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### 內皮多糖在齧齒類動物出血性休克模型中的血漿修復作用

#### Plasma Restoration of Endothelial Glycocalyx in a Rodent Model of Hemorrhagic Shock

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**背景:**在有出血性休克的創傷患者中使用以血漿為基礎的復蘇療法可降低死亡率。儘管一些人提出通過凝血蛋白替換產生有益效果，但血漿給予保護效果的確切機制仍不清楚。我們先前證實在一個細胞培養模型中血漿與晶體液相比降低了內皮細胞的通透性。由蛋白聚糖和糖蛋白組成的內皮多糖包被粘附到多配體聚糖骨架上，它們共同保護下面的內皮層。我們假設出血性休克後血漿產生的內皮細胞保護作用是部分由於其對內皮多糖包被的修復作用和多配體聚糖 1 的保護作用。

**方法:**大鼠遭受出血性休克後，達到平均動脈血壓 30mmHg 並持續 90 分鐘。隨後接受乳酸林格氏液或新鮮血漿復蘇，達到平均動脈血壓 80mmHg，並與假手術組和單純休克組作對比。2 小時後取出肺檢測多配體聚糖 mRNA、用抗多配體聚糖-1 免疫染色，或者用蘇木素和曙紅染色。為了特異性檢測血漿對內皮的作用，我們從小腸系膜灌注鑷標記的溶液來識別小靜脈，並通過電子顯微鏡使多糖包被顯影。所有資料用均數±標準誤表示。用單因素方差分析和 Tukey 後續檢驗來分析結果。

**結果:**電子顯微鏡顯示出血性休克後多糖包被降解，這被血漿而不是乳酸林格氏液所部分緩解。在接受血漿復蘇的動物組肺部多配體聚糖-1 mRNA 的表達( $2.76 \pm 0.03$ )要高於單純休克組( $1.39 \pm 0.22$ )和乳酸林格氏液組( $0.82 \pm 0.03$ )，並且和細胞表面多配體聚糖-1 免疫染色相關。組織學評分是( $1.63 \pm 0.26$ )顯示休克也導致明顯的肺部損傷，此作用可血漿復蘇減輕( $0.67 \pm 0.17$ )，而不是乳酸林格氏液( $2.0 \pm 0.25$ )。

**結論:**血漿在出血性休克後的保護效果可能是部分由於其修復內皮多糖包被和保護多配體聚糖-1 的能力。

(劉朝輝譯 馬皓琳 李士通校)

**BACKGROUND:** The use of plasma-based resuscitation for trauma patients in hemorrhagic shock has been associated with a decrease in mortality. Although some have proposed a beneficial effect through replacement of coagulation proteins, the putative mechanisms of protection afforded by plasma are unknown. We have previously shown in a cell culture model that plasma decreases endothelial cell permeability in comparison with crystalloid. The endothelial glycocalyx consists of proteoglycans and glycoproteins attached to a syndecan backbone, which together protect the underlying endothelium. We hypothesize that endothelial cell protection by plasma is due, in part, to its restoration of the endothelial glycocalyx and preservation of syndecan-1 after hemorrhagic shock.

**METHODS:** Rats were subjected to hemorrhagic shock to a mean arterial blood pressure of 30 mm Hg for 90 minutes followed by resuscitation with either lactated Ringer's (LR) solution or fresh plasma to a mean arterial blood pressure of 80 mm Hg and compared with shams or shock alone. After 2 hours, lungs were harvested for syndecan mRNA, immunostained with antisyndecan-1, or stained with hematoxylin and eosin. To specifically examine the effect of plasma on the endothelium, we infused small bowel mesentery with a lanthanum-based solution, identified venules, and visualized the glycocalyx by electron microscopy. All data are presented as mean  $\pm$  SEM. Results were analyzed by 1-way analysis of variance with Tukey post hoc tests.

**RESULTS:** Electron microscopy revealed degradation of the glycocalyx after hemorrhagic shock, which was partially restored by plasma but not LR. Pulmonary syndecan-1 mRNA expression was higher in animals resuscitated with plasma ( $2.76 \pm 0.03$ ) in comparison with shock alone ( $1.39 \pm 0.22$ ) or LR ( $0.82 \pm 0.03$ ) and correlated with cell surface syndecan-1 immunostaining. Shock also resulted in significant lung injury by histopathology scoring ( $1.63 \pm 0.26$ ), which was mitigated by resuscitation with plasma ( $0.67 \pm 0.17$ ) but not LR ( $2.0 \pm 0.25$ ).

**CONCLUSION:** The protective effects of plasma may be due in part to its ability to restore the endothelial glycocalyx and preserve syndecan-1 after hemorrhagic shock.

### 異氟烷選擇性抑制漂亮新小杆線蟲中遠端線粒體複合物 I

#### Isoflurane Selectively Inhibits Distal Mitochondrial Complex I in *Caenorhabditis Elegans*

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**背景：**線粒體電子傳遞鏈（ETC）中的複合物 I 是揮發性麻醉劑（Vas）的一個可能靶點。複合物 I 酶的活性能夠被 VAs 抑制，而複合物 I 功能障礙則能夠導致蠕蟲和人對 Vas 的超敏反應。漂亮新小杆線蟲（*C. elegans*）的突變分析提示 VAs 可以在複合物 I 底物泛醌結合部位特異性地干擾複合物 I 功能。我們假設異氟烷通過與泛醌競爭結合複合物 I 而抑制電子傳遞。

**方法：**採用野生型和突變型漂亮新小杆線蟲來研究異氟烷對離體線粒體的作用。使用確定的方法測定 ETC 的酶活性並確定劑量-反應曲線。異氟烷處理線粒體後行線粒體蛋白的平面非變性凝膠電泳。

**結果：**複合物 I 是 ETC 中對異氟烷抑制作用最敏感的組成部分；而複合物 I 近端部位（黃素蛋白）則對異氟烷相對不敏感。異氟烷和醌並不競爭結合複合物 I 上的公用位點。在體外研究中，複合物 I 酶活性的絕對比例不能預測異氟烷對動物的制動作用。異氟烷對線粒體超複合物的穩定性無可測量的影響。通過複合物 I 減少泛醌表現為不受異氟烷影響的正性協同動力學作用。

**結論：**異氟烷在遠離黃素蛋白亞複合物的一個位點直接抑制複合物 I。然而，我們推翻了先前的假設，即異氟烷和泛醌競爭結合複合物 I 上的同一個疏水性結合位點。此外，異氟烷對線蟲的制動作用並非是由於減少了離體線粒體中測得的複合物 I 電子傳遞的絕對數量。

(江繼宏 譯 馬皓琳 李士通 校)

**BACKGROUND:** Complex I of the electron transport chain (ETC) is a possible target of volatile anesthetics (VAs). Complex I enzymatic activities are inhibited by VAs, and dysfunction of complex I can lead to hypersensitivity to VAs in worms and in people. Mutant analysis in *Caenorhabditis (C.) elegans* suggests that VAs may specifically interfere with complex I function at the binding site for its substrate ubiquinone. We hypothesized that isoflurane inhibits electron transport by competing with ubiquinone for binding to complex I.

**METHODS:** Wildtype and mutant *C. elegans* were used to study the effects of isoflurane on isolated mitochondria. Enzymatic activities of the ETC were assayed and dose-response curves determined using established techniques. Two-dimensional native gels of mitochondrial proteins were performed after exposure of mitochondria to isoflurane.

**RESULTS:** Complex I is the most sensitive component of the ETC to isoflurane inhibition; however, the proximal portion of complex I (the flavoprotein) is relatively insensitive to isoflurane. Isoflurane and quinone do not compete for a common binding site on complex I. The absolute rate of complex I enzymatic activity in vitro does not predict immobilization of the animal by isoflurane. Isoflurane had no measurable effect on stability of mitochondrial supercomplexes. Reduction of ubiquinone by complex I displayed positive cooperative kinetics not disrupted by isoflurane.

**CONCLUSIONS:** Isoflurane directly inhibits complex I at a site distal to the flavoprotein subcomplex. However, we have excluded our original hypothesis that isoflurane and ubiquinone compete for a common hydrophobic binding site on complex I. In addition, immobilization of the nematode by isoflurane is not due to limiting absolute amounts of complex I electron transport as measured in isolated mitochondria.

### 肝移植手術前黃疸病人與近紅外腦組織氧飽和度低相關的實驗室指標

#### Laboratory Variables Associated with Low Near-Infrared Cerebral Oxygen Saturation in Icteric Patients Before Liver Transplantation Surgery

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**背景：**儘管局部腦組織的氧飽和度 (rSO<sub>2</sub>) 監測可以探測到腦部的氧合失調，然而其有效性在高膽紅素血症病人中受到了限制。我們在行肝移植手術前的有終末期肝病的清醒患者中，採集了 rSO<sub>2</sub> 和其他可能影響低 rSO<sub>2</sub> 解釋的實驗室指標之間的關係。

**方法：**全麻誘導前，我們對 164 名肝硬化患者 (Child 分級 A/B/C = 19/41/104) 和 8 名暴發性肝功能衰竭的患者測定了 rSO<sub>2</sub>。將 West Haven 肝性腦病評級為 3 或 4 級的患者排除。使用相關分析和多變數回歸分析以及接收者操作特徵曲線分析來評價 rSO<sub>2</sub> 與實驗室檢查指標之間的關係。

**結果：**單變數分析結果表明 rSO<sub>2</sub> (中位數 58.5%，範圍 15%~82%) 與血清總膽紅素、血紅蛋白 (Hb)、肌酐、鈉離子和鎂離子的濃度以及凝血酶原時間相關 ( $P$  均 < 0.001)，但與血清中葡萄糖、白蛋白、鉀及氨的濃度無關。多元邏輯回歸分析結果表明僅有較高的總膽紅素 (範圍為 0.4 至 66mg/dL，比值比[OR]=1.31, 95% 置信區間[CI]為 1.18 至 1.45) 和低血紅蛋白 (範圍為 5.4 至 15.7g/dL，比值比=0.21, 95% 置信區間為 0.11 至 0.43) 與 rSO<sub>2</sub> <50% 獨立相關。觀察 rSO<sub>2</sub> <50% 的最佳界值點是總膽紅素 >7.2 mg/dL (靈敏性 89%，特異性 90%) 以及血紅蛋白 <9.6 g/dL (靈敏性 70%，特異性 82%)。

**結論：**在等待肝移植手術的終末期肝病患者中，高總膽紅素和低血紅蛋白濃度與 rSO<sub>2</sub> 值低於 50% 獨立相關。本研究的結果可鑒別那些低 rSO<sub>2</sub> 可能是一種假像而非腦缺血的患者。

(劉伍 譯 馬皓琳 李士通 校)

**BACKGROUND:** Although regional cerebral oxygen saturation (rSO<sub>2</sub>) measurements can detect disturbances in cerebral oxygenation, their usefulness is limited in patients with hyperbilirubinemia. We examined the relationship between rSO<sub>2</sub> and other laboratory variables that may affect interpretation of low rSO<sub>2</sub> in awake patients with end-stage liver disease before liver transplantation surgery.

