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Mechanistic Modeling of the Effects of Acidosis on Thrombin Generation

Background: Acidosis is a common complication in trauma and complex surgery, the result of tissue hypoperfusion and venous resuscitation. Although acidosis is known to inhibit various enzyme reactions, its effect on the hemostatic system is not clear.
BACKGROUND: Acidois, a frequent complication of trauma and complex surgery, results from tissue hypoperfusion and IV resuscitation with acidic fluids. While acidosis is known to inhibit the function of distinct enzymatic reactions, its cumulative effect on the blood coagulation system is not fully understood. Here, we use computational modeling to test the hypothesis that acidosis delays and reduces the amount of thrombin generation in human blood plasma. Moreover, we investigate the sensitivity of different thrombin generation parameters to acidosis, both at the individual and population level.

METHODS: We used a kinetic model to simulate and analyze the generation of thrombin and thrombin-antithrombin complexes (TAT), which were the end points of this study. Large groups of temporal thrombin and TAT trajectories were simulated and used to calculate quantitative parameters, such as clotting time (CT), thrombin peak time, maximum slope of the thrombin curve, thrombin peak height, area under the thrombin trajectory (AUC), and prothrombin time. The resulting samples of parameter values at different pH levels were compared to assess the acidosis-induced effects. To investigate intersubject variability, we parameterized the computational model using the data on clotting factor composition for 472 subjects from the Leiden Thrombophilia Study. To compare acidosis-induced relative parameter changes in individual (“virtual”) subjects, we estimated the probabilities of relative change patterns by counting the pattern occurrences in our virtual subjects. Distribution overlaps for thrombin generation parameters at distinct pH levels were quantified using the Bhattacharyya coefficient.

RESULTS: Acidosis in the range of pH 6.9 to 7.3 progressively increased CT, thrombin peak time, AUC, and prothrombin time, while decreasing maximum slope of the thrombin curve and thrombin peak height (P < 10). Acidosis delayed the onset and decreased the amount of TAT generation (P < 10). As a measure of intrasubject variability, maximum slope of the thrombin curve and CT displayed the largest and second-largest acidosis-induced relative changes, and AUC displayed the smallest relative changes among all thrombin generation parameters in our virtual subject group (1-sided 95% lower confidence limit on the fraction of subjects displaying the patterns, 0.99). As a measure of intersubject variability, the overlaps between the maximum...
slope of the thrombin curve distributions at acidic pH levels with the maximum slope of the thrombin curve distribution at physiological pH level systematically exceeded analogous distribution overlaps for CT, thrombin peak time, and prothrombin time.

**CONCLUSIONS:** Acidosis affected all quantitative parameters of thrombin and TAT generation. While maximum slope of the thrombin curve showed the highest sensitivity to acidosis at the individual-subject level, it may be outperformed by CT, thrombin peak time, and prothrombin time as an indicator of acidosis at the subject-group level.

**Involvement of Opioid Receptors in the Lipid Rescue of Bupivacaine-Induced Cardiotoxicity**

Partownavid, Parisa MD; Sharma, Salil PhD; Li, Jignyuan MD, PhD; Umar, Soban MD, PhD; Rahman, Siamak MD; Eghbali, Mansoureh PhD

Anesthesia & Analgesia 2015 121 340–347

**BACKGROUND:** Lipid emulsion (LE) has been successfully used for resuscitation of local anesthetic cardiotoxicity caused by bupivacaine overdose. Opioid receptors have been shown to play a key role in cardio protection. We explored whether this rescue action of LE is mediated through opioid receptors.

**METHODS:** Asystole was induced by bupivacaine (10 mg/kg over 20 seconds, IV) in young male Sprague-Dawley rats, and resuscitation with LE (intralipid 20%; 5 mL/kg bolus and 0.5 mL/kg/min maintenance) was started immediately. The rats were pretreated 2 minutes before inducing asystole with nonselective opioid receptor antagonists such as naloxone and naloxone methiodide, as well as highly selective opioid receptor antagonists for subtype κ, δ, and μ or phosphate buffer solution as a control. Heart rates and ejection fractions were measured using echocardiography.

**RESULTS:** LE rescue of bupivacaine cardiotoxicity was prevented by high-dose (1 mg/kg) naloxone but not by lower doses of naloxone (1, δ, and 10 μg/kg), by naloxone methiodide (which does not cross the blood-brain barrier), and by a selective δ- and κ-opioid receptor antagonists at a higher (10 mg/kg) dose. Successful LE rescue was not affected by highly selective μ-opioid receptor antagonists. δ-Opioid receptor antagonist (10 mg/kg) pretreatment...
also resulted in reduced phosphorylation level of cardiac glycogen synthase kinase-3β in rats that were not resuscitated by LE compared with control.

CONCLUSIONS: Our data highlight the involvement of peripheral δ- and κ-opioid receptors in the rescue action of LE.
severity of residual NMB (TOF ratio <0.9) just before tracheal extubation and at arrival at the postanesthesia care unit (PACU).

RESULTS: Three hundred and two participants were enrolled. Data were available for 241 patients at tracheal extubation and for 207 patients at PACU arrival. Rocuronium was the NMB agent used in 99% of cases. Neostigmine was used for reversal of NMB in 73.9% and 72.0% of patients with TE and PACU data, respectively. The incidence of residual NMB was 63.5% (95% confidence interval, 57.4%-69.6%) at tracheal extubation and 56.5% (95% confidence interval, 49.8%-63.3%) at arrival at the PACU. In an exploratory analysis, no statistically significant differences were observed in the incidence of residual NMB according to gender, age, body mass index, ASA physical status, type of surgery, or comorbidities (all P > 0.13).

CONCLUSIONS: Residual paralysis is common at tracheal extubation and PACU arrival, despite qualitative neuromuscular monitoring and the use of neostigmine. More effective detection and management of NMB is needed to reduce the risks associated with residual NMB.

A System for Anesthesia Drug Administration Using Barcode Technology: The Codonics Safe Label System and Smart Anesthesia Manager™

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Anesthesia & Analgesia 2015 121 410–421

BACKGROUND: Many anesthetic drug errors result from vial or syringe swaps. Scanning the barcodes on vials before drug preparation, creating syringe labels that include barcodes, and scanning the syringe label barcodes before drug administration may help to prevent errors. In contrast, making syringe labels by hand that comply with the recommendations of regulatory agencies and standards-setting bodies is tedious and time consuming. A computerized system that uses vial barcodes and generates barcoded syringe labels could address both safety issues and labeling recommendations.

METHODS: We measured compliance of syringe labels in multiple operating rooms (ORs) with the recommendations of regulatory agencies and standards-setting bodies before and after the
introduction of the Codonics Safe Label System (SLS). The Codonics SLS was then combined with Smart Anesthesia Manager software to create an anesthesia barcode drug administration system, which allowed us to measure the rate of scanning syringe label barcodes at the time of drug administration in 2 cardiothoracic ORs before and after introducing a coffee card incentive. Twelve attending cardiothoracic anesthesiologists and the OR satellite pharmacy participated.

RESULTS: The use of the Codonics SLS drug labeling system resulted in >75% compliant syringe labels (95% confidence interval, 75%-98%). All syringe labels made using the Codonics SLS system were compliant. The average rate of scanning barcodes on syringe labels using Smart Anesthesia Manager was 25% (730 of 2976) over 13 weeks but increased to 58% (956 of 1645) over 8 weeks after introduction of a simple (coffee card) incentive (P < 0.001).

CONCLUSIONS: An anesthesia barcode drug administration system resulted in a moderate rate of scanning syringe label barcodes at the time of drug administration. Further, adaptation of the system will be required to achieve a higher utilization rate.

BMI與硬脊膜穿刺後頭痛在產婦中發病的關係

The Relationship of Body Mass Index with the Incidence of Postdural Puncture Headache in Parturients

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Anesthesia & Analgesia 2015 121 451–456

背景：在硬膜外或腰硬聯合麻醉之後，無意的硬膜外穿刺也有目前已知的風險，在正常體型孕婦分娩時放置硬膜外導管時它的發生率約為1%，但是在肥胖產婦中的發生率卻高達4%。醫事經驗和有限的文章裡顯示身體質量指數（BMI）和硬脊膜穿刺後頭痛（PDPH）的發生率存在著反比的關係。我們可以假設，在無意的硬脊膜穿刺後，有著更大BMI的產婦發生PDPH的幾率比那些具有較小的BMI的產婦的發病率更低。

方法：經過IRB批准，我們進行了回顧性的研究醫療記錄的審查。我們查找了從2004年1月1日到2013年12月13日機構存檔的案件，關於在進行椎管內鎮痛時發生無意識的刺破硬膜的情況。最主要的效果就是發生PDPH的幾率。我們用二進位邏輯回歸的方法對BMI和PDPH之間的關聯進行了評估，以魏氏-曼-惠特尼檢驗值為一個單核對，以發生PDPH患者的BMI值與非PDPH患者相比，計算其特性曲線下的面積。分類樹分析方法被用來確定發生PDPH的BMI臨界值。我們用Fisher精確檢驗分別對發生PDPH的產婦和未發生者進行計算，研究無意硬脊膜穿刺後鞘內導管的存在與分娩的第二產程是否存在關係。以BMI的臨界值分為兩組（低BMI和高BMI）。我們在無意刺破硬膜的時候通過控制分娩的產力和置入鞘內導管，並用Fisher精確檢驗比較了低BMI和高BMI組PDPH的發生率。次要分析評估頭痛在疼痛報導的最高數位評分，以及各個BMI組需要的硬膜外血液補充量。

結果：確定發生無意硬膜穿刺的患者有518人(0.53%) (95% CI,0.48%–0.58%)。在無意硬膜穿刺以後PDPH的發生率總體來說是51% (95% CI,46%–55%)。以隨機的BMI值對PDPH患者的BMI值與非PDPH患者相比，計算其特性曲線下的面積。分類樹分析方法被用來確定發生PDPH的BMI臨界值。我們用Fisher精確檢驗分別對發生PDPH的產婦和未發生者進行計算，研究無意硬脊膜穿刺後鞘內導管的存在與分娩的第二產程是否存在關係。以BMI的臨界值分為兩組（低BMI和高BMI組）。我們在無意刺破硬膜的時期通過控制分娩的產力和置入鞘內導管，並用Fisher精確檢驗比較了低BMI和高BMI組PDPH的發生率。次要分析評估頭痛在疼痛報導的最高數位評分，以及各個BMI組需要的硬膜外血液補充量。
BACKGROUND: Unintentional dural puncture is a known risk after epidural or combined spinal–epidural procedures, occurring in approximately 1% of labor epidural catheters placed in parturients with normal body habitus but may be as high as 4% in morbidly obese parturients. Anecdotal experience and limited publications suggest that an inverse relationship between body mass index (BMI) and postdural puncture headache (PDPH) may exist. We hypothesized that parturients with increased BMI have a lower incidence of PDPH than those with a lower BMI after unintentional dural puncture.

