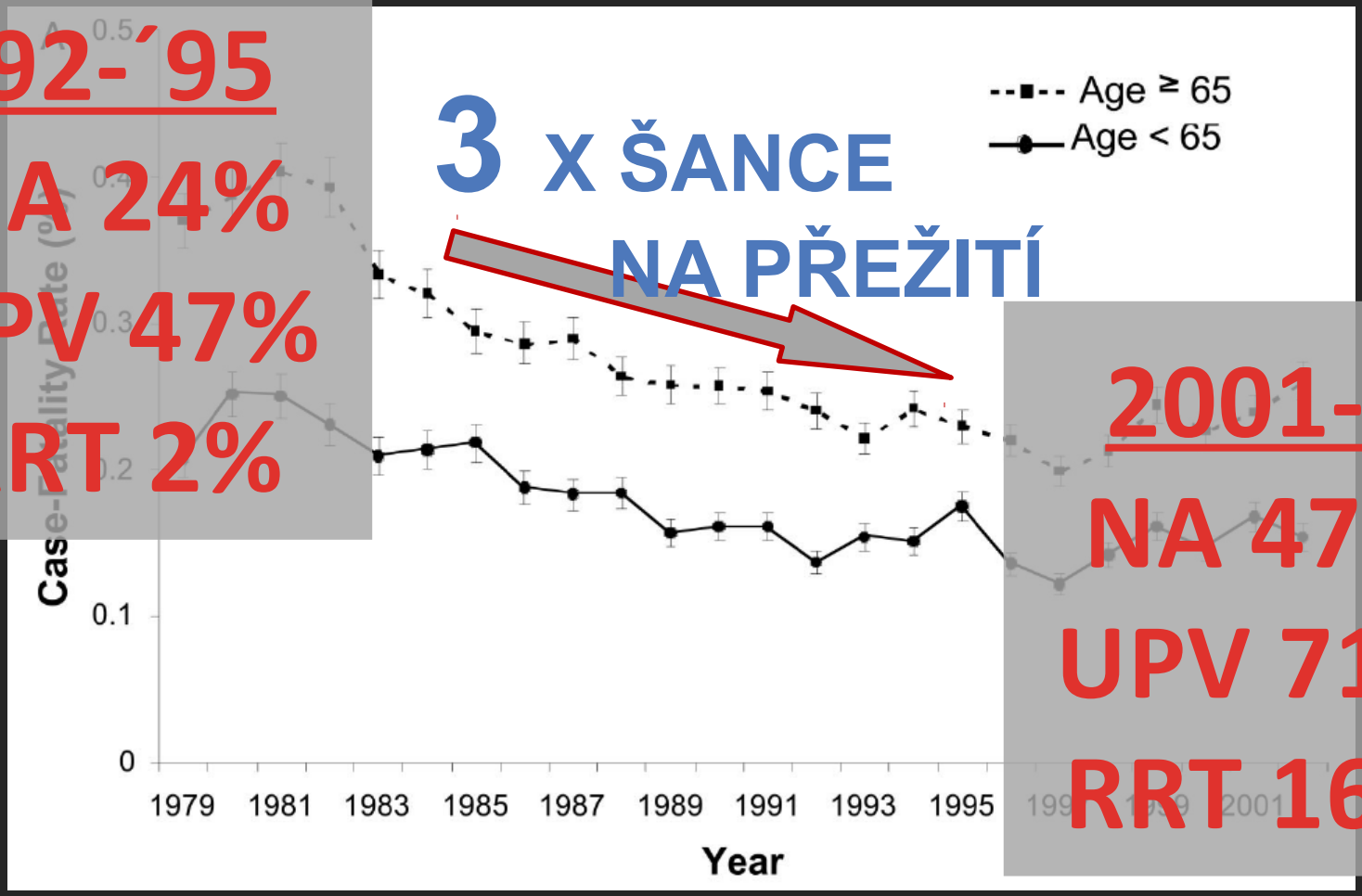
80+ let

´92-´95

NA 24%

UPV 47%

RRT 2%



2001-4

NA 47%

UPV 71%

RRT 16%

The effect of age on the development and outcome of adult sepsis*

Greg S. Martin, MD, MSc; David M. Mannino, MD; Marc Moss, MD (Crit Care Med 2006; 34:15–21)

3. Neztrácet čas

The New England Journ… …ine

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.… …M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH… …PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED… …ATIVE GROUP*

263 pts
Mortalita 46% vs 30%

… a nebát se počáteční racionální terapeutické agresivity

SEPSE / ŠOK

ODSTRANĚNÍ **PROJEVŮ** ŠOKU

ODSTRANĚNÍ **PŘÍČINY** ŠOKU

ODSTRANĚNÍ **PŘÍČINY** ŠOKU

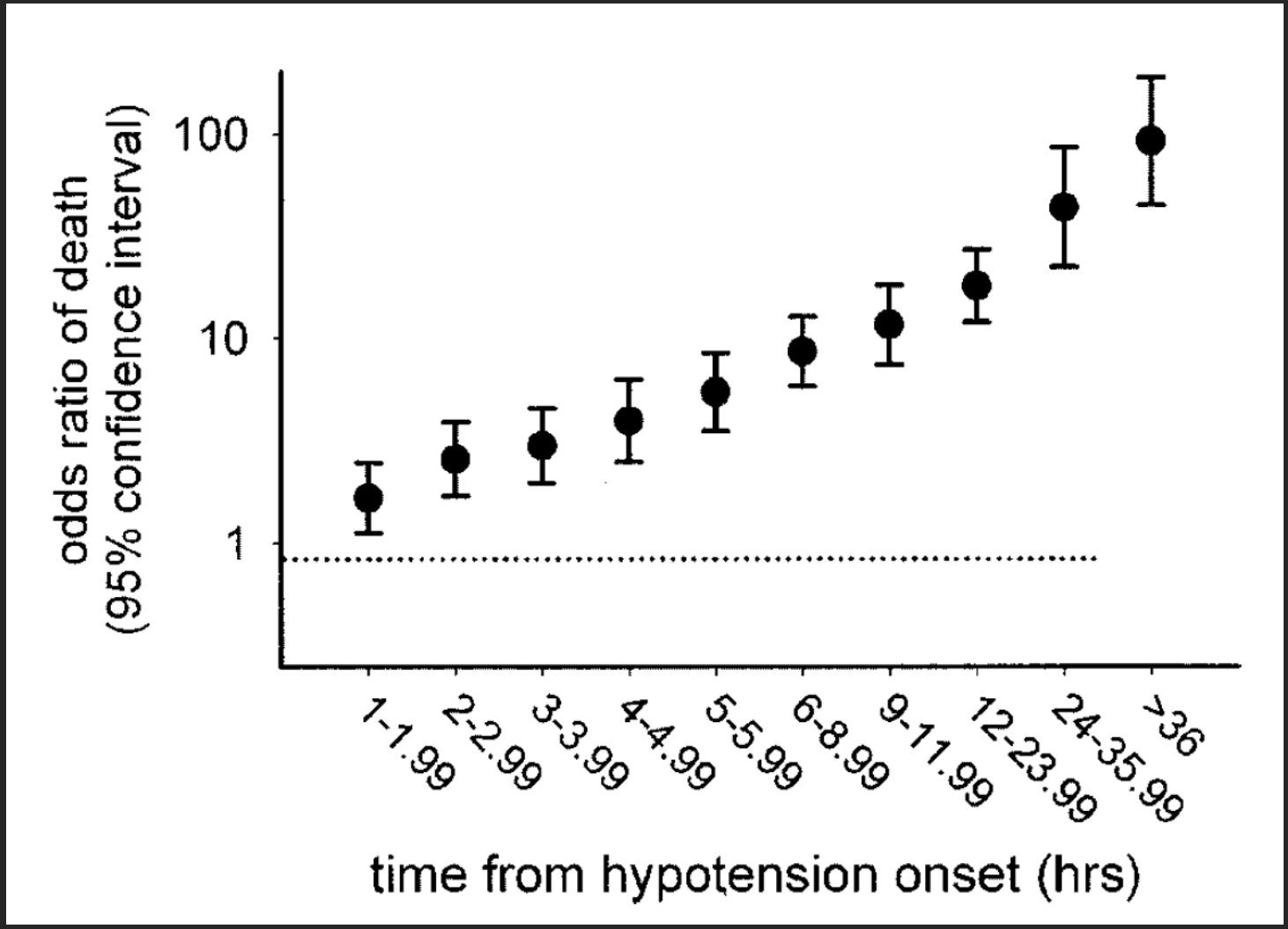
ATB

FOKUS

Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock*

(Crit Care Med 2006; 34:1589–1596)

Anand Kumar, MD; Daniel Roberts, MD; Kenneth E. Wood, DO; Bruce Light, MD; Joseph E. Parrillo, MD; Satendra Sharma, MD; Robert Suppes, BSc; Daniel Feinstein, MD; Sergio Zanotti, MD; Leo Taiberg, MD; David Gurka, MD; Aseem Kumar, PhD; Mary Cheang, MSc



