

• 标准与指南 •

中国成人 ICU 镇痛和镇静治疗指南

中华医学会重症医学分会

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Guidelines for analgesia and sedation treatment in intensive care unit of Chinese adults

Society of Critical Care Medicine Chinese Medical Association

1 前言

重症医学科(ICU)收治的患者处于强烈的应激环境之中,其常见原因包括:①自身严重疾病的影响:患者因病情严重难以自理,各种有创诊治操作,自身伤病的疼痛;②环境因素:患者被约束于病床上,灯光长明,昼夜不分,各种噪音(机器声、报警声、呼喊声等),睡眠剥夺,邻床患者的抢救或去世等;③隐匿性疼痛:气管插管及其他各种插管,长时间卧床;④对未来命运的忧虑:对疾病预后的担心,死亡的恐惧,对家人的思念与担心等。上述因素使患者感到极度的“无助”和“恐惧”,构成对患者的恶性刺激,增加了患者的痛苦,甚至使患者因为这种“无助与恐惧”而躁动挣扎,危及其生命安全。

重症医学工作者应该时刻牢记,我们在抢救生命、治疗疾病的过程中,必须同时注意尽可能减轻患者的痛苦与恐惧感,使患者不感知、不注意、不记忆或者遗忘其在危重阶段的各种痛苦,避免这些痛苦及其所引发的焦虑和躁动而增加各器官的代谢负担、加重患者的病情或影响其接受治疗。因此,镇痛和镇静应作为 ICU 患者的常规治疗。

2006 年中华医学会重症医学分会撰写了《中国重症加强治疗病房患者镇痛和镇静治疗指导意见(2006)》^[1],奠定了中国重症患者镇痛镇静的基石。近十年来国内及国际重症医学界对于疼痛、焦虑及谵妄等问题更加关注,进行了大量的工作,发表了较多文献,关于疼痛、焦虑、谵妄及其防治的理念也有逐渐的变迁,更加强调“早期干预、以镇痛治疗为基础、以患者为中心”的人文关怀,尽可能减少镇痛镇静药物治疗的不良反应^[2-4]。

鉴于上述进展,为更新重症医学工作者对镇痛、镇静及谵妄防治的认识并规范其临床应用,中华医学会重症医学分会在 2006 年指导意见的基础上,依据国内外最新的研究进展,组织专家进行讨论,归纳和构建了 5 部分内容、共 19 个在临床实践中常见的重要问题,应用目前循证医学常用的 GRADE 方法(推荐分级的评估、制定与评价)^[5-6],更新修订了本《中国成人 ICU 镇痛和镇静治疗指南》。

2 方法学

2.1 临床问题的构建:临床问题通过“PICO”原则进行构建,即人群(Patient)、干预措施(Intervention)、对照措施(Comparison)和结局(Outcome)^[6]。根据专家组的讨论,初步制定了 37 个临床问题,然后向中华医学会重症医学分会常务委员及青年委员发放问卷调查,选取了大家关注度较高的 19 个问题。

2.2 文献检索、筛选和数据整合:在文献检索工作开展前,本指南修订工作组进行了 2 次文献检索策略培训。检索的

外文数据库为 Medline、Embase 和 Cochrane library,年限为 1999 年 1 月 1 日至 2017 年 9 月 19 日;中文数据库为中国知网、万方医学和中国生物医学文献数据库,年限为 2006 年 10 月 1 日至 2017 年 9 月 19 日。检索完成后进行文献筛查,对最终选取的文献进行数据提取和质量评价[其中随机对照试验(RCT)采用 Cochrane 偏倚风险评估工具,队列研究和病例对照研究采用纽卡斯尔-渥太华(NOS)量表,诊断实验采用诊断准确性研究的质量评估(QUADAS-2)量表],最后通过 Meta 分析进行数据整合。Meta 分析应用 RevMan 5.3 软件进行数据分析,并将结果以“森林图”形式导出。期间,指南修订工作组又进行了 1 次文献质量评价培训和 2 次 Meta 分析培训。

2.3 GRADE 方法:在证据质量和推荐强度的评价中,我们采用 GRADE 方法,应用 GRADEpro 在线指南制定工具(GRADEpro Guideline Development Tool)软件进行证据质量评价和推荐强度评价^[7]。在该项目工作进行前,指南修订工作组召集全体成员进行 GRADE 方法培训;在制定指南过程中,临床专家与方法学专家共同进行证据质量和推荐强度的评价;每个临床问题的推荐意见及其推荐强度最终都须经过指南修订工作组讨论和投票表决。GRADE 方法将证据质量分级为“高”“中”“低”“极低”4 个级别,每个级别的判断主要根据以下 8 个因素进行详细评价,即研究类型、偏倚风险、一致性、间接性、精确性、发表偏倚、效应值、混杂因素和剂量-效应梯度。一般初始认为 RCT 为高质量证据,然后根据偏倚风险、一致性、间接性、精确性和发表偏倚情况进行降级处理;设计和实施较好的观察性研究初始认为是低质量证据,但可根据效应值、混杂因素和剂量-效应梯度情况进行升级处理。证据质量的评价标准见表 1。

GRADE 方法将推荐强度分为“强推荐”和“弱推荐”两类。推荐强度与证据质量、利弊间权衡、患者的意愿和价值观以及资源成本利用 4 个因素有关,具体见表 2。“强推荐”意味着利明显大于弊或弊明显大于利,大多数临床医务人员会选择或拒绝该干预措施,大多数患者亦会从中明显获益;“弱推荐”意味着利可能大于弊或弊可能大于利,指南修订工作者对此推荐意见不是很确信,此时,临床医务人员应根据证据质量评估及患者意愿和价值观进行综合选择。强推荐时,推荐意见表述为“推荐……”。弱推荐时,推荐意见表述为“建议……”,具体见表 3。

2.4 最佳实践声明:对于不能进行 GRADE 分级的强推荐,采取此种推荐方式,需要满足以下几点要求^[8]:①本声明清晰可行;②本声明有临床需求;③本声明的利益或害处明确;④证据很难收集和总结;⑤理论依据明确。

表 1 证据质量评价标准

研究设计	证据质量	具体描述	表达符号	降级因素及降级幅度	升级因素及升级幅度
随机对照试验	高级	我们非常有把握预测值接近真实值	⊕⊕⊕/A	· 偏倚风险	· 效应量大
	中级	我们对预测值有中等把握: 预测值有可能接近真实值, 但也有可能差别很大	⊕⊕⊕○/B	· -1 严重; -2 非常严重	· +1 大; +2 非常大
观察性研究	低级	我们对预测值的把握有限: 预测值可能与真实值差别很大	⊕⊕○○/C	· 不一致性	· 剂量反应
	极低级	我们对预测值几乎没有把握: 预测值与真实值可能有很大差别	⊕○○○/D	· -1 严重; -2 非常严重	· +1 梯度证据
				· 间接性	· 所有可能的混杂因素
				· 不精确性	· +1 降低所展示的效应;
				· -1 严重; -2 非常严重	· +1 当研究结果显示无效
				· 发表偏倚	· 时意味着是一种假效应
				· -1 可能; -2 非常可能	

表 2 影响推荐意见强度的因素

影响因素	解释
证据质量	证据质量越高, 强推荐可能性越大
利弊间平衡	利弊间的差别越大, 越可能做出强推荐; 净效益越小及利弊间的不确定性越小, 越可能做出弱推荐
患者的意愿和价值观	患者意愿与价值观一致和肯定, 越可能做出强推荐; 意愿和价值观可变性越大, 越可能做出弱推荐
资源成本利用	干预的成本越低, 资源利用越少, 越可能做出强推荐

表 3 推荐强度的解释及表达

推荐强度	具体描述	表达符号	指南表述
强	明确显示干预措施利大于弊或弊大于利	↑↑/I 支持某意见的强推荐 ↑↑/I 反对某意见的强推荐	“推荐……”
弱	利弊不确定或无论质量高低的证据均显示利弊相当	↑?/2 支持某意见的弱推荐 ↓?/2 反对某意见的弱推荐	“建议……”

3 指南推荐

3.1 概述

3.1.1 问题 1: 镇痛和镇静是否应作为 ICU 治疗的重要组成部分?