**METHODS:** Before induction of general anesthesia, rSO<sub>2</sub> was measured in 164 patients with liver cirrhosis (Child class A/B/C = 19/41/104) and 8 with fulminant hepatic failure. Patients with West Haven hepatic encephalopathy of grade 3 or 4 were excluded. Relationships between rSO<sub>2</sub> and laboratory variables were evaluated by correlation and multivariate regression, and by receiver operating characteristic curve analysis.

**RESULTS:** Univariate analyses showed that rSO<sub>2</sub> (median 58.5%, range 15% to 82%) correlated with serum total bilirubin, hemoglobin (Hb), creatinine, sodium, and magnesium concentrations, and prothrombin time ( $P$  < 0.001 each), but not with serum concentrations of glucose, albumin, potassium, and ammonia. Multiple logistic regression analysis showed that only elevated total bilirubin (range 0.4 to 66 mg/dL; odds ratio [OR] = 1.31; 95% confidence interval [CI] = 1.18 to 1.45) and low Hb (range 5.3 to 15.7 g/dL; OR = 0.21; 95% CI = 0.11 to 0.43) were independently related to rSO<sub>2</sub> <50%. The

optimum cutoff points for observing an  $rSO_2 < 50\%$  were total bilirubin  $> 7.2$  mg/dL (sensitivity 89%, specificity 90%) and Hb  $< 9.6$  g/dL (sensitivity 70%, specificity 82%).  
**CONCLUSIONS:** High total bilirubin and low Hb concentrations were independently associated with  $rSO_2$  values below 50% in end-stage liver disease patients awaiting liver transplantation. The results of this study identify patients in whom a low  $rSO_2$  may be an artifact rather than cerebral ischemia.

### 活性炭可有效清除現代麻醉機中的吸入麻醉藥

#### Activated Charcoal Effectively Removes Inhaled Anesthetics from Modern Anesthesia Machines

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背景：如果一名惡性高熱易感病人要接受一個麻醉藥，之前使用過揮發性麻醉藥的麻醉機必須用大流量的新鮮氣流沖洗過以後才能使用。根據以往的不一致的研究結果提出的建議是沖洗時間從 10-104 分鐘不等。曾經有研究者提出了一種淨化技術：在呼吸回路的吸氣端放置一個活性炭的濾器。

方法：我們在一些污染的麻醉機的吸氣和呼氣端都放置了活性炭濾器，並測定使輸出的異氟醚、七氟醚和地氟醚的濃度要小於 5 個兆北率 (ppm) 所需要的沖洗時間。接下來我們模擬了麻醉誘導後 90 分鐘診斷為惡性高熱的病例，並研究活性炭限制惡性高熱病人吸入麻醉藥進一步暴露的作用的大小。

結果：活性炭濾器可以在小於 2 分鐘的時間內使污染的麻醉機輸送的揮發性麻醉藥的濃度降低到一個可接受的水準，並且可以在至少 60 分鐘內維持濃度小於 5ppm。我們發現，當麻醉誘導後診斷為惡性高熱時，現在使用的麻醉機加用活性炭濾器後，在吸入麻醉藥濃度超過 5ppm 之前，至少還可以使用 67 分鐘。

結論：使用過吸入麻醉藥的麻醉機的沖洗時間一般需要 10-104 分鐘，活性炭濾器提供了一種改變了這一時間的方法。

(安光惠譯 馬皓琳 李士通校)

**INTRODUCTION:** If a malignant hyperthermia-susceptible patient is to receive an anesthetic, an anesthesia machine that has been used previously to deliver volatile anesthetics should be flushed with a high fresh gas flow. Conflicting results from previous studies recommend flush times that vary from 10 to 104 minutes. In a previously proposed alternative decontamination technique, other investigators placed an activated charcoal filter in the inspired limb of the breathing circuit.

**METHODS:** We placed activated charcoal filters on both the inspired and expired limbs of several contaminated anesthesia machines and measured the time needed to flush the machine so that the delivered concentrations of isoflurane, sevoflurane, and desflurane would be  $< 5$  parts per million (ppm). We next simulated the case for which malignant hyperthermia is diagnosed 90 minutes after induction of anesthesia and measured how well activated charcoal filters limit further exposure.

**RESULTS:** Activated charcoal filters decrease the concentration of volatile anesthetic delivered by a contaminated machine to an acceptable level in <2 minutes. The concentrations remained well below 5 ppm for at least 60 minutes. When malignant hyperthermia is diagnosed after induction of anesthesia, we found that with charcoal filters in place, the current anesthesia machine may be used for at least 67 minutes before the inspired concentration exceeds 5 ppm.

**CONCLUSIONS:** Activated charcoal filters provide an alternative approach to the 10 to 104 minutes of flushing that are normally required to prepare a machine that has been used previously to deliver a volatile anesthetic.

### 維持高危手術患者的組織灌注：一項隨機臨床試驗的系統回顧

#### Maintaining Tissue Perfusion in High-Risk Surgical Patients: A Systematic Review of Randomized Clinical Trials

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**背景：**器官儲備有限的手術患者被認為是高危病人，有更高的圍術期死亡率。為此，他們需要更嚴密的圍術期血流動力學控制方案，以避免組織低灌注。本研究中，我們系統回顧了通過運用血流動力學治療方案來對高危手術患者維持充足組織灌注的隨機對照臨床試驗。

**方法：**我們搜索了 MEDLINE、Embase、LILACS 和 Cochrane 資料庫來確認通過對高危手術患者圍術期組織灌注的血流動力學治療方案以期降低死亡率和發病率的隨機對照臨床試驗。發病的特徵為術後出現至少一個臟器功能障礙。為了明確的結果，計算出混合優勢比（POR）和 95% 可信區間（CI）。

**結果：**選出 32 項臨床試驗，包含 5056 例高危手術患者。總體的薈萃分析顯示當用血流動力學治療方案來維持組織灌注時，死亡率(POR: 0.67; 95% CI: 0.55–0.82;  $P < 0.001$ )和術後器官功能障礙發生率(POR: 0.62; 95% CI: 0.55–0.70;  $P < 0.00,001$ )顯著降低。當對照組的死亡率>20%時，血流動力學治療方案以使組織最佳化的應用進一步降低死亡率（POR: 0.32; 95% CI: 0.21–0.47;  $P < 0.00,001$ ）。通過肺動脈導管監測心輸出量及增加氧的運輸和/或減少消耗也顯著降低了死亡率(分別為 POR: 0.67; 95% CI: 0.54–0.84;  $P < 0.001$  和 POR: 0.71; 95% CI: 0.57–0.88;  $P < 0.05$ )。以增加混合或中心靜脈氧飽和度為目標的治療不能顯著降低死亡率(POR: 0.68; 95% CI: 0.22–2.10;  $P > 0.05$ )。唯一一項用乳酸作為組織灌注標誌的實驗未能顯示死亡率的統計學上顯著下降(OR: 0.33; 95% CI: 0.07–1.65;  $P > 0.05$ )。

**結論：**對高危手術病人用血流動力學治療方案來維持組織灌注可減少死亡率及術後器官衰竭。監測心輸出量計算氧的運輸和消耗有助於指導治療。有必要進行另外的隨機對照臨床試驗來分析監測混合或中心靜脈血氧飽和度以及乳酸對高危手術病人的價值。

（瞿亦楓 譯 馬皓琳 李士通校）

**BACKGROUND:** Surgical patients with limited organic reserve are considered high-risk patients and have an increased perioperative mortality. For this reason, they need a more rigorous perioperative protocol of hemodynamic control to prevent tissue hypoperfusion. In this study, we systematically reviewed the randomized controlled clinical trials that used a hemodynamic protocol to maintain adequate tissue perfusion in the high-risk surgical patient.

**METHODS:** We searched MEDLINE, Embase, LILACS, and Cochrane databases to identify randomized controlled clinical studies of surgical patients studied using a perioperative hemodynamic protocol of tissue perfusion aiming to reduce mortality and morbidity; the latter characterized at least one dysfunctional organ in the postoperative period. Pooled odds ratio (POR) and 95% confidence interval (CI) were calculated for categorical outcomes.

**RESULTS:** Thirty-two clinical trials were selected, comprising 5056 high-risk surgical patients. Global meta-analysis showed a significant reduction in mortality rate (POR: 0.67; 95% CI: 0.55–0.82;  $P < 0.001$ ) and in postoperative organ dysfunction incidence (POR: 0.62; 95% CI: 0.55–0.70;  $P < 0.00,001$ ) when a hemodynamic protocol was used to maintain tissue perfusion. When the mortality rate was  $>20\%$  in the control group, the use of a hemodynamic protocol to maintain tissue optimization resulted in a further reduction in mortality (POR: 0.32; 95% CI: 0.21–0.47;  $P < 0.00,001$ ). Monitoring cardiac output with a pulmonary artery catheter and increasing oxygen transport and/or decreasing consumption also significantly reduced mortality (POR: 0.67; 95% CI: 0.54–0.84;  $P < 0.001$  and POR: 0.71; 95% CI: 0.57–0.88;  $P < 0.05$ , respectively). Therapy directed at increasing mixed or central venous oxygen saturation did not significantly reduce mortality (POR: 0.68; 95% CI: 0.22–2.10;  $P > 0.05$ ). The only study using lactate as a marker of tissue perfusion failed to demonstrate a statistically significant reduction in mortality (OR: 0.33; 95% CI: 0.07–1.65;  $P > 0.05$ ).

**CONCLUSIONS:** In high-risk surgical patients, the use of a hemodynamic protocol to maintain tissue perfusion decreased mortality and postoperative organ failure. Monitoring cardiac output calculating oxygen transport and consumption helped to guide therapy. Additional randomized controlled clinical studies are necessary to analyze the value of monitoring mixed or central venous oxygen saturation and lactate in high-risk surgical patients.

