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老年患者与年轻患者术中输血概率的对比

Odds of Transfusion for Older Adults Compared to Younger Adults Undergoing Surgery

Brown, Charles H. IV MD, MHS[*]; Savage, William J. MD, PhD[†]; Masear, Courtney G. MD[*]; Walston, Jeremy D. MD[‡]; Tian, Jing MS[§]; Colantuoni, Elizabeth PhD[§]; Hogue, Charles W. MD[*]; Frank, Steven M. MD[*]

Anesthesia & Analgesia 2014 118 1168–1178

背景：最近的随机对照实验发现：相对于血红蛋白更低的患者，对围术期血红蛋白大于 10g/ dL 的患者输血并无益处，甚至老年患者亦如此。然而相对于年轻患者，外科医生选择给老年患者输血更随意。老年患者围术期输血概率是否较年轻患者更高并未确定。此项研究的目的是确定围术期老年患者输血的概率是否比年轻患者更高。

方法：在一个三级医疗中心进行了此项回顾性、观察队列研究，纳入了 2010 年 1 月至 2012 年 2 月期间在该中心做过外科手术的住院病人。通过多层多变量逻辑回归分析的方法，并校正了并发症、外科水平、住院期间最低血红蛋白值、性别和术中估测失血量因素和外科医生和手术综合分析，来比较大于 65 岁患者与更年轻患者输血概率的差异。

结果： 在这个分析中纳入了 20930 个患者。在校正并发症发生率、外科种类、估测外科失血量和住院期间最低血红蛋白值差异后，并以外科医生和手术类型作为随机因素的多层分析模式中，大于 65 岁患者的输血概率比年轻患者高 62%（比值比为 1.62，95%可信区间为 1.40-1.88；P<0.0001）。当把病人按住院期间最低血红蛋白值分层时（7.00–7.99, 8.00–8.99, 9.00–9.99,以及大等于 10.00 g/dL），每层中患者输血概率随着年龄增加（每十岁）而增加，住院期间最低血红蛋白不低于 10.00 g/dL 的患者除外。当比较年轻和年老患

者输血概率时，可以观察到外科种类方面的显著差异（P=0.02）而非麻醉专业差异（P=0.9）。

结论：尽管缺乏证据支持老年患者输血应有更高的血红蛋白触发值，但老年患者围术期接受红细胞输注概率比年轻患者更高。需要进一步研究确定老年患者的输血实践是否是一种改善血液管理的教育机遇。

（边文玉 译 陈杰 校）

BACKGROUND: Recent randomized controlled trials have shown no benefit for transfusion to a hemoglobin >10 g/dL compared with lower hemoglobin thresholds in the perioperative period, even among older adults. Nevertheless, physicians may choose to transfuse older adults more liberally than younger adults. It is unclear whether older patients have higher odds than younger patients of being transfused in the perioperative period. Our objective in this study was to determine whether the odds of transfusion are higher in older patients than in younger patients in the perioperative period.

METHODS: We conducted this retrospective observational cohort study at a tertiary care academic medical center. We included adults who had undergone a surgical procedure as an inpatient at our institution from January 2010 to February 2012. The primary analysis compared the odds of transfusion for patients >65 years old with the odds of transfusion in younger patients based on multilevel multivariable logistic regression analyses including adjustment for comorbidities, surgical service, lowest in-hospital hemoglobin value, gender, and estimated surgical blood loss and accounted for clustering by the surgeon and procedure.

RESULTS: We included 20,930 patients in this analysis. In multilevel models adjusted for comorbidities, surgical service, estimated surgical blood loss, and lowest in-hospital hemoglobin value, with surgeon and procedure as random effects, patients >65 years old had 62% greater odds (odds ratio, 1.62; 95% confidence interval, 1.40–1.88; P < 0.0001) of being transfused than did younger patients. When patients were stratified by lowest in-hospital hemoglobin (7.00–7.99, 8.00–8.99, 9.00–9.99, and ≥10.00 g/dL), the odds of transfusion generally increased with each additional decade of age in every stratum, except for that containing patients in whom the lowest in-hospital hemoglobin did not decrease below 10 g/dL. When the odds of transfusion were compared between younger and older patients, significant differences were observed among surgical services (P = 0.02) but not among anesthesia specialty divisions (P = 0.9).

CONCLUSIONS: Older adults have greater odds of receiving red blood cell transfusion in the perioperative period than do younger patients, despite the lack of evidence supporting higher hemoglobin triggers in elderly patients. Further research is needed to determine whether transfusion practice in the elderly is an opportunity for education to improve blood management.

关注儿童行扁桃体切除术后因睡眠呼吸暂停而导致的死亡或神经损伤：休斯敦，我们有麻烦了！

Death or Neurologic Injury after Tonsillectomy in Children with a Focus on Obstructive Sleep Apnea: Houston, We Have a Problem!

Coté, Charles J. MD[*]; Posner, Karen L. PhD[†]; Domino, Karen B. MD, MPH[†]

Anesthesia & Analgesia 2014 118 1276–1283

背景：在美国，肥胖是种流行病，因此阻塞性睡眠呼吸暂停（OSA）的发病率也随之增长。阿片药物敏感性和最近扁桃体切除术后死亡相关的证据是促成开展本次对所有儿科麻醉学会成员调查儿童行扁桃体切除术后发生不良事件的原因。

方法：共有 2377 名儿科麻醉协会成员收到电子调查表。另外也获得了美国麻醉医师协会的结案诉讼数据。扁桃体切除(伴或不伴有腺样体切除)术中或术后发生的不良事件均纳

入。通过既往有 OSA 病史或之后通过美国麻醉医师协会的 OSA 临床指南确认儿童是否存在 OSA 风险。对比率和连续变量分别采用 Fisher 精确检验和 t 检验方法比较存在风险的儿童和其他儿童之间的区别。

结果：调查回收到的 731 份回复中共有 129 例得到确认，其中 92 例数据齐全符合纳入标准。另外 45 例美国麻醉医师协会已结案诉讼数据中有 19 例数据齐全得到确认。最终共有 111 例纳入最后分析。共有 86 例（占 77%）死亡或永久性神经损伤分别发生于手术中、麻醉恢复室、病房和家中。63 位患儿（57%)符合美国麻醉医师协会的 OSA 风险标准。存在 OSA 风险的患儿相较其他儿童，肥胖和患有其他合并疾病概率更高(P < 0.0001)。风险患儿发生窒息的比例较高(P = 0.016)，反之 其他患儿不良事件中出血占的比例较高 (P = 0.006)。

结论：儿童扁桃体切除术后发生窒息相关的死亡和神经损伤表明：如果在恢复期第一、二阶段以及术后第一天夜间采用了呼吸监测，至少 16 名患儿能得到及时救助。需要一个有效的专业儿科风险评分系统协助判断患儿是否有 OSA 风险，以免被当做一个普通日间患者处理。

（陆秉玮 译 陈杰 校）

BACKGROUND: Obesity is epidemic in the United States and with it comes an increased incidence of obstructive sleep apnea (OSA). Evidence regarding opioid sensitivity as well as recent descriptions of deaths after tonsillectomy prompted a survey of all members of the Society for Pediatric Anesthesia regarding adverse events in children undergoing tonsillectomy.

METHODS: An electronic survey was sent to 2377 members of the Society for Pediatric Anesthesia. Additionally, data from the American Society of Anesthesiologists Closed Claims Project were obtained. Adverse events during or after tonsillectomy with or without adenoidectomy in children were included. Children at risk for OSA were identified as either having a positive history for OSA or a post hoc application of the American Society of Anesthesiologists OSA practice guidelines. These children were compared with all other children by Fisher exact test for proportions and t test for continuous variables.

RESULTS: A total of 129 cases were identified from the 731 replies to the survey, with 92 meeting inclusion criteria for having adequate data. Another 19 cases with adequate data were identified from the 45 from the American Society of Anesthesiologists Closed Claims Project. A total of 111 cases were included in the final analysis. Death and permanent neurologic injury occurred in 86 (77%) cases and were reported in the operating room, postanesthesia care unit, on the ward, and at home. Sixty-three (57%) children fulfilled American Society of Anesthesiologists criteria to be at risk for OSA. Children categorized as at risk for OSA were more likely than other children to be obese and to have comorbidities (P < 0.0001). A larger proportion of at risk children had the event attributed to apnea (P = 0.016), whereas all others had a larger proportion of events attributed to hemorrhage (P = 0.006).

CONCLUSIONS: Deaths or neurologic injury after tonsillectomy due to apparent apnea in children suggest that at least 16 children could have been rescued had respiratory monitoring been continued throughout first- and second-stage recovery, as well as on the ward during the first postoperative night. A validated pediatric-specific risk assessment scoring system is needed to assist with identifying children at risk for OSA who are not appropriate to be cared for on an outpatient basis.

一个通用的丙泊酚药代动力学模型

A General Purpose Pharmacokinetic Model for Propofol

Eleveld, Douglas J. PhD[*]; Proost, Johannes H. PhD[*]; Cortínez, Luis I. MD[†]; Absalom, Anthony R. MD[*]; Struys, Michel M. R. F. MD[*‡]

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背景:药代动力学(PK)模型被用于预测术中使用不同输注方案得到的药物浓度及计算靶控输注系统中的输注速率。对丙泊酚而言，文献中可查到的 PK 模型主要是由特定的患者群体或麻醉技术发展而来的，在不同病人和临床条件下该模型的精确性并未确定。本研究目的是确定一个对于不同患者和多种临床条件下有着强大预测能力的 PK 模型。

方法:汇总并分析了先前发表的 21 个丙泊酚资料集，数据包含了幼儿、儿童、成人、老年及肥胖个体。将体重、年龄、性别和病人状态作为协变量，使用 NONMEM 软件来估计一个三室异速生长模型。设计出一个术中环境相关的预测性能度量，并结合赤池信息准则来指导模型开发。

结果：数据集包括来自 660 位个体(年龄分布范围 0.25-88 岁;体重分布范围 5.2-160kg)的 10927 个药物浓度观察值。最终模型用体重、年龄、性别和患者 vs 健康志愿者作为协变量。对于一位 35 岁 70kg 的男性患者估计参数为：V1, V2, V3, CL, Q2 和 Q3 分别为 9.77, 29.0, 134 L, 1.53, 1.42, 和 0.608 L/min。预测性能优于或类似于专业模型，即使是这些模型衍生出的亚群。

结论：本研究已制定出一个通用的丙泊酚 PK 模型，适于广泛的患者群体和多种临床条件。但需要对其进一步的前瞻性评估。

（梁玉丹 译 陈杰 校）

BACKGROUND: Pharmacokinetic (PK) models are used to predict drug concentrations for infusion regimens for intraoperative displays and to calculate infusion rates in target-controlled infusion systems. For propofol, the PK models available in the literature were mostly developed from particular patient groups or anesthetic techniques, and there is uncertainty of the accuracy of the models under differing patient and clinical conditions. Our goal was to determine a PK model with robust predictive performance for a wide range of patient groups and clinical conditions.

METHODS: We aggregated and analyzed 21 previously published propofol datasets containing data from young children, children, adults, elderly, and obese individuals. A 3-compartmental allometric model was estimated with NONMEM software using weight, age, sex, and patient status as covariates. A predictive performance metric focused on intraoperative conditions was devised and used along with the Akaike information criteria to guide model development.

RESULTS: The dataset contains 10,927 drug concentration observations from 660 individuals (age range 0.25–88 years; weight range 5.2–160 kg). The final model uses weight, age, sex, and patient versus healthy volunteer as covariates. Parameter estimates for a 35-year, 70-kg male patient were: 9.77, 29.0, 134 L, 1.53, 1.42, and 0.608 L/min for V1, V2, V3, CL, Q2, and Q3, respectively. Predictive performance is better than or similar to that of specialized models, even for the subpopulations on which those models were derived.

CONCLUSIONS: We have developed a single propofol PK model that performed well for a wide range of patient groups and clinical conditions. Further prospective evaluation of the model is needed.

麻醉工作站自动检测程序在监测和处理呼吸回路梗阻方面表现各异

Automated Checkout Routines in Anesthesia Workstations Vary in Detection and Management of Breathing Circuit Obstruction

Dosch, Michael P. CRNA PhD

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虽然罕见，但麻醉呼吸系统梗阻可造成灾难性的后果。本研究在三个当前主流麻醉工作站模拟呼吸回路系统中呼气和吸气端闭塞的情况： AISYS，ADU（包括通用电气医疗集团，麦迪逊威斯康星州）和阿波罗（德尔格医疗，德福，PA）。然后开启每个麻醉机特定的自动检测程序。AISYS 允许用户接受故障，并同时启动模拟患者监护;在 ADU 和阿波罗上则无。用户必须意识到如何测试回路呼吸阻塞，以及他们自己的设备是否能在自动化检测中表现正常。

（林甲票 译 陈杰 校）

While rare, anesthesia breathing system obstruction can have devastating consequences. We created simulated occlusions of the expiratory and inspiratory limb of the circle breathing system in 3 current anesthesia workstations; Aisys, ADU (both by GE Healthcare, Madison WI), and Apollo (Draeger Medical, Telford, PA). The automated electronic checkout specific to each machine was then performed. The Aisys allowed users to accept both faults and initiate simulated patient care; the ADU and Apollo did not. Users must be aware of how to test for breathing circuit obstruction, and whether their own equipment does so adequately in the automated checkout.