METHODS: After IRB approval, we performed a retrospective cohort study by medical record review. Case logs from our institution were searched for patients with documented unintentional dural puncture during attempted neuraxial analgesia between January 1, 2004, and December 13, 2013. The primary outcome was the incidence of PDPH. The association between BMI and PDPH was assessed using binary logistic regression, and the Wilcoxon-Mann-Whitney odds and confidence intervals (CIs) for a random pair of BMI values from a PDPH subject compared with a non-PDPH subject were calculated from the area under the receiver operator characteristics curve. Classification tree analysis was used to determine the BMI cutoff value for the risk of developing a PDPH. The presence or absence of second-stage labor pushing and placement of an intrathecal catheter after unintentional dural puncture were compared in parturients with and without PDPH using the Fisher exact test. BMI groups were dichotomized at the cutoff value (low and high BMI groups). We compared the incidence of a PDPH in women who pushed during delivery was 2.4 (95% CI, 1.2–3.9, P = 0.001) compared with women who did not push. Classification tree analysis identified a BMI cutoff value of 31.5 kg/m² for prediction of a PDPH. The incidence of PDPH in parturients with a BMI ≥31.5 kg/m² (39%) was lower than in parturients with a BMI <31.5 kg/m² (56%; difference −17%; 95% CI, −7% to −26%, P = 0.0004). The odds ratio for a PDPH in the high BMI compared with the low BMI group was 0.36 (95% CI, 0.14–0.92, P = 0.04) in parturients who pushed during labor and 0.62 (95% CI, 0.41–0.97, P = 0.04) in parturients who did not push. After the unintentional dural puncture, 112 (22%) parturients had an intrathecal catheter placed. The incidence of PDPH in parturients with an epidural catheter was 59% (95% CI, 49%–68%) compared with 48% (95% CI, 43%–54%) in women with an epidural catheter (P = 0.06). Median (interquartile range) headache severity (0–10 verbal rating scale) was 8 (6–9) and did not differ between parturients in the high versus low BMI groups (P = 0.61). The rate of epidural blood patch administration for PDPH treatment was similar in BMI groups (difference −12%; 95% CI, 4 to −27, P = 0.13).

CONCLUSIONS: The findings are consistent with previous reports of decreased PDPH incidence after unintentional dural puncture in parturients with an increased BMI, even after controlling for pushing during labor. Severity of headache and need for epidural blood patch treatment were similar in low and high BMI groups.
Cell Salvage in Obstetrics

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Anesthesia & Analgesia 2015 121 465–468

術中細胞回收是減少異體輸血的一項戰略。傳統的來說，在產科手術中細胞回收一直被避
免，認爲會有羊水栓塞和誘導產婦產生同種免疫的風險。隨著細胞回收技術的不斷進步，
產科手術細胞回收的風險降低到和其他手術相似。在胎盤剝離的時候，胎兒鱗狀上皮細胞
在血液中被回收的水準可以和孕婦靜脈血液相比較。目前並沒有明確的羊水栓塞病例報
告，而且使用現代化設備也不太可能出現。細胞回收技術是符合成本效益的高利率輸血，
例如產婦胎盤異常。

（李蔚文 譯，李士通 審校）

BACKGROUND: Intraoperative cell salvage is a strategy to decrease the need for allogeneic
blood transfusion. Traditionally, cell salvage has been avoided in the obstetric population
because of the perceived risk of amniotic fluid embolism or induction of maternal
alloimmunization. With advances in cell salvage technology, the risks of cell salvage in the
obstetric population parallel those in the general population. Levels of fetal squamous cells in
salvaged blood are comparable to those in maternal venous blood at the time of placental
separation. No definite cases of amniotic fluid embolism have been reported and appear unlikely
with modern equipment. Cell salvage is cost-effective in patients with predictably high rates of
transfusion, such as parturients with abnormal placentation.

To Pretreat or Not to Pretreat: Prophylactic Anticholinergic Administration Before
Dexmedetomidine in Pediatric Imaging

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Anesthesia & Analgesia 2015 121 479–485

背景：高劑量使用右美托咪啶是目前唯一的有效用於兒科影像時的鎮靜藥，但是其造成
一過性高血壓、低血壓和心動過緩的風險卻不斷增加。但是目前沒有臨床的證據和指南來
guidance我們是否需要在麻醉前預使用抗膽鹼藥物。這項實驗的目的就是來研究右美鎮靜前是
否需要用抗膽鹼藥物預處理，以及其所造成的血流動力學改變，並比較兩者的相同和不同
點。我們對唐氏綜合症的患兒進行了一個亞組的分析。

方法：在這項回顧描述性研究中，我們回顧了163名在MRI檢查時接受了右美麻醉的患
兒。資料的分析包括了人口統計學、歷史上的唐氏綜合症、右美輸注以後的血流動力學變
化（包括心率、收縮壓、舒張壓），以及抗膽鹼能藥物的使用（阿托品或胃長寧）。

結果：小兒的平均年齡在94.5個月，其中52 (32%)名患兒有唐氏綜合症。廣義的線性混合
效應模型顯示，與預處理組相比，沒有用抗膽鹼藥物預處理組的所有患兒都出現了心率和
收縮壓的顯著降低。但兩組的舒張壓沒有明顯變化。在掃描的過程中，沒有用抗膽鹼藥物
預處理組的心率降低了26.6%，然而預處理組的心率只減少了基線的16.7% (P < 0.01)。和
基線相比，預處理組的最大心率比未預處理組有著明顯的增加(20.2% vs 10.4%,
respectively; \( P = 0.02 \)。在唐氏綜合症組，在掃描期間最大心率有著更誇張的變化，預處理組的最大心率比未預處理組增加了36倍（22% vs 0.6%，分别；\( P < 0.01 \)）。

結論：在使用右美托預防性的使用抗膽鹼能藥物沒有任何優點，除了能產生明顯的一過性的樣率和收縮壓的增加，而且和沒有用抗膽鹼能藥物預處理者相比，它在更多的患者中會造成一過性誇張的收縮壓。

（李蔚文 譯，李士通 審校）

BACKGROUND: Dexmedetomidine (Dex) appears to be very effective as a sole sedative for pediatric imaging when used at high doses, but at an increased risk of transient hypertension, hypotension, and bradycardia. There are no clinical evidence/guidelines to guide anesthesia providers as to whether patients should be pretreated with an anticholinergic. The aim of this study was to demonstrate the changes in hemodynamic parameters after Dex sedation attributed to receiving or not receiving an anticholinergic pretreatment and compare for any differences or similarities. A subgroups analysis was performed in children with Down syndrome (DS).

METHODS: In this retrospective descriptive study, we reviewed the records of 163 children receiving Dex anesthesia during MRI studies. Data analyzed included demographics, history of DS, and hemodynamics (heart rate [HR], systolic blood pressure [SBP], and diastolic blood pressure [DBP]) following Dex loading and infusion and the administration of an anticholinergic (atropine or glycopyrrolate).

RESULTS: The mean age was 94.5 months, and 52 (32%) patients had DS. The generalized linear mixed-effects regression model showed a significant reduction in HR and SBP in all patients when no anticholinergic was administered compared with when it was administered. There was no significant change with DBP. During the scan period, the HR of the no-anticholinergic group decreased 26.6%, whereas that of the anticholinergic group decreased by only 16.7% from baseline \( (P < 0.01) \). The maximal SBP increased by a significantly greater percentage, compared with baseline, in the anticholinergic group in comparison with the no-anticholinergic group \( (20.2\% \text{ vs } 10.4\%, \text{ respectively}; \ P = 0.02) \). In the DS group, the difference in the maximal SBP change during the scan period was exaggerated, with a percentage increase that was 36 times larger in the anticholinergic group compared with the no-anticholinergic group \( (22\% \text{ vs } 0.6\%, \text{ respectively}; \ P < 0.01) \).

CONCLUSIONS: Administration of a prophylactic anticholinergic with Dex shows no advantage other than a transient clinically insignificant increase in HR and SBP, and it may precipitate transient exaggerated SBP in more patients compared with not using a prophylactic anticholinergic.

血糖濃度對家兔寒戰閾值的影響

The Effects of Blood Glucose Concentration on the Shivering Threshold in Rabbits

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背景：高血糖在重病和手術患者中很常見，因爲身體的核心溫度受到了干擾。但是高血糖對體溫調節功能的影響仍是未知的。我們研究了血糖濃度對家兔寒戰閾值的影響。

方法：對27只家兔用異氟烷進行了淺麻醉，然後隨機分配到(1)鹽水輸液組、(2)胰島素滴定使血糖濃度維持在60 -100 mg/dL組和(3) 50%的葡萄糖滴定使血糖維持在200 -300 mg/dL組。在結腸放置一個塑膠管，用10°C的水灌注，使中心為溫度以2 -3°C/h的速度降低。继
結果：鹽水輸液組的家兔寒戰時的核心溫度在37.2 ± 0.5°C（平均值±標準差）。給予胰島素組的家兔的核心溫度在36.3 ± 1.1°C。給予葡萄糖組的家兔的核心溫度在38.0 ± 0.6°C。寒戰閾值的增加受血糖濃度的影響：寒顫閾值(°C) = 0.009 [血糖濃度(mg/dL)] + 35.6, r² = 0.53。血糖濃度每增加100 mg/dL，寒顫閾值因此增加約1°C。

結論：高血糖會增加家兔的寒顫閾值，而低血糖則相反。

(李蔚文譯，李士通審校)

BACKGROUND: Hyperglycemia is common in critically ill and surgical patients, as are core temperature disturbances. The effect of hyperglycemia on thermoregulatory defenses remains unknown. We determined the effect of blood glucose concentration on the shivering threshold in rabbits.

