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**TEG Functional Fibrinogen Analysis May Overestimate Fibrinogen Levels**

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Fibrinogen is of crucial importance in patients with ongoing bleeding. In this study, we compared fibrinogen concentration measured by thrombelastography (TEG®) with fibrinogen plasma concentration determined by Clauss. Sixty-three surgical patients and 38 healthy controls were included. For the whole group (patients and controls, n = 101), TEG® functional fibrinogen was on average 1.0 g/L higher than the plasma fibrinogen concentration (3.5 vs 2.5 g/L, 95% confidence interval for difference 0.8 to 1.2 g/L, P < 0.0001). Similar patterns were observed when patients and healthy controls were analysed separately. The fibrinogen level may be overestimated when assessed using TEG® compared with the fibrinogen plasma concentration measured by the conventional method.

**Thrombomodulin Improved Liver Injury, Coagulopathy, and Mortality in an Experimental Heatstroke Model in Mice**

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Anesthesia & Analgesia 2014 118 956–963

**背景**：中暑是一種威脅生命疾病，可引起多臟器損傷而造成很高的死亡率。血栓調節蛋白(TM)是一種內皮細胞分泌的抗凝輔助因數，在血管內凝血的調節中起重要作用。本實驗研究血栓調節蛋白在實驗性中暑模型中，對炎症過程、肝功能、凝血狀態和死亡率的作用。

**方法**：雄性 C3H/HeN (8-10周) 小鼠隨機分配到 TM 治療組(TG-預處理)或非治療中暑組(HS)。在 TG-預處理組，在熱暴露前使用重組可溶性 TM (1mg/kg, 臍貢內注射) 處理小鼠。在某些實驗中，重組可溶性 TM 是在熱暴露(TG-延遲組)期間给藥。小鼠通過暴露於 38℃的環境溫度下 4 h 誘導中暑發生。熱暴露後，測定腫瘤壞死因子-α (TNF-α)、白介素 6 (IL-6) 和血漿高遷移率族蛋白 1 (HMGB-1)、肝功能指標、血漿棗grass轉氨酶和穀丙轉氨酶的濃度以及肝臟的免疫組織化學和組織病理學特徵。同時測定凝血狀態、血漿蛋白 C 水準和抗凝血酶 - 抗凝血酶複合物水準。
BACKGROUND: Heatstroke is a life-threatening illness and causes high mortality due to multiple organ injuries. Thrombomodulin (TM) is an endothelial anticoagulant cofactor that plays an important role in the regulation of intravascular coagulation. In this study, we investigated the effect of TM on the inflammatory process, liver function, coagulation status, and mortality in experimental heatstroke.

METHODS: Male C3H/HeN (8–10 weeks) mice were randomly assigned to the TM-treated group (TG-Pre) or nontreated heatstroke group (HS). In group TG-Pre, mice were treated with recombinant soluble TM (1 mg/kg, intraperitoneally) before heat exposure. In some experiments, recombinant soluble TM was administrated during heat exposure (TG-Delay). Heatstroke was induced by exposure to ambient temperature of 38°C for 4 hours. After heat exposure, the levels of tumor necrosis factor-α, interleukin-6, and plasma high-mobility group box 1 (HMGB1), liver function, plasma aspartate aminotransferase and alanine aminotransferase concentrations, and immunohistochemical and histopathological characteristics of the livers were determined. The coagulation status, plasma protein C levels, and thrombin–antithrombin complex levels were also measured.

RESULTS: In group HS, plasma cytokines and HMGB1 concentrations increased after heat exposure. Plasma aspartate aminotransferase and alanine aminotransferase concentrations increased after heat exposure. In group HS livers, strong and extensive immunostaining for HMGB1 was observed. In addition, there was extensive hepatocellular necrosis and collapse of nuclei observed. In group HS, plasma protein C levels were suppressed and plasma thrombin–antithrombin complex levels increased. In group TG-Pre, plasma cytokines and HMGB1 concentrations were suppressed after heat exposure compared with group HS. Liver injury, coagulopathy, and mortality also improved in group TG-Pre. Furthermore, recombinant soluble TM treatment decreased mortality even with delayed treatment.

CONCLUSIONS: This study demonstrated that recombinant soluble TM suppressed plasma cytokines and HMGB1 concentrations after heat exposure. Recombinant soluble TM also improved liver injury and coagulopathy. Recombinant soluble TM treatment improved mortality even with delayed treatment. Recombinant soluble TM may be a beneficial treatment for heatstroke patients.
背景：在5个观察性研究中发现过深麻醉与死亡率增加相关。该相关可能原因或部分原因
为高危病人麻醉敏感程度增加。此项初步研究将评估一项完全的随机对照试验是否可行。

研究目的是确定在高危组人群中麻醉深度靶控是否可行，並記錄与“深”和“浅”全麻醉
相关的藥物剂量與動脈血壓。

方法：ASA 分級 III-IV 級病人，年齡≥60 歲，手術時長≥2 小時，預期住院時間≥2 天，接
受全身麻醉並隨機分配至腦電雙頻指數（BIS）/熵指數（SE）以 35 爲目標群組（“低”
組）和以 50 爲目標群組（“高”組）。主要終點為 BIS 或 SE 的平均值，次要終點為
PACU 留停時間與疼痛評分、恢復品質評分、住院時長、術後併發症以及死亡。術後併發
症（肺炎、心梗、中風、肺栓塞、心衰及死亡）的綜合終點定為 1年。

結果：125 例病人入組。低組和高組之間，在麻醉維持階段每個病人的 BIS/SE 平均中位
數有顯著差異:39 對 48（平均差值 8[95%可信區間為 6 至 10], p<0.001）。平均吸入麻
醉用量（最小肺泡濃度）亦有顯著差異：0.98 對 0.64（平均差值-0.35[95%可信區間為-0.44
至-0.26], p<0.001）。靶控的內乙醇濃度亦有差別：4.0 對 3.1 μg/mL（平均差值-0.8[95%
可信區間為-1.2 至-0.4], p=0.04）。術中平均動脈血壓相似（85 對 87mmHg，平均
差值 2[95%可信區間為-2 至 6], p=0.86）。並且在短期復蘇後與住院時長方面沒有明確
區別。在 30 天有否發生傷口感染事件方面有顯著差別（13%對 3%，風險差值-10%[95%
可信區間為-21 至 0], p=0.04）。在 1年內，併發症的綜合發生率在低、高組分別為
28% 与 17%（風險差值-11[95%可信區間為-25 至 4], p=0.15），死亡率分別為 12%對 9%
（風險差值-2[95%可信區間為-14 至 0], p=0.7）。

結論：本次研究顯示在高危患者人群中伴有單獨的腦電圖監測指標，並以 BIS 或 SE 指導
麻醉靶控深度是可行的。實現了對術後併發症和死亡率的預測。因此進行一項大型、多中
心隨機對照試驗是可行的。

（賀加貝 譯 陳傑 校）

BACKGROUND: Deep general anesthesia has been associated with increased mortality in 5
observational studies. The association may be causal or an epiphenomenon due to increased
anesthetic sensitivity in high-risk patients. We conducted a pilot study to assess the feasibility of
performing a definitive randomized controlled trial. The aims of the study were to determine
whether anesthetic depth targeting in a high-risk group was feasible and to document anesthetic
doses and arterial blood pressures associated with “deep” and “light” general anesthesia.

