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August, 2013

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The Influence of Laboratory Coagulation Tests and Clotting Factor Levels on Rotation Thromboelastometry (ROTEM®) During Major Surgery with Hemorrhage

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BACKGROUND: The aim of this study was to determine the association between standard laboratory tests, coagulation factor concentrations, and Rotation Thromboelastometry (ROTEM® delta, TEM® International GmbH, Munich, Germany) in patients undergoing major surgery with hemorrhage.

METHODS: In 45 patient’s fibrinogen, factor VIII, factor XIII, International Normalized Ratio (INR), activated partial thromboplastin time (aPTT), thrombin time, hemoglobin, leukocytes, and
platelet count were simultaneously measured intraoperatively with ROTEM (EXTEM, INTEM, FIBTEM, APTEM) measurements. ROTEM parameters were: clotting time (CT), clot formation time (CFT), maximum clot firmness (MCF), and α-angle. Demographic and laboratory data were expressed as mean ± SD and median [range]; nonparametric Spearman rank correlations and multiple linear regressions were performed; P-values ≤ 0.003 were considered significant.

RESULTS: Significant correlations (P ≤ 0.003) were found for CFT, α-angle, and MCF, in EXTEM, INTEM, and APTEM with platelets, INR, and fibrinogen. Factor VIII (18 measurements) showed a strong correlation (r ≥ 0.7 or r ≤ −0.7; all P ≤ 0.003) with MCF, CFT, and α-angle of EXTEM, INTEM, MCF of FIBTEM excluding CT of EXTEM, INTEM, FIBTEM and strong significant correlation for α-angle of APTEM and moderate for CFT and MCF of APTEM. A significant moderate to strong correlation of factor XIII with MCF of EXTEM, INTEM, FIBTEM, and APTEM was found. Hemoglobin was moderately correlated (r = 0.3–0.7 or r = −0.3 to −0.7) with MCF in APTEM (P = 0.003). A moderate to strong correlation of the standard coagulation tests with all ROTEM parameters was found, in particular the CT. The aPTT correlated significantly moderate to strong with CT, CFT, α-angle, and MCF of INTEM. However, multiple linear regressions were not able to show an influence of INR on ROTEM parameters except for APTEM-MCF. A significant impact of the aPTT on INTEM-CT was found. EXTEM, INTEM, and APTEM are significantly influenced by fibrinogen and platelets.

CONCLUSIONS: The results confirm the clinical assumption that EXTEM, INTEM, and APTEM are associated with fibrinogen and platelets levels; INTEM-CT significantly to aPTT; and FIBTEM significantly to fibrinogen. Factor VIII showed a significant correlation with all ROTEM parameters except CT of EXTEM, INTEM, FIBTEM, and CFT and MCF of APTEM.
BACKGROUND: In Japan, routine clinical care does not normally involve the use of a monitoring device to guide the administration of neuromuscular blocking drugs or their antagonists. Although most previous reports demonstrate that sugammadex offers more rapid and reliable antagonism from rocuronium-induced neuromuscular blockade, this advantage has not been confirmed in clinical settings when no neuromuscular monitoring is used. In this multicenter observational study, we sought to determine whether sugammadex reduces the incidence of postoperative residual weakness compared with neostigmine when the administration of rocuronium and its antagonists is not guided by neuromuscular monitoring.

METHODS: This study was conducted in two 5-month periods that preceded and followed the introduction of sugammadex into clinical practice in Japan. Five university-affiliated teaching hospitals participated in this study. Neostigmine was used to antagonize rocuronium-induced neuromuscular blockade in the first phase, and sugammadex was used in the second phase. The timing and doses of rocuronium, neostigmine, and sugammadex were determined by the attending anesthesiologists without the use of neuromuscular function monitoring devices. To ascertain the incidence of postoperative residual neuromuscular weakness, the train-of-four ratio (TOFR) was determined acceleromyographically after tracheal extubation. Since our practice also does not usually involve calibration and normalization of accelerographic responses, both TOFR <0.9 and TOFR <1.0 were used as the criteria for defining postoperative residual weakness.

RESULTS: In the first phase, 109 patients received neostigmine (average dose 33 µg/kg) and 23 patients were considered (by clinical criteria) to have adequate recovery and did not receive neostigmine (spontaneous recovery group). In the second phase, 117 patients received sugammadex (average dose 2.7 mg/kg) for antagonism of rocuronium-induced blockade. The incidence (95% confidence interval) of TOFR <0.9 under spontaneous recovery, after neostigmine, and after sugammadex, was 13.0% (2.8%–33.6%), 23.9% (16.2%–33.0%), and 4.3% (1.7%–9.4%), respectively. The incidence (95% confidence interval) of TOFR <1.0 in these groups was 69.6% (47.1%–86.6%), 67.0% (57.3%–75.7%), and 46.2% (36.9%–55.6%), respectively. The use of sevoflurane in the neostigmine group and the short interval between the administration of the last doses of rocuronium and sugammadex were associated with a higher incidence of postoperative residual weakness.

CONCLUSIONS: This study demonstrated that the risk of TOFR <0.9 after tracheal extubation after sugammadex remains as high as 9.4% in a clinical setting in which neuromuscular monitoring (objective or subjective) was not used. Our finding underscores the importance of neuromuscular monitoring even when sugammadex is used for antagonism of rocuronium-induced neuromuscular block.
Noninvasive Continuous Cardiac Output by the Nexfin Before and After Preload-Modifying Maneuvers: A Comparison with Intermittent Thermodilution Cardiac Output

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BACKGROUND: The Nexfin uses an uncalibrated pulse contour method for the continuous measurement of cardiac output (CO) in a totally noninvasive manner. Since the accuracy of pulse contour methods and their ability to track changes in CO have been repeatedly questioned, we have compared the CO measured by the Nexfin (NAPCO) with the CO measured by the pulmonary artery catheter (PACCO) in cardiosurgical patients before and after preload-modifying maneuvers.

METHODS: Twenty-eight patients who underwent on-pump cardiac surgery, of whom 18 were receiving vasopressor and/or inotropic therapy, were studied during the first postoperative hours. Preload modification, in the form of either a fluid challenge or a passive leg raising maneuver, was done whenever clinically indicated, with PACCO and NAPCO being simultaneously measured before and after each intervention.

