血管扩张剂雾化吸入治疗心脏手术患者的肺动脉高压：一项系统性评价和荟萃分析

Aerosolized Vasodilators for the Treatment of Pulmonary Hypertension in Cardiac Surgical Patients: A Systematic Review and Meta-analysis

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背景: 在心脏手术中，肺动脉高压是一个重要的预后因素，对此相继出现了一些治疗方法。在本次系统评价和荟萃分析中，作者比较了在心脏手术中雾化吸入与静脉使用血管扩张剂及安慰剂对肺动脉高压的疗效差异。搜索从开始至2015年10月MEDLINE、CENTRAL、EMBASE、Web of Science和clinicaltrials.gov数据库。主要预后指标为死亡率。次要预后指标包括住院时间和ICU停留时间以及血流动力学特征的评估。

方法: 在确认的2897项引文中，共纳入了10项研究的434例患者。

结果: 与静脉给药相比，雾化吸入显著降低肺血管阻力（-41.36dyne·s/cm，P = 0.03），有更高的平均动脉压（8.24mm Hg，P = 0.02）和右心室射血分数（7.29%，P <0.0001）。两组间没有观察到显着的血液动力学差异;然而，雾化吸入组ICU停留时间更长（0.66天，P = 0.01）。余指标未见显著差异。

结论: 与静脉给药相比，在心脏手术中雾化吸入血管扩张剂治疗肺动脉高压与改善的右心室功能相关。与安慰剂相比，应用试验药物在主要预后指标方面并无任何获益。这一领域需要进行深入研究，并着重于临床预后的显著改善。

（崔璀译 陈杰校）

BACKGROUND: In cardiac surgery, pulmonary hypertension is an important prognostic factor for which several treatments have been suggested over time. In this systematic review and meta-analysis, we compared the efficacy of inhaled aerosolized vasodilators to intravenously administered agents and to placebo in the treatment of pulmonary hypertension during cardiac surgery. We searched MEDLINE, CENTRAL, EMBASE, Web of Science, and clinicaltrials.gov databases from inception to October 2015. The incidence of mortality was assessed as the primary outcome. Secondary outcomes included length of stay in hospital and in the intensive care unit, and evaluation of the hemodynamic profile.

METHODS: Of the 2897 citations identified, 10 studies were included comprising a total of 434 patients.

RESULTS: Inhaled aerosolized agents were associated with a significant decrease in pulmonary vascular resistance (-41.36 dyne·s/cm, P= .03) and a significant increase in mean arterial pressure (8.24 mm Hg, P= .02) and right ventricular ejection fraction (7.29%, P< .0001) when compared to intravenously administered agents. No significant hemodynamically meaningful differences were observed between inhaled agents and placebo; however, an increase in length of stay in the intensive care unit was shown with the use of inhaled aerosolized agents (0.66 days, P= .01). No other differences were observed for either comparison.

CONCLUSIONS: The administration of inhaled aerosolized vasodilators for the treatment of pulmonary hypertension during cardiac surgery is associated with improved right ventricular performance when compared to intravenously administered agents. This review does not support any benefit compared to placebo on major outcomes. Further investigation is warranted in this area of research and should focus on clinically significant outcomes.

恶性高热易感者骨骼肌代谢功能障碍

Skeletal Muscle Metabolic Dysfunction in Patients With Malignant Hyperthermia Susceptibility.

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背景：恶性高热（MH）是一种骨骼肌的药理遗传疾病，表现对某些麻醉药物具有潜在致命的高代谢反应。然而，一些MH疑似患者在没有麻醉药物触发的情况下经历了肌无力，肌疲劳和运动不耐受。这项探索性研究的目的是阐明通过咖啡因-氟烷挛缩试验测定MH阳性的患者运动不耐受的病理生理学。为此，作者采用磷磁共振波谱，血氧水平依赖功能磁共振成像（MRI）和传统运动实验来比较MH阳性患者和健康对照组的骨骼肌代谢。

方法：使用磷磁共振波谱和血氧水平依赖性功能MRI评估29个MH阳性患者和20个健康对照的骨骼肌代谢情况。采用传统的体力量度测量有氧代谢能力，无氧代谢能力和肌力。

结果：在30和60秒活动期间，与健康对照相比，MH阳性患者通过氧化途径产生的ATP显著降低。与健康对照组相比，MH阳性患者的血氧水平依赖性功能MRI恢复时间更长。与健康对照相比，运动实验显示MH阳性患者的有氧代谢和无氧代谢能力较低。

结论：这项探索性研究的结果表明，与健康个体相比，MH阳性患者的有氧代谢受损。这可以解释在MH易感患者人群中表现出的运动不耐受。

（陈聪译 陈杰校）

BACKGROUND: Malignant hyperthermia (MH), a pharmacogenetic disorder of skeletal muscle, presents with a potentially lethal hypermetabolic reaction to certain anesthetics. However, some MH-susceptible patients experience muscle weakness, fatigue, and exercise intolerance in the absence of anesthetic triggers. The objective of this exploratory study was to elucidate the pathophysiology of exercise intolerance in patients tested positive for MH with the caffeine-halothane contracture test. To this end, we used phosphorus magnetic resonance spectroscopy, blood oxygen level-dependent functional magnetic resonance imaging (MRI), and traditional exercise testing to compare skeletal muscle metabolism in MH-positive patients and healthy controls.

METHODS: Skeletal muscle metabolism was assessed using phosphorus magnetic resonance spectroscopy and blood oxygen level-dependent functional MRI in 29 MH-positive patients and 20 healthy controls. Traditional measures of physical capacity were employed to measure aerobic capacity, anaerobic capacity, and muscle strength.

RESULTS: During 30- and 60-second exercise, MH-positive patients had significantly lower ATP production via the oxidative pathway compared to healthy controls. MH-positive patients also had a longer recovery time with blood oxygen level-dependent functional MRI compared to healthy controls. Exercise testing revealed lower aerobic and anaerobic capacity in MH-positive patients compared to healthy controls。
CONCLUSIONS: Results of this exploratory study suggest that MH-positive patients have impaired aerobic metabolism compared to healthy individuals. This could explain the exercise intolerance exhibited in MH-susceptible patient population.

深度镇静期间同日大量口服肠道制剂的安全性：一项前瞻性观察研究

Safety of Large-Volume, Same-Day Oral Bowel Preparations During Deep Sedation: A Prospective Observational Study.

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背景：结肠镜检查质量与肠道准备直接相关。手术当天给予部分泻药，肠道准备工作可得到很大的改善。然而，仍然存在导致较高的胃残留量(GRV)，增加肺误吸风险的顾虑。本研究目的是评估在异丙酚深度镇静下，检测手术前一天和当天行肠道准备患者的胃残留量(GRV)和胃液PH值差异。
方法:这是一项以当天接受胃肠内镜和结肠镜检查患者为对象的前瞻性观察性研究。所有纳入患者都进行大容量的聚乙二醇泻药制剂行肠道准备并接受异丙酚镇静。在胃镜下收集患者胃液，检测其容量和PH值。
结果：本研究总共纳入428名患者，其中56%的患者接受了操作当天的肠道准备，余下患者接受术前一天的肠道准备。两组胃残留量的均值 ± 标准差分别为18.1 ± 10.2毫升和16.3 ± 16.5毫升(P = .69) 。两组发生GRV≥ 25毫升或高于预期的GRV(0.4ml/kg)情况无统计学差异（分别为P=0.9和P=0.87）。以最后一次胃肠道准备的时间(3–5, 5–7, >7 小时)进行分组评估GRV，各组间也没有统计学差异（P =0 .56）。两组胃肠道准备患者的胃液PH值相似(P=0.23，分别为2.5±1.4和2.5±1.3)。但手术前一天行胃肠道准备患者其肠道准备不充分的比例更高（P =0 .001）。
结论：在结肠镜检查当天，手术前3小时完成大容量胃肠道准备不会导致胃残留量(GRV)的升高，胃液PH的下降。
（丁曦冰译 陈杰校）

BACKGROUND: Colonoscopy quality is directly related to the bowel preparation. It is well established that bowel preparations are improved when at least part of the laxative is ingested on the day of the procedure. However, there is concern that this can result in higher gastric residual volumes (GRV) and increase the risk of pulmonary aspiration. The aim of this study is to evaluate GRV and gastric pH in patients who received day-before bowel preparation versus those ingesting their laxative on the day of colonoscopy under anesthesiologist-directed propofol deep sedation.
METHODS: This is a prospective observational study for patients undergoing same-day upper endoscopy and colonoscopy. All included patients had large-volume polyethylene glycol lavage preparation and received propofol sedation. Gastric fluid was collected during the upper endoscopy for volume and pH measurement.

RESULTS: The study included 428 patients with 56% receiving same-day laxative preparation and the remainder evening-before preparation. Mean ± SD GRV was 18.1 ± 10.2 mL, 16.3 ± 16.5 mL in each of these preparation groups, respectively (P = .69). GRV ≥ 25 mL or higher than expected GRV adjusted by weight (0.4 mL/kg) were also not different among the study groups (P = .90 and P = .87, respectively). Evaluating GRV based on time since last ingestion of preparation (3–5, 5–7, >7 hours) did not result in any differences (P = .56). Gastric pH was also similar between the bowel preparation groups (P = .23), with mean ± SD of 2.5 ± 1.4 for evening-before and 2.5 ± 1.3 for the same-day preparation. There were more inadequate bowel preparations in day before bowel preparations (P = .001).
CONCLUSIONS: A large-volume bowel preparation regimen finished on the day of colonoscopy as close as 3 hours before the procedure results in no increase in GRV or decrease in gastric pH.

远端缺血预处理减轻肺叶切除后肺氧化应激损伤：一项单中心、随机、双盲、对照实验

Remote Ischemic Preconditioning Decreases Oxidative Lung Damage After Pulmonary Lobectomy: A Single-Center Randomized, Double-Blind, Controlled Trial

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背景：肺癌患者的肺叶切除手术中，术侧肺通常呈现萎陷和低灌注。当肺被重新扩张时，缺血再灌注损伤会随之发生。研究者猜测远端缺血预处理（RIPC）可以降低肺氧化应激和改善术后气体交换功能。
方法：研究者对非小细胞肺癌进行肺叶切除手术的患者进行单中心、随机、双盲实验。53位患者在麻醉诱导后随机进行肢体远端缺血预处理（在大腿使用止血带进行缺血处理，5分钟缺血／5分钟灌注，共3个循环）或对照治疗。对呼出气冷凝物和动脉血中的氧化应激标志物进行检测，采集时间分别为麻醉诱导后远端缺血预处理和手术之前（T0，基线）、术侧肺萎陷双侧肺通气之前（T1）、双侧肺通气即刻（T2）、双侧肺通气后120分钟（T3）。主要结果为T1、T2和T3三个时间点呼出气冷凝物中8-异前列腺素水平。次要结果包括以下：呼出气冷凝物和血中NO2+NO3、H2O2水平和ph值，还有肺气体交换参数（PaO2/FiO2、A-aDO2、a/A 比和呼吸指数）。
结果：在T1、T2和T3三个时间点，进行远端缺血预处理的患者的呼出气冷凝物中8-异前列腺素比对照组低，其中平均值差值和95%可信区间分别为：-15.3 (5.8-24.8), P = .002; -20.0 (5.5-34.5), P = .008; 和-10.4 (2.5-18.3), P = .011。在远端缺血预处理组，呼出气冷凝物中NO2+NO3和H2O2水平在T2和T1-T3也较对照组有所降低。处理组血液中8-异前列腺素和NO2+NO3水平在T2时间点有所降低(P < .05)。运用95%可信区间比较均值发现，远端缺血预处理组在肺叶切除后2、8、24小时相比对照组具有更好的氧合指数，分别为78 (10-146), 66 (14-118), and 58 (12-104)。

结论：肢体远端缺血预处理降低肺叶切除患者呼出气冷凝物中8-异前列腺素及其他氧化应激肺损伤标志物。通过评估氧合指数发现远端缺血预处理还可以改善术后气体交换功能。
（葛家希译 陈杰校）

BACKGROUND: During lobectomy in patients with lung cancer, the operated lung is often collapsed and hypoperfused. Ischemia/reperfusion injury may then occur when the lung is re-expanded. We hypothesized that remote ischemic preconditioning (RIPC) would decrease oxidative lung damage and improve gas exchange in the postoperative period.
METHODS: We conducted a single-center, randomized, double-blind trial in patients with nonsmall cell lung cancer undergoing elective lung lobectomy. Fifty-three patients were randomized to receive limb RIPC immediately after anesthesia induction (3 cycles: 5 minutes ischemia/5 minutes reperfusion induced by an ischemia cuff applied on the thigh) and/or control therapy without RIPC. Oxidative stress markers were measured in exhaled breath condensate (EBC) and arterial blood immediately after anesthesia induction and before RIPC and surgery (T0, baseline); during operated lung collapse, immediately before resuming two-lung ventilation (TLV) (T1); immediately after resuming TLV (T2); and 120 minutes after resuming TLV (T3). The primary outcome was 8-isoprostane levels in EBC at T1, T2, and T3. Secondary outcomes included the following: NO2+NO3, H2O2 levels, and pH in EBC and in blood (8-isoprostane, NO2+NO3) and pulmonary gas exchange variables (PaO2/FiO2, A-aDO2, a/A ratio, and respiratory index).
RESULTS: Patients subjected to RIPC had lower EBC 8-isoprostane levels when compared with controls at T1, T2, and T3 (differences between means and 95% confidence intervals): -15.3 (5.8-24.8), P = .002; -20.0 (5.5-34.5), P = .008; and -10.4 (2.5-18.3), P = .011, respectively. In the RIPC group, EBC NO2+NO3 and H2O2 levels were also lower than in controls at T2 and T1-T3, respectively (all P < .05). Blood levels of 8-isoprostane and NO2+NO3 were lower in the RIPC group at T2 (P < .05). The RIPC group had better PaO2/FiO2 compared with controls at 2 hours, 8 hours, and 24 hours after lobectomy in 95% confidence intervals for differences between means: 78 (10-146), 66 (14-118), and 58 (12-104), respectively.
CONCLUSIONS: Limb RIPC decreased EBC 8-isoprostane levels and other oxidative lung injury markers during lung lobectomy. RIPC also improved postoperative gas exchange as measured by PaO2/FiO2 ratio.

