Beta-blockers in ICU

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COLOURS OF SEPSIS
FESTIVAL INTENZIVNÍ MEDICÍNY

Disclosures

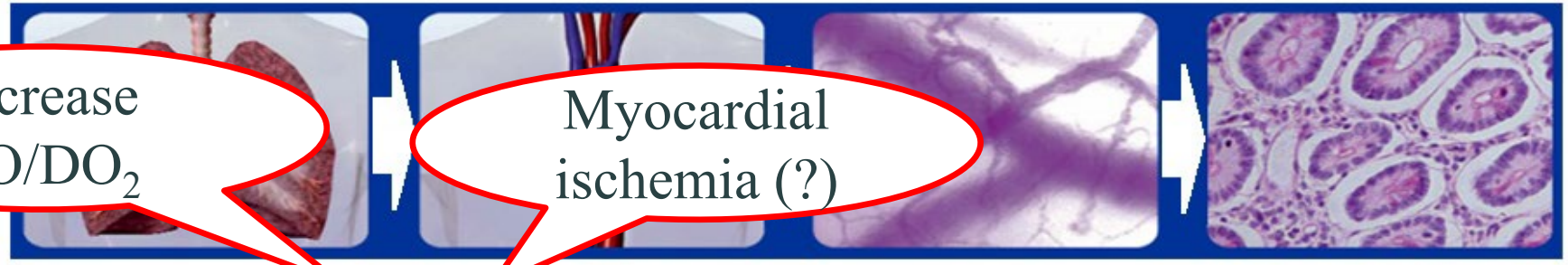
#1: I have never used beta-blockers in sepsis without a cardiovascular indication (i.e.: tachycardia hypertension)

#2: Senior Medical Director:

CytoSorbents™

Fundamentals of HD support

VO_2/DO_2



Increase CO/DO_2

Myocardial ischemia (?)

Tachycardia

$$DO_2 = (\underbrace{SV \bullet HR}_{CO}) \bullet (\underbrace{Hb \bullet 1.39 \bullet SaO_2 + 0.003 \bullet PaO_2}_{CaO_2})$$

$$VO_2 = CO \bullet (CaO_2 - CvO_2)$$

Tachycardia: double edged sword

Rationale of beta-blockers in ICU

The Effect of Heart Rate Control on Myocardial Ischemia Among High-Risk Patients After Vascular Surgery

Khether E. Raby, MD, FACC*, Sorin J. Brull, MD‡, Farris Timimi, MD†, Shamsuddin Akhtar, MD†, Stanley Rosenbaum, MD†, Cameron Naimi, BS†, and Anthony D. Whittemore, MD†

(Anesth Analg 1999;88:477–82)

Table 1. Clinical and Ischemia Characteristics Among Patients Randomized to Placebo or Esmolol

	Placebo (n = 11)	Esmolol (n = 15)
Male	4 (36)	8 (53%)
Mean age (yr)	67	69
Previous infarct or angina	4 (36)	6 (40
History of diabetes	4 (36)	3 (20
Aortic surgery	3 (27)	5 (33)
General anesthesia	10 (91)	11 (73)
Chronic β-blocker use	4 (36)	5 (3
Minimal heart rate (bpm) of ischemia occurrence	96 (60–120)	96 (71–128)
Preoperative ischemia		
Episodes	2 (1–6)	2 (1–7)
Duration (min)	22 (1–155)	40 (1–154)
Patients receiving alternative postoperative β-blockers	9 (82)	2 (13)*
Postoperative ischemia persisted	8 (73)	5 (33)*

Values are n (%) or median (range).
* $P < 0.05$, χ^2.

96 became a „magic number”

„Tachycardia – is BAD!”

Intraoperative Tachycardia and Hypertension Are Independently Associated with Adverse Outcome in Noncardiac Surgery of Long Duration

David L. Reich, MD, Elliott Bennett-Guerrero, MD, Carol A. Bodian, DrPH, Sabera Hossain, MSc, Wanda Winfree, RN, and Marina Krol, PhD

(Anesth Analg 2002;95:273–7)

Table 7. Multivariate Analysis of Negative Surgical Outcome in Long Operations (>220 minutes)

Variable	Odds ratio	*P* value
Operation duration >220 min (per minute)	1.003	0.02
POSSUM physiological score (per point of score)	1.096	0.0001
High heart rate	2.704	0.01
High systolic arterial blood pressure	2.095	0.009

Bernd Hartmann
Axel Junger
Rainer Röhrig
Joachim Klasen
Andreas Jost
Matthias Benson
Helge Braun
Carsten Fuchs
Gunter Hempelmann

Intra-operative tachycardia and peri-operative outcome

Langenbecks Arch Surg (2003) 388:255–260

Table 6 Results of the logistic regression models with the three outcome measures as dependent and all matched criteria as independent variables (*CI*: 95% confidence interval)

Variables		*P*	Odds ratio	CI
Hospital mortality	High risk surgery	0.11	1.83	(0.87; 3.83)
	Severe congestive heart failure (NYHA >II)	0.39	1.55	(0.58; 4.15)
	Severe coronary artery disease	0.79	0.87	(0.31; 2.42)
	Significant carotid artery stenosis and/or history of stroke	0.96	1.06	(0.13; 8.69)
	Renal failure	0.10	2.05	(0.87; 4.83)
	Diabetes mellitus	0.59	0.77	(0.31; 1.97)
	Urgency of surgery	<0.001	2.44	(1.60; 3.71)
	Tachycardia	0.03	2.22	(1.09; 4.53)
ICU admission	High risk surgery	<0.001	4.12	(2.80; 6.06)
	Severe congestive heart failure (NYHA >II)	0.20	1.43	(0.82; 2.50)
	Severe coronary artery disease	0.49	0.82	(0.46; 1.46)
	Significant carotid artery stenosis and/or history of stroke	0.02	0.10	(0.01; 0.74)
	Renal failure	0.11	1.56	(0.91; 2.70)
	Diabetes mellitus	0.40	0.81	(0.49; 1.33)
	Urgency of surgery	0.72	0.95	(0.73; 1.24)
	Tachycardia	<0.001	2.48	(1.70; 3.61)
Prolonged hospital stay	High-risk surgery	0.92	1.02	(0.72; 1.43)
	Severe congestive heart failure (NYHA >II)	0.99	1.00	(0.57; 1.73)
	Severe coronary artery disease	0.61	0.87	(0.50; 1.50)
	Significant carotid artery stenosis and/or history of stroke	0.40	0.81	(0.49; 1.33)
	Renal failure	0.05	1.65	(1.01; 2.71)
	Diabetes mellitus	0.65	1.10	(0.72; 1.69)
	Urgency of surgery	1.00	1.00	(0.78; 1.28)
	Tachycardia	<0.001	1.90	(1.37; 2.64)

The New England
Journal of Medicine

VOLUME 335 DECEMBER 5, 1996 NUMBER 23

EFFECT OF ATENOLOL ON MORTALITY AND CARDIOVASCULAR MORBIDITY AFTER NONCARDIAC SURGERY

DENNIS T. MANGANO, PH.D., M.D., ELIZABETH L. LAYUG, M.D., ARTHUR WALLACE, PH.D., M.D., AND IDA TATEO, M.S., FOR THE MULTICENTER STUDY OF PERIOPERATIVE ISCHEMIA RESEARCH GROUP*

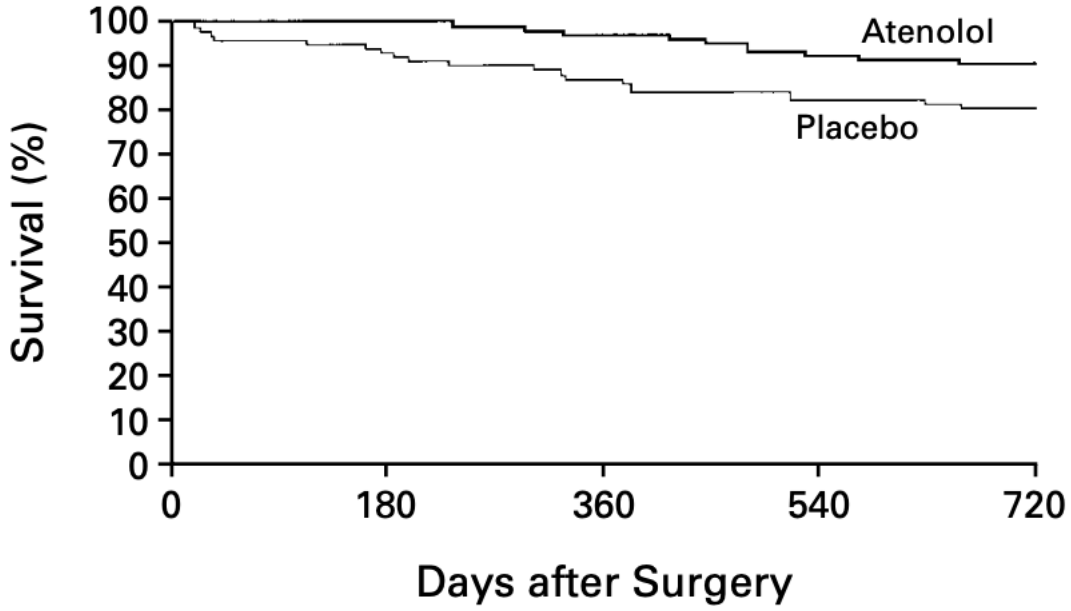


Figure 1. Overall Survival in the Two Years after Noncardiac Surgery among 192 Patients in the Atenolol and Placebo Groups Who Survived to Hospital Discharge.

