Beta blokátory v sepsi
Dobrý sluha, špatný pán

Doc MUDr Marek Nalos PhD, FCICM

Adrenaline rush

The cure of as

I know few t

Thorax 1985;**40**:887–888

Henry Hyde Salter (1823–71): a biographical sketch

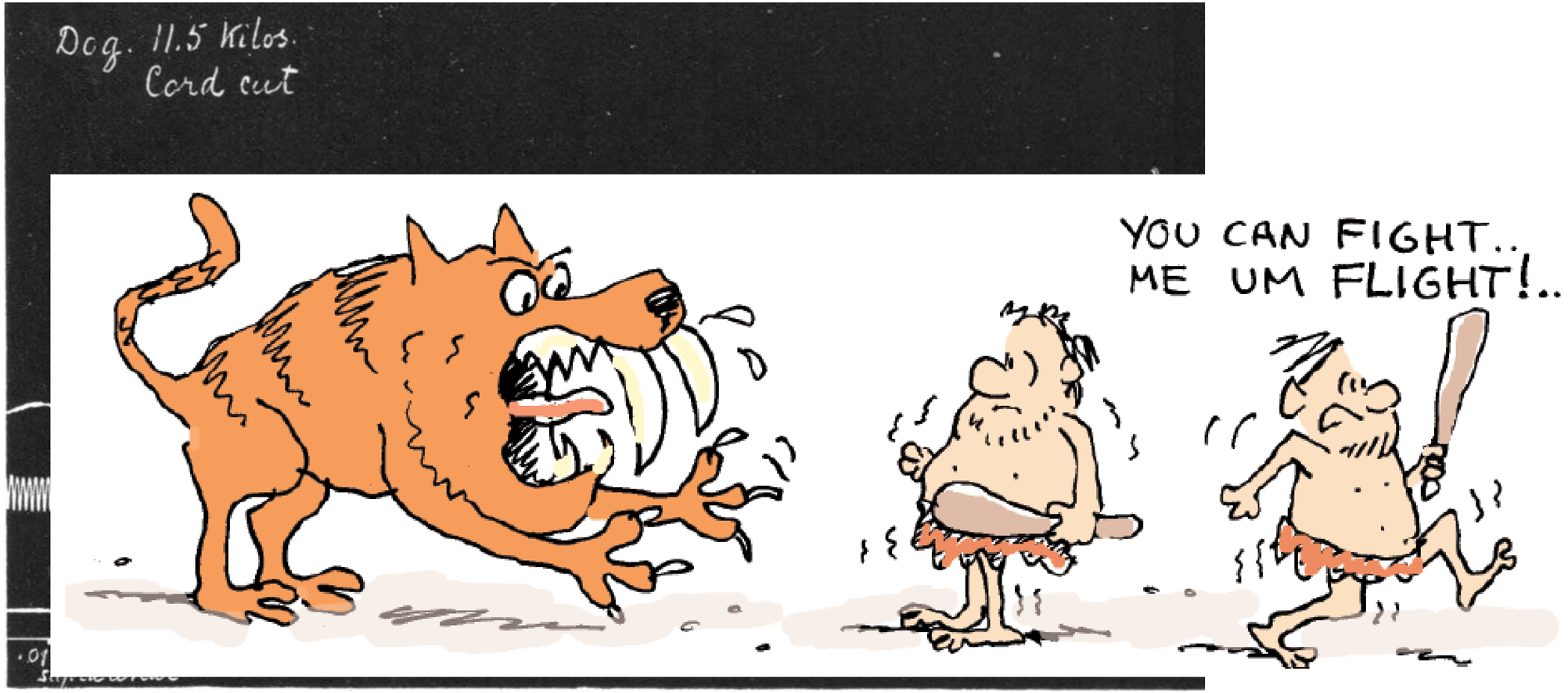
ALEX SAKULA

n as a popular teacher. In 1855 he
ssistant physician at King's College
ame full physician in 1866. He was
y being elected a fellow of King's

alter contracted whooping cough,
a developed. This was severe during
ecame less troublesome as he grew
medical studies and researches the
became his special interest. Salter
papers on asthma but he is chiefly
his magnum opus *On Asthma: Its*
reatment, which was based on his
dreds of cases and no doubt also on
ferings. The text had originally
al form, chapter by chapter, in

(1823–71). Reproduced by courtesy of the
al College of Physicians.

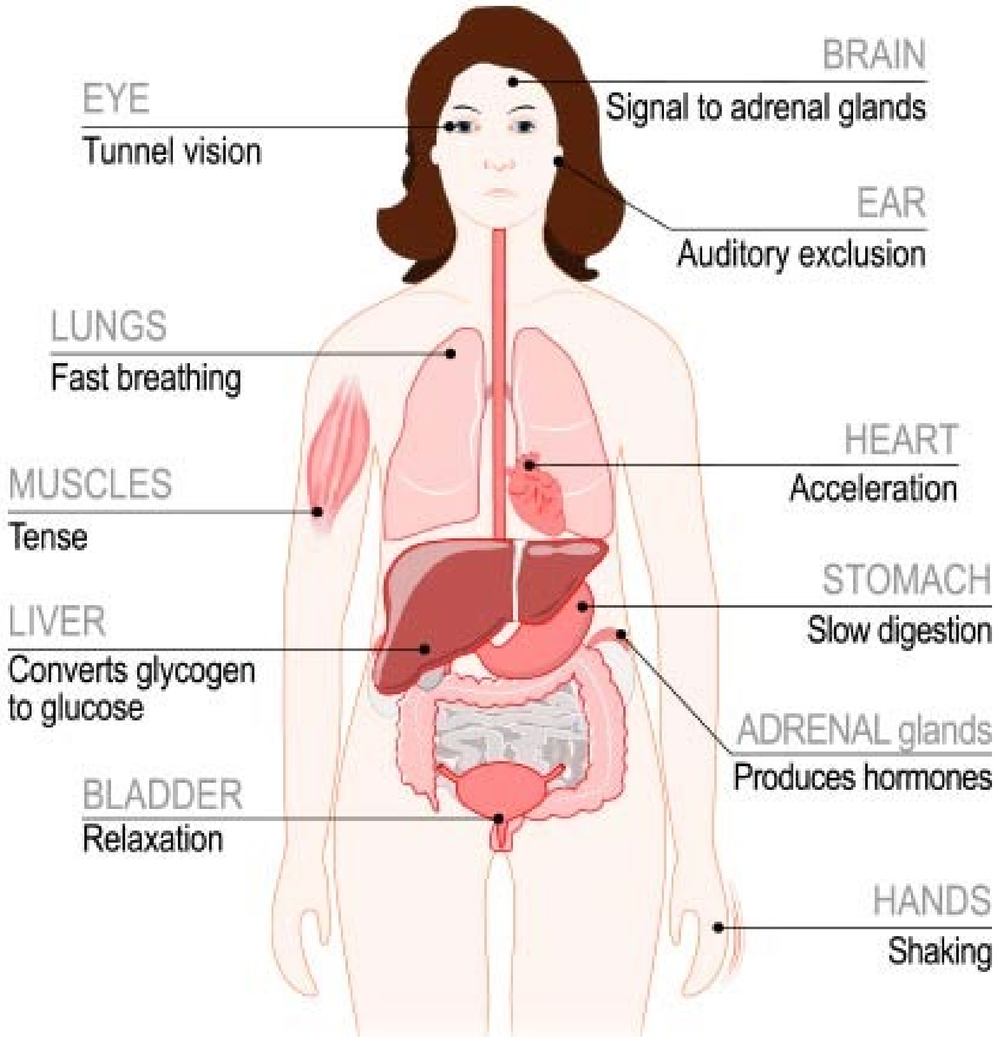
Discovery of adrenaline

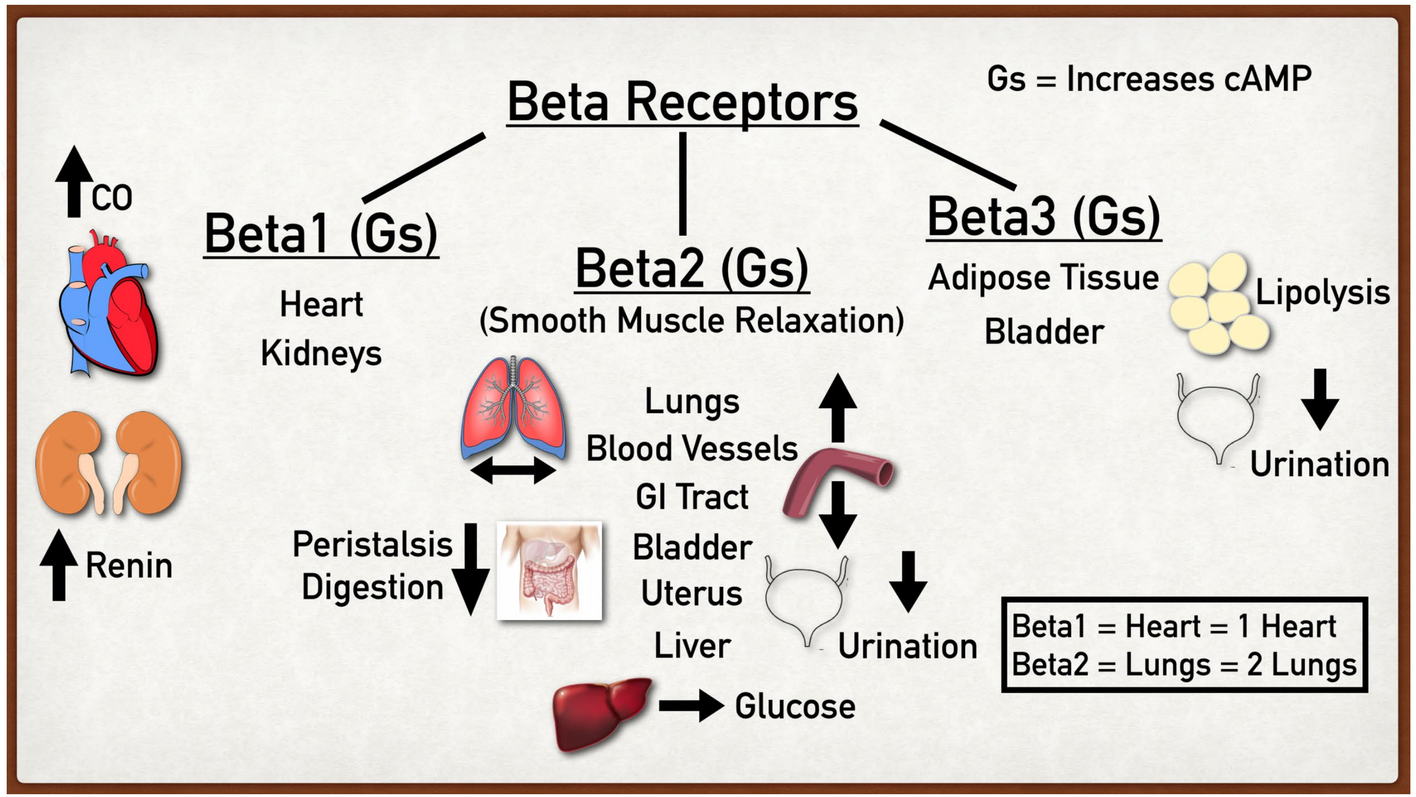


Oliver and Schäfer 1893–1894 injecting adrenal glands extract

The main function of the SNS is to stimulate the body’s fight-or-flight response.