苯二氮卓位点激动剂差异性改变大鼠杏仁核部位的乙酰胆碱释放

Benzodiazepine Site Agonists Differentially Alter Acetylcholine Release in Rat Amygdala

Hambrecht-Wiedbusch, Viviane S. PhD; Mitchell, Melinda F. BBA; Firn, Kelsie A. BS; Baghdoyan, Helen A. PhD; Lydic, Ralph PhD

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背景：苯二氮卓受体激动剂与 γ-氨基丁酸 A 型受体的苯二氮卓位点结合通过在杏仁核的作用减少焦虑和失眠。苯二氮卓位点激动剂的神经化学效应并未完全弄清。胆碱能神经传递调节杏仁核功能。本研究检验了关于苯二氮卓位点激动剂改变乙酰胆碱(ACh)在杏仁核释放的假说。

方法：利用微量透析和高性能液相色谱量化法定量测定 SD 大鼠(n = 33)的杏仁核释放的乙酰胆碱。在麻醉或非麻醉状态下，静脉给予咪达唑仑或右佐匹克隆(3mg/kg)前后测定 Ach 含量。比较林格氏溶液透析(对照)的异氟烷麻醉大鼠与包含(100μM)咪达唑仑、安定,右佐匹克隆或唑吡坦林格氏溶液透析的大鼠在透析期间释放乙酰胆碱的差异。

结果：未麻醉状态下，静脉注射咪达唑仑(−51.1%;P = 0.0029;95%可信区间(CI)−29.2% 73.0%)和右佐匹克隆(−39.6%;P = 0.0222;95%可信区间,−9.3% 69.8%)可使大鼠杏仁核内乙酰胆碱减少。麻醉状态下，静脉注射咪达唑仑(−46.2%;P = 0.0041;95%可信区间,−24.5% 67.9%)和右佐匹克隆(−34.0%;P = 0.0009;95%可信区间,−23.3% 44.7%)使大鼠杏仁核内乙酰胆碱减少；注射安定(43.2%,P = 0.0434;95%可信区间,2.1%到 84.3%)和右佐匹克隆(222.2%,P = 0.0159;95%可信区间,68.5%到 375.8%)可使大鼠杏仁核内乙酰胆碱增加。

结论：静脉注射咪达唑仑和右佐匹克隆使大鼠杏仁核内乙酰胆碱的释放减少。直接渗析到杏仁核可引起乙酰胆碱释放的增加(右佐匹克隆和安定)或无显著变化(咪达唑仑和唑吡坦)。这些 Ach 释放传递通路相关的差异性效应支持解释静脉给予咪达唑仑和右佐匹克隆引起杏仁核内乙酰胆碱的释放增加是杏仁核以外的神经系统所引发的。

（李峰日 译 陈杰 校）

BACKGROUND: Agonist binding at the benzodiazepine site of γ-aminobutric acid type A receptors diminishes anxiety and insomnia by actions in the amygdala. The neurochemical effects of benzodiazepine site agonists remain incompletely understood. Cholinergic neurotransmission modulates amygdala function, and this study tested the hypothesis that benzodiazepine site agonists alter acetylcholine (ACh) release in the amygdala.

METHODS: Microdialysis and high-performance liquid chromatography quantified ACh release in the amygdala of Sprague-Dawley rats (n = 33). ACh was measured before and after IV administration (3 mg/kg) of midazolam or eszopiclone, with and without anesthesia. ACh in isoflurane-anesthetized rats during dialysis with Ringer's solution (control) was compared with ACh release during dialysis with Ringer's solution containing (100 μM) midazolam, diazepam, eszopiclone, or zolpidem.

RESULTS: In unanesthetized rats, ACh in the amygdala was decreased by IV midazolam (−51.1%; P = 0.0029; 95% confidence interval [CI], −73.0% to −29.2%) and eszopiclone (−39.6%; P = 0.0222; 95% CI, −69.8% to −9.3%). In anesthetized rats, ACh in the amygdala was decreased by IV administration of midazolam (−46.2%; P = 0.0041; 95% CI, −67.9% to −24.5%) and eszopiclone (−34.0%; P = 0.0009; 95% CI, −44.7% to −23.3%), and increased by amygdala delivery of diazepam (43.2%; P = 0.0434; 95% CI, 2.1% to 84.3%) and eszopiclone (222.2%; P = 0.0159; 95% CI, 68.5% to 375.8%).

CONCLUSIONS: ACh release in the amygdala was decreased by IV delivery of midazolam and eszopiclone. Dialysis delivery directly into the amygdala caused either increased (eszopiclone and diazepam) or likely no significant change (midazolam and zolpidem) in ACh release. These contrasting effects of delivery route on ACh release support the interpretation that systemically administered midazolam and eszopiclone decrease ACh release in the amygdala by acting on neuronal systems outside the amygdala.

和复水化相比，脱水增强人体大脑疼痛诱发反应

Dehydration Enhances Pain-Evoked Activation in the Human Brain Compared with Rehydration

Ogino, Yuichi MD, PhD[*]; Kakeda, Takahiro RN, PHN, PhD[†]; Nakamura, Koji MD[‡]; Saito, Shigeru MD, PhD[*]

Anesthesia & Analgesia 2014 118 1317–1325

背景：脱水对于人脑组织及认知功能的负面影响已经有所报道。本研究检验了脱水情况对于疼痛阈值以及脑皮质中疼痛反应活动的影响，并与口服溶液复水化之后的功能性核磁共振做了比对。

方法：五名成年男性分别于不同的 2 天中入脱水与复水化组。各成员首日的身体情况均为随机。全员在两种情况下均经过了 12 小时禁食，之后用跑步机完成了 40min 的定量体能运动。复水化组，成员在测试日前一晚开始共服用口服溶液最多达 3000 毫升。体能运动后，于核磁共振扫描设备下，在受试者前臂内侧给予疼痛刺激（冷加压试验），并分析疼痛引起的大脑活动激活。

结果：在复水化当日，平均每位受试者服用了 2040 毫升口服溶液（从 1800-2500 毫升不等）。生理指标显示受试者经过体能训练脱水化后体重降低越明显，则其复水化后心率增加水平、鼓膜测温、尿比重也越高。受试者的数据显示受试者们反应在脱水化后感受到的口渴感比口服溶液复水化之后要更强烈，而饥饿、焦虑、情绪并未有显著不同。冷加压试验对疼痛相关的神经网络有着强烈的刺激，尤其是扣带前回、岛叶和丘脑。试验刺激在脱水化个体中的波峰群相比复水化个体更加明显，并伴随着疼痛阈值的下降（P=0.001）

结论：本研究发现说明脱水化将使机体对于疼痛刺激的大脑活动兴奋性增加，同时伴有口渴感的增强，而口服溶液能缓解口渴感，并降低大脑对于疼痛刺激的兴奋性。

（贺加贝 译 陈杰 校）

BACKGROUND: Negative effects of dehydration on the human brain and cognitive function have been reported. In this study, we examined the effects of dehydration on pain thresholds and

cortical activations in response to pain, compared with rehydration with an oral rehydration solution (ORS) by functional magnetic resonance imaging.

METHODS: Five healthy adult men were subjected to dehydration and rehydration on 2 different days. The condition on the first day was randomly assigned to each subject. They completed a 40-minute exercise protocol using a walking machine after 12 hours of fasting under both conditions. For rehydration, the subjects consumed up to 3000 mL ORS starting from the night before the test day. After exercise, a painful stimulus (cold pressor test) was applied to the subjects' medial forearm in a magnetic resonance imaging scanning gantry, and pain-evoked brain activation was analyzed.

RESULTS: On the rehydration day, each of the subjects consumed an average of 2040 mL (range; 1800–2500 mL) ORS. Physiological data revealed that subjects when dehydrated lost more weight from exercise than subjects when rehydrated had a larger heart rate increase, a higher tympanic temperature, and a higher urine osmolality. Subjective data revealed that the subjects reported significantly stronger thirst while dehydrated than while rehydrated with ORS, although the levels of hunger and anxiety and mood did not significantly differ between conditions. The cold pressor test robustly activated the pain-related neural network, notably the anterior cingulate cortex, insula, and thalamus. Such activations in the dehydrated subjects were greater than those in the rehydrated subjects in terms of peak and cluster, accompanied by a decrease in pain threshold ($P = 0.001$).

CONCLUSION: Our findings suggest that dehydration brings about increased brain activity related to painful stimuli together with enhanced thirst, whereas rehydration with ORS alleviates thirst and decreases brain activity related to painful stimuli.

小鼠鞘内注射 Myr-NR2B9c 肽通过干扰 NMDA 受体和 PSD-95 蛋白间作用减轻骨癌疼痛

Intrathecal Injection of the Peptide Myr-NR2B9c Attenuates Bone Cancer Pain Via Perturbing N-Methyl-D-Aspartate Receptor-PSD-95 Protein Interactions in Mice

Liu, Yue MD; Cui, Xinlong MD; Sun, Yu-E MD; Yang, Xuli MD; Ni, Kun MD; Zhou, Yu MD; Ma, Zhengliang MD, PhD; Gu, Xiaoping MD, PhD

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背景：N-甲基-D-天冬氨酸受体(NMDAR)性中枢致敏在癌症疼痛中具有重要作用。通过突触后 PSD-95 结合 NMDAR 亚单位 2B(NR2B)可偶联 NMDAR 激活细胞内酶如神经性一氧化氮合酶(nNOS)，激活下游信号通路并调节 NMDAR 稳定性，从而调控突触可塑性。本研究检测使用一种模拟肽是否影响脊髓内具有 NR2B 的 NMDAR 和 PSD-95 间的特殊作用，进而减轻骨癌相关的疼痛。

方法：骨肉瘤细胞被植入 C3H/HeJ 小鼠右股骨骨髓腔内诱发进展性骨癌相关性疼痛。Western blotting 检测脊髓内磷酸化 Tyr1472 NR2B、nNOS 和 PSD-95。并进一步调查鞘内注射竞争性破坏 NR2B 和 PSD-95 间作用的模拟肽 Myr-NR2B9c 对伤害性行为以及脊髓内与骨癌疼痛有关的磷酸化 Tyr1472 NR2B、nNOS 和 PSD-95 表达上调的影响。

结果：骨肉瘤细胞植入可诱发产生进展性骨癌相关性疼痛，并导致磷酸化 Tyr1472 NR2B、nNOS 和 PSD-95 表达显著上调。鞘内注射 Myr-NR2B9c 可减轻骨癌引起的机械性疼痛异常、温痛觉过敏，并降低磷酸化 Tyr1472 NR2B、nNOS 和 PSD-95 表达。

结论：鞘内注射 Myr-NR2B9c 可减轻骨癌相关性疼痛。脊髓 NR2B 细胞内摄作用和含有 NR2B 的 NMDAR 从下游 nNOS 信号活性分离可有助于 Myr-NR2B9c 的镇痛作用。此方法可能涉及与阻滞 NMDAR 相关的负性结果，可作为治疗骨癌疼痛的一种新方法。

（朱浩 译 陈杰 校）

BACKGROUND: N-methyl-D-aspartate receptor (NMDARs)-dependent central sensitization plays an important role in cancer pain. Binding of NMDAR subunit 2B (NR2B) by postsynaptic density protein-95 (PSD-95) can couple NMDAR activity to intracellular enzymes, such as neuronal nitric oxide synthase (nNOS), facilitate downstream signaling pathways, and modulate NMDAR stability, contributing to synaptic plasticity. In this study, we investigated whether perturbing the specific interaction between spinal NR2B-containing NMDAR and PSD-95, using a peptide-mimetic strategy, could attenuate bone cancer-related pain behaviors.

METHODS: Osteosarcoma cells were implanted into the intramedullary space of the right femurs of C3H/HeJ mice to induce progressive bone cancer-related pain behaviors. Western blotting was applied to examine the expression of spinal phospho-Tyr1472 NR2B, nNOS, and PSD-95. We further investigated the effects of intrathecal injection of the mimetic peptide Myr-NR2B9c, which competitively disrupts the interaction between PSD-95 and NR2B, on nociceptive behaviors and on the upregulation of phospho-Tyr1472 NR2B, nNOS, and PSD-95 associated with bone cancer pain in the spinal cord.