一氧化氮吸入用於成人和兒童的急性呼吸窘迫綜合征及急性肺損傷：一項用薈萃分析和試驗序貫分析進行的系統綜述

### **Inhaled Nitric Oxide for Acute Respiratory Distress Syndrome and Acute Lung Injury in Adults and Children: A Systematic Review with Meta-Analysis and Trial Sequential Analysis**

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**背景：**急性缺氧性呼吸衰竭（定義為急性肺損傷和急性呼吸窘迫綜合征）是一種在各年齡段病人中有較高發病率和死亡率的高危情況。吸入性一氧化氮（iNO）已被應用於改善氧合，但其作用仍具有爭議性。因此我們用薈萃分析和試驗序貫分析對臨床隨機對照試驗（RCTs）做了一個系統綜述。我們檢索了 CENTRAL、Medline、Embase、國際科學網站（International Web of Science）、LILACS、中國生物醫學文獻資料庫和 CINHAL（截止到 2010 年 1 月 31 日）。另外我們手工查閱了參考文獻，聯繫了作者和專家，並尋找了正在進行臨床試驗的登記者。其中兩位評論者獨立地選擇所有平行組的隨機對照試驗，對比了 iNO 組與安慰劑組或無干預組，並萃取了與研究方法、干預措施、資料結果、偏倚風險和不良事件相關的資料。所有試驗中，均不考慮盲法和語言環境。用循證醫學方法評估找回的試驗。討論解決意見不合處。我們的主要結果觀察指標為所有原因導致的死亡率。我們進行了分組和敏感性分析來評估 iNO 在成人和兒童以及對各種臨床和生理學指標的影響。我們通過分析試驗方法的組成評估了偏倚風險，並通過試驗序貫分析評估了隨機誤差的危險度。

**結果：**我們的研究涉及 14 項隨機對照試驗，共 1303 名參與者；其中有 10 項試驗有較高偏倚風險。iNO 在改善總體死亡率上沒有統計學顯著性差異（40.2%對 38.6%）（相對危險度為 1.06,95%可信區間為 0.93 至 1.22； $I^2 = 0$ ），但在一些分組和敏感性分析中有陽性結果。有限的資料表明 iNO 對機械通氣時間、脫離呼吸機時間、ICU 停留時間以及住院天數並無統計學顯著性作用。我們發現首個 24 小時中 iNO 對氧合有統計學顯著但暫時性改善的作用，表現在  $PO_2$  和吸入氧分數的比例(平均差[MD] 為 15.91，95%可信區間為 8.25 至 23.56； $I^2 = 25\%$ )。然而，iNO 可能會增加成人腎功能損害的風險（相對危險度為 1.59,95%可信區間為 1.17 至 2.16； $I^2 = 0$ ），但並不增加出血、高鐵血紅蛋白或二氧化氮形成的風險。

**結論：**iNO 在急性缺氧性呼吸衰竭病人中不能推薦使用。iNO 可以暫時改善氧合，但不能降低死亡率並可能有其他危害。

（張怡 譯 馬皓琳 李士通校）

**BACKGROUND:** Acute hypoxemic respiratory failure, defined as acute lung injury and acute respiratory distress syndrome, are critical conditions associated with frequent mortality and morbidity in all ages. Inhaled nitric oxide (iNO) has been used to improve oxygenation, but its role remains controversial. We performed a systematic review with meta-analysis and trial sequential analysis of randomized clinical trials (RCTs). We searched CENTRAL, Medline, Embase, International Web of Science, LILACS, the Chinese Biomedical Literature Database, and CINHAL (up to January 31, 2010). Additionally, we hand-searched reference lists, contacted authors and experts, and searched registers of ongoing trials. Two reviewers independently selected all parallel group RCTs comparing iNO with placebo or no intervention and extracted data related to study methods, interventions, outcomes, bias risk, and adverse events. All trials, irrespective of blinding or language status were included. Retrieved trials were evaluated with Cochrane methodology. Disagreements were resolved by discussion. Our primary

outcome measure was all-cause mortality. We performed subgroup and sensitivity analyses to assess the effect of iNO in adults and children and on various clinical and physiological outcomes. We assessed the risk of bias through assessment of trial methodological components. We assessed the risk of random error by applying trial sequential analysis.

**RESULTS:** We included 14 RCTs with a total of 1303 participants; 10 of these trials had a high risk of bias. iNO showed no statistically significant effect on overall mortality (40.2% versus 38.6%) (relative risks [RR] 1.06, 95% confidence interval [CI] 0.93 to 1.22;  $I^2 = 0$ ) and in several subgroup and sensitivity analyses, indicating robust results. Limited data demonstrated a statistically insignificant effect of iNO on duration of ventilation, ventilator-free days, and length of stay in the intensive care unit and hospital. We found a statistically significant but transient improvement in oxygenation in the first 24 hours, expressed as the ratio of  $PO_2$  to fraction of inspired oxygen (mean difference [MD] 15.91, 95% CI 8.25 to 23.56;  $I^2 = 25\%$ ). However, iNO appears to increase the risk of renal impairment among adults (RR 1.59, 95% CI 1.17 to 2.16;  $I^2 = 0$ ) but not the risk of bleeding or methemoglobin or nitrogen dioxide formation.

**CONCLUSION:** iNO cannot be recommended for patients with acute hypoxemic respiratory failure. iNO results in a transient improvement in oxygenation but does not reduce mortality and may be harmful.

### 某三級兒科醫院 101,885 例實施麻醉後的患兒術後死亡率

#### Postoperative Mortality in Children After 101,885 Anesthetics at a Tertiary Pediatric Hospital

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**背景：**死亡率是衡量麻醉品質及安全性的一項基本指標。目前，兒科的臨床麻醉相關死亡率資料很少。我們的研究旨在明確麻醉後 24 小時和 30 天死亡率，並明確大型三級醫院兒科臨床麻醉相關死亡的發生率及性質。

**方法：**研究選取澳大利亞墨爾本皇家兒童醫院在 2003 年 1 月 1 日到 2008 年 8 月 30 日之間接受麻醉的  $\leq 18$  歲兒童。資料通過綜合分析資料庫中所有在皇家兒童醫院實施麻醉並精確電子記錄的患兒的死亡率而得。確定麻醉後 30 天內及 24 小時內死亡的病例，檢查其病史及麻醉記錄。麻醉相關性死亡的定義是指經包含 3 名高年資麻醉醫師的專家小組一致認定麻醉或麻醉醫生控制的因子可能影響了死亡時間的那些病例。

**結果：**在為期 68 個月的時間內，共對 56,263 名患兒實施了 101,885 次麻醉。麻醉後任何原因導致的總計 24 小時死亡率為 13.4/10,000，30 天死亡率為 34.5/10,000。出生 30 天內的患兒死亡發生率最高。實施心臟手術的患兒 24 小時及 30 天的死亡率都高於實施非心臟手術的患兒。在 101,885 次麻醉中有 10 例為麻醉相關性死

亡。麻醉相關性死亡的發生率為 1/101,888 或 0.98/10,000 (95%可信區間為 0.5-1.8)。在這 10 個病例中，基礎疾病被認為是導致患兒死亡的重要因素。其中 5 例 (50%) 患兒合併肺動脈高壓。

**結論：**麻醉相關死亡率在心臟病患兒中較高，尤其是合併肺動脈高壓的患兒。無重大合併症患兒沒有麻醉相關性死亡，這支持了健康兒童中小兒麻醉的安全性。  
(陳彬彬譯 馬皓琳 李士通校)

**BACKGROUND:** Mortality is a basic measure for quality and safety in anesthesia. There are few anesthesia-related mortality data available for pediatric practice. Our objective for this study was to determine the incidence of 24-hour and 30-day mortality after anesthesia and to determine the incidence and nature of anesthesia-related mortality in pediatric practice at a large tertiary institution.

**METHODS:** Children  $\leq 18$  years old who had an anesthetic between January 1, 2003, and August 30, 2008, at the Royal Children's Hospital, Melbourne, Australia, were included for this study. Data were analyzed by merging a database for every anesthetic performed with an accurate electronic record of mortality of children who had ever been a Royal Children's Hospital patient. Cases of children dying within 30 days and 24 hours of an anesthetic were identified and the patient history and anesthetic record examined. Anesthesia-related death was defined as those cases whereby a panel of 3 senior anesthesiologists all agreed that anesthesia or factors under the control of the anesthesiologist more likely than not influenced the timing of death.

**RESULTS:** During this 68-month period, 101,885 anesthetics were administered to 56,263 children. The overall 24-hour mortality from any cause after anesthesia was 13.4 per 10,000 anesthetics delivered and 30-day mortality was 34.5 per 10,000 anesthetics delivered. The incidence of death was highest in children  $\leq 30$  days old. Patients undergoing cardiac surgery had a higher incidence of 24-hour and 30-day mortality than did those undergoing noncardiac surgery. From 101,885 anesthetics there were 10 anesthesia-related deaths. The incidence of anesthesia-related death was 1 in 10,188 or 0.98 cases per 10,000 anesthetics performed (95% confidence interval, 0.5 to 1.8). In all 10 cases, preexisting medical conditions were identified as being a significant factor in the patient's death. Five of these cases (50%) involved children with pulmonary hypertension.

**CONCLUSIONS:** Anesthesia-related mortality is higher in children with heart disease and in particular those with pulmonary hypertension. The lack of anesthesia-related deaths in children who did not have major comorbidities reinforces the safety of pediatric anesthesia in healthy children.

### 周圍神經的局部麻醉藥阻滯用於神經痛治療：系統分析

#### **Local Anesthetic Blockade of Peripheral Nerves for Treatment of Neuralgias: Systematic Analysis**

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**背景：**局部麻醉藥用於神經阻滯已被用於神經痛的診斷與治療。這些阻滯通常與皮質類固醇和其他有效藥物聯合應用。雖然神經阻滯對神經痛的長久效益被長期研究，但缺乏決定性的證據。在本系統性綜述中我們有以下目的：分析有神經痛和神經根痛綜合征的患者行局部麻醉藥周圍神經阻滯的實踐背後的證據；評估傳導阻滯作用消退後疼痛緩解的持續時間；並且評價對這些綜合症的一系列阻滯治療的效果。

**方法：**我們搜索了美國醫學索引、荷蘭醫學文摘、敘述性綜述和書籍篇章。只收集發表的英文文獻。我們共搜索到 3347 篇文章，我們全文閱讀了其中的 39 篇文章，在這其中 12 篇達到入選標準。

**結果：**我們分析了入選的 12 篇文章。每篇均為個案報告或病例系列分析，其中沒有對照研究。9 篇報告對單一神經阻滯作出評價；所有文章均記錄了超過傳導阻滯持續期間的疼痛緩解。這 9 篇報告共有 69 名患者，其中 30 名疼痛完全緩解，10 名疼痛緩解 $\geq 50\%$ 。7 篇關於行單一神經阻滯後連續評估疼痛 $\geq 1$  周的報告表明在 17 名患者中有 11 名得到完全或很大程度的疼痛緩解。所有 3 篇評價大樣本量（共 270 名）阻滯系列的報告報導了全部的陽性結果。

**結論：**因為所有綜述性文章均為個案報告或病例系列分析，所以對於神經痛用局部麻醉藥行神經阻滯的效果不能得出可靠的結論。但是，被分析的報導的 2 個特點，即結果的巨大幅度和報導結果的高度一致性，表明未來更多的研究工作是合理的。

（毛祖旻 譯 馬皓琳 李士通 校）

**BACKGROUND:** Nerve blocks with local anesthetics have been used in the diagnosis and treatment of neuralgias. Usually these blocks were administered in combination with corticosteroids and other drugs that can be effective by themselves. Although lasting benefits from nerve blocks in neuralgias have long been described, definitive evidence is lacking. We had the following objectives in this systematic review: to analyze the evidence behind the practice of peripheral nerve blockade with local anesthetics in patients with neuralgias and radicular pain syndromes; to assess the duration of pain relief after conduction block resolution; and to evaluate the effectiveness of the treatment of these syndromes with a series of blocks.