Fight or flight response





Cardiac β2-receptors - tachycardia, arrhythmias,
Peripheral β2-receptor stimulation - hypotension and reflex tachycardia

Adrenergní odpověď v sepsi

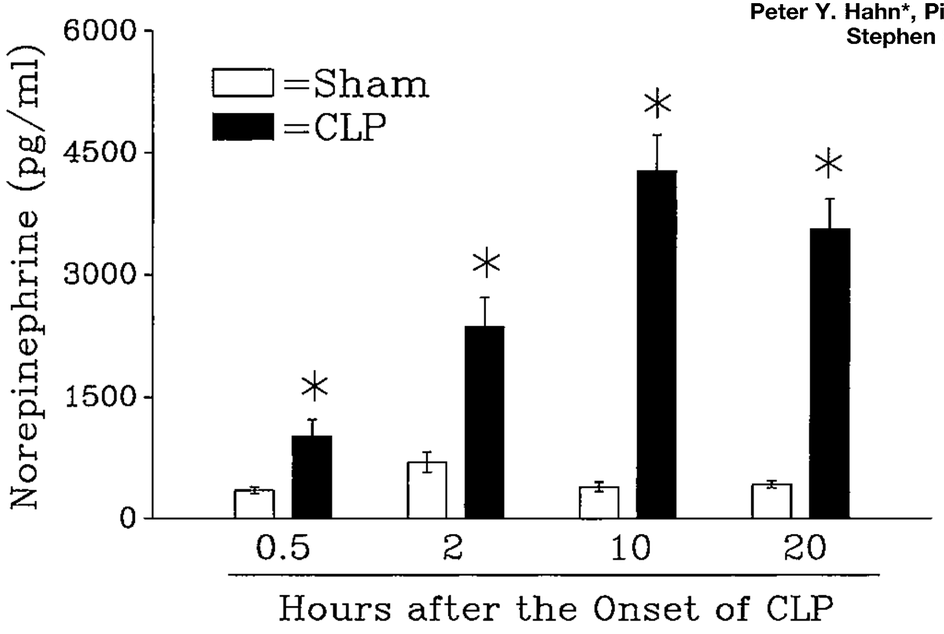
Adrenergic response to sepsis

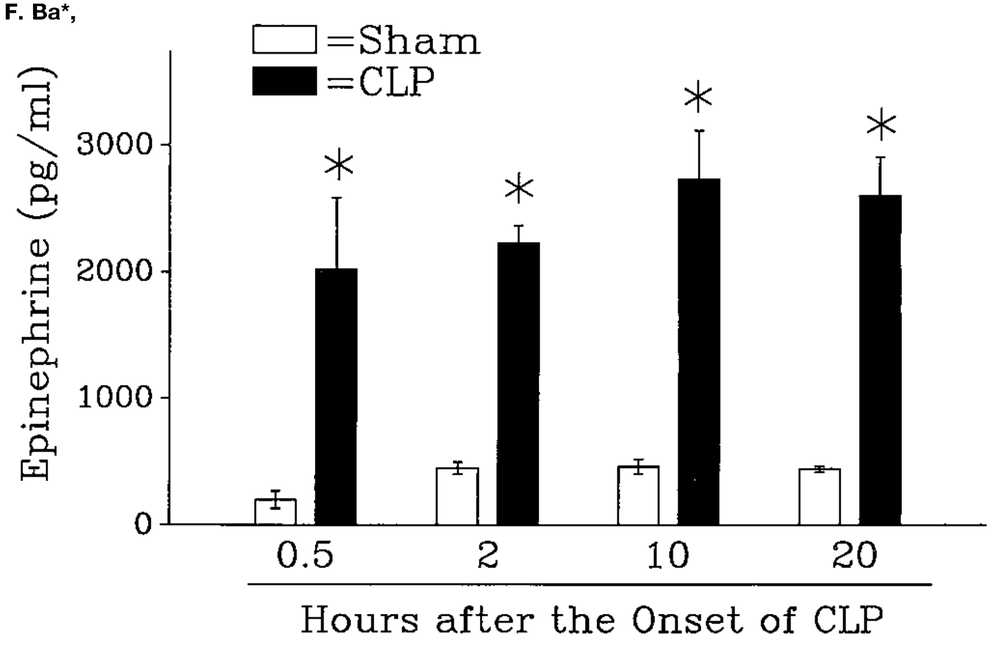
Activation of sympatoadrenal axis releases catecholamines from multiple cells

Catecholamine production increases in early sepsis - adrenal gland, autonomous nervous system, gut and white cells

SUSTAINED ELEVATION IN CIRCULATING CATECHOLAMINE LEVELS DURING POLYMICROBIAL SEPSIS

Peter Y. Hahn*, Ping Wang*‡, Stephen M. Tait‡, Zheng F. Ba*, Stephen S. Reich*, and Irshad H. Chaudry*‡





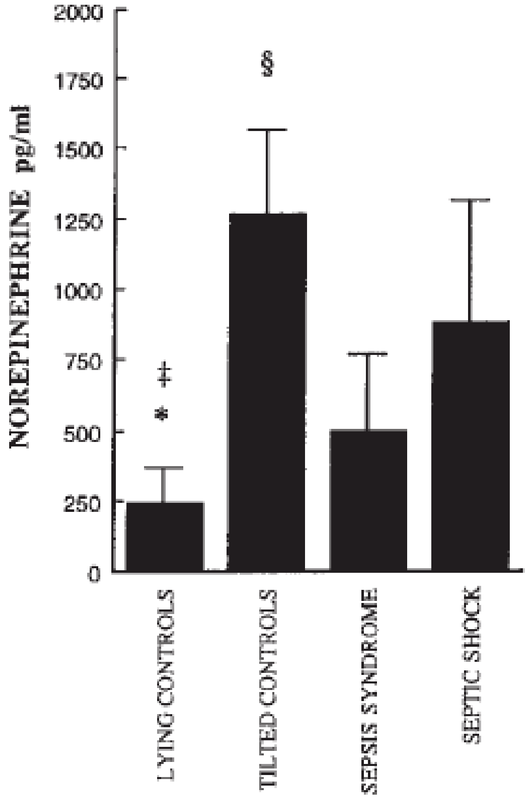
Sympathetic overstimulation

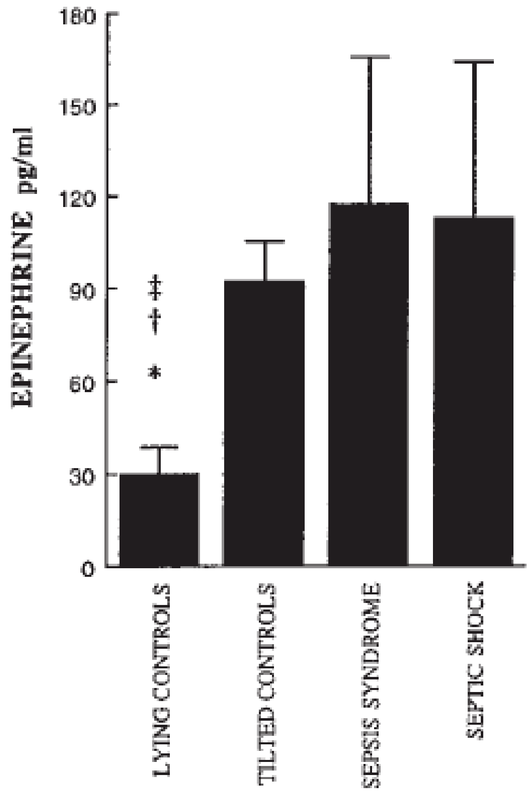
Inappropriate Sympathetic Activation at Onset of Septic Shock

A Spectral Analysis Approach

AM J RESPIR CRIT CARE MED 1999;160:458–465.

DJILLALI ANNANE, FABIEN TRABOLD, TAREK SHARSHAR, IRÈNE JARRIN, ANNE SOPHIE BLANC, JEAN CLAUDE RAPHAEL, and PHILIPPE GAJDOS





Onset of septic shock - high concentrations of circulating catecholamines

Despite high circulating catecholamine levels, adrenergic stimulation is blunted -

impaired sympathetic modulation on heart and vessels, autonomic dysfunction

Progression toward septic shock may represent the exhaustion of compensatory response such as early sympathetic nervous system stimulation due to incapability of the immune system to eliminate a pathogen and due to the persistence of systemic inflammation

Bottasso E. Toward the Existence of a Sympathetic Neuroplasticity Adaptive Mechanism Influencing the Immune Response. A Hypothetical View—Part II

Může beta blokáda ztlumit iniciální hyperaktivaci sympatického systému a následné vyčerpání adrenergní aktivace?

Rationale for beta blockade

Myocardial or organ protection?

β-blockers use may protect from the catecholamine surge of sepsis

Decrease myocardial oxygen consumption, prolong diastole and coronary perfusion reducing risk of myocardial ischaemia and improving diastolic dysfunction

β-blockers may reduce iNOS expression in vascular tissues

Wei, C., Louis, H., Schmitt, M. *et al.* Effects of low doses of esmolol on cardiac and vascular function in experimental septic shock. *Crit Care* 20, 407 (2016)

Dogs in endotoxin shock treated early with β-blockers do not develop pathological changes of severe splanchnic and pulmonary congestion and atelectasis due to excessive catecholamine stimulation.

β-blockers may restore the sepsis-induced downregulation of adrenergic receptors and suppress the proinflammatory pathways

Berk JL, Hagen JF, Beyer WH *et al.*,. The treatment of endotoxin shock by beta adrenergic blockade. Ann Surg. 1969 Jan;169(1):74-81.

Anti-inflammatory effects

RESEARCH Open Access

Hemodynamic and anti-inflammatory effects of early esmolol use in hyperkinetic septic shock: a pilot study

Bruno Levy[1,2,3,7*], Caroline Fritz[1,2,3], Caroline Piona[1,2,3], Kevin Duarte[4], Andrea Morelli[4,5], Philippe Guercl[6], Antoine Kimmoun[1,2,3] and Nicolas Girerd[4]

Beta blockade may suppress inflammatory pathways

IL8	**-0.68 (-0.83 ; -0.53)**	**0.004**
IL7	**-0.42 (-0.57 ; -0.37)**	**0.004**
IL6	**-0.50 (-1.98 ; -0.37)**	**0.012**
IL-17C	**-0.63 (-0.76 ; -0.39)**	**0.008**
IFN-gamma	**-1.08 (-1.60 ; -0.15)**	**0.020**
CXCL6	**-0.47 (-0.63 ; -0.32)**	**0.004**
IL10	**-1.02 (-1.89 ; -0.85)**	**0.008**
TNF	**-0.46 (-0.54 ; -0.06)**	**0.020**

RESEARCH Open Access

Hemodynamic and anti-inflammatory effects of early esmolol use in hyperkinetic septic shock: a pilot study

Bruno Levy[1,2,3,7*], Caroline Fritz[1,2,3], Caroline Piona[1,2,3], Kevin Duarte[4], Andrea Morelli[4,5], Philippe Guerci[6], Antoine Kimmoun[1,2,3] and Nicolas Girerd[4]

The study was terminated prior to enrollment completion due to a shift in ICU recruitment leading to a low inclusion rate. Nine consecutive stabilized tachycardic hyperkinetic septic shock patients treated with norepinephrine for a minimum of 6 h were included (Table 1).

Esmolol was infused 9 (6.4–11.6) hours after norepinephrine introduction. Esmolol was ceased early in 3 out of 9 patients due to a marked increase in norepinephrine requirement associated with a picture of persistent cardiac failure at the lowest esmolol dose (Table 1: patients 7–9).