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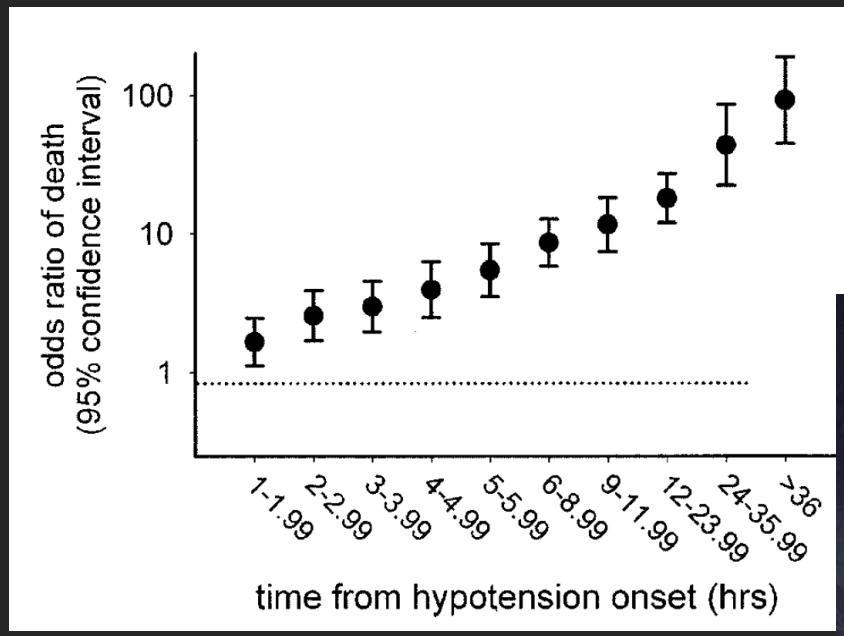


SepsEast 2016
3rd Central and Eastern European Sepsis Forum

ODSTRANĚNÍ **PŘÍČINY** ŠOKU

ODSTRANĚNÍ **PROJEVŮ** ŠOKU

ATB

PERFUZE

FOKUS

OXYGENACE

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

A. INITIAL RESUSCITATION

1. Sepsis and septic shock are medical emergencies, and we recommend that treatment and resuscitation begin immediately (BPS).
2. We recommend that, in the resuscitation from sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloid fluid be given within the first 3 hours (strong recommendation, low quality of evidence).
3. We recommend that, following initial fluid resuscitation, additional fluids be guided by frequent reassessment of hemodynamic status (BPS).

RACIONÁLNÍ ???

A Users' Guide to the 2016 Surviving Sepsis Guidelines

Application of Fluid Resuscitation in Adult Septic Shock

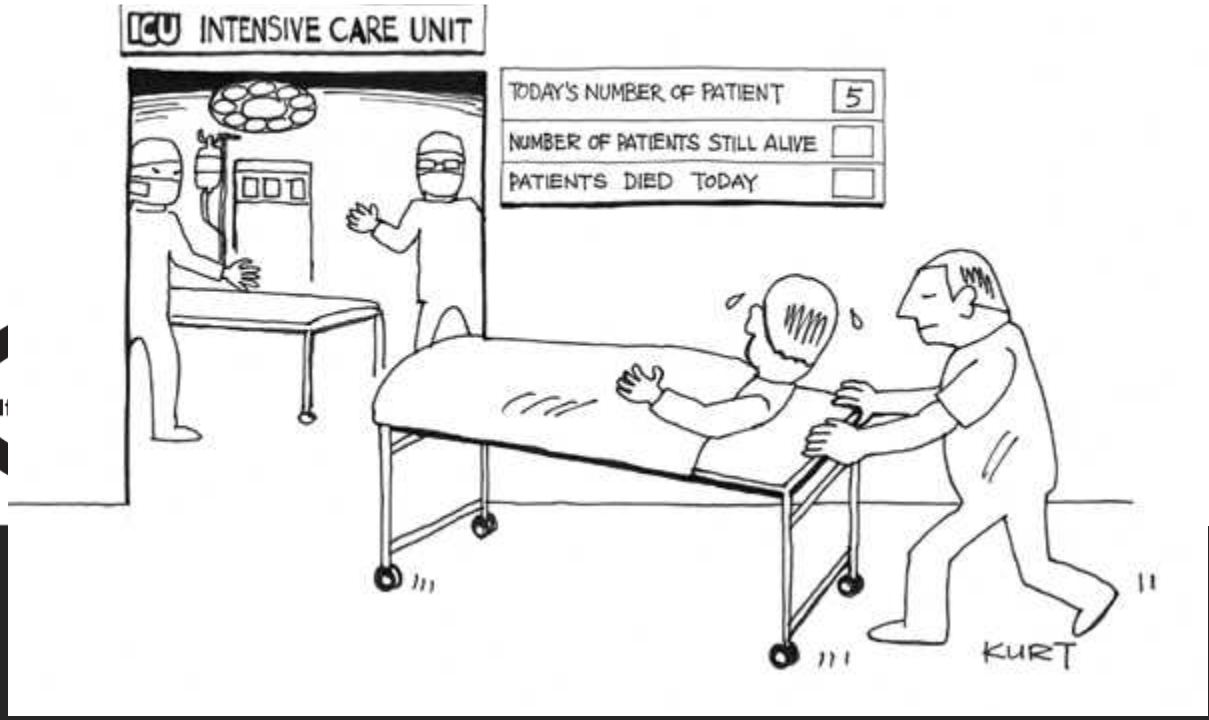
RACIONÁLNÍ ???

No high flow oxygen and
No ESRD on dialysis or CHF

↓

Rapid infusion
of 30 ml/kg
Crystalloid*

KILLING BY INTENSIVE CARE…



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Protocol-Based Care for Early Septic Shock

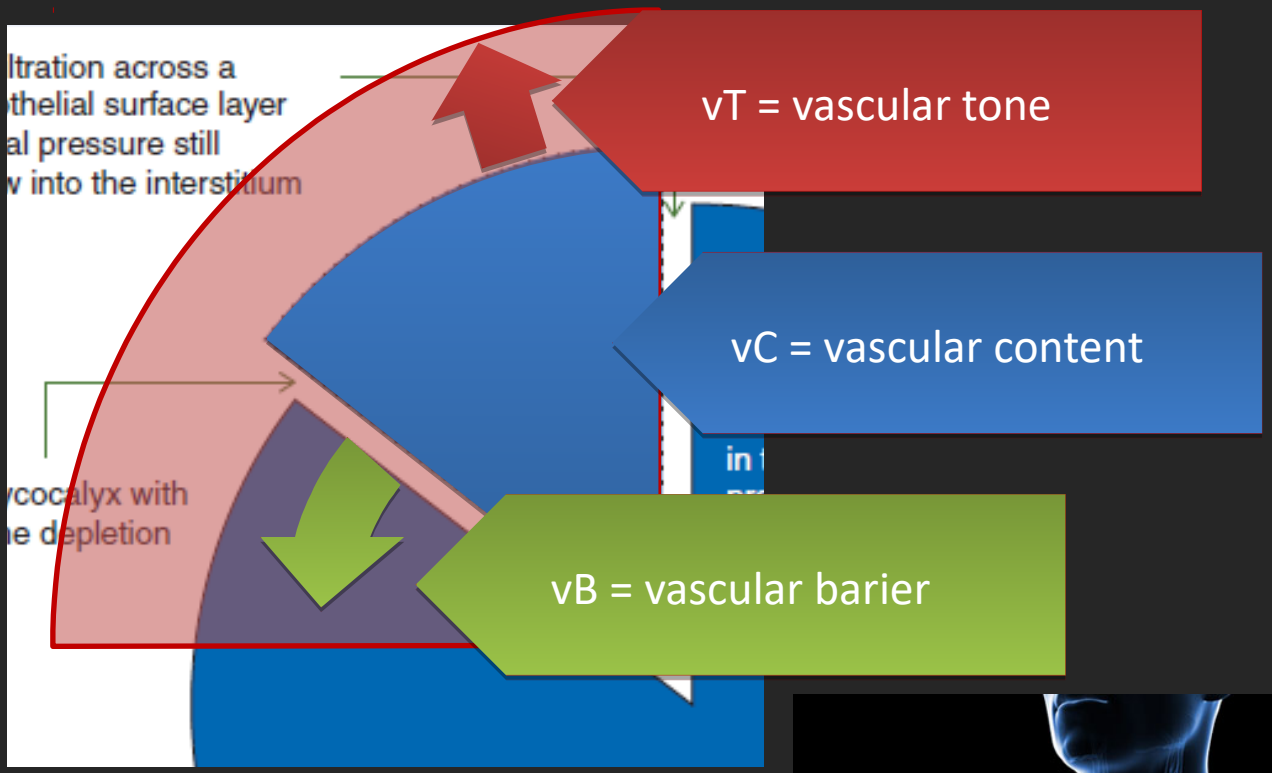
The ProCESS Investigators*

even after an intravenous fluid challenge. We initially required the fluid challenge to be 20 ml or more per kilogram of body weight, administered over the course of 30 minutes, but in April 2010, we simplified the requirement to a challenge of 1000 ml or more administered over the course of 30 minutes. Patients did not have to be in shock

