房顫：圍術期的現有證據和管理策略

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

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房顫（AF）是圍術期最常見的一種心律失常，先前認為這是一種良性、自限性疾病，但近期資料表明圍術期房顫與相當高的發病率和死亡率相關，且可預測部分患者發生長期房顫及卒中的風險。儘管存在已知的危險因素，但大部分房顫的發生依然無法預測，尤其是在非心臟手術之後。因此，將圍術期風險降至最低的策略是最有益的，其中包括避免潛在的誘發心律失常因素，以及積極治療與患者、手術相關可能導致房顫的的因素。除了處理房顫本身，臨床醫生還必須解決房顫引起的血流動力學紊亂症狀，以防止終末器官功能障礙的發生。這篇綜述旨在討論有關房顫的誘發因素、危險因素及轉歸結果的現有證據，以及在當前圍術期環境中存在的一些爭議問題。

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.

（陳思涵 譯 陳傑 校）

連續六個夜班後攝入咖啡因對麻醉住院醫師駕駛行為的影響

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

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背景：麻醉科住院醫師培訓因涉及對住院患者的監護需要通宵工作，從而導致住院醫師睡眠方式的改變以及睡眠時間不足。在通宵工作後，住院醫師通常選擇咖啡提神，為通勤回家做準備。

方法：研究在麻醉住院醫師連續通宵工作 6 天后立即飲用一種咖啡因能量飲料（含 160mg 咖啡因）後在高保真、虛擬實境駕駛模擬器（使用駕駛員導航系統的維吉尼亞駕駛安全實驗室）中駕駛表現的影響。26 名住院醫師參與了這項研究，並在駕駛模擬測試開始前 60min 將其隨機分為飲用含咖啡因或不含咖啡因的能量飲料組。在隨後的一周夜班工作結束後，兩組住院醫師進行了相同的駕駛測試（交叉試驗設計），並使用心理運動警戒任務測試（PVT）來評估其反應時間及注意力下降的程度。

結果：在連續進行 6 個夜班工作後，咖啡因能量飲料組的麻醉科住院醫師在開始行駛的前 10min 內表現出較靈活的操控油門、轉向以及加速的能力，隨後也證明了在最後駕駛的 30min 內，與非咖啡因能量飲料組相比，改善的駕駛能力與更少的障礙物碰撞相關（時期 2：0.65 vs 0.87；時期 3：0.47 vs 0.95；P= 0.03）。飲用含咖啡因能量飲料可明顯改善住院醫師在模擬駕駛中最後 30min 內的駕駛能力。兩組之間的平均反應時間存在顯著差異（278.9 ± 29.1 vs 294.0 ± 36.3 毫秒; P = 0.021），而在主要失誤次數（0.09 ± 0.43 vs 0.27 ± 0.55; P =0 .257）和次要失誤次數方面（1.05 ± 1.39 vs 2.05 ± 3.06; P = 0.197）卻沒有顯著差異。

結論：在連續 6 天夜班工作後飲用含咖啡因的能量飲料，麻醉科住院醫師在高保真駕駛模擬器的測試中可表現出改善的駕駛能力，包括顯著減少了碰撞的發生率以及更快的反應時間。

（陳思涵 譯 陳傑 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.

鞘內給予芬太尼用於剖宮產的療效評價:一項隨機對照試驗的系統回顧和薈萃分析聯合試驗序貫分析

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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背景：芬太尼和嗎啡是剖宮產手術期間行腰麻過程中加入布比卡因最常用的兩種阿片類藥物。許多臨床試驗已經評估了不同劑量芬太尼加入鞘內布比卡因用於腰麻的有效性和安全性，但其益處、危害和最佳劑量仍不清楚。本研究目的是系統地回顧芬太尼單獨加入鞘內布比卡因和聯合嗎啡加入布比卡因用於剖宮產時腰麻的有效性證據。

方法：檢索關鍵電子資料庫(PubMed、Embase 和 Cochrane 圖書館)中剖宮產人群相關的隨機對照試驗。主要結果是腰麻失敗率，這是通過轉為全麻或術中輔助鎮痛來評估的。兩位評審員使用標準化的試算表獨立地提取資料。結果以 95% 置信區間的相對風險或平均差異表示。

結果：薈萃分析納入 17 項隨機對照臨床試驗(大多數被判斷為低或不明確的偏倚風險)，共 1064 名參與者的資料。芬太尼單獨加入鞘內布比卡因可減少術中輔助鎮痛的需要(相對風險，0.18;95%置信區間,0.11 - -0.27;需治療次數 4 次),降低噁心/嘔吐發生率(相對危險度，0.41;95%置信區間,0.24 - -0.70;需治療次數 6.5 次)，且術後首次需要鎮痛時間較長(平均差值 91 分鐘;95%可信區間,69 - 113)。在轉為全身麻醉的發生率(相對危險度，0.67;95% CI, 0.12-3.57)、低血壓的發生率、感覺神經阻滯起效時間或運動阻滯的持續時間方面沒有差異。然而，鞘內加入芬太尼與較高的術中瘙癢發生率相關(相對風險，5.89;95%置信區間,2.07 - -16.79;需要加害次數，13.5)。與單純的鞘內布比卡因複合嗎啡相比，將芬太尼加入鞘內布比卡

因嗎啡具有類似的益處，顯著減少了術中輔助鎮痛的需要(相對風險，0.16;95%

置信區間,0.03 - -0.95;9)。漏斗圖分析顯示納入研究中存在發表偏倚的可能性。

結論：目前證據表明，芬太尼既可單獨作為鞘內布比卡因的添加劑，也可與嗎啡

聯合作為鞘內布比卡因的添加劑用於腰麻下的剖宮產。由於納入研究的發表偏倚、

小樣本量和高偏倚風險的可能性，故需謹慎對待此研究結果。

（蔣旭亮 譯 陳傑 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.