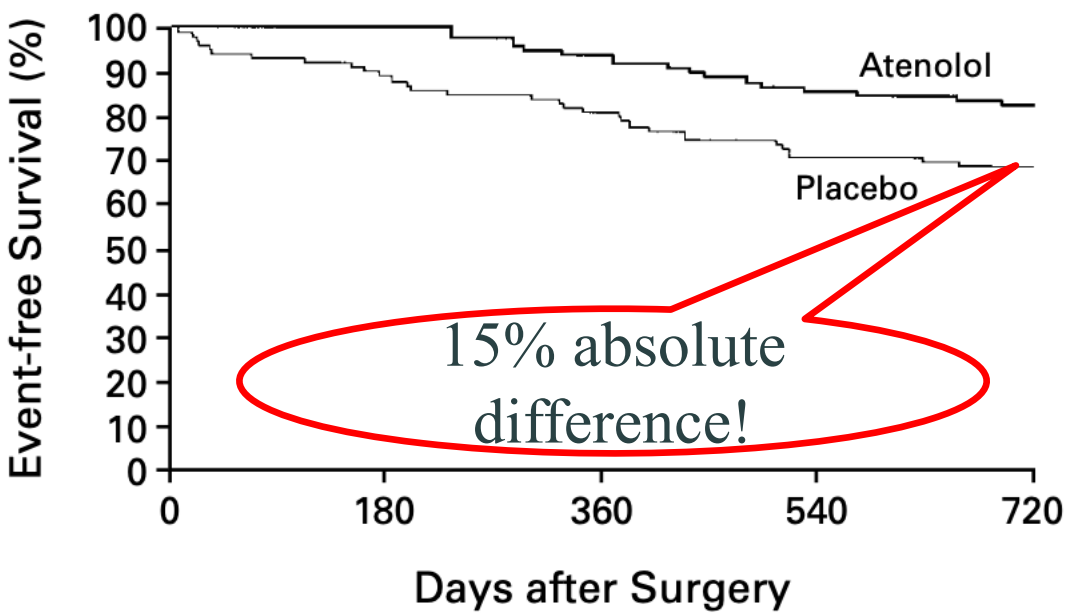


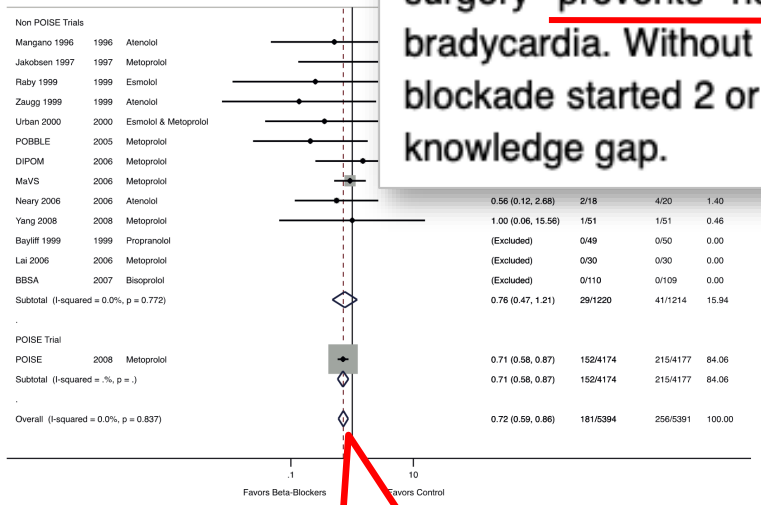
Figure 2. Event-free Survival in the Two Years after Noncardiac Surgery among 192 Patients in the Atenolol and Placebo Groups Who Survived to Hospital Discharge.

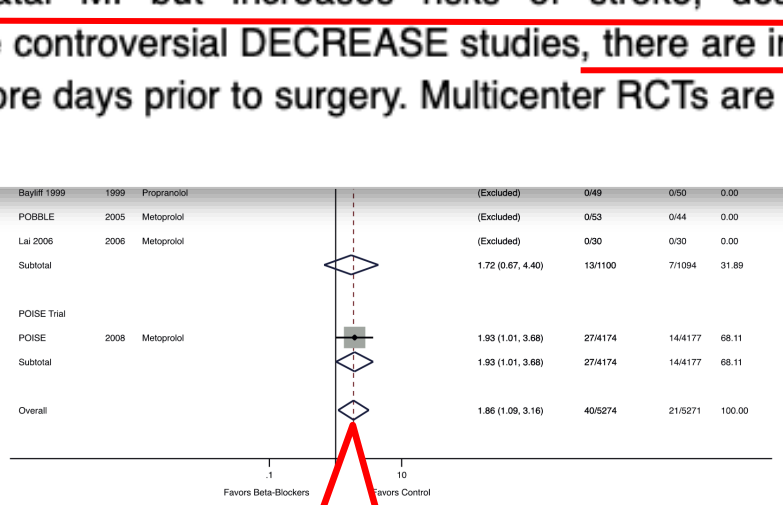
Perioperative Beta Blockade in Noncardiac Surgery: A Systematic Review for the 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery

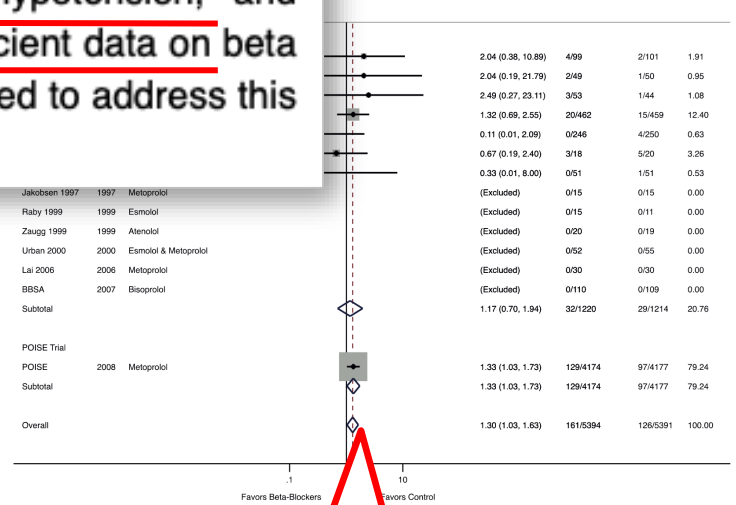
A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

(*Circulation*. 2014;130:2246-2264.)

CONCLUSIONS— Perioperative beta blockade started within 1 day or less before noncardiac surgery prevents nonfatal MI but increases risks of stroke, death, hypotension, and bradycardia. Without the controversial DECREASE studies, there are insufficient data on beta blockade started 2 or more days prior to surgery. Multicenter RCTs are needed to address this knowledge gap.