The use of esmolol was associated with a significant decrease in heart rate from 115 (110–125) to 100 (92–103) beats/min ($p = 0.004$), and a significant decrease in cardiac index from 4.2 (3.1–4.4) to 2.9 (2.5–3.7) l/min/m^{-2} ($p = 0.004$) without any change in either stroke volume or left ventricular end diastolic volume. Double

Conclusion

In the very early phase of septic shock, heart rate reduction using a fast titration of esmolol is associated with an increased risk of hypotension and decreased cardiac index despite maintained adequate tissue perfusion.

Rationale against beta blockade

β-blockers reduce cardiac output - compromise patients with preexisting cardiac dysfunction

Cardiovascular collapse may occur in patients with hypovolaemia (compensatory adrenergic response is blocked)

or

Cardiovascular collapse may occur in patients with severe left or right ventricular dysfunction

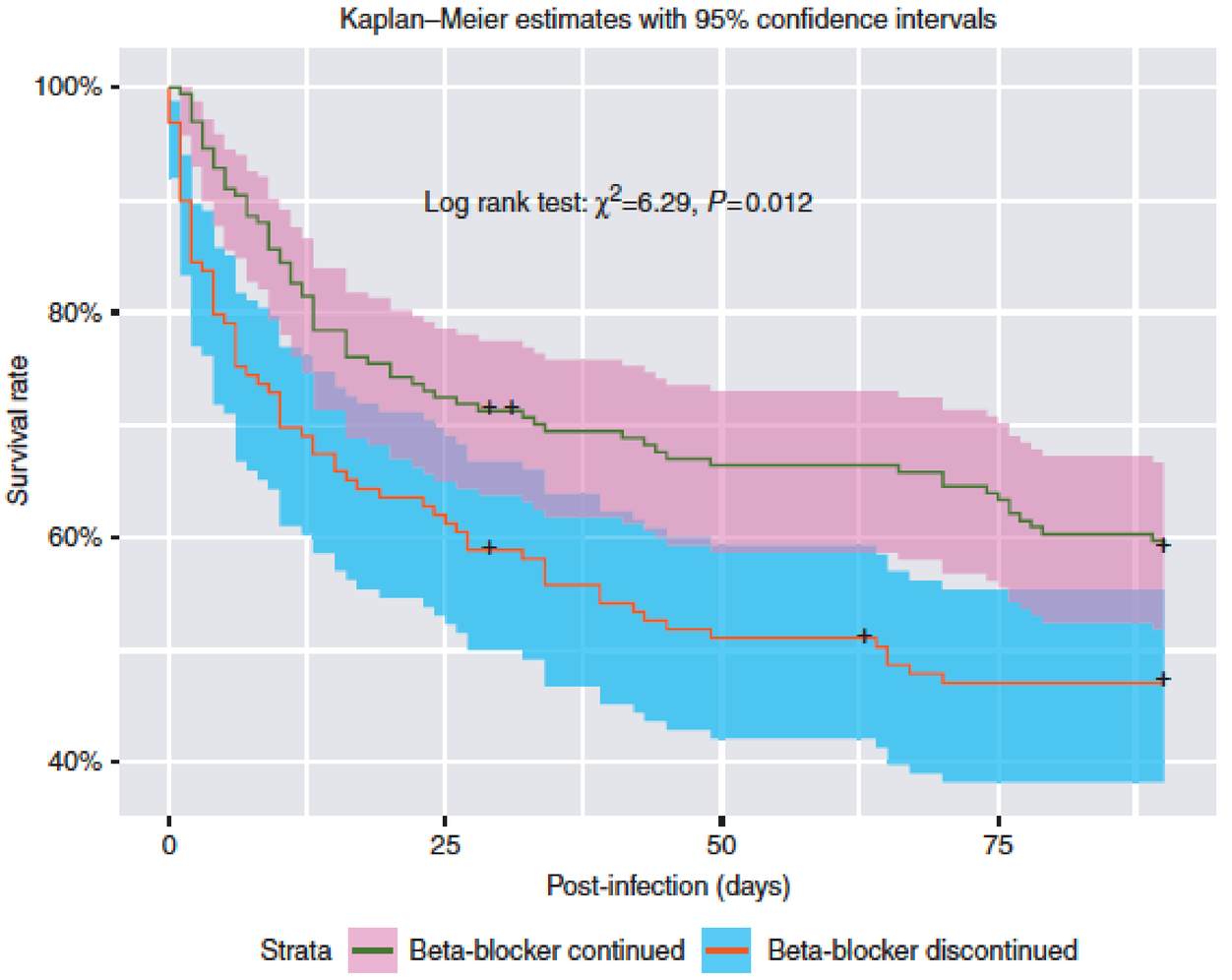
Beta blokátory – premorbidně

Continuing chronic beta-blockade in the acute phase of severe sepsis and septic shock is associated with decreased mortality rates up to 90 days

C. Fuchs[1,*,†], S. Wauschkuhn[1,†], C. Scheer[1], M. Vollmer[2], K. Meissner[1], S.-O. Kuhn[1], K. Hahnenkamp[1], A. Morelli[3], M. Gründling[1] and S. Rehberg[1]

British Journal of Anaesthesia, 119 (4): 616–25 (2017)

Baseline variables	Discontinued N=129		Continued N=167		P value
	med	*(IQR)*	*med*	*(IQR)*	
Age, yr	72.7	(60.6–77.3)	74.9	(65.9–79.4)	0.02
APACHE II score at sepsis onset	21.0	(16.2–26.0)	20.0	(15.0–24.5)	0.25
SAPS II score at sepsis onset	45.5	(39.0–58.0)	43.0	(35.0–52.0)	<0.01
Lactate (first 24 h), mmol L^{-1}	3.5	(2.0–6.5)	2.3	(1.5–3.8)	<0.01



The association between premorbid beta blocker exposure and mortality in sepsis—a systematic review

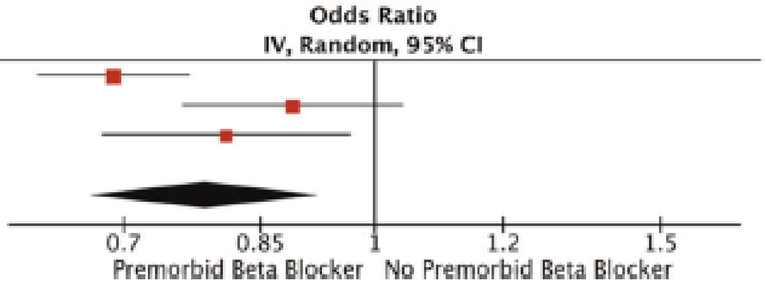
Tan *et al. Critical Care* (2019) 23:298

Kaiquan Tan[1], Martin Harazim[4], Benjamin Tang[1,3], Anthony Mclean[1,2] and Marek Nalos[1,2,4*]

9 studies included in final analysis
56414 patients with sepsis
including 6576 with premorbid beta blocker exposure

Study or Subgroup	log[Odds Ratio]	SE	Premorbid BB Total	No Premorbid BB Total	Weight	Odds Ratio IV, Random, 95% CI
Singer et al	-0.3711	0.0546	2838	4001	38.1%	0.69 [0.62, 0.77]
Hsieh et al	-0.1165	0.0795	1040	32173	32.1%	0.89 [0.76, 1.04]
Macchia et al	-0.2107	0.0893	1061	8404	29.8%	0.81 [0.68, 0.96]
Total (95% CI)			**4939**	**44578**	**100.0%**	**0.79 [0.67, 0.92]**

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 7.59$, df = 2 (P = 0.02); $I^2 = 74\%$
Test for overall effect: Z = 2.92 (P = 0.004)



Association Between Premorbid Beta-Blocker Exposure and Sepsis Outcomes—The Beta-Blockers in European and Australian/American Septic Patients (BEAST) Study

Tan, Kaiquan MD[1]; Harazim, Martin et al

Critical Care Medicine: September 2021 - Volume 49 - Issue 9 - p 1493-1503

Premorbid β-blocker exposure ↓ ICU mortality: aOR, 0.80; (95% CI, 0.66-0.97; p = 0.025)

↓ Hospital mortality aOR, 0.83; (95% CI, 0.71-0.99; p = 0.033)

Carvedilol

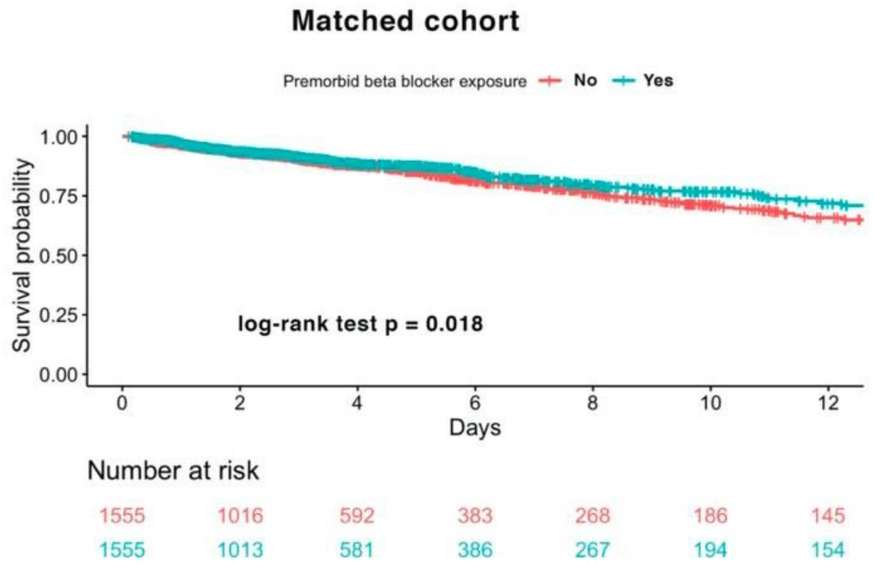
ICU mortality	**0.46 (0.29–0.73).**	**p<0.001**
Hospital mortality	**0.64 (0.46–0.91),**	**p<0.01**

Carvedilol blocks cardiac β2-receptors > β1-receptors - cardiac effects less pronounced, alpha blockade may improve peripheral perfusion

Molenaar P, et al. Cardiovasc Res. 2006;69(1):128-39

Carvedilol has potent antioxidant properties (10x > vitamin E, metabolites 1000-fold > vitamin E).
Inhibits formation of ROS in the myocardium

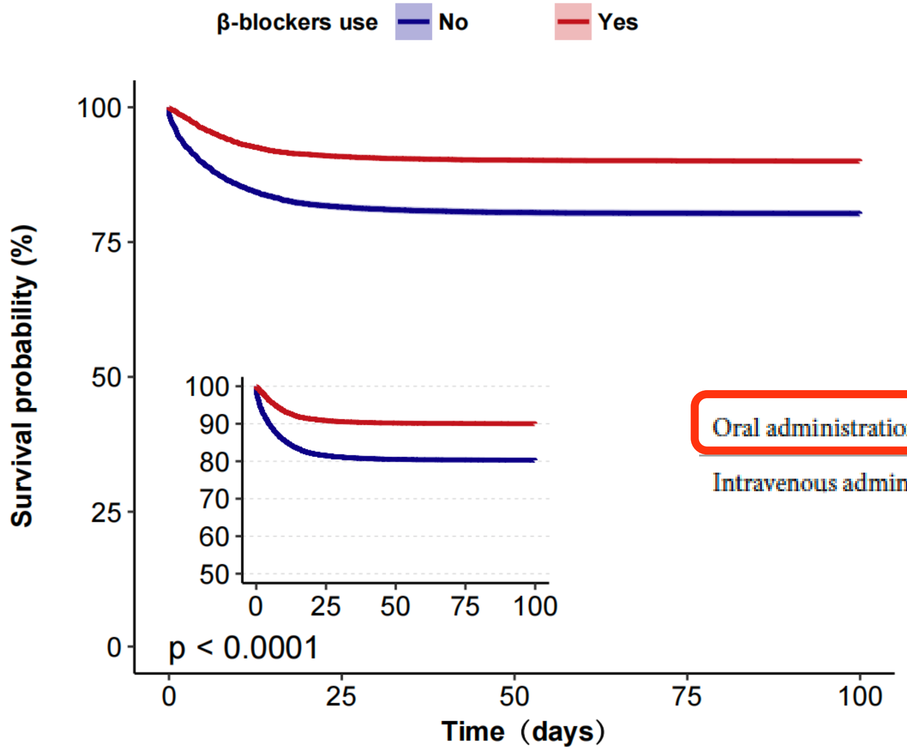
Feuerstein GZ, et al. Am J Cardiol. 1997 4;80(11A):41L-45L.



