Sedarea in TI
Sedation in ICU

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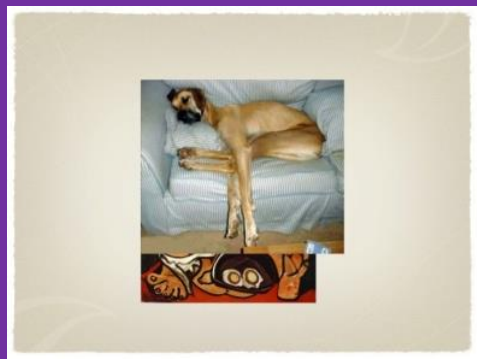
Pornim de la premisa ca…..

- Sedarea corecta in TI = unul dintre cele mai importante aspecte ale managementului pacientului
- Confortul pacientului =un scop principal in TI, include controlul durerii, al anxiolizei si prevenirea/tratamentul delirului (PAD).
- Obtinerea echilibrului intre sedare si analgezie =provocare
- Este absolut necesar sa existe niveluri tinta rationale de sedare agreate → personalul va avea obiective diferite pt acelasi pacient → ↑ sansa complicatiilor iatrogene si poate afecta recuperarea



Scopurile sedarii si/sau analgeziei in TI

- Anxioliza si amnezie fata de evenimentele –personale si ale celorlalti-
- ↓ incidenta S de stres posttraumatic (PTSD)
- Confortul si odihna pacientului
- ↓ incidenta delirului
- Analgezie adecvata
- Faciliteaza ventilatia mecanica si alte tratamente stresante
- ↓ consumul de O2 la pacientii critici
- Faciliteaza procesul de nursing/evita self-extubarea sau auto-ranirea
- ↑ eficienta tratamentului (de ex ventilatia cu rap invers I/E)
- ↓ raspunsul hemodinamic la manopere si stimuli (nursing si manopere chirurgicale, aspiratie)
- ↓ stresul pacientului cu toate consecintele sale negative (anxioliza)
- ? Influenteaza/moduleaza raspunsul inflamator?

Mirski MA, Hemstreet MK. Journal of the Neurological Sciences 2007;261: 16–34.
Patient safety council.ICU sedation guidelines of care.2009.availale at http://www.chpso.org/meds/sedation.pdf
Whitehouse T, Snelson C, Grounds M. **Intensive Care Society** Review of Best Practice for Analgesia and Sedation in the Critical Care. On Behalf of the Sedation Committee of the Intensive Care Society United Kingdom, 2014


Laughter is not
the best medicine,
Propofol is.
someecards
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EVALUAREA NIVELULUI SEDARII

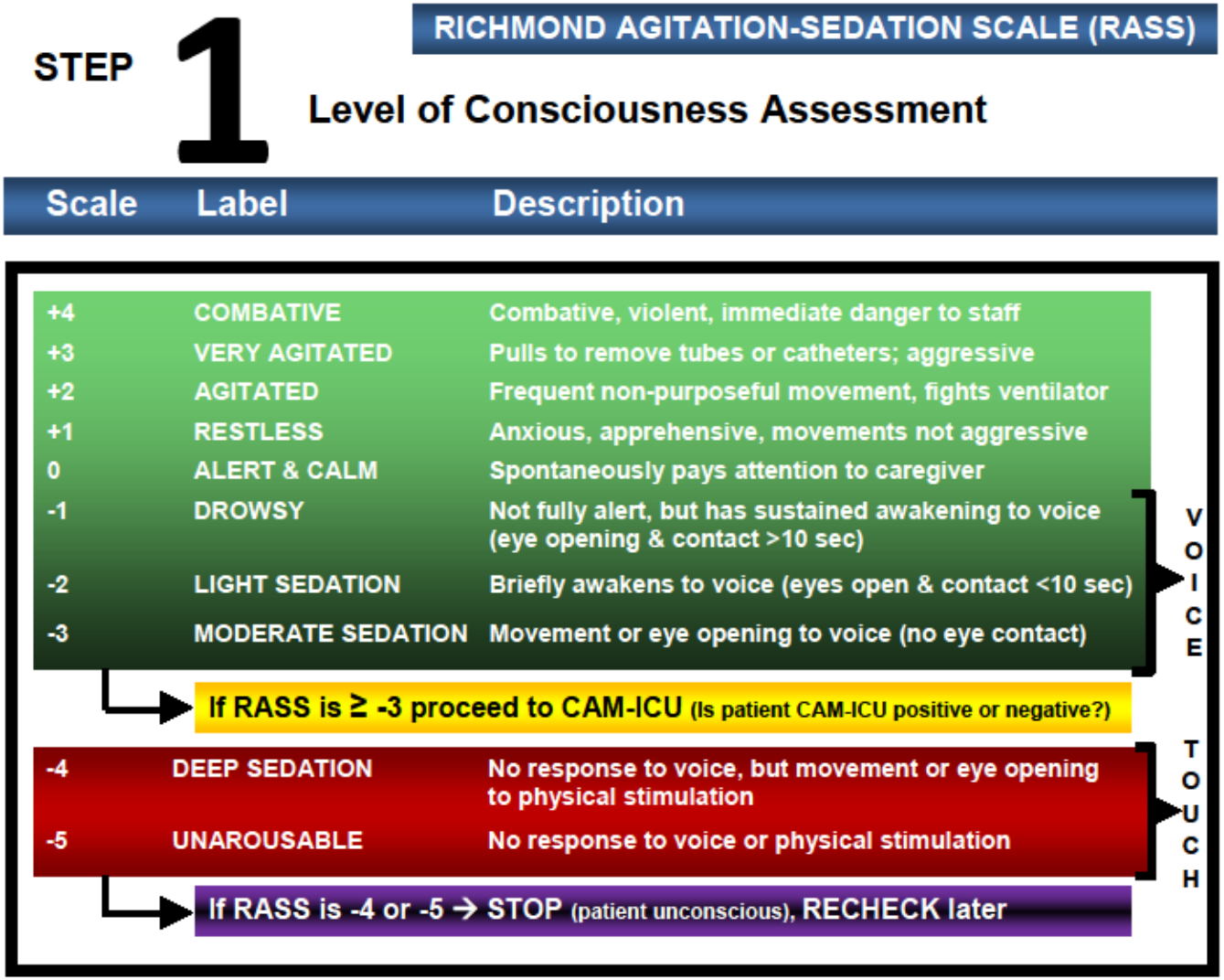
- Clinica
- Aspect pacient
- Stabilitatea CV
- Scale de sedare: OAAS, Ramsay, RASS (-2 sau mai putin) Bloomsbury, Addenbrookes
- Obs! Subiective si nu fac diferenta clara intre diverse grade de sedare
- Scale de durere inclusiv pt pacientii ventilati
- Scale de evaluare a delirului (CAM-ICU, delirium check-list)

- Monitorizare
- BIS
- Patient state index PSI
- Confortul pacientului: actigrafie

Gradele de profunzime ale sedarii in TI

- Scala Ramsay
- 1- pacient treaz, anxios, agitat si/sau nelinistit
- 2- pacient treaz, cooperant, care tolereaza ventilatia, orientat si linistit
- 3- pacient treaz, care raspunde exclusiv la comenzi
- 4- pacient adormit, raspuns scurt si prompt la atingerea zonei glabelare sau la stimuli auditivi puternici
- 5- pacient adormit, raspuns lent la atingerea zonei glabelare sau la stimuli auditivi puternici, dar raspuns prompt la stimuli durerosi
- 6- pacient adormit, fara raspuns la atingerea zonei glabelare sau la stimuli auditivi puternici

RASS



Sessler CN, Gosnell MS, Grap MJ, et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. Am J Respir Crit Care Med. 2002;166(10):1338-44.

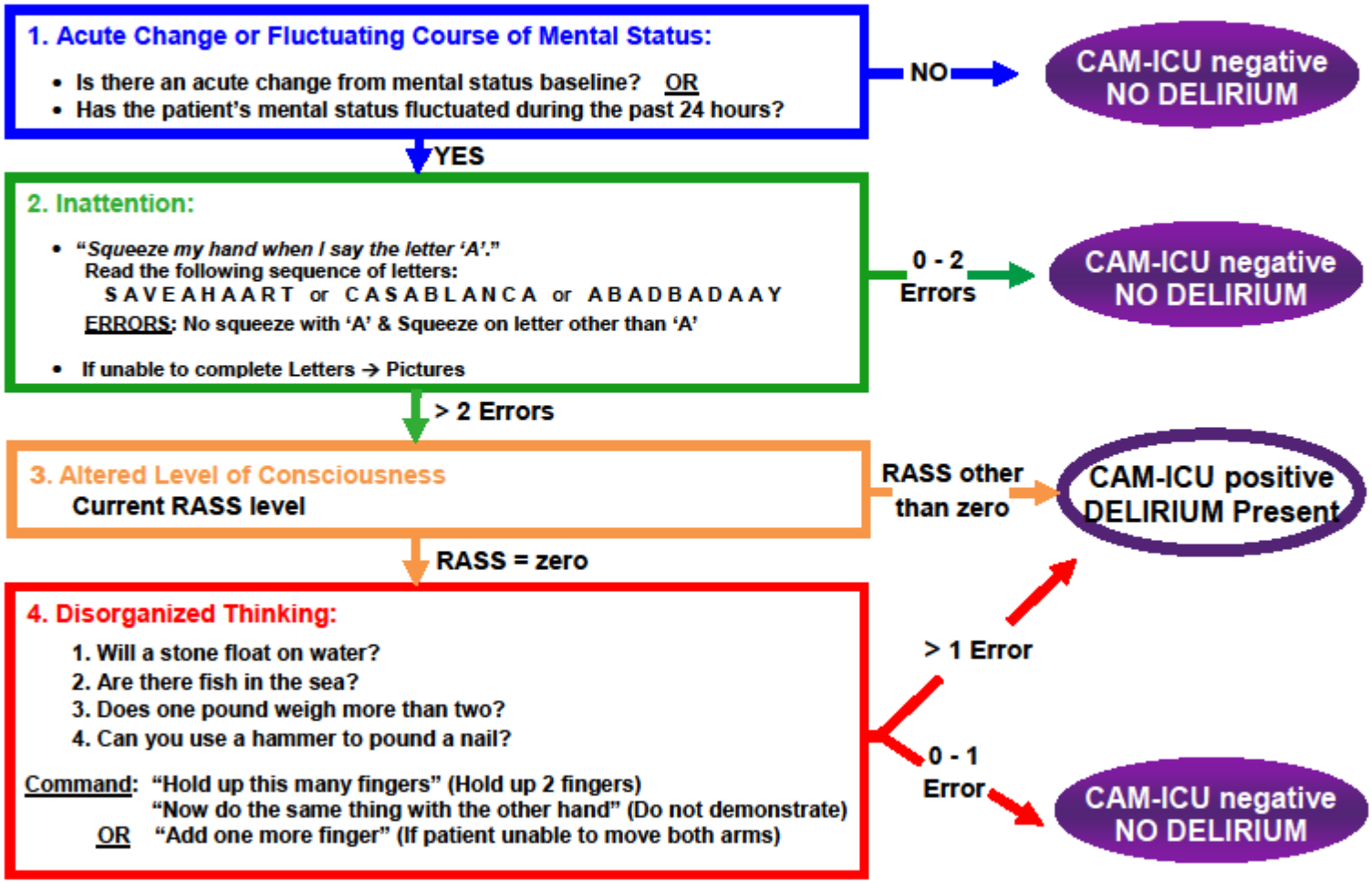
Evaluarea delirului
ICU Delirium screening checklist