METHODS: Twenty-seven rabbits lightly anesthetized with isoflurane were randomly assigned to infusions of (1) saline, (2) insulin titrated to produce blood glucose concentrations 60 to 100 mg/dL, or (3) 50% dextrose titrated to produce blood glucose concentrations 200 to 300 mg/dL. Core temperature was reduced at a rate of 2 to 3°C/h by perfusing water at 10°C through a plastic tube positioned in the colon. Cooling continued until shivering was observed by an investigator blinded to treatment or until esophageal (core) temperature reached 34°C. Core temperatures at the onset of shivering defined the threshold. All analyses were conducted using SAS version 9.3 (SAS Institute Inc., Cary, NC).

RESULTS: Rabbits given saline shivered at 37.2 ± 0.5°C (mean ± SD). Rabbits given insulin shivered at 36.3 ± 1.1°C. Rabbits given dextrose shivered at 38.0 ± 0.6°C. The shivering threshold increased as a function of blood glucose concentration: shivering threshold (°C) = 0.009 [blood glucose concentration (mg/dL)] + 35.6, r² = 0.53. The shivering threshold thus increased approximately 1°C for each 100 mg/dL increase in blood glucose concentration.

CONCLUSIONS: Hyperglycemia increases the threshold for shivering, whereas hypoglycemia lowers the threshold on rabbits.

Paravertebral Block for Inguinal Herniorrhaphy: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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背景：椎旁神經阻滯是一項安全有效的麻醉方法用於開胸和乳房切除術。然而，對於椎旁阻滯用於腹股溝疝修補術卻沒有系統的回顧和Meta分析。我們來研究比較一下椎旁阻滯和全身麻醉(135 vs 133 名患者)，椎旁阻滯和椎管內麻醉(191 vs 186 名患者)，椎旁阻滯和其他周圍神經阻滯(119 vs 117 名患者)。疼痛和鎮痛、PONV以及血流動力學變化和尿儲留的發生率這些因素。疼痛和鎮痛、PONV以及血流動力學指標都採用聯合
BACKGROUND: Paravertebral block (PVB) is a safe and effective anesthetic technique for thoracotomy and mastectomy. However, no systematic review or meta-analysis has focused on PVB for inguinal herniorrhaphy. Our study compares PVB with general anesthesia/systemic analgesia, neuraxial blocks, and other peripheral nerve blocks.

METHODS: We analyzed 14 randomized controlled trials from PubMed, MEDLINE, CENTRAL, EMBASE, and CINAHL up to February 2015, without language restriction, comparing PVB under sedation with general anesthesia/systemic analgesia (135 vs 133 patients), neuraxial blocks (191 vs 186 patients), and other peripheral nerve blocks (119 vs 117 patients). We investigated pain scores, consumption of postoperative analgesics, incidence of postoperative nausea and vomiting (PONV), length of hospital stay, postanesthesia care unit bypassing rate, time to perform blocks, intraoperative hemodynamics, and incidence of urinary retention. Joint hypothesis testing was adopted for pain and analgesics, PONV, and hemodynamic variables. All analyses were performed with RevMan 5.2.11 (Cochrane Collaboration, Copenhagen). Hartung-Knapp-Sidik-Jonkman method was used for post hoc testing.

RESULTS: PVB reduced PONV (nausea: risk ratio [RR] = 0.22; 95% confidence interval [CI], 0.05–0.93; numbers needed to treat [NNT] = 4.5; I² = 15% and vomiting: RR = 0.15; 95% CI, 0.03–0.76; NNT = 8.3; I² = 0%) compared with general anesthesia/systemic analgesia (quality of evidence [QoE]: high). Compared with neuraxial blocks, PVB resulted in less postoperative nausea (RR = 0.34 [95% CI, 0.13–0.91], NNT = 8.3, I² = 0%) and urinary retention (RR = 0.14 [95% CI, 0.05–0.42], NNT = 7.4, I² = 0%) than neuraxial blocks (QoE: high). More time was needed to perform PVB than neuraxial blocks (standardized mean difference = 1.90 [95% CI, 0.02–3.77], I² = 92%; mean difference = 5.33 minutes; QoE: moderate). However, the available data could not reject the null hypothesis of noninferiority on all pain scores and analgesic requirements for both PVB versus general anesthesia/systemic analgesia and PVB versus neuraxial blocks (QoE: low), as well as on hemodynamic outcomes for PVB versus neuraxial blocks (QoE: moderate). Our systematic review showed that PVB decreased postoperative pain scores and analgesic requirement as compared with ilioinguinal block and transversus abdominis plane block.

CONCLUSIONS: This meta-analysis shows that PVB provides an anesthesia with fewer undesirable effects for inguinal herniorrhaphy. The choice between general anesthesia/systemic analgesia, neuraxial blocks, PVB, and other peripheral nerve blocks should be based on time available to perform the block and a complete coverage over the relevant structures by the blocks.
Preoperative Aspirin Use and Lung Injury After Aortic Valve Replacement Surgery: A Retrospective Cohort Study

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BACKGROUND: Acute respiratory distress syndrome (ARDS) occurs uncommonly after cardiac surgery but has a mortality rate as high as 80%. Aspirin may prevent lung injury in at-risk patients by reducing platelet-neutrophil aggregates in the lung. We hypothesized that preoperative aspirin use would be associated with a decreased risk of ARDS after aortic valve replacement surgery.

METHODS: We performed a retrospective single-center cohort study that included all adult patients who had aortic valve replacement surgery during a 5-year period. The primary outcome variable was postoperative ARDS. The secondary outcome variable was nadir PaO2/FIO2 ratio during the first 72 hours after surgery. Both crude and propensity score-adjusted logistic regression analyses were performed to estimate the odds ratio for developing ARDS in aspirin users. Subgroups were analyzed to determine whether preoperative aspirin use might be associated with improved oxygenation in patients with specific risk factors for lung injury.

RESULTS: Of the 375 patients who had aortic valve replacement surgery during the study period, 181 patients took aspirin preoperatively (48.3%) with most taking a dose of 81 mg (72.0%). There were 22 cases of ARDS in the cohort (5.5%). There was no significant difference in the rate of ARDS between aspirin users and nonusers (5.0% vs 6.7%, P = 0.52). There was also no significant difference in the nadir PaO2/FIO2 ratio between aspirin users and nonusers (P = 0.12). The crude odds ratio for ARDS in aspirin users was 0.725 (99% confidence interval, 0.229-2.289; P = 0.47), and the propensity score-adjusted odds ratio was 0.457 (99% confidence interval, 0.120-1.730; P = 0.13).
CONCLUSIONS: Within the constraints of this analysis that included only 22 affected patients, preoperative aspirin use was not associated with a decreased incidence of ARDS after aortic valve replacement surgery or improved oxygenation.

Lung Injury After One-Lung Ventilation: A Review of the Pathophysiologic Mechanisms Affecting the Ventilated and the Collapsed Lung

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Lung injury is the leading cause of death after thoracic surgery. Initially recognized after pneumonectomy, it has since been described after any period of 1-lung ventilation (OLV), even in the absence of lung resection. Overhydration and high tidal volumes were thought to be responsible at various points; however, it is now recognized that the pathophysiology is more complex and multifactorial. All causative mechanisms known to trigger ventilator-induced lung injury have been described in the OLV setting. The ventilated lung is exposed to high strain secondary to large, nonphysiologic tidal volumes and loss of the normal functional residual capacity. In addition, the ventilated lung experiences oxidative stress, as well as capillary shear stress because of hyperperfusion. Surgical manipulation and/or resection of the collapsed lung may induce lung injury. Re-expansion of the collapsed lung at the conclusion of OLV invariably induces duration-dependent, ischemia-reperfusion injury. Inflammatory cytokines are released in response to localized injury and may promote local and contralateral lung injury. Protective ventilation and volatile anesthesia lessen the degree of injury; however, increases in biochemical and histologic markers of lung injury appear unavoidable. The endothelial glycocalyx may represent a common pathway for lung injury creation during OLV, because it is damaged by most of the recognized lung injurious mechanisms. Experimental therapies to stabilize the endothelial glycocalyx may afford the ability to reduce lung injury in the future. In the interim, protective ventilation with tidal volumes of 4 to 5 mL/kg predicted body weight, positive end-expiratory pressure of 5 to 10 cm H2O, and routine lung recruitment should be used during OLV in an attempt to minimize harmful lung stress and strain. Additional strategies to reduce lung injury include routine volatile anesthesia and efforts to minimize OLV duration and hyperoxia. (Anesth Analg 2015;121:302–18)
Rationale and Design of the Balanced Anesthesia Study: A Prospective Randomized Clinical Trial of Two Levels of Anesthetic Depth on Patient Outcome After Major Surgery

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BACKGROUND: An association between relatively deep anesthesia, as guided by the bispectral index (BIS), and increased postoperative mortality has been demonstrated in 6 of 8 published observational studies, but association does not necessarily mean causality. Small clinical trials of anesthetic depth have demonstrated increased delirium and postoperative cognitive dysfunction in patients who were relatively deeply anesthetized, but have been inadequately powered to study mortality. A large-scale randomized study is required to determine whether causality exists.

METHODS: The primary hypothesis of our study is that "light" anesthesia, defined as a BIS target of 50, will reduce all-cause mortality within 1 year of surgery in comparison with "deep" anesthesia, defined as a BIS target of 35, in patients aged ≥60 years presenting for major surgery under general anesthesia. The trial is an international multicenter, randomized, parallel-group, double-blind (patients and investigators) prospective, intention-to-treat, safety and efficacy study. The relative reduction in mortality in the light anesthesia group is expected to be 20%, giving an absolute risk reduction from 10% to 8%. Power analysis using α = 0.049 and β = 0.2 indicates that 3250 patients are required in each group.