老年创伤性颅内出血患者术前低剂量阿司匹林暴露与其急诊手术预后

Preoperative Low-Dose Aspirin Exposure and Outcomes After Emergency Neurosurgery for Traumatic Intracranial Hemorrhage in Elderly Patients

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背景：抗血小板药物通常在择期神经外科手术前停用，但在急诊神外手术中却无法得以实现。本研究对接受急诊神外手术的老年患者进行了一项回顾性队列研究，以探讨术前服用阿司匹林是否会导致更劣的预后。
方法：研究者对1级创伤中心2008～2012年间所有接受了急诊神经外科手术的创伤性颅内出血的案例进行了分析，其中对于65岁以上且术前有过阿司匹林暴露史的老年患者，研究者比较了患者的统计学特征，并发症以及结局。排除标准包括：（1）多发伤，（2）其他术前抗凝剂或抗血小板药物的联合使用，（3）手术适应症以外的硬膜下、硬膜外、或脑实质出血，以及（4）一次住院期间重复接受多次神外手术。所研究的结局包括术中预估出血量、需要再次手术的术后颅内出血、住院死亡人数，ICU住院天数，总住院时长，以及围手术期血液制品的输注。此外，作者还研究了血小板输注是否会对服用阿司匹林的患者的结局产生影响。
结果：本研究纳入了171名患者。术前服用阿司匹林的患者（n=87，其中95%的患者均为小剂量服用：81mg/d）与不服者（n = 84; 78.3 ± 7.8 vs 75.9 ± 7.9 岁, $P > 0.05$）大致年龄相仿，只是前者的格拉斯哥昏迷评分分数稍高(12.8 ± 3.4 vs 11.4 ± 4, $P = 0.02$)，以及患冠状动脉疾病的概率更高($P < 0.05$) 。校正了格拉斯哥昏迷评分分数以及冠状动脉疾病等因素后，研究者发现术前服用阿司匹林的患者围手术期血小板输注概率更高（校正后OR=9.89，95%CI为4.24 - 26.25）。两组之间在其他结局方面均没有差异。在接受阿司匹林暴露的患者中，术前或术中的血小板输注并不能导致一个较好的预后。
结论：在接受急诊手术且年龄≥65岁的创伤性颅内出血的老年患者中，术前小剂量服用阿司匹林不增加围手术期出血，住院时间和住院死亡率。
（徐侨翌译 陈杰校）
BACKGROUND: Antiplatelet medications are usually discontinued before elective neurosurgery, but this is not an option for emergent neurosurgery. We performed a retrospective cohort study to examine whether preoperative aspirin use was associated with worse outcomes after emergency neurosurgery in elderly patients.
METHODS: We analyzed all cases of emergency neurosurgical procedures for traumatic intracranial hemorrhage from 2008 to 2012 at a level 1 trauma center. Demographics, comorbidities, and outcomes were compared for patients ≥65 years by preoperative aspirin exposure. Exclusion criteria were: (1) polytrauma, (2) concomitant use of other preoperative anticoagulants or antiplatelet agents, (3) surgical indication other than subdural, extradural, or intraparenchymal hemorrhage, and (4) repeat neurosurgical procedures within a single admission. Estimated intraoperative blood loss, postprocedural intracranial bleeding requiring reoperation, death in hospital, intensive care unit, and hospital lengths of stay and perioperative blood product transfusion from 48 hours before 48 hours after surgery were the study outcomes. We also examined whether platelet transfusion had an impact on outcomes for patients on aspirin.
RESULTS: The cohort included 171 patients. Patients receiving preoperative aspirin (n = 87, 95% taking 81 mg/day) were the same age as patients not receiving aspirin (n = 84; 78.3 ± 7.8 vs 75.9 ± 7.9 years, $P > .05$), had slightly higher admission Glasgow Coma Scale scores (12.8 ± 3.4 vs 11.4 ± 4, $P = .02$) and tended to have more coronary artery disease ($P < .05$). Adjusted for Glasgow Coma Scale and coronary artery disease, patients receiving preoperative aspirin had a higher odds of perioperative platelet transfusion (adjusted odds ratio 9.89, 95% confidence interval 4.24– 26.25). There were no other

differences in outcomes between the 2 groups. Preoperative or intraoperative platelet transfusion was not associated with better outcomes among aspirin patients.
CONCLUSIONS: In patients age ≥65 years undergoing emergency neurosurgery for traumatic intracranial hemorrhage, preoperative low-dose aspirin treatment was not associated with increased perioperative bleeding, hospital lengths of stay, or in hospital mortality.

术前筛查出的阻塞性睡眠呼吸暂停与先前诊断的阻塞性睡眠呼吸暂停相比手术预后更差

Preoperatively Screened Obstructive Sleep Apnea Is Associated With Worse Postoperative Outcomes Than Previously Diagnosed Obstructive Sleep Apnea

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背景：阻塞性睡眠呼吸暂停（OSA）影响着高达26%的美国成年人，经常漏诊，增加围手术期发病率。研究者假设在手术当天筛查出来的中／高风险的OSA（S-OSA）患者与先前诊断OSA（D-OSA）患者有相同的围手术期呼吸系统并发症、医疗花费和死亡率。其次，研究假设这两组OSA患者都比未患OSA的患者有更多呼吸系统并发症。
方法:通过对1个教学医院和2个社区医院的电子医疗数据库进行回顾性调查，以研究正在接受非紧急住院治疗的成年人(2012年1月1日至2014年12月31日)。根据手术当天术前评估和呼吸暂停(打鼾、疲劳、睡眠中可观察到的呼吸暂停、高血压、体重指数超过35、年龄超过50岁、颈粗、男性)得分，病人被划分为D-OSA、S-OSA或No-OSA。观察了围手术期的呼吸事件和干预措施、医疗花费和死亡率。主要预后指标(不良呼吸事件[AREs])包括围手术期的低氧血症和困难气道管理。血氧过低被定义为持续脉搏血氧测定3分钟，外周血氧饱和度(SpO2)小于90%，或经验证和／或被手工记录入病历。轻度低氧血症被定义为最低SpO2是86%-89%，中／重度低氧血症被定义为最低SpO2小于等于85%。次要预后指标包括术后呼吸干预、ICU入住、住院时间、30天和1年的全因死亡率。使用线性和逻辑回归分析对结果进行比较。
结果:共有28912名患者接受了评估:3432名(11.9%)D-OSA患者;1546(名5.3%)S-OSA患者;以及23934(82.8%)无No-OSA患者。S-OSA患者中之前有68.0％出现不良呼吸事件;D-OSA患者中至少71.0%;No-OSA患者中至少52.1%(未经调整的P值小于0.001)，主要是出PACU后的中度或重度低血氧症事件(PACU;在S-OSA患者中有39.9%;在D-OSA 患者中有39.5%;在No-OSA患者中有27.1%)。与D-OSA患者相比，S-OSA患者在PACU中的中度/重度低氧血症率更低，但有相似的术中和术后，更高的困难面罩通气率，以及相似的困难气管插管报告。在对人群、健康、手术差异和医院类型进行调整后，在S-OSA和D-OSA患者中，发生大于等于1的不良呼吸事件率可能性并没有不同(调整后的比值比0.90[99%的置信区间，0.75-1.09];P=.15)。与D-OSA患者相比，S-OSA患者术后的术后重插管、机械通气、术后直接重症监护病房住院、住院时间和30天的全因死亡率显著增加。

结论:被归类为 S-OSA 的患者与 D-OSA 患者的不良呼吸事件率相同，但S-OSA患者术后呼吸干预、医院使用和30天的全因死亡率都有所增加。这部分比D-OSA 患者有更糟糕的术后结果的S-OSA患者，反映了出PACU后对这一临床诊断缺乏认识和适当的管理。这些高危患者需要多学科干预。

（杨柳译 陈杰校）

BACKGROUND: Obstructive sleep apnea (OSA) affects up to 26% of US adults, is often undiagnosed, and increases perioperative morbidity. We hypothesized that patients screened on the day of surgery as moderate/high risk for OSA (S-OSA) present similar perioperative respiratory complications, hospital use, and mortality than patients with previously diagnosed OSA (D-OSA). Second, we hypothesized that both OSA groups have more respiratory complications than No-OSA patients.

METHODS: The electronic medical database from 1 academic and 2 community hospitals was retrospectively queried to identify adults undergoing nonemergent inpatient surgery (January 1, 2012, to December 31, 2014). Based on the day-of-surgery preoperative assessment and STOP-BANG (Snoring, Tiredness, Observed apnea during sleep, high blood Pressure, Body mass index >35, Age >50 years, thick Neck, Gender male) score, they were classified as D-OSA, S-OSA, or No-OSA. Perioperative respiratory events and interventions, hospital use, and mortality were measured. The primary outcome composite (adverse respiratory events [AREs]) included perioperative hypoxemic events and difficult airway management. Hypoxemic event was defined as peripheral saturation of oxygen (SpO2) <90% by continuous pulse oximetry for ≥3 minutes, or if validated and/or manually entered into the medical chart. Hypoxemia was classified as mild (lowest SpO2 86%–89%) or moderate/severe (lowest SpO2 ≤85%). Secondary outcomes included postoperative respiratory interventions, intensive care unit admission, hospital length of stay, and 30-day and 1-year all-cause mortality. Outcomes were compared using linear and logistic regression analyses.

RESULTS: A total of 28,912 patients were assessed: 3432 (11.9%) D-OSA; 1546 (5.3%) S-OSA; and 23,934 (82.8%) No-OSA patients. At least 1 ARE was present in 68.0% of S-OSA; 71.0% of D-OSA; and 52.1% of No-OSA patients (unadjusted P < .001), primarily ≥1 moderate/severe hypoxemic event after discharge from the postanesthesia care unit (PACU; 39.9% in S-OSA; 39.5% in D-OSA; and 27.1% in No-OSA patients). S-OSA patients compared to D-OSA patients presented lower rates of moderate/severe hypoxemia in the PACU but similar intraoperatively and postoperatively, higher difficult mask ventilation rates, and similar difficult intubation reports. After adjusting for demographic, health, and surgical differences and hospital type, the likelihood of ≥1 ARE was not different in S-OSA and D-OSA patients (adjusted odds ratio 0.90 [99% confidence interval, 0.75–1.09]; P = .15). S-OSA patients compared to D-OSA patients had significantly increased postoperative reintubation, mechanical ventilation, direct intensive care unit admission after surgery, hospital length of stay, and 30-day all-cause mortality.

CONCLUSIONS: Patients classified as S-OSA have similar rates of AREs to D-OSA patients, but increased postoperative respiratory interventions, hospital use, and 30-day all-cause mortality. These worse postoperative outcomes in S-OSA patients than D-OSA patients could reflect the lack of awareness and appropriate management of this bedside S-OSA diagnosis after PACU discharge. Multidisciplinary interventions are needed for these high-risk patients.

神经电刺激不能正确预测肌间沟臂丛神经阻滞中针-神经的距离和局麻药物的扩散趋势。

Electric Nerve Stimulation Does Not Correctly Predict Needle-Nerve Distance and Potential Local Anesthetic Spread for Interscalene Brachial Plexus Blockade

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本研究评估了神经电刺激作为一个神经定位工具的价值。对 43 位行肩部手术的患者引发运动反应后，通过超声成像来评估针尖端的位置离相距最近的神经的距离，以及生理盐水的扩散情况。21 位患者针尖距离最近的神经 1-4mm，7 位患者针尖直接接触到了神经，另外 15 位患者针尖距离神经 6-18mm。在 21 位患者当中，随后注入的生理盐水夹层未达到臂丛。因此，神经电刺激正确识别针-神经距离的成功率为 48.8%，且仅有 51.2%的患者能够达到正确的流体扩散。

（姚雪雅译 陈杰校）

This study evaluated electric nerve stimulation as a nerve location tool. After eliciting motor response in 43 patients undergoing shoulder surgery, the needle tip's position, distance from the closest nerve, and spread of saline were evaluated using ultrasound imaging. The needle's tip resided 1 to 4 mm from the closest nerve in 21, in direct contact with it in 7, and 6 to 18 mm away in 15 patients. In 21 patients, subsequent saline dissection did not reach the brachial plexus. Thus, the success rate of electric nerve stimulation for correct needle-nerve distance identification was 48.8%, with correct fluid spread reached in only 51.2% of patients.