**METHODS:** We searched Medline, Embase, narrative reviews, and book chapters. Only articles published in English were collected. The list of 3347 identified articles was reduced to 39 articles that were read entirely, 12 of which met inclusion criteria.

**RESULTS:** Twelve included articles were analyzed. Each can be classified as a single case report or case series; there were no controlled studies among them. Nine reports assessed a single block outcome; all recorded pain relief beyond the duration of conduction blockade. Those 9 reports represented a total of 69 patients, 30 of whom had complete pain relief and 10 had relief  $\geq 50\%$ . Seven reports with the assessment of continuous pain  $\geq 1$  week after a single block reported complete or profound pain relief in 11 of 17 patients. All 3 reports with the assessment of a series of blocks in a large number of patients (total of 270) reported overall positive results.

**CONCLUSION:** Because all reviewed articles were only single case reports or case series, no reliable conclusion could be drawn concerning the effectiveness of nerve blocks with local anesthetics in neuralgia. However, 2 features of the analyzed reports—

the large magnitude of the effect and the high consistency of the reported outcome— indicate that future research efforts are warranted.

### 腹橫肌平面阻滯的新途徑對於結直腸術後鎮痛的有效性

#### The Efficacy of a Novel Approach to Transversus Abdominis Plane Block for Postoperative Analgesia After Colorectal Surgery

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**背景：**腹橫肌平面(TAP)阻滯的鎮痛效應是已在進行腹部手術患者確立。我們評估一種新的 TAP 阻滯途徑對於結直腸手術術後鎮痛的有效性。

**方法：**招募了 40 例 ASA 分級為 I 至 III 級進行結直腸手術的成年患者到這一雙盲隨機對照試驗。使用了一個標準化的全麻技術。在手術結束時，用 22G 的鈍針在臍水準和腋中線處，從腹壁內側穿刺到腹橫肌，進行 TAP 阻滯。這些患者隨機分配接受 20mL 的 0.25% 布比卡因 (TAP 組) 或生理鹽水 (對照組) 注射腹壁的每一側。每一患者在術後 0、0.5、1、2、4、8、12 和 24 小時的時候評估靜息與咳嗽時的疼痛視覺類比評分。用靜脈注射嗎啡來作為術後補救鎮痛。記錄第一次需要補救鎮痛的時間、24 小時內總嗎啡需求量、2、4、6、12 和 24 小時累積的嗎啡消耗量以及副作用情況 (呼吸抑制、嗜睡、噁心/嘔吐)。

**結果：**TAP 組 24 小時總嗎啡消耗量比對照組減少 65% ( $P < 0.0001$ )。在所有時間點上，TAP 組的累積嗎啡需求量明顯較低。雖然第一次需要嗎啡注射的時間兩組相當，但是後續嗎啡劑量所需的時間間隔 TAP 組明顯長於對照組。在所有評估的時間點上，TAP 組患者靜息和咳嗽時的疼痛評分都明顯低於對照組。在術後 1、2、4 和 6 小時時，TAP 組中嗜睡的發生率較低 ( $P < 0.05$ )。

**結論：**這一新的 TAP 阻滯方法為結直腸手術提供了有效的術後鎮痛。

(唐亮 譯 馬皓琳 李士通 校)

**BACKGROUND:** The analgesic efficacy of transversus abdominis plane (TAP) block has been established for patients undergoing abdominal surgery. We evaluated the efficacy of a novel approach to TAP block for postoperative analgesia after colorectal surgery.

**METHODS:** Forty adult ASA physical status I to III patients undergoing colorectal surgery were recruited to this double-blind randomized controlled trial. A standard general anesthetic technique was used. TAP block was performed at the end of surgery by piercing the transversus abdominis muscle from inside the abdominal wall at the midaxillary line at the level of the umbilicus with a 22-gauge blunt needle. The patients were randomly assigned to receive either 20 mL of 0.25% bupivacaine (TAP group) or normal saline (control group) on each side of the abdominal wall. Each patient was assessed at 0, 0.5, 1, 2, 4, 8, 12, and 24 hours postoperatively for pain at rest and on coughing using a visual analog scale. IV morphine was used for postoperative rescue analgesia. Time to first request for rescue analgesia, total morphine requirement in 24

hours, cumulative morphine consumption at 2, 4, 6, 12, and 24 hours, and adverse effects (respiratory depression, sedation, nausea/vomiting) were recorded.

**RESULTS:** A 65% decrease in 24-hour total morphine consumption was observed in the TAP group compared with the control group ( $P < 0.0001$ ). The cumulative morphine requirement was also significantly lower in the TAP group at all time points. Although the time to first request for morphine was comparable, the subsequent doses of morphine were required at significantly longer time intervals in the TAP group than in the control group. TAP group patients had significantly lower pain scores at rest and on coughing as compared with the control group, at all time points assessed. The incidence of sedation was also less in the TAP group at 1, 2, 4, and 6 hours postoperatively ( $P < 0.05$ ).

**CONCLUSIONS:** This new approach to the TAP block provides effective postoperative analgesia after colorectal surgery.

### 基於尿滲透壓監測通宵禁食下的機體水化狀態不改變低風險患者全身麻醉時低血壓的發生

#### Hydration Status After Overnight Fasting as Measured by Urine Osmolality Does Not Alter the Magnitude of Hypotension During General Anesthesia in Low Risk Patients

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**背景:** 細胞間隙中晶體溶液分佈增加可能會降低患者血管內容量擴充的有效性。作者研究通宵禁食患者的術前水化狀態是否會影響組織間液再分佈和全身麻醉中低血壓的發生。

**方法:** 60 例接受鼓室成形術 ASA I/II 級患者，午夜開始禁食。麻醉誘導用芬太尼、異丙酚，麻醉維持用七氟醚和瑞芬太尼。麻醉誘導時，輸注 15mL/kg 醋酸林格氏溶液 60 分鐘，之後給予 1mL/kg 醋酸林格氏液 30 分鐘。在麻醉誘導後以及實驗過程中測定尿滲透壓(pre- $U_{osm}$ , post- $U_{osm}$ )，實驗結束後測定全身細胞外液生物電阻抗與基礎值相比下降的百分比 ( $\Delta Re$ )。根據患者 pre- $U_{osm} < 25\%$  或 pre- $U_{osm} > 75\%$  分別進入水化組及脫水組。對一系列變數，包括在相對於基線 30 - 90 分鐘期間平均動脈壓和  $\Delta Re$  進行組間比較。

**結果:** 脫水組(pre- $U_{osm} > 759.5$  mOsm/kg,  $n = 15$ )相對水化組(pre- $U_{osm} < 378.5$  mOsm/kg,  $n = 15$ )，年齡較小(44vs52 歲,  $P = 0.049$ )，並有較高的 post- $U_{osm}$  (181 vs 55 mOsm/kg,  $P = 0.001$ )。且相對於基線 30 - 90 分鐘期間平均動脈壓變化 (0.67 vs 0.67,  $P = 0.85$ )，95%的置信區間 (-0.070 到 0.084) 和  $\Delta Re$  (5.6% vs 6.0%,  $P = 0.58$ )，95%的置信區間 (-1.85%至 1.06%) 方面，脫水組與水化組相似。

**結論:** 利用尿滲透壓監測術前因通宵禁食導致脫水並不改變全身麻醉期間低血壓。這一結果表明，使用晶體液對術前通宵禁食患者進行血管內容量擴充，防止全身麻醉期間低血壓的做法並無根據。

(陳毓雯 譯 陳傑 校)

**BACKGROUND:** The increased distribution of crystalloid solution into the interstitial space may decrease the effectiveness of intravascular volume loading in patients. We investigated whether preoperative hydration status after overnight fasting affects interstitial fluid redistribution and thus the magnitude of hypotension during general anesthesia.

**METHODS:** Sixty ASA physical status I/II patients undergoing tympanoplasty fasted from midnight. Anesthesia was induced by fentanyl and propofol and maintained with sevoflurane and remifentanyl. Coinciding with the induction of anesthesia, 15 mL/kg acetated Ringer solution was infused IV over 60 minutes followed by 1 mL/kg acetated Ringer solution over the next 30 minutes. Urine osmolalities after induction of anesthesia and during the study period (pre- $U_{osm}$ , post- $U_{osm}$ ) and percent decreases of whole-body bioelectrical resistance for extracellular fluid relative to baseline at the end of the study period ( $\Delta R_e$ ) were measured. Patients with a pre- $U_{osm}$  < the 25th percentile or with a pre- $U_{osm}$  > the 75th percentile of pre- $U_{osm}$  were categorized in the hydrated or the dehydrated group, respectively. A range of variables, including mean arterial blood pressure during the 30- to 90-minute period relative to baseline, and  $\Delta R_e$ , were compared between the groups.

**RESULTS:** The dehydrated group (pre- $U_{osm}$  > 759.5 mOsm/kg,  $n = 15$ ) had a lower age (44 vs 52 years,  $P = 0.049$ ) and had a higher post- $U_{osm}$  (181 vs 55 mOsm/kg,  $P = 0.001$ ) compared with the hydrated group (pre- $U_{osm}$  < 378.5 mOsm/kg,  $n = 15$ ). Mean arterial blood pressure during the 30- to 90-minute period relative to baseline (0.67 vs 0.67,  $P = 0.85$ ) with 95% confidence interval for the difference of means (-0.070 to 0.084) and  $\Delta R_e$  (5.6% vs 6.0%,  $P = 0.58$ ) with 95% confidence interval for the difference of means (-1.85% to 1.06%) were similar for the hydrated and dehydrated groups.

