KDYŽ NOR NESTAČÍ...

Jan Beneš
KARIM a Simulační centrum
Lékařská fakulta v Plzni Univerzita Karlova a FN Plzeň

COI

- Řada výzkumných grantů k problematice hemodynamiky a monitorace kardiovaskulárního systému
- Spolupráce s výrobci
  - Edwards Lifesciences Inc.
  - Pulsion Getinge
  - CNSystems
- Spolupráce/ honorované přednášky pro A.O.P.

A CO TO VLASTNĚ ZNAMENÁ ?
„že nestačí“

HYPOTENZE PŘI
NOR > 0.3
ug/kg/min

V ŠIRŠÍM SLOVA SMYSLU ...
0,25-0,5 ug/kg/min

Tzn. při ŘEDĚNÍ
0,1mg/ml = 5mg/50ml
u 80 kg pacienta
14,4 ml/h
(12-24 ml/h)

Intensive Care Med (2022) 48:638–640
https://doi.org/10.1007/s00134-022-06652-x

CORRESPONDENCE

Dose of norepinephrine: the devil is in the details

Marc Leone[1*], Isabelle Goyer[2], Bruno Levy[3], Martin W. Dünser[4], Pierre Asfar[5] and Jacob C. Jentzer[6]

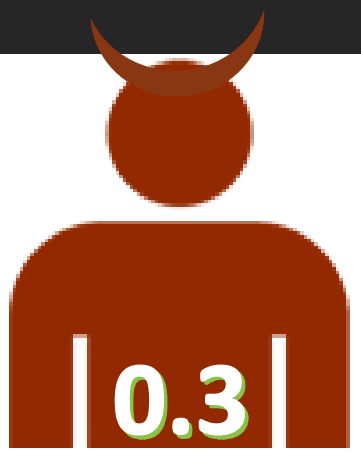


Table 1 Summary of studies with norepinephrine doses expressed in base or tartrate or hydrochloride

Authors, year of publication [ref]	Norepinephrine base (μg/kg/min)	Norepinephrine tartrate (μg/kg/min)	28-Day mortality (%)
Martin et al. 2015 [3]	0.395	0.79	48
Auchet et al. 2017 [4]	0.375	0.75	60
Asfar et al. 2014 [5] Low MAP target	0.175	0.35	38
Asfar et al. 2014 [5] High MAP target	0.2	0.4	39
Authors, year of publication [ref]	**Norepinephrine base (μg/kg/min)**	**Norepinephrine hydrochloride (μg/kg/min)**	**ICU mortality (%)**
Dünser et al. 2001 [6]	1.8	2.2	67
Dünser et al. 2003 [7]	0.5	0.61	71

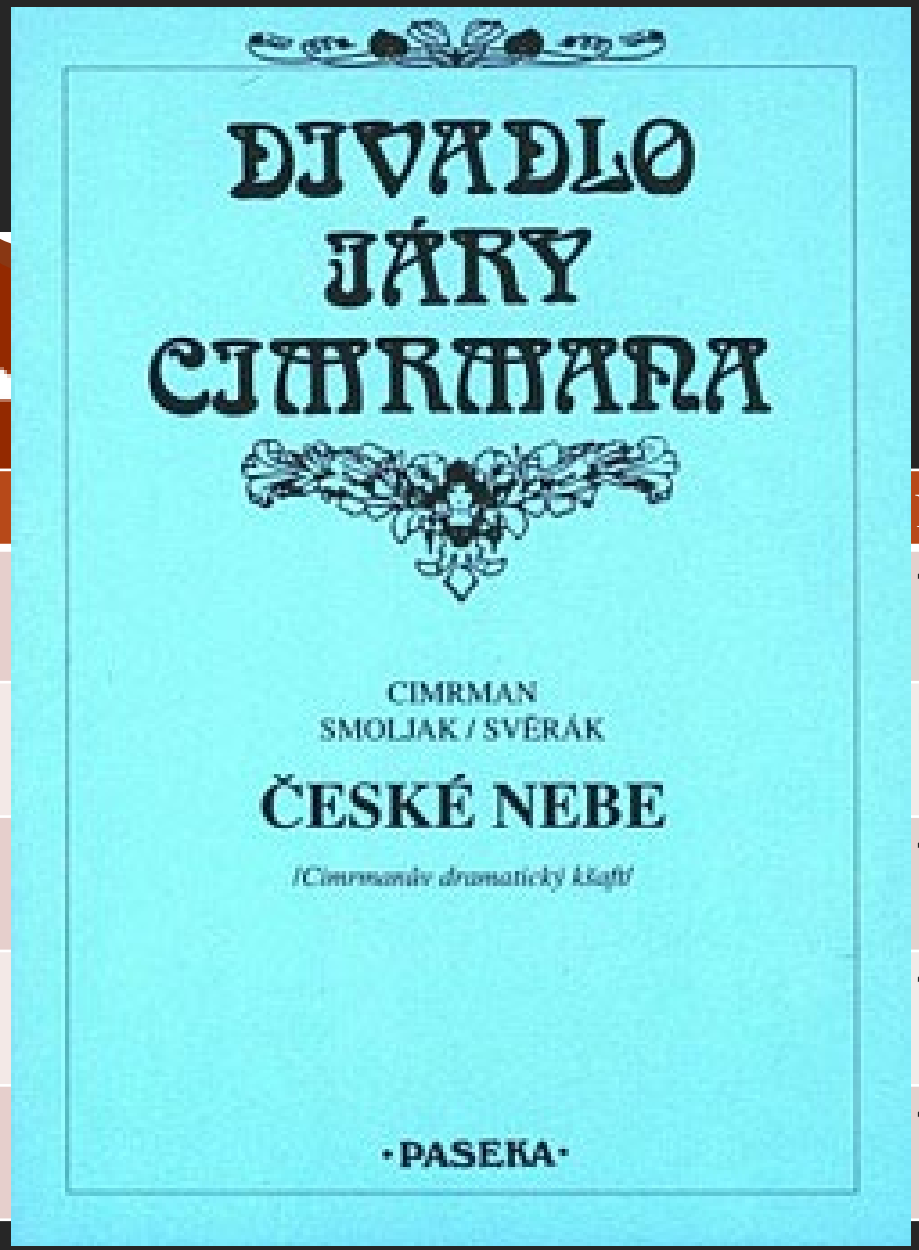
ICU intensive care unit, *MAP* mean arterial pressure

Intensive Care Med (2022) 48:638–640
https://doi.org/10.1007/s00134-022-06652-x

CORRESPONDENCE

Dose of norepinephrine: the devil is in the details

Marc Leone[1*], Isabelle Goyer[2], Bruno Levy[3], Martin W. Dünser[4], Pierre Asfar[5] and Jacob C. Jentzer[6]



		NOR base
NORADRENALIN léčiva	Norepinephrini tartras	1 mg/ml
NOREPINEPHRINE Hameln	Norepinephrini tartras	0,2 mg/ml
NOREPINEPHRINE Kabi	Norepinephrini tartras	1 mg/ml
NOREPINEPHRINE Kalceks	Norepinephrini tartras	1 mg/ml
SINORA	Norepinephrini tartras monohydricus	1 mg/ml

KAUZÁLNÍ TERAPIE

LABORATOŘ
(a opakovaně)

„TIME CONSUMING“
ECHO

KARDIOGENÍ ŠOK

CENTRÁL +
PŘÍMÉ MĚŘENÍ TK
(lépe a.femoralis)

TEKUTINOVÁ TERAPIE

MAP 65 mmHg

ZNOVU ROZVAŽ PŘÍČINU

„PRAVÉ SRDCE“

ZNÁMKY HYPOPERFUZE

HD MONITORACE

Intensive Care Med (2014) 40:1795–1815
DOI 10.1007/s00134-014-3525-z

CONFERENCE REPORTS AND EXPERT PANEL

Maurizio Cecconi
Daniel De Backer
Massimo Antonelli
Richard Beale
Jan Bakker
Christoph Hofer
Roman Jaeschke
Alexandre Mebazaa
Michael R. Pinsky
Jean Louis Teboul
Jean Louis Vincent
Andrew Rhodes

Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine

ICM Cecconi 2014

–We recommend further hemodynamic assessment (such as assessing cardiac function) to determine the type of shock if the clinical examination does not lead to a clear diagnosis. *Ungraded best practice*

–In complex patients we suggest to additionally use pulmonary artery catheterization or transpulmonary thermodilution to determine the type of shock. Level 2; QoE low (C)

–We do not recommend routine measurement of cardiac output for patients with shock responding to the initial therapy. Level 1; QoE low (C)

–We recommend measurements of cardiac output and stroke volume to evaluate the response to fluids or inotropes in patients that are not responding to initial therapy. Level 1; QoE low (C)

evaluation of cardiac function in shock. *Statement of fact*

–We do not recommend the routine use of the pulmonary artery catheter for patients in shock. Level 1; QoE high (A)

–We suggest pulmonary artery catheterization in patients with refractory shock and right ventricular dysfunction. Level 2; QoE low (C)

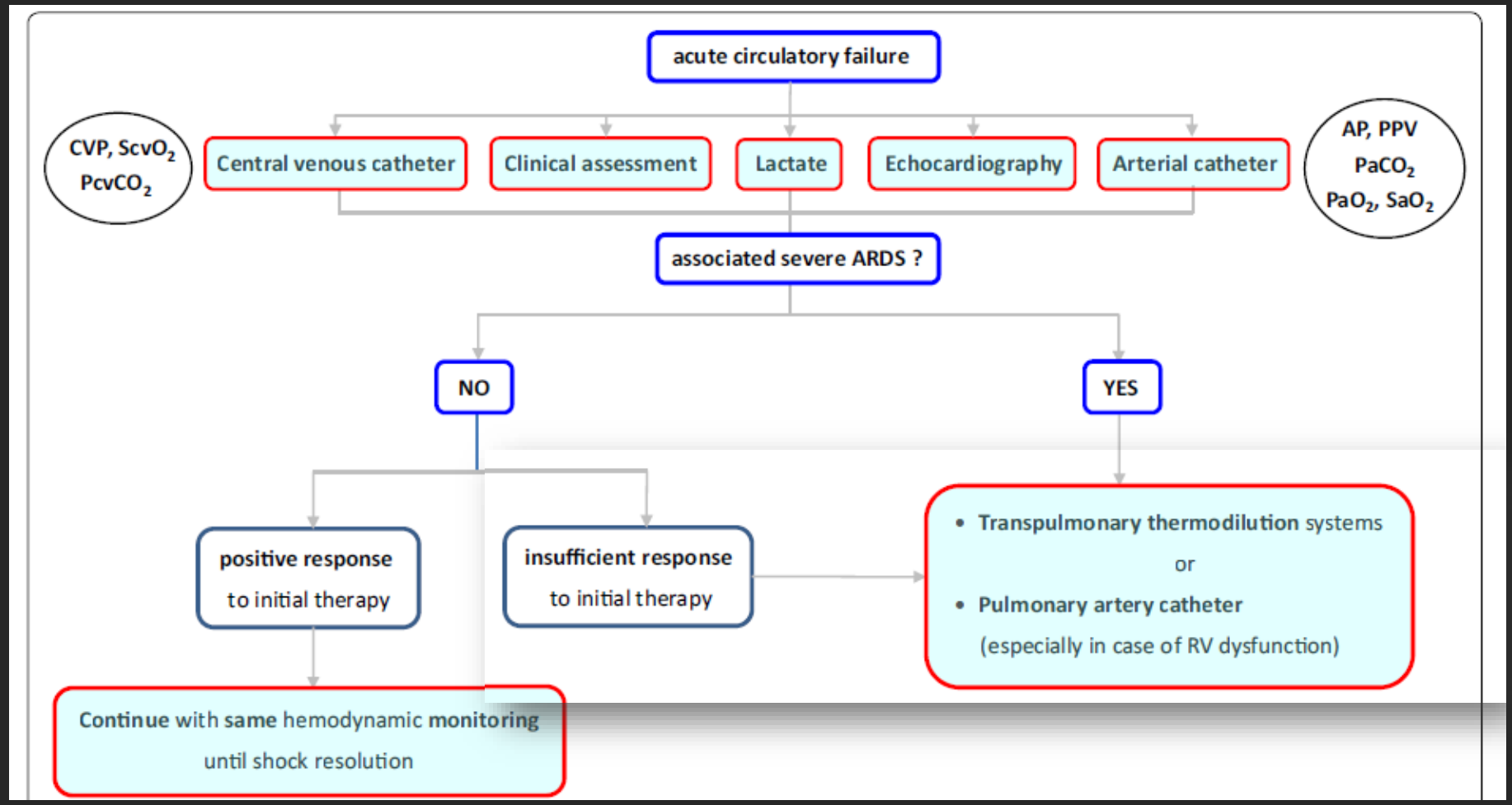
–We suggest the use of transpulmonary thermodilution or pulmonary artery catheterization in patients with severe shock especially in the case of associated acute respiratory distress syndrome. Level 2; QoE low (C)

–We recommend that less invasive devices are used, instead of more invasive devices, only when they have been validated in the context of patients with shock. *Ungraded best practice*

CONFERENCE REPORTS AND EXPERT PANEL

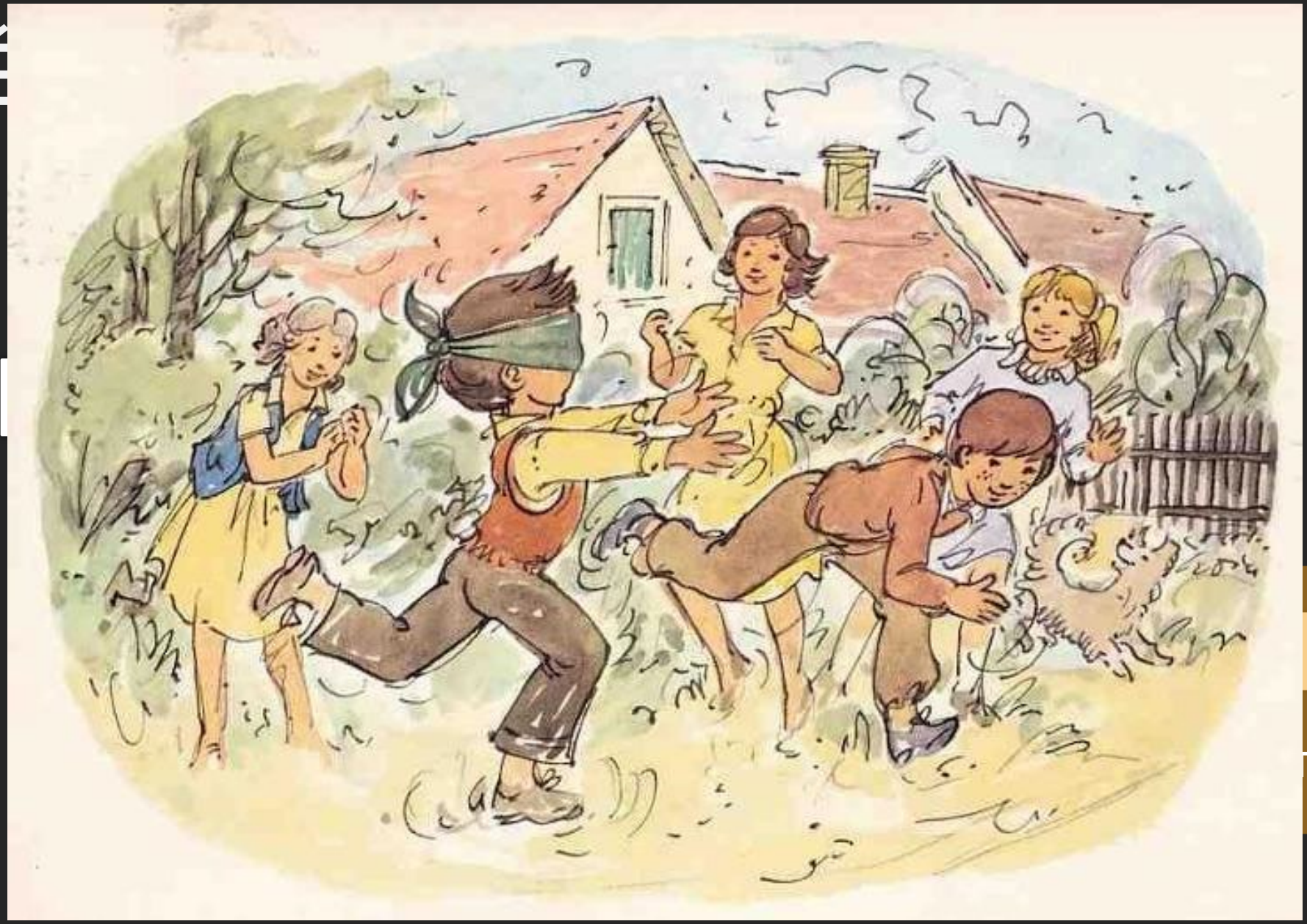
Less invasive hemodynamic monitoring in critically ill patients

Jean-Louis Teboul[1*], Bernd Saugel[2], Maurizio Cecconi[3], Daniel De Backer[4], Christoph K. Hofer[5], Xavier Monnet[1], Azriel Perel[6], Michael R. Pinsky[7], Daniel A. Reuter[2], Andrew Rhodes[3], Pierre Squara[8], Jean-Louis Vincent[9] and Thomas W. Scheeren[10]



OBĚ

MA



EF

TAŽLIVOST

ZNOVU ROZVAŽ PŘÍČINU

„PRAVÉ SRDCE“

ZNÁMKY HYPOPERFUZE

HD MONITORACE

INDIVIDUALIZACE MAP

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

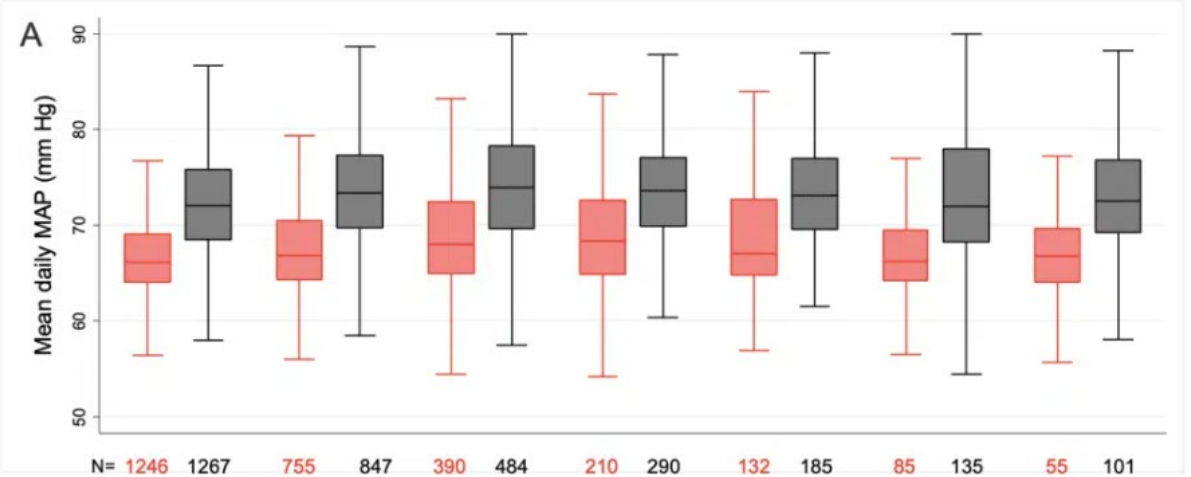
Key Points

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 intensive care unit (ICU) patients aged 65 years or older receiving vasopressors for vasodilatory hypotension?

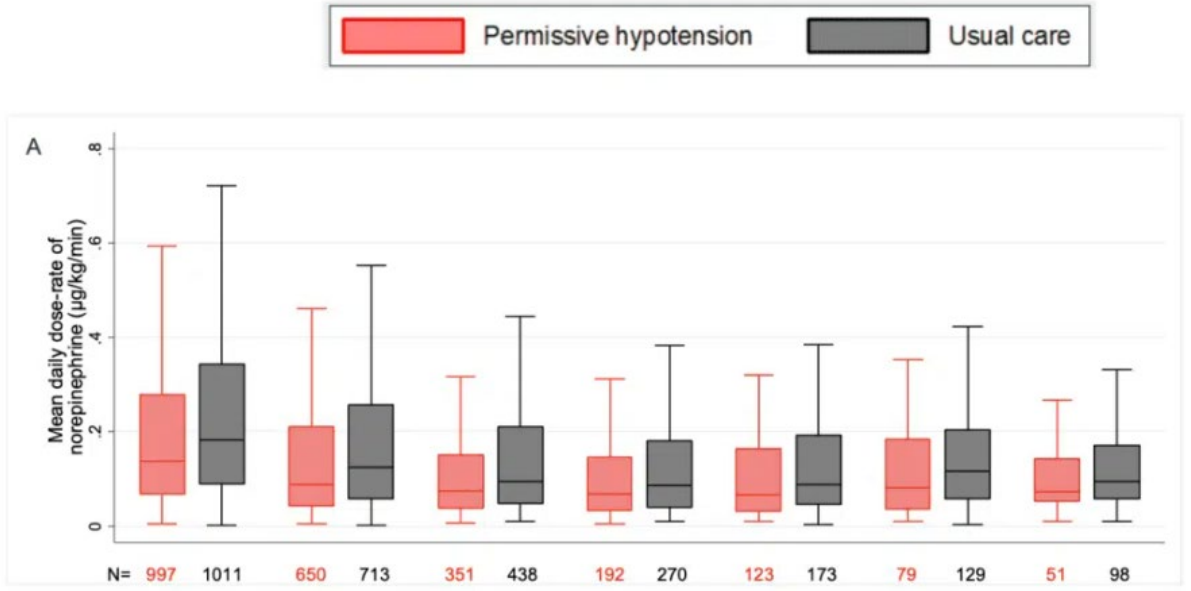
Findings In this randomized clinical trial that included 2600 patients aged 65 years or older with vasodilatory hypotension, treatment with permissive hypotension resulted in death at 90 days among 41.0% of patients compared with 43.8% of those receiving usual care, a difference that was not statistically significant.