在糖尿病神经病变大鼠模型中，二亚苯基碘鎓可通过减弱氧化应激的作用减轻布比卡因引起的坐骨神经损伤

Diphenyleneiodonium Mitigates Bupivacaine-Induced Sciatic Nerve Damage in a Diabetic Neuropathy Rat Model by Attenuating Oxidative Stress

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背景:在糖尿病神经病变(DN)大鼠模型中，局部麻醉引起的神经损伤已被证明与氧化应激的增加相关。本研究探讨了氯化二亚苯基碘鎓（DPI），一种 NADPH 氧化酶(NOX)抑制剂，对布比卡因造成糖尿病神经病变(DN)大鼠的坐骨神经损伤的影响。

方法:采用高脂饮食和链霉素注射液建立糖尿病神经病变大鼠模型。通过检测(i)血糖，(ii)后爪 von Frey 触觉反应测试，(iii) 热刺激缩足反应潜伏期(PWTL)，(iv)神经传导速度(NCV)来确定模型建立。使用布比卡因(0.2 mL,5 mg / mL)行大鼠右坐骨神经阻滞。阻滞前 24 小时与 30 分钟，于皮下注射二亚苯基碘鎓(1 mg / kg)。阻滞后 24 小时，测试神经传导速度，数种活性氧簇，以及 Caspase-3 蛋白酶以评估坐骨神经损伤的程度。

结果: 糖尿病神经病变大鼠模型建立成功。与对照组相比，布比卡因阻滞组大鼠的 VF 触觉测量值(对照组, 16.5 ± 1.3 g; 布比卡因组, 19.1 ± 1.5 g, P < .001)与热刺激缩足反应潜伏期(对照组, 13.3 ± 1.1 s; 布比卡因组, 14.6 ± 1.1 s, P = .028)增加，而坐骨神经传导速度显著下降（对照组, 38.8 ± 2.4 m/s,布比卡因组, 30.5 ± 2.0 m/s, P = .003）。且布比卡因组的坐骨神经损伤程度（由轴突面积评估）更严重(对照组, 11.6 ± 0.3 μm, 布比卡因组, 7.5 ± 0.3 μm, P < .001)。此外，DPI 注射可显著改善神经功能(VF responses, 17.3 ± 1.3 g; PWTL, 13.4 ± 1.1 seconds; NCV, 35.6 ± 3.1 m/s)，减轻轴突面积损失(9.6 ± 0.3 μm) 。与不经 DPI 注射的大鼠相比，DPI 注射组大鼠的 NOX2、NOX4 和 caspase - 3 的蛋白表达水平，脂质过氧化物和过氧化氢酶水平均明显降低(P < .05)。结论:在高脂肪饮食/链球菌诱导的糖尿病神经病变大鼠模型中，皮下注射 DPI 可以防止布比卡因神经阻滞造成的坐骨神经的功能性和神经组织学损伤。
（张金源译 陈杰校）

Background: Increased oxidative stress has been linked to local anesthetic-induced nerve injury in a diabetic neuropathy (DN) rat model. The current study explores the effects of diphenyleneiodonium (DPI) chloride, an NADPH oxidase (NOX) inhibitor, on bupivacaine-induced sciatic nerve injury in DN rats.
Methods: A rat DN model was established through high-fat diet feeding and streptozotocin injection. The model was confirmed via testing (i) blood glucose, (ii) hindpaw allodynia responses to von Frey (VF) monofilaments, (iii) paw withdrawal thermal latency (PWTL), and (iv) nerve conduction velocity (NCV). Bupivacaine (Bup, 0.2 mL, 5 mg/mL) was used to block the right sciatic nerve. DPI (1 mg/kg) was injected subcutaneously 24 hours and 30 minutes before the sciatic block. At 24 hours after the block, NCV, various reactive oxygen species, and Caspase-3 were evaluated to determine the extent of sciatic nerve injury.
Results: The DN rat model was successfully established. Compared with the DN control group, the postblock values of VF responses (DN-Con, 16.5 ± 1.3 g; DN + Bup, 19.1 ± 1.5 g, P < .001) and PWTL significantly increased (DN-Con, 13.3 ± 1.1 seconds; DN + Bup, 14.6 ± 1.1 seconds, P = .028); the NCV of sciatic nerve was significantly reduced (DN-Con, 38.8 ± 2.4 m/s, DN + Bup, 30.5 ± 2.0 m/s, P = .003), and sciatic nerve injury (as indicated by axonal area) was more severe in the bupivacaine-treated DN group (DN-Con, 11.6 ± 0.3 μm, DN + Bup, 7.5 ± 0.3 μm, P < .001). In addition, DPI treatment significantly improved nerve function (VF responses, 17.3 ± 1.3 g; PWTL, 13.4 ± 1.1 seconds; NCV, 35.6 ± 3.1 m/s) and mitigated loss of axonal area (9.6 ± 0.3 μm). Compared to the DN + Bup group (without DPI), the levels of lipid peroxides and hydroperoxides, as well as the protein expression of NOX2, NOX4, and Caspase-3, were significantly reduced in the DN + Bup + DPI group (P < .05).
Conclusions: Subcutaneous injection of DPI appears to protect against the functional and neurohistological damage of bupivacaine-blocked sciatic nerves in a high-fat diet/streptozotocin-induced DN model.

确定研究的主要结果并证明研究的次要结果：通常越少越好

Defining the Primary Outcomes and Justifying Secondary Outcomes of a Study: Usually, the Fewer, the Better

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设计和开展研究的第一步是确定主要和任何次要的研究结果。在实验，准实验或分析观察研究中，主要研究结果与主要研究目标相一致。同样，次要研究结果与次要研究目标相一致。一项特定的主要研究结果奠定了实验假设的基础，同时在字面上被纳入了假设。在方法部分，作者清楚地陈述和定义每个主要和任何次要研究结果变量。同样，在这部分，作者清楚地描述了如何测量所有主要和任何次要研究结果变量。作者会提供足够的细节，使临床医生，统计学家或信息学家能够准确地知道要测量的内容，使其他研究人员可以在各自研究场所重复测量结果。作者公布证据（最好）或其他记录以证明任何应用的测量仪器，工具或量表的有效性和可靠性。一个常见的错误（通常是致命的研究设计缺陷）是对现有测量仪器，工具或量表进行再创造（“本土化”）或修改而没有提供其有效性和可靠性的任何证据。最佳的主要结果是所采用的干预与现有或合理的证据相关联。一个实验包括太多的主要结果可能导致（a）研究无法聚焦相关问题，（b）如果治疗效果在整个结果中不同，很难给出合理的解释。在研究设计和结果中包含次要变量需要证明其合理性。如果次要结果可以为主要终点提供支持证据，那么次要结果特别有帮助。复合终点通常是由几个互相关联的结果变量组成的终点。在设计一项研究时，研究人员将复合终点的组成部分限定在感兴趣的干预最有希望产生影响的变量上，并且最好是在有初步证据的情况下。理想情况下，强复合终点的组成部分具有相似的治疗效果，频率和严重程度，最重要的是类似的严重程度。

（张松译 陈杰校）

One of the first steps in designing and conducting a research study is identifying the primary and any secondary study outcomes. In an experimental, quasi-experimental, or analytic observational research study, the primary study outcomes arise from and align directly with the primary study aim or objective. Likewise, any secondary study outcomes arise from and directly align with any secondary study aim or objective. One designated primary study outcome then forms the basis for and is incorporated literally into the stated hypothesis. In a Methods section, authors clearly state and define each primary and any secondary study outcome variable. In the same Methods section, authors clearly describe how all primary and any secondary study outcome variables were measured. Enough detail is provided so that a clinician, statistician, or informatician can know exactly what is being measured and that other investigators could duplicate the measurements in their research venue. The authors provide published substantiation (preferably) or other documented evidence of the validity and reliability of any applied measurement instrument, tool, or scale. A common pitfall—and often fatal study design flaw—is the application of a newly created (“home-grown”) or ad hoc modification of an existing measurement instrument, tool, or scale—without any supporting evidence of its validity and reliability. An optimal primary outcome is the one for which there is the most existing or plausible evidence of being associated with the exposure of interest or intervention. Including too many primary outcomes can (a) lead to an unfocused research question and study and (b) present problems with interpretation if the treatment effect differed across the outcomes. Inclusion of secondary variables in the study design and the resulting manuscript needs to be justified. Secondary outcomes are particularly helpful if they lend supporting evidence for the primary endpoint. A composite endpoint is an endpoint consisting of several outcome variables that are typically correlated with each.

In designing a study, researchers limit components of a composite endpoint to variables on which the intervention of interest would most plausibly have an effect, and optimally with preliminary evidence of an effect. Ideally, components of a strong composite endpoint have similar treatment effect, frequency, and severity—with the most important being similar severity.

一种依托咪酯类似物在大鼠实验中表现出较少抑制肾上腺皮质功能、血流动力学更稳定、行为学恢复更快的特性

An Etomidate Analogue With Less Adrenocortical Suppression, Stable Hemodynamics, and Improved Behavioral Recovery in Rats

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背景：ET-26 盐酸盐是一种依托咪酯类似物，被设计为在保留依托咪酯特性即快速起效镇静作用及血流动力学平稳的同时减少对肾上腺皮质功能的抑制作用。本研究比较了 ET-26 盐酸盐、依托咪酯以及镇静催眠药丙泊酚作用于大鼠的麻醉效能、血流动力学稳定、以及恢复特性。

方法：本实验取三只大鼠的血浆及肝组织匀浆离体进行高表达脂质层析法分析得出 ET-26 盐酸盐的代谢半衰期。"上下"实验得出三种药物的 50%催眠剂量（HD50）。应用相同剂量的三种药物评估麻醉效果和平均动脉压。血清皮质醇激素浓度应用酶联免疫法分析得到。大鼠使用均等的三种药物的恢复能力使用开放场地水迷宫实验与乳酸钠林格液进行比较。

结果：ET-26 盐酸盐在大鼠血浆和孵育肝匀浆中的代谢半衰期分别为 81±6 分钟和 126±12 分钟（平均值±标准差）。大鼠的在体实验表明，ET-26 盐酸盐使大鼠翻正能力消失的作用比依托咪酯低三倍。均等剂量下，静脉注射丙泊酚与 ET-26 盐酸盐（-10.7mmHg）和依托咪酯（-19.4mmHg）相比使平均动脉压相较于基线下降更多（-27.9mmHg）。使用均等剂量的 ET-26 盐酸盐和丙泊酚 ACTH1 激发实验 15 分钟（P＜.001）、30 分钟（P＜.001）和 60 分钟（P=.002）血清皮质醇激素浓度前者更高。静脉单次快速注射，ET-26 盐酸盐组与丙泊酚组相比空间感恢复更快，自发性活动恢复则更慢。

结论：ET-26 盐酸盐的麻醉效能和血流动力学稳定性与依托咪酯类似，但是抑制肾上腺皮质功能的副作用更小；空间感恢复较丙泊酚更快，与依托咪酯类似。（曹雪译 潘艳、薛张纲校）

BACKGROUND:ET-26 hydrochloride (ET-26HCl) is a novel etomidate analogue designedto alleviate the adrenocortical suppression caused by etomidate while retainingthe rapid sedative-hypnotic onset and stable hemodynamic features of etomidate.This study compared the anesthetic effect, hemodynamic stability, and recovery profiles of ET-26HCl, etomidate, and the sedative-hypnotic drug propofol in rats.

METHODS: The metabolic half-life of ET-26HCl was determined in vitro using highperformance liquid chromatography analysis of samples of rat plasma and liverhomogenates taken from 3 animals. Hypnotic median effective doses (HD50)

ofET-26HCl, etomidate, and propofol were determined by up-and-down methods.Anesthesia effect and mean arterial pressure were estimated using equivalentintravenous (IV) doses of propofol, etomidate, and ET-26HCl in the rats. Serum
concentrations of corticosterone were analyzed by enzyme-linked immunosorbentassay. The ability of rats to recover from the sedative-hypnotic effects of thedrugs was evaluated using open field and Morris water maze tests at equipotentdoses of propofol, etomidate, ET-26HCl, and normal saline.
RESULTS: The metabolic half-life of ET-26HCl was 81 ± 6 minutes in rat plasma and126 ± 12 minutes in incubation liver homogenate (mean ± standard deviation),respectively. In vivo experiments showed that the potency of ET-26HCl to cause a loss of righting reflex in rats was 3 times lower than that of etomidate in therats. IV propofol caused a greater decrease in mean arterial pressure relative tothe baseline (-27.9 mm Hg) than did ET-26HCl (-10.7 mm Hg) and etomidate (-19.4mm Hg) at equipotent doses. Serum corticosterone levels after drug administrationwere significantly higher in the ET-26HCl group than in the etomidate group atequivalent doses when measured 15 ($P < .001$), 30 ($P < .001$), and 60 ($P = .002$)minutes after stimulation with adrenocorticotropic hormone (ACTH1-24). Recoveryof spatial orientation from anesthesia induced by an IV bolus injection wasfaster with ET-26HCl than with propofol, but recovery of spontaneous activity wasslower.
CONCLUSIONS: ET-26HCl has anesthetic potency and hemodynamic stability similar toetomidate, but it caused less adrenocortical hormone synthesis suppression thanetomidate and faster spatial orientation recovery from anesthesia than propofol, which was similar to etomidate.

