Sedace a analgezie
v intenzivní péči

mění se úhel pohledu ?

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O čem půjde řeč

- Analgosedace obecně
- Nové strategie analgosedace
- Farmaka, která je umožní
- Co si odneseme domů

Indikace A-S

- Usnadnit kriticky nemocnému toleranci invazivního a nepohodlného monitorování a léčebných procedur
- Snížit spotřebu kyslíku omezením pacientovy bdělosti a aktivity
- Navodit amnézii na dění v prostředí IM ??
- Specifické léčebné použití u nozol. jednotek
  - status epilepticus
  - tetanus
  - delirium

Heerden PV in Oh´s Intensive Care Manual, 2009

Skaar DJ, Weinert CR in Textbook of Critical Care, 2011

Navodit amnézii na dění v prostředí IM ??

- Amnézie byla považována za neškodnou, někdy za užitečnou
- Na druhé straně je považována za potenciálně škodlivou pro dlouhodobý psychický stav pacienta – rozvoj PTSD (posttraumatické stresové poruchy)

Jones C et al. Memory, delusions and the development of acute PTSD-related symptoms after intensive care: CCM 2001

Granja C et al. Understanding PTSD-related symptoms after critical care: the early illness amnesia hypothesis. CCM 2008

Dobrodiní A-S

- Mírní bolest
- Zbavuje strachu a úzkosti
- Zajistí pacientovi klid a odpočinek
- Brání rozvoji následné psychické morbidity typu posttraumatické stresové poruchy

Heerden PV in Oh´s Intensive Care Manual, 2009
Skaar DJ, Weinert CR in Textbook of Critical Care, 2011

Nežádoucí účinky A-S

- Zvýšená morbidita
- Zvýšená mortalita

- Prodloužená doba UPV
- Rozvoj deliria
- Syndromy z odnětí
- Imunosuprese

Delirium jako NÚ A-S

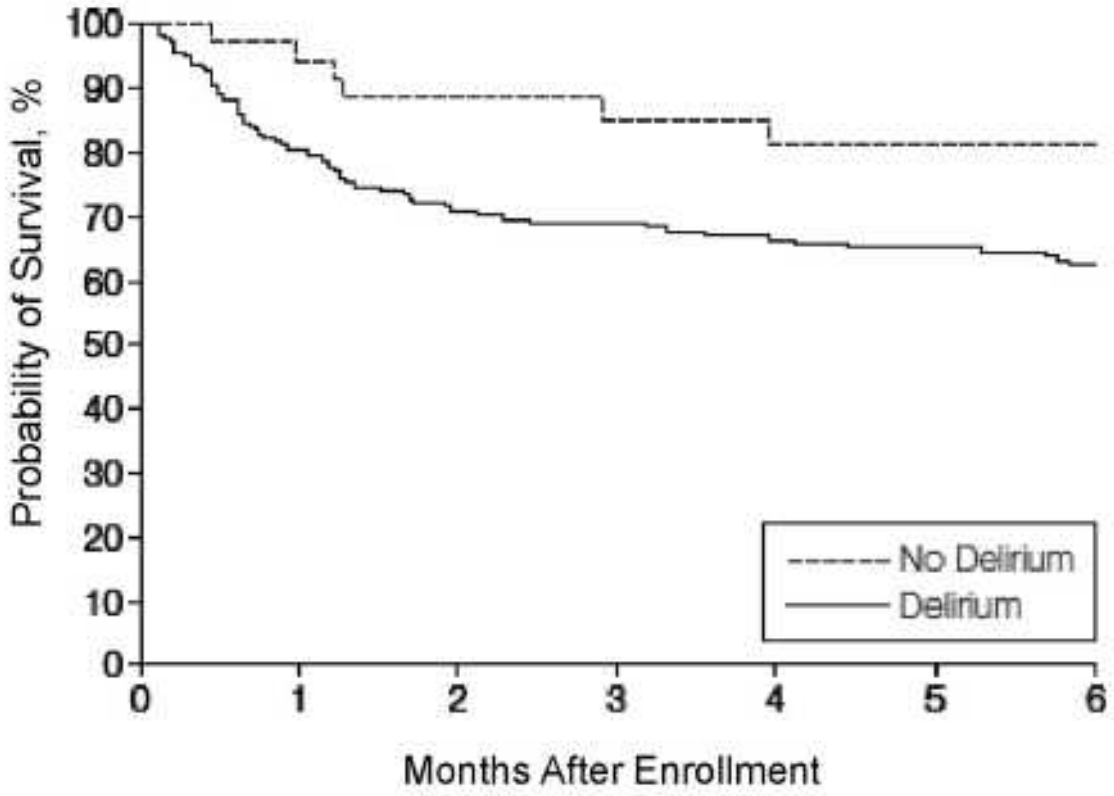
Nezávislý prediktor:

- mortality
- délky hospitalizace
- zhoršení kognitivních funkcí (trvající měsíce po propuštění)

Benzodiazepiny jsou ve vztahu ke vzniku deliria rizikovější než jiné sedativní látky

Opioidy – rozporná data. Zřejmě: přiměřené dávkování tiší bolest a snižuje d., nadměrné dávkování zvyšuje riziko deliria

McGrane S et al. Sedation in ICU. Minerva Anest 2012



No. at Risk							
No Delirium	41	34	28	25	22	21	19
Delirium	183	138	116	111	104	98	88

Figure 1. Delirium is independently associated with 6-month mortality. Multivariable Cox proportional hazards analysis demonstrated that patients who experience delirium in the intensive care unit were three times more likely to die at 6 months (hazard ratio, 3.2; 95% confidence interval, 1.4 to 7.7; $p = .008$) after adjustment for age, Charlson Comorbidity Index, modified Blessed Dementia Rating Scale score, Acute Physiology and Chronic Health Evaluation II score, Sequential Organ Failure Assessment score, sepsis, acute respiratory distress syndrome, and time-varying covariates for coma and use of sedative and analgesic medications. Reprinted with permission from Ely et al (21).

Bolest v IP

Důvody pro bolest v IP

- Vlastní onemocnění či úraz
- Převazy
- Invazivní procedury
- Ošetřovatelské postupy
- Intubace + přítomnost tracheální rourky
- Operační zákroky a stavy po operacích

Bolest v IP

Důsledky nedostatečně tlumené bolesti

- Tachykardie
- Imunosuprese
- Zvýšená produkce katecholaminů
- Zvýšená spotřeba kyslíku
- Delirium

Z uvedených důvodů jsou analgetika v první linii – před sedativy – proto analgosedace

McGrane S et al. Sedation in ICU. Minerva Anest 2012

Analgosedace

- Vývoj nových léků s rychlejším nástupem i odezněním (např. fentanyl…remifentanil)
- Důraz na titraci léků
- Důraz na použití analgetik a pouze ad hoc dotitrování sedativ

McGrane S et al. Sedation in ICU. Minerva Anest 2012

Které analgetikum ?

Není zcela jasno, neboť např.