**CONCLUSIONS:** Preoperative dehydration after overnight fasting as measured by urine osmolality did not alter the magnitude of hypotension during general anesthesia. This finding suggests that intravascular volume loading with crystalloid solution to prevent hypotension during general anesthesia is an unfounded practice for low risk patients after overnight fasting.

#### 阿替卡因的濃度依賴性神經毒性：大鼠坐骨神經電生理和體視學研究

##### Concentration-Dependent Neurotoxicity of Articaine: An Electrophysiological and Stereological Study of the Rat Sciatic Nerve

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**背景：**本研究採用大鼠坐骨神經內分別注射 50ul 的生理鹽水、2%的阿替卡因和 4%的阿替卡因的方法，定量分析阿替卡因的神經毒性。

**方法：**研究中分別在給藥前、給藥後即刻以及給藥後 3 星期記錄刺激坐骨神經的誘發脊髓電圖。試驗藥物均注射在右側坐骨神經，而未作處理的左側坐骨神經作為對照組。3 星期後將動物處死，取得坐骨神經橫斷標本進行體視學研究。

**結果：**與生理鹽水組相比，注射阿替卡因組的大鼠在注射藥物後即刻就出現誘發脊髓區域的神經電位逐漸衰減；且神經電位的衰減隨阿替卡因濃度的增加而相應增加，在給藥後 3 個星期更明顯。對照組均無明顯反應。相應處理不影響有髓鞘軸突的數量。從坐骨神經的橫斷面上看，注射 4% 阿替卡因組大鼠的軸突平均區域和髓鞘的平均厚度明顯減少。

**結論：**注射不同劑量的阿替卡因（2% 和 4%），神經損傷有明顯的區別，這說明阿替卡因的神經毒性是濃度依賴性的。而注射生理鹽水時的機械性損傷對神經傳導和組織學沒有顯著影響。

(張婷 譯 陳傑 校)

**BACKGROUND:** We performed this study to quantify the detrimental effect of intraneural injection of 50  $\mu$ L of saline, articaine 2%, or articaine 4% in the rat sciatic nerve.

**METHODS:** Lumbar-evoked electrospinograms from stimulation of the sciatic nerve were recorded before and immediately after injection and again after 3 weeks. Test substance was injected into the right sciatic nerve, and the untreated left sciatic nerve served as control. The animals were killed after the 3-week follow-up, and cross-sections of the sciatic nerve were examined stereologically.

**RESULTS:** The evoked spinal cord field potential in the articaine groups faded away immediately after injection and was concentration-dependently, significantly more reduced at the 3-week follow-up in comparison with the saline group. The response from the control sides was unaffected in all groups. The number of myelinated axons was unaffected by the treatment. The mean cross-sectional axon area and the mean myelin sheath thickness were significantly reduced in animals injected with articaine 4%.

**CONCLUSIONS:** These observations indicate concentration-dependent neurotoxic injuries after injection of articaine with a significant difference between 2% and 4% formulations. The mechanical injury of needle penetration with saline injection had no significant effect on nerve conduction or histomorphology.

#### 技術交流：關於經皮局部靜脈血氧儀的可行性研究

##### **Technical Communication: Transcutaneous Regional Venous Oximetry: A Feasibility Study**

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**背景：**動脈脈搏血氧儀是 20 世紀 70 年代引入臨床的一種方便、實用、目前普遍應用的麻醉監測設備。不幸的是，雖然動脈血氧飽和度是與心輸出量和血紅蛋白濃度

有關的三個氧供成分之一，它並不反映區域氧供是否是足夠。而借助周圍或區域靜脈氧飽和度 ( $SxvO_2$ ) 可進行區域氧供和氧需的分析。本研究目標是評估在 3 個解剖部位上使用  $SxvO_2$  經皮評估的可行性。

**方法：**將 Nonin 血氧飽和度探頭（由明尼蘇達州，普利茅茨，Nonin Medical 公司提供）直接放置在 10 名志願者前臂，頸外，頸內靜脈上，測量紅色和紅外線電磁輻射的吸收度。對這些吸收波形進行快速傅裏葉變換。將不同的頻率下紅光和紅外線輻射的脈衝吸收比與非脈衝吸收比作比較，並且基於以往經驗得出的相關性計算  $SxvO_2$ 。

**結果：**經皮  $SxvO_2$  估計範圍介於 41% 至 97%，其中在前臂、頸外和頸內靜脈處測量的平均值分別為 75%、80%、80%。總體而言，93% 的  $SxvO_2$  預測值  $<90\%$ 。

**結論：**這一技術的審定和隨後的改進需要我們將其與靜脈血氣測量的結果相關聯，其次是需要聯合相關領域氧飽和度測量技術（胎兒反射式血氧儀和近紅外光譜）和先進的信號處理技術。

(孫曉瓊 譯 陳傑 校)

**BACKGROUND:** The arterial pulse oximeter, which was introduced clinically in the 1970s, is a convenient, useful, and now ubiquitous anesthesia monitor. Unfortunately, although percent saturation of arterial hemoglobin is, along with cardiac output and concentration of hemoglobin, one of 3 components of oxygen delivery, it does not indicate whether oxygen delivery to a region of interest is adequate. Knowledge of peripheral or regional venous oxygen saturation ( $SxvO_2$ ) may lend insight into analysis of regional oxygen supply and demand. Our goal was to assess the suitability of 3 anatomic sites for the transcutaneous assessment of  $SxvO_2$ .

**METHODS:** Using a Nonin reflectance oximetry probe (provided by Nonin Medical, Plymouth, MN) placed directly over the antecubital, external jugular, and internal jugular veins in 10 volunteers, we measured the absorbance of red and infrared electromagnetic radiation. We performed fast Fourier transformation on these absorbance waveforms. The ratio of pulsatile absorbance of red and infrared radiation at different frequencies was compared with nonpulsatile absorption, and  $SxvO_2$  was calculated based on previously derived empiric correlations.

**RESULTS:** Estimates of transcutaneous  $SxvO_2$  ranged from 41% to 97%, with mean values of 75%, 80%, and 80% at the antecubital, external jugular, and internal jugular veins, respectively. Overall, 93% of predicted  $SxvO_2$  values were  $<90\%$ .

**CONCLUSION:** Validation and subsequent improvement of this technique requires correlation of our results with venous blood gas measurements, followed by incorporation of technologies from related fields in oximetry (fetal reflectance oximetry and near-infrared spectroscopy), as well as the development of advanced signal processing techniques.

通過沿中心靜脈走行的體表標誌估計右及左側中心靜脈導管置入深度的效果評估

**An Estimation of Right- and Left-Sided Central Venous Catheter Insertion Depth Using Measurement of Surface Landmarks Along the Course of Central Veins**

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**背景：**本項研究試圖尋找是否存在一種根據中心靜脈走行的局部解剖的方法，來估測中心靜脈導管置入深度。

**方法：**通過左或右頸靜脈（IJV）或鎖骨下靜脈（SCV）進行 200 例中心靜脈穿刺置管。將胸鎖乳突肌作為體表標誌進行 IJV 置管，而採用鎖骨下入路進行 SCV 插管。局部解剖學測量是隨導管的自然彎曲從皮膚褶皺的置入針刺點開始，通過同側的鎖骨切跡，直達右側第二肋軟骨及胸骨柄關節。中心靜脈置管的置入和固定深度通過局部解剖方法判定。中心靜脈導管頭端到氣管隆突的距離以及左側中心靜脈頭端到中線的成角均由術後胸片測定。

**結果：**50 例通過右頸靜脈行中心靜脈置管的頭端位置的平均值（標準差）是氣管隆突以上 0.1（1.1）cm，右側鎖骨下靜脈、左側頸靜脈、以及左鎖骨下靜脈置管的導管頭端位置距離氣管隆突分別為 0.0（0.9）cm、以上 0.3（1.0）cm，以下 0.2（0.9）cm。中心靜脈置管位置據此可預測 95% 的患者的誤差區間為隆突下 2.2cm 及隆突上 2.3cm。左側中心靜脈置管中如果與中線角度過陡（ $\geq 40^\circ$ ）則頭端在隆突上的可能（54 例中有 17 例）大於隆突下（46 例中有 2 例）。

**結論：**通過中心靜脈走行的體表標誌的方法可以估計中心靜脈的置管深度。

(陸秉璋 譯 陳傑 校)

**BACKGROUND:** In this study we sought to determine whether the topographical measurement along the course of the central veins can estimate the approximate insertion depths of central venous catheters (CVC).

**METHODS:** Two hundred central venous catheterizations were performed via the right and left internal jugular vein (IJV) or subclavian vein (SCV). The anterior approach, using the sternocleidomastoid muscle as a landmark, was used for IJV catheterization and the infraclavicular approach for SCV. Topographical measurement was performed by placing the catheter with its own curvature over the draped skin starting from the insertion point of the needle through the ipsilateral clavicular notch, and to the insertion point of the second right costal cartilage to the manubriosternal joint. The CVC was inserted and secured to a depth determined topographically. The distance between the CVC tip and the carina and the angle of the left-sided CVC tip to the vertical were measured on the postoperative chest radiograph.

**RESULTS:** The mean (SD) tip position of 50 CVCs placed via the right IJV was 0.1 (1.1) cm above the carina; right SCV, 0.0 (0.9) cm; left IJV, 0.3 (1.0) cm above the carina, and left SCV, 0.2 (0.9) cm below the carina. CVC locations could be predicted with a margin of error between 2.2 cm below the carina and 2.3 cm above the carina in 95% of patients. There were steeper ( $\geq 40^\circ$ ) angles to the vertical in the left-sided CVCs whose tips were above the carina (17 out of 54) than below the carina (2 out of 46).

**CONCLUSIONS:** The approximate insertion depth of a CVC can be estimated using measurement of surface landmarks along the pathway of central veins.

