血管擴張劑霧化吸入治療心臟手術患者的肺動脈高壓：一項系統性評價和薈萃分析

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

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背景: 在心臟手術中，肺動脈高壓是一個重要的預後因素，對此相繼出現了一些治療方法。在本次系統評價和薈萃分析中，作者比較了在心臟手術中霧化吸入與靜脈使用血管擴張劑及安慰劑對肺動脈高壓的療效差異。搜索從開始至2015年10月MEDLINE、CENTRAL、EMBASE、Web of Science和clinicaltrials.gov資料庫。主要預後指標為死亡率。次要預後指標包括住院時間和ICU停留時間以及血流動力學特徵的評估。

方法: 在確認的2897項引文中，共納入了10項研究的434例患者。

結果: 與靜脈給藥相比，霧化吸入顯著降低肺血管阻力（-41.36dyne·s/cm，P = 0.03），有更高的平均動脈壓（8.24mm Hg，P = 0.02）和右心室射血分數（7.29%，P <0.0001）。兩組間沒有觀察到顯著的血液動力學差異;然而，霧化吸入組ICU停留時間更長（0.66天，P = 0.01）。餘指標未見顯著差異。

結論: 與靜脈給藥相比，在心臟手術中霧化吸入血管擴張劑治療肺動脈高壓與改善的右心室功能相關。與安慰劑相比，應用試驗藥物在主要預後指標方面並無任何獲益。這一領域需要進行深入研究，並著重於臨床預後的顯著改善。

（崔璀譯 陳傑校）

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

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

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

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

惡性高熱易感者骨骼肌代謝功能障礙

Skeletal Muscle Metabolic Dysfunction in Patients With Malignant Hyperthermia Susceptibility.

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背景：惡性高熱（MH）是一種骨骼肌的藥理遺傳疾病，表現對某些麻醉藥物具有潛在致命的高代謝反應。然而，一些MH疑似患者在沒有麻醉藥物觸發的情況下經歷了肌無力，肌疲勞和運動不耐受。這項探索性研究的目的是闡明通過咖啡因-氟烷攣縮試驗測定MH陽性的患者運動不耐受的病理生理學。為此，作者採用磷磁共振波譜，血氧水準依賴功能磁共振成像（MRI）和傳統運動實驗來比較MH陽性患者和健康對照組的骨骼肌代謝。

方法：使用磷磁共振波譜和血氧水準依賴性功能MRI評估29個MH陽性患者和20個健康對照的骨骼肌代謝情況。採用傳統的體力量度測量有氧代謝能力，無氧代謝能力和肌力。

結果：在30和60秒活動期間，與健康對照相比，MH陽性患者通過氧化途徑產生的ATP顯著降低。與健康對照組相比，MH陽性患者的血氧水準依賴性功能MRI恢復時間更長。與健康對照相比，運動實驗顯示MH陽性患者的有氧代謝和無氧代謝能力較低。

結論：這項探索性研究的結果表明，與健康個體相比，MH陽性患者的有氧代謝受損。這可以解釋在MH易感患者人群中表現出的運動不耐受。

（陳聰譯 陳傑校）

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

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

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

深度鎮靜期間同日大量口服腸道製劑的安全性：一項前瞻性觀察研究

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

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背景：結腸鏡檢查品質與腸道準備直接相關。手術當天給予部分瀉藥，腸道準備工作可得到很大的改善。然而，仍然存在導致較高的胃殘留量(GRV)，增加肺誤吸風險的顧慮。本研究目的是評估在異丙酚深度鎮靜下，檢測手術前一天和當天行腸道準備患者的胃殘留量(GRV)和胃液PH值差異。
方法:這是一項以當天接受胃腸內鏡和結腸鏡檢查患者為物件的前瞻性觀察性研究。所有納入患者都進行大容量的聚乙二醇瀉藥製劑行腸道準備並接受異丙酚鎮靜。在胃鏡下收集患者胃液，檢測其容量和PH值。
結果：本研究總共納入428名患者，其中56%的患者接受了操作當天的腸道準備，餘下患者接受術前一天的腸道準備。兩組胃殘留量的均值 ± 標準差分別為18.1 ± 10.2毫升和16.3 ± 16.5毫升(P = .69)。兩組發生GRV≥ 25毫升或高於預期的GRV(0.4ml/kg)情況無統計學差異(分別為P=0.9和P=0.87)。以最後一次胃腸道準備的時間(3–5, 5–7, >7 小時)進行分組評估GRV，各組間也沒有統計學差異（P =0 .56）。兩組胃腸道準備患者的胃液PH值相似(P=0.23，分別為2.5±1.4和2.5±1.3)。但手術前一天行胃腸道準備患者其腸道準備不充分的比例更高（P =0 .001）。
結論：在結腸鏡檢查當天，手術前3小時完成大容量胃腸道準備不會導致胃殘留量(GRV)的升高，胃液PH的下降。
（丁曦冰譯 陳傑校）

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

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

遠端缺血預處理減輕肺葉切除後肺氧化應激損傷：一項單中心、隨機、雙盲、對照實驗

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

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背景：肺癌患者的肺葉切除手術中，術側肺通常呈現萎陷和低灌注。當肺被重新擴張時，缺血再灌注損傷會隨之發生。研究者猜測遠端缺血預處理（RIPC）可以降低肺氧化應激和改善術後氣體交換功能。
方法：研究者對非小細胞肺癌進行肺葉切除手術的患者進行單中心、隨機、雙盲實驗。53位患者在麻醉誘導後隨機進行肢體遠端缺血預處理（在大腿使用止血帶進行缺血處理，5分鐘缺血／5分鐘灌注，共3個迴圈）或對照治療。對呼出氣冷凝物和動脈血中的氧化應激標誌物進行檢測，採集時間分別為麻醉誘導後遠端缺血預處理和手術之前（T0，基線）、術側肺萎陷雙側肺通氣之前（T1）、雙側肺通氣即刻（T2）、雙側肺通氣後120分鐘（T3）。主要結果為T1、T2和T3三個時間點呼出氣冷凝物中8-異前列腺素水準。次要結果包括以下：呼出氣冷凝物和血中NO2+NO3、H2O2水準和ph值，還有肺氣體交換參數（PaO2/FiO2、A-aDO2、a/A 比和呼吸指數）。
結果：在T1、T2和T3三個時間點，進行遠端缺血預處理的患者的呼出氣冷凝物中8-異前列腺素比對照組低，其中平均值差值和95%可信區間分別為：-15.3 (5.8-24.8), P = .002; -20.0 (5.5-34.5), P = .008; 和-10.4 (2.5-18.3), P = .011。在遠端缺血預處理組，呼出氣冷凝物中NO2+NO3和H2O2水準在T2和T1-T3也較對照組有所降低。處理組血液中8-異前列腺素和NO2+NO3水準在T2時間點有所降低(P < .05)。運用95%可信區間比較均值發現，遠端缺血預處理組在肺葉切除後2、8、24小時相比對照組具有更好的氧合指數，分別為78 (10-146), 66 (14-118), and 58 (12-104)。

結論：肢體遠端缺血預處理降低肺葉切除患者呼出氣冷凝物中8-異前列腺素及其他氧化應激肺損傷標誌物。通過評估氧合指數發現遠端缺血預處理還可以改善術後氣體交換功能。

（葛家希譯 陳傑校）

BACKGROUND: During lobectomy in patients with lung cancer, the operated lung is often collapsed and hypoperfused. Ischemia/reperfusion injury may then occur when the lung is re-expanded. We hypothesized that remote ischemic preconditioning (RIPC) would decrease oxidative lung damage and improve gas exchange in the postoperative period.

METHODS: We conducted a single-center, randomized, double-blind trial in patients with nonsmall cell lung cancer undergoing elective lung lobectomy. Fifty-three patients were randomized to receive limb RIPC immediately after anesthesia induction (3 cycles: 5 minutes ischemia/5 minutes reperfusion induced by an ischemia cuff applied on the thigh) and/or control therapy without RIPC. Oxidative stress markers were measured in exhaled breath condensate (EBC) and arterial blood immediately after anesthesia induction and before RIPC and surgery (T0, baseline); during operated lung collapse, immediately before resuming two-lung ventilation (TLV) (T1); immediately after resuming TLV (T2); and 120 minutes after resuming TLV (T3). The primary outcome was 8-isoprostane levels in EBC at T1, T2, and T3. Secondary outcomes included the following: NO2+NO3, H2O2 levels, and pH in EBC and in blood (8-isoprostane, NO2+NO3) and pulmonary gas exchange variables (PaO2/FiO2, A-aDO2, a/A ratio, and respiratory index).

RESULTS: Patients subjected to RIPC had lower EBC 8-isoprostane levels when compared with controls at T1, T2, and T3 (differences between means and 95% confidence intervals): -15.3 (5.8-24.8), P = .002; -20.0 (5.5-34.5), P = .008; and -10.4 (2.5-18.3), P = .011, respectively. In the RIPC group, EBC NO2+NO3 and H2O2 levels were also lower than in controls at T2 and T1-T3, respectively (all P < .05). Blood levels of 8-isoprostane and NO2+NO3 were lower in the RIPC group at T2 (P < .05). The RIPC group had better PaO2/FiO2 compared with controls at 2 hours, 8 hours, and 24 hours after lobectomy in 95% confidence intervals for differences between means: 78 (10-146), 66 (14-118), and 58 (12-104), respectively.

CONCLUSIONS: Limb RIPC decreased EBC 8-isoprostane levels and other oxidative lung injury markers during lung lobectomy. RIPC also improved postoperative gas exchange as measured by PaO2/FiO2 ratio.