Altered LOC (level consciuousness)	1
Inattention	1
Disorientation	0
Hallucination, delusions, psychosis	0
Agitation or psychomotor retardation	1
Inappropriate speech or mood	0
Sleep/wake cycle disturbances	0
Symptom fluctuation	1

- Total score 0-8
- Normal=0, subsyndromal delirium=1-3, delirium≥ 4

Bergeron. Intensive Care Med 2001;27;859

Confusion Assessment Method for the ICU (CAM-ICU) Flowsheet



Keep Calm
and
Stay Sedated

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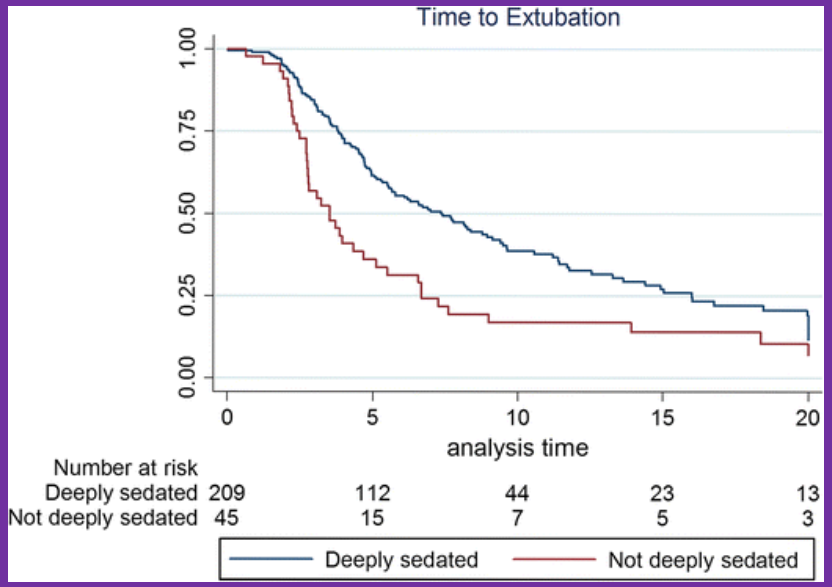
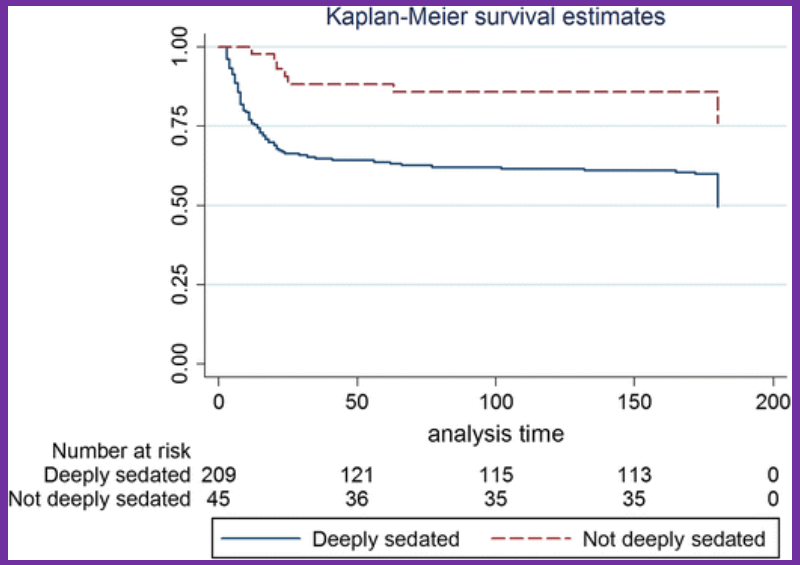
Riscurile unei sedari/analgezii inadecvate

- **Sedare exagerat de profunda**
- Alterarea activitatii centrului resp
- Incapacitatea de a mentine si proteja calea aeriana
- Instabilitate hemodinamica
- Prelungirea inutila a duratei ventilatiei mecanice
- ↑ incidentei pneumoniei de ventilator
- Risc de aparitie a depresiei
- ↑ incidenta delirului (de ex in cazul BZD)
- Amintiri false si deziluzii despre internarea in TI
- Dependenta de opioide/propofol/BZD
- Imunosupresie

Efectele/implicatiile sedarii profunde

- ↑ risc de deces la externare cu 13%/punct scor RASS
- ↑ durata pana la extubare cu 8,5 h/punct scor RASS
- ↑ mortalitatea la 180 zile
- ↑ durata spitalizarii in TI
- ↑ durata VM





Shehabi, Y., Chan, L., Kadiman, S. et al. Intensive Care Med (2013) 39: 910.
Shehabi Y, Bellomo R, Reade M et al (2012) for Sedation Practice in Intensive Care Evaluation (SPICE) Study Group and the ANZICS CTG: early intensive care sedation predicts long-term mortality in mechanically ventilated critically ill patients. Am J Respir Crit Care Med. doi:10.1164/rccm.201203-0522OC

Riscurile unei sedari/analgezii inadecvate

- **Sedare inadecvata superficiala**
- Agitatie
- Risc de detubare
- Risc de barotrauma
- Instabilitate hemodinamica: HTA, aritmii, angina, ischemie, etc
- Risc de autoleziune
- "Lupta" cu ventilatorul
- Ventilatie inadecvata (de ex pres mari, asincronie, etc)
- Hipercoagulabilitate??
- imunosupresie

Rowe K, Fletcher S. Sedation in ICU. Continuing Education in Anaesthesia. Critical care & Pain 2008;8(2):50-55.

Ce spun studiile pe grupuri largi populationale?

- 40-50% din pacientii ventilati mecanic sunt excesiv de profund sedati
- Scopurile de sedare pe termen scurt pot fi in contradictie cu evolutia pe termen lung a pacientilor (de ex distrofia musculara, angiogeneza, etc)
- Durerea este in continuare insuficient tratata

Weinert CR, Calvin AD. C*rit Care Med.* 2007;35:393-401.
Payen JF, Chanques G, Mantz J, et al. *Anesthesiology. 2007;106(4):687-695.*
Rowe K, Fletcher S. Sedation in ICU. Continuing Education in Anaesthesia. Critical care&Pain 2008;8(2):50-55.

Key points in alegerea sedarii

- Eliminati/corectati/verificati factorii/conditiile favorizanti pt agitatie
- Considerati pain-agitation-delirium (PAD)
- Ghiduri PAD
- Considerati asincronia pacient-ventilator
- Selectati agentul sedativ principal
- Selectati adjuvantele sedarii
- Protocolul de sedare dificila

Abordarea PAD

CRITICAL CARE MEDICINE

Sedation and Delirium in the Intensive Care Unit

N Engl J Med 2014;370:444-54.
DOI: 10.1056/NEJMra1208705

Michael C. Reade, M.B., B.S., D.Phil., and Simon Finfer, M.D.

Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit

Juliana Barr, MD, FCCM[1]; Gilles L. Fraser, PharmD, FCCM[2]; Kathleen Puntillo, RN, PhD, FAAN, FCCM[3]; E. Wesley Ely, MD, MPH, FACP, FCCM[4]; Céline Gélinas, RN, PhD[5]; Joseph F. Dasta, MSc, FCCM, FCCP[6]; Judy E. Davidson, DNP, RN[7]; John W. Devlin, PharmD, FCCM, FCCP[8]; John P. Kress, MD[9]; Aaron M. Joffe, DO[10]; Douglas B. Coursin, MD[11]; Daniel L. Herr, MD, MS, FCCM[12]; Avery Tung, MD[13]; Bryce R. H. Robinson, MD, FACS[14]; Dorrie K. Fontaine, PhD, RN, FAAN[15]; Michael A. Ramsay, MD[16]; Richard R. Riker, MD, FCCM[17]; Curtis N. Sessler, MD, FCCP, FCCM[18]; Brenda Pun, MSN, RN, ACNP[19]; Yoanna Skrobik, MD, FRCP[20]; Roman Jaeschke, MD[21]

Durerea

- Principalele cauze ale durerii in TI
- Incizia chirurgicala
- Cateterele si monitoarele (invazive)
- Lez tisulare det de malignitati, infectii, inflamatie
- Ischemia
- Discomfortul/durerea det de statul in pat in aceeasi pozitie h sau zile

- Assessment Tools
  - *Pain*
    - Behavioral Pain Scale (BPS)
    - Critical-Care Pain Observation Tool (CPOT)
  - *Agitation/Sedation*
    - Richmond Agitation-Sedation Scale (RASS)
    - Sedation-Agitation Scale (SAS)
  - *Delirium*
    - Confusion Assessment Method for the ICU (CAM-ICU)
    - Intensive Care Delirium Screening Checklist (ICDSC)
- "Wake Up and Breathe" Protocol
- Progressive Mobility Protocol
- Exercise/Mobility Safety Screen and Therapy
- Points to Consider When Implementing the ABCDE Bundle