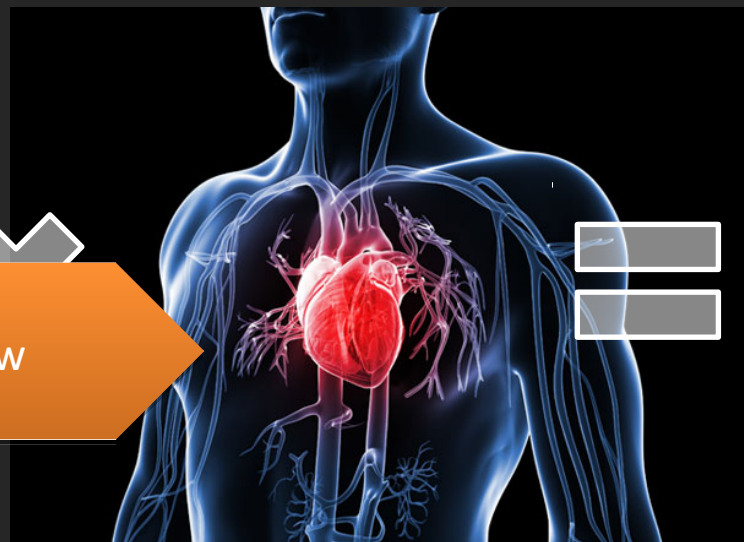
20 ml/kg/30min …

.. 1000ml/30min

Při adjustaci na odhadovanou průměrnou hmotnost 75kg ======= 13 ml/kg



BF = blood flow



Bai *et al. Critical Care* 2014, **18**:532
http://ccforum.com/content/18/5/532

CRITICAL CARE

RESEARCH Open Access

Early versus delayed administration of norepinephrine in patients with septic shock

Xiaowu Bai, Wenkui Yu*, Wu Ji, Zhiliang Lin, Shanjun Tan, Kaipeng Duan, Yi Dong, Lin Xu and Ning Li*

vT = vascular tone

administration was 3.1 ± 2.5 hours. Every 1-hour delay in norepinephrine initiation during the first 6 hours after septic shock onset was associated with a 5.3% increase in mortality. Twenty-eight day mortality rates were significantly

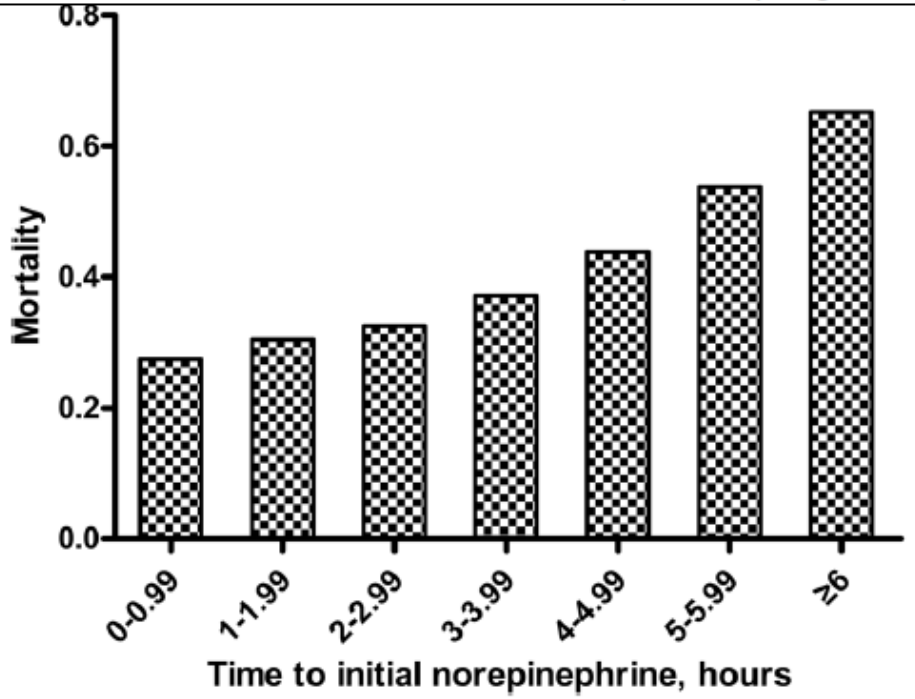


Figure 3 Mortality of patients whose initial norepinephrine administrations were within the indicated time interval.

vC = vascular content

A. INITIAL RESUSCITATION

1. Sepsis and septic shock are medical emergencies, and we recommend that treatment and resuscitation begin immediately (BPS).
2. We recommend that, in the resuscitation from sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloid fluid be given within the first 3 hours (strong recommendation, low quality of evidence).
3. We recommend that, following initial fluid resuscitation, additional fluids be guided by frequent reassessment of hemodynamic status (BPS).

F. FLUID THERAPY

1. We recommend that a fluid challenge technique be applie where fluid administration is continued as long as hemo dynamic factors continue to improve (BPS).

ŘÍZENÉ PODÁNÍ TEKUTINY

[Original Research **Critical Care**]

CHEST

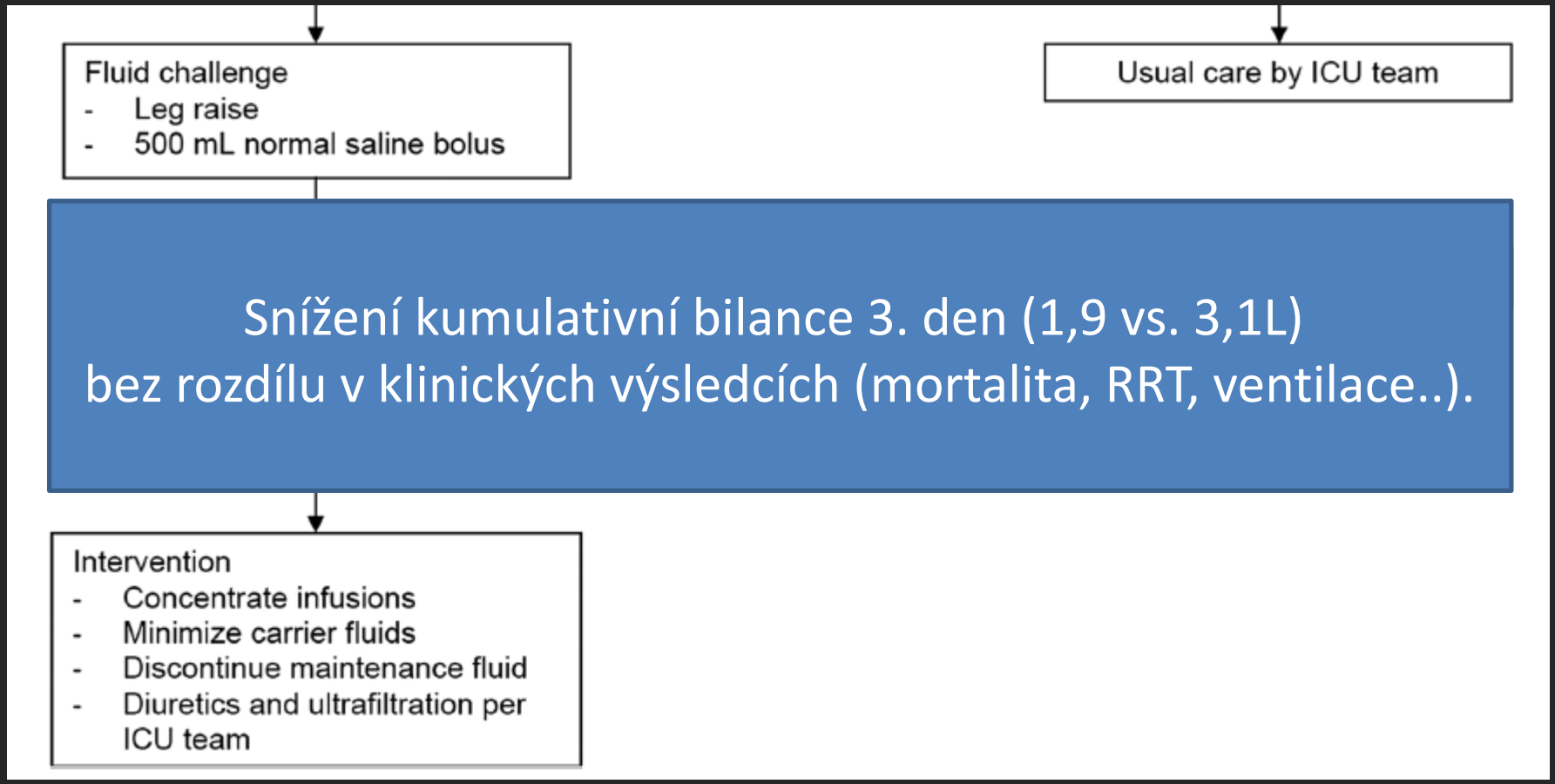
Targeted Fluid Minimization Following Initial Resuscitation in Septic Shock