- Remifentanil je snadněji titrovatelný, ale pacienti mají po extubaci větší bolest než při použití fentanylu
- Ekonomika hraje roli
- Volba v závislosti na orgánové dysfunkci, hemodynamické instabilitě

McGrane S et al. Sedation in ICU. Minerva Anest 2012

Sedace

U > 70 % pacientů na PIM je přítomna agitovanost

Důvody agitovanosti:

- strach a úzkost
- spánková deprivace
- nadbytek nevhodných stimulů (alarmy, hluk, permanentní světlo…)
- dušnost
- bolest

Jacobi J et al. Clinical practice guidelines…CCM 2002

Monitorování A-S

Tři R:

- Ramsay Scale
- Riker Sedation Agitation Scale (SAS)
- Richmond Agitation-Sedation Scale (RASS)

BIS

- Nejasný užitek
- Lze jej použít jako přídatné monitorování
- Vhodný v situacích, kdy je současná NMB

Monitorování A-S

Ramsay Scale	Sedation Agitation Scale	Richmond Agitation-Sedation Scale
Level 1: Patient awake, anxious and agitated or restless, or both	Level 7: Dangerous agitation: pulling at endotracheal tube, trying to remove catheters, climbing over bed rail, striking at staff, thrashing side to side	+4 Combative: overtly combative, violent, immediate danger to staff
Level 2: Awake, cooperative, orientated, and tranquil	Level 6: Very agitated: does not calm, despite frequent reminding of limits: requires physical restraints, biting endotracheal tube	+3 Very agitated: pulls or removes tube(s) or catheter(s); aggressive
Level 3: Awake, responds to commands only	Level 5: Agitated: anxious to mildly agitated, attempting to sit up, calms to verbal instructions	+2 Agitated: frequent non-purposeful movement, fights ventilator
Level 4: Asleep, brisk response to light glabellar tap or loud auditory stimulus	Level 4: Calm and cooperative: calm, awakens easily, follows simple commands	+1 Restless: anxious but movements not aggressive vigorous
Level 5: Asleep, sluggish response to light glabellar tape or loud auditory stimulus	Level 3: Sedated: difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off again, follows simple commands	0 Alert and calm
Level 6: Asleep, no response to light glabellar tap or loud auditory stimulus	Level 2: Very sedated: arouses to physical stimuli, but does not communicate or follow commands, may move spontaneously	-1 Drowsy: not fully alert, but has sustained awakening (eye- opening/ eye contact) to voice (>10s)
	Level 1: Unarousable: minimal or no response to noxious stimuli, does not communicate or follow commands	-2 Light sedation: briefly awakens with eye contact to voice (<10s)
		-3 Moderate sedation: movement or eye opening to voice (but no eye contact)
		-4 Deep sedation: no response to voice, but movement or eye opening to physical stimulation
		-5 Unarousable: no response to voice or physical stimulation

Podávání sedativ

- Kontinuální infuze – CIS (continuous infusion sedation)
- Bolusy
- Denní přerušování sedace – DIS (daily interruption of sedation) + titrování sedace – co nejmenší dávky po co nejmenší dobu

Kress JP et al. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. NEJM 2000

Kontinuální infuze

- Horší výsledky léčby
- Delší trvání UPV
- Delší hospitalizace na ICU i v nemocnici

Kolef et al. Chest, 1998

- Menší variabilita ve farmakokinetice a menší kolísání plazmatických hladin

Mehta et al. Crit Care Clin, 2009

Denní přerušování sedace – DIS

- dočasné přerušení infuze sedativ (propofol a midazolam) a analgetik (morfin) do doby, kdy
- pac. splní 3-4 jednoduché úkoly
- nebo se objeví agitovanost

Kress JP et al. Dailly interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. NEJM 2000

Denní přerušování sedace – DIS

- Přerušit sedaci 1x denně, pokud nejsou KI:
- Bolest
- Úzkost, strach, „distres“
  - Agitovanost
  - Hemodynamická nestabilita
  - Interference s ventilátorem
- Zvýšený nitrolební tlak
- Přetrvávající nervosvalová blokáda
- Hypotermie

Kress JP et al. NEJM 2000

Shruti BP et al. AJRCCM 2012

Crit Care Clin 25, 2009: 489-513

Protocolized and Target-based Sedation and Analgesia in the ICU

Curtis N. Sessler, MD[a,b,*], Sammy Pedram, MD[a]

A screening, prevention, and restoration model for saving the injured brain in intensive care unit survivors

Eduard E. Vasilevskis, MD; Pratik P. Pandharipande, MD, MSCI; Timothy D. Girard, MD, MSCI; E. Wesley Ely, MD, MPH

We face a profound and emerging public health problem in the form of acute and chronic brain dysfunction. This affects both young and elderly intensive care unit survivors and is altering the landscape of society. Two-thirds of intensive care unit patients develop delirium, and this is associated with longer stays, increased costs, and excess mortality. In addition, over half of intensive care unit survivors suffer a dementia-like illness that impacts their physical and cognitive functional abilities and which appears to be related to the duration of their intensive care unit delirium. A new paradigm of how intensivists handle the brain is required. We propose a three-step approach to address this emerging epidemic, which includes *S*creening, *P*revention, and *R*estoration of brain function (SPR). Screening combines risk factor identification and delirium assessment using validated instruments. Prevention of acute and chronic brain dysfunction requires implementation of a core model of care that combines evidence-based practices: awakening and breathing, coordination with target-based sedation, delirium monitoring, and exercise/early mobility (ABCDE). Restoration introduces strategies of ongoing screening and treatment for intensive care unit survivors at high risk of ongoing brain dysfunction. This practical system applying many evidence-based concepts incorporates personalized medicine, systems-based practice, and continuing research and development toward improving acute and chronic cognitive outcomes. (Crit Care Med 2010; 38[Suppl.]:S683–S691)

KEY WORDS: delirium; intensive care unit; risk factors; primary prevention; secondary prevention; tertiary prevention; quality improvement; ICU-acquired weakness; sedation; diagnosis; treatment

Strategie SPR

- **S**creening mozkové dysfunkce
  - zjištění faktorů rizikových pro vznik deliria
  - zhodnocení / vyšetření deliria
- **P**revence mozkové dysfunkce
  - strategie ABCDE
- **R**estaurace mozkové funkce

Vasilevskis E et al. Screening, prevention, and restoration model for saving the injured brain in intensive care survivors. CCM 2010

Strategie ABCDE

- **A**wakening and **B**reathing trial **C**oordination
- **C**hoice of sedatives and analgesics
- **D**aily delirium monitoring
- **E**arly mobility and **E**xercise

Vasilevskis E et al. Screening, prevention, and restoration model for saving the injured brain in intensive care survivors. CCM 2010

Morandi A et al. Sedation, delirium and mechanical ventilation: the „ABCDE“ approach. Curr Opin Crit Care 2011

Table 2. Evolution of the 'back end' of critical care: Management and recovery

Years	Concept Introduced and Published	'Back End' Process of Care	Evolutionary Step of the ABCDE Bundle
1995–1999	Spontaneous breathing trials (SBTs)	Liberation from ventilation	Step B
1999–2004	Spontaneous awakening trials (SATs)	Liberation from sedation	Step A
2001–2007	Awakening and breathing coordination (SATs + SBTs)	Liberation from sedation and ventilation	Steps ABC
2001–2008	Validation and implementation of delirium assessment/ monitoring tools	Delirium monitoring	Step D
2009–2010	Early mobility and physical therapy	Animation	Step E
2010	Awakening and breathing coordination, delirium monitoring, and early mobility	Liberation and animation	ABCDE

