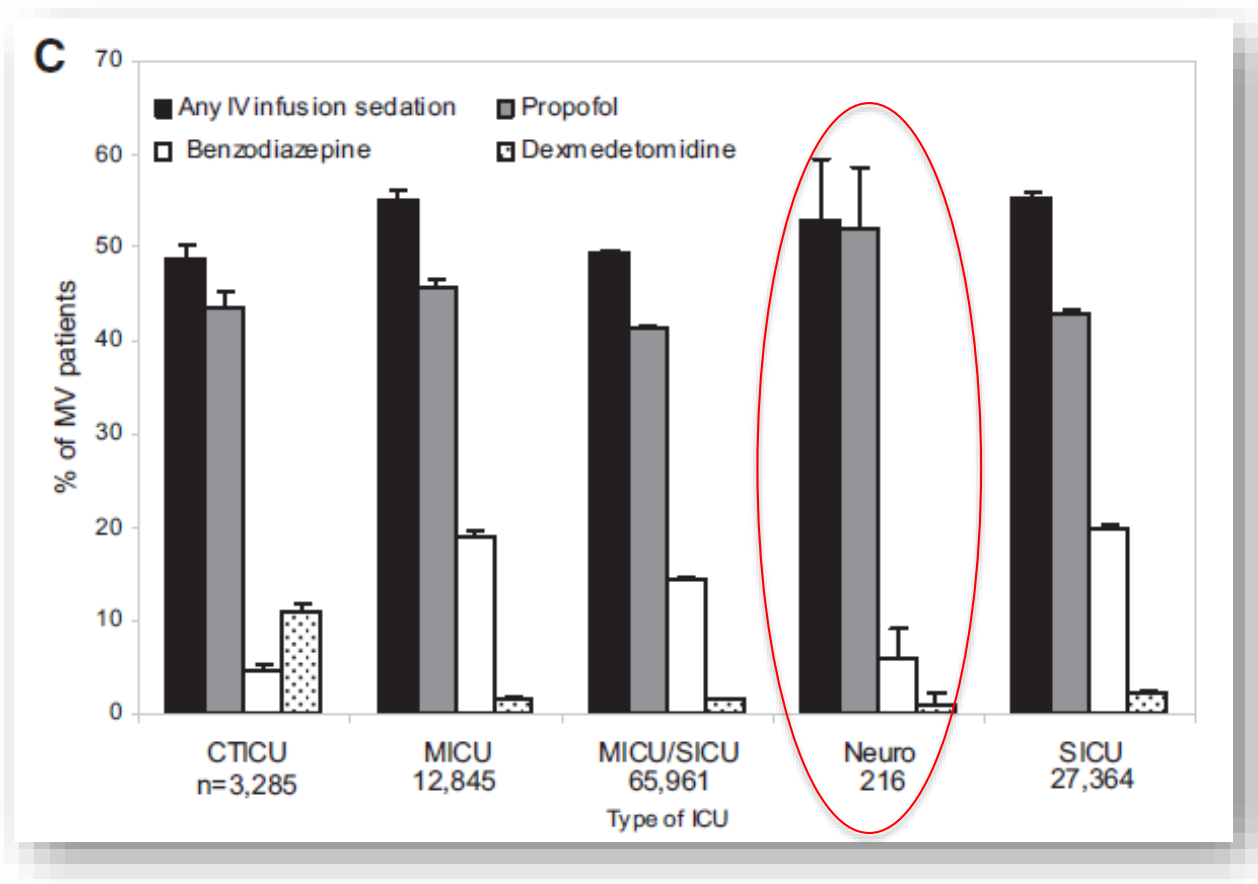


重症脑损伤患者的镇痛镇静

首都医科大学附属北京天坛医院

周建新

镇痛镇静是脑损伤治疗的重要组成部分



北美ICU机械通气调查：169 ICU、97,000例患者

镇痛镇静是脑损伤治疗的重要组成部分

TABLE 5
Treatment for patients in different ICP categories by continent

Treatment	No. of Patients (%)							
	Total		ICP <20 mm Hg		ICP 20 to <30 mm Hg		ICP ≥30 mm Hg	
	North America (757 patients)	Europe (732 patients)	North America (321 patients)	Europe (266 patients)	North America (227 patients)	Europe (225 patients)	North America (209 patients)	Europe (241 patients)
sedation	681 (90)*	688 (94)	289 (90)*	253 (95)	216 (95)	215 (96)	176 (84)*	220 (91)
paralysis	492 (65)*	393 (54)	177 (55)*	119 (45)	169 (74)*	133 (59)	146 (70)*	141 (59)
drainage	232 (31)*	106 (15)	73 (23)*	26 (9.8)	79 (35)*	30 (13)	80 (38)*	50 (21)
mannitol	350 (46)*	269 (37)	66 (21)*	36 (14)	127 (56)*	83 (37)	157 (75)*	150 (62)
hyperventilation								
intensive (≤30 mm Hg)	616 (85)*	474 (66)	239 (79)*	168 (64)	194 (87)*	144 (65)	183 (91)*	162 (69)
very intensive (≤25 mm Hg)	393 (54)*	202 (28)	140 (46)*	65 (25)	121 (55)*	65 (29)	132 (66)*	72 (31)
barbiturates	72 (9.5)	85 (12)	11 (3.4)	8 (3.0)	17 (7.5)	11 (4.9)	44 (21)	66 (27)

* p < 0.05 between continents.

北美和欧洲15国、2177例重度TBI患者的流行病学调查，
90%以上患者应用镇静治疗

脑损伤患者镇痛镇静的目的

- 控制疼痛和躁动为主要目的（轻度脑损伤 GCS 9~15）
 - 缓解疼痛、焦虑和躁动，降低应激反应
 - 减少并发症
 - 提高人工气道和机械通气的耐受性
 - 利于医疗和护理操作
- CNS保护为目的（重度脑损伤 GCS≤8）
 - 降低脑代谢、控制ICP
 - 辅助低温治疗
 - 癫痫持续状态

The **NEW ENGLAND**
JOURNAL *of* **MEDICINE**

ESTABLISHED IN 1812

DECEMBER 27, 2012

VOL. 367 NO. 26

**A Trial of Intracranial-Pressure Monitoring
in Traumatic Brain Injury**

Randall M. Chesnut, M.D., Nancy Temkin, Ph.D., Nancy Carney, Ph.D., Sureyya Dikmen, Ph.D., Carlos Rondina, M.D.,
Walter Videtta, M.D., Gustavo Petroni, M.D., Silvia Lujan, M.D., Jim Pridgeon, M.H.A., Jason Barber, M.S.,
Joan Machamer, M.A., Kelley Chaddock, B.A., Juanita M. Celix, M.D., Marianna Cherner, Ph.D., and Terence Hendrix, B.A.

