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手術前短期戒煙：一個進退兩難的困境？

Brief Preoperative Smoking Abstinence: Is There a Dilemma?

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Anesth Analg December 2011 113:1348-1351

手術前短時間停止吸煙 (<8 周) 增加手術後肺部併發症，這種憂慮為干預手術病人對煙草的應用造成了障礙。我們表明了這種擔心是如何來源於對最初的研究結果的錯誤解釋，並且不管以後累積的證據，它仍然保留在醫學文獻中。未被證實的這種概念的持續性並不是不尋常的，並且可能會對醫療實踐有明顯的影響。儘管可能需要幾個星期來從戒煙中取得對肺部的益處，對肺部併發症增加的恐懼不應該成為臨床醫生幫助病人在手術前的任何時間戒煙的障礙。

(黃麗娜 譯 馬皓琳 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.

可樂定對血管 ATP 敏感性鉀離子通道抑制作用的分子學機制

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：我們研究了 α_2 腎上腺素受體激動劑咪唑啉衍生物可樂定對大鼠的血管平滑肌細胞上的 ATP 敏感性鉀離子 (K_{ATP}) 通道和 COS-7 細胞上短暫表達的重組血管 K_{ATP} 通道的影響。

方法：我們使用膜片鉗技術，研究了可樂定在以下 4 種類型受體上的作用：1、天然的血管 K_{ATP} 通道；2、由不同種類的內向整流鉀通道(Kir6.0 家族: Kir6.1, 6.2)和

磺醯脲受體(SUR1, 2A, 2B)亞基不同組合組成的重組 K_{ATP} 通道；3、由 Kir6.2 亞基的缺失異構體(Kir6.2 Δ C36 通道)衍生成的 SUR 缺失型通道；4、ATP 敏感性降低的突變型 Kir6.2 Δ C36 通道 (Kir6.2 Δ C36-K185Q 通道)。

結果：可樂定($\geq 3 \times 10^{-8}$ M)抑制天然的 K_{ATP} 通道活性，在細胞貼附式的結構中其半數最大抑制濃度為 1.21×10^{-6} M，在膜內側翻外的結構中其半數最大抑制濃度為 0.89×10^{-6} M。在相近的效能下，可樂定 (10^{-6} 或 10^{-3} M) 同樣抑制各種 SUR/Kir6.0 重組的 K_{ATP} 通道、Kir6.2 Δ C36 通道和 Kir6.2 Δ C36-K185Q 通道的活性。

結論：臨床使用的可樂定濃度可以抑制血管平滑肌細胞中的 K_{ATP} 通道活性。這種抑制效應似乎與是其對 Kir6.0 亞基而非對 SUR 亞基作用的結果。

(劉伍 譯 馬皓琳 李士通 校)

BACKGROUND: We investigated the effects of the imidazoline-derived α_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 Δ C36 channels); and (4) mutant Kir6.2 Δ C36 channels with diminished sensitivity to ATP (Kir6.2 Δ 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 1.21×10^{-6} M and in inside-out configurations with a half-maximal inhibitory concentration value of 0.89×10^{-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 Δ C36 channel, and the Kir6.2 Δ 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.

腦狀態指數是否可以區分有意識和無意識的狀態？

Does the Cerebral State Index Separate Consciousness from Unconsciousness?

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Anesth Analg December 2011 113:1403-1410

背景：腦狀態監測 (CSM) 是一種基於腦電圖 (EEG) 的監測，用於評估全麻時的鎮靜深度。我們計算了它用於區分不同麻醉方案的手術病人有意識和無意識狀態能力的預期概率(P_K)。

方法：我們將以前研究的 40 名沒有術前用藥進行擇期手術全麻的成年病人的數位化 EEG 記錄，用 EEG 播放器重新播放並用 CSM 對其再分析。病人被隨機分成七氟醚-瑞芬太尼組和丙泊酚-瑞芬太尼組。研究設計包括慢速誘導和一次有意識地使病人蘇醒。對失去和恢復意識時的 CSM 數值進行對比。通過失去和恢復意識前後 30 秒的 CSM 數值計算 P_K 。

結果：有意識和無意識狀態之間差別的 P_K 是 0.75 ± 0.03 (平均值 \pm 標準誤)。對於七氟醚-瑞芬太尼組 P_K 是 0.71 ± 0.04 ，丙泊酚-瑞芬太尼組的 P_K 是 0.81 ± 0.03 。

結論：CSM 對於區分有意識和無意識狀態的能力與其他商業上可用的以 EEG 為基礎的參數相當。

(張怡譯 馬皓琳 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 ± 0.03 (mean \pm SE). For sevoflurane-remifentanyl, P_K was 0.71 ± 0.04 . For propofol-remifentanyl, P_K was 0.81 ± 0.03 .

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

圍術期藥品短缺：對麻醉實踐和病人安全的影響

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

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Anesth Analg December 2011 113:1429-1435;

最近，臨床圍術期使用的幾種藥物出現在國家緊缺藥物名單上。藥物的缺乏可能是因為原材料的缺乏，製造的問題和停止生產。用藥短缺對病人的醫療護理產生重大影響，並且創造了一個更易於產生用藥錯誤的環境。麻醉醫師應該積極與藥劑部門和醫院管理部門配合，提醒醫護人員，防止對病人的醫療護理和安全產生不良影響。

(安光惠譯 馬皓琳 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.