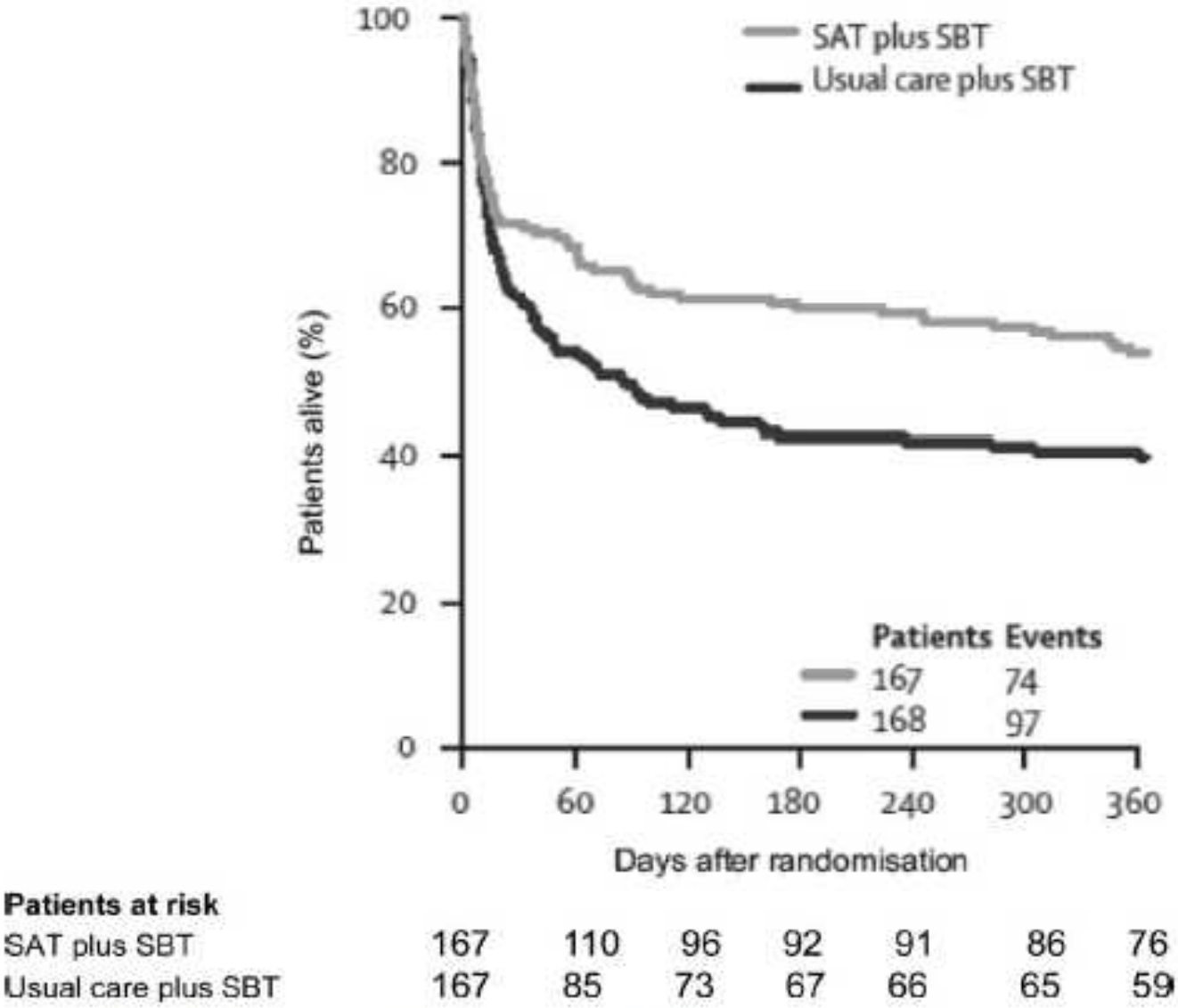
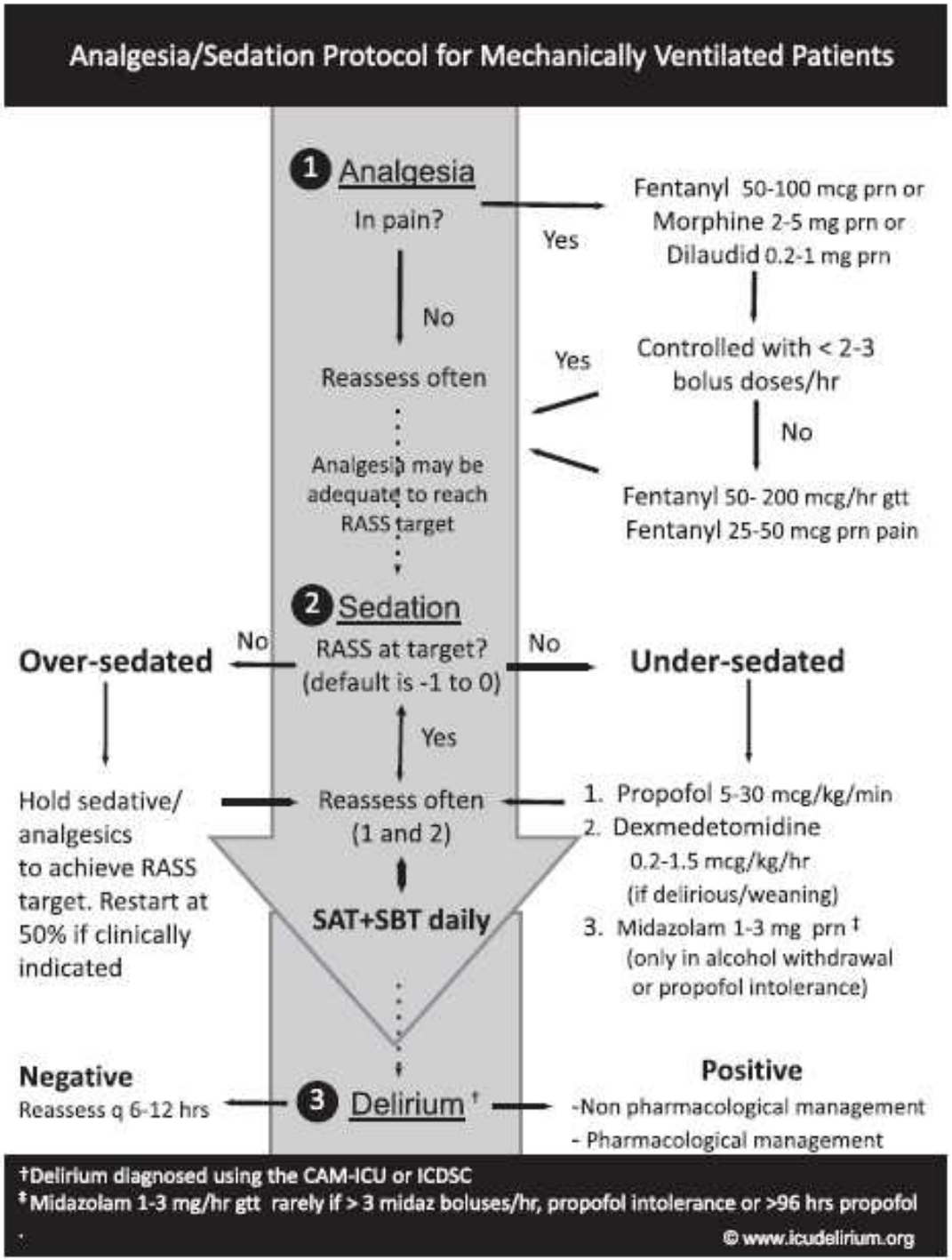


Figure 2. Paired spontaneous awakening trials (*SATs*) with spontaneous breathing trials (*SBTs*) reduce mortality at 1 yr. Multivariable Cox proportional hazards analysis demonstrated that patients in the intervention group (receiving paired daily spontaneous awakening and breathing trials) were 32% less likely to die during the next year compared with the control group. Hazard ratio = 0.68; 95% confidence interval, 1.6 to 2.9; $p < .001$. Reprinted with permission from Girard et al (49).