RESULTS: A fluid challenge was administered to 22 patients, and the passive leg raising maneuver was performed in 6 patients. These interventions were repeated in 19 patients.
producing a total of 47 pairs of measurements. At baseline, mean (±SD) CO was 4.9 ± 1.1 and 5.0 ± 1.4 L•min⁻¹, for the PACCO and NAPCO, respectively, bias 0.1 ± 1.0, 95% prediction interval −2.5 to 2.4 L•min⁻¹, and 39% of error. After preload modification, the mean CO was 5.6 ± 1.3 and 5.6± 1.5 L•min⁻¹ for the PACCO and NAPCO, respectively, bias −0.0 ± 1.1, 95% prediction interval −2.6 to 2.7 L•min⁻¹, and 38% of error. The correlation coefficients (r) between the PACCO and NAPCO before and after preload modification were 0.71 (95% confidence interval [95% CI], 0.53–0.82) and 0.70 (95% CI, 0.52–0.82), respectively. Preload modification induced similar absolute changes in PACCO and NAPCO (r = 0.9, P < 0.0001). A 4-quadrant scatter plot showed a concordance rate of 100% (95% CI, 80.5%–100%) between the changes in NAPCO and PACCO. Polar plot analysis demonstrated a small polar angle and radial limits of agreement well below the 30° benchmark. The area under a receiver operating characteristic curve, testing the ability of Nexfin to detect an increase of ≥15% in PACCO, was 0.974 (95% CI, 0.93–0.99).

CONCLUSIONS: Although the Nexfin has limited accuracy when compared with the pulmonary artery catheter, it can reliably track preload-induced changes in CO in stable patients after cardiac surgery in the presence of moderate vasopressor and inotropic therapy. This ability, combined with its total noninvasiveness, fast installation, and ease of use, make the Nexfin a suitable monitor for the perioperative continuous measurement of CO. The reliability of this monitor in tracking the CO when significant changes in peripheral resistance take place still needs to be established.

**Patient Warming Excess Heat: The Effects on Orthopedic Operating Room Ventilation Performance**

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Anesth Analg August 2013 117:406-411

**背景：**基於在普外科手術中應用的得益，使用患者保溫裝置已成爲預防術中意外低體溫發生的一項標準監護。然而，這些收益可能無法在易感染手術（例如移植手術）中完全實現，由於患者保溫裝置釋放的餘熱可能擾亂預期的從天花板到地面的氣流流通模式並使外科手術區域遭受額外污染。因此本實驗研究在整形外科手術室中，對一個模擬接受全膝置換手術鋪巾方式的人體模型採取兩項流行的患者保溫技術，暖風機和加溫毯，與對照環境比較空氣流通模式的差異。

**方法：**通過在麻醉鋪巾頭側的無菌區域釋放中性懸浮洗滌劑氣泡（“氣泡”）來評估空氣流通模式。然後監測對人體模型上半身進行加熱產生的餘熱是否會導致“氣泡”進入手術野。形式上，採取隨機化，可重複設計來評估設備（暖風機，加溫毯，對照）和麻醉鋪巾高度（低，高）對手術野上方拍攝到的“氣泡”數量的影響。

**結果：**直接的大量漂浮氣流從暖風機中排出，形成熱對流氣流，並使氣泡越過麻醉鋪巾上方進入手術野，由於患者加溫裝置的因素導致“氣泡”計數有明顯增加（P<0.001）。在各種鋪巾高度情況下，暖風機組平均“氣泡”計數為132.5，而加溫毯組為0.48（P=0.003），而對照組為0.01（P=0.008）在所有高度。在各種鋪巾高度情況下，加溫毯組與對照組之間的平均“氣泡”計數的差異忽略不計（P=0.87）鋪巾高度對“氣泡”計數無明顯影響（P=0.94）
**BACKGROUND:** Patient warming has become a standard of care for the prevention of unintentional hypothermia based on benefits established in general surgery. However, these benefits may not fully translate to contamination-sensitive surgery (i.e., implants), because patient warming devices release excess heat that may disrupt the intended ceiling-to-floor ventilation airflows and expose the surgical site to added contamination. Therefore, we studied the effects of 2 popular patient warming technologies, forced air and conductive fabric, versus control conditions on ventilation performance in an orthopedic operating room with a mannequin draped for total knee replacement.

**METHODS:** Ventilation performance was assessed by releasing neutrally buoyant detergent bubbles (“bubbles”) into the nonsterile region under the head-side of the anesthesia drape. We then tracked whether the excess heat from upper body patient warming mobilized the “bubbles” into the surgical site. Formally, a randomized replicated design assessed the effect of device (forced air, conductive fabric, control) and anesthesia drape height (low-drape, high-drape) on the number of bubbles photographed over the surgical site.

**RESULTS:** The direct mass-flow exhaust from forced air warming generated hot air convection currents that mobilized bubbles over the anesthesia drape and into the surgical site, resulting in a significant increase in bubble counts for the factor of patient warming device (P < 0.001). Forced air had an average count of 132.5 versus 0.48 for conductive fabric (P = 0.003) and 0.01 for control conditions (P = 0.008) across both drape heights. Differences in average bubble counts across both drape heights were insignificant between conductive fabric and control conditions (P = 0.87). The factor of drape height had no significant effect (P = 0.94) on bubble counts.

**CONCLUSIONS:** Excess heat from forced air warming resulted in the disruption of ventilation airflows over the surgical site, whereas conductive patient warming devices had no noticeable effect on ventilation airflows. These findings warrant future research into the effects of forced air warming excess heat on clinical outcomes during contamination-sensitive surgery.
METHODS: We performed a retrospective cohort study of adults undergoing major intraabdominal surgery from 2003 to 2010 at an academic medical center. We calculated the surgical Apgar score (SAS) for each patient based on intraoperative heart rate, mean arterial blood pressure, and estimated blood loss. Using logistic regression, we assessed the association of the SAS with the decision to admit a patient to the ICU postoperatively.

RESULTS: The cohort consisted of 8501 patients, with 72.7% having an SAS of 7 to 10 and <5% an SAS of 0 to 4. A total of 8.7% of patients were transferred immediately to the ICU postoperatively. After multivariate adjustment, there was a strong association between the SAS and the decision to admit a patient to the ICU (adjusted odds ratio 14.41 [95% confidence interval (CI), 6.88–30.19, P < 0.001] for SAS 0–2, 4.42 [95% CI, 3.19–6.13, P < 0.001] for SAS 3–4, and 2.60 [95% CI, 2.08–3.24, P < 0.001] for SAS 5–6 compared with SAS 7–8).

CONCLUSIONS: The SAS is strongly associated with clinical decisions regarding immediate ICU admission after high-risk intraabdominal surgery. These results provide an initial step toward understanding whether intraoperative hemodynamics and blood loss influence ICU triage for postsurgical patients.

全麻後早期診斷譫妄的老年患者的預後

Outcomes of Early Delirium Diagnosis After General Anesthesia in the Elderly
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BACKGROUND: Postoperative delirium in the elderly, measured days after surgery, is associated with significant negative clinical outcomes. In this study, we evaluated the prevalence and in-hospital outcomes of delirium diagnosed immediately after general anesthesia and surgery in elderly patients.