The **NEW ENGLAND**
JOURNAL *of* **MEDICINE**

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APRIL 21, 2011

VOL. 364 NO. 16

Decompressive Craniectomy in Diffuse Traumatic Brain Injury

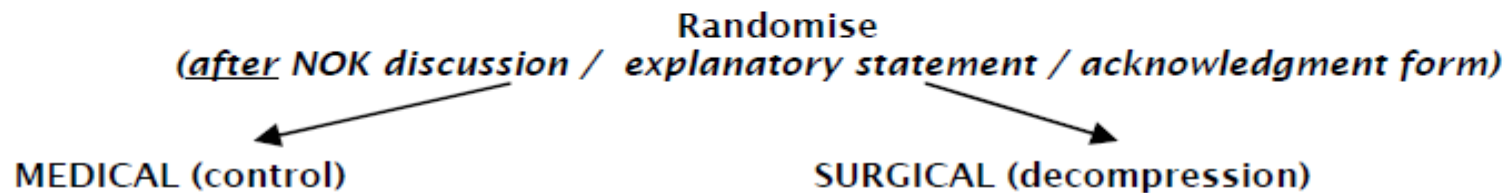
D. James Cooper, M.D., Jeffrey V. Rosenfeld, M.D., Lynnette Murray, B.App.Sci., Yaseen M. Arabi, M.D.,
Andrew R. Davies, M.B., B.S., Paul D'Urso, Ph.D., Thomas Kossmann, M.D., Jennie Ponsford, Ph.D.,
Ian Seppelt, M.B., B.S., Peter Reilly, M.D., and Rory Wolfe, Ph.D., for the DECRA Trial Investigators
and the Australian and New Zealand Intensive Care Society Clinical Trials Group*

- Arterial line and CVP
- iv Fluid to CVP 8-12
- $S_{O_2} > 95\%$; $P_{O_2} > 90$ mmHg; P_{CO_2} 36-40 mmHg
- Nurse 20-30 degrees head up, no venous obstruction
- Morphine 2-15 mg/hr, midazolam 1-15 mg/hr, \pm propofol 20-200mg/hr
- Maintain BSL 8 mmol/L and Hb close to 100g/L
- Cool to 37°C
- Serum Na 140-155 mmol/L
- Noradrenaline infusion to MAP > 90 mmHg until ICP inserted
- ICP - EVD preferred *Codman* parenchymal catheter acceptable
EVD on intermittent drainage.(monitor for 10 min drain for 5 min)
- Noradrenaline and or adrenaline infusion to keep CPP > 60 mmHg for 1st 48 hr

OPTIONAL

- f noradrenaline > 5 mcg/min - may nurse flat
- If ICP increased. - HTS/Mannitol If Na+ <152mmol/L and CVP < 12 - give 3% HTS bolus 1-200 ml
If s osmo < 315 and CVP > 12, give mannitol 20% 100 ml iv
- Cis-atracurium 10 mg iv. If ICP controlled, increase sedation.
- If *Codman* ICP - may not convert to EVD after this point
ICP becoming refractory despite above measures consider repeat CT brain scan

If: in first 72 hours post injury, and despite optimising the above
Spontaneous ICP > 20mmHg for 15 mins in 1 hr (continuous or cumulative)



新近研究提示的几点问题

- 低温中的镇痛镇静
- 冬眠合剂
- DIS

关于低温治疗中的镇静

American Society of Critical Care Anesthesiologists

Section Editor: Michael J. Murray

Anesthesia and Analgesia Protocol During Therapeutic Hypothermia After Cardiac Arrest: A Systematic Review

Carlos Chamorro, MD, PhD,* Jose M. Borrallo, MD,† Miguel A. Romera, MD,* Jose A. Silva, MD,† and Bárbara Balandín, MD*

- 咪达唑仑 57.4%: 5mg/kg~0.3mg/kg/h
- 异丙酚 19.1%: 6mg/kg/h
- 芬太尼 48.5%: 0.5~10ug/kg/h
- 吗啡 5.9%
- 肌松剂 79.4% (泮库溴铵、顺式阿曲库铵)

关于冬眠合剂

- 曾经是低温治疗的标准辅助药物
- 优点在于降低体温调定阈值
- 主要缺点在于对循环的影响

关于DIS

RESEARCH

Open Access

Effects of the neurological wake-up test on clinical examination, intracranial pressure, brain metabolism and brain tissue oxygenation in severely brain-injured patients

Raimund Helbok^{1,2*}, Pedro Kurtz¹, Michael J Schmidt¹, Morgan R Stuart¹, Luis Fernandez¹, Sander E Connolly¹, Kiwon Lee¹, Erich Schmutzhard², Stephan A Mayer¹, Jan Claassen¹ and Neeraj Badjatia^{1,3*}

CC 2012

The neurological wake-up test increases stress hormone levels in patients with severe traumatic brain injury*

Karin Skoglund, RN; Per Enblad, MD, PhD; Lars Hillered, MD, PhD; Niklas Marklund, MD, PhD

CCM 2012

The Neurological Wake-up Test Does not Alter Cerebral Energy Metabolism and Oxygenation in Patients with Severe Traumatic Brain Injury

Karin Skoglund · Lars Hillered · Karlis Purins · Parmenion P. Tsitsopoulos ·
Johanna Flygt · Henrik Engquist · Anders Lewén · Per Enblad ·
Niklas Marklund

NCC 2013

脑损伤患者镇痛镇静的目的

- 控制疼痛和躁动为主要目的（轻度脑损伤 GCS 9~15）
 - 缓解疼痛、焦虑和躁动，降低应激反应
 - 减少并发症
 - 提高人工气道和机械通气的耐受性
 - 利于医疗和护理操作
- CNS保护为目的（重度脑损伤 GCS≤8）
 - 降低脑代谢、控制ICP
 - 辅助低温治疗
 - 癫痫持续状态

神经外科术后疼痛的调查

韩如泉 李学斌 王保国 王思真

表2 各组手术入路术后 24h 疼痛程度[例(%)]

	额部	颞部	枕部及后正中	经口鼻蝶	总数
病例数	26	35	19	14	94
重度疼痛	4(15.4)	13(37.1)	5(26.3)	9(64.3)	31(33.0)
中度疼痛	10(38.5)	14(40.0)	8(42.1)	5(35.7)	37(39.4)
轻度疼痛	8(30.8)	7(20.0)	5(26.3)	0	20(21.3)
无疼痛	4(15.4)	1(2.9)	1(5.3)	0	6(6.4)

中重度疼痛
将近70%

神经外科开颅术后患者疼痛及控制状况的调查

张雪梅 侯春梅 王会文 韩如泉

【摘要】 目的 调查神经外科开颅手术患者术后疼痛及控制状况,为术后镇痛治疗提供依据。
方法 选择北京天坛医院神经外科开颅手术患者 100 例,采用疼痛视觉模拟评分(VAS)、Ramsay 镇静评分于术后 2 h 和 24 h 评估患者意识和疼痛状况,并进行术后疼痛调查问卷,记录不良事件。
结果 本组患者术后均使用静脉镇痛泵。术后 2 h 无痛 38 例(38%),轻度疼痛 49 例(49%),中度疼痛 12 例(12%),重度疼痛 1 例(1%);术后 24h 无痛 24 例(24%),轻度疼痛 30 例(30%),中度疼痛 36 例(36%),重度疼痛 10 例(10%)。
结论 神经外科开颅手术患者术后存在不同程度的疼痛,术后镇痛需要进一步深化。

