

JAN BLÁHA

Klinika anesteziologie, resuscitace
a intenzivní medicíny



INZULINOTERAPIE V INTENZIVNÍ PÉČI

... když tisíckrát
opakovaný blud
se stává pravdou

1. lékařská fakulta UK

Všeobecná fakultní nemocnice

v Praze

K danému tématu nemám žádný konflikt zájmů.

Blaħa J, et al. Perioperative tight glucose control reduces postoperative adverse events in non-diabetic cardiac surgery patients. *J Clin Endocrinol Metab.* 2015 Aug;100(8):3081-9.

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Bláħa J. Možnosti kontinuální monitorace glykémie u kriticky nemocných a léčby hyperglykémie s využitím inzulinových algoritmů. 88 s., *UK Praha, Praha, 2009*

Blaħa J, et al. Evaluation of the subcutaneous route for glucose monitoring in patients undergoing deep hypothermia. *Intensive Care Medicine, roč. 33, č. Suppl. 2, 2007, s. S263-S263*

Blaħa J, et al. Evaluation of the subcutaneous route for glucose monitoring in severe critically ill patients. *Book of abstracts, Praha, 2006, s. 12-12*



31. května - přejmenování **Ostravského kraje** na **kraj Moravskoslezský**

(Brněnského na Jihomoravský, Budějovického na Jihočeský, Jihlavského na Kraj Vysočina)



12. *prosince* - zemřel **JOSEF BICAN**, legendární fotbalový útočník (*1913)

2001



15. *ledna* - zahájen projekt Wikipedia.



11. *září* - teroristický útok na USA

7. *října* - začala válka v Afghánistánu

2001

The New England Journal of Medicine

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VOLUME 345

NOVEMBER 8, 2001

NUMBER 19



INTENSIVE INSULIN THERAPY IN CRITICALLY ILL PATIENTS

GREET VAN DEN BERGHE, M.D., Ph.D., PIETER WOUTERS, M.Sc., FRANK WEEKERS, M.D., CHARLES VERWAEST, M.D., FRANS BRUYNINCKX, M.D., MIET SCHETZ, M.D., Ph.D., DIRK VLASSELAERS, M.D., PATRICK FERDINANDE, M.D., Ph.D., PETER LAUWERS, M.D., AND ROGER BOUILLON, M.D., Ph.D.

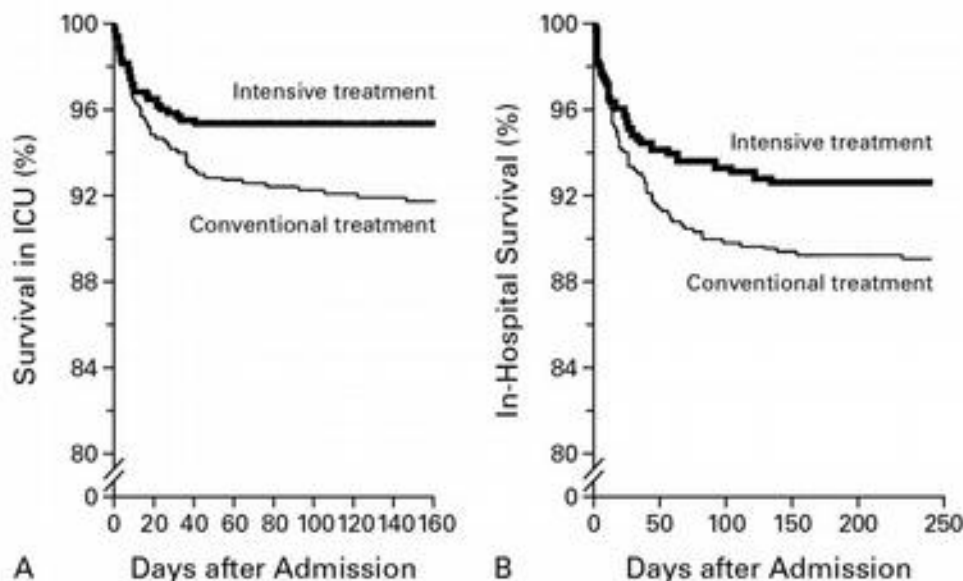


Figure 1. Kaplan-Meier Curves Showing Cumulative Survival of Patients Who Received Intensive Insulin Treatment or Conventional Treatment in the Intensive Care Unit (ICU).

Patients discharged alive from the ICU (Panel A) and from the hospital (Panel B) were considered to have survived. In both cases, the differences between the treatment groups were significant (survival in ICU, nominal $P=0.005$ and adjusted $P<0.04$; in-hospital survival, nominal $P=0.01$). P values were determined with the use of the Mantel-Cox log-rank test.

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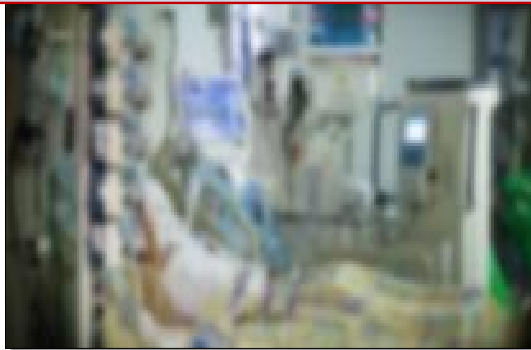
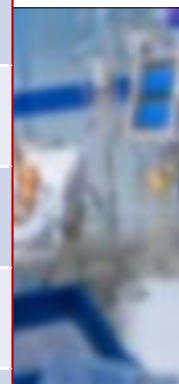
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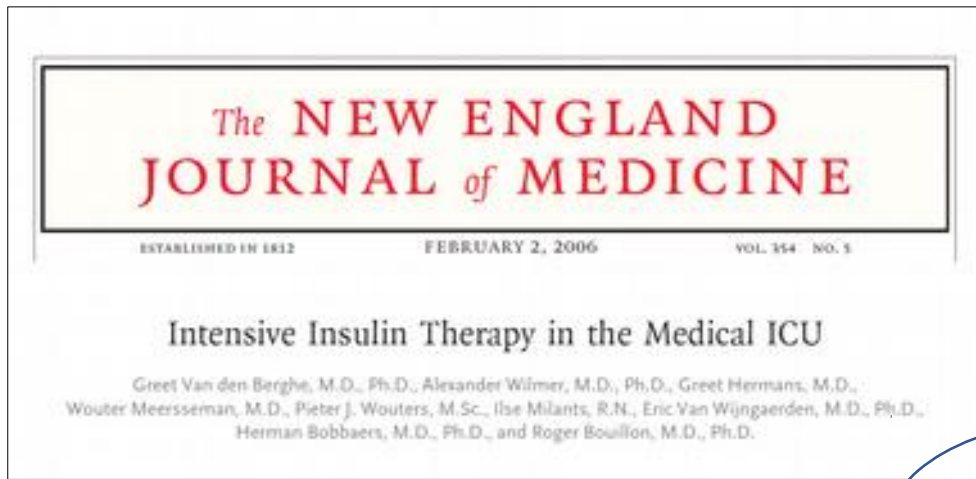
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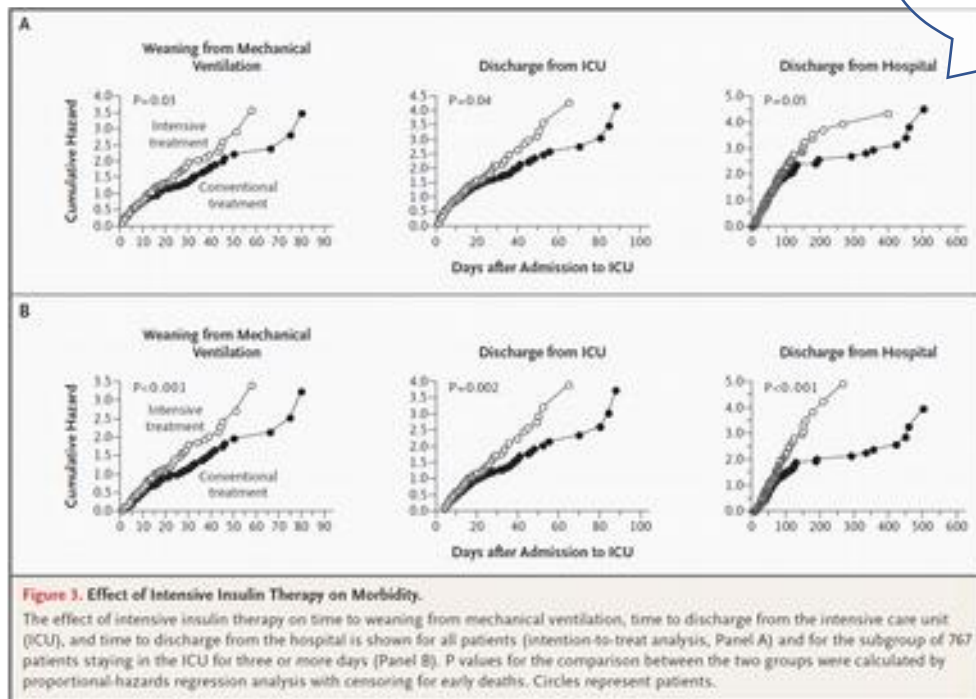
Low, Donald E.; Allum, William; De Manzoni, Giovanni; et al.
Guidelines for Perioperative Care in Esophagectomy: Enhanced Recovery After Surgery (ERAS((R))) Society Recommendations.
WORLD JOURNAL OF SURGERY (2019)



	doporučení
Surviving Sepsis Campaign	4.4-6.1 (<8.3)
American Diabetes Association	co nejbliže 6.1
American College of Endocrinology	<6.1
American College of Physicians	<10
European Society of Intensive Care Medicine	4.4-6.1



Pouze když >3 dny

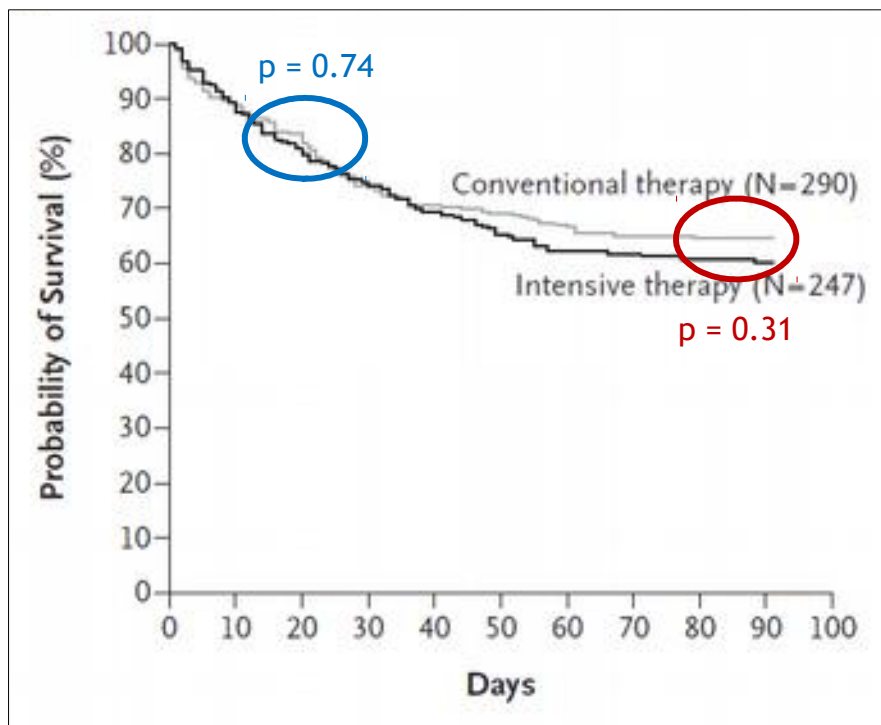


2008

ORIGINAL ARTICLE

Intensive Insulin Therapy and Pentastarch Resuscitation in Severe Sepsis

Frank M. Brunkhorst, M.D., Christoph Engel, M.D., Frank Bloos, M.D., Ph.D., Andreas Meier-Hellmann, M.D., Max Ragaller, M.D., Norbert Weiler, M.D., Onnen Moerer, M.D., Matthias Gruendling, M.D., Michael Oppert, M.D., Stefan Grond, M.D., Derk Olthoff, M.D., Ulrich Jaschinski, M.D., Stefan John, M.D., Rolf Rossaint, M.D., Tobias Welte, M.D., Martin Schaefer, M.D., Peter Kern, M.D., Evelyn Kuhnt, M.Sc., Michael Kiehntopf, M.D., Christiane Hartog, M.D., Charles Natanson, M.D., Markus Loeffler, M.D., Ph.D., and Konrad Reinhart, M.D., for the German Competence Network Sepsis (SepNet)



2008

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Table 3. Adverse and Serious Adverse Events.*

Variable	Insulin Therapy			Fluid Resuscitation		
	Conventional (N=200)	Intensive (N=247)	P Value†	Ringer's Lactate (N=275)	HES (N=262)	P Value‡
Adverse event						
Patients with at least one adverse event	80	55	<u><0.001</u>	40	40	0.81
No. of patients	80	55		40	40	
Percent (95% CI)	14.9 (11.9–17.9)	8.6 (5.4–11.9) 22.3 (17.1–27.5)		14.5 (10.4–18.7)	15.3 (10.9–19.6)	
Hypoglycemia (≤40 mg/dl)			<u><0.001</u>			0.85
No. of patients	54	42		27	27	
Percent (95% CI)	10.1 (7.5–12.6)	4.1 (1.9–6.4) 17.0 (12.3–21.7)		9.8 (6.3–13.3)	10.3 (6.6–14.0)	
Bleeding			0.30			0.45
No. of patients	23	13		10	13	
Percent (95% CI)	4.3 (2.6–6.0)	3.4 (1.4–5.6) 5.3 (2.5–8.1)		3.7 (2.1–5.9)	5.0 (2.3–7.6)	
Other§						0.11
No. of patients	10	5		8	2	
Percent (95% CI)	1.9 (0.7–3.0)	1.7 (0.2–3.2) 2.0 (0.3–3.8)		2.9 (0.9–4.9)	0.8 (0–1.8)	
Serious adverse event						
Patients with at least one serious adverse event			0.01			0.63

Počet pacientů s ≥1 nežádoucím účinkem
9 vs. 22 (%)

Počet pacientů s hypoglykémií <40 mg/dl
4 vs. 17 (%)



Jean-Charles Preiser
Philippe Devos
Sergio Ruiz-Santana
Christian Mélot
Djillali Annane
Johan Groeneveld
Gaetano Iapichino
Xavier Lefevre
Gérard Nitenberg
Pierre Singer
Jan Wernerman
Michael Joannidis
Adela Stecher
René Chiolerio

A prospective randomised multi-centre controlled trial on tight glucose control by intensive insulin therapy in adult intensive care units: the Glucontrol study

Výskyt hypoglykémie
3 vs. 9 (%)

Table 3 Outcome data, treatment-related variables, nutritional management and therapeutic variables glucose control