RESULTS: The study is underway, and 1325 patients have been recruited in 40 centers in 5 countries. It is anticipated that the study will be completed in 3 years.

CONCLUSIONS: This randomized controlled trial should definitively answer the question of whether titrating anesthetic depth makes a difference to patient outcome in a vulnerable patient group.
The Ability of esCCO™ and ECOM™ Monitors to Measure Trends in Cardiac Output During Alveolar Recruitment Maneuver After Cardiac Surgery: A Comparison with the Pulmonary Thermodilution Method

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BACKGROUND:

Alveolar recruitment maneuvers (ARMs) are known to improve perioperative morbidity but can transiently impact cardiac output (CO). This reproducible hemodynamic perturbation creates a clinical opportunity to test multiple devices during acute changes in CO. The objective of this study was to evaluate the ability of 2 minimally invasive CO monitors, the ECOM™ (Endotracheal Cardiac Output Monitor) and the esCCO™ (estimated Continuous Cardiac Output), to measure trends in CO during an ARM in postoperative cardiac surgical patients.

METHODS: Twenty-seven mechanically ventilated patients were studied in the postoperative intensive care unit setting. Hemodynamic measurements were made at 3 distinct time points: (1) before an ARM at zero end-expiratory pressure; (2) during an ARM at 15 cm H2O positive end-expiratory pressure; and (3) after the ARM again at zero end-expiratory pressure. Reference CO was obtained from intermittent bolus thermodilution (TDco) using a pulmonary artery catheter. At each of the 3 time points, mean values of 3 CO measurements from each device were collected simultaneously, as well as the corresponding changes in arterial pressure. The
coefficient of variation of the 3 sets for each patient at each time point allowed for the calculation of the precision error for each device. Differences between absolute values of CO using the 2 tested methods and TDco were assessed using a Bland-Altman plot. Additionally, the agreement and responsiveness of the changes in CO (ΔTDco, ΔESco, and ΔECco for changes in TDco, esCCO, and ECOM, respectively) and mean arterial pressure (MAP) were assessed using both a 4-quadrant plot with the coefficient of correlation concordance (CCC) and a polar plot diagram. A polar concordance rate above 80% was considered clinically acceptable.

RESULTS: Eighty-one sets of 3 CO values were analyzed. Precision error of TDco was approximately 5.1% (interquartile range: 2.8-7.1). Between esCCO and TDco, the mean bias was +0.7 L/min with limits of agreement of -2.1 L/min and +3.5 L/min. Between ECOM and TDco, the mean bias was +0.2 L/min with limits of agreement of -2.0 L/min and +2.4 L/min. The CCC between ΔECco and ΔTDco (0.82 [95% confidence interval (CI), 0.72-0.89]) was significantly higher (P = 0.0053) than the CCC between ΔESco and ΔTDco (0.42 [95% CI, 0.20-0.59]), but not statistically different (P = 0.16) than the CCC between ΔMAP and ΔTDco (0.69 [95% CI, 0.54-0.80]). Polar plot analysis showed an angular bias with radial agreement limits of -29° ± 38° between ΔESco and ΔTDco and -15° ± 29° between ΔECco and ΔTDco. Four-quadrant concordance rate was 81% (95% CI, 74-88) between ΔESco and ΔTDco and 100% between ΔECco and ΔTDco. Polar concordance rates were 41% (95% CI, 34-48) between ΔESco and ΔTDco and 85% (95% CI, 79-90) between ΔECco and ΔTDco.

CONCLUSIONS: Compared to pulmonary artery catheter thermodilution, both ECOM and esCCO underestimate changes in CO during an ARMD in postoperative cardiac surgical patients. However, ΔECco is within the angular limits of acceptable agreement and may be as efficient as invasive arterial pressure monitoring to track CO changes. In contrast, esCCO is not able to adequately track CO in these specific conditions.

藥房準備注射器麻黃堿的短缺對術中藥物使用的影響

The Impact of a Shortage of Pharmacy-Prepared Ephedrine Syringes on Intraoperative Medication Use

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Anesthesia & Analgesia 2015 121 404–409

背景：在美國與麻醉有關的用藥短缺已經越來越普遍。我們測試用供應商準備的麻黃堿取代藥房準備的注射器麻黃堿，麻黃素和去氧腎上腺素術中使用的血流動力學和患者水平的變化與供應商級別的變化有關。

方法：在藥房準備的注射器麻黃堿短缺開始的前後 1 個月，在三級醫療中心進行一般和骨科手術患者被列入範圍。最低平均動脈血壓和最慢的心率作為評估血流動力學的措施。調整後的分組採用混合效應回歸與重複測量進行測試。

結果：麻黃堿短缺前有 304 名患者，短缺後有 298 名患者。在麻黃堿短缺期間，相對於之前，至少 1 次麻黃堿的管理是更常見的(148/304 [48.7]% vs 117/298 [39.3]%; P = 0.0199)。在調整了年齡，性別，ASA 評分，手術類型，麻醉提供商，以及手術時間後，在短缺期間患者不太可能得到麻黃素( [RR] = 0.78 [95% CI], 0.61-0.96; P = 0.0198)，更容易獲得去氧腎上腺素(RR = 1.27 [95% CI], 1.02-1.51; P = 0.0357)。在短缺期間，用最慢心率或最低平均動脈血壓評估患者的血流動力學沒有顯著不同。

結論：在藥房準備的注射器麻黃堿短缺期間，用藥管理模式有了一些改變。麻黃素和去氧腎上腺素的作用是明顯的;然而對患者血流動力學影響是相當的。如本研究中觀察到的，在相對或非絕對的藥物短缺期間，供應商的使用模式是敏感的。
BACKGROUND: Anesthesia-related medication shortages have become increasingly common in the United States. We tested whether a local shortage of pharmacy-prepared ephedrine syringes, replaced by provider-prepared ephedrine, was associated with provider-level changes in ephedrine and phenylephrine use and patient-level changes in intraoperative hemodynamics.

METHODS: Consecutive patients undergoing general and orthopedic surgery at a tertiary care center were included 1 month before and 1 month after the start of the pharmacy-prepared ephedrine syringe shortage. Lowest mean arterial blood pressure and slowest heart rate were obtained as measures of hemodynamics. Adjusted associations were tested using mixed-effects regression with repeated measures.

RESULTS: Three hundred four patients before the shortage and 298 patients after the shortage began were included. The administration of at least 1 bolus of ephedrine was significantly more common before versus during the shortage (148/304 [48.7]% vs 117/298 [39.3]%; P = 0.0199). After adjusting for age, sex, ASA physical status, surgery type, anesthesia provider, and operative duration, patients were significantly less likely to receive ephedrine during the shortage (relative risk [RR] = 0.78 [95% confidence interval {CI}, 0.61-0.96]; P = 0.0198) and more likely to receive a phenylephrine bolus (RR = 1.27 [95% CI, 1.02-1.51]; P = 0.0357). Patient hemodynamics assessed by slowest heart rate or lowest mean arterial blood pressure did not differ significantly during the shortage.

CONCLUSIONS: There was an alteration in medication administration patterns during a shortage of pharmacy-prepared syringes. Changes in ephedrine and phenylephrine use were noted; however, patient hemodynamics remained comparable. Provider use patterns were sensitive even to a relative and not absolute medication shortage as observed in this study.
結論：使用IG聲門上氣道裝置作爲柔性支氣管鏡引導下氣管插管的成功率與FT喉罩類似。然而，與FT喉罩相比，IG裝置可以爲插管提供更好的聲門口視野以及縮短插管時間。

（楊曉迪譯薛張綱校）

BACKGROUND: The I-gel™ (IG) supraglottic airway device is a reliable way to establish an airway. Its large ventilation lumen allows for easy passage of an endotracheal tube. With the use of a flexible bronchoscope, the IG offers a good visualization of the laryngeal inlet. This prospective randomized study aims to compare the success rate of flexible bronchoscope-guided tracheal intubation using either the IG or the LMA-Fastrach™ (FT) laryngeal masks.

METHODS: One hundred twenty patients requiring general anesthesia were randomized to 1 of the 2 study groups: IG or FT. After anesthesia induction, the assigned laryngeal mask was inserted to obtain adequate ventilation. We then proceeded to a flexible bronchoscope-guided intubation through the supraglottic device. Tracheal intubation and laryngeal mask insertion success rates were noted, as well as the time required for these manipulations. The view of the laryngeal inlet was graded for each intubation attempt.

RESULTS: Sixty patients were assigned to each study group. The intubation success rates were similar between the IG and the FT groups (100 % vs 95.0 % at first attempt; P = 0.12). The times required for tracheal intubation were significantly lower in the IG group (30 ± 11 seconds vs 50 ± 21 seconds; P < 0.0001). Glottic visualization was better in the IG group, with a significantly higher percentage of grade 1 visualization (63.3% vs 3.3%; P < 0.0001) and a lower percentage of grade 3 visualization (1.7% vs 60.0%; P < 0.0001), than that in the FT group.

CONCLUSIONS: The use of the IG supraglottic airway device as a conduit for flexible bronchoscope-guided tracheal intubation results in a success rate equivalent to the use of the LMA-FT™. However, the IG allows for shorter intubation times and a better visualization of the glottic opening compared with the LMA-FT™.