【关键词】 术后疼痛; 镇痛; 颅脑手术; 神经外科

应用
PCA后
中重度
疼痛将
近50%

RESEARCH ARTICLE

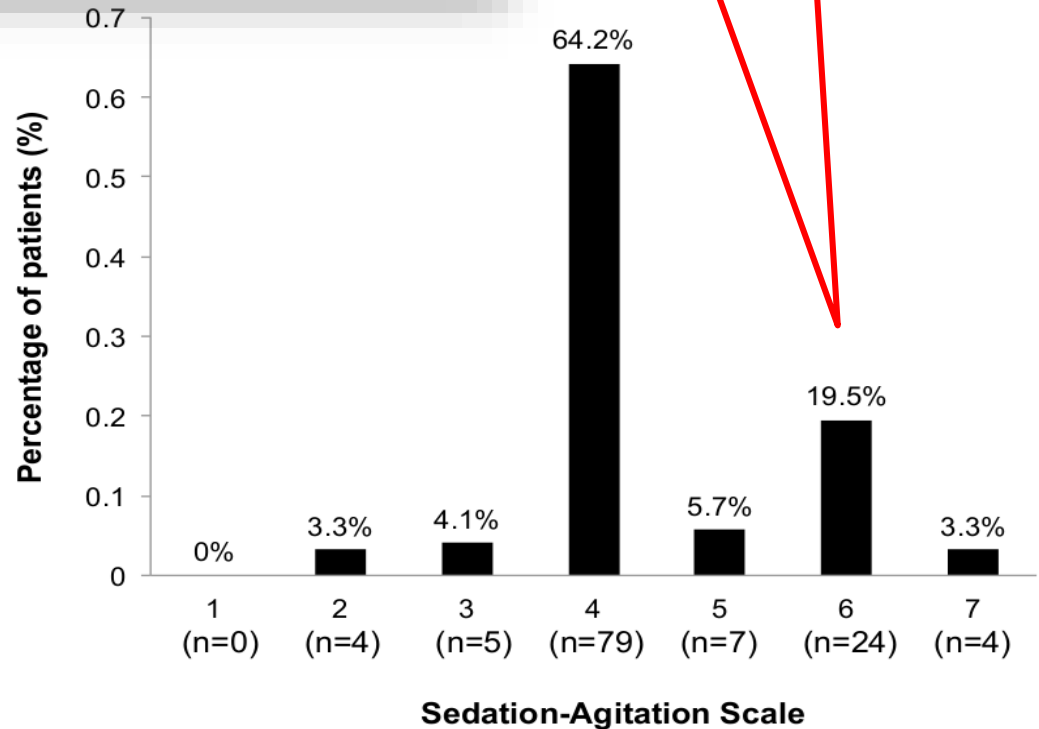
Incidence, Risk Factors and Consequences of Emergence Agitation in Adult Patients after Elective Craniotomy for Brain Tumor: A Prospective Cohort Study

Lu Chen, Ming Xu, Gui-Yun Li, Wei-Xin Cai, Jian-Xin Zhou*

Department of Critical Care Medicine, Beijing Tiantan Hospital, Capital Medical University, China National Clinical Research Center for Neurological Diseases, Beijing, 100050, China

*zhoujx.cn@gmail.com

术后第1天
躁动发生率
达30%



Knowledge of doctors and nurses on pain in patients undergoing craniotomy

The study objectives were to characterize the profile of the doctors and nurses caring for patients in the craniotomy postoperative period, checking pain assessment methods and to identify the existence of analgesia protocols. Cross-sectional and analytical study. The casuistry is constituted of 30 doctors and 30 nurses. The results revealed that 83.3 % of the nurses were female, 63.3% knew pain scales, and 16.6% said that analgesia protocols exist. Regarding doctors 60% were male, 70% knew the pain scales, 3.3% had specialization in pain treatment, 13.3% they stated that there are analgesia protocols. **The ignorance on the part of doctors and nurses about the assessment scales and pain assessment methods reveals the need for the creation of institutional policies on controlling pain, the use of instruments for the measurement of the pain phenomenon and analgesia protocols in the institution.**

神经专科对镇痛镇静持谨慎态度

- 主要担心意识评估，不能及时发现脑损伤病情变化
- 传统上，Neuro-ICU仅在下列情况时应用镇静
 - 躁动给患者带来危险
 - 躁动影响诊断、治疗和护理操作的实施

对躁动原因的鉴别非常重要

- 全身低氧低灌注的表现
- 疼痛
- 颅内压升高的早期表现
 - 颅内积气
 - 脑水肿
 - 颅内血肿
- 麻醉药的残余作用
- 额部损伤

轻度脑损伤患者

控制疼痛和躁动为主要目的：重点是评估

- RASS、SAS（信度和效度最佳）
- VAS、NRS
- BPS、CPOT（信度和效度最佳）
- GCS
- 生理指标
- EEG



Evaluating Pain, Sedation, and Delirium in the Neurologically Critically Ill—Feasibility and Reliability of Standardized Tools: A Multi-Institutional Study

Amy Yu, MD, FRCP(c)¹; Jeanne Teitelbaum MD, FRCP(C)¹; Jill Scott, RN²; Gail Gesin PharmD²; Brittany Russell, RN²; Toan Huynh, MD²; Yoanna Skrobik, MD, FRCP³

TABLE 2. Distribution of Level of Consciousness (n = 439)

Richmond Agitation-Sedation Scale Score	n (%)
−5: No response to voice or stimulation	54 (12.3)
−4: Any movement to voice or stimulation	49 (11.2)
−3: Responds to verbal commands with no eye opening	15 (3.4)
−2: Briefly (less than 10 s) awakens with eye contact to voice	36 (8.2)
−1: Awakens with eye contact of at least 10 s	25 (5.7)
0: Alert and calm	238 (54.2)
≥1: Agitated	22 (5.0)

TABLE 4. Physician/Nurse Inter-rater Reliability of Pain and Sedation Assessments