老年創傷性顱內出血患者術前低劑量阿司匹林暴露與其急診手術預後

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

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背景：抗血小板藥物通常在擇期神經外科手術前停用，但在急診神外手術中卻無法得以實現。本研究對接受急診神外手術的老年患者進行了一項回顧性佇列研究，以探討術前服用阿司匹林是否會導致更劣的預後。
方法：研究者對1級創傷中心2008～2012年間所有接受了急診神經外科手術的創傷性顱內出血的案例進行了分析，其中對於65歲以上且術前有過阿司匹林暴露史的老年患者，研究者比較了患者的統計學特徵，併發症以及結局。排除標準包括：（1）多發傷，（2）其他術前抗凝劑或抗血小板藥物的聯合使用，（3）手術適應症以外的硬膜下、硬膜外、或腦實質出血，以及（4）一次住院期間重複接受多次神外手術。所研究的結局包括術中預估出血量、需要再次手術的術後顱內出血，住院死亡人數，ICU住院天數，總住院時長，以及圍手術期血液製品的輸注。此外，作者還研究了血小板輸注是否會對服用阿司匹林的患者的結局產生影響。
結果：本研究納入了171名患者。術前服用阿司匹林的患者（n=87，其中95%的患者均為小劑量服用：81mg/d）與不服者（n = 84; 78.3 ± 7.8 vs 75.9 ± 7.9 歲, $P > 0.05$）大致年齡相仿，只是前者的格拉斯哥昏迷評分分數稍高(12.8 ± 3.4 vs 11.4 ± 4, $P = 0.02$)，以及患冠狀動脈疾病的概率更高($P < 0.05$) 。校正了格拉斯哥昏迷評分分數以及冠狀動脈疾病等因素後，研究者發現術前服用阿司匹林的患者圍手術期血小板輸注概率更高（校正後OR=9.89，95%CI為4.24 - 26.25）。兩組之間在其他結局方面均沒有差異。在接受阿司匹林暴露的患者中，術前或術中的血小板輸注並不能導致一個較好的預後。
結論：在接受急診手術且年齡≥65歲的創傷性顱內出血的老年患者中，術前小劑量服用阿司匹林不增加圍手術期出血，住院時間和住院死亡率。
（徐僑翌譯 陳傑校）
BACKGROUND: Antiplatelet medications are usually discontinued before elective neurosurgery, but this is not an option for emergent neurosurgery. We performed a retrospective cohort study to examine whether preoperative aspirin use was associated with worse outcomes after emergency neurosurgery in elderly patients.
METHODS: We analyzed all cases of emergency neurosurgical procedures for traumatic intracranial hemorrhage from 2008 to 2012 at a level 1 trauma center. Demographics, comorbidities, and outcomes were compared for patients ≥65 years by preoperative aspirin exposure. Exclusion criteria were: (1) polytrauma, (2) concomitant use of other preoperative anticoagulants or antiplatelet agents, (3) surgical indication other than subdural, extradural, or intraparenchymal hemorrhage, and (4) repeat neurosurgical procedures within a single admission. Estimated intraoperative blood loss, postprocedural intracranial bleeding requiring reoperation, death in hospital, intensive care unit, and hospital lengths of stay and perioperative blood product transfusion from 48 hours before 48 hours after surgery were the study outcomes. We also examined whether platelet transfusion had an impact on outcomes for patients on aspirin.
RESULTS: The cohort included 171 patients. Patients receiving preoperative aspirin (n = 87, 95% taking 81 mg/day) were the same age as patients not receiving aspirin (n = 84; 78.3 ± 7.8 vs 75.9 ± 7.9 years, $P > .05$), had slightly higher admission Glasgow Coma Scale scores (12.8 ± 3.4 vs 11.4 ± 4, $P = .02$) and tended to have more coronary artery disease ($P < .05$). Adjusted for Glasgow Coma Scale and coronary artery disease, patients receiving preoperative aspirin had a higher odds of perioperative platelet transfusion (adjusted odds ratio 9.89, 95% confidence interval 4.24– 26.25). There were no other

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

術前篩查出的阻塞性睡眠呼吸暫停與先前診斷的阻塞性睡眠呼吸暫停相比手術預後更差

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

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背景：阻塞性睡眠呼吸暫停（OSA）影響著高達26%的美國成年人，經常漏診，增加圍手術期發病率。研究者假設在手術當天篩查出來的中／高風險的OSA（S-OSA）患者與先前診斷OSA（D-OSA）患者有相同的圍手術期呼吸系統併發症、醫療花費和死亡率。其次，研究假設這兩組OSA患者都比未患OSA的患者有更多呼吸系統併發症。

方法:通過對1個教學醫院和2個社區醫院的電子醫療資料庫進行回顧性調查，以研究正在接受非緊急住院治療的成年人(2012年1月1日至2014年12月31日)。根據手術當天術前評估和呼吸暫停(打鼾、疲勞、睡眠中可觀察到的呼吸暫停、高血壓、體重指數超過35、年齡超過50歲、頸粗、男性)得分，病人被劃分為D-OSA 、S-OSA或No-OSA。觀察了圍手術期的呼吸事件和干預措施、醫療花費和死亡率。主要預後指標(不良呼吸事件[AREs])包括圍手術期的低氧血症和困難氣道管理。血氧過低被定義為持續脈搏血氧測定3分鐘，外周血氧飽和度(SpO2)小於90%，或經驗證和／或被手工記錄入病歷。輕度低氧血症被定義為最低SpO2是86%-89%，中／重度低氧血症被定義為最低SpO2小於等於85%。次要預後指標包括術後呼吸干預、ICU入住、住院時間、30天和1年的全因死亡率。使用線性和邏輯回歸分析對結果進行比較。

結果:共有28912名患者接受了評估:3432名(11.9%)D-OSA患者;1546(名5.3%)S-OSA患者;以及23934(82.8%)無No-OSA患者。S-OSA患者中之前有68.0％出現不良呼吸事件;D-OSA患者中至少71.0%;No-OSA患者中至少52.1%(未經調整的P值小於0.001)，主要是出PACU後的中度或重度低血氧症事件(PACU;在S-OSA患者中有39.9%;在D-OSA 患者中有39.5%;在No-OSA患者中有27.1%)。與D-OSA患者相比，S-OSA患者在PACU中的中度/重度低氧血症率更低，但有相似的術中和術後，更高的困難面罩通氣率，以及相似的困難氣管插管報告。在對人群、健康、手術差異和醫院類型進行調整後，在S-OSA和D-OSA患者中，發生大於等於1的不良呼吸事件率可能性並沒有不同(調整後的比值比0.90[99%的置信區間，0.75-1.09];P=.15)。與D-OSA患者相比，S-OSA患者術後的術後重插管、機械通氣、術後直接重症監護病房住院、住院時間和30天的全因死亡率顯著增加。

結論:被歸類為 S-OSA 的患者與 D-OSA 患者的不良呼吸事件率相同，但S-OSA患者術後呼吸干預、醫院使用和30天的全因死亡率都有所增加。這部分比D-OSA 患者有更糟糕的術後結果的S-OSA患者，反映了出PACU後對這一臨床診斷缺乏認識和適當的管理。這些高危患者需要多學科干預。

（楊柳譯 陳傑校）

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

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

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

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

神經電刺激不能正確預測肌間溝臂叢神經阻滯中針-神經的距離和局麻藥物的擴散趨勢。

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

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本研究評估了神經電刺激作為一個神經定位工具的價值。對 43 位行肩部手術的患者引發運動反應後，通過超聲成像來評估針尖端的位置離相距最近的神經的距離，以及生理鹽水的擴散情況。21 位患者針尖距離最近的神經 1-4mm，7 位患者針尖直接接觸到了神經，另外 15 位患者針尖距離神經 6-18mm。在 21 位患者當中，隨後注入的生理鹽水夾層未達到臂叢。因此，神經電刺激正確識別針-神經距離的成功率為 48.8%，且僅有 51.2%的患者能夠達到正確的流體擴散。

（姚雪雅譯 陳傑校）

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

在糖尿病神經病變大鼠模型中，二亞苯基碘鎓可通過減弱氧化應激的作用減輕布比卡因引起的坐骨神經損傷

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

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背景:在糖尿病神經病變(DN)大鼠模型中，局部麻醉引起的神經損傷已被證明與氧化應激的增加相關。本研究探討了氯化二亞苯基碘鎓(DPI)，一種 NADPH 氧化酶(NOX)抑制劑，對布比卡因造成糖尿病神經病變(DN)大鼠的坐骨神經損傷的影響。

方法:採用高脂飲食和鏈黴素注射液建立糖尿病神經病變大鼠模型。通過檢測(i)血糖，(ii)後爪 von Frey 觸覺反應測試，(iii) 熱刺激縮足反應潛伏期(PWTL)，(iv)神經傳導速度(NCV)來確定模型建立。使用布比卡因(0.2 mL,5 mg / mL)行大鼠右坐骨神經阻滯。阻滯前 24 小時與 30 分鐘，於皮下注射二亞苯基碘鎓(1 mg / kg)。阻滯後 24 小時，測試神經傳導速度，數種活性氧簇，以及 Caspase-3 蛋白酶以評估坐骨神經損傷的程度。

結果: 糖尿病神經病變大鼠模型建立成功。與對照組相比，布比卡因阻滯組大鼠的 VF 觸覺測量值(對照組, 16.5 ± 1.3 g; 布比卡因組, 19.1 ± 1.5 g, P < .001)與熱刺激縮足反應潛伏期(對照組, 13.3 ± 1.1 s; 布比卡因組, 14.6 ± 1.1 s, P = .028)增加，而坐骨神經傳導速度顯著下降（對照組, 38.8 ± 2.4 m/s,布比卡因組, 30.5 ± 2.0 m/s, P = .003）。且布比卡因組的坐骨神經損傷程度（由軸突面積評估）更嚴重(對照組, 11.6 ± 0.3 μm, 布比卡因組, 7.5 ± 0.3 μm, P < .001)。此外，DPI 注射可顯著改善神經功能(VF responses, 17.3 ± 1.3 g; PWTL, 13.4 ± 1.1 seconds; NCV, 35.6 ± 3.1 m/s)，減輕軸突面積損失(9.6 ± 0.3 μm)。與不經 DPI 注射的大鼠相比，DPI 注射組大鼠的 NOX2、NOX4 和 caspase - 3 的蛋白表達水準，脂質過氧化物和過氧化氫酶水平均明顯降低(P < .05)。

結論:在高脂肪飲食/鏈球菌誘導的糖尿病神經病變大鼠模型中，皮下注射 DPI 可以防止布比卡因神經阻滯造成的坐骨神經的功能性和神經組織學損傷。

（張金源譯 陳傑校）

Background: Increased oxidative stress has been linked to local anesthetic-induced nerve injury in a diabetic neuropathy (DN) rat model. The current study explores the effects of diphenyleneiodonium (DPI) chloride, an NADPH oxidase (NOX) inhibitor, on bupivacaine-induced sciatic nerve injury in DN rats.