一項關於血流動力學的預處理改善中高危患者的手術轉歸的系統回顧和薈萃分析

## **A Systematic Review and Meta-Analysis on the Use of Preemptive Hemodynamic Intervention to Improve Postoperative Outcomes in Moderate and High-Risk Surgical Patients**

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**背景：**大手術的併發症往往令人生厭、較為常見、卻可避免的。短期手術併發症帶來的長期症狀被公認為對倖存者的壽命和生活品質有重大影響。在過去的 30 年中，有大量研究在努力嘗試通過預先人為地對圍術期血流動力學進行干預來減少術中死亡率和發病率。早期研究因對照組死亡率較高而遭詬病並認為其在現行實踐沒有代表性，因此反對其應用於常規醫療。本回顧旨在更新此領域研究成果，通過調查現行實踐和醫療品質改善的有效性，以瞭解先前此領域的定量分析結論是否仍然有效。

**方法：**通過多種方法選取關於評估血流動力學的預處理來改善手術轉歸的隨機臨床實驗。在電子資料庫（聯機醫學文獻分析和檢索系統，荷蘭醫學文摘資料庫，循證醫學對照臨床試驗登記）篩查潛在試驗，檢查選取研究的參考目錄，另外還有來自專家和產業代表的額外資源。符合入選標準的研究必須通過完全核查並進行相對應的定量分析，亞組分析或靈敏度分析。

**結果：**共有 29 個研究入選，其中 23 個報導了手術併發症。29 個研究包括 4805 例患者，總死亡率為 7.6%。血流動力學的預處理減少了死亡率（比值比【95%可信區間】為 0.48 [0.33–0.78];  $P = 0.0002$ ）和手術併發症（優勢比 0.43 [0.34–0.53];  $P < 0.0001$ ）。亞組分析顯示相對單獨應用補液，使用肺動脈導管、超常復蘇目標、研究應用心臟指數或者氧供為目標，並且應用補液和升壓藥可顯著降低死亡率。四次亞組分析中每組的併發症率都有明顯的下降。

**結論：**血流動力學的預處理策略和伴隨治療可減少手術死亡率和併發症發生率。  
(楊秋娟 譯 陳傑 校)

**BACKGROUND:** Complications from major surgery are undesirable, common, and potentially avoidable. The long-term consequences of short-term surgical complications have recently been recognized to have a profound influence on longevity and quality of life in survivors. In the past 30 years, there have been a number of studies conducted attempting to reduce surgical mortality and morbidity by deliberately and preemptively manipulating perioperative hemodynamics. Early studies had a high control-group mortality rate and were criticized for this as being unrepresentative of current practice and raised opposition to its implementation as routine care. We performed this review to update this body of literature and to examine the effect of changes in current practice and quality of care to see whether the conclusions from previous quantitative analyses of this field remain valid.

**METHODS:** Randomized clinical trials evaluating the use of preemptive hemodynamic intervention to improve surgical outcome were identified using multiple methods. Electronic databases (MEDLINE, EMBASE, and the Cochrane Controlled Clinical Trials register) were screened for potential trials, reference lists of identified trials were

examined, and additional sources were sought from experts and industry representatives. Identified studies that fulfilled the entry criteria were examined in full and subjected to quantifiable analysis, subgroup analysis, and sensitivity analysis where possible.

**RESULTS:** There were 29 studies identified, 23 of which reported surgical complications. In total, the 29 trials involved 4805 patients with an overall mortality of 7.6%. The use of preemptive hemodynamic intervention significantly reduced mortality (pooled odds ratio [95% confidence interval] of 0.48 [0.33–0.78];  $P = 0.0002$ ) and surgical complications (odds ratio 0.43 [0.34–0.53];  $P < 0.0001$ ). Subgroup analysis showed significant reductions in mortality for studies using a pulmonary artery catheter, supranormal resuscitation targets, studies using cardiac index or oxygen delivery as goals, and the use of fluids and inotropes as opposed to fluids alone. By contrast, there was a significant reduction in morbidity for each of the 4 subgroups analyzed.

**CONCLUSION:** The use of a preemptive strategy of hemodynamic monitoring and coupled therapy reduces surgical mortality and morbidity.

### 椎管內麻醉下的分娩鎮痛對兒童學習障礙的影響

#### Neuraxial Labor Analgesia for Vaginal Delivery and Its Effects on Childhood Learning Disabilities

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**背景：**先前研究表明椎管內麻醉進行剖宮產的兒童學習障礙的發病率較低於陰道分娩。作者推測，椎管內麻醉能夠減少分娩中的應激反應，而應激則與以後的神經發育相關。爲了進一步探討這種可能性，作者在以人口爲基礎的陰道分娩出生兒童的佇列中分析了椎管內麻醉下鎮痛分娩與兒童學習障礙的關係。

**方法：**作者回顧了在 Olmsted County, 明尼蘇達州的 5 個小鎮從 1976 到 1982 年出生並在原社區居住至 5 歲的兒童的所有教育和醫療記錄，篩選出在此人群中確診爲有學習障礙的對象。Cox 回歸模型被用於比較在分娩中使用或不使用椎管內麻醉的兒童成長後學習障礙的發生率，包括對那些與臨床有潛在相關性的因素或者單變數分析 2 組之間存在差異進行校準的分析。

**結果：**在這個研究佇列中，4686 名產婦經過陰道分娩，其中 1495 例接受了椎管內麻醉鎮痛。在這個佇列中兒童學習障礙的發生與椎管內麻醉鎮痛的使用沒有相關性。（校準危險比 1.05；95% 可信區間，0.85-1.31， $P=0.63$ ）

**討論：**分娩期間是否使用椎管內鎮痛與在 19 歲之前確診的學習障礙沒有獨立的相關性。未來的研究需要評估早先發表的關於學習障礙的發生率在椎管內麻醉下剖宮產的兒童低於經陰道自然順產的兒童的潛在的機制。

(張蕾 譯 陳傑 校)

### Abstract

**BACKGROUND:** In prior work, children born to mothers who received neuraxial anesthesia for cesarean delivery had a lower incidence of subsequent learning disabilities compared with vaginal delivery. The authors speculated that neuraxial anesthesia may reduce stress responses to delivery, which could affect subsequent neurodevelopmental outcomes. To further explore this possibility, we examined the association between the use of neuraxial labor analgesia and development of childhood learning disabilities in a population-based birth cohort of children delivered vaginally.

**METHODS:** The educational and medical records of all children born to mothers residing in the area of 5 townships of Olmsted County, Minnesota from 1976 to 1982 and remaining in the community at age 5 years were reviewed to identify those with learning disabilities. Cox proportional hazards regression was used to compare the incidence of learning disabilities between children delivered vaginally with and without neuraxial labor analgesia, including analyses adjusted for factors of either potential clinical relevance or that differed between the 2 groups in univariate analysis.

**RESULTS:** Of the study cohort, 4684 mothers delivered children vaginally, with 1495 receiving neuraxial labor analgesia. The presence of childhood learning disabilities in the cohort was not associated with use of labor neuraxial analgesia (adjusted hazard ratio, 1.05; 95% confidence interval, 0.85–1.31;  $P = 0.63$ ).

**CONCLUSION:** The use of neuraxial analgesia during labor and vaginal delivery was not independently associated with learning disabilities diagnosed before age 19 years. Future studies are needed to evaluate potential mechanisms of the previous finding indicating that the incidence of learning disabilities is lower in children born to mothers via cesarean delivery under neuraxial anesthesia compared with vaginal delivery.

### 機械通氣下的嬰幼兒肺萎陷對鎖骨下靜脈位置和大小影響

#### The Effect of Lung Deflation on the Position and Size of the Subclavian Vein in Mechanically Ventilated Infants and Children

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**背景：**如果肺的萎陷增加了鎖骨下靜脈（SCV）到胸膜的距離以及靜脈的直徑，那麼它可能減少氣胸的風險並增加鎖骨下靜脈穿刺置管的成功率。本研究評估機械通氣的小兒患者肺壓縮對鎖骨下靜脈到胸膜的距離和對鎖骨下靜脈橫截面積的影響。**方法：**50名患者（25名不到一歲的嬰兒和25名一到八歲的兒童）取肩部墊高仰臥位，機械通氣的潮氣量為6到7 mL/kg。將氣管連通大氣實現肺的萎陷。用超聲分別在肺膨脹末期及肺萎陷後的0，30，60，90和120秒測量鎖骨下靜脈到胸膜的距離和鎖骨下靜脈的橫截面積。P值<0.05被認為有統計學意義。距離增加5%及橫截面積增加25%被認為有臨床相關性。

**結果：**分析了 43 名病人包括 22 名嬰兒和 21 名兒童的資料。沒有發現肺的萎陷對鎖骨下靜脈到胸膜的距離及鎖骨下靜脈的橫截面積的改變有臨床相關性。鎖骨下靜脈到胸膜的距離和鎖骨下靜脈的橫截面積並沒有隨著時間進一步增加。

**結論：**肺萎陷不能增加鎖骨下靜脈到胸膜的距離及鎖骨下靜脈的橫截面積，且未必能有利於避免氣胸及增加鎖骨下靜脈穿刺置管的成功率。

(唐穎 譯 陳傑 校)

**BACKGROUND:** If lung deflation increases the distance from the subclavian vein (SCV) to the pleura and the diameter of the vein, it might decrease the risk of pneumothorax and increase the success rate of subclavian venous cannulation. We evaluated the effect of lung deflation on the distance from the SCV to the pleura (SCV-pleura distance) and on the cross-sectional area (CSA) of the SCV in mechanically ventilated pediatric patients.

**METHODS:** Fifty patients (25 infants younger than 1 year and 25 children aged 1 to 8 years) were placed supine over a shoulder roll, and their lungs were ventilated with a tidal volume of 6 to 7 mL/kg. Lung deflation was achieved by opening the endotracheal tube to the atmosphere. The SCV-pleura distances and the SCV CSAs were measured using ultrasound at the end of inflation and 0, 30, 60, 90, and 120 seconds after lung deflation. A *P* value <0.05 was considered statistically significant. Increases of 5% in the distance and 25% in the CSA were defined as clinically relevant.

**RESULTS:** The available data from 43 patients, 22 infants and 21 children, were analyzed. No clinically relevant changes in the SCV-pleura distance or in the SCV CSA were induced by lung deflation. Neither the SCV-pleura distance nor the CSA showed any further increase with time.

**CONCLUSIONS:** Lung deflation failed to increase the SCV-pleura distance and the CSA of the SCV. Its application is unlikely to be advantageous in avoiding pneumothorax or improving the success rate of subclavian venous cannulation.

