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### 手术前短期戒烟：一个进退两难的困境？

#### **Brief Preoperative Smoking Abstinence: Is There a Dilemma?**

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*Anesth Analg December 2011 113:1348-1351*

手术前短时间停止吸烟 (<8 周) 增加手术后肺部并发症，这种忧虑为干预手术病人对烟草的应用造成了障碍。我们表明了这种担心是如何来源于对最初的研究结果的错误解释，并且不管以后累积的证据，它仍然保留在医学文献中。未被证实的这种概念的持续性并不是不寻常的，并且可能会对医疗实践有明显的影响。尽管可能需要几个星期来从戒烟中取得对肺部的益处，对肺部并发症增加的恐惧不应该成为临床医生帮助病人在手术前的任何时间戒烟的障碍。

(黄丽娜 译 马皓琳 李士通 校)

The concern that stopping smoking shortly (<8 weeks) before surgery increases postoperative pulmonary complications poses a barrier to tobacco use interventions in surgical patients. We show how this concern arose from a misinterpretation of initial studies and has remained in the medical literature despite the accumulation of later evidence. The persistence of unsubstantiated concepts is not uncommon and can have a significant impact on medical practice. Although it may take several weeks to derive pulmonary benefit from quitting, fear of an increase in pulmonary complications should not be a barrier for clinicians to help their patients quit smoking at any time before surgery.

### 可乐定对血管 ATP 敏感性钾离子通道抑制作用的分子学机制

#### **Molecular Mechanisms of the Inhibitory Effects of Clonidine on Vascular Adenosine Triphosphate-Sensitive Potassium Channels**

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*Anesth Analg December 2011 113:1374-1380*

**背景：**我们研究了  $\alpha_2$  肾上腺素受体激动剂咪唑啉衍生物可乐定对大鼠的血管平滑肌细胞上的 ATP 敏感性钾离子 ( $K_{ATP}$ ) 通道和 COS-7 细胞上短暂表达的重组血管  $K_{ATP}$  通道的影响。

**方法：**我们使用膜片钳技术，研究了可乐定在以下 4 种类型受体上的作用：1、天然的血管  $K_{ATP}$  通道；2、由不同种类的内向整流钾通道(Kir6.0 家族: Kir6.1, 6.2)和

磺酰脲受体(SUR1, 2A, 2B)亚基不同组合组成的重组  $K_{ATP}$  通道；3、由 Kir6.2 亚基的缺失异构体(Kir6.2 $\Delta$ C36 通道)衍生成的 SUR 缺失型通道；4、ATP 敏感性降低的突变型 Kir6.2 $\Delta$ C36 通道 (Kir6.2 $\Delta$ C36-K185Q 通道)。

**结果：**可乐定( $\geq 3 \times 10^{-8}$  M)抑制天然的  $K_{ATP}$  通道活性，在细胞贴附式的结构中其半数最大抑制浓度为  $1.21 \times 10^{-6}$  M，在膜内侧翻外的结构中其半数最大抑制浓度为  $0.89 \times 10^{-6}$  M。在相近的效能下，可乐定 ( $10^{-6}$  或  $10^{-3}$  M) 同样抑制各种 SUR/Kir6.0 重组的  $K_{ATP}$  通道、Kir6.2 $\Delta$ C36 通道和 Kir6.2 $\Delta$ C36-K185Q 通道的活性。

**结论：**临床使用的可乐定浓度可以抑制血管平滑肌细胞中的  $K_{ATP}$  通道活性。这种抑制效应似乎与是其对 Kir6.0 亚基而非对 SUR 亚基作用的结果。

(刘伍 译 马皓琳 李士通 校)

**BACKGROUND:** We investigated the effects of the imidazoline-derived  $\alpha_2$ -adrenoceptor agonist clonidine on vascular adenosine triphosphate-sensitive potassium ( $K_{ATP}$ ) channel activity in rat vascular smooth muscle cells and recombinant vascular  $K_{ATP}$  channels transiently expressed in COS-7 cells.

**METHODS:** Using the patch-clamp method, we investigated the effects of clonidine on the following: (1) native vascular  $K_{ATP}$  channels; (2) recombinant  $K_{ATP}$  channels with different combinations of various types of inwardly rectifying potassium channel (Kir6.0 family: Kir6.1, 6.2) and sulfonylurea receptor (SUR1, 2A, 2B) subunits; (3) SUR-deficient channels derived from a truncated isoform of the Kir6.2 subunit (Kir6.2 $\Delta$ C36 channels); and (4) mutant Kir6.2 $\Delta$ C36 channels with diminished sensitivity to ATP (Kir6.2 $\Delta$ C36-K185Q channels).

**RESULTS:** Clonidine ( $\geq 3 \times 10^{-8}$  M) inhibited native  $K_{ATP}$  channel activity in cell-attached configurations with a half-maximal inhibitory concentration value of  $1.21 \times 10^{-6}$  M and in inside-out configurations with a half-maximal inhibitory concentration value of  $0.89 \times 10^{-6}$  M. With similar potency, clonidine ( $10^{-6}$  or  $10^{-3}$  M) also inhibited the activities of various recombinant SUR/Kir6.0  $K_{ATP}$  channels, the Kir6.2 $\Delta$ C36 channel, and the Kir6.2 $\Delta$ C36-K185Q channel.

**CONCLUSIONS:** Clinically relevant concentrations of clonidine inhibit  $K_{ATP}$  channel activity in vascular smooth muscle cells. This inhibition seems to be the result of its effect on the Kir6.0 subunit and not on the SUR subunit.

### 脑状态指数是否可以区分有意识和无意识的状态？

#### Does the Cerebral State Index Separate Consciousness from Unconsciousness?

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**背景：**脑状态监测 (CSM) 是一种基于脑电图 (EEG) 的监测，用于评估全麻时的镇静深度。我们计算了它用于区分不同麻醉方案的手术病人有意识和无意识状态能力的预期概率( $P_K$ )。

**方法：**我们将以前研究的 40 名没有术前用药进行择期手术全麻的成年病人的数字化 EEG 记录，用 EEG 播放器重新播放并用 CSM 对其再分析。病人被随机分成七氟醚-瑞芬太尼组和丙泊酚-瑞芬太尼组。研究设计包括慢速诱导和一次有意识地使病人苏醒。对失去和恢复意识时的 CSM 数值进行对比。通过失去和恢复意识前后 30 秒的 CSM 数值计算  $P_K$ 。

**结果：**有意识和无意识状态之间差别的  $P_K$  是  $0.75 \pm 0.03$  (平均值  $\pm$  标准误)。对于七氟醚-瑞芬太尼组  $P_K$  是  $0.71 \pm 0.04$ ，丙泊酚-瑞芬太尼组的  $P_K$  是  $0.81 \pm 0.03$ 。

**结论：**CSM 对于区分有意识和无意识状态的能力与其他商业上可用的以 EEG 为基础的参数相当。

(张怡译 马皓琳 李士通校)

**BACKGROUND:** The Cerebral State Monitor™ (CSM) is an electroencephalogram (EEG)-based monitor that is claimed to measure the depth of hypnosis during general anesthesia. We calculated the prediction probability ( $P_K$ ) for its ability to separate consciousness from unconsciousness in surgical patients with different anesthetic regimens.

**METHODS:** Digitized EEG recordings of a previous study of 40 nonpremedicated, adult patients undergoing elective surgery under general anesthesia were replayed using an EEG player and reanalyzed using the CSM. Patients were randomly assigned to receive either sevoflurane-remifentanyl or propofol-remifentanyl. The study design included a slow induction of anesthesia and an episode of intended wakefulness. CSM values at loss and return of consciousness were compared.  $P_K$  was calculated from values 30 seconds before and 30 seconds after loss and return of consciousness.

**RESULTS:** The  $P_K$  for the differentiation between consciousness and unconsciousness was  $0.75 \pm 0.03$  (mean  $\pm$  SE). For sevoflurane-remifentanyl,  $P_K$  was  $0.71 \pm 0.04$ . For propofol-remifentanyl,  $P_K$  was  $0.81 \pm 0.03$ .

**CONCLUSIONS:** The ability of CSM for separation of consciousness and unconsciousness was comparable to other commercially available EEG-based indices.

### 围术期药品短缺：对麻醉实践和病人安全的影响

#### Shortage of Perioperative Drugs: Implications for Anesthesia Practice and Patient Safety

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Anesth Analg December 2011 113:1429-1435;

最近，临床围术期使用的几种药物出现在国家紧缺药物名单上。药物的缺乏可能是因为原材料的缺乏，制造的问题和停止生产。用药短缺对病人的医疗护理产生重大影响，并且创造了一个更易于产生用药错误的环境。麻醉医师应该积极与药剂部门和医院管理部门配合，提醒医护人员，防止对病人的医疗护理和安全产生不良影响。

(安光惠译 马皓琳 李士通校)

Several medications used in clinical perioperative medicine are currently cited on the national shortage list. Medication shortages may be attributed to lack of raw materials,

manufacturing issues, and discontinuation of production. Medication shortage has a substantial impact on patient care, and is responsible for creating an environment conducive to an increase in medication errors. Anesthesiologists should be taking an active role with the pharmacy and hospital management to alert caregivers and help to prevent adverse effects on patient care and safety.