	Group 1 BG target 7.8–10.0 mmol/L N = 542	Group 2 BG target 4.4–6.1 mmol/L N = 536	p Value
Glucose control and insulin therapy			
Blood glucose concentrations calculated from all readings (mmol/L) [median (IQR)]	8.0 (7.1–9.0)	6.5 (6.0–7.2)	<0.0001
Blood glucose concentrations calculated from morning readings (mmol/L) [median (IQR)]	7.7 (6.7–8.8)	6.1 (5.5–6.8)	<0.0001
Rate of hypoglycaemia calculated from BG % (n)	2.7 (13)	8.7 (44)	<0.0001
Estimated duration of hypoglycaemia (min) in patients presenting hypoglycaemic episode [median (IQR)]	59 (37–76)	52 (13–135)	0.887
Proportion of time in range (% of all BG readings)	34.7 (164)	42.8 (196)	0.0118
(% of morning BG)	39.5 (187)	45.1 (207)	0.0856
p value (difference between all readings and morning BG)	NS	NS	
Median of the proportion of time in range (%) (IQR)	34.3 (18.5–50.1)	39.3 (26.2–53.6)	
Proportion of time below the range (% of all BG readings)	50.3 (238)	5.9 (27)	<0.0001
(% of morning BG)	51.2 (242)	5.2 (24)	<0.0001
p value (difference between all readings and morning BG)	NS	NS	<0.0001
Median of the proportion of time below range (%) (IQR)	44.7 (24.3–75.8)	5.1 (1.1–9.2)	
Proportion of time above the range (% of all BG readings)	14.9 (71)	51.3 (236)	<0.0001
(% of morning BG)	9.3 (44)	49.7 (228)	<0.0001
p value (difference between all readings and morning BG)	0.0072	NS	<0.0001
Median of the proportion of time above range (%) (IQR)	7.6 (0.0–25.3)	52.6 (39.2–67.4)	
AUC _{high} (hour mmol L ⁻¹) [median(IQR)]	4.1 (0–40.2)	79.3 (25.9–181.1)	<0.0001
AUC _{low} (hour mmol L ⁻¹) [median(IQR)]	42.3 (12.8–125.9)	2.1 (0.2–6.1)	<0.0001
Hyperglycaemic index (mmol L ⁻¹) [median(IQR)]	0.06 (0.00–0.33)	0.78 (0.39–1.39)	<0.0001
Hypoglycaemic index (mmol L ⁻¹) [median (IQR)]	0.44 (0.22–0.94)	0.33 (0.03–0.85)	<0.0001

2009

The NEW ENGLAND
JOURNAL of MEDICINE

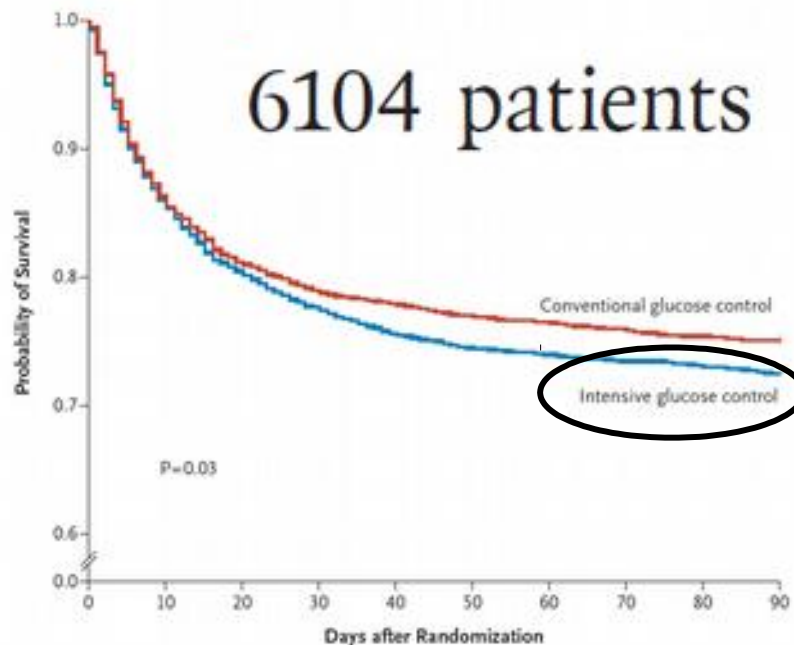
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MARCH 26, 2009

VOL. 360 · NO. 13

Intensive versus Conventional Glucose Control
in Critically Ill Patients

The NICE-SUGAR Study Investigators*



No. at Risk

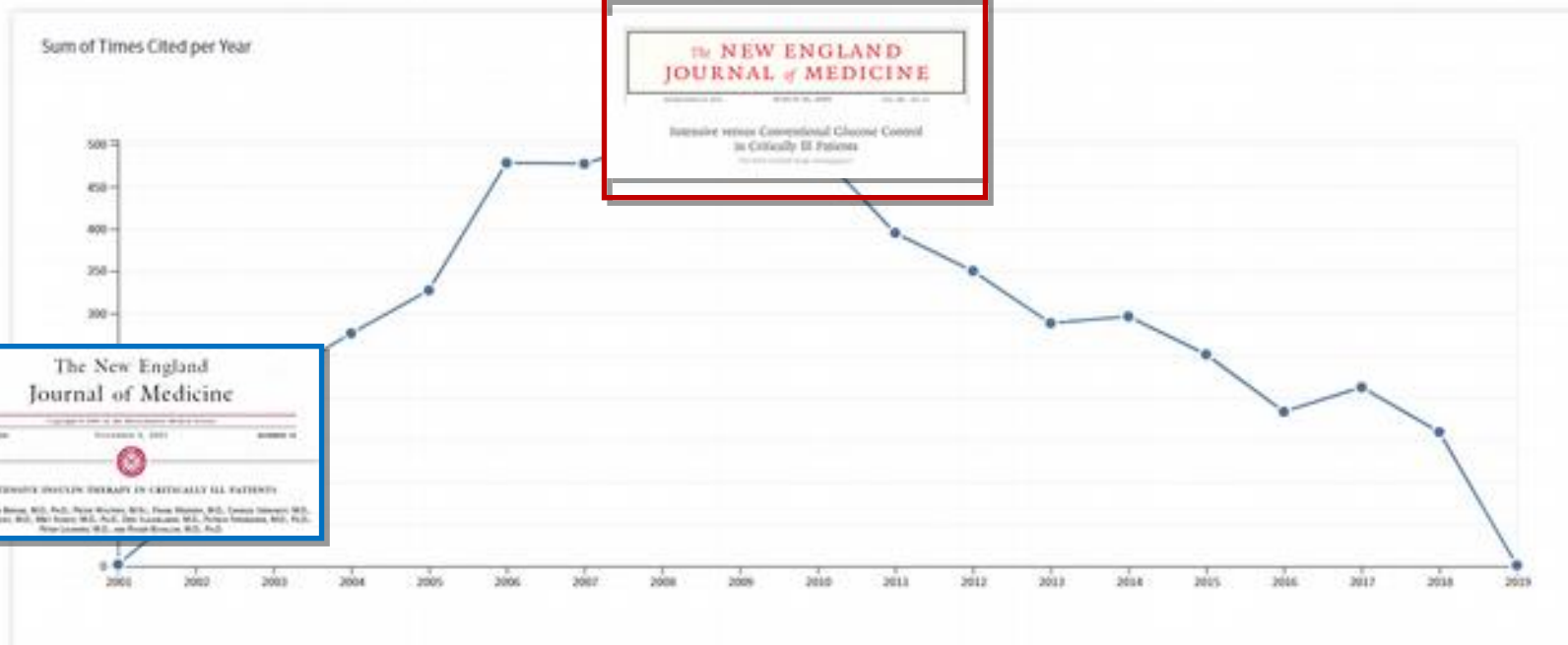
Conventional control	3014	2379	2304	2261
Intensive control	3016	2337	2227	2182

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CONFERENCE REPORTS AND EXPERT PANEL



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

Andrew Rhodes^{1*}, Laura E. Evans², Waleed Alhazzani³, Mitchell M. Levy⁴, Massimo Antonelli⁵, Ricard Ferrer⁶, Anand Kumar⁷, Jonathan E. Sevransky⁸, Charles L. Sprung⁹, Mark E. Nunnally², Bram Rochwerg³, Gordon D. Rubenfeld¹⁰, Derek C. Angus¹¹, Djillali Annane¹², Richard J. Beale¹³, Geoffrey J. Bellinghan¹⁴, Gordon R. Bernard¹⁵, Jean-Daniel Chiche¹⁶, Craig Coopersmith⁸, Daniel P. De Backer¹⁷, Craig J. French¹⁸, Seitaro Fujishima¹⁹, Herwig Gerlach²⁰, Jorge Luis Hidalgo²¹, Steven M. Hollenberg²², Alan E. Jones²³, Dilip R. Karnad²⁴, Ruth M. Kleinpell²⁵, Younsuk Koh²⁶, Thiago Costa Lisboa²⁷, Flavia R. Machado²⁸, John J. Marini²⁹, John C. Marshall³⁰, John E. Mazuski³¹, Lauralyn A. McIntyre³², Anthony S. McLean³³, Sangeeta Mehta³⁴, Rui P. Moreno³⁵, John Myburgh³⁶, Paolo Navalesi³⁷, Osamu Nishida³⁸, Tiffany M. Osborn³¹, Anders Perner³⁹, Colleen M. Plunkett²⁵, Marco Ranieri⁴⁰, Christa A. Schorr²², Maureen A. Seckel⁴¹, Christopher W. Seymour⁴², Lisa Shieh⁴³, Khalid A. Shukri⁴⁴, Steven Q. Simpson⁴⁵, Mervyn Singer⁴⁶, B. Taylor Thompson⁴⁷, Sean R. Townsend⁴⁸, Thomas Van der Poll⁴⁹, Jean-Louis Vincent⁵⁰, W. Joost Wiersinga⁴⁹, Janice L. Zimmerman⁵¹ and R. Phillip Dellinger²²

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

O. GLUCOSE CONTROL

zahájit při >10 mmol/l
a držet <10 mmol/l

1. We recommend a protocolized approach to blood glucose management in ICU patients with sepsis, commencing insulin dosing when two consecutive blood glucose levels are >180 mg/dL. This approach should target an upper blood glucose level ≤ 180 mg/dL rather than an upper target blood glucose level ≤ 110 mg/dL (strong recommendation, high quality of evidence).

Several medical organizations, including the American Association of Clinical Endocrinologists, American Diabetes Association, American Heart Association, American College of Physicians, and Society of Critical Care Medicine, have published consensus statements for glycemic control of hospitalized patients [463, 465]. These statements usually targeted glucose levels between 140 and 180 mg/dL. Because there is no evidence that targets between 140 and 180 mg/dL are different from targets of 110–140 mg/dL, the present recommendations use an upper target blood glucose ≤ 180 mg/dL without a lower target other than hypoglycemia. Stricter ranges, such as 110–140 mg/dL, may be appropriate for selected patients if this can be achieved without significant hypoglycemia [463, 465].

Protože není evidence, že by rozmezí 7.8-10 bylo lepší než 6.1-7.8...

463. American Diabetes Association (2014) Standards of medical care in diabetes—2014. Diabetes Care 37(Suppl 1):S14–S80

465. Qaseem A, Chou R, Humphrey LL (2014) Shekelle P; Clinical Guidelines Committee of the American College of Physicians. Inpatient glycemic control: best practice advice from the Clinical Guidelines Committee of the American College of Physicians. Am J Med Qual 29(2):95–98

mmol/l	mg/dl
4.4	= 80
6.1	= 110
7.8	= 140
8.3	= 150
10	≈ 180

	Před NICE-SUGAR	Po NICE-SUGAR
Surviving Sepsis Campaign	4.4-6.1 (<8.3)	<10
Society of Critical Care Medicine		začít při 8.3
American Diabetes Association	co nejblíže 6.1	7.8-10
American College of Endocrinology	<6.1	7.8-10
American College of Physicians	<10	7.8-11
European Society of Intensive Care Medicine	4.4-6.1	4.4-7.8 (??)

Dellinger *et al*: *Crit Care Med* 2013, 41(2):580-637.

Jacobi *et al*: *Crit Care Med* 2012, 40(12):3251-3276.

Krinsley JS, *et al*. *Crit Care* 2013, 17(2):R37.

ADA. *Diabetes Care* 2013, 36 Suppl 1:S11-66.

Handelsman Y *et al*: *Endocr Pract* 2015, 21 Suppl 1:1-87.

Standards of medical care in diabetes—2014. American Diabetes Association. *Diabetes Care* 37(Suppl 1):S14-S80

V TOMTO DOMĚ ZCELA
JISTĚ A PROKAZATELNĚ
NIKDY NEŽIL A NETVOŘIL
PAN
JÁRA CIMRMAN

**Můžete s tím nesouhlasit,
dá se o tom pochybovat,
ale to je jediné, co se s tím dá dělat...**



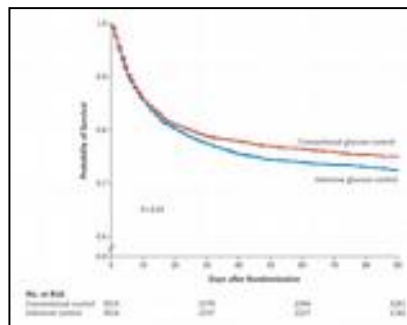
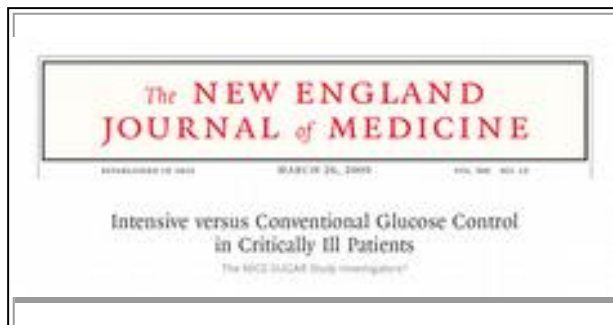
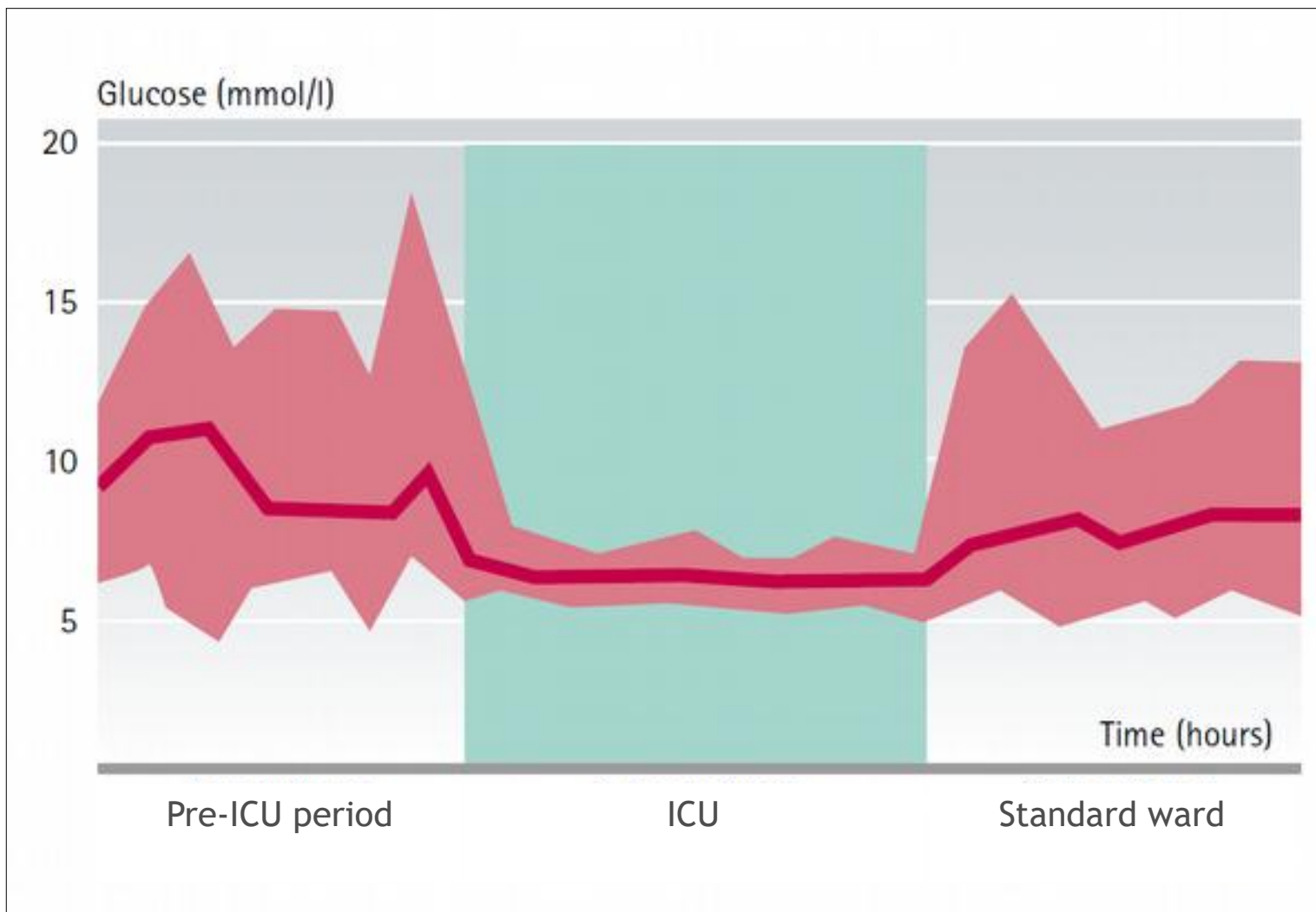