剖宫产严重产后出血的危险因素：病例对照研究

Risk Factors for Severe Postpartum Hemorrhage AfterCesarean Delivery: Case-Control Studies

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背景：与分娩前行剖宫产术的女性相比，分娩过程中行剖宫产的女性发生产后出血的风险增加了。为了明确在行分娩前剖宫产女性及行分娩中剖宫产的女性两组间的个体危险因素和严重产后出血之间是否存在联系及联系的强度，需要依据剖宫产的亚型来进行分层分析。
方法：为了确定分娩前剖宫产及分娩中剖宫产两组女性人群的严重产后出血的危险因素，我们进行了两项病例对照研究。研究队列纳入人群是在 2002 至 2012 年在美国第三产科中心分娩的女性人群。每一项研究中，所有的病例都是出血量超过 1500 毫升或者是在术中或术后输血持续到术后 48 小时。对行分娩前或分娩中剖宫产的女性发生严重产后出血的危险因素采用分离逻辑回归模型进行验证。
结果：分娩前剖宫产组，实验组纳入 269 个病例，对照组 550 个病例。分娩前剖宫产中严重产后出血具有最高校正比值比的临床因素是全麻（校正比值比是 22.3，95%的置信区间是 4.9-99.9；参照组是椎管内麻醉），多胎妊娠（校正比值比是 8.0，95%置信区间是 4.2-15.0；参照组是单胎妊娠），前置胎盘（校正比值比是 6.3，95%

置信区间 3.4-11.8）。分娩中剖宫产组，实验组纳入 278 个病例，对照组 572 个病例 ◦分娩中剖宫产中发生严重产后出血具有最高校正比值比的临床因素是全麻（校正比值比是 5.4，95%置信区间 1.7-17.1），多胎妊娠（校正比值比是 3.2，95%置信区间 1.7-6.3），产前血色素小于等于 9.9g/dL（校正比值比是 3.0，95%置信区间 1.3-6.9；参照组是产前血色素大于等于 11g/dL）。

结论：行分娩前及分娩中剖宫产的女性人群拥有共同的严重产后出血的危险因素（全麻和多胎妊娠）。然而，两组中严重产后出血的危险因素不同，当计划对行分娩前或分娩中剖宫产的高危病人进行干预时,识别出这些不同可能是重要的。

（胡翔翔译 潘艳、薛张纲校）

BACKGROUND: Women who undergo intrapartum caesarean delivery (CD) are at increased risk of postpartum hemorrhage (PPH) compared with those undergoing prelabor CD. To determine whether the presence and strength of the associations between individual risk factors and severe PPH vary among women undergoing prelabor CD or intrapartum CD, stratified analyses are needed according to CD subtype.

METHODS: To identify risk factors for severe PPH within 2 distinct CD populations, prelabor CD and intrapartum CD, we performed 2 case-control studies. Women in each study cohort delivered at a tertiary obstetric center in the United States between 2002 and 2012. For each study, cases were women who had a blood loss ≥1500 mL or who received an intraoperative or postoperative transfusion up to 48 hours after delivery. Risk factors for severe PPH among women undergoing prelabor CD or intrapartum CD were examined in separate logistic regression models.

RESULTS: For prelabor CD, we identified 269 cases and 550 controls. Clinical factors with the highest adjusted odds for severe PPH during prelabor CD were general anesthesia (adjusted odds ratio [aOR] = 22.3; 95% confidence interval [CI], 4.9–99.9; reference group = spinal anesthesia), multiple pregnancies (aOR = 8.0; 95% CI, 4.2–15.0; reference group = singleton pregnancy), and placenta previa (aOR = 6.3; 95% CI, 3.4–11.8). For intrapartum CD, we identified 278 cases and 572 controls. Clinical factors with the highest adjusted odds for severe PPH during intrapartum CD were general anesthesia (aOR = 5.4; 95% CI, 1.7–17.1), multiple pregnancies (aOR = 3.2; 95% CI, 1.7–6.3), and a predelivery hemoglobin ≤ 9.9 g/dL (aOR = 3.0; 95% CI, 1.3–6.9; reference group = predelivery hemoglobin ≥ 11 g/dL).

CONCLUSIONS: Women who undergo prelabor CD and intrapartum CD have several shared risk factors for severe PPH (general anesthesia and multiple pregnancies). However, the risk factor profiles for severe PPH differed between these CD cohorts. Recognizing these differences may be important when planning resources and interventions for high-risk patients undergoing either prelabor or intrapartum CD. (Anesth Analg 2017;125:523–32)

病态胎盘附着患者的标准化输血治疗方法

A Standardized Approach for Transfusion Medicine Support in Patients With Morbidly Adherent Placenta.

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Anesthesia & Analgesia 2017 125 603-608.

背景：在美国，由于剖宫产率的升高（2014 年 32.2%），粘连性胎盘的发病率从每千人 0.8 增加至 3.0。粘连性胎盘患者分娩时，平均失血范围在 2000 到 5000 毫升，常需大量输血治疗。我们报道了本机构针对这类患者的多学科治疗方法，以及 5 年期间的输血治疗结果。
方法：我们回顾了 2009 年 7 月 1 日至 2014 年 7 月 1 日符合研究条件的胎盘疾病的患者数据，我们通过术前胎盘疾病清单来优化围产期出血患者的治疗。
结果：136 名患者的胎盘在术后接受了检查，其中 21 名有粘连性胎盘，39 名有显微镜下粘连性胎盘，17 名有植入性胎盘，17 名有穿透性胎盘，42 名无胎盘粘连（其中 11 名有前置胎盘）。对于每种类型，患者接受血制品输注的比率为 71%（粘连性胎盘），28%（显微镜下粘连性胎盘），82%（植入性胎盘），82%（穿透性胎盘），19%（无胎盘粘连）。对于这些患有胎盘粘连相关疾病的患者，其中 89%进行了分娩后子宫切除，而没有胎盘粘连或仅有显微镜下粘连性胎盘的患者分娩后子宫切除率为 5%。
结论：基于我们的经验和回顾性分析得出的结果，无论是有分娩前影像学证据还是临床怀疑病态胎盘附着的患者，均可从标准化临床处理流程，包括输血治疗中受益。我们发现分娩前已发现的异常胎盘形成患者的大出血是可以预测的，并且无论胎盘粘连程度多少，输血量都很大。本机构的流程可迅速为高危患者在出现危及生命的产科大出血时提供充足的血制品数量和类型。因此，对于已经确诊的病态胎盘粘连患者，计划行剖宫产且可能进行子宫切除，一份程序化的多学科团队制定的清单，包括前瞻性输血治疗等，是最佳的临床实践。
（刘雯珺译 潘艳、薛张纲校）
BACKGROUND: The incidence of placenta accreta (PA) has increased from 0.8 to 3.0 in 1000 pregnancies, driven by increased rates of cesarean deliveries (32.2% in 2014) of births in the United States. The average blood loss for a delivery complicated by PA ranges from 2000 to 5000 mL, frequently requiring substantial transfusion medicine support. We report our own institutional multidisciplinaryapproach for managing such patients, along with transfusion medicine outcomes, in this setting over a 5-year period.
METHODS:We reviewed records for patients referred to our program in placental disorders from July 1, 2009, to July 1, 2014. A placental disorders preoperative checklist was implemented to ensure optimal management of patients with peripartum hemorrhage.
RESULTS:Of 136 patients whose placentas were reviewed postpartum, 21 had PA, 39 had microscopic PA, 17 had increta, 17 had percreta, and 42 had no accreta (of which 11 had placenta previa). For each subtype, the percentage of patients receiving blood products were 71% (PA), 28% (microscopic PA), 82% (increta), 82% (percreta), and 19% (no accreta). Among patients with PA or variants, 89% of patients with PA or variants underwent postpartum hysterectomy, compared to only 5% of patients with no or microscopic PA.
CONCLUSIONS:Based on our experience and on the findings of our retrospective analysis, patients presenting with either antepartum radiological evidence or clinical suspicion of morbidly adherent placenta will benefit from a standardized protocol for clinical management, including transfusion medicine support. We found that massive hemorrhage is predictable when abnormal placentation is identified predelivery and that

blood product support is substantial regardless of the degree of placental invasiveness. The protocol at our institution provides immediate access to sufficient volumes and types of blood products at delivery for patients at highest risk for life-threatening obstetric hemorrhage. Therefore, for patients with a diagnosis of morbidly adherent placenta scheduled for planned cesarean delivery with possible hysterectomy, a programmatic checklist that mobilizes a multidisciplinary team, including proactivetransfusion medicine support, represents best practices.

世界卫生组织建议围手术期进行吸氧管理来预防手术部位感染：一个危险的简化策略？

The New World Health Organization Recommendations on Perioperative Administration of Oxygen to Prevent Surgical Site Infections: A Dangerous Reductionist Approach?

Manuel Wenk, MD, PhD, Hugo Van Aken, MD, PhD, and Alexander Zarbock, MD, PhD
Anesthesia & Analgesia 2017 125 682-687

2016 年 10 月，世界卫生组织（World Health Organization，WHO）发布了关于预防手术部位感染（surgical site infections，SSIs）的建议。其中包括了建议术中至术后 6 小时内吸氧浓度为 80%。SSIs 已成为一个全球性的健康问题，WHO 这次的建议值得赞赏。然而这项建议仅仅只关注手术病人的“切口”，却忽视了高浓度吸氧对病人其他器官系统的影响并可能恶化病人的预后。

WHO 强烈建议高浓度吸氧，尽管证据水平仅为中度。然而，忽视高浓度吸氧潜在的致命的并发症来实现这一目标似乎是不合适的，特别是高浓度吸氧预防 SSI 的证据水平还不足。因此，这一策略在麻醉医师和手术医师间引起激烈的讨论。

在大多数临床情况下，正常血容量、正常血压、正常血糖、正常体温、正常通气显然可以安全应用于大多数病人。然而，像 WHO 建议的那样，任意地在术中至术后 6 小时内进行高浓度吸氧，这一策略在麻醉学和围手术医学上还有待商榷，这将在本文中进一步讨论。

（王雨婷译 潘艳、薛张纲校）

In October 2016, the World Health Organization (WHO) published recommendations for preventing surgical site infections (SSIs). Among those measures is a recommendation to administer oxygen at an inspired fraction of 80% intra- and postoperatively for up to 6 hours. SSIs have been identified as a global health problem, and the WHO should be commended for their efforts. However, this recommendation focuses only on the patient’s “wound,” ignores other organ systems potentially affected by hyperoxia, and may ultimately worsen patient outcomes.

The WHO advances a “strong recommendation” for the use of a high inspired oxygen fraction even though the quality of evidence is only moderate. However, achieving this goal by disregarding other potentially lethal complications seems inappropriate, particularly in light of the weak evidence underpinning the use of high fractions of oxygen to prevent SSI. Use of such a strategy thus should be intensely discussed by anesthesiologists and perioperative physicians.

Normovolemia, normotension, normoglycemia, normothermia, and normoventilation can clearly be safely applied to most patients in most clinical scenarios. But the liberal

application of hyperoxemia intraoperatively and up to 6 hours postoperatively, as suggested by the WHO, is questionable from the viewpoint of anesthesia and perioperative medicine, and its effects will be discussed in this article.

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儿童全麻苏醒期躁动风险量表的研制与验证：一项前瞻性观察研究

Development and Validation of a Risk Scale for Emergence Agitation After General Anesthesia in Children: A Prospective Observational Study

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背景：苏醒期躁动是小儿全麻术后常见的并发症。阶段 2 的研究目标是在行七氟醚麻醉的小儿中建立预测模型（EA 风险量表）预测小儿 EA 的发发病率，通过我们之前阶段 1 和阶段 2 的回顾性分析研究数据，确定阶段 2 前瞻性观察性队列研究中的 EA 风险量表的有效性。

方法：利用我们以前研究中 120 例患者的数据，采用 logistic 回归分析预测 1 期 EA 的发病率。通过使用 Akaike 信息准则逐步选择程序确定了预测的最优组合。计算出选定预测因子的 β 系数，并确定预测因子的得分。EA 的风险规模的预测能力是由接受者操作特性曲线（ROC）、ROC 区曲线下（指数）和 95%可信区间（CI）计算而得。在第 2 阶段，使用另一组 100 名患者（在全身麻醉下进行小手术）证实了 EA 风险量表的有效性。分别计算 ROC 曲线、指数、最佳临界点，点的敏感性和特异性。此外，我们计算了灰色区域，这两个点之间的敏感性和特异性分别 90%。

结果：在 1 期的多变量 Logistic 回归分析最终的模型包括以下 4 个预测因子：年龄（OR:-0.38；95% CI=-0.81- 0.00），小儿麻醉行为评分（OR:0.65；95% CI=-0.09-1.40），麻醉时间（OR,0.60；95% CI=-0.18 -1.19），手术过程（斜视手术 OR:2.53；95% CI=1.30-3.75,扁桃体手术 OR:2.71；95% CI=0.99-4.45）。EA 风险量表包括这 4 个预测因子，从 1 到 23 分不等。在第 2 阶段，EA 的发生率为 39%。1 阶段的 OR 指数为 0.84（95% CI=0.74-0.94），2 阶段的 OR 指数为 0.81（95% CI=0.72-0.89）。EA 风险量表的最佳截止点为 11（灵敏度＝87%，特异性＝61%）。灰色区域从 10 到 13 分，包括 38%的病人。

结论：我们研制并验证了行七氟醚麻醉的儿童的 EA 风险量表。在验证队列，该量表具有良好的预测性能（OR 指数大于 0.8）。EA 风险量表可用于预测儿童的 EA，并为高危人群采取预防策略。这种基于评分的预防性方法应该进行前瞻性研究，以评估这种策略的

（吴俊梅译 潘艳、薛张纲校）

BACKGROUND: Emergence agitation (EA) is a common complication in children after general anesthesia. The goal of this 2-phase study was (1) to develop a predictive model (EA risk scale) for the incidence of EA in children receiving sevoflurane anesthesia by performing a retrospective analysis of data from our previous study (phase 1) and (2) to determine the validity of the EA risk scale in a prospective observational cohort study (phase 2).