普通喉鏡與可視喉鏡用於氣管導管交換的對比:高風險呼吸道障礙病人的聲門視覺化，成功率，併發症以及救援方案

Conventional Versus Video Laryngoscopy for Tracheal Tube Exchange: Glottic Visualization, Success Rates, Complications, and Rescue Alternatives in the High-Risk Difficult Airway Patient

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背景：氣管導管交換是一項簡單的概念然而並不是一種簡單的過程，因爲低氧血症，導管誤入食道，以及失去氣道都有致命的影響。將喉鏡與呼吸道交換導管（AEC）結合用於氣管導管交換可能能夠減少風險。喉鏡可用於交換前檢查和開出一條氣管內導管通道（ETT）。直接喉鏡（DL）因為“視線”而受到限制；因此，會造成氣道評估和氣管導管交換的盲操作。這樣也造成了交換導管的難度以及併發症。我們假設曾經用過直接喉鏡用於氣管導管交換的氣道高風險患者，當用可視喉鏡（VL）時，相對於直接喉鏡（DL），可爲氣道評估提供更好地聲門暴露，以及用視覺化氣道交換導管方法交換氣管內導管可減少導致氣道和血流動力學併發症的風險。

方法：危重病人在氣管導管交換前需要在直接喉鏡的輔助下進行氣道評估。假如在直接喉鏡輔助下交換前氣道評估為“暴露差”，這些患者在用可視喉鏡氣道評估後可用可視喉鏡進行氣管導管交換。我們將直接喉鏡下的氣道評估與可視喉鏡下的氣道評估進行比較。我們分析了用於氣管內導管交換所做的嘗試，併發症及救援設備。然後，這些交換結果將與一组歷史對照組病人作對比，這些病人在直接喉鏡（DL）輔助預交換呼吸道評估中被評
定為暴露不佳，並採用了直接喉鏡（DL）+呼吸道交換導管（AEC）輔助交換。這種呼吸道評估方法及氣管內導管通道（ETT）由一個來自麻醉部門的或有麻醉援助能力的職業麻醉醫生執行。

結果：328 個在原先的採用直接喉鏡（DL）評估中被認定為暴露不佳的病人與在歷史對照組（DL+AEC）中視線清晰的 337 個病人對比，之後做了可視喉鏡（VL）。大部分（88%）的病人可以在可視喉鏡檢查中可以做到完全或者接近完全的暴露。氣管內導管通道（ETT）交換的初步成功率在 VL 組中更大（跟 DL 對比為 91.5%對 67.7%，P=0.0001）。

需要嘗試 3 次以上的病人的數量更低（與 DL 對比為 1.2%對 6.8%，P=0.0003）。在與歷史對照 DL+AEC 組病人對比時，中度及重度低氧血症的發病率的相對差異，氣管導管誤入食道，心動過緩以及呼吸道援救設備干預需求將在 VL 交換過程中被監測。

結論：這些發現支持了這樣的假設：可視喉鏡在呼吸道評估中可以更好的暴露聲門，並能減少氣管內導管（ETT）交換過程中的呼吸道及血流動力學的併發症。

BACKGROUND: Tracheal tube exchange is a simple concept but not a simple procedure because hypoxemia, esophageal intubation, and loss of airway may occur with life-threatening ramifications. Combining laryngoscopy with an airway exchange catheter (AEC) may lessen the exchange risk. Laryngoscopy is useful for a pre-exchange examination and to open a pathway for endotracheal tube (ETT) passage. Direct laryngoscopy (DL) is hampered by a restricted “line of sight”; thus, airway assessment and exchange may proceed blindly and contribute to difficulty and complications. We hypothesized that video laryngoscopy (VL), when compared with DL, will improve glottic viewing for airway assessment, and the VL-AEC method of ETT exchange will result in a reduction in airway and hemodynamic complications in high-risk patients when compared with a historical group of patients who underwent DL + AEC-assisted exchange.

METHODS: Critically ill patients requiring an ETT exchange underwent DL-assisted pre-exchange airway assessment. If the DL-assisted pre-exchange assessment rendered a “poor view,” these patients underwent a VL-based airway assessment followed by a VL-assisted ETT exchange procedure. The DL and VL pre-exchange assessments were compared. The attempts, complications, and rescue devices required for ETT exchange were analyzed. These exchange results were then compared with a historical control group of patients who (1) were classified as a poor view on DL-assisted pre-exchange airway assessment; and (2) underwent a DL + AEC-assisted exchange. The airway assessment and ETT exchange were performed by a board-certified anesthesiologist from the Department of Anesthesiology alone or with anesthesia resident assistance.

RESULTS: Three hundred twenty-eight patients with a poor view on initial DL examination underwent a subsequent VL with comparison of views with the 337 patients in the historical control group (DL + AEC). A majority (88%) had a “full or near-full view” on VL examination. The first-pass success rate for ETT exchange was greater in the VL group (91.5% vs 67.7% with DL; P = 0.0001) and the number of patients requiring 3+ attempts was lower (1.2% vs 6.8% with DL; P = 0.0003). A commensurate difference in the incidence of mild and severe hypoxemia, esophageal intubation, bradycardia, and the need for rescue airway device intervention was also observed with VL exchange procedures when compared with the historical DL + AEC group.

CONCLUSIONS: These findings support the hypothesis that VL may result in better glottic viewing for airway assessment and may permit the ETT exchange procedure to be performed with fewer airway and hemodynamic complications. Execution of the ETT exchange over an
AEC was augmented by improved glottic visualization to allow more efficient and timely ETT passage. Multiple attempts to resecure the airway increased the number of exchange complications. VL + AEC exchange led to fewer attempts and is consistent with the recommendation of the American Society of Anesthesiologists Difficult Airway Task Force to limit laryngoscopic attempts and, as a consequence, decrease complications. A VL-based pre-exchange airway assessment may be a valuable procedure for both planning the exchange and uncovering unrecognized airway maladies, for example, partial or complete self-extubation.

Dexmedetomidine Does Not Affect Evoked Potentials During Spine Surgery

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BACKGROUND: The effect of dexmedetomidine on evoked potentials (EPs) has not been elucidated. We aimed to investigate the effect of dexmedetomidine on somatosensory, motor, and visual EPs.

METHODS: After IRB approval, 40 adult patients scheduled for elective spine surgery using total IV anesthesia with propofol and remifentanil were randomly assigned to receive either dexmedetomidine (n = 20) or placebo (n = 20) in a double-blind, placebo-controlled trial. After obtaining informed consent, positioning, and baseline EPs recording, patients were randomly assigned to either IV dexmedetomidine 0.6 μg/kg infused over 10 minutes, followed by 0.6 μg/kg/h, or a corresponding volume of IV normal saline (placebo). EP measures at 60 ± 30 minutes after initiation of study drug were defined as T1 and at 150 ± 30 minutes were defined as T2.
T2. Changes from baseline to T1 (primary end point) and from baseline to T2 (secondary end point) in EP latencies (milliseconds) and amplitudes (microvolts) were compared between groups. Data presented as mean ± SD (95% confidence interval).

RESULTS: Data from 40 patients (dexmedetomidine: n = 20; age, 54 ± 3 years; 10 males; placebo: n = 20; age, 52 ± 2 years; 5 males) were analyzed. There was no difference between dexmedetomidine versus placebo groups in primary end points: change of somatosensory EPs at T1, latency: 0.01 ± 1.3 (-0.64, 0.65) vs 0.01 ± 1.3 (-0.64, 0.65), P = 0.43 (-1.24, 0.45); amplitude: 0.03 ± 0.14 (-0.06, 0.02) vs -0.01 ± 0.13 (-0.07, 0.05), P = 0.76 (-0.074, 0.1); motor EPs amplitude at T1: 65.1 ± 194.8 (-35, 165; n = 18) vs 109.2 ± 241.4 (-24, 243; n = 16), P = 0.57 (-113.5, 241.57); visual EPs at T1 (right eye), amplitude: 2.3 ± 3.6 (-0.4, 5.1; n = 11) vs 0.3 ± 6.0 (-3.3, 3.9; n = 16), P = 0.38 (-6.7, 2.6); latency N1: 2.3 ± 3.6 (-0.4, 5.1) vs 0.3 ± 6.0 (-3.3, 3.9), P = 0.38 (-6.7, 2.6); latency P1: -1.6 ± 13.4 (-11.9, 8.7) vs -1.4 ± 8.1 (-6.3, 3.5), P = 0.97 (-9.3, 9.7) or secondary end points. There were no differences between right and left visual EPs either at T1 or at T2.

CONCLUSIONS: In clinically relevant doses, dexmedetomidine as an adjunct to total IV anesthesia does not seem to alter EPs and therefore can be safely used during surgeries requiring monitoring of EPs.

出生早期全身性使用黃體酮改變成年後術後的痛覺過敏反應: 一項雌性大鼠研究
Systemic Progesterone Administration in Early Life Alters the Hyperalgesic Responses to Surgery in the Adult: A Study on Female Rats
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背景：目前早產兒的存活率有顯著上升，而進行宮內手術的量也有所增加。新生兒時期受到的有害刺激會引起成年後對疼痛反應的改變。已知孕婦體內含有高濃度的黃體酮，而黃體酮同時是一種有效的抗痛覺過敏藥物。因而，我們研究出生早期使用黃體酮對成年大鼠術後的影響。

方法：選擇雌性新生大鼠在出生後的 1 到 7 天內（P1-P7）分別注射黃體酮或溶劑。第二對照組則不進行注射。每組中一半的大鼠在 P3 時接受後爪切割手術而另一半則沒有。在 P60 時大鼠成年，所有組內的大鼠都受到一次後爪切割手術。我們對大鼠進行觸覺敏感性和熱敏感性的測試，在 P14-P42 每週進行一次（第一階段），在 P60 受到第二次損傷刺激前進行一次以及在 P61-P70 每兩天進行一次（第二階段）。在 P67，將大鼠注射多聚甲醛固定後取出脊髓染色並通過免疫細胞化學方法分析活化 p-p38 絲裂原活化蛋白激酶。

結果：在 P3 時接受手術的大鼠在第一階段的觸覺和熱敏感性都高於非手術大鼠，但在注射黃體酮的大鼠組內則沒有這種差異。P3 時受到的切割刺激也導致在 P60 的切割刺激後（第二階段）持續的觸覺和熱的高敏性，而在早期注射黃體酮的組內，疼痛的程度顯著降低並且疼痛消退的速度更快。即使在第一階段沒有接受手術刺激的大鼠中，出生時注射黃體酮減弱了第二階段中的觸覺高敏感性。脊髓細胞染色中，溶劑注射組的大鼠表現出更多的 p-p38 絲裂原活化的蛋白質。

結論：我們的結果提示子宮內的高內源性黃體酮水準可能有相同的保護作用以及新生兒的黃體酮水準能極大地影響傷害性刺激傳導通路的發展。

（施芸岑 譯 薛張綱 校）

BACKGROUND: There has recently been a substantial increase in the survival of prematurely born neonates and an increase of in utero surgeries. Noxious stimulation in the newborn alters the pain response to injury in adult life. Progesterone, an effective antihyperalgesic agent in the
adult, is at high concentration in the pregnant mother. Therefore, we investigated the effects of early-life progesterone on postsurgical outcomes in adult rats.