METHODS: Consecutive English-speaking surgical candidates, aged 70 years or older, were prospectively enrolled during July to August 2010. After surgery, each participant was evaluated for a Diagnostic and Statistical Manual of Mental Disorders IV diagnosis of delirium in the postanesthesia care unit (PACU) and repeatedly thereafter while hospitalized. Delirium in the PACU was evaluated for an independent association with change in cognitive function from preoperative baseline testing and discharge disposition.

RESULTS: Ninety-one (58% female) patients, 78% of whom were living independently before surgery, were found to have a prevalence of delirium in the PACU of 45% (41/91); 74% (14/19) of all delirium episodes detected during subsequent hospitalization started in the PACU. Early delirium was independently associated with impaired cognition (i.e., decreased category word fluency) relative to presurgery baseline testing (adjusted difference [95% confidence interval] for change in T-score: −6.02 [−10.58 to −1.45]; P = 0.01). Patients whose delirium had resolved by postoperative day 1 showed negative outcomes that were intermediate in severity between those who were never delirious during hospitalization and those whose delirium in the PACU persisted after transfer to hospital wards (adjusted probability [95% confidence interval] of discharge to institution: 3% [0%–10%], 26% [1%–51%], 39% [0%–81%] for the 3 groups, respectively).

CONCLUSIONS: Delirium in the PACU is common, but not universal. It is associated with subsequent delirium on the ward, and potentially with a decline in cognitive function and increased institutionalization at hospital discharge.

The Analgesic Efficacy of Subcostal Transversus Abdominis Plane Block Compared with Thoracic Epidural Analgesia and Intravenous Opioid Analgesia After Radical Gastrectomy
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Anesth Analg August 2013 117:507-513

背景: 腹橫肌平面 (TAP) 阻滯已經被證實在下腹部手術中可提供有效的術後鎮痛, 肋下 TAP 阻滯也已同樣被證明是一種對於臍以上腹部提供鎮痛作用的新技術。本文比較單次肋下 TAP 阻滯與持續胸段硬膜外、靜脈阿片類藥物給予的鎮痛效應的差異。

方法: 90 例擇期行根治性胃切除術的病人隨機分為三組: 接受全麻聯合肋下 TAP 阻滯（TAP 組）、全麻聯合硬膜外麻醉 (EA 組) 或全麻 (GA 組)。在 TAP 組，全麻誘導後以 0.375% 羅呱卡因行雙側肋下 TAP 阻滯。在 EA 組，全麻誘導前 T8、T9 水平行硬膜外置管，給予 8ml 0.25% 羅呱卡因作為負荷劑量。術中硬膜外維持量為 0.25% 羅呱卡因 5ml/h。GA 組接受標準的全身麻醉。在復 conseguir 醫院 (PACU)，所有組在 VAS>3 時接受靜脈嗎啡。所有病人在 PACU 開始接受含有嗎啡的靜脈病人自控鎮痛，而 EA 組為 0.125% 布比卡因 5ml/h 的硬膜外鎮痛。在 PACU，術後 1, 3, 6, 24, 48 和 72h 對病人進行疼痛評估，主要預後指標為 24h 內嗎啡消耗量和所有 VAS 疼痛評分。

結果: 90 例中有 82 例患者納入了研究 (91.1%)。TAP 組顯示 24h 累計嗎啡消耗量減少 (98.75% 可信區間, -29 to -9 mg) 且所有時點 VAS 疼痛評分均非劣于進行標準阿片藥鎮痛的 GA 組，而 EA 組為 0.125% 布比卡因 5ml/h 的硬膜外鎮痛，在 PACU，術後 1, 3, 6, 24, 48 和 72h 對病人進行疼痛評估，主要預後指標為 24h 內嗎啡消耗量和所有 VAS 疼痛評分。

結論: 單次肋下 TAP 阻滯比靜脈阿片藥鎮痛藥有效，而持續胸段硬膜外鎮痛比單次肋下 TAP 阻滯更有效。

（瞿亦楓 譯 陳傑 校）

BACKGROUND: The transversus abdominis plane (TAP) block has been shown to provide effective postoperative analgesia in lower abdominal surgery. Subcostal TAP block has also been proposed as a new technique to provide analgesia for the supraumbilical abdomen. We compared the analgesic and opioid-sparing effects of a single-injection subcostal TAP block with continuous thoracic epidural analgesia and IV opioid analgesia.

METHODS: Ninety patients undergoing elective radical gastrectomy were randomized to receive either combined general–subcostal TAP anesthesia (group TAP), combined general–epidural anesthesia (group EA), or general anesthesia (group GA), and were analyzed on an intention-to-treat basis. In group TAP, a bilateral subcostal TAP block was performed after induction of general anesthesia using 20 mL of 0.375% ropivacaine. In group EA, a thoracic epidural was placed between T8 and T9 and bolused with 8 mL of 0.25% ropivacaine before induction of general anesthesia. The epidural was maintained with 5 mL/h of 0.25% ropivacaine during the surgery. Group GA received standard general anesthesia. In the postanesthesia care unit (PACU), all groups received IV morphine titration for visual analog scale (VAS) pain scores >3. All patients were started on IV patient-controlled analgesia with morphine after morphine titration in the PACU, while group EA also had their epidural maintained with 5 mL/h of 0.125% bupivacaine with 8 μg/mL morphine. Patients were assessed in the PACU and at 1, 3, 6, 24, 48, and 72 hours postoperatively. Primary outcomes measured were morphine consumption at 24 hours and all VAS pain scores.
RESULTS: Data from 82 of 90 (91.1%) patients were included in the study. Group TAP demonstrated decreased cumulative morphine consumption at 24 hours (98.75% confidence intervals, −29 to −9 mg) and noninferiority on VAS pain scores at all measurement times, as compared with group GA with standard opioid analgesia. However, group EA was superior to group TAP regarding cumulative morphine consumption at 24 hours (98.75% confidence intervals, −23 to −4 mg) and noninferior to group TAP on VAS pain scores at all comparison points. Group TAP had reduced morphine consumption from PACU admission to 6 hours as compared with group GA, but increased morphine consumption for 6 to 24 hours as compared with group EA.

CONCLUSION: Single-injection subcostal TAP block was more effective than IV opioid analgesia, while continuous thoracic epidural analgesia was more effective than the single-injection subcostal TAP block.