推荐意见 1: 推荐镇痛、镇静作为 ICU 治疗的重要组成部分 (最佳实践声明)。

本指南中, 镇痛镇静治疗特指应用药物手段减轻 / 解除患者的疼痛、焦虑及躁动。

理论依据: 疼痛是因损伤或炎症刺激, 或者因情感痛苦而产生的一种不适的躯体感觉及精神体验^[9]。疼痛在 ICU 中普遍存在, 其来源包括原发疾病、手术、创伤、烧伤、癌性疼痛和翻身、吸痰、气管插管、伤口护理、引流管拔除和导管插入等相关治疗操作以及长时间制动、炎症反应等因素^[10-12]。除 ICU 住院期间的急性疼痛外, 疾病相关的物理性损伤及相关精神因素可能导致患者出现慢性 ICU 相关疼痛 (CIRP)^[13]。疼痛导致机体应激、器官做功负荷增加、睡眠不足和代谢改变, 进而出现疲劳和定向力障碍, 导致心动过速、组织氧耗增加、凝血功能异常、呼吸功能障碍、免疫抑制和分解代谢增加等。镇痛是为了减轻或消除机体对痛觉刺激的应激及病理生理损伤所采取的药物措施, 对于 ICU 患者具有很重要的意义。

焦虑是一种强烈的忧虑、不确定或恐惧状态。50% 以

上的 ICU 患者可能出现焦虑症状, 其特征包括躯体症状 (如心慌、出汗) 和紧张感。ICU 患者焦虑的原因包括^[14-15]:

① 病房环境: 包括噪音、灯光刺激、室温过高或过低; ② 对自己疾病和生命的担忧; ③ 高强度的医源性刺激 (频繁的监测、治疗, 被迫更换体位); ④ 各种疼痛; ⑤ 原发疾病本身的损害; ⑥ 对诊断和治疗措施的不了解与恐惧; ⑦ 对家人和亲朋的思念, 等。减轻焦虑的方法包括: 保持患者舒适, 提供充分镇痛, 完善环境和使用镇静药物等。因此对焦虑患者应在充分镇痛和去除可逆性因素基础上开始镇静治疗。

躁动是一种伴有不停动作的易激惹状态, 或是一种伴随着挣扎动作的极度焦虑状态。在综合 ICU 中, 70% 以上的患者发生过躁动。引起焦虑的原因均可以导致躁动; 另外, 某些药物的不良反应、休克、低氧血症、低血糖、酒精及其他药物的戒断反应、机械通气不同步等也是引起躁动的常见原因。研究显示, 最易使重症患者焦虑、躁动的原因依次为: 疼痛、失眠、经鼻或经口腔的各种插管、失去支配自身能力的恐惧感以及身体其他部位的各种管道限制等。躁动可导致患者与呼吸机对抗, 耗氧量增加, 意外拔除身上的各种装置和导管, 甚至危及生命^[11, 15-16]。

睡眠障碍: 睡眠是人体不可或缺的生理过程, 睡眠障碍可能会延缓组织修复、降低细胞免疫功能。睡眠障碍的类型包括: 失眠、过度睡眠和睡眠-觉醒节律障碍等。失眠是一种睡眠质量或数量达不到正常需要的主观感觉体验, 失眠或睡眠被打扰 (碎片化睡眠) 在 ICU 患者中极为常见。原因包括: ① 多种原因造成的持续噪音; ② 灯光刺激; ③ 高强度的医源性刺激 (如频繁的测量生命体征、查体, 被迫更换体位); ④ 疾病本身的损害以及患者对自身疾病的担心和了解。患者在 ICU 睡眠的特点是短暂睡眠、觉醒和快速动眼睡眠交替。患者快动眼睡眠明显减少, 睡眠质量下降, 使得患者焦虑、抑郁或恐惧, 甚至躁动, 延缓疾病的恢复^[17-19]。

镇痛和镇静的目的和意义在于: ① 消除或减轻患者的疼痛及躯体不适感, 减少不良刺激及交感神经系统的过度兴奋; ② 帮助和改善患者睡眠, 诱导遗忘, 减少或消除患者对其在 ICU 治疗期间病痛的记忆; ③ 减轻或消除患者焦虑、躁动甚至谵妄, 防止患者的无意识行为 (例如挣扎) 干扰治疗, 保护患者的生命安全; ④ 减轻器官应激负荷, 保护器官储备功能, 维持机体内环境稳定。镇痛镇静可以降低患者的代谢速率, 减少其氧耗氧需, 使机体组织氧耗的需求变化尽可能适应受到损害的氧输送状态, 并减轻各器官的代谢负担, 从而减轻强烈病理因素所造成的损伤, 为器官功能的恢复赢得时间创造条件^[1]。

3.1.2 问题 2: 需要尽可能祛除 ICU 中导致疼痛、焦虑和躁动的诱因吗?

推荐意见 2: 需尽可能祛除 ICU 中导致疼痛、焦虑和躁动的诱因 (最佳实践声明)。

理论依据: ICU 患者处于强烈的应激环境中, 无论躯体或精神上都常常经历很多导致疼痛、焦虑和躁动的诱因, 在镇痛镇静治疗中应首先尽量设法祛除上述诱因, 并积极采用非药物治疗。研究表明, 非药物治疗能降低患者疼痛评分及其所需要的镇痛和镇静药物的剂量^[20-21]。

推荐意见 3: 推荐在 ICU 通过改善患者环境、降低噪音、集中进行护理及医疗干预、减少夜间声光刺激等策略, 促进睡眠, 保护患者睡眠周期 (强推荐, 中级证据质量)。

理论依据: 睡眠剥夺不仅易于造成患者精神障碍, 还可损害组织修复及免疫机制^[18], 导致危重患者焦虑甚至谵妄^[22-24], 并增加机体的应激反应, 而睡眠剥夺在 ICU 中非常普遍^[18-19]。关于非药物干预手段对 ICU 患者睡眠的影响, 2016 年 Litton 等^[25]的一项荟萃分析整合了 5 篇相关文献, 其中包括 3 篇 RCT 和 2 篇队列研究, 荟萃分析后发现, 对 ICU 患者应用耳罩可改善患者的睡眠, 证据质量为中级。Hu 等^[26]的系统性综述对其他非药物干预措施进行总结评价, 指出集中进行护理及医疗干预可以改善部分患者睡眠状况, 减少谵妄的发生, 但证据强度较低, 仍需进行大规模研究验证并观察有无负面影响。噪音也是影响患者睡眠的重要因素, 监护仪、呼吸机等设备的报警声、电话铃声、医护人员的大声言语和行为的声、甚至频繁开关门以及患者和设备的搬动转运均可能是 ICU 噪音的来源, 世界卫生组织建议医院白天的噪音不超过 40~45 dB, 晚上不超过 35 dB^[27-29]。另外, 其他改善睡眠的措施, 如: 音乐^[30-31]、足部按摩等放松疗法^[32], 对重症患者睡眠影响暂未得出具有统计学意义的结论且证据等级偏低, 尚需进一步验证。

推荐意见 4: 建议在可能导致疼痛的操作前, 预先使用止痛药或非药物干预, 以减轻疼痛 (弱推荐, 中级证据质量)。

理论依据: 目前的证据表明, 在翻身之前给予镇痛药物能显著降低患者的疼痛评分。Robleda 等^[33]进行的一项 RCT 研究入选 ICU 机械通气患者, 随机分为芬太尼组 (39 例) 和安慰剂组 (36 例), 翻身前给予芬太尼或安慰剂发现, 芬太尼组翻身时的疼痛发生率较低 [74% (95% 可信区间, 95%CI=58%~87%) 比 94% (95%CI=81%~99%), $P=0.026$], 芬太尼组行为疼痛量表评分 (BPS) 的曲线下面积 (AUC) 明显低于安慰剂组 [132 (108, 150) 比 147 (125, 180), $P=0.016$], 且芬太尼组与安慰剂组不良事件发生率差异无统计学意义 (23% 比 14%, $P=0.381$)。de Jong 等^[34]的前瞻性干预研究同样显示, 翻身前给予计划性的镇痛治疗能将翻身前后严重疼痛发生率从 16% 降至 6% [优势比 (OR)=0.33, 95%CI=0.11~0.98, $P=0.04$], 严重不良事件发生率从 37% 降至 17%。由此提示, 在其他导致疼痛的操作前 (如伤口处理、穿刺置管等) 给予镇痛干预, 可以减轻患者的疼痛。

此外, 在进行导致疼痛的操作前给予音乐治疗、情绪舒缓及物理方法也能达到一定的缓解疼痛的效果。Jaber 等^[35]的随机交叉试验研究表明, 音乐治疗能减轻气管插管患者拔除气管导管时的疼痛程度。其他 2 项在冠状动脉旁路移植术后患者中的研究则表明, 拔除胸腔引流管前给予患者深呼吸

吸情绪舒缓治疗能降低患者的疼痛程度^[21, 36]。

另外, 拔出胸腔引流管前使用冰袋也能起到较好的缓解疼痛的效果, 目前有 3 项研究比较了预先使用冰袋能否减少拔除胸腔引流管的疼痛^[21, 37-38], 整合该 3 项研究进行荟萃分析结果显示, 预先使用冰袋能减少拔除胸腔引流管的疼痛 [拔除胸腔引流管后疼痛评分降低, 加权均数差 (SMD)=0.30, 95%CI=0.01~0.59, $P=0.04$, $I^2=0\%$]。进行 GRADE 分级后证据质量为中级。

3.1.3 问题 3: 实施镇痛镇静治疗是否应该常规评估患者的器官功能状态和器官储备能力?