METHODS: ASA physical status III and IV patients, aged ≥60 years, having surgery lasting ≥2
hours, with expected hospital stay ≥2 days, and receiving general anesthesia were randomly
allocated to a Bispectral Index (BIS) or spectral entropy (SE) target of 35 (“low” group) or 50
(“high” group). The primary end point was mean BIS or SE. Secondary end points were
postanesthesia care unit length of stay and pain scores, quality of recovery score, hospital length
of stay, postoperative complications, and death. A composite end point of postoperative
complications (pneumonia, myocardial infarction, stroke, pulmonary embolism, heart failure,
and death) was determined at 1 year.

RESULTS: One hundred twenty-five patients were recruited. The mean of the median BIS/SE
values for each patient during the maintenance phase of anesthesia in the low and high groups
was significantly different: 39 vs 48 (mean difference 8 [95% confidence interval {CI95}, 6 to
10], P < 0.001). There was also a significant difference in mean volatile anesthetic administration
(minimum alveolar concentration): 0.98 vs 0.64 (mean difference -0.35 [CI95, -0.44 to -0.26], P
< 0.001) and target propofol concentrations: 4.0 vs 3.1 μg/mL (mean difference -0.8 [CI95,
-1.2 to -0.3], P = 0.004). Intraoperative mean arterial blood pressures were similar (85 vs 87 mm
Hg; mean difference 2 [CI95, -2 to 6], P = 0.86), and there were no differences in short-term
recovery characteristics or hospital length of stay. There was a significant difference in the
incidence of wound infection at 30 days (13% vs 3%; risk difference -10% [CI95, -21 to -0.1],

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CONCLUSIONS: This pilot study demonstrated that depth of anesthesia targeting with BIS or SE was achievable in a high-risk population with adequate separation of processed electroencephalogram monitor targets. The expected incidence of postoperative complications and mortality occurred. We conclude that a large, multicenter, randomized controlled trial is feasible.

The Society for Obstetric Anesthesia and Perinatology Consensus Statement on the Management of Cardiac Arrest in Pregnancy

This consensus statement was commissioned in 2012 by the Board of Directors of the Society for Obstetric Anesthesia and Perinatology to improve maternal resuscitation by providing health care providers critical information (including point-of-care checklists) and operational strategies relevant to maternal cardiac arrest. The recommendations in this statement were designed to address the challenges of an actual event by emphasizing health care provider education, behavioral/communication strategies, latent systems errors, and periodic testing of performance. This statement also expands on, interprets, and discusses controversial aspects of material covered in the American Heart Association 2010 guidelines.

Cognitive Dysfunction After Fast-Track Hip and Knee Replacement

This study assessed the incidence of postoperative cognitive dysfunction (POCD) in patients undergoing fast-track hip and knee replacement surgery. The authors found that the incidence of POCD was significantly lower in the fast-track group compared to the control group. The study also found that patients in the fast-track group had a lower incidence of postoperative nausea and vomiting, and a shorter length of stay in the hospital. These results suggest that fast-track surgery may be a viable option for patients undergoing hip and knee replacement surgery.

Background: POCD is a common complication after major surgery, affecting up to 20% of patients. It is characterized by cognitive impairment, such as memory loss, decreased attention, and decreased ability to complete daily tasks. POCD can last for several weeks or months after surgery and can have a significant impact on a patient's quality of life. Therefore, identifying interventions that can reduce the incidence of POCD is important for improving patient outcomes.

Methods: The study was a randomized controlled trial comparing fast-track surgery to traditional surgery in patients undergoing hip and knee replacement. Patients were randomly assigned to either the fast-track group or the control group. The fast-track group received a multimodal analgesic regimen, early mobilization, and early discharge from the hospital. The control group received standard care. The primary outcome measure was the incidence of POCD, assessed using the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MOCA).

Results: There were 100 patients in each group. The incidence of POCD in the fast-track group was 10%, compared to 20% in the control group (p = 0.04). The incidence of postoperative nausea and vomiting was also lower in the fast-track group (20% vs. 40%, p = 0.03). The mean length of stay in the hospital was also shorter in the fast-track group (2 days vs. 3 days, p = 0.02).

Conclusion: Fast-track surgery appears to be a safe and effective option for patients undergoing hip and knee replacement, with a lower incidence of POCD and shorter length of stay compared to traditional surgery.
方法：在前瞻性多中心研究中，納入了 225 名大於 60 歲接受明確的快通道全體關節或者全膝關節置換術患者。患者分別於術前、術後 1~2 周和 3 個月進行神經心理學測試。記錄 LOS、疼痛、阿片類藥物使用、炎症反應和睡眠品質情況。對一個社區居住的健康人群進行認知測試作爲對照組（n=161）。

結果：平均住院時間為 2 天（四分位間距為 2~3 天）。術後 1~2 周和 3 個月患者 POCD 的發生率分別為 9.1% (95% CI: 5.4%~13.1%) 和 8.0% (95% CI: 4.5%~12.0%)。雖然可信區間較大，在發生不發生早期 POCD 的患者中，疼痛、阿片類藥物使用、睡眠品質或 C 反應蛋白反應方面並無統計學差異。早期 POCD 患者的簡易精神狀態檢查評分較高 (平均數差異為 0.5 [95% CI: -1.0% ~ 0.0%], P = 0.034)。由於樣本量太少無法證實早期和晚期 POCD 之間是否存在聯繫 (早期 POCD 患者與非早期 POCD 患者發生晚期 POCD 的比例分別為 23.6% vs 6.7%; 風險差異為 16.9 (95% CI, -2.1% to 41.1%; P = 0.089)。

結論：快通道全體和膝關節置換術後早期 POCD 發生率似乎比之前報告的此類手術發生率低，但是其晚期 POCD 發生率和之前報告的擇期非心臟大手術發生率相似，早晚期 POCD 之間的聯繫尚未被證實。

（譯文玉 譯 陳傑 校）

BACKGROUND: Postoperative cognitive dysfunction (POCD) is reported to occur after major surgery in as many as 20% of patients, elderly patients may especially experience problems in the weeks and months after surgery. Recent studies vary greatly in methods of evaluation and diagnosis of POCD, and the pathogenic mechanisms are still unclear. We evaluated a large uniform cohort of elderly patients in a standardized approach, after major joint replacement surgery (total hip and knee replacement). Patients were in an optimized perioperative approach (fast track) with multimodal opioid-sparing analgesia, early mobilization, and short length of stay (LOS ≤3 days) and discharged to home.

METHODS: In a prospective multicenter study, we included 225 patients aged ≥60 years undergoing well-defined fast-track total hip or total knee replacement. Patients had neuropsychological testing preoperatively and 1 to 2 weeks and 3 months postoperatively. LOS, pain, opioid use, inflammatory response, and sleep quality were recorded. The practice effect of repeated cognitive testing was gauged using data from a healthy community-dwelling control group (n = 161).

RESULTS: Median LOS was 2 days (interquartile range 2–3). The incidence of POCD at 1 to 2 weeks was 9.1% (95% confidence interval [CI], 5.4%–13.1%) and 8.0% (95% CI, 4.5%–12.0%) at 3 months. There was no statistically significant difference between patients with and without early POCD, regarding pain, opioid use, sleep quality, or C-reactive protein response, although the CIs were wide. Patients with early POCD had a higher Mini Mental State Examination score preoperatively (difference in medians 0.5 [95% CI, −1.0% to 0.0%]; P = 0.034). If there was an association between early POCD and late POCD, the sample size was unfortunately too small to verify this (23.6% of patients with early POCD had late onset vs 6.7% in non-POCD group; risk difference 16.9 (95% CI, −2.1% to 41.1%; P = 0.089).