**METHODS:** Female rat pups were administered progesterone or vehicle during the first 7 days postpartum (P1-P7). A control group had no injections. Half of each of these groups received an incision of the hindpaw at P3 and the other half did not. At P60, all groups of these now adult rats received a second paw incision. Tactile sensitivity and thermal sensitivity were measured weekly at P14-P42 (period I), at P60 (just before the second incision), and every 2 days of P61-P70 (period II). At P67, rats were fixed by systemic paraformaldehyde perfusion and their spinal cords taken for staining and immunocytochemical analysis of activated p-p38 mitogen-activated protein kinase.

**RESULTS:** Rats with surgery at P3 had greater tactile and thermal hyperalgesia in period I than the nonoperated rats, a difference abolished by progesterone treatment. P3 incision also resulted in long-lasting tactile and thermal hyperalgesia after the P60 incision (period II), both of which were markedly smaller in degree and faster to resolve in rats receiving early progesterone. Even in rats that were not operated on in period I, neonatal progesterone lessened the tactile hyperalgesia in period II. More spinal cells showed p-p38 staining in vehicle-treated rats as a result of the early-life incision but not in those treated with progesterone.

**CONCLUSIONS:** These findings suggest that endogenously high progesterone in utero may have a similarly protective action and that the development of nociceptive circuitry can be strongly influenced by neonatal progesterone.

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**黏彈性參數α角能否鑒別纖維蛋白原和血小板缺乏並指導纖維蛋白原補充?**

Can the Viscoelastic Parameter α-Angle Distinguish Fibrinogen from Platelet Deficiency and Guide Fibrinogen Supplementation?

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作爲一項床邊檢驗項目，全血的黏彈性試驗，例如血栓彈力圖 (TEG®, Haemoscope Inc., Niles, IL) 和血栓彈力測定 (ROTEM®, Tem International GmbH, Munich, Germany)，正在被越來越多地運用於描述凝血障礙狀態和指導止血治療。TEG® 專利 (發表於 2004 年) 提出了基於單一分析（高嶺土活化分析）的一種演算法，其得出的 α-斜率和最大振幅參數分別用來指導纖維蛋白原補充和血小板管理。雖然 TEG® 和 ROTEM® 的儀器都能做到多重分析，但是基於 TEG® 的單一分析演算法仍然在很多機構中使用。最近研究討論了單一分析方法的局限性和不準確性。研究表明 α-角和最大振幅參數都反映了纖維蛋白原和血小板形成血栓強度的綜合作用。因此，雖然 TEG® 單一分析可用於識別凝血障礙狀態，但無法被用於鑒別纖維蛋白原（纖維蛋白原）和（或）血小板的缺陷。反之，兩種黏彈性方法同時進行測定，一項加入而不另一項不加血小板抑制劑，能切實辨別特定的凝血障礙狀態，如纖維蛋白形成不足或血小板形成血栓強度不足。這些資訊是選擇適當止血治療的關鍵。

（劉洋 譯 陳傑 校）

Viscoelastic tests such as thrombelastography (TEG®, Haemoscope Inc., Niles, IL) and thromboelastometry (ROTEM®, Tem International GmbH, Munich, Germany), performed in whole blood, are increasingly used at the point-of-care to characterize coagulopathic states and guide hemostatic therapy. An algorithm, based on a mono-analysis (kaolin-activated assay) approach, was proposed in the TEG® patent (issued in 2004) where the α-angle and the maximum amplitude parameters are used to guide fibrinogen supplementation and platelet administration, respectively. Although multiple assays for both the TEG® and ROTEM devices are now available, algorithms based on TEG® mono-analysis are still used in many institutions.
In light of more recent findings, we discuss here the limitations and inaccuracies of the mono-analysis approach. Research shows that both $\alpha$-angle and maximum amplitude parameters reflect the combined contribution of fibrinogen and platelets to clot strength. Therefore, although TEG® mono-analysis is useful for identifying a coagulopathic state, it cannot be used to discriminate between fibrin/fibrinogen and/or platelet deficits, respectively. Conversely, the use of viscoelastic methods where 2 assays can be run simultaneously, one with platelet inhibitors and one without, can effectively allow for the identification of specific coagulopathic states, such as insufficient fibrin formation or an insufficient contribution of platelets to clot strength. Such information is critical for making the appropriate choice of hemostatic therapy.

A Comparison of Differences Between the Systemic Pharmacokinetics of Levobupivacaine and Ropivacaine During Continuous Epidural Infusion: A Prospective, Randomized, Multicenter, Double-Blind Controlled Trial

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**背景**：與靜脈注射阿片類藥物相比，硬膜外輸注左旋布比卡因和羅呱卡因可以為患者提供足夠的術後鎮痛同時減少藥物副作用，並提高患者預後。藥代動力學比藥物的客觀副作用能更好地評價不同藥物的安全性。由於左旋布比卡因和羅呱卡因的藥代動力學特性不同，本研究主要目的是研究兩種藥物在同一人群的硬膜外持續輸注過程中是否具有不同藥代動力學特性。此項隨機對照雙盲多中心試驗，比較對接受大型腹部、泌尿外科、婦科手術的成年患者進行 0.125%左旋布比卡因或 0.2%羅呱卡因持續硬膜外輸注作為術後鎮痛管理的藥代動力學特徵。本研究主要通過變異係數（CV）評估左旋布比卡因和羅呱卡因的系統風險和個體差異的等效值，及預測兩種藥物在持續硬膜外輸注後血漿藥物濃度的可能差異。

**方法**：181 名接受腹部大手術的成年患者隨機分成兩組，分別接受硬膜外輸注 0.125%左旋布比卡因 +0.75 μg/mL 舒芬太尼或 0.2%羅呱卡因 +0.75 μg/mL 舒芬太尼，持續 48 小時。主要終點指標是在 48 小時持續硬膜外輸注期間，通過在 15%變異係數範圍內的曲線下面積分析左旋布比卡因和羅呱卡因的血漿藥物濃度變異性。變異係數反映局麻藥物相對中值濃度的離散情況，從而提示預測血漿藥物濃度的可靠程度。次要終點指標是評價包括平均血漿藥物濃度峰值分析在內的局麻藥藥理學特性，同時評價血漿清除率、副作用、疼痛程度（通過數位化量表評估，比如，靜態數位化量表和動態數位化量表）和需要解救劑量的次數。

**結果**：兩組 CV 的差異無統計學意義：即曲線下面積的差異在 15%範圍內。左旋布比卡因的變異係數為 0.54，羅呱卡因為 0.51 ($p=0.725$)。羅呱卡因的血漿藥物濃度達峰比左旋布比卡因更迅速。羅呱卡因的清除速率隨病人年齡的增長而降低。兩組之間的靜態數位評定量表、動態數位評定量表分數、解救次數以及副作用情況均無統計學意義。

**結論**：考慮變異係數，成年患者接受持續硬膜外輸注左旋布比卡因和羅呱卡因的血漿藥物濃度個體差異性是相同的。本研究發現羅呱卡因的清除隨著患者年齡增長而減弱，但是這個發現也有一些局限性。48 小時的輸注時間並未達到穩態血漿濃度。由於可能達到中毒水準，左旋布比卡因和羅呱卡因持續輸注 48 小時以上的血漿藥物濃度特性還需進一步研究。總之，兩種藥物局部麻醉在臨床效能和副作用發生率兩方面均無顯著差異。

（楊中偉 譯 陳傑 校）
BACKGROUND: Epidural infusion of levobupivacaine and ropivacaine provides adequate postoperative pain management by minimizing side effects related to IV opioids and improving patient outcome. The safety profile of different drugs can be better estimated by comparing their pharmacokinetic profiles than by considering their objective side effects. Because levobupivacaine and ropivacaine have different pharmacokinetic properties, our aim was to investigate whether there is a difference in the pharmacokinetic variability of the 2 drugs in a homogeneous population undergoing continuous epidural infusion. This double-blind, multicenter, randomized, controlled trial study was designed to compare the pharmacokinetics of continuous thoracic epidural infusion of levobupivacaine 0.125% or ropivacaine 0.2% for postoperative pain management in adult patients who had undergone major abdominal, urological, or gynecological surgery. This study is focused on the evaluation of the coefficient of variation (CV) to assess the equivalence in the systemic exposure and interindividual variability between levobupivacaine and ropivacaine and, therefore, the possible differences in the predictability of the plasmatic concentrations of the 2 drugs during thoracic epidural infusion.

METHODS: One hundred eighty-one adults undergoing major abdominal surgery were enrolled in the study. Patients were randomized to receive an epidural infusion of levobupivacaine 0.125% + sufentanil 0.75 μg/mL or of ropivacaine 0.2% + sufentanil 0.75 μg/mL at 5 mL/h for 48 hours. The primary end point of this study was to analyze the variability of plasma concentration of levobupivacaine and ropivacaine via an area under the curve within a range of 15% of the CV during 48 hours of continuous epidural infusion. The CV shows how the concentration values of local anesthetics are scattered around the median concentration value, thus indicating the extent to which plasma concentration is predictable during infusion. Secondary end points were to assess the pharmacologic profile of the local anesthetics used in the study, including an analysis of mean peak plasma concentrations, and also to assess plasma clearance, side effects, pain intensity (measured with a verbal numeric ranging score, i.e., static Numeric Rating Scale [NRS] and dynamic NRS), and the need for rescue doses.

RESULTS: The comparison between the 2 CVs showed no statistical difference: the difference between area under the curve was within the range of 15%. The CV was 0.54 for levobupivacaine and 0.51 for ropivacaine (P = 0.725). The plasma concentrations of ropivacaine approached the Cmax significantly faster than those of levobupivacaine. Clearance of ropivacaine decreases with increasing patient age. There were no significant differences in NRS, dynamic NRS scores, the number of rescue doses, or in side effects between groups.