推荐意见 5: 推荐实施镇痛镇静治疗前后应该常规评估患者的器官功能状态和器官储备能力 (最佳实践声明)。

理论依据: 镇痛和镇静治疗是一把“双刃剑”, 在降低应激、保护器官功能的同时, 也可能抑制某些器官的重要生理功能 (如呼吸、循环) 或加重某些器官 (如肝脏、肾脏) 的代谢负担而导致器官功能损伤或失衡。镇痛镇静药物对患者各器官功能的影响是 ICU 医生必须重视的问题之一。在实施镇痛和镇静之前应对患者的基本生命体征 (意识、心率、呼吸、血压、尿量以及体温) 进行严密监测, 以选择合适的药物及其剂量, 确定观察监测的疗效目标, 制定最好的个体化治疗方案, 达到最小的不良反应和最佳的疗效。镇痛和镇静不足时, 患者可能出现人机对抗、呼吸浅促、潮气量减少、心率增快、血氧饱和度降低等; 镇痛和镇静过深时, 患者可能表现为呼吸频率过慢、幅度减小、心率过慢、血压下降、缺氧和 (或) 二氧化碳蓄积等, 应结合患者病情及器官功能状态, 及时调整镇痛和镇静治疗方案, 避免不良事件发生。对于血流动力学不稳定的患者, 需要评估导致血流动力学不稳定的病因, 选择对循环影响相对小的镇痛镇静药物, 并在镇痛镇静的同时积极处理循环问题。对于肝肾功能不全的患者, 需要积极评估肝肾功能, 并选择合适的药物及其剂量和给药方式, 同时根据肝肾功能情况对药物的剂量及时进行调整。对于呼吸衰竭而自主呼吸代偿性驱动很强的患者, 需要合适的镇痛镇静深度, 以尽可能减少患者的自主呼吸驱动、减轻对肺组织的牵张损伤。

3.2 疼痛的评估、治疗与监测

3.2.1 问题 4: ICU 患者是否应常规进行疼痛评估?

推荐意见 6: 推荐 ICU 患者应常规进行疼痛评估 (强推荐, 中级证据质量)。

理论依据: Georgiou 等^[39]的系统综述详细总结了疼痛评估对 ICU 重症患者的作用, 但由于异质性太大未能进一步行荟萃分析。该综述指出, 对患者定时进行疼痛评估, 有助于进行恰当的镇痛治疗^[40-41], 并可以减少镇痛药物的使用剂量^[42-44]。其中, 纳入的一些文献显示, 对患者定时进行疼痛评估, 疼痛的发生率及疼痛程度均较未评估组显著降低^[11, 45-46]。同时, 有部分文献还表明, 进行常规的疼痛评估有助于缩短 ICU 住院时间^[40-43]和机械通气时间^[40], 并降低呼吸机相关性肺炎 (VAP) 的发生率^[11]。一项队列研究则表明, 进行常规的疼痛评估还有助于降低病死率^[47]。由此可见, 应对 ICU 患者常规进行疼痛评估, 选择恰当的方法定时评估疼痛程度及治疗反应并进行记录。

3.2.2 问题 5: 关于疼痛评估的方法应如何选择?

推荐意见 7: 建议对于能自主表达的患者应用数字评

分表(NRS)评分,对于不能表达但具有躯体运动功能、行为可以观察的患者应用重症监护疼痛观察量表(CPOT)或BPS评分量表(弱推荐,中级证据质量)。

理论依据:疼痛评估应包括疼痛的部位、特点、加重及减轻因素和强度,最可靠有效的评估指标是患者的自我描述。使用各种评分方法来评估疼痛程度和治疗反应,应该定期进行、完整记录。常用的评分方法有:NRS、面部表情评分表(FPS)、BPS及CPOT等。对于能自主表达的患者目前较常应用的方法是NRS评分^[3], Rahu等^[48]的前瞻性研究表明,对于接受机械通气治疗且能自主表达的患者,NRS评分具有较好的疼痛评价效果。在不能表达、具有躯体运动功能、行为可以观察的患者,BPS和CPOT对于疼痛程度的评价具有较高的可信性和一致性,虽然BPS易于记忆,但两者差异无统计学意义^[49],同时清醒患者的BPS或CPOT评分与NRS评分具有较好的相关性^[50]。近年来也有一些在特殊人群中的研究,如心脏外科重症患者^[51]、创伤患者和神经外科患者^[52]、未昏迷谵妄患者^[53],表明CPOT评分是一种有效的疼痛评估工具^[54]。以下是3种常用疼痛评估工具的详细介绍。

3.2.2.1 NRS: NRS是一个从0~10的点状标尺,0代表不痛,10代表疼痛难忍,由患者从上面选一个数字描述疼痛(图1)。用NRS评价老年患者急、慢性疼痛的有效性及其可靠性已获得证实。



图1 数字疼痛评分尺

3.2.2.2 BPS: 即从面部表情、上肢运动及机械通气顺应性3个疼痛相关行为指标方面进行评估(表4),评估患者的疼痛程度时,每个条目根据患者的反应情况分别赋予1~4分,将3个条目的得分相加,总分为3~12分,总分越高说明患者的疼痛程度越高,一般使用BPS完成对患者的疼痛评估约需要2~5 min。但该评分有一定的局限性,在未行机械通气的患者中无法使用,所以Chanques等^[49]对该量表进行了改良,将原量表中“机械通气顺应性”这个条目更换为“增加非插管患者发声”这一指标,另外2个条目保留不变,发展为BPS-NI,每个条目同样根据患者的反应情况分别赋予1~4分,将3个条目的得分相加,总分为3~12分,总分越高说明患者的疼痛程度越高。

3.2.2.3 CPOT: 该量表包括面部表情、动作、肌张力、发声/对机械通气的顺应性4个疼痛行为,每个条目0~2分,总分0~8分;其中0分代表不痛,8分代表最痛(表5)。CPOT是一种特别为无法交流的ICU患者开发的疼痛行为客观量表。

3.2.3 问题6: 镇痛是否应该作为镇静的基石?

推荐意见8: 推荐在镇静治疗的同时或之前需给予镇痛治疗(强推荐,中级证据质量)。

理论依据:大部分患者烦躁的首要原因是疼痛和不适感,故重症患者应首先考虑镇痛治疗,镇痛应作为镇静的基石^[55]。研究表明,联合镇痛治疗的镇静方案能减少疼痛发生、降低患者镇痛评分、降低机械通气的使用率^[56]、缩短气管插管时间^[57]及住院时间。使用镇痛为先的镇静方法也要权衡镇痛药可干扰呼吸动力、减少胃动力及为提供肠内营养提高难度,同时还要考虑停药所导致的疼痛复发。

表4 行为疼痛量表(BPS)

疼痛行为相关指标	1分	2分	3分	4分
面部表情	放松	部分紧张	完全紧张	扭曲
上肢运动	无活动	部分弯曲	手指、上肢完全弯曲	完全回缩
机械通气顺应性(插管)	完全能耐受	呛咳,大部分时间能耐受	对抗呼吸机	不能控制通气
发声(非插管)	无疼痛相关发声	呻吟 ≤ 3 次/min且每次持续时间 ≤ 3 s	呻吟 > 3 次/min或每次持续时间 > 3 s	咆哮或使用“哦”“哎哟”等言语抱怨,或握住呼吸

表5 重症监护疼痛观察量表(CPOT)

疼痛行为相关指标	描述	状态	评分(分)
面部表情	未观察到肌肉紧张	自然、放松	0
	表现出皱眉、眉毛放低、眼眶紧绷和提肌收缩	紧张	1
	以上所有的面部变化加上眼睑轻度闭合	扮怪相	2
动作	不动(并不代表不存在疼痛)	无体动	0
	缓慢、谨慎的运动,触碰或抚摸疼痛部位,通过运动寻求关注	保护性体动	1
	拉拽管道,试图坐起来,运动肢体/猛烈摆动,不遵从指令,攻击工作人员,试图从床上爬出来	烦乱不安	2
肌张力(通过被动的弯曲和伸展来评估)	对被动的运动不作抵抗	放松	0
	对被动的运动动作抵抗	紧张和肌肉僵硬	1
	对被动的运动动作剧烈抵抗,无法将其完成	非常紧张或僵硬	2
对机械通气顺应性(气管插管患者)	无警报发生,舒适地接受机械通气	耐受呼吸机或机械通气	0
	警报自动停止	咳嗽但是耐受	1
	不同步:机械通气阻断,频繁报警用	对抗呼吸机	2
或发声(拔管后的患者)	正常腔调讲话或不发声	正常腔调讲话或不发声	0
	叹息,呻吟	叹息,呻吟	1
	喊叫,啜泣	喊叫,啜泣	2

3.2.4 问题 7: 常用的阿片类药物有哪些? 其药理特性、使用方法、不良作用如何?