在產科麻醉裏什麼是新的？2011年 Gerard W. Ostheimer 講座

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

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Anesth Analg December 2011 113:1450-1458

“產科麻醉裏什麼是新的”講座由產科麻醉於圍生醫學協會始辦於1975年，以更新其成員上一年的醫學文獻。在1995年這個講座重新命名以紀念 Gerard W. Ostheimer，這位來自 Brigham 和女子醫院的產科麻醉醫師對產科麻醉知識和實踐做出了顯著貢獻。Ostheimer 的講座者綜述了產科麻醉、產科、圍生醫學和健康服務方面的文獻來確定與產科麻醉實踐相關的文章。這篇綜述總結了2010年文獻中最相關的刊物。

（劉朝輝譯，馬皓琳，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.

椎管內麻醉與全身麻醉技術在腹式子宮切除術後恢復品質及鎮痛效果方面的比較：一項前瞻性、隨機化對照試驗

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：經歷腹式子宮切除術的患者經常有明顯的術後疼痛，即使同時使用多模式鎮痛處理也不能緩解。與全身麻醉相比，椎管內麻醉有節省阿片類藥物的作用，並

且可能使患者獲得更好的術後恢復。本研究的主要目的是比較椎管內麻醉和全身麻醉對腹式子宮切除術後恢復品質的影響。

方法：本研究是一項前瞻性、隨機化、對照的臨床試驗。招募了 70 名健康女性並隨機分配以全身麻醉或椎管內麻醉技術為主要麻醉方案。主要觀察指標是總體恢復品質——術後 24 小時 40 問卷法 (QoR-40)。其他收集的資料包括術後疼痛評分和阿片類藥物的消耗量。用 Mann-Whitney *U* 檢驗、Fisher 精確核對總和線性回歸進行分析資料。 $P < 0.05$ 被認為有統計學意義。

結果：椎管內麻醉組與全身麻醉組術後 24 小時總體 QoR-40 評分的差異中位數 (95% 可信區間) 為 17 (11-21.5) ($P < 0.001$)。椎管內麻醉組患者的各項 QoR-40 亞成分中的恢復品質評分均優於全身麻醉組 (所有 $P < 0.005$)。椎管內麻醉組與全身麻醉組術後 48 小時總體 QoR-40 評分的差異中位數為 8 (6-10) ($P < 0.001$)。全身麻醉組術後阿片類藥物的消耗量和疼痛評分高於椎管內麻醉組。術後 24 小時 ($r^2 = 0.67$ [$P < 0.0001$, 95% 可信區間 0.77 - 0.51]) 和 48 小時 ($r^2 = 0.58$ [$P < 0.0001$, 95% 可信區間 0.72- 0.42]) 阿片類藥物的消耗量與術後恢復品質均存在反線性關係。

結論：椎管內麻醉比全身麻醉使腹式子宮切除術後患者獲得更好的恢復品質。椎管內麻醉的阿片類藥物節省作用與術後患者恢復品質更好有關。如排除禁忌症，椎管內麻醉可能更適用於這些患者。

(陳彬彬譯 馬皓琳 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.

抑制小鼠脊髓神經元中的 KCC2 能導致對熱刺激有超敏反應

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

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背景：KCC2 是特異性的神經元鉀氯離子協同轉運蛋白，是通過其影響脊髓神經元突觸後抑制來參與疼痛知覺的生理。我們將一種新被鑒定的、非常強效的 KCC2 選擇性抑制劑（D4）、有一個無活性的結構變異體（D4.14）和 Na-K-2Cl 協同轉運蛋白（NKCC1）抑制劑布美他尼，注入小鼠的鞘內腔來監測它們對熱誘發傷害性反應的影響。

方法：我們對商用鞘內導管進行了修改並通過手術放置到 2 組的 10 只小鼠中。手術恢復後，通過導管對這些小鼠注射 D4、D4.14 和布美他尼。注射每個測試藥物後進行傷害性測量（熱板法，甩尾法）並和媒介對照進行比較。

結果：每組中都有 2 只老鼠因為術後的併發症而被剔除。用 55°C 熱板法進行測量結果顯示，注射活性 KCC2 抑制劑後退縮潛伏期有統計學意義的顯著性縮短（ <0.01 ），但注射無活性化合物後並沒有變化（ $=0.78$ ）。在同一溫度下注射布美他尼後退縮潛伏期顯著延長（ $P=0.02$ ）。這些結果在 49°C 下用甩尾試驗可以確認。

結論：用熱板法和甩尾試驗進行測試證實，通過 D4 抑制 KCC2 可導致小鼠熱誘發的潛伏期縮短，而這兩個傷害性試驗都證實了布美他尼抑制 NKCC1 可導致對熱刺激有反應的潛伏期延長。

（唐亮 譯 馬皓琳 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.