RESULTS: Inoculation of osteosarcoma cells induced progressive bone cancer pain and resulted in a significant upregulation of phospho-Tyr1472 NR2B, nNOS, and PSD-95. Intrathecal administration of Myr-NR2B9c attenuated bone cancer-evoked mechanical allodynia, thermal hyperalgesia, and reduced spinal phospho-Tyr1472 NR2B, nNOS, and PSD-95 expression.

CONCLUSIONS: Intrathecal administration of Myr-NR2B9c reduced bone cancer pain. Internalization of spinal NR2B and dissociation NR2B-containing NMDARs activation from downstream nNOS signaling may contribute to the analgesic effects of Myr-NR2B9c. This approach may circumvent the negative consequences associated with blocking NMDARs, and may be a novel strategy for the treatment of bone cancer pain.

超声引导下内收肌管连续阻滞用于全膝关节置换术：一项随机双盲实验

Continuous Ultrasound-Guided Adductor Canal Block for Total Knee Arthroplasty: A Randomized, Double-Blind Trial

Hanson, Neil A. MD[*]; Allen, Cindy Jo RN[*]; Hostetter, Lucy S. MD[†]; Nagy, Ryan MD[*]; Derby, Ryan E. MD, MPH[*]; Slee, April E. MS[‡]; Arslan, Alex BS[‡]; Auyong, David B. MD[*]

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背景：在减少全膝关节置换术患者术后疼痛方面，内收肌管阻滞已经展现了其潜力。然而没有任何随机对照研究评估在内收肌管中连续输注 0.2%罗哌卡因是否能减少阿片类药物的使用。本文假设连续内收肌管阻滞可以减少术后阿片类药物的使用。

方法：80 例初次行单侧全膝关节置换术患者随机接受超声引导下连续 0.2%罗哌卡因内收肌管阻滞或者接受假导管放置。术前所有患者都接受单次股神经阻滞和脊麻，这是本机构的一项标准麻醉方式。在调整基线后，协方差分析评价术后 48 小时累积 IV 吗啡消耗量。次要结果包括静息疼痛评分（numeric rating scale），术后 1 天和 2 天物理治疗时的疼痛高峰评分，股四头肌最大等长收缩，物理治疗时的走动距离，术后恶心、呕吐和对镇痛的满意度。

结果：80 名受试者被随机分配，76 名完成了协议研究。48h 累计吗啡消耗量（阻滞−对照）的最小均方差为−16.68mg（95%置信区间，-29.78- -3.59，P = 0.013）。两组 24h 和 48h（预测的股神经阻滞效应消失后）之间的吗啡使用总量也有不同，最小均方差为−11.17mg（95%可信区间：-19.93 至 2.42，P = 0.013）。ITT 分析类似于 PP 分析结果。功能结果显示在术后第 2 天，内收肌管导管组患者有更佳的股四头肌力量（P = 0.010）和更远的走动距离（P = 0.034）。

结论：在全膝关节置换术后第一个 48h，与使用安慰剂相比，使用连续内收肌管阻滞可减少阿片类药物使用。其它结果包括：在全膝关节置换术后，股四头肌力量，行走距离和疼痛评分都可以从内收肌管导管获益，但这一结果若要作为结论还需进一步研究。

（谈睛华 译 陈杰 校）

BACKGROUND: Adductor canal blocks have shown promise in reducing postoperative pain in total knee arthroplasty patients. No randomized, controlled studies, however, evaluate the opioid-sparing benefits of a continuous 0.2% ropivacaine infusion at the adductor canal. We hypothesized that a continuous adductor canal block would decrease postoperative opioid consumption.

METHODS: Eighty subjects presenting for primary unilateral total knee arthroplasty were randomized to receive either a continuous ultrasound-guided adductor canal block with 0.2% ropivacaine or a sham catheter. All subjects received a preoperative single-injection femoral nerve block with spinal anesthesia as is standard of care at our institution. Cumulative IV morphine consumption 48 hours after surgery was evaluated with analysis of covariance, adjusted for baseline characteristics. Secondary outcomes included resting pain scores (numeric rating scale), peak pain scores during physical therapy on postoperative days 1 and 2, quadriceps maximum voluntary isometric contraction, distance ambulated during physical therapy, postoperative nausea and vomiting, and satisfaction with analgesia.

RESULTS: Eighty subjects were randomized, and 76 completed the study per-protocol. The least-square mean difference in cumulative morphine consumption over 48 hours (block − sham) was −16.68 mg (95% confidence interval, −29.78 to −3.59, P = 0.013). Total morphine use between 24 and 48 hours (after predicted femoral nerve block resolution) also differed by least-square mean −11.17 mg (95% confidence interval,: −19.93 to −2.42, P = 0.013). Intention-to-treat analysis was similar to the per-protocol results. Functional outcomes revealed subjects in the adductor canal catheter group had better quadriceps strength (P = 0.010) and further distance ambulated (P = 0.034) on postoperative day 2.

CONCLUSIONS: A continuous adductor canal block for total knee arthroplasty reduces opioid consumption compared with that of placebo in the first 48 hours after surgery. Other outcomes including quadriceps strength, distance ambulated, and pain scores all show benefit from an adductor canal catheter after total knee arthroplasty but require further study before being interpreted as conclusive.

单次低剂量地塞米松对围手术期患者血糖的影响（一项针对妇科手术患者的随机对照研究）

The effect of single low-dose dexamethasone on blood glucose concentrations in the perioperative period: a randomized, placebo-controlled investigation in gynecologic surgical patients.

Murphy GS1, Szokol JW, Avram MJ, Greenberg SB, Shear T, Vender JS, Gray J, Landry E.

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背景：单次低剂量地塞米松对围手术期患者血糖的影响至今尚未明确阐述。本研究我们在麻醉诱导期采取两种不同剂量的地塞米松（4mg 和 8mg）进行注射，并在注射后 24 小时内进行血糖监测。

方法：对 200 例女性患者进行随机分组，共 6 组：早期对照组（生理盐水）；早期试验组-4mg（4mg 地塞米松）；早期试验组-8mg（8mg 地塞米松）；晚期对照组（生理盐水）；晚期试验组-4mg（4mg 地塞米松）；晚期试验组-8mg（8mg 地塞米松）。对于早期研究组，血糖监测时间设在给药后 0h，1h，2h，3h 和 4h；对于晚期研究组，则设在给

药后 8h 和 24h。对于给药后发生高血糖患者要进行数量统计（高血糖定义为血糖浓度>180mg/ dL）。

结果：所有对照组和试验组的患者血糖浓度值均在围手术期出现明显增高（由血糖基础值 94mg/dL~102 mg/dL 增高到峰值 141mg/dL~161.5 mg/dL，P < 0.001）。不论给予地塞米松的剂量高低（4mg 或 8mg），在不同时间点测定对照组和试验组血糖后，结果未出现明显差异。此外，在早期组和晚期组发生高血糖的发生率也未出现明显差异（早期组：21%-28%, P = 0.807；晚期组：13%-24%, P = 0.552）。

结论：在围手术期给予单次低剂量地塞米松后，24 小时内患者血糖浓度并没有出现明显差异，故建议临床麻醉医生利用地塞米松预防患者恶心呕吐时，没有必要顾虑反应性高血糖。

（王嘉兴译 薛张纲校）

BACKGROUND: The effect of single low-dose dexamethasone therapy on perioperative blood glucose concentrations has not been well characterized. In this investigation, we examined the effect of 2 commonly used doses of dexamethasone (4 and 8 mg at induction of anesthesia) on blood glucose concentrations during the first 24 hours after administration.

METHODS: Two hundred women patients were randomized to 1 of 6 groups: Early-control (saline); Early-4 mg (4 mg dexamethasone); Early-8 mg (8 mg dexamethasone); Late-control (saline); Late-4 mg (4 mg dexamethasone); and Late-8 mg (8 mg dexamethasone). Blood glucose concentrations were measured at baseline and 1, 2, 3, and 4 hours after administration in the early groups and at baseline and 8 and 24 hours after administration in the late groups. The incidence of hyperglycemic events (the number of patients with at least 1 blood glucose concentration >180 mg/dL) was determined.

RESULTS: Blood glucose concentrations increased significantly over time in all control and dexamethasone groups (from median baselines of 94 to 102 mg/dL to maximum medians ranging from 141 to 161.5 mg/dL, all P < 0.001). Blood glucose concentrations did not differ significantly between the groups receiving dexamethasone (either 4 or 8 mg) and those receiving saline at any measurement time. The incidence of hyperglycemic events did not differ in any of the early (21%-28%, P = 0.807) or late (13%-24%, P = 0.552) groups.

CONCLUSIONS: Because blood glucose concentrations during the first 24 hours after administration of single low-dose dexamethasone did not differ from those observed after saline administrations, these results suggest clinicians need not avoid using dexamethasone for nausea and vomiting prophylaxis out of concerns related to hyperglycemia.

使用地塞米松预防术后恶心呕吐与肿瘤复发和高血糖：更多争议？

Cancer Recurrence and Hyperglycemia with Dexamethasone for Postoperative Nausea and Vomiting Prophylaxis: More Moot Points?

Colin, Brian MD; Gan, Tong J. MD, MHS, FRCA

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常规使用地塞米松来预防术后呕心呕吐（PONV），在麻醉医师和麻醉供应商之间争论了很多年。为什么？有明确的资料表明，地塞米松低价高效，是预防术后恶心呕吐的优选药物，被 PONV 共识指南所推荐。与可能是最常用的预防和治疗 PONV 的 5-HT-3 受体阻滞剂昂丹司琼相比较，预防 PONV 的需治疗指数为 4，而昂丹司琼为 6。理想的预防剂量是在麻醉诱导期以 4mg 静脉注射，但是，因为阿片类药物的封顶效应和短暂的恢复期，8mg 静脉注射能够产生额外的缓解疼痛的好处。

争论的原因在于地塞米松是糖皮质激素，用于围术期的患者时会产生令人担忧的副作用。这些顾虑包括伤口感染，伤口愈合，围术期出血，皮质醇抑制，神经肌肉无力，高血糖，甚至肿瘤复发。在本期的 Anesthesia & Analgesia，使用地塞米松的两个顾虑，类固醇激素与肿瘤复发和围术期高血糖的关系，都会讨论到。

糖皮质激素和它们在肿瘤患者的使用早已是围术期关注到的话题。手术切除是许多类肿瘤的确切治疗方法，肿瘤复发和转移性疾病是肿瘤手术患者死亡最重要的原因。围术期宿主防御的抑制，麻醉技术和药物选择，它们对宿主免疫的影响越来越受到关注。已经显示出地塞米松对 T 细胞功能和自然杀伤细胞的抑制，它们都参与了抗肿瘤免疫反应。尽管有这些发现，关于使用皮质醇激素和肿瘤复发的资料很少。

在这个问题上，De Oliveira 等发表了一个回顾性观察研究，分析了围手术期地塞米松 4~8mg 用于预防术后恶心呕吐对接受原发性卵巢肿瘤细胞减灭术的妇女对卵巢癌和卵巢癌的复发风险的影响。主要目的是通过对围手术期接受地塞米松和没有接受治疗的妇女相比较，卵巢癌复发的风险是否增加。在研究纳入的 260 例妇女中，178 例癌症复发，这些患者中的 102 例注射过地塞米松。这项研究最终发现在主要手术治疗后，围手术期使用地塞米松和卵巢癌复发之间没有显著的关联，因此不支持避免使用单剂量地塞米松预防术后恶心呕吐。有一些公认有缺陷的研究，如样本量小，缺乏术中和术后镇痛管理的规范化。这是特别重要的，因为一些研究表明，在围手术期使用阿片类药物可能对血管生成和癌症结果产生影响。已发现阿片样物质通过细胞增殖和细胞凋亡的调制的生长来调节肿瘤细胞；它们引起免疫抑制，以及调节血管形成，通过激活血管生长细胞受体如血管内皮生长因子和血小板衍生的生长因子来协助肿瘤的转移和生长。另一项研究提出的证据表明，阿片类药物通过 μ-阿片受体的相互影响可能对肺癌的进展有直接影响。单剂量地塞米松与癌症复发，在文献中，没有临床证据反驳上述结论。事实上，Egberts 等创建了一个动物模型，使用地塞米松能预防胰腺癌的复发和转移。Munstedt 等发现，化疗使用地塞米松并不影响卵巢癌的结果，但可能对骨髓有保护作用。

