

## 神经重症的血流动力学治疗要点

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**摘要:**神经重症血流动力学治疗的目的在于改善脑功能,其核心为优化脑灌注,终止原发或继发脑损伤。需关注以下要点:以基于近红外光谱技术测量的脑氧水平间接判断脑灌注的充足性,作为调整脑血流的启动点,进而优化颅脑血流状态。经颅多普勒超声是目前床旁评估脑血流、脑血管阻力的关键手段,并可通过测量视神经鞘警示颅内压增高。血流动力学目标包括血压、心输出量、氧输送等需要更高层次的管理以促进脑功能的恢复。脑功能监测指标的含义是双面的,过低水平的脑活动提示脑灌注不足,而异常活跃的脑电活动则提示过高的脑氧耗。脑氧、脑血流、脑功能为整体“三位一体”的颅脑血流动力学三角是神经重症患者管理的关键。

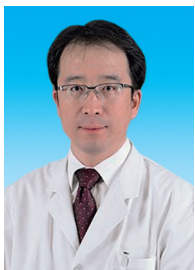
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**Key-points of cerebral hemodynamic therapy in neuro critical cases.** LIU Yang, CHEN Huan, LIU Da-wei, WANG Xiao-ting, Chinese Critical Hypothermia-Sedation Therapy Study Group. Department of Critical Care Medicine, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing 100730, China  
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**Abstract:** Cerebral hemodynamic therapy has the ultimate goal of brain function improvements. The therapeutic endpoint is to optimize cerebral perfusion in order to stop primary or secondary injury and promote brain function recovery. Clinically, cerebral perfusion can be indirectly measured by brain oxygenation instruments including Near-infrared spectroscopy. Cerebral blood flow optimization should be the core target of cerebral hemodynamic therapy. Transcranial Color-Coded Duplex and Transcranial Doppler sonography are essential techniques to quantify cerebral blood flow, evaluate vascular resistance, and alert for increased intracranial pressure non-invasively by bedside measurements of optic nerve sheath diameter. Hemodynamic targets including blood pressure, cardiac output, and oxygen delivery require extra considerations beyond traditional hemodynamic therapy in order to promote cerebral function. Brain electricity monitoring should be read with caution where low brain activity might indicate insufficient cerebral perfusion, whereas overactive brain function shows high oxygen consumption. In clinical practice, the integrated monitoring of cerebral blood flow, brain oxygenation and brain function would improve the management of neurocritical patients.

**Keywords:** cerebral hemodynamic therapy; neurocritical cases; cerebral perfusion; brain oxygenation



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近年来,有关血流动力学治疗的临床与基础研究进展迅速,相较于传统的血流动力学监测,目前的重症血流动力学治疗更加强调其“治疗”理念。脑作为人体最重要的器官之一,需要额外的关注。神经重症,既包括原发神经系统重症损伤,也囊括其他重症疾患延伸至神经系统的继发改变,包括脑血管事件、谵妄、短期或长期认知损伤、意识障碍等,在重症监护病房(ICU)中常见,与重症患者的不良预后密切相关。因此,所有ICU都应重视神经重症血流动力学治疗,需贯穿于重症患者的诊疗始

终,包括重大手术后、脓毒症和体外膜氧合(ECMO)辅助的患者等。

### 1 在ICU中常规以脑氧监测脑灌注的充足性

脑细胞正常工作需要的氧是通过颅脑血流输送而来,脑氧饱和度是判断脑血流充足性的重要指标,由氧供及脑氧耗量共同决定。只有脑组织氧输送和氧消耗平衡协同,才能达到合适的局部组织氧饱和度状态。评估脑氧有三种方法:(1)颈静脉球氧饱和度  $S_{jv}O_2$ ; (2)颅内导管直接测得脑组织氧分压 ( $P_{bt}O_2$ ); (3)基于近红外光谱技术(NIRS)的局部脑氧饱和度 ( $rScO_2$ )或脑组织氧合指数(TOI)。