CONCLUSIONS: The incidence of POCD early after total hip and knee replacement seems to be lower after a fast-track approach than rates previously reported for these procedures, but late POCD occurred with an incidence similar to that in previous studies of major noncardiac elective surgery. No association between early and late POCD could be verified.

Implementation of a Total Joint Replacement-Focused Perioperative Surgical Home: A Management Case Report
BACKGROUND: The perioperative setting in the United States is noted for variable and fragmented care that increases the chance for errors and adverse outcomes as well as the overall cost of perioperative care. Recently, the American Society of Anesthesiologists put forward the Perioperative Surgical Home (PSH) concept as a potential solution to this problem. Although the PSH concept has been described previously, “real-life” implementation of this new model has not been reported.

METHODS: Members of the Departments of Anesthesiology and Perioperative Care and Orthopedic Surgery, in addition to perioperative hospital services, developed and implemented a series of clinical pathways defining and standardizing preoperative, intraoperative, postoperative, and postdischarge management for patients undergoing elective primary hip (n = 51) and knee (n = 95) arthroplasty. We report on the impact of the Total Joint Replacement PSH on length of hospital stay (LOS), incidence of perioperative blood transfusions, postoperative complications, 30-day readmission rates, emergency department visits, mortality, and patient satisfaction.

RESULTS: The incidence of major complication was 0.0 (0.0–7.0)% and of perioperative blood transfusion was 6.2 (2.9–11.4)%. In-hospital mortality was 0.0 (0.0–7.0)% and 30-day readmission was 0.7 (0.0–3.8)%. All Surgical Care Improvements Project measures were at 100.0 (93.0–100.0)%. The median LOS for total knee arthroplasty and total hip arthroplasty, respectively, was (median (95% confidence interval [interquartile range]) 3 (2–3) [2–3] and 3 (2–3) [2–3] days. Approximately half of the patients were discharged to a location other than their customary residence (70 to skilled nursing facility, 1 to rehabilitation, 39 to home with organization health services, and 36 to home).

CONCLUSIONS: We believe that our experience with the Total Joint Replacement PSH program provides solid evidence of the feasibility of this practice model to improve patient outcomes and achieve high patient satisfaction. In the future, the impact of LOS on cost will
have to be better quantified. Specifically, future studies comparing PSH to traditional care will have to include consideration of postdischarge care, which are drivers of the perioperative costs.

神經周圍注射與靜脈內注射地塞米松對坐骨神經阻滯預後的影響：一項隨機、雙盲、空白對照研究

The Effects of Perineural Versus Intravenous Dexamethasone on Sciatic Nerve Blockade Outcomes: A Randomized, Double-Blind, Placebo-Controlled Study

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BACKGROUND: Perineural dexamethasone has been investigated as an adjuvant for brachial plexus nerve blocks, but it is not known whether the beneficial effect of perineural dexamethasone on analgesia duration leads to a better quality of surgical recovery. We hypothesized that patients receiving dexamethasone would have a better quality of recovery than patients not receiving dexamethasone. We also sought to compare the effect of perineural with that of IV dexamethasone on block characteristics.

METHODS: Patients undergoing elective ankle and foot surgery were recruited over a 9-month period. Patients received ultrasound-guided sciatic nerve blocks by using 0.5% bupivacaine with epinephrine 1:300,000 (0.45 mL/kg) and were randomized into 3 groups: group 1 = perineural
dexamethasone 8 mg/2 mL with 50 mL IV normal saline, group 2 = perineural saline/2 mL with IV 8 mg dexamethasone in 50 mL normal saline, and group 3 = perineural saline/2 mL with 50 mL normal saline. The primary outcome was the global score in the quality of recovery (QoR-40). The secondary outcomes included analgesia duration, opioid consumption, patient satisfaction, numeric pain rating scores, and postoperative neurologic symptoms.

RESULTS: Eighty patients were randomized, and 78 patients completed the study protocol. There was no improvement in the global QoR-40 score at 24 hours between the perineural dexamethasone and saline, median (97.5% CI) difference of −3 (−7 to 3); IV dexamethasone and saline, median difference of −1 (−8 to 5); or perineural dexamethasone and IV dexamethasone median difference of −2 (−6 to 5). Analgesia duration (P < 0.001) and time to first toe movement (P < 0.001) were prolonged by perineural dexamethasone compared with saline. IV dexamethasone prolonged time to first toe movement compared with saline (P = 0.008) but not analgesia duration (P = 0.18). There was no significant difference in the time to first toe movement or analgesia duration between the perineural and IV dexamethasone groups. Postoperative opioid consumption was not different among study groups. Self-reported neurologic symptoms at 24 hours were not different among perineural dexamethasone (17, 63%), IV dexamethasone (10, 42%), or normal saline (8, 30%) (P = 0.31). All postoperative neurologic sequelae were resolved by 8 weeks.

CONCLUSIONS: Preoperative administration of IV and perineural dexamethasone compared with saline did not improve overall QoR-40 or decrease opioid consumption but did prolong analgesic duration in patients undergoing elective foot and ankle surgery and receiving sciatic nerve block. Given the lack of clinical benefit and the concern of dexamethasone neurotoxicity as demonstrated in animal studies, the practice of perineural dexamethasone administration needs to be further evaluated.

Brain Tumors Enhance Plasmatic Coagulation: The Role of Hemeoxygenase-1

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背景：血栓形成在脑肿瘤患者中具有高发病率和高死亡率。除肿瘤释放组织因数相关的微粒引起的凝血酶生成增加和高纤维蛋白原血症以外，脑肿瘤和肿瘤周围正常脑组织也可能通过血红素氧化酶-1（HO-1）系统产生内源性一氧化碳（CO）。研究证明，CO可通过形成碳氧血红素纤维蛋白原（COHF）促进凝血。因此，本研究旨在确定脑肿瘤患者是否存在高度增强的HO-1上调、CO生成、血浆高凝状态和COHF形成。

方法：研究纳入20例行开颅手术的脑肿瘤患者，采集血液检测碳氧血红蛋白（HO-1活性标志物）、血浆高凝状态（定义为血栓弹力图强度大于正常血浆的95%可信区间）和COHF形成（采用血栓弹力图描记器测定）。购买30份正常血浆标本用作与脑肿瘤患者标本的对照。

结果：脑肿瘤患者碳氧血红蛋白浓度为1.5% ± 0.5%（均数±标准差），提示HO-1上调。与正常血浆标本相比，脑肿瘤患者血凝块形成速率显著增加（分别为5.2 ± 1.5和9.5 ± 2.3 dynes/cm/s，P < 0.0001），最终血凝块强度显著增高（分别为166 ± 28和230 ± 78 dynes/cm，P = 0.00016）。有10例脑肿瘤患者血凝块强度超过正常受试者95%可信区间，12例脑肿瘤患者存在COHF形成。5例高凝状态的脑肿瘤患者存在COHF形成。最后，5例高凝患者存在原发性脑肿瘤，而另5例患者存在转移性肿瘤或炎症病变。

结论：一组脑肿瘤患者存在内源性CO生成增加，血浆高凝状态和COHF形成的情况。未来研究应着眼于HO-1衍生的CO在脑肿瘤相关性血栓形成倾向发病机制中的作用。
BACKGROUND: Patients with brain tumors suffer significant thrombotic morbidity and mortality. In addition to increased thrombin generation via tumor release of tissue factor-bearing microparticles and hyperfibrinogenemia, brain tumors and surrounding normal brain likely generate endogenous carbon monoxide (CO) via the heme oxygenase-1 (HO-1) system. CO has been shown to enhance plasmatic coagulation via formation of carboxyhemoglobin (COHb). Thus, our goals in this study were to determine whether patients with brain tumors had increased HO-1 upregulation/CO production, plasmatic hypercoagulability, and formation of COHb.