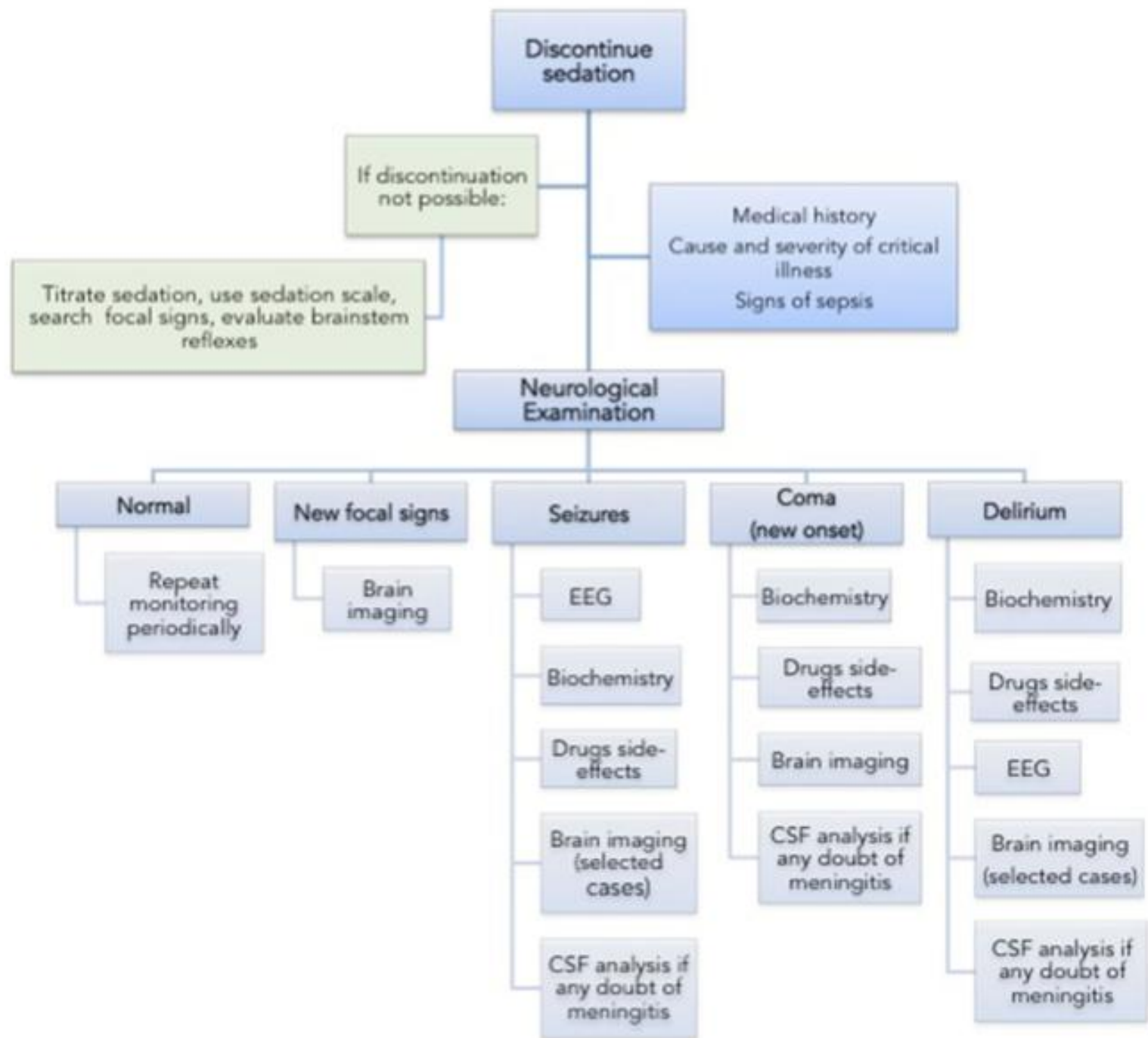
Assessment Item	No. of Evaluations	Intraclass Correlation Coefficient
Numeric Rating Scale	121	0.92
Behavioral Pain Scale	47	0.83
Richmond Agitation-Sedation Scale	200	0.92
Total Intensive Care Delirium Screening Checklist score	161	0.86

Tarek Sharshar
Giuseppe Citerio
Peter J. D. Andrews
Arturo Chierigato
Nicola Latronico
David K. Menon
Louis Puybasset
Claudio Sandroni
Robert D. Stevens

Neurological examination of critically ill patients: a pragmatic approach. Report of an ESICM expert panel

Intensive Care Med 2014 ahead of print

- 神经系统体检应列为**常规监测**
- 应包括：**意识、认知、脑干功能、运动功能**
- **镇静的实施应尽可能减少对神经系统体检的影响（除非减浅镇静深度会导致颅内压升高）**
- 神经系统体检是实施其他进一步监测的依据
- 神经系统体检对部分患者群体的预后评估具有帮助（CA、TBI）



停用镇静剂后的神经系统体检项目

□ 意识、认知、脑干功能、运动功能

	影像学	生化	脑脊液	药物筛查	EEG
局灶体征	✓				
coma	✓	✓	✓	✓	
谵妄	✓	✓	✓	✓	✓
癫痫	✓	✓	✓	✓	✓

镇痛镇静剂选择原则

- 对CNS无附加损害
- 快速苏醒

Comparison of the safety and efficacy of propofol with midazolam for sedation of patients with severe traumatic brain injury: A meta-analysis☆☆☆

Jian-wen Gu, MD, PhD*, Tao Yang, MD, Yong-qin Kuang, MD, PhD, Hai-dong Huang, MD, Bin Kong, MD, Hai-feng Shu, MD, PhD, Si-xun Yu, MD, PhD, Jun-hai Zhang, MD

Department of Neurosurgery, Chengdu Military General Hospital, Chengdu 610083, China

Results: Seven relevant studies were identified. Three of these studies were excluded: one was a single-arm study, one compared morphine and propofol, and for one the full text article could not be obtained. The remaining 4 studies were included in the meta-analysis. The results of the meta-analysis showed that propofol and midazolam have similar effects on the Glasgow Outcome Scale score, mortality, intracranial pressure, and cerebral perfusion pressure.

Conclusion: Our meta-analysis of 4 studies showed that there are no important differences between propofol and midazolam when administered to provide sedation for patients with severe traumatic brain injury. Further randomized, controlled trials comparing propofol with midazolam for sedation of such patients are needed.

Dexmedetomidine in Patients After Intracranial Surgery

This study has been completed.

Sponsor:

Capital Medical University

Information provided by (Responsible Party):

Jian-Xin Zhou, Capital Medical University

ClinicalTrials.gov Identifier:

NCT01445639

First received: September 30, 2011

Last updated: January 25, 2014

Last verified: January 2014

[History of Changes](#)

Zhao *et al. Trials* 2013, **14**:251

<http://www.trialsjournal.com/content/14/1/251>



STUDY PROTOCOL

Open Access

Use of dexmedetomidine for prophylactic analgesia and sedation in delayed extubation patients after craniotomy: a study protocol and statistical analysis plan for a randomized controlled trial

Li-Hong Zhao, Zhong-Hua Shi, Ning-Ning Yin and Jian-Xin Zhou*

Prophylactic Analgesia and Sedation Trial (PASTrial I & II)

纳入：开颅术后保留气管插管的成年患者

- 年龄<18岁
- 孕产妇
- 急诊或24小时内二次手术
- 延髓手术
- 术前意识障碍或癫痫
- 肝肾功能不全
- 入室GCS-M=1~4
- 入室BPs<90mmHg、HR<50bpm、或需血管活性药物维持
- 入室表现房室传导阻滞、急性心肌梗死