綜述：β-腎上腺素能受體生理及其回饋 β-受體阻滯劑的藥物基因組學

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

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心肌 β-腎上腺素能受體 (βARs) 在變更心率、心肌收縮力及心肌舒張功能方面起了重要作用。啟動 β1AR 與 β2AR 可增加環磷腺苷濃度，並通過級聯反應產生心肌收縮；相反，啟動 β3AR 卻導致心肌收縮力下降。心衰患者由於 β1ARs 下調及 β3AR 活性與密度增高，導致環磷腺苷轉化減少，心肌收縮力下降。βAR 拮抗劑常用於冠心病及心衰患者的一般治療，但圍術期是否使用仍存有爭議。過去 20 年，β-受體阻滯劑的個體化反應一直為研究熱點，除藥代動力學、藥效動力學及種族差異外，基因變異也在其中扮演了重要角色。單核苷酸多態性 (SNP) 是人類最常見的基因變異。與 β1AR 臨床相關的 SNP 有 2 個 (Ser49Gly, Arg389Gly)，與 β2AR 相關的有 3 個 (Arg16Gly, Gln27Glu, Thr164Ile)，與 β3AR 相關的有 1 個 (Trp64Arg)。儘管結果存在爭議，但大量研究資料普遍顯示 βAR SNPs 與臨床結局 (例如心衰、冠心病、血管反應性、高血壓、哮喘、肥胖及糖尿病等疾病的臨床進展) 間存在潛在聯繫。雖然 βAR SNPs 並不直接導致疾病發生，但其似乎是某些疾病及應激與藥物反應的危險因素與修飾因數。相關圍術期研究也已證實，具有 Arg389Gly β1AR 多態性的患者其甘氨酸存有變異，發生圍術期不良事件的概率顯著增高。當瞭解基因變異的重要性後，圍術期藥物使用可能從簡單的治療干預轉變為更加個體化的腎上腺素能受體調節。

(范羽譯 薛張綱校)

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 β 1AR (Ser49Gly, Arg389Gly), 3 for the β 2AR (Arg16Gly, Gln27Glu, Thr164Ile), and 1 for the β 3AR (Trp64Arg). Although results are somewhat controversial, generally large datasets have the potential to show a relationship between β AR SNPs and outcomes such as development and progression of heart failure, coronary artery disease, vascular reactivity, hypertension, asthma, obesity, and diabetes. Although β 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 β 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.

關於嗎啡導致非小細胞肺癌的表皮生長因數路徑啓動的研究

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

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背景：表皮生長因數受體(EGFR)和 μ -型阿片受體(MOR)表達於非小細胞型肺癌(NSCLC)細胞和人類肺癌上，共同被激動。我們假設臨床上使用阿片類藥物，它是 MOR 激動劑且同時啓動 EGFR，可促進生長及存活的信號傳導。

方法：我們用 H2009，一種人類腺癌 NSCLC 細胞系，有組成性 EGFR 磷酸化作用，通過逆轉錄酶聚合酶鏈反應增加了 H2009 上 μ -型和 δ -型阿片受體的表達。我們運用 Western 蛋白印跡法，生物複合體細胞活素磁珠試驗，免疫螢光染色，BrdU 結合酶聯免疫吸附法，和 BioCoat™ Matrigel™ 侵入試驗分別檢驗細胞信號，細胞活素的表達，人類肺癌上 MOR 和 EGFR 的螢光定位分析，及細胞增殖與侵犯。

結果：類似於 EGF，嗎啡刺激 H2009 細胞上的 EGFR 的磷酸化作用，蛋白激酶 B，和 MAPK/ERK。OR 拮抗劑，納洛酮，EGFR 絡氨酸激酶抑制劑，埃羅替尼，MOR 和 δ -型阿片受體沉默使嗎啡和 EGF 誘導的信號磷酸化作用消失，意味著 OR 共啓動 EGFR。與 Beas2B 上皮細胞相比，H2009 細胞最主要分泌高水準細胞活素。意味著 H2009 細胞上分泌的細胞活素可能與 OR 的表達增加有關係。我們觀察了人類 NSCLC 組織的 EGFR 和 MOR 的螢光定位分析。功能上，嗎啡和上皮增長因數誘導 H2009 細胞增值和入侵，可以像埃羅替尼一樣被納洛酮逆轉。

結論：嗎啡通過 ORs 使 EGFR 磷酸化，導致瀑布式下游的 MAPK/ERK，Akt 磷酸化，細胞增殖和入侵。特別是，ORs 也與上皮因數誘導的 EGFR 的磷酸化有關係。人類肺癌 MOR 和 EGFR 共表達的增加表明嗎啡也許有促生長作用。

(侯文婷譯 薛張綱校)

BACKGROUND:Epidermal growth factor receptor (EGFR) is coactivated by the μ -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 δ -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 δ -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.