推荐意见 9: ICU 患者非神经性疼痛, 建议首选阿片类药物作为镇痛药物(弱推荐, 低级证据质量)。

阿片类药物为强效中枢镇痛剂之一, 具有镇痛效果强、起效快、可调性强、价格低廉等优点, 是 ICU 患者疼痛管理中的基本药物^[33, 55-56, 58-60]。但不同阿片类药物作用的阿片类受体及药理特点不同, 应根据患者具体情况选择合适的药物。ICU 常用的阿片类药物包括吗啡、芬太尼、瑞芬太尼、舒芬太尼、二氢吗啡酮、美沙酮、布托啡诺以及地佐辛等^[55]。主要药物的特性见表 6。

3.2.4.1 芬太尼: 镇痛效价是吗啡的 100~180 倍, 研究表明芬太尼应用于 ICU 中, 能明显降低疼痛评分^[56]和疼痛发生率^[33]。但由于芬太尼的表现分布容积较大, 反复多次给药易于蓄积, 不宜作为长期镇痛治疗的药物。

3.2.4.2 瑞芬太尼: 为芬太尼类 μ 型阿片受体激动剂, 主要与 α -1-酸性糖蛋白结合, 在组织和血液中被迅速水解, 故起效快, 维持时间短。正因为上述优势, 有研究显示, 瑞芬太尼能明显缩短机械通气时间及 ICU 住院时间^[59, 61-65]。通过整合 6 篇关于瑞芬太尼与芬太尼、吗啡等其他阿片类镇痛药物在 ICU 患者镇痛应用比较的研究^[57, 59, 61, 63-65]进行荟萃分析后发现, 瑞芬太尼能够缩短机械通气时间〔均数差(MD)=-0.42, 95%CI=-0.71~-0.13, $P=0.004$ 〕和 ICU 住院时间(MD=-0.82, 95%CI=-1.48~-0.16, $P=0.01$)。进行 GRADE 分级后证据质量为低级。瑞芬太尼在重症患者镇痛治疗中的应用逐渐增加。

3.2.4.3 舒芬太尼: 镇痛作用很强, 为芬太尼的 5~10 倍。国内一项研究表明舒芬太尼在 ICU 镇痛治疗中能减少镇静药物剂量^[60]。因其镇痛效果明确、起效快、蓄积小、对呼吸抑制作用小^[58], 近年来在 ICU 重症患者中的应用逐渐增多。

阿片类药物的不良反应主要是引起呼吸抑制、血压下降和胃肠蠕动减弱, 在老年人尤其明显。吗啡类衍生物氢吗啡酮^[66]和阿片受体激动剂布托啡诺^[67]可能在降低呼吸抑制及胃肠道不良反应方面具有一定的优势, 但仍需进一步的临床试验验证。

3.2.5 问题 8: 镇痛治疗是否需要联合应用非阿片类镇痛药物?

推荐意见 10: 建议联合应用非阿片类镇痛药物以减少阿片类药物的用量及相关不良反应(弱推荐, 高级证据质量)。

对于非神经性疼痛, 近年来有研究表明氯胺酮^[68-71]、非甾体类抗炎药^[72-74]、奈布啡^[75-76]和加巴喷丁^[77]等非阿片类镇痛药物能有效减轻重症患者的非神经性疼痛^[78]。而对于神经性疼痛, 加巴喷丁^[79-80]和卡马西平^[81]具有

较好的镇痛作用。非阿片类药物可以用来减少阿片类药物的用量和减少阿片类药物的不良反应。目前共有 8 项 RCT 研究涉及在重症患者中应用非阿片类镇痛药物能否减少阿片类镇痛药物的应用^[69-70, 72, 77, 81-84], 整合其中 3 项 RCT^[73, 82-83]的结果进行荟萃分析后发现, 非阿片类镇痛药物的应用能显著减少阿片类药物的用量(MD=-12.68, 95%CI=-15.61~-9.76, $P<0.00001$)。进行 GRADE 分级后证据质量为中级。另外, 目前共有 5 项 RCT 研究涉及在重症患者中应用非阿片类镇痛药物能否减少阿片类镇痛药物相关不良反应^[76, 79, 82-84], 整合这 5 项 RCT 结果进行荟萃分析后同样发现, 应用非阿片类镇痛药物能显著降低恶心、呕吐等阿片类不良反应的发生($OR=0.42$, 95%CI=0.26~0.67, $P=0.0004$), 进行 GRADE 分级后证据质量分别为高级和中级。

3.2.6 问题 9: 实施镇痛后, 还需要对镇痛效果进行密切评估吗?

推荐意见 11: 推荐在实施镇痛后, 要对镇痛效果进行密切评估, 并根据评估结果进一步调整治疗方案(最佳实践声明)。

理论依据: 镇痛治疗的目的在于减轻甚至消除机体器官因为疼痛而导致的过度代偿作功, 保护器官储备功能。因此, 实施镇痛后必须密切监测镇痛效果和循环呼吸等器官功能, 根据镇痛的效果随时调整药物的剂量, 以免镇痛不足或过量。镇痛不足则达不到预期的镇痛效果, 而镇痛过量则可能引起呼吸抑制、抑制胃肠道运动等不良反应, 最终延长机械通气时间、ICU 住院时间, 甚至增加病死率。一般而言, 镇痛效果评估的方法及预期目标: 对于能自主表达的患者应用 NRS 评分, 其目标值为 <4 分; 对于不能表达、运动功能良好、行为可以观察的患者应用 BPS 评分或 CPOT 评分, 其目标值为 BPS <5 分和 CPOT <3 分。

3.3 焦虑和躁动的评估、治疗及监测

3.3.1 问题 10: ICU 患者镇静的深度应如何选择?

推荐意见 12: 建议 ICU 患者根据器官功能状态个体化选择镇静深度, 实施目标指导的镇静策略(弱推荐, 中级证据质量)。

理论依据: 所谓目标指导的镇静策略, 即 ICU 患者根据器官功能状态, 个体化确立镇静程度的目标, 并根据目标连续评估、随时调整治疗方案, 以尽可能使镇静治疗扬利抑弊。

在保证患者器官功能处于适度代偿范围的基础上, 调节镇静药物剂量, 维持患者处于最合适的镇静状态。镇静的深浅程度应根据病情变化和患者器官储备功能程度而调节变化。对于器官功能相对稳定、恢复期的患者, 应给予浅镇静, 以缩短机械通气时间和 ICU 住院时间^[85]。但对处于应激

表 6 阿片类药物的药理学特性

阿片类药物	起效时间	半衰期	负荷剂量	维持剂量	不良反应
芬太尼	1~2 min	2~4 h	0.35~0.50 $\mu\text{g}/\text{kg}$	0.7~10.0 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$	比吗啡更少的低血压; 累积有肝损害
吗啡	5~10 min	3~4 h	2~4 mg	2~30 mg/h	累计用量有肝肾损害; 有一定的组织胺释放
瑞芬太尼	1~3 min	3~10 min	0.5~1.0 $\mu\text{g}/\text{kg}$ iv (>1 min)	0.02~0.15 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$	没有肝肾损害; 如果体重 $>130\%$ 理想体重, 使用理想体重计算
舒芬太尼	1~3 min	784 min 左右	0.2~0.5 $\mu\text{g}/\text{kg}$	0.2~0.3 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$	剂量个体差异性较大, 分布半衰期短, 代谢半衰期长, 长期使用可能延长机械通气时间