A Pilot Study

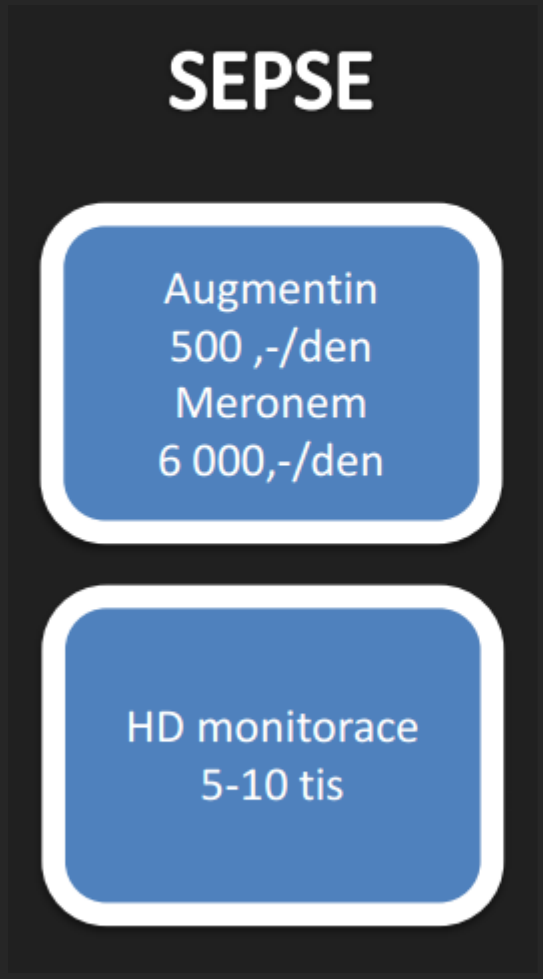
Catherine Chen, MD; and Marin H. Kollef, MD

CHEST 2015; 148(6):1462-1469

82 RANDOMIZOVANÝCH PACIENTŮ SE SEPSÍ

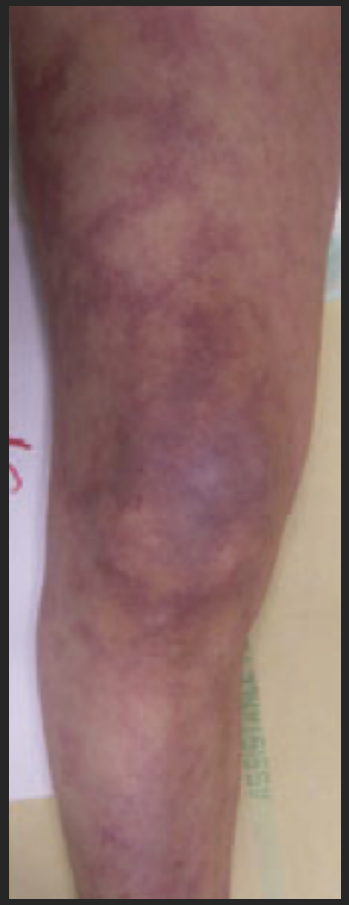


4. … a její ekonomické / personální náročnosti



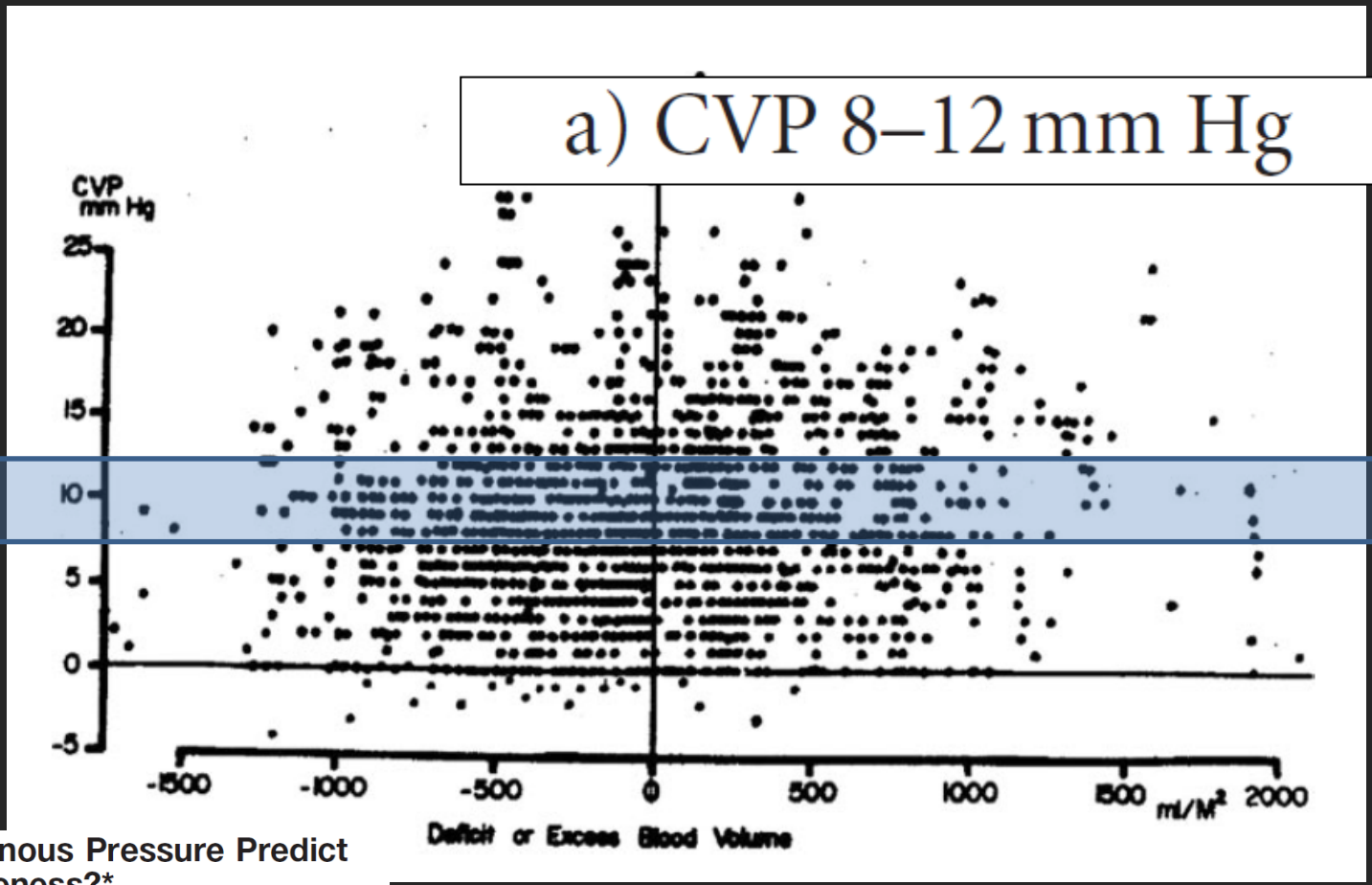
5. Nedělat léčebnou kosmetiku

110/60 (76)	99%
36,5C	85 ml



Spec. bioch. vyšetře		
P-Laktat		7,59

… a vyvarovat se neracionálních léčebných cílů



Does Central Venous Pressure Predict Fluid Responsiveness?*

A Systematic Review of the Literature and the Tale of Seven Mares

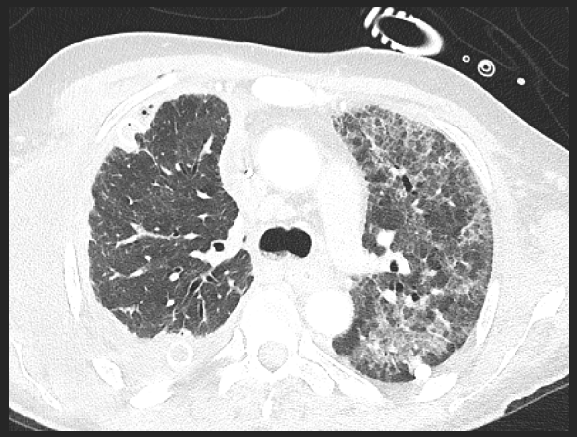
(CHEST 2008; 134:172–178)

Paul E. Marik, MD, FCCP; Michael Baram, MD, FCCP; and Bobbak Vahid, MD

O_2/CO_2

+

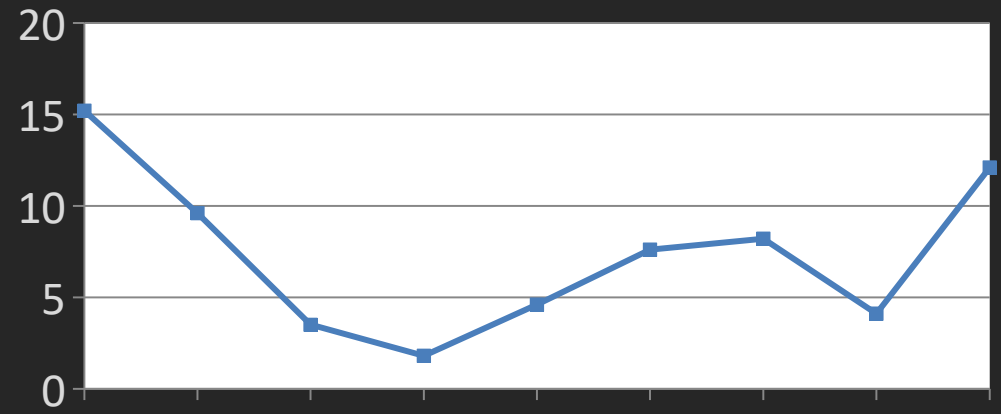
AGRESIVNÍ VENTILACE



GLY

+

TĚSNÁ KONTROLA



http://emcrit.org/pulmcrit/vanish-renoresuscitation-vasopressin-vepinephrine/

6. A když něco nefunguje…

… zopakovat to !!!