Analgesia/Sedation Protocol for Mechanically Ventilated Patients
1 Analgesia
In pain?
Yes
Fentanyl 50-100 mcg prn or
Morphine 2-5 mg prn or
Dilaudid 0.2-1 mg prn
No
Reassess often
Yes
Controlled with < 2-3 bolus doses/hr
No
Analgesia may be adequate to reach RASS target
Fentanyl 50- 200 mcg/hr gtt
Fentanyl 25-50 mcg prn pain
2 Sedation
No
Over-sedated
RASS at target?
(default is -1 to 0)
No
Under-sedated
Yes
Hold sedative/ analgesics to achieve RASS target. Restart at 50% if clinically indicated
Reassess often
(1 and 2)
1. Propofol 5-30 mcg/kg/min
2. Dexmedetomidine
0.2-1.5 mcg/kg/hr
(if delirious/weaning)
3. Midazolam 1-3 mg prn ‡
(only in alcohol withdrawal or propofol intolerance)
SAT+SBT daily
Negative
Reassess q 6-12 hrs
3 Delirium †
Positive
-Non pharmacological management
- Pharmacological management
†Delirium diagnosed using the CAM-ICU or ICDSC
‡Midazolam 1-3 mg/hr gtt rarely if > 3 midaz boluses/hr, propofol intolerance or >96 hrs propofol
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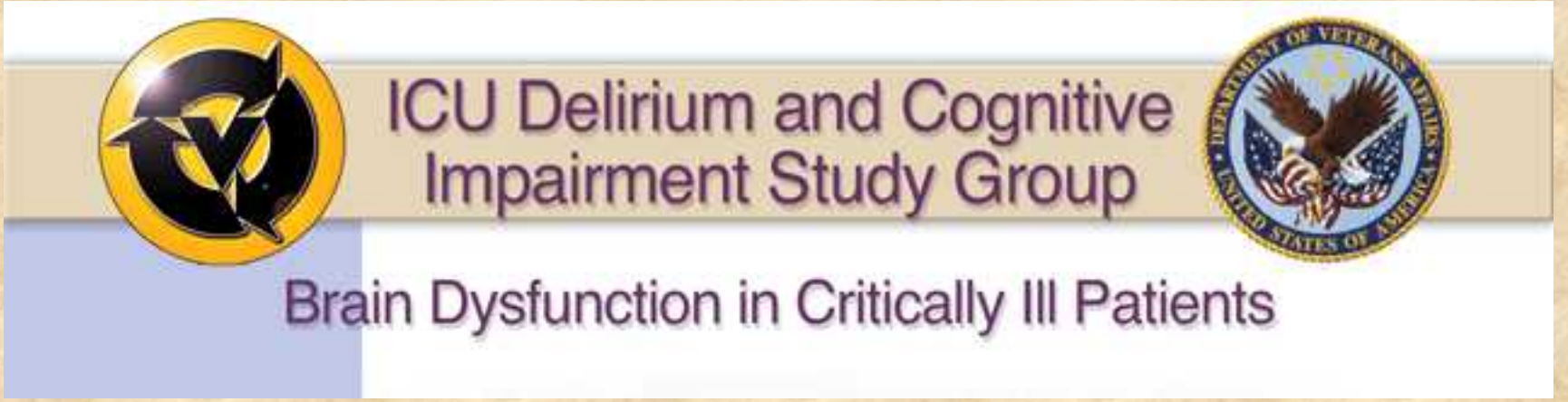
Vanderbilt University Medical Center
Veteran Affairs TN Valley Geriatric Research Education and Clinical Center, Nashville, Tennessee



Ideální preparát pro sedaci

- Levný
- Minimální ovlivnění hemodynamiky
- Minimální útlum dechu
- Bez lékových interakcí
- Bez aktivních metabolitů
- Bez orgánové toxicity
- Krátký kontext-senzitivní poločas
- Eliminace nezávislá na orgánových funkcích

Používaná sedativa

- GABA agonisté
  - propofol
  - benzodiazepiny
- Alfa-2 agonisté
  - dexmedetomidin
  - klonidin
- (antipsychotika – haloperidol, atypická)
- (ketamin)
- (volatilní anestetika)

Propofol

- GABA agonista
- Velký distribuční objem
- 98% vazba na bílkoviny
- Krátký poločas
- Je-li užíván formou bolusů nebo infuzně pro lehkou sedaci, má krátkodobý účinek
- Při dlouhodobé infuzi se nasytí periferní tkáně a zvyšuje se úloha metabolismu na úkor redistribuce

Propofol - NÚ

- Hypotenze (vazodilatace + deprese myokardu)
- Dechový útlum
- Je energeticky „výživný“ – 1,1 kcal/ml
- Hypertriglyceridemie → propofol infusion sy
  - prolongované infuze
  - vysoké celkové dávky
  - děti
  - sledovat pH, laktát, CK, TGl, ekg
  - současné německé doporučení – po 7 dnech vyměnit za jiné sedativum

Diedrich DA et al. ICM 2011
Martin J et al. Ger Med Sci 2010

Propofol versus benzodiazepiny

- Kratší hospitalizace byla prokázána pouze ve vztahu k sedaci dlouhodobými BDZ – diazepam, lorazepam
- K midazolamu – není významný rozdíl v LOS
- Ceny ICU pobytu jsou srovnatelné

Barreintos-Vega R et al. CCM 1997

Ho KM et al. ICM 2008

Alfa-2 agonisté

- Alfa-2 receptor – „nejdůležitější presynaptický receptor v lidském těle“

Gregoretti et al, Current Drug Targets 2009

- Alfa-2 agonismus (zejm. α-2a) - účinek:
  - sympatikolytický
  - hypnotický
  - sedativní
  - analgetický
  - neuroprotektivní

Panzer et al. Crit Care Clinics 2009

Hossain MD et al. Eur J Pharmacol 2004

Effect of Sedation With Dexmedetomidine vs Lorazepam on Acute Brain Dysfunction in Mechanically Ventilated Patients

The MENDS Randomized Controlled Trial

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Context Lorazepam is currently recommended for sustained sedation of mechanically ventilated intensive care unit (ICU) patients, but this and other benzodiazepine drugs may contribute to acute brain dysfunction, ie, delirium and coma, associated with prolonged hospital stays, costs, and increased mortality. Dexmedetomidine induces sedation via different central nervous system receptors than the benzodiazepine drugs and may lower the risk of acute brain dysfunction.

Objective To determine whether dexmedetomidine reduces the duration of delirium and coma in mechanically ventilated ICU patients while providing adequate sedation as compared with lorazepam.

Design, Setting, Patients, and Intervention Double-blind, randomized controlled trial of 106 adult mechanically ventilated medical and surgical ICU patients at 2 tertiary care centers between August 2004 and April 2006. Patients were sedated with dexmedetomidine or lorazepam for as many as 120 hours. Study drugs were titrated to achieve the desired level of sedation, measured using the Richmond Agitation-Sedation Scale (RASS). Patients were monitored twice daily for delirium using the Confusion Assessment Method for the ICU (CAM-ICU).

Main Outcome Measures Days alive without delirium or coma and percentage of days spent within 1 RASS point of the sedation goal.