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Crit Care Med. 2013;41:263-306. (Complete Guidelines)
Am J Health-Syst Pharm. 2013;70:53-58. (Executive Summary)

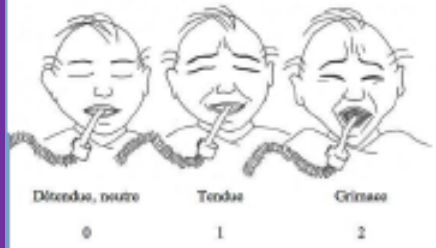
San Diego *Patient Safety Council*

Tool Kit

ICU Sedation Guidelines of Care

December 2009

Figure 7: The Critical-Care Pain Observation Tool (CPOT)

Indicator	Score		Description
Facial expression  Caroline Arbour, RN, B.Sc., M.Sc.A(c) School of Nursing, McGill University	Relaxed, neutral	0	No muscle tension observed
	Tense	1	Presence of frowning, brow lowering, orbit tightening and levator contraction or any other change (e.g., opening eyes or tearing during nociceptive procedures)
	Grimacing	2	All previous facial movements plus eyelid tightly closed (the patient may present with mouth open or biting the endotracheal tube)
Body movements (Puntillo et al., 1997 ; Devlin et al., 1999)	Absence of movements or normal position	0	Does not move at all (doesn't necessarily mean absence of pain) or normal position (movements not aimed toward the pain site or not made for the purpose of protection)
	Protection	1	Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements
	Restlessness	2	Pulling tube, attempting to sit up, moving limbs/thrashing, not following commands, striking at staff, trying to climb out of bed
Compliance with the ventilator (intubated patients) (Harris et al. 1991. Payen et al., 2001) **OR** **Vocalization (extubated patients)** (Mateo et Krenzischek, 1992)	Tolerating ventilator or movement	0	Alarms not activated, easy ventilation
	Coughing but tolerating	1	Coughing, alarms may be activated but stop spontaneously
	Fighting ventilator	2	Asynchrony: blocking ventilation, alarms frequently activated
	Talking in normal tone or no sound	0	Talking in normal tone or no sound
	Sighing, moaning	1	Sighing, moaning
	Crying out, sobbing	2	Crying out, sobbing
Muscle tension Evaluation by passive flexion and extension of upper limbs when patient is at rest (Ambuel et al., 1992) or when patient is being turned	Relaxed	0	No resistance to passive movements
	Tense, rigid	1	Resistance to passive movements
	Very tense or rigid	2	Strong resistance to passive movements, incapacity to complete them

Behavioral Pain Scale (BPS)

Item	Description	Score
Facial expression	Relaxed	1
	Partially tightened (e.g., brow lowering)	2
	Fully tightened (e.g., eyelid closing)	3
	Grimacing	4
Upper limb movements	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with mechanical ventilation	Tolerating movement	1
	Coughing but tolerating ventilation for the most of time	2
	Fighting ventilator	3
	Unable to control ventilation	4

BPS score ranges from 3 (no pain) to 12 (maximum pain).

Agitatie vs delirium

- Agitatia fara delir este mai des intalnita; poate apare daca pacientul are durere, disconfort sau anxietate.
- Agitatia nu necesita trat special (de obicei)→ dispare cu rezolvarea cauzei (spre deosebire de delir care poate frecvent persista)
- Trebuie evaluate cauzele posibile de agitatie si indepartate inainte de a seda pacientul
- Cu importanta la fel de mare pt "tratamentul" agitatiei: discutati cu pacientul si explicati-i tot ce se intampla!!!
- Ideal, one-to-one nursing pt pacientul critic → confera asistentei posibilitatea de a comunica cu pacientul si de a rezolva agitatia fara necesar de imobilizare fizica sau farmacologica

Whitehouse T, Snelson C, Grounds M. **Intensive Care Society** Review of Best Practice for Analgesia and Sedation in the Critical Care. On Behalf of the Sedation Committee of the Intensive Care Society United Kingdom, 2014

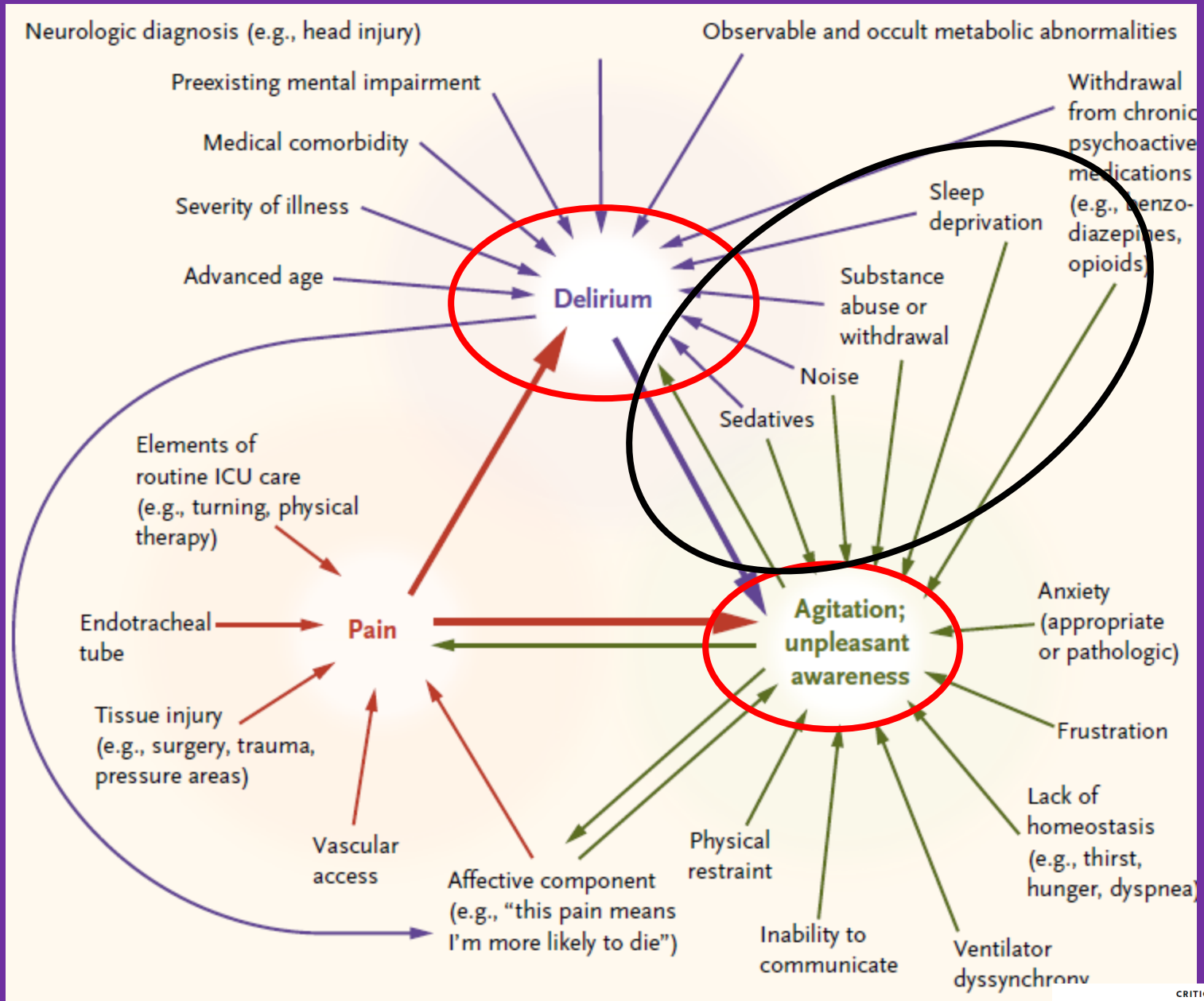


Figure 1. Causes and Interactions of Pain, Agitation, and Delirium.

CRITICAL CARE MEDICINE

Sedation and Delirium in the Intensive Care Unit

Michael C. Reade, M.B., B.S., D.Phil., and Simon Finfer, M.D.

Ghiduri generale pt abordarea sedarii/analgeziei (PAD, 2013)

- Durerea = se va monitoriza de rutina la toti pacientii adulti in TI (+1B) utilizand NRS 0-10 self-report.
- The Behavioral Pain Scale (BPS) si Critical-Care Pain Observation Tool (CPOT) sunt cele mai valide si fidele instrumente de evaluarea a comportamentului la durere
- Nu recomandam ca semnele vitale (sau scalele observationale pt durere care utilizeaza semnele vitale) sa fie utilizate ca singur instrument pt evaluarea durerii la pac adulti in TI (-2C), ci doar ca orientare pt instrumentele propriu-zise (+1C).

Pain

c. Treatment of pain

i. We recommend that preemptive analgesia and/or nonpharmacologic interventions (e.g., relaxation) be administered to alleviate pain in adult ICU patients prior to chest tube removal (+1C).

ii. We suggest that for other types of invasive and potentially painful procedures in adult ICU patients, preemptive analgesic therapy and/or nonpharmacologic interventions may also be administered to alleviate pain (+2C).

iii. We recommend that intravenous (IV) opioids be considered as the first-line drug class of choice to treat non-neuropathic pain in critically ill patients (+1C).

iv. All available IV opioids, when titrated to similar pain intensity endpoints, are equally effective (C).

v. We suggest that nonopioid analgesics be considered to decrease the amount of opioids administered (or to eliminate the need for IV opioids altogether) and to decrease opioid-related side effects (+2C).

vi. We recommend that either enterally administered gabapentin or carbamazepine, in addition to IV opioids, be considered for treatment of neuropathic pain (+1A).

We recommend that thoracic epidural anesthesia/analgesia be considered for postoperative analgesia in patients undergoing abdominal aortic aneurysm surgery (+1B).

We provide no recommendation for using a lumbar epidural over parenteral opioids for postoperative analgesia in patients undergoing abdominal aortic aneurysm surgery, due to a lack of benefit of epidural over parenteral opioids in this patient population (0,A).

We provide no recommendation for the use of thoracic epidural analgesia in patients undergoing either intrathoracic or nonvascular abdominal surgical procedures, due to insufficient and conflicting evidence for this mode of analgesic delivery in these patients (0,B).

We suggest that thoracic epidural analgesia be considered for patients with traumatic rib fractures (+2B).