Table 3. Outcomes and Adverse Events.[☆]

Outcome Measure	Intensive Glucose Control	Conventional Glucose Control	Odds Ratio or Absolute Difference (95% CI) [†]	Statistical Test	P Value
Death — no. of patients/total no. (%)				Logistic regression	
At day 90	829/3010 (27.5)	751/3012 (24.9)	1.14 (1.02 to 1.28)		0.02
At day 28	670/3010 (22.3)	627/3012 (20.8)	1.09 (0.96 to 1.23)		0.17
Days in ICU — median (IQR)	6 (2 to 11)	6 (2 to 11)	0	Log-rank test	0.84
Days in hospital — median (IQR)	17 (8 to 35)	17 (8 to 35)	0	Log-rank test	0.86
Mechanical ventilation — no. of patients/total no. (%)	2894/3014 (96.0)	2872/3014 (95.3)	0.7 (-0.3 to 1.76)	Pearson's test	0.17
Days of mechanical ventilation	6.6±6.6	6.6±6.5	0	Wilcoxon rank-sum test	0.56
Renal-replacement therapy — no. of patients/total no. (%)	465/3014 (15.4)	438/3014 (14.5)	0.9 (-0.9 to 2.7)	Pearson's test	0.34
Days of renal-replacement therapy	0.8±2.6	0.8±2.8	0	Wilcoxon rank-sum test	0.39



Adaptováno z Amrein K, Glucose Management; Berlin 2011)

ORIGINAL ARTICLE

Hypoglycemia and Risk of Death in Critically Ill Patients

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pulmonary & critical care

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Sep
23
2012

Intensive glucose control probably kills, says NICE-SUGAR post-hoc (NEJM)

Critical Care, GI and Nutrition, Randomized Controlled Trials

Add comments

sociation exhibits a dose-response relationship and is strongest for death from distributive shock. However, these data cannot prove a causal relationship. (Funded by the Australian National Health and Medical Research Council and others; NICE-SUGAR ClinicalTrials.gov number, NCT00220987.)



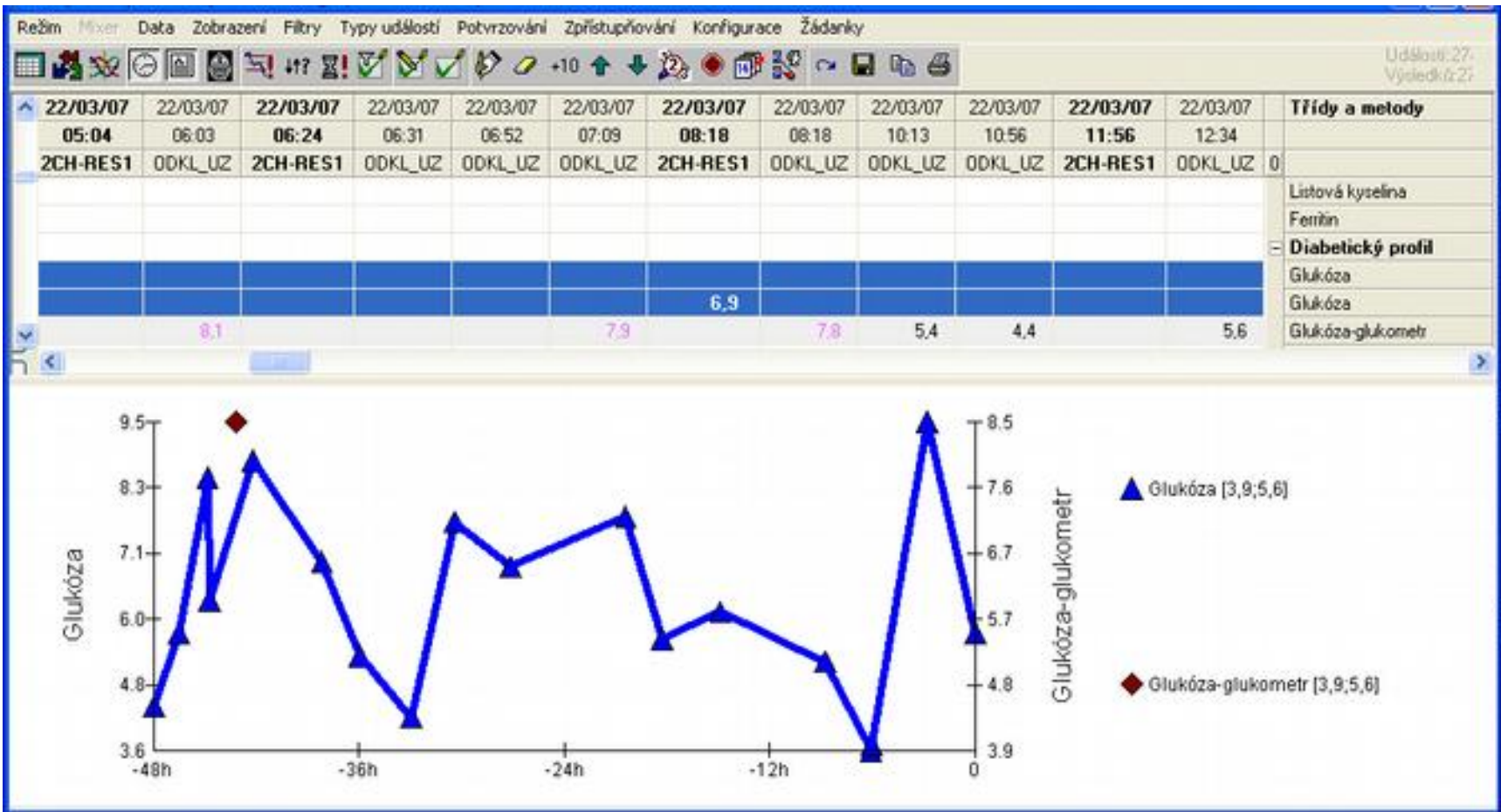
Kardiochirurgie (2007-8)

Výskyt hypoglykémie u 985 nonDM pacientů (%)

Pooperační JIP		
hypoglykémie <4.4	hypoglykémie <3.3	hypoglykémie <2.2
10,5	1,4	0,02

Standardní oddělení		
hypoglykémie <4.4	hypoglykémie <3.3	hypoglykémie <2.2
3,9	2,3	0,1

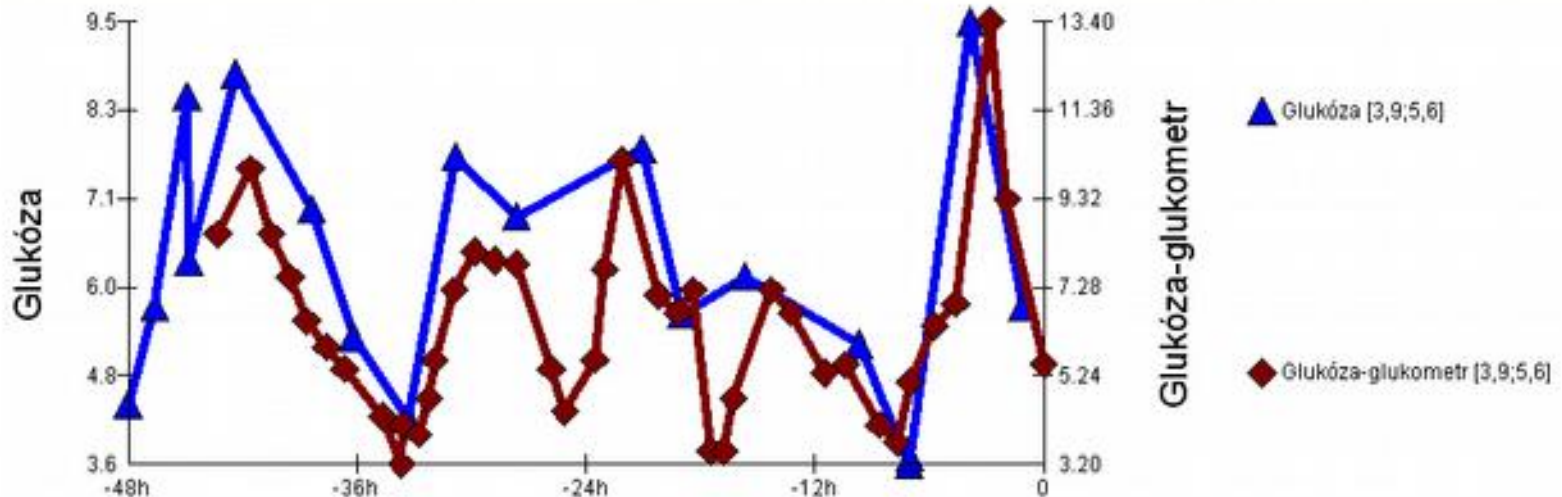
(hladiny glykémie v mmol/l)

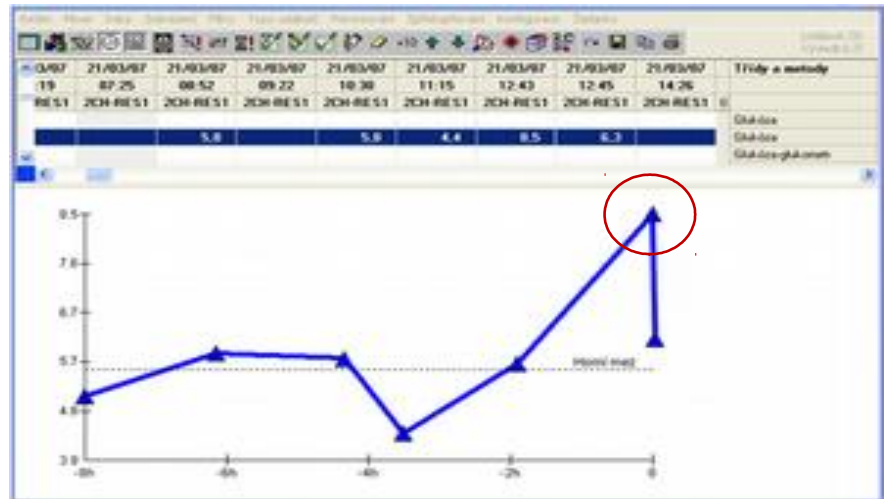
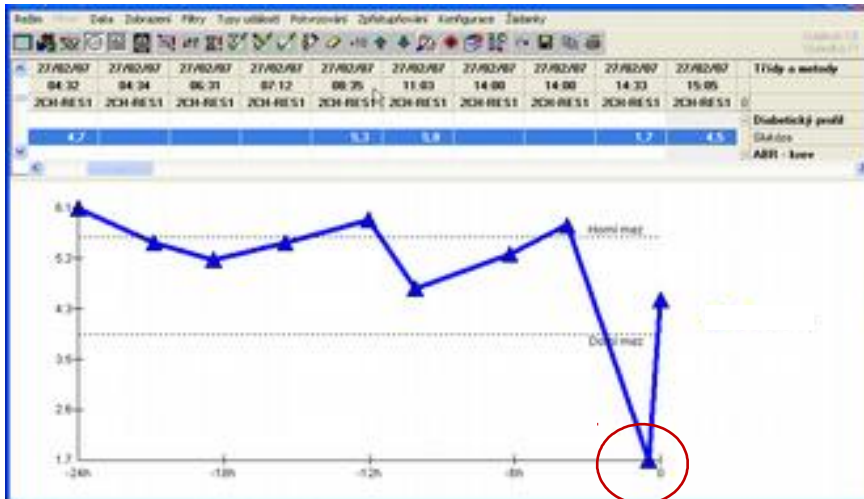
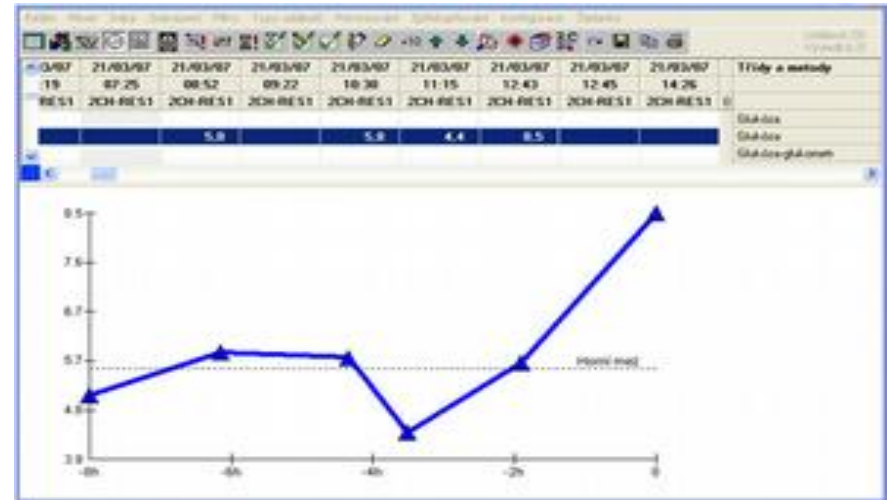
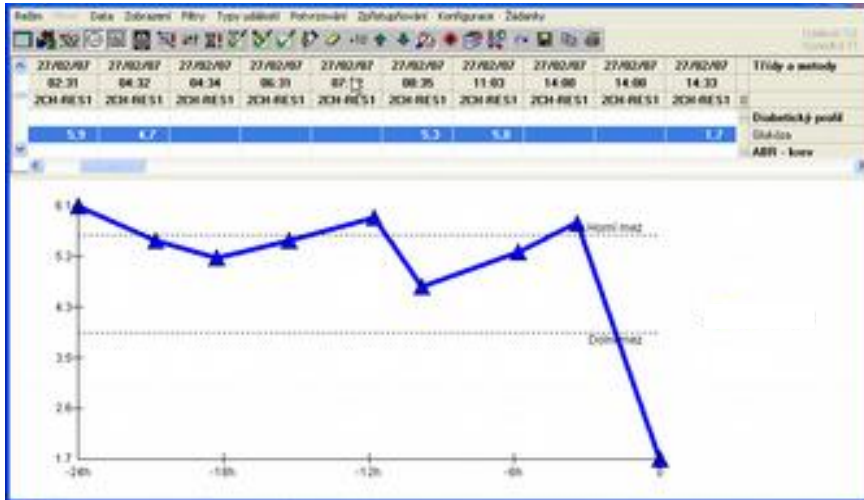