Association between the β-blocker use and patients with sepsis: a cohort study

Qilin Yang†, Tianyu Kong†, Ziping Bao†, Shanshan Yang, Xiaohua Chen, Jiezhao Zheng, Xuming Xiong, Deliang Wen* and Zhenhui Zhang*

MIMIC IV and eICU database - ~ 60000 patients



Number at risk

No	13390	10405	9880	9576	9369
Yes	10438	9153	8815	8577	8450

	No. of patients	Crude coefficient	Crude *p*-value	Adjusted coefficient[a]	
Oral administration	567(7.4)	0.35 (0.32~0.38)	<0.001	0.46 (0.42~0.51)	<0.001
Intravenous administration	465(17)	0.85 (0.77~0.93)	0.001	0.75 (0.68~0.84)	<0.001

Subgroup	NO.of patients	HR (95%CI)	P for interaction
Heart Rate			
HR<95	7738	0.54 (0.49~0.59)	0.063
95≤HR<120	2415	0.6 (0.53~0.69)	
HR≥120	285	0.59 (0.42~0.83)	

Měli bychom pacientům předepsat beta blokátor při dimisi z intenzivní péče???

Long-Term Mortality and Major Adverse Cardiovascular Events in Sepsis Survivors

A Nationwide Population-based Study

Am J Respir Crit Care Med Vol 194, Iss 2, pp 209–217 2016

Shuo-Ming Ou[1,2,3*], Hsi Chu[2,4*], Pei-Wen Chao[5,6], Yi-Jung Lee[2,7], Shu-Chen Kuo[2,8,9], Tzeng-Ji Chen[10], Ching-Min Tseng[2,11], Chia-Jen Shih[2,12,13‡], and Yung-Tai Chen[2,14‡]

Long term follow up in ~ 94000 patients

	Sepsis Cohort			Matched Population Control Cohort			Propensity Score–matched: Crude	
	No. of Events	Person-Years	Incidence Rate*	No. of Events	Person-Years	Incidence Rate*	HR (95% CI)	*P* Value
Major adverse cardiovascular events†	9,875	361,291	27.33	9,690	500,165	19.37	1.37 (1.34–1.41)	<0.001
Ischemic stroke	5,930	366,672	16.17	6,234	505,636	12.33	1.27 (1.23–1.32)	<0.001
Hemorrhagic stroke	1,491	380,513	3.92	1,467	521,969	2.81	1.36 (1.26–1.46)	<0.001
Myocardial infarction	1,820	380,391	4.78	2,039	521,034	3.91	1.22 (1.14–1.30)	<0.001
Heart failure	7,951	364,533	21.81	7,252	508,288	14.27	1.48 (1.43–1.53)	<0.001
Sudden cardiac death/ventricular arrhythmia	3,051	381,430	8.00	2,503	522,934	4.79	1.65 (1.57–1.74)	<0.001
All-cause mortality	37,902	384,001	98.70	22,717	525,318	43.24	2.18 (2.14–2.22)	<0.001

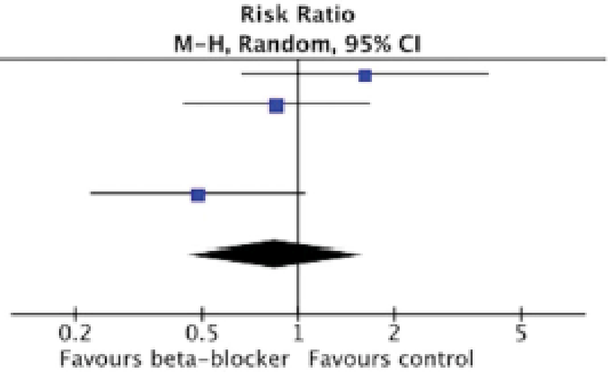
Beta-blocker treatment in the critically ill: a systematic review and meta-analysis

ANNALS OF MEDICINE
2022, VOL. 54, NO. 1, 1994–2010
https://doi.org/10.1080/07853890.2022.2098376

Maria Heliste[a], Ville Pettilä[a], David Berger[b], Stephan M. Jakob[b] and Erika Wilkman[a]

Study or Subgroup	Beta-blocker Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Ali 2015	10	35	6	34	28.6%	1.62 [0.66, 3.96]
Balser 1998	11	34	11	29	38.0%	0.85 [0.44, 1.67]
Brunner 2000	0	59	0	57		Not estimable
Connolly 2003	0	500	0	500		Not estimable
Khalili 2020	8	99	20	120	33.4%	0.48 [0.22, 1.05]
Total (95% CI)		**727**		**740**	**100.0%**	**0.85 [0.45, 1.60]**
Total events	29		37			

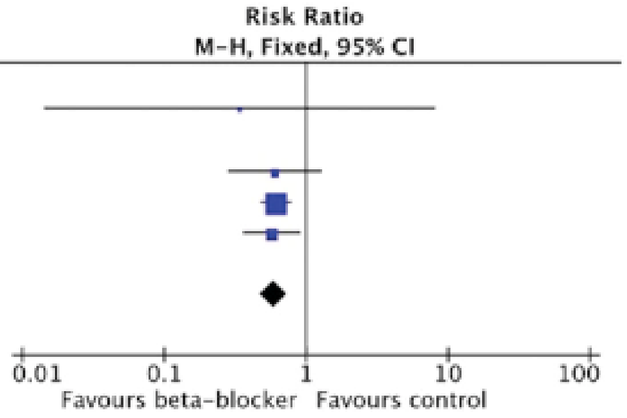
Heterogeneity: $Tau^2 = 0.16$; $Chi^2 = 4.02$, df = 2 (P = 0.13); $I^2 = 50\%$
Test for overall effect: Z = 0.51 (P = 0.61)



Forest plot of short-term mortality.

Study or Subgroup	Beta-blocker Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bible 2014	0	25	0	20		Not estimable
Er 2016	0	50	1	51	1.4%	0.34 [0.01, 8.15]
Hanada 2012	0	47	0	49		Not estimable
Kakihana 2020	9	75	15	75	14.1%	0.60 [0.28, 1.29]
Morelli 2013	38	77	62	77	58.2%	0.61 [0.48, 0.79]
Wang 2015	12	30	42	60	26.3%	0.57 [0.36, 0.91]
Total (95% CI)		**304**		**332**	**100.0%**	**0.60 [0.48, 0.74]**
Total events	59		120			

Heterogeneity: $Chi^2 = 0.20$, df = 3 (P = 0.98); $I^2 = 0\%$
Test for overall effect: Z = 4.56 (P < 0.00001)



. Forest plot of long-term mortality.

Beta blokátory - podávat během sepse na JIP?

Practice Patterns and Outcomes of Treatments for Atrial Fibrillation During Sepsis

A Propensity-Matched Cohort Study

Allan J. Walkey, MD, MSc; Stephen R. Evans, MPH; Michael R. Winter, MPH; and Emelia J. Benjamin, MD, ScM

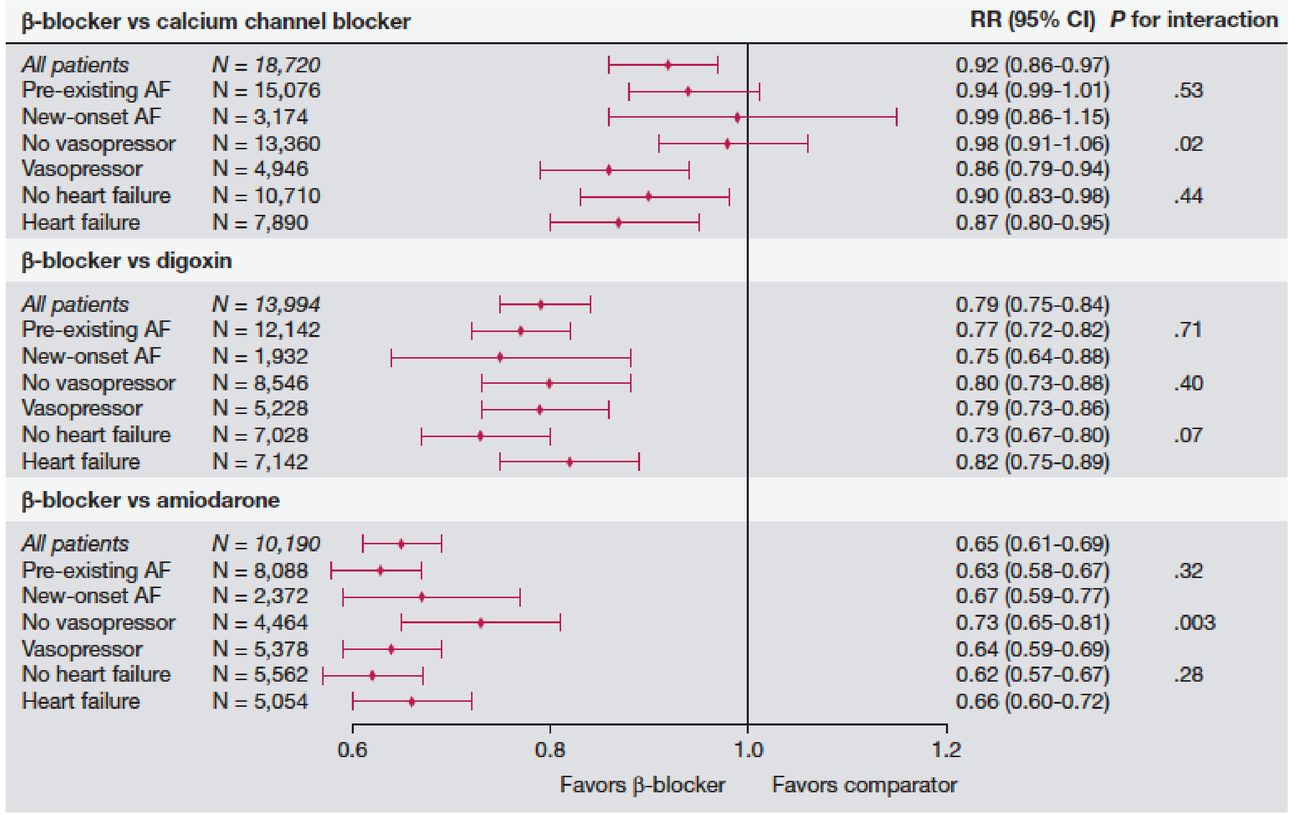
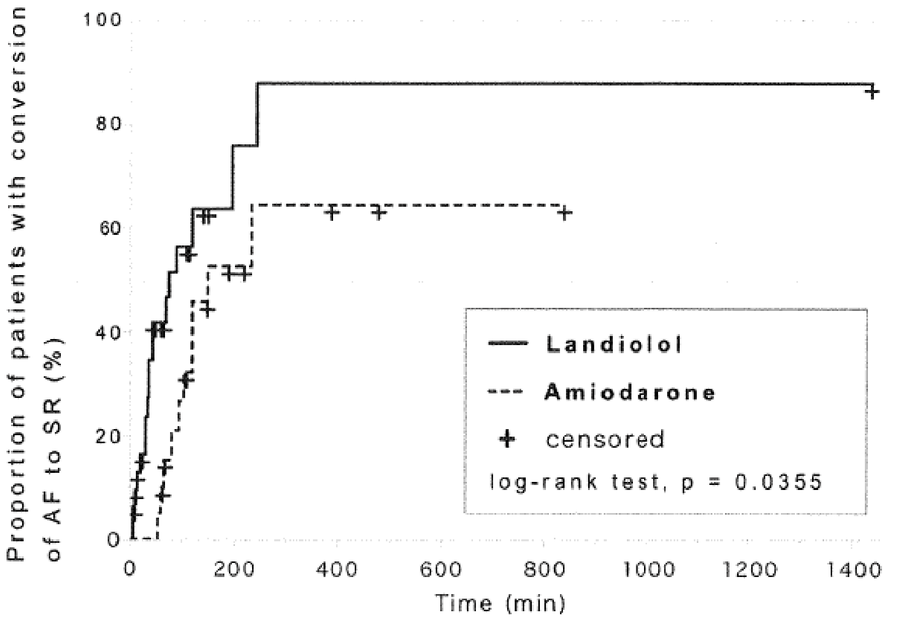