### 三磷酸腺苷敏感性鉀通道阻滯劑減弱了 R-PIA 對神經損傷性大鼠的抗痛覺異常效應

#### Adenosine Triphosphate-Sensitive Potassium Channel Blockers Attenuate the Antiallodynic Effect of R-PIA in Neuropathic Rats

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Abstract

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**背景：**神經損傷可產生神經性疼痛。鞘內注射腺苷可減弱其伴隨的機械性痛覺敏化。腺苷神經保護作用是由三磷酸腺苷 (ATP) 敏感性鉀通道( $K_{ATP}$ ) 所介導。作者使用大鼠神經結紮為神經病理性疼痛的損傷模型評估腺苷 A1 受體激動劑，N6-(1-

苯基-2-丙醇)腺苷 (R - PIA) 和  $K_{ATP}$  通道關係，以確定是否 R - PIA 的抗痛覺異常療效也由  $K_{ATP}$  通道介導。

**方法：**由牢固結紮左腰椎第五和第六脊椎神經誘發機械性痛敏。左後爪的機械痛敏以 von Frey 暗條測痛法測量縮爪閾值來評估。鞘內注射 R - PIA (0.5, 1 或 2ug) 誘導抗痛覺異常療效。我們評估  $K_{ATP}$  通道阻滯劑格列本脲或 5-羥色胺(5-HT) 預處理是否能逆轉 R - PIA 的抗痛覺異常效果。此外，作者評估了  $K_{ATP}$  通道開放劑二氮嗪是否有抗痛覺異常效果並促進了 R - PIA 的作用。最後，研究電壓依賴的鉀通道阻斷劑 4 - 氨基吡啶是否削弱了 R - PIA 的效果。

**結果：**鞘內注射 R - PIA 濃度為 2ug 時能產生最大的抗痛覺異常效應 ( $P < 0.05$ )。鞘內注射格列本脲預處理和腹腔內預注 5-HT 顯著降低了 R - PIA 的抗痛覺異常效應。二氮嗪產生了抗痛覺異常效果，也增強了 R - PIA 的作用。4 - 氨基吡啶並沒有對 R - PIA 的作用有影響。

**結論：**在大鼠結紮神經損傷模型中，腺苷 A1 受體刺激的抗痛覺異常效果可能與  $K_{ATP}$  通道的活動有關。

(鄒巧群 譯 陳傑 校)

**BACKGROUND:** Nerve injury can generate neuropathic pain. The accompanying mechanical allodynia may be reduced by the intrathecal administration of adenosine. The neuroprotective effects of adenosine are mediated by the adenosine triphosphate (ATP)-sensitive potassium ( $K_{ATP}$ ) channel. We assessed the relationship between the adenosine A1 receptor agonist,  $N^6$ -(R)-phenylisopropyl adenosine (R-PIA), and  $K_{ATP}$  channels to determine whether the antiallodynic effects of R-PIA are also mediated through  $K_{ATP}$  channels in a rat nerve ligation injury model of neuropathic pain.

**METHODS:** Mechanical allodynia was induced by tight ligation of the left lumbar fifth and sixth spinal nerves. Mechanical allodynia in the left hindpaw was evaluated using von Frey filaments to measure withdrawal thresholds. R-PIA (0.5, 1, or 2  $\mu$ g) was administered intrathecally to induce antiallodynia. We assessed whether pretreatment with the  $K_{ATP}$  channel blockers glibenclamide or 5-hydroxydecanoate reversed the antiallodynic effect of R-PIA. Also, we evaluated whether diazoxide, a  $K_{ATP}$  channel opener, had an antiallodynic effect and promoted the antiallodynic effect of R-PIA. Lastly, we investigated whether the voltage-activated K channel blocker 4-aminopyridine attenuated the effect of R-PIA.

**RESULTS:** Intrathecal R-PIA produced maximal antiallodynia at 2  $\mu$ g ( $P < 0.05$ ). Intrathecal pretreatment with glibenclamide and intraperitoneal pretreatment 5-hydroxydecanoate significantly reduced the antiallodynic effect of R-PIA. Diazoxide produced an antiallodynic effect and also enhanced the antiallodynic action of R-PIA. 4-Aminopyridine had no effect on the antiallodynic action of R-PIA.

**CONCLUSIONS:** The antiallodynic effects of adenosine A1 receptor stimulation may be related to  $K_{ATP}$  channel activity in a rat model of nerve ligation injury.

短互動式動畫視頻資訊對麻醉前焦慮、麻醉知識瞭解及術前訪視時間的影響：一項隨機對照試驗

**The Effects of Short Interactive Animation Video Information on Preanesthetic Anxiety, Knowledge, and Interview Time: A Randomized Controlled Trial.**

Kakinuma A, Nagatani H, Otake H, Mizuno J, Nakata Y

**背景：**此研究設計的互動式動畫視頻提供了包括風險、效益及供選方案在內的麻醉實施過程基本說明。本研究假設這段視頻將增進患者對於麻醉過程的瞭解、減輕術前焦慮及縮短訪視時間。

**方法：**將 211 名術前入院至少 1 天並計畫擇期於全麻或硬膜外複合全麻下行腫瘤手術的患者隨機分配至視頻組 (n=106) 或非視頻組 (n=105)。視頻組患者要求在病房觀看短互動式動畫視頻。看完視頻後，麻醉醫師將對該組患者進行術前訪視並例行風險評估。非視頻組患者也由麻醉醫師實施術前訪視，但不要求觀看視頻。在麻醉醫師訪視前與手術日當天，兩組患者均要求完成狀態-特質焦慮量表及共 14 分值的知識測驗。此外，本研究還對術前訪視時間進行了測算。

**結果：**兩組患者無人口統計學差異。較非視頻組患者而言，視頻組患者的訪視時間縮短了 34.4% (視頻組 12.2±5.3 分鐘，非視頻組 18.6±6.4 分鐘；縮短時間百分比的 95% 置信區間[CI]：32.7%-44.3%)，且麻醉知識的知曉度增進了 11.6% (視頻組得分 12.5±1.4，非視頻組得分 11.2±1.7；知識增長百分比的 95% 置信區間[CI]：32.7%-44.3%)。然而，對於麻醉前焦慮，兩組患者間無統計學差異。

**結論：**本研究的短互動式動畫視頻幫助患者瞭解麻醉並縮短了麻醉醫師的訪視時間。

(范羽譯 薛張綱校)

**Background:** We designed an interactive animated video that provides a basic explanation-including the risks, benefits, and alternatives-of anesthetic procedures. We hypothesized that this video would improve patient understanding of anesthesia, reduce anxiety, and shorten the interview time.

**Methods:** Two hundred eleven patients scheduled for cancer surgery under general anesthesia or combined general and epidural anesthesia, who were admitted at least 1 day before the surgery, were randomly assigned to the video group (n = 106) or the no-video group (n = 105). The patients in the video group were asked to watch a short interactive animation video in the ward. After watching the video, the patients were visited by an anesthesiologist who performed a preanesthetic interview and routine risk assessment. The patients in the no-video group were also visited by an anesthesiologist, but were not asked to watch the video. In both groups, the patients were asked to complete the State-Trait Anxiety Inventory and a 14-point scale of knowledge test before the anesthesiologist's visit and on the day of surgery. We also measured interview time.

**Results:** There was no demographic difference between the 2 groups. The interview time was 34.4% shorter (video group, 12.2 ± 5.3 minutes, vs. no-video group, 18.6 ± 6.4 minutes; 95% confidence interval [CI] for the percentage reduction in time: 32.7%-44.3%), and knowledge of anesthesia was 11.6% better in the video group (score 12.5 ± 1.4 vs. no-video group score 11.2 ± 1.7; 95% CI for the percentage increase in knowledge: 8.5%-13.9%). However, there was no difference in preanesthetic anxiety between the 2 groups.

**Conclusion:** Our short interactive animation video helped patients' understanding of anesthesia and reduced anesthesiologists' interview time.

## 異丙酚誘發血管舒張並通過血管周圍脂肪組織和內皮細胞進行調節的機制

### The Mechanisms of Propofol-Induced Vascular Relaxation and Modulation by Perivascular Adipose Tissue and Endothelium

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**背景：**異丙酚作為直接或間接的血管擴張劑導致平滑肌細胞鬆弛從而引起低血壓。血管周圍脂肪組織（PVAT）及內皮削弱血管收縮作用，並且高血壓及糖尿病改變了PVAT的功能。PVAT是否影響麻醉劑對血管功能的作用尚不清楚。我們研究了有關血管周圍的脂肪組織和血管內皮參與的丙泊酚誘發血管擴張的機制。

**方法：**準備 Wistar 老鼠的胸主動脈環——PVAT+、PVAT-、E+、E-，用於功能研究。

**結果：**經新福林收縮後的血管，異丙酚誘發的血管擴張在 PVAT+ 及 E+ 的血管最明顯，兩者均缺如的血管擴張作用最不明顯。丙泊酚通過內皮細胞依賴和非依賴兩種機制介導血管張作用。對異丙酚引起的血管舒張反應，一氧化氮合酶抑制劑、鉀通道阻斷劑（四乙銨及格列本脲）對 E+ 和 E- 血管均顯著減弱，可溶性鳥氨酸環化酶抑制劑 1H-〔1,2,4〕惡二唑〔4,3-a〕喹啉-1-酮及過氧化氫清除劑（過氧化氫酶）對 E- 的血管顯著減弱。PVAT 的存在顯著的增強了對異丙酚誘導的血管舒張作用。經新福林預收縮後，PVAT+ 或 E+ 的血管對異丙酚誘發的舒張有作用，相比之下，經 KCl 預收縮後，四種類型的血管對異丙酚誘發的舒張作用相似。

**結論：**PVAT 通過內皮依賴性及非內皮依賴性兩種途徑增強異丙酚誘發的老鼠主動脈舒張效應，因此突顯了 PVAT 的臨床重要性。

（侯文婷譯 薛張綱校）

**Background:** Propofol causes hypotension due to relaxation of vascular smooth muscle cells through its direct or indirect vasodilator effects. Perivascular adipose tissue (PVAT) and endothelium attenuate vascular contraction, and the function of PVAT is altered in hypertension and diabetes. Whether PVAT affects the action of anesthetics on vascular function is unknown. We studied the mechanisms of propofol-induced relaxation in relation to the involvement of PVAT and endothelium.

**Methods:** Thoracic aortic rings from Wistar rats were prepared with or without PVAT (PVAT+ and PVAT-), intact endothelium (E+), or both, or with the endothelium removed (E-) for functional studies.

**Results:** In phenylephrine precontracted vessels, propofol-induced relaxation was highest with both PVAT and E+ and lowest in vessels denuded of both PVAT and endothelium. Propofol-induced relaxation occurred via both endothelium-dependent and -independent mechanisms. The relaxation response induced by propofol was significantly reduced by nitric oxide synthase inhibitor (L-NNA), K(+) channel blockers (tetraethylammonium and glibenclamide) in E+ and E- vessels, and by soluble guanylyl cyclase inhibitor 1H-(1,2,4)oxadiazolo(4,3-A)quinazoline-1-one and hydrogen peroxide scavenger (catalase) in E- vessels. The presence of PVAT significantly enhanced the relaxation response induced by propofol. In contrast to phenylephrine precontracted vessels in which the presence of PVAT or endothelium had an effect, in vessels precontracted with KCl, propofol-induced relaxation was similar among the 4 types of vessel preparation.

**Conclusions:** PVAT enhances the relaxation effect induced by propofol in rat aorta through both endothelium-dependent and endothelium-independent pathways thus highlighting the clinical importance of PVAT.

