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TEG® Functional Fibrinogen Analysis May Overestimate Fibrinogen Levels

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

Background: Heatstroke is a lethal disease that can cause multi-organ injury and high mortality. Thrombomodulin (TM), a group of endothelial cells that secrete anticoagulant factors, plays an important role in regulation of intravascular coagulation. This study investigated the effect of TM on liver injury, coagulopathy, and mortality in an experimental heatstroke model.

Methods: Male C3H/HeN (8-10 week) mice were randomly assigned to TM treatment group (TG treatment) or untreated heatstroke group (HS). In the TG group, mice were given recombinant TM (1 mg/kg, intraperitoneally) before exposure to heat stress. In the HS group, mice were exposed to heat stress for 4 hours. Blood samples were collected and analyzed for TNF-α, IL-6, HMGB-1, transaminases, and liver histology.

Results: Mice in the TG group had lower TNF-α, IL-6, and HMGB-1 levels compared to the HS group. The TG group also showed improved liver function and histology compared to the HS group.

Conclusion: Thrombomodulin administration before heatstroke reduces liver injury, coagulopathy, and mortality in a mouse model of heatstroke.
结果：中暑组热暴露后血浆细胞因子和 HMGB1 的浓度增加，血浆谷草转氨酶和谷丙转氨酶浓度升高。肝脏有强烈而广泛 HMGB1 免疫表达。此外，有大量的肝细胞坏死和细胞核的裂解。在中暑组中，血浆蛋白 C 水平被抑制，血浆凝血酶 - 抗凝血酶复合物水平增高。

在 TG 预处理组中，血浆细胞因子和 HMGB1 含量的升高与 HS 组相比受到抑制；肝损伤、凝血功能障碍、死亡率也有所改善。此外，重组可溶性 TM 治疗甚至能延缓治疗时机，降低死亡率。

结论：本研究表明重组可溶性 TM 抑制热暴露后血浆细胞因子和 HMGB1 浓度的升高。重组可溶性 TM 也改善了肝损伤和凝血功能障碍，降低死亡率甚至延长治疗时机。重组可溶性 TM 对于中暑病人可能是一种有益的治疗。

（林甲票 译 陈杰 校）

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.

A Pilot Study for a Prospective, Randomized, Double-Blind Trial of the Influence of Anesthetic Depth on Long-Term Outcome

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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，并记录与“深”和“浅”全麻中
相关的药物剂量与动脉血压。

方法：ASA 分级 III-IV 级病人，年龄≥60 岁，手术时长≥2 小时，接收全身麻醉并随机分配至脑电双频指数（BIS）/熵指数（SE）以 35 为目标组（“低”
组）和以 50 为目标组（“高”组）。主要终点为 BIS 或 SE 的平均值，次要终点为 PACU
停留时间与疼痛评分、恢复质量评分、住院时长、术后并发症以及死亡。术后并发症（肺
炎、心梗、中风、肺栓塞、心衰及死亡）的综合终点定为 1 年。

结果：125 例病人入组。低组和高组之间，在麻醉维持阶段每个病人的 BIS/SE
平均中位数有显著差异：39 对 48（平均差值 8 [95% 可信区间为 6 至 8]，p < 0.001）。平均吸入麻醉用量（最小肺泡浓度）亦有显著差异：0.98 对 0.64（平均差值 -0.35 [95% 可信区间为 -0.44 至 -0.26]，p < 0.001）。靶控的丙泊酚浓度亦有差别：4.0 对 3.1 μg/mL（平均差值
0.8 [95% 可信区间为 -1.2 至 0.3]，p = 0.004）。术中平均动脉血压相似（85 对 87mmHg，平均
diffference 2 [95% 可信区间为 -2 至 6]，p = 0.86），并且在短期复苏特征与住院时长方面没有明显
区别。在 30 天有否发生伤口感染事件方面有显著差别（13% 对 3%，风险差值 -10% [95%
可信区间为 -21 至 -0.1]，p = 0.04）。在 1 年内，并发症的综合发生率在低、高组分别为
28% 与 17%（风险差值 -11 [95% 可信区间为 -25 至 4]，p = 0.15），死亡率分别为 12% 对 9%
（风险差值 -2 [95% 可信区间为 -14 至 9]，p = 0.7）。

结论：本次研究显示在高危患者人群中伴有单独的脑电图监测指标，并以 BIS 或 SE 指导
麻醉靶控深度是可行的。实现了对术后并发症和死亡率的预测。因此进行一项大型、多中
心随机对照试验是可行的。

(贺加贝 译 陈杰 校)
At 1 year, the composite rates of complications in the low and high groups were 28% and 17% (risk difference $-11$ [CI95, $-25$ to $-4$], $P = 0.15$) and mortality rates were 12% and 9%, respectively (risk difference $-2$ [CI95, $-14$ to $-9$], $P = 0.70$).