Figure 2 – *Summary of analyses for AF treatments during sepsis and relative risk for mortality. The number of subjects and weighted average of RR in*

Efficacy and Safety of Landiolol Compared to Amiodarone for the Management of Postoperative Atrial Fibrillation in Intensive Care Patients

Sho C. Shibata, MD, PhD, Akinori Uchiyama, MD, PhD, Noriyuki Ohta, MD, PhD, and Yuji Fujino, MD, PhD



Efficacy and safety of landiolol, an ultra-short-acting β1-selective antagonist, for treatment of sepsis-related tachyarrhythmia (J-Land 3S): a multicentre, open-label, randomised controlled trial

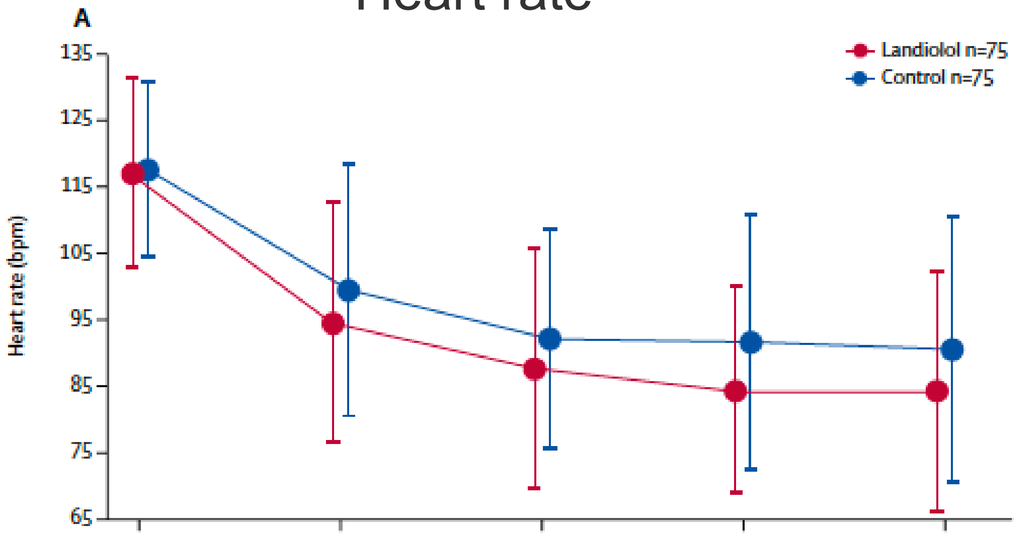
Lancet Respir Med 2020

Published Online
March 31, 2020

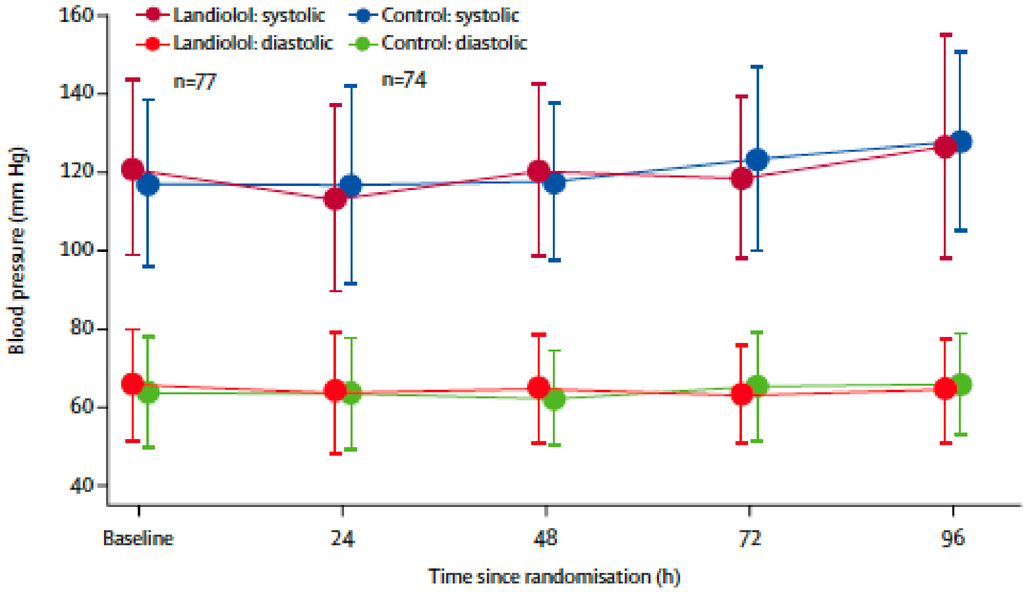
*Yasuyuki Kakihana, Osamu Nishida, Takumi Taniguchi, Masaki Okajima, Hiroshi Morimatsu, Hiroshi Ogura, Yoshitsugu Yamada, Tetsuji Nagano, Eiichiro Morishima, Naoyuki Matsuda, on behalf of the J-Land 3S Study Group**

Inclusion criteria: Septic shock
Catecholamine to maintain MAP > 65mmHg
Heart rate > 100 bpm for at least 10min with diagnosis of AF or sinus tachycardia.

Heart rate



BP

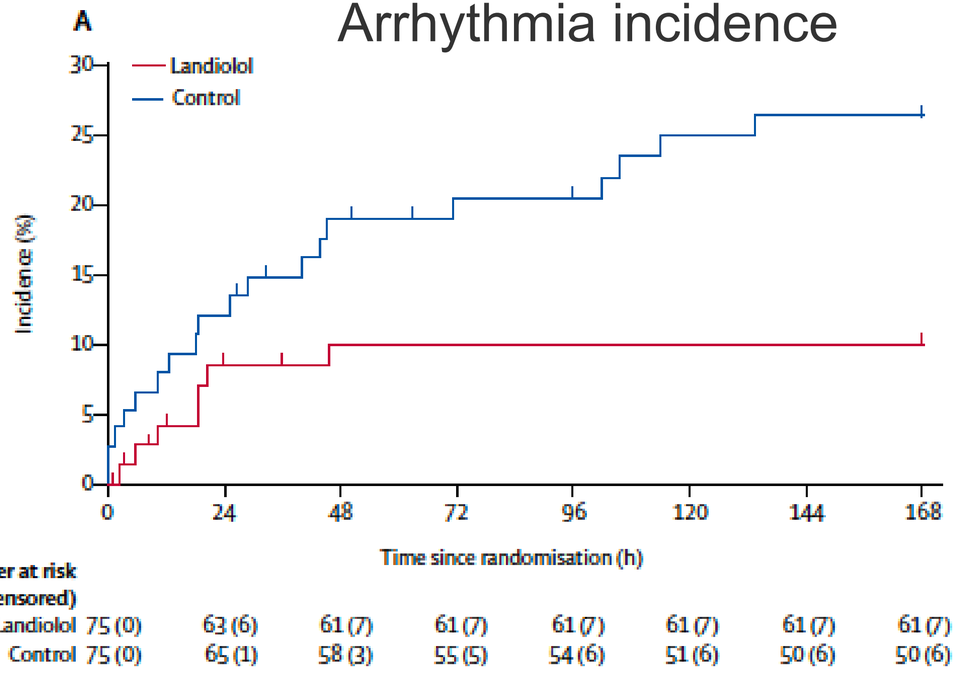


Efficacy and safety of landiolol, an ultra-short-acting β1-selective antagonist, for treatment of sepsis-related tachyarrhythmia (J-Land 3S): a multicentre, open-label, randomised controlled trial

*Yasuyuki Kakihana, Osamu Nishida, Takumi Taniguchi, Masaki Okajima, Hiroshi Morimatsu, Hiroshi Ogura, Yoshitsugu Yamada, Tetsuji Nagano, Eiichiro Morishima, Naoyuki Matsuda, on behalf of the J-Land 3S Study Group**

www.thelancet.com/respiratory **Published online March 31, 2020**

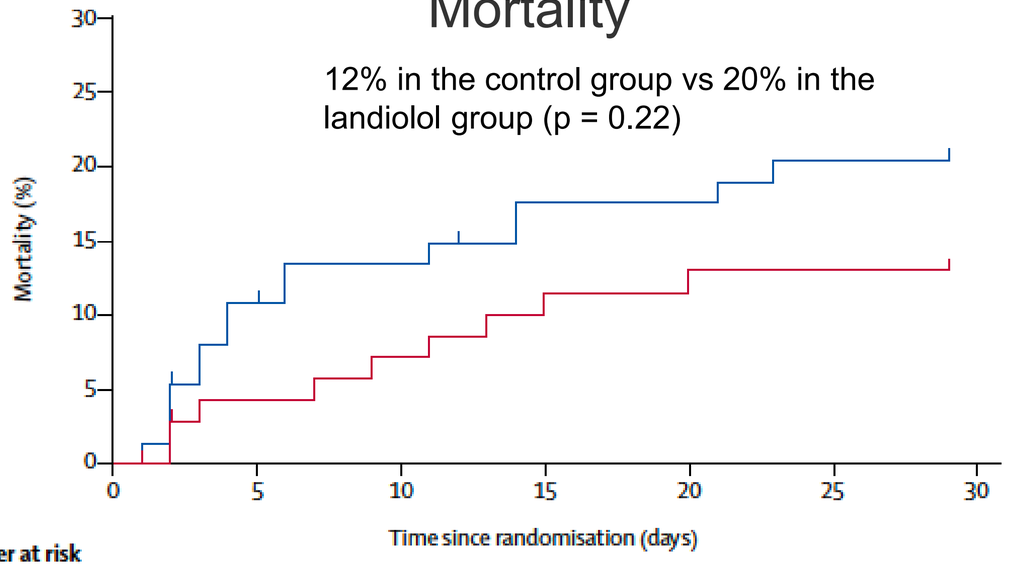
Arrhythmia incidence



Number at risk (number censored)								
Landiolol	75 (0)	63 (6)	61 (7)	61 (7)	61 (7)	61 (7)	61 (7)	61 (7)
Control	75 (0)	65 (1)	58 (3)	55 (5)	54 (6)	51 (6)	50 (6)	50 (6)

Mortality

12% in the control group vs 20% in the landiolol group (p = 0.22)