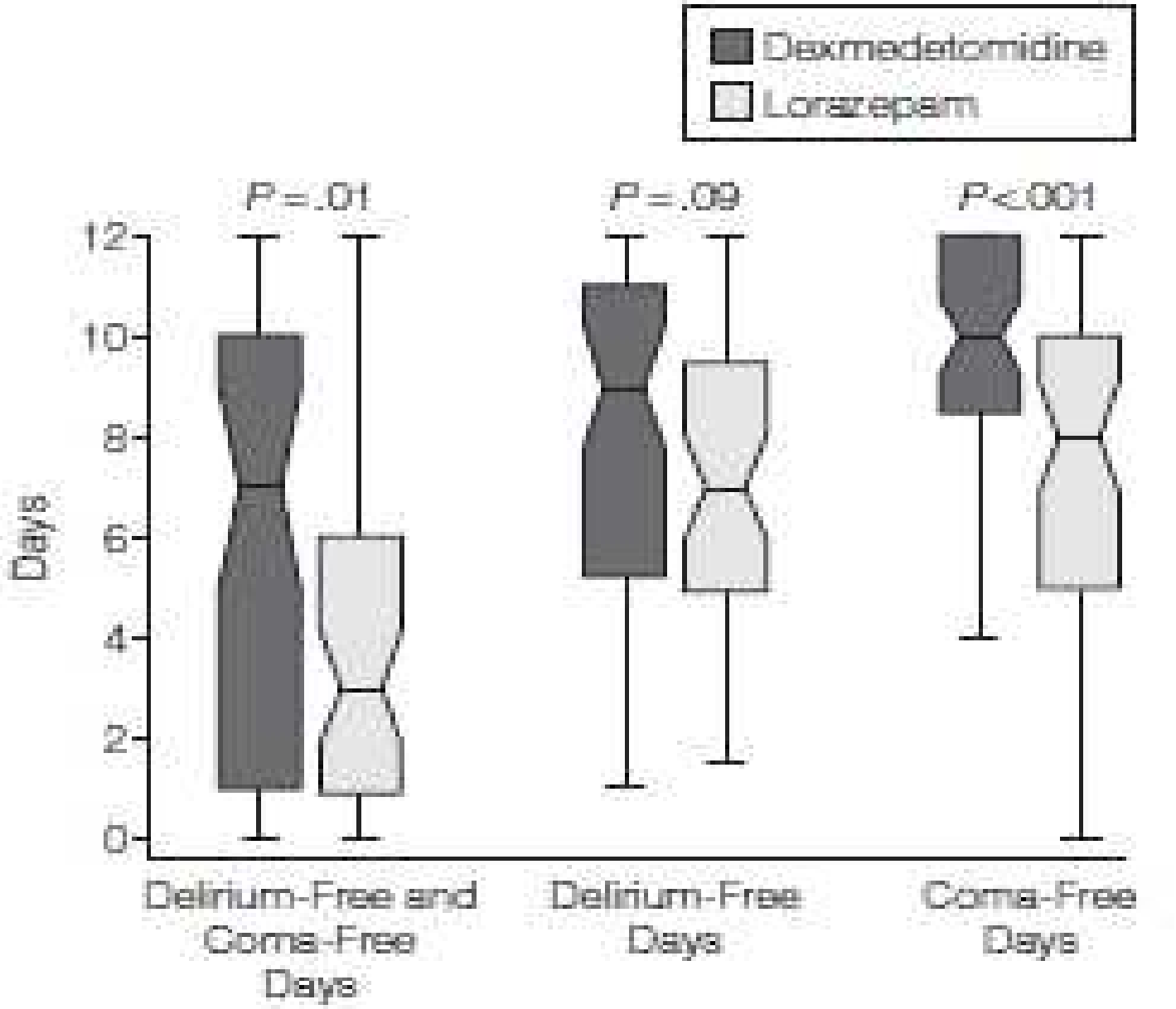
Sedace – DEX vs. BDZ

- Pandharipande et al, JAMA 2007 – srovnání dex a lorazepamu na výskyt deliria u UPV
  - Sedace dexmedetomidinem
    - 0,15-1,5 µg/kg/hod, max. 120 hod.
  - Sedace lorazepamem
    - 1-10 mg/kg/hod., max. 120 hod.

  Závěr – sedace dexmedetominidem u pac.na UPV v prostředí ICU – signifikantně více dní bez deliria nebo komatu při srovnatelných nákladech na léčbu.

  Byl to první RCT, který ukázal, že akutní mozková dysfunkce může být omezena výběrem sedativa.

Figure 2. Delirium-Free and Coma-Free Days During Study



Dexmedetomidine and the Reduction of Postoperative Delirium after Cardiac Surgery

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CRAIG MILLER, M.D., BRUCE A. REITZ, M.D.

Background: *Delirium is a neurobehavioral syndrome caused by the transient disruption of normal neuronal activity secondary to systemic disturbances.* **Objective:** *The authors investigated the effects of postoperative sedation on the development of delirium in patients undergoing cardiac-valve procedures.* **Methods:** *Patients underwent elective cardiac surgery with a standardized intraoperative anesthesia protocol, followed by random assignment to one of three postoperative sedation protocols: dexmedetomidine, propofol, or midazolam.* **Results:** *The incidence of delirium for patients receiving dexmedetomidine was 3%, for those receiving propofol was 50%, and for patients receiving midazolam, 50%. Patients who developed postoperative delirium experienced significantly longer intensive-care stays and longer total hospitalization.* **Conclusion:** *The findings of this open-label, randomized clinical investigation suggest that postoperative sedation with dexmedetomidine was associated with significantly lower rates of postoperative delirium and lower care costs.*

(Psychosomatics 2009; 50:206–217)

Sedace – DEX vs. PROP vs. BDZ

- Maldonado, Psychosomatics 2009 – delirium po KCH operacích:
  - Sedace dexmedetomidinem **3 %** pacientů
    - Úv. 0,4 μg/kg následována 0,2-0,7 μg/kg/h, max. 24 h
  - Sedace propofolem **50 %** pacientů
    - 25-50 μg/kg/min
  - Sedace midazolamem **50 %** pacientů
    - 0,5-2 mg/hod.

  Závěr – sedace dexmedetomidinem – signifikantně méně pooperačních delirií, nižší léčebné náklady (zkrácení doby hospitalizace)

Critical Care

CRITICAL CARE

Effect of dexmedetomidine versus lorazepam on outcome in patients with sepsis: an a priori-designed analysis of the MENDS randomized controlled trial

Critical Care 2010, **14**:R38 doi:10.1186/cc8916

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Sedace – DEX vs. BDZ

- Pandharipande et al, CC 2010-11 – srovnání dex a lorazepamu na celkové výsledky léčby u septických pacientů
  - Sedace dexmedetomidinem
    - 0,15-1,5 μg/kg/hod, max. 120 hod.
  - Sedace lorazepamem
    - 1-10 mg/kg/hod., max. 120 hod.

  Závěr – sedace dexmedetominidem u septických pac.
  – signifikantně více dní bez mozkové dysfunkce a UPV, menší úmrtnost

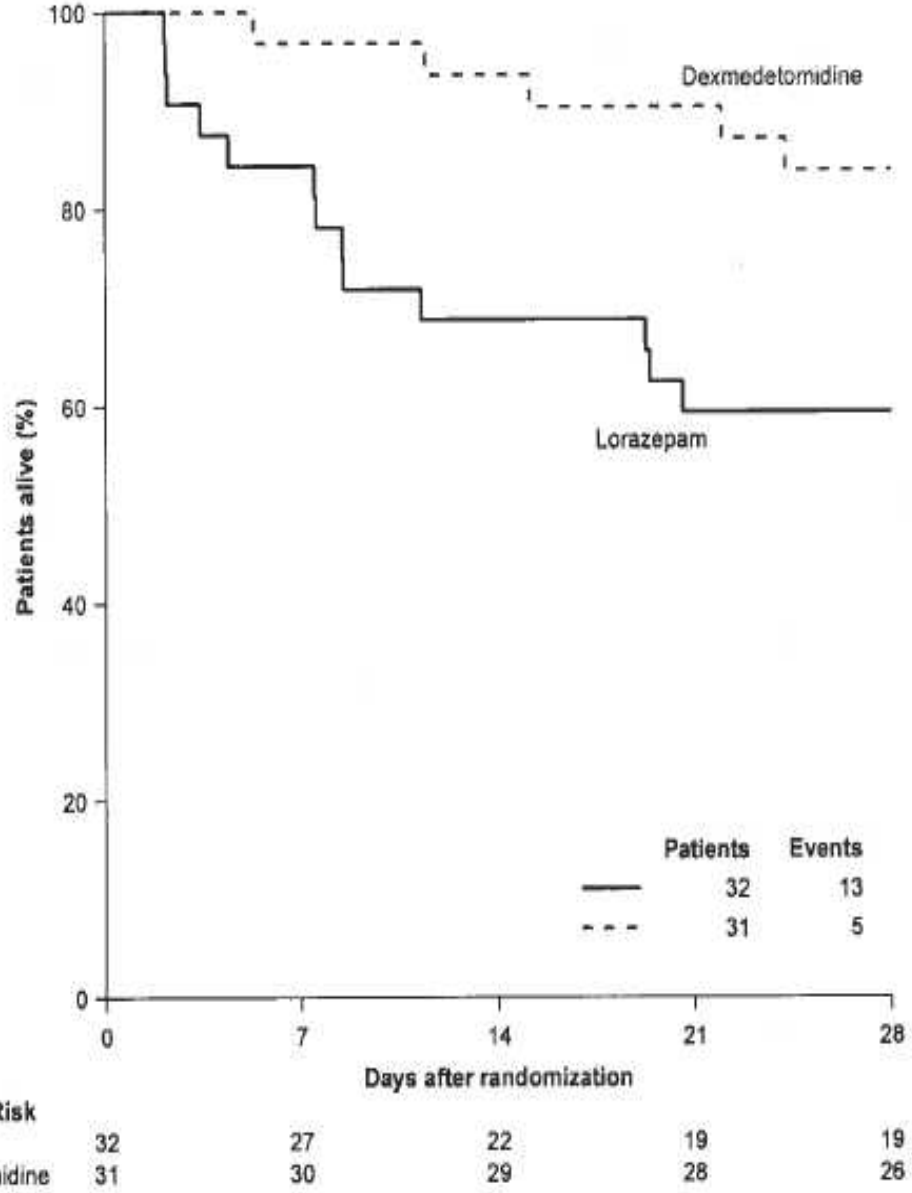

Figure 3. Kaplan-Meier curve showing probability of survival during the first 28 days according to treatment group, among patients with sepsis. Dexmedetomidine decreased the probability of dying within 28 days by 70%; this beneficial effect was not seen in patients who were not septic (*P* value for interaction = 0.11 implying an interaction between sepsis and the treatment groups).