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**

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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**

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背景：据报道大手术术后患者的认知功能障碍（POCD）发生率高达20%，尤其是老年患者。在术后的几周和几个月都可能存在此类问题。最近的研究中关于POCD的评估和诊断方法众说纷纭，其发病机制仍然不详。本研究采用标准方法评估了一个由大关节置换术（全髋和膝关节置换术）后老年病人组成的平衡队列。给予患者最优围术期管理（快速
道），包括减少阿片药物的多模式镇痛、早期活动和缩短住院时间（LOS≤3天）尽快出院。

方法：前瞻性多中心研究中，纳入了225名大于60岁接受明确的快通道全髋关节或者全膝关节置换术患者。患者分别于术前、术后1-2周和3个月进行神经心理学测试。记录LOS、疼痛、阿片类药物使用、炎症反应和睡眠质量情况。对一个社区居住的健康人群进行认知测试作为对照组（n=161）。

结果：平均住院时间为2天（四分位间距为2-3天）。术后1-2周和3个月患者POCD的发生率分别为9.1%（95%CI：5.4%-13.1%）和8.0%（95%CI：4.5%-12.0%）。虽然可信区间较大，在发生和不发生早期POCD的患者中，疼痛、阿片类药物使用、睡眠质量或C反应蛋白反应方面并无统计学差异。早期POCD患者术前的简易精神状态检查评分较高（平均数差异为0.5 [95% CI：-1.0%～0.0%]，P = 0.034）。由于样本量太少无法证实早期和晚期POCD之间是否存在联系（早期POCD患者与非早期POCD患者发生晚期POCD的比例分别为23.6% vs 6.7%；风险差异为16.9（95% CI，-2.1% to 41.1%；P = 0.089）。

结论：快通道全髋和膝关节置换术后早期POCD发生率似乎比之前报道的此类手术发生率低，但是其晚期POCD发生率和之前报道的择期非心脏大手术发生率相似，早期和晚期POCD之间的联系尚未被证实。

（边文玉 译 陈杰 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.

一个以全关节置换为重点的外科围手术期家庭医疗模式的实施：一项管理案例报道

Implementation of a Total Joint Replacement-Focused Perioperative Surgical Home: A Management Case Report
背景：在美国，围术期的管理较为多样和独立，而这种特点会增加错误和不良后果的发生，同时增加围术期治疗的成本。近年来，美国麻醉医师协会提出了外科围术期家庭医疗模式（PSH）这一观念作为这个问题的潜在处理方法。尽管PSH观念已有描述，但这种新模式的实际应用未曾被报道。

方法：围术期医疗工作者与麻醉科、围术期护理及骨科相关人员一起研发并制定了一系列临床监护方案来界定并规范对接受选择性髋关节或膝关节成形术的病人术前、术中、术后及出院后的管理。本研究报道全关置换术PSH对住院时间（LOS）、围术期输血发生率、术后并发症、30天再住院率、急诊入院、死亡率及病人的满意度。

结果：主要并发症的发生率为0.0 (0.0–7.0)%，围术期输血率为6.2 (2.9–11.4)%，院内死亡率为0.0 (0.0–7.0)%。术后30天再住院率为0.7 (0.0–3.8)%。所有外科监护改进项目实施为100 (93.0–100.0)%。全膝置换及全髋置换住院时间中位数（95%可信区间）分别为3 (2–3) [2–3]和3 (2–3) [2–3]天。大约一半的病人出院后转入当地护理中心而不是他们住所（70例入特殊疗养院，1例入康复中心，39例入卫生服务中心，36例回家）。

结论：在全关节置换中采用外科围术期家庭医疗模式所获得的经验为提高病人的预后及获得病人高满意度方面提供了确实的证据。将来，住院成本的影响将会更好地量化。将来进行的比较PSH与传统监护的研究需要把出院后监护考虑在内，因为后者也是围术期费用的重要影响因素。

（梁玉丹 译 陈杰 校）

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 care 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.