We provide no recommendation for neuraxial/regional analgesia over systemic analgesia in medical ICU patients, due to lack of evidence in this patient population (0, No Evidence).

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4. Strategies for Managing Pain, Agitation, and Delirium to Improve ICU Outcomes
   a. We recommend either daily sedation interruption or a light target level of sedation be routinely used in mechanically ventilated adult ICU patients (+1B).
   b. We suggest that analgesia-first sedation be used in mechanically ventilated adult ICU patients (+2B).
   c. We recommend promoting sleep in adult ICU patients by optimizing patients' environments, using strategies to control light and noise, clustering patient care activities, and decreasing stimuli at night to protect patients' sleep cycles (+1C).
   d. We provide no recommendation for using specific modes of mechanical ventilation to promote sleep in mechanically ventilated adult ICU patients, as insufficient evidence exists for the efficacy of these interventions (0, No Evidence).
   e. We recommend using an interdisciplinary ICU team approach that includes provider education, preprinted and/or computerized protocols and order forms, and quality ICU rounds checklists to facilitate the use of pain, agitation, and delirium management guidelines or protocols in adult ICUs (+1B).

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Ghiduri generale pt abordarea sedarii/analgeziei (PAD, 2013)

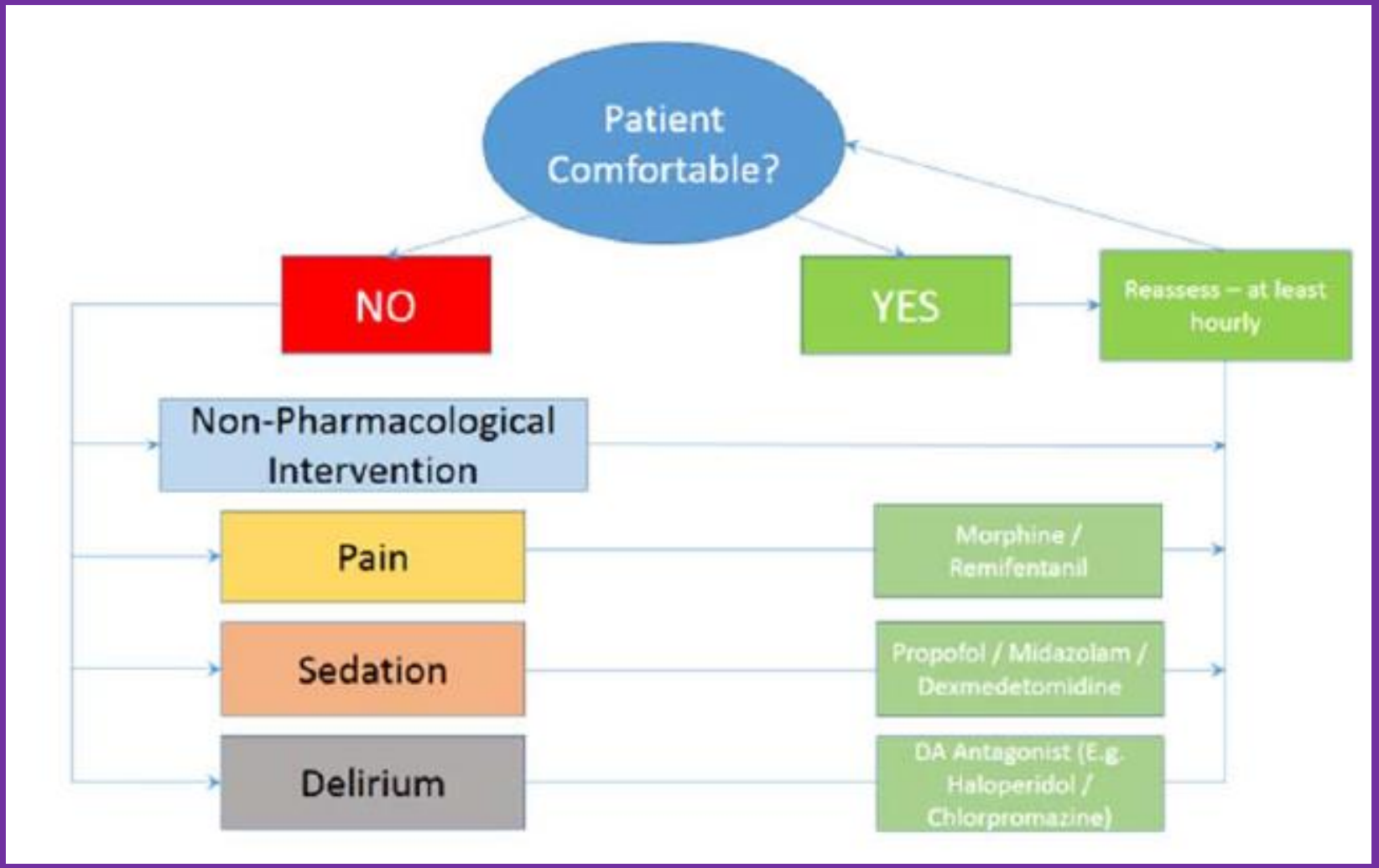
- RASS si SAS sunt cele mai fidele scale de evaluare a profunzii si calitatii sedarii la pac din TI (B).
- Metodele obiective de monitorizare a functiei cerebrale (AEP, BIS, Narcotrend, PSI, or state entropy) nu vor fi uitilizate ca monitorizare primara a profunzimii sedarii la pac non-comatosi, necurarizati. Aceste metode sunt substituenti neadecvati a sistemelor de scor (-1B).
- Aceste metode de monitorizare vor fi utilizate la pacientii curarizati in TI (+2B).

PAD Guidelines 2013

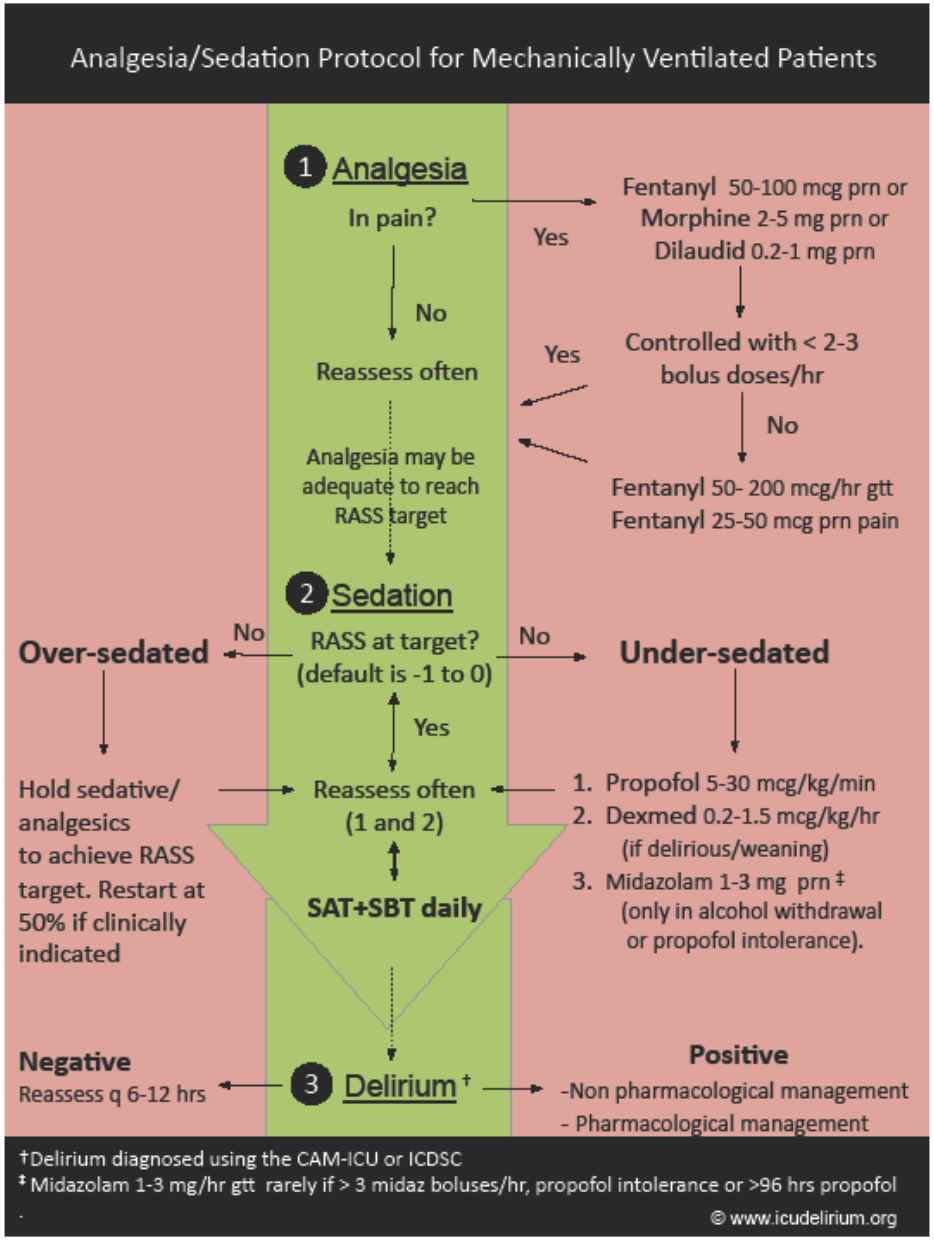
Ghiduri generale pt abordarea sedarii/analgeziei (PAD, 2013)