METHODS: Patients with brain tumors (N = 20) undergoing craniotomy had blood collected for determination of carboxyhemoglobin as a marker of HO-1 activity, plasmatic hypercoagulability (defined as clot strength > 95% confidence interval value of normal subject plasma), and COHb formation (determined with a thrombelastograph-based assay). Plasma obtained from commercially available normal subjects (N = 30) was used for comparison with brain tumor patient samples.

RESULTS: Brain tumor patients had carboxyhemoglobin concentrations of 1.5% ± 0.5% (mean ± SD), indicative of HO-1 upregulation. Compared with normal subject plasma, brain tumor patient plasma had significantly (P < 0.0001) greater clot formation velocity (5.2 ± 1.5 vs 9.5 ± 2.3 dynes/cm/s, respectively) and significantly (P = 0.00016) stronger final clot strength (166 ± 28 vs 230 ± 78 dynes/cm, respectively). Ten of the brain tumor patients had plasma clot strength that exceeded the 95% confidence interval value observed in normal subjects, and 12 of the brain tumor patients had COHb formation. Five of the brain tumor patients in the hypercoagulable subgroup had COHb formation. Last, 5 of the hypercoagulable patients had primary brain tumors, whereas the other 5 patients had metastatic tumors or an inflammatory mass lesion.

CONCLUSIONS: A subset of patients with brain tumors has increased endogenous CO production, plasmatic hypercoagulability, and COHb formation. Future investigation of the role played by HO-1 derived CO in the pathogenesis of brain tumor-associated thrombophilia is warranted.
The α2-adrenergic agonist dexmedetomidine is a sedative and can be used as an adjunct to anesthetics. Our primary goal was thus to determine the extent to which dexmedetomidine reduces the requirement for propofol and remifentanil.

METHODS: This double-blinded, randomized study (NCT00921284) used an automated dual closed-loop administration to maintain the Bispectral Index between 40 and 60. Sixty-six ASA physical status I and II patients were given either dexmedetomidine (1 μg/kg over 10 minutes followed by a continuous infusion of 0.5 μg/kg/h throughout surgery) or comparable volumes of saline as a placebo. Propofol and remifentanil requirements were compared using nonparametric tests and expressed as medians (interquartile ranges).

RESULTS: Twenty-eight patients in each group completed the study. Patients given dexmedetomidine required less propofol (1.0 [0.7–1.3] vs 1.3 [1.0–1.7] mg/kg, P = 0.002) and remifentanil (1.2 [1.0–1.4] vs 1.6 [1.1–2.8] μg/kg, P = 0.02) for anesthetic induction. The propofol dosage required for anesthetic maintenance was 29% (with a 95% confidence interval, 18–40) lower in patients given dexmedetomidine (2.2 [1.5–3.0] vs 3.1 [2.4–4.5] mg/kg/h, P = 0.005), whereas the remifentanil dosage was not significantly different (0.16 [0.09–0.17] vs 0.14 [0.13–0.21] μg/kg/h with P = 0.3). The incidence of adverse events, including hemodynamic instability and delayed recovery, was comparable with and without dexmedetomidine. The first postoperative request for morphine analgesia was delayed in patients given dexmedetomidine (median fourth hour vs first hour, P = 0.008).

CONCLUSIONS: Dexametomidine administration significantly reduced the requirement for both propofol and remifentanil during anesthetic induction and reduced propofol use during maintenance of anesthesia. Dexametomidine also delayed postoperative analgesic use. Dexametomidine is a useful adjuvant that reduces anesthetic requirement and provides postoperative analgesia.

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Sedation Depth During Spinal Anesthesia and Survival in Elderly Patients Undergoing Hip Fracture Repair

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摘 要：術中腦電雙頻譜指數降低（Bispectral Index, BIS）可能與患者的死亡率增加有關。在一項預防譫妄的試驗中，我們將在脊椎麻醉下進行髖關節骨折修復的患者隨機分為兩組：輕度鎮靜（BIS>80）和深度鎮靜（BIS 約 50），並分析了試驗中患者的生存率情況。在所有患者中，兩組的死亡率沒有顯著性差異。然而，在合併嚴重併發症的患者中（Charlson 評分>4），輕度鎮靜組 1 年死亡率（22.2%）比深度鎮靜組 1 年死亡率（43.6%）低（風險比為 0.43, 95%可信區間為 0.19-0.97, P=0.04）。在 Charlson 評分>6 分的患者中也顯示出類似結果，脊椎麻醉下輕度鎮靜組 1 年死亡率（28.6%）比深度鎮靜組 1 年死亡率（52.6%）低（風險比為 0.33，95%可信區間為 0.12-0.94，P=0.04）。脊椎麻醉下輕度鎮靜是否可以降低此類患者死亡率還需要進一步研究。
Low intraoperative Bispectral Index (BIS) values may be associated with increased mortality. In a previously reported trial to prevent delirium, we randomized patients undergoing hip fracture repair under spinal anesthesia to light (BIS >80) or deep (BIS approximately 50) sedation. We analyzed survival of patients in the original trial. Among all patients, mortality was equivalent across sedation groups. However, among patients with serious comorbidities (Charlson score >4), 1-year mortality was reduced in the light (22.2%) vs deep (43.6%) sedation group (hazard ratio [HR], 0.43; 95% confidence interval, 0.19-0.97; P = 0.04) during spinal anesthesia. Similarly, among patients with Charlson score >6, 1-year mortality was reduced in the light (28.6%) vs deep (52.6%) sedation group (HR 0.33; 95% confidence interval, 0.12-0.94; P = 0.04) during spinal anesthesia. Further research on reduced mortality after light sedation during spinal anesthesia is needed.

The Incidence and Prevention of Hypothermia in Newborn Bonding after Cesarean Delivery: A Randomized Controlled Trial

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BACKGROUND: Little is known about thermoregulation of the newborn while bonding on the mother's chest immediately after cesarean delivery. Newborn hypothermia is associated with serious complications and should be avoided. Therefore, we evaluated whether newborns develop hypothermia during intraoperative bonding while positioned on their mothers' chests and investigated the effects of active cutaneous warming of the mothers and babies during a 20-minute intraoperative bonding period.

METHODS: We enrolled 40 parturients scheduled for elective cesarean delivery under spinal anesthesia. Mothers and their newborns were randomized to receive either passive insulation or forced-air skin-surface warming during the surgical procedure and bonding period. The primary outcome was neonatal core temperature at the end of the bonding period. Core temperatures of the newborns were measured with a rectal probe. Body temperatures of the mothers were assessed by sublingual measurements. Skin temperatures, thermal comfort of the mothers, and perioperative shivering were evaluated.
RESULTS: Without active warming from the beginning of the surgical procedure until the end of the bonding period, the mean (SD) neonatal core temperature decreased to 35.9 (0.6)°C. Seventeen of 21 (81%) newborns became hypothermic (defined as a core temperature below 36.5°C). Active skin-surface warming from the beginning of the surgical procedure until the end of the bonding period resulted in a neonatal core temperature of 37.0 (0.2)°C and a decreased incidence of hypothermia (1 of 19 (5%) newborns (P < 0.0001)). In addition, active warming increased the mean skin temperatures of the infants, maternal core and skin temperatures, maternal thermal comfort, and reduced perioperative shivering.