Meaning Reducing the exposure to vasopressors through permissive hypotension did not significantly reduce mortality at 90 days.

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



eFigure 6. Vasopressor dose-rates days 1 to 7 post-randomization.



ZNOVU ROZVAŽ PŘÍČINU

„PRAVÉ SRDCE“

ZNÁMKY HYPOPERFUZE

HD MONITORACE

INDIVIDUALIZACE MAP
(vasopressor challenge)

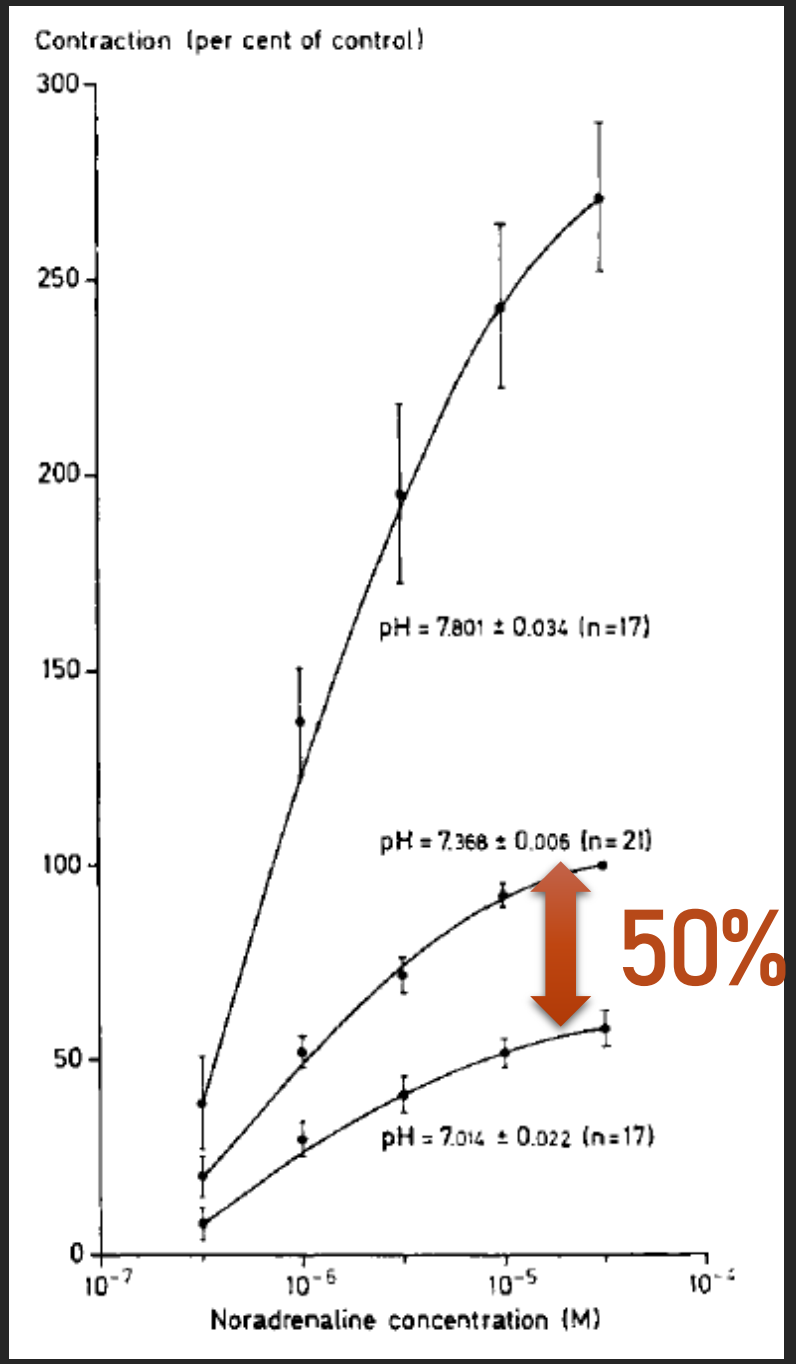
pH a HOMEOSTÁZA

Influence of pH and pCO_2 on Alpha-Receptor Mediated Contraction in Brain Vessels

By

Lars Edvinsson and Richard Sercombe

Received 8 December 1975



ZNOVU ROZVAŽ PŘÍČINU

„PRAVÉ SRDCE“

ZNÁMKY HYPOPERFUZE

HD MONITORACE

INDIVIDUALIZACE MAP
(vasopressor challenge)

pH a HOMEOSTÁZA

„PŘÍSADY“

Na et al. Journal of Intensive Care (2021) 9:75
https://doi.org/10.1186/s40560-021-00589-x

Journal of Intensive Care

RESEARCH Open Access

Hydrocortisone, ascorbic acid, and thiamine (HAT) for sepsis and septic shock: a meta-analysis with sequential trial analysis

Weilan Na[1], Huili Shen[2], Yichu Li[1] and Dong Qu[1*]

MORTALITY 30D

Study or Subgroup	Events	Total	Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Fujii2020	25	107	21	104	19.5%	1.16 [0.69, 1.93]
Iglesias2020	11	68	13	69	9.6%	0.86 [0.41, 1.78]
Mohamed2020	26	45	23	43	36.7%	1.08 [0.74, 1.57]
Moskowitz2020	28	101	23	99	22.6%	1.19 [0.74, 1.92]
Wani2020	12	50	14	50	11.6%	0.86 [0.44, 1.66]
Total (95% CI)		**371**		**365**	**100.0%**	**1.07 [0.85, 1.34]**
Total events	102		94			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.07$, df = 4 (P = 0.90); $I^2 = 0\%$

Risk Ratio M-H, Random, 95% CI

0.5 0.7 1 1.5 2

Favours [intervention] Favours [control]

VASOPRESSOR LOAD

Study or Subgroup	Events	Total	Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Chang2020	11	40	14	40	7.6%	0.79 [0.41, 1.52]
Fujii2020	24	106	21	103	12.2%	1.11 [0.66, 1.87]
Hussein2021	17	47	21	47	13.4%	0.81 [0.49, 1.33]
Moskowitz2020	35	101	29	99	19.9%	1.18 [0.79, 1.78]
Sevransky2021	55	252	60	249	31.9%	0.91 [0.66, 1.25]
Wani2020	20	50	21	50	14.9%	0.95 [0.59, 1.52]
Total (95% CI)		**596**		**588**	**100.0%**	**0.96 [0.80, 1.15]**
Total events	162		166			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.26$, df = 5 (P = 0.81); $I^2 = 0\%$

Test for overall effect: Z = 0.42 (P = 0.67)

Risk Ratio M-H, Random, 95% CI

0.2 0.5 1 2 5

Favours [intervention] Favours [control]

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Intravenous Vitamin C in Adults with Sepsis in the Intensive Care Unit

Lamontagne F et al. DOI: 10.1056/NEJMoa2200644

CLINICAL PROBLEM

Intravenous vitamin C has been hypothesized to mitigate tissue injury due to oxidative stress in patients with sepsis. Studies to date have shown mixed results with regard to patient outcomes.

CLINICAL TRIAL

Design: A phase 3, multicenter, randomized, controlled trial examined the efficacy and safety of a high dose of intravenous vitamin C in adults with sepsis who were receiving vasopressor therapy in the intensive care unit (ICU).

Intervention: 872 patients were assigned to receive an infusion of vitamin C (50 mg/kg of body weight) or placebo every 6 hours for up to 4 days. The primary outcome was a composite of death or persistent organ dysfunction on day 28.

RESULTS

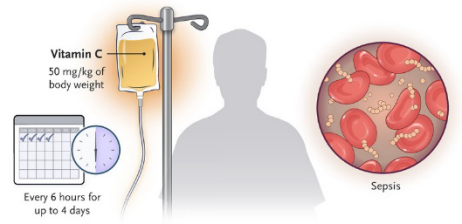
Efficacy: Among 863 patients in the analysis population, the incidence of primary outcome events was greater in the vitamin C group than in the placebo group.

Safety: There were no significant differences between the groups in prespecified safety outcomes (stage 3 acute kidney injury, acute hemolysis, and hypoglycemia). In the vitamin C group, one patient had a severe hypoglycemic episode and another had a serious anaphylaxis event.

LIMITATIONS AND REMAINING QUESTIONS

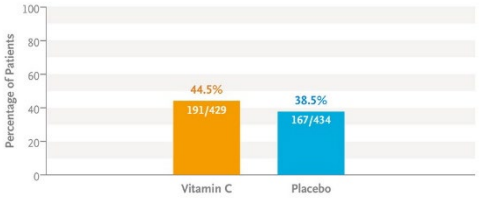
- Secondary analyses did not determine a possible mechanism for the worse outcomes seen with intravenous vitamin C.
- It is not known which patients had acute respiratory distress syndrome (ARDS) at baseline; thus, whether patients with ARDS had a different response to vitamin C is unclear.
- The patient population was representative of high-income countries, rather than low- and middle-income countries where the incidence of sepsis is highest.

Links: Full Article | NEJM Quick Take

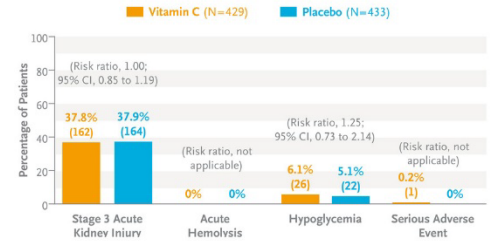


Death or Persistent Organ Dysfunction at 28 Days

Risk ratio, 1.21; 95% CI, 1.04 to 1.40; P = 0.01



Safety Outcomes



CONCLUSIONS

In adults with sepsis who were receiving vasopressor therapy in the ICU, the risk of death or persistent organ dysfunction was higher with intravenous vitamin C than with placebo.

ORIGINAL ARTICLE

Patient-Level Meta-Analysis of Low-Dose Hydrocortisone in Adults with Septic Shock

Authors: Romain Pirracchio, M.D., M.P.H., Ph.D., Djillali Annane, M.D., Ph.D., Andre K. Waschka, Ph.D., François Lamontagne, M.D., M.Sc., Yaseen M. Arabi, M.D., Pierre-Edouard Bollaert, M.D., Laurent Billot, M.D., +18, and Anthony Delaney, M.D., Ph.D. Author Info & Affiliations

Published May 22, 2023 | NEJM Evid 2023;2(6) | DOI: 10.1056/EVIDoa2300034 | VOL. 2 NO. 6

RESULTS

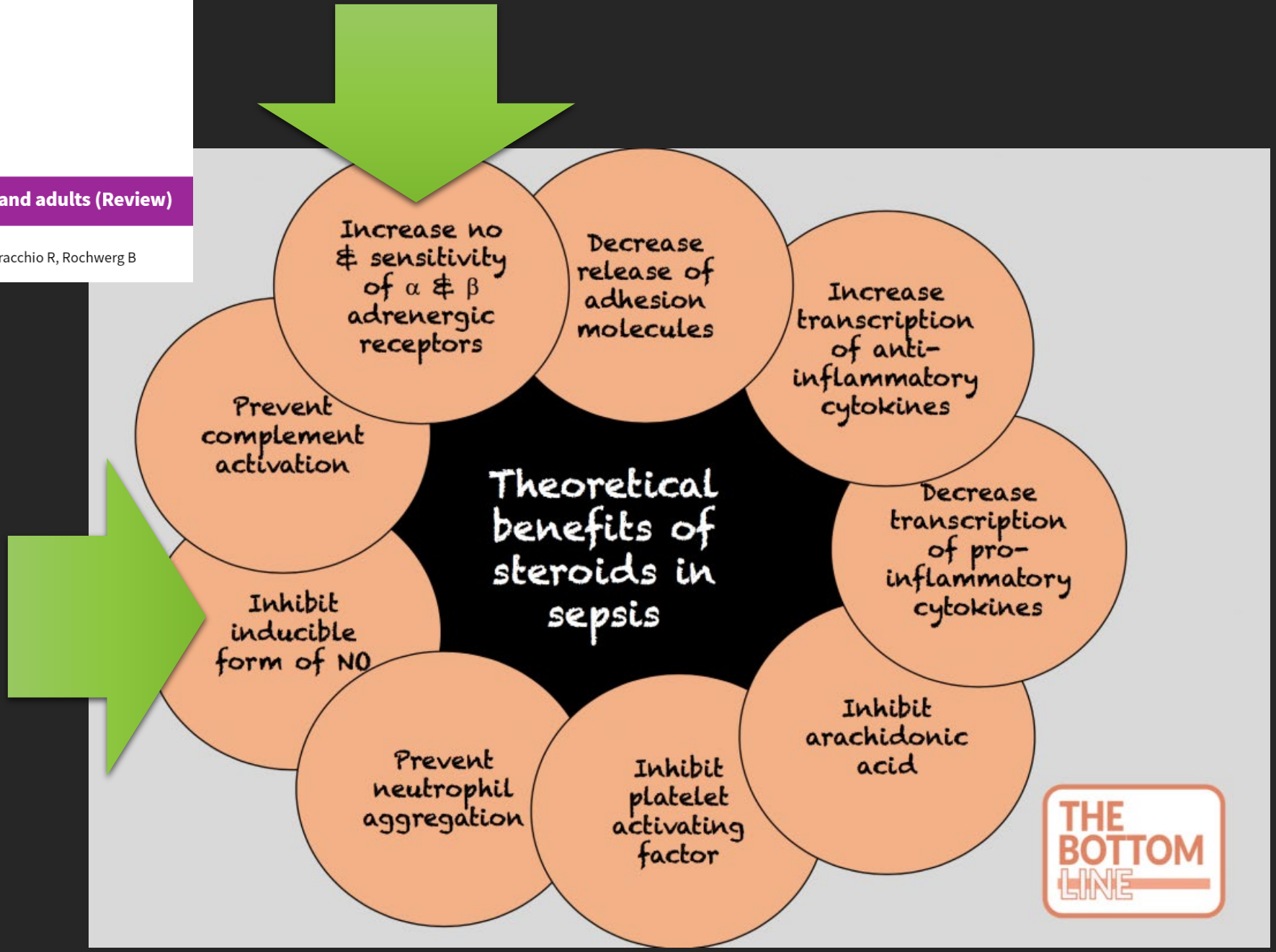
Of 24 eligible trials (n=8528), 17 (n=7882) provided individual patient data, and 7 (n=5929) provided 90-day mortality. The marginal relative risk (RR) for 90-day mortality of hydrocortisone versus placebo was 0.93 (95% confidence interval [CI], 0.82 to 1.04; P=0.22; moderate certainty). It was 0.86 (95% CI, 0.79 to 0.92) for hydrocortisone with fludrocortisone and 0.96 (95% CI, 0.82 to 1.12) without fludrocortisone. There was no significant differential treatment effect across subgroups. Hydrocortisone was associated with little to no difference in any of the secondary outcomes except vasopressor-free days (mean difference, 1.24 days; 95% CI, 0.74 to 1.73; high certainty). Hydrocortisone may not be associated with an increase in the risk of superinfection (RR, 1.04; 95% CI, 0.95 to 1.15; low certainty), hyperglycemia (RR, 1.05; 95% CI, 0.98 to 1.12; low certainty), or gastroduodenal bleeding (RR, 1.11; 95% CI, 0.83 to 1.48; low certainty). Hydrocortisone may be associated with an increase in the risk of hypernatremia (RR, 2.01; 95% CI, 1.56 to 2.60; low certainty) and muscle weakness (n=2647; RR, 1.73; 95% CI, 1.49 to 1.99; low certainty).

Cochrane Library

Cochrane Database of Systematic Reviews

Corticosteroids for treating sepsis in children and adults (Review)

Annane D, Bellissant E, Bollaert PE, Briegel J, Keh D, Kupfer Y, Pirracchio R, Rochwerg B



ZNOVU ROZVAŽ PŘÍČINU

„PRAVÉ SRDCE“

ZNÁMKY HYPOPERFUZE

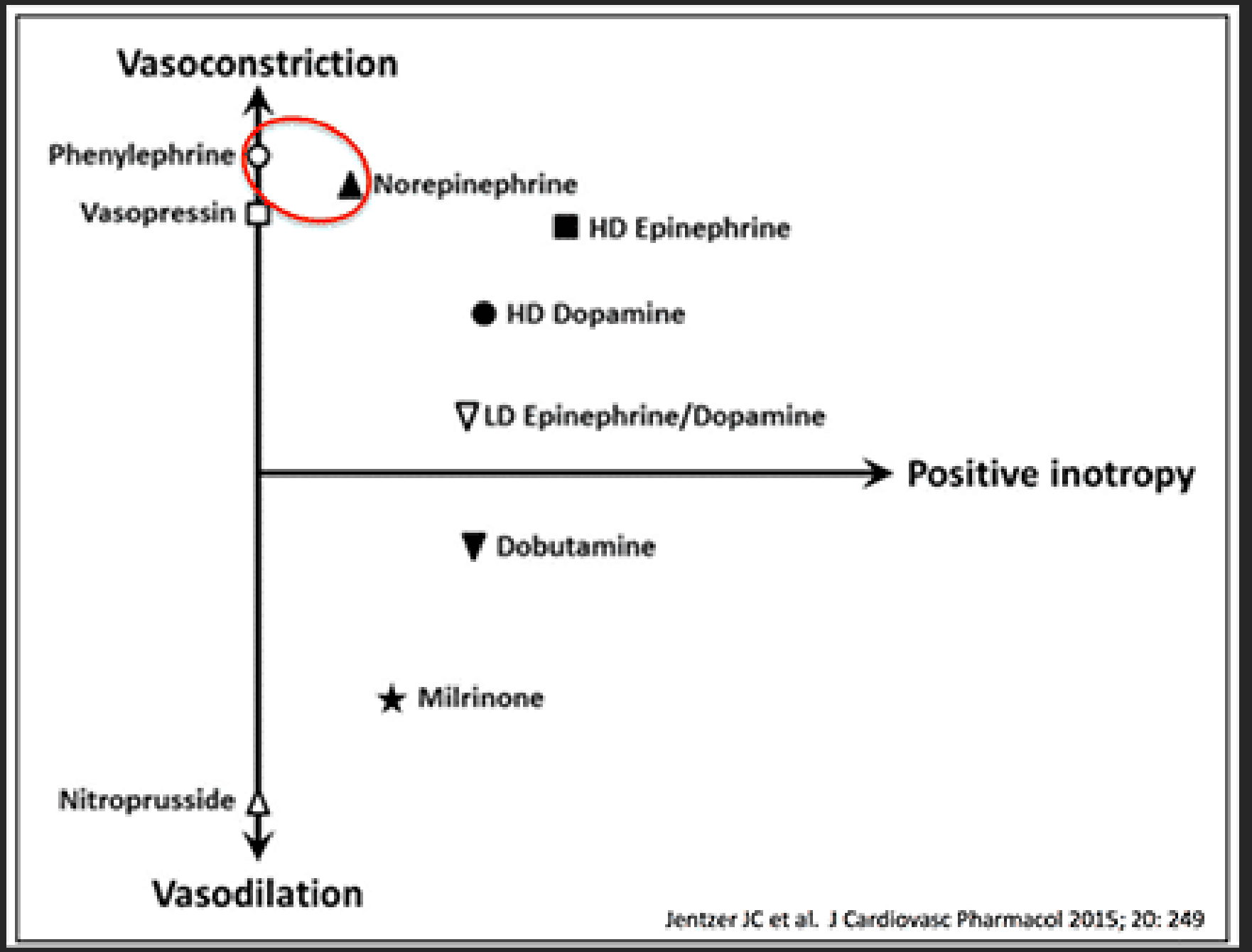
HD MONITORACE

INDIVIDUALIZACE MAP
(vasopressor challenge)

pH a HOMEOSTÁZA

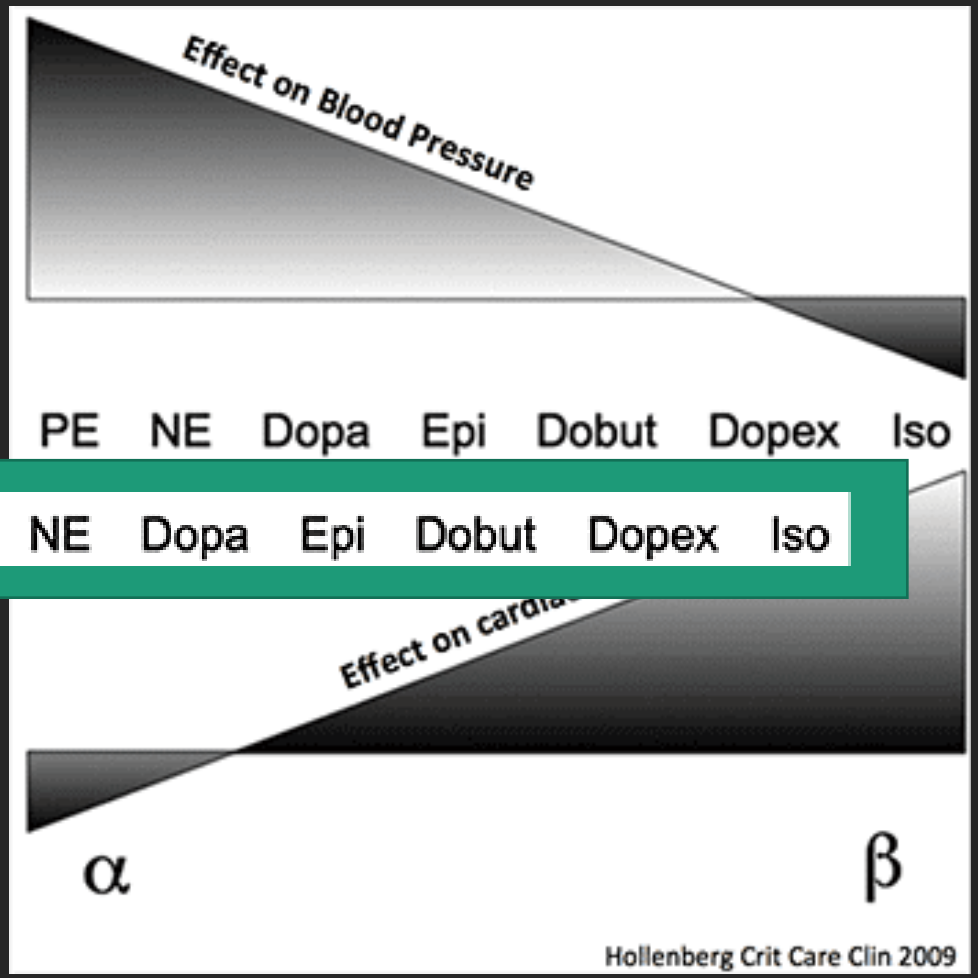
KORTIKOSTEROID

PŘI DOBRÉM „VÝDEJI“
JINÝ VAZOPRESOR


Vasoconstriction
Phenylephrine
Norepinephrine
Vasopressin
HD Epinephrine
HD Dopamine
LD Epinephrine/Dopamine
Positive inotropy
Dobutamine
Milrinone
Nitroprusside
Vasodilation
Jentzer JC et al. J Cardiovasc Pharmacol 2015; 20: 249