使用地塞米松经常受到关注的风险是术中和术后的高血糖，有一些以前的研究表明使用糖皮质激素引起短暂的血糖水平的升高。糖皮质激素已知会增加肝脏葡萄糖生成，同时增加胰岛素抵抗和降低葡萄糖的氧化和摄取。高血糖作的这些用可能与危重和术后病人的不良反应相关，如抑制免疫功能，增加促炎性细胞因子，增加全身血管阻力，渗透性利尿，电解质以及酸碱失衡。

IMurphy 等为解决这个问题进行了一个随机，安慰剂对照试验，以确定地塞米松用于妇科手术病人在围术期对血糖浓度的影响。主要的结果是在给予单次的低剂量地塞米松治疗（4 和 8 毫克）后，记录第一个 24 小时的血糖浓度和高血糖事件的发生率（血糖水平> 180 毫克/分升）。患者行子宫切除术，随机分为接受生理盐水，地塞米松 4 毫克，地塞米松 8 mg 三组，在围手术期 24 小时内的指定时间点为每个组测量血糖。该研究发现，尽管血糖浓度在对照组和地塞米松组均显著增加，但地塞米松组和生理盐水对照组之间在围术期 24 小时的任意时间点之间没有显著性差异。结论表明，围术期不应因考虑高血糖事件而避免给予低剂量地塞米松来预防术后的恶心呕吐。这一发现在其它文献中的证据得到支持。Abdelmalak 等人的一项研究表明，进行重大非心脏手术后，接受地塞米松 8 毫克组与安慰剂组均有较高的血糖水平，不管是糖尿病还是非糖尿病患者，其效果都是非常有限的。在一项类似研究中，Nazar 等调查了 40 例非糖尿病和 30 例 2 型糖尿病行腹腔镜胆囊切除术的患者。患者被随机分为生理盐水组和地塞米松 8 毫克组，结果表明，在使用地塞米松预防术后恶心呕吐后，2 型糖尿病患者围术期高血糖的敏感性不比非糖尿病患者高。

我们团队最近在本杂志发表了一篇编者按，名字为：使用地塞米松预防术后恶心呕吐和伤口并发症：一个有争议的问题？我们的结论是，目前的文献不支持如下观点：围术期单次剂量的地塞米松在统计学上显著增加伤口并发症的发生率和最终伤口愈合时间。这和使用单次剂量地塞米松预防术后恶心呕吐与肿瘤复发和术中高血糖进行的上述评估，再次表明麻醉医师能够安全的使用 4~8mg 的地塞米松预防术后恶心呕吐。

（吴赤译 薛张纲校）

The routine use of dexamethasone for the prophylaxis of postoperative nausea and vomiting (PONV) has been controversial and debated among anesthesiologists and anesthesia providers

for many years. Why is this? There are clear data to support that dexamethasone, with its relative low cost and high efficacy, is a preferred antiemetic for the prevention of PONV, as recommended by the PONV Consensus Guidelines. Compared with ondansetron, a 5-HT-3 receptor antagonist, which is likely the most commonly used antiemetic to prevent and treat PONV, the number needed-to-treat to prevent PONV for dexamethasone is 4, compared with 6 to 7 for ondansetron. The ideal prophylactic dosage appears to be 4 mg IV at induction of anesthesia; however, 8 mg IV may provide the additional benefit of pain relief because of opioid-sparing effects as well as shorten recovery time.

The reason for this controversy, of course, is that dexamethasone is a glucocorticoid with many feared side effects when used in the perioperative patient population. There have been concerns regarding the risk of wound infections, wound healing, perioperative bleeding, cortisol suppression, neuromuscular weakness, high blood glucose levels, and even cancer recurrence.In this issue of Anesthesia & Analgesia, 2 concerns of dexamethasone, the association with steroids and the recurrence of cancer, as well as the concern for the induction of perioperative hyperglycemia, are examined.

Glucocorticoids and their use in cancer patients have long been a topic of concern in the perioperative setting. Surgical excision is the primary definitive treatment for many forms of cancer, with tumor recurrence and metastatic disease being the most important cause of mortality in surgical cancer patients. The suppression of host defenses in the perioperative period, as well as the role of anesthetic techniques and drug choices, are becoming increasingly scrutinized regarding their effect on host immunity. Dexamethasone has been shown to suppress T cell function as well as natural killer cell development, both of which are known to participate in antitumor immune responses. Despite these findings, there are few data at this point regarding corticosteroid use and cancer recurrence.

In this issue, De Oliveira et al. present a retrospective observational study that analyzes the effect of perioperative systemic dexamethasone (4–10 mg) for PONV prophylaxis in women who underwent primary ovarian cytoreductive surgery for ovarian cancer and the risk of ovarian cancer recurrence. The primary aim was to determine the overall increase in the risk of ovarian cancer recurrence in these patients by determining tumor recurrence in women given perioperative dexamethasone versus those who did not receive the medication. Of 260 women included in the study, 178 had cancer recurrence; 102 of these patients received dexamethasone. The study ultimately found no significant association between perioperative dexamethasone use and ovarian cancer recurrence after primary surgical treatment and therefore does not support the avoidance of single-dose dexamethasone for PONV prophylaxis. There are some acknowledged weaknesses to the study, such as a small sample size and a lack of standardization of intraoperative and postoperative analgesic management. This is particularly important in that several studies have suggested that the use of opioids in the perioperative setting may have an effect on angiogenesis and cancer outcomes. Opioids have been found to regulate the growth of neoplastic cells through the modulation of cell proliferation and apoptosis; they cause immunosuppression, as well as modulate angiogenesis, aiding tumor metastasis and growth through activation of vascular growth cell receptors such as vascular endothelial growth factor and platelet derived growth factor. Another study presented evidence that opioids may have a direct effect on lung cancer progression through interaction with the μ-opioid receptor. In cancer recurrence from single-dose dexamethasone, there is no clinical evidence in the literature to refute the above findings. In fact, Egberts et al. created an animal model in which dexamethasone had utility in preventing the recurrence and metastasis of pancreatic cancer. A study by Munstedt et al. found that dexamethasone used along with chemotherapy did not affect ovarian cancer outcomes but may have protective effects on bone marrow.

Another often-touted risk of dexamethasone use is the concern for intraoperative and postoperative hyperglycemia, with several previous studies demonstrating a transient rise in glucose levels with the use of glucocorticoids. Glucocorticoids are known to increase hepatic glucose production, while increasing insulin resistance and decreasing glucose oxidation and

uptake. These hyperglycemic effects may be associated with adverse outcomes in the critically ill and postsurgical patients, such as suppression of immune function, increase in proinflammatory cytokines, increased systemic vascular resistance, osmotic diuresis, and electrolyte as well as acid–base imbalances.

Murphy et al. address this concern in this issue with a randomized, placebo-controlled trial to address the effect of dexamethasone on blood glucose concentration in the perioperative environment for gynecologic surgical patients. The primary outcome was to determine the effect of a single low-dose dexamethasone therapy (4 and 8 mg) on blood glucose concentrations during the first 24 hours following administration and to record the incidence of hyperglycemic events (blood glucose level >180 mg/dL). Patients presenting for elective hysterectomies were randomized to receive saline, dexamethasone 4 mg, or dexamethasone 8 mg, with blood glucose measurements at specified times for each group within a 24-hour perioperative period. The study found that while blood glucose concentrations increased significantly in all control and dexamethasone groups, they did not differ significantly between the dexamethasone and saline control groups at any time within the 24-hour perioperative period. Therefore, the results suggest that low-dose dexamethasone used for PONV prophylaxis should not be avoided because of concerns for hyperglycemic events. This finding is supported by other evidence in the literature. One study by Abdelmalak et al. showed that while patients undergoing major noncardiac surgery had higher blood glucose levels after receiving dexamethasone 8 mg versus placebo, the effect was very limited in both diabetic and nondiabetic patients. A similar study by Nazar et al. investigated a group of 40 nondiabetic and 30 type-2 diabetic patients undergoing laparoscopic cholecystectomy. Patients were randomized to receive either saline or dexamethasone 8 mg, and the results showed that there was no higher susceptibility in the type-2 diabetic patients than the nondiabetic patients to develop perioperative hyperglycemia following PONV doses of dexamethasone.

Our group recently wrote an editorial in this journal with the title: Wound complications with dexamethasone for postoperative nausea and vomiting prophylaxis: a moot point? We concluded that the current literature does not support the concern that single-dose use of intraoperative dexamethasone contributes to a statistically significant increase in the incidence of wound complications or time to complete wound healing. This, along with the above evaluations of the concerns of the use of single-dose dexamethasone for PONV and the recurrence of cancer or intraoperative hyperglycemia, suggest again that anesthesiologists can safely use dexamethasone 4 to 8 mg doses for PONV prophylaxis.

心脏外科病人中输注储存的同种异体血而非自体血回收后损伤红细胞的可塑性

Impaired Red Blood Cell Deformability after Transfusion of Stored Allogeneic Blood but Not Autologous Salvaged Blood in Cardiac Surgery Patients

Salaria, Osman N. MD; Barodka, Viachaslau M. MD; Hogue, Charles W. MD; Berkowitz, Dan E. MD; Ness, Paul M. MD; Wasey, Jack O. MD; Frank, Steven M. MD

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背景：心肺转流和红细胞长时间的储存都与红细胞结构、功能的损害性改变密切相关，进而影响组织氧运输。我们假设，在心外科病人中，红细胞的可塑性和聚集性受自体血回收的单一影响很小，但同种异体血输注起负面影响。

方法：在这项前瞻性队列研究中，32 位行心肺转流术的病人根据输血方式分为 3 组：单独输注自体血红细胞组（Auto，n=12），输注自体血红细胞和少量（<5 单位）同种异体血红细胞组(Auto+Allo min; n=10)，和输注自体血红细胞与中等量（>5 单位）同种异体血红细胞(Auto+Allo mod; n=10)。在术前、术中和术后 3 天分别利用激光衍射法检测红细胞的伸长指数（可塑性）和临界剪切应力（聚集性）。

结果：在 Auto 组，红细胞伸长指数和术前比并没有明显变化。在 Auto+Allo min 组，平均伸长指数从术前的 32.31 ± 0.02 下降为术后第 1 天的 30.47 ± 0.02(P = 0.003)。在 Auto+Allo mod 组，平均伸长指数从术前的 32.7 ± 0.02 下降为术后第 1 天的 28.14 ± 0.01。可塑性剂量依赖性的由术前向术后 3 天慢慢恢复。聚集性的变化在各组之间无差异，与输血类型无关。3 组的平均临界剪切应力从 359 ± 174 mPa 降为 170 ± 141 mPa（P = 0.01），手术结束时为最低，术后第 1 天又恢复为术前水平。

结论：在心脏外科病人中，输注同种异体血红细胞，而不是自体血红细胞，与红细胞细胞膜的可塑性降低呈剂量依赖性相关，并持续到术后三天。以上结果表明自体血红细胞比储存的红细胞质量更高，因为后者会导致所谓的储存损伤。

（吕越昌译 薛张纲校）

BACKGROUND: Both cardiopulmonary bypass (CPB) and red blood cell (RBC) storage are associated with detrimental changes in RBC structure and function that may adversely affect tissue oxygen delivery. We tested the hypothesis that in cardiac surgery patients, RBC deformability and aggregation are minimally affected by CPB with autologous salvaged blood alone but are negatively affected by the addition of stored allogeneic blood.

METHODS: In this prospective cohort study, 32 patients undergoing cardiac surgery with CPB were divided into 3 groups by transfusion status: autologous salvaged RBCs alone (Auto; n = 12), autologous salvaged RBCs + minimal (<5 units) stored allogeneic RBCs (Auto+Allo min; n = 10), and autologous salvaged RBCs + moderate (≥5 units) stored allogeneic RBCs (Auto+Allo mod; n = 10). Ektacytometry was used to measure RBC elongation index (deformability) and critical shear stress (aggregation) before, during, and for 3 days after surgery.

RESULTS: In the Auto group, RBC elongation index did not change significantly from the preoperative baseline. In the Auto+Allo min group, mean elongation index decreased from 32.31 ± 0.02 (baseline) to 30.47 ± 0.02 (nadir on postoperative day 1) (P = 0.003, representing a 6% change). In the Auto+Allo mod group, mean elongation index decreased from 32.7 ± 0.02 (baseline) to 28.14 ± 0.01 (nadir on postoperative day 1) (P = 0.0001, representing a 14% change). Deformability then dose-dependently recovered toward baseline over the first 3 postoperative days. Changes in aggregation were unrelated to transfusion (no difference among groups). For the 3 groups combined, mean critical shear stress decreased from 359 ± 174 mPa to 170 ± 141 mPa (P = 0.01, representing a 54% change), with the nadir at the end of surgery and returned to baseline by postoperative day 1.