Intensive Care Med
DOI 10.1007/s00134-015-3850-x

SEVEN-DAY PROFILE PUBLICATION

Maurizio Cecconi
Christoph Hofer
Jean-Louis Teboul
Ville Pettila
Erika Wilkman
Zsolt Molnar

Fluid challenges in intensive care: the FENICE study

A global inception cohort study

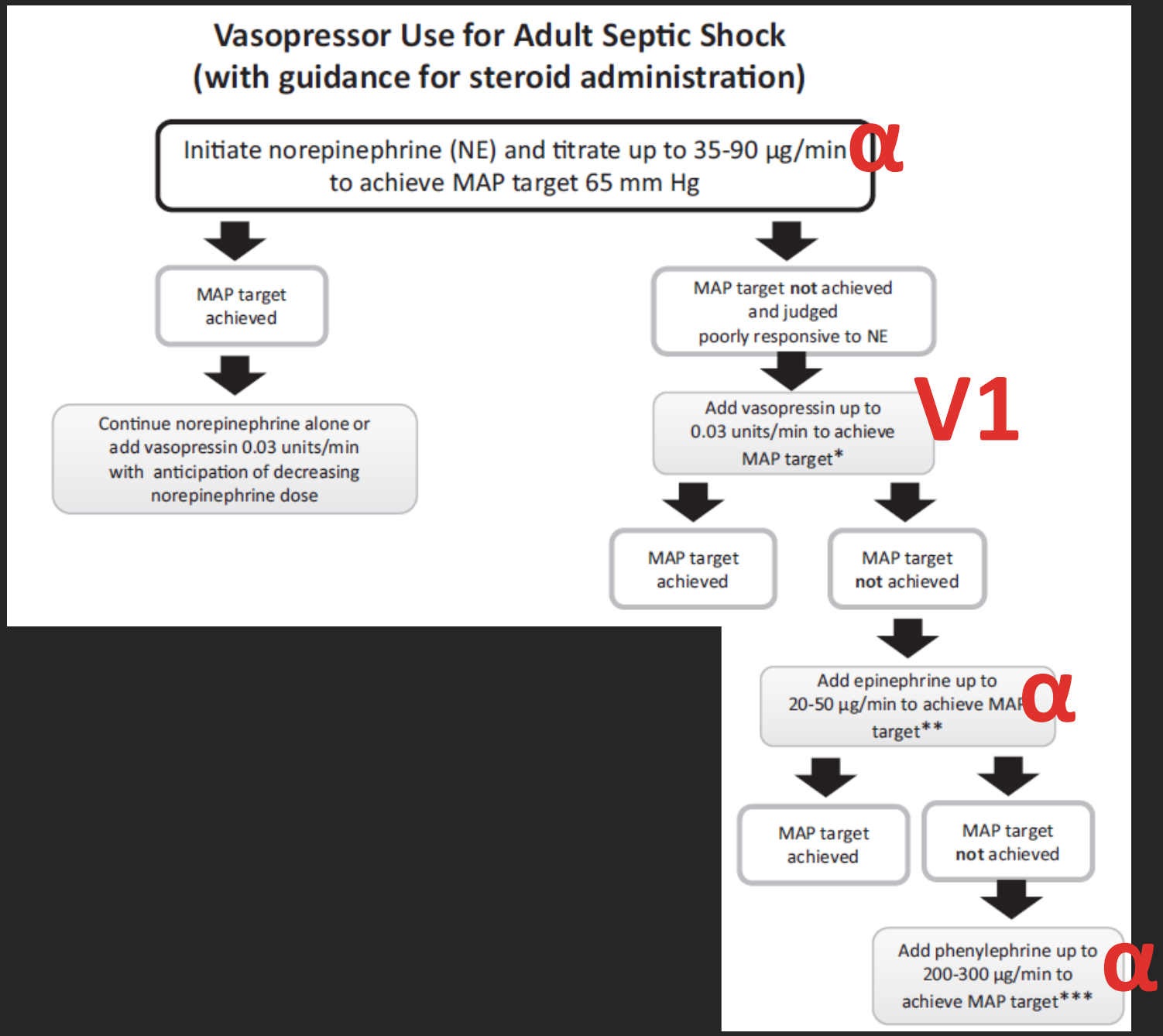
Hemodynamic variable used to predict fluid responsiveness	*n*	% Of category	% All
No variable used	945		42.7 [40.6–44.8]
Any variable used	1268		57.3 [55.2–59.4]
Static	785		35.5 [33.5–37.5]
CVP	572	89.9 [87.8–92.0]	25.8 [24.0–27.6]

Co je použito k predikci reakce na tekutinu:

1. NIC (43%)
2. CVP (26%)

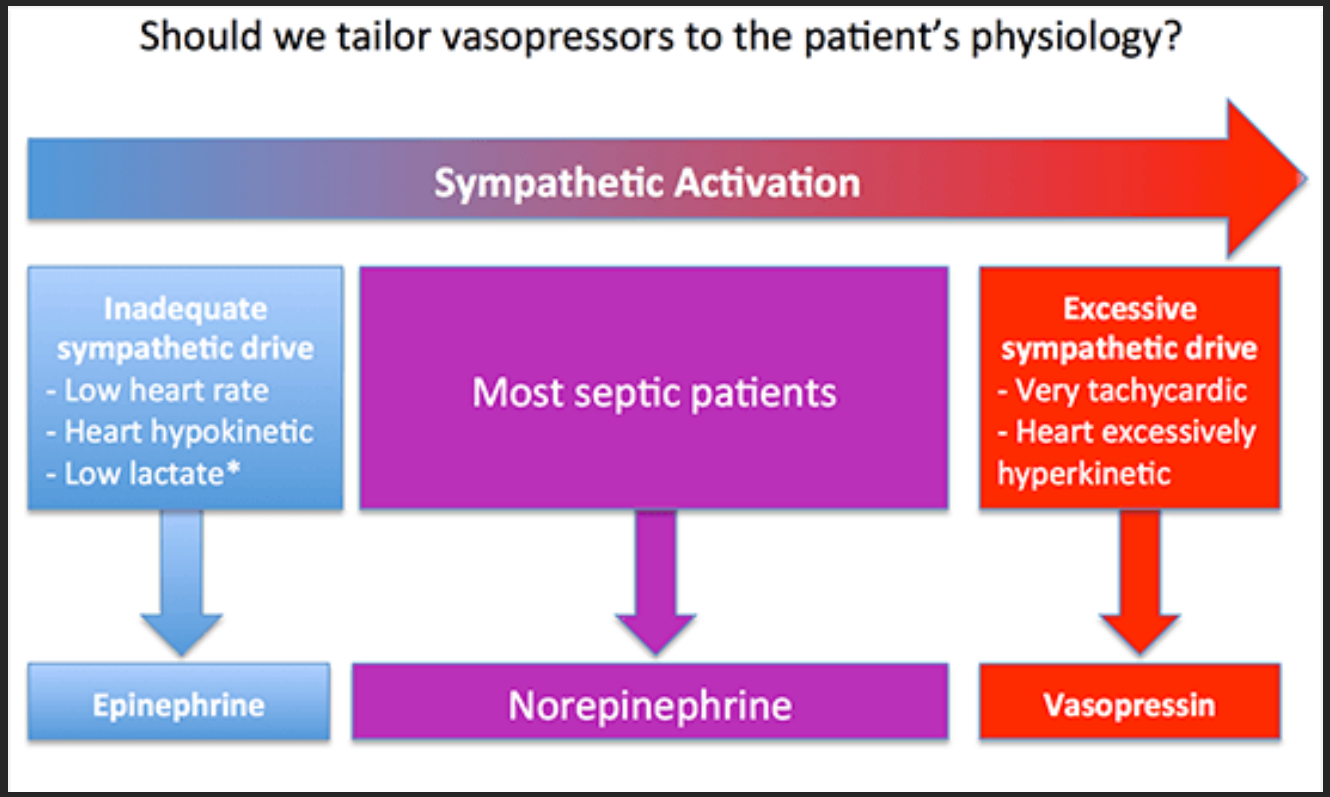
Further fluid administration – n (%)	1050 (47.4 ± 2.5)	
with an initial positive response n (%) OR	739 (47.9 ± 2.5)	Ref
with an initial negative response n (%) OR	212 (49.4 ± 6.6)	OR 0.94 (0.76-1.16)
with an initial uncertain response n (%) OR	99 (52.4 ± 7.1)	OR 0.83 (0.62-1.13)

U 49,4 % případů bylo pokračováno v podání tekutiny i přes negativní reakci na podání tekutiny


Vasopressor Use for Adult Septic Shock
(with guidance for steroid administration)
Initiate norepinephrine (NE) and titrate up to 35-90 µg/min
to achieve MAP target 65 mm Hg
α
MAP target achieved
Continue norepinephrine alone or add vasopressin 0.03 units/min with anticipation of decreasing norepinephrine dose
MAP target not achieved and judged poorly responsive to NE
Add vasopressin up to 0.03 units/min to achieve MAP target*
V1
MAP target achieved
MAP target not achieved
Add epinephrine up to 20-50 µg/min to achieve MAP target**
α
MAP target achieved
MAP target not achieved
Add phenylephrine up to 200-300 µg/min to achieve MAP target***
α

??? RŮZNÉ FENOTYPY ???