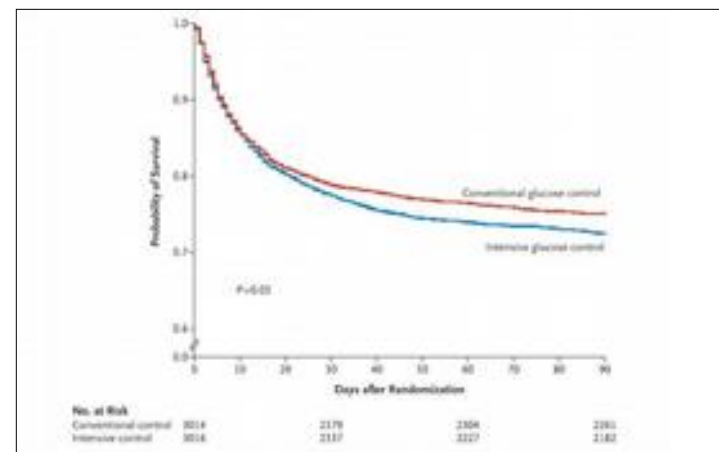
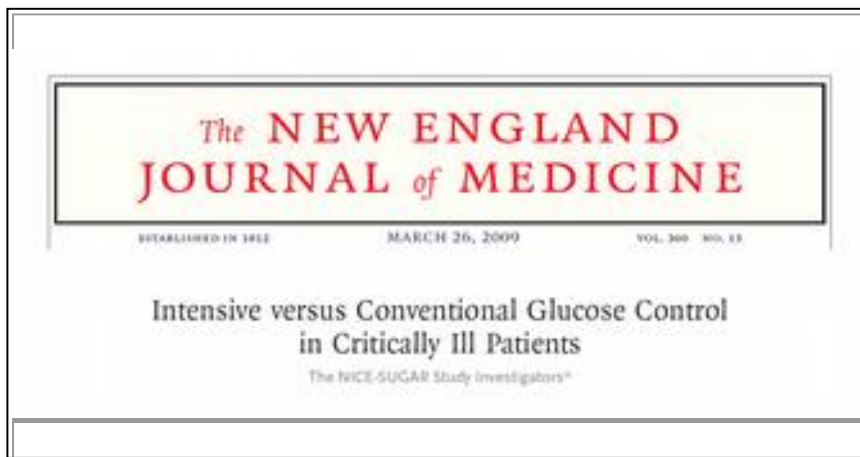
Režim Mixer Data Zobrazení Filtry Typy událostí Potvrzování Zpřístupňování Konfigurace Žádanky

Událost: 27
Výsledek: 0,27

22/03/07	22/03/07	22/03/07	22/03/07	22/03/07	22/03/07	22/03/07	22/03/07	22/03/07	22/03/07	22/03/07	22/03/07	Třídy a metody
02:08	02:28	03:01	03:33	03:53	04:57	05:02	05:04	06:03	06:24	06:31	06:52	
ODKL_UZ	ZCH-RES1	ODKL_UZ	ODKL_UZ	ODKL_UZ	ODKL_UZ	ZCH-RES1	ZCH-RES1	ODKL_UZ	ZCH-RES1	ODKL_UZ	ODKL_UZ	0
	4.2					7.7						Diabetický profil
												Glukóza
												Glukóza
												Glukóza-glukometr
4.1		3.9	4.7	5.6	7.2			8.1				







173 of all 288 episodes (60.1%) were confirmed by a laboratory measurement, 112 (38.9%) were unconfirmed bedside readings, and 3 (1.0%) were of unknown confirmation status.

ODBĚR KREVNÍHO VZORKU



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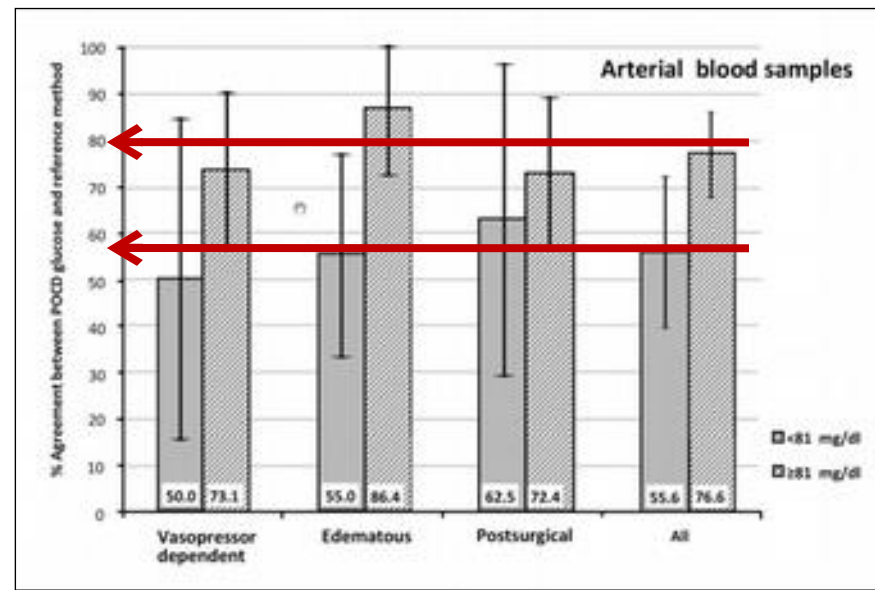
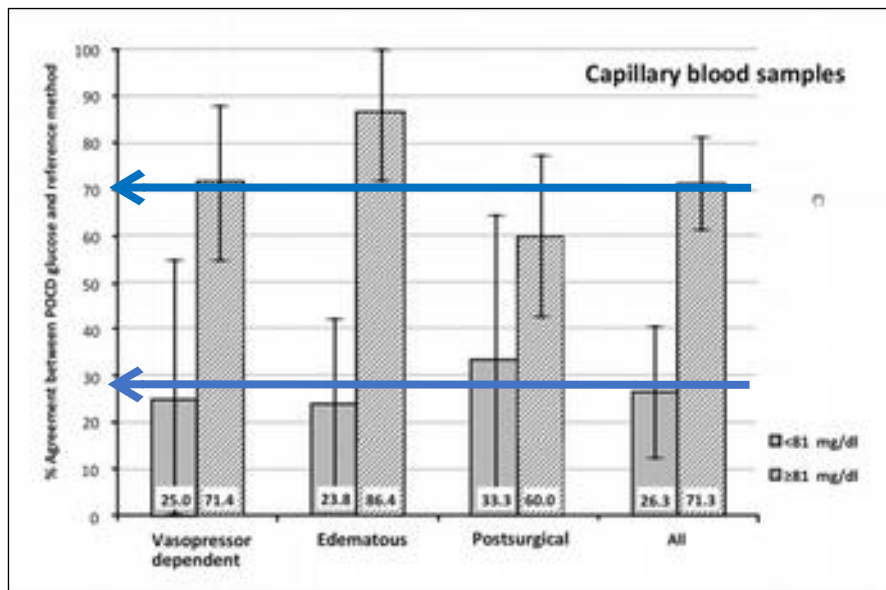
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Fekih Hassen M. Diabetes Res Clin Pract. 2010 Jan;87(1):87-91
Critchell CD et al. Intensive Care Med. 2007 Dec;33(12):2079-84
Hassen FM. Diabetes Res Clin Pract. 2010 Jan;87(1):87-91



Point-of-care glucose monitoring devices (POCGMDs) glucose measurement agreement with reference method during hypoglycemia versus nonhypoglycemia in critically ill patients. The POCGMD glucose measurement were said to agree with the reference method (CLD) if both measurements resulted in a similar clinical intervention.

The original data source: Kanji S, et al. Reliability of point-of-care testing for glucose measurement in critically ill adults. Crit Care Med. 2005;33(12):2778–2785.

Rebel A et al. Accuracy of point-of-care glucose measurements. J Diabetes Sci Technol. 2012 March; 6(2): 396-411

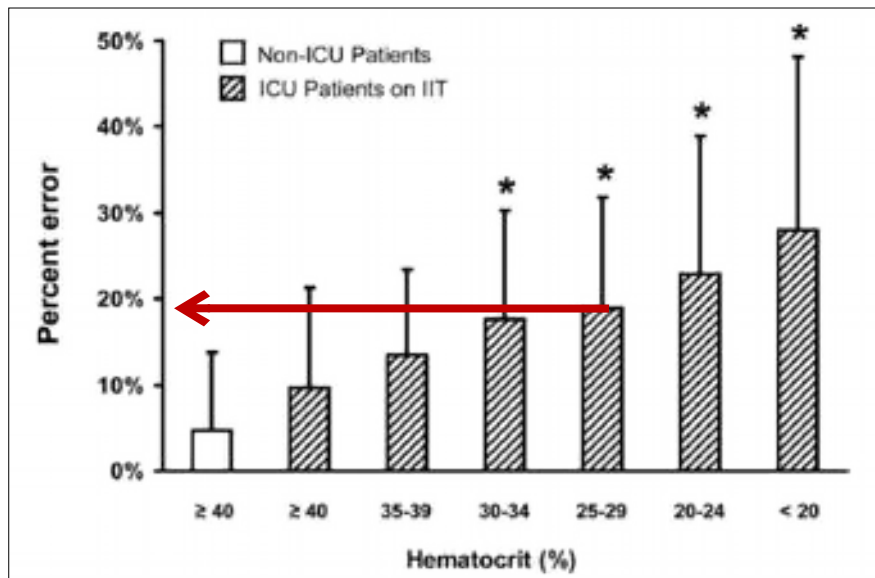


Figure 1. Percent error in glucometer measurements (reference = laboratory glucose) inversely correlated with degree of anemia in intensive care unit (ICU) patients; the lowest hematocrit group, significantly different from that of normal hematocrit in non-ICU patient samples collected during same time period ($p < .001$). *IIT*, intensive insulin therapy.

Pidcock et al. Crit Care Med 2010; 38:471- 476

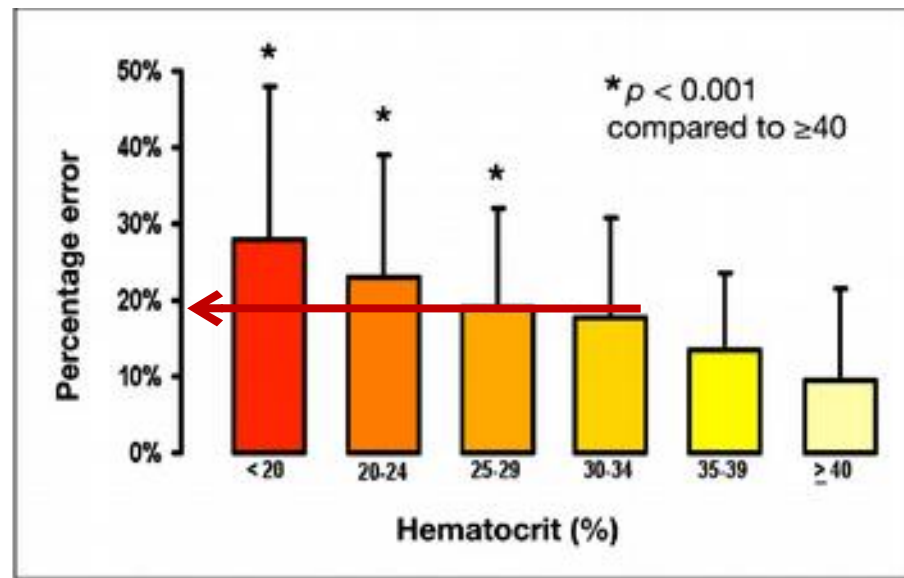


Figure 3. Glucometer error increases in a linearly as HCT decreases.

Mann AE et al. J Diabetes Sci Technol 2009;3(6):1319-1329

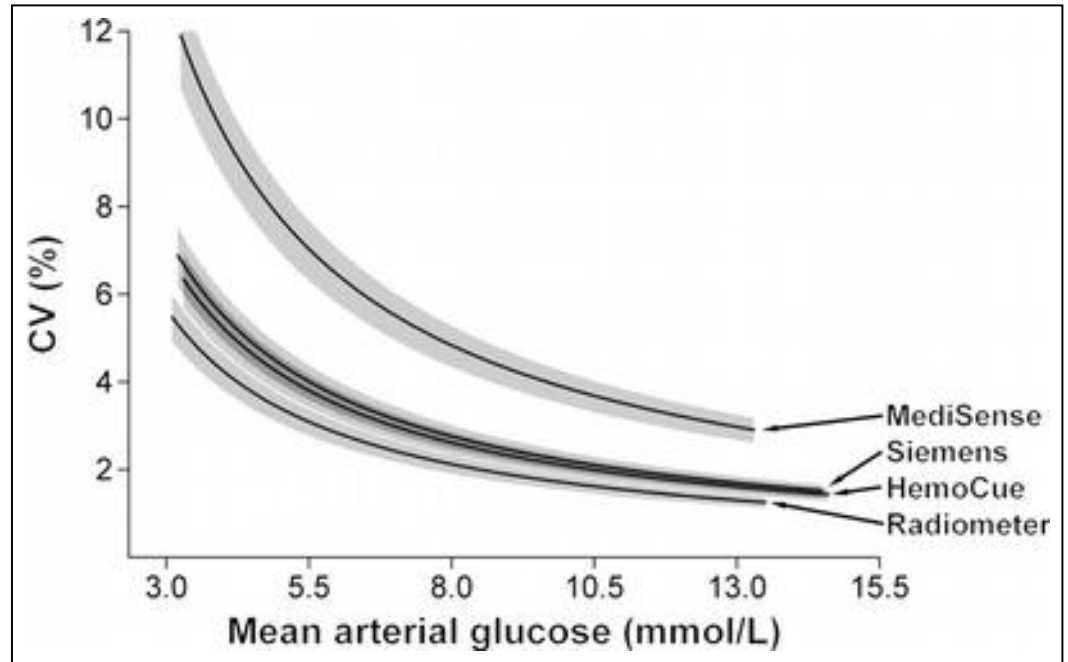


Figure 1

Arterial glucose concentration imprecision profiles for MediSense PC_χ, Siemens ADVIA, HemoCue DM and Radiometer 700 instruments. Shaded areas represent approximate 95% confidence intervals

REVIEW

Clinical review: Consensus recommendations on measurement of blood glucose and reporting glycemic control in critically ill adults

Simon Finfer¹, Jan Wernerman², Jean-Charles Preiser^{*3}, Tony Cass⁴, Thomas Desaive⁵, Roman Hovorka⁶, Jeffrey I Joseph⁷, Mikhail Kosiborod⁸, James Krinsley⁹, Iain Mackenzie¹⁰, Dieter Mesotten¹¹, Marcus J Schultz¹², Mitchell G Scott¹³, Robbert Slingerland¹⁴, Greet Van den Berghe¹¹ and Tom Van Herpe^{1,15}

Appropriate standards for Intermittent measurement of blood glucose in the ICU

Blood sampling

1. Patients whose severity of illness justifies invasive vascular monitoring
 - a. All blood samples should be drawn from an arterial line
 - b. If an arterial line is temporarily or permanently unavailable, sample from a venous line
 - c. Capillary (needle stick) samples are inaccurate and should not be used

Choice of blood glucose analyzer in clinical practice in critical care units

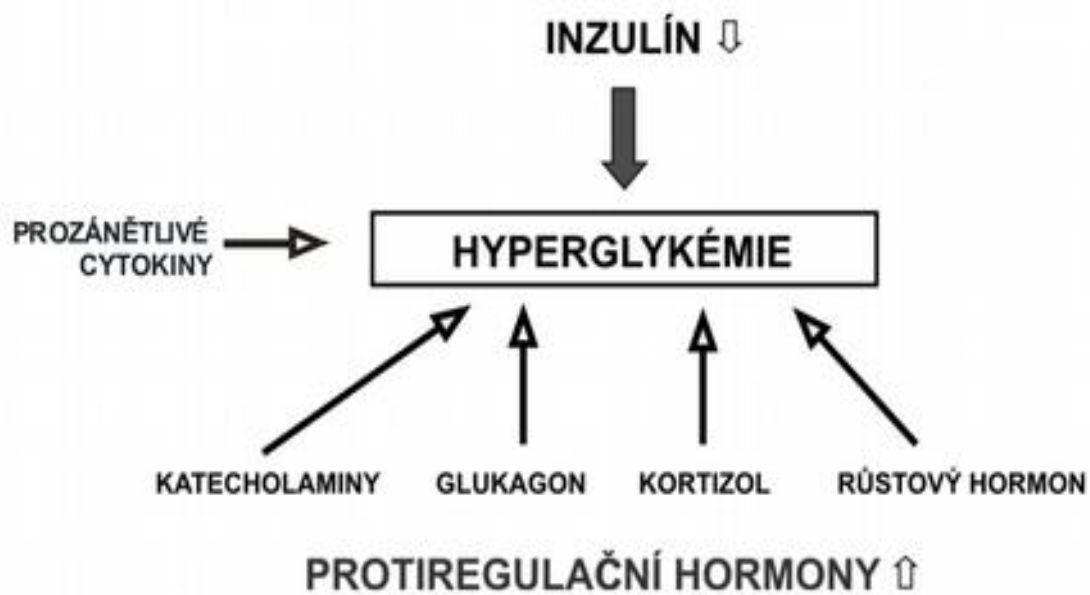
1. Patients whose severity of illness justifies invasive vascular monitoring
 - a. Samples taken from arterial or central venous catheters should be analyzed in a central laboratory or blood gas analyzer; a blood gas analyzer should be the default analyzer, central laboratory measurements should only be used if results can be obtained without delay

LIDSKÝ FAKTOR !