CONCLUSIONS: In cardiac surgery patients, transfusion with stored allogeneic RBCs, but not autologous salvaged RBCs, is associated with a decrease in RBC cell membrane deformability that is dose-dependent and may persist beyond 3 postoperative days. These findings suggest that autologous salvaged RBCs may be of higher quality than stored RBCs, since the latter are subject to the so-called storage lesions.

合成大麻素 Ajulemic 酸对电压门控钠通道的阻滞

Inhibition of Voltage-Gated Na+ Channels by the Synthetic Cannabinoid Ajulemic Acid

Foadi, Nilufar MD*; Berger, Christian MD*; Pilawski, Igor VMD*; Stoetzer, Carsten MD*; Karst, Matthias MD*; Haeseler, Gertrud MD*; Wegner, Florian MD†; Leffler, Andreas MD*; Ahrens, Jörg MD*

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背景：合成大麻素 ajulemic 酸已被证实可以缓解患者慢性神经性疼痛。大麻素可与疼痛机制环路中数个分子相互作用，包括对电压门控钠通道的强效抑制作用。在本研究中，我们在神经细胞及非神经细胞钠通道中深入研究了这个特性。

方法：我们在体外研究了 ajulemic 酸对于内向钠离子电流的抑制作用。人胚胎肾 293t 细胞用于 Nav1.2, 1.3, 1.4, 1.5, 1.5N406K, 1.5F1760A 及 1.7 的表达系统。Nav1.8 仅短暂表达于 ND7/23 细胞中。Nav1.2, Nav1.3 及 Nav 1.8 来源于大鼠，Nav1.4, Nav1.5 及 Nav1.7 则来源于人。应用全细胞膜片钳技术进行钠离子电流的分析。研究中使用的 ajulemic 酸的浓度分别为 0.1, 0.3, 1, 3, 10 和 30 μmol/L。

结果：Ajulemic 酸浓度依赖性的可逆的抑制研究中观察的所有亚型的电压门控钠离子通道（Nav），包括 Nav1.2, 1.3, 1.4, 1.5, 1.7 和 1.8。对静息通道产生半数最大紧张性阻滞的浓度值在 2 到 9 μmol/L 之间，并且在失活通道中的阻滞作用增强，提示 ajulemic 酸的钠通道阻滞作用依赖于通道所处的功能状态。紧张性阻滞在分别在通道 Nav1.2 和 Nav1.3, Nav1.4 和 Nav1.5, 以及 Nav1.7 和 Nav1.8 的对比中并无显著性差异。通过方差分析对其它亚型组合（比如 Nav1.2 和 Nav1.4）的阻滞进行的统计分析结果差异有显著统计学意义。虽然我们并未研究任何相关的功能依赖性的阻滞，ajulemic 酸可引起电压依赖通道快速失活的强烈的超级化改变，以及缓慢失活的轻度超级化改变。对局麻药不敏感的 Nav1.5 构成 N406K 以及 F1760A，对 ajulemic 酸的阻滞作用表现出内在的敏感性。最后，我们发现低浓度的 ajulemic 酸可有效抑制 Nav1.5 中由 Navβ4 肽段介导的再生电流。

结论：我们的研究数据表明 ajulemic 酸可能通过阻滞钠离子通道的相关机制来缓解神经性疼痛。对于再生电流的强效的阻滞作用以及对局麻药不敏感通道的内在阻滞表明 ajulemic 酸与一些尚未被知晓的钠通道位点相互作用。

(杜芳译 薛张纲校)

BACKGROUND: The synthetic cannabinoid ajulemic acid has been demonstrated to alleviate pain in patients suffering from chronic neuropathic pain. Cannabinoids interact with several molecules within the pain circuit, including a potent inhibition of voltage-gated sodium channels. In this study, we closely characterized this property on neuronal and nonneuronal sodium channels.

METHODS: The inhibition of sodium inward currents by ajulemic acid was studied in vitro. Human embryonic kidney 293t cells were used as the expression system for Nav1.2, 1.3, 1.4, 1.5, 1.5N406K, 1.5F1760A, and 1.7; Nav1.8 was transiently expressed in ND7/23 cells. Nav1.2, Nav1.3, and Nav 1.8 were from rats, and Nav1.4, Nav1.5, and Nav1.7 were of human origin. Sodium currents were analyzed by means of the whole cell patch-clamp technique. The investigated concentrations of ajulemic acid were 0.1, 0.3, 1, 3, 10, and 30 μmol/L.

RESULTS: Ajulemic acid reversibly and concentration-dependently inhibited all voltage-gated sodium channel (Nav) isoforms investigated in this study, including Nav1.2, 1.3, 1.4, 1.5, 1.7, and 1.8. Tonic block of resting channels yielded half-maximal inhibitory concentration values between 2 and 9 μmol/L and was strongly enhanced on inactivated channels, suggesting state-dependent inhibition by ajulemic acid. Tonic block did not differ significantly when comparing Nav1.2 and Nav1.3, Nav1.4 and Nav1.5, and Nav1.7 and Nav1.8. Statistical analysis of other combinations of subunits (e.g., Nav1.2 and Nav1.4) by analysis of variance yielded a significant difference in block. Although we did not observe any relevant use-dependent block, ajulemic acid induced a strong hyperpolarizing shift of the voltage dependency of fast inactivation and modest shift of slow inactivation. The local anesthetic-insensitive Nav1.5 constructs N406K and F1760A displayed a preserved sensitivity to block by ajulemic acid. Finally, we found that low concentrations of ajulemic acid efficiently inhibited Navβ4 peptide-mediated resurgent currents in Nav1.5.

CONCLUSIONS: Our data suggest that block of sodium channels can be a relevant mechanism by which ajulemic acid alleviates neuropathic pain. The potent inhibition of resurgent currents and the preserved block on local anesthetic-insensitive channels indicates that ajulemic acid interacts with a conserved but yet unknown site of sodium channels.

可视喉镜辅助可弯曲气管镜对预测为困难气道的患者进行气管插管是否可行？一项前瞻性、随机临床试验

Is Video Laryngoscope-Assisted Flexible Tracheoscope Intubation Feasible for Patients with Predicted Difficult Airway? A Prospective, Randomized Clinical Trial

Lenhardt, Rainer MD[*†]; Burkhart, Mary Tyler MD[*]; Brock, Guy N. PhD[‡]; Kanchi-Kandadai, Sunitha MD[*]; Sharma, Rachana MD[*]; Akça, Ozan MD, FCCM[*†]

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背景：插管失败有可能会增加患者的发病率和死亡率。可视喉镜联合可弯曲气管镜相当于一个可弯曲的可视管芯，可以提高困难气道插管的成功率。我们通过研究检验了这种组合方法，发现这不仅易化了预测为困难气道的患者的气管插管，还可以缩短插管时间、减少插管尝试次数。

方法：我们随机、前瞻性地对 140 例行择期或急诊手术预期为困难气道的患者进行了试验。插入可视喉镜后，患者被随机分配到放置预成型管芯组（对照组）或可弯曲气管镜组（干预组）。研究主要观察的指标是插管成功的时间和气管插管尝试的次数。

结果：研究表明两组间需要 2 次或以上尝试插管次数的患者人数相似（对照组为 14%，干预组为 13%，P = 1.0）；两组间需要 3 次或以上尝试插管次数的患者人数没有显著差异（对照组为 8.6%，干预组为 1.4%，P = 0.12）。两组间插管时间的分布曲线也没有明显差异（对照组：中位数为 66 秒，四分位数间距 47-89 秒；干预组：中位数为 71 秒，四分位数间距 52-100 秒，P = 0.35）。在对照组中，4 例颈椎病患，在使用可视喉镜和硬质管芯尝试插管失败 3 次后，采用可视喉镜联合可弯曲气管镜插管成功。对于这 4 例患者，从决定改变插管方法至可弯曲气管镜成功插管用时为 36±14 秒。干预组中颈椎患者插管的总体成功概率为 100%（20/20），而对照组为 80%（16/20），95%置信区间分别为 1.4%和 44%，P = 0.04。

结论：对于预测为困难气道的患者，可弯曲气管镜辅助可视喉镜插管是仅使用可视喉镜的一个可行的替代方案。可弯曲气管镜联合可视喉镜还可能进一步增加明确有困难气道的择期手术患者气管插管的成功率，特别是当需要保持线性稳定时。

（江凌慧译 薛张纲校）

BACKGROUND: Failed intubation may result in both increased morbidity and mortality. The combination of a video laryngoscope and a flexible tracheoscope used as a flexible video stylet may improve the success rate of securing a difficult airway. We tested the hypothesis that this combination is a feasible way to facilitate intubation in patients with a predicted difficult airway in that it will shorten intubation times and reduce the number of intubation attempts.

METHODS: We conducted a randomized, prospective trial in 140 patients with anticipated difficult airways undergoing elective or urgent surgery. After insertion of video laryngoscope, patients were randomly assigned to either having their tube placed with the use of a preformed stylet (control group) or with a flexible tracheoscope (intervention group). The primary outcome measures were time to successful intubation and number of intubation attempts.

RESULTS: The number of intubations requiring 2 or more intubation attempts was similar in the 2 groups (14% control vs 13% intervention, *P* = 1.0); the number of patients requiring 3 or more intubation attempts was not significantly different (8.6% control vs 1.4% intervention, *P*= 0.12). Distribution for time to intubation also did not differ between the control (median of 66 seconds, interquartile range 47–89) and the intervention group (median of 71 seconds, interquartile range 52–100; *P* = 0.35). In the control group, 4 patients, all with cervical spine pathology, had the trachea intubated successfully with the video laryngoscope plus flexible tracheoscope after 3 failed attempts with video laryngoscope and rigid stylet. For these 4 patients, time from the decision to change the intubation method to successful intubation with a flexible tracheoscope was 36 ± 14 seconds. Overall success probability for cervical spine patients was

100% (20/20) in the intervention group and 80% (16/20) in the control group, with an exact 95% confidence interval for the difference of 1.4% to 44%, *P* = 0.04.

CONCLUSIONS: Flexible tracheoscope-assisted video laryngoscopic intubation is a feasible alternative to video laryngoscope only intubation in patients with predicted difficult airways. A flexible tracheoscope used in combination with video laryngoscope may also further increase the success rate of intubation in select patients with a proven difficult airway, particularly when in-line stabilization is required.

输血观念：面向外科病人及其麻醉和外科医生的一项调查

Perceptions about bloodtransfusion: a survey of surgicalpatients and their anesthesiologists and surgeons.

Vetter TR1,Adhami LF, Porterfield JR Jr, Marques MB.

From the Department of Anesthesiology, University of Alabama at Birmingham, Birmingham, Alabama.

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背景：虽然输血较常见并且是治疗外科失血的主要措施，但是患者及其医师可能会认为其有发生不良反应的风险。以患者为中心的医疗要求临床医生充分了解每位病人对输血的认识，并且将其纳入共同医疗决策内容中。

方法：患者在门诊进行常规术前评估时完成纸质问卷。同时该医疗机构中将为其实施麻醉和手术的医生在网上完成问卷。这两份问卷用于评估患者和医生对输血的认识，包括输血的整体风险、对输血的 5 项特定不良反应的担忧程度以及对这些不良反应的发生率的认识。组别差异用常规统计学进行计算。

结果：总共 294 位患者和 73 位医师完成问卷。在被调查的患者中 20%（95%可信区间 15%-25%）认为输血“很容易发生风险”或者“经常发生风险”。认为输血整体风险较大与非裔美国人（P=0.028）及受到高中及以下教育（P=0.022）有关。认为过敏反应（P = 0.001)）、发热(P < 0.001),和呼吸困难(P = 0.001)风险较大与非裔美国人有关。认为过敏反应（P = 0.009)）、发热(P=0.039)、呼吸困难(P = 0.004)、HIV/AIDS 和肝炎(P = 0.003)和医疗错误(P = 0.039)风险较大与受到高中及以下教育（P=0.022）有关。患者及医师问卷也有显著差异：医师比患者认为输血更有风险(P = 0.001)。

结论：尽管在美国和其他发达国家输血安全得到改善，但是本研究结果表明相当大比例的患者仍然认为输血具有较大的风险。而且患者和他们的麻醉医生/外科医生对输血相关风险和并发症的认识有较大差异。充分了解患者对输血的认识、识别那些认为输血风险忧虑较多的患者可以使专业医护人员在知情同意和建议患者输血时充分考虑个体患者的价值观、信仰、害怕或者担心，以求更好地处理风险。

(盖晓冬译 薛张纲校))

BACKGROUND: Although bloodtransfusion is a common therapeutic intervention and a mainstay of treating surgicalblood loss, it may be perceived by patients and their physicians as having associated risk of adverse events. Practicing patient-centered care necessitates that clinicians have an understanding of an individual patient's perceptions of transfusion practice and incorporate this into shared medical decision-making.