随机、双盲、安慰剂对照

SAS» 5: (Mida)(Prop) bolus or bump
疼痛主诉: Fent 0.05mg IV

- 理想镇静百分比
- 给药期间躁动频次, 镇静剂量
- 给药期间疼痛主诉频次, 镇痛剂量
- 次要转归和并发症

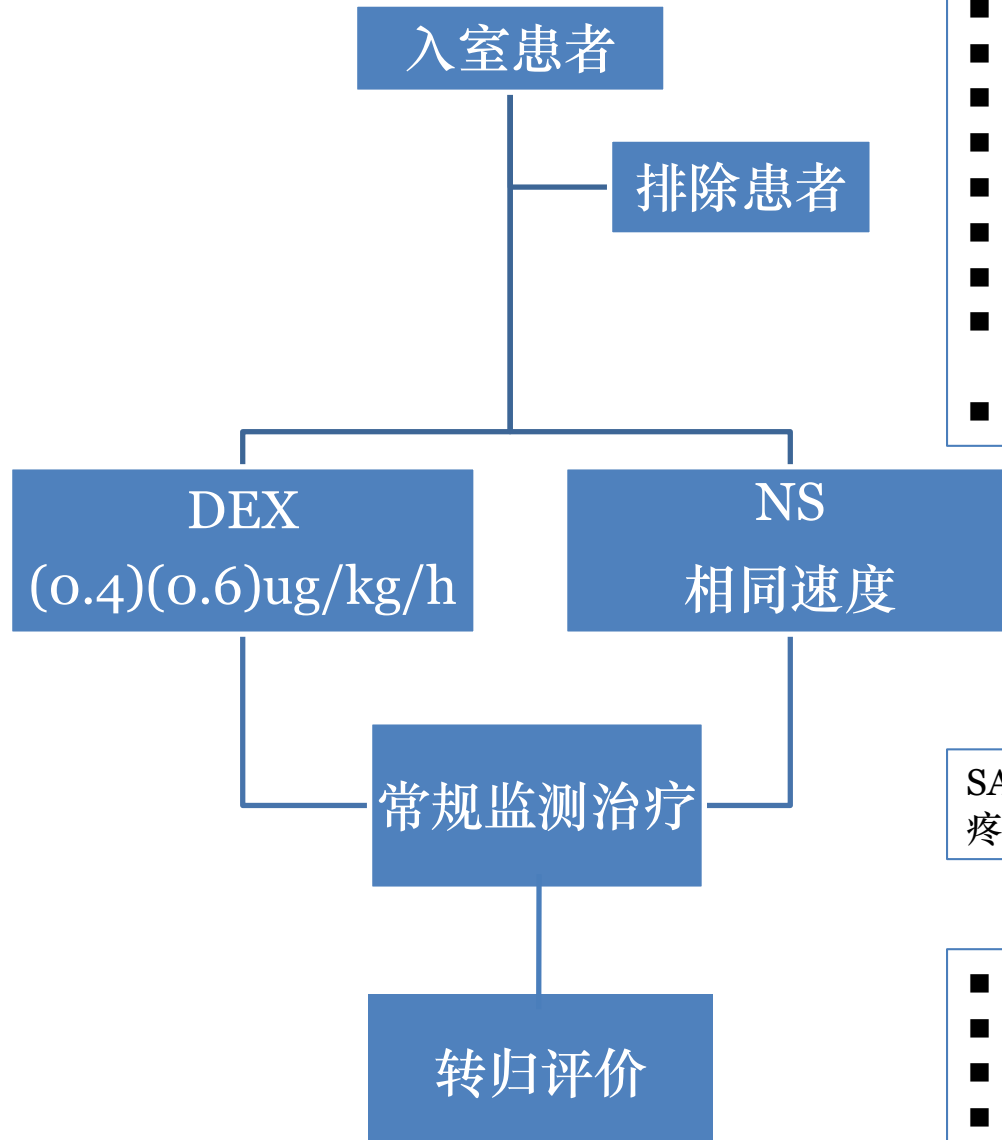


Table 2. Efficacy of sedation.

	DEX group (n=71)	NS group (n=75)	p
Length of agents infusion, hr	12.5±4.3	13.4±3.1	0.322
Percentage of time in optimal sedation, (%)	99.0±3.6	93.0±16.2	0.003
Agitation, n (%)	6(8.5)	22(29.7)	0.001
Rescue propofol, n (%)	3(4.2)	10(13.3)	0.048
Continuous infusion of propofol, n (%)	0(0)	5(6.7)	0.036
Total dose of propofol, mg/pts	2.08±11.03	28.29±109.73	0.000