Methods: A rat DN model was established through high-fat diet feeding and streptozotocin injection. The model was confirmed via testing (i) blood glucose, (ii) hindpaw allodynia responses to von Frey (VF) monofilaments, (iii) paw withdrawal thermal latency (PWTL), and (iv) nerve conduction velocity (NCV). Bupivacaine (Bup, 0.2 mL, 5 mg/mL) was used to block the right sciatic nerve. DPI (1 mg/kg) was injected subcutaneously 24 hours and 30 minutes before the sciatic block. At 24 hours after the block, NCV, various reactive oxygen species, and Caspase-3 were evaluated to determine the extent of sciatic nerve injury.

Results: The DN rat model was successfully established. Compared with the DN control group, the postblock values of VF responses (DN-Con, 16.5 ± 1.3 g; DN + Bup, 19.1 ± 1.5 g, P < .001) and PWTL significantly increased (DN-Con, 13.3 ± 1.1 seconds; DN + Bup, 14.6 ± 1.1 seconds, P = .028); the NCV of sciatic nerve was significantly reduced (DN-Con, 38.8 ± 2.4 m/s, DN + Bup, 30.5 ± 2.0 m/s, P = .003), and sciatic nerve injury (as indicated by axonal area) was more severe in the bupivacaine-treated DN group (DN-Con, 11.6 ± 0.3 μm, DN + Bup, 7.5 ± 0.3 μm, P < .001). In addition, DPI treatment significantly improved nerve function (VF responses, 17.3 ± 1.3 g; PWTL, 13.4 ± 1.1 seconds; NCV, 35.6 ± 3.1 m/s) and mitigated loss of axonal area (9.6 ± 0.3 μm). Compared to the DN + Bup group (without DPI), the levels of lipid peroxides and hydroperoxides, as well as the protein expression of NOX2, NOX4, and Caspase-3, were significantly reduced in the DN + Bup + DPI group (P < .05).

Conclusions: Subcutaneous injection of DPI appears to protect against the functional and neurohistological damage of bupivacaine-blocked sciatic nerves in a high-fat diet/streptozotocin-induced DN model.

確定研究的主要結果並證明研究的次要結果：通常越少越好

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

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設計和開展研究的第一步是確定主要和任何次要的研究結果。在實驗，准實驗或分析觀察研究中，主要研究結果與主要研究目標相一致。同樣，次要研究結果與次要研究目標相一致。一項特定的主要研究結果奠定了實驗假設的基礎，同時在字面上被納入了假設。在方法部分，作者清楚地陳述和定義每個主要和任何次要研究結果變數。同樣，在這部分，作者清楚地描述了如何測量所有主要和任何次要研究結果變數。作者會提供足夠的細節，使臨床醫生，統計學家或資訊學家能夠準確地知道要測量的內容，使其他研究人員可以在各自研究場所重複測量結果。作者公佈證據（最好）或其他記錄以證明任何應用的測量儀器，工具或量表的有效性和可靠性。一個常見的錯誤（通常是致命的研究設計缺陷）是對現有測量儀器，工具或量表進行再創造（“本土化”）或修改而沒有提供其有效性和可靠性的任何證據。最佳的主要結果是所採用的干預與現有或合理的證據相關聯。一個實驗包括太多的主要結果可能導致（a）研究無法聚焦相關問題，（b）如果治療效果在整個結果中不同，很難給出合理的解釋。在研究設計和結果中包含次要變數需要證明其合理性。如果次要結果可以為主要終點提供支持證據，那麼次要結果特別有幫助。複合終點通常是由幾個互相關聯的結果變數組成的終點。在設計一項研究時，研究人員將複合終點的組成部分限定在感興趣的干預最有希望產生影響的變數上，並且最好是在有初步證據的情況下。理想情況下，強複合終點的組成部分具有相似的治療效果，頻率和嚴重程度，最重要的是類似的嚴重程度。

（張松譯 陳傑校）

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

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

一種依託咪酯類似物在大鼠實驗中表現出較少抑制腎上腺皮質功能、血流動力學更穩定、行為學恢復更快的特性

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

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背景：ET-26 鹽酸鹽是一種依託咪酯類似物，被設計為在保留依託咪酯特性即快速起效鎮靜作用及血流動力學平穩的同時減少對腎上腺皮質功能的抑制作用。本研究比較了 ET-26 鹽酸鹽、依託咪酯以及鎮靜催眠藥丙泊酚作用於大鼠的麻醉效能、血流動力學穩定、以及恢復特性。

方法：本實驗取三隻大鼠的血漿及肝組織勻漿離體進行高表達脂質層析法分析得出 ET-26 鹽酸鹽的代謝半衰期。“上下”實驗得出三種藥物的 50%催眠劑量（HD50）。應用相同劑量的三種藥物評估麻醉效果和平均動脈壓。血清皮質醇激素濃度應用酶聯免疫法分析得到。大鼠使用均等的三種藥物的恢復能力使用開放場地水迷宮實驗與乳酸鈉林格液進行比較。

結果：ET-26 鹽酸鹽在大鼠血漿和孵育肝勻漿中的代謝半衰期分別為 81±6 分鐘和 126±12 分鐘（平均值±標準差）。大鼠的在體實驗表明，ET-26 鹽酸鹽使大鼠翻正能力消失的作用比依託咪酯低三倍。均等劑量下，靜脈注射丙泊酚與 ET-26 鹽酸鹽（-10.7mmHg）和依託咪酯（-19.4mmHg）相比使平均動脈壓相較於基線下降更多（-27.9mmHg）。使用均等劑量的 ET-26 鹽酸鹽和丙泊酚 ACTH1 激發實驗 15 分鐘（P＜.001）、30 分鐘（P＜.001）和 60 分鐘（P=.002）血清皮質醇激素濃度前者更高。靜脈單次快速注射，ET-26 鹽酸鹽組與丙泊酚組相比空間感恢復更快，自發性活動恢復則更慢。

結論：ET-26 鹽酸鹽的麻醉效能和血流動力學穩定性與依託咪酯類似，但是抑制腎上腺皮質功能的副作用更小；空間感恢復較丙泊酚更快，與依託咪酯類似。（曹雪譯 潘豔、薛張綱校）

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

METHODS: The metabolic half-life of ET-26HCl was determined in vitro using highperformance liquid chromatography analysis of samples of rat plasma and

liverhomogenates taken from 3 animals. Hypnotic median effective doses (HD50) ofET-26HCl, etomidate, and propofol were determined by up-and-down methods.Anesthesia effect and mean arterial pressure were estimated using equivalentintravenous (IV) doses of propofol, etomidate, and ET-26HCl in the rats. Serum
concentrations of corticosterone were analyzed by enzyme-linked immunosorbentassay. The ability of rats to recover from the sedative-hypnotic effects of thedrugs was evaluated using open field and Morris water maze tests at equipotentdoses of propofol, etomidate, ET-26HCl, and normal saline.
RESULTS: The metabolic half-life of ET-26HCl was 81 ± 6 minutes in rat plasma and126 ± 12 minutes in incubation liver homogenate (mean ± standard deviation),respectively. In vivo experiments showed that the potency of ET-26HCl to cause a loss of righting reflex in rats was 3 times lower than that of etomidate in therats. IV propofol caused a greater decrease in mean arterial pressure relative tothe baseline (-27.9 mm Hg) than did ET-26HCl (-10.7 mm Hg) and etomidate (-19.4mm Hg) at equipotent doses. Serum corticosterone levels after drug administrationwere significantly higher in the ET-26HCl group than in the etomidate group atequivalent doses when measured 15 ($P < .001$), 30 ($P < .001$), and 60 ($P = .002$)minutes after stimulation with adrenocorticotropic hormone (ACTH1-24). Recoveryof spatial orientation from anesthesia induced by an IV bolus injection wasfaster with ET-26HCl than with propofol, but recovery of spontaneous activity wasslower.
CONCLUSIONS: ET-26HCl has anesthetic potency and hemodynamic stability similar toetomidate, but it caused less adrenocortical hormone synthesis suppression thanetomidate and faster spatial orientation recovery from anesthesia than propofol, which was similar to etomidate.

剖宮產嚴重產後出血的危險因素：病例對照研究

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

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Anesthesia & Analgesia: 2017 125 523–532.