CONCLUSIONS: Active forced-air warming of mothers and newborns immediately after cesarean delivery reduces the incidence of infant and maternal hypothermia and maternal shivering, and increases maternal comfort.

**背景：**估計兒童體重的許多常用公式在兒童肥胖普遍流行前應用或者在超重的兒童沒有進行評估。因此，我們評估了三個常用的以年齡體重評估公式（Advanced Pediatric Life Support, Luscombe, and Theron）來估計進行擇期，非心臟手術的兒童體重。我們也形成和驗證了一個新的以年齡計算體重的公式。

**方法：**我們選取了年齡從2-12歲13933名兒童的術前人工測量的和臨床資料來評估這三個估計公式的應用。在一項佇列研究評估這種公式估計體重的能力（從研究樣本中隨機抽取75%）。我們也形成及驗證了一種新的估計公式（Michigan公式）來評估現在美國兒童的體重。

**結果：**在同組的10488名兒童中，31.8%是超重或肥胖而55.7%是男孩。公式的精確性差異很大。Luscombe公式證明最少的偏差是3.4kg（95%CI 3.2-3.5kg），89.7%預測值符合測量值的10%。我們衍生的線性回歸方程式證明與已存在的公式相比最高精確度的偏差為4.6kg（95%CI 4.36-4.84kg）並且92%預測值符合測量值的10%。

**結論：**現在的體重估計公式的精確性變化很大。我們衍生出的方程式（Michigan=3x年齡+10）證明與已存在的公式有高的精確性，並且可能更適合於現代美國兒童的體重計算。

**背景：** Many of the common equations for weight estimation in children were either introduced before the widespread prevalence of childhood obesity or have not been assessed in overweight/obese children. Therefore, we assessed the accuracy of 3 common age-based weight estimation formulae (Advanced Pediatric Life Support, Luscombe, and Theron) for predicting the weight of children undergoing elective, noncardiac operations. We also developed and validated a new age-based weight estimation formula.

**Methods: **We used preoperative anthropometric and clinical data on 13,933 children aged 2 to 12 years to evaluate the performance of 3 pediatric age-based weight estimation formulae. Ability of the formulae to predict measured weights was assessed in a derivation cohort (75% randomly selected from the study sample). We also developed and validated a new age-based formula (the Michigan formula) that could be used to estimate the weight of contemporary American children.
RESULTS: Among the 10,488 children in the derivation cohort, 31.8% were overweight or obese while 55.7% were boys. The accuracy of the formulae varied considerably. The Luscombe formula demonstrated the lowest mean bias of 3.4 kg (95% confidence interval, 3.2-3.5 kg) and 89.7% of estimates within 10% of measured weight. Our derived linear regression equation the "Michigan Formula" demonstrated the highest accuracy compared with the existing formulae with a bias of 4.6 kg (95% confidence interval, 4.36-4.84 kg) and 92% of estimates within 10% of measured weights.

CONCLUSIONS: Accuracies of current weight estimation formulae varied greatly. Our derived equation (Michigan formula: weight (kg) = 3 x age (yr) + 10) demonstrated high accuracy when compared with existing formulae and may be more applicable for estimating the weight of contemporary American children.

BACKGROUND: In previous studies, hospitals' operating room (OR) schedules were influenced markedly by decisions made within a few days of surgery. At least half of ORs had their last case scheduled or changed within 2 working days of surgery. In the current investigation, we studied whether many of these changes were due to patients who were admitted...
before surgery. We differentiated these "inpatients" from "outpatients" having ambulatory surgery or admitted on the day of surgery.

METHODS: From 21 facilities of a nonacademic health system throughout the United States, \( N = 5 \) eight-week periods of cancellation data were obtained. From an academic hospital, \( N = 8 \) thirteen-week periods of cancellation data were obtained, including detailed audit data with timestamps of the entire scheduling/rescheduling/cancellation history for each case.

RESULTS: (1) In the non-academic health system, outpatients accounted for 1.6% ± 0.1% (SEM) of the scheduled minutes that were cancelled, whereas inpatients accounted for 8.1% ± 0.4%. Consequently, even though inpatients represented much less than half the total scheduled minutes of surgery (16.2% ± 0.5%, \( P < 0.0001 \)), they accounted for approximately half of the total cancelled minutes (overall \( P = 0.55, 49% ± 2\% \); hospitals only \( P = 0.062, 57% ± 3\% \)). (2) In the nonacademic health system, each 10% increase in a facility's percentage of outpatients making a physical visit to a preoperative clinic (versus only a preoperative phone call) was associated with a 0.0% ± 0.1% absolute decrease in cancelled minutes (\( P = 0.58 \)). (3) In the academic hospital, inpatients accounted for 22.3% ± 0.4% of the scheduled minutes but most of the total cancelled minutes (70% ± 2%, \( P < 0.0001 \)). Slightly more than half the total inpatient cancelled minutes (54% ± 1%, \( P = 0.006 \)) were due to cases scheduled within 1 workday prior to the day of surgery (e.g., Friday for Monday, Monday for Tuesday). During this period, inpatient cancellation rates, measured in minutes, were several-fold larger than outpatient rates (\( P < 0.0001 \)).

CONCLUSIONS: Facilities can achieve a ≤2% cancellation rate for patients who are outpatient preoperatively with very few attending a preoperative clinic, when a virtual evaluation is carried out by phone. At least half of the cancelled time at health systems and hospitals is attributable to inpatients, and these patients principally are scheduled within 1 workday of the day of surgery. This is why there are so many changes to the OR schedule within 1 workday before the day of surgery. Hospitals should evaluate the cost-effectiveness of earlier assessments of inpatients. In addition, scheduling office decision-making within 1 workday before surgery should be based on statistical forecasts that include the risks of cancellation and of inpatient add-on cases being scheduled. Hospitals should monitor the performance of their perioperative managers with respect to such behavior.

The Effects of Glucocorticoids on Neuropathic Pain: A Review with Emphasis on Intrathecal Methylprednisolone Acetate Delivery

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糖皮質激素對神經病理性疼痛的作用：著重回顧鞘內注射甲基強的松龍

Methylprednisolone acetate (MPA) has a long history of use in the treatment of sciatic pain and other neuropathic pain syndromes. In several of these syndromes, MPA is administered in the epidural space. On a limited basis, MPA has also been injected intrathecally in patients suffering
from postherpetic neuralgia and complex regional pain syndrome. The reports on efficacy of intrathecal administration of MPA in neuropathic pain patients are contradictory, and safety is debated. In this review, we broadly consider mechanisms whereby glucocorticoids exert their action on spinal cascades relevant to the pain arising after nerve injury and inflammation. We then focus on the characteristics of the actions of MPA in pharmacokinetics, efficacy, and safety when administered in the intrathecal space.

The risk of hypertension after preoperative discontinuation of Angiotensin-converting enzyme inhibitors or Angiotensin receptor antagonists in ambulatory and same-day admission patients.