一種未經校正的脈搏波形測量心排量的方法在主動脈內球囊反搏患者中的應用

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

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背景：無創監測系統，如脈搏波形法等，正越來越多地應用於估測心排量。然爾主動脈內球囊反搏可能會使動脈血壓的波形產生諸多變異從而影響由脈搏波形估測

心排量的準確性。MostCare系統是一種由未經校準的脈搏波形估測心排量的方法。我們的研究將心衰並接受主動脈內球囊反搏患者中MostCare系統的結果與間斷地熱稀釋法測得的心排量進行比較，從而探討MostCare系統的可信度如何。

方法：研究包含了15名冠狀動脈搭橋術後需要主動脈內球囊反搏進行血流動力學支持的患者。放置肺動脈導管並且通過熱稀釋法測量心排量(ThD-CO)。MostCare系統直接連接在標準監護系統中，並通過橈動脈壓力波形計算出心排量(MostCare-CO)。資料獲取自三種不同的主動脈內球囊反搏比(1:1, 1:2, 1:4)以及移除球囊後。

結果：本次研究共分析了106對ThD-CO和MostCare-CO資料。ThD-CO與MostCare-CO之間具有良好的相關性($r=0.90$, 95%可信區間為0.86-0.93; $P<0.001$)。經過重複測量得到的平均心排量測量的誤差為-0.2L/min(-1.31至0.91L/min, 下限的95%可信區間為-1.72至-0.9; 上限的95%可信區間為0.5至1.32)，相對比百分比誤差為24。在不同主動脈內球囊反搏的設定頻率下，ThD-CO與MostCare-CO之間的結果非常一致。心排量的變化分別由2種不同方法進行計算。資料結果顯示相關性達到0.82(95%可信區間為0.76-0.87; $P<0.001$)平均誤差為0.14L/min(-1.31至1.59L/min, 下限95%可信區間為-1.62至-1.0; 上限95%可信區間為1.28至1.90)。

結論：MostCare系統可以在主動脈內球囊反搏的患者中監測心排量，並且結果可與熱稀釋法相媲美。球囊充氣和放氣所產生的動脈形態變化對MostCare系統並無顯著影響。

(黃劍譯 薛張綱校)

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.

使用全自動電腦確定氣管導管的位置：一項動物模型的評估

Automatic Computerized Endotracheal Tube Position Verification: An Animal Model Evaluation

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背景：氣管插管位置不當是發病率和死亡率的高危因素，核查和確認氣管插管位置是必要的。我們提出了使用影像學分析的方法，用電腦系統自動確定氣管插管位置。終端產品將不包含一台監視器，而是用一個小型的電子處理器自動分析所獲得的圖像。

方法：自動分析影像系統已經取得進展：它可以區分食管，氣管和隆突的圖像。在重組模式的相似性的基礎上，圖像處理包括把圖像轉換為灰度，提取，劃分到一個級別。在氣管插管的鋼絲上組裝有一個視頻感測器。這個鋼絲被放入到 10 個牛的喉嚨，並收集了視頻圖像。對所有影像進行分析，區分隆突，氣管或食管。影像被轉入新的系統。在每個測試週期中，9 個影像都使用該系統，第 10 個影像作為基準。該過程重複 10 次，所以每部影像有 9 次進行教學，一次進行測試。

結果：十個記錄的影像，其中 1600 圖像被提取（氣管：490 圖像;隆突：550 圖像;和食道：560 張）。只有 1 食管影像被誤認為氣管（假陽性 0.001%）。2 個隆突的影像和 22 個氣管的影像被誤列為食道（假陰性 0.041%），靈敏度：0.98，特異性：0.99。20 張隆突的圖像被誤列為氣管，25 張氣管圖像被誤列為隆突（假陽性 0.045%，假陰性 0.041%，靈敏度：0.96 和特異性：0.95）。

結論：對潛在的氣管插管位置的核查系統進行了評估。使用無灌注的生物組織顯示分析系統的高精度，有待進一步研究證實。

（劉珏瑩譯 薛張綱校）

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.

發生腸道缺血再灌注之後異氟烷吸入麻醉可保留肝肺的線粒體氧化功能

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

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背景：腸道的缺血再灌注（IR）發生之後可導致肝肺的功能障礙，繼而出現多器官功能衰竭。我們的研究是比較在發生 IR 之後，氫胺酮和異氟烷對於肝、肺線粒體氧化功能的影響各自不同之處。

方法：本實驗中成年雄性 Wistar 大鼠被隨機分配在四組中（對照組和 IR 組的大鼠或是經腹膜給予氫胺酮或是吸入異氟烷）。實驗將會測定肝和肺各自的線粒體最大耗氧量以及呼吸鏈效能。

結果：應用氫胺酮的時候腸道 IR 會確實會對肝和肺的線粒體氧化功能造成損害，而異氟烷則不然。

結論：在腸道 IR 之後，異氟烷吸入麻醉可保留肝肺的線粒體氧化功能。

（陸麗虹譯 薛張綱校）

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.