呼氣末屏氣試驗預測容量反應性不適合開腹手術

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

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背景:呼氣末屏氣試驗可預測重症監護患者的容量反應性;然而，它在手術室應用的效力受到質疑。本研究評估開腹手術中呼氣末屏氣試驗來預測擴容的效果。

方法:本研究納入46例患者:第一階段(n = 26)持續15秒的呼氣末屏氣測試,隨之擴容,即 5min 內給予 250ml 膠體和第二階段(n = 20)持續 25 秒呼氣末屏氣測試，隨之擴容。最後 10 例病人進行橫膈壓監測。擴容後心指數增加> 15%的患者為有效應答者。分析脈壓變異度、每搏量（SV）指數、心臟指數。以擴容的應答者狀態為預後指標，建立呼氣末屏氣試驗引起的 SV 和脈壓變化和脈壓變化的受試者工作特徵曲線。

結果:共有 44 次(38%)擴容被視為有效應答。呼氣末屏氣試驗 15 秒後，血流動力學變數無明顯增加。呼氣末屏氣試驗 25 秒後，有效應答者的 SV 指數升高(呼氣末屏氣試驗 25 秒後，有效應答者 vs 無效應答者 37.1±8.8 mL/m vs 35.7 ± 8.6;P<.0001)。呼氣末屏氣試驗不能區分有效和無效應答者。只有脈壓變異度在曲線下面積與偶然預期有顯著差異(0.7 [0.57-0.81];15 秒呼氣末屏氣試驗 P = .002;和 0.78 (0.64 - -0.89);呼氣末屏氣試驗 25 秒 P = .0001)。開腹後胃壓明顯下降(4 [2.75-5]vs 2 [2-4] cm H2O;P = .0417);橫膈壓梯度無明顯差異。

結論:在開腹手術中，呼氣末試驗在區分擴容後有效和無效反應者是不可靠的。

（劉碧瑩 譯 陳傑 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 屏氣 clusion test was not reliable to

discriminate responders from nonresponders after volume expansion during laparotomic surgery

配備醫師的急救直升機上初始格拉斯評分 8 分以上的患者出現鎮痛不足情況：一項 10 萬餘例院外急診的多中心二次數據分析

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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背景：鎮痛不足與其他不良事件一樣，在院外急救初次鎮痛治療期間較為常見，甚至是在醫師在場的情況下。作者分析了格拉斯昏迷評分(GCS)8 分以上的患者在配備醫師的急救直升機(p-HEMS)上進行院外救治期間鎮痛不足的影響因素。

方法：此項多中心的二次數據分析納入 2005 年 1 月 1 日至 2017 年 12 月 31 日的在 p-HEMS 上接受急救的有意識的患者。篩選標準是:患者當場的疼痛數字評分（NRS）大於 4 分，GCS 大於 8 分，未行心肺復蘇且美國國家諮詢航空委員會（NACA）評分小於 6。研究應用多變數的二元回歸分析來研究鎮痛不足（交接 NRS≥4 或疼痛評分降低<3）的特點。研究期間使用線性回歸分析來描述疼痛治療中的變化。

結果：作者分析了 106,730 名患者的資料（3.6% 資料缺失）。其中 82.9%患者在現場接受了鎮痛治療；79.1%患者接受了鎮痛藥物，38.6%則接受了非藥物干預，其中 37.4%的患者同時接受兩種治療。而 18.4%的患者出現了鎮痛不足（置信區間為 18.1-18.6）。與此相關的因素有低 NACA 評分、低 NRS 評分以及出現中樞神經系統或婦產相關的主訴。無臨床證據顯示，相較于強中效阿片藥物、非阿片鎮痛藥或氯胺酮，使用弱阿片藥物（比值比 [OR]）=1.05，95%置信區間 CI,0.68-1.57）與鎮痛不足相關。作者觀察了這項 12 年的研究中鎮痛藥物使用的變化，特別是強效阿片藥物（芬太尼或舒芬太尼）的使用率從 30.3%增至 42.3%（P 值<0.001）。其中 17.1%的患者（95% CI,16.9-17.3）並未接受任何疼痛治療。

結論：在這項佇列研究中，18.4%的患者出現鎮痛不足。特殊主訴，低 NACA 評分、低 NRS 評分與鎮痛不足相關。然而，17.1%患者並未行任何鎮痛治療，這提示仍需改進入院前的鎮痛治療。無論何時應啟動藥物及非藥物的鎮痛治療。

（劉碧瑩 譯 陳傑 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

兒科患者腰叢神經的深度預測：一項回顧性磁共振研究

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

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背景：腰叢神經（LP）阻滯常用於下肢鎮痛中。如果腰叢神經深度（LPD）可預