..trocha FYZIOLOGIE

	alpha1 (α_1R)	alpha2 (α_2R)	beta1 (β_1R)	beta2 (β_2R)	Dopamine (DA_{1-5}R)
	Vasoconstriction Inotropy		Inotropy Dromotropy Chronotropy	Inotropy Bronchodilation Vasodilation	Natriuresis Splanchnic vasodilation
Adrenaline	++	+	++++	+++	
Noradrenaline	++++	+	++	+	
Phenylephrine and Metaraminol	++++	+			
Ephedrine			++++		
Dopamine	>10 µg/kg/min		5–10 µg/kg/min	5–10 µg/kg/m	
Dobutamine	+		++++	++	
Isoprenaline			++++	+++	



LIFE IN THE FASTLANE

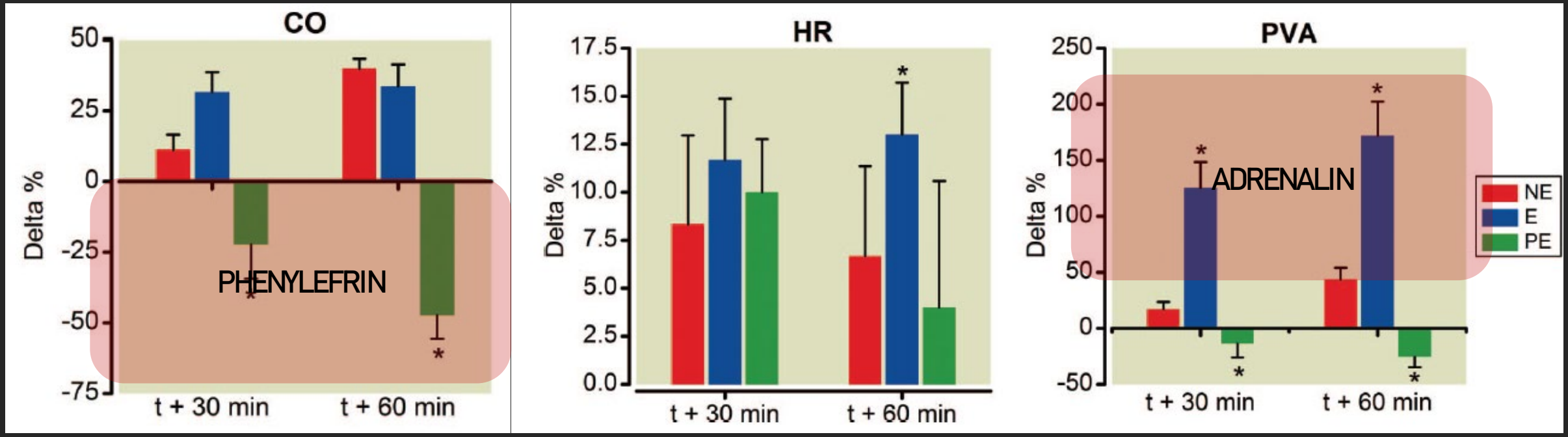
https://litfl.com/inotropes-vasopressors-and-other-vasoactive-agents/

Comparison of Equipressor Doses of Norepinephrine, Epinephrine, and Phenylephrine on Septic Myocardial Dysfunction

Nicolas Ducrocq, M.D.,* Antoine Kimmoun, M.D.,* Anna Furmaniuk, M.Sc.,† Zerin Hekalo, M.Sc.,† Fatiha Maskali, Ph.D.,‡ Sylvain Poussier, Ph.D.,‡ Pierre-Yves Marie, M.D., Ph.D.,§ Bruno Levy, M.D., Ph.D.‖

What This Article Tells Us That Is New

- Norepinephrine and epinephrine improved global hemodynamics and myocardial function during experimental septic shock but epinephrine increased myocardial oxygen consumption, whereas phenylephrine decreased ventricular performance

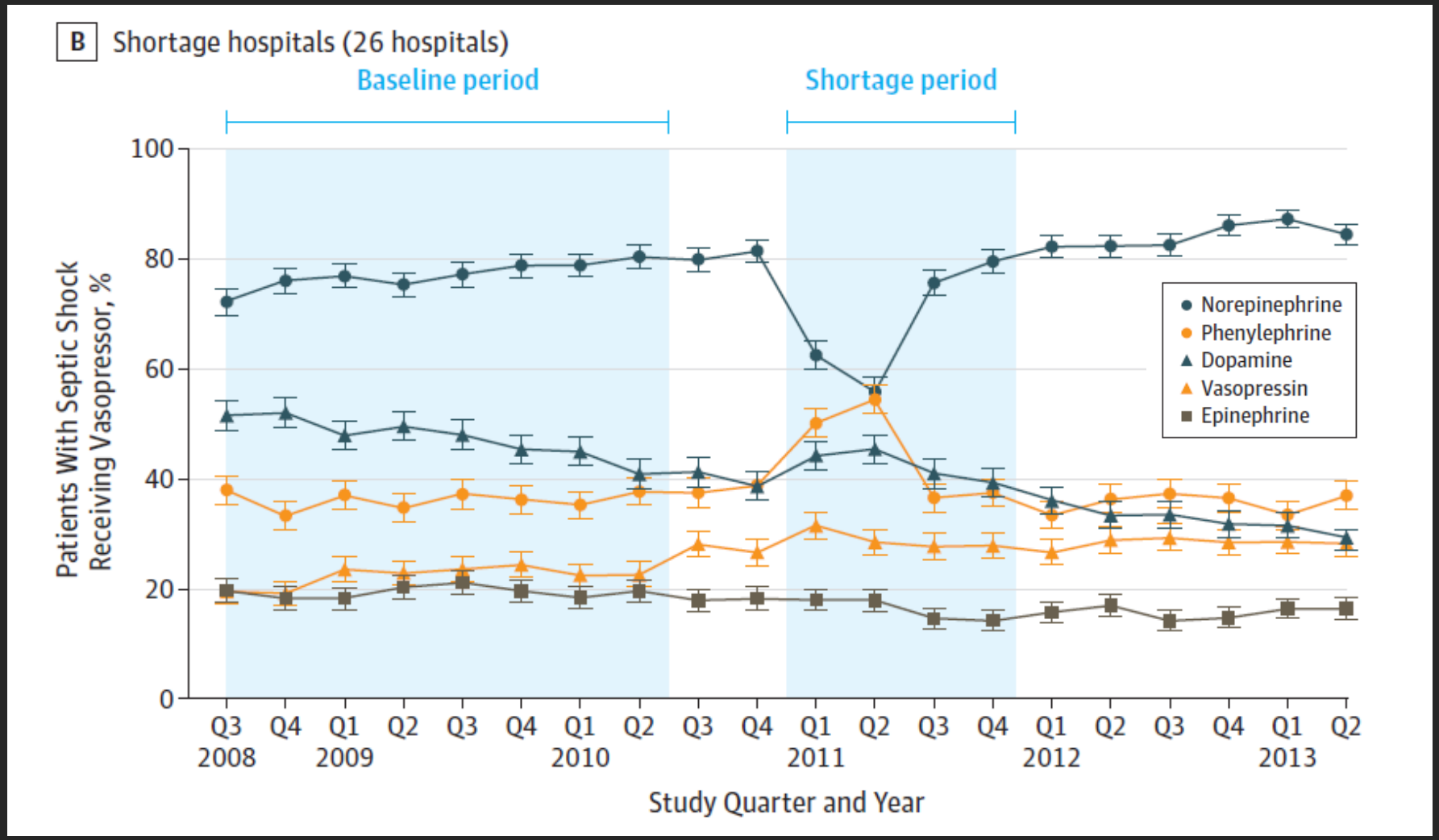


JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Association Between US Norepinephrine Shortage and Mortality Among Patients With Septic Shock

Emily Vail, MD; Hayley B. Gershengorn, MD; May Hua, MD, MSc; Allan J. Walkey, MD, MSc; Gordon Rubenfeld, MD, MSc; Hannah Wunsch, MD, MSc

DESIGN, SETTING, AND PARTICIPANTS Retrospective cohort study of 26 US hospitals in the Premier Healthcare Database with a baseline rate of norepinephrine use of at least 60% for patients with septic shock. The cohort included adults with septic shock admitted to study hospitals between July 1, 2008, and June 30, 2013 (n = 27 835).



JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Association Between US Norepinephrine Shortage and Mortality Among Patients With Septic Shock

Emily Vail, MD; Hayley B. Gershengorn, MD; May Hua, MD, MSc; Allan J. Walkey, MD, MSc; Gordon Rubenfeld, MD, MSc; Hannah Wunsch, MD, MSc

Cohort	Deaths, No./Total Patients, No. (%)	Absolute Mortality Difference, % (95% CI)[a]	Adjusted Odds Ratio (95% CI)[b]	*P* Value
Patients with septic shock receiving vasopressors				
Primary model[c]				
Admission to shortage hospitals during a nonshortage quarter	9283/25 874 (35.9)	NA	1 [Reference]	
Admission to shortage hospitals during a quarter of 2011 in which norepinephrine use decreased >20% below baseline	777/1961 (39.6)	3.7 (1.5-6.0)	1.15 (1.01-1.30)	.03
Difference-in-differences model[d]				
Difference-in-differences estimator for shortage and consistent-use hospitals	NA	NA	1.17 (1.06-1.31)	.003

CONCLUSIONS AND RELEVANCE Among patients with septic shock in US hospitals affected by the 2011 norepinephrine shortage, the most commonly administered alternative vasopressor was phenylephrine. Patients admitted to these hospitals during times of shortage had higher in-hospital mortality.

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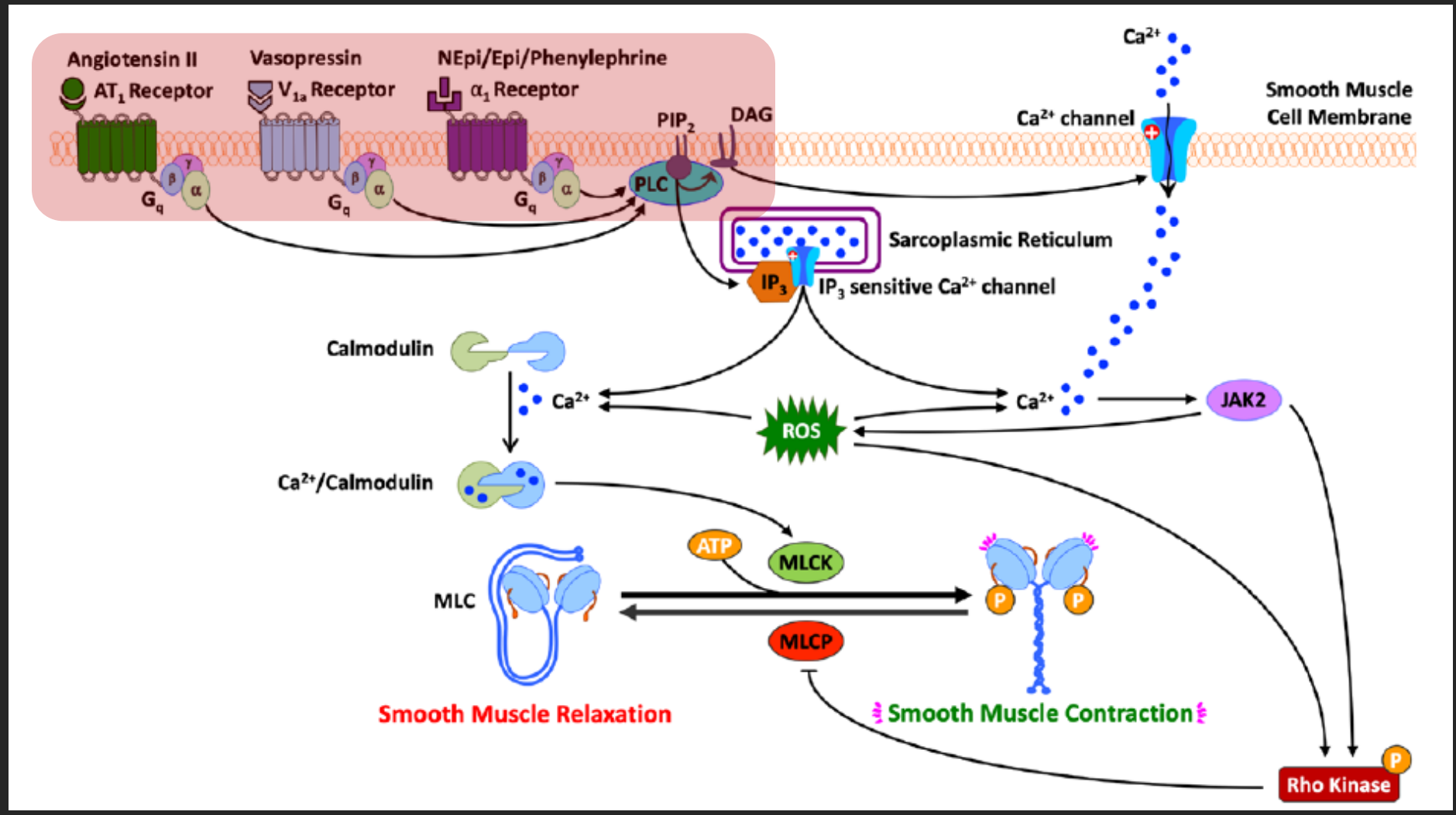
NARRATIVE REVIEW ARTICLE

CME

Reversal of Vasodilatory Shock: Current Perspectives on Conventional, Rescue, and Emerging Vasoactive Agents for the Treatment of Shock

Jonathan H. Chow, MD,* Ezeldeen Abuelkasem, MBBCh, MSc,† Susan Sankova, MD,*
Reney A. Henderson, MD,* Michael A. Mazzeffi, MD, MPH,* and Kenichi A. Tanaka, MD, MSc*

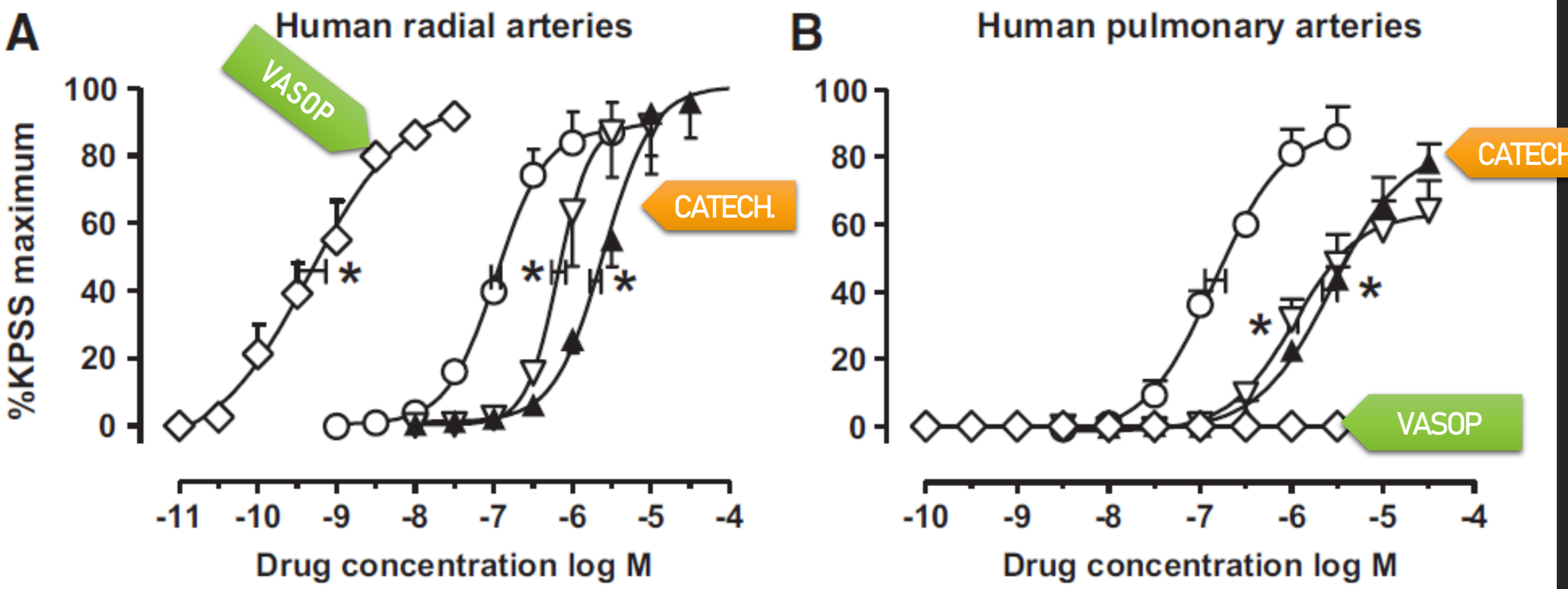


..trocha FYZIOLOGIE

Vasoconstrictor Responses to Vasopressor Agents in Human Pulmonary and Radial Arteries

An In Vitro Study

Dale A. Currigan, M.B.B.S., Richard J. A. Hughes, B.Sc.Hons., M.Phil., Christine E. Wright, B.Sc.Hons., Ph.D., James A. Angus, B.Sc.Hons., Ph.D., Paul F. Soeding, B.Sc.Hons., Ph.D., M.B.B.S.



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 28, 2008 VOL. 358 NO. 9

Vasopressin versus Norepinephrine Infusion in Patients with Septic Shock

James A. Russell, M.D., Keith R. Walley, M.D., Joel Singer, Ph.D., Anthony
Paul C. Hébert, M.D., D. James Cooper, B.M., B.S., M.D., Cheryl L. Holme
John T. Granton, M.D., Michelle M. Storms, B.Sc.N., Deborah J. Cook, M.D.,
and Dieter Ayers, M.Sc., for the VASST Investiga

Vl/V2 = 1
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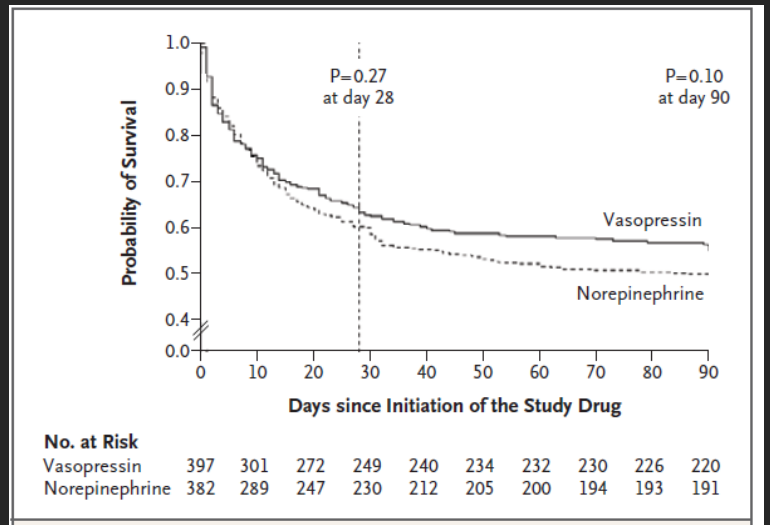


Figure 2. Kaplan–Meier Survival Curves for Patients Who Underwent Randomization and Infusion.

The dashed vertical line marks day 28. P values were calculated with the use of the log-rank test.