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

**RESULTS:**

- **QoR-40:**
  - Placebo: mean difference 3.95, 95% CI -7 to -3
  - Intravenous dexamethasone: mean difference 1.95, 95% CI -8 to -5
  - Perineural dexamethasone: mean difference 2.95, 95% CI -6 to -5

- **Duration of Analgesia:**
  - Placebo vs Intravenous dexamethasone: significant difference (P < 0.001)
  - Placebo vs Perineural dexamethasone: trend toward significance (P = 0.08)
  - Intravenous dexamethasone vs Perineural dexamethasone: no difference (P = 0.31)

**CONCLUSIONS:**

- **QoR-40:** No significant improvement
- **Analgesia Duration:**
  - Placebo vs Intravenous dexamethasone: significant difference
  - Placebo vs Perineural dexamethasone: trend toward significance
  - Intravenous dexamethasone vs Perineural dexamethasone: no difference

- **Footdrop:** Placebo vs Intravenous dexamethasone: significant difference
- **Postoperative Morbidity:**
  - All patients recovered by 8 weeks.
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。除肿瘤释放组织因子相关微粒引起的凝血酶产生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过度增强的 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（定义为血凝块强度大于正常血浆的 95%可信区间）和 COHF 形成（采用血栓弹性描记器测定）。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高（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 例高凝亚组的脑肿瘤患者存在 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 hemeoxygenase-1 (HO-1) system. CO has been shown to enhance plasmatic coagulation via formation of carboxyhemefibrinogen (COHF). 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 COHF.

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 COHF 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 COHF formation. Five of the brain tumor patients in the hypercoagulable subgroup had COHF 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 COHF formation. Future investigation of the role played by HO-1 derived CO in the pathogenesis of brain tumor-associated thrombophilia is warranted.

Dexmedetomidine Reduces Propofol and Remifentanil Requirements During Bispectral Index-Guided Closed-Loop Anesthesia: A Double-Blind, Placebo-Controlled Trial

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背景：α2-受体选择性激动剂右美托咪定被用作麻醉辅助用药。因此，此项研究试图确定在何种情况下，右美托咪定可以减少丙泊酚和瑞芬太尼的用量。

方法：这项双盲随机对照研究（注册号 00921284）使用一个自动化闭环管理保持熵电双频指数在40和60之间。66名ASA I和II级患者给予右美托咪定（在手术中给予1ug/kg超过10分钟的，连续输注0.5ug/kg/h）或者同等剂量的生理盐水作为安慰剂。丙泊酚和瑞芬太尼用量采用非参数检验和中位数（四分位数）的方法比较。

结果：每组中有28名患者完成了此项研究，在麻醉诱导中，右美托咪定组患者需要较少的丙泊酚（1.0 [0.7-1.3] vs 1.3 [1.0-1.7] mg/kg, P=0.002）和瑞芬太尼（1.2 [1.0-1.4] vs 1.6 [1.1-2.8] μg/kg, P = 0.02）。麻醉维持过程中，右美托咪定组（2.2 [1.5-3.0] vs 3.1 [2.4-4.5] mg/kg/h, P = 0.005）患者需要较少剂量丙泊酚 29%（95%可信区间，18-40），而瑞芬太尼
结论：右美托咪定可以有效减少麻醉诱导过程中丙泊酚和瑞芬太尼剂量，以及减少麻醉维持过程中丙泊酚的使用量。同时，右美托咪定也可以延缓术后镇痛药的使用。右美托咪定是一种有效的辅助用药，可以用于减少麻醉药的使用量以及术后镇痛。

(B) 静 译  李士通 校)

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

评估儿科常用的以年龄估算体重公式的精确性
Assessing the Accuracy of Common Pediatric Age-Based Weight Estimation Formulae
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BACKGROUND: 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

 Relative Influence on Total Cancelled Operating Room Time from Patients Who Are Inpatients or Outpatients Preoperatively

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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.
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.