帶有突變基因 p.4894 的斯里蘭卡肉碱受體與惡性高熱、先天性神經肌肉疾病（帶有統一1型纖維）有關。

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: 斯里蘭卡肉碱受體1(RyR1)是一種 Ca^{2+} 釋放通道,位於骨骼肌肌漿網膜上。在患有惡性高熱和先天性肌病的患者中發現,在 DNA 水準 RyR1 有超過200多種差異。只有30種差異被充分認為是引起惡性高熱的突變因素。日本患者中攜帶 Ala4894Thr RyR1 更容易患惡性高熱和一種罕見的肌病(一種先天的神經肌肉肌病帶有統一的1型纖維)。我們假設不同的 RyR1 Ala4894 差異導致了不同的病理生理改變,其對 RyR1 激動劑有不同的藥理學敏感性。

方法: 表達 RYR1 突變基因的媒介物感染人體胚胎的腎293細胞。經過72小時的感染,我們發現在咖啡因和4CmC 的作用下細胞內 Ca^{2+} 發生了變化。

結果: 感染 Ala4894Th 和 rAla4894Ser 的細胞比野生株對咖啡因更加敏感。感染 Ala4894Thr 的細胞比野生株對4CmC 更加敏感。然而,感染 Ala4894Pro 的細胞對咖啡因和4CmC 都沒有反應。感染 Ala4894Gly 的細胞比野生株對咖啡因敏感度低。另外,感染 Ala4894Thr, Ala4894Ser 的細胞對咖啡因的反應會被丹曲林所抑制。

結論: 我們發現不同的 RyR1Ala4894 基因差異會導致其對激動劑或拮抗劑的敏感性不同,可能預示著 RYR1 在興奮收縮偶聯功能上的不同與對惡性高熱的敏感性不同。高敏感性的 Ala4894Thr-RyR1 與惡性高熱、低功能的 Ala4894Pro-RyR1 (帶有統一的1型纖維) 聯繫密切。

(翁梅琳譯 薛張綱校)

BACKGROUND: Ryanodine receptor 1 (RyR1) is a 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.

鞘內注射不含聚乙二醇的甲強龍來增加醫療安全

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

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背景：先前的研究證實鞘內注射甲強龍對於治療帶狀皰疹後神經痛非常有效。然而以聚乙二醇作為防腐劑限制了鞘內甲強龍的廣泛使用。本研究中，我們打算減少聚乙二醇的濃度，目的是精確計算出醋酸甲強龍中所需的聚乙二醇濃度。

方法：單劑量 80 毫克的醋酸甲強龍用於提取聚乙二醇部分。在兩相反應後，我們小心的提取出只含有類固醇的部分。我們在不同的時間點提取，通過液相色譜和質譜法計算聚乙二醇和甲強龍的量。小樣本採用 PH 試紙測定 PH 值。

結果：使用單側檢驗以及 Bonferroni 校正顯示在不同時間蒸餾後和基線值之間存在統計學差異。蒸餾 2 至 4 小時得到聚乙二醇的最小量 78%，最大量為 85%。然而，我們沒有改變溶液的 PH 值和甲強龍的濃度。

結論：通過我們的方法降低聚乙二醇的濃度，甲強龍相關併發症會減少，在帶狀皰疹後神經痛患者對其他治療無反應後應該考慮給予他們這個治療方法，因為他們有可能接受反復的鞘內給藥。

(姚敏敏譯 薛張綱校)

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.

鞘內注射低劑量納洛酮通過增加坐骨神經橫斷大鼠的脊髓突觸間隙的興奮性氨基酸的重吸收增強嗎啡的鎮痛效果

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：在這個研究中，我們試驗了低劑量納洛酮對嗎啡鎮痛效果的影響和對有神經痛的大鼠的脊髓背角谷氨酸轉運體表達的影響。

方法：通過部分橫斷的 Wistar 大鼠的左側坐骨神經來誘發神經病理性疼痛，同時鞘內置管用來給藥；一些大鼠鞘內放置微透析探針來收集腦脊液。疼痛用腳底測試——一種哈格裏夫斯熱輻射裝置——來評估，也可用 von Frey 測試來評估。用 Western 標記法和免疫組化法來測定左側脊髓背角谷氨酸轉運蛋白的表達。興奮性氨基酸（EAAs）谷氨酸和腦脊液中天門冬氨酸的水準用高液相色譜法來測定。

結果：減少與坐骨神經橫斷（PST）同側的脊髓背角的板層 I 和 II 內星形細胞谷氨酸轉運體的表達（GLT-1 和 GLAST 水準分別為 55% 和 53%，在假手術大鼠中），可觀察到疼痛過敏和 PST 後肢痛。高劑量納洛酮（15 微克）減少嗎啡（10 微克）抗疼痛過敏和鎮痛效果。相反，小劑量（15 納克）納洛酮增強嗎啡（10 微克）鎮痛效果，與單用嗎啡治療相比熱刺激的避退反射閾值增加（19% 上升至 35%），觸覺刺激的避退反射閾值也增加（33% 上升至 55%），這與恢復同坐骨神經橫斷（PST）同側的脊髓背角的板層 I 和 II 內星形細胞的 GLAST 和 GLT-1 表達水準（分別為 102% 和 114%）和降低腦脊液中 EAA 水準（谷氨酸 10 μ M，天門冬氨酸 1.1 μ M）相關。

結論：低劑量納洛酮增強嗎啡在 PST 大鼠中的鎮痛效果，可能是通過修復星形膠質細胞表達的 GLAST 和 GLT-1，這些物質抑制突觸間隙中 EAAs 的積聚，獲得神經保護作用。

（張玥琪譯，薛張綱校）

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 μ g) attenuated the antihyperalgesia and antiallodynia effects of the morphine (10 μ g). In contrast, ultra-low dose (15 ng) naloxone enhanced the antinociceptive effect of morphine (10 μ g), 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 μ M; aspartate: 1.1 μ 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.