我们推荐在重症患者入住ICU早期开始监测脑氧水平。有多项研究结果支持其临床价值。首先,脑氧可警示脑组织氧合不足。 $P_{bt}O_2$ 导向( $P_{bt}O_2 > 20$  mmHg)的治疗策略给颅脑创伤(TBI)患者带来长期获益<sup>[1]</sup>。对于重型TBI患者,基于颅内压(ICP)和脑氧联合监测的治疗流程优于仅关注ICP的治疗<sup>[2]</sup>。然而, $P_{bt}O_2$ 测量创伤性较强,极少用于非TBI患者。 $S_{jv}O_2$ 正常值为55%~75%,多研究支持 $S_{jv}O_2$ 目标值应维持在50%以上,当 $S_{jv}O_2$ 低于目标值时提示患者存在相对氧供障碍,预后不佳<sup>[3]</sup>。NIRS监测无创,可床旁操作,与 $S_{jv}O_2$ 一致性较好<sup>[4]</sup>,在ICU应用潜力最高。重症患者入室24 h内脑氧水平过低可增加谵妄发生风险<sup>[5]</sup>。近期一项系统性综述中,四项研究探讨了脑氧饱和度与重症患者(脓毒症或呼吸衰竭)的神经系统结局的关系,提示 $rScO_2$ 较低者更容易发生谵妄<sup>[6]</sup>。急性肝衰竭患者的异常 $S_{jv}O_2$ 水平及 $S_{jv}O_2$ 变异性与肝性脑病的发生密切相关<sup>[7]</sup>。NIRS监测还可以发现子痫患者的脑氧合异常,而硫酸镁输注可以促进脑氧饱和度的恢复<sup>[8]</sup>。静脉动脉体外膜肺氧合(VA-ECMO)辅助的患者若最初1周内 $rScO_2$ 水平低于58%(右)或57%(左),则28天内死亡风险更高<sup>[9]</sup>。其次,NIRS可早期识别脑血流过灌注。研究表明NIRS监测可在ICP升高之前发现过灌注,避免继发性脑缺血发生<sup>[10]</sup>。

保证大循环氧输送是保证脑氧充足性的前提。心外术后患者和脓毒症休克患者的中心静脉氧饱和度( $ScvO_2$ )和 $rScO_2$ 均显著正相关<sup>[11]</sup>。TBI患者 $ScvO_2$ 低于65%是死亡率增加的危险因素<sup>[12]</sup>。必要的氧疗、俯卧位治疗<sup>[13]</sup>有助于维持脑氧。

### 2 优化脑血流是重症颅脑血流动力学治疗的核心

脑自身几乎没有代谢储备,需脑血流持续输送氧与营养,故优化脑血流是颅脑血流动力学治疗的基础,保证恰当的脑血流量是关键。但评估脑血流量的手段通常是有创的或需要大型医疗设备,难以在ICU实现。临床当中常通过测量脑血流速(FV)来间接反映血流量,经颅多普勒超声(TCD)是主要方法<sup>[14]</sup>。大脑中动脉(MCA)的M1段流经同侧大脑半球血流的40%,是最常用的TCD监测位点<sup>[14]</sup>。从同一位置可持续监测脑血流速,判断血流方向。通过多普勒波形可直接测得大脑动脉收缩期峰流速和舒张期末流速,计算获得脑血流指数(CBFi)、平均流速(MV)、阻力指数(RI)和搏动指数(PI)等。血流流速减低提示缺血状态。TCD频谱形态同样有临床意义,在脑死亡发展过程中,可见震荡波、钉子波,最终无信号。除此之外,FV也与血管病理状态有关,在解读FV异常值时需额外注意:FV增快提示脑充血状态或脑血管痉挛状态;MCA血流速与同侧颅外段颈内动脉血流速的比值(LR)可鉴别二者—— $LR < 3$ 提示脑充血状态, $LR > 3$ 提示脑血管痉挛, $LR > 6$ 为严重脑血管痉挛<sup>[15]</sup>。

脑血流由平均动脉压(MAP)与静脉间的压力差(即脑灌注压, CPP)和脑血管阻力决定。但颅骨是刚性结构,脑组织、脑脊液和血液的总体积一定,若其一体积增加,将引起颅内压(ICP)升高,使其他组分体积受限。此外,脑血管自调节能力(CA)保证脑血流在一定压力范围内相对稳定。脑血流的优化从以下几点着手。

2.1 MAP目标需关注CA 重症患者的MAP应在CA的MAP低限(LLA)和高限(ULA)之间,最佳MAP(MAPopt)对应CA最强的位点。动脉血压在MAPopt之上的大幅度波动可引起更多更严重的围术期谵妄<sup>[16]</sup>;若MAP长时间低于LLA,则围术期脑梗死<sup>[17]</sup>、认知障碍、死亡率<sup>[18]</sup>显著增加。通常认为LLA和ULA分别为50~60 mmHg<sup>[19]</sup>、(90 ± 12) mmHg<sup>[20]</sup>,但重症患者LLA个体差异很大。全身炎症反应、颅脑损伤、脑梗死等可改变全身血流与脑血流之间的关系。缺氧缺血性脑损伤患者MAPopt为(75 ± 10) mmHg<sup>[21]</sup>;SAH患者CA范围显著缩窄<sup>[22]</sup>;Berg等<sup>[23]</sup>发现脓毒症早期CA范围与健康对照并不