急性期、器官功能不稳定的患者,宜给予较深镇静以保护器官功能,这些情况主要包括:①机械通气人机严重不协调;②严重急性呼吸窘迫综合征(ARDS)早期短疗程神经-肌肉阻滞剂、俯卧位通气、肺复张等治疗时作为基础;③严重颅脑损伤有颅内高压;④癫痫持续状态;⑤外科需严格制动者;⑥任何需要应用神经-肌肉阻滞剂治疗的情况,都必须以充分的深度镇痛镇静为基础。

通过检索文献,目前共有 5 篇 RCT 研究比较了采用目标指导镇静与不采用目标指导镇静对 ICU 患者机械通气时间、ICU 住院时间、总住院时间、住院病死率、ICU 病死率、意外拔管率、再插管率和气管切开率等 8 项临床指标的影响^[85-89],荟萃分析显示:目标指导镇静可以缩短总住院时间($MD=-3.67$, $95\%CI=-5.31 \sim -2.03$, $P<0.00001$)和 ICU 住院时间($MD=-1.52$, $95\%CI=-2.57 \sim -0.48$, $P=0.004$),但对机械通气时间、住院病死率和 ICU 病死率无影响;另外,目标指导镇静不增加意外拔管率、再插管率和气管切开率。进行 GRADE 分级后总住院时间和 ICU 住院时间的证据质量为中级。

3.3.2 问题 11: ICU 患者镇静中应常规实施每日镇静中断(DSI)吗?

推荐意见 13: 应根据镇静状态的评估结果随时调整镇静深度,对于深度镇静患者宜实施 DSI(弱推荐,中级证据质量)。

理论依据:DSI 是指在连续性使用镇静药物的过程中,每日进行短时间的停用镇静药物,待患者恢复出现基本的遵嘱反应和神经肌肉动作后再重新给予镇静治疗。具体标准为满足以下 4 项中的 3 项:遵嘱睁眼、眼神追踪、遵嘱握拳、遵嘱动脚趾。DSI 的目的是限制镇静药物的过量使用,通过对患者每日短时间的中断镇静药物输注以减少其体内的镇静药物蓄积,进而缩短机械通气时间,改善临床结局。但近年来关于 DSI 的研究众说纷纭,最初发现 DSI 能改善预后的研究,研究对象多为深镇静的患者,而近些年随着新型镇静药物的推广及临床医生对镇静深度认识的变迁,关于 DSI 的研究则多为阴性结果。对于无需深镇静的患者,更需要强调的是随时调整镇静深度,而不仅仅是 DSI,但对于深镇静的患者,仍需实施 DSI 以减少镇静药物的过量使用。

目前,已经有多项 RCT 评价了实施 DSI 的效果,但其结果各异。通过文献检索,本指南修订小组共纳入 9 篇 RCT 评价 DSI 在 ICU 患者中对机械通气时间、ICU 住院时间、

住院总时间、ICU 病死率等影响的文献^[90-98]。其中 7 篇文献^[90-91, 93-95, 97-98]结局指标包含机械通气时间,进行荟萃分析后发现,DSI 不能缩短 ICU 患者的机械通气时间($MD=-0.30$, $95\%CI=-1.25 \sim 0.65$, $P=0.54$)。有部分文献采用了 28 d 内无机械通气时间作为结局指标^[92-93, 96-97],荟萃分析显示,DSI 不能延长 ICU 患者 28 d 内无机械通气时间($MD=-0.22$, $95\%CI=-4.24 \sim 3.80$, $P=0.91$)。另外荟萃分析还显示,DSI 对 ICU 患者的 ICU 住院时间^[90-98]无影响($MD=-0.94$, $95\%CI=-2.91 \sim 1.03$, $P=0.35$),对总住院时间^[90-98]无影响($MD=-1.35$, $95\%CI=-3.26 \sim 5.96$, $P=0.57$),对 ICU 病死率^[90-94, 97-98]无影响[相对危险度(RR)=0.99, $95\%CI=0.77 \sim 1.27$, $P=0.93$],对意外拔管率^[91-93, 95-96, 98]无影响($RR=1.17$, $95\%CI=0.71 \sim 1.91$, $P=0.55$),对拔管后 48 h 内再插管率^[92, 95-96, 98]无影响($RR=0.94$, $95\%CI=0.68 \sim 1.31$, $P=0.71$),但是,DSI 能降低 ICU 患者的气管切开率^[91-93, 95-96, 98]($RR=0.74$, $95\%CI=0.58 \sim 0.93$, $P=0.01$)。进行 GRADE 分级后机械通气时间和气管切开率的证据质量为中级,其余为低级。

3.3.3 问题 12: ICU 患者镇静药物应如何选择?

推荐意见 14: 苯二氮草类和丙泊酚仍然应作为目前镇静治疗的基本药物(最佳实践声明)。

右美托咪定通过拮抗中枢及外周儿茶酚胺的作用,兼具轻度镇静和镇痛效果,与其他镇痛镇静药物具有协同作用,可以缩短机械通气时间和 ICU 住院时间(弱推荐,低级证据质量)。

理论依据:目前 ICU 临床上常用的镇静药物有苯二氮草类、丙泊酚和右美托咪定,具体药理机制、用法用量及不良反应见表 7。

3.3.3.1 苯二氮草类药物: 苯二氮草类药物是中枢神经系统 γ 氨基丁酸(GABA)受体激动剂,具有抗焦虑、遗忘、镇静、催眠和抗惊厥作用。ICU 最常用的苯二氮草类药物为咪唑安定,其作为该类物质中相对水溶性最强的物质,具有起效快、持续时间相对短、血浆清除率较高的特点。苯二氮草类药物是 ICU 患者重要的镇静药物之一,特别是用于焦虑、癫痫发作以及酒精戒断治疗。并且苯二氮草类药物在深度镇静、不注意、不记忆(遗忘)或联合其他镇痛镇静药使用以降低彼此不良反应方面仍具有很重要的作用^[4]。

但近年来的研究表明,苯二氮草类药物容易引起蓄积、代谢较慢、增加镇静深度,从而进一步延长机械通气时间及

表 7 常用镇静药物特点

镇静药物	首剂后起效时间	清除半衰期	首次剂量	维持剂量	不良反应	备注
咪唑安定	2~5 min	3~11 h	0.01~0.05 mg/kg	0.02~0.10 mg·kg ⁻¹ ·h ⁻¹	呼吸抑制、低血压、可能导致谵妄	对循环影响小;酒精、药物戒断反应的一线选择
地西泮	2~5 min	20~120 h	5~10 mg	0.03~0.10 mg/kg	呼吸抑制、低血压	半衰期过长,不容易实现“浅镇静”策略;不推荐作为镇静一线选择
丙泊酚	1~2 min	快速清除 34~64 min, 缓慢清除 184~382 min	5 μg·kg ⁻¹ ·min ⁻¹	1~4 mg·kg ⁻¹ ·h ⁻¹	低血压、呼吸抑制、高甘油三酯、输注点疼痛、丙泊酚输注综合征	儿童镇静时要特别注意丙泊酚输注综合征;高甘油三酯血症患者慎用;可以降低颅内压;谵妄发生率较低
右美托咪定	5~10 min	1.8~3.1 h	1 μg/kg, 超过 10 min 缓慢输注	0.2~0.7 μg·kg ⁻¹ ·min ⁻¹	心动过缓、低血压	可以预防、治疗谵妄;对循环影响小

住院时间。通过文献检索及筛查,纳入了 10 篇 RCT^[99-108] 的 11 项研究(其中郭丰等^[107] 包含 2 项研究)。11 项研究均比较了苯二氮草类药物与非苯二氮草类药物对 ICU 住院时间的影响,进行荟萃分析后显示,苯二氮草类药物会明显延长 ICU 住院时间($MD=2.10$, $95\%CI=3.17 \sim 1.03$, $P=0.0001$)和机械通气时间^[99-104, 106-108] ($MD=1.60$, $95\%CI=2.35 \sim 0.85$, $P<0.0001$)。相对于苯二氮草类药物,非苯二氮草类药物可以降低谵妄的发生率^[101-104, 108] ($RR=0.67$, $95\%CI=0.49 \sim 0.93$, $P=0.02$),但对病死率^[99-100, 103-104, 106-107] 并无影响($RR=1.03$, $95\%CI=0.85 \sim 1.25$, $P=0.77$)。进行 GRADE 分级后证据质量级别为低级。