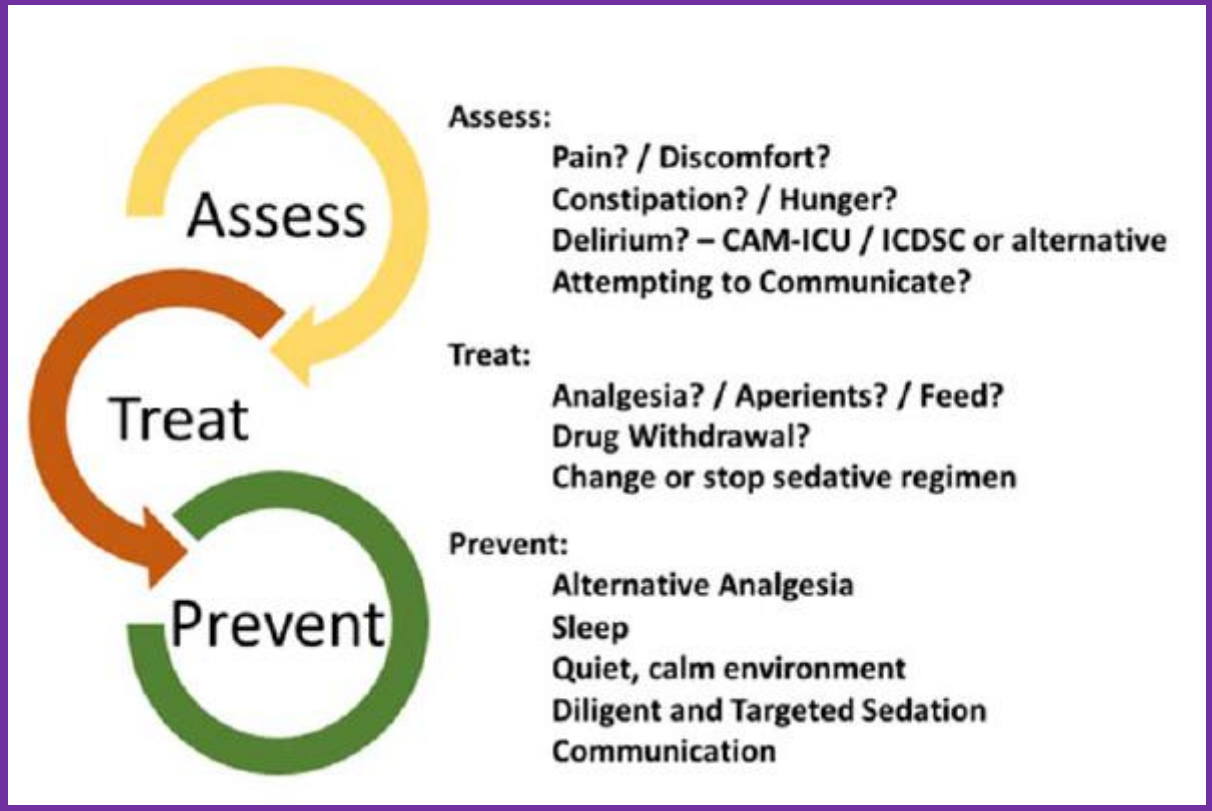
- Sedarea cu non-BZD (propofol or dex) vs BZD (midaz/lorazepam) amelioreaza evolutia clinica la pac ventilati mecanic in TI (+2B)
- Delirul este asoc cu ↑ mortalitatii (A), ↑ ICU si HLOS (A), si cu aparitia alterarilor cognitive post-ICU la pacientii adulti (B)
- Monitorizarea de rutina a delirului cu CAM-ICU sau Intensive Care Delirium Screening Checklist (ICDSC) –cele mai validate si fidele instrumente de monitorizare la pacientii adulti din TI (A).
- Coma = factor independent pt delir la pacientii din TI.
- BZD= factor de risc pt dezv delirului in TI (B).
- Nu exista suficiente date pt relatia propofol-delir in TI (C), iar relatia dex- ↓ delir nu este unanim acceptata desi cele mai multe studii sustin acest lucru (C).

Chen K, Lu Z, Xin Y, Cai Y, Chen Y, Pan S. Alpha-2 agonists for long-term sedation during mechanical ventilation in critically ill patients. Cochrane Database of Systematic Reviews 2015, Issue 1. Art. No.: CD010269. DOI: 10.1002/14651858.CD010269.pub2



Intensive Care Society Review of Best Practice for Analgesia and Sedation in the Critical Care


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
Over-sedated
No
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)
SAT+SBT daily
1. Propofol 5-30 mcg/kg/min
2. Dexmed 0.2-1.5 mcg/kg/hr
(if delirious/weaning)
3. Midazolam 1-3 mg prn ‡
(only in alcohol withdrawal
or propofol intolerance).
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
© www.icudelirium.org



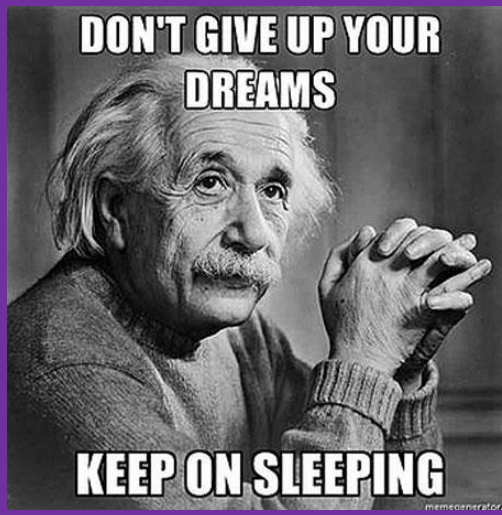
Intensive Care Society Review of Best Practice for Analgesia and Sedation in the Critical Care

Care sunt cele mai folosite substante pentru sedare/analgezie?

- Benzodiazepine: midazolam, lorazepam
- Propofol
- α -2 agonisti: dexmedetomidina, clonidina
- Opioide: mofina, fentanyl, remifentanil, sufentanil
- Barbiturice
- Inhalatorii: sevo, isofluran (Anaconda)

- OBS! Aceste substante se pot folosi ca unice substante sau in combinatii!

Propofolul



- Pro
- Sedare de calitate
- Durata scurta de act
- Permite ferestre de sedare
- Profil de imunitate superior; efect antiinflamator
- Nu cumuleaza
- Amnezie
- Efecte antiemetice
- Con/ef sec:
- S perfuziei cu propofol (48-72 h, copii, adulti critici)
- Bradicardie, depresie miocardica
- ↓RVP
- Colorarea in verde a urinei
- Aport caloric/trigliceride ↑
- Risc contaminare/soc septic

Rowe K, Fletcher S. Sedation in ICU. Continuing Education in Anaesthesia. Critical care&Pain 2008;8(2):50-55.

Benzodiazepinele

- Pro
- Anxioliza
- amnezie
- Stabilitate hemodinamca
- Ieftin

- Con/ef sec
- Dependenta
- S de sevraj la intreruperea sedarii
- Durata lunga de act
- Cumulare (diazepam)
- Profil imunologic fevorabil depresiei imune ; exista raportari asupra ↑ infectiilor la pacienti sedati cu BZD
- Asoc cu delir

Rowe K, Fletcher S. Sedation in ICU. Continuing Education in Anaesthesia. Critical care&Pain 2008;8(2):50-55.

Tiopentalul si ketamina

- Tiopental adm in perfuzie continua in managementul statusului epileptic refractar si al afect cu HTIC severa si refractara
- Ef sec
- Cumulare
- Depresie miocardica
- Depresie imuna
- la doze mari cinetica de ordin O

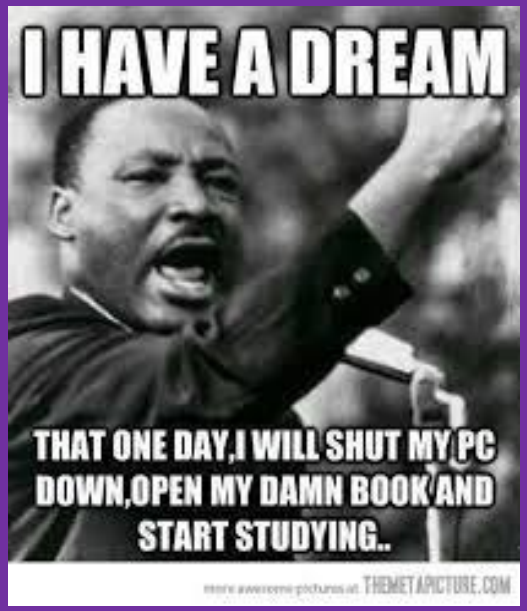
- Ketamina
- Adm in asoc cu propofol, morfina,
- Un rol in status astmaticus
- Neuroprotectie ?
- Ef sec
- Stim S, tahicardie, efortului cardiac
- Halucinatii, delir, PONV

Rowe K, Fletcher S. Sedation in ICU. Continuing Education in Anaesthesia. Critical care & Pain 2008;8(2):50-55.

Dexmedetomidina/clonidina

- Analgezie
- Anxioliza
- depresie respiratorie minima
- Profil imunologic favorabil
- Nu determina/tratament delir
- Amnezie partiala
- Sedare 24 h, dar sunt deja publicate studii pe durata mai lunga (72h)

- Ef sec
- HTA rebound
- hTA
- Bradicardie
- Eliminare intarziata in Insuf ren
- Adesea trebuie asociata cu opioide



Rowe K, Fletcher S. Sedation in ICU. Continuing Education in Anaesthesia. Critical care&Pain 2008;8(2):50-55.

Lin et al. Critical Care 2012, 16:R169
http://ccforum.com/content/16/5/R169

CRITICAL CARE

RESEARCH Open Access

Can dexmedetomidine be a safe and efficacious sedative agent in post-cardiac surgery patients? a meta-analysis

Yi Yun Lin[1†], Bin He[2†], Jian Chen[1] and Zhi Nong Wang[1*]

Conclusions: Dexmedetomidine was associated with shorter length of mechanical ventilation and lower risk of delirium following cardiac surgery. Although the risk of bradycardia was significantly higher compared with traditional sedatives, it may not increase length of hospital stay and hospital mortality. Moreover, dexmedetomidine may decrease the risk of ventricular tachycardia and hyperglycemia. Thus, dexmedetomidine could be a safe and efficacious sedative agent in cardiac surgical patients

Intensive Care Med (2010) 36:926–939
DOI 10.1007/s00134-010-1877-6

REVIEW

Jen A. Tan
Kwok M. Ho

Use of dexmedetomidine as a sedative and analgesic agent in critically ill adult patients: a meta-analysis

agents. *Conclusions:* Significant heterogeneity existed between the pooled studies. The limited evidence suggested that dexmedetomidine might reduce length of ICU stay in some critically ill patients, but the risk of bradycardia was significantly higher when both a loading dose and high maintenance doses (>0.7 μg kg^{-1} h^{-1}) were used.