- chybný odběr krevního vzorku
- 5% všech hodnot glykémie zadaných do protokolu se neshoduje s naměřenými hodnotami
- nastavená rychlost inzulínu se od doporučení protokolu liší o 2% - 23%
- 83% ignorovaných doporučení bylo pro „obavy z hypoglykémie“
- riziko „nenastavení infusních pump“ (např. při souběžné akutní situaci)

Campion TR et al. International Journal Of Medical Informatics 80 (2011) 863-871
Campion TR et al. J. Am. Med. Inform. Assoc. 18 (May (3)) (2011) 251-258.
Anger KE et al. Pharmacotherapy 26 (February (2)) (2006) 214-228.



Marik and Bellomo *Critical Care* 2013, 17:305
<http://ccforum.com/content/17/2/305>



VIEWPOINT

Stress hyperglycemia: an essential survival response!

Paul E Marik^{1,*} and Rinaldo Bellomo²

NICE-SUGAR, a large randomized, multi-center trial performed in 6,104 ICU patients, demonstrated that intensive glucose control (81 to 108 mg/dl) increased mortality when compared to conventional glucose control [9].

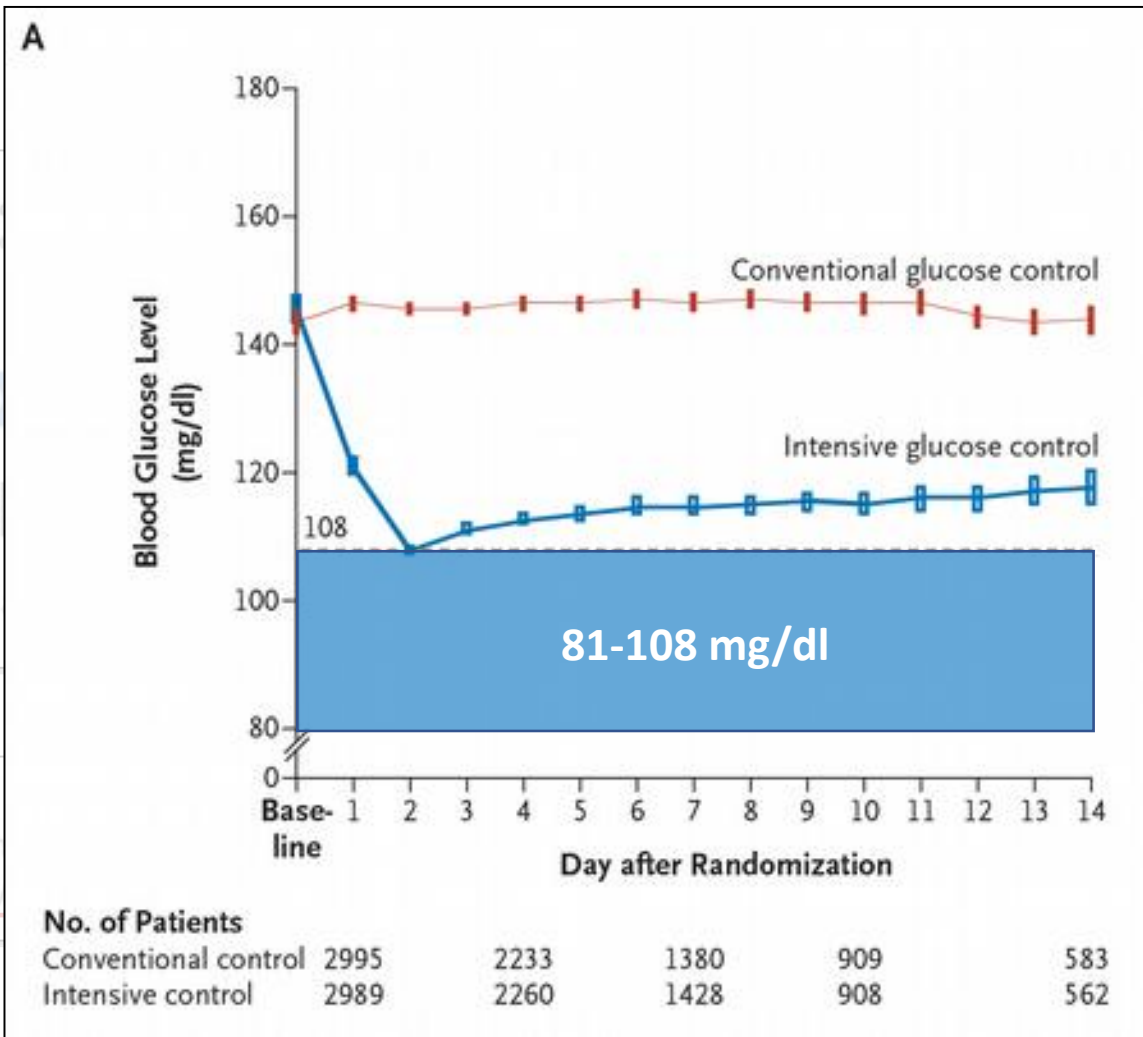
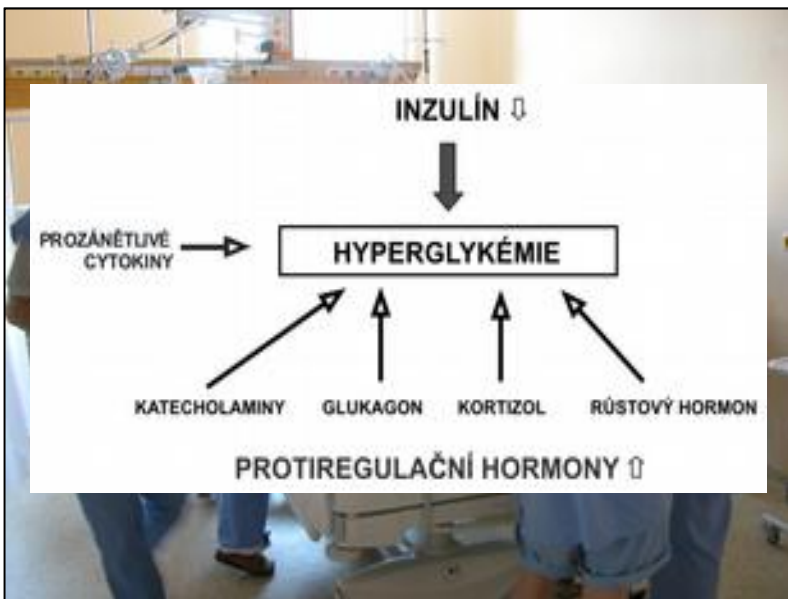


Figure 2. Data on Blood Glucose Level, According to Treatment Group.



HYPERGLYKÉMIE

- ♥ destabilizuje atheromové pláty a vede k akutnímu koronárnímu syndromu
- ♥ zvětšuje rozsah myokardiální nekrózy a redukuje koronární kolaterální průtok
- ♥ zhoršuje ischemicko-reperfúzní postižení

(Marfella, Diabetes Care 2000; Marfella, Diabetologia 2000; Kersten, Am J Physiol 1998; Kersten, Am J Physiol Heart Circ Physiol 2001; Verma, J Thorac Cardiovasc Surg 2002)

zvyšuje riziko trombózy

(Sakamoto, Thromb Haemost 2000; Knobler, Thromb Res 1998; Gesele, J Am Coll Cardiol 2003)

způsobuje endoteliální dysfunkci a aktivuje rozvoj systémového zánětu

(Beckman, Circulation 2001; Williams, Circulation 1998; Title, J Am Coll Cardiol 2000)

snižuje cerebrální krevní průtok, zhoršuje ischemické poškození CNS

(Lin B, Acta Neuropathologica 1998; Gisselsson, J Cereb Blood Flow Metab 1999; Hoxworth, Brain Res 1999; Li, Stroke 2000; Capes, Stroke 2001)

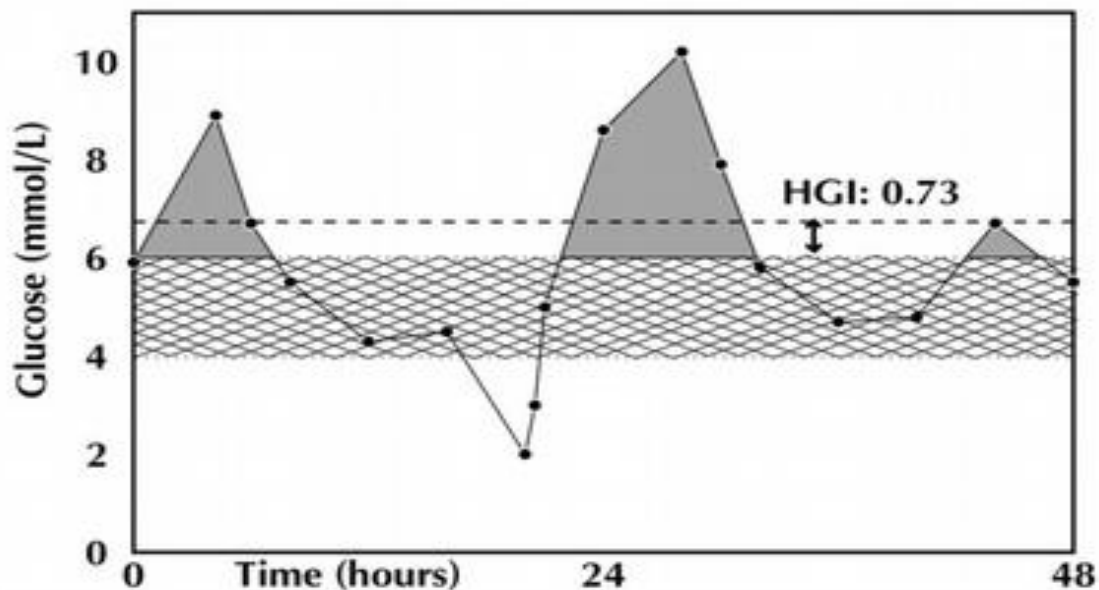
zhoršuje rozsah renálního postižení u pacientů po kardiochirurgické operaci

(Meldrum, J Surg Res 1999; Van den Berghe, N Engl J Med 2001)

zvyšuje počet infekčních pooperačních komplikací

(Butler, Pharmacotherapy 2005; Van den Berghe, N Engl J Med 2006; Van den Berghe, N Engl J Med 2001; Gale, Am Surg 2007)

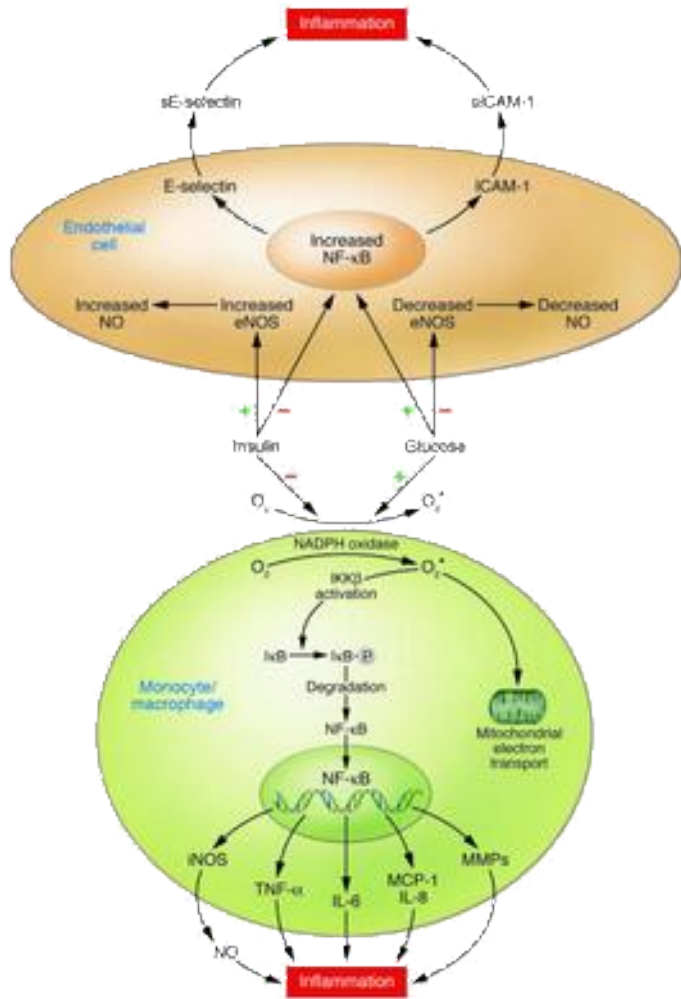
HYPERGLYKÉMIE



Characteristics for surviving and non-surviving patients and results of univariate analysis of glucose indices

Characteristic	Survivors	Nonsurvivors	<i>P</i>
Mean glucose (mmol/l)	6.9 (6.0–8.4)	7.7 (6.4–9.5)	<0.001
Morning glucose (mmol/l)	6.6 (5.9–7.9)	7.5 (6.2–8.8)	<0.001
Admission glucose (mmol/l)	7.2 (5.8–9.5)	7.9 (6.0–10.9)	0.07
Maximum glucose (mmol/l)	10.2 (8.0–14.2)	12.3 (9.5–16.4)	<0.001
HGI (mmol/l)	0.9 (0.3–2.1)	1.8 (0.7–3.4)	<0.001

HYPERGLYKÉMIE



Dandona et al. J Clin Invest. 2005

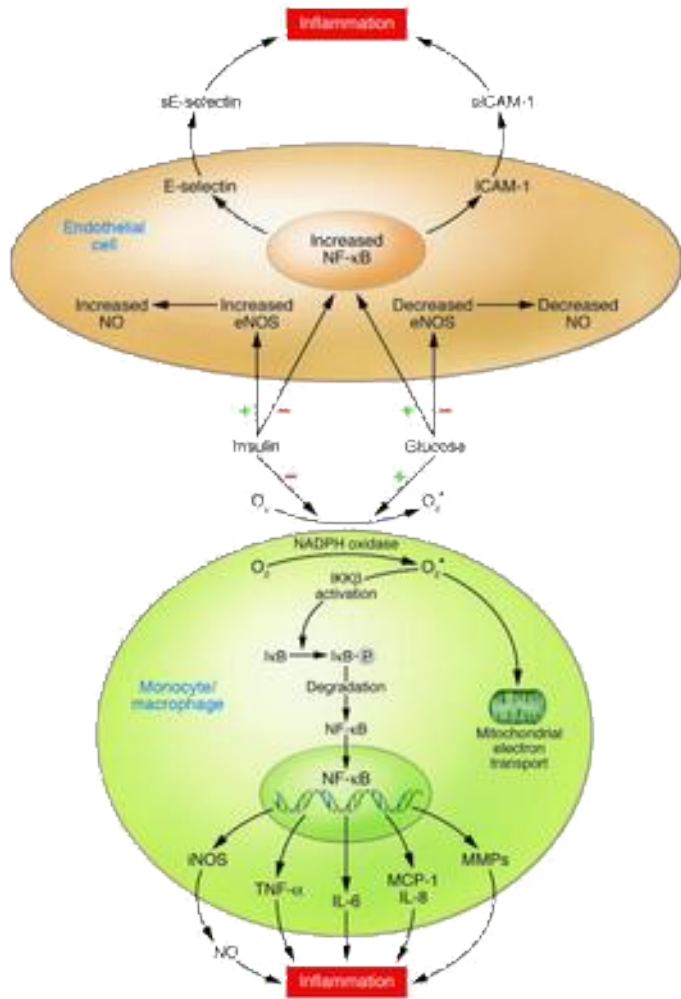
- přímý toxický vliv glukózy
- cestou zvýšení intracelulárního oxidativního stresu při vyšší produkci mitochondriálních peroxidů

Quijano, Am J Physiol Heart Circ Physiol 2007; Vanhorebeek, Lancet 2005; Beal, JAMA 1994; Corstjens, Crit Care 2006; Henderson, CJEM 2006; Turina, Crit Care Med 2006

- větší poškození než vlastní hypoglykémie způsobí rychlá reperfuze glukózou !