MI
(RR:0.72)

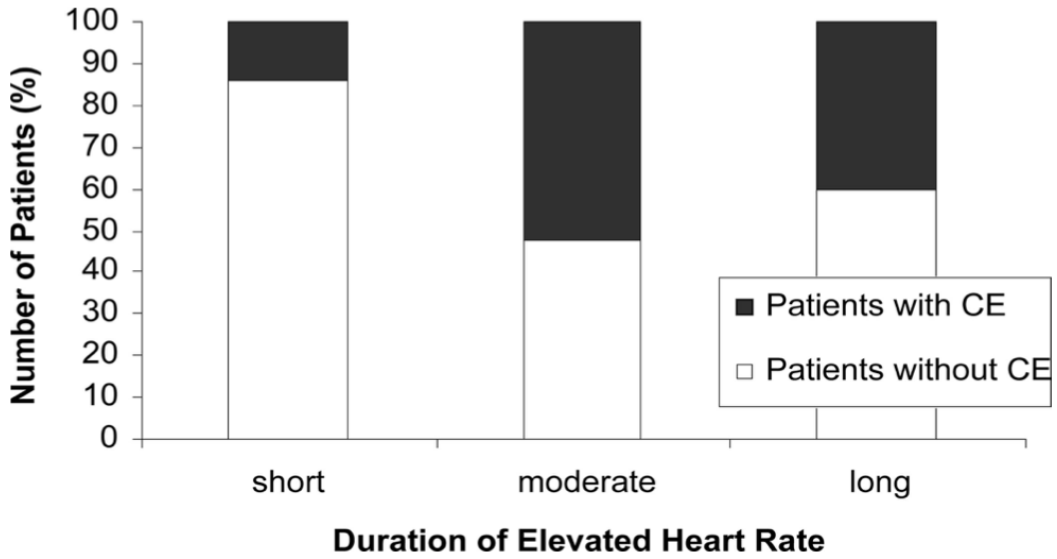
Stroke
(RR: 1.86)

Mortality
(RR: 1.30)

Impact of prolonged elevated heart rate on incidence of major cardiac events in critically ill patients with a high risk of cardiac complications*

Crit Care Med 2005 Vol. 33, No. 1

Olaf Sander, MD; Ingeborg D. Welters, MD, PhD; Pierre Foëx, MD, DPhil; John W. Sear, MD, BSc, PhD



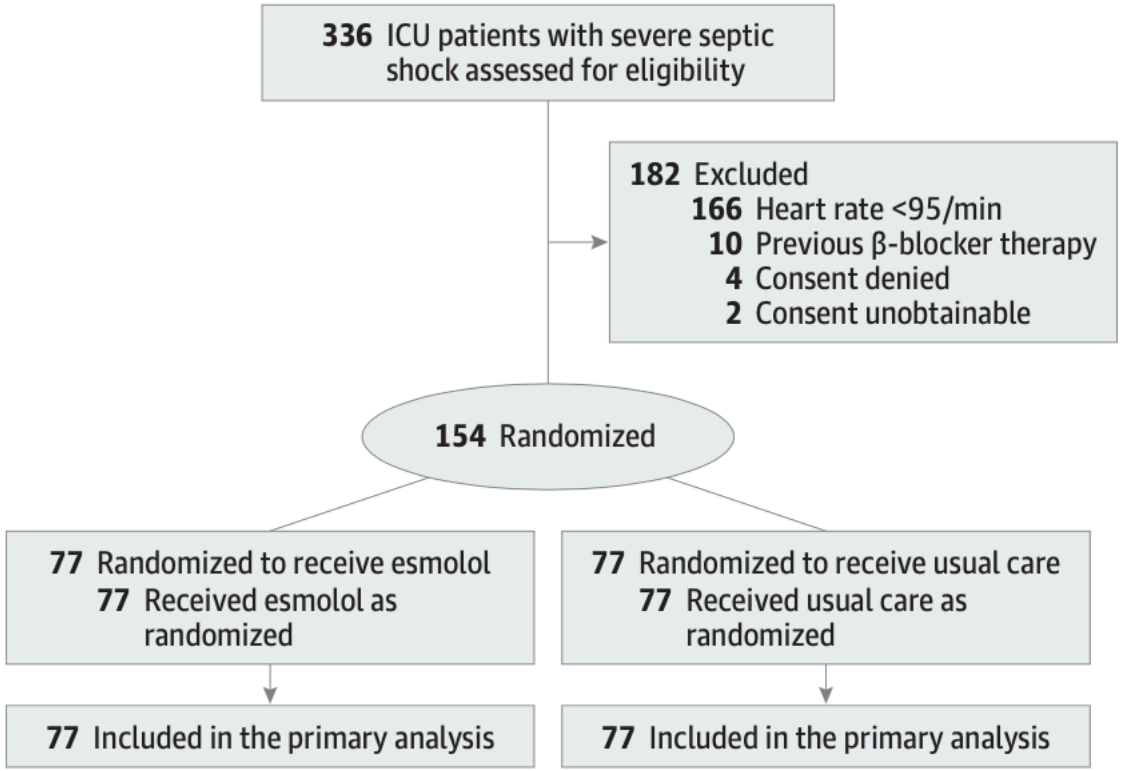
Our data provide evidence for an increased incidence of major cardiac events in critically ill, cardiac high-risk patients with an elevated heart rate of >95 beats/min for a prolonged period of at least 12 hrs within their intensive care unit stay.

Effect of Heart Rate Control With Esmolol on Hemodynamic and Clinical Outcomes in Patients With Septic Shock
A Randomized Clinical Trial

Andrea Morelli, MD; Christian Ertmer, MD; Martin Westphal, MD; Sebastian Rehberg, MD; Tim Kampmeier, MD; Sandra Ligges, PhD; Alessandra Orecchioni, MD; Annalia D'Egidio, MD; Fiorella D'Ippoliti, MD; Cristina Raffone, MD; Mario Venditti, MD; Fabio Guarracino, MD; Massimo Girardis, MD; Luigi Tritapepe, MD; Paolo Pietropaoli, MD; Alexander Mebazaa, MD; Mervyn Singer, MD, FRCP

JAMA. 2013;310(16):1683-1691.

Figure 1. Flow Chart



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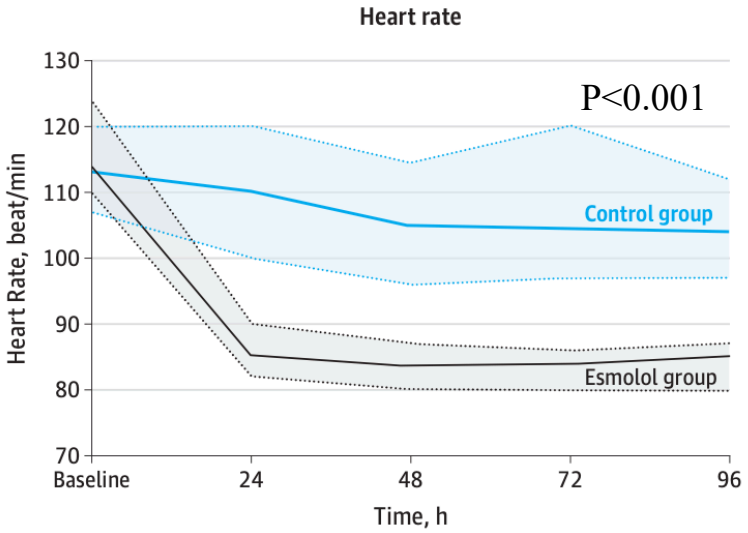

