房颤：围术期的现有证据和管理策略

Atrial Fibrillation: Current Evidence and Management Strategies During the Perioperative Period

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Anesthesia & Analgesia: 2020 130 2-13

房颤（AF）是围术期最常见的一种心律失常，先前认为这是一种良性、自限性疾病，但近期数据表明围术期房颤与相当高的发病率和死亡率相关，且可预测部分患者发生长期房颤及卒中的风险。尽管存在已知的危险因素，但大部分房颤的发生依然无法预测，尤其是在非心脏手术之后。因此，将围术期风险降至最低的策略是最有益的，其中包括避免潜在的诱发心律失常因素，以及积极治疗与患者、手术相关可能导致房颤的的因素。除了处理房颤本身，临床医生还必须解决房颤引起的血流动力学紊乱症状，以防止终末器官功能障碍的发生。这篇综述旨在讨论有关房颤的诱发因素、危险因素及转归结果的现有证据，以及在当前围术期环境中存在的一些争议问题。

Atrial fibrillation (AF) is the most common arrhythmia in the perioperative period. Previously considered a benign and self-limited entity, recent data suggest that perioperative AF is associated with considerable morbidity and mortality and may predict long-term AF and stroke risk in some patients. Despite known risk factors, AF remains largely unpredictable, especially after noncardiac surgery. As a consequence, strategies to minimize perioperative risk are mostly supportive and include avoiding potential arrhythmogenic triggers and proactively treating patient- and surgery-related factors that might precipitate AF. In addition to managing AF itself, clinicians must also address the hemodynamic perturbations that result from AF to prevent end-organ dysfunction. This review will discuss current evidence with respect to causes, risk factors, and outcomes of patients with AF, and address current controversies in the perioperative setting.

（陈思涵 译 陈杰 校）

连续六个夜班后摄入咖啡因对麻醉住院医师驾驶行为的影响

Impact of Caffeine Ingestion on the Driving Performance of Anesthesiology Residents After 6 Consecutive Overnight Work Shifts

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Anesthesia & Analgesia: 2020 130 66-75

背景：麻醉科住院医师培训因涉及对住院患者的监护需要通宵工作，从而导致住院医师睡眠方式的改变以及睡眠时间不足。在通宵工作后，住院医师通常选择咖啡提神，为通勤回家做准备。

方法：研究在麻醉住院医师连续通宵工作 6 天后立即饮用一种咖啡因能量饮料（含 160mg 咖啡因）后在高保真、虚拟现实驾驶模拟器（使用驾驶员导航系统的弗吉尼亚驾驶安全实验室）中驾驶表现的影响。26 名住院医师参与了这项研究，并在驾驶模拟测试开始前 60min 将其随机分为饮用含咖啡因或不含咖啡因的

能量饮料组。在随后的一周夜班工作结束后，两组住院医师进行了相同的驾驶测试（交叉试验设计），并使用心理运动警戒任务测试（PVT）来评估其反应时间及注意力下降的程度。

结果：在连续进行 6 个夜班工作后，咖啡因能量饮料组的麻醉科住院医师在开始行驶的前 10min 内表现出较灵活的操控油门、转向以及加速的能力，随后也证明了在最后驾驶的 30min 内，与非咖啡因能量饮料组相比，改善的驾驶能力与更少的障碍物碰撞相关（时期 2：0.65 vs 0.87；时期 3：0.47 vs 0.95；P= 0.03）。饮用含咖啡因能量饮料可明显改善住院医师在模拟驾驶中最后 30min 内的驾驶能力。两组之间的平均反应时间存在显著差异（278.9 ± 29.1 vs 294.0 ± 36.3 毫秒; P = 0.021），而在主要失误次数（0.09 ± 0.43 vs 0.27 ± 0.55; P =0 .257）和次要失误次数方面（1.05 ± 1.39 vs 2.05 ± 3.06; P = 0.197）却没有显著差异。

结论：在连续 6 天夜班工作后饮用含咖啡因的能量饮料，麻醉科住院医师在高保真驾驶模拟器的测试中可表现出改善的驾驶能力，包括显著减少了碰撞的发生率以及更快的反应时间。

（陈思涵 译 陈杰 校）

BACKGROUND: Residency training in anesthesiology involves care of hospitalized patients and necessitates overnight work, resulting in altered sleep patterns and sleep deprivation. Caffeine consumption is commonly used to improve alertness when fatigued after overnight work, in preparation for the commute home.

METHODS: We studied the impact of drinking a caffeinated energy drink (160 mg of caffeine) on driving performance in a high-fidelity, virtual reality driving simulator (Virginia Driving Safety Laboratory using the Driver Guidance System) in anesthesiology resident physicians immediately after 6 consecutive night-float shifts. Twenty-six residents participated and were randomized to either consume a caffeinated or noncaffeinated energy drink 60 minutes before the driving simulation session. After a subsequent week of night-float work, residents performed the same driving session (in a crossover fashion) with the opposite intervention. Psychomotor vigilance task (PVT) testing was used to evaluate reaction time and lapses in attention.

RESULTS: After 6 consecutive night-float shifts, anesthesiology residents who consumed a caffeinated energy drink had increased variability in driving for throttle, steering, and speed during the first 10 minutes of open-road driving but proceeded to demonstrate improved driving performance with fewer obstacle collisions (epoch 2: 0.65 vs 0.87; epoch 3: 0.47 vs 0.95; P = .03) in the final 30 minutes of driving as compared to driving performance after consumption of a noncaffeinated energy drink. Improved driving performance was most apparent during the last 30 minutes of the simulated drive in the caffeinated condition. Mean reaction time between the caffeine and noncaffeine states differed significantly (278.9 ± 29.1 vs 294.0 ± 36.3 milliseconds; P = .021), while the number of major lapses (0.09 ± 0.43 vs 0.27 ± 0.55; P = .257) and minor lapses (1.05 ± 1.39 vs 2.05 ± 3.06; P = .197) was not significantly different.

CONCLUSIONS: After consuming a caffeinated energy drink on conclusion of 6 shifts of night-float work, anesthesiology residents had improved control

of driving performance variables in a high-fidelity driving simulator, including a significant reduction in collisions as well as slightly faster reaction times.

鞘内给予芬太尼用于剖宫产的疗效评价:一项随机对照试验的系统回顾和荟萃分析联合试验序贯分析

Efficacy of Intrathecal Fentanyl for Cesarean Delivery: A Systematic Review and Meta-analysis of Randomized Controlled Trials With Trial Sequential Analysis

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Anesthesia & Analgesia: 2020 130 111-125

背景：芬太尼和吗啡是剖宫产手术期间行腰麻过程中加入布比卡因最常用的两种阿片类药物。许多临床试验已经评估了不同剂量芬太尼加入鞘内布比卡因用于腰麻的有效性和安全性，但其益处、危害和最佳剂量仍不清楚。本研究目的是系统地回顾芬太尼单独加入鞘内布比卡因和联合吗啡加入布比卡因用于剖宫产时腰麻的有效性证据。

方法：检索关键电子数据库(PubMed、Embase 和 Cochrane 图书馆)中剖宫产人群相关的随机对照试验。主要结果是腰麻失败率，这是通过转为全麻或术中辅助镇痛来评估的。两位评审员使用标准化的电子表格独立地提取数据。结果以 95% 置信区间的相对风险或平均差异表示。

结果：荟萃分析纳入 17 项随机对照临床试验(大多数被判断为低或不明确的偏倚风险)，共 1064 名参与者的数据。芬太尼单独加入鞘内布比卡因可减少术中辅助镇痛的需要(相对风险，0.18;95%置信区间,0.11 - -0.27;需治疗次数 4 次),降低恶心/呕吐发生率(相对危险度，0.41;95%置信区间,0.24 - -0.70;需治疗次数 6.5 次)，且术后首次需要镇痛时间较长(平均差值 91 分钟;95%可信区间,69 - 113)。在转为全身麻醉的发生率(相对危险度，0.67;95% CI, 0.12-3.57)、低血压的发生率、感觉神经阻滞起效时间或运动阻滞的持续时间方面没有差异。然而，鞘内加入芬太尼与较高的术中瘙痒发生率相关(相对风险，5.89;95%置信区间,2.07 - -16.79;需要加害次数，13.5)。与单纯的鞘内布比卡因复合吗啡相比，将芬太尼加入鞘内布比卡因吗啡具有类似的益处，显著减少了术中辅助镇痛的需要(相对风险，0.16;95%置信区间,0.03 - -0.95;9)。漏斗图分析显示纳入研究中存在发表偏倚的可能性。

结论：目前证据表明，芬太尼既可单独作为鞘内布比卡因的添加剂，也可与吗啡联合作为鞘内布比卡因的添加剂用于腰麻下的剖宫产。由于纳入研究的发表偏倚、小样本量和高偏倚风险的可能性，故需谨慎对待此研究结果。

（蒋旭亮 译 陈杰 校）

BACKGROUND: Fentanyl and morphine are the 2 most commonly added opioids to bupivacaine for spinal anesthesia during cesarean delivery. Numerous clinical trials have assessed efficacy and safety of different doses of fentanyl added to intrathecal bupivacaine for spinal anesthesia, yet its benefit, harm, and optimal dose remain unclear. This study aimed to systematically review the evidence of the efficacy of fentanyl when added to intrathecal bupivacaine alone and when added to bupivacaine with morphine for spinal anesthesia during cesarean delivery.

METHODS: Key electronic databases (PubMed, Embase, and Cochrane Library) were searched for randomized controlled trials in the cesarean delivery population. The primary outcome was the failure rate of spinal anesthesia, as assessed by the need for either conversion to general anesthesia or intraoperative analgesic supplementation. Two reviewers independently extracted the data using a standardized electronic form. Results are expressed as relative risks or mean differences with 95% CIs.
RESULTS: Seventeen randomized controlled clinical trials (most judged as low or unclear risk of bias) with 1064 participants provided data for the meta-analysis. Fentanyl added to intrathecal bupivacaine alone reduced the need for intraoperative supplemental analgesia (relative risk, 0.18; 95% CI, 0.11-0.27; number needed to treat, 4) and the incidence of nausea/vomiting (relative risk, 0.41; 95% CI, 0.24-0.70; number needed to treat, 6.5), with longer time to first postoperative analgesia request (mean difference, 91 minutes; 95% CI, 69-113). No difference was observed regarding the need for conversion to general anesthesia (relative risk, 0.67; 95% CI, 0.12-3.57), the incidence of hypotension, the onset of sensory block, or the duration of motor block. However, the addition of intrathecal fentanyl was associated with higher incidence of intraoperative pruritus (relative risk, 5.89; 95% CI, 2.07-16.79; number needed to harm, 13.5). The inclusion of fentanyl to intrathecal bupivacaine-morphine compared to intrathecal bupivacaine-morphine alone conferred a similar benefit, with a significantly reduced need for intraoperative supplemental analgesia (relative risk, 0.16; 95% CI, 0.03-0.95; number needed to treat, 9). Analysis using a funnel plot indicated a possibility of publication bias in included studies.
CONCLUSIONS: Current evidence suggests a benefit of using fentanyl as both an additive to intrathecal bupivacaine alone and to intrathecal bupivacaine combined with morphine for cesarean delivery under spinal anesthesia. The possibility of publication bias, small sample size, and high risk of bias in some of the included studies warrant treating the results with caution.