CONCLUSIONS: Considering the CV, the interindividual variability of plasma concentration for levobupivacaine and ropivacaine is equivalent after thoracic epidural infusion in adults. We found a reduction in clearance of ropivacaine depending on patient age, but this finding could be the result of some limitations of our study. The steady-state concentration was not reached during the 48-hour infusion and the behavior of plasma concentrations of ropivacaine and levobupivacaine during continuous infusions lasting more than 48 hours remains to be investigated, because they could reach toxic levels. Finally, no differences in the clinical efficacy or in the incidence of adverse effects between groups were found for either local anesthetic.

關於七氟烷麻醉下Sugammadex逆轉呱庫溴銨介導的中度神經肌肉阻滯的一項隨機試驗
Reversal of Pipecuronium-Induced Moderate Neuromuscular Block with Sugammadex in the Presence of a Sevoflurane Anesthetic: A Randomized Trial
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Anesthesia & Analgesia 2015 121 373–380
BACKGROUND: Pipecuronium is a steroidal neuromuscular blocking agent. Sugammadex, a relaxant binding \( \gamma \)-cyclodextrin derivative, reverses the effect of rocuronium, vecuronium, and pancuronium. We investigated whether sugammadex reverses moderate pipecuronium-induced neuromuscular blockade (NMB) and the doses required to achieve reversal.

METHODS: This single-center, randomized, double-blind, 5-group parallel-arm study comprised 50 patients undergoing general anesthesia with propofol, sevoflurane, fentanyl, and pipecuronium. Neuromuscular monitoring was performed with acceleromyography (TOF-Watch SX®) according to international standards. When the NMB recovered spontaneously to train-of-four count 2, patients randomly received 1.0, 2.0, 3.0, or 4.0 mg/kg of sugammadex or placebo. Recovery time from sugammadex injection to normalized train-of-four (TOF) ratio 0.9 was the primary outcome variable. The recovery time from the sugammadex injection to final T1 was the secondary end point. Postoperative neuromuscular functions were also assessed.

RESULTS: Each patient who received sugammadex recovered to a normalized TOF ratio of 0.9 within 5.0 minutes (95% lower confidence interval for the lowest dose 70.1%; for all doses 90.8%) and 79% of these patients reached a normalized TOF ratio 0.9 within 2.0 minutes (95% lower confidence interval for the lowest dose 26.7%; for all doses 63.7%). T1 recovered several minutes after the TOF ratio. No residual postoperative NMB was observed.

CONCLUSIONS: Sugammadex adequately and rapidly reverses pipecuronium-induced moderate NMB during sevoflurane anesthesia. Once the train-of-four count has spontaneously returned to 2 responses following pipecuronium administration, a dose of 2.0 mg/kg of sugammadex is sufficient to reverse the NMB.

The Surgical Care Improvement Project Antibiotic Guidelines: Should We Expect More Than Good Intentions?

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Anesthesiology 2015 121 397–403
Since 2006, the Surgical Care Improvement Project (SCIP) has promoted 3 perioperative antibiotic recommendations designed to reduce the incidence of surgical site infections. Despite good evidence for the efficacy of these recommendations, the efforts of SCIP have not measurably improved the rates of surgical site infections. We offer 3 arguments as to why SCIP has fallen short of expectations. We then suggest a reorientation of quality improvement efforts to focus less on reporting, and incentivizing adherence to imperfect metrics, and more on creating local and regional quality collaboratives to educate clinicians about how to improve practice. Ultimately, successful quality improvement projects are behavioral interventions that will only succeed to the degree that they motivate individual clinicians, practicing within a particular context, to do the difficult work of identifying failures and iteratively working toward excellence.

Predictors of Delayed Postoperative Respiratory Depression Assessed from Naloxone Administration

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**Background:** This study aimed to determine patient and surgical characteristics associated with naloxone use following delayed post-anesthesia respiratory depression.

**Methods:** In 2008–2010, patients undergoing anesthesia were monitored for delayed respiratory depression using naloxone administration. A logistic regression approach was used to evaluate factors associated with naloxone use.

**Results:** Among 134 patients receiving naloxone, 58% (95% CI 1.3–1.9) were found to have obstructive sleep apnea. Factors associated with naloxone use included higher BMI, lower baseline respiratory rate, and a history of respiratory depression.

**Conclusions:** The use of naloxone following anesthesia was associated with respiratory depression, and may be a useful tool in identifying patients at risk for respiratory depression.
BACKGROUND: The aim of this study was to identify patient and procedural characteristics associated with postoperative respiratory depression or sedation requiring naloxone intervention.

METHODS: We identified patients who received naloxone to reverse opioid-induced respiratory depression or sedation within 48 hours after discharge from anesthetic care (transfer from the postanesthesia care unit or transfer from the operating room to postoperative areas) between July 1, 2008, and June 30, 2010. Patients were matched to 2 control subjects based on age, sex, and exact type of procedure performed during the same year. A chart review was performed to identify patient, anesthetic, and surgical factors that may be associated with risk for intervention requiring naloxone. In addition, we identified all patients who developed adverse respiratory events (hypoventilation, apnea, oxyhemoglobin desaturation, pain/sedation mismatch) during phase 1 anesthesia recovery. We performed conditional logistic regression taking into account the 1:2 matched set case-control study design to assess patient and procedural characteristics associated with naloxone use.

RESULTS: We identified 134 naloxone administrations, 58% within 12 hours of discharge from anesthesia care, with an incidence of 1.6 per 1000 (95% confidence interval [CI], 1.3–1.9) anesthetics. The presence of obstructive sleep apnea (odds ratio [OR] = 2.45; 95% CI, 1.27–4.66; P = 0.008) and diagnosis of an adverse respiratory event in the postanesthesia recovery room (OR = 5.11; 95% CI, 2.32–11.27; P < 0.001) were associated with an increased risk for requiring naloxone to treat respiratory depression or sedation after discharge from anesthesia care. After discharge from anesthesia care, patients administered naloxone used a greater median dose of opioids (10 [interquartile range, 0–47.1] vs 5 [0–24.8] IV morphine equivalents, P = 0.020) and more medications with sedating side effects (n = 41 [31%] vs 24 [9%]; P < 0.001).

CONCLUSIONS: Obstructive sleep apnea and adverse respiratory events in the recovery room are harbingers of increased risk for respiratory depression or sedation requiring naloxone after discharge from anesthesia care. Also, patients administered naloxone received more opioids and other sedating medications after discharge from anesthetic care. Our findings suggest that these patients may benefit from more careful monitoring after being discharged from anesthesia care.

Expecting the Unexpected: Perspectives on Stillbirth and Late Termination of Pregnancy for Fetal Anomalies

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准媽媽和她們的配偶們準備了幾個月來熱切地歡迎他們期待已久的寶寶來到他們的家庭。而死產或可能危及胎兒生命的胎兒畸形的診斷結果對受其影響的母親和她們的家庭來說是一個可怕的事故。從診斷到採取干預措施（即引產死胎或對畸形胎兒終止晚期妊娠），患者經常感到無助和被拋棄，會對許多人有長期的心理和情緒的影響。產科知識管理，道德和醫學的挑戰，心理學方面近幾年來有所發展。熟悉相關新興知識使產科麻醉醫生更好地提供有效的移情關懷。考慮到臨產婦的復蘇需要，碰到這類經歷過死胎或致命胎兒畸形的婦女促使麻醉醫生對臨產關懷的現有證據進行總結陳述。

Expectant mothers and their spouses spend months preparing to eagerly welcome their much-anticipated baby into their family. Stillbirth or a diagnosis of life-limiting fetal anomalies comes as a devastating turn of events for affected women and their families. From the time of diagnosis to intervention (i.e., induction of labor for stillbirth or late termination of pregnancy for fetal
anomalies), affected women often feel vulnerable and abandoned, with many experiencing long-
term psychological and emotional effects. Knowledge of obstetric management, ethical and 
medical challenges, and psychological aspects have evolved in recent years. Familiarity with this 
emerging knowledge better prepares the obstetric anesthesiologist to deliver effective and 
empathic care. Encounters with women experiencing stillbirth and life-limiting fetal anomalies 
prompted this review of current evidence regarding parturient’ perspectives on their care as they 
set out on the road to recovery.

Transversus Abdominis Plane Block Versus Caudal Epidural for Lower Abdominal 
Surgery in Children: A Double-Blinded Randomized Controlled Trial

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Anesthesia & Analgesia 2015 121 471–478

BACKGROUND: Transversus abdominis plane block (TAPB) has emerged as a safe and 
effective regional anesthesia technique for providing postoperative lower abdominal analgesia. 
Complications associated with TAPB are rare and pose a lower overall risk to the patient 
receiving a TAPB versus a caudal block, which is considered the gold standard for pediatric 
lower abdominal regional anesthesia. Our study hypothesis was that TAPB would initially be 
equivalent to caudal block in providing postoperative pain control but would also show improved 
pain relief beyond the anticipated caudal duration.

METHODS: This study was a double-blinded randomized controlled trial. Forty-five children 
between the ages of 1 and 9 undergoing bilateral ureteral reimplantation surgery through a low 
transverse incision were enrolled. Narcotic requirement, pain scores (FLACC/Wong-Baker 
FACES), episodes of emesis, and antispasmodic requirement were recorded in the postanesthesia
care unit (PACU) and at 6-hour intervals for 24 hours from the time of block placement. Our protocol used a multimodal approach toward pain management in all children, including randomized regional technique, scheduled ketorolac, morphine as needed, and the antispasmodic, oxybutynin, as needed.

RESULTS: Morphine requirement showed no statistical difference during the initial 12 hours (all P ≥ 0.68 at PACU, 6 and 12 hours). However, at 24 hours those patients randomized to receive the TAPB required less cumulative morphine than the caudal group (0.05 mg/kg ± 0.06 vs 0.09 mg/kg ± 0.07, P = 0.03). There was a trend toward fewer episodes of emesis in the TAPB group which reached statistical significance at 18 and 24 hours (6 vs 1 episodes, P = 0.03; and 9 vs 2 episodes, P = 0.02). Pain scores (0–10) were higher in the TAPB group in the PACU (3.46 ± 2.69 vs 1.71 ± 2.1, P = 0.02), but there were no significant differences at all subsequent time points (all P ≥ 0.10). The TAPB group also had a higher requirement for the bladder antispasmodic oxybutynin at 24 hours (0.49 ± 0.58 vs 0.28 ± 0.17, P = 0.003).