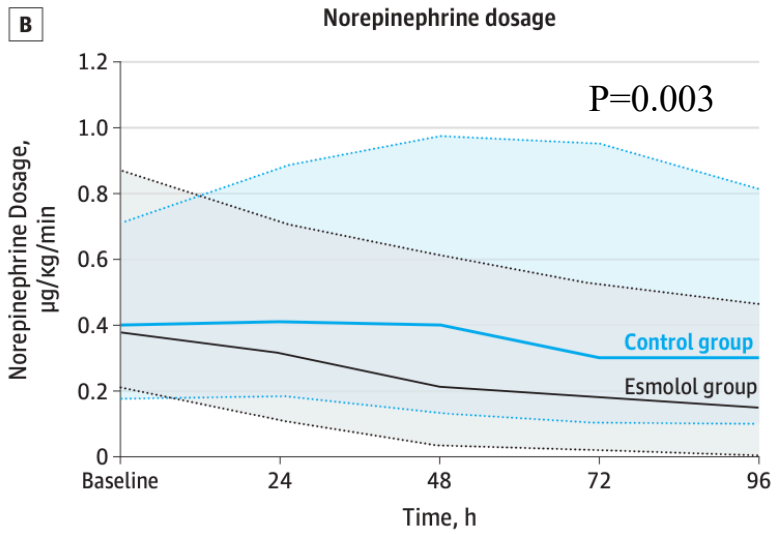

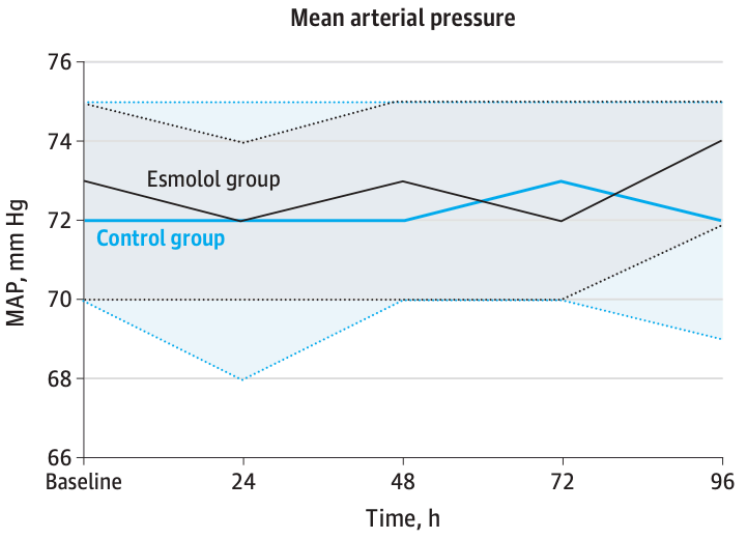

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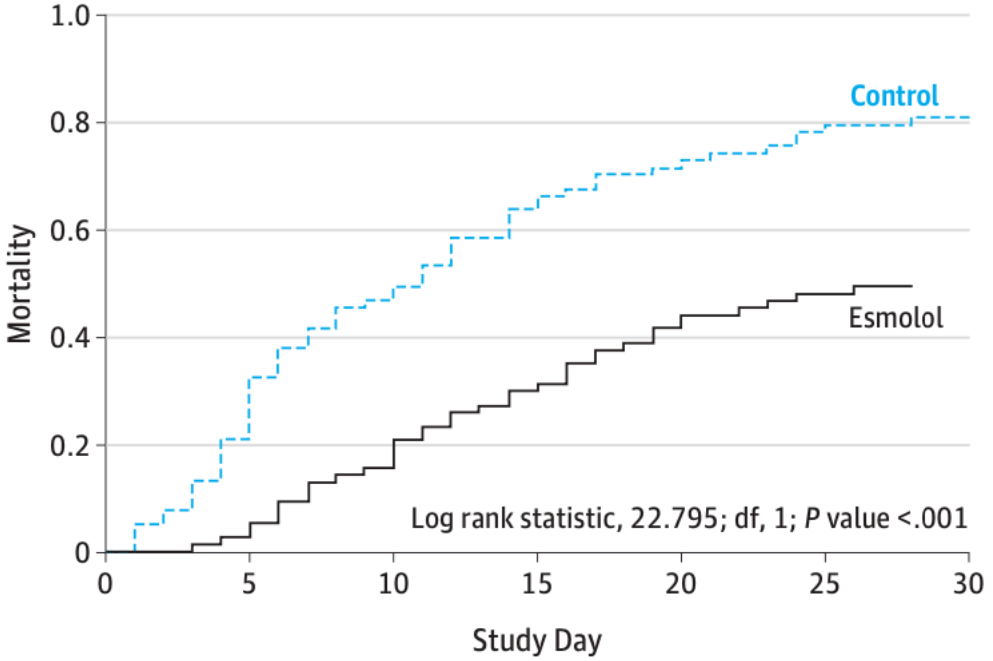

CONCLUSIONS AND RELEVANCE For patients in septic shock, open-label use of esmolol vs standard care was associated with reductions in heart rates to achieve target levels, without increased adverse events. The observed improvement in mortality and other secondary clinical outcomes warrants further investigation.

Effect of Ultrashort-Acting β-Blockers on Mortality in Patients With Sepsis With Persistent Tachycardia Despite Initial Resuscitation

A Systematic Review and Meta-analysis of Randomized Controlled Trials

Daisuke Hasegawa, MD; Ryota Sato, MD; Narut Prasitlumkum, MD; Kazuki Nishida, MD; Kunihiko Takahashi, PhD; Tomoaki Yatabe, MD, PhD; and Osamu Nishida, MD, PhD

CHEST 2021; 159(6):2289-2300

Study		Age, y	Men, %	APACHE II Score	Norepinephrine Dose at Baseline, μg/kg/min	28-d Mortality[a]
Kakihana et al[23]	Landiolol	67.8 ± 13.8	68.4	23.1 ± 8.9	0.2 ± 0.2	9/75 (12)
	Control	66.4 ± 15.2	50.7	22.2 ± 8.6	0.2 ± 0.2	15/75 (20)
Liu et al[21]	Esmolol	58.0 ± 15.0	58.0	18.8 ± 6.5	1.06 ± 1.43	31/50 (62.0)
	Control	57.0 ± 18.0	56.0	19.1 ± 7.5	0.76 ± 0.79	34/50 (68.0)
Wang et al[20]	Esmolol	67.2 ± 12.5	70.0	18.4 ± 6.3	Not reported	9/30 (30/0)
	Control	62.5 ± 14.5	60.0	15.7 ± 6.3	Not reported	11/30 (36.7)
Xinqiang et al[18]	Esmolol	61.4 ± 6.9	58.3	20.8 ± 3.1	0.38 ± 0.04	6/24 (25.0)
	Control	61.2 ± 6.4	54.2	21.2 ± 2.7	0.39 ± 0.04	15/24 (62.5)
Wang et al[19]	Esmolol	34 (21-60)[b]	63.3	21.2 ± 5.7	0.25 ± 0.16	12/30 (40.0)
	Control	38 (20-57)[b]	63.3	20.8 ± 5.6	0.28 ± 0.21	20/30 (66.7)
Yang et al[24]	Esmolol	51.0 ± 22.6	Not reported	20.1 ± 9.2	Not reported	Not reported
	Control	55.0 ± 25.4	Not reported	21.3 ± 8.3	Not reported	Not reported
Morelli et al[22]	Esmolol	66 (52-75)[c]	70.1	Not reported	0.38 (0.21-0.87)[d]	38/77 (49.4)
	Control	69 (58-78)[c]	68.8	Not reported	0.40 (0.18-0.71)[d]	62/77 (80.5)

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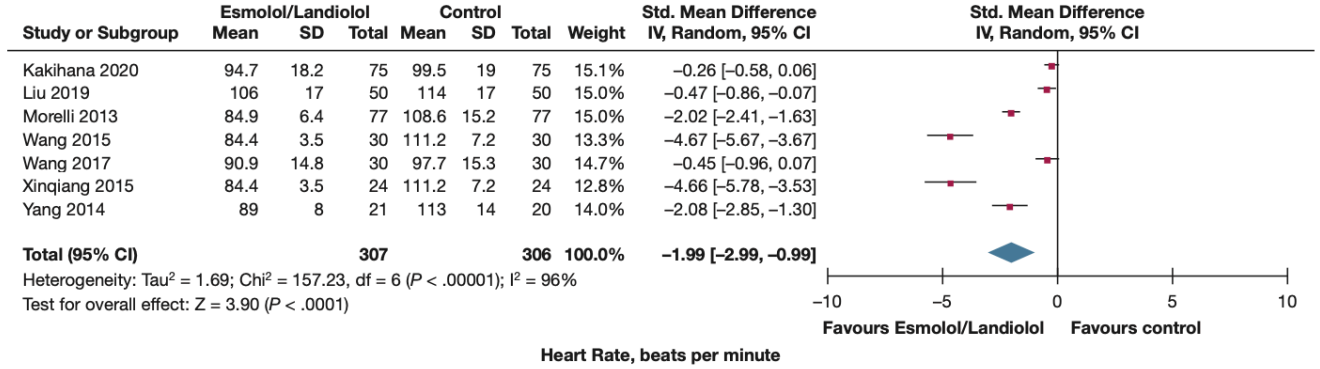