Dexmedetomidine vs Midazolam for Sedation of Critically Ill Patients

Conclusions There was no difference between dexmedetomidine and midazolam in time at targeted sedation level in mechanically ventilated ICU patients. At comparable sedation levels, dexmedetomidine-treated patients spent less time on the ventilator, experienced less delirium, and developed less tachycardia and hypertension. The most notable adverse effect of dexmedetomidine was bradycardia.

Trial Registration clinicaltrials.gov Identifier: NCT00216190

JAMA. 2009;301(5):489-499 www.jama.com

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Effects	Dexmedetomidine	Benzodiazepines	Propofol	Opioids	Haloperidol
Sedation	X	X	X	X	X
Alleviation of anxiety	X	X			
Analgesic properties	X			X	
Promotion of arousability during sedation	X				
Facilitation of ventilation during weaning	X				
No respiratory depression	X				X
Control of delirium	X				X
Organ protection	X		X		
Control of stress response	X				
Reduction of shivering	X				
Cooperative sedation	X				
Mimicking of natural sleep	X				

[a] Based on data from Pandharipande et al.[13]

patient is alert. Dexmedetomidine is as effective as propofol and midazolam for sedation of critically ill patients.[4,6,10] In this study, patients receiving dexmedetomidine were calm, in stable hemodynamic status, and able to participate in the

weaning process more quicker than were patients given midazolam or propofol.

An incidental discovery was that the rate of ventilator-associated pneumonia was 0% during the time dexmedetomidine was used. Previ-

Use of Dexmedetomidine for Primary Sedation in a General Intensive Care Unit

Jenni Short, RN, MSN, ARNP-BC

Sedation & Immunomodulation

Robert D. Sanders, BSc, MBBS, FRCA[a,b,*], Tracy Hussell, BSc, PhD[b], Mervyn Maze, MBChB, FRCP, FRCA, FMedSci[a]

Crit Care Clin 25 (2009) 551–570

Table 1
Summarized effects of sedatives on the innate and adaptive immune response (↓ represents immunodepression; ↑ represents immune potentiation; –, unknown effect)

Drug Class	Innate Immune Response	Adaptive Immune Response
Propofol	↓	–
Benzodiazepines	↓	–
Opioids	↓	↓
α_2-Adrenoceptor agonists	↑	–

Opioidele

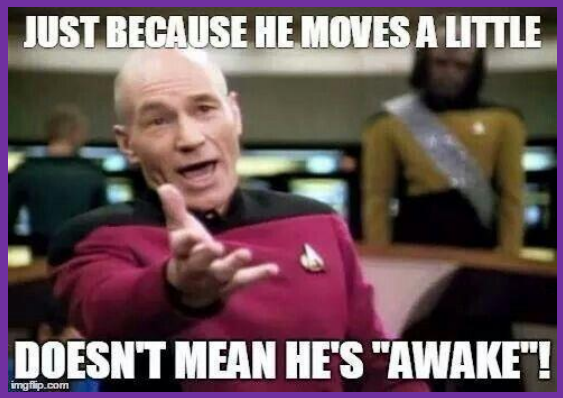
- Analgezie
- Anxioliza
- Uneori (remifentanil) usoara sedare
- Remifentanil de electie, dar cost ridicat si necesita analgezie de fond
- Ef sec
- Depresie respiratorie
- Bradicardie
- hTA
- Greata
- Constipatie
- Imunosupresie (infectii, oncogeneza, angiogeneza)
- Dependenta
- Nu amnezie a evenimentelor

Rowe K, Fletcher S. Sedation in ICU. Continuing Education in Anaesthesia. Critical care&Pain 2008;8(2):50-55.

Curare

- Indicatii

- Moduri de ventilatie invazive/f invazive (ex ARDS sever)
- Controlul ventilatiei a pacientii cu necesar de sedare ridicat
- ↓ cons de O2 la pacientii cu hipoxemie critica
- Controlul PIC ↑



Sedarea inhalatorie

- In TI Iso/sevo in special la pac cu afect resp, dar nu numai
- Este posibila atingerea unor niveluri suficiente de sedare la pacientii cu afect cerebrovasc in TI prin aplicarea sedarii inhalatorii cu isoflurane long-term fara o ↑ relevanta a ICP, daca PIC de baseline are val scazute sau doar moderat ↑.
- Precautii se vor lua fata de efectul isofluranului de a reduce MAP si CPP.
- Neuromonitorizarea multimodala este recomandata la aplicarea acestei metode.

Sackey PV, Martling C-R, Granath F, Radell PJ. Prolonged isoflurane sedation of intensive care unit patients with the Anesthetic Conserving Device. Critical Care Medicine 2004(32);11:2241-2246
Bösel J, Purrucker JC, Nowak F, Renzland J, Schiller P, Pérez EB, Poli S, Brunn B, Hacke W, Steiner T. Volatile isoflurane sedation in cerebrovascular intensive care patients using AnaConDa(®): effects on cerebral oxygenation, circulation, and pressure. Intensive Care Med 2012;38(12):1955-64.

threatening asthma. Both the use of volatile agent and the AnaConDa have been described for ICU sedation [2, 3] but in the light of the practicalities, familiarity, efficacy, cost and safety of intravenous sedation regimes in the ICU, we wanted to be able to justify volatile use. Suffice to say the only valid alternative we have come up with so far was its use for postoperative sedation following cardiac surgery. This was in an elderly, NYHA grade II, patient with type I hypersensitivity to egg who underwent elective aortic valve replacement and single coronary artery bypass graft. He was administered conventional volatile anaesthesia during the operation. Afterwards he was commenced on an isoflurane-primed AnaConDa with the expired concentration kept at around 0.5% for transfer and for maintenance on ICU. Analgesia was maintained by epidural bupivacaine. The

Review Article

A review of the practice of sedation with inhalational anaesthetics in the intensive care unit with the AnaConDa® device

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Indian Journal of Anaesthesia | Vol. 56| Issue 6 | Nov-Dec 2012

ELSEVIER

Best Practice & Research Clinical Anaesthesiology
Vol. 19, No. 3, pp. 523–538, 2005
doi:10.1016/j.bpa.2005.02.006
available online at http://www.sciencedirect.com

BEST PRACTICE & RESEARCH

15

Inhalational anaesthetics in the ICU: theory and practice of inhalational sedation in the ICU, economics, risk-benefit

Andreas Meiser* Dr Med

Sevoflurane in very low concentrations seems to interfere with engraving of emotionally disturbing information in the amygdaloid bodies. When volunteers are shown a mixture of emotionally disturbing and emotionally neutral pictures, they will predominantly memorize the first ones. Low-dose sevoflurane inhalation abolishes this predominance (personal communication, G. Schelling, San Diego, USA).

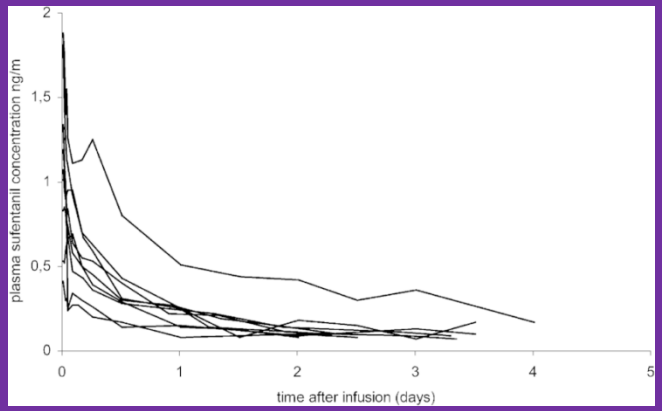
Volatile anaesthetics give excellent control over their action. Onset of action is usually quick, especially when injection techniques are used as in the AnaConDa® or Zeus® (see below). The end-tidal fraction (F_{et}) of the volatile anaesthetics can be monitored, representing a precise indicator of the drug's concentration in the target organ much more reliable than any target-controlled infusion algorithm. Emergence times are shorter and more predictable than after intravenous sedation. This has been shown in many clinical trials.[11–15] Volatile anaesthetics accumulate very little, and

halothane, the newer volatile anaesthetics interfere very little with haemodynamics, especially in low concentrations. By lowering or increasing blood pressure with nitroprusside or phenylephrine in volunteers, Ebert et al showed that regulation of heart rate (baroreceptor reflex) and of peripheral sympathetic nerve activity was hardly disturbed at 0.5 MAC desflurane compared to the awake state.[16] The sympatho-adrenergic stimulation seen after a first sudden increase in desflurane concentration from 1 to 1.5 MAC[17] is not relevant for ICU sedation as such high concentrations are not indicated. In fact we found heart rate to be more often in the normal range in patients sedated with desflurane compared to propofol.[15]

Volatile anaesthetics are potent bronchodilators. Unlike ketamine and most other agents, they do not act via acetylcholine or β_2-receptors[18] and thus may be tried when other agents have failed. The mechanism seems to involve nitric oxide as well as prostaglandins released by the epithelium.[19] The bronchoconstriction seen in inhalational induction with desflurane is due to its pungent odour and is short-lived. Volatile anaesthetics have been used successfully for the treatment of status asthmaticus when other therapies have failed.[20–25]

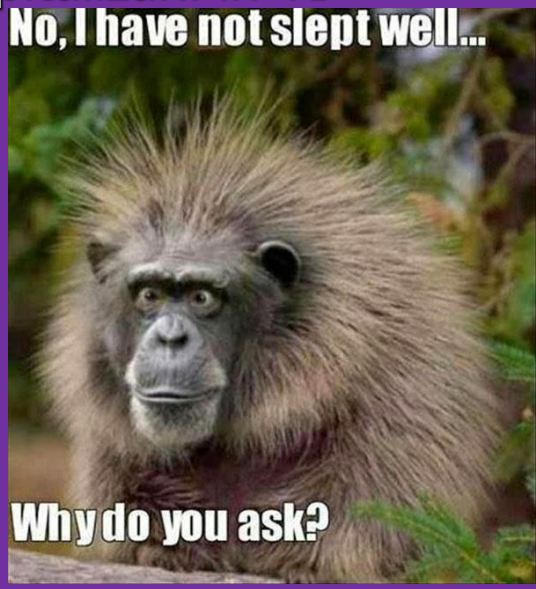
Combinatii de substante folosite pentru sedare

- Propofol+ remifentanil/fentanyl
- Midazolam + morfina
- Dexmedetomidina ± remifentanil/fentanyl
- Dexmedetomidina± propofol
- Inhalatorie
- OBS! Sufentanil este f rar rec pt sedare in ICU!!