CONCLUSIONS: TAPB provided superior analgesia compared with the caudal block at 6 to 24 hours after block placement, as demonstrated by a statistically significant decrease in cumulative opioid requirement, which was the primary end point. The lower incidence of emesis in the TAPB group likely reflected the decreased opioid consumption. Although TAPB appears to be less effective than the caudal block in preventing viscerally mediated bladder spasms, as evidenced by the higher PACU pain scores and increased oxybutynin requirement at 24 hours, this effect may be counteracted in future clinical practice by scheduled administration of the antispasmodic medications. Considering the overall safety advantages of the TAPB over the caudal block, this should be considered a preferred regional technique for lower abdominal surgeries.

利用血栓彈力計對小兒先心病患者行速率曲線測量以量化纖維蛋白溶解程度

Quantification of Fibrinolysis Using Velocity Curves Measured with Thromboelastometry in Children with Congenital Heart Disease

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背景：本研究假設血栓彈力計（ROTEM®, Tem International GmbH, Munich, Germany）測得的血凝塊振幅（A）和彈性（E）變化擬合得到的速率參數可以更準確地檢測接受先天性心臟病糾治術患兒全血的纖溶風險。

方法：在全身麻醉誘導後獲得患者的全血標本。對以下七種狀態進行了研究：正常對照血（作為基線）和含不同漸進濃度的組織型纖溶酶原啟動物（t-PA）（102, 255, 512, 1024, 1535, 2539 單位/毫升）的樣血。使用 ROTEM 資料，在基於不同時間點間血凝塊振幅和彈性變化來計算速率曲線。分析得出以下參數：基於血栓幅度的血栓形成最大速率（MTA），基於血栓振幅的血栓形成凝固時間（MTT），基於血栓振幅的血栓裂解最大速率（MTLe），基於血栓彈性變化的血栓裂解最大速率（MTLe）。將這些參數與最大血凝的裂解參數進行比較並一直觀察到凝固時間後的 30 分鐘（LI30，百分率）。

結果：當 t-PA 大於 255 單位/毫升時，LI30（平均差，255 單位/ mL 相較於基線，-31.05％，P <0.0001）和基於血栓振幅的血栓形成凝固時間（平均差，255 単位/ mL 相較於基線，-7.5，P = 0.005）開始減小。當 t-PA 大於 512 單位/毫升時，基於血栓振幅的血栓形成凝固時間（平均差，512 單位/ mL 相較於基線，-10.9，P = 0.010）、MTL（平均差，255 單位/毫升相對於基線，-3.2，P = 0.016）和 MTLe（平均差，255 單位/ mL 相對於基線，-7.8，P = 0.004）發生變化。當 t-PA 濃度≥512 單位/毫升，血栓不再形成。為了檢測最小的
織溶活化，LI30、MTL 和 MTLE 之間的受試者特徵曲線下面積沒有顯著差異（102 單位/mL 分別為 0.74、0.75 和 0.72，P = 0.708），而靈敏度和特異性的極值：LI30 以 97% 為界值，MTL 以 0.3 為界值及 MTLE 以 0.5 為界值，它們的敏感度和特異度分別為 52% 和 85%、83% 和 45% 及 83% 和 45%。

結論：基於血栓振幅或血栓彈性變化的速率曲線可為血液中血凝塊形成和溶解提供客觀的動力學量度指標，並能檢測即使是輕微的纖溶。但還需要進一步研究，以評估這些參數的臨床意義。

（袁亞偉 譯 陳傑 校）

BACKGROUND: In this pilot study, we hypothesized that velocity parameters obtained from changes in clot amplitude (A) and clot elasticity (E) measured with thromboelastometry (ROTEM®. Tem International GmbH, Munich, Germany) could improve detection of fibrinolysis in whole blood obtained from children undergoing surgery for congenital heart disease.

METHODS: Whole blood samples were obtained after induction of general anesthesia. Seven conditions were studied: native whole blood (baseline) and samples with progressive tissue-type plasminogen activator (t-PA) concentrations (102, 255, 512, 1024, 1535, and 2539 units/mL). We calculated velocity curves based on changes in clot amplitude and elasticity between different time points using ROTEM data. The analysis allowed for the determination of the following parameters: the maximum rate of thrombus formation based on amplitude or elasticity and the maximum rate of thrombus lysis measured based on amplitude (MTL) or maximum rate of thrombus lysis measured based on elasticity (MTLe). We compared these parameters with the lysis in relation to maximal clotting firmness and measured 30 minutes after the clotting time (LI30, in percent).

RESULTS: Concentrations of t-PA ≥ 255 units/mL resulted in a decrease in LI30 (mean difference, 255 units/mL versus baseline, −31.05%, P < 0.0001) and the maximum rate of thrombus formation based on amplitude (mean difference, 255 units/mL versus baseline, −7.5, P = 0.005). Concentrations of t-PA ≥ 512 units/mL resulted in changes in maximum rate of thrombus formation based on elasticity (mean difference, 512 units/mL versus baseline, −10.9, P = 0.010), MTL (mean difference, 255 units/mL versus baseline, −3.2, P = 0.016), and MTLe (mean difference, 255 units/mL versus baseline, −7.8, P = 0.004). For t-PA concentrations ≥ 512 units/mL, clot formation was abolished. The area under the receiver operating characteristics curves did not differ between LI30, MTL, and MTLe for the detection of minimal fibrinolytic activation (102 units/mL; 0.74, 0.75, and 0.72, respectively, P = 0.708), whereas sensitivity and specificity of the cutoff values 97% for LI30, −0.3 for MTL, and −0.5 for MTLe were 52% and 85%, 83% and 45%, and 83% and 45%, respectively.

CONCLUSIONS: Velocity curves based on the amplitudes or clot elasticity could provide objective measurement of clot growth and clot lysis kinetics, allowing detection of even minor fibrinolysis. Further studies are needed to assess the clinical relevance of these parameters.

運用大鼠皮膚切口模型研究度洛西丁對痛覺異常和痛覺過敏局部和全身的作用

The Local and Systemic Actions of Duloxetine in Allodynia and Hyperalgesia Using a Rat Skin Incision Pain Model

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背景：度洛西丁是一種對重度抑鬱症有效的抗抑鬱劑，同時也是糖尿病性周圍神經病變、慢性骨骼肌疼痛和纖維組織肌痛患者緩解疼痛的良藥。度洛西丁在緩解疼痛方面的作
用機制尚不清楚。本次研究提出，度洛西丁是否可通過全身以及局部機制起到鎮痛作用。

方法：在大鼠的皮膚作切口後，對在切口處皮下注射布比卡因和度洛西丁後抑制術後疼
痛的療效進行比較。對側和腹膜內的注射是用來評估度洛西丁全身的效果。局麻作用是通
過對大鼠坐骨神經功能的阻滯來分析的。度洛西丁對納通道的抑制作用主要表現在外鼠的
GH3細胞上。

結果：研究顯示，在皮膚作切口後，皮下注射2mg的度洛西丁可以減輕幾天的痛覺異常
和痛覺過敏，而皮下注射2mg布比卡因並無此作用。在對側注射10mg度洛西丁對術後疼
痛緩解只有極小的作用。只有用了較高劑量（10到20mg），腹膜內注射度洛西丁才可以
減輕痛覺異常和痛覺過敏。通過坐骨神經阻滯，度洛西丁（2mg）可以抑制運動和疼痛感
覺功能大約24小時，同時也可以用50％的抑制濃度30.4±1.2μM和4.26±0.19μM（n=8）分
別使通道靜止和快速滅活來減少電流。此外當受到5Hz刺激時，度洛西丁（10μM）
產生阻斷近70％的納電流峰。結論：此研究顯示度洛西丁可以起到局麻的作用，也是一種可以全身和局部應用的鎮痛
劑。由於度洛西丁可以高效地抑制神經元的納電流，當它作用於許多中樞神經系統和外周
靶點時，可以通過抑制由神經末梢損傷引起的自發神經衝動，發揮其抵抗痛覺過敏的作
用。

（李悅譯 陳傑校）

BACKGROUND: Duloxetine is an antidepressant effective for major depressive disorder and
also the alleviation of pain for patients with diabetic peripheral neuropathy, chronic
musculoskeletal pain, and fibromyalgia. How duloxetine works in pain relief remains unknown.
In this study, we address whether duloxetine could act as an analgesic via systemic and local
applications.

METHODS: Efficacies of bupivacaine and duloxetine applied subcutaneously at the incision
site against acute postoperative pain were compared after rat skin incision. Contralateral and
intraperitoneal injections were used to assess systemic efficacy of duloxetine. Local anesthetic
actions were assayed through functional block of the rat sciatic nerve. Inhibition by duloxetine of
neuronal Na+ channels was characterized in rat GH3 cells.

RESULTS: Our studies showed that subcutaneous duloxetine (2 mg) reduced hyperalgesia and
allodynia for several days after skin incision, whereas subcutaneous bupivacaine (2 mg) did not.
Contralaterally injected duloxetine (10 mg) had minimal effects on postoperative pain. Intraperitoneal
injection duloxetine also reduced both allodynia and hyperalgesia, albeit at higher doses
(10–20 mg). Duloxetine (2 mg) inhibited motor and nociceptive functions via sciatic nerve block
for approximately 24 hours. It also reduced Na+ currents with 50% inhibitory concentrations of
30.4 ± 1.2 μM and 4.26 ± 0.19 μM (n = 8) for resting and fast-inactivated channels, respectively.
Furthermore, duloxetine (10 μM) elicited additional use-dependent block of peak Na+ currents
by approximately 70% when stimulated at 5 Hz.

CONCLUSIONS: Our results demonstrate that duloxetine can act as a local anesthetic and an
analgesic drug via both local and systemic applications. Because duloxetine inhibits neuronal
Na+ currents with high potency, it may exert its antihyperalgesic effects through inhibition of the
spontaneous nerve impulses that result from peripheral injury, encompassing its actions on
multiple central nervous system and peripheral targets.