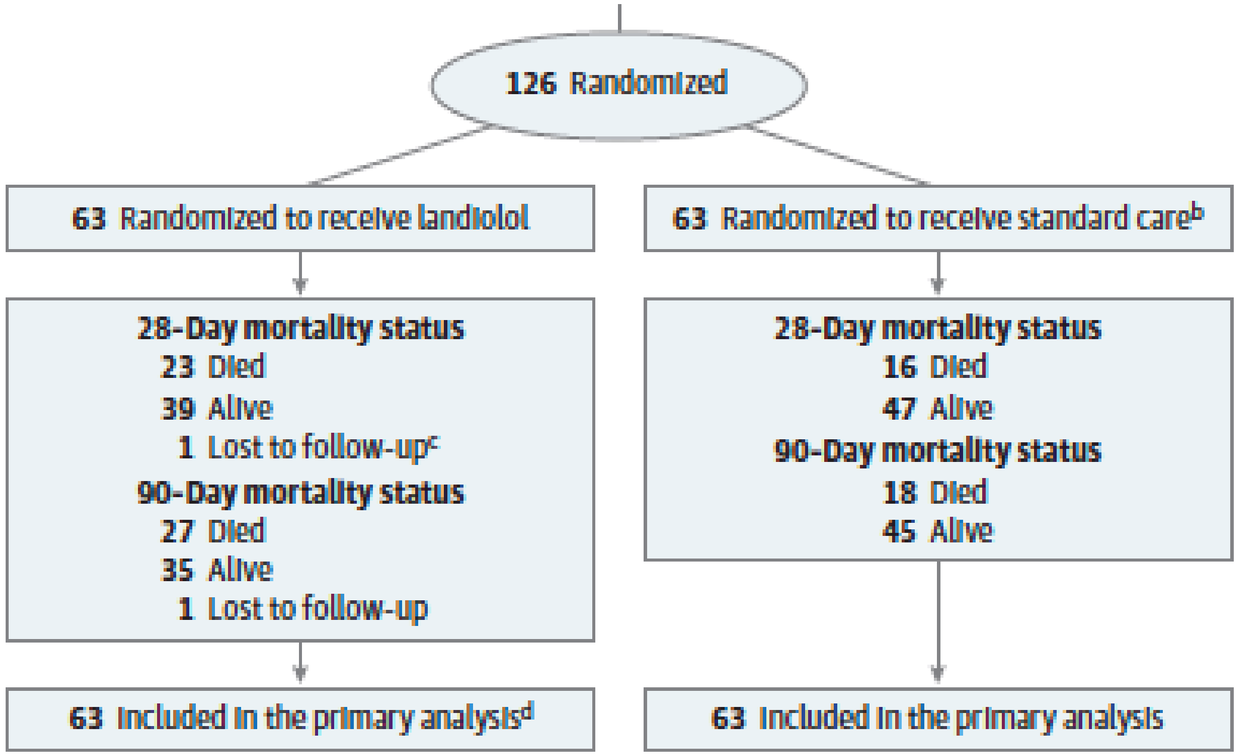
Number at risk (number censored)							
Landiolol	75 (0)	66 (6)	64 (6)	62 (6)	61 (6)	60 (6)	0 (66)
Control	75 (0)	66 (1)	63 (2)	59 (3)	59 (3)	57 (3)	0 (60)

SAE related to landiolol occurred in 6% of patients, hypotension in 4%
cardiac arrest, severe bradycardia, ejection fraction decrease occurred in one patient each

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Landiolol and Organ Failure in Patients With Septic Shock
The STRESS-L Randomized Clinical Trial

Tony Whitehouse, MD; Anower Hossain, PhD; Gavin D. Perkins, MD; Anthony C. Gordon, MD; Julian Bion, MD; Duncan Young, MD; Danny McAuley, MD; Mervyn Singer, MD; Janet Lord, PhD; Simon Gates, PhD; Tonny Veenith, MD; Niall S. MacCallum, PhD; Joyce Yeung, MD; Richard Innes, MD; Ingeborg Welters, MD; Nafisa Boota, MSc; Emma Skilton, BSc; Belinder Ghuman, BSc; Maddy Hill, MPH; Scott E. Regan, BA; Dipesh Mistry, PhD; Ranjit Lall, PhD; for the STRESS-L Collaborators



Inclusion/randomization

septic shock - adequate fluid resuscitation, with > 0.1 µg/kg/min of norepinephrine (for >24 hours but <72 hours) and tachycardia heart rate of > 95/min.

The continuous i.v. landiolol - started at 1.0µg/kg/min, increasing every 15 minutes by 1.0 µg/kg/min to reach the target heart rate of 80-94/min within 6hours

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Landiolol and Organ Failure in Patients With Septic Shock
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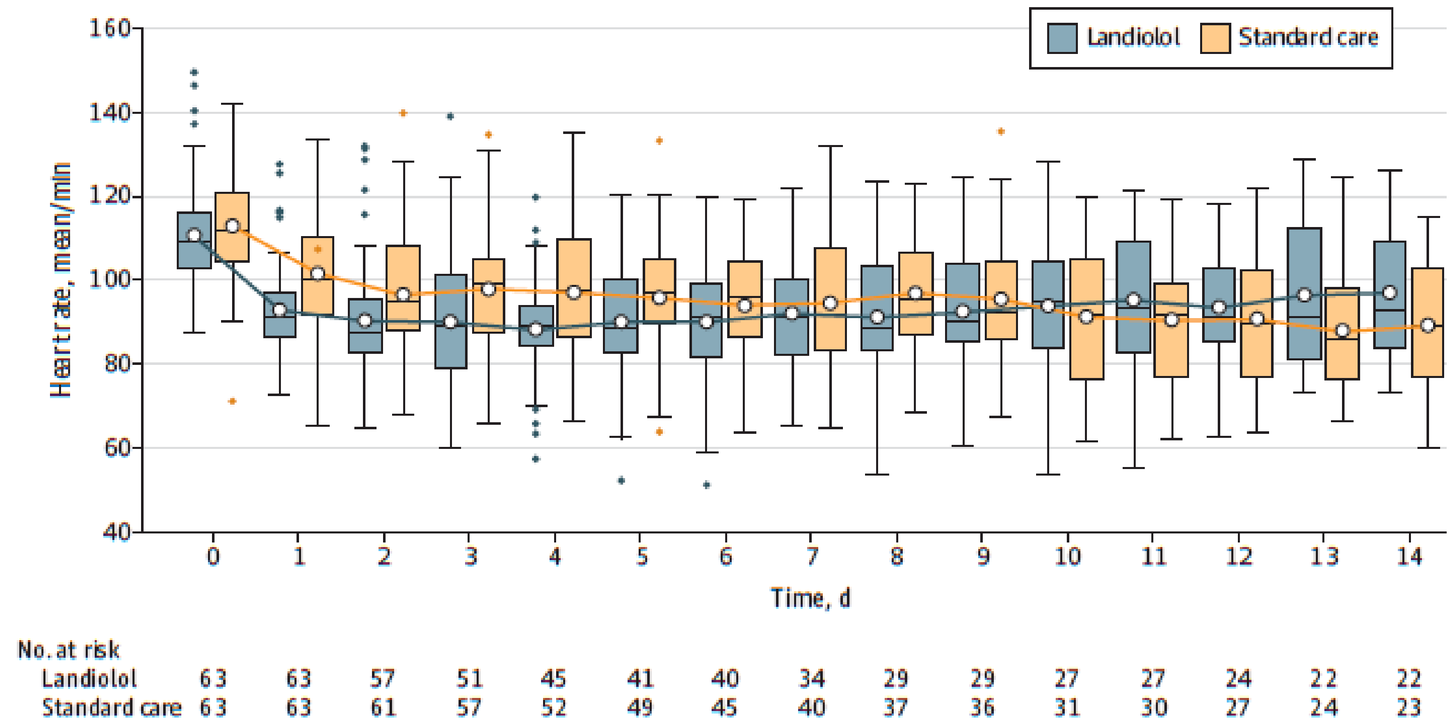
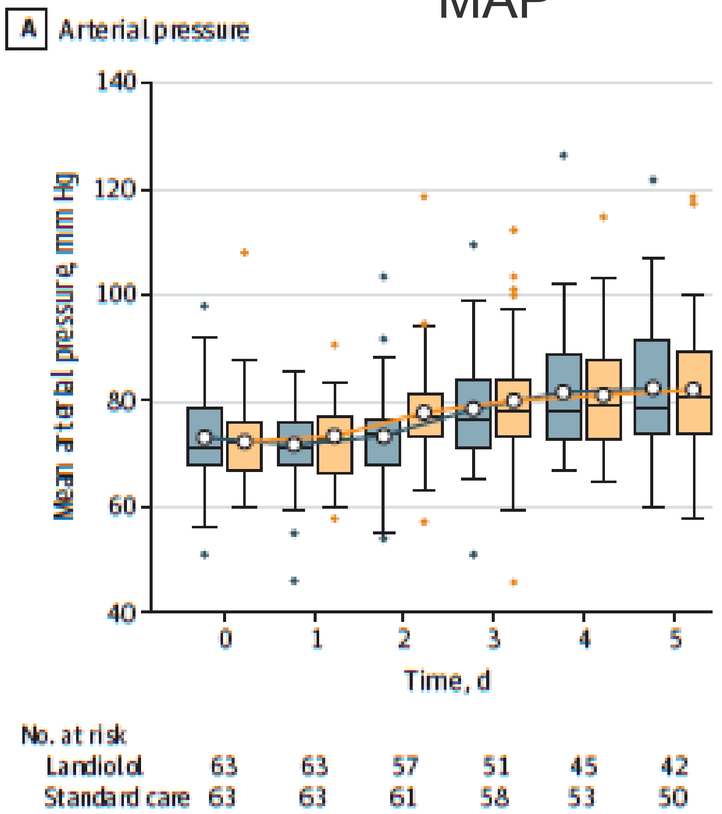
Heart rate



MAP



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The trial was stopped prematurely on the advice of the independent data monitoring committee because of increased mortality

Only 126 (37% of planned) patients were enrolled

Mortality at day 28

Landiolol - 37.1% (23 of 62) **vs.** 25.4% (16 of 63) - Standard care

Mortality at day 90

Landiolol - 43.5% (27 of 62) **vs.** 28.6% (18 of 63) - Standard care group

β-Blockers in Patients With Sepsis

Putting the Puzzle Together, Piece by Piece

Steven M. Hollenberg, MD

cardiomyopathy and may not tolerate β-blockade. Cardiac output monitoring was left to the discretion of the investigators for pragmatic reasons, and this is an important limitation of the trial. It is hard to exclude the possibility that at least some of the patients in the landiolol group may have had decreased cardiac output, with or without a vasodilatory effect, a possibility that is supported by decreased blood pressure, elevated lactate levels, and increased norepinephrine requirements in this group. It is conceivable that closer hemodynamic monitoring, at least in selected patients, would have allowed more careful titration of β-blockers so as to minimize decreases in cardiac output. In this respect, dif-

The patients receiving landiolol had higher mean lactate and norepinephrine requirements - indicate a reduction in cardiac output.