關於冠狀動脈搭橋或脊椎手術患者術前服糖的研究
Preoperative Carbohydrate Loading in Patients Undergoing Coronary Artery Bypass or Spinal Surgery
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Anesth Analg August 2013 117:305-313;

研究背景：手術應激引發的腸島素抵抗反應可能導致高血糖症，並由此發起術後併發症。術前給患者口服糖類可能改善病人對腸島素的敏感性，並減少高血糖症。本研究探討了給冠狀動脈搭橋手術和脊椎減壓手術病人補充糖類對於患者腸島素抵抗反應的影響。

方法：26個冠狀動脈搭橋手術病人和12個脊椎手術病人，隨機分兩組：CHO組為術前一晚口服800mL，術前2小時口服400mL糖；FAST組為按照標準的醫院方案執行禁食。採用腸島素短時耐受實驗和體內平衡模型評估（HOMA）對病人的腸島素敏感度的基礎值和術後值進行評估。分別記錄術前和術後24小時、48小時、72小時時的白細胞介素-6、C反應蛋白和游離脂肪酸水準；測得脂聯素的基礎值。在手術前即刻測量病人的良好自我感覺，並記錄術中及術後の預後。

結果：無論是短時腸島素耐受實驗，還是體內平衡模型評估（HOMA），FAST和CHO兩組的術後腸島素敏感度並無明顯區別。短時腸島素耐受實驗結果為：血糖消失速度為0.29%/分鐘比0.38%/分鐘，差異的99%置信區間为-0.17～0.32，P=0.41；HOMA結果為：值大於1時的腸島素耐受值2.3比3.3，差異的99%置信區間为-0.8～2.8，P=0.14。CHO組術後迴圈血糖水準6.2mmol/L，比FAST組6.9mmol/L有降低趨勢（差異的99%置信區間为-1.7～0.25，P=0.05）。而CHO組由HOMA-β測得的術後β細胞功能（值<100%時的損壞β細胞功能）87%比FAST組的47.5%有增高趨勢（99%置信區間下，-9.4～88.4）。但這些差異並不顯著。兩組的脂聯素水準在基線上並無差異；游離脂肪酸水準、白細胞介素-6 及C反應蛋白不受處理影響。

結論：術前服糖並不提高術後腸島素敏感度。但是，本研究所觀察到的術後血糖水準、β細胞功能及發病性的預後需要進一步的研究以重新評估手術患者的傳統禁食措施。

（趙曉譯 李皓琳 李士通校）
BACKGROUND: Surgical stress creates a state of insulin resistance which may contribute to the development of hyperglycemia and, subsequently, postoperative complications. Consumption of an oral carbohydrate supplement before surgery may improve insulin sensitivity and reduce hyperglycemia. In this trial, we investigated the effects of carbohydrate supplementation on insulin resistance in coronary artery bypass graft and spinal decompression and fusion surgical patients.

METHODS: Twenty-six patients undergoing coronary artery bypass graft and 12 undergoing spine surgery were randomized to receive 800 mL of an oral carbohydrate supplement the evening before and 400 mL 2 hours before surgery (CHO) or to fasting per standard hospital protocol (FAST). Baseline and postoperative measurements of insulin sensitivity were assessed using the short insulin tolerance test and homeostasis model assessment (HOMA). Interleukin-6, C-reactive protein, and free fatty acid levels were determined at baseline, postoperatively, and 24, 48, and 72 hours after surgery. Adiponectin was measured at baseline. Subjective feelings of well-being were measured immediately before surgery, and intra- and postoperative outcomes were documented.

RESULTS: Postoperative insulin sensitivity did not differ significantly between the FAST and CHO groups whether measured by the short insulin tolerance test (rate of disappearance of blood glucose: 0.29%/min vs 0.38%/min; 99% confidence interval [CI] for difference, −0.17 to 0.32, P = 0.41) or HOMA (insulin resistance at values >1: 2.3 vs 3.3; 99% CI for difference, −0.8 to 2.8, P = 0.14). Circulating blood glucose levels after surgery in the CHO group, 6.9 mmol/L, tended to be lower than the FAST group, 6.9 mmol/L (99% CI for difference, −1.7 to 0.25, P = 0.05) and postoperative β-cell function, measured by HOMA-β (impaired β-cell function at values <100%), tended to be higher in the CHO group, 87%, vs 47.5% in the FAST group (99% CI for difference, −9.4 to 88.4), but these differences were not significant. Adiponectin levels were not different between groups at baseline, and levels of free fatty acid, interleukin-6 and C-reactive protein were not affected by treatment.

CONCLUSIONS: Preoperative carbohydrate loading did not improve postoperative insulin sensitivity. However, the observed postoperative blood glucose levels and β-cell function as well as secondary outcomes warrant further study to reevaluate traditional fasting practices in surgical patients.

對雷莫司瓊預防術後噁心嘔吐效用的再評價：系統回顧和 meta 分析

Reevaluation of the Effectiveness of Ramosetron for Preventing Postoperative Nausea and Vomiting: A Systematic Review and Meta-Analysis

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背景：先前的 meta 分析結果顯示，雷莫司瓊對術後噁心嘔吐（PONV）有很好的預防作用。然而，這些先前的 meta 分析包括 Fujii 等的很多研究，而 Fujii 等的很多研究現在已被證實是捏造的。本次 meta 分析在除外 Fujii 等人的隨機對照試驗之後，再次對雷莫司瓊預防術後 PONV 的效用進行評估。

方法：我們検索了 Medline、Cochrane、對照臨床試驗的中央寄存器（CENTRAL）、Embase 和科學網。選取所有與安慰劑或者作爲對照的其他藥物作對比來檢驗雷莫司瓊對 PONV 預防作用的雙盲隨機對照試驗。手術後的第一個 24h 被劃分為早期（0-6 小時）和晚期（6-24 小時）兩個時間段，並分別收集相關資料。
**BACKGROUND:** Ramosetron has been shown to have a very strong effect for preventing postoperative nausea and vomiting (PONV) in previous meta-analyses. However, these previous meta-analyses included a number of studies by Fujii et al. which have now been proven to have been fabricated. In the present meta-analysis, we reevaluated the effectiveness of ramosetron in preventing PONV after excluding Fujii et al.’s randomized controlled trials.

**METHODS:** We searched MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), Embase, and Web of Science. All double-blind randomized controlled trials that tested the efficacy of ramosetron compared with a placebo or other drugs as a control in the prophylaxis of PONV were considered to be eligible. The first postoperative 24 hours were divided into early (0–6 hours) and late (6–24 hours) time periods, and we collected these data separately.

**RESULTS:** A total of 1372 patients were included in the final analysis. Compared with a placebo, ramosetron reduced the incidence of early postoperative nausea (PON) (relative risk [RR] [95% confidence interval] 0.59 [0.47–0.73]; number needed to treat [NNT] [95% confidence interval] 6.0 [4.3–9.7]), late PON (RR 0.65 [0.49–0.85]; NNT 7.2 [4.6–16.6]), early postoperative vomiting (POV) (RR 0.48 [0.31–0.74]; NNT 14.8 [8.3–70.4]), and late POV (RR 0.50 [0.35–0.73]; NNT 12.3 [7.1–47.6]). Compared with ondansetron, ramosetron reduces early POV (RR 0.50 [0.28–0.90]; NNT 24.1 [10.7–98.0]) and late POV (RR 0.53 [0.34–0.81]; NNT 27.2 [12.0–102.0]) but not PON.