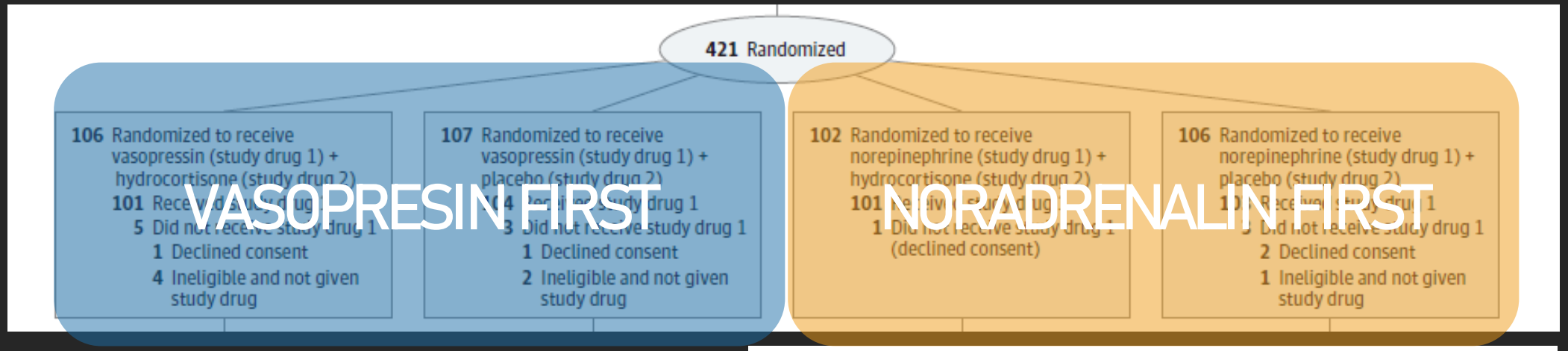
Table 4. Rates and Risks of Death from Any Cause According to the Severity of Shock.*

Stratum	Norepinephrine Group	Vasopressin Group	P Value†	Absolute Risk Reduction (95% CI)	Relative Risk (95% CI)
	no./total no. (%)			%	
More severe septic shock					
28-day mortality	85/200 (42.5)	88/200 (44.0)	0.76	−1.5 (−11.2 to 8.2)	1.04 (0.83 to 1.3)
90-day mortality	105/199 (52.8)	103/199 (51.8)	0.84	1.0 (−8.8 to 10.8)	0.98 (0.81 to 1.18)
Less severe septic shock					
28-day mortality	65/182 (35.7)	52/196 (26.5)	0.05	9.2 (−0.1 to 18.5)	0.74 (0.55 to 1.01)
90-day mortality	83/180 (46.1)	69/193 (35.8)	0.04	10.4 (0.4 to 20.3)	0.78 (0.61 to 0.99)

* Patients with more severe septic shock were defined as those who required at least 15 μg of norepinephrine per minute or the equivalent at the time of randomization. Those with less severe septic shock were defined as those who required 5 to 14 μg of norepinephrine per minute or the equivalent at the time of randomization.

???

FUNGUJE VÍCE U NIŽŠÍ ZÁVAŽNOSTI ŠOKU



JAMA | Original Investigation

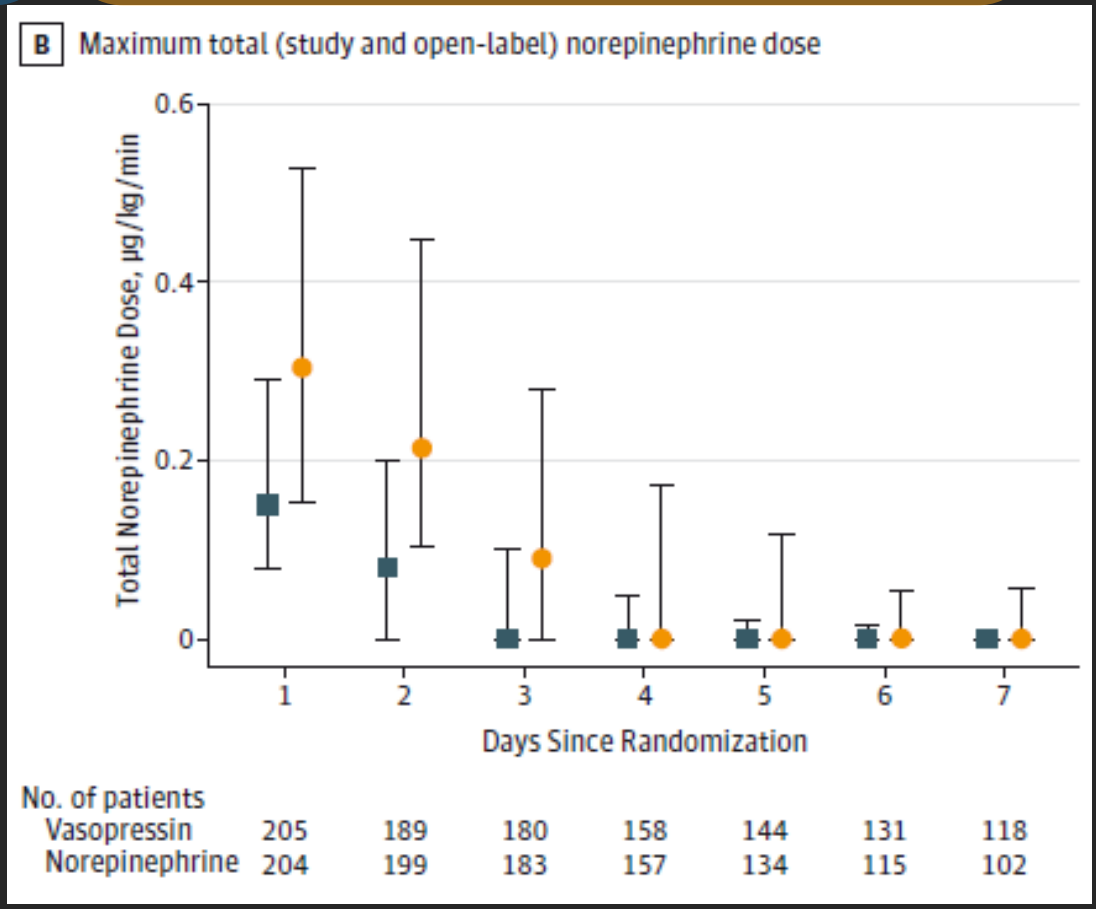
Effect of Early Vasopressin vs Norepinephrine on Kidney Failure in Patients With Septic Shock

The VANISH Randomized Clinical Trial

Anthony C. Gordon, MD; Alexina J. Mason, PhD; Neeraja Thirunavukkarasu, MSc; Gavin D. Perkins, MD; Maurizio Cecconi, MD; Magda Cepkova, MD; David G. Pogson, MB BCh; Hollmann D. Aya, MD; Aisha Anjum, BSc; Gregory J. Frazier, MSc; Shalini Santhakumaran, MSc; Deborah Ashby, PhD; Stephen J. Brett, MD; for the VANISH Investigators

Conclusions

Among adults with septic shock, the early use of vasopressin compared with norepinephrine did not improve the number of kidney failure–free days. Although these findings do not support the use of vasopressin to replace norepinephrine as initial treatment in this situation, the confidence interval included a potential clinically important benefit for vasopressin, and larger trials may be warranted to assess this further.



Surviving Sepsis Campaign

Vasoactive Agent Management

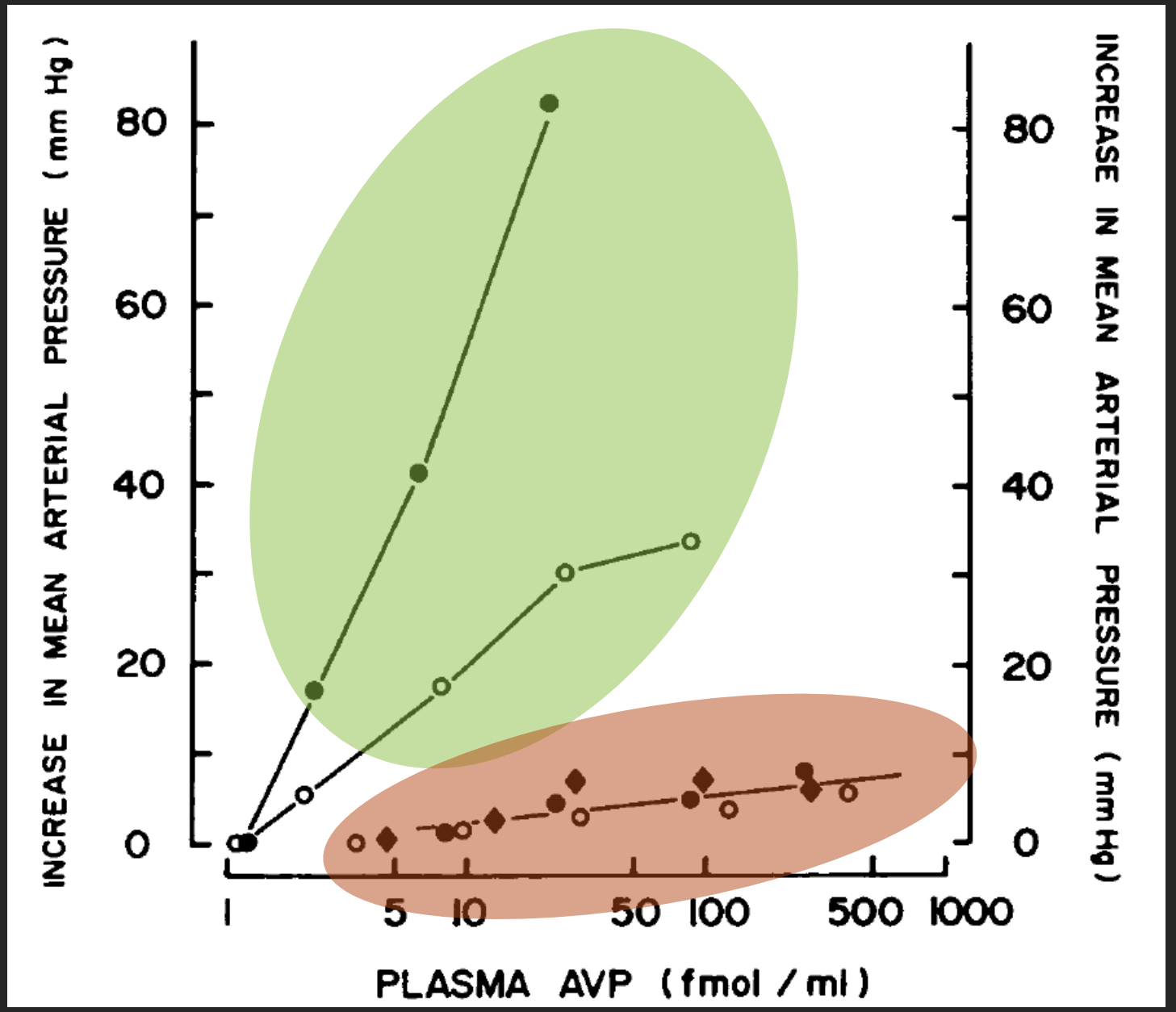
	☑ Use norepinephrine as first-line vasopressor.
For patients with septic shock on vasopressors	☑ Target a MAP of 65 mm Hg. ⚠ **Consider** invasive monitoring of arterial blood pressure.
If central access is not yet available	⚠ **Consider** initiating vasopressors peripherally.*
If MAP is inadequate despite low-to-moderate norepinephrine	⚠ **Consider** adding vasopressin.

0,01-0,03 IU/min
NEstandardní ředění 40IU/40ml
0,6-1,2-1,8 ml/h

Journal of Cardiovascular Pharmacology
2:367–376 © 1980 Raven Press, New York

Greatly Enhanced Pressor Response to Antidiuretic Hormone in Patients with Impaired Cardiovascular Reflexes Due to Idiopathic Orthostatic Hypotension

*J. Möhring,[1] †K. Glänzer, ‡J. A. Maciel Jr., †R. Düsing, †H. J. Kramer, *R. Arbogast, and *J. Koch-Weser



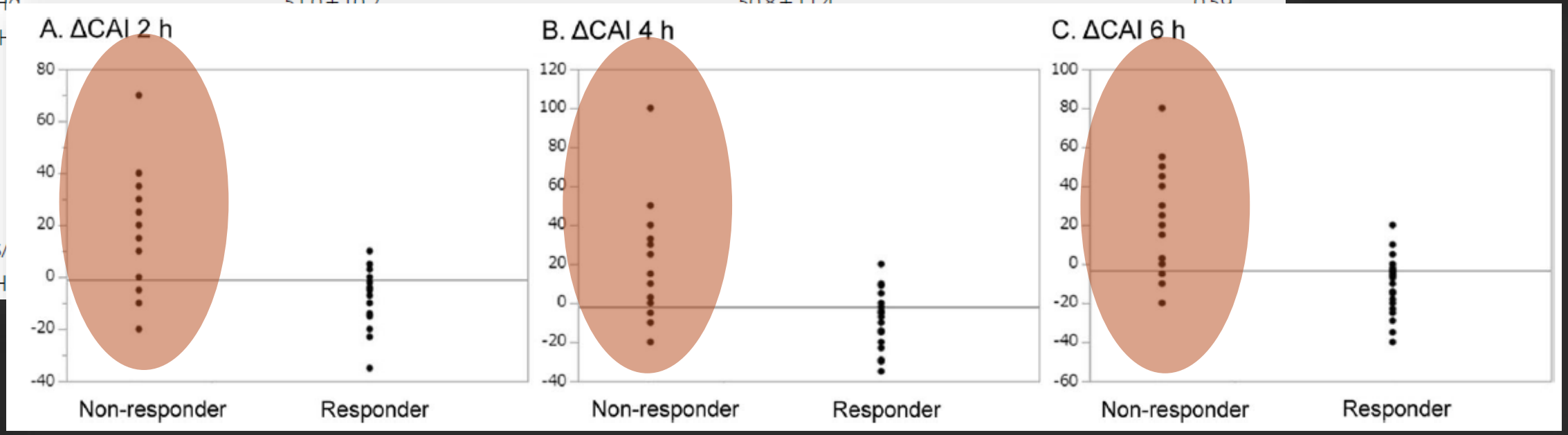
RESEARCH Open Access

The Vasopressin Loading for Refractory septic shock (VALOR) study: a prospective observational study

Kensuke Nakamura[1,2*], Hidehiko Nakano[2], Daisuke Ikechi[2], Masaki Mochizuki[2], Yuji Takahashi[2], Yasuaki Koyama[2], Hideki Hashimoto[2], Toshikazu Abe[3,4], Mineji Hayakawa[5] and Kazuma Yamakawa[6]

BOLUS 1IU u pacientů s dávkou NOR 0,2 ug/kg/min A NÁSLEDNÁ INFUZE 1U/hod

n	Responder MAP change > 22 mmHg 62	Non-responder MAP change ≤ 22 mmHg 30	p value
Pre SBP mm Hg	107.3 ± 22.2	104.8 ± 22.2	0.59
Pre DBP mm Hg	51.0 ± 10.2	50.8 ± 11.4	0.59
Pre MAP mm H			
Pre HR /min			
Pre CO l/min			
Pre SV ml			
Pre SVV %			
Pre dPmx			
Pre SVR dynes/			
Pre CVP mm H			



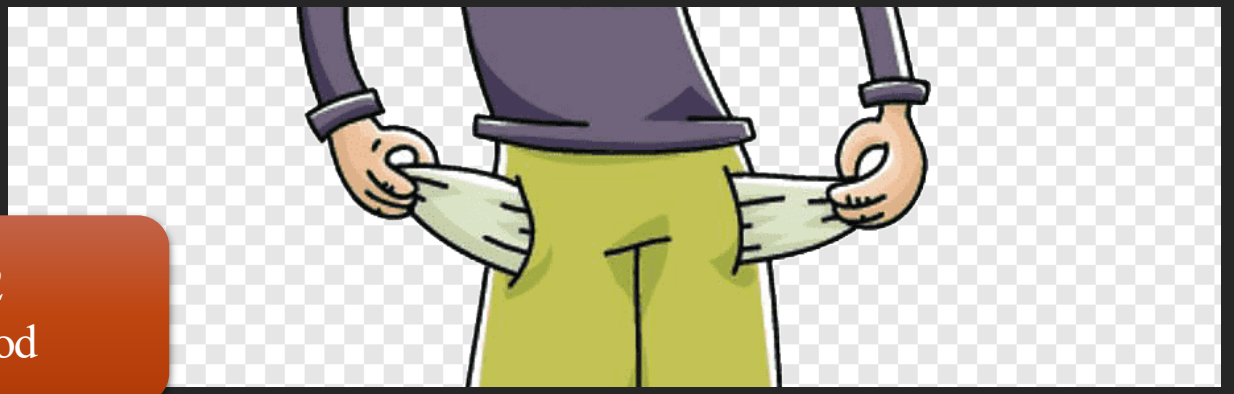
Citation:
Huang P, Guo Y, Li B and Liu Q (2019) Terlipressin Versus Norepinephrine for Septic Shock: A Systematic Review and Meta-Analysis. Front. Pharmacol. 10:1492. doi: 10.3389/fphar.2019.01492

Terlipressin Versus Norepinephrine for Septic Shock: A Systematic Review and Meta-Analysis

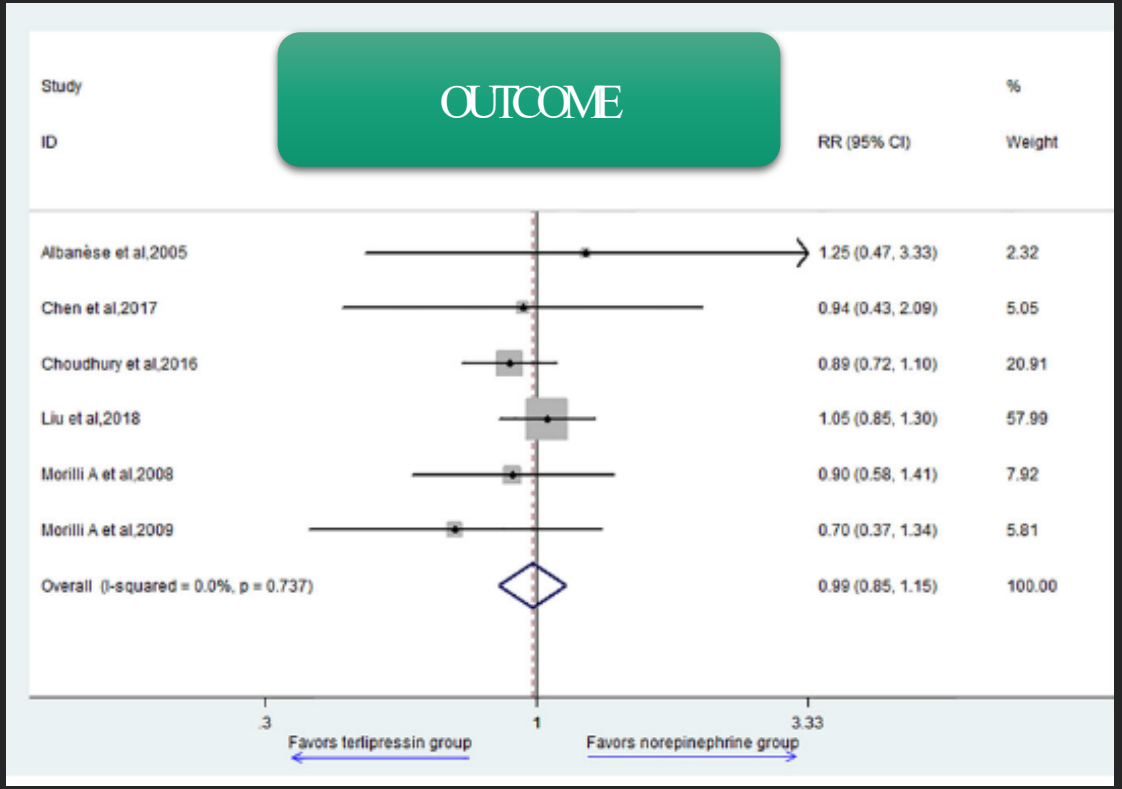
Po Huang[1], Yuhong Guo[1], Bo Li[1,2] and Qingquan Liu[1,2,3]*

[1] Beijing Hospital of Traditional Chinese Medicine, Capital Medical University, Beijing, Chin
Laboratory, Beijing Institute of Traditional Chinese Medicine, Beijing, China, [3] Infection and
Laboratory of Basic Research With Traditional Chinese Medicine on Infectious Diseases, E

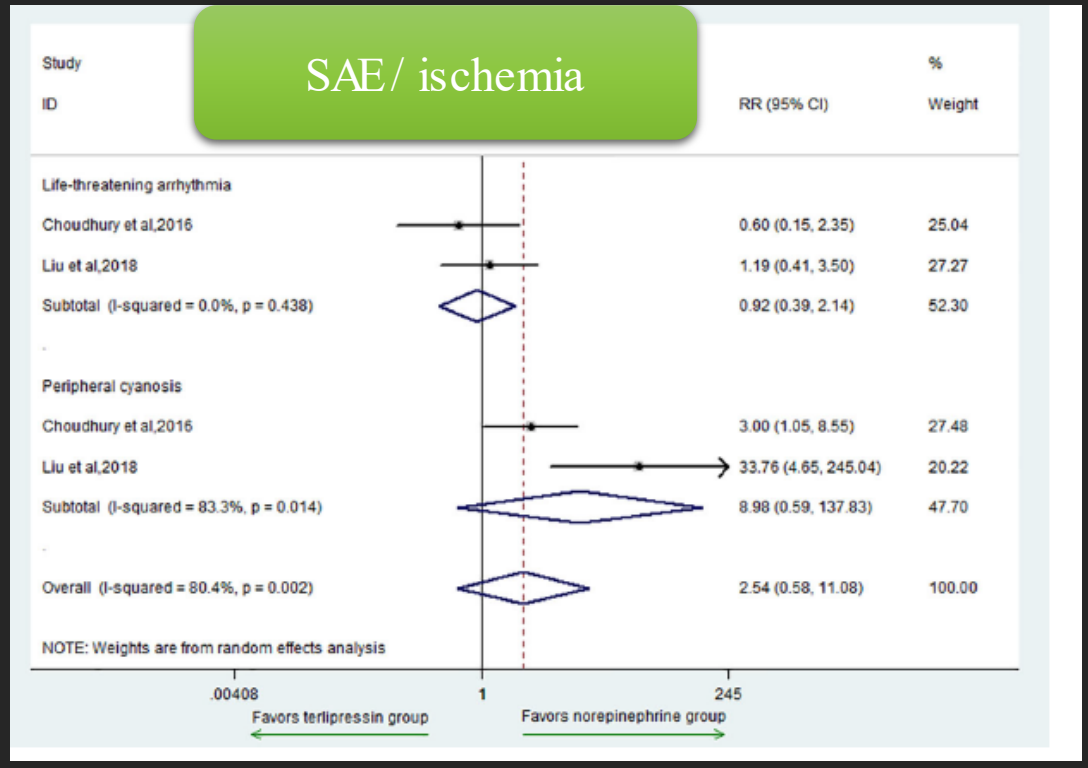
VI/V2 =2,2
Počas 6 hod



OUTCOME



SAE / ischemia



ZNOVU ROZVAŽ PŘÍČINU

„PRAVÉ SRDCE“

ZNÁMKY HYPOPERFUZE

HD MONITORACE

INDIVIDUALIZACE MAP
(vasopressor challenge)