Available online http://ccforum.com/content/13/3/R75

Research

Open Access

Dexmedetomidine vs. haloperidol in delirious, agitated, intubated patients: a randomised open-label trial

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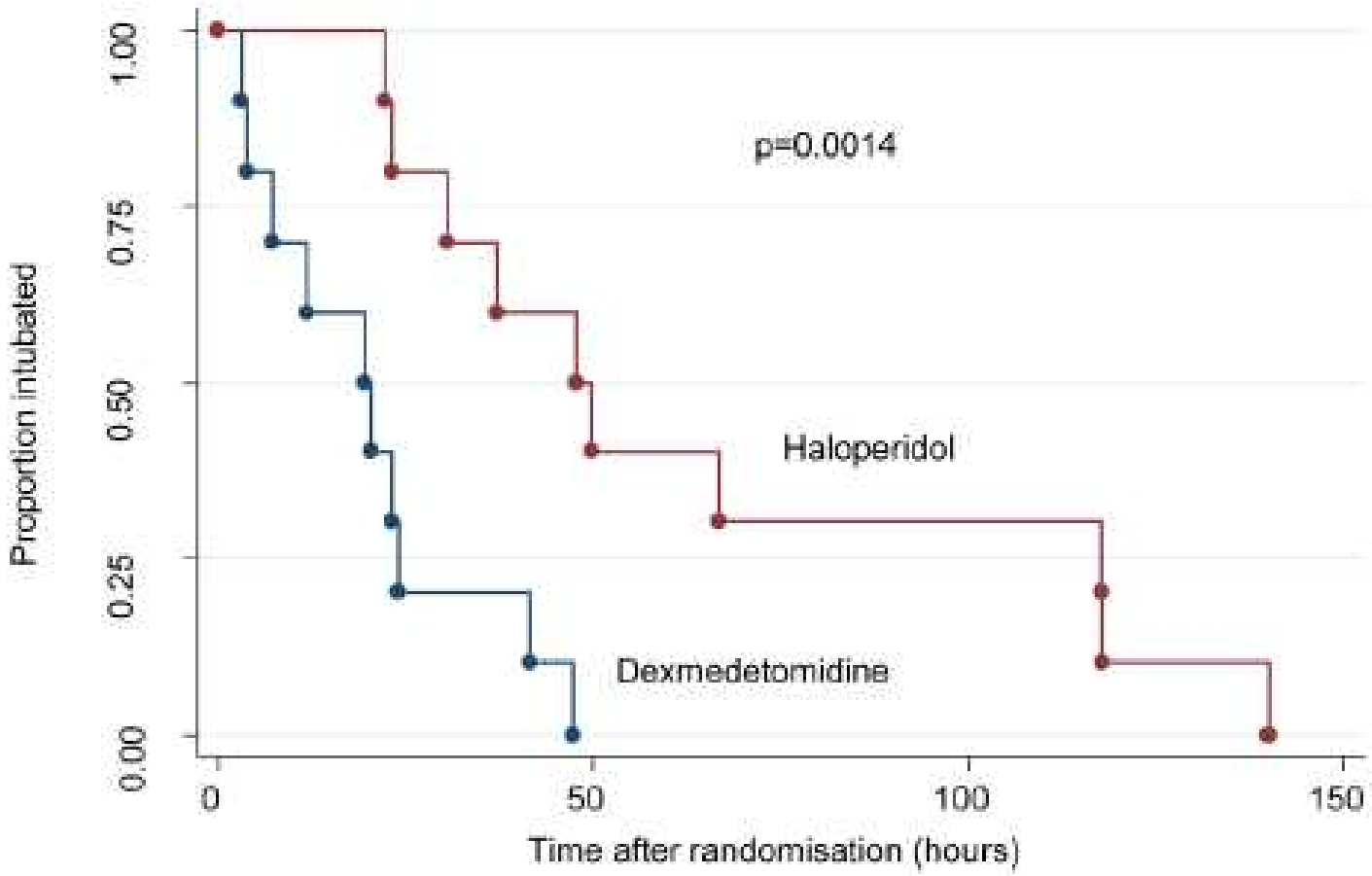
Critical Care 2009, **13**:R75 (doi:10.1186/cc7890)
This article is online at: http://ccforum.com/content/13/3/R75

Sedace – DEX vs. haloperidol

- Reade et al, CC 2009 – srovnání dex a haloperidolu u agitovaných intub. pacientů
  - – Sedace dexmedetomidinem
    - 0,2-0,7 μg/kg/hod
  - – Sedace haloperidolem
    - 0,5-2 mg/hod

  Závěr – sedace dexmedetomidinem – signifikantně časnější extubace (19,9 vs. 24,0 h), dex významně zkrátil dobu hospitalizace na ICU ze 6,5 na 1,5 dne

Figure 2



Graph showing time to extubation.

JAMA®

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current as of February 2, 2009.

Dexmedetomidine vs Midazolam for Sedation of Critically Ill Patients: A Randomized Trial

Richard R. Riker; Yahya Shehabi; Paula M. Bokesch; et al.

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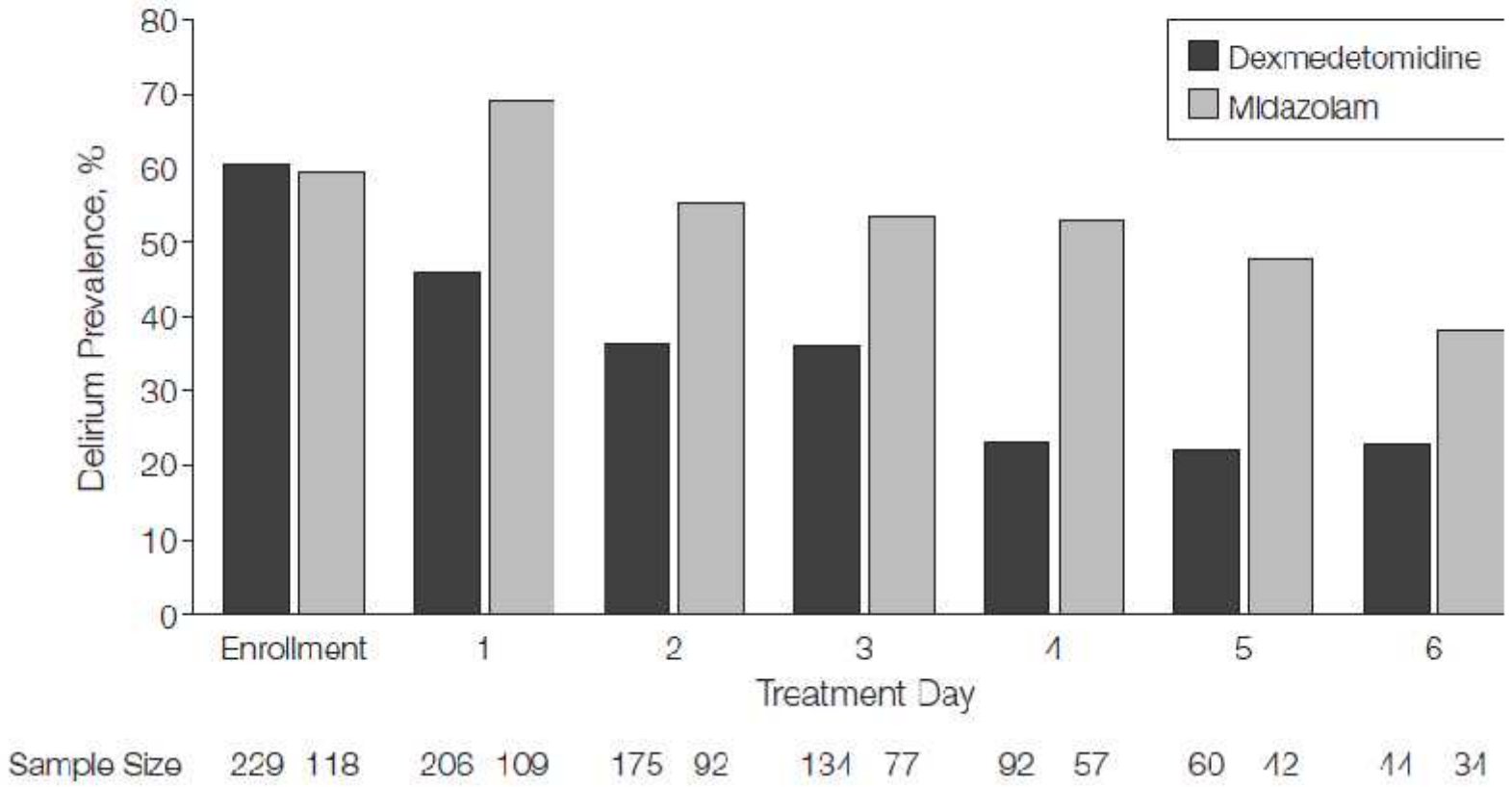
http://jama.ama-assn.org/cgi/content/full/2009.56v1