**CONCLUSIONS:** Ramosetron has a significant effect for preventing PONV compared with a placebo, but less than that reported in previous analyses. Ramosetron also has statistically significant differences in preventing early and late POV compared with ondansetron, but the clinical significance may be questioned because the NNTs are large.

**Propofol Stimulates Noradrenalin-Inhibited Neurons in the Ventrolateral Preoptic Nucleus by Reducing GABAergic Inhibition**

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Anesth Analg August 2013 117:358-363
興奮性中間神經元（NA(+)神經元）。我們之前的工作表明正常情況下 NA(−)神經元是處於 NA(+)神經元的抑制性調控。先前的研究同樣表明通過對 GABA 能神經元起作用的試劑如丙泊酚啓動 VLPO 的 GABA 促投射性神經元，從而產生對結節乳頭核上的覺醒產生核的抑制和鎮靜作用。然而丙泊酚如何啓動 VLPO 神經元仍然不清楚。我們研究了丙泊酚通過抑制包括來自於 VLPO NA(+)神經元的 GABA 能神經傳遞間接啓動 NA(−)神經元的可能性。

方法：記錄大鼠急性腦片中的 VLPO 細胞的電生理活動。

結果：丙泊酚促進 NA(−)神經元的放電，並減少 NA(−)神經元中自發性 GABA 能抑制性突觸後電流的頻率，但不降低其幅度。相反，丙泊酚抑制 NA(+)神經元的放電。

結論：丙泊酚通過減少 GABA 能神經傳遞來興奮 VLPO 上的 NA(−)神經元，至少部分通過抑制 VLPO 上的 NA(+)神經元。這可能是丙泊酚產生鎮靜作用的一個關鍵機制。

（楊禮 譯 馬皓琳 李士通 校）

BACKGROUND: The cellular mechanisms underlying the sedative effect of general anesthetics are not completely understood. Accumulating evidence indicates that the ventrolateral preoptic area (VLPO) of the hypothalamus plays a critical role. The VLPO contains 2 major types of neurons, the noradrenalin-inhibited GABAergic projecting neurons (NA(−) neurons) and the noradrenalin-excited interneurons (NA(+) neurons) which are probably also γ-aminobutyric acid (GABA)-containing neurons. Our previous work suggests that NA(−) neurons are normally under the inhibitory control of NA(+) neurons. Previous studies also show that GABAergic agents including propofol activate GABAergic projecting neurons in the VLPO, which is believed to lead to the inhibition of the arousal-producing nuclei in the tuberomammillary nucleus and sedation. However, how propofol activates VLPO neurons remains unclear. We explored the possibility that propofol activates NA(−) neurons indirectly, by inhibiting GABAergic transmission including those from VLPO NA(+) neurons.

METHODS: Electrophysiological activities were recorded from VLPO cells in acute brain slices of rats.

RESULTS: Propofol facilitates the discharges of NA(−) neurons and reduces the frequency, but not the amplitude of spontaneous GABAergic inhibitory postsynaptic currents in NA(−) neurons. Conversely, propofol suppressed the discharges of NA(+) neurons.

CONCLUSION: Propofol excites VLPO NA(−) neurons by reducing GABAergic transmission, at least in part by inhibiting VLPO NA(+) neurons. This may be a critical mechanism contributing to propofol-induced sedation.
背景：围手术期监测系统提供了大量未解释的资料，使用易于产生假象的阈值警报，并且依赖临床医生连续性地肉眼追踪生理资料中的变化。为了避免这些缺陷，我们开发了一项能够提供即时临床决定以识别关键事件的专家系统。我们评估了在模拟环境下这套专家系统提高关键事件识别的效率。假设在这套专家系统的帮助下麻醉医师将会更加迅速并准确地识别关键性通气事件。

方法：我们使用了高保真人模拟器来模拟一个手术室的环境，参与者以随机的顺序管理了4个场景（麻醉气体过量、张力性气胸、过敏反应和气管内导管气囊泄露）。在其中2个场景中，参与者随机分配到这项提供趋势性警报和潜在诊断的专家系统。测定发生到识别的时间和发生到处理的时间。每项场景结束后完成工作量问卷调查和结构化述职报告，研究期结束后完成可用性问卷调查。资料分析使用了混合线性回归模型；工作量分数使用了Fisher’s精确检验。

结果：20名麻醉实习生和15名麻醉医师参与了试验，年龄的混合中位数为36岁（29-66岁），麻醉经验年限中位数为6年（1-38年）。在气管内导管气囊泄露场景中，专家系统将事件发生到识别的时间缩短了128秒（99%可信区间，54-202秒），事件发生到处理的时间缩短了140秒（99%可信区间，79-200秒）。在其他3个场景中，最好的案例是将过敏反应发生到诊断的时间减少了97秒（99%可信区间下限），最差的案例是将麻醉气体过量发生到处理的时间增加了63秒（99%可信区间上限）。参与者对这项专家系统非常满意（评分中位数2分，1-7分制）。在参与者述职报告的基础上，我们确认了避免任务固定、再次确保才开始有创治疗及确认可能诊断是3项保障安全的关键点。

结论：在气管内导管气囊泄露的场景中使用专家系统，事件发生到诊断和事件发生到处理的时间有临床意义及统计学显著意义地缩短。在其他3个场景中观察到的差别要小得多，也无统计学显著意义。需要进一步的评估以确定即时专家系统用於麻醉的临床实用性。

（盛嘉君 谯、马皓琳、李士通审校）

BACKGROUND: Perioperative monitoring systems produce a large amount of uninterpreted data, use threshold alarms prone to artifacts, and rely on the clinician to continuously visually track changes in physiological data. To address these deficiencies, we developed an expert system that provides real-time clinical decisions for the identification of critical events. We hypothesized that anesthesiologists would identify critical ventilatory events more rapidly and accurately with the expert system.

METHODS: We used a high-fidelity human patient simulator to simulate an operating room environment. Participants managed 4 scenarios (Anesthetic Vapor Overdose, Tension Pneumothorax, Anaphylaxis, and Endotracheal Tube Cuff Leak) in random order. In 2 of their 4 scenarios, participants were randomly assigned to the expert system, which provided trend-based alerts and potential differential diagnoses. Time to detection and time to treatment were measured. Workload questionnaires and structured debriefings were completed after each scenario, and a usability questionnaire at the conclusion of the session. Data were analyzed using a mixed-effects linear regression model; Fisher exact test was used for workload scores.