急诊手术和日间手术患者术前停用 ACEI/ARB 类药物后高血压的风险评估

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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背景：已有报道称术前持续使用 ACEI/ARB 类药物与术中对升压药物无反应的低血压相关。因此，一些研究者建议术前应停用该类药物，但是尚无关于停药后不良后果的报道。我们组织了一个前瞻性，单盲，随机试验来观察这类药物对术前动脉血压的作用。入选包括急诊手术和日间手术的患者。

方法：前瞻性地入选 2006 年至 2011 年间 644 名急诊手术和日间手术的患者，根据是否持续服用 ACEI/ARB 类药物随机分成 2 组。使用了意向性治疗分析。主要终点是术前立即出现高血压。次要终点包括因高血压手术取消，住院时间延长，不良临床事件和术后高血压。

结果：最终分析了 526 名患者的数据。其中 262 名为不持续服用 ACEI/ARB 类药物，264 名为持续服用的患者。手术当天不服用 ACEI/ARB 类药物与术前高血压的发病率无关（P=0.775）。研究组中 1 级和 2 级高血压的不同发病率的 95% 置信区间（CI）的上界显示，停用 ACEI/ARB 类药物与 1 级高血压发病率无关（>4.8%），与 2 级高血压发病率亦无关（>5.8%）。停用 ACEI/ARB 类药物与术后高血压发病率增高，住院时间延长、不良临床事件发生无关。

结论：手术当天停用 ACEI/ARB 类药物与持续服用药物相比，事实上并不增加围术期高血压的发病率。研究结果为手术当天停用药物提供了基础研究证据，说明其并不增加血流动力学不良事件。

(陈实玉译 薛张纲校)

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.

在结直肠手术患者的目标导向液体治疗中无创心输出量与食管多普勒监测的前瞻性对比

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: 目标导向液体治疗（GDFT）与手术后改善预后有关。食管多普勒监测（EDM）被广泛使用，但也有一些局限性。NICOM，一种完全无创之心输出量监测仪（Cheetah 医疗），可适当指导GDFT。目前尚没有前瞻性研究比较NICOM和EDM对GDFT的指导。我们假设，NICOM在指导GDFT中与EDM无显著差别。

方法: 100位成年择期结直肠手术患者参加了这项研究。在第一研究组中的患者（N=50）在术中GDFT由EDM引导，而NICOM被连接。在第二研究组中的患者（N=50）在术中GDFT由NICOM引导，而EDM被连接。用250毫升胶体每搏量进行优化。研究对两种测量方式的数据进行了比较；并对患者的治疗效果（术后疼痛，恶心，肠功能恢复），并发症（肾，肺，感染和伤口并发症）和住院时间（LOS）进行比较。

结果：使用增加10%心搏量液体优化后，两种测量方式的数据变化分别是5分钟60%，10分钟61%，15分钟66%，在任何时间点无显著系统性的分歧（McNemar P＞0.05）。相比NICOM，EDM有显著更多的丢失的数据，没有临床中发现总LOS或其他成果显著差异。平均住院天数分别为组一6.56±4.32天，组二6.07±2.85天，差异95%可信限分别为0.96至1.95天（P=0.5016）。

结论：NICOM在指导GDFT中与EDM相似，结果上没有显著临床差异，并且其使用方便且数据丢失较少。该NICOM可能是一个可选择的指导GDFT的监测方法。

（陈婉南译 薛张纲校）

**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 分级与其他术后 ICU 危险分层的联系**

The Association Between ASA Status and Other Risk Stratification Models on Postoperative Intensive Care Unit Outcomes

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**背景：**关于术后危险分层方法与 SICU 转归之间联系的文献报道较少。我们的假设主张常规的评估如 ASA 身体状态评估，美国心脏协会指南定义的外科风险，简易 SRCI 评分与 SICU 转归密切相关。

**方法：**我们用表格回顾了 2010 年 10 月 1 日至 2011 年 3 月 1 日进入 SICU 的病人。我们收集了病人一般情况和术后临床数据：年龄，性别，ASA 病人体质状况和手术风险评估，以及 SRCI 评分。结点数据包括我们初设的终结点、SICU 停留时间，以及第二终点：机械通气和血管活性药物使用时程，获得性器官功能障碍的数量，7 天内再入 ICU，SICU 内死亡，以及 30 天内死亡。我们应用回归分析和无参数统计，P 小于 0.05 表示有很大差异。