呼气末屏气试验预测容量反应性不适合开腹手术

End-Expiratory Occlusion Test to Predict Fluid Responsiveness Is Not Suitable for Laparotomic Surgery

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Anesthesia & Analgesia: 2020 130 151-158

背景:呼气末屏气试验可预测重症监护患者的容量反应性;然而，它在手术室应用的效力受到质疑。本研究评估开腹手术中呼气末屏气试验来预测扩容的效果。
方法:本研究纳入46例患者:第一阶段(n = 26)持续15秒的呼气末屏气测试,随之扩容,即 5min 内给予 250ml 胶体和第二阶段(n = 20)持续 25 秒呼气末屏气测试，随之扩容。最后 10 例病人进行横膈压监测。扩容后心指数增加> 15%的患者为有效应答者。分析脉压变异度、每搏量（SV）指数、心脏指数。以扩容的应答者状态为预后指标，建立呼气末屏气试验引起的 SV 和脉压变化和脉压变化的受试者工作特征曲线。

结果:共有 44 次(38%)扩容被视为有效应答。呼气末屏气试验 15 秒后，血流动力学变量无明显增加。呼气末屏气试验 25 秒后，有效应答者的 SV 指数升高(呼气末屏气试验 25 秒后，有效应答者 vs 无效应答者 37.1±8.8 mL/m vs 35.7 ± 8.6;P<.0001)。呼气末屏气试验不能区分有效和无效应答者。只有脉压变异度在曲线下面积与偶然预期有显著差异(0.7 [0.57-0.81];15 秒呼气末屏气试验 P = .002;和 0.78 (0.64 - -0.89);呼气末屏气试验 25 秒 P = .0001)。开腹后胃压明显下降(4 [2.75-5]vs 2 [2-4] cm H2O;P = .0417);横膈压梯度无明显差异。
结论:在开腹手术中，呼气末试验在区分扩容后有效和无效反应者是不可靠的。（刘碧莹 译 陈杰 校）

BACKGROUND: The end-expiratory occlusion test predicts fluid responsiveness in ventilated intensive care patients; however, its utility in the operating room is questioned. We assessed end-expiratory occlusion test in laparotomic surgery for predicting volume expansion.
METHODS: Forty-six patients were included in this study: stage 1 (n = 26) with an end-expiratory occlusion test of 15 seconds, followed by volume expansion, which consisted of 250 mL of colloid over 5 minutes and stage 2 (n = 20) with an end-expiratory occlusion test of 25 seconds followed by volume expansion. The last 10 patients had transdiaphragmatic pressures probed. Patients with an increase in cardiac index >15% after volume expansion were responders. Pulse pressure variation, stroke volume (SV) index, and cardiac index were analyzed. Receiver operating characteristic curves were established for changes in SV and pulse pressure induced by end-expiratory occlusion test and pulse pressure variation using the responders status for volume expansion as outcome.
RESULTS: A total of 44 (38%) volume expansions were deemed responders. After end-expiratory occlusion test of 15 seconds, no hemodynamic variables were significantly increased. After end-expiratory occlusion test of 25 seconds, SV index increased in responders (37.1 ± 8.8 mL/m after end-expiratory occlusion test of 25 seconds versus 35.7 ± 8.6 before; P < .0001). End-expiratory occlusion test could not discriminate responders from nonresponders. Only pulse pressure variation had significantly different area under the curve from that expected by chance (0.7 [0.57-0.81]; P = .002 for end-expiratory occlusion test of 15 seconds; and 0.78 [0.64-0.89]; P = .0001 for end-expiratory occlusion test of 25 seconds). After laparotomy, gastric pressure decreased significantly (4 [2.75-5] vs 2 [2-4] cm H2O; P = .0417); no difference was noticed in the transdiaphragmatic gradient.
CONCLUSIONS: End-expiratory oc 屏气 clusion test was not reliable to discriminate responders from nonresponders after volume expansion during laparotomic surgery

配备医师的急救直升机上初始格拉斯评分 8 分以上的患者出现镇痛不足情况：一项 10 万余例院外急诊的多中心二次数据分析

Oligoanalgesia in Patients With an Initial Glasgow Coma Scale Score ≥8 in a Physician-Staffed Helicopter Emergency Medical Service: A Multicentric Secondary Data Analysis of >100,000 Out-of-Hospital Emergency Missions

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Anesthesia & Analgesia: 2020 130 176-186

背景：镇痛不足与其他不良事件一样，在院外急救初次镇痛治疗期间较为常见，甚至是在医师在场的情况下。作者分析了格拉斯昏迷评分(GCS)8 分以上的患者在配备医师的急救直升机(p-HEMS)上进行院外救治期间镇痛不足的影响因素。
方法：此项多中心的二次数据分析纳入 2005 年 1 月 1 日至 2017 年 12 月 31 日的在 p-HEMS 上接受急救的有意识的患者。筛选标准是:患者当场的疼痛数字评分（NRS）大于 4 分，GCS 大于 8 分，未行心肺复苏且美国国家咨询航空委员会（NACA）评分小于 6。研究应用多变量的二元回归分析来研究镇痛不足（交接 NRS≥4 或疼痛评分降低<3）的特点。研究期间使用线性回归分析来描述疼痛治疗中的变化。
结果：作者分析了 106,730 名患者的数据（3.6% 数据缺失）。其中 82.9%患者在现场接受了镇痛治疗；79.1%患者接受了镇痛药物，38.6%则接受了非药物干预，其中 37.4%的患者同时接受两种治疗。而 18.4%的患者出现了镇痛不足（置信区间为 18.1-18.6）。与此相关的因素有低 NACA 评分、低 NRS 评分以及出现中枢神经系统或妇产相关的主诉。无临床证据显示，相较于强中效阿片药物、非阿片镇痛药或氯胺酮，使用弱阿片药物（比值比 [OR]）=1.05，95%置信区间 CI,0.68-1.57）与镇痛不足相关。作者观察了这项 12 年的研究中镇痛药物使用的变化，特别是强效阿片药物（芬太尼或舒芬太尼）的使用率从 30.3%增至 42.3%（P 值<0.001）。其中 17.1%的患者（95% CI,16.9-17.3）并未接受任何疼痛治疗。
结论：在这项队列研究中，18.4%的患者出现镇痛不足。特殊主诉，低 NACA 评分、低 NRS 评分与镇痛不足相关。然而，17.1%患者并未行任何镇痛治疗，这提示仍需改进入院前的镇痛治疗。无论何时应启动药物及非药物的镇痛治疗。
（刘碧莹 译 陈杰 校）

BACKGROUND: Oligoanalgesia, as well as adverse events related to the initiated pain therapy, is prevalent in out-of-hospital emergency medicine, even when a physician is present. We sought to identify factors involved in insufficient pain therapy of patients presenting with an initial Glasgow Coma Scale (GCS) score of ≥8 in the out-of-hospital phase, when therapy is provided by a physician-staffed helicopter emergency medical service (p-HEMS).
METHODS: This was a multicenter, secondary data analysis of conscious patients treated in primary p-HEMS missions between January 1, 2005, and December 31, 2017. Patients with a numeric rating scale (NRS) pain score ≥4, GCS score ≥8 on the scene, without cardiopulmonary resuscitation (CPR), and a National Advisory Committee for Aeronautics (NACA) score <VI were included. Multivariable logistic binary regression analyses were used to identify characteristics of oligoanalgesia (NRS ≥4 at handover or pain reduction <3). Linear regression analysis was used to identify changes in pain treatment within the study period.
RESULTS: We analyzed data from 106,730 patients (3.6% missing data at variable level). Of these patients, 82.9% received some type of analgesic therapy on scene; 79.1% of all patients received analgesic drugs, and 38.6% received nonpharmacological interventions, while 37.4% received both types of intervention.

Oligoanalgesia was identified in 18.4% (95% confidence interval [CI], 18.1–18.6) of patients. Factors associated with oligoanalgesia were a low NACA score and a low NRS score, as well as central nervous system or gynecological/obstetric complaints. The use of weak opioids (odds ratio [OR] = 1.05; 95% CI, 0.68–1.57) had no clinically relevant association with oligoanalgesia, in contrast to the use of strong or moderate opioids, nonopioid analgesics, or ketamine. We observed changes in the analgesic drugs used over the 12-year study period, particularly in the use of strong opioids (fentanyl or sufentanil), from 30.3% to 42.3% (P value <.001). Of all patients, 17.1% (95% CI, 16.9–17.3) did not receive any type of pain therapy.
CONCLUSIONS: In the studied p-HEMS cohort, oligoanalgesia was present in 18.4% of all cases. Special presenting complaints, low NACA scores, and low pain scores were associated with the occurrence of oligoanalgesia. However, 17.1% of patients received no type of pain therapy, which suggests a scope for further improvement in prehospital pain therapy. Pharmacological and nonpharmaceutical pain relief should be initiated whenever indicated

儿科患者腰丛神经的深度预测：一项回顾性磁共振研究

Predicting the Depth of the Lumbar Plexus in Pediatric Patients: A Retrospective Magnetic Resonance Imaging Study

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Anesthesia & Analgesia: 2020 130 201-208