Care substanta/combinatie?

- Nici un agent de sedare este ideal
- Alegerea se bazeaza pe nevoile pacientului, traditie, protocoale locale
- Dexmedetomidine- or propofol-based sedation ↓ durata admisiei in TI si ↓ durata VM
- Propofol vs dex nu sunt diferente in durata VM si a spitalizarii in TI



Fraser GL, Devlin JW, Worby CP, et al. Benzodiazepine versus nonbenzodiazepine-based sedation for mechanically ventilated, critically ill adults: a systematic review and meta-analysis of randomized trials. Crit Care Med. 2013;41(9 Suppl 1):S30-8.
Jakob SM, Ruokonen E, Grounds RM, et al. Dexmedetomidine vs midazolam or propofol for sedation during prolonged mechanical ventilation: two randomized controlled trials. JAMA 2012;307:1151-1160

Tehnici de administrare a substantelor pentru sedare

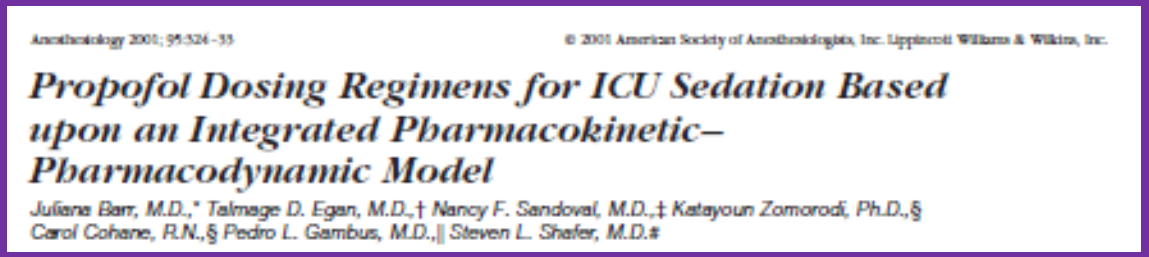
- Bolusuri i.v. rar in TI
- Morfina, rar fentanyl, BZD
- Obs! Concentr plasmatice variabile, inconstante, risc awareness

- Perfuzie continua cu dispozitive automate
- Cel mai frecvent folosita
- Majoritatea substantelor cumuleaza
- Propofol: 0,5-6 mg/kg/h
- Remifentanil: 0.1–0.15 mcg/kg/min si titrare la 5 min interval cu 0.025 mcg/kg/min. La peste 0.2 mcg/kg/min, se adauga un alt sedativ
- Dex 0,2-0,7 mcg/kg/h, max 1,5
- Fentanyl/morfina

Rowe K, Fletcher S. Sedation in the intensive care unit. Contin Educ Anaesth Crit Care Pain (2008) 8 (2): 5055

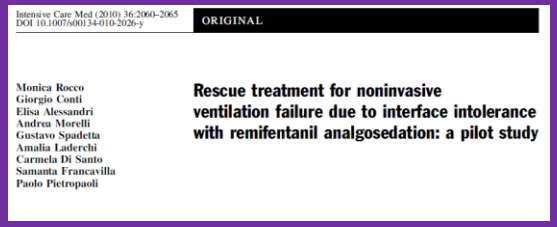
Tehnici de administrare a substantelor pentru sedare

- TCI
- Remifentanil ± propofol
- Concentr plasmatica fixa/exact titrabila si rapid ajustabila
- Remifentanil
- 0,025 mcg/kg/min, steps de 0,01mcg/kg/min
- Unii recomanda doze max de 0,12 sau 0,2 mcg/kg/min dupa care se adauga o alta substanta
- TCI 0,025 ng/ml →2,5ng/ml
- Propofol
- 0,5mcg/ml → 4mcg/ml, steps 0,25-0,5mcg/ml


Anesthesiology 2001; 95:324–33 © 2001 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

Propofol Dosing Regimens for ICU Sedation Based upon an Integrated Pharmacokinetic–Pharmacodynamic Model

Juliana Barr, M.D.,* Talmage D. Egan, M.D.,† Nancy F. Sandoval, M.D.,‡ Katayoun Zomorodi, Ph.D.,§ Carol Cohane, R.N.,§ Pedro L. Gambus, M.D.,‖ Steven L. Shafer, M.D.#


Intensive Care Med (2010) 36:2060–2065
DOI 10.1007/s00134-010-2026-y

ORIGINAL

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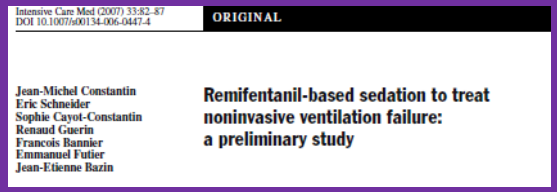
Carmela Di Santo
Samanta Francavilla
Paolo Pietropaoli

Rescue treatment for noninvasive ventilation failure due to interface intolerance with remifentanil analgosedation: a pilot study


Intensive Care Med (2007) 33:82–87
DOI 10.1007/s00134-006-0447-4

ORIGINAL

Jean-Michel Constantin
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Francois Bannier
Emmanuel Futier
Jean-Etienne Bazin

Remifentanil-based sedation to treat noninvasive ventilation failure: a preliminary study


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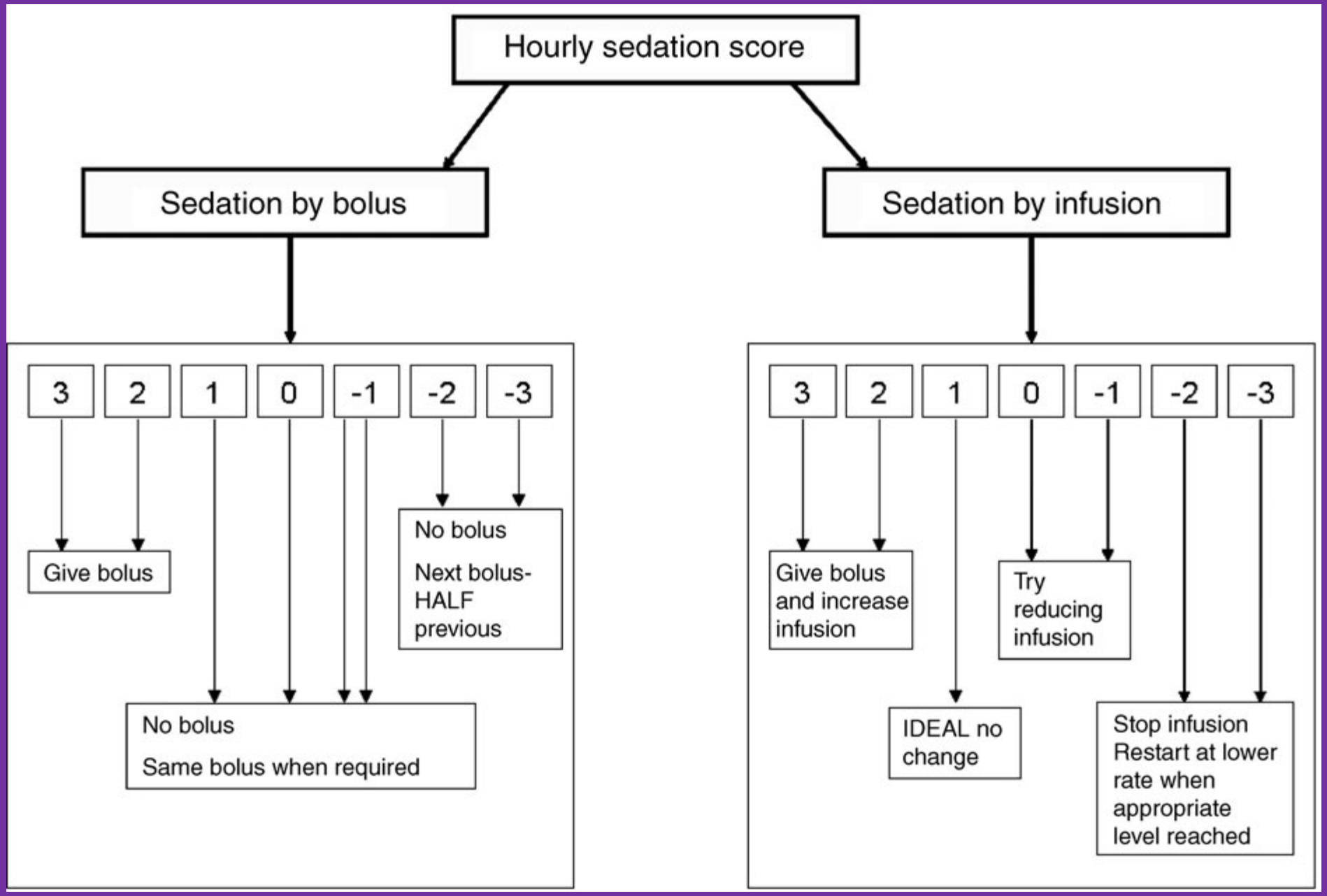
Origi

Remifentanil sedation: a five year retrospective case series focusing on its role in non-invasive ventilation

N Smallwood, B Peringathara, S Twigg


Hourly sedation score
Sedation by bolus
Sedation by infusion
3
2
1
0
-1
-2
-3
Give bolus
No bolus
Next bolus-HALF previous
No bolus
Same bolus when required
3
2
1
0
-1
-2
-3
Give bolus and increase infusion
Try reducing infusion
IDEAL no change
Stop infusion
Restart at lower rate when appropriate level reached

Strategii de sedare

- SEDAREA SE VA AJUSTA LA NEVOILE FIECARUI PACIENT SI A AFECTIUNILOR SALE!!!!!
- Dupa "natura" pacientului
- Pacient operat si ventilat → sedare si analgezie
- Pacient ventilat pt afectiune "medicala" → sedare (incl remi)
- Dupa durata sedarii
  - Durata scurta

    Propofol+remifentanil

    Propofol+fentanyl

    Dexmedetomidina+ opioid/propofol
  - Durata lunga

    Midazolam+morfina/fentanyl

Strategii de sedare pentru ventilatie mecanica

- Ventilatie controlata→ sedare profunda (propofol ± opioide) ± curarizare care:
  - Sa inhibe complet respiratiile spontane
  - Sa elimine lupta cu ventilatorul
  - Sa protejeze (cons de O2, HTIC, odihna, etc)
- Ventilatie asistata/controlata → grade variabile de sedare care:
  - Sa nu inhibe respiratia pacientului
  - Sa nu determine/agraveze asincronia pacient-ventilator
  - Sa nu favorizeze extubarea accidentala
- Ventilatie spontana (CPAP), sevraj → sedare usoara care:
  - Sa nu deprime respiratia
  - Daca este cazul

Strategii de sedare pentru ventilatie mecanica

- Suficient de profunda/evaluare scor/consemnare
- Scurta durata/durata minim necesara pt a evita complicatiile
- Reducere treptata/ferestre de sedare pt evaluarea starii pacientului
- Rotatie regim de sedare pt evitarea dependentei
- Pe primul plan analgezia si apoi sedarea (analgezia scade considerabil necesarul de sedare)
- De preferinta multimodala
- Costuri
- Atentie si la efectele secundare pe termen lung

Ce este nou/reiterat/reevaluat?