3.3.3.2 丙泊酚: 丙泊酚也是 ICU 常用的镇静药物之一,其特点是起效快、作用时间短、撤药后能快速清醒、且镇静深度呈剂量依赖性,丙泊酚亦可产生遗忘作用和抗惊厥作用。另外,丙泊酚具有减少脑血流、降低颅内压(ICP)和脑氧代谢率(CMRO₂)的作用,用于颅脑损伤患者的镇静可减少 ICP 的升高。丙泊酚单次注射时可出现暂时性呼吸抑制和血压下降、心动过缓,尤见于心脏储备功能差、低血容量的患者。其他的不良反应包括高甘油三酯血症、急性胰腺炎和横纹肌损伤。丙泊酚使用时可出现外周静脉注射痛,因此临床多采用持续缓慢静脉输注方式。另外,部分患者长期使用后可能出现诱导耐药。

因巨大的分布容积所致的短效性,丙泊酚较苯二氮草类药物能改善患者 ICU 住院时间等指标,共纳入了 4 篇 RCT 比较了应用丙泊酚与苯二氮草类药物对 ICU 住院时间的影响^[99, 105-107],进行荟萃分析后发现,应用丙泊酚能缩短 ICU 住院时间($MD=-3.33$, $95\%CI=-5.26 \sim -1.41$, $P=0.0007$)。其中 3 篇比较了应用丙泊酚与苯二氮草类药物对机械通气时间和短期病死率的影响^[99, 106-107],进行荟萃分析后发现,与苯二氮草类药物相比,应用丙泊酚能缩短机械通气时间($MD=-2.57$, $95\%CI=-3.65 \sim -1.49$, $P<0.0001$),但对短期病死率无影响($RR=0.94$, $95\%CI=0.52 \sim 1.68$, $P=0.83$)。进行 GRADE 分级后,机械通气时间的证据质量级别为中级,其余 2 项指标为低级。

3.3.3.3 右美托咪定: 右美托咪定是选择性 α_2 受体激动剂,通过抑制蓝斑核去甲肾上腺素释放和竞争性拮抗 α_2 受体,起到减轻交感兴奋风暴、冷静、抗焦虑和轻度的镇痛镇静作用,没有抗惊厥作用。由于不作用于中脑网状上行系统和 GABA 受体,使用右美托咪定镇静的患者更容易唤醒,呼吸抑制较少。右美托咪定一般在给药 15 min 内起效,镇静高峰出现在静脉给药后 1 h 内,能快速分布于周围组织并被肝脏代谢。对于肝功能正常的患者来说,清除半衰期大约为 3 h。重度肝功能障碍的患者,会延长右美托咪定的清除,应适当降低剂量。右美托咪定最常见的不良反应是低血压和心动过缓,静脉负荷剂量过快给予可引起血压及心率波动,故在 ICU 给予负荷剂量时一定要注速,必要时可适当延长输注时间。另外,右美托咪定兼具镇痛作用,可减少阿片类药物的需求。

目前,共有 23 篇针对非心脏手术 ICU 患者的 RCT 研究^[90, 100, 102-104, 109-126],分析右美托咪定是否可缩短 ICU 患者的机械通气时间和 ICU 住院时间、降低谵妄发生率、增加心动过缓及低血压事件的发生。整合这些 RCT 结果进行荟萃分析后发现,相比苯二氮草类和丙泊酚等镇静药物,应用右美

托咪定可以明显缩短 ICU 住院时间^[100, 102-104, 112-113, 115-120, 126] ($MD=-2.17$, $95\%CI=-3.06 \sim -1.27$, $P<0.0001$)和机械通气时间^[100, 102, 104, 110, 113-114, 117, 121, 122-126] ($MD=-6.08$, $95\%CI=-9.86 \sim -2.30$, $P=0.002$);但是应用右美托咪定确实会增加心动过缓^[100, 102-104, 109, 116-117, 119, 122, 126] ($RR=2.02$, $95\%CI=1.64 \sim 2.49$, $P<0.0001$)及低血压^[100, 102, 104, 109, 117, 123, 126] ($RR=1.48$, $95\%CI=1.10 \sim 1.98$, $P=0.009$)事件的发生。进行 GRADE 分级后证据质量级别为低级。

另外,我们还整合了 5 篇成人心脏术后 ICU 患者的 RCT 研究^[127-131],进行荟萃分析后显示,相比丙泊酚和苯二氮草类药物,应用右美托咪定在机械通气时间($MD=-0.53$, $95\%CI=-1.74 \sim 0.68$, $P=0.39$)和 ICU 住院时间($MD=-0.36$, $95\%CI=-0.98 \sim 0.26$, $P=0.26$)的比较上差异并无统计学意义。进行 GRADE 分级后机械通气时间的证据质量级别为中级,ICU 住院时间为低级。

3.3.4 问题 13: ICU 患者中神经-肌肉阻滞剂应用指征与时机是什么?

推荐意见 15: 所有神经-肌肉阻滞剂必须在充分镇痛镇静治疗的基础上加以使用(最佳实践声明)。

推荐意见 16: 对于重度 ARDS 早期患者,在充分镇痛镇静治疗的基础上可以考虑使用神经-肌肉阻滞剂(弱推荐,中级证据质量)。

理论依据: 清醒肌松是一种等同于麻醉时“术中知晓”的极度危险状态,它可以使患者出现严重交感风暴、应激状态和濒死感,显著加大循环呼吸等器官的代谢负担。因此神经-肌肉阻滞剂必须在充分镇痛镇静的前提下应用。目前主要应用在某些特定的危重疾病状态,例如:重度 ARDS 早期、哮喘持续状态、癫痫持续状态、严重惊厥以及破伤风等肌肉强烈痉挛的病症。目前关于重度 ARDS 早期神经-肌肉阻滞剂应用的证据主要来自法国的同一个研究团队发表的 3 项 RCT^[132-134],Neto 等^[135] 对上述 3 项 RCT 数据整合进行荟萃分析,结果显示,与安慰剂相比,早期短时间(48 h 内)应用神经-肌肉阻滞剂能显著降低中重度 ARDS 患者的 ICU 病死率($RR=0.71$, $95\%CI=0.55 \sim 0.90$, $P=0.005$)、28 d 病死率($RR=0.68$, $95\%CI=0.51 \sim 0.92$, $P=0.01$)和气压伤的风险($RR=0.45$, $95\%CI=0.22, 0.92$, $P=0.03$),且不增加 ICU 获得性肌无力(ICUAW)的发生风险($RR=1.13$, $95\%CI=0.76 \sim 1.67$, $P=0.54$)。进行 GRADE 分级之后,ICU 病死率的证据质量级别为中级,其余为低级。

另外,鉴于神经-肌肉阻滞剂易导致患者神经肌肉耦联损伤和肌无力、痰液引流障碍及肺不张等不良反应^[136-138],故临床上应用神经-肌肉阻滞剂仍需慎重。

3.3.5 问题 14: 实施镇静后,需要对镇静深度进行密切监测吗?

推荐意见 17: 推荐实施镇静后要对镇静深度进行密切监测,Richmond 躁动-镇静评分(RASS)和镇静-躁动评分(SAS)是常用可靠的镇静评估工具(强推荐,中级证据质量)。

理论依据: 镇痛镇静治疗的目的是在维持机体基本灌注氧合的基础上,尽可能保护器官储备功能,减轻器官过度代偿的氧耗作功。同时,保持危重症患者处于最舒适和安全的镇静状态是 ICU 镇静治疗的重要目标之一。因此,需要定时评估患者的镇静程度以便于调整镇静药物及其剂量以达到预期目标。目前临床常用的主观镇静评分法有 RASS

(表8)、Ramsay评分、SAS(表9),客观评估方法有脑电双频指数(BIS)、肌肉活动评分法(MAAS)等,但目前没有证据证明客观评估方法对于非肌松治疗的患者有益。

表8 Richmond躁动-镇静评分(RASS评分)

评分(分)	分级	描述
4	有攻击性	非常有攻击性,暴力倾向,对医务人员造成危险
3	非常躁动	非常躁动,拔出各种导管
2	躁动	焦虑 身体激烈移动,无法配合呼吸机
1	不安焦虑	焦虑紧张,但身体活动不剧烈
0	清醒平静	清醒自然状态
-1	昏昏欲睡	没有完全清醒,声音刺激后有眼神接触,可保持清醒超过10s
-2	轻度镇静	声音刺激后能清醒,有眼神接触,<10s
-3	中度镇静	声音刺激后能睁眼,但无眼神接触
-4	深度镇静	声音刺激后无反应,但疼痛刺激后能睁眼或运动
-5	不可唤醒	对声音及疼痛刺激均无反应