METHODS: Using data collected from 120 patients in our previous study, logistic

regression analysis was used to predict the incidence of EA in phase 1. The optimal combination of the predictors was determined by a stepwise selection procedure using Akaike information criterion. The beta-coefficient for the selected predictors was calculated, and scores for predictors determined. The predictive ability of the EA risk scale was assessed by a receiver operating characteristic (ROC) curve, and the area under the ROC curve (c-index) was calculated with a 95% confidence interval (CI). In phase 2, the validity of the EA risk scale was confirmed using another data set of 100 patients (who underwent minor surgery under general anesthesia). The ROC curve, the c-index, the best cutoff point, and the sensitivity and specificity at the point were calculated. In addition, we calculated the gray zone, which ranges between the two points where sensitivity and specificity, respectively, become 90%.
RESULTS: In phase 1, the final model of the multivariable logistic regression analysis included the following 4 predictors: age (logarithm odds ratios [OR], -0.38; 95% CI, -0.81 to 0.00), Pediatric Anesthesia Behavior score (logarithm OR, 0.65; 95% CI, -0.09 to 1.40), anesthesia time (logarithm OR, 0.60; 95% CI, -0.18 to 1.19), and operative procedure (logarithm OR, 2.53; 95% CI, 1.30-3.75 for strabismus surgery and logarithm OR, 2.71; 95% CI, 0.99-4.45 for tonsillectomy). The EA risk scale included these 4 predictors and ranged from 1 to 23 points. In phase 2, the incidence of EA was 39%. The c-index of phase 1 was 0.84 (95% CI, 0.74-0.94), and the c-index of phase 2 was 0.81 (95% CI, 0.72-0.89). The best cutoff point for the EA risk scale was 11 (sensitivity = 87% and specificity = 61%). The gray zone ranged from 10 to 13 points, and included 38% of patients.
CONCLUSIONS: We developed and validated an EA risk scale for children receiving sevoflurane anesthesia. In our validation cohort, this scale has excellent predictive performance (c-index > 0.8). The EA risk scale could be used to predict EA in children and adopt a preventive strategy for those at high risk. This score-based preventive approach should be studied prospectively to assess the safety and efficacy of such a strategy.

围术期静脉血栓栓塞：综述

Perioperative Venous Thromboembolism: A Review.

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Anesthesia & Analgesia. 2017 125 403-412.

静脉血栓栓塞（VTE）是围手术期增加患者的发病率、死亡率和医疗费用的一个重要问题。它也被认为是最可预防的术后并发症。在过去的 20 年内尽管广泛的采用指南预防，它的发病率并没有实质性的改变。目前的预防工作还不够这是越来越明显的。使用强效抗凝药可降低静脉血栓栓塞的发生率，但增加出血和感染的风险。随着近年来对静脉血栓形成的病理生理学的更多学习。人们越来越重视除了抗凝剂所调控的“传统凝血级联反应”之外的组织因子、单核细胞、中性粒细胞、中性粒细胞外的携带物、微泡和血小板血栓的形成和扩展。这些最近的研究在一定程度上解释了为什么阿司匹林在防止血栓传播方面表现出显著的效果。血管内皮功能障碍，传统上认为是动脉血栓形成的危险因素，静脉瓣尖端独特的环境为静脉血栓的形成起着重要的作用，这表明新的治疗方式，如他汀类药物的作用。并不是所有的患者都有同等的风险患静脉血栓栓塞，即使在接受高危手术时，也需要更好的工具来准确

预测静脉血栓栓塞的风险。只有这样我们才能有效的个体化预防和权衡静脉血栓栓塞的风险与治疗相关的风险。由于细胞类型和参与血栓形成的途径的不同，使用低安全剂量止血调节疗法如抗凝剂，抗血栓和抗血小板药物的综合治疗方案可能会更有效。

(叶志祥译 潘艳、薛张纲校)

Venous thromboembolism (VTE) is a significant problem in the perioperative period, increasing patient morbidity, mortality, and health care costs. It is also considered the most preventable of the major postoperative complications. Despite widespread adoption of prophylaxis guidelines, it appears that morbidity from the disease has not substantially changed within the past 2 decades. It is becoming clear that current prophylaxis efforts are not sufficient. Using more potent anticoagulants may decrease the incidence of VTE, but increase the risk for bleeding and infection. Much has been learned about the pathophysiology of venous thrombogenesis in recent years. Beyond the "traditional coagulation cascade," which anticoagulants modulate, there is a growing appreciation for the roles of tissue factor, monocytes, neutrophils, neutrophil extracellular traps, microvesicles, and platelets in thrombus initiation and propagation. These recent studies explain to some degree why aspirin appears to be remarkably effective in preventing thrombus propagation. Endothelial dysfunction, traditionally thought of as a risk factor for arterial thrombosis, plays an important role within the cusps of venous valves, a unique environment where the majority of venous thrombi originate. This suggests a role for newer treatment modalities such as statins. Not all patients have an equal likelihood of experiencing a VTE, even when undergoing high-risk procedures, and better tools are required to accurately predict VTE risk. Only then will we be able to effectively individualize prophylaxis by balancing the risks for VTE against the risks associated with treatment. Given the different cell types and pathways involved in thrombogenesis, it is likely that multimodal treatment regimens will be more effective, enabling the use of lower and safer doses of hemostatic modulating therapies such as anticoagulants, antithrombotics, and antiplatelet medications.

左旋布比卡因减少瑞芬太尼、丙泊酚消费闭环滴定的脑电双频指数引导下进行胸段硬膜外镇痛：一项双盲安慰剂对照研究

Thoracic Epidural Analgesia With Levobupivacaine Reduces Remifentanil and Propofol Consumption Evaluated by Closed-Loop Titration Guided by the Bispectral Index: A Double-Blind Placebo-Controlled Study

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背景：当血流动力学被用于滴定麻醉深度时，胸段硬膜外镇痛（TEA）联合全身麻醉可以使得全麻的用量减半。因此我们确定 TEA 对麻醉需要量的影响，使用闭环控制器通过监测脑电双频指数来自动调控丙泊酚和瑞芬太尼的用量。

方法：采用单中心双盲研究，选择择期行后外侧开胸手术的患者。患者被随机分配接受注射后持续输注 0.5%布比卡因（左旋组）或 0.9%生理盐水溶液（生理盐水组）。全麻是由同一个自动控制器进行的。经食道多普勒探头引导的卒中体积优化在随机化之前进行。主要结果变量是瑞芬太尼在切皮和缝合皮肤之间的自动释放量。记录

到的大动脉低血压。数据以中位数[四分位距]或数量表示（%）
结果：每组十九例患者完成了研究。对脑电双频指数范围在 40-60 的患者进行比较(85 [77-88] vs 83 [72-87]; P = .39),与单纯全麻相比，椎管内阻滞需要较少的瑞芬太尼(0.15 [0.10-0.20] vs 0.23 [0.14-0.25], microg.kg.min; P = .03)和丙泊酚用量(4.3 [3.7-4.9] vs 5.7 [4.6-7.3] mg.kg.h; P = .005) 。两组主要动脉低血压均相似（左旋与生理盐水组，分别为 6 [32%] vs 5 [25%]; P = .46 ；）。
结论：左旋布比卡因硬膜外给药可以减少瑞芬太尼的用量减少三分之一。卒中体积优化后，两组主要的动脉低血压放生率相似。
（刘娟兰译 潘艳、薛张纲校）
BACKGROUND: Thoracic epidural analgesia (TEA) combined with general anesthesia decreases anesthetic requirements by half when hemodynamic criteria are used for the titration of analgesia. We therefore determined the impact of TEA on anesthetic requirements, when a closed-loop controller was used allowing the automated coadministration of propofol-remifentanil guided solely by the Bispectral index.
METHODS: This single-center double-blind study enrolled patients scheduled for elective posterolateral thoracotomy using TEA. Patients were randomly assigned to receive a bolus followed by a continuous infusion of levobupivacaine 0.5% (levo group) or saline 0.9% solution (saline group). General anesthesia was performed by the same automated controller. Stroke volume optimization guided by an esophageal Doppler probe was performed before randomization. The primary outcome variable was the amount of remifentanil delivered by the automated controller between skin incision and closure. Major arterial hypotension was recorded. Data are presented as medians [interquartile range] or number (%)
RESULTS:: Nineteen adult patients per group completed the study. At similar depth of anesthesia evaluated by the percentage of time with the Bispectral index in the range 40-60 (85 [77-88] vs 83 [72-87]; P = .39), patients with neuraxial block required less remifentanil (0.15 [0.10-0.20] vs 0.23 [0.14-0.25], microg.kg.min; P = .03) and propofol (4.3 [3.7-4.9] vs 5.7 [4.6-7.3] mg.kg.h; P = .005). Major arterial hypotension was similar in both groups (6 [32%] vs 5 [25%]; P = .46; levo versus saline group, respectively).
CONCLUSIONS: Epidurally administered levobupivacaine allowed a decrease by one-third of remifentanil requirement. After stroke volume optimization, major arterial hypotension was similar between groups.

在完全弗氏佐剂诱发的炎症疼痛模型中 σ-1 受体/ p38 MAPK 抑制穴位埋线调节疼痛的作用

Role of Sigma-1 Receptor/p38 MAPK Inhibition in Acupoint Catgut Embedding-Mediated Analgesic Effects in Complete Freunds Adjuvant-Induced Inflammatory Pain.

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背景：
内质网伴侣蛋白质 Sigma-1 受体（σ-1 受体）和丝裂原活化蛋白激酶（MAPKs）参与了疼痛机制。穴位刺激在炎性疼痛中发挥了确切的抗痛觉过敏作用。然而，σ-1

受体和 MAPKs 是否与穴位刺激诱导的镇痛作用相关联尚不清楚。本研究探讨了穴位埋线（ACE）的镇痛效果以及抑制 σ-1 和 MAPKs 在穴位埋线镇痛中的作用。

方法：

小鼠进行鞘内置管准备。在炎性疼痛小鼠模型的（完全弗氏佐剂足底注射）双侧昆仑穴（BL60），足三里穴（ST36）和三阴交（SP6）穴位进行穴位埋线。然后，每日注射 σ-1 受体激动剂 PRE-084 或生理盐水 。在完全弗氏佐剂注射前和注射后的 1,3 和 5 天时测量缩爪反应的阈值和爪水肿程度。使用蛋白免疫印迹来评估脊髓 σ-1 受体，p38MAPK 和细胞外信号调节激酶（ERK）的蛋白表达，并在完全弗氏佐剂注射后 1,3 和 5 天利用免疫组化检测 σ-1 受体。

结果：

穴位埋线表现出特定的镇痛作用。穴位埋线增加了小鼠缩爪反应的阈值，并在 1,3 和 5 天显著降低完全弗氏佐剂诱发的爪水肿。穴位埋线降低 σ-1 受体的蛋白表达，其在注射完全弗氏佐剂后 1,3 和 5 天显着增加。除第 5 天，第 1、3 天穴位埋线降低 p38 MAPK 和 ERK 的表达。然而，除了不改变 ERK 的表达，注射 σ-1 受体激动剂 PRE-084 显着逆转了这些改变，。

结论：

本研究表明，在完全弗氏佐剂诱发炎症性疼痛的小鼠模型中，除 ERK 外，穴位埋线通过抑制 σ-1 受体对 p38 MAPK 调节的表达，发挥了抗痛觉过敏作用。

（吴静怡译 潘艳、薛张纲校）

BACKGROUND: The endoplasmic reticulum chaperone protein Sigma-1 receptor (Sig-1 R) and mitogen-activated protein kinases (MAPKs) are involved in the mechanism of pain. Acupoint stimulation exerts an exact antihyperalgesic effect in inflammatory pain. However, whether Sig-1 R and MAPKs are associated with the acupoint stimulation-induced analgesic effects is not clear. This study investigated the analgesic effect of acupoint catgut embedding (ACE) and the inhibition of Sig-1 R and MAPKs in ACE analgesia.

METHODS: Rats were prepared with intrathecal catheter implantation. ACE was applied to bilateral "Kunlun" (BL60), "Zusanli" (ST36), and "Sanyinjiao" (SP6) acupoints in the rat model of inflammatory pain (complete Freund's adjuvant [CFA] intraplantar injection). Then, Sig-1R agonist PRE084 or saline was intrathecally given daily. The paw withdrawal thresholds and paw edema were measured before CFA injection and at 1, 3, and 5 day after CFA injection. Western bolt was used to evaluate the protein expression of spinal Sig-1R, p38MAPK, and extracellular signal-regulated kinase (ERK), and immunohistochemistry of Sig-1R was detected at 1, 3, and 5 days after CFA injection.

RESULTS:ACE exhibited specific analgesic effects. ACE increased paw withdrawal thresholds and markedly decreased CFA-induced paw edema at 1, 3, and 5 days. ACE downregulated the protein expression of Sig-1R, which was increased significantly at 1, 3, and 5 days after CFA injection. ACE decreased the expression of p38 MAPK and ERK at 1 and 3 days but not at 5 days. However, an injection of Sig-1R agonist PRE084 markedly reversed these alterations, except ERK expression.