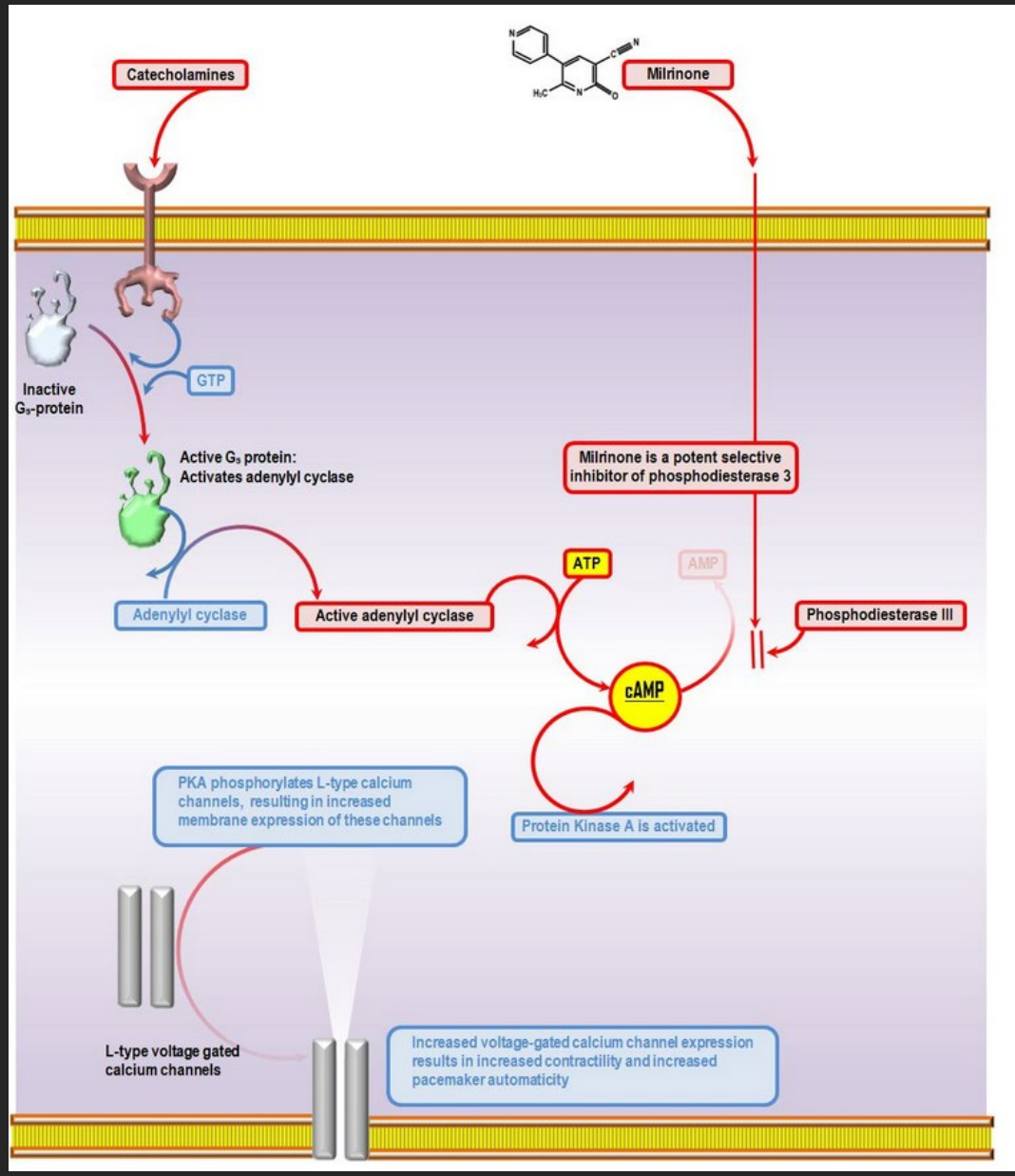
pH a HOMEOSTÁZA

KORTIKOSTEROID

PŘI ŠPATNÉM „VÝDEJI“
INOTROPIKUM ???

5. We suggest using dobutamine in patients who show evidence of persistent hypoperfusion despite adequate fluid loading and the use of vasopressor agents (weak recommendation, low quality of evidence).

If cardiac dysfunction with persistent hypoperfusion is present despite adequate volume status and blood pressure	⚠ **Consider** adding dobutamine or switching to epinephrine.



REVIEW Open Access

Levosimendan in the light of the results of the recent randomized controlled trials: an expert opinion paper

Bernard Cholley[1,2,3*], Bruno Levy[4], Jean-Luc Fellahi[5,6], Dan Longrois[7,8], Julien Amour[9,10], Alexandre Ouattara[11,12,13] and Alexandre Mebazaa[8,14]

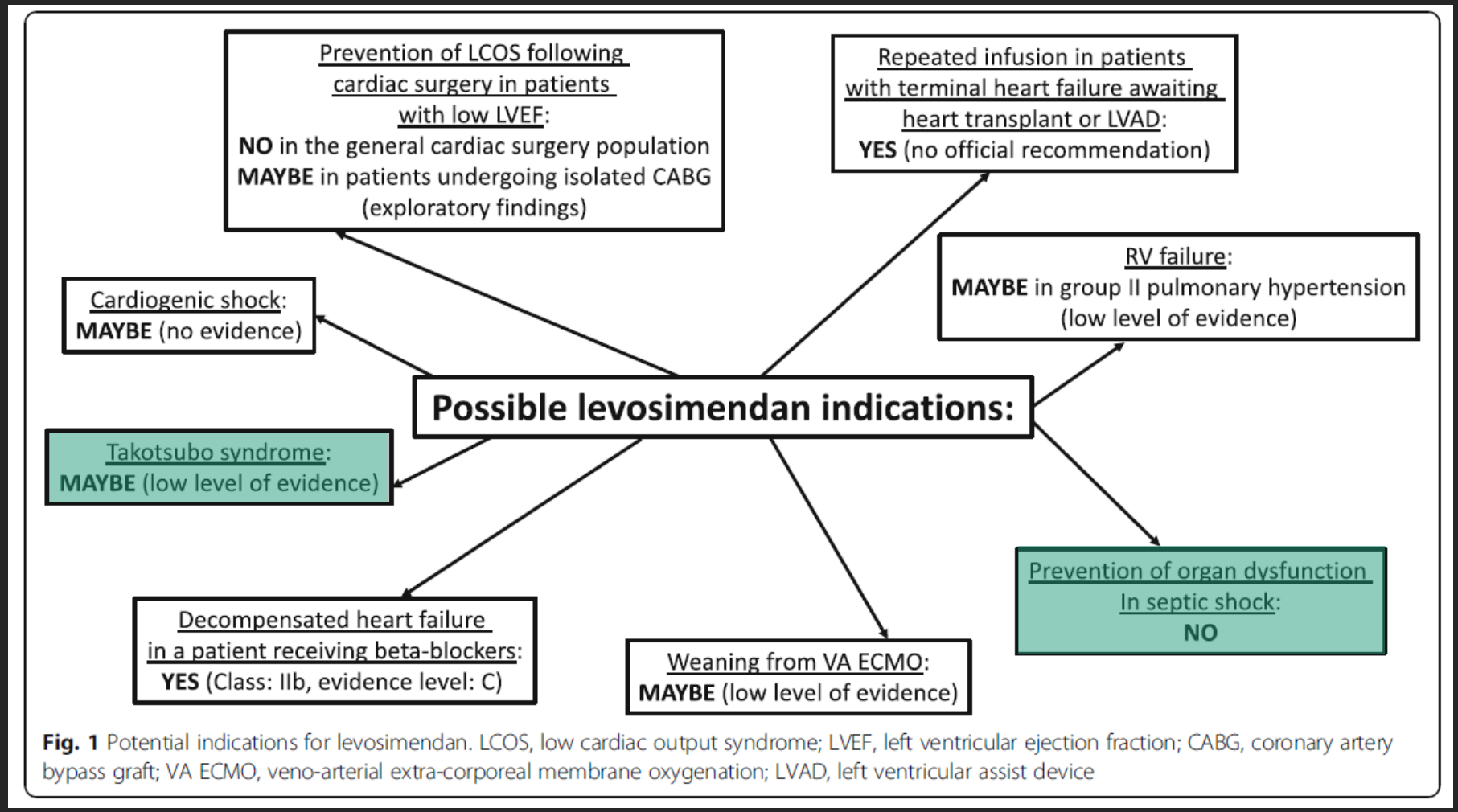


Fig. 1 Potential indications for levosimendan. LCOS, low cardiac output syndrome; LVEF, left ventricular ejection fraction; CABG, coronary artery bypass graft; VA ECMO, veno-arterial extra-corporeal membrane oxygenation; LVAD, left ventricular assist device

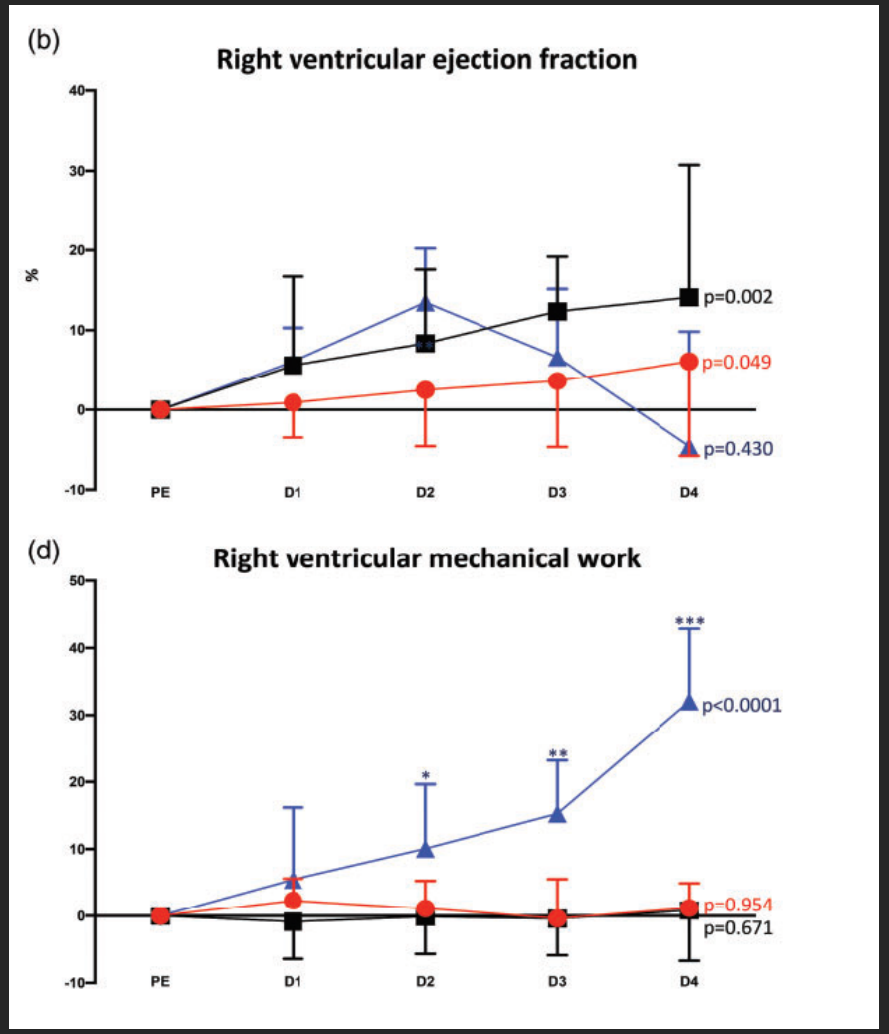
Original Research Article

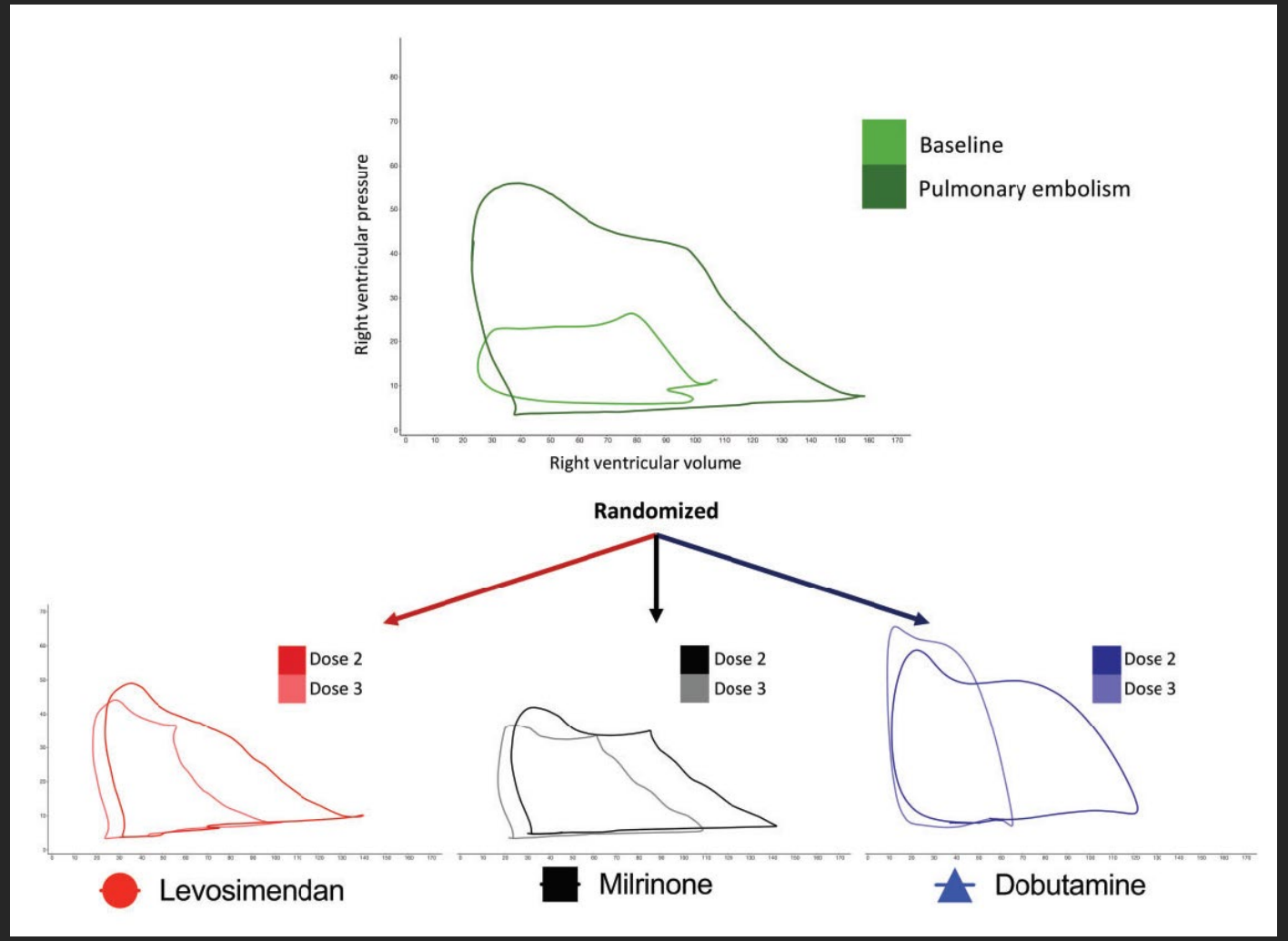
Pulmonary Circulation

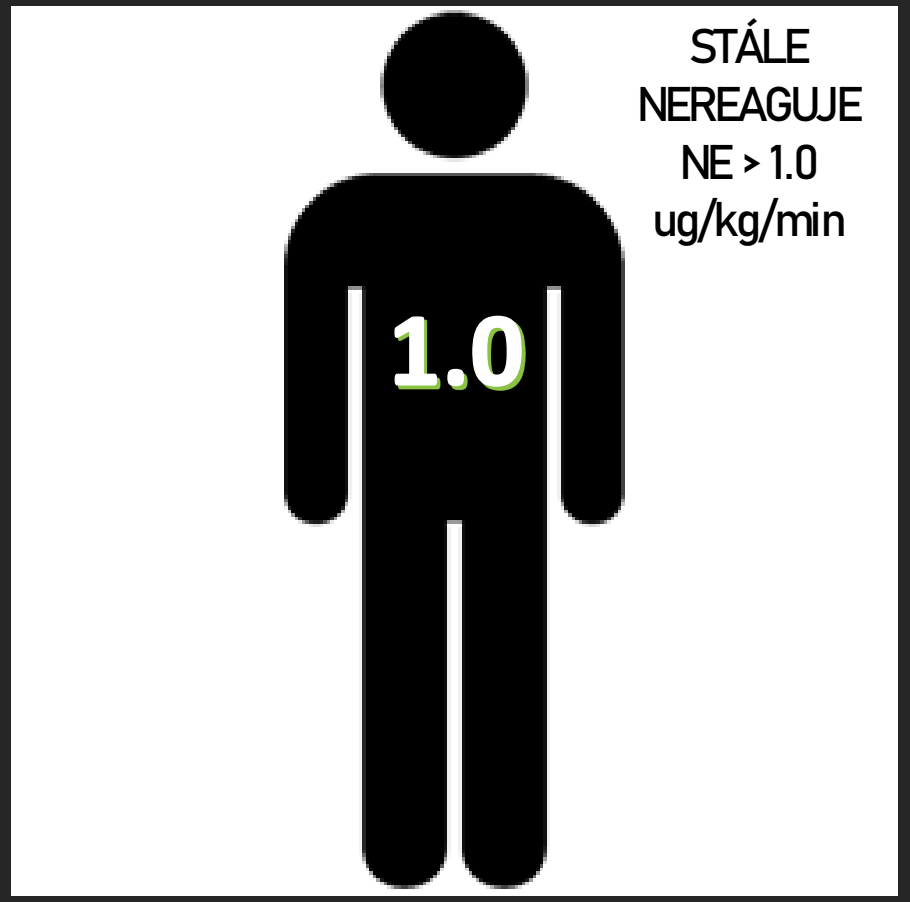
Levosimendan, milrinone, and dobutamine in experimental acute pulmonary embolism

Mads D. Lyhne, Simone J. Dragsbaek, Jacob V. Hansen, Jacob G. Schultz, Asger Andersen and Jens Erik Nielsen-Kudsk

Department of Cardiology, Aarhus University Hospital, Aarhus, Denmark; Department of Clinical Medicine, Aarhus University, Aarhus, Denmark