表9 镇静-躁动评分(SAS评分)

评分(分)	分级	描述
7	危险躁动	拉拽气管内插管,试图拔除各种导管,翻越栏杆,攻击医护人员,在床上辗转挣扎
6	非常躁动	需要保护性束缚并反复语言,提示劝阻咬气管插管
5	躁动	焦虑或身体躁动,经言语提示劝阻可安静
4	安静合作	容易唤醒,服从指令
3	镇静	嗜睡,语言刺激或轻轻摇动可唤醒并能服从简单指令,但又迅速入睡
2	非常镇静	对躯体刺激有反应,不能交流及服从指令,有自主运动
1	不能唤醒	对恶性刺激无或仅有轻微反应,不能交流及服从指令

理想的镇静评分法应符合易于评估和记录,有助于镇静程度的准确判断并指导治疗,即:简单、准确、相对客观易重复。目前临床应用的多种镇静评分系统中,RASS和SAS评分法因其简单、易操作、对镇静目标具有良好的指示性而被广泛应用于临床,并能指导镇静药物剂量的调整^[139-140]。2013年的一篇综述^[141]共纳入36篇文章,包含了11种镇静评分法,该研究制定了1项0~20分的评分系统(15~20分为非常好,12~14.9分为中等,10~11.9分为差,低于10分为非常差),囊括了项目选择和内容验证、可靠性、真实性、可行性及对患者实施结果的相关性和影响等5个方面的内容,来评估这11种评分法的有效性及其可行性。结果显示,对于ICU患者,众多镇静评分法中RASS和SAS是评估患者镇静深度及镇静质量最有效和可靠的方法(RASS:19.5分,SAS:19分)。另一项研究对比了格拉斯哥昏迷评分(GCS)、Ramsay、RASS、SAS 4种评分方法,结果显示,RASS与SAS的相关性最好,并且便于医护人员床旁评估,这两种评估方法可用于日常临床评估、指导镇静治疗,并可避免过度使用镇静药物、减少镇静药物相关并发症^[142]。此外,SAS和RASS评分还有助于对谵妄的筛查与评估,且相关性良好^[143]。

建议实施镇静后,宜连续评估镇静深度,调整治疗,趋近目标。浅镇静时,镇静深度的目标值为RASS -2~-1分,SAS 3~4分;较深镇静时,镇静深度的目标值为RASS -3~-4分,SAS 2分;当合并应用神经-肌肉阻滞剂时,镇静深度的目

标值应为RASS -5分,SAS 1分。

推荐意见 18:对于联合使用神经-肌肉阻滞剂患者的镇静程度评估,建议使用客观脑功能监测(弱推荐,低级证据质量)。

理论依据:接受神经-肌肉阻滞剂治疗的患者,因其达到一定肌松深度后将失去神经肌肉运动反应,难以通过主观镇静评分对其进行镇静深度的评估,此时,客观脑功能监测将是一种补充措施^[144]。研究表明,包括BIS、麻醉趋势指数(NI)、状态熵(SE)、患者状态指数(PSI)等在内的多种原来在麻醉中应用的客观脑功能监测,可作为ICU患者镇静评估的客观标准^[145-159]。也有研究提出客观脑功能监测设备增加了费用和人力消耗,与主观评分系统相比,在评价镇静深度方面,客观评价方法并无显著益处^[160-164]。但对于ICU肌松患者存在镇静不全的风险、而肌松患者主观镇静评分无法获得时,BIS等监测可作为一种补充手段帮助识别这些问题^[153,165]。

3.4 谵妄及其防治:谵妄是多种原因引起的一过性的意识混乱状态伴有认知功能障碍。短时间内出现意识障碍和认知能力改变是谵妄的临床特征,意识清晰度下降或觉醒程度降低是诊断的关键。ICU患者因焦虑、麻醉、代谢异常、缺氧、循环不稳定或神经系统病变等原因,可以出现谵妄症状,且长时间置身于陌生而嘈杂的ICU环境会加重谵妄的症状。谵妄分为兴奋型、缄默型和混合型,缄默型因不易被识别往往预后更差。

3.4.1 问题 15:谵妄是ICU患者预后不佳的危险因素吗?

推荐意见 19:谵妄是ICU患者预后不佳的危险因素,推荐密切关注并早期发现ICU患者的谵妄(强推荐,中级证据质量)。

理论依据:近年来的研究表明,老年谵妄患者的住院时间明显延长,每日住院费用及病死率均显著增加^[166-169]。关于谵妄对ICU患者的影响共筛选出10项队列研究^[166-175],进行荟萃分析后显示,谵妄可显著增加ICU患者的病死率($OR=3.42$, $95\%CI=2.45\sim4.76$, $P<0.00001$),延长ICU住院时间($MD=2.66$, $95\%CI=1.83\sim2.69$, $P<0.000001$)。进行GRADE分级后病死率的证据质量级别为低级,ICU住院时间为中级。

3.4.2 问题 16:谵妄的相关因素包括哪些?

关于谵妄的危险因素共纳入中、英文文献96篇^[176-271],均为队列和观察性研究,对其中118个变量进行了荟萃分析,结果显示,谵妄相关危险因素包括高龄、慢性阻塞性肺疾病病史、高血压病史、高血糖及糖尿病病史、心力衰竭、抑郁病史、谵妄病史、脑血管病史、酗酒病史、脓毒症、肾功能不全、美国纽约心脏协会(ASA)心功能分级 $\geq$ Ⅲ级、急诊手术、苯二氮草类药物等镇静药物应用、阿片类药物应用、皮质醇水平升高、低氧血症、机械通气、贫血、电解质紊乱、认知损伤、体外循环、束缚及心律失常等。另外,2015年Zaal等^[272]的荟萃分析纳入了33项研究,最终总结出11个谵妄的独立危险因素,包括:年龄、痴呆、高血压、急诊手术、创伤、急性生理学及慢性健康状况评分Ⅱ(APACHE Ⅱ)评分、机械通气、代谢性酸中毒、谵妄病史、昏迷、多器官功能衰竭,而右美托咪定应用为谵妄的保护因素。

3.4.3 问题 17:哪些ICU患者需要进行谵妄评估?如何选择评估工具?

推荐意见 20: 建议对于 RASS ≥ -2 分、且具有谵妄相关危险因素的 ICU 患者应常规进行谵妄评估。建议使用 ICU 患者意识模糊评估法 (CAM-ICU) 或重症监护谵妄筛查量表 (ICDSC) 作为 ICU 患者的谵妄评估工具 (弱推荐, 低级证据质量)。

理论依据: 谵妄在 ICU 中, 尤其是机械通气患者中有较高的发生率^[273-274]。ICU 工作人员容易忽视非躁动型谵妄, 而正如前所述, 谵妄是 ICU 患者预后不佳的独立危险因素, 因此监测谵妄具有重要意义。而对于深度镇静的患者 (RASS ≤ -3 分), 其无法与工作人员进行有效的交流和配合, 从而无法完成评估。综上所述, 对于 RASS ≥ -2 分、具有谵妄相关危险因素的 ICU 患者应常规进行谵妄监测, 从而达到早期预警、早期防治的效果。

谵妄的诊断主要依据临床检查及病史。2012 年 Gusmao-Flores 等^[275] 的荟萃分析共纳入了 9 篇文献^[175, 276-283], 结果显示, CAM-ICU (表 10) 和 ICDSC 具有较高的敏感性及特异性, 为可靠的监测方法。2013 年 Shi 等^[284] 的荟萃分析纳入了 22 项研究, 评估 CAM 和 CAM-ICU 对谵妄的评估效果, 结果发现两者均具有较高的敏感性和特异性。

表 10 ICU 患者意识模糊评估法 (CAM-ICU) 谵妄评分表

临床特征	评价指标
1. 精神状态突然改变或波动	任一问题回答“是”, 该特征为阳性 • 与基础水平相比患者的精神状态是否有突然变化? • 患者的精神状态 (如 RASS、GCS 评分或以往的谵妄评估) 在过去的 24 h 内有无起伏波动?
2. 注意力不集中	注意力筛查试验, 错误 ≥ 3 个该特征为阳性 数字测验: “我读 10 个数字, 你听到 1 时就握我的手。” 用正常语调读数: 8、1、7、5、1、4、1、1、3、6。 • 在读“1”时患者未握手为错误。 • 在读“1”以外的数字时患者握手也为错误。
3. 意识水平变化	完全清醒以外的任何意识状态 (即 RASS $\neq 0$), 该特征为阳性 • 正常——对周围环境完全知道, 并且有适当的互动; • 警惕——过度的警戒状态; • 嗜睡; • 昏睡; • 昏迷。
4. 思维无序	错误 ≥ 2 个, 该特征为阳性 A 组问题: B 组问题: ① 石头会飘在水面上吗? ① 树叶会飘在水面上吗? ② 海里有鱼吗? ② 海里有大象吗? ③ 1 斤比 2 斤重吗? ③ 2 斤比 1 斤重吗? ④ 你能用锤子砸钉子吗? ④ 你能用锤子砍木头吗? ⑤ 指令: • 对患者说: “举起这么多手指” (在患者面前举起 2 根手指), “现在用另一只手做同样的事” (不重复手指的数目)。 • 如果患者不能移动手臂, 要求患者“比这个多举一根手指”。
诊断	临床特征 1+2+3 或 4, 可诊断患者存在谵妄

注: ICU 为重症医学科, RASS 为 Richmond 躁动-镇静评分, GCS 为格拉斯哥昏迷评分

3.4.4 问题 18: 如何预防 ICU 谵妄?