測，操作時間及操作併發症可以大大減少。

方法：作者研究了 361 例兒科患者（<18 歲）的磁共振影像。使用單一及多重因素線性回歸分析預測腰叢深度，包括患者年齡、體重、身高、正中線與髂後上棘間距。計算正中線與腰叢最外側（midline-LP）及髂後上棘間距（midline-PSIS）的比率，結果顯示針的穿刺點應位於第四、第五腰椎間隙水準（L4/L5）。同時在第四腰椎水準發現腎臟。

結果：在兒科患者中（<18 歲）L4/L5 水準推測腰叢深度公式為：LPD=0.844×體重(kg) + 25.8 (mm)，(卡方檢驗 r2 = 0.791; r2 的 95% 置信區間[CI], 0.753–0.829)。總體 midline-LP/midline-PSIS 比值為 0.87 (95% CI, 0.86–0.89)，而在嬰幼兒中該比值更高，為 0.87 (95% CI, 0.86–0.89)。在兒科患者中，腎下極在 L4 水準更為常見(嬰幼兒為 43.7% ，學齡前兒童為 13.7%)。此項研究中，有 6 名患者（1.7%）在 L4/L5 水準觀察到腎臟。

結論：為對兒科患者實行安全有效的腰叢神經阻滯，應考慮腰叢深度及腎臟損傷的風險。

（劉碧瑩 譯 陳傑 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.

靜息腦功能連接預測老年患者靜注小劑量咪達唑侖後的腦連接變化

Baseline Functional Connectivity Predicts Connectivity Changes Due to a Small Dose of Midazolam in Older Adults

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背景：苯二氮卓類藥物在圍術期作為抗焦慮藥物被廣泛使用。一般來說，該類藥物會影響認知功能，然而能否對小劑量短效苯二氮卓類藥物咪達唑侖的作用進行客觀評估尚未可知。為研究該問題，作者對 55-73 歲成人進行了一項前瞻性觀察研究。通過有效的心理測驗和功能影像技術，研究靜脈注射 2mg 咪達唑侖是否影響認知功能。

方法：作者通過使用完善可重複的神經心理狀態測試和靜息功能磁共振(rs-fMRI)來評估靜注 2mg 咪達唑侖的效果。

結果： 咪達唑侖減少即時和延遲記憶，極大的影響了靜息功能磁共振的結果。靜注咪達唑侖後，基準靜息連接顯示記憶減退。

結論：即使受試者樣本量小，咪達唑侖對腦網路活動的影響在統計學上也有顯著意義。若研究者繼續完善，靜息腦連接功能可能作為評估咪達唑侖對老年患者影響的一個有效手段。

（劉碧瑩 譯 陳傑 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.

術中呼吸機管理與術後氧合、肺部併發症和死亡率的關係

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

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背景：“肺保護通氣”描述了一種包括低潮氣量（VTs）和/或低驅動壓/平臺壓的通氣策略，並與機械通氣後改善的預後相關。 我們評估了術中通氣參數（包括呼氣末正壓[PEEP]，驅動壓和潮氣量）與 3 個術後結局之間的關係：（1）Pao2/Fio2，（2）術後肺部併發症，（3）30 天死亡率。

方法:我們回顧性分析了從 2006 年至 2015 年在美國單中心接受非心臟大手術並在術後維持機械通氣的成年患者。 使用多元回歸分析，我們研究了術中呼吸機設置與術後插管時最低 Pao2 / Fio2、出院診斷包括肺部併發症以及院內 30 天死亡率的相關性。

結果：在一個佇列的 2096 例病例中，中位 PEEP 為 5 cm H_2O（四分位範圍= 4 - 6），中位 VT 為 520 mL（四分位範圍= 460 - 580），中位驅動壓為 15 cm H_2O（13-19）。經過多變數調整後，術中 PEEP（線性回歸估計[B] = -6.04； 95％CI，從-8.22 至-3.87； P <.001），中位 Fio2（B = -0.30；95％CI，從-0.50 至- 0.10；P = .003），以及驅動壓> 16 cm H_2O 的小時數（B = -5.40； 95％CI，-7.2 至-4.2； P <.001）與術後 Pao2 / Fio2 降低有關。較高的術後 Pao2 / Fio2 比值與降低肺部併發症的風險（每 100 mm Hg 的校正比值比= 0.495； 95％CI 為 0.331 - 0.740； P = 0.001，模型 C 統計值為 0.852）和死亡率（調整後的優勢比= 0.495； 95％CI 為 0.366-0.606； P <.001，模型 C 統計量為 0.820）相關。術中 VT> 500 mL 的時間也與術後發生肺部並 ；P = .042）。

結論：在非心臟手術後需要術後插管的患者中，中位 Fio2 升高、中位 PEEP 升高以及持續時間長且驅動壓升高可預示術後 Pao2 / Fio2 較低。術中 VT> 500 mL 的持續時間是術後肺部併發症增加的獨立相關因素。較低的術後 Pao2 / Fio2 比值與肺部併發症和死亡率獨立相關。 我們的研究結果表明，術後 Pao2 / Fio2 可能是未來前瞻性研究的潛在目標，該研究旨在研究特定通氣策略對減少呼吸機相關肺損傷的影響。