相同。CA的定量监测技术为颅脑血流动力学精准治疗打开了全新的窗口。由不同的脑血流监测手段和数据处理方法,可得到多种CA指数,包括(1)传递函数分析法;(2)相关分析法:指各种脑血流的等效参数与动脉血压之间的相关系数,不受线性关系的限制,主要参数包括:①基于TCD监测的脑血流流速相关指数,因专业操作性强、探头固定要求较高,临床应用有一定局限性。②压力反应指数PRx是颅内压和血压间的相关系数,正值提示CA缺失。③基于脑氧监测的组织血氧指数TOx操作简单而无创,可连续监测,且与其他参数相关性较好,在重症患者CA监测中应用前景较高。

**2.2 颅内压管理** ICP升高会继发脑灌注不足。当ICP超过20mmHg时,CA受损风险高<sup>[24]</sup>,MAP的选择需更谨慎。脑室内导管测压是颅内压监测的金标准,但创伤较大。超声测量视神经鞘直径(ONSD)可间接反映ICP<sup>[25]</sup>,其相关性在CT、MRI和有创ICP监测的研究中得到验证。通过TCD测得脑血管RI、PI与ICP间有较高相关性<sup>[15]</sup>,PI急性升高反映颅内压增高<sup>[26]</sup>,可作为启动干预的警戒线。

**2.3 评估脑血管阻力** 静态脑血管PI值可反映脑血管外周阻力,间接指示脑血管微循环情况。脓毒症患者大部分在早期出现脑微循环障碍。Pierrakos等<sup>[27]</sup>发现脓毒症早期PI>1.3的患者发生谵妄的比例显著升高。Taccone等<sup>[28]</sup>的动物实验结果表明,在脓毒症早期脑血管阻力增加时,若维持MAP高于65mmHg(65~70mmHg),脑组织低氧的发生显著减少。因此对于PI升高的患者,应适当提高MAP目标,保证脑灌注压、脑血流。ECMO辅助患者的PI参考价值有限<sup>[29]</sup>。脑血管阻力对动脉二氧化碳分压(PaCO<sub>2</sub>)非常敏感,随着PaCO<sub>2</sub>升高脑阻力血管扩张,脑血流增多,可引起ICP增高、CPP降低,故对于TBI患者常采用过度通气治疗。

**2.4 评估大循环血流** 重症患者心输出量的急、慢性改变均会引起脑血流显著变化。SAH患者心指数(CI)过低可增加延迟性脑梗死风险<sup>[12]</sup>。神经重症也可导致全身血流动力学异常。强烈应激引起急性可逆性左心室收缩功能障碍,即应激性心肌病,SAH、脑出血和急性缺血性脑梗死等神经重症应激是最重要的病因之一,患者预后较差<sup>[30-31]</sup>。

### 3 脑功能指标的双面含义

脑功能是判断氧供与氧需是否平衡的最终指标,ICU医生可通过神经查体、意识评估及床旁脑电活动监测来判断重症患者的脑功能状态。但脑功能指标的含义是双方面的,过低水平的脑活动提示脑灌注不足,而异常活跃的脑电活动和精神状态则提示过高的脑氧耗。二者需辩证看待,并予以针对性的干预。一方面,随着脑血流逐渐减少,脑电图(EEG)首先表现为快波减少,之后慢波逐渐增多,提示严重缺氧导致神经元跨膜电位消失,细胞死亡,进而脑组织梗死<sup>[32]</sup>,EEG可比其他诊断手段提早识别脑梗死。一经发现,ICU医生应根据脑氧、脑血流状态及时优化脑灌注。另一方面,重症患者是癫痫发作<sup>[33]</sup>包括非痉挛性癫痫发作(NCSz)/非痉挛性癫痫持续状态(NCSE)的高危人群。上述异常脑电活动使脑氧耗显著增加。ICU的昏迷患者中,NCSz发生率为8%,其中,缺氧性脑病为最主要的病因,其次为缺血性脑梗死、中枢神经系统感染、TBI、代谢性脑病等。在非原发性脑损伤的患者中,脓毒症患者大多数存在脑电活动异常,Hosokawa等<sup>[34]</sup>系统回顾了脓毒症患者脑电图(EEG)及诱发电位(Ep)研究,脓毒症患者可见NCSz、NCSE、EEG背景异常、三相波等异常脑电活动。Merceron等<sup>[35]</sup>通过观察昏迷患者的脑血流与脑电活动发现,脑血流速增快与NCSE的发生显著相关。因此在ICU中,对于GCS<8分并存在危险因素颅脑创伤患者、持续难以解释的意识改变的SAH患者和脓毒症患者,均应进行EEG检查,并给予针对性的药物治疗及镇静处理。RASS评分和脑电双频指数(BIS)在ICU中用于定量监测镇静深度,指导降低脑耗氧的冷静治疗。