**结果：**我们一共监测了 239 名病人，其中有 220 名进入本研究组研究范围。病人的平均年龄为 58±16 岁。其中有 32% 的急症手术病人，5% 的 7 天内再入院至 SICU。SICU 死亡率为 3.2%，在 SICU 住院时间（2.9 ± 2.1 vs 5.9 ± 7.4, P = 0.007），呼吸机辅助通气（0.9 ± 2.0 vs 3.4 ± 6.8, P = 0.001）和基于 ASA 分级（≤ 2 vs ≥ 3）的获得性器官功能障碍数（0 [0-2] vs 1 [0-5], P < 0.001）等因素有显著差异。同 ASA 分级明显相关的混合因素：SICU 住院时间（意外发生比例 [IRR] = 1.79, 95% 置信区间 [CI], 1.35-2.39, P < 0.001），呼吸机辅助通气（IRR = 2.57, 95% CI, 1.69-3.92, P < 0.001），血管加压药物治疗（IRR = 3.57, 95% CI, 1.84-6.94, P < 0.001），获得性器官功能障碍数（IRR = 1.71, 95% CI, 1.46-1.99, P < 0.001），和再次收治 ICU（发生率= 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% 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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A novel method for ultrasound-guided radial arterial catheterization in pediatric patients.


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一种超声引导下儿科患者中桡动脉置管的新方法

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


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方法：评估的早期，我们对102名儿科患者进行了多因素Logistic回归分析。因变量包括首次尝试和整体的成功或失败；变量包括收缩压，体重，ASA分级，动脉直径和桡动脉皮下深度(<2, 2-4, ≥4 mm)。使用Kaplan-Meier曲线与对数秩和Dunn检验来评价动脉皮下深度对置管成功率的影响。然后我们评价了60名置管成功的患者。这些患者随机分为皮下注射生理盐水组和对照组，并且必要时，将动脉皮下深度从小于2毫米增加到2至4毫米。

结果：从多因素Logistic回归分析中得出：动脉皮下深度在2至4毫米之间是首次尝试和总体成功的重要独立预测因子。对数秩检测结果显示：动脉皮下深度2至4毫米这一组的穿刺置管时间显著短于其他两组(2-4 vs <2 mm组，P = 0.01而2-4 vs ≥4 mm组，P < 0.001)；并且首次尝试的成功率也较高(<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)。总体成功率也较高(<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)。皮下注射生理盐水使动脉深度从小于2毫米变为2至4毫米可以显著缩短穿刺置管时间(P=0.002)，提高首次尝试置管的成功率(注射生理盐水[85.0%] vs <2 mm [30.0%], P < 0.001)，以及总体成功率(注射生理盐水[90.0%] vs <2 mm [55.0%], P = 0.02)。

结论：当动脉皮下深度为2至4毫米时，儿科患者超声引导下桡动脉置管是一种快速可靠的方法。对于动脉位于皮下深度小于2毫米者，皮下注射生理盐水使之深度变为2至4毫米可以减少置管时间和提高成功率。

瑞芬太尼在未成熟发育的小鼠大脑上的抗细胞凋亡效果：一个活体外研究
The antiapoptotic effect of remifentanil on the immature mouse brain: an exvivo study

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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 glutamateergic 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.

在小鼠慢性挤压损伤模型中孟鲁司特减少神经疼痛通过抑制 P38 分裂素活化蛋白激酶和 KAPPA B 核因子

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.

超声引导下锁骨上臂丛神经阻滞:单次与三次注射技术在上肢动静脉瘘成形术的比较

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

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背景：虽然超声引导下锁骨上臂丛神经营阻具有良好的成功率，但目前尚不明确多次注射是否优于单次注射（SI）。因此我们比较了单次注射（SI）与三次注射（TI）的感觉阻滞成功率。

方法：在本项随机双盲研究中，将96例终末期肾病拟行动静脉瘘成形术的患者随机分组后，分别采用SI或TI方案进行神经阻滞。主要观察指标为注射5, 10, 15, 20分钟后，5条神经的感觉阻滞综合评分（正中神经，尺神经，桡神经，前臂内侧皮神经和肌皮神经）。次要观察指标是阻滞起效时间，操作时间（完成神经阻滞的时间），上述各神经的独立成功率，手术麻醉的成功率，及并发症发生率。
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.