背景：腰丛神经（LP）阻滞常用于下肢镇痛中。如果腰丛神经深度（LPD）可预测，操作时间及操作并发症可以大大减少。
方法：作者研究了 361 例儿科患者（<18 岁）的磁共振影像。使用单一及多重因素线性回归分析预测腰丛深度，包括患者年龄、体重、身高、正中线与髂后上棘间距。计算正中线与腰丛最外侧（midline-LP）及髂后上棘间距（midline-PSIS）的比率，结果显示针的穿刺点应位于第四、第五腰椎间隙水平（L4/L5）。同时在第四腰椎水平发现肾脏。
结果：在儿科患者中（<18 岁）L4/L5 水平推测腰丛深度公式为：LPD=0.844×体重(kg) + 25.8 (mm)，(卡方检验 r2 = 0.791; r2 的 95% 置信区间[CI], 0.753–0.829)。总体 midline-LP/midline-PSIS 比值为 0.87 (95% CI, 0.86–0.89)，而在婴幼儿中该比值更高，为 0.87 (95% CI, 0.86–0.89)。在儿科患者中，肾下极在 L4 水平更为常见(婴幼儿为 43.7% ，学龄前儿童为 13.7%)。此项研究中，有 6 名患者（1.7%）在 L4/L5 水平观察到肾脏。
结论：为对儿科患者实行安全有效的腰丛神经阻滞，应考虑腰丛深度及肾脏损伤的风险。
（刘碧莹 译 陈杰 校）
BACKGROUND: The lumbar plexus (LP) block is commonly used for analgesia for lower extremities. If the depth of the LP (LPD) can be predicted, the performance time and procedure-related complications could be reduced.
METHODS: Three hundred sixty-one magnetic resonance images of pediatric patients (<18 years of age) were analyzed. Simple linear regression and multiple

linear regression analyses were performed to predict the LPD using patient age, weight, height, and the distance between the midline and posterior superior iliac spine (midline-PSIS). The ratio of the distance between the midline and the most lateral aspect of the LP (midline-LP) to midline-PSIS (midline-LP/midline-PSIS ratio) was calculated to suggest a needle insertion point at the L4/L5 intervertebral level. The presence of the kidney at the L4 level and the L4/L5 intervertebral level was determined.
RESULTS: The LPD at the L4/L5 intervertebral levels was predicted using the equation LPD = 0.844 × weight (kg) + 25.8 (mm) in pediatric patients <18 years of age (r2 = 0.791; 95% confidence interval [CI] of r2, 0.753–0.829). The overall midline-LP/midline-PSIS ratio was 0.87 (95% CI, 0.86–0.89), and the ratio was higher in neonates and infants (0.98 [95% CI, 0.95–1.02]) than in the other age groups. The presence of the lower kidney pole at the L4 level was common in pediatric patients (43.7% of neonates and infants and 13.7% of toddlers and preschool-aged children). The lower kidney pole was observed at the L4/L5 level in 6 patients (1.7%).
CONCLUSIONS: When LP block is performed in pediatric patients, the LPD and risk of renal injury should be considered for successful and safe analgesic block.

静息脑功能连接预测老年患者静注小剂量咪达唑仑后的脑连接变化
Baseline Functional Connectivity Predicts Connectivity Changes Due to a Small Dose of Midazolam in Older Adults
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Anesthesia & Analgesia: 2020 130 224-232

背景：苯二氮卓类药物在围术期作为抗焦虑药物被广泛使用。一般来说，该类药物会影响认知功能，然而能否对小剂量短效苯二氮卓类药物咪达唑仑的作用进行客观评估尚未可知。为研究该问题，作者对 55-73 岁成人进行了一项前瞻性观察研究。通过有效的心理测验和功能影像技术，研究静脉注射 2mg 咪达唑仑是否影响认知功能。
方法：作者通过使用完善可重复的神经心理状态测试和静息功能磁共振(rs-fMRI)来评估静注 2mg 咪达唑仑的效果。
结果： 咪达唑仑减少即时和延迟记忆，极大的影响了静息功能磁共振的结果。静注咪达唑仑后，基准静息连接显示记忆减退。
结论：即使受试者样本量小，咪达唑仑对脑网络活动的影响在统计学上也有显著意义。若研究者继续完善，静息脑连接功能可能作为评估咪达唑仑对老年患者影响的一个有效手段。
（刘碧莹 译 陈杰 校）
BACKGROUND: In the perioperative context, benzodiazepines are widely used as anxiolytics. They affect cognition in general, but it is unclear whether the effects of a small dose of the short-acting benzodiazepine midazolam can be assessed objectively. To address this scientific question, we conducted a prospective observational study in adults 55–73 years of age. Using both validated psychometric and functional imaging techniques, we determined whether a 2-mg intravenous (IV) dose of midazolam

affects cognitive function.
METHODS: We measured the effect of 2 mg IV of midazolam with both the well-established Repeatable Battery for the Assessment of Neuropsychological Status test and resting-state functional magnetic imaging (rs-fMRI) in older adults.
RESULTS: Midazolam reduces immediate and delayed memory and has a profound and robust effect on rs-fMRI. Baseline resting-state connectivity predicts memory decline after midazolam administration.
CONCLUSIONS: Observed effects of midazolam on brain networks were statistically significant even in a small group of volunteers. If validated by other investigators, resting-state brain connectivity may have utility as a measure to predict sensitivity to midazolam in older adults.

术中呼吸机管理与术后氧合、肺部并发症和死亡率的关系

Association of Intraoperative Ventilator Management With Postoperative Oxygenation, Pulmonary Complications, and Mortality

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Anesthesia & Analgesia: 2020 130 165-175

背景：“肺保护通气”描述了一种包括低潮气量（VTs）和/或低驱动压/平台压的通气策略，并与机械通气后改善的预后相关。 我们评估了术中通气参数（包括呼气末正压[PEEP]，驱动压和潮气量）与 3 个术后结局之间的关系：（1）Pao2/Fio2，（2）术后肺部并发症，（3）30 天死亡率。
方法：我们回顾性分析了从 2006 年至 2015 年在美国单中心接受非心脏大手术并在术后维持机械通气的成年患者。 使用多元回归分析，我们研究了术中呼吸机设置与术后插管时最低 Pao2 / Fio2、出院诊断包括肺部并发症以及院内 30 天死亡率的相关性。
结果：在一个队列的 2096 例病例中，中位 PEEP 为 5 cm H_2O（四分位范围= 4 - 6），中位 VT 为 520 mL（四分位范围= 460 - 580），中位驱动压为 15 cm H_2O（13-19）。经过多变量调整后，术中 PEEP（线性回归估计[B] = -6.04； 95％CI，从-8.22 至-3.87；P <.001），中位 Fio2（B = -0.30；95％CI，从-0.50 至- 0.10；P = .003），以及驱动压> 16 cm H_2O 的小时数（B = -5.40；95％CI，-7.2 至-4.2；P <.001）与术后 Pao2 / Fio2 降低有关。较高的术后 Pao2 / Fio2 比值与降低肺部并发症的风险（每 100 mm Hg 的校正比值比= 0.495；95％CI 为 0.331 - 0.740；P = 0.001，模型 C 统计值为 0.852）和死亡率（调整后的优势比= 0.495； 95％CI 为 0.366-0.606； P <.001，模型 C 统计量为 0.820）相关。术中 VT> 500 mL 的时间也与术后发生肺部并 ；P = .042）。
结论：在非心脏手术后需要术后插管的患者中，中位 Fio2 升高、中位 PEEP 升高以及持续时间长且驱动压升高可预示术后 Pao2 / Fio2 较低。术中 VT> 500 mL 的持续时间是术后肺部并发症增加的独立相关因素。较低的术后 Pao2 / Fio2 比值与肺部并发症和死亡率独立相关。 我们的研究结果表明，术后 Pao2 / Fio2 可能是未来前瞻性研究的潜在目标，该研究旨在研究特定通气策略对减少呼吸机相关肺损伤的影响。

（吴兆艺 译 潘艳、薛张纲）

Abstract

BACKGROUND: “Lung-protective ventilation” describes a ventilation strategy involving low tidal volumes (VTs) and/or low driving pressure/plateau pressure and has been associated with improved outcomes after mechanical ventilation. We evaluated the association between intraoperative ventilation parameters (including positive end-expiratory pressure [PEEP], driving pressure, and VT) and 3 postoperative outcomes: (1) Pao2/fractional inspired oxygen tension (Fio2), (2) postoperative pulmonary complications, and (3) 30-day mortality.

METHODS: We retrospectively analyzed adult patients who underwent major noncardiac surgery and remained intubated postoperatively from 2006 to 2015 at a single US center. Using multivariable regressions, we studied associations between intraoperative ventilator settings and lowest postoperative Pao2/Fio2 while intubated, pulmonary complications identified from discharge diagnoses, and in-hospital 30-day mortality.

RESULTS: Among a cohort of 2096 cases, the median PEEP was 5 cm H2O (interquartile range = 4–6), median delivered VT was 520 mL (interquartile range = 460–580), and median driving pressure was 15 cm H2O (13–19). After multivariable adjustment, intraoperative median PEEP (linear regression estimate [B] = −6.04; 95% CI, −8.22 to −3.87; P < .001), median Fio2 (B = −0.30; 95% CI, −0.50 to −0.10; P = .003), and hours with driving pressure >16 cm H2O (B = −5.40; 95% CI, −7.2 to −4.2; P < .001) were associated with decreased postoperative Pao2/Fio2. Higher postoperative Pao2/Fio2 ratios were associated with a decreased risk of pulmonary complications (adjusted odds ratio for each 100 mm Hg = 0.495; 95% CI, 0.331–0.740; P = .001, model C-statistic of 0.852) and mortality (adjusted odds ratio = 0.495; 95% CI, 0.366–0.606; P < .001, model C-statistic of 0.820). Intraoperative time with VT >500 mL was also associated with an increased likelihood of developing a postoperative pulmonary complication (adjusted odds ratio = 1.06/hour; 95% CI, 1.00–1.20; P = .042).

CONCLUSIONS: In patients requiring postoperative intubation after noncardiac surgery, increased median Fio2, increased median PEEP, and increased time duration with elevated driving pressure predict lower postoperative Pao2/Fio2. Intraoperative duration of VT >500 mL was independently associated with increased postoperative pulmonary complications. Lower postoperative Pao2/Fio2 ratios were independently associated with pulmonary complications and mortality. Our findings

suggest that postoperative Pao2/Fio2 may be a potential target for future prospective trials investigating the impact of specific ventilation strategies for reducing ventilator-induced pulmonary injury.