Suh SW. J. Clin. Invest 2007. 117(4):910-918

HYPERGLYKÉMIE



Dandona et al. J Clin Invest. 2005

HYPEROXÉMIE

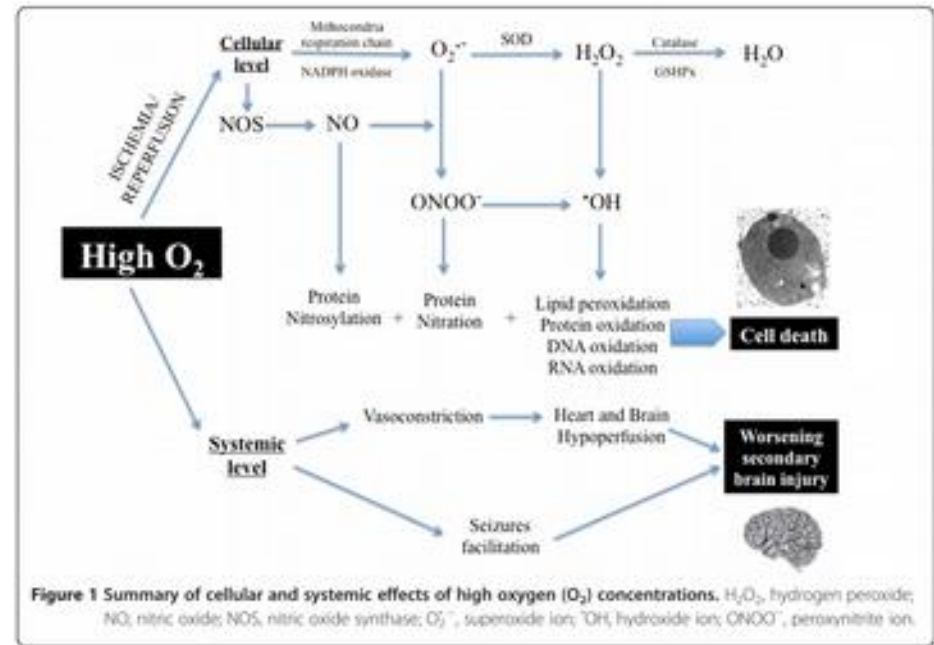


Figure 1 Summary of cellular and systemic effects of high oxygen (O_2) concentrations. H_2O_2 , hydrogen peroxide; NO, nitric oxide; NOS, nitric oxide synthase; $O_2^{\cdot-}$, superoxide ion; $^{\cdot}OH$, hydroxide ion; $ONOO^{\cdot-}$, peroxynitrite ion.

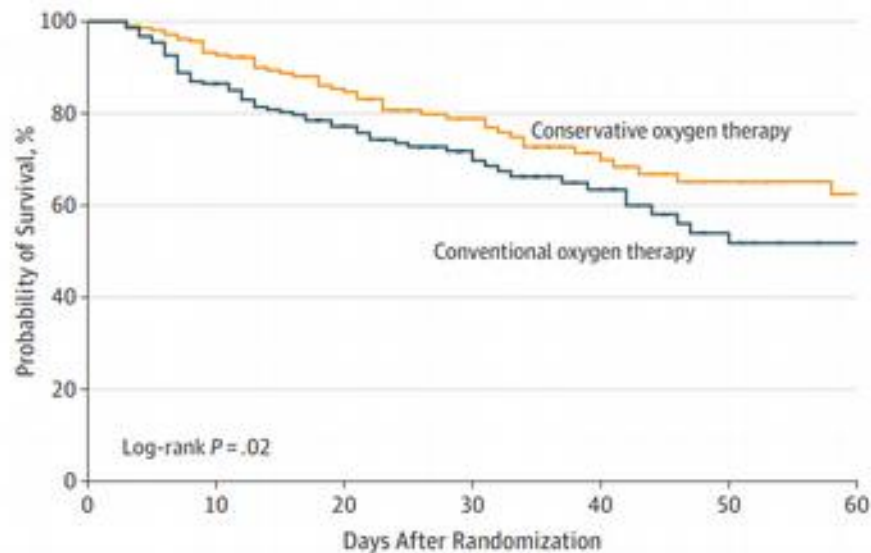
Dell'Anna et al. Critical Care 2014, 18:555

Effect of Conservative vs Conventional Oxygen Therapy on Mortality Among Patients in an Intensive Care Unit

The Oxygen-ICU Randomized Clinical Trial

Massimo Girardis, MD; Stefano Busani, MD; Elisa Damiani, MD; Abele Donati, MD; Laura Rinaldi, MD; Andrea Marudi, MD; Andrea Morelli, MD; Massimo Antonelli, MD; Mervyn Singer, MD, FRCA

Figure 2. Probability of Survival From Study Inclusion (Day 0) Through Day 60 for Patients in the Conservative and Conventional Oxygen Strategy Groups



No. at risk		0	10	20	30	40	50	60
Conservative oxygen therapy		216	201	188	181	173	170	169
Conventional oxygen therapy		218	189	172	163	158	152	152

Patients discharged alive from the hospital were considered to have survived, and their median follow-up was 22 days for the conservative group (interquartile range, 13-37) and 24 days for the conventional group (interquartile range, 15-35).

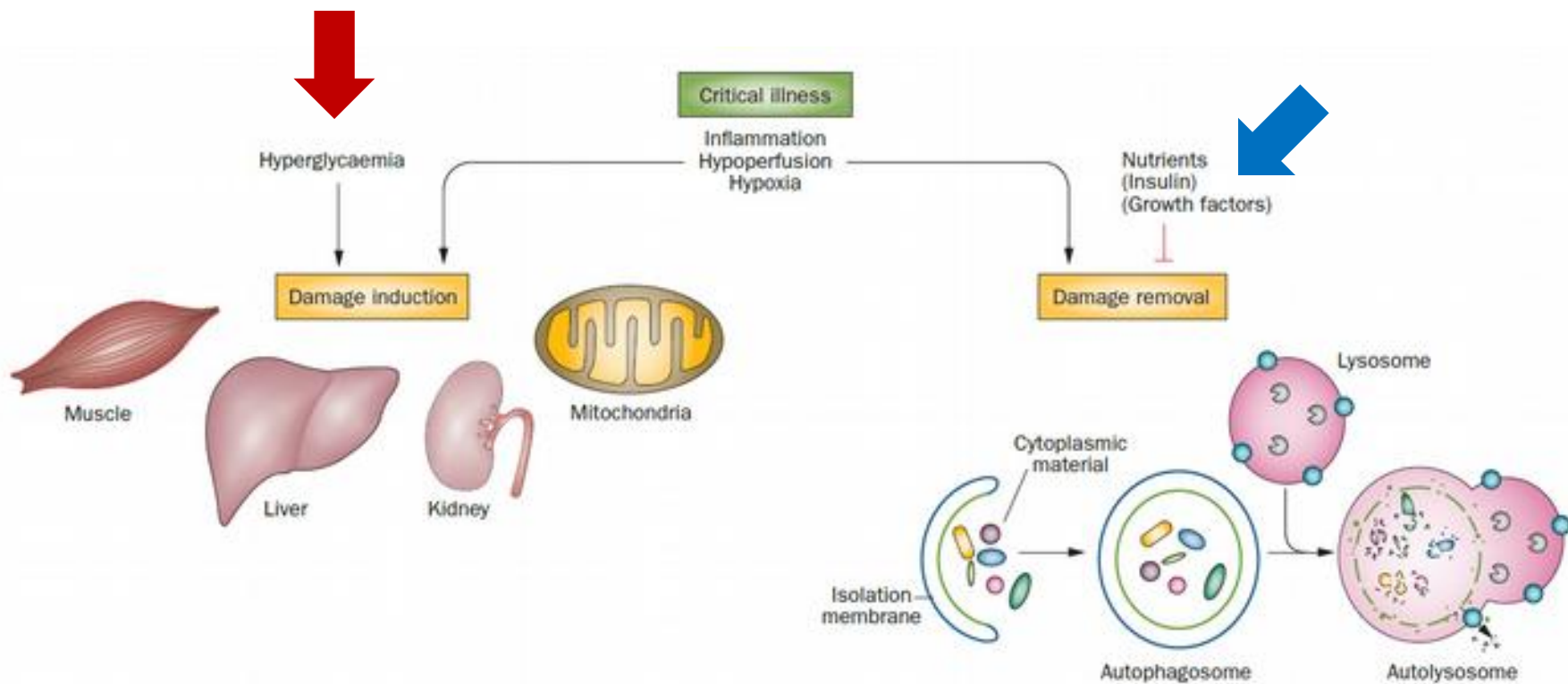


Figure 2 | Balance between damage induction and removal in critical illness. Critical illness represents a 'multiple hit' insult on cells, with damage induced by hypoxia, hypoperfusion and inflammation. Hyperglycaemia adds to such cell damage. Removal of cell damage (by autophagy) is essential for recovery. Suppressive effects by nutrients early during critical illness could compromise such damage removal systems. Conversely, when cell damage removal systems are fully functional, perhaps the damage evoked by moderate hyperglycaemia could be dealt with. This hypothesis remains to be investigated.

Česká diabetologická společnost ČLS JEP
Doporučený postup péče o diabetes mellitus 2. typu
Za ČDS: J. Škrha, T. Pelikánová, M. Kvapil
Revize ze dne: 1. 8. 2017

Tab. 1: Cíle léčby nemocného s diabetem

Ukazatel	Požadovaná hodnota
HbA1c (mmol/mol)*	< 45 (< 60)
Glykémie v žilní plazmě nalačno/před jídlem (mmol/l)	≤ 6,0 (< 7,0)
Hodnoty glykémie v plné kapilární krvi (selfmonitoring)	
nalačno/před jídlem (mmol/l)	4,0–6,0 (< 8,0)
postprandiální (mmol/l)	5,0–7,5 (< 9,0)
Krevní tlak (mmHg)	< 130/80 (< 140/90)

Association between intensive care unit–acquired dysglycemia and in-hospital mortality*

Omar Badawi, PharmD; Michael D. Waite, MD; Steven A. Fuhrman, MD; Ilene H. Zuckerman, PharmD, PhD

Design: Retrospective, observational study.

Setting: eICU Research Institute participating hospitals with an active tele-ICU program.

Patients: A total of 194,772 patients with length of stay >48 hrs.

Interventions: None.

Table 5. Relative risk of hospital mortality by categories of dysglycemia (n = 98,011)

	Unadjusted RR Hospital Mortality (95% CI)	Adjusted ^a RR Hospital Mortality (95% CI)	Glucocorticoid Adjusted ^b RR Hospital Mortality (95% CI)
Maximum average daily glucose, mg/dL			
<80	1.45 (0.95–2.24)	1.40 (0.90–2.18)	0.99 (0.49–2.03)
80–110	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
110–150	1.62 (1.50–1.76)	1.13 (1.04–1.58)	1.12 (1.01–1.24)
150–180	3.20 (2.94–3.48)	1.43 (1.30–1.58)	1.38 (1.22–1.55)
180–240	4.71 (4.33–5.12)	1.63 (1.47–1.81)	1.51 (1.33–1.72)
240–300	6.01 (5.43–6.65)	1.76 (1.55–1.99)	1.57 (1.34–1.84)
>300	7.05 (6.23–7.98)	1.89 (1.62–2.19)	1.78 (1.48–2.15)
Lowest glucose level, mg/dL			
<20	4.85 (3.99–5.88)	1.67 (1.37–2.03)	1.69 (1.35–2.12)
20–40	4.52 (4.14–4.93)	1.53 (1.37–1.70)	1.55 (1.37–1.76)
40–60	2.75 (2.58–2.94)	1.12 (1.04–1.21)	1.10 (1.00–1.20)
60–80	1.62 (1.55–1.69)	1.06 (1.01–1.11)	1.04 (0.98–1.10)
80–110	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
>110	1.36 (1.29–1.44)	1.50 (1.42–1.59)	1.42 (1.32–1.53)
Glucose variability (quintiles) ^c			
0–20th percentile	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
20–40th percentile	1.58 (1.46–1.72)	1.27 (1.17–1.38)	1.21 (1.10–1.34)
40–60th percentile	2.11 (1.95–2.27)	1.41 (1.30–1.53)	1.38 (1.25–1.53)
60–80th percentile	2.72 (2.53–2.93)	1.45 (1.33–1.59)	1.36 (1.22–1.52)
80–100th percentile	3.94 (3.67–4.23)	1.61 (1.47–1.78)	1.56 (1.39–1.75)

*Adjusted for age, sex, race, operative admission diagnosis, history of diabetes, Acute Physiology and Chronic Health Evaluation IV score, admission glucose, admission temperature, number of glucose values per patient day, highest temperature, white blood cell count, serum sodium, and serum creatinin throughout the intensive care unit (ICU) stay, duration of mechanical ventilation, year of ICU admission, and ICU-acquired acute renal injury, respiratory failure and sepsis. ^aAdjusted for glucocorticoids in addition to primary model (n = 69,596). ^bThresholds for percentiles of glucose variability (coefficient of variation) were 20th percentile = 0.19; 40th percentile = 0.15; 60th percentile = 0.19; 80th percentile = 0.25; and 100th percentile = 1.67.

Badawi et al.
Crit Care Med 2012; 40:3180-3188

Hyperglycemia-related mortality in critically ill patients varies with admission diagnosis*

Mercedes Falciglia, MD; Ron W. Freyberg, MS; Peter L. Almenoff, MD; David A. D'Alessio, MD; Marta L. Render, MD

Design: Retrospective cohort study.

Setting: 173 U.S. medical, surgical, and cardiac intensive care units.

Patients: 259,040 admissions; unadjusted mortality rate, 11.2%.

Interventions: None.