### 4 多模态血流动力学监测

神经重症整合监测尚无标准化模式,选择哪些指标、何种监测手段以及何时启动多模块监测,需个体化分析。近年较多研究致力于开发新型多参数监测设备,将脑血流、脑氧、颅内压等参数的监测整合于单个探头中,并在动物实验中小有成效<sup>[36]</sup>。神经重症多模态监测可获得大量临床数据,对于巨大数据量的高效分析处理能力,是多模态监测用于

临床的难点。机器学习、大数据与神经重症的结合,将是实现患者个体导向精准化治疗的重要基础。

## 5 结论

所有ICU均应重视颅脑血流动力学治疗,其核心为优化脑灌注,改善脑功能。临床实践中,以脑氧、脑血流、脑功能为整体“三位一体”的颅脑血流动力学治疗,可显著提高神经重症患者的诊疗水平。多模态监测、大数据与神经重症的结合是未来实现患者个体导向精准化治疗的重要方向。

## 参考文献

- [1] Narotam PK, Morrison JF, Nathoo N. Brain tissue oxygen monitoring in traumatic brain injury and major trauma: outcome analysis of a brain tissue oxygen-directed therapy [J]. *J Neurosurg*, 2009, 111(4):672-682.
- [2] Okonkwo DO, Shutter LA, Moore C, et al. Brain oxygen optimization in severe traumatic brain injury phase-II: a Phase II randomized trial [J]. *Crit Care Med*, 2017, 45(11):1907-1914.
- [3] Tang Y, Liu W, Xu F. Research progress of monitoring methods of cerebral oxygen metabolism after craniocerebral operations [J]. *Int J Pediatr*, 2018, 45(2):141-144.
- [4] Green MS, Sehgal S, Tariq R. Near-infrared spectroscopy: the new must have tool in the intensive care unit? [J]. *Semin Cardiothorac Vasc Anesth*, 2016, 20(3):213-224.
- [5] Wood MD, Maslove DM, Muscedere JG, et al. Low brain tissue oxygenation contributes to the development of delirium in critically ill patients: a prospective observational study [J]. *J Crit Care*, 2017, 41:289-295.
- [6] Bendahan N, Neal O, Ross-White A, et al. Relationship between near-infrared spectroscopy-derived cerebral oxygenation and delirium in critically ill patients: a systematic review [J]. *J Intensive Care Med*, 2019, 34(6):514-520.
- [7] Sawhney R, Holland-Fischer P, Rosselli M, et al. Role of ammonia, inflammation, and cerebral oxygenation in brain dysfunction of acute-on-chronic liver failure patients [J]. *Liver Transpl*, 2016, 22(6):732-742.
- [8] Guerci P, Vial F, Feugeas J, et al. Cerebral oximetry assessed by near-infrared spectrometry during preeclampsia: an observational study: impact of magnesium sulfate administration [J]. *Crit Care Med*, 2014, 42(11):2379-2386.
- [9] Kim HS, Ha SO, Yu KH, et al. Cerebral oxygenation as a monitoring parameter for mortality during venoarterial extracorporeal membrane oxygenation [J]. *ASAIO J*, 2019, 65(4):342-348.
- [10] Nielsen HB, Tofteng F, Wang LP, et al. Cerebral oxygenation determined by near-infrared spectrophotometry in patients with fulminant hepatic failure [J]. *J Hepatol*, 2003, 38(2):188-192.
- [11] Al Tayar A, Abouelela A, Mohiuddeen K. Can the cerebral regional oxygen saturation be a perfusion parameter in shock? [J]. *J Crit Care*, 2017, 38:164-167.
- [12] Taccone FS, Citerio G. Advanced monitoring of systemic hemodynamics in critically ill patients with acute brain injury [J]. *Neurocrit Care*, 2014, 21 Suppl 2:S38-63.
- [13] Roth C, Ferbert A, Deinsberger W, et al. Does prone positioning increase intracranial pressure? A retrospective analysis of patients with acute brain injury and acute respiratory failure [J]. *Neurocrit Care*, 2014, 21(2):186-191.
- [14] Edmonds HL Jr, Isley MR, Sloan TB, et al. American Society of Neurophysiologic Monitoring and American Society of Neuroimaging joint guidelines for transcranial doppler ultrasonic monitoring [J]. *J Neuroimaging*, 2011, 21(2):177-183.
- [15] White H, Venkatesh B. Applications of transcranial Doppler in the ICU: a review [J]. *Intensive Care Med*, 2006, 32(7):981-994.
- [16] Hori D, Max L, Laffam A, et al. Blood pressure deviations from optimal mean arterial pressure during cardiac surgery measured with a novel monitor of cerebral blood flow and risk for perioperative delirium: a pilot study [J]. *J Cardiothorac Vasc Anesth*, 2016, 30(3):606-612.
- [17] Hori D, Nomura Y, Ono M, et al. Optimal blood pressure during cardiopulmonary bypass defined by cerebral autoregulation monitoring [J]. *J Thorac Cardiovasc Surg*, 2017, 154(5):1590-1598. e1592.