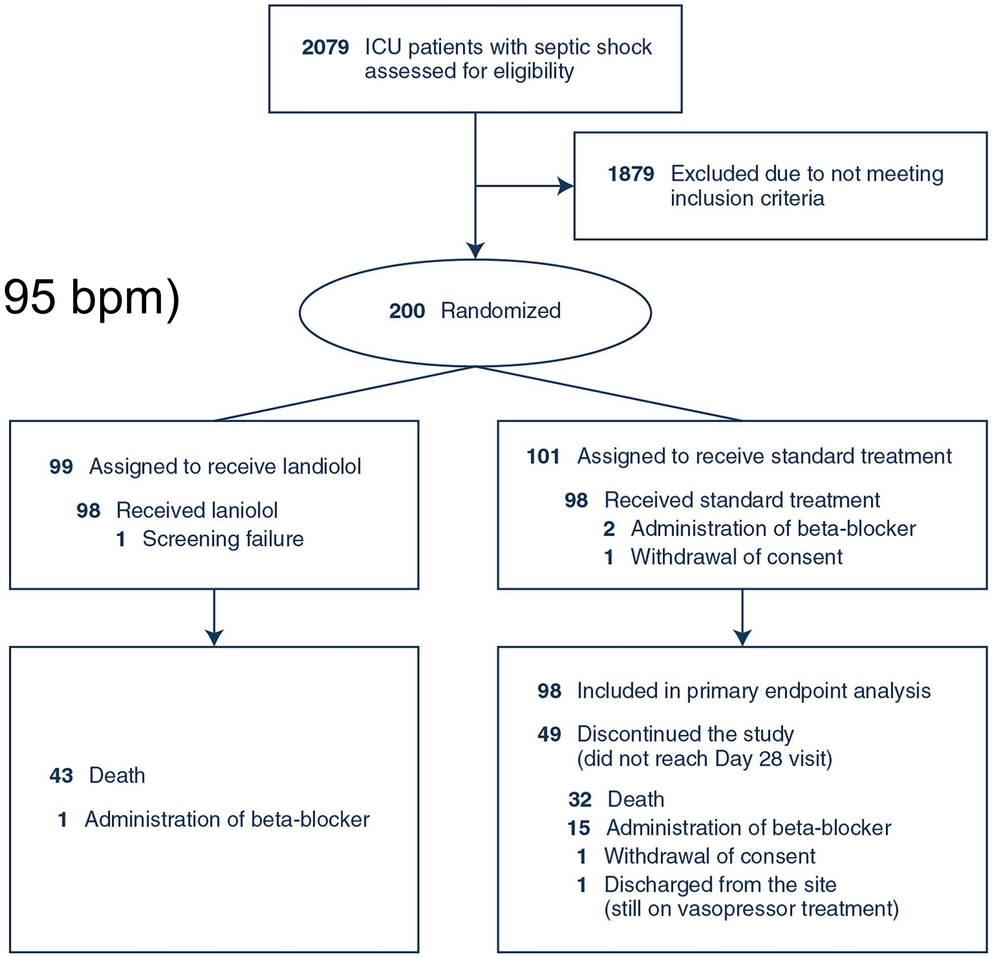
Landiolol for heart rate control in patients with septic shock and persistent tachycardia. A multicenter randomized clinical trial (Landi-SEP)

Sebastian Rehberg[1*], Sandra Frank[2], Vladimír Černý[3,4,12,23,24], Radek Cihlář[5], Rainer Borgstedt[1], Gianni Biancofiore[6], Fabio Guarracino[7], Andreas Schober[8], Helmut Trimmel[9], Thomas Pernerstorfer[10], Christian Siebers[11], Pavel Dostál[12,24], Andrea Morelli[13], Michael Joannidis[14], Ingrid Pretsch[15], Christian Fuchs[16], Tim Rahmel[17], Matej Podbregar[18,25], Éva Duliczki[19], Kadri Tamme[20], Martin Unger[21], Jan Sus[21], Christoph Klade[21], Kurt Krejcy[21], Nairi Kirchbaumer-Baroian[21], Günther Krumpl[22] and František Duška[3] on behalf of the LANDI-SEP Study Group

Intensive Care Med
https://doi.org/10.1007/s00134-024-07587-1

Inclusion criteria: septic shock with persistent tachycardia (HR ≥ 95 bpm) despite a hemodynamic optimization phase of 12 - 36hrs.

Sepsis standard treatment (SSC guidelines)
Continuous infusion of landiolol (1 µg/kg/min).
Titration phase (0–24 h), the dose was increased at increments of 1 µg/kg/min to reach a target HR of 80–94 bpm.
Then Landiolol was administered at any dose to maintain target HR until discontinuation of vasopressor infusion,
death, or serious adverse event (SAE).



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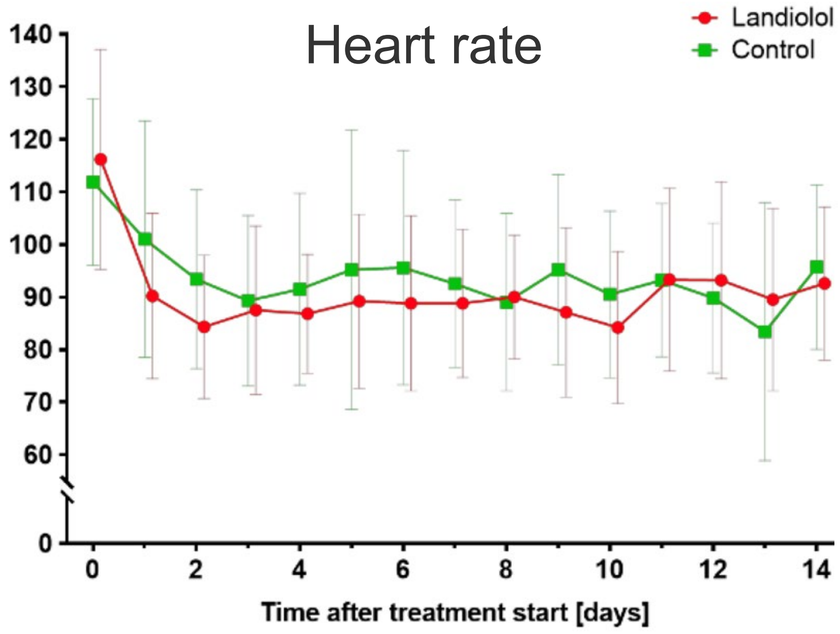

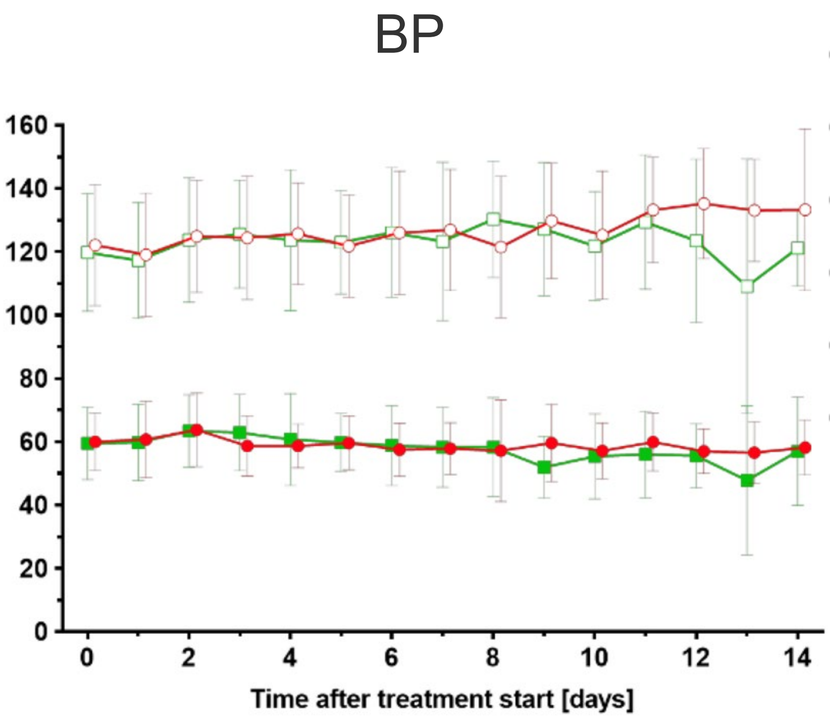

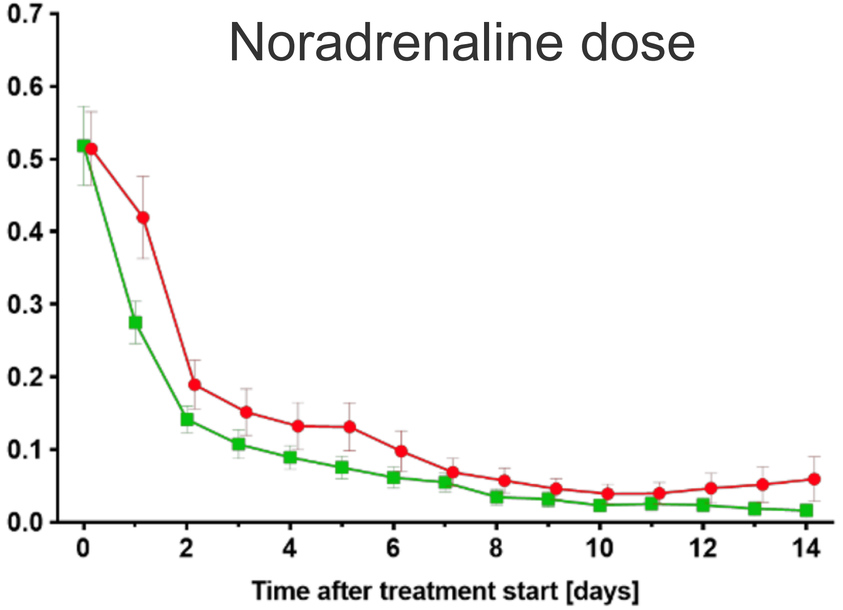

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Table 3 Secondary efficacy analyses

Response	Landiolol group ($n=98$)	Control group ($n=98$)	Overall	Effect estimate (95% CI)	*P* value
28-day mortality, n (%)[a]	43 (43.9)	39 (40.2)	82 (42.1)	MD, 3.8% (−9.9 to 17.3%)	0.60
ICU mortality, n (%)[b]	43 (43.9)	33 (34)	76 (39)	MD, 9.9% (−3.8 to 23%)	0.16
Duration of ICU stay for patients alive on day 28, median (95% CI), days	14 (10.2–15.3)	13.9 (10.2–20.4)	–	HR, 1.17 (0.70–1.94)	0.55

Post hoc subgroup analysis
showed higher mortality risk for the landiolol group
(47%) vs control group (40%)
in patients with sinus tachycardia

opposite was observed in patients with AF (34% vs 42%)

Combined milrinone and enteral metoprolol therapy in patients with septic myocardial depression

Christian A Schmittinger[1], Martin W Dünser[1], Maria Haller[2], Hanno Ulmer[3], Günter Luckner[1], Christian Torgersen[1], Stefan Jochberger[1] and Walter R Hasibeder[2]

Critical Care 2008, 12:R99

Retrospective analysis - clinical experience with the combined use of milrinone and enteral metoprolol therapy in 40 patients with septic shock and cardiac depression.

β-blockers initiated only after stabilization of cardiovascular function (18 ± 16 hrs after shock onset) to decrease the heart rate < 95/min.

Heart rate significantly decreased; 65- 95/min achieved in 97.5% of patients.

MAP increased despite decreasing norepinephrine, vasopressin, and milrinone dosages.

Cardiac output maintained with a lower heart rate and a higher stroke volume.

Enteral metoprolol therapy - no major adverse effects on cardiovascular or organ function.