CONCLUSIONS: The present study demonstrated that ACE exhibited antihyperalgesic effects via the inhibition of the Sig-1R that modulated p38 MAPK, but not ERK, expression in the CFA-induced inflammatory pain model in rats.

在心脏手术病人中，一个有组织的护理过程可以减少围手术期并发症的发生

A Structured Transfer of Care Process Reduces Perioperative Complications in Cardiac Surgery Patients

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Anesthesia & Analgesia: 2017 125 477–482

严重的并发症在术后心脏手术病人的重症监护中很常见。其中的一些并发症可能会在从手术室向重症监护病房(重症监护病房)移交过程中受到影响。护理过程的结构化转移可能会降低通信错误和围手术期并发症的发生率。我们假设，从术中团队到重症监护小组的合作、全面、结构化的护理将减少一组特定的术后并发症。我们通过开发和引进一个综合的多学科的护理过程来检验这一假说。我们在干预前后使用两个护理数据库之间的联系来测量病人的结果:麻醉信息管理系统和关键的护理并发症登记数据库。在研究期间，共有 1127 名术后心脏外科手术的患者，在干预后的 550 名和 577 名患者中。干预前后的总体并发症(P=.154)之间没有统计学上的差异。然而，干预治疗后可预防并发症的减少(P=.023)。这项调查的主要发现是，从手术室到重症监护室的合作全面的护理过程的引入，与那些可预防的并发症的患者有关。(潘艳、薛张纲校）

Serious complications are common during the intensive care of postoperative cardiac surgery patients. Some of these complications may be influenced by communication during the process of handover of care from the operating room to the intensive care unit (ICU) team. A structured transfer of care process may reduce the rate of communication errors and perioperative complications.We hypothesized that a collaborative, comprehensive, structured handover of care from the intraoperative team to the ICU team would reduce a specific set of postoperative complications. We tested this hypothesis by developing and introducing a comprehensive multidisciplinary transfer of care process. We measured patient outcomes before and after the intervention using a linkage between 2 care databases: an Anesthesia Information Management System and a critical care complication registry database.There were 1127 total postoperative cardiac surgery admissions during the study period, 550 before and 577 after the intervention. There was no statistical difference between overall complications before and after the intervention (P = .154). However, there was a statistically significant reduction in preventable complications after the intervention (P = .023).The main finding of this investigation is that the introduction of a collaborative, comprehensive transfer of care process from the operating room to the ICU was associated with patients suffering fewer preventable complications.

住院患者的院内死亡率和脓毒症干预手段之间的关系：一项具体数据的回顾性研究

Relationship Between a Sepsis Intervention Bundle and In-Hospital Mortality Among Hospitalized Patients: A Retrospective Analysis of Real-World Data.

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Anesthesia & Analgesia: 2017 125 507-513.

背景:脓毒症是全身对感染产生的可以导致组织损伤、气管衰竭甚至死亡的一种反应。

为了减少脓毒症相关并发症发生率和死亡率，目前已经有很多研究致力于形成一套有循证依据的可以在脓毒症早期对其进行识别和处理的干预手段。我们对最小创伤性脓毒症干预手段和院内死亡率之间的关系进行了评估。

方法:我们对旧金山加利福利亚大学医学中心的成年患者进行了回顾性队列研究。这些患者的出院时间限定在 2012 年 1 月 1 日至 2014 年 12 月 31 日之间，并且均曾诊断为重症脓毒症或者脓毒症休克。脓毒症干预手段包括：测量血乳酸，抗生素使用前进行血液培养，发生脓毒症表现 3 小时内（急诊室）和 1 小时内（病房）开始使用广谱抗生素，低血压或者乳酸水平高于 4mmol/L 的患者给予静脉液体复苏，液体复苏后仍然低血压的患者给予血管加压药物。我们使用 Poisson 回归对发病率比（IRR）和需要治疗的人数（NNT）进行评估。

结果:完整的干预可以使死亡率降低 30%（调整后的发病率比 IRR 为 0.69，95%置信区间，0.53-0.91）。主要对急诊室发生的重症脓毒症、入院时发生的重症脓毒症、年龄、入院时疾病的严重程度和死亡风险、机体免疫功能不全和入院时的充血性心力衰竭进行了调整。避免 1 例死亡的治疗人数（NNT）为 15（置信区间 ，8-69）。其他死亡独立危险因素包括入院时发生的重症脓毒症（调整后的 IRR 为 0.55，置信区间 ，0.32-0.92）和年龄增加（每增加 10 岁调整后的 IRR 为 1.13 ，置信区间 ，1.03-1.24）。

结论:在调整风险后 ，脓毒症干预可以降低院内死亡率 。调整后的需要治疗人数（NNT）为重症脓毒症患者的结局改善的量化评价提供了合理且可以达到的目标值。

（赵明晔译 潘艳、薛张纲校）

BACKGROUND: Sepsis is a systemic response to infection that can lead to tissue damage, organ failure, and death. Efforts have been made to develop evidence-based intervention bundles to identify and manage sepsis early in the course of the disease to decrease sepsis-related morbidity and mortality. We evaluated the relationship between a minimally invasive sepsis intervention bundle and in-hospital mortality using robust methods for observational data.

METHODS: We performed a retrospective cohort study at the University of California, San Francisco, Medical Center among adult patients discharged between January 1, 2012, and December 31, 2014, and who received a diagnosis of severe sepsis/septic shock (SS/SS). Sepsis intervention bundle elements included measurement of blood lactate; drawing of blood cultures before starting antibiotics; initiation of broad spectrum antibiotics within 3 hours of sepsis presentation in the emergency department or 1 hour of presentation on an inpatient unit; administration of intravenous fluid bolus if the patient was hypotensive or had a lactate level >4 mmol/L; and starting intravenous vasopressors if the patient remained hypotensive after fluid bolus administration. Poisson regression for a binary outcome variable was used to estimate an adjusted incidence-rate ratio (IRR) comparing mortality in groups defined by bundle compliance measured as a binary predictor, and to estimate an adjusted number needed to treat (NNT).

RESULTS: Complete bundle compliance was associated with a 31% lower risk of mortality (adjusted IRR, 0.69, 95% confidence interval [CI], 0.53-0.91), adjusting for SS/SS presentation in the emergency department, SS/SS present on admission (POA), age, admission severity of illness and risk of mortality, Medicaid/Medicare payor status, immunocompromised host status, and congestive heart failure POA. The adjusted NNT to save one life was 15 (CI, 8-69). Other factors independently associated with mortality included SS/SS POA (adjusted IRR, 0.55; CI, 0.32-0.92) and increased age (adjusted IRR,

1.13 per 10-year increase in age; CI, 1.03-1.24).
CONCLUSIONS: The University of California, San Francisco, sepsis bundle was associated with a decreased risk of in-hospital mortality across hospital units after robust control for confounders and risk adjustment. The adjusted NNT provides a reasonable and **achievable goal to observe measureable improvements in outcomes for patients diagnosed with SS/SS.**

活体供肝肝切除术中每搏输出量变异度引导与中心静脉引导的低中心静脉压指导米力农应用：一项随机双盲临床试验

Stroke Volume Variation–Guided Versus Central Venous Pressure–Guided Low Central Venous Pressure With Milrinone During Living Donor Hepatectomy: A Randomized Double-Blinded Clinical Trial

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背景：我们以前曾证明米力农在活体供肝肝切除术的作用。然而，具有较低侵入性的替代中心静脉导管的另一个选择和影响良好的手术预后的围手术期因素尚未确定。目前的研究评估了是否每搏输出量变异度（SVV）引导的方法可以在米力农引起的复杂血管舒张时代替中心静脉置管。
方法：我们随机分配 42 例活体肝移植供体分别接受 SVV 指导或中心静脉压（CVP）指导获得米力农诱导的低 CVP。应用目标 SVV 9%代替 CVP5 毫米汞柱。分别由 2 名外科主治医师应用 4 点法比较 CVP 和 SVV 指导组（n = 19，每组总得分= 38）手术区域的等级评估作为一个主要的结果变量。进行多变量分析，以确定与最佳手术领域相关的独立因素作为事后分析。
结果：通过 Mann-Whitney U 检验皮评价两组间外科领域的评分，或为 1 或 2，发现两组之间没有差异（P = .358）。在血管舒张如 CVP≤5 mm Hg 时 SVV 和 CVP 之间有很弱的相关性（R = -0.06；95%置信区间，-0.09 -0.04；P <0.001）。事后分析表明，年轻人、基线较低 CVP、持续时间较长的米力农可能对提供最佳的手术视野是有帮助的。
结论：米力农诱导的血管舒张功能在活体肝切除术中提供良好的手术环境，不管是否应用低 CVP 的指导方法。然而，SVV 在提示低 CVP 方面并不是一个有用的指标，因为在血管舒张时 SVV 和 CVP 之间很弱的相关性。此外，提供最佳手术视野的因素如供体年龄，主动禁食，适当剂量米力农需要进行进一步的研究，并最好是通过前瞻性研究。
（陆晓斐译 李士通校）

BACKGROUND: We previously demonstrated the usefulness of milrinone for living donor hepatectomy. However, a less-invasive alternative to central venous catheterization and perioperative contributors to good surgical outcomes remain undetermined. The current study evaluated whether the stroke volume variation (SVV)-guided method can substitute central venous catheterization during milrinone-induced profound vasodilation.
METHODS: We randomly assigned 42 living liver donors to receive either SVV guidance or central venous pressure (CVP) guidance to obtain milrinone-induced low

CVP. Target SVV of 9% was used as a substitute for CVP of 5 mm Hg. The surgical field grade evaluated by 2 attending surgeons on a 4-point scale was compared between the CVP- and SVV-guided groups (n = 19, total number of scores = 38 per group) as a primary outcome variable. Multivariable analysis was performed to identify independent factors associated with the best surgical field as a post hoc analysis.
RESULTS: Surgical field grades, which were either 1 or 2, were not found to be different between the 2 groups via Mann-Whitney U test (P = .358). There was a very weak correlation between SVV and CVP during profound vasodilation such as CVP ≤ 5 mm Hg (R = -0.06; 95% confidence interval, -0.09 to -0.04; P < .001). Additional post hoc analysis suggested that younger age, lower baseline CVP, and longer duration of milrinone infusion might be helpful in providing the best surgical field.
CONCLUSIONS: Milrinone-induced vasodilation resulted in favorable surgical environment regardless of guidance methods of low CVP during living donor hepatectomy. However, SVV was not a useful indicator of low CVP because of very weak correlation between SVV and CVP during profound vasodilation. In addition, factors contributing to the best surgical field such as donor age, proactive fasting, and proper dosing of milrinone need to be investigated further, ideally through prospective studies.

仰卧位病人应用挤压式喷雾器鼻腔内给药时导致超量

Intranasal Medication Administration Using a Squeeze Bottle Atomizer Results in Overdosing if Deployed in Supine Patients

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背景：血管收缩剂和局部麻醉剂，通常使用挤压式喷雾器应用在鼻腔黏膜上以消肿、止血和镇痛。尽管广泛使用，但很少有涉及安全管理技术细节的临床指南。本研究的目的是量化，通过模拟病人在仰卧位和直立位时的位置和管理参数，能够可靠地提供每次喷雾到鼻腔粘膜所需药物的液体量。
方法：对 10 名麻醉患者进行了样本的研究。提供者被指示使用 25 mL 蘸和管鼻挤压瓶将测试溶液（无菌水）应用到直立位（90°仰角）和仰卧位（0°仰角）的人体模型上。在人体模型试验的基础上，分别在 0°、15°、30°、45°和 90°的条件下对喷雾瓶进行了附加试验，确定了喷头工作角度与液体分配量的关系。
结果：与垂直位置相比（0.041±0.02 mL），在仰卧位时每喷雾平均体积明显较大（0.56±0.22 mL，差异为 0.52 mL，95%可信区间[CI]，0.37-0.67 mL，P<0.001）。使用标准 0.25%的溶液，将给药体积转化为肾上腺素剂量，仰卧位和直立位相比每喷估计增加 1300μg（95% CI，925-1675μg，P<0.001）。随着给药角度≤30°，与瓶身从 90°角开始，药物体积明显增加。45°时的给药体积与 90°的体积无差别（0.032～0.006 ml，0.030～0.005 ml，p＝.34）。
结论：我们发现，在人体模型上应用鼻腔挤压瓶时，仰卧位时每喷的体积（即剂量）比直立位增加了 14 倍。由于在临床实践中使用挤压瓶使用雾化器时，曾报道经鼻给药的药物毒性和意外过量的发生，我们的数据表明，所有滴鼻药物应给予精确的计量装置。如果没有计量设备，用药应在≥45°角度时给予；然而，我们推荐给药时病

人为坐位，瓶身呈 90°，因为当角度小于 45°时，只有一个小的变化会导致药物剂量大幅提高。
（陆晓斐 译 李士通 校）

BACKGROUND: Vasoconstrictors and local anesthetics are commonly administered using a squeeze bottle atomizer to the nasal mucosa to reduce edema, limit bleeding, and provide analgesia. Despite widespread use, there are few clinical guidelines that address technical details related to safe administration. The purpose of this study was to quantify, via simulation, the amount of liquid delivered to the nasal mucosa when patients are in the supine and upright positions and administration parameters that would reliably provide the desired amount of medication per spray.
METHODS: A convenience sample of 10 anesthesia residents was studied. Providers were instructed to use a 25-mL dip and tube nasal squeeze bottle to administer the test solution (sterile water) to a mannequin in the upright (90° elevation) and supine (0° elevation) position. After mannequin testing, additional testing was completed with the spray bottles at 0°, 15°, 30°, 45°, and 90° to determine the relationship between the angles of administration and the amount of liquid dispensed.
RESULTS: The mean volume delivered per spray was substantially greater when administered in the supine position (0.56 ± 0.22 mL) compared with the upright position (0.041 ± 0.02 mL, difference = 0.52 mL, 95% confidence interval [CI], 0.37-0.67 mL, P < .001). Converting the administered volume to the dose of phenylephrine that would be administered using our standard 0.25% solution, an estimated additional 1300 mcg is delivered per spray in the supine position compared with the upright position (95% CI, 925-1675 mcg, P < .001). Administration with a delivery angle of ≤30° resulted in significantly more volume than when the bottle was oriented at a 90° angle. The volume dispensed at 45° was not different from the volume delivered at 90° (0.032 ± 0.006 mL vs 0.030 ± 0.005 mL, P = .34).
CONCLUSIONS: We found a 14-fold increase in the volume (ie, dose) delivered per spray when a nasal squeeze bottle was used with a mannequin in the supine position compared with the upright position. Given the reported toxicity from the use of intranasal medication and the inadvertent overdosing that occurs when squeeze bottle atomizers are used in clinical practice, our data suggest that all intranasal drugs should be administered with a precise, metered-dose device. If a metered-dose device is unavailable, the medication should be delivered at an angle of ≥45°; however, we recommend administering the drug with the patient in the sitting position and the bottle at 90° because only a small change in angle below 45° will result in a substantial increase in medication delivered.