背景：與分娩前行剖宮產術的女性相比，分娩過程中行剖宮產的女性發生產後出血的風險增加了。為了明確在行分娩前剖宮產女性及行分娩中剖宮產的女性兩組間的個體危險因素和嚴重產後出血之間是否存在聯繫及聯繫的強度，需要依據剖宮產的亞型來進行分層分析。
方法：為了確定分娩前剖宮產及分娩中剖宮產兩組女性人群的嚴重產後出血的危險因素，我們進行了兩項病例對照研究。研究佇列納入人群是在 2002 至 2012 年在美國第三產科中心分娩的女性人群。每一項研究中，所有的病例都是出血量超過 1500 毫升或者是在術中或術後輸血持續到術後 48 小時。對行分娩前或分娩中剖宮產的女性發生嚴重產後出血的危險因素採用分離邏輯回歸模型進行驗證。
結果：分娩前剖宮產組，實驗組納入 269 個病例，對照組 550 個病例。分娩前剖宮產中嚴重產後出血具有最高校正比值比的臨床因素是全麻（校正比值比是 22.3，95%的置信區間是 4.9-99.9；參照組是椎管內麻醉），多胎妊娠（校正比值比是 8.0，

95%置信區間是 4.2-15.0；參照組是單胎妊娠），前置胎盤（校正比值比是 6.3，95%置信區間 3.4-11.8）。分娩中剖宮產組，實驗組納入 278 個病例，對照組 572 個病例。分娩中剖宮產中發生嚴重產後出血具有最高校正比值比的臨床因素是全麻（校正比值比是 5.4，95%置信區間 1.7-17.1），多胎妊娠（校正比值比是 3.2，95%置信區間 1.7-6.3），產前血色素小於等於 9.9g/dL（校正比值比是 3.0，95%置信區間 1.3-6.9；參照組是產前血色素大於等於 11g/dL）。

結論：行分娩前及分娩中剖宮產的女性人群擁有共同的嚴重產後出血的危險因素（全麻和多胎妊娠）。然而，兩組中嚴重產後出血的危險因素不同，當計畫對行分娩前或分娩中剖宮產的高危病人進行干預時,識別出這些不同可能是重要的。

（胡翔翔譯 潘豔、薛張綱校）

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

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

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

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

病態胎盤附著患者的標準化輸血治療方法

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

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Anesthesia & Analgesia 2017 125 603-608.

背景：在美國，由於剖宮產率的升高（2014 年 32.2%），粘連性胎盤的發病率從每千人 0.8 增加至 3.0。粘連性胎盤患者分娩時，平均失血範圍在 2000 到 5000 毫升，常需大量輸血治療。我們報導了本機構針對這類患者的多學科治療方法，以及 5 年期間的輸血治療結果。
方法：我們回顧了 2009 年 7 月 1 日至 2014 年 7 月 1 日符合研究條件的胎盤疾病的患者資料，我們通過術前胎盤疾病清單來優化圍產期出血患者的治療。
結果：136 名患者的胎盤在術後接受了檢查，其中 21 名有粘連性胎盤，39 名有顯微鏡下粘連性胎盤，17 名有植入性胎盤，17 名有穿透性胎盤，42 名無胎盤粘連（其中 11 名有前置胎盤）。對於每種類型，患者接受血製品輸注的比率為 71%（粘連性胎盤），28%（顯微鏡下粘連性胎盤），82%（植入性胎盤），82%（穿透性胎盤），19%（無胎盤粘連）。對於這些患有胎盤粘連相關疾病的患者，其中 89%進行了分娩後子宮切除，而沒有胎盤粘連或僅有顯微鏡下粘連性胎盤的患者分娩後子宮切除率為 5%。
結論：基於我們的經驗和回顧性分析得出的結果，無論是有分娩前影像學證據還是臨床懷疑病態胎盤附著的患者，均可從標準化臨床處理流程，包括輸血治療中受益。我們發現分娩前已發現的異常胎盤形成患者的大出血是可以預測的，並且無論胎盤粘連程度多少，輸血量都很大。本機構的流程可迅速為高危患者在出現危及生命的產科大出血時提供充足的血製品數量和類型。因此，對於已經確診的病態胎盤粘連患者，計畫行剖宮產且可能進行子宮切除，一份程式化的多學科團隊制定的清單，包括前瞻性輸血治療等，是最佳的臨床實踐。
（劉雯珺譯 潘豔、薛張綱校）

BACKGROUND: The incidence of placenta accreta (PA) has increased from 0.8 to 3.0 in 1000 pregnancies, driven by increased rates of cesarean deliveries (32.2% in 2014) of births in the United States. The average blood loss for a delivery complicated by PA ranges from 2000 to 5000 mL, frequently requiring substantial transfusion medicine support. We report our own institutional multidisciplinaryapproach for managing such patients, along with transfusion medicine outcomes, in this setting over a 5-year period.
METHODS:We reviewed records for patients referred to our program in placental disorders from July 1, 2009, to July 1, 2014. A placental disorders preoperative checklist was implemented to ensure optimal management of patients with peripartum hemorrhage.
RESULTS:Of 136 patients whose placentas were reviewed postpartum, 21 had PA, 39 had microscopic PA, 17 had increta, 17 had percreta, and 42 had no accreta (of which 11 had placenta previa). For each subtype, the percentage of patients receiving blood products were 71% (PA), 28% (microscopic PA), 82% (increta), 82% (percreta), and 19% (no accreta). Among patients with PA or variants, 89% of patients with PA or variants underwent postpartum hysterectomy, compared to only 5% of patients with no or microscopic PA.
CONCLUSIONS:Based on our experience and on the findings of our retrospective analysis, patients presenting with either antepartum radiological evidence or clinical suspicion of morbidly adherent placenta will benefit from a standardized protocol for clinical management, including transfusion medicine support. We found that massive

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

世界衛生組織建議圍手術期進行吸氧管理來預防手術部位感染：一個危險的簡化策略？

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

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Anesthesia & Analgesia 2017 125 682-687

2016 年 10 月，世界衛生組織（World Health Organization，WHO）發佈了關於預防手術部位感染（surgical site infections，SSIs）的建議。其中包括了建議術中至術後 6 小時內吸氧濃度為 80%。SSIs 已成為一個全球性的健康問題，WHO 這次的建議值得讚賞。然而這項建議僅僅只關注手術病人的“切口”，卻忽視了高濃度吸氧對病人其他器官系統的影響並可能惡化病人的預後。

WHO 強烈建議高濃度吸氧，儘管證據水準僅為中度。然而，忽視高濃度吸氧潛在的致命的併發症來實現這一目標似乎是不合適的，特別是高濃度吸氧預防 SSI 的證據水準還不足。因此，這一策略在麻醉醫師和手術醫師間引起激烈的討論。

在大多數臨床情況下，正常血容量、正常血壓、正常血糖、正常體溫、正常通氣顯然可以安全應用于大多數病人。然而，像 WHO 建議的那樣，任意地在術中至術後 6 小時內進行高濃度吸氧，這一策略在麻醉學和圍手術醫學上還有待商榷，這將在本文中進一步討論。

（王雨婷譯 潘豔、薛張綱校）

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

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

Normovolemia, normotension, normoglycemia, normothermia, and normoventilation can clearly be safely applied to most patients in most clinical scenarios. But the liberal application of hyperoxemia intraoperatively and up to 6 hours postoperatively, as suggested by the WHO, is questionable from the viewpoint of anesthesia and perioperative medicine, and its effects will be discussed in this article.

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兒童全麻蘇醒期躁動風險量表的研製與驗證：一項前瞻性觀察研究

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

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Anesthesia & Analgesia. 2017 125 550–555

背景：蘇醒期躁動是小兒全麻術後常見的併發症。階段 2 的研究目標是在行七氟醚麻醉的小兒中建立預測模型（EA 風險量表）預測小兒 EA 的發發病率，通過我們之前階段 1 和階段 2 的回顧性分析研究資料，確定階段 2 前瞻性觀察性佇列研究中的 EA 風險量表的有效性。

方法：利用我們以前研究中 120 例患者的資料，採用 logistic 回歸分析預測 1 期 EA 的發病率。通過使用 Akaike 資訊準則逐步選擇程式確定了預測的最優組合。計算出選定預測因數的 β 係數，並確定預測因數的得分。EA 的風險規模的預測能力是由接受者操作特性曲線（ROC）、ROC 區曲線下（指數）和 95%可信區間（CI）計算而得。在第 2 階段，使用另一組 100 名患者（在全身麻醉下進行小手術）證實了 EA 風險量表的有效性。分別計算 ROC 曲線、指數、最佳臨界點，點的敏感性和特異性。此外，我們計算了灰色區域，這兩個點之間的敏感性和特異性分別 90%。

結果：在 1 期的多變數 Logistic 回歸分析最終的模型包括以下 4 個預測因數：年齡（OR:-0.38；95% CI=-0.81- 0.00），小兒麻醉行為評分（OR:0.65；95% CI=-0.09-1.40），麻醉時間（OR,0.60；95% CI=-0.18 -1.19），手術過程（斜視手術 OR:2.53；95% CI=1.30-3.75,扁桃體手術 OR:2.71；95% CI=0.99-4.45）。EA 風險量表包括這 4 個預測因數，從 1 到 23 分不等。在第 2 階段，EA 的發生率為 39%。1 階段的 OR 指數為 0.84（95% CI=0.74-0.94），2 階段的 OR 指數為 0.81（95% CI=0.72-0.89）。EA 風險量表的最佳截止點為 11（靈敏度＝87%，特異性＝61%）。灰色區域從 10 到 13 分，包括 38%的病人。

結論：我們研製並驗證了行七氟醚麻醉的兒童的 EA 風險量表。在驗證佇列，該量表具有良好的預測性能（OR 指數大於 0.8）。EA 風險量表可用于預測兒童的 EA，並為高危人群採取預防策略。這種基於評分的預防性方法應該進行前瞻性研究，以評估這種策略的