綜述：體外迴圈期間止血系統的啓動

Review Articles: Activation of the Hemostatic System During Cardiopulmonary Bypass

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體外迴圈是一個獨特的臨床環節，它會導致止血系統的廣泛啓動。但是手術也會啓動凝血、血小板以及纖溶系統，這些都與受傷時的止血機制有關。一般的體外迴圈主要通過稀釋凝血細胞和凝血酶來影響正常的凝血機制，通過自體血回輸以及啓動血液中各種系統，包括血小板系統，激肽釋放酶激肽系統和纖溶系統。激肽釋放酶激肽系統的啓動能增加刺激 XIIa 因數，激肽釋放酶，緩激肽和血漿纖溶酶原活化水準，但是幾乎對凝血酶的啓動無作用。血漿纖維蛋白原的啓動和迴圈纖維蛋白單體的增加會引起纖溶酶的產生，它可以去除纖維蛋白。體外迴圈的非內皮表面，連同迴圈中的凝血酶和纖溶酶，可以引起血小板的啓動。血小板受體缺失以及降低血小板對於損傷的反應。本綜述重點在體外迴圈引起止血系統啓動的機制和文獻中報導中標誌物的監測。此外，還討論了抑制啓動的方法，包括限制心臟切開術的吸引，增加迴圈生物相容性，抗凝血酶和抗纖溶的使用。決定哪一類病人將會從這種療法中受益最終需要凝血蛋白表達基因表型的調查。但是，到目前為止，聯合使用上述方法來抑制體外迴圈凝血系統啓動似乎是合理的。

(範逸辰 譯 陳傑 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 cardiomy 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.

布比卡因使長 QT 綜合征的細胞和計算模型的動作電位不穩定

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

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背景：局部麻醉藥布比卡因對心肌動作電位（APs）的影響主要歸因於抑制心臟 Na⁺通道。與之相關的誘導阻滯高親和力 hERG 通道的能力目前尚不清楚。作者研究了這種相互作用是否對長 QT 綜合征的細胞和計算模型作用更顯著。

方法：從成年豚鼠心分離左心室心肌細胞出來的，並使用膜片鉗技術研究布比卡因誘導的動作電位效應。藥理學中 LQT 樣狀態由抑制 I_{ks}（LQT1，10μmol/L 色原烷醇 293B）或 I_{kr}（LQT2，10μmol/L E4031）引起。布比卡因效應的計算分析是基於 Luo-Rudy 動態模型。

結果：布比卡因導致心肌細胞的劑量依賴型動作電位縮短。然而，應用 1—30μmol/L 的布比卡因時，觀察到延長的 AP 持續時間的變異度高達 40%。這種 AP 持續時間不穩定效應在類 LQT1 心肌細胞中顯著增加，但在類 LQT2 心肌細胞中則不明顯。類似的，在應用 3μmol/L 的布比卡因時類 LQT1 AP 延長的發生率由 6% 顯著增加至 24%，類 LQT2 心肌細胞並非如此。計算模型支援了這種概念，即這種在對照心肌細胞和類 LQT1 心肌細胞中由布比卡因誘導的 AP 不穩定和 AP 延長是由於抑制 hERG 通道而造成。

結論：這項研究提供的證據表明，布比卡因誘導了 hERG 通道的抑制，這在正常情況下是功能沉默的而在類 LQT1 狀態下變得更加相關，在類 LQT1 狀態下複極化更大程度上依賴 hERG 通道。因此，布比卡因在心臟離子電流的正常平衡改變時心臟鈉離子通道以外的作用決定其心臟淨效應。

（孫曉瓊 譯 陳傑 校）

BACKGROUND: The effects of the local anesthetic bupivacaine on cardiac action potentials (APs) are mainly attributed to inhibition of cardiac Na⁺ 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 Na^+ channels may, therefore, determine the net cardiac effects of bupivacaine when the normal balance of ionic currents is altered.

在複雜的脊柱外科手術中連續無創血紅蛋白的監測

Continuous Noninvasive Hemoglobin Monitoring During Complex Spine Surgery

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背景：目前在手術室中血紅蛋白的監測需要反復抽血，多個步驟，延遲一段不確定的時間才能得到結果。因此對於是否需要輸血的管理可能會推遲或在結果出來前就已決定是否輸血。連續無創的血紅蛋白監測可以更及時地評估患者的病情和更適當地進行血液的管理。有一項新的技術，即 CO-脈搏血氧飽和度 (SpHb)，通過在手指上放置一個感測器來提供連續的無創血紅蛋白濃度監測。作者評估了 SpHb 與實驗室 CO 血氧儀測量的血紅蛋白值 (tHb) 相比，在具有失血高風險的複雜性脊柱手術中的準確性。