- [18] Ono M, Brady K, Easley RB, et al. Duration and magnitude of blood pressure below cerebral autoregulation threshold during cardiopulmonary bypass is associated with major morbidity and operative mortality [J]. *J Thorac Cardiovasc Surg*, 2014, 147(1):483-489.
- [19] Goodson CM, Rosenblatt K, Rivera-Lara L, et al. Cerebral blood flow autoregulation in sepsis for the intensivist: why its monitoring may be the future of individualized care [J]. *J Intensive Care Med*, 2018, 33(2):63-73.
- [20] Hori D, Brown C, Ono M, et al. Arterial pressure above the upper cerebral autoregulation limit during cardiopulmonary bypass is associated with postoperative delirium [J]. *Br J Anaesth*, 2014, 113(6):1009-1017.
- [21] Sekhon MS, Griesdale DE. Individualized perfusion targets in hypoxic ischemic brain injury after cardiac arrest [J]. *Crit Care*, 2017, 21(1):259.
- [22] Santos GA, Petersen N, Zamani AA, et al. Pathophysiologic differences in cerebral autoregulation after subarachnoid hemorrhage [J]. *Neurology*, 2016, 86(21):1950-1956.
- [23] Berg RM, Plovsing RR, Bailey DM, et al. The dynamic cerebral autoregulatory adaptive response to noradrenaline is attenuated during systemic inflammation in humans [J]. *Clin Exp Pharmacol Physiol*, 2015, 42(7):740-746.

- [24] de-Lima-Oliveira M, Salinet ASM, Nogueira RC, et al. Intracranial hypertension and cerebral autoregulation: a systematic review and meta-analysis[J]. *World Neurosurg*, 2018, 113:110-124.
- [25] Robba C, Santori G, Czosnyka M, et al. Optic nerve sheath diameter measured sonographically as non-invasive estimator of intracranial pressure: a systematic review and meta-analysis[J]. *Intensive Care Med*, 2018, 44(8):1284-1294.
- [26] de Riva N, Budohoski KP, Smielewski P, et al. Transcranial Doppler pulsatility index: what it is and what it isn't[J]. *Neurocrit Care*, 2012, 17(1):58-66.
- [27] Pierrakos C, Attou R, Decorte L, et al. Transcranial Doppler to assess sepsis-associated encephalopathy in critically ill patients[J]. *BMC Anesthesiol*, 2014, 14:45.
- [28] Taccone FS, Su F, De Deyne C, et al. Sepsis is associated with altered cerebral microcirculation and tissue hypoxia in experimental peritonitis[J]. *Crit Care Med*, 2014, 42(2):e114-122.
- [29] Kavi T, Esch M, Rinsky B, et al. Transcranial doppler changes in patients treated with extracorporeal membrane oxygenation [J]. *J Stroke Cerebrovasc Dis*, 2016, 25(12):2882-2885.
- [30] Pelliccia F, Kaski JC, Crea F, et al. Pathophysiology of Takotsubo syndrome[J]. *Circulation*, 2017, 135(24):2426-2441.
- [31] Nasr DM, Tomasini S, Prasad A, et al. Acute brain diseases as triggers for stress cardiomyopathy: clinical characteristics and outcomes[J]. *Neurocrit Care*, 2017, 27(3):356-361.
- [32] Sharbrough FW, Messick JM Jr, Sundt TM Jr. Correlation of continuous electroencephalograms with cerebral blood flow measurements during carotid endarterectomy [J]. *Stroke*, 1973, 4(4):674-683.
- [33] Claassen J, Taccone FS, Horn P, et al. Recommendations on the use of EEG monitoring in critically ill patients: consensus statement from the neurointensive care section of the ESICM[J]. *Intensive Care Med*, 2013, 39(8):1337-1351.
- [34] Hosokawa K, Gaspard N, Su F, et al. Clinical neurophysiological assessment of sepsis-associated brain dysfunction: a systematic review[J]. *Crit Care*, 2014, 18(6):674.
- [35] Merceron S, Geeraerts T, Montlahuc C, et al. Assessment of cerebral blood flow changes in nonconvulsive status epilepticus in comatose patients: a pathophysiological transcranial Doppler study[J]. *Seizure*, 2014, 23(4):284-289.
- [36] Mader MM, Leidorf A, Hecker A, et al. Evaluation of a new multi-parameter brain probe for simultaneous measurement of brain tissue oxygenation, cerebral blood flow, intracranial pressure, and brain temperature in a porcine model[J]. *Neurocrit Care*, 2018, 29(2):291-301.