（吳俊梅譯 潘豔、薛張綱校）

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

observational cohort study (phase 2).
METHODS: Using data collected from 120 patients in our previous study, logistic regression analysis was used to predict the incidence of EA in phase 1. The optimal combination of the predictors was determined by a stepwise selection procedure using Akaike information criterion. The beta-coefficient for the selected predictors was calculated, and scores for predictors determined. The predictive ability of the EA risk scale was assessed by a receiver operating characteristic (ROC) curve, and the area under the ROC curve (c-index) was calculated with a 95% confidence interval (CI). In phase 2, the validity of the EA risk scale was confirmed using another data set of 100 patients (who underwent minor surgery under general anesthesia). The ROC curve, the c-index, the best cutoff point, and the sensitivity and specificity at the point were calculated. In addition, we calculated the gray zone, which ranges between the two points where sensitivity and specificity, respectively, become 90%.
RESULTS: In phase 1, the final model of the multivariable logistic regression analysis included the following 4 predictors: age (logarithm odds ratios [OR], -0.38; 95% CI, -0.81 to 0.00), Pediatric Anesthesia Behavior score (logarithm OR, 0.65; 95% CI, -0.09 to 1.40), anesthesia time (logarithm OR, 0.60; 95% CI, -0.18 to 1.19), and operative procedure (logarithm OR, 2.53; 95% CI, 1.30-3.75 for strabismus surgery and logarithm OR, 2.71; 95% CI, 0.99-4.45 for tonsillectomy). The EA risk scale included these 4 predictors and ranged from 1 to 23 points. In phase 2, the incidence of EA was 39%. The c-index of phase 1 was 0.84 (95% CI, 0.74-0.94), and the c-index of phase 2 was 0.81 (95% CI, 0.72-0.89). The best cutoff point for the EA risk scale was 11 (sensitivity = 87% and specificity = 61%). The gray zone ranged from 10 to 13 points, and included 38% of patients.
CONCLUSIONS: We developed and validated an EA risk scale for children receiving sevoflurane anesthesia. In our validation cohort, this scale has excellent predictive performance (c-index > 0.8). The EA risk scale could be used to predict EA in children and adopt a preventive strategy for those at high risk. This score-based preventive approach should be studied prospectively to assess the safety and efficacy of such a strategy.

圍術期靜脈血栓栓塞：綜述

Perioperative Venous Thromboembolism: A Review.

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Anesthesia & Analgesia. 2017 125 403-412.

靜脈血栓栓塞（VTE）是圍手術期增加患者的發病率、死亡率和醫療費用的一個重要問題。它也被認為是最可預防的術後併發症。在過去的 20 年內儘管廣泛的採用指南預防，它的發病率並沒有實質性的改變。目前的預防工作還不夠這是越來越明顯的。使用強效抗凝藥可降低靜脈血栓栓塞的發生率，但增加出血和感染的風險。隨著近年來對靜脈血栓形成的病理生理學的更多學習。人們越來越重視除了抗凝劑所調控的“傳統凝血級聯反應”之外的組織因數、單核細胞、中性粒細胞、中性粒細胞外的攜帶物、微泡和血小板血栓的形成和擴展。這些最近的研究在一定程度上解釋了為什麼阿司匹林在防止血栓傳播方面表現出顯著的效果。血管內皮功能障礙，傳統上認為是動脈血栓形成的危險因素，靜脈瓣尖端獨特的環境為靜脈血栓的形成起

著重要的作用，這表明新的治療方式，如他汀類藥物的作用。並不是所有的患者都有同等的風險患靜脈血栓栓塞，即使在接受高危手術時，也需要更好的工具來準確預測靜脈血栓栓塞的風險。只有這樣我們才能有效的個體化預防和權衡靜脈血栓栓塞的風險與治療相關的風險。由於細胞類型和參與血栓形成的途徑的不同，使用低安全劑量止血調節療法如抗凝劑，抗血栓和抗血小板藥物的綜合治療方案可能會更有效。

(葉志祥譯 潘豔、薛張綱校)

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

左旋布比卡因減少瑞芬太尼、丙泊酚消費閉環滴定的腦電雙頻指數引導下進行胸段硬膜外鎮痛：一項雙盲安慰劑對照研究

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

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背景：當血流動力學被用於滴定麻醉深度時，胸段硬膜外鎮痛（TEA）聯合全身麻醉可以使得全麻的用量減半。因此我們確定 TEA 對麻醉需要量的影響，使用閉環控制器通過監測腦電雙頻指數來自動調控丙泊酚和瑞芬太尼的用量。

方法：採用單中心雙盲研究，選擇擇期行後外側開胸手術的患者。患者被隨機分配接受注射後持續輸注 0.5%布比卡因（左旋組）或 0.9%生理鹽水溶液（生理鹽水組）。

全麻是由同一個自動控制器進行的。經食道多普勒探頭引導的卒中體積優化在隨機化之前進行。主要結果變數是瑞芬太尼在切皮和縫合皮膚之間的自動釋放量。記錄到的大動脈低血壓。資料以中位數[四分位距]或數量表示（%）
結果：每組十九例患者完成了研究。對腦電雙頻指數範圍在 40-60 的患者進行比較(85 [77-88] vs 83 [72-87]; P = .39),與單純全麻相比，椎管內阻滯需要較少的瑞芬太尼(0.15 [0.10-0.20] vs 0.23 [0.14-0.25], microg.kg.min; P = .03)和丙泊酚用量(4.3 [3.7-4.9] vs 5.7 [4.6-7.3] mg.kg.h; P = .005)。兩組主要動脈低血壓均相似（左旋與生理鹽水組，分別為 6 [32%] vs 5 [25%]; P = .46；）。
結論：左旋布比卡因硬膜外給藥可以減少瑞芬太尼的用量減少三分之一。卒中體積優化後，兩組主要的動脈低血壓放生率相似。
（劉娟蘭譯 潘豔、薛張綱校）
BACKGROUND: Thoracic epidural analgesia (TEA) combined with general anesthesia decreases anesthetic requirements by half when hemodynamic criteria are used for the titration of analgesia. We therefore determined the impact of TEA on anesthetic requirements, when a closed-loop controller was used allowing the automated coadministration of propofol-remifentanil guided solely by the Bispectral index.
METHODS: This single-center double-blind study enrolled patients scheduled for elective posterolateral thoracotomy using TEA. Patients were randomly assigned to receive a bolus followed by a continuous infusion of levobupivacaine 0.5% (levo group) or saline 0.9% solution (saline group). General anesthesia was performed by the same automated controller. Stroke volume optimization guided by an esophageal Doppler probe was performed before randomization. The primary outcome variable was the amount of remifentanil delivered by the automated controller between skin incision and closure. Major arterial hypotension was recorded. Data are presented as medians [interquartile range] or number (%)
RESULTS:: Nineteen adult patients per group completed the study. At similar depth of anesthesia evaluated by the percentage of time with the Bispectral index in the range 40-60 (85 [77-88] vs 83 [72-87]; P = .39), patients with neuraxial block required less remifentanil (0.15 [0.10-0.20] vs 0.23 [0.14-0.25], microg.kg.min; P = .03) and propofol (4.3 [3.7-4.9] vs 5.7 [4.6-7.3] mg.kg.h; P = .005). Major arterial hypotension was similar in both groups (6 [32%] vs 5 [25%]; P = .46; levo versus saline group, respectively).
CONCLUSIONS: Epidurally administered levobupivacaine allowed a decrease by one-third of remifentanil requirement. After stroke volume optimization, major arterial hypotension was similar between groups.

在完全弗氏佐劑誘發的炎症疼痛模型中 σ-1 受體/ p38 MAPK 抑制穴位埋線調節疼痛的作用

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

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背景：

內質網伴侶蛋白質 Sigma-1 受體（σ-1 受體）和絲裂原活化蛋白激酶（MAPKs）參與了疼痛機制。穴位刺激在炎性疼痛中發揮了確切的抗痛覺過敏作用。然而，σ-1 受體和 MAPKs 是否與穴位刺激誘導的鎮痛作用相關聯尚不清楚。本研究探討了穴位埋線（ACE）的鎮痛效果以及抑制 σ-1 和 MAPKs 在穴位埋線鎮痛中的作用。

方法：

小鼠進行鞘內置管準備。在炎性疼痛小鼠模型的（完全弗氏佐劑足底注射）雙側昆侖穴（BL60），足三裡穴（ST36）和三陰交（SP6）穴位進行穴位埋線。然後，每日注射 σ-1 受體激動劑 PRE-084 或生理鹽水。在完全弗氏佐劑注射前和注射後的 1,3 和 5 天時測量縮爪反應的閾值和爪水腫程度。使用蛋白免疫印跡來評估脊髓 σ-1 受體，p38MAPK 和細胞外信號調節激酶（ERK）的蛋白表達，並在完全弗氏佐劑注射後 1,3 和 5 天利用免疫組化檢測 σ-1 受體。

結果：

穴位埋線表現出特定的鎮痛作用。穴位埋線增加了小鼠縮爪反應的閾值，並在 1,3 和 5 天顯著降低完全弗氏佐劑誘發的爪水腫。穴位埋線降低 σ-1 受體的蛋白表達，其在注射完全弗氏佐劑後 1,3 和 5 天顯著增加。除第 5 天，第 1、3 天穴位埋線降低 p38 MAPK 和 ERK 的表達。然而，除了不改變 ERK 的表達，注射 σ-1 受體激動劑 PRE-084 顯著逆轉了這些改變，。

結論：

本研究表明，在完全弗氏佐劑誘發炎症性疼痛的小鼠模型中，除 ERK 外，穴位埋線通過抑制 σ-1 受體對 p38 MAPK 調節的表達，發揮了抗痛覺過敏作用。

（吳靜怡譯 潘豔、薛張綱校）

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

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

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

CONCLUSIONS: The present study demonstrated that ACE exhibited antihyperalgesic effects via the inhibition of the Sig-1R that modulated p38 MAPK, but not ERK,

expression in the CFA-induced inflammatory pain model in rats.