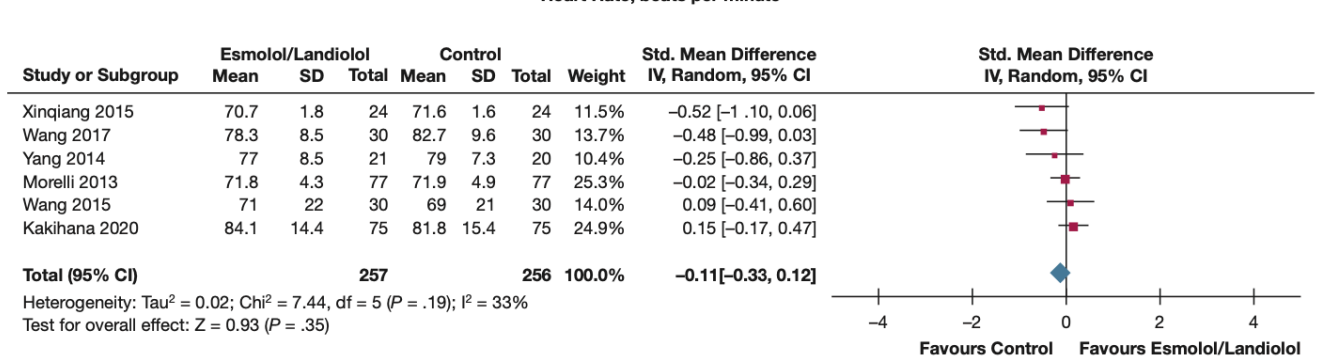
Study or Subgroup	Esmolol/Landiolol Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Kakihana 2020	94.7	18.2	75	99.5	19	75	15.1%	−0.26 [−0.58, 0.06]
Liu 2019	106	17	50	114	17	50	15.0%	−0.47 [−0.86, −0.07]
Morelli 2013	84.9	6.4	77	108.6	15.2	77	15.0%	−2.02 [−2.41, −1.63]
Wang 2015	84.4	3.5	30	111.2	7.2	30	13.3%	−4.67 [−5.67, −3.67]
Wang 2017	90.9	14.8	30	97.7	15.3	30	14.7%	−0.45 [−0.96, 0.07]
Xinqiang 2015	84.4	3.5	24	111.2	7.2	24	12.8%	−4.66 [−5.78, −3.53]
Yang 2014	89	8	21	113	14	20	14.0%	−2.08 [−2.85, −1.30]
Total (95% CI)			**307**			**306**	**100.0%**	**−1.99 [−2.99, −0.99]**

Heterogeneity: Tau² = 1.69; Chi² = 157.23, df = 6 (*P* < .00001); I² = 96%
Test for overall effect: Z = 3.90 (*P* < .0001)

Std. Mean Difference IV, Random, 95% CI
−10 −5 0 5 10
Favours Esmolol/Landiolol Favours control

Heart Rate, beats per minute

HR



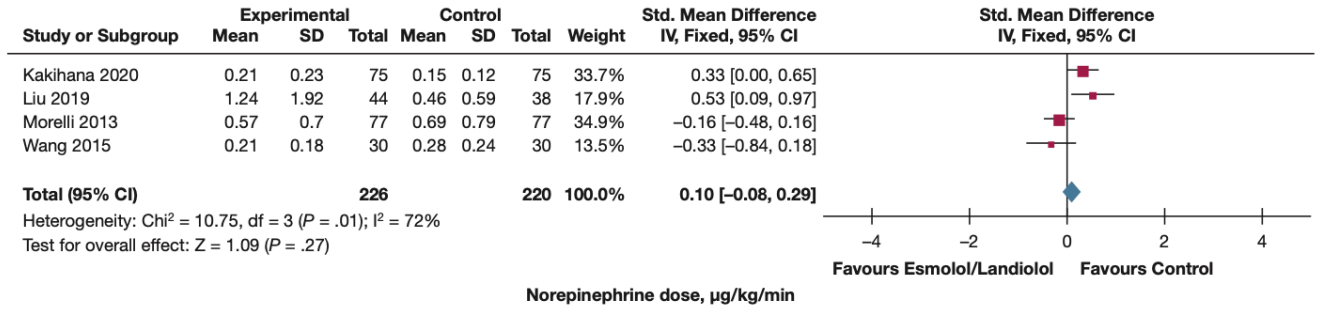
Study or Subgroup	Esmolol/Landiolol Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Xinqiang 2015	70.7	1.8	24	71.6	1.6	24	11.5%	−0.52 [−1 .10, 0.06]
Wang 2017	78.3	8.5	30	82.7	9.6	30	13.7%	−0.48 [−0.99, 0.03]
Yang 2014	77	8.5	21	79	7.3	20	10.4%	−0.25 [−0.86, 0.37]
Morelli 2013	71.8	4.3	77	71.9	4.9	77	25.3%	−0.02 [−0.34, 0.29]
Wang 2015	71	22	30	69	21	30	14.0%	0.09 [−0.41, 0.60]
Kakihana 2020	84.1	14.4	75	81.8	15.4	75	24.9%	0.15 [−0.17, 0.47]
Total (95% CI)			**257**			**256**	**100.0%**	**−0.11[−0.33, 0.12]**

Heterogeneity: Tau² = 0.02; Chi² = 7.44, df = 5 (*P* = .19); I² = 33%
Test for overall effect: Z = 0.93 (*P* = .35)

Std. Mean Difference IV, Random, 95% CI
−4 −2 0 2 4
Favours Control Favours Esmolol/Landiolol

Mean Arterial Pressure, mmHg

MAP



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Kakihana 2020	0.21	0.23	75	0.15	0.12	75	33.7%	0.33 [0.00, 0.65]
Liu 2019	1.24	1.92	44	0.46	0.59	38	17.9%	0.53 [0.09, 0.97]
Morelli 2013	0.57	0.7	77	0.69	0.79	77	34.9%	−0.16 [−0.48, 0.16]
Wang 2015	0.21	0.18	30	0.28	0.24	30	13.5%	−0.33 [−0.84, 0.18]
Total (95% CI)			**226**			**220**	**100.0%**	**0.10 [−0.08, 0.29]**

Heterogeneity: Chi² = 10.75, df = 3 (*P* = .01); I² = 72%
Test for overall effect: Z = 1.09 (*P* = .27)

Std. Mean Difference IV, Fixed, 95% CI
−4 −2 0 2 4
Favours Esmolol/Landiolol Favours Control

Norepinephrine dose, μg/kg/min

NE

CHEST 2021; 159(6):2289-2300

Effect of Ultrashort-Acting β-Blockers on Mortality in Patients With Sepsis With Persistent Tachycardia Despite Initial Resuscitation

A Systematic Review and Meta-analysis of Randomized Controlled Trials

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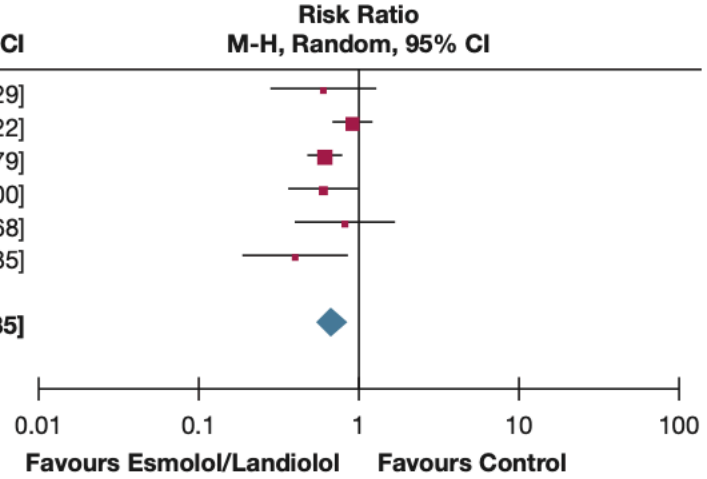
Mortality

Study or Subgroup	Esmolol/Landiolol Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Kakihana 2020	9	75	15	75	7.4%	0.60 [0.28, 1.29]
Liu 2019	31	50	34	50	29.3%	0.91 [0.68, 1.22]
Morelli 2013	38	77	62	77	33.2%	0.61 [0.48, 0.79]
Wang 2015	12	30	20	30	14.5%	0.60 [0.36, 1.00]
Wang 2017	9	30	11	30	8.2%	0.82 [0.40, 1.68]
Xinqiang 2015	6	24	15	24	7.5%	0.40 [0.19, 0.85]
Total (95% CI)		**286**		**286**	**100.0%**	**0.68 [0.54, 0.85]**
Total events	105		157			

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 7.21$, df = 5 ($P = .21$); $I^2 = 31\%$

Test for overall effect: $Z = 3.40$ ($P = .0007$)



INTERPRETATION: The use of ultrashort-acting β-blockers such as esmolol and landiolol in patients with sepsis with persistent tachycardia despite initial resuscitation was associated with significantly lower 28-day mortality.

CONFERENCE REPORTS AND EXPERT PANEL

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

GUIDELINES

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021

Intensive Care Med (2021) 47:1181–1247
https://doi.org/10.1007/s00134-021-06506-y

93 recommendations
0 on beta-blockade

EDITORIAL

Editorials represent the opinions of the authors and *JAMA* and not those of the American Medical Association.

Is There a Role for β-Blockade in Septic Shock?

Michael R. Pinsky, MD

important, caution needs to be stressed before applying these results to all patients in septic shock. The reasons for

ond, more than half of the septic shock candidates for this trial were excluded because they did not have tachycardia. It is un-

degree of sinoatrial node blockade. Third, because out-patient use of β-blockers is common, it is unknown how such patients, who were excluded from the trial, might have fared.

tant to define the patients for whom use of β-blockers is most indicated and those for whom these medications should be avoided.