RESULTS: Twenty anesthesiology trainees and 15 staff anesthesiologists with a combined median (range) of 36 (29–66) years of age and 6 (1–38) years of anesthesia experience participated. For the Endotracheal Tube Cuff Leak, the expert system caused mean reductions of 128 (99% confidence interval [CI], 54–202) seconds in time to detection and 140 (99% CI, 79–200) seconds in time to treatment. In the other 3 scenarios, a best-case decrease of 97 seconds (lower 99% CI) in time to diagnosis for Anaphylaxis and a worst-case increase of 63 seconds (upper 99% CI) in time to treatment for Anesthetic Vapor Overdose were found. Participants were highly satisfied with the expert system (median score, 2 on a scale of 1–7). Based on participant debriefings, we identified avoidance of task fixation, reassurance to initiate invasive treatment, and confirmation of a suspected diagnosis as 3 safety-critical areas.
CONCLUSION: When using the expert system, clinically important and statistically significant decreases in time to detection and time to treatment were observed for the Endotracheal Tube Cuff Leak scenario. The observed differences in the other 3 scenarios were much smaller and not statistically significant. Further evaluation is required to confirm the clinical utility of real-time expert systems for anesthesia.

Endotracheal Tube Cuff Leaks: Causes, Consequences, and Management
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Anesth Analg August 2013 117:428-434

The consequences of endotracheal tube (ETT) cuff leak may range from a bubbling noise to a life-threatening ventilatory failure. Although the definitive solution is ETT replacement, this is often neither needed nor safe to perform. Frequently, the leak is not caused by a structural defect in the ETT. Cuff underinflation, cephalad migration of the ETT (partial tracheal extubation), misplaced orogastric or nasogastric tubes, wide discrepancy between ETT and tracheal diameters, or increased peak airway pressure can cause leaks around intact cuffs. Correction of these problems will stop the leak without ETT replacement. Alternatively, ETT cuff, pilot balloon, and inflation system damage due to inadvertent trauma or manufacturing defects may be responsible. Conservative management ideas (management without ETT replacement) were previously published to solve the problem. However, when a large structural defect is identified or conservative measures fail, ETT replacement becomes necessary. This can be performed with direct laryngoscopy if laryngeal visualization is adequate. A difficult exchange with possible airway loss should be anticipated, and prepared for, when there are signs and/or history of difficult intubation. A risk/benefit analysis of each individual situation is warranted before decisions are made on how best to proceed. Alternative back-up ventilation plans should be preformulated and the necessary equipment ready before the exchange. In this review, various management concerns and plans are discussed, and a simple algorithm to manage leaky ETT cuff situations is presented.
Novel Measurements of the Length of the Subglottic Airway in Infants and Young Children

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Anesth Analg August 2013 117:462-470

BACKGROUND: To date, the lengths of the subglottic and tracheal airway segments have been measured from autopsy specimens. Images of the head and neck obtained from computerized tomography (CT) provide an alternate method. Our objective in this study was to identify anatomic landmarks from CT scans in infants and young children to estimate the lengths of the subglottic airway segments and to correlate these lengths with age.

METHODS: We performed a retrospective analysis of CT images of the neck for various diagnostic indications in children ≤3 years. We obtained planes of reconstruction at the level of the vocal cords (VCSs), cricoid cartilage, and carina (C) which were parallel to each other and perpendicular to sagittal long axis of the trachea. The lengths of the subglottic airway (LengthSG) and total length of the laryngotracheal airway (LengthVC–C) were measured from the distance between, respectively, the VC versus cricoid cartilage and the VC versus C planes of reconstruction. Tracheal length was then calculated as the difference between LengthVC–C and LengthSG.

RESULTS: Fifty-six children met the inclusion criteria. There were 29 boys. The median weight was 10.7 kg (range 3.1-19.0 kg). Regression analysis yielded mean LengthSG (mm) = 7.8 + 0.03•corrected age (months), r² = 0.07, P = 0.056; lower and upper 95% confidence interval for β = 0.03 were −0.001 and 0.0061. The mean LengthSG was 8.4 mm with a SD of 1.4 mm. The 95th percentile for LengthSG was 10.8 mm, and the 5% to 95% interquartile range was 4.9 mm. The estimate for the 95% confidence interval of the 95th percentile was between 10.2 and 11.3 mm.

CONCLUSION: Through our study of 56 infants and children, we reported a new method for estimating the length of the subglottic airway and suggested that subglottic and tracheal airway growth patterns may differ.
(months), \( r^2 = 0.7, P < 0.001 \). Tracheal length also increased with age: mean tracheal length (cm) = 4.5 + 0.05 \times \text{corrected age (months)}, \( r^2 = 0.6, P < 0.001 \).

CONCLUSION: We report a novel estimate method for the lengths of the airway segments between the VC and C in 56 infants and young children and suggest that the growth characteristics of the subglottic and tracheal airway may differ.

Horace Wells, a contender for recognition as the discoverer of anesthesia, is celebrated in the town where he conducted most of his work, Hartford, CT. His only descendant was his son, Charles Thomas Wells (1839–1909), an influential and successful business executive at Aetna Insurance Company. He was a man of considerable influence, and he worked tirelessly with city officials and the Connecticut Dental Association in celebrating the 50th anniversary of his father’s contribution to medicine. This discovery is unique because events and individuals in 1 country, the United States, contributed entirely to the birth of a medical specialty. Sites in Jefferson, GA; Hartford, CT; and Boston, MA and their environs celebrate this most precious contribution to modern medicine, especially since the introduction of safe anesthesia permitted the development of surgical specialties and obstetrics. We trace the history and relationship between Horace Wells and several sites and artifacts in Hartford, CT. These sites span the most important, distinctive, and attractive parts of the city: Bushnell Park, Trinity College, Cedar Hill Cemetery, the Athenaeum, and the Connecticut Historical Society.
背景：吸入麻醉藥的藥效通過最小肺泡濃度(MAC)來量化，是指50%的患者在疼痛刺激時的肺泡濃度。吸入麻醉藥抑制體動的機制尚未完全闡述，但有些藥物會影響MAC。在這個試驗中，我們研究了單個劑量靜脈注射的利多卡因對七氟醚MAC值的影響。

方法：我們使用Dixon“up-and-down”法來確定七氟醚的MAC值。入選行擇期手術的患者，分成3組，每組30人，年齡30至65歲。3組分別給予安慰劑，0.75mg/kg利多卡因，1.5mg/kg利多卡因，誘導後15分鐘平衡期，然後應用試驗藥物，3分鐘後切皮，記錄有無體動。