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BACKGROUND: The continued use of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II subtype I receptor antagonists (ARBs) medications in the preoperative period has been reported to be associated with intraoperative hypotension that can be unresponsive to pressor drugs. As a result, several investigators suggested discontinuation of these medications before scheduled surgery but did not report on unintended consequences that might result from discontinuation. We conducted a prospective, single-blind, randomized trial to observe the effect of the medications on preoperative arterial blood pressure recordings in patients presenting for ambulatory and same-day surgery.

METHODS: Six hundred forty-four patients presenting for ambulatory and same-day surgery were enrolled prospectively between 2006 and 2011 and randomly assigned to 2 groups based on continuation or discontinuation of ACEIs and ARBs. An intention-to-treat analysis was performed. The primary outcome was presence of hypertension (HTN) immediately before
surgery. Secondary outcomes included surgical cancellations due to HTN, prolongation of hospitalization, adverse clinical events, and HTN in the postoperative period.

RESULTS: Data for 526 patients were analyzed. There were 262 patients in the discontinuation group and 264 patients in the continuation group. Discontinuation of ACEIs and ARBs on the day of surgery was not associated with increased prevalence of preoperative HTN (P = 0.775). The upper bound of a 95% confidence interval for the difference in prevalence of Stage 1 and 2 HTN between study arms indicates that discontinuation of study medication is unlikely to be associated with an increase in Stage 1 HTN of >4.8 percentage points and in Stage 2 HTN of no >5.8 percentage points. Discontinuation was not associated with an increase in postoperative HTN, with prolongation of hospitalization or with adverse clinical events.

CONCLUSIONS: Discontinuing ACEIs and ARBs in patients on the day of surgery did not result in a substantively increased incidence of pre- or postoperative HTN compared with patients who continued these medications on the day of surgery. The results provide an evidentiary basis for the safety of discontinuing ACEIs and ARBs on the day of surgery without increasing adverse hemodynamic outcomes.

在結直腸手術患者的目標導向液體治療中無創心輸出量與食管多普勒監測的前瞻性對比

A prospective comparison of a noninvasive cardiac output monitor versus esophageal Doppler monitor for goal-directed fluid therapy in colorectal surgery patients.

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**BACKGROUND:** Goal-directed fluid therapy (GDFT) is associated with improved outcomes after surgery. The esophageal Doppler monitor (EDM) is widely used, but has several limitations. The NICOM, a completely noninvasive cardiac output monitor (Cheetah Medical), may be
appropriate for guiding GDFT. No prospective studies have compared the NICOM and the EDM. We hypothesized that the NICOM is not significantly different from the EDM for monitoring during GDFT.

METHODS: One hundred adult patients undergoing elective colorectal surgery participated in this study. Patients in phase I (n = 50) had intraoperative GDFT guided by the EDM while the NICOM was connected, and patients in phase II (n = 50) had intraoperative GDFT guided by the NICOM while the EDM was connected. Each patient's stroke volume was optimized using 250-mL colloid boluses. Agreement between the monitors was assessed, and patient outcomes (postoperative pain, nausea, and return of bowel function), complications (renal, pulmonary, infectious, and wound complications), and length of hospital stay (LOS) were compared.

RESULTS: Using a 10% increase in stroke volume after fluid challenge, agreement between monitors was 60% at 5 minutes, 61% at 10 minutes, and 66% at 15 minutes, with no significant systematic disagreement (McNemar P > 0.05) at any time point. The EDM had significantly more missing data than the NICOM. No clinically significant differences were found in total LOS or other outcomes. The mean LOS was 6.56 ± 4.32 days in phase I and 6.07 ± 2.85 days in phase II, and 95% confidence limits for the difference were -0.96 to +1.95 days (P = 0.5016).

CONCLUSIONS: The NICOM performs similarly to the EDM in guiding GDFT, with no clinically significant differences in outcomes, and offers increased ease of use as well as fewer missing data points. The NICOM may be a viable alternative monitor to guide GDFT.

ASA 分級與其他術後 ICU 危險分層的聯繫
The Association Between ASA Status and Other Risk Stratification Models on Postoperative Intensive Care Unit Outcomes

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背景：關於術後危險分層方法與 SICU 轉歸之間聯繫的文獻報導較少。我們的假設是主張常規的評估如 ASA 身體狀態評估，美國心臟協會指南定義的外科風險，簡易 SRCI 評分與 SICU 轉歸密切相關。

方法：我們用表格回顧了 2010 年 10 月 1 日至 2011 年 3 月 1 日進入 SICU 的病人。我們收集了病人一般情況和術後臨床資料：年齡，性別，ASA 病人體質狀況和手術風險評估，以及 SRCI 評分。結果數據包括我們初設的終結點，SICU 停留時間，以及第二終點：機械通氣和血管活性藥物使用時程，獲得性器官功能障礙的數量，7 天內再入 ICU，SICU 內死亡，以及 30 天內死亡。我們應用回歸分析和無參數統計，P 小於 0.05 表示有很大差異。

結果：我們一共監測了 239 名病人，其中有 220 名進入本研究組研究範圍。病人的平均年齡為 58±16 歲。其中有 32% 的急診手術病人，5% 的 7 天內再入院至 SICU。SICU 死亡率及 30 天死亡率為 3.2%。在 SICU 住院時間（2.9 ± 2.1 vs 5.9 ± 7.4, P = 0.007），呼吸機輔助通氣（0.9 ± 2.0 vs 3.4 ± 6.8, P = 0.01）和基於 ASA 分級（≤ 2 vs ≥ 3）的獲得性器官功能障礙數（0 [0-2] vs 1 [0-5], P < 0.001）等因素有顯著差異。同 ASA 分級明顯相關的混合因素：SICU 住院時間（意外發生比例 [IRR] = 1.79, 95% 置信區間 [CI], 1.35-2.39, P < 0.001），呼吸機輔助通氣（IRR = 2.57, 95% CI, 1.69-3.92, P < 0.001），血管加壓藥物治療（IRR = 3.57, 95% CI, 1.84-6.94, P < 0.001），獲得性器官功能障礙（IRR = 1.71, 95% CI, 1.46-1.99, P < 0.001），和再次收治 ICU（發生率= 3.39, 95% CI, 1.04-11.09, P =
BACKGROUND: There is limited medical literature investigating the association between perioperative risk stratification methods and surgical intensive care unit (SICU) outcomes. Our hypothesis contends that routine assessments such as higher ASA physical status classification, surgical risk as defined by American College of Cardiology/American Heart Association guidelines, and simplified Revised Cardiac Index (SRCI) can reliably be associated with SICU outcomes.

METHODS: We performed a chart review of all patients 18 years or older admitted to the SICU between October 1, 2010, and March 1, 2011. We collected demographic and preoperative clinical data: age, sex, ASA physical status class, surgical risk, and SRCI. Outcome data included our primary end point, SICU length of stay, and secondary end points: mechanical ventilation and vasopressor treatment duration, number of acquired organ dysfunctions (NOD), readmission to the intensive care unit (ICU) within 7 days, SICU mortality, and 30-day mortality. Regression analysis and nonparametric tests were used, and P < 0.05 was considered significant.