（吳兆藝 譯 潘豔、薛張綱）

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

催眠深度監測：源於聽覺誘發電位指數（aepEX）的潛伏中期聽覺誘發電位在接受地氟烷-瑞芬太尼複合麻醉的兒童患者中的應用

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背景：聽覺誘發電位指數（aepEX+）監測系統利用潛伏中期聽覺誘發電位測定催眠深度，本研究在接受地氟烷-瑞芬太尼複合麻醉的兒童患者中評價了該系統的應用。

方法：75 例 1-18 歲（按年齡分組：分為 1-3 歲,3-6 歲,6-18 歲年齡組，用於亞組分析）的患者被納入此項前瞻性觀察性研究。研究同時記錄了 aepEX 和 BIS 數值，其中後者用於對照。研究將 aepEX 區分不同意識水準的能力作為主要研究指標，並根據密西根大學鎮靜評分表定義意識水準的程度，同時使用預測概率 Pk 和 ROC 曲線進行分析。呼末地氟烷濃度和 aepEX、BIS 的關係作為次要結局指標，其關係將使用非線性回歸模型進行評價。

結果：aepEX 和 BIS 的預測概率值分別為 0.68（95%可信區間，0.53-0.82），0.85（95%可信區間，0.73-0.96，P 值=0.02）。aepEX 和 BIS 的 ROC 曲線下麵積分別為 0.89(95%可信區間，0.8-0.95)，0.76(95%可信區間，0.68-0.84，P 值=0.04)。當 aepEX 的截斷值大於 52 時，其最大敏感度和特異度分別為 81%(95%可信區間，61%-93%），86%（95%可信區間 ，74%-94%）；當 BIS 的截斷值大於 65 時，其最大敏感度和特異度分別為 69%（95%可信區間，56%-81%），70%（95%可信區間，57%-81%）。調整年齡的呼末地氟烷濃度的 EC50 值對 aepEX 和 BIS 而言，分別為 0.59MAC（四分位間距，0.38-0.85），0.58MAC（四分位間距，0.41-0.7）。亞組分析表明在 ROC 曲線下面積和 EC50 值上年齡間沒有差異。

結論：在接受地氟烷-瑞芬太尼複合麻醉的兒童患者中，aepEX 可以作為區分清醒狀態與非清醒狀態的可靠指標。

（王沛 譯 潘豔、薛張綱）

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.

與含有 n6 脂肪酸的脂肪乳劑相比，富含 n3 脂肪酸的脂肪乳劑對大鼠心臟取胰島素信號和攝取葡萄糖有保護作用

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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背景：當前我們尚不清楚，與急性暴露於含 n6 脂肪酸的大豆油脂乳劑相比，暴露於 n3 脂肪酸的魚油脂乳劑是否對整個心臟的胰島素信號轉導和葡萄糖攝取更有利。

方法:給 SD 大鼠正常活動的心臟輸注含有 11mm 的葡萄糖和結合白蛋白的 1.2 mM 棕櫚酸鹽 90 分鐘，在起始 30 分鐘內不使用胰島素，後 60 分鐘內給與 50 mU/L 的胰島素。這些大鼠的心臟被隨機分配到 100uM 的脂肪乳組、ω-3 魚油脂肪乳組、無脂肪乳（僅用胰島素治療）組 60 分鐘三組。通過應用[5-3H]葡萄糖放射性追蹤劑測定糖酵解和糖原合成從而計算葡萄糖攝取情況。採用免疫印跡法測定蛋白磷酸酶 2A (PP2A)、前蛋白激酶 Akt 和磷酸化的果糖激酶(PFK)-2。應用特定酶法測定糖酵解的代謝產物。採用質譜法建立醯基肉堿圖譜。應用 κB 核因數(NFκB)易位情況作為活性氧(ROS)的生物感測器。

結果：胰島素介導的葡萄糖攝取由於脂內糖酵解和糖原合成而減少(4.9 ± 0.4 vs 3.7 ± 0.3 μmol/gdw•min;；P = .047)。相反，ω-3 魚油脂肪乳治療組對胰島素介導的葡萄糖攝取並不顯著影響糖酵解和糖原合成(5.1 ± 0.3 vs 4.9 ± 0.4 μmol/gdw•min; P = .94)。雖然脂質不影響 PP2A 的磷酸化狀態，但 ω-3 魚油脂肪乳可顯著增強酪氨酸的磷酸化並可以抑制 PP2A。同時由於 Akt 選擇性的蘇氨酸磷酸化增加，可使得下游靶蛋白 PFK-2 S483 水準升高。由於 1、6-二磷酸果糖與 6-磷酸果糖比率的增加使得 PFK-1 活性與脂質相比也增加(ω-3 魚油脂肪乳組 0.60 ± 0.11 versus 脂質組 0.47 ± 0.09; P = .023)，與 PFK2 增強果糖 2,6-二磷酸化一致，PFK2 為其主要變構啟動劑。NFκB 核因數的易位和啟動可證實 ω-3 魚油脂肪乳可能會導致醯基肉堿的積累和促氧化反應。

結論:與脂質相比，ω-3 魚油脂肪乳通過 PP2A-Akt-PFK 途徑攝取葡萄糖後可對整個活動的心臟產生保護作用。n3 脂肪酸通過降低脂肪酸的 β 氧化效率從而導致醯基肉堿聚集和促氧化反應，這說明 n3 脂肪酸可能會通過抑制氧化還原敏感的 PP2A，從而保護心臟對胰島素信號的傳導和葡萄糖的攝取。