Monitoring Depth of Hypnosis: Mid-Latency Auditory Evoked Potentials Derived aepEX in Children Receiving Desflurane-Remifentanil Anesthesia
催眠深度监测：源于听觉诱发电位指数（aepEX）的潜伏中期听觉诱发电位在接受地氟烷-瑞芬太尼复合麻醉的儿童患者中的应用

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Anesthesia & Analgesia: 2020 130 194-200

背景：听觉诱发电位指数（aepEX+）监测系统利用潜伏中期听觉诱发电位测定催眠深度，本研究在接受地氟烷-瑞芬太尼复合麻醉的儿童患者中评价了该系统的应用。
方法：75 例 1-18 岁（按年龄分组：分为 1-3 岁,3-6 岁,6-18 岁年龄组，用于亚组分析）的患者被纳入此项前瞻性观察性研究。研究同时记录了 aepEX 和 BIS 数值，其中后者用于对照。研究将 aepEX 区分不同意识水平的能力作为主要研究指标，并根据密歇根大学镇静评分表定义意识水平的程度，同时使用预测概率 Pk 和 ROC 曲线进行分析。呼末地氟烷浓度和 aepEX、BIS 的关系作为次要结局指标，其关系将使用非线性回归模型进行评价。
结果：aepEX 和 BIS 的预测概率值分别为 0.68（95%可信区间，0.53-0.82），0.85（95%可信区间，0.73-0.96，P 值=0.02）。aepEX 和 BIS 的 ROC 曲线下面积分别为 0.89（95%可信区间，0.8-0.95），0.76（95%可信区间，0.68-0.84，P 值=0.04）。当 aepEX 的截断值大于 52 时，其最大敏感度和特异度分别为 81%（95%可信区间，61%-93%），86%（95%可信区间 ，74%-94%）；当 BIS 的截断值大于 65 时，其最大敏感度和特异度分别为 69%（95%可信区间，56%-81%），70%（95%可信区间，57%-81%）。调整年龄的呼末地氟烷浓度的 EC50 值对 aepEX 和 BIS 而言，分别为 0.59MAC（四分位间距，0.38-0.85），0.58MAC（四分位间距，0.41-0.7）。亚组分析表明在 ROC 曲线下面积和 EC50 值上年龄间没有差异。
结论：在接受地氟烷-瑞芬太尼复合麻醉的儿童患者中，aepEX 可以作为区分清醒状态与非清醒状态的可靠指标。
（王沛 译 潘艳、薛张纲）

BACKGROUND: The aepEXplus monitoring system, which uses mid-latency auditory evoked potentials to measure depth of hypnosis, was evaluated in pediatric patients receiving desflurane-remifentanil anesthesia.
METHODS: Seventy-five patients, 1–18 years of age (stratified for age; 1–3, 3–6, 6–18 years, for subgroup analyses), were included in this prospective observational study. The aepEX and the bispectral index (BIS) were recorded simultaneously, the latter serving as a reference. The ability of the aepEX to detect different levels of consciousness, defined according to the University of Michigan Sedation Scale, investigated using prediction probability (Pk), and receiver operating characteristic (ROC) analysis, served as the primary outcome parameter. As a secondary

outcome parameter, the relationship between end-tidal desflurane and the aepEX and BIS values were calculated by fitting in a nonlinear regression model.
RESULTS: The Pk values for the aepEX and the BIS were, respectively, .68 (95% CI, 0.53–0.82) and .85 (95% CI, 0.73–0.96; P = .02). The aepEX and the BIS had an area under the ROC curve of, respectively, 0.89 (95% CI, 0.80–0.95) and 0.76 (95% CI, 0.68–0.84; P = .04). The maximized sensitivity and specificity were, respectively, 81% (95% CI, 61%–93%) and 86% (95% CI, 74%–94%) for the aepEX at a cutoff value of >52, and 69% (95% CI, 56%–81%) and 70% (95% CI, 57%–81%) for the BIS at a cutoff value of >65. The age-corrected end-tidal desflurane concentration associated with an index value of 50 (EC50) was 0.59 minimum alveolar concentration (interquartile range: 0.38–0.85) and 0.58 minimum alveolar concentration (interquartile range: 0.41–0.70) for, respectively, the aepEX and BIS (P = .69). Age-group analysis showed no evidence of a difference regarding the area under the ROC curve or EC50.
CONCLUSIONS: The aepEX can reliably differentiate between a conscious and an unconscious state in pediatric patients receiving desflurane-remifentanil anesthesia.

与含有 n6 脂肪酸的脂肪乳剂相比，富含 n3 脂肪酸的脂肪乳剂对大鼠心脏取胰岛素信号和摄取葡萄糖有保护作用

Lipid Emulsion Containing High Amounts of n3 Fatty Acids (Omegaven) as Opposed to n6 Fatty Acids (Intralipid) Preserves Insulin Signaling and Glucose Uptake in Perfused Rat Hearts

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Anesthesia & Analgesia: 2020 130 37-48
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背景：当前我们尚不清楚，与急性暴露于含 n6 脂肪酸的大豆油脂乳剂相比，暴露于 n3 脂肪酸的鱼油脂乳剂是否对整个心脏的胰岛素信号转导和葡萄糖摄取更有利。
方法：给 SD 大鼠正常活动的心脏输注含有 11mm 的葡萄糖和结合白蛋白的 1.2 mM 棕榈酸盐 90 分钟，在起始 30 分钟内不使用胰岛素，后 60 分钟内给与 50 mU/L 的胰岛素。这些大鼠的心脏被随机分配到 100uM 的脂肪乳组、ω-3 鱼油脂肪乳组、无脂肪乳（仅用胰岛素治疗）组 60 分钟三组。通过应用[5-3H]葡萄糖放射性追踪剂测定糖酵解和糖原合成从而计算葡萄糖摄取情况。采用免疫印迹法测定蛋白磷酸酶 2A (PP2A)、前蛋白激酶 Akt 和磷酸化的果糖激酶(PFK)-2。应用特定酶法测定糖酵解的代谢产物。采用质谱法建立酰基肉碱图谱。应用 κB 核因子(NFκB)易位情况作为活性氧(ROS)的生物传感器。
结果：胰岛素介导的葡萄糖摄取由于脂内糖酵解和糖原合成而减少(4.9 ± 0.4 vs 3.7 ± 0.3 μmol/gdw•min;; P = .047)。相反，ω-3 鱼油脂肪乳治疗组对胰岛素介导的葡萄糖摄取并不显著影响糖酵解和糖原合成(5.1 ± 0.3 vs 4.9 ± 0.4 μmol/gdw•min; P = .94)。虽然脂质不影响 PP2A 的磷酸化状态，但

ω-3 鱼油脂肪乳可显著增强酪氨酸的磷酸化并可以抑制 PP2A。同时由于 Akt 选择性的苏氨酸磷酸化增加，可使得下游靶蛋白 PFK-2 S483 水平升高。由于 1、6-二磷酸果糖与 6-磷酸果糖比率的增加使得 PFK-1 活性与脂质相比也增加(ω-3 鱼油脂肪乳组 0.60 ± 0.11 versus 脂质组 0.47 ± 0.09; P = .023)，与 PFK2 增强果糖 2,6-二磷酸化一致，PFK2 为其主要变构激活剂。NF κ B 核因子的易位和激活可证实 ω-3 鱼油脂肪乳可能会导致酰基肉碱的积累和促氧化反应。

结论:与脂质相比，ω-3 鱼油脂肪乳通过 PP2A-Akt-PFK 途径摄取葡萄糖后可对整个活动的心脏产生保护作用。n3 脂肪酸通过降低脂肪酸的 β 氧化效率从而导致酰基肉碱聚集和促氧化反应，这说明 n3 脂肪酸可能会通过抑制氧化还原敏感的 PP2A，从而保护心脏对胰岛素信号的传导和葡萄糖的摄取。

（石平 译 潘艳、薛张纲）

Lipid Emulsion Containing High Amounts of n3 Fatty Acids (Omegaven) as Opposed to n6 Fatty Acids (Intralipid) Preserves Insulin Signaling and Glucose Uptake in Perfused Rat Hearts

Phing-How Lou, PhD,* Eliana Lucchinetti, PhD,† Martin Hersberger, PhD,‡

BACKGROUND: It is currently unknown whether acute exposure to n3 fatty acidcontaining fish oil–based lipid emulsion Omegaven as opposed to the n6 fatty acid–containing soybean oil–based lipid emulsion Intralipid is more favorable in terms of insulin signaling and glucose uptake in the intact beating heart.

METHODS: Sprague–Dawley rat hearts were perfused in the working mode for 90 minutes in the presence of 11 mM glucose and 1.2 mM palmitate bound to albumin, the first 30 minutes without insulin followed by 60 minutes with insulin (50 mU/L). Hearts were randomly allocated to 100 μM Intralipid, 100 μM Omegaven, or no emulsion (insulin treatment alone) for 60 minutes.Glycolysis and glycogen synthesis were measured with the radioactive tracer [5-3H]glucose, and glucose uptake was calculated. Phosphorylation of protein phosphatase 2A (PP2A), protein kinase Akt, and phosphofructokinase (PFK)-2 was measured by immunoblotting. Glycolytic metabolites were determined by enzymatic assays. Mass spectrometry was used to establish acylcarnitine profiles. Nuclear factor κB (NFκB) nuclear translocation served as reactive oxygen species (ROS) biosensor.

RESULTS: Insulin-mediated glucose uptake was decreased by Intralipid (4.9 ± 0.4 vs 3.7 ± 0.3 μmol/gram dry heart weight [gdw]•min; P = .047) due to both reduced glycolysis and glycogen synthesis. In contrast, Omegaven treatment did not affect insulin-mediated glycolysis or glycogen synthesis and thus preserved glucose uptake (5.1 ± 0.3 vs 4.9 ± 0.4 μmol/gdw•min; P= .94). While Intralipid did not affect PP2A phosphorylation status, Omegaven resulted in significantly enhanced tyrosine phosphorylation and inhibition of PP2A. This was accompanied by increased selective threonine phosphorylation of Akt and the downstream target PFK-2 at S483. PFK-1 activity was increased when compared with Intralipid as measured by the ratio of fructose 1,6-bisphosphate to

fructose 6-phosphate (Omegaven 0.60 ± 0.11 versus Intralipid 0.47 ± 0.09; P = .023), consistent with increased formation of fructose 2,6-bisphosphate by PFK2, its main allosteric activator. Omegaven lead to accumulation of acylcarnitines and fostered a prooxidant response as evidenced by NFκB nuclear translocation and activation.
CONCLUSIONS: Omegaven as opposed to Intralipid preserves glucose uptake via the PP2A–Akt–PFK pathway in intact beating hearts. n3 fatty acids decelerate β-oxidation causing accumulation of acylcarnitine species and a prooxidant response, which likely inhibits redox-sensitive PP2A and thus preserves insulin signaling and glucose uptake.