方法：研究物件入選標準為行複雜脊柱外科手術需有創動脈、中心靜脈監測和每小時血紅蛋白測量的患者。每小時採取一次血液樣本（若有臨床指征可增加次數），使用實驗室 CO-血氧飽和度測量血紅蛋白，即許多醫院測量血紅蛋白的標準方法。同一個時刻 tHb 和 SpHb 的測量結果進行比較。

結果：21 名患者入選研究。tHb 的平均值為 6.9-13.9g/dl，SpHb 的平均值為 6.9-13.4g/dl。共有 186 對資料 (tHb/SpHb) 進行了分析，排除 SpHb 信號差的資料後

剩下 130 對資料的偏差（定義為 tHb 和 SpHb 之間的差異）和精確度（定義為差值的一個標準差）分別為 $-0.1 \text{ g/dL} \pm 1.0 \text{ g/dL}$ 。Bland-Altman 分析法表明 tHb 和 SpHb 之間關係良好，差異範圍為 -2.0 to 1.8 g/dL 。絕對的偏差和精確度為 $0.8 \pm 0.6 \text{ g/dL}$ 。

結論：在複雜性脊柱外科手術中，連續無創的 CO-脈搏血氧血紅蛋白監測與標準實驗室儀器進行的血紅蛋白監測精確度的偏差是在臨床可接受的範圍內，為 1.5 g/dL 之內。這種技術可提供與間歇性血液樣本分析相比更即時的血紅蛋白值的監測，這樣我們可以在手術中提高對血液的管理。

（滕凌雅 譯 陳傑 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 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 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.

普外科擇期手術的手術時機以及術後 30 天死亡率

Operation Timing and 30-Day Mortality After Elective General Surgery

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背景：疲勞、晝夜節律、作息時間以及配備人員等人為因素可能影響患者在醫療期間的照顧。交通運輸業的研究發現輪班工作制、晝夜節律紊亂以及加班可使人的工作效率有所降低。作者猜測：是否普外科手術的手術時機（尤其增加了時間、周數以及七月或者八月對比其他月份）以及月相與 30 天死亡率獨立相關。住院患者比較的次要結果也被評估。

方法：對克裏蘭夫診所在 2005 年 1 月至 2010 年 9 月行擇期普外科手術的 32,001 例患者進行手術時間（上午六點至下午七點），工作日的時間，月份，以及月相的二進位結果分析。30 天死亡率通過多變數邏輯回歸方法被作為一個二進位端點，在 ICD 編碼（國際疾病分類標準）的基礎上增加了風險指數。

結論：死亡率與工作日的手術時間並無差別。一周中工作日的差別也未被發現 (0.99 [0.83, 1.17])。七月以及八月手術的死亡率與其他月份相比無明顯差別 (OR=0.72 [0.36, 1.43], $P = 0.22$) 月相和死亡率沒有明顯相關 ($P = 0.72$)。對照組別種時間的分割沒有明顯的意義。

結論：普外科擇期手術在一天中的任何時間、一周中的任何天數以及一年中的任何月份進行都是安全的。

（龔寅 譯 陳傑 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 (9th 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.

應用 Rasch 模型制定簡化版多屬性效用量表評估產婦硬膜外鎮痛的認知程度

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應基於保健行為理論，如多屬性效用判斷理論等，這對解釋心理因素和分娩疼痛之間的複雜關係是必要的。在此研究中，作者旨在使用 Rasch 分析簡化以往 20 項的多屬性問卷，依靠多屬性效用理論來評估分娩後硬膜外鎮痛的認知程度。

方法：使用 Rasch 分析選擇性減縮分類，排除不適合的專案和患者，生成線性的分娩硬膜外鎮痛認知評分（ATLEA）。問卷中的專案屬性和分類閾值也進行評估。進一步，將簡化量表和完全量表進行可靠性和經驗上的有效性的比較。

結果：167 名產婦完成問卷。最初的 10 項分級量表整合成 4 項，並未影響可靠性。3 名被調查者和 11 個專案因為不適合被排除。簡化版和完全版的可靠性指數分別為 0.68 和 0.74。簡化版和完全版問卷的 ATLEA 評分關聯係數為 0.89。通過計算受試者工作特徵曲線（ROC 曲線）下面積，得出簡化版和完全版的 ATLEA 評分對決定分娩後硬膜外鎮痛的實證效度分別為 0.80 和 0.81。

結論：研究論證了採用 Rasch 分析簡化多屬性效用量表並未影響可靠性，需要進一步研究證明簡化問卷在臨床實際中的有效性。

（陸秉璋 譯 陳傑 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 人神經膠質細胞體外培養模型中 2-去氧-D 葡萄糖可減弱異氟醚導致的細胞毒性作用