METHODS: A paper survey was completed by patients during routine outpatient preoperative evaluation. An online survey was completed by attending anesthesiologists and surgeons at the same institution. Both surveys evaluated perceptions of the overall risk of transfusions, level of concern regarding 5 specific adverse events with transfusion, and perceptions of the frequency of

those adverse events. Group differences were evaluated with conventional inferential biostatistics.

RESULTS:A total of 294 patients and 73 physicians completed the surveys. Among the surveyed patients, 20% (95% confidence interval, 15%-25%) perceived blood transfusions as "very often risky" or "always risky." Greater perceived overall bloodtransfusion risk was associated with African American race (P = 0.028) and having a high school or less level of education (P = 0.022). Greater perceived risk of allergic reaction (P = 0.001), fever (P < 0.001), and dyspnea (P = 0.001) were associated with African American race. Greater perceived risk of allergic reaction (P = 0.009), fever (P = 0.039), dyspnea (P = 0.004), human immunodeficiency virus/acquired immune deficiency syndrome and hepatitis (P = 0.003), and medical error (P = 0.039) were associated with having a high school or less level of education. Patients and physicians also differed significantly in their survey responses, with physicians reporting greater overall perceived risk with a bloodtransfusion (P = 0.001).

CONCLUSIONS: Despite improvements in bloodtransfusion safety in the United States and other developed countries, the results of this study indicate that a sizeable percentage of patients still perceive transfusion as having significant associated risk. Furthermore, patients and their anesthesiologists/surgeons differ in their perceptions about transfusion-related risks and complications. Understanding patients' perceptions of bloodtransfusion and identifying groups with the greater specific concerns will better enable health care professionals to address risk during the informed consent process and recommend blood management in accordance with the individual patient's values, beliefs, and fears or concerns.

注射 A 型肉毒素治疗颈部和肩胛带筋膜疼痛综合征的疗效观察

Botulinum Toxin Type A Injections for Cervical and Shoulder Girdle Myofascial Pain Using an Enriched Protocol Design

Nicol, Andrea L. MD, MS; Wu, Irene I. MD; Ferrante, F. Michael MD

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背景：肌筋膜疼痛综合症表现为局部肌肉疼痛和强直，其典型特征为存在受累肌肉组织的触发点。A 型肉毒素（BoNT-A）已被证实具有镇痛特性，并可诱导持续的肌肉松弛，因此 BoNT-A 比传统的治疗方案有更好的缓解疗效。我们旨在了解疼痛肌肉组织中直接注射 BoNT-A 是否对治疗颈部和肩胛带筋膜疼痛综合症有效。

方法：本研究按照严格精简设计标准纳入颈部和肩胛带筋膜疼痛综合症患者 114 例，接受 BoNT-A 注射并观察其对药物的反应。其中 54 例有反应者被纳入一项 12 周的随机、双盲、安慰剂对照的研究。基线资料记录疼痛评分和生活质量，常规随访至本研究结束后 26 周。

结果：相对于注射安慰剂的对照组，疼痛肌肉群中再次注射 BoNT-A 组患者可提高平均数值视觉疼痛评分(P = 0.019 [0.26, 2.78])。再次接受注射 BoNT-A 组患者每周出现头痛的比例减少(P = 0.04 [0.07, 4.55])。同时此组患者在平日活动和睡眠中的简明疼痛量表评分较安慰剂组有明显改善（P = 0.046 [0.038,3.700]，P=0.02 [0.37,4.33]）。

结论：在颈部和肩胛带筋膜疼痛患者的疼痛肌肉群中直接注射 BoNT-A 可提高平均疼痛评分和改善生活质量。

(郭宝磊译 薛张纲校)

BACKGROUND: Myofascial pain syndrome is a regional condition of muscle pain and stiffness and is classically characterized by the presence of trigger points in affected musculature. Botulinum toxin type A (BoNT-A) has been shown to have antinociceptive properties and elicit sustained muscle relaxation, thereby possibly affording even greater relief than traditional

strategies. Our goal was to determine whether direct injection of BoNT-A into painful muscle groups is effective for cervical and shoulder girdle myofascial pain.

METHODS: An enriched protocol design was used, wherein 114 patients with cervical and shoulder girdle myofascial pain underwent injection of BoNT-A to determine their response to the drug. Fifty-four responders were then enrolled in a 12-week, randomized, double-blind, placebo-controlled trial. Pain scales and quality of life measures were assessed at baseline and at routine follow-up visits until completion of the study after 26 weeks.

RESULTS: Injection of BoNT-A into painful muscle groups improved average visual numerical pain scores in subjects who received a second dose of BoNT-A compared to placebo (P = 0.019 [0.26, 2.78]). Subjects who received a second dose of BoNT-A had a reduced number of headaches per week (P = 0.04 [0.07, 4.55]). Brief Pain Inventory interference scores for general activity and sleep were improved (P = 0.046 [0.038, 3.700] and 0.02 [0.37, 4.33], respectively) in those who received a second dose of BoNT-A.

CONCLUSION: BoNT-A injected directly into painful muscle groups improves average pain scores and certain aspects of quality of life in patients experiencing severe cervical and shoulder girdle myofascial pain.

纳米麻醉：一项由磁石导向的经静脉给予含罗哌卡因纳米颗粒进行鼠踝关节阻滞的新技术

Nanoanesthesia: a novel, intravenous approach to ankle block in the rat by magnet-directed concentration of ropivacaine-associated nanoparticles.

Mantha VR[1], Nair HK, Venkataramanan R, Gao YY, Matyjaszewski K, Dong H, Li W, Landsittel D, Cohen E, Lariviere WR.

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背景：我们研究联合静脉注射含罗哌卡因的有磁性的纳米颗粒及踝部磁性导向进行鼠踝关节阻滞作为目前局部神经阻滞的替代方法的可行性。

方法：我们通过测量鼠足部对热刺激的撤药潜伏期来观察磁性导向的含罗哌卡因的磁性纳米颗粒的麻醉效果。含罗哌卡因的磁性纳米颗粒复合体由 0.7%罗哌卡因（重量/容积）和含 12%磁性物质（Fe3O4，重量/重量）的 0.8%磁性纳米颗粒（重量/容积）构成。我们在注射该复合体 15、30 及 60min 时对有磁性导向的右足及没有磁性导向的左足及传统应用 0.1%或 0.2%罗哌卡因进行的踝关节阻滞进行比较，并在 30min 时对单纯注射该复合体的右足与联合磁性导向的右足进行比较。另外，我们还测定了含罗哌卡因的磁性纳米颗粒复合体的药代动力学。

结果：与经过预处理的同侧足掌及没有磁性导向的对侧足掌相比较，静脉注射含罗哌卡因的磁性纳米颗粒联合足部磁性导向可显著增加足掌对热刺激的撤药潜伏期（p < 0.0001。磁性导向 30min 后踝部组织罗哌卡因绝对浓度及踝部组织/血浆浓度比例均高于单纯注射含罗哌卡因的磁性纳米颗粒复合体(均值 ± 标准差, 150 ± 10 ng/g vs 105 ± 15 ng/g 及 6.1 ± 0.8 vs 4.2 ± 0.7)。

结论：我们的研究表明通过静脉注射含罗哌卡因的磁性纳米颗粒复合体联合踝部磁性导向进行踝关节阻滞是可行的，并推荐对该方法进行深入研究。

（郝光伟译 薛张纲校）

BACKGROUND: As an alternative to current methods of local nerve block, we studied the feasibility of producing ankle block in the rat with IV injection of magnetic nanoparticles (MNPs) associated with ropivacaine and application of a magnet at the ankle.

METHODS: The anesthetic effect of magnet-directed ropivacaine-associated MNPs (MNP/Ropiv) was tested in the rat using paw withdrawal latencies from thermal stimuli applied to the hindpaw. The MNP/Ropiv complexes consisted of 0.7% w/v ropivacaine and 0.8% w/v MNPs containing 12% w/w magnetite (Fe3O4). The effect of IV injection of MNP/Ropiv with 15, 30, and 60-minute magnet application to the right ankle was compared with the effect without magnet application on the left hindpaw, to conventional ankle block with 0.1% or 0.2% ropivacaine, and to IV injection of MNPs alone with 30-minute magnet application to the right ankle. In addition, the pharmacokinetics of the MNP/Ropiv complexes were determined.

RESULTS: IV injection of MNP/Ropiv with magnet application at the ankle significantly increased paw withdrawal latencies from thermal stimuli compared with pretreatment baselines in the same paw ($P < 0.0001$) and compared with the contralateral paw without magnet application ($P < 0.0001$). IV injection of MNPs alone had no significant effect on paw withdrawal latency. Absolute ropivacaine concentrations in ankle tissue, and ankle tissue-to-plasma concentration ratios were higher in the MNP/Ropiv group with 30-minute magnet application compared with MNP/Ropiv group without magnet application (mean ± SEM, 150 ± 10 ng/g vs 105 ± 15 ng/g, respectively, and 6.1 ± 0.8 vs 4.2 ± 0.7, respectively).

CONCLUSIONS: The current study establishes proof of principle that it is possible to produce ankle block in the rat by IV injection of MNP/Ropiv complexes and magnet application at the ankle. The results indicate that further study of this approach is warranted.

地塞米松与卵巢癌复发有关吗？

Is Dexamethasone Associated with Recurrence of Ovarian Cancer?

De Oliveira, Gildasio S. Jr MD, MSCI[*†]; McCarthy, Robert PharmD[*]; Turan, Alparsalan MD[†]; Schink, Julian C. MD[‡]; Fitzgerald, Paul C. MS[*]; Sessler, Daniel I. MD[†]

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背景：基础科学研究表明在经过可能具有疗效的手术治疗后，围术期免疫损伤可能增加肿瘤复发的风险。尽管地塞米松具有免疫抑制的特性，但为了减少术后恶心呕吐的发生，地塞米松仍普遍应用于肿瘤患者。因此我们对围术期使用地塞米松增加卵巢癌复发风险的假设进行了验证。

方法：我们使用了由西北大学妇产科肿瘤部门建立的数据库，从中选取了 1997 年 1 月至 2007 年 10 月行原发性卵巢肿瘤细胞减灭术的女性患者。我们将肿瘤复发患者中围术期全身性使用地塞米松（4-10mg）与未使用地塞米松的患者进行比较。研究的主要终点是倾向性匹配到肿瘤复发的时间。复发被定义为癌抗原 125＞21 U/mL 或 CT 发现肿瘤组织并经过病理证实。我们使用了 10000 个样本的自助法来计算倾向性配对组间的差值中位数和 95%可信区间。

结果：260 名行原发性肿瘤细胞减灭术的卵巢癌女性患者符合入选标准，其中 102 名患者围术期全身性使用了地塞米松。178 名患者被发现肿瘤复发，肿瘤复发时间的总体未调整中位数（IQR）为 18（7-50）个月。87 例患者与 87 名对照患者进行倾向性匹配来调整混杂变量。经过倾向性匹配分组，地塞米松组复发时间的 IQR 为 23（6-46）个月，对照组为 18（8-53）个月（P=0.63），地塞米松组与对照组间复发时间的差值中位数（95%可信区间）为 5（-8 至 17）个月。

结论：我们并未发现围术期全身性使用地塞米松与原发性肿瘤细胞减灭术后卵巢癌复发之间有联系的证据。本研究结果不支持避免卵巢癌患者围术期使用低剂量地塞米松来预防术后恶心呕吐和疼痛。

（张怡译 李士通 审校）

BACKGROUND: Basic science studies suggest that perioperative immune impairment may augment the risk of cancer recurrence after otherwise potentially curative surgery. Despite its immunosuppressant properties, dexamethasone is commonly given to oncologic patients in an effort to reduce postoperative nausea and vomiting. We therefore tested the hypothesis that perioperative dexamethasone administration increases the risk of ovarian cancer recurrence.

METHODS: Women who had primary ovarian cytoreductive surgery between January 1997 and October 2007 were identified using a database maintained by the division of Gynecologic Oncology at Northwestern University. Tumor recurrence in women given perioperative systemic dexamethasone (4-10 mg) was compared with those who did not receive dexamethasone. The primary outcome was the propensity-matched time to cancer recurrence. Recurrence was defined by a carcinoantigen 125 >21 U/mL or computerized tomography evidence of the disease followed by tissue confirmation. Median difference and 95% confidence interval between the propensity-matched groups were calculated using a 10,000 sample bootstrap.

RESULTS: Among 260 women having primary cytoreductive surgery for ovarian cancer that met our inclusion criteria, 102 subjects were given perioperative systemic dexamethasone. Cancer recurrence was observed in 178 subjects, and the overall unadjusted median (IQR) time to recurrence was 18 (7-50) months. Eighty-seven cases and 87 controls were propensity matched to adjust for confounding covariates. After propensity matching the groups for confounding covariates, the median (IQR) time to recurrence in the dexamethasone group was 23 (6-46) compared with 18 (8-53) months in the control group (P = 0.63) with a median (95% confidence interval) difference of time to recurrence between the dexamethasone and the control group of 5 (-8 to 17) months.