在心臟手術病人中，一個有組織的護理過程可以減少圍手術期併發症的發生

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

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嚴重的併發症在術後心臟手術病人的重症監護中很常見。其中的一些併發症可能會在從手術室向重症監護病房(重症監護病房)移交過程中受到影響。護理過程的結構化轉移可能會降低通信錯誤和圍手術期併發症的發生率。我們假設，從術中團隊到重症監護小組的合作、全面、結構化的護理將減少一組特定的術後併發症。我們通過開發和引進一個綜合的多學科的護理過程來檢驗這一假說。我們在干預前後使用兩個護理資料庫之間的聯繫來測量病人的結果:麻醉資訊管理系統和關鍵的護理併發症登記資料庫。在研究期間，共有 1127 名術後心臟外科手術的患者，在干預後的 550 名和 577 名患者中。干預前後的總體併發症(P=.154)之間沒有統計學上的差異。然而，干預治療後可預防併發症的減少(P=.023)。這項調查的主要發現是，從手術室到重症監護室的合作全面的護理過程的引入，與那些可預防的併發症的患者有關。

(潘豔、薛張綱校）

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

住院患者的院內死亡率和膿毒症干預手段之間的關係：一項具體資料的回顧性研究

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

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Anesthesia & Analgesia: 2017 125 507-513.

背景:膿毒症是全身對感染產生的可以導致組織損傷、氣管衰竭甚至死亡的一種反應。為了減少膿毒症相關併發症發生率和死亡率，目前已經有很多研究致力於形成一套有循證依據的可以在膿毒症早期對其進行識別和處理的干預手段。我們對最小創傷性膿毒症干預手段和院內死亡率之間的關係進行了評估。
方法:我們對三藩市加利福利亞大學醫學中心的成年患者進行了回顧性佇列研究。這些患者的出院時間限定在 2012 年 1 月 1 日至 2014 年 12 月 31 日之間，並且均曾診斷為重症膿毒症或者膿毒症休克。膿毒症干預手段包括：測量血乳酸，抗生素使用前進行血液培養，發生膿毒症表現 3 小時內（急診室）和 1 小時內（病房）開始使用廣譜抗生素，低血壓或者乳酸水準高於 4mmol/L 的患者給予靜脈液體復蘇，液體復蘇後仍然低血壓的患者給予血管加壓藥物。我們使用 Poisson 回歸對發病率比（IRR）和需要治療的人數（NNT）進行評估。
結果:完整的干預可以使死亡率降低 30%（調整後的發病率比 IRR 為 0.69，95%置信區間，0.53-0.91）。主要對急診室發生的重症膿毒症、入院時發生的重症膿毒症、年齡、入院時疾病的嚴重程度和死亡風險、機體免疫功能不全和入院時的充血性心力衰竭進行了調整。避免 1 例死亡的治療人數（NNT）為 15（置信區間 ，8-69）。其他死亡獨立危險因素包括入院時發生的重症膿毒症（調整後的 IRR 為 0.55，置信區間，0.32-0.92）和年齡增加（每增加 10 歲調整後的 IRR 為 1.13，置信區間，1.03-1.24）。
結論:在調整風險後，膿毒症干預可以降低院內死亡率。調整後的需要治療人數（NNT）為重症膿毒症患者的結局改善的量化評價提供了合理且可以達到的目標值。
（趙明曄譯 潘豔、薛張綱校）

BACKGROUND: Sepsis is a systemic response to infection that can lead to tissue damage, organ failure, and death. Efforts have been made to develop evidence-based intervention bundles to identify and manage sepsis early in the course of the disease to decrease sepsis-related morbidity and mortality. We evaluated the relationship between a minimally invasive sepsis intervention bundle and in-hospital mortality using robust methods for observational data.
METHODS: We performed a retrospective cohort study at the University of California, San Francisco, Medical Center among adult patients discharged between January 1, 2012, and December 31, 2014, and who received a diagnosis of severe sepsis/septic shock (SS/SS). Sepsis intervention bundle elements included measurement of blood lactate; drawing of blood cultures before starting antibiotics; initiation of broad spectrum antibiotics within 3 hours of sepsis presentation in the emergency department or 1 hour of presentation on an inpatient unit; administration of intravenous fluid bolus if the patient was hypotensive or had a lactate level >4 mmol/L; and starting intravenous vasopressors if the patient remained hypotensive after fluid bolus administration. Poisson regression for a binary outcome variable was used to estimate an adjusted incidence-rate ratio (IRR) comparing mortality in groups defined by bundle compliance measured as a binary predictor, and to estimate an adjusted number needed to treat (NNT).
RESULTS: Complete bundle compliance was associated with a 31% lower risk of mortality (adjusted IRR, 0.69, 95% confidence interval [CI], 0.53-0.91), adjusting for SS/SS presentation in the emergency department, SS/SS present on admission (POA),

age, admission severity of illness and risk of mortality, Medicaid/Medicare payor status, immunocompromised host status, and congestive heart failure POA. The adjusted NNT to save one life was 15 (CI, 8-69). Other factors independently associated with mortality included SS/SS POA (adjusted IRR, 0.55; CI, 0.32-0.92) and increased age (adjusted IRR, 1.13 per 10-year increase in age; CI, 1.03-1.24).
CONCLUSIONS: The University of California, San Francisco, sepsis bundle was associated with a decreased risk of in-hospital mortality across hospital units after robust control for confounders and risk adjustment. The adjusted NNT provides a reasonable and **achievable goal to observe measureable improvements in outcomes for patients diagnosed with SS/SS.**

活體供肝肝切除術中每搏輸出量變異度引導與中心靜脈引導的低中心靜脈壓指導米力農應用：一項隨機雙盲臨床試驗

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

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Anesthesia & Analgesia: 2017 125 423–430

背景：我們以前曾證明米力農在活體供肝肝切除術的作用。然而，具有較低侵入性的替代中心靜脈導管的另一個選擇和影響良好的手術預後的圍手術期因素尚未確定。目前的研究評估了是否每搏輸出量變異度（SVV）引導的方法可以在米力農引起的複雜血管舒張時代替中心靜脈置管。
方法:我們隨機分配 42 例活體肝移植供體分別接受 SVV 指導或中心靜脈壓(CVP）指導獲得米力農誘導的低 CVP。應用目標 SVV 9%代替 CVP5 毫米汞柱。分別由 2 名外科主治醫師應用 4 點法比較 CVP 和 SVV 指導組（n = 19，每組總得分= 38）手術區域的等級評估作為一個主要的結果變數。進行多變數分析，以確定與最佳手術領域相關的獨立因素作為事後分析。
結果：通過 Mann-Whitney U 檢驗皮評價兩組間外科領域的評分，或為 1 或 2，發現兩組之間沒有差異（P = .358）。在血管舒張如 CVP≤5 mm Hg 時 SVV 和 CVP 之間有很弱的相關性（R = -0.06；95%置信區間，-0.09 -0.04；P <0.001）。事後分析表明，年輕人、基線較低 CVP、持續時間較長的米力農可能對提供最佳的手術視野是有幫助的。
結論：米力農誘導的血管舒張功能在活體肝切除術中提供良好的手術環境，不管是否應用低 CVP 的指導方法。然而，SVV 在提示低 CVP 方面並不是一個有用的指標，因為在血管舒張時 SVV 和 CVP 之間很弱的相關性。此外，提供最佳手術視野的因素如供體年齡，主動禁食，適當劑量米力農需要進行進一步的研究，並最好是通過前瞻性研究。
（陸曉斐譯 李士通校）

BACKGROUND: We previously demonstrated the usefulness of milrinone for living donor hepatectomy. However, a less-invasive alternative to central venous catheterization and perioperative contributors to good surgical outcomes remain undetermined. The

current study evaluated whether the stroke volume variation (SVV)-guided method can substitute central venous catheterization during milrinone-induced profound vasodilation.
METHODS: We randomly assigned 42 living liver donors to receive either SVV guidance or central venous pressure (CVP) guidance to obtain milrinone-induced low CVP. Target SVV of 9% was used as a substitute for CVP of 5 mm Hg. The surgical field grade evaluated by 2 attending surgeons on a 4-point scale was compared between the CVP- and SVV-guided groups (n = 19, total number of scores = 38 per group) as a primary outcome variable. Multivariable analysis was performed to identify independent factors associated with the best surgical field as a post hoc analysis.
RESULTS: Surgical field grades, which were either 1 or 2, were not found to be different between the 2 groups via Mann-Whitney U test (P = .358). There was a very weak correlation between SVV and CVP during profound vasodilation such as CVP ≤ 5 mm Hg (R = -0.06; 95% confidence interval, -0.09 to -0.04; P < .001). Additional post hoc analysis suggested that younger age, lower baseline CVP, and longer duration of milrinone infusion might be helpful in providing the best surgical field.
CONCLUSIONS: Milrinone-induced vasodilation resulted in favorable surgical environment regardless of guidance methods of low CVP during living donor hepatectomy. However, SVV was not a useful indicator of low CVP because of very weak correlation between SVV and CVP during profound vasodilation. In addition, factors contributing to the best surgical field such as donor age, proactive fasting, and proper dosing of milrinone need to be investigated further, ideally through prospective studies.