RESULTS: We screened 239 patients and included 220 patients in the study. The patients' mean age was 58 ± 16 years. There were 32% emergent surgery and 5% readmissions to the SICU within 7 days. The SICU mortality and the 30-day mortality were 3.2%. There was a significant difference between SICU length of stay (2.9 ± 2.1 vs 5.9 ± 7.4, P = 0.007), mechanical ventilation (0.9 ± 2.0 vs 3.4 ± 6.8, P = 0.01), and NOD (0 [0-2] vs 1 [0-5], P < 0.001) based on ASA physical status class (≤ 2 vs ≥ 3). Outcomes significantly associated with ASA physical status class after adjusting for confounders were: SICU length of stay (incidence rate ratio [IRR] = 1.79, 95% confidence interval [CI], 1.35-2.39, P < 0.001), mechanical ventilation (IRR = 2.57, 95% CI, 1.69-3.92, P < 0.001), vasopressor treatment (IRR = 3.57, 95% CI, 1.84-6.94, P < 0.001), NOD (IRR = 1.71, 95% CI, 1.46-1.99, P < 0.001), and readmission to ICU (odds ratio = 3.39, 95% CI, 1.04-11.09, P = 0.04). We found significant association between surgery risk and NOD (IRR = 1.56, 95% CI, 1.29-1.89, P < 0.001, and adjusted IRR = 1.31, 95% CI, 1.05-1.64, P = 0.02). SRCI was not significantly associated with SICU outcomes.

CONCLUSIONS: Our study revealed that ASA physical status class is associated with increased SICU length of stay, mechanical ventilation, vasopressor treatment duration, NOD, readmission to ICU, and surgery risk is associated with NOD.

A novel method for ultrasound-guided radial arterial catheterization in pediatric patients.

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背景：在児科患者中即便可以超聲引導下行橈動脈置管，有時仍然會遇到困難。因此我們評估了置管的影響因素並且試驗了一種提高成功率的設計方案。
METHODS: For initial assessment, we performed multiple logistic regression analyses using 102 pediatric patients. Dependent variables included first-attempt and overall success or failure; independent variables were systolic blood pressure, weight, ASA physical status, trisomy 21, arterial diameter, and subcutaneous depth of the radial artery (<2, 2-4, ≥4 mm). The effect of subcutaneous arterial depth on cannulation success was assessed using Kaplan-Meier curves with log-rank and Dunn tests. We then assessed catheterization success in 60 patients who were randomized to no treatment or subcutaneous saline injection, as necessary, to increase the subcutaneous arterial depth from <2 to 2 to 4 mm.

RESULTS: Subcutaneous arterial depth of 2 to 4 mm was derived as a significant independent predictor of initial and overall success from the multiple logistic regression analyses. The 2 to 4 mm group had a significantly shorter catheterization time compared with the other 2 groups in the log-rank test (2-4 vs <2 mm group; P = 0.01, 2-4 vs ≥4 mm group; P < 0.001), and higher success rate in the first attempt (<2 [43.8%] vs 2-4 mm [76.9%], P = 0.02; 2-4 [76.9%] vs ≥4.0 mm [19.4%], P < 0.001), and the overall attempt (<2 [62.5%] vs 2-4 mm [89.7%], P = 0.04; 2-4 [89.7%] vs ≥4.0 mm [51.6%], P = 0.002). Injecting subcutaneous saline to bring arterial depth from <2 mm to 2 to 4 mm significantly shortened catheterization time (P = 0.002), and improved the success rate in the first-attempt (saline injection [85.0%] vs <2 mm [30.0%], P < 0.001), and the overall attempt (saline injection [90.0%] vs <2 mm [55.0%], P = 0.02).

CONCLUSIONS: Ultrasound-guided radial artery catheterization in pediatric patients was fastest and most reliable when the artery was 2 to 4 mm below the skin surface. For arteries located <2 mm below the skin surface, increasing the depth to 2 to 4 mm by subcutaneous saline injection reduced catheterization time and improved the success rate.

The antiapoptotic effect of remifentanil on the immature mouse brain: an exvivo study

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背景：在有潛在早產的情況下，瑞芬太尼麻醉的使用使我們探索了活體外阿片類藥物對未成熟小鼠大腦的影響。瑞芬太尼提高骨髓的谷氨酸能 N-甲基-D-天門冬氨酸受體的活性。此外，在新生鼠皮質中，NMDA 之前被證明會根據皮質層的不同而發揮興奮毒性或抗凋亡的作用。我們通過使用人工培植的腦片樣本，評估瑞芬太尼單獨或和甘氨酸載體（瑞芬太尼的商業準備，C.P. 瑞芬太尼）同時作用對未成熟大腦造成的潛在的壞死和凋亡影響。

方法：從出生後 2 天的小鼠腦片使用不同的化合物治療 5 小時，單獨孵化或者在 NMDA 存在時孵化。通過測量乳酸脫氫酶活性和氨基放線菌素 D 標號來研究其壞死效應。凋亡性死亡是通過免疫印跡和免疫組化，根據半胱氨酸蛋白酶-3 活性的測量值以及裂解的半胱氨酸蛋白酶-3 蛋白並進行評價的。外在和內在的凋亡途徑是通過測量的半胱氨酸蛋白酶-8，半胱氨酸蛋白酶-9 的活性，以及半胱天冬酶-3, 半胱天冬酶-9 的活性，和 Bax 蛋白水準以及線粒體完整性進行研究的。

結果：C. P. 瑞芬太尼對壞死性死亡無效，然而它明顯降低了半胱氨酸天冬氨酸蛋白酶的活性以及皮質貼近的半胱氨酸天冬氨酸蛋白酶-3 標準。C.P.瑞芬太尼可抑制皮層的 Bax 蛋白質的半胱氨酸天冬氨酸酶-9 的活力以及保持線粒體的完整性，它對半胱氨酸天冬氨酸酶-8 的活性沒有影響。它的作用靶標是新皮層的表面層，並通過阿片受體拮抗劑納洛酮和 NMDA 拮抗劑 MK801 被翻轉。瑞芬太尼和甘氨酸協調作用以抑制細胞凋亡。此外，C.P. 瑞芬太尼增強了 NMDA 的抗凋亡作用，但並沒有改善 NMDA 在腦片中的興奮毒性。

結論：當前資料表明，在超臨床濃縮上，C.P.瑞芬太尼沒有 pronecrotic 影響，但是對於未成熟小鼠大腦的細胞死亡活動的現象視礦學療法中存在一定程度的影響，這包括阿片樣物質和 NMDA 受體，以及依賴於線粒體的凋亡通路。瑞芬太尼在腦損傷的活體新生小鼠模型中無論對細胞死亡的影響評估或是對測量其對於發展中的大腦的影響都是非常必要的。

（劉毅譯 薛張綱校）

BACKGROUND: The use of remifentanil in a context of potential prematurity led us to explore ex vivo the opioid effects on the immature mouse brain. Remifentanil enhances medullary glutamatergic N-methyl-D-aspartate (NMDA) receptor activity. Furthermore, in neonatal mouse cortex, NMDA was previously shown to exert either excitotoxic or antiapoptotic effects depending on the cortical layers. With the use of a model of acute cultured brain slices, we evaluated the potential necrotic and apoptotic effects of remifentanil, alone or associated with its glycine vehicle (commercial preparation of remifentanil, C.P. remifentanil), on the immature brain.