Table 2. Hyperglycemia is associated with increased mortality for the entire cohort and across all intensive care unit types, levels of severity of illness, and length of stay

Cohort	No.	p	Adjusted Odds Ratio (95% Confidence Interval) ^a Mean Glucose, mg/dL			
			111–145	146–199	200–300	>300
Total	259,040	<.0001	1.31 (1.26–1.36)	1.82 (1.74–1.90)	2.13 (2.03–2.25)	2.85 (2.58–3.14)
Diabetes	77,850	<.0001	1.13 (1.02–1.26)	1.49 (1.35–1.65)	1.88 (1.69–2.08)	2.76 (2.38–3.20)
No diabetes	180,084	<.0001	1.35 (1.30–1.41)	2.14 (2.04–2.24)	2.91 (2.71–3.11)	4.04 (3.44–4.75)
Intensive care unit						
Cardiac	20,359	<.0001	1.68 (1.43–1.97)	2.27 (1.91–2.69)	2.42 (1.97–2.98)	3.85 (2.63–5.62)
Medical	19,501	<.0001	1.40 (1.25–1.57)	1.86 (1.65–2.10)	2.08 (1.80–2.40)	2.39 (1.79–3.18)
Surgical	71,672	<.0001	1.06 (0.96–1.16)	1.56 (1.42–1.73)	1.86 (1.63–2.12)	2.92 (2.20–3.89)
Medical/cardiac	60,212	<.0001	1.38 (1.28–1.48)	1.77 (1.64–1.91)	2.01 (1.83–2.21)	2.70 (2.26–3.23)
Mixed	87,296	<.0001	1.36 (1.27–1.45)	1.96 (1.83–2.10)	2.36 (2.16–2.56)	2.98 (2.55–3.48)
Severity of illness: predicted mortality (% likelihood of death)						
<2.5%	116319	<.0001	1.71 (1.41–2.08)	2.32 (1.89–2.85)	2.85 (2.22–3.65)	3.10 (1.91–5.01)
2.5–5%	42765	<.0001	1.46 (1.26–1.69)	2.20 (1.89–2.56)	2.38 (1.97–2.87)	3.58 (2.57–4.98)
5–10%	34978	<.0001	1.52 (1.37–1.69)	2.00 (1.79–2.24)	2.50 (2.18–2.86)	2.72 (2.07–3.56)
10–30%	38214	<.0001	1.43 (1.33–1.52)	1.95 (1.82–2.09)	2.21 (2.03–2.41)	2.71 (2.30–3.19)
>30%	26764	<.0001	1.05 (0.99–1.12)	1.49 (1.39–1.59)	1.79 (1.65–1.94)	2.89 (2.44–3.43)
Length of stay						
1 day	2,153	<.0001	1.52 (1.02–2.27)	1.56 (1.03–2.36)	1.79 (1.18–2.71)	4.08 (2.52–6.59)
2 days	51,171	<.0001	1.14 (1.02–1.28)	1.58 (1.39–1.78)	1.87 (1.62–2.16)	2.67 (2.15–3.31)
3 days	64,693	<.0001	1.28 (1.16–1.41)	1.65 (1.49–1.83)	1.97 (1.74–2.23)	2.89 (2.32–3.60)
3–6 days	88,121	<.0001	1.19 (1.11–1.27)	1.73 (1.61–1.87)	1.91 (1.74–2.10)	2.33 (1.92–2.83)
>6 days	52,902	<.0001	1.27 (1.18–1.35)	1.80 (1.68–1.93)	2.31 (2.11–2.52)	3.09 (2.44–3.92)

^aReference group is the mean glucose category with normoglycemia (70–110 mg/dL).

Krinsley and Preiser *Critical Care* (2015) 19:179
DOI 10.1186/s13054-015-0908-7



RESEARCH

Open Access

Time in blood glucose range 70 to 140 mg/dl >80% is strongly associated with increased survival in non-diabetic critically ill adults

James S Krinsley^{1*} and Jean-Charles Preiser²

OPEN

Perioperative Blood Glucose Levels <150 mg/dL are Associated With Improved 5-Year Survival in Patients Undergoing On-Pump Cardiac Surgery

A Prospective, Observational Cohort Study

Ashham Mansur, MD, Aron Frederik Popov, MD, Ameen Abu Hanna, PhD, Ingo Bergmann, MD, Ivo Florian Brandes, MD, Tim Beissbarth, PhD, Martin Bauer, PhD, and José Hinz, PhD

Abstract: Hyperglycemia is common during and after Coronary Artery Bypass Graft Surgery (CABGS) and has been shown to be associated with poor clinical outcomes. In this study, we hypothesized that a moderate perioperative mean blood glucose level of <150 mg/dL improves long-term survival in cardiac surgery patients. We conducted a prospective, observational cohort study in the heart center of the University Medical Center of Goettingen, Germany. Patients undergoing on-pump cardiac surgery were enrolled in this investigation. After evaluating perioperative blood glucose levels, patients were classified into 2 groups based on mean glucose levels: Glucose ≥ 150 mg/dL and Glucose <150 mg/dL. Patients were followed up for 5 years, and mortality within this period was recorded as the primary outcome parameter. Secondary outcome parameters included the length of ICU stay, the use of inotropic agents, the length of hospital stay, and the in-hospital mortality. A total of 455 consecutive patients who underwent cardiac surgery with cardiopulmonary bypass were enrolled in this investigation. A Kaplan–Meier survival analysis of the 5-year mortality risk revealed a higher mortality risk among patients with glucose levels ≥ 150 mg/dL ($P=0.0043$, log-rank test). After adjustment for confounders in a multivariate Cox regression model, the association between glucose ≥ 150 mg/dL and 5-year mortality remained significant (hazard ratio, 2.10; 95% CI, 1.30–3.39; $P=0.0023$). This association was corroborated by propensity score matching, in which Kaplan–Meier survival analysis demonstrated significant improvement in the 5-year survival of patients with glucose

levels <150 mg/dL ($P=0.0339$). Similarly, in-hospital mortality was significantly higher in patients with glucose ≥ 150 mg/dL compared with patients with glucose <150 mg/dL. Moreover, patients in the Glucose ≥ 150 mg/dL group required significantly higher doses of the inotropic agent Dobutamine (mg/d) compared with patients in the Glucose <150 mg/dL group (20.6 ± 62.3 and 10.5 ± 40.7 , respectively; $P=0.0104$). Moreover, patients in the Glucose ≥ 150 mg/dL group showed a significantly longer hospital stay compared with patients in the Glucose <150 mg/dL group (28 ± 23 and 24 ± 19 , respectively; $P=0.0297$). We conclude that perioperative blood glucose levels <150 mg/dL are associated with improved 5-year survival in patients undergoing cardiac surgery. More studies are warranted to explain this effect.

(*Medicine* 94(45):e2035)

Abbreviations: APACHE II = Acute Physiology and Chronic Health Evaluation Score, BMI = body mass index, CABGS = coronary artery bypass graft surgery, CI = cardiac index, CVP = central venous pressure, ECMO = extracorporeal membrane oxygenation, HR = heart rate, IABP = intra-aortic balloon pump, ICU = intensive care unit, MAP = mean arterial pressure, PAP = mean pulmonary artery pressure, PCWP = pulmonary capillary wedge pressure, PVRI = pulmonary vascular resistance index, SAPS II = Simplified Acute Physiology Score, SVRI = systemic vascular resistance index.

Table 2. ICU Glucose Control (From the Beginning of Operation to the End of ICU Stay)

	Nondiabetic Subjects		Diabetic Subjects	
	PERI Group	POST Group	PERI Group	POST Group
No. of patients	869	910	265	339
Average blood glucose, mmol/L				
Whole period	6.5 ± 0.6	6.6 ± 0.8	6.9 ± 1.0	7.1 ± 0.8 ^b
Intraoperative period	6.8 ± 1.1	7.0 ± 1.2 ^a	7.7 ± 1.9	8.3 ± 1.8 ^b
Time in TGC target range (4.4–6.1 mmol/L), %	40.8 ± 13.6	39.7 ± 13.8	34.3 ± 12.7 ^d	30.8 ± 11.5
Time in GC range (4.4–8.3 mmol/L), %	82.5 ± 11.1 ^a	79.7 ± 12.5	68.8 ± 14.6 ^d	65.2 ± 13.9
Time above target range (>8.3 mmol/L), %	12.5 ± 10.2	13.9 ± 11.8 ^b	21.1 ± 15.6	26.1 ± 13.8 ^a
Time below target range (<4.4 mmol/L), %	5.0 ± 5.2	6.4 ± 5.6 ^a	10.1 ± 5.7 ^c	8.7 ± 5.9
Moderate hypoglycemia (2.2–3.2 mmol/L), no. of measurements/ all measurements, %	267/40 766 (0.7)	419/45 100 (0.9) ^b	241/15 553 (1.5)	266/17 755 (1.5)
Severe hypoglycemia <2.2 mmol/L (no. of measurements/all measurements), %	20/40 766 (0.1)	33/45 100 (0.1)	24/15 553 (0.2)	28/17 755 (0.2)

Table 4. Perioperative Morbidity and Mortality: Nondiabetic and Diabetic Subjects

	Nondiabetic Subjects			Diabetic Subjects		
	PERI Group	POST Group	AD or RR(95% CI)	PERI Group	POST Group	AD or RR(95% CI)
No. of patients	869	910	41	265	339	74
Perioperative mortality, no of patients (%)	19 (2.2)	33 (3.6)	0.60 (0.35 to 1.05)	18 (6.8)	15 (4.4)	1.54 (0.79–2.99)
Perioperative morbidity, no of patients (%)	185 (21.3)	307 (33.7) ^c	0.63 (0.54 to 0.74)	78 (29.4)	119 (35.1)	0.84 (0.66–1.06)
Complications, no. of events (%)						
Cardiovascular	109 (12.5)	193 (21.2) ^c	0.59 (0.48 to 0.73)	26 (9.8)	64 (18.9) ^b	0.52 (0.34–0.80)
Respiratory	56 (6.4)	69 (7.6)	0.85 (0.60 to 1.19)	16 (6.0)	25 (7.4)	0.82 (0.45–1.50)
Renal	54 (6.2)	92 (10.1) ^b	0.61 (0.45 to 0.85)	34 (12.8)	39 (11.5)	1.12 (0.72–1.72)
Gastrointestinal	22 (2.5)	46 (5.1) ^b	0.50 (0.30 to 0.83)	11 (4.2)	20 (5.9)	0.70 (0.34–1.44)
Neurological	8 (0.9)	60 (6.6) ^c	0.14 (0.07 to 0.29)	22 (8.3)	22 (6.5)	1.28 (0.72–2.26)
Infectious	24 (2.7)	60 (6.6) ^c	0.42 (0.26 to 0.67)	12 (4.5)	29 (8.6)	0.53 (0.28–1.02)

Data are expressed as means ± SD or absolute number with relative percentage. The difference between the groups was expressed as absolute difference (AD) for numerical data or relative risk (RR) for categorical data, both with 95% CI. The AD and RR values are unadjusted. ^a $P < .05$. ^b $P < .01$. ^c $P < .001$.

ORIGINAL RESEARCH

Trends in Glycemic Control Over a 2-Year Period in 126 US Hospitals

Sophie Bersoux, MD, MPH¹; Curtiss B. Cook, MD²; Gail L. Kongable, RN, MSN, FNP³; Jianfen Shu, MS⁴

¹Division of Community Internal Medicine Mayo Clinic, Scottsdale, Arizona; ²Divisions of Endocrinology and Preventive, Occupational, and Aerospace Medicine, Mayo Clinic, Scottsdale, Arizona; ³Department of Neurosurgery and Department of Neurology, University of Virginia, Charlottesville, Virginia; ⁴Department of Statistics, University of Virginia, Charlottesville, Virginia.

OBJECTIVE: Report data on glucose control from 126 U.S. hospitals (Jan -Dec 2009)

RESULTS: The **mean BG** was **166 mg/dL**

The prevalence of **hyperglycemia** (>180 mg/dL) was **28%**

BENCHMARKING GLYCEMIC CONTROL IN U.S. HOSPITALS

*Sophie Bersoux, MD, MPH¹; Curtiss B. Cook, MD²; Gail L. Kongable, RN, MSN, FNP³;
Jianfen Shu, PhD³; Denise R. Zito, BS, MT (ASCP)⁴*

OBJECTIVE: Report data on glucose control from 635 U.S. hospitals (Jan -Dec 2012)

RESULTS: In total, 12,178,002 POC-BG measurements from 575,084 ICU patients were analyzed.

The **mean BG** was **170 mg/dL**

The prevalence of **hyperglycemia** (>180 mg/dL) was **28.2%**

The prevalence of **hypoglycemia** (<70 mg/dL) was **5.6%**

The patient-day-weighted mean glucose and prevalence of hypoglycemia were highest in the smallest hospitals, in rural hospitals, and in hospitals located in the Northeast (all $P < .01$).

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INTENSIVE INSULIN THERAPY IN CRITICALLY ILL PATIENTS

GREET VAN DEN BERGHE, M.D., Ph.D., PETER WOUTERS, M.Sc., FRANK WEKERS, M.D., CHARLES VERWAEST, M.D., FRANS BRUYNINCKX, M.D., MET SCHETZ, M.D., Ph.D., DIRK VLASSELAERS, M.D., PATRICK FERDINAND, M.D., Ph.D., PETER LAUWERS, M.D., AND ROGER BOULLON, M.D., Ph.D.

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Intensive versus Conventional Glucose Control in Critically Ill Patients

The NICE-SUGAR Study Investigators*

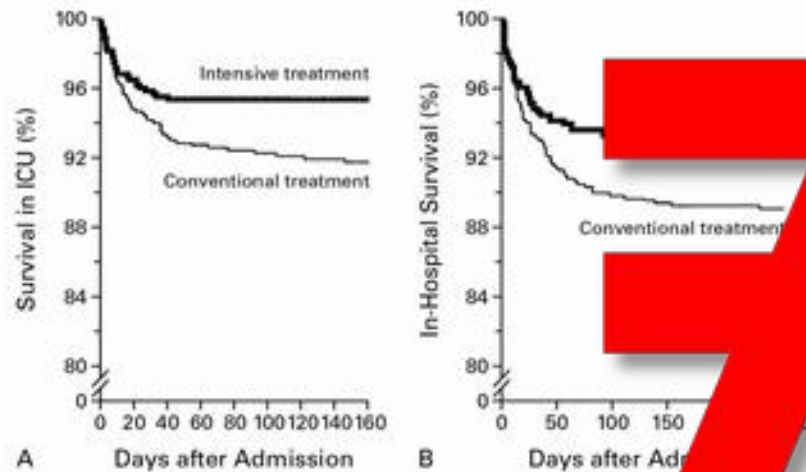
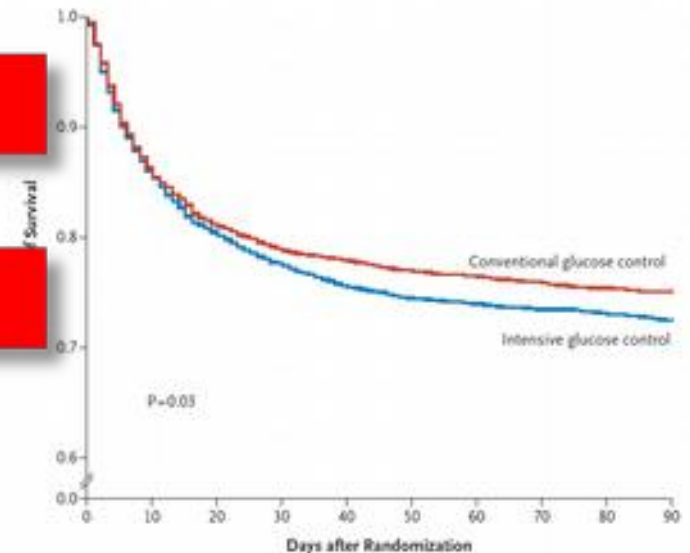


Figure 1. Kaplan-Meier Curves Showing Cumulative Survival of Patients Who Received Intensive Insulin Treatment or Conventional Treatment in the Intensive Care Unit (ICU).

Patients discharged alive from the ICU (Panel A) and from the hospital (Panel B) were considered to have survived. In both cases, the differences between the treatment groups were significant (survival in ICU, nominal $P=0.005$ and adjusted $P<0.04$; in-hospital survival, nominal $P=0.011$). P values were determined with the use of the Mantel-Cox log-rank test.