ECMO



beta-blokáda

http://emcrit.org/pulmcrit/sepsis-myths/

7. Opomíjet limitace klinických studií

Představte si phase 3 studii noradrenalinu …

… pacient se sepsí indukovanou refrakterní hypotenzí (STK pod 90mmHg po podání 1000ml) dostane 0,25ug/kg/min testovaná látky…

Bude tohle fungovat ?

BAD DESIGN

The NEW ENGLAND JOURNAL of MEDICINE

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

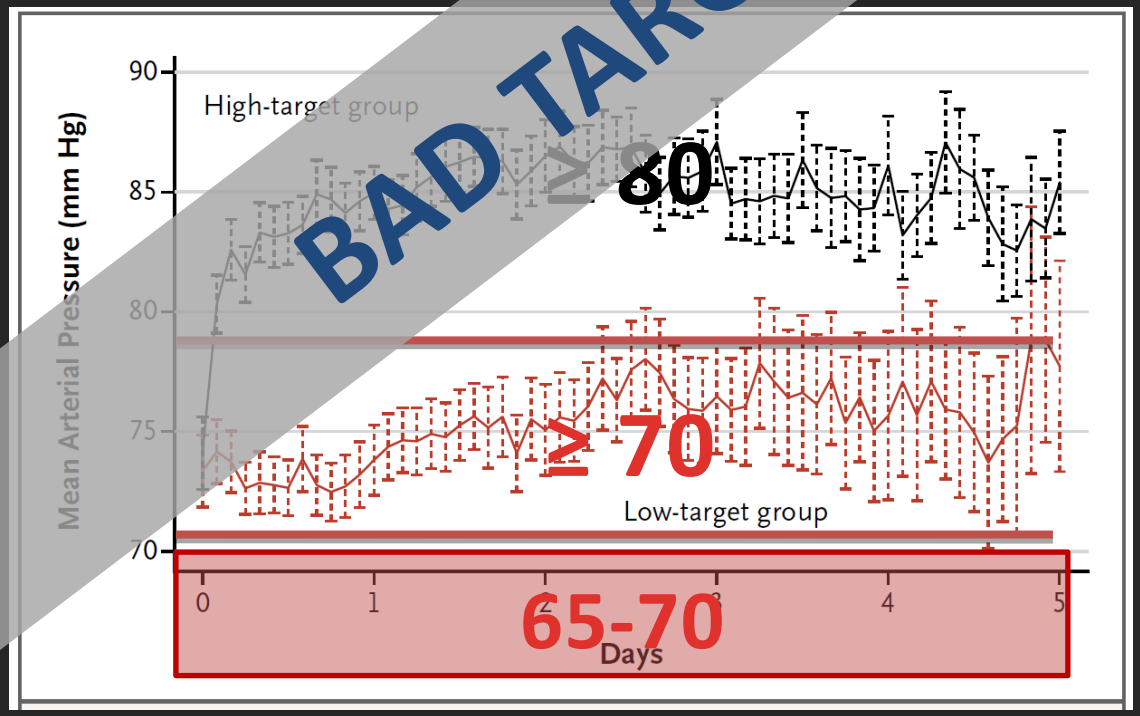
High versus Low Blood-Pressure Target in Patients with Septic Shock

Pierre Asfar, M.D., Ph.D., Ferhat Meziani, M.D., Ph.D., Jean-François Hamel, M.D., Fabien Grelon, M.D.,

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.)

BAD TARGET



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Pierre Asfar, M.D., Ph.D., Ferhat Meziani, M.D., Ph.D., Jean-François Hamel, M.D., Fabien Grelon, M.D.,

BAD POPULATION

Secondary outcomes — no./total no. (%)			
Death at day 90†	16 (42.1)	170 (43.8)	0.74
Survival at day 28 without organ support‡	241 (62.1)	235 (60.6)	0.66
Doubling of plasma creatinine	161 (41.5)	150 (38.7)	0.42
No chronic hypertension	71/215 (33.0)	85/221 (38.5)	0.32
Chronic hypertension	90/173 (52.0)	65/167 (38.9)	0.02
Renal-replacement therapy from day 1 to day 7	139 (35.8)	130 (33.5)	0.50
No chronic hypertension	66/215 (30.7)	77/221 (34.8)	0.36
Chronic hypertension	73/173 (42.2)	53/167 (31.7)	0.046

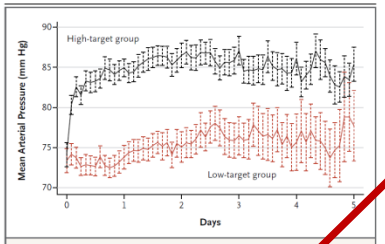


Figure 2. Mean Arterial Pressure during the 5-Day Study Period.
Mean arterial pressures were significantly lower in the low-target group than in the high-target group during the 5 protocol-specified days (P=0.02 by repeated-measures regression analysis), although the values exceeded the target values of 80 to 85 mm Hg in the high-target group and 65 to 70 mm Hg in the low-target group. The I bars represent 95% confidence intervals.

fluid balance, and the fluid balance was lower than those reported previously,[7,8] possibly because our population of patients differed from those in previous studies or because of more restrictive protocols for fluid administration in France. In addition, there were no significant between-group differences in the overall rates of organ dysfunction or death at 90 days. However, in patients with a history of chronic arterial hypertension, targeting a mean arterial pressure of 80 to 85 mm Hg reduced both the incidence of a doubling of the blood creatinine level and the rate of renal-replacement therapy. There was no significant between-group difference in the overall rate of serious adverse events, but patients in the high-target group had significantly more episodes of atrial fibrillation.

No differences in the primary and secondary outcomes were observed between the two groups. Our study was prospectively powered to detect an absolute difference of 10 percentage points in the rate of death on the basis of an expected rate of 45% in the low-target group, at an alpha level of 0.05 and a beta level of 0.20, with the use of a two-tailed test. The expected overall death rate in our study was consistent with the rates among patients with septic shock that were reported in previous multicenter trials (37%,[5] 39%,[8] 47%,[4] and 49%[6]) at the time the trial was designed. The absolute reduction of 10 percentage points in mo... our study because the ... in the literature when the ... in 2008 had tested the hy... reductions of 2... percentag... age points, and 10 percen... of death. Two other trials ... after ... started recruitin... hypothesis of an absolute ... percentage points[7,15] and ... Hence, the anticipated r... study was close to the risk... previous studies. However, ... death at 28 days was lower ... other studies, although it ... rate in more recent trials, ... ranging from 25 to 57%. Nevertheless, the lower-t... death led to an underpow... we may not have detected ... cidence of some adverse ... events such as myocardial ...

Septic shock is a major ... fibrillation,[17] and in our st... was significantly more co... target group than in the l... adverse effect might be r... cantly higher doses of catecholamine and the longer duration of catecholamine infusions in the high-target group. However, given the small number of episodes of atrial fibrillation, other confounding factors cannot be ruled out. The association between atrial fibrillation and septic shock should be considered only as a hypothesis-generating concept for future trials.