CONCLUSION: We could not find evidence for an association between perioperative systemic dexamethasone administration and ovarian cancer recurrence after primary cytoreductive surgery. Our results do not support avoiding low-dose perioperative dexamethasone for prevention of postoperative nausea, vomiting, and pain in ovarian cancer patients.

亚临床的一氧化碳限制暴露于异氟烷的发育中大脑的凋亡。

Subclinical Carbon Monoxide Limits Apoptosis in the Developing Brain After Isoflurane Exposure

Cheng, Ying; Levy, Richard J. MD

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背景：挥发性麻醉药会造成广泛发育中大脑细胞凋亡。一氧化碳有抗凋亡特性。婴儿及儿童通常在低流量麻醉有呼出的内源性一氧化碳重复吸入，导致了亚临床的一氧化碳暴露。因此，我们旨在确定一氧化碳是否会限制异氟烷在发育中大脑的诱导细胞凋亡。

方法：将 7 天的雄性 CD-1 幼鼠暴露于含有 0，5 或 10ppm 一氧化碳的空气中，用含或不含 2%异氟醚处理 1h。我们评估碳氧血红蛋白水平，细胞色素 C 过氧化物酶活性及接触后前脑线粒体过氧化物 C 的释放，测量活化的 capspase-3 阳性细胞及皮质、海马和下丘脑/丘脑中的 TUNEL 阳性细胞核的数量。

结果：碳氧血红蛋白水平近似于人类暴露于一氧化碳相同时间。异氟烷显著增加暴露于空气中的大鼠的细胞色素 C 过氧化物酶的活性，细胞色素 C 的释放，活化的 caspase-3 阳性细胞及前脑中 TUNEL 阳性细胞核的数量。然而在同时暴露于异氟烷后，一氧化碳消除了异氟烷诱导的细胞色素 C 过氧化物酶活性及细胞色素 C 从前脑线粒体的释放，降低了活化的 caspase-3 阳性细胞及 TUNEL 阳性细胞核的数量。

结论：综上所诉，数据显示一氧化碳通过浓度依赖性抑制细胞色素 C 过氧化物酶来减少暴露于异氟烷后的细胞凋亡。尽管还不确定一氧化碳是否直接抑制异氟烷诱导的细胞凋亡，但设定低流量麻醉以达到重复吸入特定浓度的一氧化碳可能是防止麻醉药诱发的婴幼儿神经毒性的未来发展策略。

（邢怡安译 李士通 审校）

BACKGROUND: Volatile anesthetics cause widespread apoptosis in the developing brain. Carbon monoxide (CO) has antiapoptotic properties, and exhaled endogenous CO is commonly rebreathed during low-flow anesthesia in infants and children, resulting in subclinical CO exposure. Thus, we aimed to determine whether CO could limit isoflurane-induced apoptosis in the developing brain.

METHODS: Seven-day-old male CD-1 mouse pups underwent 1-hour exposure to 0 (air), 5, or 100 ppm CO in air with or without isoflurane (2%). We assessed carboxyhemoglobin levels, cytochrome c peroxidase activity, and cytochrome c release from forebrain mitochondria after exposure and quantified the number of activated caspase-3 positive cells and TUNEL positive nuclei in neocortex, hippocampus, and hypothalamus/thalamus.

RESULTS: Carboxyhemoglobin levels approximated those expected in humans after a similar time-weighted CO exposure. Isoflurane significantly increased cytochrome c peroxidase activity, cytochrome c release, the number of activated caspase-3 cells, and TUNEL positive nuclei in the forebrain of air-exposed mice. CO, however, abrogated isoflurane-induced cytochrome c peroxidase activation and cytochrome c release from forebrain mitochondria and decreased the number of activated caspase-3 positive cells and TUNEL positive nuclei after simultaneous exposure with isoflurane.

CONCLUSIONS: Taken together, the data indicate that CO can limit apoptosis after isoflurane exposure via inhibition of cytochrome c peroxidase depending on concentration. Although it is unknown whether CO directly inhibited isoflurane-induced apoptosis, it is possible that low-flow anesthesia designed to target rebreathing of specific concentrations of CO may be a desired strategy to develop in the future in an effort to prevent anesthesia-induced neurotoxicity in infants and children.

经食道超声心动图在 Mitraclip 术的应用

Transesophageal Echocardiography During MitraClip® Procedure

Guarracino, Fabio MD[*]; Baldassarri, Rubia MD[*]; Ferro, Baldassare MD[*]; Giannini, Cristina MD, PhD[†]; Bertini, Pietro MD[*]; Petronio, Anna Sonia MD[†]; Di Bello, Vitantonio MD[†]; Landoni, Giovanni MD[‡]; Alfieri, Ottavio MD[§]

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经皮二尖瓣（MV）修补程序与 MitraClip 输送系统越来越多地被用于治疗高危重度二尖瓣返流。治疗过程包括经皮插入和 MV 传单之间夹定位。经食管超声（TEE）起着关键的作用，在过程中提供关于夹导航信息，对 MV 接合线夹定位，系统的把握，单张二尖瓣进步，阀门组织捕捉确认，和最终结果的评价。实时三维 TEE 在经皮二尖瓣修复提供了两个心脏和血管内装置的高品质的可视化图像。通过三维 TEE 最佳的可视化是通过两个心房和心室方面获得的。在 MV 外科手术中， TEE 用于置换前的评估。而在 MitraClip 修复过程中必须要 TEE 的指导。心脏麻醉医师在手术中除了实施麻醉，还可以为介入心脏病学家提供更多的帮助用于指导 MV 修复。

（王晓莉 译，李士通 审校）

The percutaneous mitral valve (MV) repair procedure performed with the MitraClip delivery system is increasingly used to treat severe mitral regurgitation in high-risk patients. The treatment involves percutaneous insertion and positioning of a clip between the MV leaflets. Transesophageal echocardiography (TEE) plays a key role in the procedure by providing information regarding clip navigation, clip alignment to the MV coaptation line, transmitral advancement of the system, leaflet grasping, confirmation of valve tissue catching, and assessment of the final result. Real-time 3-dimensional TEE has increasing value in percutaneous MV repair providing high-quality visualization of both the heart and the intravascular devices. Optimal visualization by 3-dimensional TEE is obtained through both the atrial and ventricular aspects. In contrast to MV surgery, where TEE is involved in the prebypass assessment phase and in evaluation of the final repair, TEE is mandatory to guide management during MitraClip repair. Cardiac anesthesiologists may provide assistance to interventional cardiologists during the procedure itself in addition to their anesthetic-related tasks.

通过多感官知觉训练来提高麻醉医生对氧饱和度声响变化的敏感度

Improving Pulse Oximetry Pitch Perception with Multisensory Perceptual Training.

Schlesinger, Joseph J. MD; Stevenson, Ryan A. PhD; Shotwell, Matthew S. PhD; Wallace, Mark T. PhD

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为了提高患者的术中安全，脉搏氧饱和度已成为临床麻醉中的常规监测项目。在这里，我们给大家介绍一个视听训练课程，通过这个训练，麻醉医生可提升对指脉氧饱和度的监控能力。在知觉训练之前和之后，我们分别对 15 个麻醉科住院医师的听觉能力（通过感知氧饱和度音响变化来判断氧饱和度的变化）进行了测试。结果显示，在模拟的类似于手术室的嘈杂环境中，训练之后麻醉医生判断氧饱和度变化的准确性提高了 9%（95% 的可信区间, 4%-14%, P = 0.0004, t166 = 3.60）；判断的时间快了 72 毫秒（95% 的可信区间，40-103 毫秒, P < 0.0001, t166 = -4.52)。本研究阐明了多感官知觉训练的有益之处，从而为临床更好地定义多感官知觉训练奠定了基础。

（王慧娟 译 李士通 校）

The pulse oximeter is a critical monitor in anesthesia practice designed to improve patient safety. Here, we present an approach to improve the ability of anesthesiologists to monitor arterial oxygen saturation via pulse oximetry through an audiovisual training process. Fifteen residents' abilities to detect auditory changes in pulse oximetry were measured before and after perceptual training. Training resulted in a 9% (95% confidence interval, 4%-14%, P = 0.0004, t166 = 3.60) increase in detection accuracy, and a 72-millisecond (95% confidence interval, 40-103 milliseconds, P < 0.0001, t166 = -4.52) speeding of response times in attentionally demanding and noisy conditions that were designed to simulate an operating room. This study illustrates the benefits of multisensory training and sets the stage for further work to better define the role of perceptual training in clinical anesthesiology.

一项利用核磁共振成像技术反应口服营养补充剂和口服补液溶液对胃排空及糖原负荷影响的交叉研究

The Effects on Gastric Emptying and Carbohydrate Loading of an Oral Nutritional Supplement and an Oral Rehydration Solution: A Crossover Study with Magnetic Resonance Imaging

Nakamura, Makoto MD[*]; Uchida, Kanji MD, PhD[*]; Akahane, Masaaki MD, PhD[†]; Watanabe, Yasushi[†]; Ohtomo, Kuni MD, PhD[†]; Yamada, Yoshitsugu MD, PhD[*]

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背景：近日术前口服清亮液体成为了提高手术后转归的一种方法。一种复合电解质或蛋白质的糖原饮料可能对患者有好处。然而，这种饮料对患者胃储留，恶心呕吐和水合状态的影响并不明确。

方法：在给予 10 位健康的志愿者口服 500mL 含有 1.8%葡萄糖和电解质口服补液溶液（ORS）前后，我们通过核磁共振成像技术来评估不同时程的胃容量，并测量血糖水平。同样人数的受试者摄入 500mL 含 18%葡萄糖和精氨酸(545 mOsm/kg)的口服营养溶液（ONS）作为交叉对照组。

结果：口服溶液 1 小时以后 ORS 组的平均胃液量（中位数，95%可信区间）是 55.0 (55.3, 39.0-70.9) mL ，而 ONS 组是 409.2 (410.9, 371.4-447.0) mL ，(P = 0.0002)。摄入 90 分钟后 ORS 组所有受试者胃液量降至 1mL/kg 以下，而 ONS 组 120 分钟以后没有一位受试者降至 1mL/kg 以下。口服溶液后 ONS 组血糖水平持续性上升(30、60、120 分钟，P < 0.0001)，而 ORS 组仅初期有血糖升高(30 分钟 P < 0.0001, 60 分钟 P = 0.01, 120 分钟 P = 0.205)。

结论：含少量葡萄糖的 ORS 溶液胃排空较快，适合用于术前。虽然含有精氨酸的 ONS 溶液能维持高血糖水平，但相对渗透压较低，胃排空较慢。

（盛嘉君 译，李士通 审校）

BACKGROUND: Preoperative administration of clear fluids by mouth has recently been endorsed as a way to improve postoperative outcomes. A carbohydrate-containing beverage supplemented with electrolytes or proteins may have additional benefits for patients' satisfaction. However, effects on gastric residual, nausea, and emesis and the effectiveness of these beverages for improving patients' hydration status have not been well defined.

METHODS: We evaluated changes in gastric volume over time by magnetic resonance imaging, as well as blood glucose levels, before and after administration of 500 mL oral rehydration solution (ORS) containing 1.8% glucose and electrolytes in 10 healthy volunteers. The same volume of an oral nutritional supplement (ONS) containing 18% glucose and supplemental arginine (545 mOsm/kg) was given to the same population using a crossover design.

RESULTS: The mean (median, 95% confidence interval) gastric fluid volume at 1 hour after oral ingestion was 55.0 (55.3, 39.0-70.9) mL in the ORS group, whereas 409.2 (410.9, 371.4-447.0) mL in the ONS group (P = 0.0002). The gastric fluid volume of all participants in the ORS group returned to <1 mL/kg at 90 minutes after ingestion, whereas none reached <1 mL/kg at 120 minutes in the ONS group. The ONS group showed a sustained increase in the blood glucose level after ingestion (P < 0.0001 to baseline at 30, 60, 120 minutes), while the ORS group showed an initial increase (P < 0.0001, P = 0.01, P = 0.205 at each time point).

CONCLUSIONS: ORS supplemented with a small amount of glucose showed faster gastric emptying, which may make it suitable for preoperative administration. In contrast, ONS supplemented with arginine with a relatively low osmolality was associated with a longer time for gastric emptying, although it showed a sustained increase in blood glucose level.