結果：安慰劑組MAC值1.86%±0.40%，0.75mg/kg利多卡因組MAC值1.87%±0.45%(P=1.00)。1.5mg/kg利多卡因組MAC值1.63%±0.24%(P=0.022)，明顯小於安慰劑組，七氟醚的平均濃度差0.23%，95%CI 0.03-0.43。安慰劑組和0.75mg/kg利多卡因組兩者之間沒有顯著差異，七氟醚的平均濃度差-0.01%，95%CI -0.27 to 0.25，P=1.00。

結論：靜脈注射1.5mg/kg利多卡因降低至少0.03%七氟醚MAC(平均濃度差0.23%，95%CI 0.03-0.43)。我們沒有觀察到0.75mg/kg利多卡因有相似的效果。

(陳實玉譯薛張綱校)
背景：尽管预先经皮给予局麻药被通常应用於减少皮膚手術導致的疼痛，由於角質層和較厚的表皮層的阻撓，這些預處理並不能有效地滲透表皮組織。基於醇質體的熱力學穩定性，小分子，包裹率高以及其經皮滲透性，它可以有效地運送藥物穿過皮膚。本研究評估了利多卡因基醇質體的體外負載劑量，包裹率，熱力學穩定性以及經皮滲透性以及體內的效能以及皮膚刺激作用。

方法：利多卡因醇質體通過注射超聲濾過法制得。其大小，負載效能，包裹率以及穩定性通過遙射細微性儀和高效液相色譜法評估。劑型由正交試驗中測得的最大包裹率決定。應用弗朗茲型擴散細胞實驗分析其體外經皮滲透效率。應用針刺實驗分析藥物有效性。使用白色豚鼠進行皮膚刺激性試驗，後進行組織病理學分析。該結果將會與利多卡因脂質體以及利多卡因乙醇溶液進行比較。

結果：利多卡因基醇質體由5%雞蛋磷脂醯膽鹼，35%乙醇，0.2%膽固醇，5%利多卡因基，超純水的平均最大包裹率為51% ±4%，平均粒徑為31 ± 3 nm，平均負載效率95.0% ± 0.1%。利多卡因基醇質體的包裹率在25°C ± 1°C情況下保持60天的穩定性（95%可信區間[CI]，-1.12% to 1.34%; P = 0.833）。三種基質利多卡因的皮膚滲透性有顯著差異（F = 120, P < 0.001），醇質體顯著高於脂質體（95%修正度，1129-1818 µg/(cm²•h); P < 0.001），醇質體也顯著高於乙醇溶液（95%修正度，1468-2157 µg/(cm²•h); P < 0.001）。相較於利多卡因脂質體以及利多卡因乙醇溶液，利多卡因基醇質體在體內起效時間更快而且作用時間更長。沒有證據顯示利多卡因基醇質體對豚鼠表皮有刺激作用。

結論：醇質體是可以作爲局麻藥經皮給藥的潜在的載體並可用於其它需要經皮快速起效的藥物。

(陳婉南譯 薛張綱校)
duration in vivo than did lidocaine base liposomes or lidocaine delivered in a hydroethanolic solution. Lidocaine base ethosomes showed no evidence of dermal irritation in guinea pigs.

**CONCLUSIONS:** Ethosomes are potential carriers of local anesthetics across the skin and may have applicability for other percutaneous drugs that require rapid onset.

**BACKGROUND:** Residual neuromuscular block is defined as a mechanomyography (MMG) or electromyography (EMG) train-of-four (TOF) ratio <0.90, and is common in patients receiving neuromuscular blocking drugs. Objective neuromuscular monitoring is the only reliable way to detect and exclude residual neuromuscular block. Acceleromyography (AMG) is commercially available and easy to use in the clinical setting. However, AMG is not interchangeable with MMG or EMG. Currently, it is unclear what value must be reached by AMG TOF ratio to reliably exclude residual neuromuscular block.

**METHODS:** During spontaneous recovery from neuromuscular block, we monitored TOF ratio on the same arm using AMG at the adductor pollicis and EMG at the first dorsal interosseous. AMG and EMG TOF ratios were compared by the Bland–Altman analysis for repeated measurements. The precision of each device was assessed by the repeatability coefficient. A small repeatability coefficient indicates high precision of the device. The agreement between the

**RESULTS:** In 26 patients, 261 AMG and EMG TOF ratio comparisons were made. The AMG and EMG TOF ratio repeatability coefficients were 0.094 and 0.051, respectively. The AMG and EMG TOF ratio agreement range was -0.045 to 0.396.

**CONCLUSIONS:** AMG has less precision than EMG and may exceed EMG TOF ratio by at least 0.15. This result does not differ significantly from the baseline or due to the different methods. When AMG reaches 1.0, residual muscle block cannot be excluded.
devices was assessed by the bias and the 95% limits of agreement. Small bias and narrow limits of agreement indicate strong agreement. We defined clinically acceptable agreement between AMG and EMG as a bias <0.025 and limits of agreement within −0.050 to 0.050, provided that the control comparison between EMG and itself can fulfill these criteria.

RESULTS: In 26 patients, 261 comparisons between AMG and EMG were made. The repeatability coefficient of AMG and EMG were 0.094 (95% confidence interval [CI], 0.088–0.100) and 0.051 (95% CI, 0.048–0.055), respectively. The bias between AMG and EMG TOF ratio was 0.176 (95% CI, 0.162–0.190), with limits of agreement −0.045 to 0.396 (95% CI, −0.067 to 0.419).

CONCLUSIONS: AMG is less precise than EMG and overestimates EMG TOF ratio by at least 0.15. The lack of agreement cannot be attributed to instrumental imprecision or the baseline difference between successive measurements during spontaneous recovery of neuromuscular function. Residual neuromuscular block cannot be excluded on reaching an AMG TOF ratio of 1.00.
hyperchloremia (serum chloride >110 mEq/L) and whether this electrolyte disturbance is associated with an increase in length of hospital stay, morbidity, or 30-day postoperative mortality.

METHODS: Data were retrospectively collected on consecutive adult patients (>18 years of age) who underwent inpatient, noncardiac, nontransplant surgery between January 1, 2003 and December 31, 2008. The impact of postoperative hyperchloremia on patient morbidity and length of hospital stay was examined using propensity-matched and logistic multivariable analysis.

RESULTS: The dataset consisted of 22,851 surgical patients with normal preoperative serum chloride concentration and renal function. Acute postoperative hyperchloremia (serum chloride >110 mmol/L) is quite common, with an incidence of 22%. Patients were propensity-matched based on their likelihood to develop acute postoperative hyperchloremia. Of the 4955 patients with hyperchloremia after surgery, 4266 (85%) patients were matched to patients who had normal serum chloride levels after surgery. These 2 groups were well balanced with respect to all variables collected. The hyperchloremic group was at increased risk of mortality at 30 days postoperatively (3.0% vs 1.9%; odds ratio = 1.58; 95% confidence interval, 1.25-1.98) (relative risk 1.6 or risk increase of 1.1%) and had a longer hospital stay (7.0 days [interquartile range 4.1-12.3] compared with 6.3 [interquartile range 4.0-11.3]) than patients with normal postoperative serum chloride levels. Patients with postoperative hyperchloremia were more likely to have postoperative renal dysfunction. Using all preoperative variables and measured outcome variables in a logistic regression analysis, hyperchloremia remained an independent predictor of 30-day mortality with an odds ratio of 2.05 (95% confidence interval, 1.62-2.59).