### 在产科麻醉里什么是新的？2011年 Gerard W. Ostheimer 讲座

#### **What's New in Obstetric Anesthesia? The 2011 Gerard W. Ostheimer Lecture**

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“产科麻醉里什么是新的”讲座由产科麻醉于围生医学协会始办于1975年，以更新其成员上一年的医学文献。在1995年这个讲座重新命名以纪念 Gerard W. Ostheimer，这位来自 Brigham 和女子医院的产科麻醉医师对产科麻醉知识和实践做出了显著贡献。Ostheimer 的讲座者综述了产科麻醉、产科、围生医学和健康服务方面的文献来确定与产科麻醉实践相关的文章。这篇综述总结了2010年文献中最相关的刊物。

（刘朝辉译，马皓琳，李士通校）

The “What's New in Obstetric Anesthesia” lecture was established by the Society for Obstetric Anesthesia and Perinatology in 1975 to update members on the preceding year's medical literature. In 1995, the lecture was renamed in honor of Gerard W. Ostheimer, an obstetric anesthesiologist from Brigham and Women's Hospital who contributed significantly to the knowledge and practice of obstetric anesthesia. The Ostheimer lecturer reviews the obstetric anesthesia, obstetric, perinatology, and health services literature to identify articles that are relevant to the practice of obstetric anesthesiology. This review summarizes the most relevant publications from the 2010 literature.

### 椎管内麻醉与全身麻醉技术在腹式子宫切除术后恢复质量及镇痛效果方面的比较：一项前瞻性、随机化对照试验

#### **The Effect of Neuraxial Versus General Anesthesia Techniques on Postoperative Quality of Recovery and Analgesia After Abdominal Hysterectomy: A Prospective, Randomized, Controlled Trial**

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**背景：**经历腹式子宫切除术的患者经常有明显的术后疼痛，即使同时使用多模式镇痛处理也不能缓解。与全身麻醉相比，椎管内麻醉有节省阿片类药物的作用，并

且可能使患者获得更好的术后恢复。本研究的主要目的是比较椎管内麻醉和全身麻醉对腹式子宫切除术后恢复质量的影响。

**方法：**本研究是一项前瞻性、随机化、对照的临床试验。招募了 70 名健康女性并随机分配以全身麻醉或椎管内麻醉技术为主要麻醉方案。主要观察指标是总体恢复质量——术后 24 小时 40 问卷法 (QoR-40)。其他收集的数据包括术后疼痛评分和阿片类药物的消耗量。用 Mann-Whitney *U* 检验、Fisher 精确检验和线性回归进行分析数据。 $P < 0.05$  被认为有统计学意义。

**结果：**椎管内麻醉组与全身麻醉组术后 24 小时总体 QoR-40 评分的差异中位数 (95% 可信区间) 为 17 (11-21.5) ( $P < 0.001$ )。椎管内麻醉组患者的各项 QoR-40 亚成分中的恢复质量评分均优于全身麻醉组 (所有  $P < 0.005$ )。椎管内麻醉组与全身麻醉组术后 48 小时总体 QoR-40 评分的差异中位数为 8 (6-10) ( $P < 0.001$ )。全身麻醉组术后阿片类药物的消耗量和疼痛评分高于椎管内麻醉组。术后 24 小时 ( $r^2 = 0.67 [P < 0.0001, 95\% \text{ 可信区间 } 0.77 - 0.51]$ ) 和 48 小时 ( $r^2 = 0.58 [P < 0.0001, 95\% \text{ 可信区间 } 0.72 - 0.42]$ ) 阿片类药物的消耗量与术后恢复质量均存在反线性关系。

**结论：**椎管内麻醉比全身麻醉使腹式子宫切除术后患者获得更好的恢复质量。椎管内麻醉的阿片类药物节省作用与术后患者恢复质量更好有关。如排除禁忌症，椎管内麻醉可能更适用于这些患者。

(陈彬彬译 马皓琳 李士通校)

**BACKGROUND:** Patients undergoing abdominal hysterectomy often have significant postoperative pain despite the use of concurrent multimodal pain strategies. Neuraxial anesthesia has opioid-sparing effects and may provide better postoperative recovery to patients when compared with general anesthesia. Our main objective in this study was to compare the effects of neuraxial and general anesthesia on postoperative quality of recovery after abdominal hysterectomy.

**METHODS:** The study was a prospective, randomized, controlled clinical trial. Seventy healthy females were recruited and randomized to a general anesthesia or neuraxial technique as their primary anesthetic regimen. The primary outcome was the global quality of recovery—40 questionnaire (QoR-40) at 24 hours after the surgical procedure. Other data collected included postoperative pain scores and opioid consumption. Data were analyzed using the Mann-Whitney *U* test, Fisher's exact test, and linear regression. A *P* value  $< 0.05$  was considered statistically significant.

**RESULTS:** The median difference (95% confidence interval [CI]) in the global QoR-40 score at 24 hours between the neuraxial and general anesthesia groups was 17 (11 to 21.5) ( $P < 0.001$ ). Patients in the neuraxial anesthesia group had better quality of recovery scores in all the QoR-40 subcomponents than did the general anesthesia group (all  $P < 0.005$ ). The median difference in global QoR-40 scores at 48 hours between the neuraxial anesthesia and the general anesthesia groups was 8 (6–10) ( $P < 0.001$ ). Postoperative opioid consumption and pain scores were higher in the general anesthesia group than in the neuraxial anesthesia group. There was an inverse linear relationship between opioid consumption and postoperative quality of recovery at 24 hours,  $r^2 = 0.67$  ( $P < 0.0001$ , 95% CI of 0.77 to 0.51), and at 48 hours,  $r^2 = 0.58$  ( $P < 0.0001$ , 95% CI of 0.72 to 0.42).

**CONCLUSION:** Neuraxial anesthesia provides better quality of recovery than does general anesthesia for patients undergoing abdominal hysterectomy. The opioid-sparing effects of neuraxial anesthesia were associated with a better quality of recovery in patients after the surgical procedure. In the absence of contraindications, neuraxial anesthesia seems to be a better anesthetic plan for those patients.

### 抑制小鼠脊髓神经元中的 KCC2 能导致对热刺激有超敏反应

#### **Inhibition of KCC2 in Mouse Spinal Cord Neurons Leads to Hypersensitivity to Thermal Stimulation**

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**背景：**KCC2 是特异性的神经元钾氯离子协同转运蛋白，是通过其影响脊髓神经元突触后抑制来参与疼痛知觉的生理。我们将一种新被鉴定的、非常强效的 KCC2 选择性抑制剂（D4）、有一个无活性的结构变异体（D4.14）和 Na-K-2Cl 协同转运蛋白（NKCC1）抑制剂布美他尼，注入小鼠的鞘内腔来监测它们对热诱发伤害性反应的影响。

**方法：**我们对商用鞘内导管进行了修改并通过手术放置到 2 组的 10 只小鼠中。手术恢复后，通过导管对这些小鼠注射 D4、D4.14 和布美他尼。注射每个测试药物后进行伤害性测量（热板法，甩尾法）并和媒介对照进行比较。

**结果：**每组中都有 2 只老鼠因为术后的并发症而被剔除。用 55°C 热板法进行测量结果显示，注射活性 KCC2 抑制剂后退缩潜伏期有统计学意义的显著性缩短（ $<0.01$ ），但注射无活性化合物后并没有变化（ $=0.78$ ）。在同一温度下注射布美他尼后退缩潜伏期显著延长（ $P=0.02$ ）。这些结果在 49°C 下用甩尾试验可以确认。

**结论：**用热板法和甩尾试验进行测试证实，通过 D4 抑制 KCC2 可导致小鼠热诱发的潜伏期缩短，而这两个伤害性试验都证实了布美他尼抑制 NKCC1 可导致对热刺激有反应的潜伏期延长。

（唐亮 译 马皓琳 李士通 校）

**BACKGROUND:** KCC2, a neuronal-specific K-Cl cotransporter, is involved in pain perception physiology through its effects on postsynaptic inhibition in spinal cord neurons. We injected a newly identified, highly potent and selective inhibitor of KCC2 (D4), an inactive structural variant (D4.14), and the Na-K-2Cl cotransporter (NKCC1) inhibitor, bumetanide, into the intrathecal space of mice to measure their effect on heat-evoked nociceptive responses.

**METHODS:** Commercially available intrathecal catheters were modified and surgically placed into 2 cohorts of 10 mice. After recovery from the procedure, the mice were injected with D4, D4.14, and bumetanide through this catheter. Nociceptive measurements (hotplate assay, tail flick assay) were performed after injection of each of the test drugs and compared with vehicle controls.

**RESULTS:** Two mice in each cohort were omitted because of postprocedure complications. There was a statistically significant decrease ( $P < 0.01$ ) in withdrawal

latency after injection of the active KCC2 inhibitor but not after injection of the inactive compound ( $P = 0.78$ ), as measured by hotplate assay at 55°C. Injection of bumetanide significantly increased withdrawal latency ( $P = 0.02$ ) at the same temperature. These results were confirmed using tail flick assays performed at 49°C.

**CONCLUSIONS:** Inhibition of KCC2 by D4 led to decreased heat-evoked withdrawal latency in mice, as measured by hotplate and tail flick assays, whereas inhibition of NKCC1 by bumetanide resulted in increased response latencies to heat stimuli as measured by both of these nociceptive tests.