（石平 譯 潘豔、薛張綱）

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藥的使用與麻醉後噁心嘔吐的處理減少有關：一項傾向匹配的回顧性觀察研究

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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背景： 非典型抗精神病藥可有效預防化療引起的噁心和嘔吐，但圍手術期研究很少。 我們試圖驗證慢性非典型抗精神病藥物與術後噁心和嘔吐之間的關係。

方法： 在這項單中心，傾向匹配，回顧性，觀察性研究中，對 2014 年 1 月至 2017 年 12 月的非心臟擇期外科手術病例進行了調查，瞭解麻醉後護理部門對於術後噁心嘔吐患者給予止吐藥的主要結果如下： 長期服用奧氮平，阿立呱唑和利培酮是人們關注的重點。 其他引數包括門診止吐藥，改良的 Apfel 評分，年齡，美國麻醉醫師學會身體狀況評分，病例長度以及接觸致嘔藥和化學預防藥的情況。 使用病例級數據進行邏輯回歸。 在按 1：2 的傾向匹配後進行條件 logistic 回歸，無需替換即可進行抽樣。 進行了蒙特卡洛模擬，以計算平均水準的治療效果。

結果： 在 13,660 例患者中，有 154 例接受非典型抗精神病藥物治療的患者與 308 例未接受抗精神病藥物治療的患者相匹配，分別代表 115 例和 273 例的獨特患者。 在一個均衡的佇列中，接受典型抗精神病藥的患者的嘔吐機率水準與未服用非典型抗精神病藥的患者相比，長期服用 3 種非典型抗精神病藥的患者的嘔吐率更低，優勢比為 0.29（95%CI，0.11-0.75； P = .015）。

結論： 慢性非典型抗精神病藥治療與麻醉後止吐給藥的降低有關。 這些發現支援需要進行前瞻性研究來確定使用這些藥物進行術後噁心和嘔吐化學預防的安全性和有效性。

（王碩 譯 潘豔、薛張綱）

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.

呼吸機模式不影響脊柱外科手術中失血或輸血的需求：一項回顧性研究

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

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背景：

成人脊柱畸形手術中失血是多因素的。麻醉相關因素，如機械通氣方式，可能導致術中失血。本研究旨在探討呼吸機模式及呼吸機參數對俯臥位脊柱手術患者術中失血量及輸血需求的影響。

方法：

這項單中心回顧性研究調查了 2015 年 5 月至 2016 年 6 月期間接受選擇性俯臥位脊柱手術的 18 歲以上患者的電子病歷。採用多元線性回歸模型控制年齡、性別、美國麻醉師學會（ASA）身體狀況評分、體重指數（BMI）、術前凝血參數和實驗室值、手術水準、籠結構、截骨術、經椎間孔腰椎錐間融合術、椎板切除術、二次手術、脊柱手術侵襲性指數和手術時間，研究呼吸機模式和呼吸機參數與術中估計失血量（EBL）、填充紅細胞（PRBCs）、新鮮冰凍血漿（FFP）、冷沉澱和血小板輸注、引流量的關係。在二次分析中，比較了壓力控制通氣（PCV）和容量控制通氣（VCV）傾向評分匹配佇列的 EBL、輸血量和術後引流量。

結果：

回顧了 946 份記錄，822 份被納入分析。調整混雜因素後，在通氣模式和術中 EBL（估計值，-2；95%CI，-248 至 245；P=.99）或血製品輸注（PRBC：估計值，-9；95%CI，-154 至 135；P=.90；FFP：估計值，-3；95%CI，-59 至 54；P=.93；冷沉澱：估計值，-14；95%CI，-70 至 43；P=.63；血小板：-7；95%CI，-39 至 24；P=.64）之間未觀察到具有統計學意義的關聯。傾向性評分匹配後（每組 n=27），PVC 組與 VCV 組在 EBL（平均差 525 mL；95%CI，-15 至 1065；P=.056）或血製品輸注（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）；冷沉澱（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）方面無顯著差異。

結論：

在俯臥位脊柱手術中，機械通氣和氣道壓力與術中失血或異體輸血無關。使用肺保護技術的現代通氣策略可以緩解先前觀察到的 PCV 和 VCV 模式之間的失血差異。

（魏婉婷 譯 潘豔、薛張綱）

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

切口損傷調節嗎啡獎賞作用和嗎啡複用：Kappa 阿片受體啟動的作用

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背景:在手術恢復期之後持續使用處方類阿片藥物是美國當前阿片危機相關公共衛生問題的一重要部分。然而，很少有研究來研究嗎啡獎賞作用是否受到急性疼痛和損傷的影響。

方法：在小鼠切口損傷和輕微創傷模型中，小鼠接受了嗎啡的建模、消退和藥物複用，以分別檢驗嗎啡在急性切口損傷和藥物複用下的獎賞作用特性。此外，我們還試圖確定這些行為是否受到 kappa 阿片受體信號傳導通路的影響，因此在用嗎啡和切口損傷建模之後以及在複用藥物之前，我們檢測了前強啡肽信使 RNA 在伏隔核和內側前額葉皮質中的表達。