慢性非典型抗精神病药的使用与麻醉后恶心呕吐的处理减少有关：一项倾向匹配的回顾性观察研究

Chronic Atypical Antipsychotic Use Is Associated With Reduced Need for Postoperative Nausea and Vomiting Rescue in the Postanesthesia Care Unit: A PropensityMatched Retrospective Observational Study

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Anesthesia & Analgesia: 2020 130 141-150

背景： 非典型抗精神病药可有效预防化疗引起的恶心和呕吐，但围手术期研究很少。 我们试图验证慢性非典型抗精神病药物与术后恶心和呕吐之间的关系。
方法： 在这项单中心，倾向匹配，回顾性，观察性研究中，对 2014 年 1 月至 2017 年 12 月的非心脏择期外科手术病例进行了调查，了解麻醉后护理部门对于术后恶心呕吐患者给予止吐药的主要结果如下： 长期服用奥氮平，阿立哌唑和利培酮是人们关注的重点。 其他自变量包括门诊止吐药，改良的 Apfel 评分，年龄，美国麻醉医师学会身体状况评分，病例长度以及接触致呕药和化学预防药的情况。 使用病例级数据进行逻辑回归。 在按 1：2 的倾向匹配后进行条件 logistic 回归，无需替换即可进行抽样。 进行了蒙特卡洛模拟，以计算平均水平的治疗效果。
结果： 在 13,660 例患者中，有 154 例接受非典型抗精神病药物治疗的患者与 308 例未接受抗精神病药物治疗的患者相匹配，分别代表 115 例和 273 例的独特患者。 在一个均衡的队列中，接受典型抗精神病药的患者的呕吐机率水平与未服用非典型抗精神病药的患者相比，长期服用 3 种非典型抗精神病药的患者的呕吐率更低，优势比为 0.29（95％CI，0.11-0.75； P = .015）。
结论： 慢性非典型抗精神病药治疗与麻醉后止吐给药的降低有关。 这些发现支持需要进行前瞻性研究来确定使用这些药物进行术后恶心和呕吐化学预防的安全性和有效性。
（王硕 译 潘艳、薛张纲）
BACKGROUND: Atypical antipsychotics are efficacious for chemoprophylaxis against chemotherapy-induced nausea and vomiting, but perioperative investigations have been scant. We sought to examine the association

between chronic atypical antipsychotic therapy and the likelihood of postoperative nausea and vomiting.

METHODS: In this single-center, propensity-matched, retrospective, observational study, elective noncardiac surgical cases from January 2014 to December 2017 were examined with regard to the primary outcome of rescue antiemetic administration in the postanesthesia care unit as a measure of postoperative nausea and vomiting. Chronic administration of olanzapine, aripiprazole, and risperidone was the exposure of interest. Other independent variables included outpatient antiemetics, modified Apfel score, age, American Society of Anesthesiologists physical status score, case length, and exposures to emetogenic and chemoprophylactic agents. Logistic regression was performed using case-level data. Conditional logistic regression was performed after 1:2 propensity matching, sampling without replacement. Monte Carlo simulation was performed to compute the mean patient-level treatment effect on the treated.

RESULTS: Of 13,660 cases, 154 cases with patients receiving atypical antipsychotics were matched against 308 cases without, representing 115 and 273 unique patients, respectively. In a well-balanced cohort, the mean patient-level odds of being administered rescue antiemetic was lower for patients chronically taking the 3 atypical antipsychotics under consideration as compared to those not on atypical antipsychotics, with an odds ratio of 0.29 (95% CI, 0.11 - 0.75; P = .015).

CONCLUSIONS: Chronic atypical antipsychotic therapy is associated with reduced risk of postanesthesia care unit antiemetic administration. These findings support the need for prospective studies to establish the safety and efficacy of postoperative nausea and vomiting chemoprophylaxis with these agents.

呼吸机模式不影响脊柱外科手术中失血或输血的需求：一项回顾性研究

Ventilator Mode Does Not Influence Blood Loss or Transfusion Requirements During Major Spine Surgery: A Retrospective Study

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Anesthesia & Analgesia: 2020 130 100-110

背景：

成人脊柱畸形手术中失血是多因素的。麻醉相关因素，如机械通气方式，可能导致术中失血。本研究旨在探讨呼吸机模式及呼吸机参数对俯卧位脊柱手术患者术中失血量及输血需求的影响。

方法：

这项单中心回顾性研究调查了2015年5月至2016年6月期间接受选择性俯卧位脊柱手术的18岁以上患者的电子病历。采用多元线性回归模型控制年龄、性别、美国麻醉师学会（ASA）身体状况评分、体重指数（BMI）、术前凝血参数和实验室值、手术水平、笼结构、截骨术、经椎间孔腰椎锥间融合术、椎板切除术、二次手术、脊柱手术侵袭性指数和手术时间，研究呼吸机模式和呼吸机参数与术中估计失血量（EBL）、填充红细胞（PRBCs）、新鲜冰冻血浆（FFP）、冷沉淀和血小板输注、引流量的关系。在二次分析中，比较了压力控制通气（PCV）和容量控制通气（VCV）倾向评分匹配队列的EBL、输血量和术后引流量。

结果：

回顾了946份记录，822份被纳入分析。调整混杂因素后，在通气模式和术中EBL（估计值，-2；95%CI，-248至245；P=.99）或血制品输注（PRBC：估计值，-9；95%CI，-154至135；P=.90；FFP：估计值，-3；95%CI，-59至54；P=.93；冷沉淀：估计值，-14；95%CI，-70至43；P=.63；血小板：-7；95%CI，-39至24；P=.64）之间未观察到具有统计学意义的关联。倾向性评分匹配后（每组n=27），PVC组与VCV组在EBL（平均差525 mL；95%CI，-15至1065；P=.056）或血制品输注（PRBC：平均差208 mL；95%CI，-23至439；P=.077；FFP平均差34 mL；95%CI，-17至84；P=.19）；冷沉淀（平均差55 mL；95%CI，-24至133；P=0.17）；或血小板（平均差，26ml；95%CI，-12至64；P=0.18）方面无显著差异。

结论：

在俯卧位脊柱手术中，机械通气和气道压力与术中失血或异体输血无关。使用肺保护技术的现代通气策略可以缓解先前观察到的PCV和VCV模式之间的失血差异。

（魏婉婷 译 潘艳、薛张纲）

BACKGROUND: Blood loss during adult spinal deformity surgery is multifactorial. Anesthetic-related factors, such as mode of mechanical ventilation, may contribute to intraoperative blood loss. The aim of this study was to determine the influence of ventilator mode and ventilator parameters on intraoperative blood loss and transfusion requirements in patients undergoing prone position spine surgery.

METHODS: This single-center retrospective study examined electronic medical records of patients ≥18 years of age who underwent elective prone position spine surgery between May 2015 and June 2016. Associations between ventilator mode and ventilator parameters with intraoperative estimated blood loss (EBL), packed red blood cells (PRBCs), fresh-frozen plasma (FFP), cryoprecipitate and platelet transfusions, and subfascial drain output were examined using multiple linear regression models controlling for age, sex, American Society of Anesthesiologist (ASA) physical status score, body mass index (BMI), preoperative blood coagulation parameters and laboratory values, operative levels, cage constructs, osteotomies, transforaminal lumbar interbody fusions, laminectomies, reoperation, spine surgery invasiveness index, and operative time. In a secondary analysis, EBL, blood product transfusions, and postoperative drain output were compared between pressure-controlled ventilation (PCV) and volume-controlled ventilation (VCV) propensity score–matched cohorts.

RESULTS: Nine hundred forty-six records were reviewed, and 822 were included in the analysis. After adjusting for confounding, no statistically significant associations were observed between mode of ventilation and intraoperative EBL (estimate, −2; 95% confidence interval [CI], −248 to 245; P = .99) or blood product transfusions (PRBC: estimate, −9; 95% CI, −154 to 135; P = .90; FFP: estimate, −3; 95% CI, −59 to 54; P = .93; cryoprecipitate: estimate, −14; 95% CI, −70 to 43; P = .63; platelets: −7; 95% CI, −39 to 24; P = .64). After propensity score matching (n = 27 per group), no significant differences were observed in EBL (mean difference, 525 mL; 95% CI, −15 to 1065; P = .056) or blood transfusions (PRBC: mean difference, 208 mL; 95% CI, −23 to 439; P = .077; FFP (mean difference, 34 mL; 95% CI, −17 to 84; P = .19); cryoprecipitate (mean difference, 55 mL; 95% CI, −24 to 133; P = .17); or platelets (mean difference, 26 mL; 95% CI, −12 to 64; P = .18) between PCV and VCV groups.

CONCLUSIONS: In prone position spine surgery, neither mode of mechanical ventilation nor airway pressure is associated with intraoperative blood loss or need for allogeneic transfusion. Use of modern ventilation strategies using lung protective techniques may mitigate differences in blood loss previously observed between PCV and VCV modes.

Incisional Injury Modulates Morphine Reward and Morphine-Primed Reinstatement: A Role of Kappa Opioid Receptor Activation
切口损伤调节吗啡奖赏作用和吗啡复用：Kappa 阿片受体激活的作用

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Anesthesia & Analgesia: 2020 130 248-257

背景：在手术恢复期之后持续使用处方类阿片药物是美国当前阿片危机相关公共卫生问题的一重要部分。然而，很少有研究来研究吗啡奖赏作用是否受到急性疼痛和损伤的影响。

方法：在小鼠切口损伤和轻微创伤模型中，小鼠接受了吗啡的建模、消退和药物复用，以分别检验吗啡在急性切口损伤和药物复用下的奖赏作用特性。此外，我们还试图确定这些行为是否受到 kappa 阿片受体信号传导通路的影响，因此在用

吗啡和切口损伤建模之后以及在复用药物之前，我们检测了前强啡肽信使 RNA 在伏隔核和内侧前额叶皮质中的表达。

结果：在存在切口损伤的小鼠中，我们观察到吗啡奖赏作用的增强，其更偏好设置为吗啡相关的位置，但这种增强在复用吗啡时就减弱了。这种适应性减弱效应在切口损伤后 12 天组的小鼠中没有出现，此时疼痛敏感化已经消退；反而它们显示了吗啡复用时的增强效应。前强啡肽在切口损伤和吗啡处理小鼠的伏隔核和内侧前额叶皮质中的表达明显增加，并持续升高至药物复用。 在切口损伤后 12 天后组的小鼠中未观察到这些变化。此外，在复用吗啡前用 Nor-BNI 阻断 kappa 阿片受体逆转了损伤所致的减弱效应。

结论：这些发现表明，由于切口损伤，吗啡的奖赏作用有所增强，但反常的是，这也是一种对在切口损伤下由奖赏回路中 kappa 阿片受体激活导致的药物复用的保护性适应。远期的损伤不能提供这种保护，反而表现为增强药物复用。

（叶姗姗 译 潘艳、薛张纲）

Background: Persistent use of prescription opioids beyond the period of surgical recovery is a large part of a public health problem linked to the current opioid crisis in the United States. However, few studies have been conducted to examine whether morphine reward is influenced by acute pain and injury.