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- [23] Young GB, Bolton CF, Archibald YM, et al. The electroencephalogram in sepsis-associated encephalopathy [J]. *J Clin Neurophysiol*, 1992, 9(1):145-152.
- [24] Claassen J, Taccone FS, Horn P, et al. Recommendations on the use of EEG monitoring in critically ill patients: consensus statement from the neurointensive care section of the ESICM[J]. *Intensive Care Med*, 2013, 39(8):1337-1351.
- [25] Sandroni C, Cariou A, Cavallaro F, et al. Prognostication in comatose survivors of cardiac arrest: an advisory statement from the European Resuscitation Council and the European Society of Intensive Care Medicine[J]. *Intensive Care Med*, 2014, 40(12):1816-1831.
- [26] Chunhua X, Shiyue S, Chuxiong P, et al. Different effects of propofol and dexmedetomidine sedation on electroencephalogram patterns: wakefulness, moderate sedation, deep sedation and recovery[J]. *PLoS One*, 2018, 13(6):e0199120.
- [27] Roustan JP, Valette S, Aubas P, et al. can electroencephalographic analysis be used to determine sedation levels in critically ill patients?[J]. *Anesth Analg*, 2005, 101(4):1141-1151.
- [28] Maksimow A, Snapir A, Särkelä M, et al. Assessing the depth of dexmedetomidine-induced sedation with electroencephalogram (EEG)-based spectral entropy [J]. *Acta Anaesthesiologica Scandinavica*, 2007, 51(1):22-30.
- [29] Vanluchene AL, Struys MM, Heyse BE, et al. Spectral entropy measurement of patient responsiveness during propofol and remifentanyl. A comparison with the bispectral index[J]. *Br J Anaesth*, 2004, 93(5):645-654.
- [30] Kilbride RD, Costello DJ, Chiappa KH. How seizure detection by continuous electroencephalographic monitoring affects the prescribing of antiepileptic medications [J]. *Arch Neurol*, 2009, 66(6):723-728.
- [31] Jordan KG. Continuous EEG monitoring in the neuroscience intensive care unit and emergency department [J]. *J Clin Neurophysiol*, 1999, 16(1):14-39.
- [32] Vespa PM, Nenov V, Nuwer MR. Continuous EEG monitoring in the intensive care unit: early findings and clinical efficacy [J]. *J Clin Neurophysiol*, 1999, 16(1):1-13.
- [33] Abend NS, Dlugos DJ, Hahn CD, et al. Use of EEG monitoring and management of non-convulsive seizures in critically ill patients: a survey of neurologists[J]. *Neurocrit Care*, 2010, 12(3):382-389.
- [34] Herman ST, Abend NS, Bleck TP, et al. Consensus statement on continuous EEG in critically ill adults and children, part II: personnel, technical specifications, and clinical practice [J]. *J Clin Neurophysiol*, 2015, 32(2):96-108.
- [35] Young GB, Campbell VC. EEG monitoring in the intensive care unit: pitfalls and caveats [J]. *J Clin Neurophysiol*, 1999, 16(1):40-45.

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