結果：在存在切口損傷的小鼠中，我們觀察到嗎啡獎賞作用的增強，其更偏好設置為嗎啡相關的位置，但這種增強在複用嗎啡時就減弱了。這種適應性減弱效應在切口損傷後 12 天組的小鼠中沒有出現，此時疼痛敏感化已經消退；反而它們顯示了嗎啡複用時的增強效應。前強啡肽在切口損傷和嗎啡處理小鼠的伏隔核和內側前額葉皮質中的表達明顯增加，並持續升高至藥物複用。 在切口損傷後 12 天后組的小鼠中未觀察到這些變化。此外，在複用嗎啡前用 Nor-BNI 阻斷 kappa 阿片受體逆轉了損傷所致的減弱效應。

結論：這些發現表明，由於切口損傷，嗎啡的獎賞作用有所增強，但反常的是，這也是一種對在切口損傷下由獎賞回路中 kappa 阿片受體啟動導致的藥物複用的保護性適應。遠期的損傷不能提供這種保護，反而表現為增強藥物複用。

（葉姍姍 譯 潘豔、薛張綱）

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.

彈性增強喉罩與氣管插管在甲狀腺手術中封閉氣道效果的比較:一項隨機對照試驗

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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背景:FLMA 在甲狀腺手術中得到廣泛應用，但仍存在漏氣、移位等問題。

方法:在這個隨機、單盲、非劣效性的對照試驗中，我們將擇期行甲狀腺根治術的患者隨機分為氣管內插管組(ETT)和 FLMA 組。主要結果為通氣洩漏量、氣道壓

力峰值和呼吸末二氧化碳分壓(PetCO2)。在插入 ETT/FLMA 時，劃皮時，以及手術期間每間隔 10 分鐘收集主要結果的資料。並分別以 10ml、5cm H2O 和 10mm Hg 作為通氣洩露量、氣道峰值壓力和 PetCO2 非劣效 δ 值。我們使用線性混合效應模型評估了相對于 ETT 組患者，FLMA 組患者主要結果資料的非劣效性。我們術前、術後均評估 FLMA 面罩位置，並記錄氣道併發症。

結果:132 例患者中，ETT 組 65 例，FLMA 組 67 例。混合效應模型(FLMA 組- ETT 組)在通氣漏量、氣道峰值壓力和 PetCO2 方面的差異分別為 2.09 mL(98.3%置信區間[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)。術後 FLMA 的光纖位置評分明顯高於術前。FLMA 組無嚴重移位、面罩密封性喪失、返流或誤吸。FLMA 組有 1 例患者出現短暫且易於控制的喉痙攣。

結論:在甲狀腺手術中，儘管在操作過程中可能出現輕微到中度的面罩移位，但 FLMA 在氣道壓力峰值和 PetCO2 方面並不劣於 ETT。沒有證據表明使用 FLMA 時併發症發生率更高。

（王甲利 譯 潘豔、薛張綱）

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.

血管擴張性休克的逆轉：治療休克的常規、搶救和新型血管活性藥物的研究現狀

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

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瞭解血管收縮藥的不同機制對於它們在臨床不同休克狀態下的最佳應用至關重要。我們全面回顧了常規的、搶救的和新型的血管活性藥物，包括它們的藥理作用和支持它們在血管擴張性休克中使用的證據。本文討論了每種藥物與膿毒症存活指南中的關係，以提供每種藥物如何適用於治療血管擴張性休克的演算法的環境。當常規藥物無效時，可以使用救援劑，儘管關於它們的臨床有效性的證據程度不同。此外，最近出現了抗壞血酸和血管緊張素 II 等治療血管擴張性休克的新藥物。抗壞血酸在血管麻痹的治療中取得了一定的成功，目前正在對其有效性進行更嚴格的評估。血管緊張素 II(Ang-2)是治療血管擴張性休克的最新血管增壓藥。除了節約了兒茶酚胺，它已被證明在某些危重患者亞群中可以降低死亡率。

（許芳霞譯 李金寶校）

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.

髖部骨折患者術後譫妄的危險預測評分的建立

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

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背景：髖部骨折術後譫妄（PHFD）是老年患者一個重要的臨床問題，但尚缺少合適的簡易的風險預測模型用於術前。

方法：我們查閱了 2016 年美國外科醫生學院國家外科品質改進計畫髖部骨折手術目標參與者使用資料檔案，獲得一項 60 歲以上髖部骨折患者的佇列研究（n=8871，隨機分配至推導組[70%]或驗證組[30%]）。通過採用逐步多變數 losistic 回歸分析，進一步除去變數，然後評估受試者-操作者特徵曲線下面積（AUC）的變化，在推導組中建立了 PHFD 的簡約預測模型。從最終的多變數模型得出風險評分。

結果：在 6210 例推導組患者中，有 1816 例發生 PHFD（29.2%）。在 32 個候選變數中，9 個被納入最終的模型：（1）術前譫妄（校正比值比[aOR]，8.32 [95%