CONCLUSION: This retrospective cohort trial demonstrates an association between hyperchloremia and poor postoperative outcome. Additional studies are required to demonstrate a causal relationship between these variables.

先天性心臟病患兒應用心導管檢查及術後急性腎功能不全

Cardiac catheterization and postoperative acute kidney failure in congenital heart pediatric patients.

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Anesth Analg August 2013 117:455-461

背景：急性腎功能（ARF）不全是兒科病人心臟手術後的嚴重併發症。血管造影使用的造影劑是ARF的危險因素。在我們的研究中，我們研究了患兒行心臟手術後ARF的發生率與血管造影劑的使用時間、劑量的關係。

方法：我們採用回顧性研究的方法。我們收集了277名年齡小於12歲的患兒血管造影方面的資料及其它變數的資訊，他們接受血管造影檢查與心臟手術間隔時間相同。評價腎功能分為損傷、不全、功能喪失、終末期腎病。

結果：64%的患者術後腎功能不全的情況相似，55名（20%）患者出現ARF（終末期腎病）。相比于其他患者ARF的患者（2.8±2.2 g/kg），ARF患者接受較大劑量的碘造影劑（4.6±2.6 g/kg）（P<0.001），每增加1 g/kg劑量的碘劑，ARF的風險增加31%。多因素模型提示，年齡小於2歲的患兒ARF的風險增加20倍，術後低心排患者ARF的風險增加3
BACKGROUND: Acute renal failure (ARF) is a severe complication of cardiac operations in pediatric patients. Angiography with the exposure to contrast media is a risk factor for ARF. In the present study, we explored the association between timing of angiography, dose of contrast media, and the incidence of ARF after cardiac operations in pediatric patients.

METHODS: We performed a retrospective analysis of prospectively collected data. Angiographic data and other covariates were collected in 277 patients aged ≤12 years receiving angiography and cardiac operations during the same hospital stay. Renal outcome was assessed according to the pediatric Risk, Injury, Failure, Loss of function, End stage score (pRIFLE).

RESULTS: One hundred seventy-seven (64%) patients suffered some degree of postoperative renal dysfunction, and 55 (20%) had ARF (pRIFLE stage Failure). Patients with ARF received a significantly (P < 0.001) larger dose of iodine contrast media (4.6 ± 2.6 g/kg) with respect to the other patients (2.8 ± 2.2 g/kg), with a relative risk increase for ARF of 31% per each incremental iodine dose of 1 g/kg at the univariate analysis. A multivariable risk model demonstrated that the risk for ARF is 20 times higher in patients aged younger than 2 years and 3 times higher in case of postoperative low cardiac output. Within this model, the iodine dose on angiography is confirmed as an independent risk factor for ARF, with a relative risk increase for ARF of 16% per each incremental iodine dose of 1 g/kg.

CONCLUSIONS: Angiography before cardiac surgery is an important risk factor for ARF in pediatric patients. Being a modifiable risk factor, the contrast media dose should be limited to the lowest possible value, avoiding large doses of iodine which, together with other factors (age and postoperative low cardiac output), concur in the determinism of postoperative ARF.
modalities, electrocardiography is still used in approximately 60% to 70% of the epilepsy centers in North America to guide surgical resection of the epileptogenic lesion and to assess for completeness of surgery. In this review, we discuss the principles and intraoperative use of electrocorticography, the effect of anesthetic drugs on electrocorticography, and the use of pharmacoactivation for intraoperative localization of epileptogenic zone.

布比卡因，羅呱卡因，甲呱卡因對人體軟骨細胞和軟骨的細胞毒性。
The cytotoxicity of bupivacaine, ropivacaine, and mepivacaine on human chondrocytes and cartilage.

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Anesth Analg August 2013 117:514-522

BACKGROUND: Intraarticular injections of local anesthetics are frequently used as part of multimodal pain regimens. However, recent data suggest that local anesthetics affect chondrocyte viability. In this study, we assessed the chondrotoxic effects of mepivacaine, ropivacaine, and bupivacaine. We hypothesized that specific cytotoxic potencies directly correlate with analgesic potencies, and that cytotoxic effects in intact cartilage are different than in osteoarthritic tissue.

METHODS: Human articular chondrocytes were exposed to equal and equipotent concentrations of bupivacaine, ropivacaine, and mepivacaine for 1 hour. Cell viability, apoptosis, and necrosis were determined at predefined time points using flow cytometry, live-dead staining, and caspase detection. Intact and osteoarthritic human cartilage explants were treated with equipotent concentrations of named drugs to determine cell viability applying fluorescence microscopy.
RESULTS: Chondrotoxic effects increased from ropivacaine to mepivacaine to bupivacaine in a time-dependent and concentration-dependent manner. Compared with control, bupivacaine 0.5% decreased chondrocyte viability to 78% ± 9% (P = 0.0183) 1 hour and 16% ± 10% (P < 0.0001) 24 hours later, as determined by live-dead staining in monolayer cultures. Viability rates were reduced to 80% ± 7% (P = 0.0475) 1 hour and 80% ± 10% (P = 0.0095) 24 hours after treatment with ropivacaine 0.75%. After exposure to mepivacaine 2%, viable cells were scored 36% ± 6% (P < 0.0001) after 1 hour and 30% ± 11% (P < 0.0001) after 24 hours. Ropivacaine treatment was less chondrotoxic than bupivacaine (P = 0.0006) and mepivacaine exposure (P = 0.0059). Exposure to concentrations up to 0.25% of bupivacaine, 0.5% of ropivacaine, and 0.5% of mepivacaine did not reveal significant chondrotoxicity in flow cytometry. However, chondrotoxicity did not correlate with potency of local anesthetics. Immediate cell death was mainly due to necrosis followed by apoptosis. Cellular death rates were clearly higher in osteoarthritic compared with intact cartilage after bupivacaine, mepivacaine, and ropivacaine treatment in a decreasing order.

CONCLUSION: Bupivacaine, ropivacaine, and mepivacaine are chondrotoxic in a time-dependent, concentration-dependent, and drug-dependent manner. Chondrotoxic and analgesic potencies do not directly correlate. Cellular death rates were higher in osteoarthritic compared with intact cartilage after local anesthetic treatment.