### 综述：β-肾上腺素能受体生理及其反馈 β-受体阻滞剂的药物基因组学

#### Review Articles: Pharmacogenomics of β-Adrenergic Receptor Physiology and Response to β-Blockade.

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心肌 β-肾上腺素能受体 (βARs) 在变更心率、心肌收缩力及心肌舒张功能方面起了重要作用。激活 β1AR 与 β2AR 可增加环磷腺苷浓度，并通过级联反应产生心肌收缩；相反，激活 β3AR 却导致心肌收缩力下降。心衰患者由于 β1ARs 下调及 β3AR 活性与密度增高，导致环磷腺苷转化减少，心肌收缩力下降。βAR 拮抗剂常用于冠心病及心衰患者的一般治疗，但围术期是否使用仍存有争议。过去 20 年，β-受体阻滞剂的个体化反应一直为研究热点，除药代动力学、药效动力学及种族差异外，基因变异也在其中扮演了重要角色。单核苷酸多态性 (SNP) 是人类最常见的基因变异。与 β1AR 临床相关的 SNP 有 2 个 (Ser49Gly, Arg389Gly)，与 β2AR 相关的有 3 个 (Arg16Gly, Gln27Glu, Thr164Ile)，与 β3AR 相关的有 1 个 (Trp64Arg)。尽管结果存在争议，但大量研究数据普遍显示 βAR SNPs 与临床结局 (例如心衰、冠心病、血管反应性、高血压、哮喘、肥胖及糖尿病等疾病的临床进展) 间存在潜在联系。虽然 βAR SNPs 并不直接导致疾病发生，但其似乎是某些疾病及应激与药物反应的危险因素与修饰因子。相关围术期研究也已证实，具有 Arg389Gly β1AR 多态性的患者其甘氨酸存有变异，发生围术期不良事件的概率显著增高。当了解基因变异的重要性后，围术期药物使用可能从简单的治疗干预转变为更加个体化的肾上腺素能受体调节。

(范羽译 薛张纲校)

Myocardial β-adrenergic receptors (βARs) are important in altering heart rate, inotropic state, and myocardial relaxation (lusitropy). The β1AR and β2AR stimulation increases cyclic adenosine monophosphate concentration with the net result of myocyte contraction, whereas β3AR stimulation results in decreased inotropy. Downregulation of β1ARs in heart failure, as well as an increased β3AR activity and density, lead to decreased cyclic adenosine monophosphate production and reduced inotropy. The βAR antagonists are commonly used in patients with coronary artery disease and heart failure; however, perioperative use of βAR antagonists is controversial. Individual patient's response to beta-blocker therapy is an area of intensive research, and apart from pharmacokinetics, pharmacodynamics, and ethnic differences, genetic alterations have become more

important in the last 20 years. The most common genetic variants in humans are single nucleotide polymorphisms (SNPs). There are 2 clinically relevant SNPs for the  $\beta$ 1AR (Ser49Gly, Arg389Gly), 3 for the  $\beta$ 2AR (Arg16Gly, Gln27Glu, Thr164Ile), and 1 for the  $\beta$ 3AR (Trp64Arg). Although results are somewhat controversial, generally large datasets have the potential to show a relationship between  $\beta$ AR SNPs and outcomes such as development and progression of heart failure, coronary artery disease, vascular reactivity, hypertension, asthma, obesity, and diabetes. Although  $\beta$ AR SNPs may not directly cause disease, they appear to be risk factors for, and modifiers of, disease and the response to stress and drugs. In the perioperative setting, this has specifically been demonstrated for the Arg389Gly  $\beta$ 1AR polymorphism with which patients with the Gly variant had a higher incidence of adverse perioperative events. Knowing that genetic variants play an important role, perioperative medicine will likely change from simple therapeutic intervention to a more personalized way of adrenergic receptor modulation.

### 关于吗啡导致非小细胞肺癌的表皮生长因子途径激活的研究

#### Morphine-induced epidermal growth factor pathway activation in non-small cell lung cancer

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**背景：**表皮生长因子受体(EGFR)和  $\mu$ -型阿片受体(MOR)表达于非小细胞型肺癌(NSCLC)细胞和人类肺癌上，共同被激动。我们假设临床上使用阿片类药物，它是 MOR 激动剂且同时激活 EGFR，可促进生长及存活的信号传导。

**方法：**我们用 H2009，一种人类腺癌 NSCLC 细胞系，有组成性 EGFR 磷酸化作用，通过逆转录酶聚合酶链反应增加了 H2009 上  $\mu$ -型和  $\delta$ -型阿片受体的表达。我们运用 Western 蛋白印迹法，生物复合体细胞活素磁珠试验，免疫荧光染色，BrdU 结合酶联免疫吸附法，和 BioCoat™ Matrigel™ 侵入试验分别检验细胞信号，细胞活素的表达，人类肺癌上 MOR 和 EGFR 的荧光定位分析，及细胞增殖与侵犯。

**结果：**类似于 EGF，吗啡刺激 H2009 细胞上的 EGFR 的磷酸化作用，蛋白激酶 B，和 MAPK/ERK。OR 拮抗剂，纳洛酮，EGFR 络氨酸激酶抑制剂，埃罗替尼，MOR 和  $\delta$ -型阿片受体沉默使吗啡和 EGF 诱导的信号磷酸化作用消失，意味着 OR 共激活 EGFR。与 Beas2B 上皮细胞相比，H2009 细胞最主要分泌高水平细胞活素。意味着 H2009 细胞上分泌的细胞活素可能与 OR 的表达增加有关系。我们观察了人类 NSCLC 组织的 EGFR 和 MOR 的荧光定位分析。功能上，吗啡和上皮生长因子诱导 H2009 细胞增值和入侵，可以像埃罗替尼一样被纳洛酮逆转。

**结论：**吗啡通过 ORs 使 EGFR 磷酸化，导致瀑布式下游的 MAPK/ERK，Akt 磷酸化，细胞增殖和入侵。特别是，ORs 也与上皮因子诱导的 EGFR 的磷酸化有关系。人类肺癌 MOR 和 EGFR 共表达的增加表明吗啡也许有促生长作用。

(侯文婷译 薛张纲校)

**BACKGROUND:**Epidermal growth factor receptor (EGFR) is coactivated by the  $\mu$ -opioid receptor (MOR), expressed on non-small cell lung cancer (NSCLC) cells and human lung cancer. We hypothesized that clinically used opioid analgesics that are MOR agonists coactivate EGFR, resulting in growth- and survival-promoting signaling.

**METHODS:**We used H2009, a human adenocarcinoma NSCLC cell line, with constitutive EGFR phosphorylation, which showed increased expression of MOR and the  $\delta$ -opioid receptor by reverse transcriptase polymerase chain reaction. We used Western immunoblotting, magnetic bead-based Bio-Plex cytokine assay, immunofluorescent staining, BrdU incorporation enzyme-linked immunosorbent assay, (ELISA)and BioCoat™ Matrigel™ invasion assay to examine cell signaling, cytokine expression, colocalization of MOR and EGFR in human lung cancer, and cell proliferation and invasion, respectively.

**CONCLUSION:**Morphine-induced phosphorylation of EGFR occurs via ORs, leading to downstream MAPK/ERK, Akt phosphorylation, cell proliferation, and increased invasion. Notably, ORs are also associated with EGF-induced phosphorylation of EGFR. Increased coexpression of MOR and EGFR in human lung cancer suggests that morphine may have a growth-promoting effect in lung cancer.

**RESULTS:**Similar to epidermal growth factor (EGF), morphine stimulated phosphorylation of EGFR, Akt/protein kinase B (Akt), and mitogen-activated protein kinase/extracellular signal regulated kinase (MAPK/ERK) signaling in H2009 cells. Opioid receptor (OR) antagonist, naloxone, EGFR tyrosine kinase inhibitor, erlotinib, and silencing of MOR and  $\delta$ -opioid receptor abrogated morphine- and EGF-induced phosphorylation of signaling, suggestive of OR-mediated coactivation of EGFR. H2009 cells secreted significantly higher levels of cytokines compared with control Beas2B epithelial cells. H2009-conditioned medium stimulated MOR expression in Beas2B cells, suggesting that cytokines secreted by H2009 may be associated with increased OR expression in H2009. We observed colocalization of EGFR and MOR, in human NSCLC tissue. Functionally, morphine- and EGF-induced proliferation and invasion of H2009 cells was ameliorated by naloxone as well as erlotinib.

**一种未经校正的脉搏波形测量心排量的方法在主动脉内球囊反搏患者中的应用**

**An uncalibrated pulse contour method to measure cardiac output during aortic counterpulsation.**

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**背景：**无创监测系统，如脉搏波形法等，正越来越多地应用于估测心排量。然尔主动脉内球囊反搏可能会使动脉血压的波形产生诸多变异从而影响由脉搏波形估测

心排量的准确性。MostCare系统是一种由未经校准的脉搏波形估测心排量的方法。我们的研究将心衰并接受主动脉内球囊反搏患者中MostCare系统的结果与间断地热稀释法测得的心排量进行比较，从而探讨MostCare系统的可信度如何。

**方法：**研究包含了15名冠状动脉搭桥术后需要主动脉内球囊反搏进行血流动力学支持的患者。放置肺动脉导管并且通过热稀释法测量心排量(ThD-CO)。MostCare系统直接连接在标准监护系统中，并通过桡动脉压力波形计算出心排量(MostCare-CO)。数据采集自三种不同的主动脉内球囊反搏比(1:1, 1:2, 1:4)以及移除球囊后。

**结果：**本次研究共分析了106对ThD-CO和MostCare-CO数据。ThD-CO与MostCare-CO之间具有良好的相关性( $r=0.90$ , 95%可信区间为0.86-0.93;  $P<0.001$ )。经过重复测量得到的平均心排量测量的误差为-0.2L/min(-1.31至0.91L/min, 下限的95%可信区间为-1.72至-0.9; 上限的95%可信区间为0.5至1.32)，相对比百分比误差为24。在不同主动脉内球囊反搏的设定频率下，ThD-CO与MostCare-CO之间的结果非常一致。心排量的变化分别由2种不同方法进行计算。数据结果显示相关性达到0.82(95%可信区间为0.76-0.87;  $P<0.001$ )平均误差为0.14L/min(-1.31至1.59L/min, 下限95%可信区间为-1.62至-1.0; 上限95%可信区间为1.28至1.90)。

**结论：**MostCare系统可以在主动脉内球囊反搏的患者中监测心排量，并且结果可与热稀释法相媲美。球囊充气 and 放气所产生的动脉形态变化对MostCare系统并无显著影响。

(黄剑译 薛张纲校)

**BACKGROUND:** Less-invasive monitoring systems, such as pulse contour methods, are increasingly being used to estimate cardiac output (CO). However, alterations in the arterial waveform caused by intraaortic balloon pump counterpulsation may affect the ability of pulse contour algorithms to determine CO. We investigated the reliability of an uncalibrated pulse contour method, the MostCare system, in patients with cardiac failure receiving intraaortic balloon pump counterpulsation by comparing its measurements of CO with those determined by an intermittent thermodilution method.