仰臥位病人應用擠壓式噴霧器鼻腔內給藥時導致超量

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

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背景:血管收縮劑和局部麻醉劑,通常使用擠壓式噴霧器應用在鼻腔黏膜上以消腫、止血和鎮痛。儘管廣泛使用，但很少有涉及安全管理技術細節的臨床指南。本研究的目的是量化，通過類比病人在仰臥位和直立位時的位置和管理參數，能夠可靠地提供每次噴霧到鼻腔粘膜所需藥物的液體量。
方法：對 10 名麻醉患者進行了樣本的研究。提供者被指示使用 25 mL 蘸和管鼻擠壓瓶將測試溶液（無菌水）應用到直立位（90°仰角）和仰臥位（0°仰角）的人體模型上。在人體模型試驗的基礎上，分別在 0°、15°、30°、45°和 90°的條件下對噴霧瓶進行了附加試驗，確定了噴頭工作角度與液體分配量的關係。
結果：與垂直位置相比（0.041±0.02 mL），在仰臥位時每噴霧平均體積明顯較大（0.56±0.22 mL，差異為 0.52 mL，95%可信區間[CI]，0.37-0.67 mL，P<0.001）。使用標準 0.25%的溶液，將給藥體積轉化為腎上腺素劑量，仰臥位和直立位相比每噴估計增加 1300μg（95% CI，925-1675μg，P<0.001）。隨著給藥角度≤30°，與瓶身從 90°角開始，藥物體積明顯增加。45°時的給藥體積與 90°的體積無差別（0.032～0.006 ml，0.030～0.005 ml，p＝.34）。

結論：我們發現，在人體模型上應用鼻腔擠壓瓶時，仰臥位時每噴的體積（即劑量）比直立位增加了 14 倍。由於在臨床實踐中使用擠壓瓶使用霧化器時，曾報導經鼻給藥的藥物毒性和意外過量的發生，我們的資料表明，所有滴鼻藥物應給予精確的計量裝置。如果沒有計量設備，用藥應在≥45°角度時給予；然而，我們推薦給藥時病人為坐位，瓶身呈 90°，因為當角度小於 45°時，只有一個小的變化會導致藥物劑量大幅提高。
（陸曉斐 譯 李士通 校）

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

隨機交叉試驗比較應用兩種光棒插管技術比較模擬頸椎制動患者插管過程中的頸椎移動：喉鏡輔助與傳統光棒插管

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

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背景：在頸椎制動的患者中，推下頜可以引起頸椎運動。同時使用喉鏡可以幫助光棒插管，使中線位置固定，光棒在口腔自由運動而無顎推力。我們比較了喉鏡輔助光棒插管（LALI）與常規光棒插管（CLI）對模擬頸椎固定氣管插管患者頸椎運動的影響。

方法：在這項隨機交叉研究，對 20 例模擬頸部制動的患者在插管前和插管過程中測量枕骨- C1、C1-C2 和 C2-C5 節段的頸椎夾角，插管分別使用 LALI 和 CLI 技術。頸椎運動的定義是指在插管過程中頸段測量角度的變化。

結果：當使用 LALI 和 CLI 技術時，枕骨- C1 段的頸椎運動分別為 5.6°（4.3）和 9.3°（4.5），（平均差異[98.33%CI]；3.8°[7.2 - 0.3]；P = .007）。在其他頸段，兩種技術之間的差異不顯著（C1-C2 節段-0.1°[- 2.6 - 2.5]； P =.911 和 C2-C5 節段-0.2°[- 2.8- 2.5]；P =.795）。

結論：在模擬頸椎制動患者的氣管插管過程中，與 CLI 技術相比，LALI 技術產生較少的上頸椎運動。

（張秋麗 譯 李士通 校）

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

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

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

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

與異氟醚相比，七氟醚減少急性呼吸窘迫綜合征大鼠肺內而不是肺外肺損傷

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

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背景：揮發性麻醉藥可調節急性呼吸窘迫綜合征（ARDS）的炎症反應。然而，目前尚不清楚他們是否根據 ARDS 病因不同而反應不同。我們推測，七氟醚和異氟醚在體內和體外對肺內（P）和肺外（EXP）急性呼吸窘迫綜合征的肺損傷影響並無差異。

方法：24 只 wistar 大鼠，隨機分為應用七氟醚和異氟醚全身麻醉（1-2 分鐘）。動物再隨機接受大腸桿菌脂多糖（LPS）氣管內（ARDSp）或腹腔注射（ARDSexp），誘導 ARDS 後 24 小時，再接受 1 個最小肺泡濃度的七氟烷或異氟烷麻醉 60 分鐘。主要觀察指標為肺組織中白細胞介素（IL）-6 mRNA 的表達。次要終點包括氣體交換、肺力學、組織學和 IL-10 mRNA 的表達，核因數相關因數 2（Nrf2），表面活性蛋白（SP）-B、血管細胞黏附分子-1，內皮阿米洛利敏感鈉通道亞單位 α 和 γ，和鈉-鉀-ATPα 泵亞基 α1（α1-NA，K-ATPase）1、β（β1-NA，K-ATPase）。另外的 ARDSp 和 ARDSexp 大鼠（n = 6）應用硫噴妥鈉麻醉而不進行機械通氣（NV）作為對照組。另外，為了確定如何七氟醚和異氟醚作用於 II 型上皮細胞，A549 人肺上皮細胞受 LPS 刺激 24 小時後（20μ 克/毫升），進一步暴露於七氟烷或異氟烷後（1 最小肺泡濃度）60 分鐘，並進行了 SP-B 表達的量化。

結果：在 ARDSp 組，與異氟醚相比，七氟醚可在更大程度上降低 IL-6 的表達（P = .04）。與異氟醚組相比，七氟醚組的肺靜態順應性（P = .0049）和肺泡萎陷（P = .033）均更低。而 Nrf2（P = .036），SP-B（P = .042）和 β1-NA，K-ATP 酶（P = 038）在七氟醚均顯著高表達。在 ARDSexp，七氟醚和異氟醚之間在肺泡萎陷、肺力學以及分子參數，均沒有觀察到顯著差異。在體外，七氟醚組 SP-B 的表達明顯比異氟醚高（P =. 026）。

結論：與異氟醚相比，七氟醚並沒有影響 ARDSexp 的肺部炎症，但它確實降低了 ARDSp 的肺部炎症。

（張秋麗 譯 李士通 校）

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

METHODS: Twenty-four Wistar rats were randomized to undergo general anesthesia (1-2 minutes) with sevoflurane and isoflurane. Animals were then further randomized to receive Escherichia coli lipopolysaccharide (LPS) intratracheally (ARDSp) or intraperitoneally (ARDSexp), and 24 hours after ARDS induction, they were subjected to 60 minutes of sevoflurane or isoflurane anesthesia at 1 minimal alveolar concentration. The primary outcome measure was interleukin (IL)-6 mRNA expression in lung tissue. Secondary outcomes included gas exchange, lung mechanics, histology, and mRNA

expression of IL-10, nuclear factor erythroid 2-related factor-2 (Nrf2), surfactant protein (SP)-B, vascular cell adhesion molecule-1, epithelial amiloride-sensitive Na-channel subunits α and γ, and sodium-potassium-adenosine-triphosphatase pump subunits α1 (α1-Na,K-ATPase) and β1 (β1-Na,K-ATPase). Additional ARDSp and ARDSexp animals (n = 6 per group) were anesthetized with sodium thiopental but not mechanically ventilated (NV) to serve as controls. Separately, to identify how sevoflurane and isoflurane act on type II epithelial cells, A549 human lung epithelial cells were stimulated with LPS (20 μg/mL) for 24 hours, and SP-B expression was quantified after further exposure to sevoflurane or isoflurane (1 minimal alveolar concentration) for 60 minutes.
RESULTS: In ARDSp, sevoflurane reduced IL-6 expression to a greater degree than isoflurane (P = .04). Static lung elastance (P = .0049) and alveolar collapse (P = .033) were lower in sevoflurane than isoflurane, whereas Nrf2 (P = .036), SP-B (P = .042), and β1-Na,K-ATPase (P = .038) expressions were higher in sevoflurane. In ARDSexp, no significant differences were observed in lung mechanics, alveolar collapse, or molecular parameters between sevoflurane and isoflurane. In vitro, SP-B expression was higher in sevoflurane than isoflurane (P = .026).
CONCLUSIONS: Compared with isoflurane, sevoflurane did not affect lung inflammation in ARDSexp, but it did reduce lung inflammation in ARDSp.