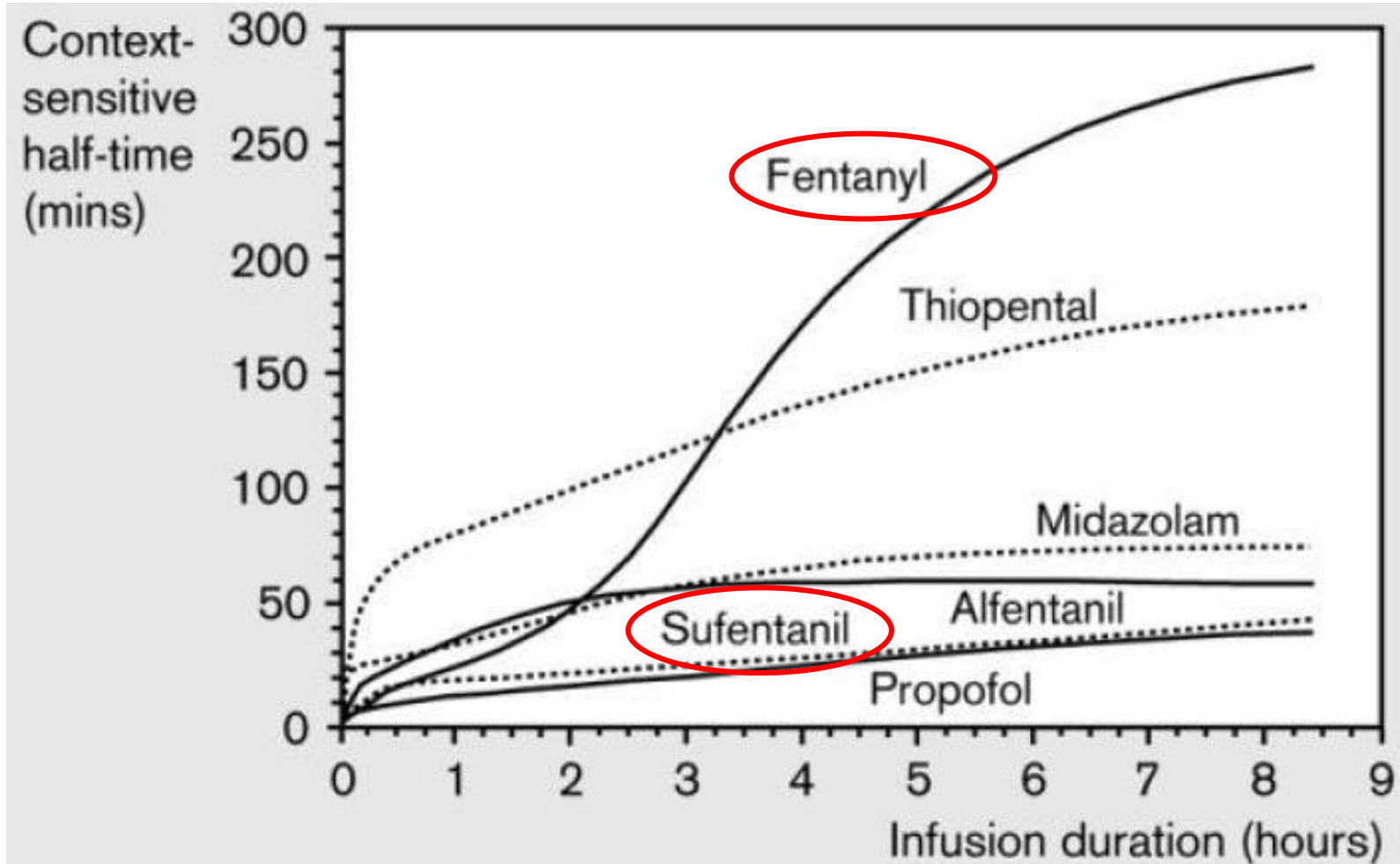
PAD指南

- ICU患者镇痛治疗一线药物：阿片类药物
- 拔除胸腔引流管前预先镇痛，可推广到其他创伤性操作

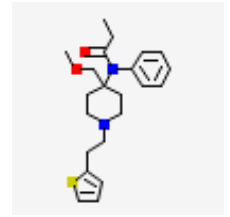
ICU常用阿片类药物

	$T_{1/2\beta}$ (h)	Cl (ml/kg/min)	费用	代谢	主要副作用
吗啡	1.5-5	14	\$	脱甲基	HR/BP↓、支气管痉挛
芬太尼	1.3-3	13	\$	脱甲基	呼吸抑制、肌肉僵硬
舒芬	13	14	\$	脱甲基	HR↓、肌肉僵硬
瑞芬	0.05	50	\$\$	非特异酯酶	HR/BP↓、肌肉僵硬

Context-sensitive half time



舒芬太尼 (sufentanil)



- 芬太尼的衍生物
- 脂溶性高，极易透过血脑屏障，并能迅速在脑内达到有效浓度。但由于与阿片受体的亲和力较芬太尼强，故镇痛强度大，效价约为芬太尼的5~10倍，作用持续时间也更长
- 有较宽的安全阈范围。大鼠研究的治疗指数为25211，高于芬太尼(277) 和吗啡(69.5)
- 尤其适用于脑损伤患者
 - 呼吸抑制发生率低，且残留呼吸抑制作用较少
 - 对颅内血流动力学影响小

国内开展的多中心研究

· 94 ·

中华危重病急救医学 2014 年 2 月第 26 卷第 2 期 Chin Crit Care Med, February 2014, Vol.26, No.2

· 论著 ·

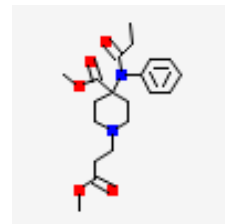
舒芬太尼对重症监护病房危重患者镇痛 / 镇静治疗的多中心随机对照临床研究

杨宏富 孙荣青 常银江 付云 李保林 秦秉玉 芦乙滨 焦宪法
张振平 孙立冬 刘小军 胡亚兰 毛峥嵘

【摘要】 **目的** 评价舒芬太尼在重症监护病房(ICU)重症患者中的镇痛 / 镇静效果和安全性,并与芬太尼进行比较。**方法** 采用多中心随机对照临床研究。选择 2011 年 6 月至 2012 年 1 月河南省 11 家医院 ICU 需镇痛的重症成人患者,按各医院编号和进入试验的时间顺序编号,采用信封法随机分为两组,每组 300 例。剔除持续镇痛时间 < 48 h 及镇痛期间行连续性肾脏替代治疗(CRRT)者,最终纳入的 544 例患者中舒芬太尼组 282 例,芬太尼组 262 例。用药前两组年龄、体质量、急性生理学及慢性健康状况评分系统 II (APACHE II)评分、格拉斯哥昏迷评分(GCS)差异无统计学意义,具有可比性。镇痛目标为面部表情评分法(FPS) ≤ 2 分,若超过镇痛药限定剂量(舒芬太尼 $0.3 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$,芬太尼 $2 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$)仍不能达标,则维持镇痛限定剂量并加用咪达唑仑,满足 FPS ≤ 2 分或 Ramsay 3 分即为达标。所有病例持续镇痛时间为 48 ~ 168 h。收集相关资料,进行统计学分析。**结果** ① 与镇痛前比较,舒芬太尼镇痛后各时间点平均动脉压(MAP)明显下降($F=6.061, P<0.001$),且

结论: 与芬太尼比较,舒芬太尼的镇痛效能强、生理干扰轻、不良反应低

瑞芬太尼 (remifentanyl)



- 肝脏外代谢：非特异性酯酶
- 时量相关半衰期短，撤药后迅速清除
- 呼吸抑制作用呈剂量依赖性
- 对颅内血流动力学影响小

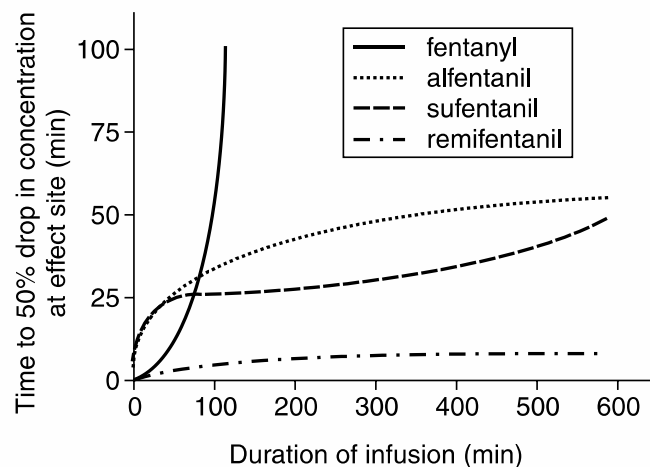
Review

The place for short-acting opioids: special emphasis on remifentanyl

Wolfram Wilhelm¹ and Sascha Kreuer²

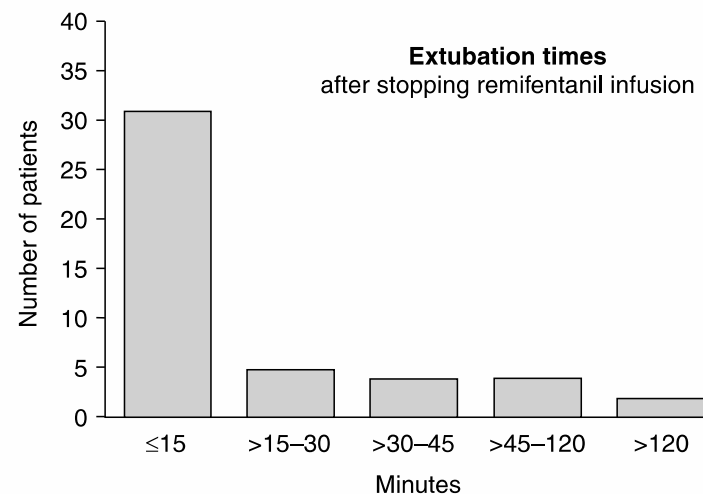
Critical Care 2008, **12(Suppl 3)**:S5 (doi:10.1186/cc6152)