**METHODS:** The study included 15 patients requiring hemodynamic support with an intraaortic balloon pump after coronary artery bypass graft surgery. A pulmonary artery catheter was inserted and CO was determined by bolus thermodilution (ThD-CO). The MostCare device was directly connected to the standard monitoring system for analysis of the radial artery pressure wave and computation of CO (MostCare-CO). Data were collected at 3 different intraaortic balloon pump rates (1:1, 1:2, 1:4) and after intraaortic balloon pump removal.

**RESULTS:** One hundred six pairs of ThD-CO and MostCare-CO measurements were analyzed. There was a good correlation between ThD-CO and MostCare-CO ( $r = 0.90$ , 95% confidence interval [CI] = 0.86-0.93;  $P < 0.001$ ). The mean bias of all CO measurements corrected for repeated measures was -0.2 L/min with limits of agreements of -1.31 to 0.91 L/min (lower 95% CI, -1.72 to -0.90; upper 95% CI, 0.50-1.32) and a relative percentage error of 24. There were close agreements between ThD-CO and MostCare-CO at the different intraaortic balloon pump rate settings. Changes in CO were calculated separately for the 2 methods and data comparison showed a correlation of 0.82 (95% CI = 0.76-0.87;  $P < 0.001$ ) and a mean bias of 0.14 L/min with limits of agreement of -1.31 to 1.59 L/min (lower 95% CI, -1.62 to -1.00; upper 95% CI, 1.28-1.90).

**CONCLUSION:**The MostCare system provided measurements of CO that were comparable to ThD-CO in patients assisted with an intraaortic balloon pump. The reliability of the MostCare system is not significantly affected by changes in arterial waveform morphology caused by inflation and deflation of the intraaortic balloon pump.

### 使用全自动计算机确定气管导管的位置：一项动物模型的评估

#### **Automatic Computerized Endotracheal Tube Position Verification: An Animal Model Evaluation**

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**背景：**气管插管位置不当是发病率和死亡率的高危因素，核查和确认气管插管位置是必要的。我们提出了使用影像学分析的方法，用计算机系统自动确定气管插管位置。终端产品将不包含一台监视器，而是用一个小型的电子处理器自动分析所获得的图像。

**方法：**自动分析影像系统已经取得进展：它可以区分食管，气管和隆突的图像。在重组模式的相似性的基础上，图像处理包括把图像转换为灰度，提取，划分到一个级别。在气管插管的钢丝上组装有一个视频传感器。这个钢丝被放入到10个牛的喉咙，并收集了视频图像。对所有影像进行分析，区分隆突，气管或食管。影像被转入新的系统。在每个测试周期中，9个影像都使用该系统，第10个影像作为基准。该过程重复10次，所以每部影像有9次进行教学，一次进行测试。

**结果：**十个记录的影像，其中1600图像被提取（气管：490图像；隆突：550图像；和食道：560张）。只有1食管影像被误认为气管（假阳性0.001%）。2个隆突的影像和22个气管的影像被误列为食道（假阴性0.041%），灵敏度：0.98，特异性：0.99。20张隆突的图像被误列为气管，25张气管图像被误列为隆突（假阳性0.045%，假阴性0.041%，灵敏度：0.96和特异性：0.95）。

**结论：**对潜在的气管插管位置的核查系统进行了评估。使用无灌注的生物组织显示分析系统的高精度，有待进一步研究证实。

（刘珏莹译 薛张纲校）

**BACKGROUND:** Improper endotracheal tube positioning carries a high risk for morbidity and mortality; verification and confirmation of correct placement is necessary. We propose a computer-automated identification of endotracheal tube positioning using image analysis. The end product will not retain a monitor; rather, the acquired image will be automatically analyzed by a mini electronic processor.

**METHODS:** An algorithm that automatically analyzes images has been developed: it classifies images into esophagus, trachea, and carina. Image processing includes

converting the image to grayscale and extracting and classifying into 1 class, on the basis of similarity to pretrained patterns. A prototypical video sensor mounted on an intubating stylet has also been assembled. This stylet was introduced into 10 bovine throats, and video images were gathered. Videos were analyzed and classified as carina, trachea, or esophagus. The videos were then introduced to the new algorithm. In each test cycle, 9 videos were used to train the algorithm, and the 10th was used as a benchmark. This procedure was repeated 10 times so that each video was used 9 times for teaching and 1 time for testing.

**RESULTS:** Ten videos were recorded, of which 1600 images were extracted (trachea: 490 images; carina: 550 images; and esophagus: 560 images). Only 1 esophageal image was classified as trachea (false positive 0.001%). Two carinal images and 22 tracheal images were recognized as esophagus (false negative 0.041%), sensitivity 0.98 and specificity 0.99. Twenty images of the carina were identified as trachea, and 25 images of the trachea were identified as the carina (false positive 0.045%, false negative 0.041%, sensitivity 0.96 and specificity 0.95).

**CONCLUSION:** A potential tube position verification system was assessed. High accuracy of the analysis algorithm was shown using nonperfused biological tissue, justifying further research.

### 发生肠道缺血再灌注之后异氟烷吸入麻醉可保留肝肺的线粒体氧化功能

#### Isoflurane Anesthesia Preserves Liver and Lung Mitochondrial Oxidative Capacity After Gut Ischemia–Reperfusion

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**背景：**肠道的缺血再灌注（IR）发生之后可导致肝肺的功能障碍，继而出现多器官功能衰竭。我们的研究是比较在发生 IR 之后，氨胺酮和异氟烷对于肝、肺线粒体氧化功能的影响各自不同之处。

**方法：**本实验中成年雄性 Wistar 大鼠被随机分配在四组中（对照组和 IR 组的大鼠或是经腹膜给予氨胺酮或是吸入异氟烷）。实验将会测定肝和肺各自的线粒体最大耗氧量以及呼吸链效能。

**结果：**应用氨胺酮的时候肠道 IR 会确实会对肝和肺的线粒体氧化功能造成损害，而异氟烷则不然。

**结论：**在肠道 IR 之后，异氟烷吸入麻醉可保留肝肺的线粒体氧化功能。

（陆丽虹译 薛张纲校）

**BACKGROUND:** Lung and liver dysfunction is involved in gut ischemia–reperfusion (IR)–induced multiple organ failure. We compared the effects of ketamine and isoflurane on liver and lung mitochondrial oxidative capacity after gut IR.

**METHODS:** Adult male Wistar rats were randomized into 4 groups (controls and gut IR receiving either intraperitoneal ketamine or inhaled isoflurane). Maximal oxygen consumption and the activity of respiratory chain complexes were measured on isolated liver and lung mitochondria.

**RESULTS:** Gut IR significantly impaired liver and lung mitochondrial oxidative capacity when using ketamine but not isoflurane.

**CONCLUSION:** Isoflurane preserved liver and lung mitochondrial oxidative capacity after gut IR.

带有突变基因 p.4894 的斯里兰卡肉碱受体与恶性高热、先天性神经肌肉疾病（带有统一1型纤维）有关。

### Mutated p.4894 RyR1 Function Related to Malignant Hyperthermia and Congenital Neuromuscular Disease with Uniform Type 1 Fiber (CNMDU1)

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**背景:** 斯里兰卡肉碱受体1(RyR1)是一种  $\text{Ca}^{2+}$  释放通道,位于骨骼肌肌浆网膜上。在患有恶性高热和先天性肌病的患者中发现,在 DNA 水平 RyR1 有超过200多种差异。只有30种差异被充分认为是引起恶性高热的突变因素。日本患者中携带 Ala4894Thr RyR1 更容易患恶性高热和一种罕见的肌病(一种先天性的神经肌肉肌病带有统一的1型纤维)。我们假设不同的 RyR1 Ala4894 差异导致了不同的病理生理改变,其对 RyR1 激动剂有不同的药理学敏感性。

**方法:** 表达 RYR1 突变基因的媒介物感染人体胚胎的肾293细胞。经过72小时的感染,我们发现在咖啡因和4CmC 的作用下细胞内  $\text{Ca}^{2+}$  发生了变化。

**结果:** 感染 Ala4894Th 和 rAla4894Ser 的细胞比野生株对咖啡因更加敏感。感染 Ala4894Thr 的细胞比野生株对4CmC 更加敏感。然而,感染 Ala4894Pro 的细胞对咖啡因和4CmC 都没有反应。感染 Ala4894Gly 的细胞比野生株对咖啡因敏感度低。另外,感染 Ala4894Thr, Ala4894Ser 的细胞对咖啡因的反应会被丹曲林所抑制。

**结论:** 我们发现不同的 RyR1Ala4894 基因差异会导致其对激动剂或拮抗剂的敏感性不同,可能预示着 RYR1 在兴奋收缩偶联功能上的不同与对恶性高热的敏感性不同。高敏感性的 Ala4894Thr-RyR1 与恶性高热、低功能的 Ala4894Pro-RyR1 (带有统一的1型纤维) 联系密切。

(翁梅琳译 薛张纲校)

**BACKGROUND:** Ryanodine receptor 1 (RyR1) is a  $\text{Ca}^{2+}$  release channel located in the sarcoplasmic reticulum membrane of skeletal muscle. More than 200 variants in RyR1

have been identified in DNA from patients with malignant hyperthermia (MH) and congenital myopathies; only 30 have been sufficiently studied so as to be identified as MH-causative mutations. The Ala4894Thr RyR1 variant was found in a Japanese patient with susceptibility to MH, and the Ala4894Pro variant in a rare case of myopathy: congenital neuromuscular disease with uniform type 1 fiber (CNMDU1). We hypothesized that different Ala4894 variants of RyR1 cause different pathophysiological changes that are identifiable by having differing pharmacological sensitivities to RYR1 agonists.