Methods: In a mouse model of incisional injury and minor trauma, animals underwent conditioning, extinction, and drug-primed reinstatement with morphine to examine the rewarding properties of morphine in the presence of acute incisional injury and drug-induced relapse, respectively. In addition, we sought to determine whether these behaviors were influenced by kappa opioid receptor signaling and measured expression of prodynorphin messenger RNA in the nucleus accumbens and medial prefrontal cortex after conditioning and before reinstatement with morphine and incisional injury.

Results: In the presence of incisional injury, we observed enhancement of morphine reward with morphine-conditioned place preference but attenuated morphine-primed reinstatement to reward. This adaptation was not present in animals conditioned 12 days after incisional injury when nociceptive sensitization had resolved; however, they showed enhancement of morphine-primed reinstatement. Prodynorphin expression was greatly enhanced in the nucleus accumbens and medial prefrontal cortex of mice with incisional injury and morphine conditioning and remained elevated up to drug-primed reinstatement. These changes were not observed in mice conditioned 12 days after incisional injury. Further, kappa opioid receptor blockade with norbinaltorphimine before reinstatement reversed the attenuation induced by injury.

Conclusions: These findings suggest enhancement of morphine reward as a result of incisional injury but paradoxically a protective adaptation with incisional injury from drug-induced relapse resulting from kappa opioid receptor activation in the reward circuitry. Remote injury conferred no such protection and appeared to enhance reinstatement.

弹性增强喉罩与气管插管在甲状腺手术中封闭气道效果的比较:一项随机对照试验

Performance of Air Seal of Flexible Reinforced Laryngeal Mask Airway in Thyroid Surgery Compared With Endotracheal Tube: A Randomized Controlled Trial

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Anesthesia & Analgesia: 2020 130 217-223

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背景:FLMA 在甲状腺手术中得到广泛应用，但仍存在漏气、移位等问题。

方法:在这个随机、单盲、非劣效性的对照试验中，我们将择期行甲状腺根治术的患者随机分为气管内插管组(ETT)和 FLMA 组。主要结果为通气泄漏量、气道压力峰值和呼吸末二氧化碳分压(PetCO2)。在插入 ETT/FLMA 时，划皮时，以及手术期间每间隔 10 分钟收集主要结果的数据。并分别以 10ml、5cm H2O 和 10mm Hg 作为通气泄露量、气道峰值压力和 PetCO2 非劣效 δ 值。我们使用线性混合效应模型评估了相对于 ETT 组患者，FLMA 组患者主要结果数据的非劣效性。我们术前、术后均评估 FLMA 面罩位置，并记录气道并发症。

结果:132 例患者中，ETT 组 65 例，FLMA 组 67 例。混合效应模型(FLMA 组- ETT 组)在通气漏量、气道峰值压力和 PetCO2 方面的差异分别为 2.09 mL(98.3%置信区间[CI]， -6.46 ~ 10.64)、-0.60 cm H2O (98.3% CI， -2.15 ~ 0.96)和 1.02 mm Hg (98.3% CI, 0.04 ~ 1.99)。术后 FLMA 的光纤位置评分明显高于术前。FLMA 组无严重移位、面罩密封性丧失、返流或误吸。FLMA 组有 1 例患者出现短暂且易于控制的喉痉挛。

结论:在甲状腺手术中，尽管在操作过程中可能出现轻微到中度的面罩移位，但 FLMA 在气道压力峰值和 PetCO2 方面并不劣于 ETT。没有证据表明使用 FLMA 时并发症发生率更高。

（王甲利 译 潘艳、薛张纲）

BACKGROUND: Flexible reinforced laryngeal mask airway (FLMA®) has gained popularity in thyroid surgery, but air leak and displacement are still concerns.

METHODS: In this randomized, single-blinded, noninferiority, controlled trial, we randomized patients scheduled for elective radical thyroidectomy to an endotracheal tube (ETT) group or a FLMA group. The primary outcomes were ventilation leak volume, peak airway pressure, and partial pressure of end-tidal carbon dioxide (PetCO2). Data for primary outcomes were collected after insertion of ETT/FLMA, at incision, and at 10-minute intervals during surgery. Ten milliliters, 5 cm H2O, and 10 mm Hg were used as the noninferiority deltas for ventilation leak volume, peak airway pressure, and PetCO2, respectively. We assessed noninferiority of FLMA to ETT on the primary outcomes over time using the results of a linear mixed-effects model. The position of FLMA mask was evaluated before and after surgery, and the airway complications were recorded.

RESULTS: A total of 132 patients were included: 65 in ETT group and 67 in FLMA group. Differences (FLMA group minus ETT group) of ventilation leak volume, peak airway pressure, and PetCO2 from the mixed-effects models were 2.09 mL (98.3% confidence interval [CI], -6.46 to 10.64), -0.60 cm H2O (98.3% CI, -2.15 to 0.96), and 1.02 mm Hg (98.3% CI, 0.04-1.99), respectively. Score of fiber-optic position of FLMA was significantly higher after surgery than before. There was no severe shift, loss of the mask seal, regurgitation, or aspiration in the FLMA group. One patient in the FLMA group experienced brief and easily controlled laryngospasm.
CONCLUSIONS: In thyroid surgery, FLMA is noninferior to ETT in the peak airway pressure and PetCO2 although mild to moderate mask shift could occur during surgical manipulation. There is no evidence for a higher complication rate when FLMA is used.

血管扩张性休克的逆转：治疗休克的常规、抢救和新型血管活性药物的研究现状

Reversal of Vasodilatory Shock: Current Perspectives on Conventional, Rescue, and Emerging Vasoactive Agents for the Treatment of Shock

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了解血管收缩药的不同机制对于它们在临床不同休克状态下的最佳应用至关重要。我们全面回顾了常规的、抢救的和新型的血管活性药物，包括它们的药理作用和支持它们在血管扩张性休克中使用的证据。本文讨论了每种药物与脓毒症存活指南中的关系，以提供每种药物如何适用于治疗血管扩张性休克的算法的环境。当常规药物无效时，可以使用救援剂，尽管关于它们的临床有效性的证据程度不同。此外，最近出现了抗坏血酸和血管紧张素 II 等治疗血管扩张性休克的新药物。抗坏血酸在血管麻痹的治疗中取得了一定的成功，目前正在对其有效性进行更严格的评估。血管紧张素 II(Ang-2)是治疗血管扩张性休克的最新血管增压药。除了节约了儿茶酚胺，它已被证明在某些危重患者亚群中可以降低死亡率。
（许芳霞译 李金宝校）

Understanding the different mechanisms of vasoconstrictors is crucial to their optimal application to clinically diverse shock states. We present a comprehensive review of conventional, rescue, and novel vasoactive agents including their pharmacology and evidence supporting their use in vasodilatory shock. The role of each drug in relation to the Surviving Sepsis Guidelines is discussed to provide a context of how each one fits into the algorithm for treating vasodilatory shock. Rescue agents can be utilized when conventional medications fail, although there are varying levels of evidence on their clinical effectiveness. In addition, novel agents for the treatment of vasodilatory shock have recently emerged such as ascorbic acid and angiotensin II. Ascorbic acid has been used with some success in vasoplegia and is currently undergoing a more rigorous evaluation of its utility. Angiotensin II (Ang-2) is the newest available

vasopressor for the treatment of vasodilatory shock. In addition to its catecholamine-sparing properties, it has been shown to hold promising mortality benefits in certain subsets of critically ill patients.

髋部骨折患者术后谵妄的危险预测评分的建立

Development of a Risk Score to Predict Postoperative Delirium in Patients With Hip Fracture

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Anesthesia & Analgesia: 2020 130 79-86

背景：髋部骨折术后谵妄（PHFD）是老年患者一个重要的临床问题，但尚缺少合适的简易的风险预测模型用于术前。

方法：我们查阅了 2016 年美国外科医生学院国家外科质量改进计划髋部骨折手术目标参与者使用数据文件，获得一项 60 岁以上髋部骨折患者的队列研究（n=8871，随机分配至推导组[70%]或验证组[30%]）。通过采用逐步多变量 losistic 回归分析，进一步除去变量，然后评估受试者-操作者特征曲线下面积（AUC）的变化，在推导组中建立了 PHFD 的简约预测模型。从最终的多变量模型得出风险评分。

结果：在 6210 例推导组患者中，有 1816 例发生 PHFD（29.2%）。在 32 个候选变量中，9 个被纳入最终的模型：（1）术前谵妄（校正比值比[aOR]，8.32 [95%可信区间]{CI}6.78-10.2，8 分）；（2）术前痴呆（aOR，2.38 [95%CI,2.05-2.76]，3 分）；（3）年龄（参考，60-69 岁）（70-79 岁：aOR，1.60[95%CI，1.20-2.12]，2 分；80-89 岁：aOR，2.09[95%CI，1.59-2.74]，2 分；≥90 岁：aOR，2.43[95%CI，1.82-3.23]，3 分）；（4）医疗管理（aOR，1.43[95%CI，1.31-1.81]，1 分）；（5）美国麻醉医师协会（ASA）身体状况分级 III-V 级（aOR，1.40[95%CI，1.14-1.72]，1 分）；（6）功能依赖（aOR，1.37[95%CI，1.17-1.61]，1 分）；（7）吸烟（aOR，1.36[95%CI，1.07-1.72]，1 分）；（8）全身炎症反应综合征/脓毒症/脓毒性休克（aOR，1.34[95%CI，1.09-1.65]，1 分）；（9）术前使用助行器（aOR，1.32[95%CI，1.14-1.52]，1 分），风险评分总分在 0-20 分之间。Logistic 回归和风险评估模型的 AUCs 分别为 0.77（95%CI，0.76-0.78）和 0.77（95%CI，0.76-0.78），与验证队列的结果相似。

结论：以这 9 个术前危险因素为基础的危险评分对老年人 PHFD 的预测有良好的准确性。

（许芳霞译 李金宝校）

BACKGROUND: Post-hip fracture surgery delirium (PHFD) is a significant clinical problem in older patients, but an adequate, simple risk prediction model for use in the preoperative period has not been developed.