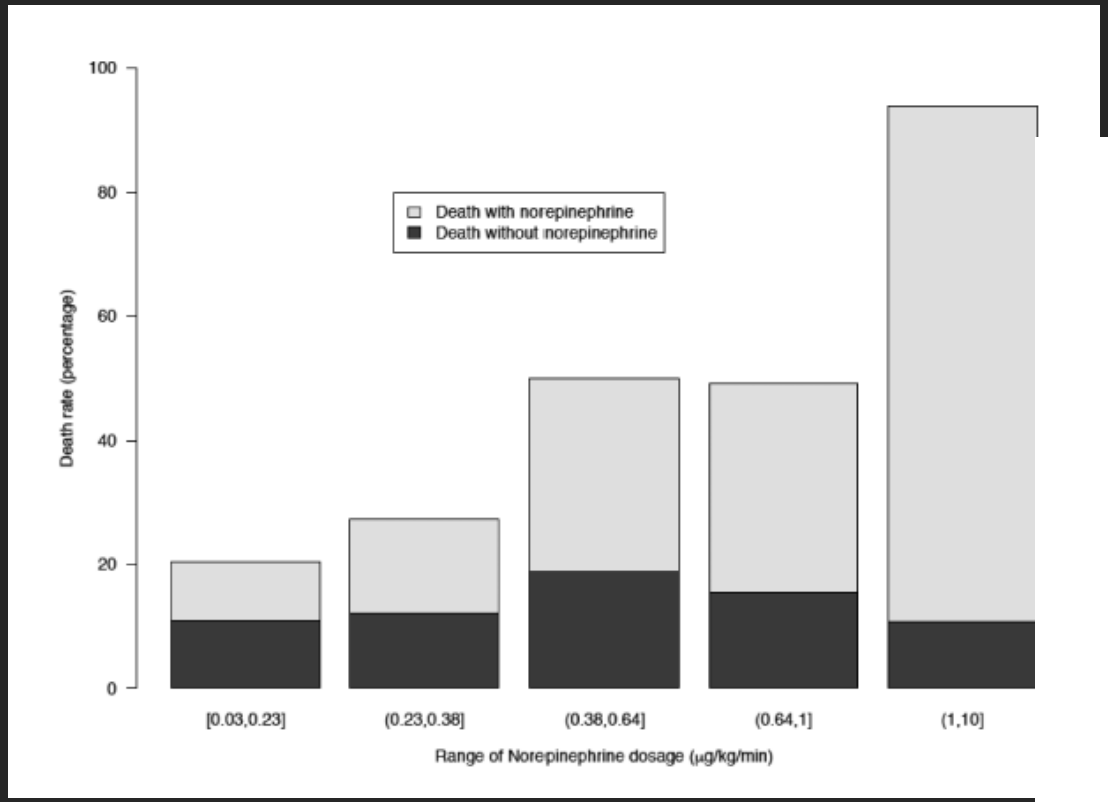

1.0
STÁLE
NEREAGUJE
NE > 1.0
ug/kg/min

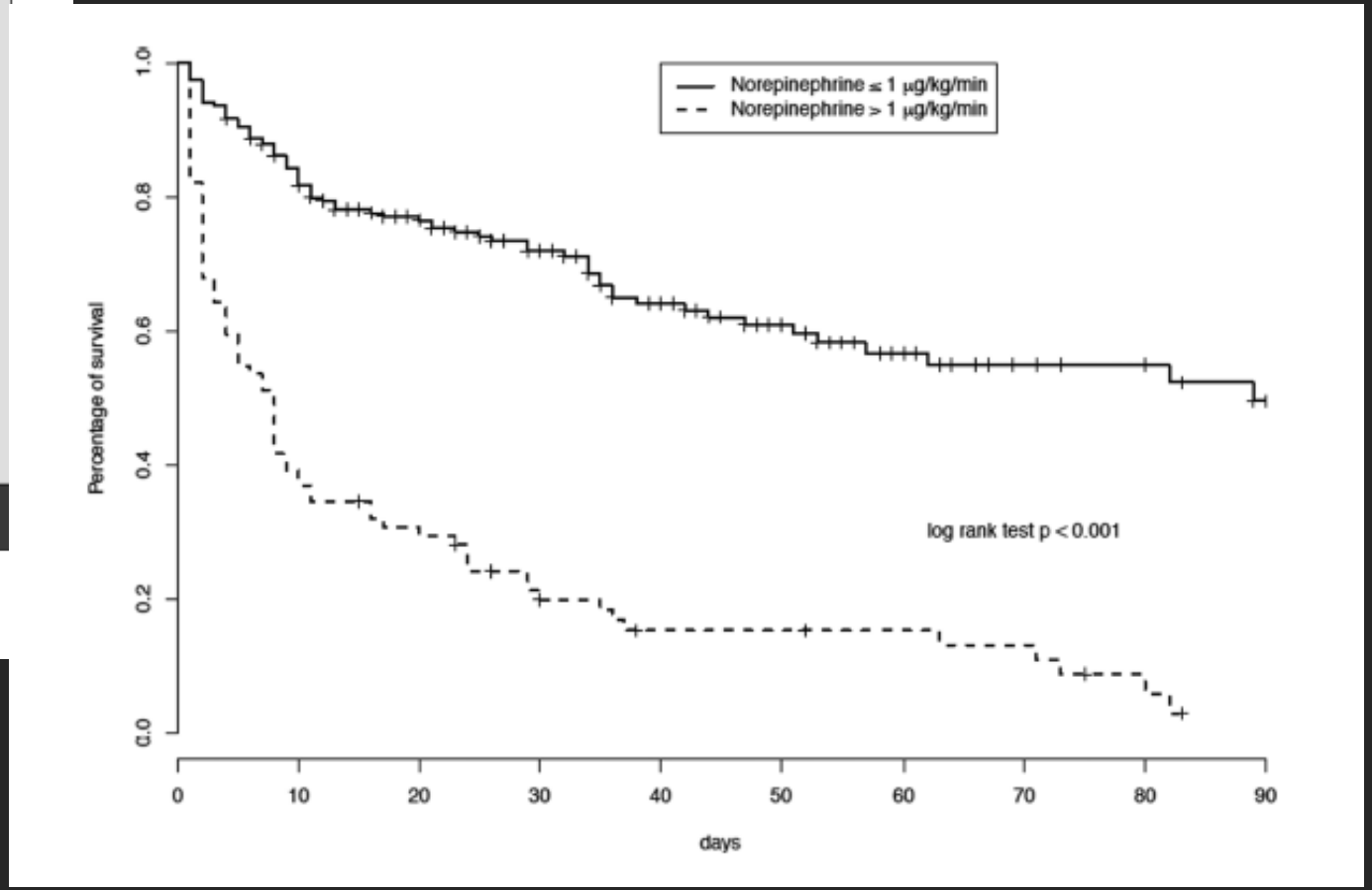
SHOCK, Vol. 44, No. 4, pp. 305–309, 2015

NOREPINEPHRINE: NOT TOO MUCH, TOO LONG

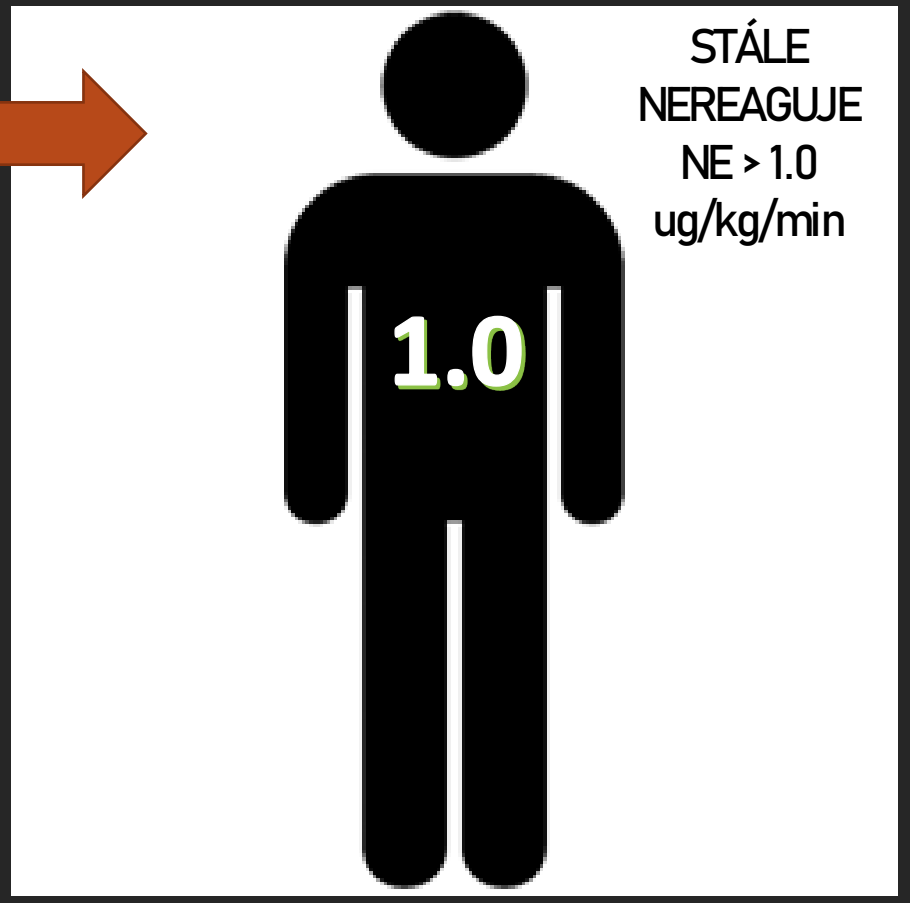
Claude Martin, Sophie Medam, François Antonini, Julie Alingrin, Malik Haddam, Emmanuelle Hammad, Bertrand Meyssignac, Coralie Vigne, Laurent Zieleskiewicz, and Marc Leone

Service d'Anesthésie et de Réanimation, Hôpital Nord, Assistance Publique Hôpitaux de Marseille, and Aix Marseille Université, Marseille, France





ADRENALIN

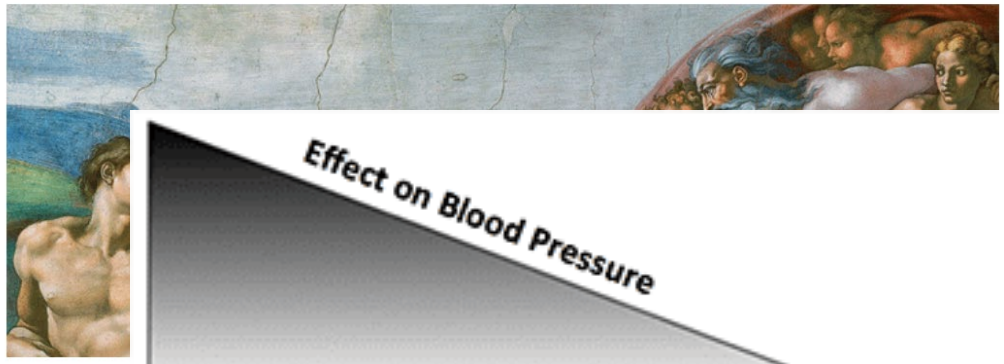


TREAT-CHALLENGE ≈ 4 mcg/min
tzn cca 0,05 ug/kg/min

ADRENALIN 2mg/20ml
cca 4 ml/h (4,2)

PulmCrit- Epinephrine challenge in sepsis: An empiric approach to catecholamines

April 25, 2016 by **Josh Farkas** — 15 Comments

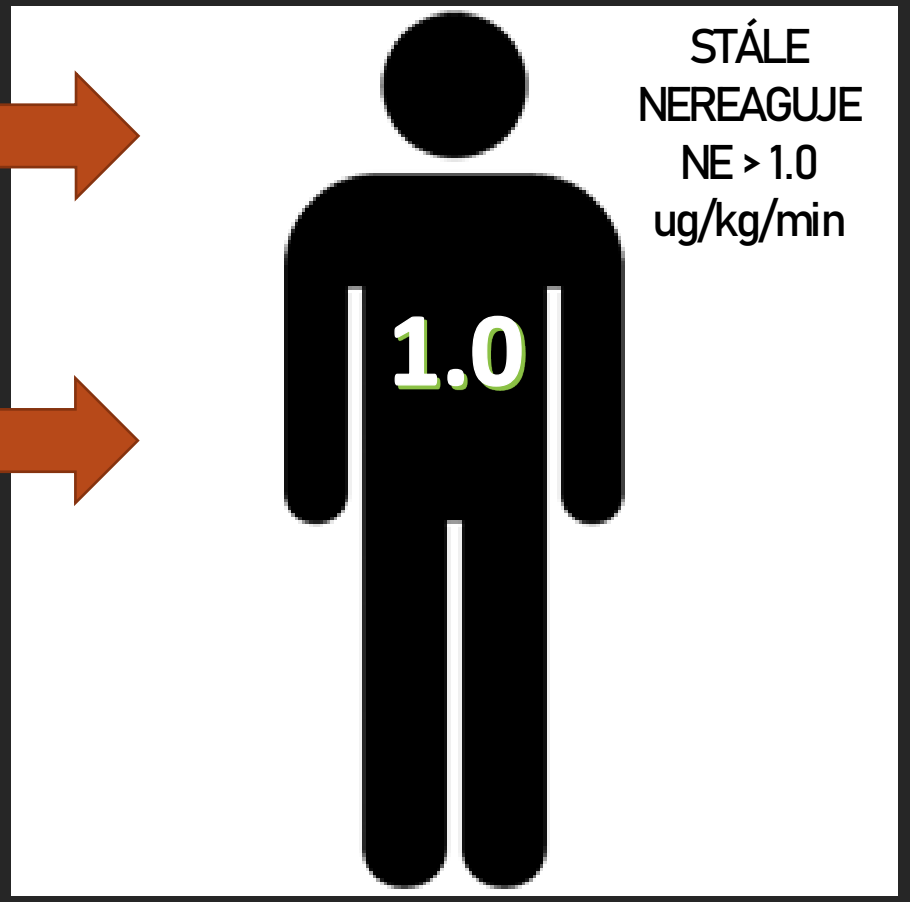


Evaluating responsiveness to epinephr

	Favorable response	
MAP	**- Increased** **- Able to wean down norepinephrine by >> 5 mcg/min**	**- Unchanged**
HR	**- HR ends up in "appropriately tachycardic" range (? 90-110)**	**- HR increase** **potentially d**
UOP	**- Increased urine output**	**- Unchanged**
Skin	**- Extremities warmer** **- Skin mottling disappears** **- Capillary refill improved**	**- Unchanged**

ADRENALIN

ANGIOTENSIN II



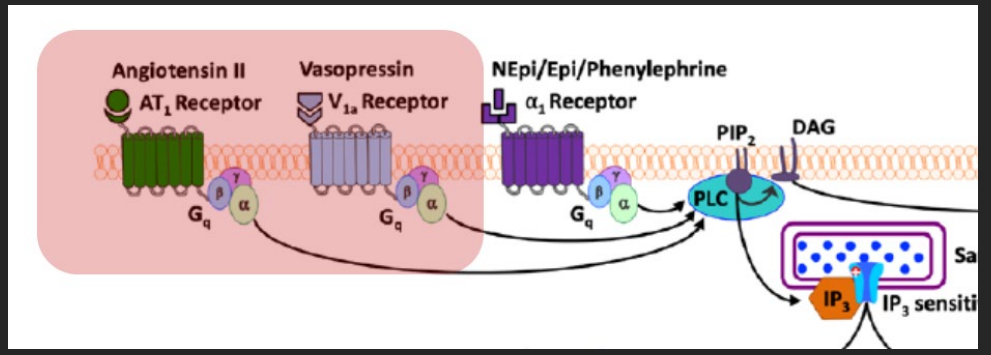
STÁLE NEREAGUJE
NE > 1.0 ug/kg/min

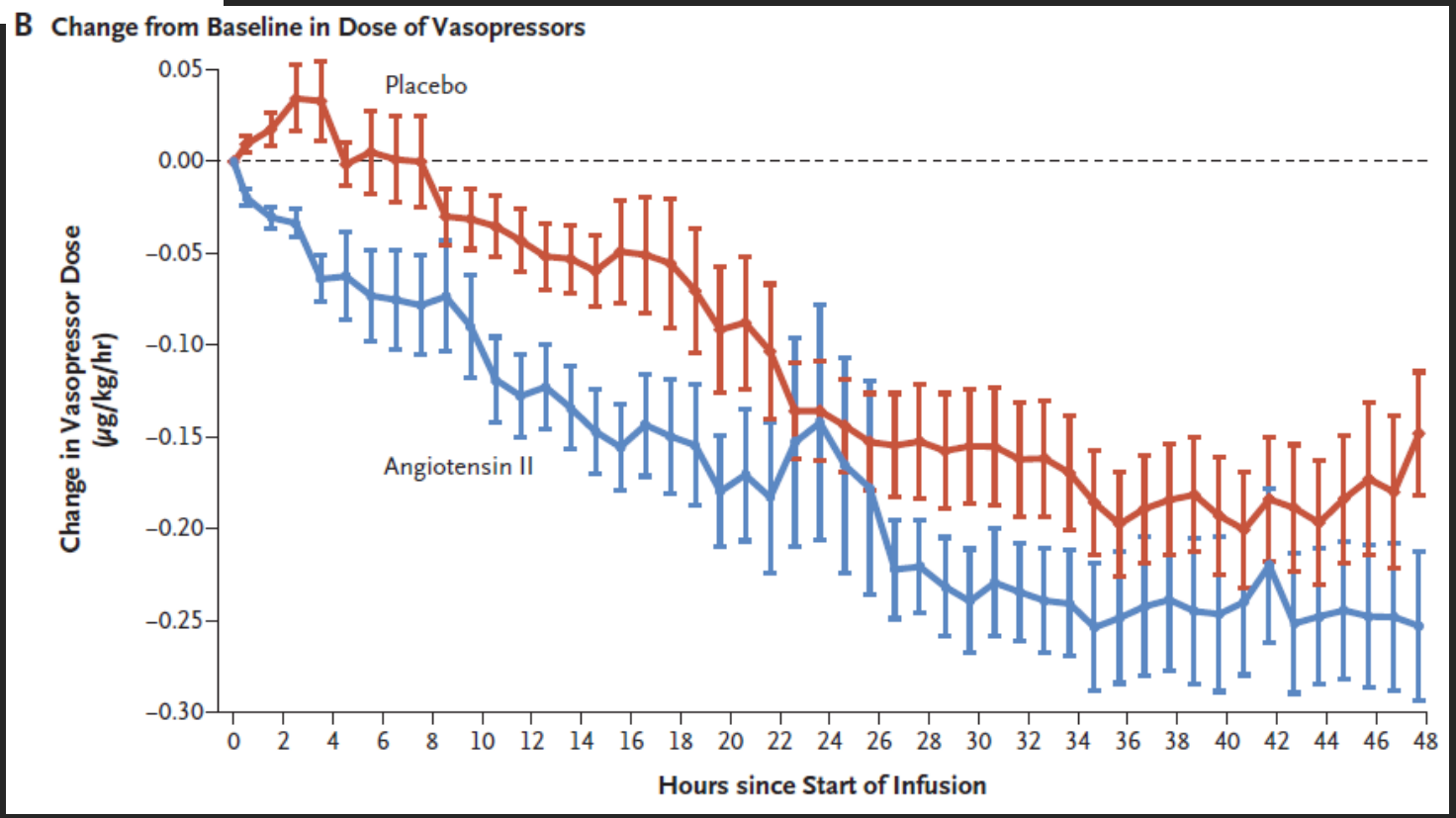
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 3, 2017 VOL. 377 NO. 5

Angiotensin II for the Treatment of Vasodilatory Shock

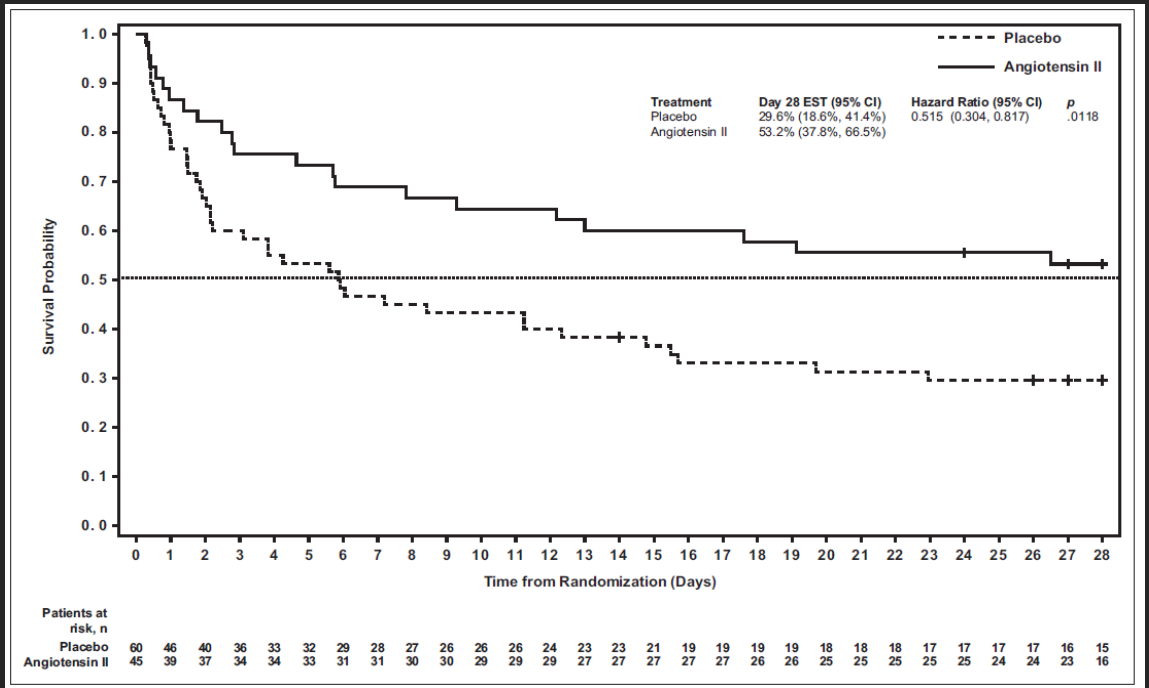
Ashish Khanna, M.D., Shane W. English, M.D., Xueyuan S. Wang, M.D., Kealy Ham, M.D., James Tumlin, M.D., Harold Szerlip, M.D., Laurence W. Busse, M.D., Laith Altaweel, M.D., Timothy E. Albertson, M.D., M.P.H., Ph.D., Caleb Mackey, M.D., Michael T. McCurdy, M.D., David W. Boldt, M.D., Stefan Chock, M.D., Paul J. Young, M.B., Ch.B., Ph.D., Kenneth Krell, M.D., Richard G. Wunderink, M.D., Marlies Ostermann, M.D., Ph.D., Raghavan Murugan, M.D., Michelle N. Gong, M.D., Rakshit Panwar, M.D., Johanna Hästbacka, M.D., Ph.D., Raphael Favory, M.D., Ph.D., Balasubramanian Venkatesh, M.D., B. Taylor Thompson, M.D., Rinaldo Bellomo, M.D., Jeffrey Jensen, B.S., Stew Kroll, M.A., Lakhmir S. Chawla, M.D., George F. Tidmarsh, M.D., Ph.D., and Adam M. Deane, M.D., for the ATHOS-3 Investigators*





Outcomes in Patients with Vasodilatory Shock and Renal Replacement Therapy Treated with Intravenous Angiotensin II

James A. Tumlin, MD[1]; Raghavan Murugan, MD, MS, FRCP, FCCM[2]; Adam M. Deane, MD, PhD[3];



6

EFFECT OF DISEASE SEVERITY ON SURVIVAL IN PATIENTS RECEIVING ANGIOTENSIN II FOR VASODILATORY SHOCK

Harold Szerlip, Azra Bihorac, Steven Chang, Kevin Chung, Johanna Hästbacka, Raghavan Murugan, Raphael Favory, James Tumlin, Balasubramanian Venkatesh, Lakhmir Chawla, George Tidmarsh

Greater mortality was seen in the placebo group than the Ang II group in patients with more severe disease at baseline: 28-day mortality, comparing the Ang II and placebo groups respectively, was 51.8% (n = 58) and 70.8% (n = 65) (HR 0.62; 95% CI = 0.39- 0.98; $P = .037$) in patients with APACHE II scores > 30