可信區間]{CI}6.78-10.2，8 分）；（2）術前癡呆（aOR，2.38 [95%CI,2.05-2.76]，3 分）；（3）年齡（參考，60-69 歲）（70-79 歲：aOR，1.60[95%CI，1.20-2.12]，2 分；80-89 歲：aOR，2.09[95%CI，1.59-2.74]，2 分；≥90 歲：aOR，2.43[95%CI，1.82-3.23]，3 分）；（4）醫療管理（aOR，1.43[95%CI，1.31-1.81]，1 分）；（5）美國麻醉醫師協會（ASA）身體狀況分級 III-V 級（aOR，1.40[95%CI，1.14-1.72]，1 分）；（6）功能依賴（aOR，1.37[95%CI，1.17-1.61]，1 分）；（7）吸煙（aOR，1.36[95%CI，1.07-1.72]，1 分）；（8）全身炎症反應綜合征/膿毒症/膿毒性休克（aOR，1.34[95%CI，1.09-1.65]，1 分）；（9）術前使用助行器（aOR，1.32[95%CI，1.14-1.52]，1 分），風險評分總分在 0-20 分之間。Logistic 回歸和風險評估模型的 AUCs 分別為 0.77（95%CI，0.76-0.78）和 0.77（95%CI，0.76-0.78），與驗證佇列的結果相似。

結論：以這 9 個術前危險因素為基礎的危險評分對老年人 PHFD 的預測有良好的準確性。

（許芳霞譯 李金寶校）

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. 兒童電休克的麻醉管理：對現有文獻的系統回顧

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

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電休克療法（ECT）被越來越廣泛應用于兒童的各種精神疾病。但尚缺乏文獻報導相關麻醉管理的臨床特點。本系統綜述的目的是描述兒科 ECT 麻醉問題的現有文獻。對原始出版物進行篩選，納入標準是：（1）英文手稿；（2）18 歲以下人群；（3）使用 ECT。資料表包括人口統計資訊，麻醉管理和 ECT 過程的細節以及不良事件。平均年齡為 15 歲，90%為 12-17 歲，沒有＜6 歲的案例。最常見的精神病診斷為重度抑鬱（n=185）和精神分裂症/分裂性情感障礙（n=187）。ECT 同樣被用來治療很多其它疾病。所有病例中有 16%存在併發症。常見併發症為發育遲緩（n=21）和孤獨症（n=18）。主要的 ECT 指征為嚴重的精神疾病（n=190），藥物治療無效的症狀（n=154），自殺傾向（n=153）。每個患者的 ECT 療程從 2-156 不等，平均持續時間為 91.89±144.3s。最常見的誘導藥物為丙泊酚和甲硫氨酸，最常見的肌松藥物為琥珀膽鹼。報告的不良事件包括頭痛、噁

心、鎮靜和短期遺忘，以及罕見的良性心律失常和長時間癲癇發作。消極的認知和獲得護理的機會減少可導致治療延誤，因此，這些兒童就會處於疾病的晚期。在檢查 592 名兒童的現代化 ECT 細節中，沒有出息嚴重的麻醉併發症。進一步研究應該從回顧性分析 ECT 期間的麻醉資料開始，從而比較麻醉藥物和技術對不良事件和結果的各種影響。

（許芳霞譯 李金寶校）

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.加速血管置管檢測的體外刺激研究

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

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背景：一些操作者用 0.9%的氯化鈉對小型靜脈血管導管針頭進行預處理，稱這種改進在置管過程中可加快檢測血管置入導管時目測的回血速度。

方法：我們使用人類血液比較了生理鹽水灌注和未灌注生理鹽水的 24 和 22 號血管導管針頭回血所需的時間（Introcan Safety IV 導管； B.Braun，伯利恒，賓夕法尼亞州）。注射泵（Medfusion 4000，北卡羅來納州卡裡）穿刺針通過矽膠膜穿入裝有新鮮捐贈的人類血液的靜脈輸液“ t 型管”（Microbore Extension Set，5 英寸； Hospira，Lake Forest，IL）。當血管導管針頭接觸血液時電路傳導就完成了，從而發光二極體被照亮。通過視頻回顧，我們確定了從發光二極體照亮到視覺檢測血液回流導管的時間。我們在 24 和 22 規格的血管導管（共 420 個導管）中測試了 105 個生理鹽水灌注的血管導管和 105 個未灌注的血管導管。我們使用 R（http://www.R-project.org/）中的非參數 Wilcoxon 秩和檢驗分析了中位時間以使回血視覺化。斯坦福大學醫學研究中的人類受試者行政管理小組指出該項目不符合人類受試者研究的要求，因此不需要機構審查委員會的監督。

結果：在 24 號血管導管組中，血液通過未灌注血管導管針的中位時間（和四分位間距）為 1.14（0.61-1.47）秒，而生理鹽水灌注組為 0.76（0.41-1.20）秒（P ＝ 0.006）。在 22 號導管組中，血液通過未灌注血管導管針的時間的中位時間（四分位間距）為 1.80（1.23-2.95）秒，而生理鹽水灌注組為 1.46（1.03-2.54）秒（ P = .046）。

結論：這些結果表明，與未灌注的血管導管針相比，用 0.9%氯化鈉灌注小的血管導管針，特別是 24 號導管，可以更早地檢測到血管置管。

（許芳霞譯 李金寶校）

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. 腰硬聯合麻醉中 4 種基於體重給藥的苯腎對預防剖宮產低血壓的量效研究

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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背景：預防性靜脈輸注苯腎上腺素是預防腰麻剖宮時低血壓的有效措施。然而最佳輸注劑量尚不清楚。本研究的目的是確定 50%（ED50）和 90%（ED90）的患