虽然导致谵妄的诱因很多, 其具体机制仍尚未完全清楚, 但谵妄所表现的意识与认知功能损伤, 一定有脑组织损伤

作为物质基础。因此, 预防和及时纠正各种可能导致脑组织灌注氧合损害的因素非常重要。如前所述, 谵妄的危险因素包括脓毒症、疾病严重程度、低灌注、机械通气等, 因此积极治疗原发病、尽量减少引起谵妄的诱发因素、改善组织和脑灌注, 将有利于谵妄的预防。

推荐意见 21: 推荐通过改善睡眠及早期活动等措施减少 ICU 患者谵妄的发生 (强推荐, 中级证据质量)。

理论依据: 睡眠剥夺是 ICU 患者发生谵妄的因素之一, 因此改善睡眠的时间及质量有助于降低谵妄的发生率。目前有 3 项 RCT 研究了耳塞对谵妄发生率的影响^[285-287], 进行荟萃分析后发现, 耳塞的使用可降低谵妄的发生率 ($RR=0.56$, $95\%CI=0.38 \sim 0.81$, $P=0.002$)。进行 GRADE 分级后证据质量级别为中级。另外, 集中进行护理及医疗干预等措施亦可以减少谵妄的发生, 但证据强度较低^[26]。Schweickert^[288] 及 Needham^[289] 等进行 RCT 研究还表明, 对 ICU 患者进行早期康复锻炼能降低谵妄的发生率及持续时间。

推荐意见 22: 右美托咪定可以减少 ICU 谵妄的发生 (弱推荐, 中级证据质量)。

理论依据: 对于非心脏术后 ICU 重症患者, 共有 9 项 RCT 评价了右美托咪定对谵妄发生率的影响^[100, 102-104, 113, 115, 121, 123, 126], 进行荟萃分析后发现, 右美托咪定可以降低谵妄的发生率 ($RR=0.64$, $95\%CI=0.46 \sim 0.88$, $P=0.006$)。进行 GRADE 分级后证据级别为低级。另外, 对于心脏术后患者的影响, 共纳入了 3 项 RCT^[128, 130-131], 荟萃分析后发现, 右美托咪定同样能明显降低谵妄的发生率 ($RR=0.31$, $95\%CI=0.13 \sim 0.76$, $P=0.01$)。进行 GRADE 分级后证据级别为中级。目前关于右美托咪定对谵妄治疗效果的研究较少, 2016 年 Reade 等^[119] 的 RCT 研究显示, 对于躁动型谵妄患者, 右美托咪定能缩短谵妄的持续时间。

还有文献显示, 褪黑素也具有减少 ICU 谵妄发生的作用。褪黑素是一种调整睡眠节律的激素, 外源性应用可以改善睡眠质量。目前有 2 项 RCT 评价了褪黑素对 ICU 重症患者谵妄发生率的影响^[290-291], 进行荟萃分析后发现, 口服褪黑素可以降低谵妄的发生率 ($RR=0.20$, $95\%CI=0.09 \sim 0.47$, $P=0.0002$)。进行 GRADE 分级后证据级别为中级。

推荐意见 23: 不建议应用氟哌啶醇、他汀类药物、多奈哌齐和抗精神病药物来预防及治疗谵妄 (弱推荐, 中级证据质量)。

理论依据: 有 8 项 RCT 研究分析了在重症患者中应用氟哌啶醇能否有效防治谵妄^[115, 292-298], 整合这 8 项 RCT 结果进行荟萃分析显示, 应用氟哌啶醇并不能降低谵妄发生率 ($RR=0.7$, $95\%CI=0.49 \sim 1.04$, $P=0.08$), 同时对谵妄持续时间 ($MD=-0.05$, $95\%CI=-0.75 \sim 0.66$, $P=0.9$) 也无影响。进行 GRADE 分级后对谵妄发生率的证据质量级别为低级, 对谵妄持续时间的证据质量级别为中级。

他汀类药物对谵妄预防作用的文献共 3 篇^[299-301], 2 篇前瞻性队列研究, 1 篇前瞻性研究, 荟萃分析后同样发现他汀类药物不能降低谵妄的发生率 ($OR=0.89$, $95\%CI=0.69 \sim 1.16$, $P=0.14$), 进行 GRADE 分级后对谵妄发生率的证据质量级别为低级。

多奈哌齐属六氧吡啶类氧化物, 是第二代特异的不可逆性中枢乙酰胆碱酯酶 (AChE) 抑制剂, 对外周 AChE 作用很小。本品通过抑制 AChE 活性, 使突触间隙乙酰胆碱 (ACh) 的分

关于抗精神病药物对谵妄的预防及治疗作用, Girard 等^[295]的 RCT 研究显示, 齐拉西酮不能降低谵妄的持续时间及病死率。Weaver 等^[304]的回顾性研究同样发现抗精神病药物不能减少谵妄的持续时间。但也有回顾性研究提出喹硫平能减少谵妄的持续时间^[305]。Neufeld 等^[306]的荟萃分析纳入了 19 项临床研究, 进行荟萃分析后指出抗精神病药物不能降低谵妄的发生率或持续时间。

问题 20: 镇痛镇静治疗可能会带来哪些并发症?

积极处理原发病、尽量减少或避免引起肌无力的药物、早期康复训练、充足的营养支持等均有助于肌无力的预防及恢复。

3.5.5 其他:镇痛镇静后患者自主活动减少,加之疼痛感觉变弱,会导致患者较长时间不改变体位,继而容易造成压疮、深静脉血栓等并发症,因此对于镇痛镇静的重症患者应采取加强体疗、变换体位、早期活动等方式以减少上述并发症的发生。

```

graph TD
    A[改善ICU患者舒适性的非药物措施：  
减少声光刺激、改善睡眠、早期活动] --> B{疼痛评估  
基础状态}
    B --> C{可交流：NRS<4  
不可交流：BPS<5分、  
CPOT<3分}
    C -- 是 --> D{镇静评估  
基础状态}
    C -- 否 --> E[镇痛治疗：  
阿片类/非阿片类药物]
    D -- 有 --> F[RASS：-3~-4分  
SAS：2分]
    D -- 无 --> G[RASS：-2~1分  
SAS：3~4分]
    F --> H[是]
    F --> I[否]
    G --> H
    G --> I
    H --> J[非药物措施]
    I --> K[镇静治疗：  
非苯二氮草类/苯二氮草类]
    K --> L[半小时内心镇静评估  
密切监测镇静程度]
    L --> M[深镇静患者需每日镇静中断]
    M --> N[意识状态突然改变]
    E --> O[半小时内心镇痛评估  
密切监测镇痛程度]
    O --> N
    N --> P{谵妄评估  
Qd-bid}
    P --> Q{CMA-ICU阳性  
或ICDSC>4分}
    Q -- 是 --> R[去除谵妄危险因素  
避免苯二氮草类药物  
右美托咪定]
    Q -- 否 --> S[非药物措施]
  
```

注:ICU 为重症医学科,NRS 为数字评分表,BPS 为行为疼痛量表,COPT 为重症监护疼痛观察量表,RASS 为 Richmond 躁动-镇静评分,SAS 为镇静-躁动评分,CMA-ICU 为 ICU 患者意识模糊评估法,ICDSC 为重症监护谵妄筛查量表

图2 镇痛镇静实施流程

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