**METHODS:** Expression vector with a mutation in RYR1 corresponding to the Ala4894Thr, Ala4894Pro, Ala4894Ser, or Ala 4894Gly variant of human RyR1 was transfected into human embryonic kidney 293 cells. At 72 hours after transfection, we determined the intracellular  $Ca^{2+}$  changes induced by caffeine and 4-chloro-m-cresol (4CmC), in the presence or absence of dantrolene.

**RESULTS:** Ala4894Thr-transfected cells and Ala4894Ser-transfected cells were more sensitive to caffeine than the wild type, and Ala4894Thr-transfected cells were also more sensitive to 4CmC than the wild type, whereas Ala4894Pro-transfected cells had no response to caffeine or 4CmC. Ala4894Gly-transfected cells were significantly less sensitive to caffeine than the wild type. In addition, the responses of -transfected cells and Ala4894Ser-transfected cells to caffeine were suppressed by dantrolene.

**CONCLUSION:** We concluded that different Ala4894 variants of RyR1 lead to different agonist/antagonist sensitivities, which may predict differing RYR1 functionality during excitation-contraction coupling and sensitivity to MH. The hypersensitive Ala4894Thr-RyR1 is associated with MH and the poorly functional Ala4894Pro-RyR1 with CNMDU1.

### 鞘内注射不含聚乙二醇的甲强龙来增加医疗安全

#### Enhancing the Relative Safety of Intentional or Unintentional Intrathecal Methylprednisolone Administration by Removing Polyethylene Glycol

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**背景：**先前的研究证实鞘内注射甲强龙对于治疗带状疱疹后神经痛非常有效。然而以聚乙二醇作为防腐剂限制了鞘内甲强龙的广泛使用。本研究中，我们打算减少聚乙二醇的浓度，目的是精确计算出醋酸甲强龙中所需的聚乙二醇浓度。

**方法：**单剂量 80 毫克的醋酸甲强龙用于提取聚乙二醇部分。在两相反应后，我们小心的提取出只含有类固醇的部分。我们在不同的时间点提取，通过液相色谱和质谱法计算聚乙二醇和甲强龙的量。小样本采用 PH 试纸测定 PH 值。

**结果：**使用单侧检验以及 Bonferroni 校正显示在不同时间蒸馏后和基线值之间存在统计学差异。蒸馏 2 至 4 小时得到聚乙二醇的最小量 78%，最大量为 85%。然而，我们没有改变溶液的 PH 值和甲强龙的浓度。

**结论：**通过我们的方法降低聚乙二醇的浓度，甲强龙相关并发症会减少，在带状疱疹后神经痛患者对其他治疗无反应后应该考虑给予他们这个治疗方法，因为他们有可能接受反复的鞘内给药。

(姚敏敏译 薛张纲校)

**BACKGROUND:** Previous studies have shown that intrathecal methylprednisolone is a very effective treatment for postherpetic neuralgia. However, widespread use of intrathecal methylprednisolone is limited by the presence of polyethylene glycol (PEG) as a preservative in the commercial formulation. In this study, we are proposing a method to reduce the concentration of PEG in the methylprednisolone acetate (MPA) suspension by inverting a vial before sterilely aspirating the contents into a syringe for subsequent injection. The purpose of this brief study was to precisely quantify the concentration of PEG in the MPA suspension.

**METHODS:** Single-dose vials containing 80 mg of MPA suspension were inverted to promote partition of the PEG away from the steroid component. After achieving 2 phases, we carefully extracted and aspirated only the steroid component. We kept the vials inverted for different time points (from 0 to 480 minutes), and we measured the concentration of PEG and methylprednisolone by using liquid chromatography and mass spectrometry. We also measured the pH of samples by using the pH meter for small samples.

**RESULTS:** The 1-way analysis of variance with post hoc analysis and Bonferroni correction showed statistically significant differences ( $P < 0.0001$ ) between baseline concentrations and concentrations after inverting the vials for different times. We removed a minimum of 78% of PEG (the Bonferroni-corrected lower confidence limit for overall reduction in PEG) by keeping the vials inverted from 2 to 4 hours, and the average amount removed was 85% per vial. However, we did not change the concentration of methylprednisolone or the pH of the solution.

**CONCLUSIONS:** We believe that by decreasing the PEG concentration using our method, MPA-related complications will potentially be reduced, and this should be considered in patients with postherpetic neuralgia refractory to other treatments who might be candidates for repeated intrathecal injections.

鞘内注射低剂量纳洛酮通过增加坐骨神经横断大鼠的脊髓突触间隙的兴奋性氨基酸的重吸收增强吗啡的镇痛效果

**Intrathecal Ultra-Low Dose Naloxone Enhances the Antinociceptive Effect of Morphine by Enhancing the Reuptake of Excitatory Amino Acids from the Synaptic Cleft in the Spinal Cord of Partial Sciatic Nerve–Transected Rats**

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**背景：**在这个研究中，我们试验了低剂量纳洛酮对吗啡镇痛效果的影响和对有神经痛的大鼠的脊髓背角谷氨酸转运体表达的影响。

**方法：**通过部分横断的 Wistar 大鼠的左侧坐骨神经来诱发神经病理性疼痛，同时鞘内置管用来给药；一些大鼠鞘内放置微透析探针来收集脑脊液。疼痛用脚底测试——一种哈格里夫斯热辐射装置——来评估，也可用 von Frey 测试来评估。用 Western 标记法和免疫组化法来测定左侧脊髓背角谷氨酸转运蛋白的表达。兴奋性氨基酸（EAAs）谷氨酸和脑脊液中天门冬氨酸的水平用高效液相色谱法来测定。

**结果：**减少与坐骨神经横断（PST）同侧的脊髓背角的板层 I 和 II 内星形细胞谷氨酸转运体的表达（GLT-1 和 GLAST 水平分别为 55% 和 53%，在假手术大鼠中），可观察到疼痛过敏和 PST 后肢痛。高剂量纳洛酮（15 微克）减少吗啡（10 微克）抗疼痛过敏和镇痛效果。相反，小剂量（15 纳克）纳洛酮增强吗啡（10 微克）镇痛效果，与单用吗啡治疗相比热刺激的避退反射阈值增加（19% 上升至 35%），触觉刺激的避退反射阈值也增加（33% 上升至 55%），这与恢复同坐骨神经横断（PST）同侧的脊髓背角的板层 I 和 II 内星形细胞的 GLAST 和 GLT-1 表达水平（分别为 102% 和 114%）和降低脑脊液中 EAA 水平（谷氨酸 10uM，天门冬氨酸 1.1uM）相关。

**结论：**低剂量纳洛酮增强吗啡在 PST 大鼠中的镇痛效果，可能是通过修复星形胶质细胞表达的 GLAST 和 GLT-1，这些物质抑制突触间隙中 EAAs 的积聚，获得神经保护作用。

（张玥琪译，薛张纲校）

**BACKGROUND:** In this study, we examined the effects of ultra-low dose naloxone on the antinociceptive effect of morphine and on spinal cord dorsal horn glutamate transporter expression in rats with neuropathic pain.

**METHODS:** Neuropathic pain was induced in male Wistar rats by partial transection of the left sciatic nerve and an intrathecal catheter was implanted for drug administration; in some rats, an intrathecal microdialysis probe for cerebrospinal fluid (CSF) dialysate collection was also implanted. Nociception was assessed using the plantar test, a Hargreaves radiant heat apparatus, and by the von Frey test, using a dynamic plantar anesthesiometer. Glutamate transporter protein expression in the left spinal cord dorsal horn was examined by Western blotting and immunohistochemistry. Levels of the excitatory amino acids (EAAs) glutamate and aspartate in the CSF dialysate were measured using high-performance liquid chromatography.

**RESULTS:** Reduced astrocyte expression of glutamate transporters (GLT-1 and GLAST levels were 55% and 53%, respectively, of that in sham-operated rats) in laminae I and II of the spinal cord dorsal horn ipsilateral to the partial sciatic nerve transection (PST), and hyperalgesia and allodynia in the PST hindlimb were observed. High-dose naloxone (15 µg) attenuated the antihyperalgesia and antiallodynia effects of the morphine (10 µg). In contrast, ultra-low dose (15 ng) naloxone enhanced the antinociceptive effect of morphine (10 µg), with an increase in the paw withdrawal threshold to thermal stimulus (from 19% to 35%) and to tactile stimulus (from 33% to 55%) compared with morphine treatment alone, and this was associated with restoration of GLAST and GLT-1

expression to control levels (102% and 114%, respectively) in the astrocytes of laminae I and II in the spinal cord dorsal horn ipsilateral to the PST hindlimb and a decrease in EAA levels in the CSF dialysate (glutamate: 10.0  $\mu$ M; aspartate: 1.1  $\mu$ M).