Combined milrinone and enteral metoprolol therapy in patients with septic myocardial depression

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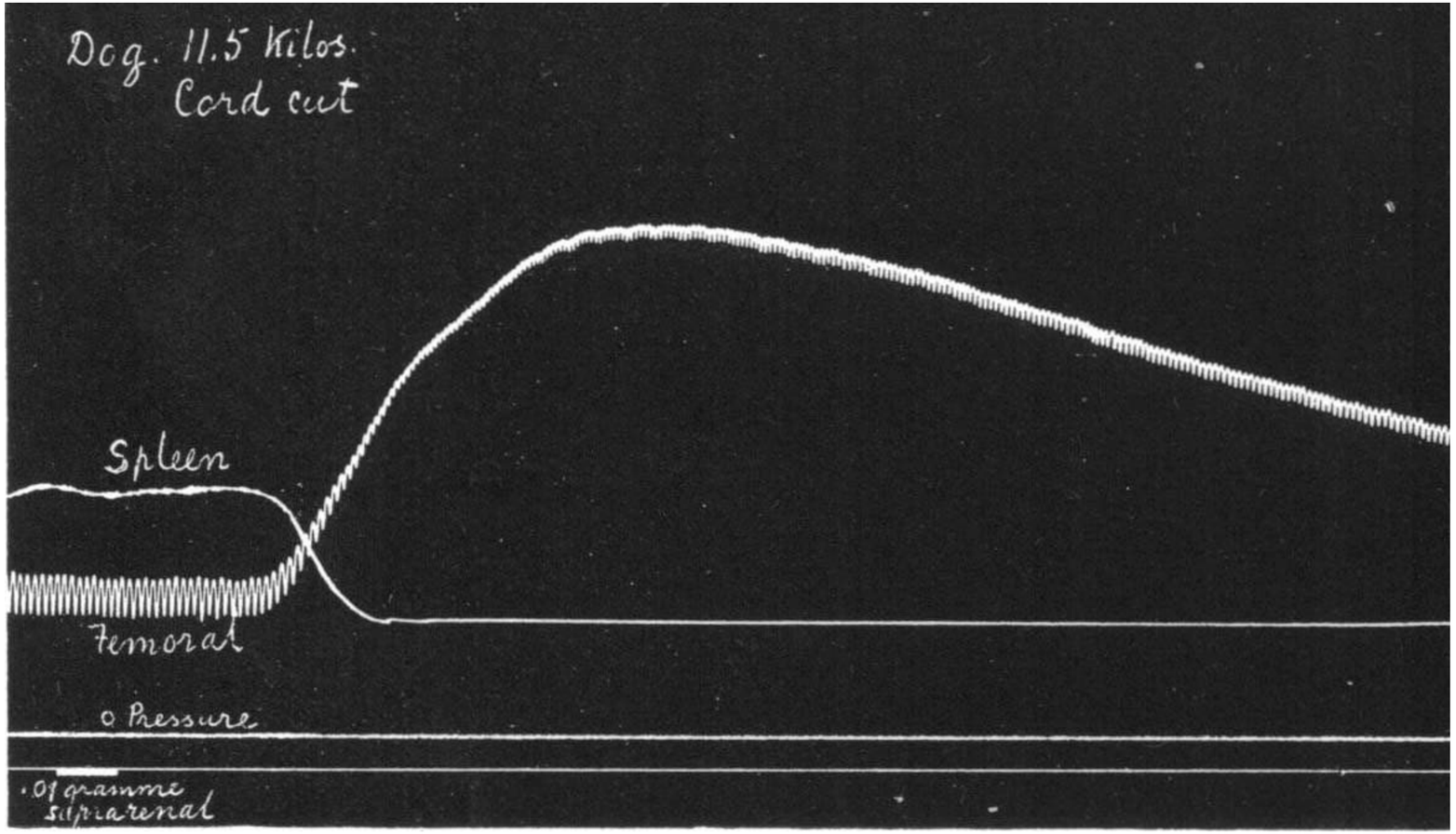
Adverse events during the observation period

	Number (percentage)
Asymptomatic bradycardia	2 (5)
Symptomatic bradycardia	0 (0)
Increase in norepinephrine dosage	9 (22.5)
Decrease in cardiac index	7 (17.5)
Decrease in cardiac index and $ScvO_2$	1 (2.5)
Decrease in stroke volume index	2 (5)
Increase in milrinone dosage	6 (15)

Administration of β-blockers with concomitant catecholamine treatment does not compromise hemodynamics, when given enterally to stabilised sepsis patients

Splanchnic perfusion is reduced in shock
Enteral beta blocker absorption will be reduced



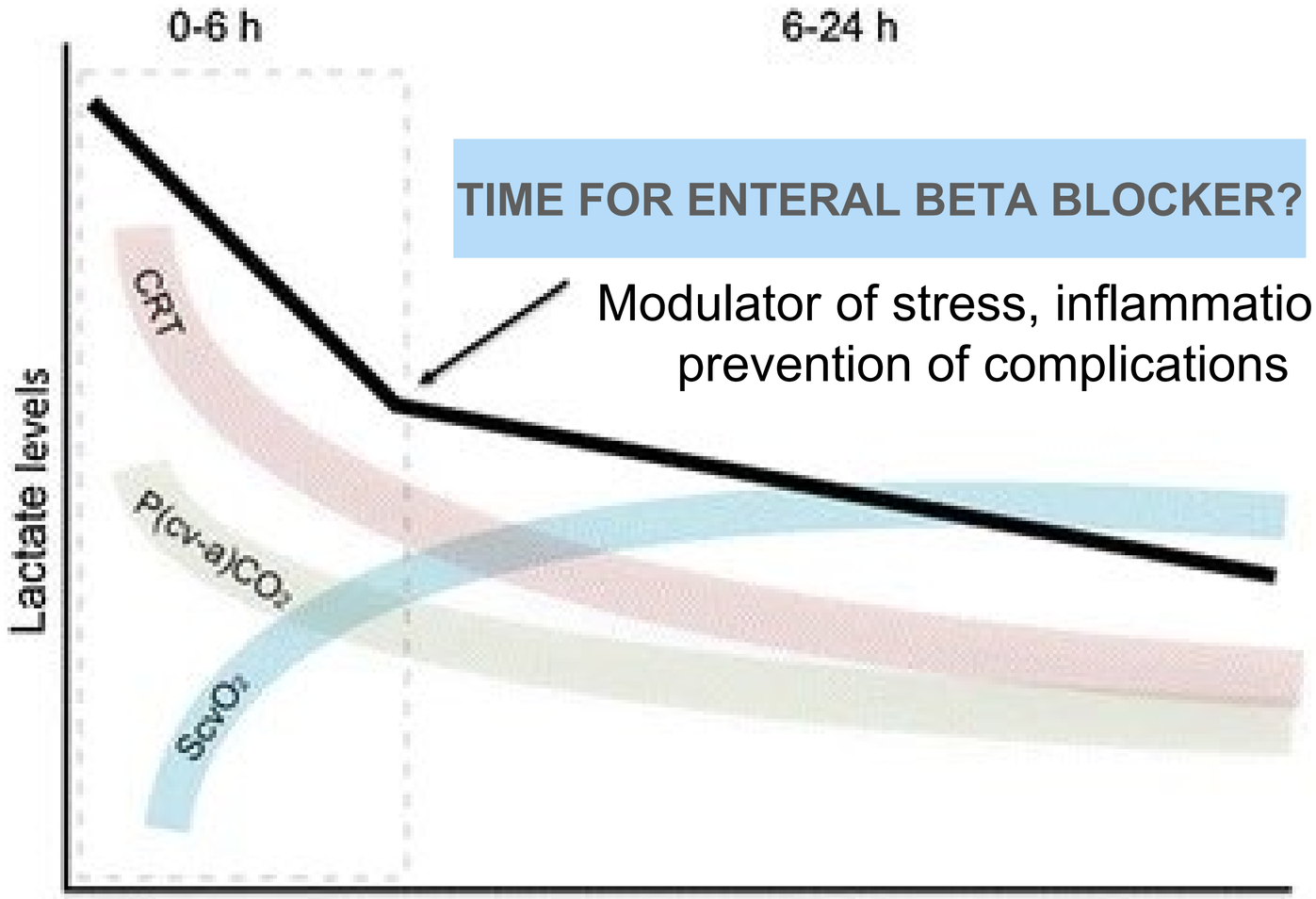
Beta blokátory v sepsi- praktický návrh k použití

β-blockers for rapid atrial fibrillation, SVT, frequent arrhythmia

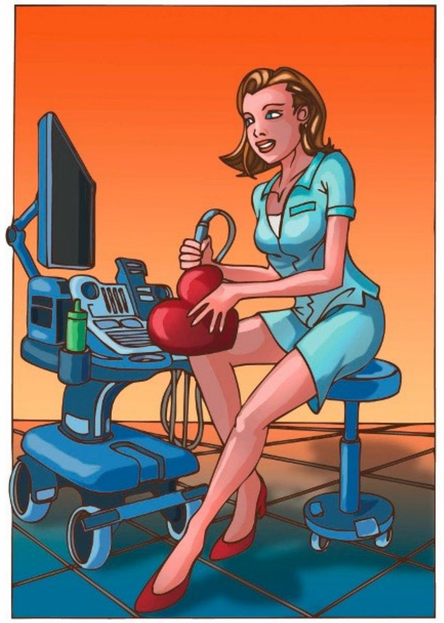
Early septic shock

Fluid resuscitation
Vasopressors
Steroids

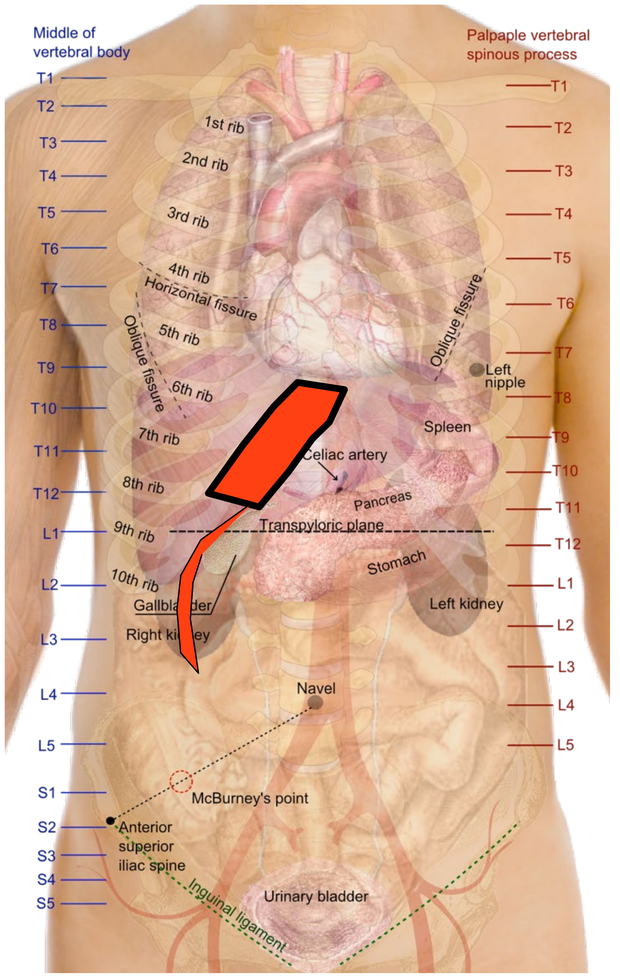
Treat pain, fever, dyspnoea



Echo to confirm normal CO



ECHO
BREWING COMPANY



Conclusions

- Early adrenergic surge and catecholamine excess in septic shock
- Dysregulation of adrenergic signalling
- Beta blockade may be beneficial in sepsis
- Which patients?
- Cardiac output monitoring preferably by echocardiography is vital
- Enteral administration may be preferable
- We don’t know which beta blocker is best to use

- We need more studies


Thank you