随机交叉试验比较应用两种光棒插管技术比较模拟颈椎制动患者插管过程中的颈椎移动：喉镜辅助与传统光棒插管

A Randomized Crossover Study Comparing Cervical Spine Motion During Intubation Between Two Lightwand Intubation Techniques in Patients With Simulated Cervical Immobilization: Laryngoscope-Assisted Versus Conventional Lightwand Intubation

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背景：在颈椎制动的患者中，推下颌可以引起颈椎运动。同时使用喉镜可以帮助光棒插管，使中线位置固定，光棒在口腔自由运动而无颚推力。我们比较了喉镜辅助光棒插管（LALI）与常规光棒插管（CLI）对模拟颈椎固定气管插管患者颈椎运动的影响。

方法：在这项随机交叉研究，对 20 例模拟颈部制动的患者在插管前和插管过程中测量枕骨- C1 、C1-C2 和 C2-C5 节段的颈椎夹角 插管分别使用 LALI 和 CLI 技术。颈椎运动的定义是指在插管过程中颈段测量角度的变化。

结果：当使用 LALI 和 CLI 技术时，枕骨- C1 段的颈椎运动分别为 5.6°（4.3）和 9.3°（4.5），（平均差异[98.33%CI]；3.8°[7.2 - 0.3]；P = .007）。在其他颈段，两种技术之间的差异不显著（C1-C2 节段-0.1°[- 2.6 - 2.5]； P =.911 和 C2-C5 节段-0.2°[- 2.8- 2.5]；P =.795）。

结论：在模拟颈椎制动患者的气管插管过程中，与 CLI 技术相比，LALI 技术产生较少的上颈椎运动。

（张秋丽 译 李士通 校）

BACKGROUND: In patients with cervical immobilization, jaw thrust can cause cervical spine movement. Concurrent use of a laryngoscope may facilitate lightwand intubation, allowing midline placement and free movement of the lightwand in the oral cavity without jaw thrust. We compared the effects of laryngoscope-assisted lightwand intubation (LALI) versus conventional lightwand intubation (CLI) on cervical spine motion during intubation in patients with simulated cervical immobilization.

METHODS: In this randomized crossover study, the cervical spine angle was measured before and during intubation at the occiput-C1, C1-C2, and C2-C5 segments in 20 patients with simulated cervical immobilization who underwent intubation using both the LALI and CLI techniques. Cervical spine motion was defined as the change from baseline in angle measured at each cervical segment during intubation.

RESULTS: Cervical spine motion at the occiput-C1 segment was 5.6° (4.3) and 9.3° (4.5) when we used the LALI and CLI techniques, respectively (mean difference [98.33% CI]; -3.8° [-7.2 to -0.3]; P = .007). At other cervical segments, it was not significantly different between the 2 techniques (-0.1° [-2.6 to 2.5]; P = .911 in the C1-C2 segment and -0.2° [-2.8 to 2.5]; P = .795 in the C2-C5 segment).

CONCLUSIONS: The LALI technique produces less upper cervical spine motion during intubation than the CLI technique in patients with simulated cervical immobilization.

与异氟醚相比，七氟醚减少急性呼吸窘迫综合征大鼠肺内而不是肺外肺损伤

Sevoflurane, Compared With Isoflurane, Minimizes Lung Damage in Pulmonary but Not in Extrapulmonary Acute Respiratory Distress Syndrome in Rats

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背景：挥发性麻醉药可调节急性呼吸窘迫综合征（ARDS）的炎症反应。然而，目前尚不清楚他们是否根据 ARDS 病因不同而反应不同。我们推测，七氟醚和异氟醚在体内和体外对肺内（P）和肺外（EXP）急性呼吸窘迫综合征的肺损伤影响并无差异。

方法：24 只 wistar 大鼠，随机分为应用七氟醚和异氟醚全身麻醉（1-2 分钟）。动物再随机接受大肠杆菌脂多糖（LPS）气管内（ARDSp）或腹腔注射（ARDSexp），诱导 ARDS 后 24 小时，再接受 1 个最小肺泡浓度的七氟烷或异氟烷麻醉 60 分钟。主要观察指标为肺组织中白细胞介素（IL）-6 mRNA 的表达。次要终点包括气体交换、肺力学、组织学和 IL-10 mRNA 的表达，核因子相关因子 2（Nrf2），表面活性蛋白（SP）-B、血管细胞黏附分子-1，内皮阿米洛利敏感钠通道亚单位 α 和 γ，和钠-钾-ATPα 泵亚基 α1（α1-NA，K-ATPase）1、β（β1-NA，K-ATPase）。另外的 ARDSp 和 ARDSexp 大鼠（n = 6）应用硫喷妥钠麻醉而不进行机械通气（NV）作为对照组。另外，为了确定如何七氟醚和异氟醚作用于 II 型上皮细胞，A549 人肺上皮细胞受 LPS 刺激 24 小时后（20μ 克/毫升），进一步暴露于七氟烷或异氟烷后（1 最小肺泡浓度）60 分钟，并进行了 SP-B 表达的量化。

结果：在 ARDSp 组，与异氟醚相比，七氟醚可在更大程度上降低 IL-6 的表达(P = .04)。与异氟醚组相比，七氟醚组的肺静态顺应性（P = .0049）和肺泡萎陷（P = .033）均更低。而 Nrf2（P = .036），SP-B（P = .042）和 β1-NA，K-ATP 酶（P = 038）在七氟醚均显著高表达。在 ARDSexp，七氟醚和异氟醚之间在肺泡萎陷、肺力学以及分子参数，均没有观察到显著差异。在体外，七氟醚组 SP-B 的表达明显比异氟醚高（P =. 026）。

结论：与异氟醚相比，七氟醚并没有影响 ARDSexp 的肺部炎症，但它确实降低了 ARDSp 的肺部炎症。

（张秋丽 译 李士通 校）

BACKGROUND: Volatile anesthetics modulate inflammation in acute respiratory distress syndrome (ARDS). However, it is unclear whether they act differently depending on ARDS etiology. We hypothesized that the in vivo and in vitro effects of sevoflurane and isoflurane on lung damage would not differ in pulmonary (p) and extrapulmonary (exp) ARDS.

METHODS: Twenty-four Wistar rats were randomized to undergo general anesthesia (1-2 minutes) with sevoflurane and isoflurane. Animals were then further randomized to receive Escherichia coli lipopolysaccharide (LPS) intratracheally (ARDSp) or intraperitoneally (ARDSexp), and 24 hours after ARDS induction, they were subjected to 60 minutes of sevoflurane or isoflurane anesthesia at 1 minimal alveolar concentration. The primary outcome measure was interleukin (IL)-6 mRNA expression in lung tissue. Secondary outcomes included gas exchange, lung mechanics, histology, and mRNA expression of IL-10, nuclear factor erythroid 2-related factor-2 (Nrf2), surfactant protein (SP)-B, vascular cell adhesion molecule-1, epithelial amiloride-sensitive Na-channel subunits α and γ, and sodium-potassium-adenosine-triphosphatase pump subunits α1 (α1-Na,K-ATPase) and β1 (β1-Na,K-ATPase). Additional ARDSp and ARDSexp animals (n = 6 per group) were anesthetized with sodium thiopental but not mechanically ventilated (NV) to serve as controls. Separately, to identify how sevoflurane and isoflurane act on type II epithelial cells, A549 human lung epithelial cells were stimulated

with LPS (20 μg/mL) for 24 hours, and SP-B expression was quantified after further exposure to sevoflurane or isoflurane (1 minimal alveolar concentration) for 60 minutes.
RESULTS: In ARDSp, sevoflurane reduced IL-6 expression to a greater degree than isoflurane (P = .04). Static lung elastance (P = .0049) and alveolar collapse (P = .033) were lower in sevoflurane than isoflurane, whereas Nrf2 (P = .036), SP-B (P = .042), and β1-Na,K-ATPase (P = .038) expressions were higher in sevoflurane. In ARDSexp, no significant differences were observed in lung mechanics, alveolar collapse, or molecular parameters between sevoflurane and isoflurane. In vitro, SP-B expression was higher in sevoflurane than isoflurane (P = .026).
CONCLUSIONS: Compared with isoflurane, sevoflurane did not affect lung inflammation in ARDSexp, but it did reduce lung inflammation in ARDSp.

资源匮乏地区急诊剖宫产术乳酸林格式液与生理盐水选择：一项务实的临床试验

Ringer's Lactate Versus Normal Saline in Urgent Cesarean Delivery in a Resource-Limited Setting: A Pragmatic Clinical Trial

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背景：晶体的常规用于在剖宫产术围手术期的液体管理。很少有研究确定在产科麻醉中晶体液的选择。我们比较了 Ringer 乳酸（RL）与 0.9%生理盐水（NS）对产妇和新生儿血液 pH 值的影响 ,以及在低资源环境下紧急剖宫产术后 24 小时的发病率。我们的假设是，RL 将导致低于 NS 组 30%的酸中毒率。
方法：这是一个务实的前瞻性随机双盲对照试验，纳入在穆拉戈国家转诊医院病房从 2011 年 9 月到 2012 年 5 月的产妇。对五百例产妇进行了研究；随机分为 252 例生理盐水组和 248 例 RL 组。分析术前、术后母体静脉血气及胎盘脐动脉血气。主要结果是母亲酸中毒的发生率，如术后静脉血 pH 值低于 7.32 或之前正常孕妇的碱剩余低于-3。母亲 24 小时术后发病率、新生儿酸碱度和新生儿碱剩余是主要次要结局。这项研究是在 ClinicalTrials.gov 官网注册 NCT01585740。
结果：产妇酸中毒的总发生率为 NS 组 38%，RL 组 29%（相对风险，1.29；95%置信区间，1.01-1.66；P = .04）。NS 组 32%产妇术后静脉 pH 值下降至低于 7.32，在 RL 组为 19%（相对风险，1.65；95%置信区间，1.18-2.31；P = .003）两组术后碱剩余相对下降低于-3 无统计学意义。两组产妇 24 小时术后发病率和新生儿结局的发生率无显著差异。
结论：NS 可作为紧急剖宫产术中的液体治疗替代 RL 的安全选择，尽管代谢性酸中毒的发生率增加。
（沈辰 译 李士通 校）
BACKGROUND: Crystalloids are used routinely for perioperative fluid management in cesarean delivery. Few studies have determined the crystalloid of choice in obstetric anesthesia. We compared the effects of Ringer's lactate (RL) versus 0.9% normal saline (NS) on maternal and neonatal blood pH and 24-hour postoperative morbidity in urgent cesarean delivery in a low-resource setting. Our hypothesis was that RL would result in 30% less acidosis than NS.