Figure 1



Context-sensitive half-times of remifentanyl and the other 4-anilidopiperidine opioids. Remifentanyl has a context-sensitive half-time of 3 to 4 minutes, regardless of the duration of infusion, whereas continuous infusion of the other opioids results in accumulation and considerable prolongation of effect, making these opioids intermediate-acting or long-acting agents, depending on the duration of infusion. Figure adapted with permission from Egan TD, Lemmens HJ, Fiset P, Hermann DJ, Muir KT, Stanski DR, Shafer SL: The pharmacokinetics of the new short-acting opioid remifentanyl (Gl87084B) in healthy adult male volunteers. *Anesthesiology* 1993, 79:881-892.

Figure 3



Extubation times after remifentanyl infusion. Shown are extubation times in 46 intensive care unit patients after sedation with a remifentanyl infusion (mean duration 9.8 hours, mean dosage $0.14 \pm 0.08 \mu\text{g}/\text{kg}$ per minute). Two-thirds of all patients could be extubated within 15 minutes and 87% within 45 minutes after cessation of remifentanyl infusion. Figure adapted with permission from: Wilhelm W, Dorscheid E, Schlaich N, Niederprüm, Deller D: The use of remifentanyl in critically ill patients. Clinical findings and early experience. *Anaesthetist* 1999, 48:625-629. © Springer.

BMJ Open Short-term use of remifentanyl during endotracheal extubation for prophylactic analgesia in neurosurgical patients after craniotomy (SURE after Craniotomy Study): a study protocol and statistical analysis plan for a randomised controlled trial