者在以固定比例根據體重進行預防性輸注時，有效預防低血壓的苯腎上腺素的劑量。

方法：80 例擇期剖宮產的產婦隨機分為 4 組（每組 20 人），在鞘內注射 10mg 高壓布比卡因和 5μg 舒芬太尼後，立即開始以 0.25、0.375、0.5 和 0.625 μg/kg/min 的速度輸注苯腎上腺素。有效劑量的定義是，在開始腰麻到分娩期間，未出現低血壓（收縮壓低于基線水準≥20%或＜90 mmHg）。用 probit 分析計算預防性苯腎上腺素的 ED50 和 ED90 值。

結果：在苯腎上腺素輸注速度分別為 0.25、0.375、0.5 和 0.625 μg/kg/min 的 4 組中，低血壓的發生率分別為 13/20、8/20、2/20 和 1/20。ED50 和 ED90 的計算值分別為 0.31（95%CI，0.24-0.36）和 0.54（95%CI，0.46-0.76）。各組的不良反應和新生兒結局均無顯著性差異。

結論：在本研究條件下，以恒速輸注苯腎上腺素從而預防腰麻剖宮產術中低血壓時， ED50 和 ED90 值分別是 0.31（95%CI，0.24-0.36）和 0.54（95%CI，0.46-0.76）μg/kg/min。

（許芳霞譯 李金寶校）

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. 右美托咪定在嬰幼兒原味肝移植術後的藥動學研究

Pharmacokinetics of Dexmedetomidine in Infants and Children After Orthotopic Liver Transplantation
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背景：右美托咪定（DEX）是小兒肝移植術後常用的鎮靜藥物。肝功能不全，包括藥物清除率改變，在肝移植術後很常見。然而，這部分人群DEX的藥動學（PK）尚不清楚。本研究旨在探討小兒肝移植術後 DEX 的 PK 譜。

方法：採用單中心、開放標記的右美托咪定藥動學研究，靜脈負荷劑量為 0.5μg/kg，持續泵注劑量為 0.5μg/kg/h。一共有 20 例年齡為 1 月-18 歲，行肝移植術後進入重症監護室的患兒納入本研究。採集全血，用幹血紙片法分析 DEX 的濃度。採用非線性混合效應模型對 DEX 的藥動學特點進行描述。

結果：右美托咪定的藥動學以一級消除二室模型為佳。一個典型的兒童肝移植後，國際標準化比值（INR）為 1.8，全血 DEX 清除率為 52L/h（95%可信區間[CI]，31-73 L/h）。此外，組間清除率為 246L/h（95%可信區間[CI]，139-391 L/h），中心分佈容積為 186 L/70kg（95%可信區間[CI]，140-301L/kg），外周分佈容積為 203 L（95%可信區間[CI]，123-338L）所有參數的個體間變異度在 11%-111%。

清除率與體重無關，而與 INR 成反比。INR 增加至 3.2 可導致 DEX 清除率降低 50%。體重與分佈中心容積呈線性相關。所有其它協變數，包括年齡、缺血時間、總膽紅素和丙氨酸轉移酶，都不是預測 DEX 分佈的顯著因數。

結論：肝移植術後接受 DEX 治療的兒童肝臟清除率有很大的變異度，它與體重無關，但受肝功能影響，比如受 INR 影響。在這群人中，根據臨床效應來滴定 DEX 的劑量可能很重要，因為基於體重的劑量與血濃度相關性較差。當 INR 發生變化時，DEX 鎮靜的品質需要更加注意。

（許芳霞譯 李金寶校）

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. 增殖物啟動受體 γ 輔啟動子 1α 單倍劑量不足可促進燒傷後的疼痛慢性化

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

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背景：手術和創傷等組織損傷常伴隨急性疼痛的發生，並通常隨著組織癒合而消失。但在很多情況下，儘管組織已修復，但急性疼痛並沒有消失，而是轉化成了慢性疼痛。本研究中，我們檢測了增殖物啟動受體 γ 輔啟動子 1α（PGC-1α），一個線粒體生物合成的主要調節因數，是否與小鼠燒傷後的疼痛慢性化有關。

方法：採用 PGC-1α$^{+/+}$和同窩的 PGC-1α$^{+/-}$小鼠，雌雄均有。對這些小鼠進行燒傷實驗。檢測後爪機械縮足閾值和熱縮足潛伏期。

結果：PGC-1α$^{+/-}$和 PGC-1α$^{+/+}$小鼠的爪肢機械縮足閾值和熱縮足潛伏期的基線水準想差不多。燒傷後第 3 天和第 5 天，PGC-1α$^{+/+}$和 PGC-1α$^{+/-}$小鼠均表現出明顯的縮足參數下降。當 PGC-1α$^{+/+}$小鼠在第 11-14 天完全恢復至其燒傷前水準時，PGC-1α$^{+/-}$小鼠並未在同一時間內恢復這些參數，與性別無關。此外，我們通過運用化學發光依賴的活性氧成像技術，發現 PGC-1α$^{+/-}$小鼠和 PGC-1α$^{+/+}$小鼠組織炎症的恢復程度相似。

結論：綜上，我們結果提示 PGC-1α 單倍體劑量不足可促進燒傷後疼痛的慢性化。

（許芳霞譯 李金寶校）

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.