Is there anything beyond the HR?

Journal of Intensive Care Medicine
Volume 24 Number 5
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10.1177/0885066609340519
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Sympathetic Overstimulation During Critical Illness: Adverse Effects of Adrenergic Stress

Martin W. Dünser, MD, and Walter R. Hasibeder, MD

during evolution. However, in critical illness an overshooting stimulation of the sympathetic nervous system may well exceed in time and scope its beneficial effects. Comparable to the overwhelming immune response during sepsis, adrenergic stress in critical illness may get out of control and cause adverse effects. Several organ systems may be affected. The heart seems to be most susceptible to sympathetic overstimulation. Detrimental effects include impaired diastolic function, tachycardia and tachyarrhythmia, myocardial ischemia, stunning, apoptosis and necrosis. Adverse catecholamine effects have been

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observed in other organs such as the lungs (pulmonary edema, elevated pulmonary arterial pressures), the coagulation (hypercoagulability, thrombus formation), gastrointestinal (hypoperfusion, inhibition of peristalsis), endocrinologic (decreased prolactin, thyroid and growth hormone secretion) and immune systems (immunomodulation, stimulation of bacterial growth), and metabolism (increase in cell energy expenditure, hyperglycemia, catabolism, lipolysis, hyperlactatemia, electrolyte changes), bone marrow (anemia), and skeletal muscles (apoptosis).

„Sympathetic Dysautonomia Syndrome (SDS)”

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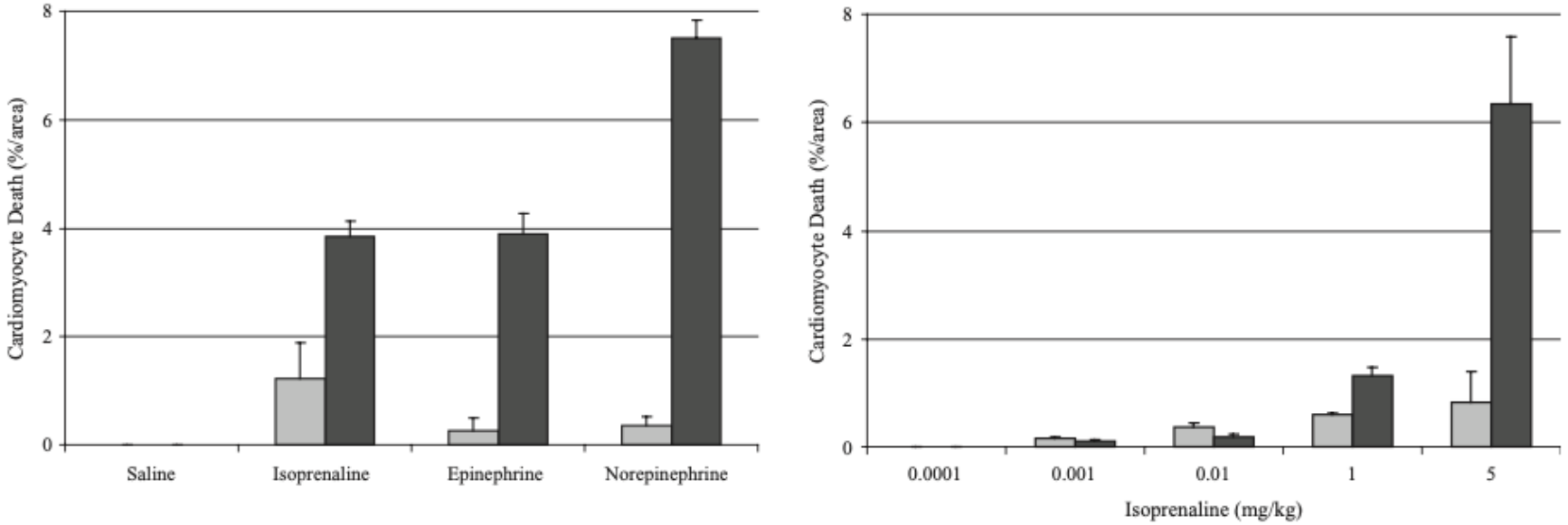


Figure 1. Extent of cardiomyocyte apoptosis (light grey) and necrosis (dark grey) in the left ventricular subendocardium after subcutaneous injection of various catecholamines at 20 mmol/kg each (left) and increasing dosages of isoprenaline (right) in male wistar rats (modified after Goldspink DF et al[70,71]). Apoptosis and necrosis were measured at their temporal (3 hours and 18 hours) and spatial (2 mm from apex) peaks. Data are mean values ± SEM. The rate of cardiomyocyte apoptosis was higher in nonsurvivors than in survivors after acute myocardial infarction[72] and predicted complications and adverse outcome after aortic valve replacement in patients with severe left ventricular hypertrophy.[73]

Are you surprised?

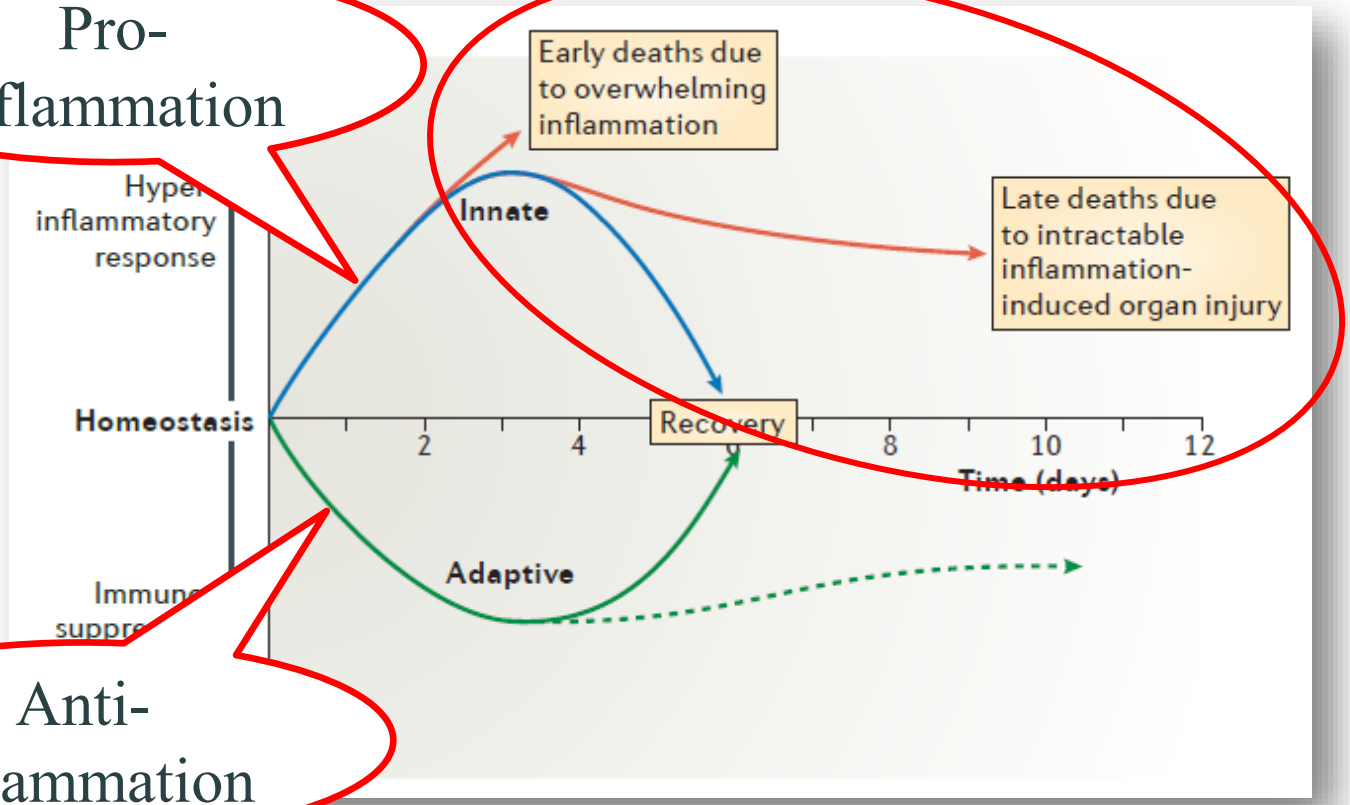
Sympathetic Dysautonomia Syndrome and/or Dysregulated Immune Response?