Yuan-Xing Wu, Han Chen, Jian-Xin Zhou

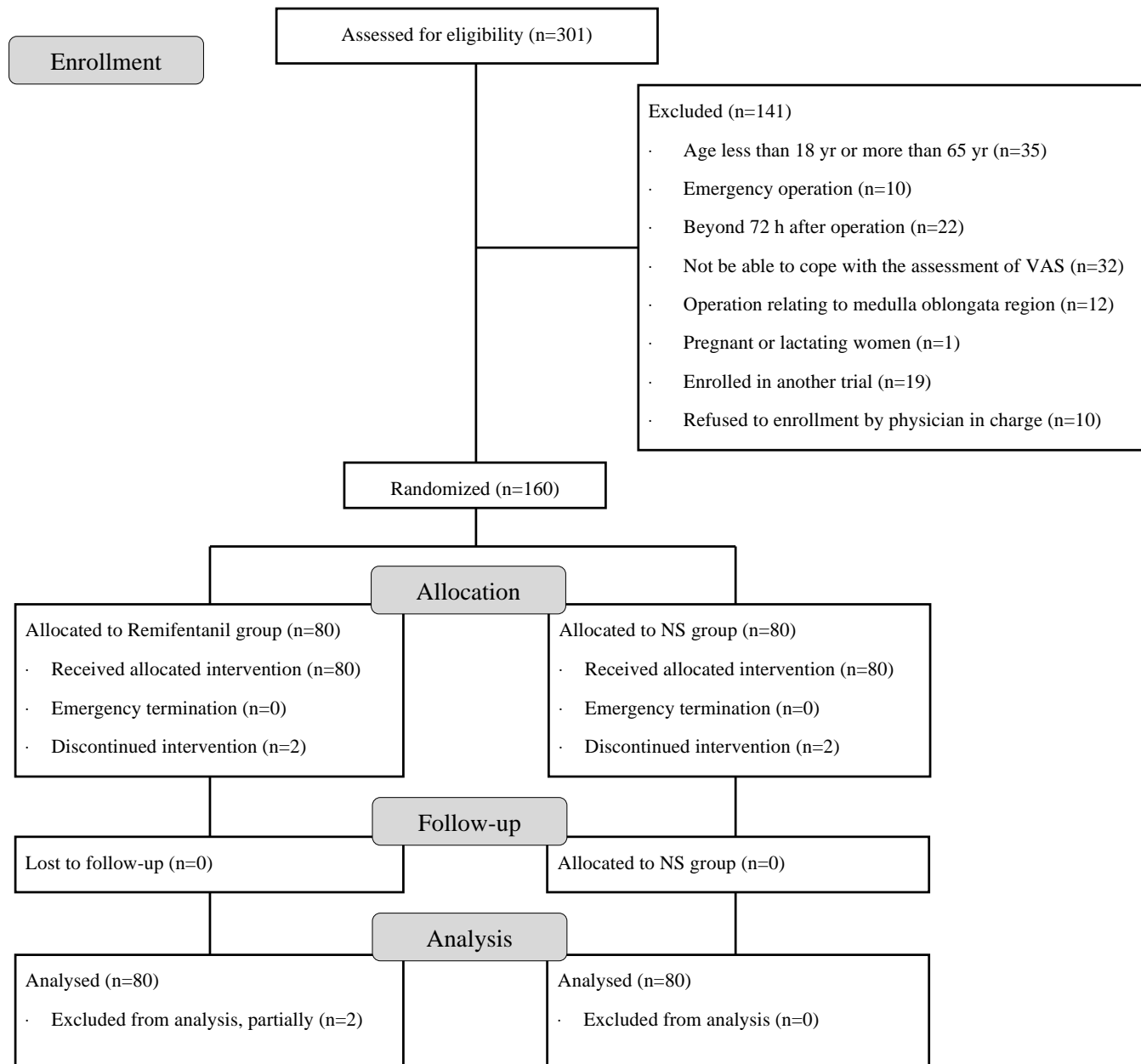
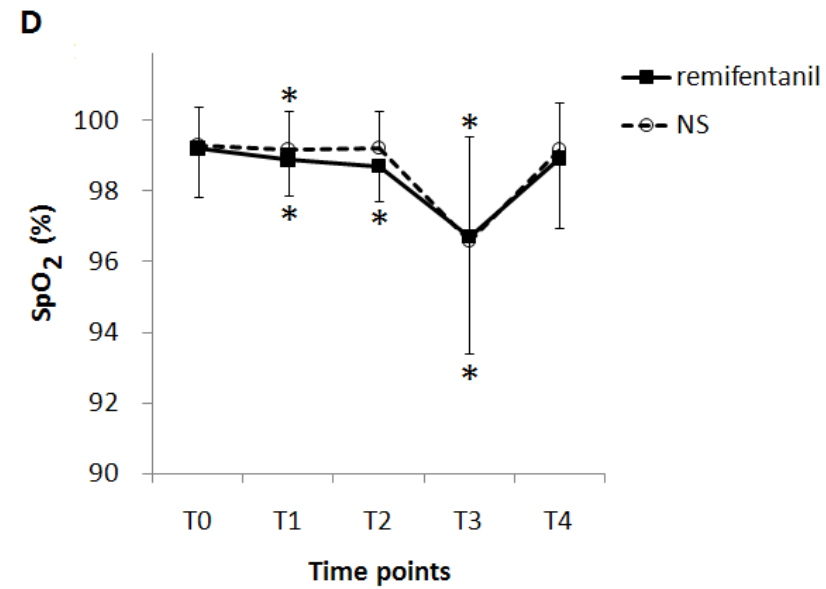
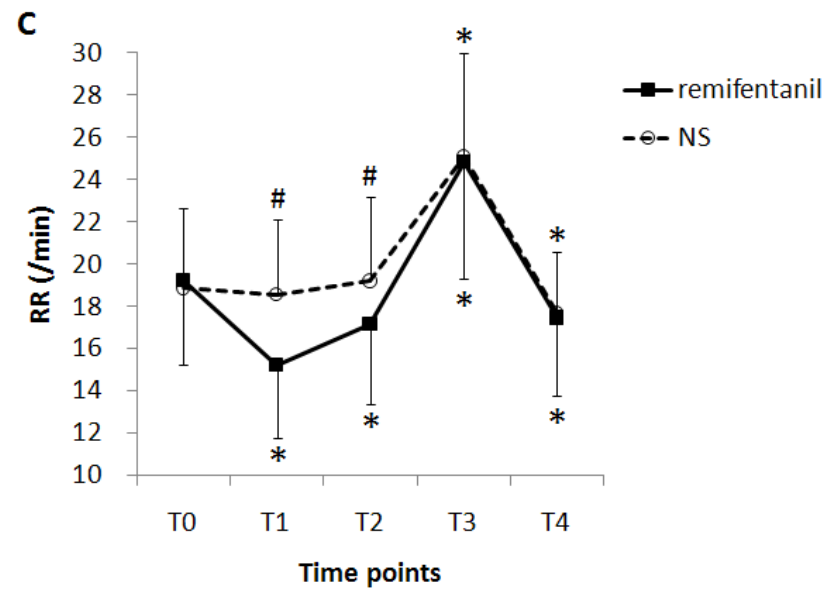
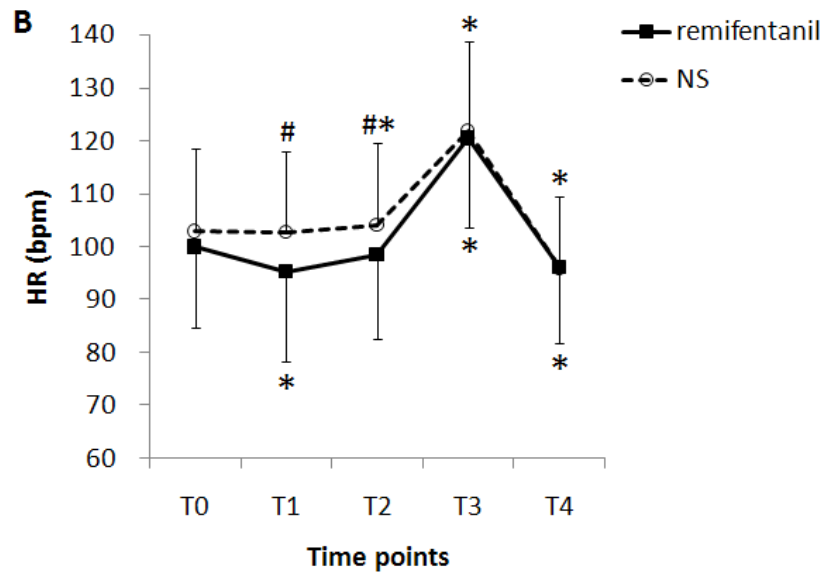
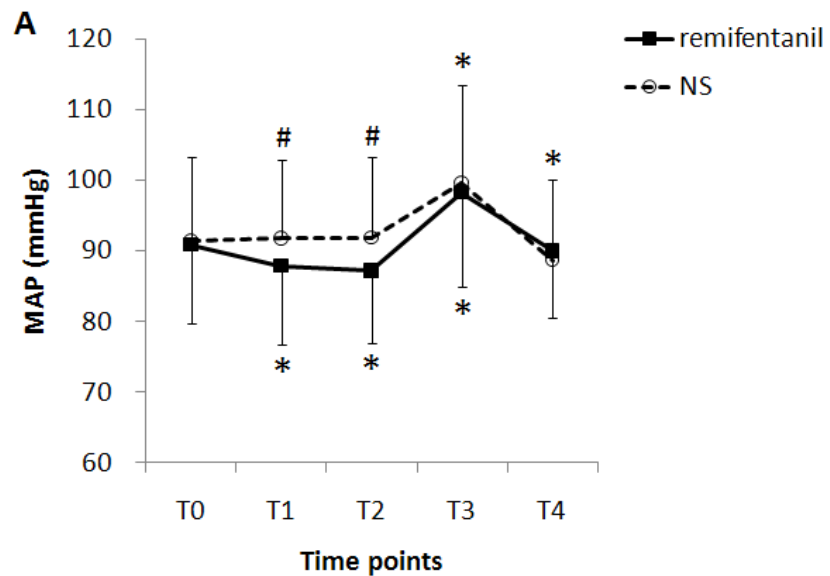


Table 2. Incidence of Severe and Moderate Pain during Peri-extubation Period

	Remifentanyl	NS	<i>P</i> Value
Intention-to-treat	n=80	n=80	
Severe pain	20 (25.0)	33 (41.3)	0.029
Severe and moderate pain	29 (36.3)	50 (62.5)	0.001
Pre-protocol	n=78	n=80	
Severe pain	19 (24.4)	33 (41.3)	0.024
Severe and moderate pain	28 (35.9)	50 (62.5)	0.001

Data are shown as no. (%).



脑损伤患者镇痛方案

- 短期应用(术后患者): 瑞芬有助于拔管
- <24h: 舒芬→瑞芬有助于快速消除
- >24h: 芬太尼, 疗效+经济学考虑

·标准与指南·

重症脑损伤患者镇痛镇静专家共识

中国医师协会神经外科医师分会神经重症专家委员会



小结

- 脑损伤患者是躁动和疼痛的高危群体
- 恰当镇痛镇静的基础是评估
 - 建立常规
 - 意识障碍患者的疼痛评价具有研究前景
- 药物选择原则
 - 对CNS无附加损害
 - 快速起效和消除