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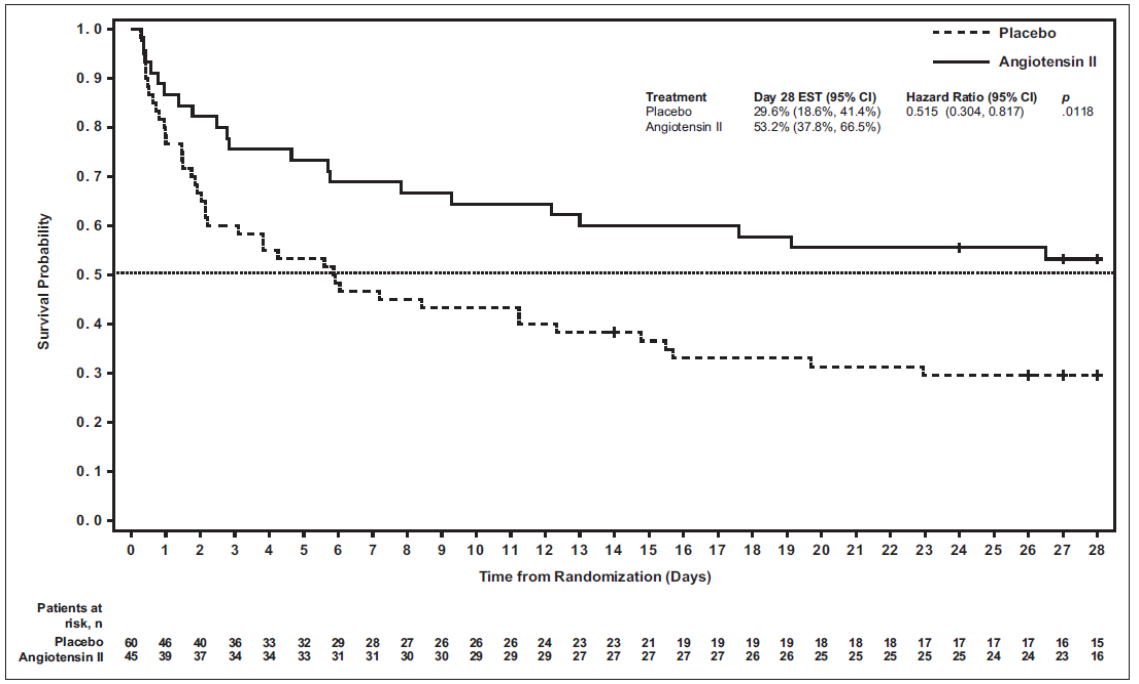

6

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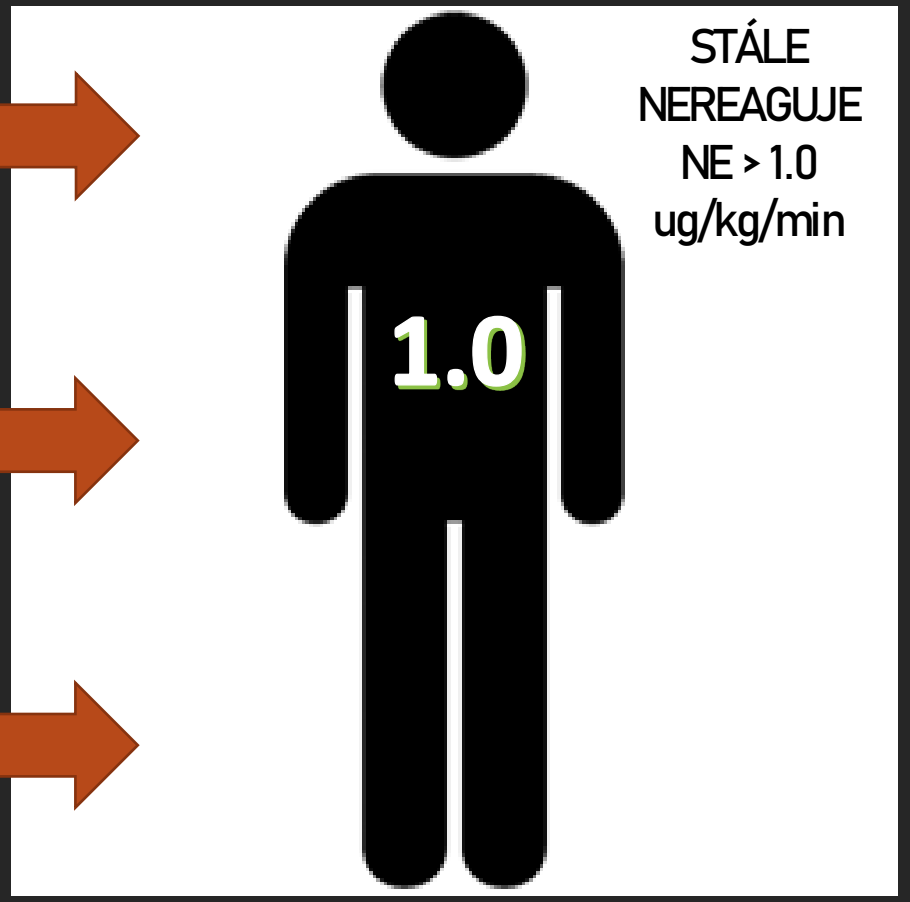
???

EFEKTIVNĚJŠÍ U „ZÁVAŽNĚJŠÍCH“ PACIENTŮ

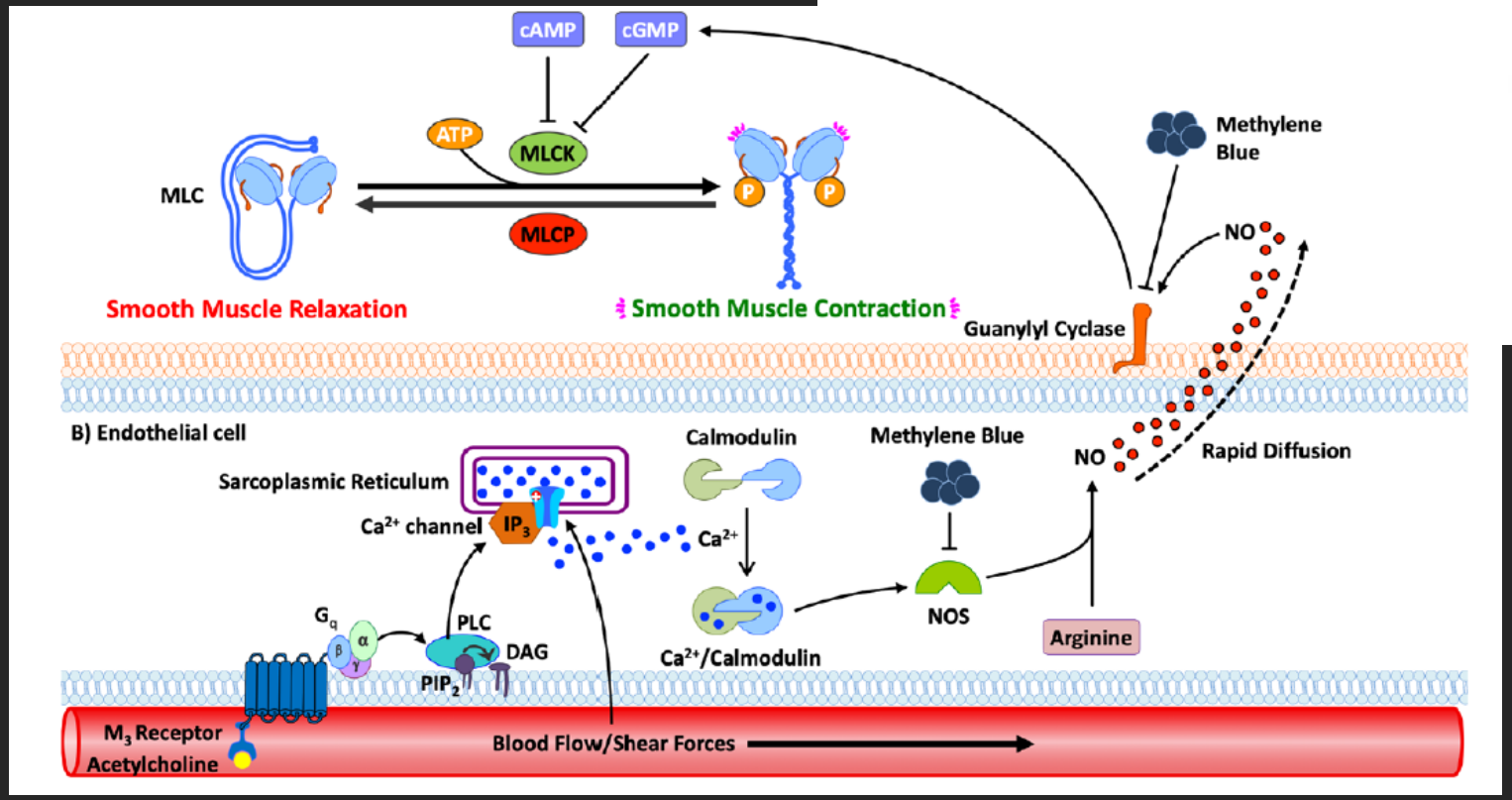
ADRENALIN

ANGIOTENSIN II

METHYLENOVÁ MODŘ



STÁLE NEREAGUJE
NE > 1.0 ug/kg/min

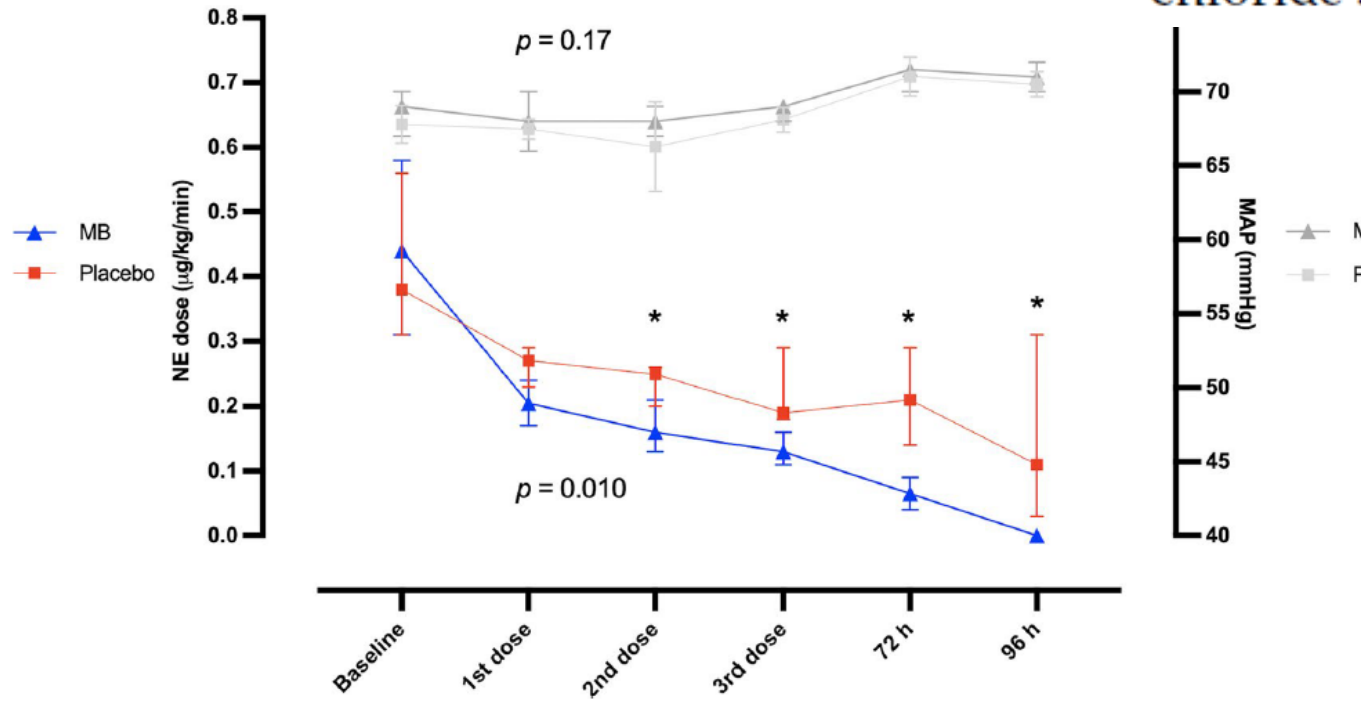

cAMP
cGMP
ATP
MLCK
MLC
MLCP
P
P
Methylene Blue
NO
Smooth Muscle Relaxation
Smooth Muscle Contraction
Guanylyl Cyclase
B) Endothelial cell
Calmodulin
Methylene Blue
NO
Rapid Diffusion
Sarcoplasmic Reticulum
Ca2+ channel
IP3
Ca2+
Gq
α
β
γ
PLC
DAG
PIP2
NOS
Arginine
Ca2+/Calmodulin
M3 Receptor
Acetylcholine
Blood Flow/Shear Forces

RESEARCH Open Access

Early adjunctive methylene blue in patients with septic shock: a randomized controlled trial

Miguel Ibarra-Estrada[1,2,3*], Eduardo Kattan[3,4], Pavel Aguilera-González[2], Laura Sandoval-Plascencia[5], Uriel Rico-Jauregui[1], Carlos A. Gómez-Partida[1], Iris X. Ortiz-Macías[1], José A. López-Pulgarín[1], Quetzalcóatl Chávez-Peña[1], Julio C. Mijangos-Méndez[1], Guadalupe Aguirre-Avalos[1†] and Glenn Hernández[3,4]

Patient
(IV) infu
chloride



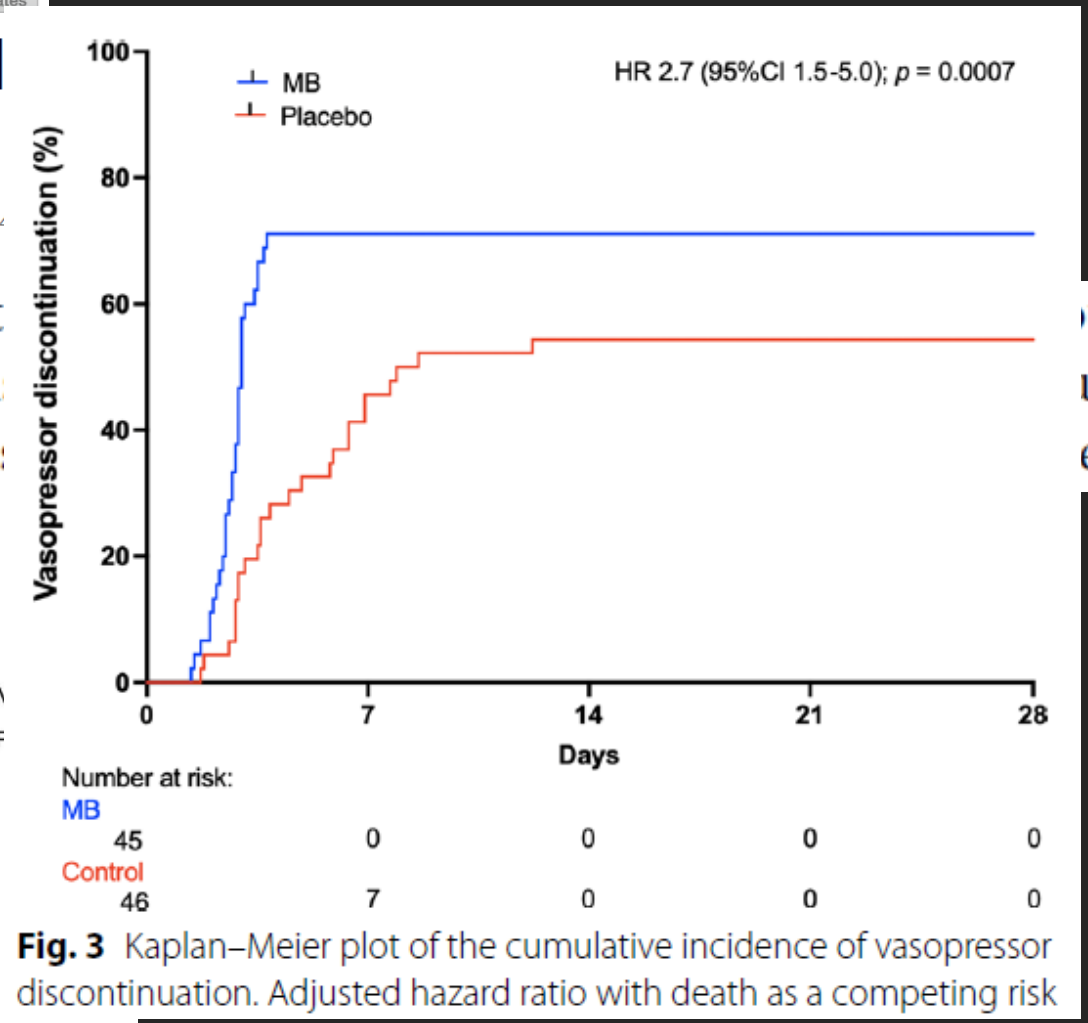


Fig. 3 Kaplan–Meier plot of the cumulative incidence of vasopressor discontinuation. Adjusted hazard ratio with death as a competing risk

us
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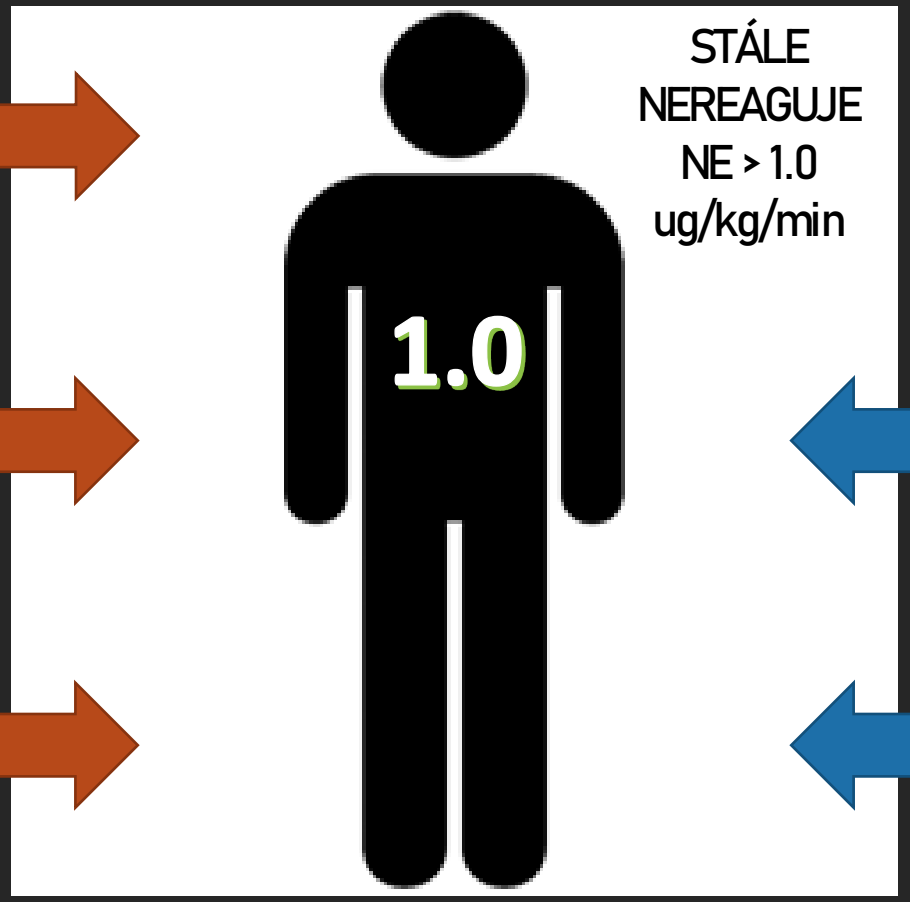
ADRENALIN

ANGIOTENSIN II

METHYLENOVÁ MODŘ



RESCUE TERAPIE ??