At ra... cording ... hyperte... reporte... sion, wh... ies.[18] A... sion, a ... pressur... means ... could h... perfus... rates. N... betwee... those w... dent. T...

organ dysfunction or death at 90 days. However, in patients with a history of chronic arterial hypertension, targeting a mean arterial pressure of 80 to 85 mm Hg reduced both the incidence of a doubling of the blood creatinine level and the rate of renal-replacement therapy. There was no

BAD CONCLUSIONS

Studie	Relativní riziko
CHEST	1,21 (1,00-1,45)
6 S	1,28 (0,96-1,72)
SEPSISPAM	1,23 (0,91-1,67)

8. Nepodléhat módním trendům

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 26, 2009 VOL. 360 NO. 13

Intensive versus Conventional Glucose Control in Critically Ill Patients

The NICE-SUGAR Study Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydroxyethyl Starch 130/0.42 versus Ringer's Acetate in Severe Sepsis

Anders Perner, M.D., Ph.D., Nicolai Haase, M.D.,

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 22, 2009 VOL. 361 NO. 17

Intensity of Continuous Renal-Replacement Therapy in Critically Ill Patients

The RENAL Replacement Therapy Study Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 31, 2012 VOL. 366 NO. 22

Drotrecogin Alfa (Activated) in Adults with Septic Shock

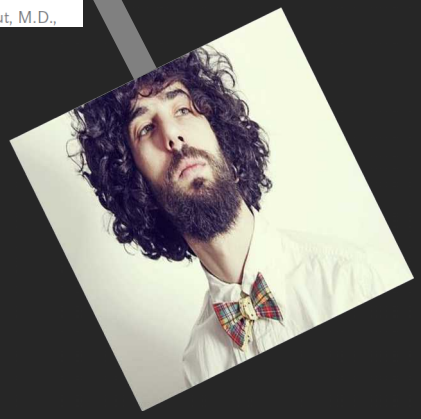
V. Marco Ranieri, M.D., B. Taylor Thompson, M.D., Philip S. Barie, M.D., M.B.A., Jean-François Dhainaut, M.D.,

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 1, 2014 VOL. 370 NO. 18

A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*



Intensive Care Med (2015) 41:1703–1706
DOI 10.1007/s00134-015-3733-1

WHAT'S NEW IN INTENSIVE CARE

Anders Perner
John Myburgh

Ten 'short-lived' beliefs in intensive care medicine

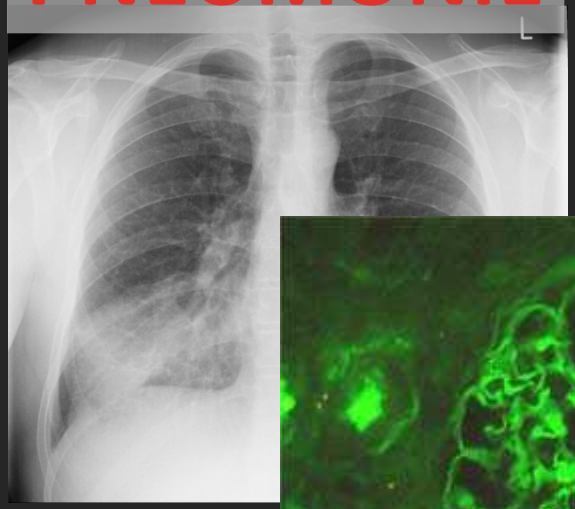
1. Albumin
2. Časná a cílená hemodynamická resuscitace u pacientů se septickým šokem
3. Podávání aktivovaného proteinu C
4. Kortikosteroidy v nízké dávce
5. Intenzivní kontrola glykemie
6. Podávání škrobů
7. Dekompresní kraniektomie
8. Indukovaná hypotermie
9. Komplexní transfuzní strategie
10. Podpora funkce ledvin vysokoobjemovou eliminací

Sorry, there's no magic bullet. You gotta eat healthy and live healthy to be healthy and look healthy. End of story.

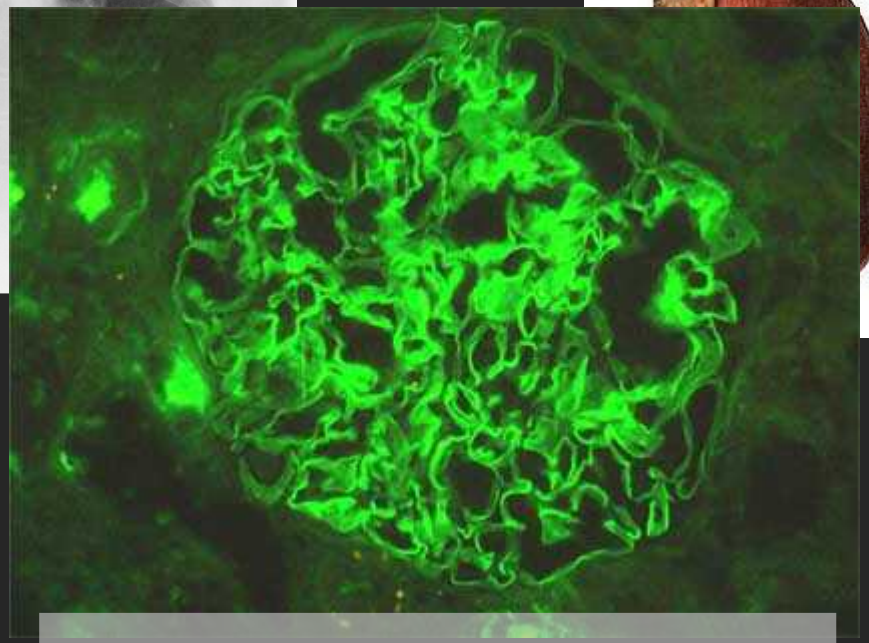
Morgan Spurlock

9. Nemyslet si, že už vím o pacientově stavu všechno

PNEUMONIE



S -AKI



GOODPASTURE SY.