Sepsis-induced immunosuppression: from cellular dysfunctions to immunotherapy

Richard S. Hotchkiss[1], Guillaume Monneret[2] and Didier Payen[3]

Nature Reviews | Immunology Volume 13 | December 2013 | 862-874

Pro-inflammation

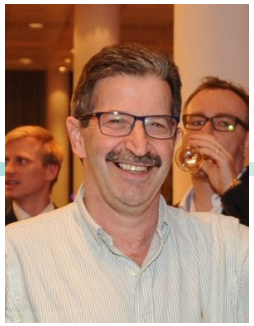


Anti-inflammation

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH



Organ dysfunction
+
dysregulated host response

Table 2. Terminology and *International Classification of Diseases* Coding

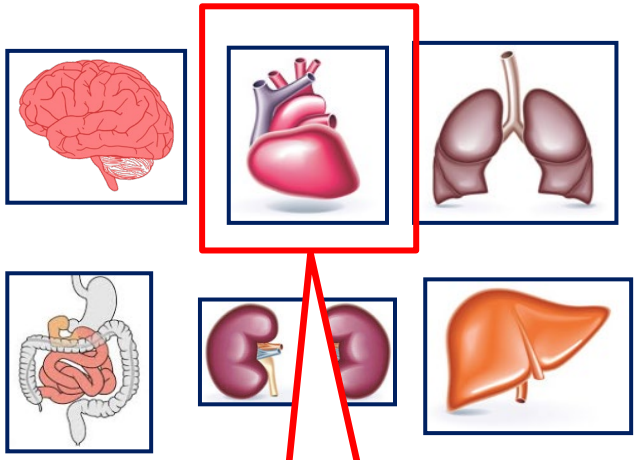
Current Guidelines and Terminology	Sepsis	Septic Shock
1991 and 2001 consensus terminology[9,10]	Severe sepsis Sepsis-induced hypoperfusion	Septic shock[13]
2015 Definition	Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection	Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality
ical[a]	Suspected or documented infection and an acute increase of ≥2 SOFA points (a proxy for organ dysfunction)	Sepsis[a] and vasopressor therapy needed to elevate MAP ≥65 mm Hg and lactate >2 mmol/L (18 mg/dL) despite adequate fluid resuscitation[13]
mended ary *ICD* des[a]		
ICD-9	995.92	785.52
ICD-10[a]	R65.20	R65.21
Framework for implementation for coding and research	Identify suspected infection by using concomitant orders for blood cultures and antibiotics (oral or parenteral) in a specified period[b] Within specified period around suspected infection[c]: 1. Identify sepsis by using a clinical criterion for life-threatening organ dysfunction 2. Assess for shock criteria, using administration of vasopressors, MAP <65 mm Hg, and lactate >2 mmol/L (18 mg/dL)[d]	

Life threatening organ dysfunction due to SDS?

Metabolism

Endocrinology

Skeletal Muscle



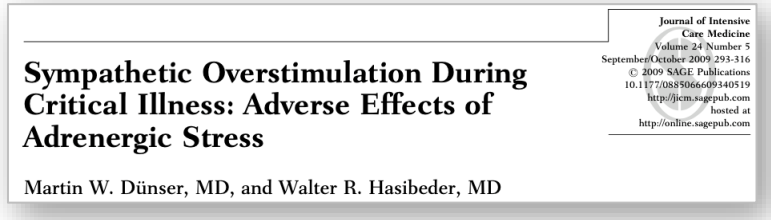
Coagulation System

Immune System

Bone Marrow

CIP

Heart ≠ CVS



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It is all: Dysregulated host response?

Metabolic phenotype of skeletal muscle in early critical illness

Zudin A Puthucheary,[1,2,3,4] Ronan Astin,[1,2] Mark J W Mcphail,[5,6] Saima Saeed,[7] Yasmin Pasha,[5] Danielle E Bear,[4,8,9,10] Despina Constantin,[11] Cristiana Velloso,[4] Sean Manning,[12,13,14] Lori Calvert,[15] Mervyn Singer,[3,7] Rachel L Batterham,[12,13] Maria Gomez-Romero,[16] Elaine Holmes,[16] Michael C Steiner,[17] Philip J Atherton,[11] Paul Greenhaff,[11] Lindsay M Edwards,[18] Kenneth Smith,[11] Stephen D Harridge,[4] Nicholas Hart,[10,19] Hugh E Montgomery[1,2]

Thorax 2018;**0**:1–10.

Table 2 Intramuscular cytokine concentrations on day 1 and day 7 of critical illness (n=29)

Cytokine	Day 1	Day 7	P values
TNF-α	11.2 (0.6–32.0)	0.6 (0.6–24.0)	0.375
TNFR1	0.34 (0.0–1.5)	1.1 (0.0–3.5)	**0.042***
TNFR2	0.01 (0.01–1.1)	1.4 (0.01–2.7)	0.083
IL-1α	6.8 (5.2–9.8)	7.6 (6.4–10.2)	0.715
HIF-1α	14.0 (9.8–22.5)	26.0 (21.0–69.8)	**<0.001***
IL-1β	28.4 (21.6–44.0)	30.8 (27.2–37.2)	0.229
IL-2	51.2 (0.9–66.0)	48.8 (0.9–56.8)	0.294
IL-4	150.0 (88.6–370.0)	242.0 (152.2–719.4)	0.206
IL-6	19.2 (6.8–59.8)	37.2 (12.2–84.2)	0.495
IL-8	21.6 (7.4–58.2)	52.8 (10.6–177.0)	0.100
IL-10	11.2 (0.37–41.8)	24.8 (14.8–298.4)	**0.005***
IFN-γ	6.8 (0.4–8.8)	8.4 (3.0–9.2)	0.353
MCP-1	84.8 (18.1–122.2)	116.0 (88.4–267.2)	0.168
EGF	22.8 (2.0–40.6)	21.2 (1.0–29.6)	0.301

Why read on?

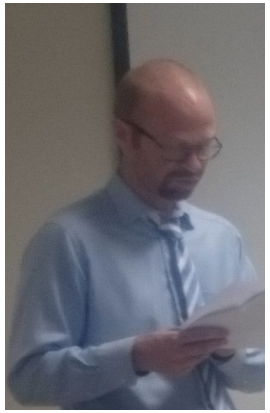
- Skeletal muscle wasting in critical care is associated with impaired lipid oxidation and reduced ATP bioavailability, driven by intramuscular inflammation and altered hypoxic signalling, which may account for the inconsistent outcome observed in the nutrition and exercise clinical trials.