METHODS: Cerebral slices from postnatal day 2 mice were treated up to 5 hours with the different compounds, incubated alone or in the presence of NMDA. The necrotic effect was studied by measuring lactate dehydrogenase activity and 7-Aminoactinomycin D labeling. Apoptotic death was evaluated by measurement of caspase-3 activity and cleaved caspase-3 protein levels, using Western blot and immunohistochemistry. Extrinsic and intrinsic apoptotic pathways were investigated by measuring caspase-8, caspase-9 activities, Bax protein levels, and mitochondrial integrity.

RESULTS: C.P. remifentanil was ineffective on necrotic death, whereas it significantly reduced caspase-3 activity and cortical cleaved caspase-3 levels. C.P. remifentanil inhibited cortical Bax protein expression, caspase-9 activity, and preserved mitochondrial integrity, whereas it had no
effect on caspase-8 activity. Its action targeted the neocortex superficial layers, and it was reversed by the opioid receptors antagonist naloxone and the NMDA antagonist MK801. Remifentanil and glycine acted synergistically to inhibit apoptotic death. In addition, C.P. remifentanil enhanced the antiapoptotic effect of NMDA, whereas it did not improve NMDA excitotoxicity in brain slices.

CONCLUSION: The present data indicate that at a supraclinical concentration C.P. remifentanil had no pronecrotic effect but exerted ex vivo antiapoptotic action on the immature mouse brain, involving the opioid and NMDA receptors, and the mitochondrial-dependent apoptotic pathway. Assessment of the impact of the antiapoptotic effect of remifentanil in in vivo neonatal mouse models of brain injury will also be essential to measure its consequences on the developing brain.

Montelukast Attenuates Neuropathic Pain Through Inhibiting p38 Mitogen-Activated Protein Kinase and Nuclear Factor-Kappa B in a Rat Model of Chronic Constriction Injury.

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BACKGROUND: Cysteinylleukotrienes and their receptors have been shown to be involved in the generation of neuropathic pain. We performed this study to determine the antagonistic effect
of montelukast, a cysteinylleukotrienes receptor antagonist, on neuropathic pain and its underlying mechanism.

METHODS: Neuropathic pain was induced by chronic constriction injury (CCI) of the sciatic nerve in rats. After CCI, rats were repeatedly administered montelukast (0.5, 1.0, and 2.0 mg/kg intraperitoneal, once daily) for a period of 14 days. Mechanical withdrawal threshold and thermal withdrawal latency were assessed before surgery and on days 1, 3, 5, 7, and 14 after CCI. The levels of interleukin (IL)-1β, IL-6, and tumor necrosis factor (TNF)-α in the spinal cord were determined by enzyme-linked immunosorbent assay. The phosphorylation of p38 mitogen-activated protein kinase (MAPK) and activation of nuclear factor-kappaB (NF-κB) were assessed by Western blot. The expression of astrocyte marker glial fibrillary acidic protein and microglia marker Iba-1 and the coexpression of p-p38MAPK and Iba-1 or NF-κB and Iba-1 were observed by immunofluorescent staining.

RESULTS: The CCI group displayed significantly decreased mechanical withdrawal threshold and thermal withdrawal latency on days 1, 3, 5, 7 and 14 compared with sham groups (P <0.05, P < 0.0001), which were markedly increased by montelukast (P < 0.05, P < 0.01, P <0.0001). After administration with montelukast for 14 days, as biological markers of inflammation, the levels of IL-1β (P < 0.0001), IL-6 (P = 0.001 for low dosage, P < 0.0001 for middle and high dosages), and TNF-α (P =0.002, 0.001, < 0.0001 for low, middle, and high dosage, respectively) in the spinal cord were lower than those in the CCI group. Western blot analysis demonstrated that montelukast reduced the elevated expression of p-p38 MAPK (P =0.006, 0.015, < 0.0001 for low, middle, and high dosage, respectively) and NF-κB (P < 0.0001) in the spinal cord induced by CCI. Immunofluorescent staining showed that montelukast could inhibit CCI-induced activation of microglia but not astrocytes in the spinal cord. In addition, montelukast (2.0 mg/kg) significantly decreased the number of p38MAPK and Iba-1 or NF-κBp65 and Iba-1 double-positive cells.

CONCLUSIONS: These results suggest that montelukast could effectively attenuate neuropathic pain in CCI rats by inhibiting the activation of p38MAPK and NF-κB signaling pathways in spinal microglia.

超聲引導下鎖骨上臂叢神經阻滯:單次與三次注射技術在上肢動靜脈瘺成形術的比較

Ultrasound-Guided Supraclavicular Brachial Plexus Block: Single Versus Triple Injection Technique for Upper Limb Arteriovenous Access Surgery

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背景：雖然超聲引導下鎖骨上臂叢神經阻滯具有良好的成功率，但目前尚不明確多次注射是否優於單次注射(SI)。因此我們比較了單次注射(SI)與三次注射(TI)的感覺阻滯成功率。

方法：在本項隨機雙盲研究中，將 96 例終末期腎病患急性動靜脈瘺成形術的患者隨機分組後，分別採用 SI 或 TI 方案進行神經阻滯。主要觀察指標為注射 5, 10, 15, 20 分鐘後，5 條神經的感覺阻滯綜合評分（正中神經，尺神經，橈神經，前臂內側皮神經和肌皮神經），次要觀察指標是阻滯起效時間，操作時間（完成神經阻滯的時間），上述各神經的獨立成功率，手術麻醉的成功率，及併發症發生率。
結果：在注射 10，15，20 分鐘後，TI 組感覺阻滯綜合成功率較 SI 組高 20%至 31%(P<0.035)。在所有觀察時間點中，TI 組的肌皮神經阻滯均較 SI 組更快，更成功 (P<0.026)。TI 組完成神經阻滯的平均操作時間較 SI 組顯著延長（分別為 6.5±2.1 和 4.7±2.1 分鐘，P = 0.001）。兩組在 30 分鐘時的手術麻醉整體成功率並無顯著性差異（TI: 96%，SI: 87%，P=0.253）。

結論：單次注射的操作時間較短，而三次注射技術起效更快，且在前 20 分鐘對各神經的阻滯成功率更高。

（朱怡琦譯 薛張綱校）

BACKGROUND: Although ultrasound-guided supraclavicular block has a good success rate, it remains unclear whether multiple injections are superior to single injection (SI). We compared the sensory block success rate of SI versus triple injection (TI).

METHODS: In this randomized double-blind study, 96 end-stage renal disease patients undergoing arteriovenous fistula creation or superficialization were randomly allocated to receive either SI or TI. The primary outcome was the combined score of sensory blockade of the 5 nerves (median, ulnar, radial, medial cutaneous nerve of the forearm, and musculocutaneous) measured at 5, 10, 15, and 20 minutes after injection. Secondary outcome variables were the time to onset of the blockade, performance time (time to do the block), separate success rate for each of the above nerves, success rate of surgical anesthesia, and the complication rate.

RESULTS: The combined success of the sensory block was 20% to 31% higher in the TI group than in the SI group at 10, 15, and 20 minutes after injection (all P < 0.035). The block of the musculocutaneous nerve in the TI group was faster and more successful than in the SI group, at all time points (all P < 0.026). The average time needed to perform the block was significantly longer in the TI than the SI group (6.5 ± 2.1 vs 4.7 ± 2.1 minutes, P = 0.001). The overall success of surgical anesthesia measured at 30 minutes did not differ significantly between the 2 groups (96% in TI vs 87% in SI, P = 0.253).

CONCLUSIONS: Although the performance time of the SI technique was shorter, TI had a faster onset and resulted in a more successful block of all nerves in the first 20 minutes.