长期存活的肝癌切除术后长期存活：与术后镇痛选择有关的潜在风险

Long-Term Survival after Resection of Hepatocelluar Carcinoma: A Potential Risk Associated with the Choice of Postoperative Analgesia

Cao, Longhui MD, PhD; Chang, Yi MD; Lin, Wenqian MD; Zhou, Jianhua MD, PhD; Tan, Hongying MD, PhD; Yuan, Yunfei MD, PhD; Zeng, Weian MD, PhD

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背景：麻醉管理与癌症复发或长期生存率之间相关关系仍不确定的。在这项研究中，我们比较了术后硬膜外吗啡镇痛与术后芬太尼静脉镇痛对行肝癌切除患者肿瘤复发和长期存活的影响。

方法：对本机构在 1997 年至 2007 年间行肝癌切除术的患者 1846 例进行回顾性队列研究进行。采用 Kaplan-Meiser 生存预测法评估复发率和长期生存率，使用多变量 Cox 风险回归进行比较并用倾向性评分进行调整。

结果：819 例患者符合纳入标准，随机分为 2 组：吗啡术后硬膜外镇痛的患者（EA，N = 451）和芬太尼术后静脉镇痛患者（IA，N = 368）。所有患者中位随访时间为 4.2 年（2-9）。硬膜外镇痛组癌症复发率（37.7%比 30.7%，P = 0.036）和死亡率（40.6%比 30.4%，P = 0.003）明显高静脉镇痛组。两组当中无复发生存率类似（风险比 2.224，95%可信区间为 0.207-23.893，P = 0.509）。采用多变量 Cox 比例风险回归分析显示，肝癌切除术后影响长期生存的独立风险因素包括： ASA 分级,肿瘤大小，术前 α 甲胎蛋白以及吗啡术后硬膜外镇痛。

结论：术后静脉芬太尼镇痛相比，硬膜外吗啡术后镇痛与肝癌切除患者的癌症复发率和死亡率增加有关，但对无复发生存率无显著影响。

（杨斌 译，李士通 审校）

BACKGROUND: Associations between anesthetic management and cancer recurrence or long-time survival remain uncertain. In this study, we compared the effects of postoperative epidural morphine analgesia with that of postoperative IV fentanyl analgesia on cancer recurrence and long-term survival in patients undergoing resection of hepatocellular carcinoma.

METHODS: A retrospective cohort study was performed on patients with hepatocellular carcinoma receiving hepatic resection at this institution (n = 1846, 1997-2007). Recurrence-free survival and long-term survival were assessed using Kaplan-Meier survival estimates and compared using a multivariate Cox proportional hazards regression, adjusted with propensity scores.

RESULTS: Eight hundred nineteen patients met the inclusion criteria and were divided into 2 groups: patients receiving postoperative epidural analgesia with morphine (EA, n = 451) and

patients receiving postoperative IV analgesia with fentanyl (IA, n = 368). The median time of follow-up for all patients was 4.2 years (2-9). The rates of recurrence of cancer (37.7% vs 30.7%, P = 0.036) and death (40.6% vs 30.4%, P = 0.003) were higher in the EA group versus IA group. Recurrence-free survival was similar in both the EA and IA groups (hazards ratio 2.224, 95% confidence interval, 0.207-23.893, P = 0.509). Using a multivariate Cox proportional hazards regression adjusted with propensity scores, independent risk factors for long-term survival in patients after resection of hepatocellular carcinoma were ASA physical status, tumor diameter, preoperative α-fetoprotein (+) as well as postoperative epidural analgesia with morphine.

CONCLUSION: Compared with postoperative IV analgesia with fentanyl, postoperative epidural analgesia with morphine was associated with increased cancer recurrence and death but had no significant effect on recurrence-free survival in patients undergoing resection of hepatocellular carcinoma.

姜黄素可减轻切口疼痛及增进功能恢复

Curcumin Treatment Attenuates Pain and Enhances Functional Recovery after Incision

Sahbaie, Peyman MD; Sun, Yuan MD, PhD; Liang, De-Yong PhD; Shi, Xiao-You MD; Clark, J. David MD, PhD

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背景：尽管阿片类药物、辅助药物及区域麻醉不断进步，仍有 20%～30%的患者术后发生中至重度疼痛。根据不同手术类型，10%～50%的患者术后持续性疼痛，而目前并没有建立预防方法。姜黄素（diferuloylmethane）是姜黄中的一种酚类成分，在东方传统医学中作为防腐剂，抗氧化剂，抗炎药，镇痛剂使用。它可能对治疗术后疼痛有效果。

方法：我们使用 C57BL / 6 小鼠后爪切口模型，记术后 7 天内对机械和热刺激的敏感度以及水肿程度和温度。条件性位置偏爱实验（CPP）用于评估切口自发痛，而多参数数字步态分析则评估步态功能的改变。

结果：姜黄素（50 mg/kg）显著降低后爪切口小鼠对机械和热的敏感性。姜黄素对基线疼痛阈值无影响。姜黄素也减轻后爪切口肿胀，提示其有抗炎效果。此外，围手术期姜黄素治疗减轻小鼠后爪切口用前列腺素 E2 所诱发的痛觉过敏。此外，CPP 提示对照组小鼠切口 48 小时后有自发疼痛，而姜黄素治疗小鼠无持续性疼痛。同时，小鼠后爪切口引发数个步态相关指数变化，但姜黄素治疗组小鼠正常。姜黄素治疗组小鼠在术后 1 至 3 天，体内早期痛觉免疫介质，包括白细胞介素（IL）-1β，IL-6，肿瘤坏死因子α和巨噬细胞炎性蛋白-1α，其围切口期水平没有减少甚至还增强了。相同条件下，抗炎细胞因子 IL-10 不变，而转化生长因子-β水平增强。

结论：我们的研究表明，姜黄素治疗有效缓解切口诱发的炎症，痛觉过敏，自发痛，和功能步态异常。转化生长因子-β水平增强提示了一种可能的机制。这些临床研究结果表明姜黄素可能用于预防治疗术后疼痛。

（魏薇 译，李士通 审校）

BACKGROUND: Acute pain after surgery remains moderate to severe for 20% to 30% of patients despite advancements in the use of opioids, adjuvant drugs, and regional anesthesia. Depending on the type of surgery, 10% to 50% of patients experience persistent pain postoperatively, and there are no established methods for its prevention. Curcumin (diferuloylmethane) is one of the phenolic constituents of turmeric that has been used in Eastern traditional medicine as an antiseptic, antioxidant, anti-inflammatory, and analgesic agent. It may be effective for treating postoperative pain.

METHODS: We used the hindpaw incision model with C57BL/6 mice. Sensitization to mechanical and thermal stimuli as well as effects on edema and temperature were measured up

to 7 days after surgery. Spontaneous pain after incision was assessed by using conditioned place preference (CPP), and alterations in gait function were assessed using multiparameter digital gait analysis.

RESULTS: Curcumin (50 mg/kg) significantly reduced the intensity of mechanical and heat sensitization after hindpaw incision in mice. No effects of curcumin on baseline nociceptive thresholds were observed. Curcumin also reduced hindpaw swelling after incision, suggesting an anti-inflammatory effect. In addition, perioperative curcumin treatment attenuated hyperalgesic priming due to incision when mice were subsequently challenged with hindpaw prostaglandin E2 application. Furthermore, while vehicle-treated mice had evidence of spontaneous pain 48 hours after incision in the CPP paradigm, no evidence of ongoing pain was observed in the mice treated with curcumin. Likewise, hindpaw incision caused changes in several gait-related indices, but most of these were normalized in the curcumin-treated animals. The peri-incisional levels of several pronociceptive immune mediators including interleukin (IL)-1β, IL-6, tumor necrosis factor α, and macrophage inflammatory protein-1α were either not reduced or were even augmented 1 and 3 days after incision in curcumin-treated mice. The anti-inflammatory cytokine IL-10 was unchanged, while transforming growth factor-β levels were enhanced under the same conditions.

CONCLUSIONS: Our studies suggest that curcumin treatment is effective in alleviating incision-induced inflammation, nociceptive sensitization, spontaneous pain, and functional gait abnormalities. Augmented transforming growth factor-β production provides one possible mechanism. These preclinical findings demonstrate curcumin's potential as a preventative strategy in postoperative pain treatment.

随机对照比较双注射法和定向丛内注射法超声引导下锁骨上臂丛神经阻滞

A randomized comparison between double-injection and targeted intracluster-injection ultrasound-guided supraclavicular brachial plexus block.

Techasuk, Wallaya MD; González, Andrea P. MD; Bernucci, Francisca MD; Cupido, Tracy DO, FRCPC; Finlayson, Roderick J. MD, FRCPC; Tran, De QH MD, FRCPC

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背景：在这项前瞻性、随机、观察者盲法的研究中，我们比较了双注射法（DI）超声引导下锁骨上臂丛神经阻滞和新的定向丛内注射法技术（TII），这项技术是将局麻药注射在神经束及其周围内（臂丛神经干和分支的汇集处）。

方法：90 个病人随机分为两组：DI 和 TII，每组 45 人，分别接受超声引导下锁骨上臂丛神经阻滞。所有病人局麻药均采用 1.5%利多卡因配伍 5 μg/ml 肾上腺素，用量均为 32 ml。两组病人都注射半量局麻药（16 ml）至主要的神经丛内，在 DI 组，另外半量局麻药注射在第一肋和锁骨下动脉交叉处，在 TII 组，余下半量局麻药等量注射到每个神经节。结果根据总的麻醉相关时间评估（总的操作时间和起效时间）。

结果：与 DI 组相比，TII 组麻醉起效时间更快（均数±标准差：10.1 ± 6.4 vs 18.5 ± 8.3 minutes; P < 0.0001),，总的麻醉时间也更短（(21.2 ± 7.7 vs 27.7 ± 9.0 minutes; P = 0.001，95%置信区间为 2.90-10.08 minutes)。TII 组没有失败病例，DI 组有三例失败。因此两组具有可比性。神经阻滞相关疼痛评分和不良反应事件在两组均没有组内差异。与 TII 组相比，DI 组需要更少的穿刺途径(平均数 ± 四分位距: 4 ± 2 vs 7 ± 3; P < 0.0001)和更短的穿刺时间(8.4 ± 2.9 vs 10.7 ± 2.7 minutes 以及操作时间(9.0 ± 3.2 vs 11.2 ± 3.0 minutes; P = 0.001)。

结论：虽然 DI 法和 TII 法超声引导下锁骨上臂丛神经阻滞似乎成功率相似，但是我们不排除有 17.9%的组内差异可能未被检测出。由于起效时间短，TII 技术可以提供更短的总麻醉相关时间。

（汤唯香 译，李士通 审校）

BACKGROUND: In this prospective, randomized, observer-blinded study, we compared double-injection (DI) ultrasound-guided supraclavicular block to a novel targeted intracluster-injection (TII) technique, whereby local anesthetic is injected inside the main and satellite neural clusters (confluences of trunks and divisions of the brachial plexus).

METHODS: Ninety patients were randomly allocated to receive a DI (n = 45) or TII (n = 45) technique for ultrasound-guided supraclavicular block. The local anesthetic drug (lidocaine 1.5% with epinephrine 5 μg/mL) and total volume (32 mL) were identical in all subjects. In both groups, half the volume (16 mL) was injected inside the main neural cluster. For the DI technique, the second half (16 mL) was deposited at the "corner pocket" (intersection of the first rib and subclavian artery). In contrast, for the TII technique, the remaining half was divided into equal aliquots and injected inside every single satellite cluster. The main outcome variable was the total anesthesia-related time (sum of performance and onset times).

RESULTS: Due to a quicker onset (mean ± standard deviation (SD): 10.1 ± 6.4 vs 18.5 ± 8.3 minutes; $P < 0.0001$), the total anesthesia-related time was shorter with the TII technique (21.2 ± 7.7 vs 27.7 ± 9.0 minutes; $P = 0.001$; 95% confidence interval for the difference of the means: 2.90-10.08 minutes). There were 0 (of 45) and 3 (of 45) surgical failures for the TII and DI group, respectively. Thus, the 2 methods achieved comparable rates of surgical anesthesia (93.3%-100.0%; 95% confidence interval for the difference of the success rates: -2.3% to 17.9%). No intergroup differences were observed in block-related pain scores and adverse events. The DI group required fewer needle passes (median ± interquartile range: 4 ± 2 vs 7 ± 3; $P < 0.0001$) as well as shorter needling (8.4 ± 2.9 vs 10.7 ± 2.7 minutes; $P < 0.0001$) and performance (9.0 ± 3.2 vs 11.2 ± 3.0 minutes; $P = 0.001$) times.

CONCLUSION: Although DI and TII ultrasound-guided supraclavicular blocks seem to provide comparable success rates, we cannot exclude the possibility that an intergroup difference of 17.9% might have gone undetected. Due to its quick onset, the TII technique results in a shorter total anesthesia-related time.