METHODS: The 2016 American College of Surgeons National Surgical Quality Improvement Program Hip Fracture Procedure Targeted Participant Use Data File was used to obtain a cohort of patients ≥60 years of age who underwent hip fracture surgery (n = 8871; randomly assigned to derivation [70%] or validation [30%] cohorts). A parsimonious prediction model for PHFD was developed in the derivation cohort using stepwise multivariable logistic regression with further removal of

variables by evaluating changes in the area under the receiver operator characteristic curve (AUC). A risk score was developed from the final multivariable model.

RESULTS: Of 6210 patients in the derivation cohort, PHFD occurred in 1816 (29.2%). Of 32 candidate variables, 9 were included in the final model: (1) preoperative delirium (adjusted odds ratio [aOR], 8.32 [95% confidence interval {CI}, 6.78-10.21], 8 risk score points); (2) preoperative dementia (aOR, 2.38 [95% CI, 2.05-2.76], 3 points); (3) age (reference, 60-69 years of age) (age 70-79: aOR, 1.60 [95% CI, 1.20-2.12], 2 points; age 80-89: aOR, 2.09 [95% CI, 1.59-2.74], 2 points; and age ≥90: aOR, 2.43 [95% CI, 1.82-3.23], 3 points); (4) medical comanagement (aOR, 1.43 [95% CI, 1.13-1.81], 1 point); (5) American Society of Anesthesiologists (ASA) physical status III-V (aOR, 1.40 [95% CI, 1.14-1.73], 1 point); (6) functional dependence (aOR, 1.37 [95% CI, 1.17-1.61], 1 point); (7) smoking (aOR, 1.36 [95% CI, 1.07-1.72], 1 point); (8) systemic inflammatory response syndrome/sepsis/septic shock (aOR, 1.34 [95% CI, 1.09-1.65], 1 point); and (9) preoperative use of mobility aid (aOR, 1.32 [95% CI, 1.14-1.52], 1 point), resulting in a risk score ranging from 0 to 20 points. The AUCs of the logistic regression and risk score models were 0.77 (95% CI, 0.76-0.78) and 0.77 (95% CI, 0.76-0.78), respectively, with similar results in the validation cohort.

CONCLUSIONS: A risk score based on 9 preoperative risk factors can predict PHFD in older adult patients with fairly good accuracy.

3. 儿童电休克的麻醉管理：对现有文献的系统回顾

Anesthetic Management During Electroconvulsive Therapy in Children: A Systematic Review of the Available Literature

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Anesthesia & Analgesia: 2020 130 126-140

电休克疗法（ECT）被越来越广泛应用于儿童的各种精神疾病。但尚缺乏文献报道相关麻醉管理的临床特点。本系统综述的目的是描述儿科 ECT 麻醉问题的现有文献。对原始出版物进行筛选，纳入标准是：（1）英文手稿；（2）18 岁以下人群；（3）使用 ECT。数据表包括人口统计信息，麻醉管理和 ECT 过程的细节以及不良事件。平均年龄为 15 岁，90%为 12-17 岁，没有＜6 岁的案例。最常见的精神病诊断为重度抑郁（n=185）和精神分裂症/分裂性情感障碍（n=187）。ECT 同样被用来治疗很多其它疾病。所有病例中有 16%存在并发症。常见并发症为发育迟缓（n=21）和孤独症（n=18）。主要的 ECT 指征为严重的精神疾病（n=190），药物治疗无效的症状（n=154），自杀倾向（n=153）。每个患者的 ECT 疗程从 2-156 不等，平均持续时间为 91.89±144.3s。最常见的诱导药物为丙泊酚和甲硫氨酸，最常见的肌松药物为琥珀胆碱。报告的不良事件包括头痛、恶心、镇静和短期遗忘，以及罕见的良性心律失常和长时间癫痫发作。消极的认知和获得护理的机会减少可导致治疗延误，因此，这些儿童就会处于疾病的晚期。在检查 592 名儿童的现代化 ECT 细节中，没有出息严重的麻醉并发症。进一步研究应该从回顾性分析 ECT 期间的麻醉数据开始，从而比较麻醉药物和技术对不良事件和结果的各种影响。

（许芳霞译 李金宝校）

Electroconvulsive therapy (ECT) is indicated in a myriad of pediatric psychiatric conditions in children, and its use is increasing. Literature on the clinical features salient to anesthetic care is lacking. The objective of this systematic review is to describe the available literature on the anesthetic considerations of pediatric ECT. Original publications were screened for inclusion criteria: (1) manuscript written in English; (2) persons under 18 years of age; and (3) use of ECT. Data tabulation included demographic information, details of anesthetic management and ECT procedure, and adverse events. The mean age was 15 years, 90% were 12-17 years of age, and no cases involving children <6 years of age were identified. The psychiatric diagnoses most commonly represented were major depressive disorder (n = 185) and schizophrenia/schizoaffective disorders (n = 187). ECT was also used to treat many neurological disorders. Medical comorbidities were reported in 16% of all cases. Common coexisting conditions included developmental delay (n = 21) and autism (n = 18). Primary ECT indications included severe psychosis (n = 190), symptoms refractory to pharmacotherapy (n = 154), and suicidality (n = 153). ECT courses per patient ranged from 2 to 156. Duration averaged 91.89 ± 144.3 seconds. The most commonly reported induction agents were propofol and methohexital, and the most commonly reported paralytic agent was succinylcholine. Reported adverse events included headache, nausea, sedation, and short-term amnesia, as well as rare cases of benign dysrhythmias and prolonged seizure. Negative perception and diminished access to care result in treatment delays; thus, these children present in an advanced state of disease. In examining the details of modern ECT performed in 592 children, no major anesthetic morbidity was identified. Further study should start with retrospective analysis of anesthesia data during ECT to compare various effects of anesthesia medications and technique on adverse events and outcomes.

4.加速血管置管检测的体外刺激研究

Speeding the Detection of Vessel Cannulation: An In-Vitro Stimulation Study

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Anesthesia & Analgesia: 2020 130 159-164

背景：一些操作者用 0.9%的氯化钠对小型静脉血管导管针头进行预处理，称这种改进在置管过程中可加快检测血管置入导管时目测的回血速度。

方法：我们使用人类血液比较了生理盐水灌注和未灌注生理盐水的 24 和 22 号血管导管针头回血所需的时间（Introcan Safety IV 导管； B.Braun，伯利恒，宾夕法尼亚州）。注射泵（Medfusion 4000，北卡罗来纳州卡里）穿刺针通过硅胶膜穿入装有新鲜捐赠的人类血液的静脉输液“ t 型管”（Microbore Extension Set，5 英寸； Hospira，Lake Forest，IL）。当血管导管针头接触血液时电路传导就完成了，从而发光二极管被照亮。通过视频回顾，我们确定了从发光二极管照亮到视觉检测血液回流导管的时间。我们在 24 和 22 规格的血管导管（共 420 个导管）中测试了 105 个生理盐水灌注的血管导管和 105 个未灌注的血管导管。我们

使用 R（http://www.R-project.org/）中的非参数 Wilcoxon 秩和检验分析了中位时间以使回血可视化。斯坦福大学医学研究中的人类受试者行政管理小组指出该项目不符合人类受试者研究的要求，因此不需要机构审查委员会的监督。

结果：在 24 号血管导管组中，血液通过未灌注血管导管针的中位时间（和四分位间距）为 1.14（0.61-1.47）秒，而生理盐水灌注组为 0.76（0.41-1.20）秒（P ＝ 0.006）。在 22 号导管组中，血液通过未灌注血管导管针的时间的中位时间（四分位间距）为 1.80（1.23-2.95）秒，而生理盐水灌注组为 1.46（1.03-2.54）秒（ P = .046）。

结论：这些结果表明，与未灌注的血管导管针相比，用 0.9％氯化钠灌注小的血管导管针，特别是 24 号导管，可以更早地检测到血管置管。

（许芳霞译 李金宝校）

BACKGROUND: Some practitioners "prime" small IV angiocatheter needles with 0.9% sodium chloride-claiming this modification speeds visual detection of blood in the angiocatheter flash chamber on vessel cannulation.

METHODS: We compared the time required for human blood to travel the length of saline-primed and saline-unprimed 24- and 22-gauge angiocatheter needles (Introcan Safety IV Catheter; B. Braun, Bethlehem, PA). A syringe pump (Medfusion 4000, Cary, NC) advanced each angiocatheter needle through the silicone membrane of an IV tubing "t-piece" (Microbore Extension Set, 5 Inch; Hospira, Lake Forest, IL) filled with freshly donated human blood. When the angiocatheter needle contacted the blood, an electrical circuit was completed, illuminating a light-emitting diode. We determined the time from light-emitting diode illumination to visual detection of blood in the flash chamber by video review. We tested 105 saline-primed angiocatheters and 105 unprimed angiocatheters in the 24- and 22-gauge angiocatheter sizes (420 catheters total). We analyzed the median time to visualize the flash using the nonparametric Wilcoxon rank sum test in R (http://www.R-project.org/). The Stanford University Administrative Panel on Human Subjects in Medical Research determined that this project did not meet the definition of human subjects research and did not require institutional review board oversight.

RESULTS: In the 24-gauge angiocatheter group, the median (and interquartile range) time for blood to travel the length of the unprimed angiocatheter needle was 1.14 (0.61-1.47) seconds compared with 0.76 (0.41-1.20) seconds in the saline-primed group (P = 0.006). In the 22-gauge catheter group, the median (interquartile range) time for blood to travel the length of the unprimed angiocatheter needle was 1.80 (1.23-2.95) seconds compared with 1.46 (1.03-2.54) seconds in the saline-primed group (P = .046).

CONCLUSIONS: These results support the notion that priming small angiocatheter needles, in particular 24-gauge catheters, with 0.9% sodium chloride may provide earlier detection of vessel cannulation than with the unprimed angiocatheter.