Sedace DEX vs. BDZ

- Riker et al, JAMA 2009 – srovnání dex a midazolamu v sedaci kriticky nemocných
  - Sedace dexmedetomidinem
    - 0,8 µg/kg/hod, dále titrace dle RASS
  - Sedace midazolamem
    - 0,06 mg/kg/hod, dále titrace dle RASS

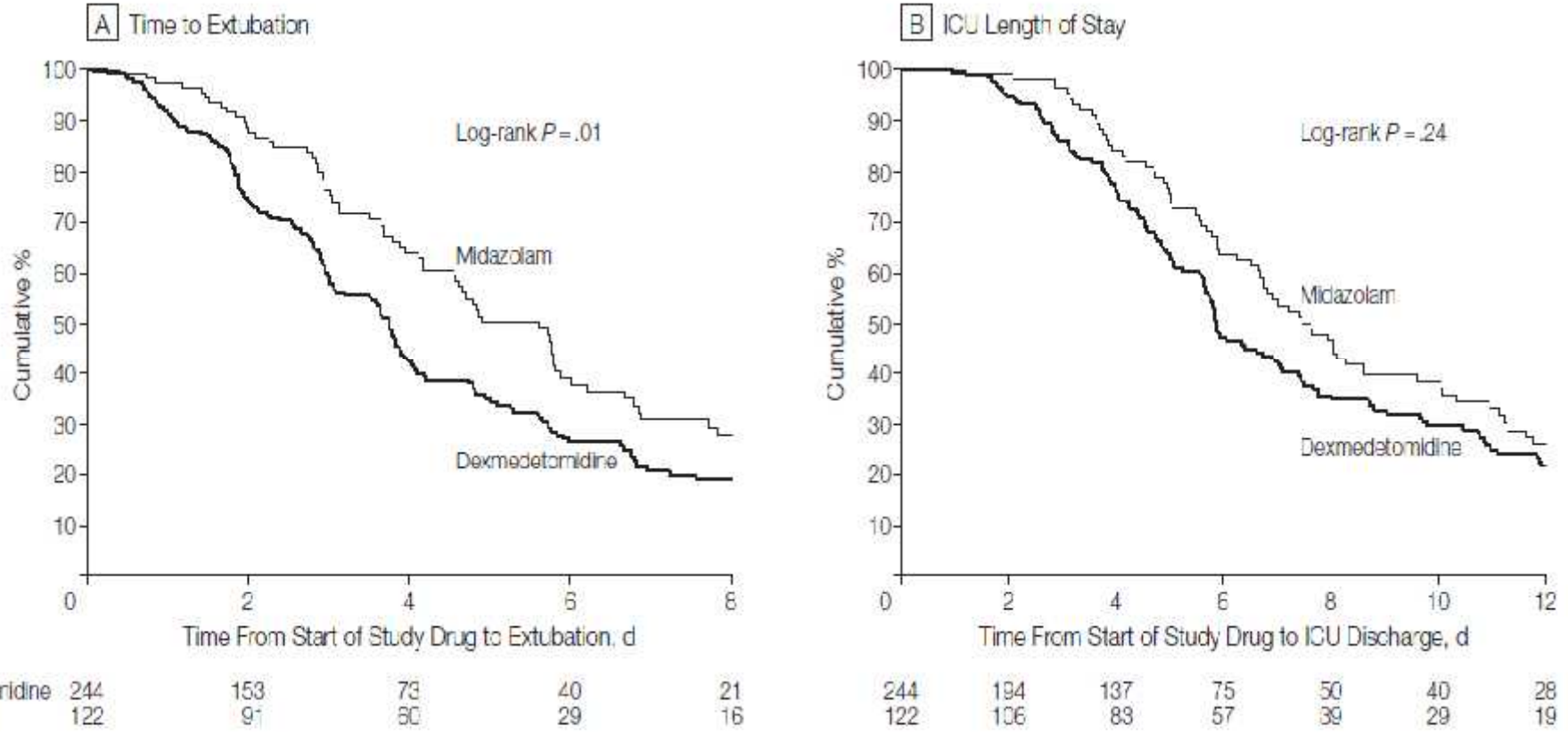
  Závěr – sedace dexmedetominidem – signifikantně méně delirií (54% vs. 76,6%), dex významně zkrátil dobu hospitalizace na ICU 5,9 vs. 7,6 dne. Pac. s dex měli častěji bradykardii, ale méně často tachykardii a hypertenzi.

Figure 2. Daily Prevalence of Delirium Among Intubated Intensive Care Unit Patients Treated With Dexmedetomidine vs Midazolam



Delirium was diagnosed using the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU).[24] At baseline, 60.3% of dexmedetomidine-treated patients and 59.3% of midazolam-treated patients were CAM-ICU–positive ($P=.82$). The effect of dexmedetomidine treatment was significant in the generalized estimating equation[27] analysis, with a 24.9% decrease (95% confidence interval, 16%-34%; $P<.001$) relative to midazolam treatment. Numbers differ from those for primary analysis because patients were extubated, discharged from the intensive care unit, or had missing delirium assessments.

Figure 3. Time to Extubation and Intensive Care Unit (ICU) Length of Stay Among Patients Treated With Dexmedetomidine vs Midazolam



A, Time to extubation was calculated from the start of study drug to the time of extubation after which no reintubation occurred. Patients not extubated were censored at time of study drug discontinuation. The median time to extubation was 1.9 days shorter for the dexmedetomidine group than for the midazolam group (3.7 days [95% confidence interval {CI}, 3.1-4.0] vs 5.6 days [95% CI, 4.6-5.9]; P=.01 by log-rank test). B, Length of ICU stay was calculated from start of study drug to time of order for ICU transfer. Patients without discharge were censored at the time of study drug discontinuation. The median length of ICU stay was similar between the dexmedetomidine and midazolam groups (5.9 days [95% CI, 5.7-7.0] vs 7.6 days [95% CI, 6.7-8.6]; *P*= .24 by log-rank test).

Dexmedetomidine vs Midazolam or Propofol for Sedation During Prolonged Mechanical Ventilation

Two Randomized Controlled Trials

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Context Long-term sedation with midazolam or propofol in intensive care units (ICUs) has serious adverse effects. Dexmedetomidine, an α_2-agonist available for ICU sedation, may reduce the duration of mechanical ventilation and enhance patient comfort.

Objective To determine the efficacy of dexmedetomidine vs midazolam or propofol (preferred usual care) in maintaining sedation; reducing duration of mechanical ventilation; and improving patients' interaction with nursing care.