METHODS: This was a pragmatic prospective double-blind randomized controlled trial in the Mulago National Referral Hospital Labor Ward Theater from September 2011 to May 2012. Five hundred parturients were studied; 252 were randomly assigned to NS and 248 to RL groups. Preoperative and postoperative maternal venous blood gases and placental umbilical arterial cord blood gases were analyzed. The primary outcome was incidence of maternal acidosis, as defined by a postoperative drop in venous pH below 7.32 or reduction in base excess below -3 in a previously normal parturient. Maternal 24-hour postoperative morbidity, neonatal pH, and neonatal base excess were the main secondary outcomes. The study was registered in ClinicalTrials.gov as NCT01585740.
RESULTS: The overall incidence of maternal acidosis was 38% in NS and 29% in RL (relative risk, 1.29; 95% confidence interval, 1.01-1.66; P = .04). Thirty-two percent of parturients in NS experienced a drop in venous pH below 7.32 postoperatively, compared with 19% in RL (relative risk, 1.65; 95% confidence interval, 1.18-2.31; P = .003). The comparative drop in base excess postoperatively below -3 between the 2 groups was not statistically significant. There were no significant differences in the incidence of maternal 24-hour postoperative morbidity events and neonatal outcomes between the 2 groups.
CONCLUSIONS: NS may be a safe choice for intraoperative fluid therapy in urgent cesarean delivery as RL, albeit with an increased incidence of metabolic acidosis

严重术中高血糖与开颅术后复合感染的发生无关：一项观察性研究

Severe Intraoperative Hyperglycemia Is Independently Associated With Postoperative Composite Infection After Craniotomy: An Observational Study

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背景：开颅术后感染增加了致残率和死亡率的风险。危险因素的识别和纠正应优先考虑。术中高血糖与开颅术后感染的相关性研究不足。
方法：共 2 个主要的医疗中心的 224 例患者进行前瞻性研究，以评估术中严重高血糖（SIH，血糖≥180 mg/dL）与接受开颅手术患者术后感染的高风险相关。麻醉诱导后立即采血并行动脉血气分析，拔管前再进行动脉血气分析。并确定开颅术后 7 天内出现的任何类型的感染。
结果：开颅术后第一周内新术后复合感染发生率为 10%（n＝22）。体重、性别、美国麻醉医师协会（ASA）评分，术前和/或术中使用类固醇，和糖尿病与术后感染没有相关性。拟合多因素 logistic 回归模型调整为急诊外科、手术时间长、年龄≥65 年后，SIH 与术后感染的独立相关（比值比[95%置信区间]，4.17[1.50-11.56]，P = .006）。
结论：SIH 与行开颅手术治疗患者术后新发复合感染独立相关。是否在开颅手术中预防 SIH 对降低术后感染的风险是未知的，需要进一步研究评价。
（沈辰 译 李士通 校）
BACKGROUND: Postoperative infection after craniotomy carries an increased risk of morbidity and mortality. Identification and correction of the risk factors should be

prioritized. The association of intraoperative hyperglycemia with postoperative infections in patients undergoing craniotomy is inadequately studied.
METHODS: A total of 224 patients were prospectively enrolled in 2 major medical centers to assess whether severe intraoperative hyperglycemia (SIH, blood glucose ≥180 mg/dL) is associated with an increased risk of postoperative infection in patients undergoing craniotomy. Arterial blood samples were drawn and analyzed immediately after anesthetic induction and again before tracheal extubation. The new onset of any type of infection within 7 days after craniotomy was determined.
RESULTS: The incidence of new postoperative composite infection was 10% (n = 22) within the first week after craniotomy. Weight, sex, American Society of Anesthesiologists score, preoperative and/or intraoperative steroid use, and diabetes mellitus were not associated with postoperative infection. SIH was independently associated with postoperative infection (odds ratio [95% confidence interval], 4.17 [1.50-11.56], P = .006) after fitting a multiple logistic regression model to adjust for emergency surgery, length of surgery, and age ≥65 years.
CONCLUSIONS: SIH is independently associated with postoperative new-onset composite infections in patients undergoing craniotomy. Whether prevention of SIH during craniotomy results in a reduced postoperative risk of infection is unknown and needs to be appraised by further study.

肝移植患者血浆凝血酶生成的恢复

Restoration of Thrombin Generation in Plasma From Liver Transplant Recipients

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背景：在大多数国家，血浆输注仍然是肝移植（LT）的主要止血治疗。然而，需要大量的血浆来达到临床相关因素的增加。凝血酶原复合物（PCC）在华法林逆转过程中是一种低剂量的血浆替代品，但其疗效一直没有得到很好的研究。
方法：收集 28 例 LT 患者在移植前（T0）和移植后 30 分钟（T1）的血标本，测定 X 因子及抗凝血酶水平。比较 LT 和华法林血浆患者， PCC（0.2 和 0.4 IU/mL）和正常血浆置换 10%容量的体外作用，使用凝血酶生成（TG）测定测量滞后时间、凝血酶的峰值相比与内源性凝血酶潜能（ETP）。
结果：随着国际标准化率从 1.7 上升到 3，凝血状态在 T1 时恶化，X 因子从 49%下降到 28%。TG 测量在 T0 和 T1 显示正常的滞后时间和 ETP，但 T0 为正常低峰，T1 为低于正常峰值。两剂量 PCC 均增加峰值和 ETP，而 10%体积的血浆置换对 TG 的影响最小。由于低抗凝血酶，在 LT 血浆中加入 0.40.4 IU/mL 的 PCC 后，凝血酶抑制率似乎非常缓慢。相同剂量的 PCC 和血浆对华法林逆转作用均表现不足。
结论：PCC 较血浆能更有效地降低 LT 患者的 TG。由于较慢凝血酶抑制，LT 患者所需的 PCC 剂量似乎比逆转华法林的剂量低。
（顾明露 译 李士通 校）
BACKGROUND: Plasma transfusion remains the mainstay hemostatic therapy during liver transplantation (LT) in most countries. However, a large volume is required for

plasma to achieve clinically relevant factor increases. Prothrombin complex concentrate (PCC) is a low-volume alternative to plasma in warfarin reversal, but its efficacy has not been well studied in LT.
METHODS: Blood samples were collected from 28 LT patients at baseline (T0) and 30 minutes after graft reperfusion (T1). Factor X and antithrombin levels were measured. Ex vivo effects of PCC (0.2 and 0.4 IU/mL) and 10% volume replacement with normal plasma were compared in LT and warfarin plasma by measuring lag time, thrombin peak, and endogenous thrombin potential (ETP) using thrombin generation (TG) assay.
RESULTS: Coagulation status was worsened at T1 as international normalized ratio increased from 1.7 to 3.0, and factor X was decreased from 49% to 28%. TG measurements showed normal lag time and ETP at T0 and T1, but low-normal peak at T0, and below-normal peak at T1. Both doses of PCC increased peak and ETP, while 10% volume plasma had minimal effects on TG. Thrombin inhibition appears to be very slow after adding 0.4 IU/mL of PCC in LT plasma due to low antithrombin. The same doses of PCC and plasma were insufficient for warfarin reversal.
CONCLUSIONS: Reduced TG in LT can be more effectively restored by using PCC rather than plasma. The required doses of PCC for LT patients seem to be lower than warfarin reversal due to slow thrombin inhibition.

神经病理性痛的干预：一项系统性评价概述

Interventions for Neuropathic Pain: An Overview of Systematic Reviews

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神经病理性疼痛的众多干预（NEUP）是可用的，但其治疗仍不满意。我们系统地总结了随机对照试验中干预措施为 NEUP 的证据并系统评价（SRs）。截至 2015 年 3 月，共检索到五个电子数据库。使用测量工具 A 评估系统评价的研究质量。包含在 SRs 中的 97 项研究中，其中最常见的干预措施包括药物治疗（59%）和外科治疗（15%）。分析的 SRs 多数为中等质量。摘要的结论中超过 50%的关于功效的和大约 80%的关于安全性的结论是不确定的。有效的干预措施，阐述了糖尿病痛性神经病变（普瑞巴林，加巴喷丁，某些三环类抗抑郁药[TCAs]，阿片类药物，抗抑郁药和抗惊厥药）、带状疱疹后遗神经痛（加巴喷丁、普瑞巴林、某些抗抑郁药，抗抑郁药和抗惊厥药、阿片类药物，丙戊酸钠，辣椒碱，利多卡因），根性神经痛（硬膜外皮质类固醇，重复经颅磁刺激[rTMS]，髓核摘除术），颈神经根性疼痛（rTMS），腕管综合征（腕管综合征、肘管综合征）（简单的减压和尺神经转位）、三叉神经痛（卡马西平、拉莫三嗪、和匹莫齐特治疗难治性病例，rTMS），HIV 相关的神经病变（局部辣椒碱），和中枢 NeuP（某些三环类抗抑郁药，普瑞巴林，大麻，和 rTMS）。证据表明 NeuP 的干预常常是不确定的或完全缺乏的。关于 NeuP 治疗的新的随机对照试验是必要的，他们应当是安全和使用明确的诊断标准。
（顾明露 译 李士通 校）
Numerous interventions for neuropathic pain (NeuP) are available, but its treatment remains unsatisfactory. We systematically summarized evidence from systematic reviews

(SRs) of randomized controlled trials on interventions for NeuP. Five electronic databases were searched up to March 2015. Study quality was analyzed using A Measurement Tool to Assess Systematic Reviews. The most common interventions in 97 included SRs were pharmacologic (59%) and surgical (15%). The majority of analyzed SRs were of medium quality. More than 50% of conclusions from abstracts on efficacy and approximately 80% on safety were inconclusive. Effective interventions were described for painful diabetic neuropathy (pregabalin, gabapentin, certain tricyclic antidepressants [TCAs], opioids, antidepressants, and anticonvulsants), postherpetic neuralgia (gabapentin, pregabalin, certain TCAs, antidepressants and anticonvulsants, opioids, sodium valproate, topical capsaicin, and lidocaine), lumbar radicular pain (epidural corticosteroids, repetitive transcranial magnetic stimulation [rTMS], and discectomy), cervical radicular pain (rTMS), carpal tunnel syndrome (carpal tunnel release), cubital tunnel syndrome (simple decompression and ulnar nerve transposition), trigeminal neuralgia (carbamazepine, lamotrigine, and pimozide for refractory cases, rTMS), HIV-related neuropathy (topical capsaicin), and central NeuP (certain TCAs, pregabalin, cannabinoids, and rTMS). Evidence about interventions for NeuP is frequently inconclusive or completely lacking. New randomized controlled trials about interventions for NeuP are necessary; they should address safety and use clear diagnostic criteria.

辐射药理分析鞘内注射 BRL52537（κ-阿片受体激动剂）、Pregabalin（钙通道调节剂）、AF 353（P2X3 受体拮抗剂）和 A804598（P2X7 受体拮抗剂）等药物组合治疗神经病理性痛大鼠

Isobolographic Analysis of Drug Combinations With Intrathecal BRL52537 (κ-Opioid Agonist), Pregabalin (Calcium Channel Modulator), AF 353 (P2X3 Receptor Antagonist), and A804598 (P2X7 Receptor Antagonist) in Neuropathic Rats

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背景：神经病理性疼痛应采用多种药物联合治疗，因为神经病理性疼痛的机制涉及多种生理原因，并由多种途径介导。在这项研究中，我们定义了 BRL52537 药理作用（κ-阿片受体激动剂），普瑞巴林（钙通道调节剂），AF 353（P2X3 受体拮抗剂），和 A804598（P2X7 受体拮抗剂）的药理相互作用。

方法：雄性 Sprague Dawley 大鼠通过脊神经结扎（SNL）建立神经病理性疼痛模型，并用 von Frey 细丝测定机械刺激的反应。通过鞘内注射途径给药，观察药物效果，以及辐射分析评价药物相互作用等。应用实时聚合酶链反应评价空白组、SNL 组和药物治疗的 SNL 组大鼠的脊髓或背根神经节疼痛相关受体 mRNA 的表达水平。

结果：鞘内给予 BRL52537，普瑞巴林，AF 353，和 A804598 对 SNL 大鼠有治疗效果。关于联合用药的研究，鞘内联合应用 BRL52537 与普瑞巴林或 A804598 具有协同作用，与其他药物的组合表现出相加作用。观察效能的排名顺序如下：BRL52537 +普瑞巴林> BRL52537 + A804598 >普瑞巴林+ AF 353 > A804598 +普瑞巴林>

BRL52537＋AF 353 > AF 353 +A804598。实时聚合酶链反应表明 P2X3 受体和钙通道 mRNA 表达水平的变化，而 P2X7 受体和 κ-阿片受体的表达水平没有改变。
结论：这些结果表明，鞘内联合应用 BRL 52537、普瑞巴林、AF 353 和 A804598 有协同或相加作用减少 SNL 诱发的疼痛，这一结果表明提高单药疗效的可能性。（徐燕伊方译 李士通校）

BACKGROUND: Neuropathic pain should be treated with drug combinations exhibiting multiple analgesic mechanisms of action because the mechanism of neuropathic pain involves multiple physiological causes and is mediated by multiple pathways. In this study, we defined the pharmacological interaction of BRL52537 (κ-opioid agonist), pregabalin (calcium channel modulator), AF 353 (P2X3 receptor antagonist), and A804598 (P2X7 receptor antagonist).
METHODS: Animal models of neuropathic pain were established by spinal nerve ligation (SNL) in male Sprague-Dawley rats, and responses to the mechanical stimulation using von Frey filaments were measured. Drugs were administered by intrathecal route and were examined for antiallodynic effects, and drug interactions were evaluated using isobolographic analysis. The mRNA expression levels of pain-related receptors in each spinal cord or dorsal root ganglion of naïve, SNL, and drug-treated SNL rats were evaluated using real-time polymerase chain reaction.
RESULTS: Intrathecal BRL52537, pregabalin, AF 353, and A804598 produced antiallodynic effects in SNL rats. In the drug combination studies, intrathecal coadministration of BRL52537 with pregabalin or A804598 exhibited synergistic interactions, and other drugs combinations showed additivity. The rank order of potency was observed as follows: BRL52537 + pregabalin > BRL52537 + A804598 > pregabalin + AF 353 > A804598 + pregabalin > BRL52537 + AF 353 > AF 353 + A804598. Real-time polymerase chain reaction indicated that alterations of P2X3 receptor and calcium channel mRNA expression levels were observed, while P2X7 receptor and κ-opioid receptor expression levels were not altered.
CONCLUSIONS: These results demonstrated that intrathecal combination of BRL52537, pregabalin, AF 353, and A804598 synergistically or additively attenuated allodynia evoked by SNL, which suggests the possibility to improve the efficacy of single-drug administration.