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：β-澱粉樣蛋白 (Aβ) 累積以及細胞凋亡蛋白酶顯示參與阿茲海默病的神經發病機理。Aβ 通過天冬氨酸蛋白酶 β-位點產生澱粉樣前體蛋白水解酶 (BACE)，裂解澱粉樣前體蛋白而產生。吸入異氟醚可以減少 caspase 活化並增加 BACE 和 Aβ 的水準。然而，異氟醚導致的神經毒性的機制仍需要進一步研究。類似葡萄糖的 2-DG 有神經保護作用。因此，作者設法證明是否 2-DG 能減少異氟醚導致的 caspase-3 的活化並增加 BACE 的水準。

方法：H4 人神經膠質瘤細胞用生理鹽水或者 2-DG (5 mM) 處理 1 個小時，然後作對照組或 2% 異氟醚持續 6 個小時。監測 caspase-3 水準，BACE，細胞內鈣水準和 ROS。使用方差分析評估 2-DG 和異氟醚的交互作用。

結果：在 H4 人神經膠質瘤細胞，2-DG 減少 caspase-3 啟動(477% vs 186%, $F = 8.68$; $P = 0.019$) 並增加 BACE 水準(345% vs 123%, $F = 42.24$; $P = 0.0002$)。2-DG 減少細胞內鈣水準及 ROS(100% vs 66%, $F = 1.94$; $P = 0.014$)。

結論：2-DG 可能氧化應激並增加細胞內鈣水準，這樣可以減少異氟醚導致的神經毒性。

(丁佳 譯 陳傑 校)

BACKGROUND: β-Amyloid protein (Aβ) accumulation and caspase activation have been shown to contribute to Alzheimer disease neuropathogenesis. Aβ is produced from amyloid precursor protein through proteolytic processing by aspartyl protease β-site amyloid precursor protein-cleaving enzyme (BACE). The inhaled anesthetic isoflurane has been shown to induce caspase activation and increase levels of BACE and Aβ. 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.

大鼠突觸支架蛋白 Homer 1b/c 降解可減弱由 CFA 誘導的繼發痛覺過敏

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: 早先的研究證明了 Homer 1b/c 作為一種突觸後分子的支架蛋白在神經突觸鏈結、聚集親代謝性谷氨酸受體，對其信號傳遞有很大作用。本研究中作者調查了由完全弗氏佐劑 (CFA) 誘導的在繼發的痛覺過敏中 Homer 1b/c 可能的參與作用。

方法: 對 Wistar 大鼠的左後踝關節注射 CFA 來誘導慢性炎症。從炎症開始向鞘內注射 Homer 1b/c 反義或錯義寡核苷酸(反義, 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; 錯義, 10 $\mu\text{g}/10 \mu\text{L}$) 5 到 8 天。在鞘內注射之前和之後就確定停藥的閾值和其對機械或溫覺刺激的潛伏期。應用免疫技術檢測脊髓內 Homer 1b/c 的表達與分佈。

結果: 大鼠在 CFA 注射後 24 小時內出現機械性異常疼痛和溫覺過敏，且持續超過 2 周。在炎症後 7 天 Homer 1b/c 的表達到達高峰，28 天回到基線水準。Homer 1b/c 反義寡核苷酸的鞘內注射顯著減少了 Homer 1b/c 蛋白在脊髓的表達。另外，Homer 1b/c 反義寡核苷酸的注射減弱了第 2 到 5 天的繼發性機械性痛覺超敏，並且減輕了第 3 到 4 天的溫覺超敏。錯義寡核苷酸對 Homer 1b/c 的表達和超敏化沒有影響。而幼鼠，Homer 1b/c 反義寡核苷酸並沒有影響其機械性和溫覺反應以及自主活動。

結論: 這些最新結果顯示脊髓的 Homer 1b/c 參與了 CFA 誘導的繼發痛覺過敏，它可能成一種疼痛治療新的靶目標。

(俞劼晶 譯 陳傑 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.

上止血帶或神經阻滯後小腿的體位能加強臑窩徑路坐骨神經阻滯的效果

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，作者假設小腿的體位及止血帶的應用與普通小腿中立位相比能改變兩點刺激法坐骨神經阻滯的阻滯效果。

方法：隨機連續入組骨科患者 90 例，ASA 分級 I-II 級，擇期臑窩阻滯麻醉下行足部及腳踝部手術（患者俯臥位，應用兩點刺激法）。患者隨機分為三組，組 1 中患者神經阻滯完成後翻身平臥後立即將小腿置於中立位，組 2 中患者大腿屈曲 45 度角並維持該體位 15 分鐘，組 3 中將患者小腿置於中立位並上止血帶，患者仰臥位注射局麻藥物時止血帶充氣。局麻藥為常規 2% 丙胺卡因 15mL 及 0.5% 左旋布比卡因 15mL 混合液。

結果：組 2 及組 3 患者的感覺阻滯及運動阻滯起效時間有所縮短，阻滯恢復時間有所延長。

結論：在日常麻醉中應用以上兩種方法包括注射時上止血帶及兩點刺激法膕窩徑路坐骨神經阻滯後立即仰臥位並使小腿旋後位也許能同樣的增加麻醉阻滯的效果。作者認為坐骨神經阻滯時小腿的特殊體位及止血帶的應用能使阻滯神經周圍局麻藥分佈增加並導致起效時間縮短及作用時程的延長。

(陳毓雯 譯 陳傑 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.