„EXOTICKÁ“ PNEUMONIE

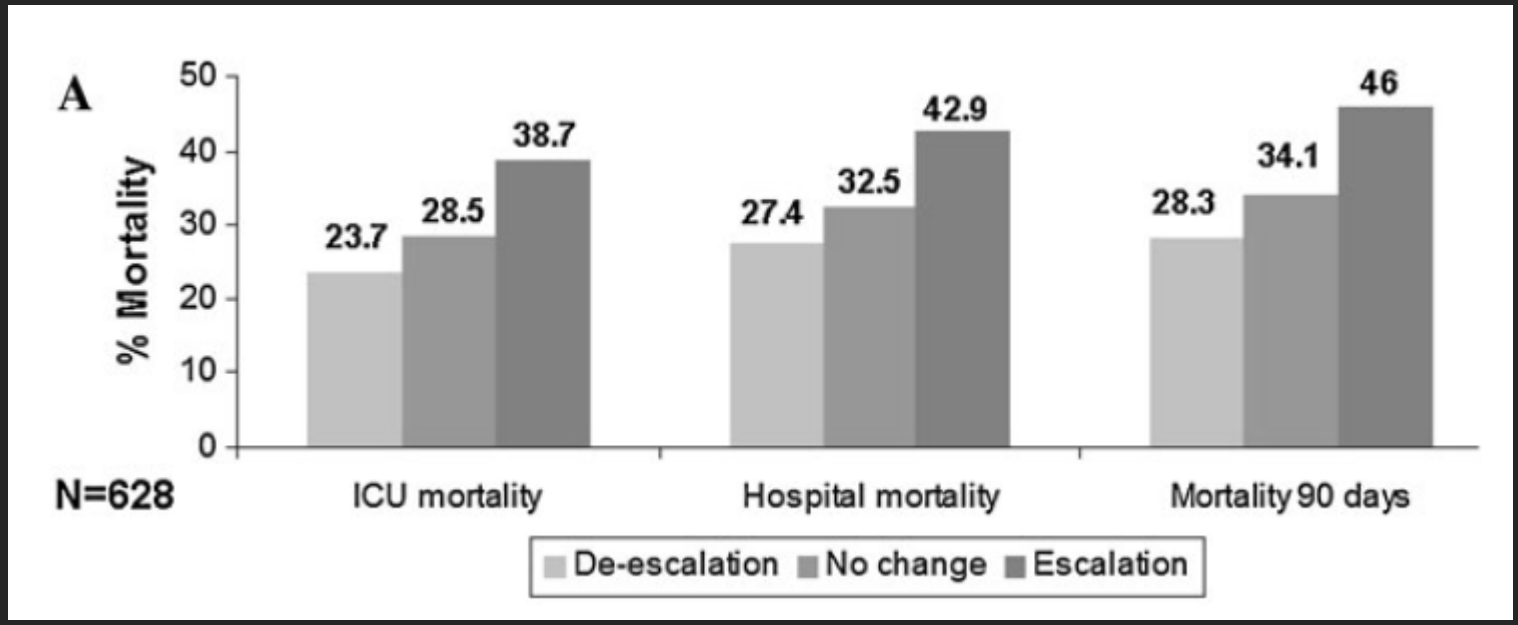
10. Neopomenout brzdit

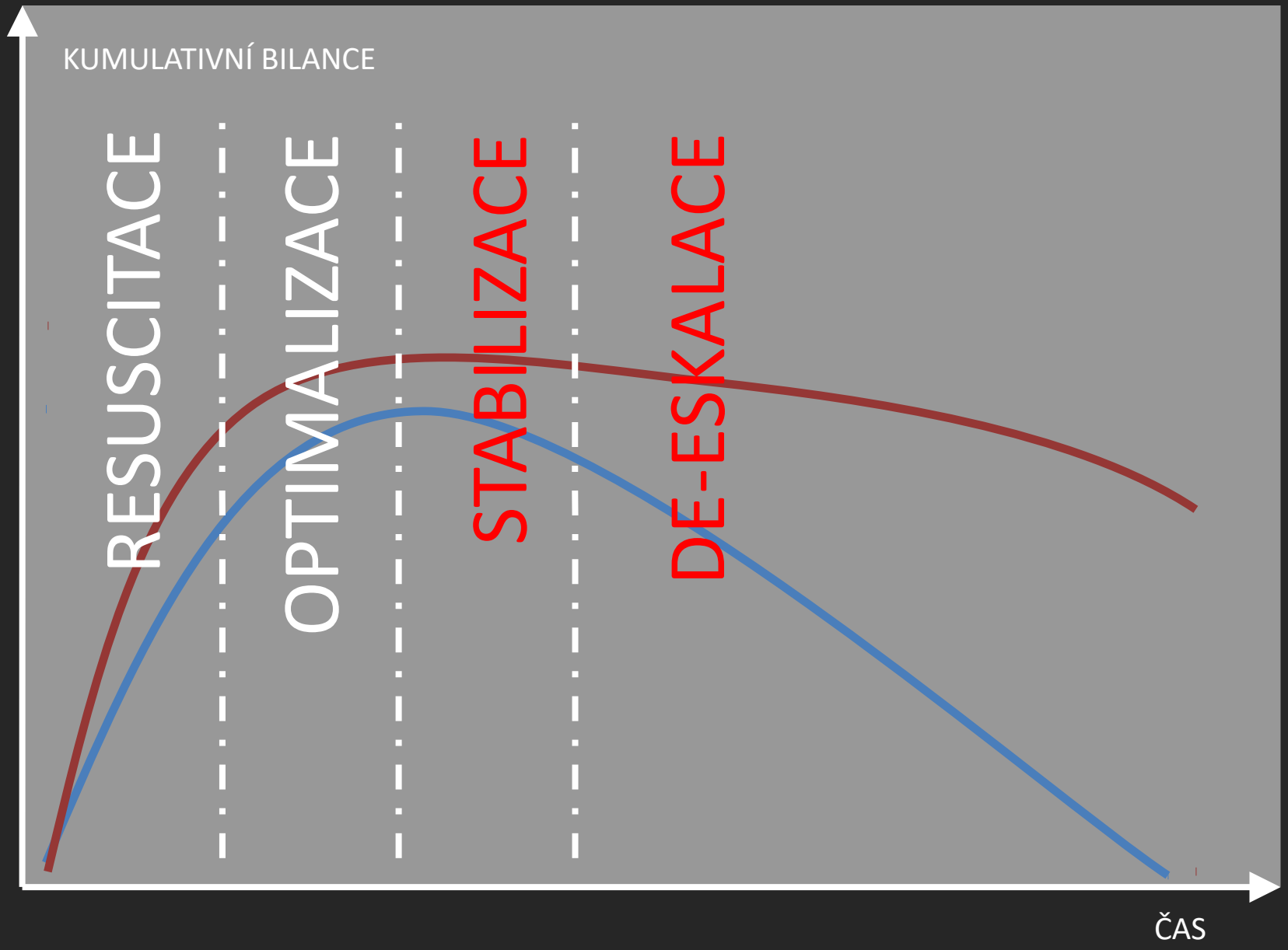
Intensive Care Med (2014) 40:32–40
DOI 10.1007/s00134-013-3077-7

ORIGINAL ARTICLE

J. Garnacho-Montero
A. Gutiérrez-Pizarraya
A. Escoresca-Ortega
Y. Corcia-Palomo
Esperanza Fernández-Delgado
I. Herrera-Melero
C. Ortiz-Leyba
J. A. Márquez-Vácaro

De-escalation of empirical therapy is associated with lower mortality in patients with severe sepsis and septic shock




KUMULATIVNÍ BILANCE
RESUSCITACE
OPTIMALIZACE
STABILIZACE
DE-ESKALACE
ČAS

Silva *et al. Critical Care* 2013, **17**:R288
http://ccforum.com/content/17/6/R288

CRITICAL CARE

RESEARCH Open Access

The effect of excess fluid balance on the mortality rate of surgical patients: a multicenter prospective study

Kumulativní bilance nad 2L

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

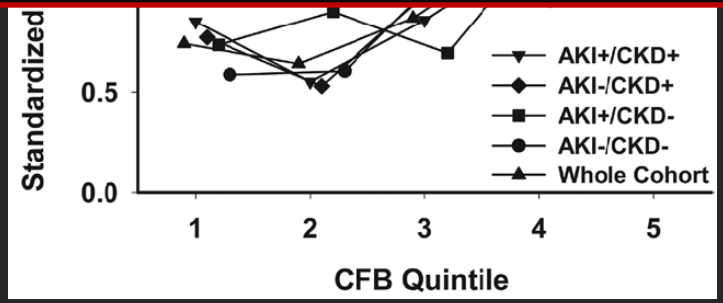
ELSEVIER

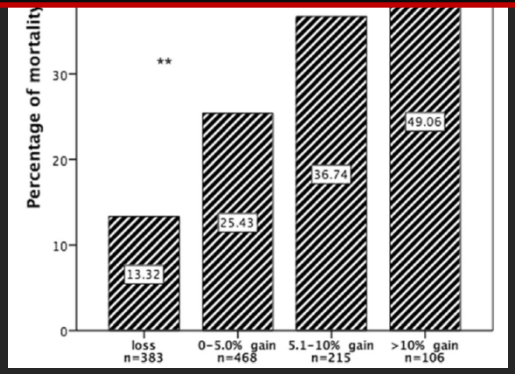
Impact of positive fluid balance on critically ill surgical patients: A prospective observational study

Galinos Barmparas, MD [a], Douglas Liou, MD [a], Debora Lee, BS [a], Nicole Fierro, BS [a], Matthew Bloom, MD [a], Eric Ley, MD [a], Ali Salim, MD [b], Marko Bukur, MD [c,d,*]

Vyrovnaná kumulativní bilance
5.den – 70% redukce mortality

POČÍNAJE 3. DNEM ZHORŠUJE POZITIVNÍ KUMULATIVNÍ BILANCE PROGNOZU PACIENTA O cca 1,05-1,1 NA 1 LITR





10 times NEVER AGAIN

1. Neléčit sepsi - sepse je syndrom …
2. Nevzdávat to předčasně
3. Neztrácet čas,
   nebát se počáteční racionální terapeutické agresivity
4. … a její ekonomické / personální náročnosti
5. Nedělat léčebnou kosmetiku
   … a vyvarovat se neracionálních léčebných cílů
6. Když něco nefunguje, zopakovat to
7. Opomíjet limitace klinických studií
8. Nepodléhat módním trendům
9. Nemyslet si, že už vím o pacientově stavu všechno
10. Neopomenout de-eskalovat

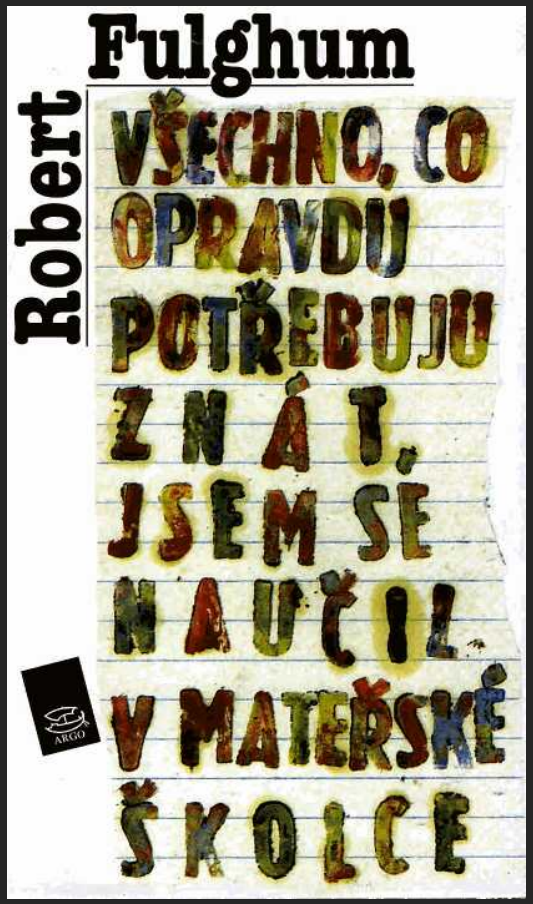
+1 nepřestat být ČLOVĚKEM

„… a přiznat si, že námi to nekončí …

Truog R. et al. Critical Care Medicine 2008; 36: 953-963

CÍLEM INTENZIVNÍ PÉČE BY MĚLO BÝT POMOCI NEMOCNÉMU PŘEŽÍT AKUTNÍ OHROŽENÍ JEHO ŽIVOTA ZA SOUČASNÉHO UCHOVÁNÍ ŠANCE NA UDRŽENÍ DOSTATEČNÉ KVALITY ŽIVOTA

+2 … a nebát se použít
trochu selského rozumu.“



DĚKUJI ZA POZORNOST