資源匱乏地區急診剖宮產術乳酸林格式液與生理鹽水選擇：一項務實的臨床試驗
Ringer's Lactate Versus Normal Saline in Urgent Cesarean Delivery in a Resource-Limited Setting: A Pragmatic Clinical Trial

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背景：晶體的常規用於在剖宮產術圍手術期的液體管理。很少有研究確定在產科麻醉中晶體液的選擇。我們比較了 Ringer 乳酸（RL）與 0.9%生理鹽水（NS）對產婦和新生兒血液pH值的影響，以及在低資源環境下緊急剖宮產術後24小時的發病率。我們的假設是，RL 將導致低於 NS 組 30%的酸中毒率。
方法：這是一個務實的前瞻性隨機雙盲對照試驗，納入在穆拉戈國家轉診醫院病房從 2011 年 9 月到 2012 年 5 月的產婦。對五百例產婦進行了研究；隨機分為 252 例生理鹽水組和 248 例 RL 組。分析術前、術後母體靜脈血氣及胎盤臍動脈血氣。主要結果是母親酸中毒的發生率，如術後靜脈血 pH 值低於 7.32 或之前正常孕婦的城剩餘低於-3。母親 24 小時術後發病率、新生兒酸鹼度和新生兒城剩餘是主要次要結局。這項研究是在 ClinicalTrials.gov 官網註冊 NCT01585740。
結果：產婦酸中毒的總發生率為 NS 組 38%，RL 組 29%（相對風險，1.29；95%置信區間，1.01-1.66；P = .04）。NS 組 32%產婦術後靜脈 pH 值下降至低於 7.32，在 RL 組為 19%（相對風險，1.65；95%置信區間，1.18-2.31；P = .003）兩組術後城剩餘相對下降低於-3 無統計學意義。兩組產婦 24 小時術後發病率和新生兒結局的發生率無顯著差異。
結論：NS 可作為緊急剖宮產術中的液體治療替代 RL 的安全選擇，儘管代謝性酸中毒的發生率增加。

（沈辰 譯 李士通 校）

BACKGROUND: Crystalloids are used routinely for perioperative fluid management in cesarean delivery. Few studies have determined the crystalloid of choice in obstetric anesthesia. We compared the effects of Ringer's lactate (RL) versus 0.9% normal saline (NS) on maternal and neonatal blood pH and 24-hour postoperative morbidity in urgent cesarean delivery in a low-resource setting. Our hypothesis was that RL would result in 30% less acidosis than NS.

METHODS: This was a pragmatic prospective double-blind randomized controlled trial in the Mulago National Referral Hospital Labor Ward Theater from September 2011 to May 2012. Five hundred parturients were studied; 252 were randomly assigned to NS and 248 to RL groups. Preoperative and postoperative maternal venous blood gases and placental umbilical arterial cord blood gases were analyzed. The primary outcome was incidence of maternal acidosis, as defined by a postoperative drop in venous pH below 7.32 or reduction in base excess below -3 in a previously normal parturient. Maternal 24-hour postoperative morbidity, neonatal pH, and neonatal base excess were the main secondary outcomes. The study was registered in ClinicalTrials.gov as NCT01585740.

RESULTS: The overall incidence of maternal acidosis was 38% in NS and 29% in RL (relative risk, 1.29; 95% confidence interval, 1.01-1.66; P = .04). Thirty-two percent of parturients in NS experienced a drop in venous pH below 7.32 postoperatively, compared with 19% in RL (relative risk, 1.65; 95% confidence interval, 1.18-2.31; P = .003). The comparative drop in base excess postoperatively below -3 between the 2 groups was not statistically significant. There were no significant differences in the incidence of maternal 24-hour postoperative morbidity events and neonatal outcomes between the 2 groups.

CONCLUSIONS: NS may be a safe choice for intraoperative fluid therapy in urgent cesarean delivery as RL, albeit with an increased incidence of metabolic acidosis

嚴重術中高血糖與開顱術後複合感染的發生無關：一項觀察性研究

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

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背景：開顱術後感染增加了致殘率和死亡率的風險。危險因素的識別和糾正應優先考慮。術中高血糖與開顱術後感染的相關性研究不足。

方法：共 2 個主要的醫療中心的 224 例患者進行前瞻性研究，以評估術中嚴重高血糖（SIH，血糖≥180 mg/dL）與接受開顱手術患者術後感染的高風險相關。麻醉誘導後立即采血並行動脈血氣分析，拔管前再進行動脈血氣分析。並確定開顱術後 7 天內出現的任何類型的感染。

結果：開顱術後第一周內新術後複合感染發生率為 10%（n＝22）。體重、性別、美國麻醉醫師協會（ASA）評分，術前和/或術中使用類固醇，和糖尿病與術後感染沒有相關性。擬合多因素 logistic 回歸模型調整為急診外科、手術時間長、年齡≥65 年後，SIH 與術後感染的獨立相關（比值比[95%置信區間]，4.17[1.50-11.56]，P = .006）。

結論：SIH 與行開顱手術治療患者術後新發複合感染獨立相關。是否在開顱手術中預防 SIH 對降低術後感染的風險是未知的，需要進一步研究評價。
（沈辰 譯 李士通 校）

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

肝移植患者血漿凝血酶生成的恢復

Restoration of Thrombin Generation in Plasma From Liver Transplant Recipients

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背景：在大多數國家，血漿輸注仍然是肝移植（LT）的主要止血治療。然而，需要大量的血漿來達到臨床相關因素的增加。凝血酶原複合物（PCC）在華法林逆轉過程中是一種低劑量的血漿替代品，但其療效一直沒有得到很好的研究。
方法：收集 28 例 LT 患者在移植前（T0）和移植後 30 分鐘（T1）的血標本，測定 X 因數及抗凝血酶水準。比較 LT 和華法林血漿患者， PCC（0.2 和 0.4 IU/mL）和正常血漿置換 10%容量的體外作用，使用凝血酶生成（TG）測定測量滯後時間、凝血酶的峰值相比與內源性凝血酶潛能（ETP）。
結果：隨著國際標準化率從 1.7 上升到 3，凝血狀態在 T1 時惡化，X 因數從 49%下降到 28%。TG 測量在 T0 和 T1 顯示正常的滯後時間和 ETP，但 T0 為正常低峰，T1 為低於正常峰值。兩劑量 PCC 均增加峰值和 ETP，而 10%體積的血漿置換對 TG 的影響最小。由於低抗凝血酶，在 LT 血漿中加入 0.40.4 IU/mL 的 PCC 後，凝血酶抑制率似乎非常緩慢。相同劑量的 PCC 和血漿對華法林逆轉作用均表現不足。

結論：PCC 較血漿能更有效地降低 LT 患者的 TG。由於較慢凝血酶抑制，LT 患者所需的 PCC 劑量似乎比逆轉華法林的劑量低。
（顧明露 譯 李士通 校）

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

神經病理性痛的干預：一項系統性評價概述

Interventions for Neuropathic Pain: An Overview of Systematic Reviews

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神經病理性疼痛的眾多干預（NEUP）是可用的，但其治療仍不滿意。我們系統地總結了隨機對照試驗中干預措施為 NEUP 的證據並系統評價（SRs）。截至 2015 年 3 月，共檢索到五個電子資料庫。使用測量工具 A 評估系統評價的研究品質。包含在 SRs 中的 97 項研究中，其中最常見的干預措施包括藥物治療（59%）和外科治療（15%）。分析的 SRs 多數為中等品質。摘要的結論中超過 50%的關於功效的和大約 80%的關於安全性的結論是不確定的。有效的干預措施，闡述了糖尿病痛性神經病變（普瑞巴林，加巴噴丁，某些三環類抗抑鬱藥[TCAs]，阿片類藥物，抗抑鬱藥和抗驚厥藥）、帶狀皰疹後遺神經痛（加巴噴丁、普瑞巴林、某些抗抑鬱藥，抗抑鬱藥和抗驚厥藥、阿片類藥物，丙戊酸鈉，辣椒堿，利多卡因），根性神經痛（硬膜外皮質類固醇，重複經顱磁刺激[rTMS]，髓核摘除術），頸神經根性疼痛（rTMS），腕管綜合征（腕管綜合征、肘管綜合征）（簡單的減壓和尺神經轉位）、三叉神經痛（卡馬西平、拉莫三嗪、和匹莫齊特治療難治性病例，rTMS），HIV 相關的神經病變（局部辣椒堿），和中樞 NeuP（某些三環類抗抑鬱藥，普瑞巴林，大麻，和

rTMS）。證據表明 NeuP 的干預常常是不確定的或完全缺乏的。關於 NeuP 治療的新的隨機對照試驗是必要的，他們應當是安全和使用明確的診斷標準。
（顧明露 譯 李士通 校）

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

輻射藥理分析鞘內注射 BRL52537（κ-阿片受體激動劑）、Pregabalin（鈣通道調節劑）、AF 353（P2X3 受體拮抗劑）和 A804598（P2X7 受體拮抗劑）等藥物組合治療神經病理性痛大鼠

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

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背景：神經病理性疼痛應採用多種藥物聯合治療，因為神經病理性疼痛的機制涉及多種生理原因，並由多種途徑介導。在這項研究中，我們定義了 BRL52537 藥理作用（κ-阿片受體激動劑），普瑞巴林（鈣通道調節劑），AF 353（P2X3 受體拮抗劑），和 A804598（P2X7 受體拮抗劑）的藥理相互作用。

方法：雄性 Sprague Dawley 大鼠通過脊神經結紮（SNL）建立神經病理性疼痛模型，並用 von Frey 細絲測定機械刺激的反應。通過鞘內注射途徑給藥，觀察藥物效果，以及輻射分析評價藥物相互作用等。應用即時聚合酶鏈反應評價空白組、SNL 組和藥物治療的 SNL 組大鼠的脊髓或背根神經節疼痛相關受體 mRNA 的表達水準。

結果：鞘內給予 BRL52537，普瑞巴林，AF 353，和 A804598 對 SNL 大鼠有治療效果。關於聯合用藥的研究，鞘內聯合應用 BRL52537 與普瑞巴林或 A804598 具有協同作用，與其他藥物的組合表現出相加作用。觀察效能的排名順序如下：BRL52537 +普瑞巴林> BRL52537 + A804598 >普瑞巴林+ AF 353 > A804598 +普瑞巴林> BRL52537＋AF 353 > AF 353 +A804598。即時聚合酶鏈反應表明 P2X3 受體和鈣通道 mRNA 表達水準的變化，而 P2X7 受體和 κ-阿片受體的表達水準沒有改變。
結論：這些結果表明，鞘內聯合應用 BRL 52537、普瑞巴林、AF 353 和 A804598 有協同或相加作用減少 SNL 誘發的疼痛，這一結果表明提高單藥療效的可能性。（徐燕伊方譯 李士通校）

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