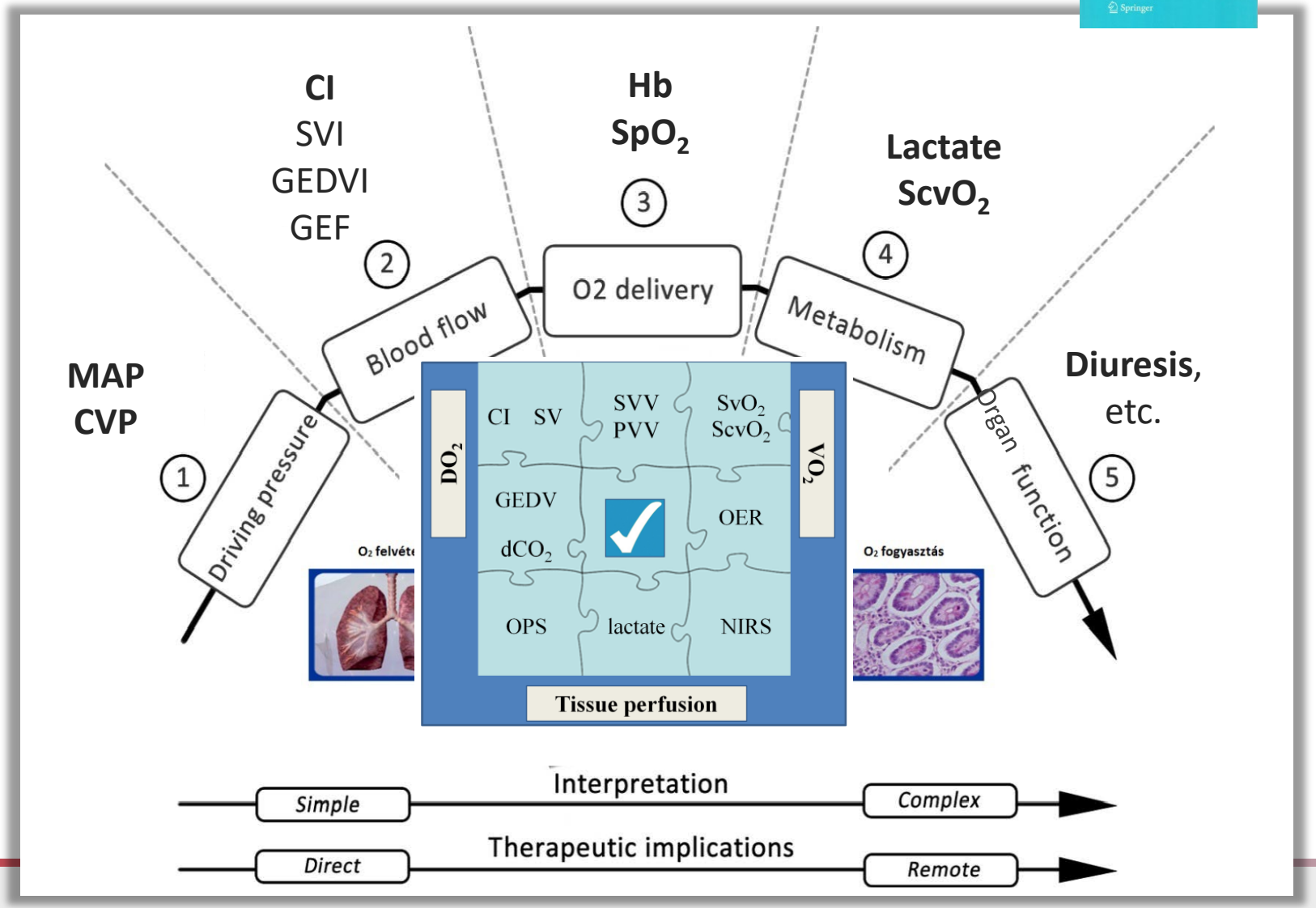
Final words on hemodynamics

The Hemodynamic Puzzle: Solving the Impossible?

K. Tánczos, M. Németh, and Z. Molnár

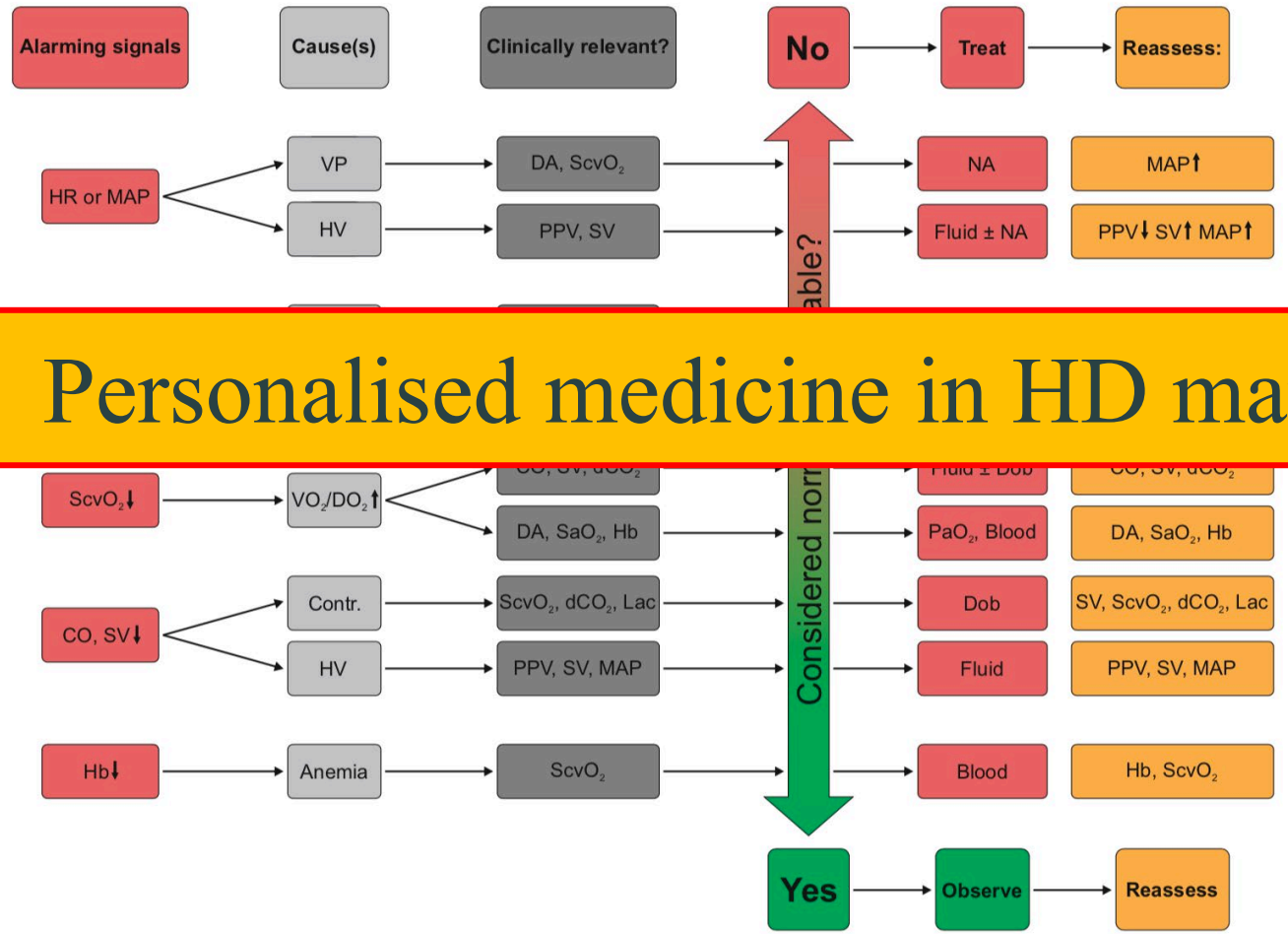
2014, pp 355-365





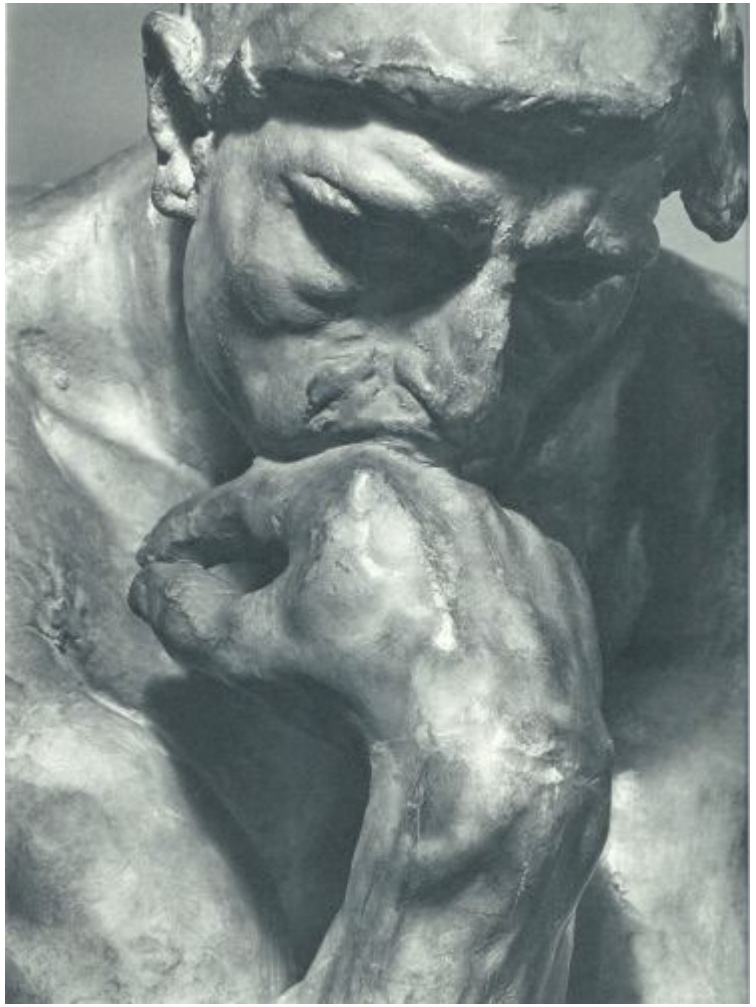
Intraoperative hypotension is just the tip of the iceberg: a call for multimodal, individualised, contextualised management of intraoperative cardiovascular dynamics

Zsolt Molnar[1,2], Jan Benes[3,4,5] and Bernd Saugel[6,7,*]



Personalised medicine in HD management

There is no replacement (yet):



Auguste Rodin: The Thinker