- Necesitatea existentei in fiecare TI a protocoalelor/instrumentelor de evaluare pt PAD
- Must! Protocoale de pain management
- Must! Protocoale pt managementul sedarii
- Must! Protocoale pt managementul delirului

- Obs! Protocoalele vor include atat profilaxia cat si tratamentul !
- Exista protocoale care recomanda evaluarea durerii cel putin orar

Ce este nou/reiterat/reevaluat?

- Ferestre de sedare zilnica (daca nu este cind) pt evaluare si instituirea la timp a sevrajului de ventilator
- Rotatia agentului sedativ principal, in functie de durata sedarii

B

Summary of PAD Guidelines

PAIN AND ANALGESIA

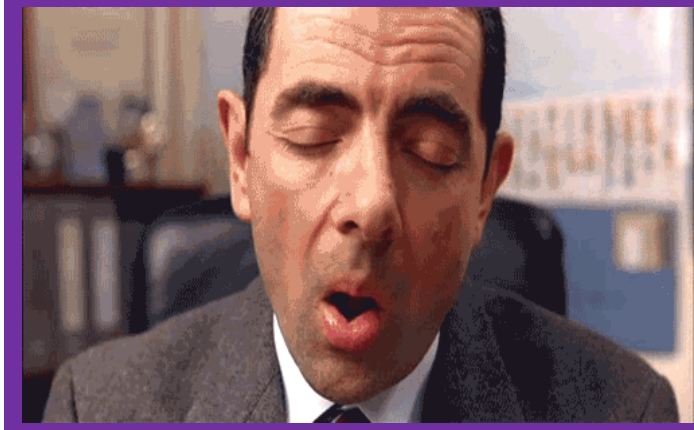
1. ICU patients routinely experience pain at rest and with ICU care (B). Pain in cardiac surgery patients, especially women, is poorly treated (B). Procedural pain is common in ICU patients (B).
2. Perform routine pain assessment in all patients (1B). In motor intact patients unable to self report, we suggest using behavioral pain scales rather than vital signs to assess pain (2C). The BPS and CPOT are the most valid and reliable behavioral pain scales (B). Vital signs should only be used as a cue for further pain assessment (2C).
3. For non-neuropathic pain, use intravenous opioids as first line analgesic therapy (1C); use non-opioid analgesics to reduce opioid side effects (1C); and use either gabapentin or carbamazepine in conjunction with intravenous opioids for neuropathic pain (1A).
4. Suggest preemptively treating procedural pain (2C), especially chest tube removal (1C).
5. Use thoracic epidural analgesia for abdominal aortic surgery (1B), and suggest also using for traumatic rib fractures (2B). No evidence guides the use of lumbar epidural analgesia for abdominal aneurysm surgery (0A), or thoracic epidural analgesia for either intrathoracic or nonvascular abdominal surgical procedures (0B). No evidence guides the use of regional vs. systemic analgesia in medical ICU patients (0).

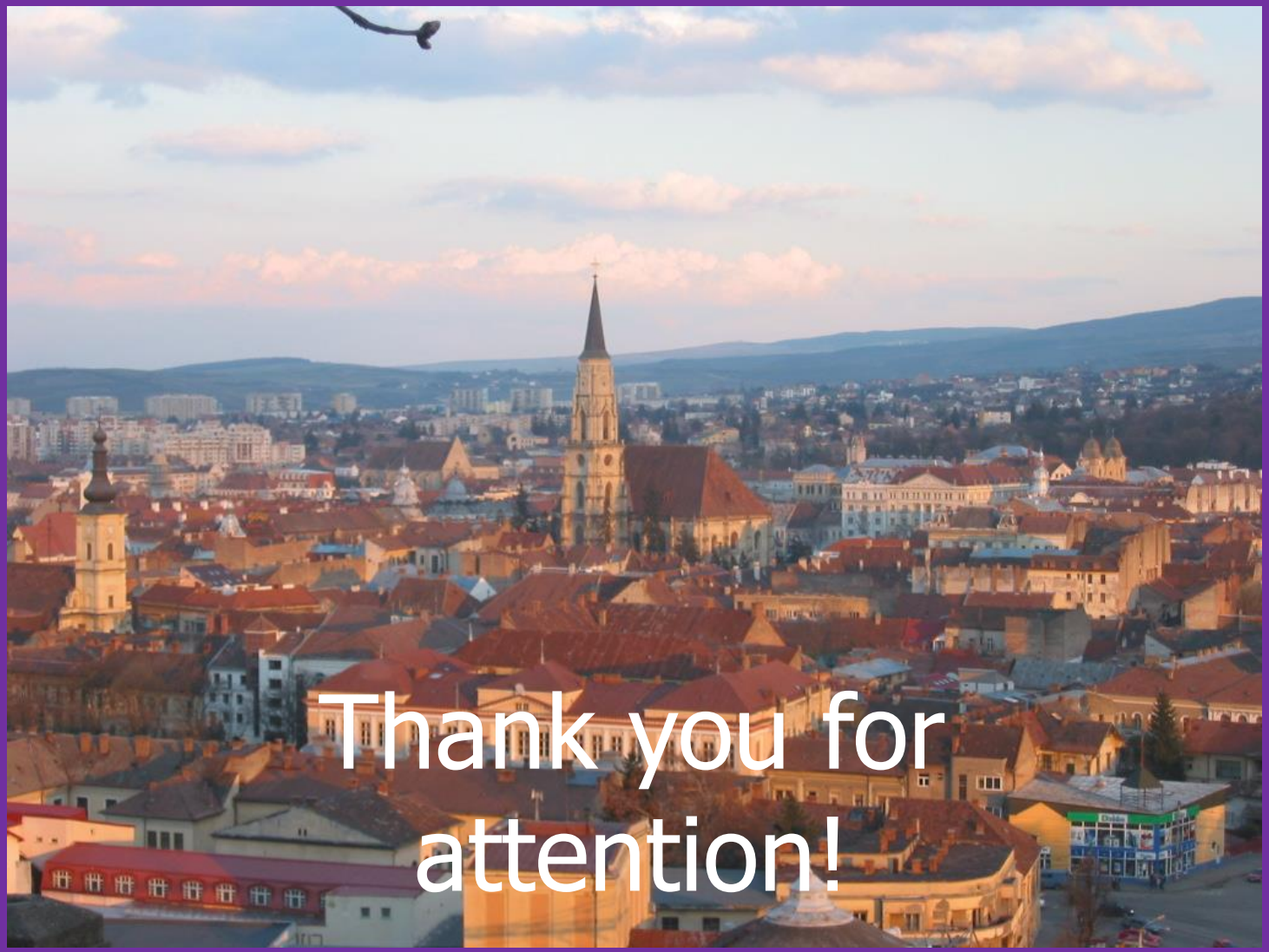
AGITATION AND SEDATION

1. Maintaining lighter levels of sedation in ICU patients is associated with improved clinical outcomes (B); light levels of sedation should be maintained in these patients (1B).
2. The RASS and SAS scales are most valid and reliable instruments for assessing adequacy and depth of sedation (B).
3. Use Brain Function monitors only as adjuncts to subjective sedation scales in unparalyzed patients (1B), but suggest using brain function monitors to primarily monitor depth of sedation in patients receiving neuromuscular blocking agents (2B).
4. Use EEG monitoring to monitor non-convulsive seizure activity in ICU patients at risk for seizures, and to titrate burst suppression therapy in ICU patients with elevated intracranial pressure (1A).
5. Use either use daily sedative interruption or titrate sedative medications to maintain light levels of sedation (1B). Suggest using Analgesia-first sedation (2B). Suggest using non-benzodiazepines rather than benzodiazepine infusions for sedation (2B). Use sedation protocols and daily checklists to integrate and to facilitate management of pain, sedation, and delirium in ICU patients (1B).

DELIRIUM

1. Delirium is associated with increased mortality (A), prolonged ICU and hospital LOS (A), and post-ICU cognitive impairment (B).
2. Delirium risk factors include: pre-existing dementia, HTN, history of alcoholism, and a high severity of illness at baseline (B); coma (B); and benzodiazepine use (B). Mechanically ventilated ICU patients at risk for delirium have a lower delirium prevalence when treated with dexmedetomidine rather than with benzodiazepines (B).
3. Routinely monitor ICU patients for delirium (1B). The CAM-ICU and ICDSC are the most valid and reliable instruments for this purpose (A).
4. Pursue early mobilization to reduce the incidence and duration of delirium (1B).
5. Suggest not using either haloperidol or atypical antipsychotics prophylactically to prevent delirium (2C).
6. Promote sleep in adult ICU patients by optimizing patients' environments, using strategies to control light and noise, to cluster patient care activities, and to decrease stimuli at night in order to protect patients' sleep cycles (1C).
7. Do not use rivastigmine to reduce the duration of delirium in ICU patients (1C).
8. Suggest withholding antipsychotics in patients with baseline QT prolongation, a history of Torsades de Pointes, or in those receiving concomitant medications known to prolong the QT interval (2C).
9. When sedation is required in delirious ICU patients, suggest using dexmedetomidine rather than benzodiazepine infusions for sedation in these patients, unless delirium is related to either alcohol or benzodiazepine withdrawal (2B).




Thank you for
attention!