No. at Risk				
Conventional control	3014	2379	2304	2261
Intensive control	3016	2337	2227	2182

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Intensive versus Conventional Glucose Control in Critically Ill Patients

The NICE-SUGAR Study Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intensive Insulin Therapy and Pentastarch Resuscitation in Severe Sepsis

Frank M. Brunkhorst, M.D., Christoph Engel, M.D., Frank Bloos, M.D., Ph.D.,

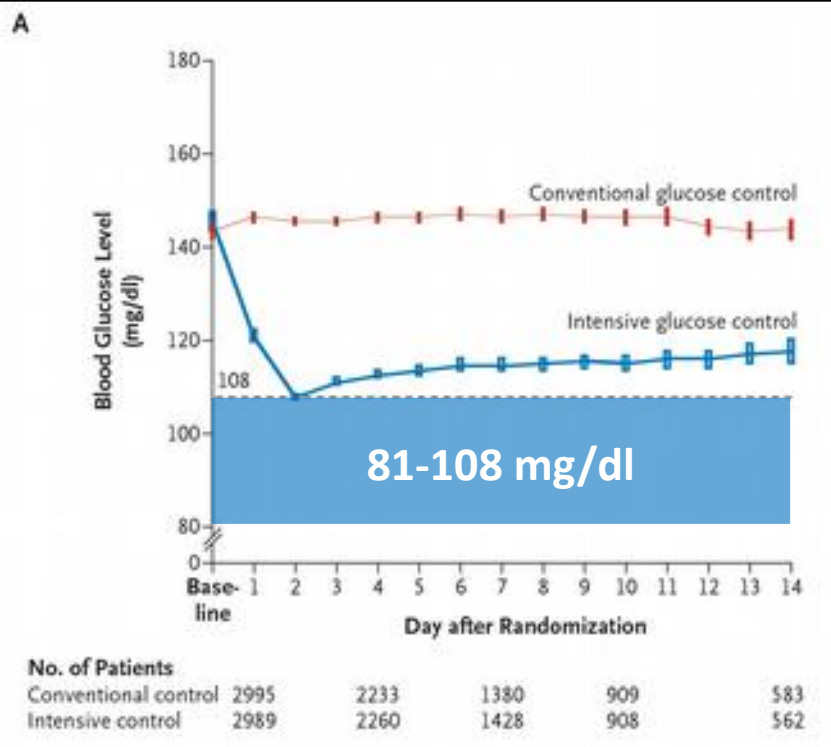


Figure 2. Data on Blood Glucose Level, According to Treatment Group.

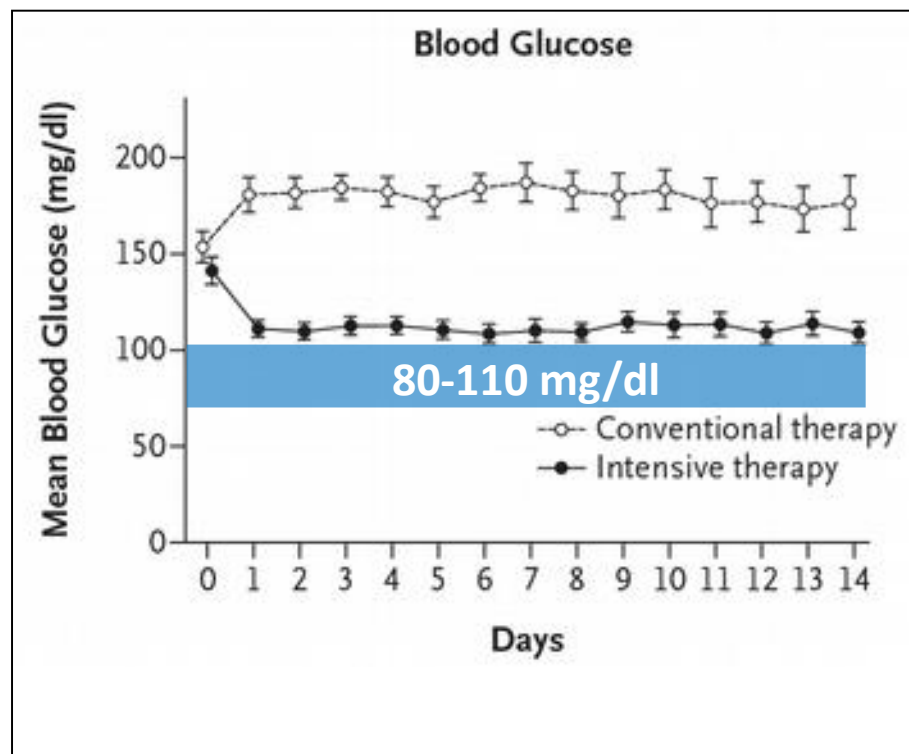


Figure 1. The mean morning blood glucose level.

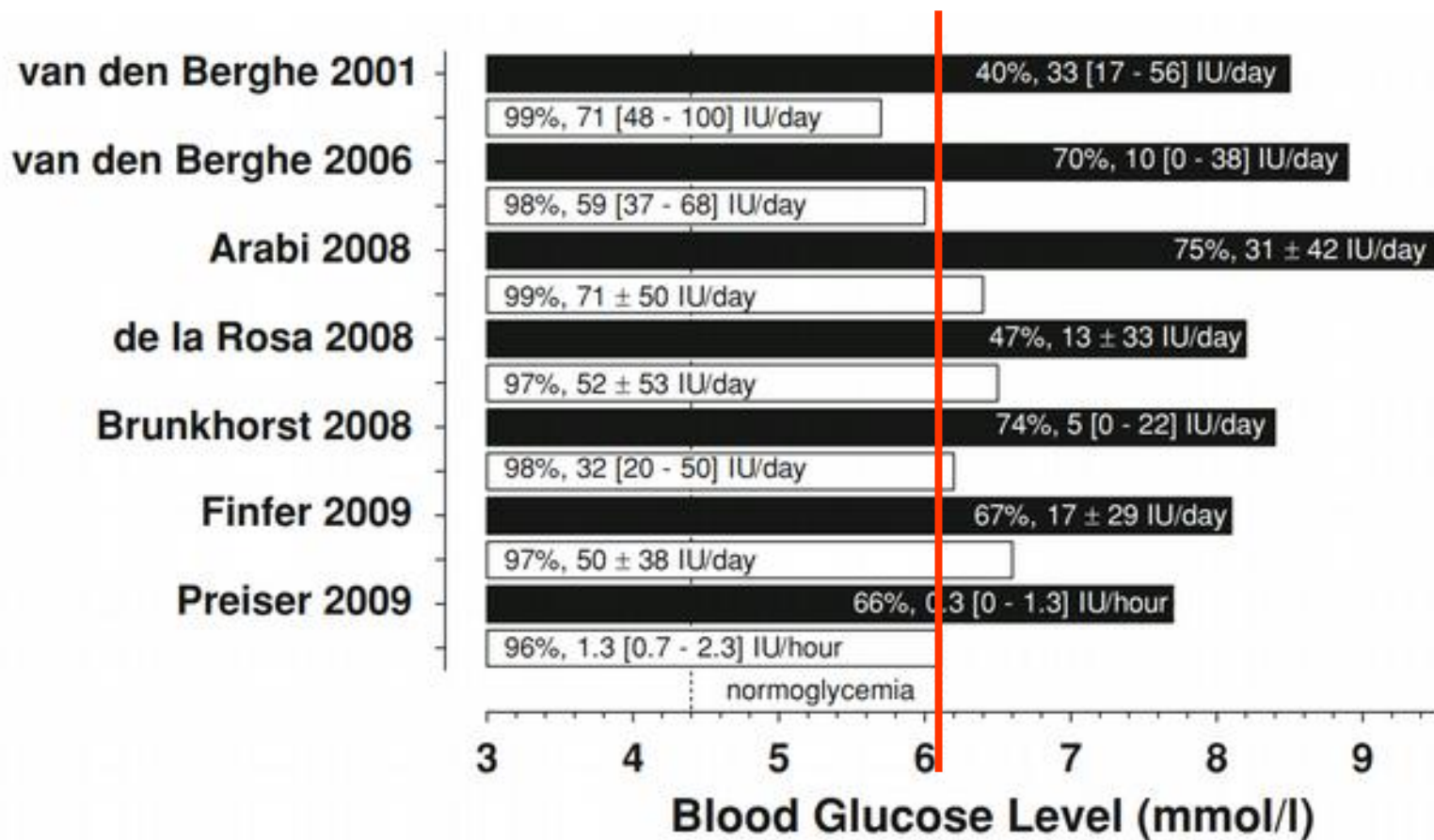


Fig. 1 Blood glucose levels, percentage of patients treated with insulin and insulin dose (mean \pm standard deviation or median [interquartile range] in the control or conventional group (*filled bars*) and tight glycemic control group (*open bars*) of seven randomized controlled trials

SOUHRN

- 1.** Koncept kontroly glykémie je správný, ale v současné době ho nedokážeme bezpečně realizovat,
- 2.** ani neznáme optimální hladiny glykémie pro jednotlivé skupiny pacientů.
- 3.** Ale neexistuje žádný důvod tolerovat hladiny nad 8.3 mmol/l.
- 4.** Kontinuální měření glykémie je nepochybně nutností.

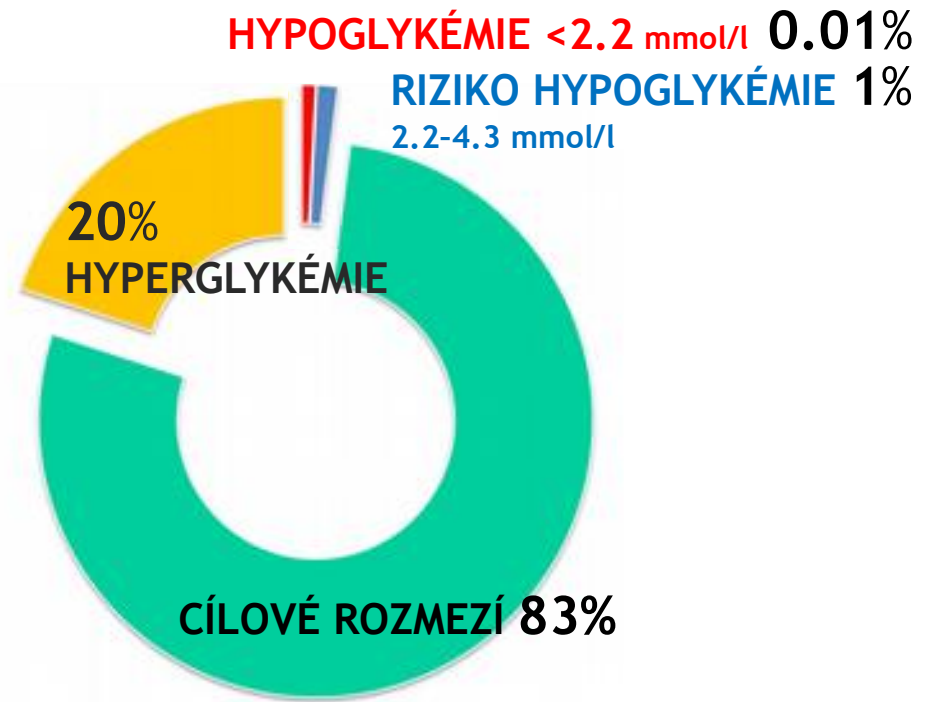
Space GlucoseControl system for blood glucose control in intensive care patients - a European multicentre observational study

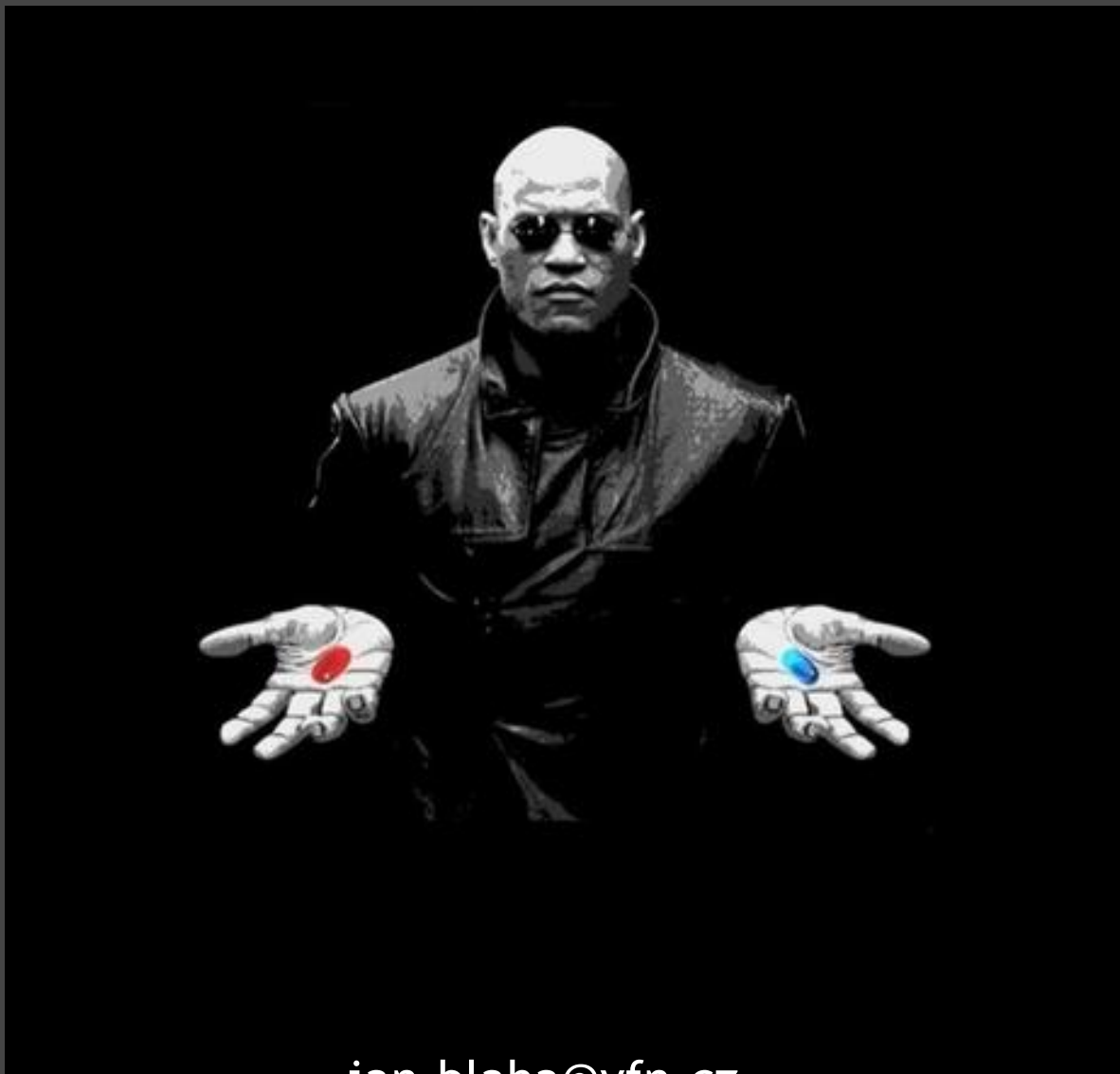
Jan Blaha^{1*}, Barbara Barteczko-Grajek², Pawel Berezowicz³, Jiri Charvat⁴, Jiri Chvojka⁵, Teodoro Grau⁶, Jonathan Holmgren⁷, Ulrich Jaschinski⁸, Petr Kopecky¹, Jan Manak⁹, Mette Moehl¹⁰, Jonathan Paddle¹¹, Marcello Pasculli¹², Johan Petersson¹³, Sirak Petros¹⁴, Danilo Radrizzani¹⁵, Vinodkumar Singh¹⁶ and Joel Starkopf¹⁷

Table 2 Blood glucose control characteristics (508 patients)

Blood glucose level at entry [mmol.l ⁻¹]	9.3 (6.8–12.3)
Time to reach target range [hours]	4.5 (2.3–8.3)
Mean insulin infusion rate [U/h]	3.3 (2.3–5.1)
<i>Whole study period</i>	
Mean blood glucose level [mmol.l ⁻¹]	6.9 (6.6–7.7)
Severe hypoglycaemia <2.2 mmol.l ⁻¹ [Number of patients/number of episodes]	4 (0.8)/4 (0.01)
Hypoglycaemia 2.2–4.3 mmol.l ⁻¹ [% of time]	0.2 (0–1.4)
Target range [% of time]	83.0 (68.7–93.1)
Hyperglycaemia >8.3 mmol.l ⁻¹ [% of time]	14.7 (6.1–29.5)

Data are presented as median (IQR) or number (%)





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