**CONCLUSIONS:** Ultra-low dose naloxone enhanced the antinociceptive effect of morphine in PST rats, possibly by restoration of GLAST and GLT-1 expression in astrocytes, which inhibited the accumulation of EAAs in the synapses, resulting in a neuroprotective effect.

### 综述：体外循环期间止血系统的激活

#### Review Articles: Activation of the Hemostatic System During Cardiopulmonary Bypass

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体外循环是一个独特的临床环节，它会导致止血系统的广泛激活。但是手术也会激活凝血、血小板以及纤溶系统，这些都与受伤时的止血机制有关。一般的体外循环主要通过稀释凝血细胞和凝血酶来影响正常的凝血机制，通过自体血回输以及激活血液中各种系统，包括血小板系统，激肽释放酶激肽系统和纤溶系统。激肽释放酶激肽系统的激活能增加刺激 XIIa 因子，激肽释放酶，缓激肽和血浆纤溶酶原活化水平，但是几乎对凝血酶的激活无作用。血浆纤维蛋白原的激活和循环纤维蛋白单体的增加会引起纤溶酶的产生，它可以去除纤维蛋白。体外循环的非内皮表面，连同循环中的凝血酶和纤溶酶，可以引起血小板的激活。血小板受体缺失以及降低血小板对于损伤的反应。本综述重点在体外循环引起止血系统激活的机制和文献中报道中标志物的监测。此外，还讨论了抑制激活的方法，包括限制心脏切开术的吸引，增加循环生物相容性，抗凝血酶和抗纤溶的使用。决定哪一类病人将会从这种疗法中受益最终需要凝血蛋白表达基因表型的调查。但是，到目前为止，联合使用上述方法来抑制体外循环凝血系统激活似乎是合理的。

(范逸辰 译 陈杰 校)

Cardiopulmonary bypass (CPB) is a unique clinical scenario that results in widespread activation of the hemostatic system. However, surgery also results in normal increases in coagulation activation, platelet activation, and fibrinolysis that are associated with normal wound hemostasis. Conventional CPB interferes with normal hemostasis by diluting hemostatic cells and proteins, through reinfusion of shed blood, and through activation on the bypass circuit surface of multiple systems including platelets, the kallikrein-kinin system, and fibrinolysis. CPB activation of the kallikrein-kinin system increases activated factor XIIa, kallikrein, bradykinin, and tissue plasminogen activator levels, but has little effect on thrombin generation. Increased tissue plasminogen activator and circulating fibrin result in increased plasmin generation, which removes hemostatic fibrin. The nonendothelial surface of the bypass circuit, along with circulating thrombin and plasmin,

lead to platelet activation, platelet receptor loss, and reduced platelet response to wounds. In this review, we highlight the major mechanisms responsible for CPB-induced activation of the hemostatic system and examine some of the markers described in the literature. Additionally, strategies used to reduce this activation are discussed, including limiting cardiotomy suction, increasing circuit biocompatibility, antithrombin supplementation, and antifibrinolytic use. Determining which patients will most benefit from specific therapies will ultimately require investigation into genetic phenotypes of coagulation protein expression. Until that time, however, a combination of approaches to reduce the hemostatic activation from CPB seems warranted.

### 布比卡因使长 QT 综合症的细胞和计算模型的动作电位不稳定

#### **Bupivacaine Destabilizes Action Potential Duration in Cellular and Computational Models of Long QT Syndrome 1**

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**背景：**局部麻醉药布比卡因对心肌动作电位（APs）的影响主要归因于抑制心脏 Na<sup>+</sup>通道。与之相关的诱导阻滞高亲和力 hERG 通道的能力目前尚不清楚。作者研究了这种相互作用是否对长 QT 综合症的细胞和计算模型作用更显著。

**方法：**从成年豚鼠心分离左心室心肌细胞出来的，并使用膜片钳技术研究布比卡因诱导的动作电位效应。药理学中 LQT 样状态由抑制 I<sub>ks</sub>（LQT1，10 μmol/L 色原烷醇 293B）或 I<sub>kr</sub>（LQT2，10 μmol/L E4031）引起。布比卡因效应的计算分析是基于 Luo-Rudy 动态模型。

**结果：**布比卡因导致心肌细胞的剂量依赖型动作电位缩短。然而，应用 1—30 μmol/L 的布比卡因时，观察到延长的 AP 持续时间的变异度高达 40%。这种 AP 持续时间不稳定效应在类 LQT1 心肌细胞中显著增加，但在类 LQT2 心肌细胞中则不明显。类似的，在应用 3 μmol/L 的布比卡因时类 LQT1 AP 延长的发生率由 6% 显著增加至 24%，类 LQT2 心肌细胞并非如此。计算模型支持了这种概念，即这种在对照心肌细胞和类 LQT1 心肌细胞中由布比卡因诱导的 AP 不稳定和 AP 延长是由于抑制 hERG 通道而造成。

**结论：**这项研究提供的证据表明，布比卡因诱导了 hERG 通道的抑制，这在正常情况下是功能沉默的而在类 LQT1 状态下变得更加相关，在类 LQT1 状态下复极化更大程度上依赖 hERG 通道。因此，布比卡因在心脏离子电流的正常平衡改变时心脏钠离子通道以外的作用决定其心脏净效应。

（孙晓琼 译 陈杰 校）

**BACKGROUND:** The effects of the local anesthetic bupivacaine on cardiac action potentials (APs) are mainly attributed to inhibition of cardiac Na<sup>+</sup> channels. The relevance of its ability to also induce high-affinity blockade of human *ether-à-gogo*-related gene (hERG) channels is unclear. We investigated whether this interaction may

functionally become more significant in cellular and computational models of long (L)QT syndromes.

**METHODS:** Left ventricular cardiomyocytes were isolated from adult guinea pig hearts, and bupivacaine-induced effects on APs were investigated using the patch-clamp technique. LQT-like states were pharmacologically induced by either blocking  $I_{Ks}$  (LQT1-like, 10  $\mu\text{mol/L}$  chromanol 293B), or  $I_{Kr}$  (LQT2-like, 10  $\mu\text{mol/L}$  E4031). Computational analysis of bupivacaine's effects was based on the Luo-Rudy dynamic model.

**RESULTS:** Bupivacaine induced dose-dependent AP shortening in control myocytes. However, in the presence of 1 to 30  $\mu\text{mol/L}$  bupivacaine, a high variability in AP duration with AP prolongations of up to 40% was observed. This destabilizing effect on AP duration was significantly increased in LQT1-like but not in LQT2-like myocytes. Similarly, the incidence of AP prolongations in the presence of 3  $\mu\text{mol/L}$  bupivacaine was significantly increased from 6% in control myocytes to 24% in LQT1-like but not in LQT2-like myocytes. Computational modeling supported the concept that this bupivacaine-induced AP instability and the AP prolongations in the control and LQT1-like myocytes were caused by inhibition of hERG channels.

**CONCLUSIONS:** This study provides evidence that bupivacaine induces inhibition of hERG channels, which is functionally silent under normal conditions but will become more relevant in LQT1-like states in which repolarization relies to a larger degree on hERG channels. Interactions with ion channels other than cardiac  $\text{Na}^+$  channels may, therefore, determine the net cardiac effects of bupivacaine when the normal balance of ionic currents is altered.

### 在复杂的脊柱外科手术中连续无创血红蛋白的监测

#### Continuous Noninvasive Hemoglobin Monitoring During Complex Spine Surgery

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**背景:** 目前在手术室中血红蛋白的监测需要反复抽血, 多个步骤, 延迟一段不确定的时间才能得到结果。因此对于是否需要输血的管理可能会推迟或在结果出来前就已决定是否输血。连续无创的血红蛋白监测可以更及时地评估患者的病情和更适当地进行血液的管理。有一项新的技术, 即 CO-脉搏血氧饱和度 (SpHb), 通过在手指上放置一个传感器来提供连续的无创血红蛋白浓度监测。作者评估了 SpHb 与实验室 CO 血氧仪测量的血红蛋白值 (tHb) 相比, 在具有失血高风险的复杂性脊柱手术中的准确性。

**方法:** 研究对象入选标准为行复杂脊柱外科手术需有创动脉、中心静脉监测和每小时血红蛋白测量的患者。每小时采取一次血液样本 (若有临床指征可增加次数), 使用实验室 CO-血氧饱和度测量血红蛋白, 即许多医院测量血红蛋白的标准方法。同一个时刻 tHb 和 SpHb 的测量结果进行比较。

**结果:** 21 名患者入选研究。tHb 的平均值为 6.9-13.9g/dl, SpHb 的平均值为 6.9-13.4g/dl。共有 186 对数据 (tHb/SpHb) 进行了分析, 排除 SpHb 信号差的数据后

剩下 130 对数据的偏差（定义为 tHb 和 SpHb 之间的差异）和精确度（定义为差值的一个标准差）分别为  $-0.1 \text{ g/dL} \pm 1.0 \text{ g/dL}$ 。Bland-Altman 分析法表明 tHb 和 SpHb 之间关系良好，差异范围为  $-2.0$  to  $1.8 \text{ g/dL}$ 。绝对的偏差和精确度为  $0.8 \pm 0.6 \text{ g/dL}$ 。

**结论：**在复杂性脊柱外科手术中，连续无创的 CO-脉搏血氧血红蛋白监测与标准实验室仪器进行的血红蛋白监测精确度的偏差是在临床可接受的范围内，为  $1.5 \text{ g/dL}$  之内。这种技术可提供与间歇性血液样本分析相比更实时的血红蛋白值的监测，这样我们可以在手术中提高对血液的管理。

（滕凌雅 译 陈杰 校）

**BACKGROUND:** Monitoring hemoglobin levels in the operating room currently requires repeated blood draws, several steps, and a variable time delay to receive results. Consequently, blood transfusion management decisions may be delayed or made before hemoglobin results become available. The ability to measure hemoglobin continuously and noninvasively may enable a more rapid assessment of a patient's condition and more appropriate blood management. A new technology, Pulse CO-Oximetry, provides a continuous, noninvasive estimate of hemoglobin concentration (SpHb) from a sensor placed on the finger. We evaluated the accuracy of SpHb compared with laboratory CO-Oximetry measurements of total hemoglobin (tHb) during complex spine procedures in patients at high risk for blood loss.