Design, Setting, and Patients Two phase 3 multicenter, randomized, double-blind trials carried out from 2007 to 2010. The MIDEX trial compared midazolam with dexmedetomidine in ICUs of 44 centers in 9 European countries; the PRODEX trial compared propofol with dexmedetomidine in 31 centers in 6 European countries and 2 centers in Russia. Included were adult ICU patients receiving mechanical ventilation who needed light to moderate sedation for more than 24 hours (midazolam, n=251, vs dexmedetomidine, n=249; propofol, n=247, vs dexmedetomidine, n=251).

JAMA, March 21, 2012—Vol 307, No. 11

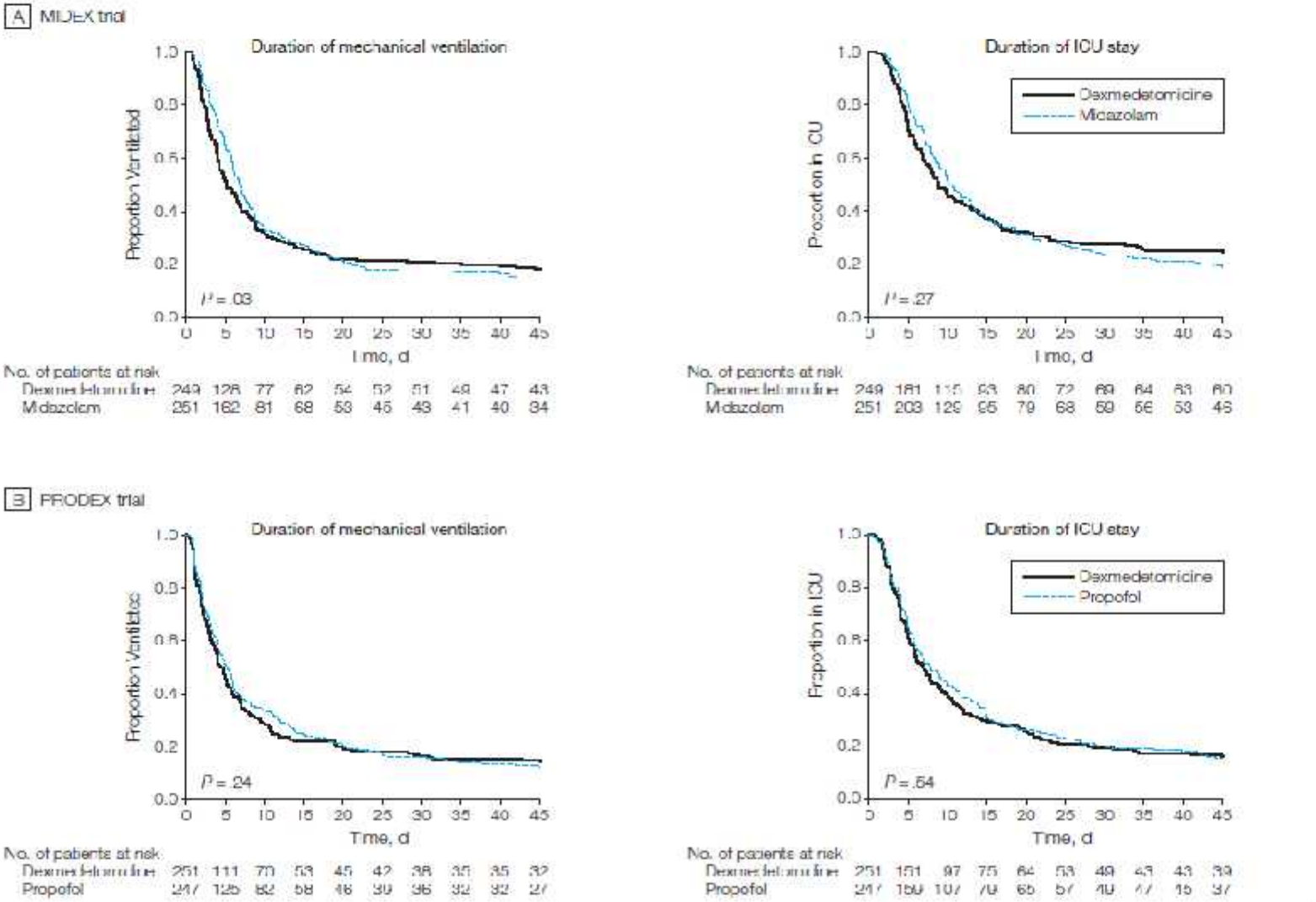
Sedace DEX vs. MIDAZ vs. PROP

- Jakob et al, JAMA 2012 – srovnání dex a midaz a dex a propof v sedaci u dlouhodobé UPV (MIDEX a PRODEX trial)
  - Sedace dexmedetomidinem
    - 0,2-1,4 µg/kg/hod, titrace dle RASS
  - Sedace midazolamem
    - 0,03-0,2 mg/kg/hod, titrace dle RASS
  - Sedace poropofolem
    - 0,3-4,0 mg/kg/hod, titrace dle RASS

Sedace DEX vs. MIDAZ vs. PROP -

- nebyla zjištěna inferiorita dexmedetomidinu vůči midazolamu ani propofolu pro zajištění lehké až střední sedace u dlouhodobé UPV
- DEX ve srovnání s MIDAZ zkrátil trvání UPV (123 vs. 164 hod.)
- nebyl rozdíl v LOS na ICU a v mortalitě
- DEX ve srovnání s MIDAZ i PROP zlepšil pacientovu schopnost sdělovat bolest
- u DEXu ve srv. s MIDAZ bylo více hypotenzí (20,6 vs. 11,6%) a bradykardií (14,2 vs. 5,2%)

Figure 2. Duration of Mechanical Ventilation and Intensive Care Unit Stay



In the MIDEX trial (midazolam vs dexmedetomidine), the median duration of mechanical ventilation was, for dexmedetomidine, 123 hours (interquartile range [IQR], 67-337 hours) and, for midazolam, 164 hours (IQR, 92-380 hours) (Gehan-Wilcoxon $P=.03$). The median length of stay in the intensive care unit (ICU) from randomization until the patient was medically fit for discharge was, for dexmedetomidine, 211 hours (IQR, 115-831 hours) and, for midazolam, 243 hours (IQR, 140-630 hours; Gehan-Wilcoxon $P=.27$). In the PRODEX trial (propofol vs dexmedetomidine), the median duration of mechanical ventilation was, for dexmedetomidine, 97 hours (IQR, 45-257 hours) and, for propofol, 118 hours (IQR, 48-327 hours) (Gehan-Wilcoxon $P=.24$). The median length of stay in the ICU from randomization until the patient was medically fit for discharge was, for dexmedetomidine, 164 hours (IQR, 90-480 hours) and, for propofol, 185 hours (93-520 hours, Cox's proportional hazards test $P=.54$). Study drugs were given for a maximum of 336 hours in both trials.

Dex v.s. benzodiazepiny a delirium

- Nabízí se otázka, zda k významnému omezení výskytu deliria vede:
  - vyvarování se GABA-agonistů
  - nebo pozitivní vliv α-2 agonistů ?

Hipp DM et al. Neurotherapeutics 2012

Killing them softly with sedatives: do we have better alternatives?

Pratik Pandharipande, Nashville

Berlin – ESICM, X. 2011

- Vyvažovat dobrodiní a škodlivé účinky A-S
- BDZ jsou rizikovým faktorem deliria a dalších konsekvencí, které jsou potenciálně ovlivnitelné
- Zvažujte redukci používání BDZ, poskytujte adekvátní úlevu od bolesti
- Protokolizovaná cílená sedace s denními periodami buzení a SBT zlepšuje výsledky léč.
- Dex a propofol jsou pro ICU pacienty nadějné

Take home message

Take home message (=malá domů)

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Mojžíš Zákon je nade vše

Take home message (=malá domů)

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A-S	**ABCDE strategie je nade vše**

VÁŠ JEŠTĚ SOULOŽÍ? MŮJ UŽ JENOM PUBLIKUJE...