5. 腰硬联合麻醉中 4 种基于体重给药的苯肾对预防剖宫产低血压的量效研究

Dose–Response Study of 4 Weight-Based Phenylephrine Infusion Regimens for Preventing Hypotension During Cesarean Delivery Under Combined Spinal–Epidural Anesthesia

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Anesthesia & Analgesia: 2020 130 187-193

背景：预防性静脉输注苯肾上腺素是预防腰麻剖宫时低血压的有效措施。然而最佳输注剂量尚不清楚。本研究的目的是确定 50%（ED50）和 90%（ED90）的患者在以固定比例根据体重进行预防性输注时，有效预防低血压的苯肾上腺素的剂量。

方法：80 例择期剖宫产的产妇随机分为 4 组（每组 20 人），在鞘内注射 10mg 高压布比卡因和 5μg 舒芬太尼后，立即开始以 0.25、0.375、0.5 和 0.625 μg/kg/min 的速度输注苯肾上腺素。有效剂量的定义是，在开始腰麻到分娩期间，未出现低血压（收缩压低于基线水平≥20%或＜90 mmHg）。用 probit 分析计算预防性苯肾上腺素的 ED50 和 ED90 值。

结果：在苯肾上腺素输注速度分别为 0.25、0.375、0.5 和 0.625 μg/kg/min 的 4 组中，低血压的发生率分别为 13/20、8/20、2/20 和 1/20。ED50 和 ED90 的计算值分别为 0.31（95%CI，0.24-0.36）和 0.54（95%CI，0.46-0.76）。各组的不良反应和新生儿结局均无显著性差异。

结论：在本研究条件下，以恒速输注苯肾上腺素从而预防腰麻剖宫产术中低血压时， ED50 和 ED90 值分别是 0.31（95%CI，0.24-0.36）和 0.54（95%CI，0.46-0.76）μg/kg/min。

（许芳霞译 李金宝校）

BACKGROUND: Prophylactic IV infusion of phenylephrine has been recommended to prevent hypotension during spinal anesthesia for cesarean delivery. However, the optimal infusion dose is unknown. This study aimed to determine the infusion dose of phenylephrine that would be effective in preventing hypotension in 50% (ED50) and 90% (ED90) of patients when administered as a prophylactic infusion at a fixed rate based on the individual body weight.

METHODS: Eighty parturients scheduled for elective cesarean delivery were randomly allocated to receive IV infusion of prophylactic phenylephrine at 0.25, 0.375, 0.5, or 0.625 μg/kg/min (n = 20 per group) started immediately after intrathecal injection of 10 mg hyperbaric bupivacaine and 5 μg sufentanil using a combined spinal-epidural technique. An effective dose was defined by the occurrence of no hypotension (defined as a decrease in systolic blood pressure by ≥20% below baseline and to <90 mm Hg) during the interval from the initiation of spinal anesthesia to delivery of the infant. Values for ED50 and ED90 of prophylactic phenylephrine were calculated using probit analysis.

RESULTS: Hypotension occurred in 13/20, 8/20, 2/20, and 1/20 patients in the groups that received phenylephrine infusion at 0.25, 0.375, 0.5, or 0.625 μg/kg/min, respectively. The calculated values for ED50 and ED90 were 0.31 (95% CI, 0.24-0.36) and 0.54 (95% CI, 0.46-0.76) μg/kg/min, respectively. No difference was found in the incidence of adverse effects and neonatal outcomes among groups.

CONCLUSIONS: Under the conditions of this study, when phenylephrine was given as a fixed-rate prophylactic infusion during spinal anesthesia for cesarean delivery to

prevent hypotension, the values for ED50 and ED90 were 0.31 (95% CI, 0.24-0.36) and 0.54 (95% CI, 0.46-0.76) μg/kg/min, respectively.

6. 右美托咪定在婴幼儿原味肝移植术后的药动学研究

Pharmacokinetics of Dexmedetomidine in Infants and Children After Orthotopic Liver Transplantation

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Anesthesia & Analgesia: 2020 130 209-216

背景：右美托咪定（DEX）是小儿肝移植术后常用的镇静药物。肝功能不全，包括药物清除率改变，在肝移植术后很常见。然而，这部分人群DEX的药动学（PK）尚不清楚。本研究旨在探讨小儿肝移植术后 DEX 的 PK 谱。

方法：采用单中心、开放标记的右美托咪定药动学研究，静脉负荷剂量为 0.5μg/kg，持续泵注剂量为 0.5μg/kg/h。一共有 20 例年龄为 1 月-18 岁，行肝移植术后进入重症监护室的患儿纳入本研究。采集全血，用干血纸片法分析 DEX 的浓度。采用非线性混合效应模型对 DEX 的药动学特点进行描述。

结果：右美托咪定的药动学以一级消除二室模型为佳。一个典型的儿童肝移植后，国际标准化比值（INR）为 1.8，全血 DEX 清除率为 52L/h（95%可信区间[CI]，31-73 L/h）。此外，组间清除率为 246L/h（95%可信区间[CI]，139-391 L/h），中心分布容积为 186 L/70kg（95%可信区间[CI]，140-301L/kg），外周分布容积为 203 L（95%可信区间[CI]，123-338L）所有参数的个体间变异度在 11%-111%。清除率与体重无关，而与 INR 成反比。INR 增加至 3.2 可导致 DEX 清除率降低 50%。体重与分布中心容积呈线性相关。所有其它协变量，包括年龄、缺血时间、总胆红素和丙氨酸转移酶，都不是预测 DEX 分布的显著因子。

结论：肝移植术后接受 DEX 治疗的儿童肝脏清除率有很大的变异度，它与体重无关，但受肝功能影响，比如受 INR 影响。在这群人中，根据临床效应来滴定 DEX 的剂量可能很重要，因为基于体重的剂量与血浓度相关性较差。当 INR 发生变化时，DEX 镇静的质量需要更加注意。

（许芳霞译 李金宝校）

BACKGROUND: Dexmedetomidine (DEX) is a sedative and analgesic medication that is frequently used postoperatively in children after liver transplantation. Hepatic dysfunction, including alterations in drug clearance, is common immediately after liver transplantation. However, the pharmacokinetics (PK) of DEX in this population is unknown. The objective of this study was to determine the PK profile of DEX in children after liver transplantation.

METHODS: This was a single-center, open-label PK study of DEX administered as an intravenous loading dose of 0.5 μg/kg followed by a continuous infusion of 0.5 μg/kg/h. Twenty subjects, 1 month to 18 years of age, who were admitted to the pediatric intensive care unit after liver transplantation were enrolled. Whole blood was collected and analyzed for DEX concentration using a dried blood spot method. Nonlinear mixed-effects modeling was used to characterize the population PK of DEX.

RESULTS: DEX PK was best described by a 2-compartment model with first-order elimination. A typical child after liver transplantation with an international normalized ratio (INR) of 1.8 was found to have a whole blood DEX clearance of 52 L/h (95% confidence interval [CI], 31-73 L/h). In addition, intercompartmental clearance was 246 L/h (95% CI, 139-391 L/h), central volume of distribution was 186 L/70 kg (95% CI, 140-301 L/70 kg), and peripheral volume of distribution was 203 L (95% CI, 123-338 L). Interindividual variability ranged from 11% to 111% for all parameters. Clearance was not found to be associated with weight but was found to be inversely proportional to INR. An increase in INR to 3.2 resulted in a 50% decrease in DEX clearance. Weight was linearly correlated with central volume of distribution. All other covariates, including age, ischemic time, total bilirubin, and alanine aminotransferase, were not found to be significant predictors of DEX disposition.
CONCLUSIONS: Children who received DEX after liver transplantation have large variability in clearance, which was not found to be associated with weight but is influenced by underlying liver function, as reflected by INR. In this population, titration of DEX dosing to clinical effect may be important because weight-based dosing is poorly associated with blood concentrations. More attention to quality of DEX sedation may be warranted when INR values are changing.

7. 增殖物激活受体 γ 辅激活子 1α 单倍剂量不足可促进烧伤后的疼痛慢性化

Proliferator-Activated Receptor-Gamma Coactivator-1α Haploinsufficiency Promotes Pain Chronification After Burn Injury

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Anesthesia & Analgesia: 2020 130 240-247

背景：手术和创伤等组织损伤常伴随急性疼痛的发生，并通常随着组织愈合而消失。但在很多情况下，尽管组织已修复，但急性疼痛并没有消失，而是转化成了慢性疼痛。本研究中，我们检测了增殖物激活受体 γ 辅激活子 1α（PGC-1α），一个线粒体生物合成的主要调节因子，是否与小鼠烧伤后的疼痛慢性化有关。
方法：采用 PGC-1α$^{+/+}$和同窝的 PGC-1α$^{+/-}$小鼠，雌雄均有。对这些小鼠进行烧伤实验。检测后爪机械缩足阈值和热缩足潜伏期。
结果：PGC-1α$^{+/-}$和 PGC-1α$^{+/+}$小鼠的爪肢机械缩足阈值和热缩足潜伏期的基线水平想差不多。烧伤后第 3 天和第 5 天，PGC-1α$^{+/+}$和 PGC-1α$^{+/-}$小鼠均表现出明显的缩足参数下降。当 PGC-1α$^{+/+}$小鼠在第 11-14 天完全恢复至其烧伤前水平时，PGC-1α$^{+/-}$小鼠并未在同一时间内恢复这些参数，与性别无关。此外，我们通过运用化学发光依赖的活性氧成像技术，发现 PGC-1α$^{+/-}$小鼠和 PGC-1α$^{+/+}$小鼠组织炎症的恢复程度相似。
结论：综上，我们结果提示 PGC-1α 单倍体剂量不足可促进烧伤后疼痛的慢性化。
（许芳霞译 李金宝校）

BACKGROUND: Tissue injuries such as surgery and trauma are usually accompanied by simultaneous development of acute pain, which typically resolves along with tissue healing. However, in many cases, acute pain does not resolve

despite proper tissue repair; rather, it transitions to chronic pain. In this study, we examined whether proliferator-activated receptor-gamma coactivator-1α (PGC-1α), a master regulator of mitochondria biogenesis, is implicated in pain chronification after burn injury in mice.

METHODS: We used PGC-1α and littermates PGC-1α mice of both sex. Burn injury was induced on these mice. Hindpaw mechanical withdrawal thresholds and thermal withdrawal latency were examined.

RESULTS: Hindpaw mechanical withdrawal thresholds and thermal withdrawal latencies were comparable at baseline between PGC-1α and PGC-1α mice. After burn injury, both PGC-1α and PGC-1α mice exhibited an initial dramatic decrease of withdrawal parameters at days 3 and 5 after injury. While PGC-1α mice fully recovered their withdrawal parameters to preinjury levels by days 11-14, PGC-1α mice failed to recover those parameters during the same time frame, regardless of sex. Moreover, we found that PGC-1α mice resolved tissue inflammation in a similar fashion to PGC-1α mice using a chemiluminescence-based reactive oxygen species imaging technique.

CONCLUSIONS: Taken together, our data suggest that PGC-1α haploinsufficiency promotes pain chronification after burn injury.