**METHODS:** Patients eligible for the study were undergoing complex spine surgery with planned invasive arterial or central venous monitoring and hourly blood draws for hemoglobin measurement. During each surgery, blood samples were obtained hourly (or more often if clinically indicated) and analyzed by the central laboratory with CO-Oximetry, a standard method of hemoglobin measurement in many hospitals. The tHb measurements were compared with SpHb obtained at the time of the blood draw.

**RESULTS:** Twenty-nine patients were included in the study. The tHb values ranged from 6.9 to 13.9 g/dL, and the SpHb values ranged from 6.9 to 13.4 g/dL. A total of 186 data pairs (tHb/SpHb) were analyzed; after removal of SpHb readings with low signal quality, the bias (defined as the difference between SpHb and tHb) and precision (defined as 1 SD of the bias) were  $-0.1 \text{ g/dL} \pm 1.0 \text{ g/dL}$  for the remaining 130 data pairs. Bland-Altman analysis showed good agreement of SpHb to tHb values over the range of values; limits of agreement were  $-2.0$  to  $1.8 \text{ g/dL}$ . The absolute bias and precision were  $0.8 \pm 0.6 \text{ g/dL}$ .

**CONCLUSIONS:** Continuous, noninvasive hemoglobin measurement via Pulse CO-Oximetry demonstrated clinically acceptable accuracy of hemoglobin measurement within  $1.5 \text{ g/dL}$  compared with a standard laboratory reference device when used during complex spine surgery. This technology may provide more timely information on hemoglobin status than intermittent blood sample analysis and thus has the potential to improve blood management during surgery.

### 普外科择期手术的手术时机以及术后 30 天死亡率

#### Operation Timing and 30-Day Mortality After Elective General Surgery

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**背景：**疲劳、昼夜节律、作息时间以及配备人员等人为因素可能影响患者在医疗期间的照顾。交通运输业的研究发现轮班工作制、昼夜节律紊乱以及加班可使人的工作效率有所降低。作者猜测：是否普外科手术的手术时机（尤其增加了时间、周数以及七月或者八月对比其他月份）以及月相与 30 天死亡率独立相关。住院患者比较的次要结果也被评估。

**方法：**对克里兰夫诊所在 2005 年 1 月至 2010 年 9 月择期普外科手术的 32,001 例患者进行手术时间（上午六点至下午七点），工作日的时间，月份，以及月相的二进制结果分析。30 天死亡率通过多变量逻辑回归方法被作为一个二进制端点，在 ICD 编码（国际疾病分类标准）的基础上增加了风险指数。

**结论：**死亡率与工作日的手术时间并无差别。一周中工作日的差别也未被发现 (0.99 [0.83, 1.17])。七月以及八月手术的死亡率与其他月份相比无明显差别 (OR=0.72 [0.36, 1.43],  $P = 0.22$ ) 月相和死亡率没有明显相关 ( $P = 0.72$ )。对照组别种时间的分割没有明显的意义。

**结论：**普外科择期手术在一天中的任何时间、一周中的任何天数以及一年中的任何月份进行都是安全的。

（龚寅 译 陈杰 校）

**BACKGROUND:** Human factors such as fatigue, circadian rhythms, scheduling, and staffing may have an impact on patient care over the course of a day across all medical specialties. Research by the transportation industry concludes that human performance is degraded by shift work, circadian rhythm disturbances, and prolonged duty. We investigated whether the timing of general surgery (specifically, increasing time of day, increasing day of week, July/August cases versus other months), and moon phase is independently related to 30-day mortality. A secondary outcome of composite in-hospital complications was also evaluated.

**METHODS:** The binary outcomes of 32,001 elective general surgical patients at the Cleveland Clinic between January 2005 and September 2010 were analyzed according to the hour of the day (6 am to 7 pm), day of the workweek, month of the year, and moon phase in which the surgery started. Thirty-day mortality was modeled as a binary endpoint using a multivariable logistic regression, adjusting for a risk stratification index based on International Classification of Diseases (9<sup>th</sup> rev.) codes.

**RESULTS:** The adjusted odds ratio ([Bonferroni-adjusted 95% CI]) associated with a relative increase in time of day of 4 h was 1.23 [0.91, 1.67],  $P = 0.09$ . Similarly, no association was found for day of week (0.99 [0.83, 1.17]) for a relative increase of 1 day,  $P = 0.85$ . Mortality was not significantly more frequent in July and August than in other months (adjusted odds ratio = 0.72 [0.36, 1.43],  $P = 0.22$ ). Moon phase was not significantly related to mortality ( $P = 0.72$ ). There were also no significant time-dependent differences in composite complications.

**CONCLUSIONS:** Elective general surgery appears to be comparably safe at any time of the workday, any day of the workweek, and in any month of the year.

## 应用 Rasch 模型制定简化版多属性效用量表评估产妇硬膜外镇痛的认识程度

### Application of the Rasch Model to Develop a Simplified Version of a Multiattribute Utility Measurement on Attitude Toward Labor Epidural Analgesia

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**背景：**有效可靠的量表制定应基于保健行为理论，如多属性效用判断理论等，这对解释心理因素和分娩疼痛之间的复杂关系是必要的。在此研究中，作者旨在使用 Rasch 分析简化以往 20 项的多属性问卷，依靠多属性效用理论来评估分娩后硬膜外镇痛的认知程度。

**方法：**使用 Rasch 分析选择性减缩分类，排除不适合的项目和患者，生成线性的分娩硬膜外镇痛认知评分（ATLEA）。问卷中的项目属性和分类阈值也进行评估。进一步，将简化量表和完全量表进行可靠性和经验上的有效性的比较。

**结果：**167 名产妇完成问卷。最初的 10 项分级量表整合成 4 项，并未影响可靠性。3 名被调查者和 11 个项目因为不适合被排除。简化版和完全版的可靠性指数分别为 0.68 和 0.74。简化版和完全版问卷的 ATLEA 评分关联系数为 0.89。通过计算受试者工作特征曲线（ROC 曲线）下面积，得出简化版和完全版的 ATLEA 评分对决定分娩后硬膜外镇痛的实证效度分别为 0.80 和 0.81。

**结论：**研究论证了采用 Rasch 分析简化多属性效用量表并未影响可靠性，需要进一步研究证明简化问卷在临床实际中的有效性。

（陆秉玮 译 陈杰 校）

**BACKGROUND:** Valid and reliable measures based on health behavior theory, such as multiattribute utility decision theory, are essential to elucidate complex relationships between psychological factors and labor pain. In this study we aimed to use Rasch analysis to simplify a previously developed 20-item multidimensional questionnaire on attitude toward labor epidural analgesia using multiattribute utility theory.

**METHODS:** The Rasch analysis was performed to condense item selection categories, to exclude misfit items and persons, and to generate a unidimensional attitude toward labor epidural analgesia (ATLEA) score. Item characteristics and thresholds of rating categories in the questionnaire were also estimated. Reliability and empirical validity of the simplified version were further compared with those of the full version.

**RESULTS:** One hundred sixty-seven postpartum women completed the questionnaire. The original 10 rating scale categories were combined to make 4 without compromising reliability. Three respondents and 11 items were excluded because of misfit. Reliability indices of the simplified and full versions were 0.68 and 0.74, respectively. The correlation coefficient between ATLEA scores from the simplified and full versions was 0.89. Empirical validity values of ATLEA scores from the simplified and full versions for labor epidural analgesia decision, as assessed by area under the receiver operating characteristic curves, were 0.80 and 0.81, respectively.

**CONCLUSIONS:** We demonstrated application of the Rasch analysis to simplifying a multiattribute utility questionnaire without compromising reliability. Further study is necessary to determine whether the simplified questionnaire is valid for use in clinical practice.