ECMO
(jiná mechanická podpora)

EXPERIMENTY

Relationship between norepinephrine dose, tachycardia and outcome in septic shock: A multicentre evaluation

Roberta Domizi [a,b], Sara Calcinaro [a,b], Steve Harris [a,c], Christian Beilstein [d], Christiaan Boerma [e], Jean-Daniel Chiche [f], Annalia D'Egidio [g], Elisa Damiani [b], Abele Donati [b,*], Peter M. Koetsier [e], Mary P. Madden [h], Daniel F. McAuley [h], Andrea Morelli [g], Paolo Pelaia [b], Patrick Royer [f], Manu Shankar-Hari [i], Nadine Wickboldt [d], Parjam Zolfaghari [d], Mervyn Singer [a,c]

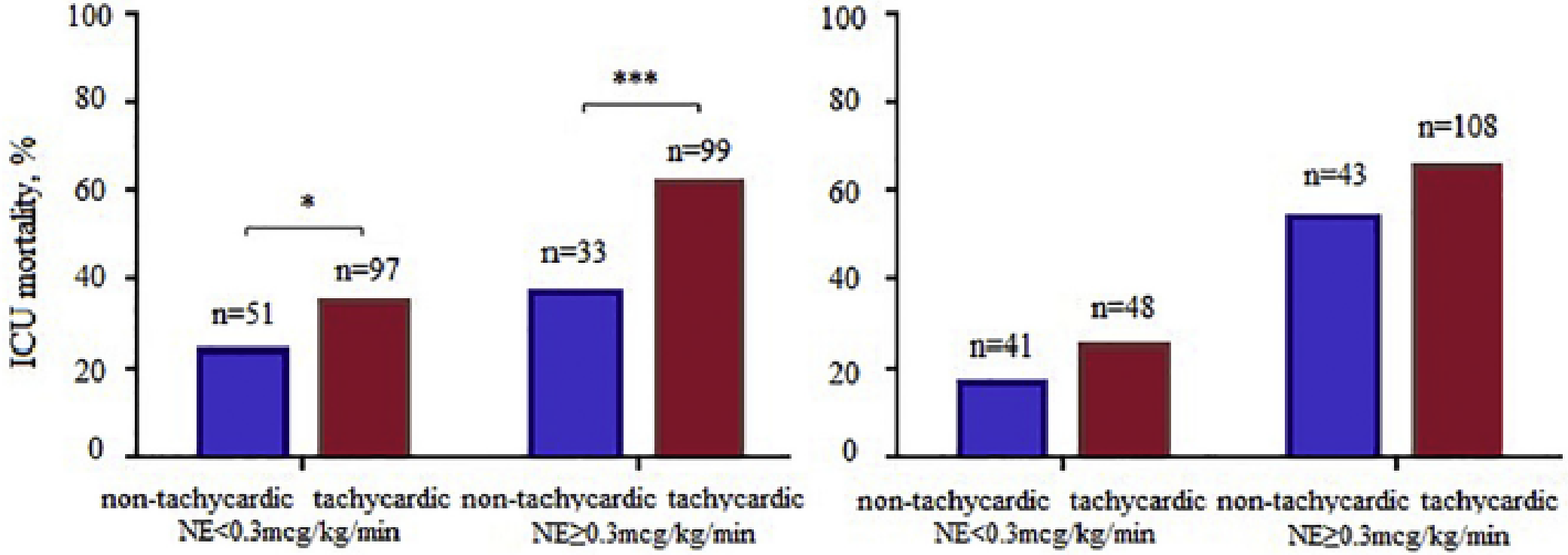
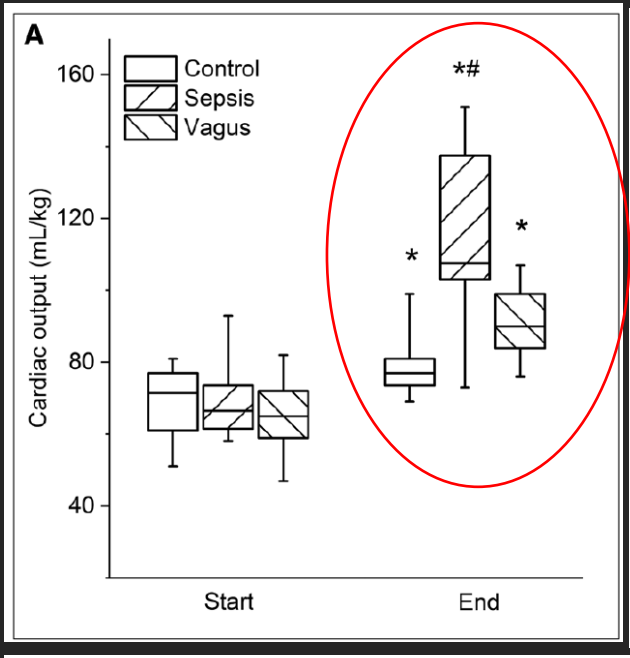
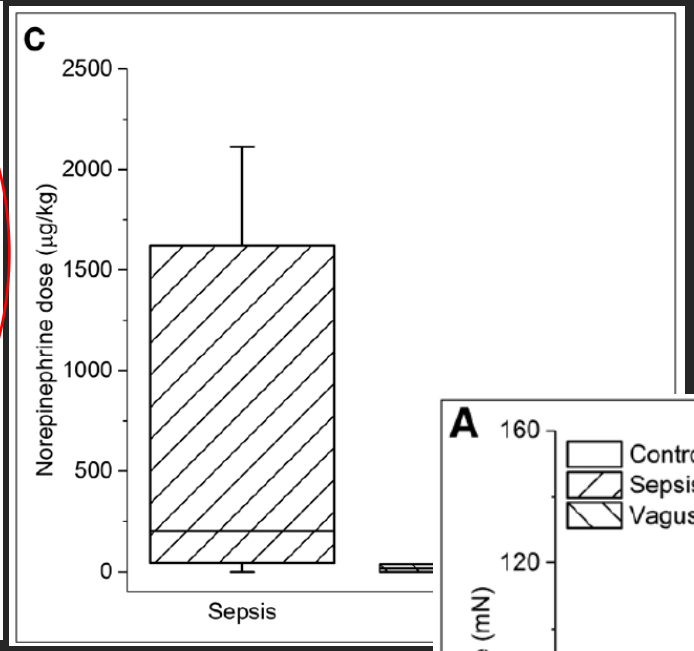


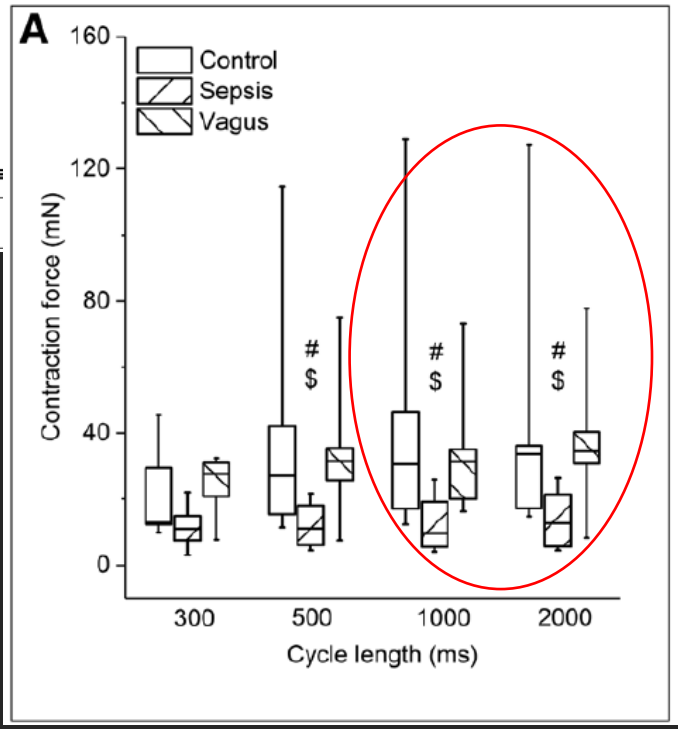
Fig. 2. Tachycardia and mortality rates in low- and high-dose norepinephrine groups at T1 and T24.

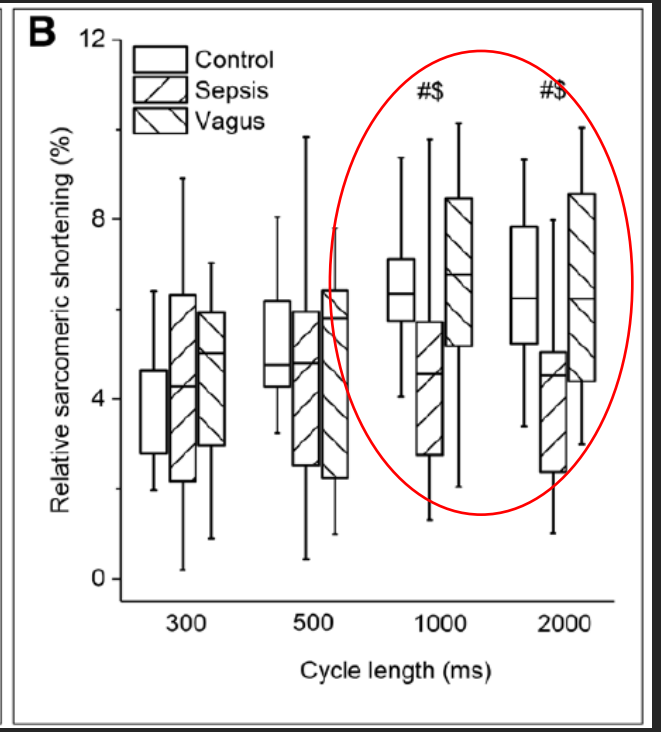
Vagus Nerve Stimulation Attenuates Multiple Organ Dysfunction in Resuscitated Porcine Progressive Sepsis

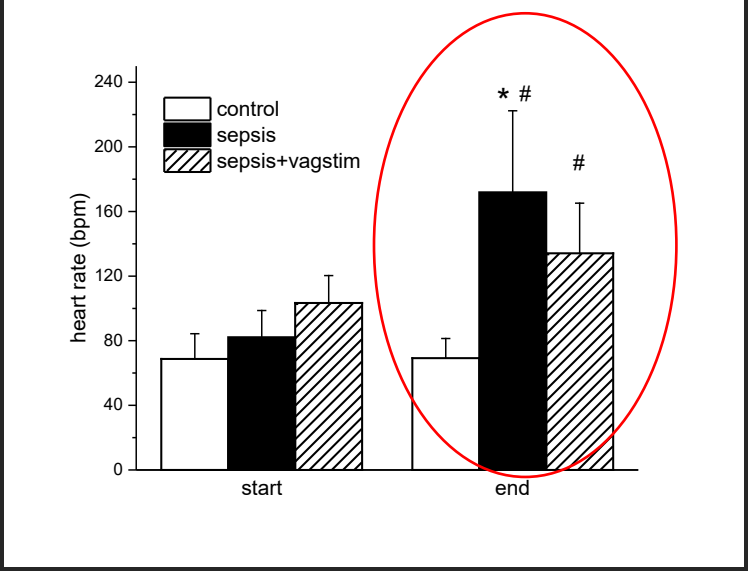
Michaela Kohoutova, MSc[1,2]; Jan Horak, MD[2,3]; Dagmar Jarkovska, Ing, PhD[1,2]; Vendula Martinkova, MD[2,4]; Vaclav Tegl, MD[2,5]; Lukas Nalos, MD, PhD[1,2]; Lucie Vistejnova, Ing, PhD[2]; Jan Benes, MD, PhD[2,5]; Jitka Sviglerova, MD, PhD[1,2]; Jitka Kuncova, MD, PhD[1,2]; Martin Matejovic, MD, PhD[2,3]; Milan Stengl, MD, PhD[1,2]









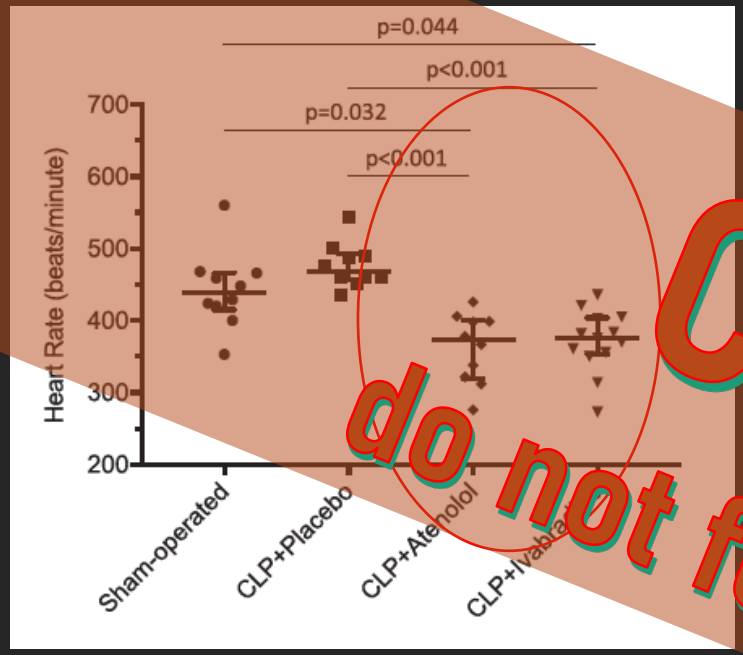


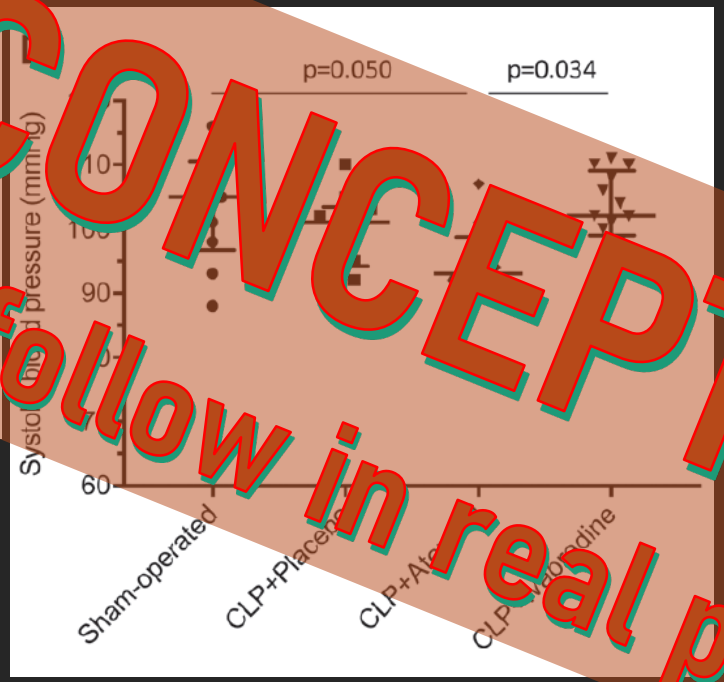
ANESTHESIOLOGY

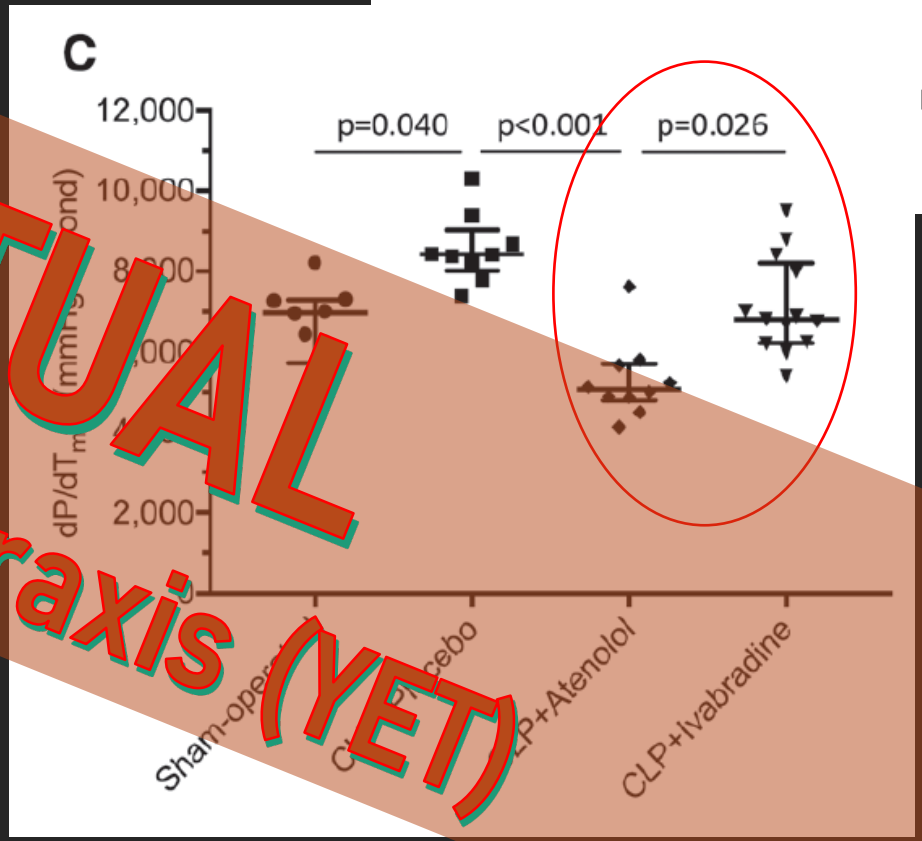
Heart Rate Control during Experimental Sepsis in Mice

Comparison of Ivabradine and β-Blockers

Ph.D.,





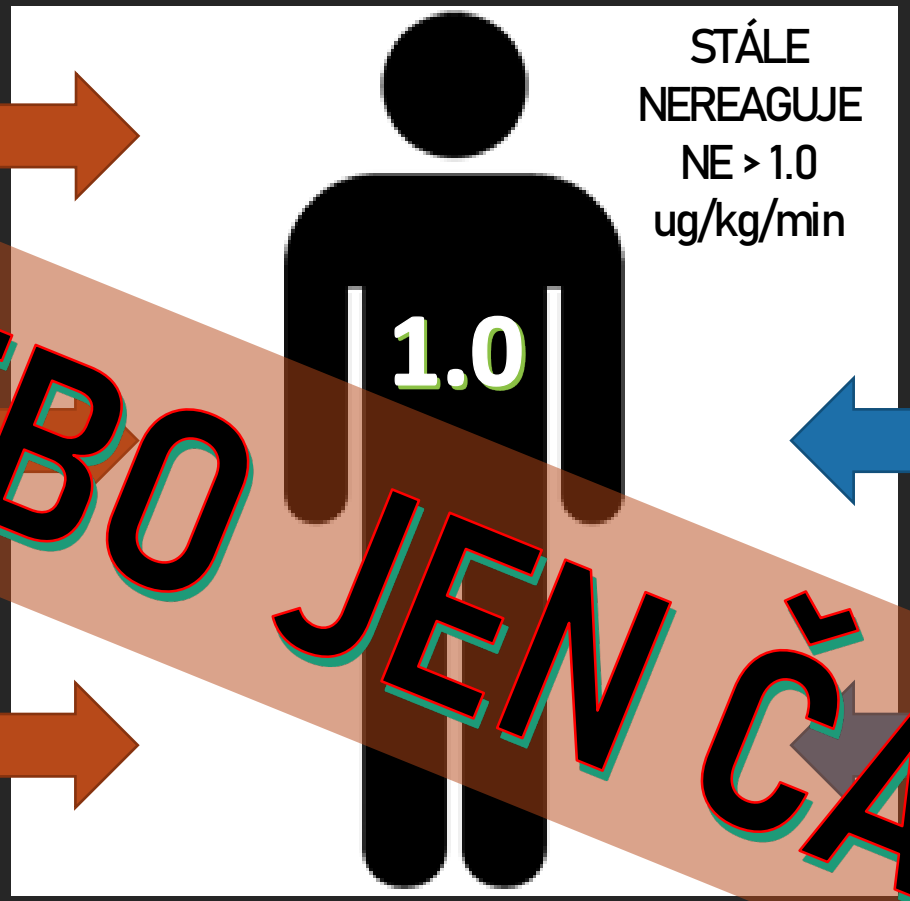


CONCEPTUAL
do not follow in real praxis (YET)

ADRENALIN

ANGIOTENSIN II

METHYLENOVÁ MODŘ



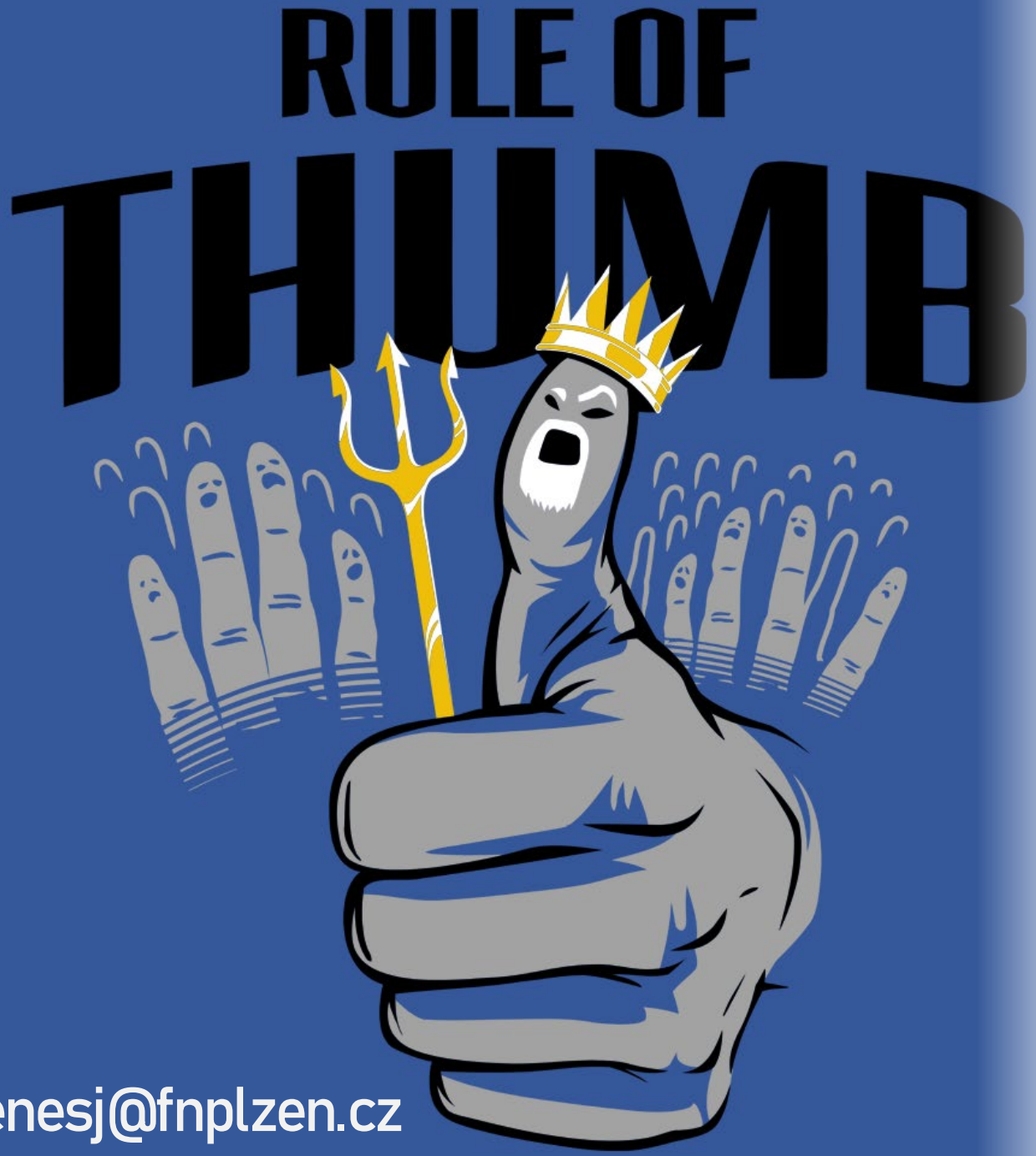
STÁLE NEREAGUJE
NE > 1.0 ug/kg/min

RESCUE TERAPIE ??

ECMO
(...mechanická podpora)

EXPERIMENTY

NEBO JEN ČAS...



benesj@fnplzen.cz

KDYŽ NEVÍTE

a

PACIENT MÁ HYPOTENZI

-

NOREPINEPHRINE

JE VAŠE VOLBA

DĚKUJI

ZA

POZORNOST