**在 H4 人神经胶质细胞体外培养模型中 2-脱氧-D 葡萄糖可减弱异氟醚导致的细胞毒性作用**

**2-Deoxy-D-Glucose Attenuates Isoflurane-Induced Cytotoxicity in an In Vitro Cell Culture Model of H4 Human Neuroglioma Cells**

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**背景:**  $\beta$ -淀粉样蛋白 ( $A\beta$ ) 累积以及细胞凋亡蛋白酶显示参与阿兹海默病的神经发病机理。 $A\beta$  通过天冬氨酸蛋白酶  $\beta$ -位点产生淀粉样前体蛋白水解酶 (BACE)，裂解淀粉样前体蛋白而产生。吸入异氟醚可以减少 caspase 活化并增加 BACE 和  $A\beta$  的水平。然而，异氟醚导致的神经毒性的机制仍需要进一步研究。类似葡萄糖的 2-DG 有神经保护作用。因此，作者设法证明是否 2-DG 能减少异氟醚导致的 caspase-3 的活化并增加 BACE 的水平。

**方法:** H4 人神经胶质瘤细胞用生理盐水或者 2-DG (5 mM) 处理 1 个小时，然后作对照组或 2% 异氟醚持续 6 个小时。监测 caspase-3 水平，BACE，细胞内钙水平和 ROS。使用方差分析评估 2-DG 和异氟醚的交互作用。

**结果:** 在 H4 人神经胶质瘤细胞，2-DG 减少 caspase-3 激活 (477% vs 186%,  $F = 8.68$ ;  $P = 0.019$ ) 并增加 BACE 水平 (345% vs 123%,  $F = 42.24$ ;  $P = 0.0002$ )。2-DG 减少细胞内钙水平及 ROS (100% vs 66%,  $F = 1.94$ ;  $P = 0.014$ )。

**结论:** 2-DG 可能氧化应激并增加细胞内钙水平，这样可以减少异氟醚导致的神经毒性。

(丁佳 译 陈杰 校)

**BACKGROUND:**  $\beta$ -Amyloid protein ( $A\beta$ ) accumulation and caspase activation have been shown to contribute to Alzheimer disease neuropathogenesis.  $A\beta$  is produced from amyloid precursor protein through proteolytic processing by aspartyl protease  $\beta$ -site amyloid precursor protein-cleaving enzyme (BACE). The inhaled anesthetic isoflurane has been shown to induce caspase activation and increase levels of BACE and  $A\beta$ . However, the underlying mechanisms and interventions of the isoflurane-induced

neurotoxicity remain largely to be determined. The glucose analog 2-deoxy-D-glucose (2-DG) has neuroprotective effects. Therefore, we sought to determine whether 2-DG can reduce caspase-3 activation and the increase in the levels of BACE and reactive oxygen species (ROS) induced by isoflurane.

**METHODS:** H4 human neuroglioma cells were treated with saline or 2-DG (5 mM) for 1 hour followed by a control condition or 2% isoflurane for 6 hours. The levels of caspase-3 cleavage (activation), BACE, cytosolic calcium, and ROS were determined. Two-way analysis of variance was used to assess the interactions of 2-DG and isoflurane on caspase-3 activation, and levels of BACE and ROS.

**RESULTS:** In H4 human neuroglioma cells, 2-DG reduced the caspase-3 activation (477% vs 186%,  $F = 8.68$ ;  $P = 0.019$ ) and the increase in BACE levels (345% vs 123%,  $F = 42.24$ ;  $P = 0.0002$ ) induced by isoflurane. 2-DG decreased the levels of cytosolic calcium and ROS (100% vs 66%,  $F = 1.94$ ;  $P = 0.014$ ).

**CONCLUSIONS:** These results suggest that 2-DG may decrease oxidative stress and increase cytosolic calcium levels, thus attenuating isoflurane-induced neurotoxicity.

### 大鼠突触支架蛋白 Homer 1b/c 降解可减弱由 CFA 诱导的继发痛觉过敏

#### Knockdown of Synaptic Scaffolding Protein Homer 1b/c Attenuates Secondary Hyperalgesia Induced by Complete Freund's Adjuvant in Rats

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**背景:** 早先的研究证明了 Homer 1b/c 作为一种突触后分子的支架蛋白在神经突触链接、聚集亲代谢性谷氨酸受体, 对其信号传递有很大作用。本研究中作者调查了由完全弗氏佐剂 (CFA) 诱导的在继发的痛觉过敏中 Homer 1b/c 可能的参与作用。

**方法:** 对 Wistar 大鼠的左后踝关节注射 CFA 来诱导慢性炎症。从炎症开始向鞘内注射 Homer 1b/c 反义或错义寡核苷酸(反义, 10  $\mu\text{g}/10 \mu\text{L}$ , 5  $\mu\text{g}/10 \mu\text{L}$ , or 2.5  $\mu\text{g}/10 \mu\text{L}$ , 每天一次; 错义, 10  $\mu\text{g}/10 \mu\text{L}$ ) 5 到 8 天。在鞘内注射之前和之后就确定停药阈值和其对机械或温觉刺激的潜伏期。应用免疫技术检测脊髓内 Homer 1b/c 的表达与分布。

**结果:** 大鼠在 CFA 注射后 24 小时内出现机械性异常疼痛和温觉过敏, 且持续超过 2 周。在炎症后 7 天 Homer 1b/c 的表达到达高峰, 28 天回到基线水平。Homer 1b/c 反义寡核苷酸的鞘内注射显著减少了 Homer 1b/c 蛋白在脊髓的表达。另外, Homer 1b/c 反义寡核苷酸的注射减弱了第 2 到 5 天的继发性机械性痛觉超敏, 并且减轻了第 3 到 4 天的温觉超敏。错义寡核苷酸对 Homer 1b/c 的表达和超敏化没有影响。而幼鼠, Homer 1b/c 反义寡核苷酸并没有影响其机械性和温觉反应以及自主活动。

**结论:** 这些最新结果显示脊髓的 Homer 1b/c 参与了 CFA 诱导的继发痛觉过敏, 它可能成一种疼痛治疗新的靶目标。

(俞劼晶 译 陈杰 校)

**BACKGROUND:** Previous studies have demonstrated that Homer 1b/c, a postsynaptic molecular scaffolding protein that binds and clusters metabotropic glutamate receptors at neuronal synapses, has an important role in the metabotropic glutamate receptor signaling process. In the current study, we investigated the possible involvement of Homer 1b/c in secondary hyperalgesia induced by complete Freund's adjuvant (CFA).

**METHODS:** Chronic inflammation was induced by injecting CFA into the left hind ankle of Wistar rats. Homer 1b/c antisense or missense oligonucleotides were intrathecally administered (antisense, 10 µg/10 µL, 5 µg/10 µL, or 2.5 µg/10 µL, once a day; missense, 10 µg/10 µL) from 5 to 8 days after the onset of inflammation. The withdrawal threshold and withdrawal latency to mechanical or thermal stimuli were determined before and after the intrathecal administration. The expression and distribution of Homer 1b/c were examined in the spinal cord using immunological techniques.

**RESULTS:** Mechanical allodynia and thermal hyperalgesia were induced within 24 hours and maintained for >2 weeks after the CFA injection. The expression of Homer 1b/c reached the highest level 7 days after inflammation and returned to baseline at day 28. Intrathecal administration of Homer 1b/c antisense oligonucleotides markedly reduced the expression of Homer 1b/c protein in the spinal cord. Additionally, administration of Homer 1b/c antisense oligonucleotides attenuated secondary mechanical hypersensitization on days 2 to 5 and reduced thermal hypersensitization on days 3 to 4. There were no effects of missense oligonucleotides on hypersensitization and the expression of Homer 1b/c. In the naïve rats, Homer 1b/c antisense oligonucleotides did not affect the mechanical and thermal responses or locomotor activity.

**CONCLUSIONS:** These novel results demonstrate that Homer 1b/c in the spinal cord contributes to the maintenance of secondary hyperalgesia induced by CFA and suggest that Homer 1b/c may be a novel target for pain therapy.

### 上止血带或神经阻滞小腿的体位能加强腓窝径路坐骨神经阻滞的效果

#### Distal Tourniquet or Leg Position After Injection Enhances the Efficacy of Sciatic Nerve Blockade by the Popliteal Approach

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**背景：**在此次研究中，作者假设小腿的体位及止血带的应用与普通小腿中立位相比能改变两点刺激法坐骨神经阻滞的阻滞效果。

**方法：**随机连续入组骨科患者 90 例，ASA 分级 I-II 级，择期腓窝阻滞麻醉下行足部及脚踝部手术（患者俯卧位，应用两点刺激法）。患者随机分为三组，组 1 中患者神经阻滞完成后翻身平卧后立即将小腿置于中立位，组 2 中患者大腿屈曲 45 度角并维持该体位 15 分钟，组 3 中将患者小腿置于中立位并上止血带，患者仰卧位注射局麻药物时止血带充气。局麻药为常规 2% 丙胺卡因 15mL 及 0.5% 左旋布比卡因 15mL 混合液。

**结果：**组 2 及组 3 患者的感觉阻滞及运动阻滞起效时间有所缩短，阻滞恢复时间有所延长。

**结论：**在日常麻醉中应用以上两种方法包括注射时上止血带及两点刺激法腓窝径路坐骨神经阻滞后立即仰卧位并使小腿旋后位也许能同样的增加麻醉阻滞的效果。作者认为坐骨神经阻滞时小腿的特殊体位及止血带的应用能使阻滞神经周围局麻药分布增加并导致起效时间缩短及作用时程的延长。

（陈毓雯 译 陈杰 校）

**BACKGROUND:** In this study, we hypothesized that leg positioning and distal tourniquet application, when compared with neutral positioning of the leg, alters the efficacy of sciatic nerve block performed by the double-stimulation technique.

**METHODS:** Ninety randomized, consecutive, ASA physical status I to III patients undergoing foot and ankle surgery with a popliteal fossa block (using a double-stimulation technique with the patient in prone position) were prospectively studied. Patients were randomized to have the blocked leg either kept in a neutral position immediately after the patient was turned supine (group 1), flexed 45 degrees at the thigh and maintained in that position for 15 minutes (group 2), or have a distal tourniquet applied with the leg in a neutral position and inflated during injection of the local anesthetic with the patient supine (group 3). A standardized local anesthetic mixture containing 15 mL of 2% prilocaine and 15 mL of 0.5% levobupivacaine was used in all study groups.

**RESULTS:** The onset times for sensory and motor blocks were shorter, and the time to recovery of blocks was longer, postprocedure in both group 2 and 3.

**CONCLUSIONS:** Similar beneficial effects might be reached with the application of a distal tourniquet during injection or elevating the patient's leg turned supine immediately after sciatic nerve block with a popliteal approach by a double-injection technique. We suggest that using the leg-up position or application of a distal tourniquet for sciatic nerve block may lead to a more proximal distribution of the local anesthetic and may result in a faster onset of sensory and motor blocks as well as longer duration of blockade.