**簡短報告：間距緊密雙極感應可以抑制燒灼引起的電磁干擾對心臟植入式電設備的干擾**

**Brief report: suppression of cautery-induced electromagnetic interference of cardiac implantable electrical devices by closely spaced bipolar sensing.**

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**背景：**手術中使用電刀等設備產生的電磁干擾可以使心臟起搏器或植入式除顫器受抑制或者高敏而導致心律失常。特別需要指出的是，頻繁使用廣泛間距傳感裝置(如整合的雙極傳感)可以使植入式除顫器對電磁干擾更加敏感性。因此通常會使用無創程式在手術前關閉自動除顫功能並且在手術後重新開啓。間距緊密傳感裝置(如真正的雙極)受電磁干擾的影響最小，因此手術中使用雙極電凝可以儘量避免手術前對植入式除顫器的重新編程並且保護起搏裝置的功能。

**方法：**我們的研究物件包括了23名新接受植入式除顫器或者正在接受植入式除顫脈衝發生器治療的患者。每個病人都分別嘗試電灼引起的電磁干擾對於間距緊密傳感裝置和廣泛間距傳感裝置的影響。

**結果：**比較這兩種感應模式，在廣泛間距雙極感應時，心電圖右心室振幅明顯增大並且電磁干擾的雜訊幅度也較大。此外，廣泛間距雙極感應時，有22人發生了植入式除顫器起搏功能抑制，並且有17人檢出了錯誤的"心室顫動"。相反，緊密雙極感應則不伴有起搏抑制或者錯誤的心室顫動感知。

**結論：**間隔緊密的雙極感應(即真正的雙極性)可以很好地屏除電灼引起的電磁干擾。對於植入式起搏裝置採用間隔緊密的雙極感應可以減少圍手術期重新編程同時保持手術中的正常功能。

(黃劍譯 薛張綱校)

**BACKGROUND :** Electromagnetic interference (EMI) induced by electrocautery during surgery in patients with cardiac pacemakers or implanted cardioverter-defibrillators (ICDs) may inhibit pacing and cause inappropriate tachyarrhythmia oversensing. In particular, susceptibility to EMI may be enhanced in ICDs by frequently used wide interelectrode sensing (i.e., integrated bipolar sensing). Consequently, ICD function is usually disabled preoperatively and restored later by noninvasive programming. Because sensing by closely spaced electrodes (i.e., true bipolar) may be less susceptible to EMI, preoperative programming to a true bipolar mode may minimize the need for perioperative programming while preserving device function.

**METHODS** : Our study population consisted of 23 consecutive patients either receiving a new ICD or undergoing ICD pulse generator change. In each patient, electrocautery-induced EMI was initiated with the ICD in the closely spaced sensing configuration and again during widely spaced sensing.

**RESULTS** : In comparing the 2 sensing modes, right ventricular electrogram amplitude was significantly greater and EMI noise amplitude tended to be greater with widely spaced bipolar sensing. Furthermore, widely spaced bipolar sensing was associated with ICD pacing inhibition in 22 of 23 patients and incorrect "ventricular fibrillation" detection in 17 of 23 patients. Conversely, closely spaced bipolar sensing was not accompanied by either pacing inhibition or incorrect ventricular fibrillation sensing.

**CONCLUSION** : Closely spaced bipolar sensing (i.e., true bipolar) appropriately rejects electrocautery-induced EMI. Programming implanted devices to closely spaced bipolar sensing may minimize the need for perioperative reprogramming while preserving intraoperative device operation.

### 慢性腎臟疾病與擇期整形手術術後死亡率得關係

#### Chronic Kidney Disease and Postoperative Morbidity After Elective Orthopedic Surgery

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**背景** : eGFR 被認為與增加心血管的風險和各種原因的死亡聯繫緊密。擇期中危的非心血管的手術的風險沒有被發現有相關性。我們假設 CKD 與擇期中危的整形科的手術的高發病率相關。

**方法** : 研究擇期整形手術的關節的置換術後，顯示在大部分全球的手術過程，麻醉和手術操作的特徵都是及其相似的。eGFR 是用修改後的腎臟疾病的飲食的公式，從常規的肌酐酸酐的測量結果中計算出來的。CKD 是  $eGFR < 60 \text{ mL/min/1.73 m}^2$ 。心臟風險（修改後的心臟風險指南），循證醫學，圍手術期的因素與圍手術期的發病率（手術的時間，失血量，手術時的溫度）的相關性也是有記錄的。主要的要點是手術後的發病率，儘量用手術後的發病率的調查來報告。發病率的差異是在有 CKD 的病人和腎臟功能正常的病人（用 X2 的測試）用 HR 或 OR 或 95% Cis 進行分析的。第二個要點是在有 ckd 和腎功能正常的病人中比較出院的時間和變成沒有發病的時間（用 log-rank 的測試來分析）。多元還原分析顯示 ckd，圍手術期的因素和發病率，和住院的時間都相關

**結果** : 手術後的發病率的調查結果記錄了 526 個進行擇期的整形手術的病人中。Ckd 的病人 ( $n = 142$ ; 27%) 在手術後的第 5 日 (OR 2.1 [95% CI: 1.2–3.7];  $P < 0.0001$ ) 有很高發病率。ckd 得病人用更長的時間 (HR 1.6 [95% CI: 1.2–1.9]) 去變成復發的病人

(HR 1.4 [95% CI: 1.2–1.7];  $P = 0.0001$ ; log-rank test).ckd 病人的出院時間被延誤 4 日。ckd 病人患肺部疾病，感染，心血管疾病，腎臟疾病，神經系的疾病，還有疼痛的發病是較為持久的。進一步將 ckd 得病人分層後顯示術前 eGFR  $\leq 50$  mL/min/1.73 m<sup>2</sup> 與高發病率，住院時間長相關，與年齡無關。多元還原分析顯示術前 ckd ( $P = 0.006$ ) 和充血性心衰( $P = 0.002$ )與住院時間延長相關。

**結論：**大致上小部分的有 ckd 的病人進行擇期整形科手術是有長時間發病和長時間的住院時間的比例是增加的。術前 eGFR 可能比其餘的危險因素更增加圍術期的風險。

(劉珏瑩譯 薛張綱校)

**BACKGROUND:** Reduced estimated glomerular filtration rate (eGFR) is strongly associated with increased cardiovascular risk and all-cause mortality. Associations with morbidity in elective, moderate-risk noncardiac surgery have not been explored. We hypothesized that chronic kidney disease (CKD) would be associated with excess morbidity after elective, moderate-risk orthopedic surgery.

**Methods:** Patients undergoing elective orthopedic joint replacement procedures were studied, representing a large proportion of global surgical procedures and characterized by highly homogeneous anesthetic and surgical practice. eGFR was calculated from routine creatinine measurements using the Modification of Diet in Renal Disease equation. CKD was defined as eGFR  $< 60$  mL/min/1.73 m<sup>2</sup>. Cardiac risk (Revised Cardiac Risk Index) and evidence-based, perioperative factors associated with perioperative morbidity (operative time, blood loss, perioperative temperature) were also recorded prospectively. The primary end point was postoperative morbidity, recorded prospectively using the postoperative morbidity survey. Morbidity differences were analyzed between patients with CKD and normal preoperative renal function ( $\chi^2$  test for trend) and presented as hazard ratio (HR) or odds ratio (OR) with 95% confidence intervals (95% CIs). The secondary end points were time to hospital discharge and time to become morbidity free (analyzed by log-rank test), both between and within CKD compared with normal renal function patients. Multiple regression analysis was performed to assess the association of CKD, perioperative factors with morbidity, and length of hospital stay.

**Results:** Postoperative morbidity survey was recorded in 526 patients undergoing elective orthopedic surgery. CKD patients ( $n = 142$ ; 27%) sustained excess morbidity on postoperative day 5 (OR 2.1 [95% CI: 1.2–3.7];  $P < 0.0001$ ). CKD patients took longer (HR 1.6 [95% CI: 1.2–1.9]) to become morbidity free (log-rank test,  $P < 0.0001$ ). Time to hospital discharge was delayed by 4 days in CKD patients (HR 1.4 [95% CI: 1.2–1.7];  $P = 0.0001$ ; log-rank test). CKD patients sustained more pulmonary (OR 2.2 [95% CI: 1.3–3.6];  $P = 0.002$ ), infectious (OR 1.7 [95% CI: 1.1–2.7];  $P = 0.01$ ), cardiovascular (OR 2.4 [95% CI: 1.2–4.8];  $P = 0.01$ ), renal (OR 2.3 [95% CI: 1.5–3.5];  $P < 0.00,001$ ), neurological (OR 4.3 [95% CI: 1.3–17.7];  $P = 0.005$ ), and pain (OR 1.8 [95% CI: 1.03–3.1];  $P = 0.04$ ) morbidities. Further stratification of CKD revealed preoperative eGFR  $\leq 50$  mL/min/1.73 m<sup>2</sup> to be associated with more frequent morbidity and longer hospital stay, independent of age. Multiple regression analysis identified CKD ( $P = 0.006$ ) and congestive cardiac failure ( $P = 0.002$ ) as preoperative factors associated with prolonged hospital stay.

**Conclusions:** A substantial minority of patients with CKD undergoing elective orthopedic procedures are at increased risk of prolonged morbidity and hospital stay. Preoperative eGFR may enhance perioperative risk stratification beyond traditional risk factors.

## 腺病毒依附的血管生成素-1 加速內毒素誘導的急性肺損傷小鼠模型對炎症的反應

### Adenovirus-Delivered Angiotensin 1 Accelerates the Resolution of Inflammation of Acute Endotoxic Lung Injury in Mice

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**背景：**免疫系統在保護機體免受感染中起著關鍵的作用。免疫系統可以及時處理炎症反應，在保護機體返回內環境穩態，保持正常的器官功能中起至關重要的作用。血管生成素-1 可以防止作為炎症反應的病原體的一部分的內皮細胞的啟動，並在急性肺損傷中起抗炎作用。我們設計這項研究，通過增加血清血管生成素-1 的含量，研究是否可以加速內毒素誘導的急性肺損傷小鼠模型對炎症的反應。

**方法：**氣管內注入脂多糖誘導動物急性肺損傷模型，這些小鼠 24 小時前分別用腺病毒載體或腺病毒 GFP- GFP – 血管生成素-1 預處理過。每組額外的 6 只已預處理過小鼠在滴入脂多糖前被處死作為對照。分析他們的炎症指數。用螢光啟動細胞分選測定凋亡多形核白細胞和巨噬細胞的吞噬功能。對組織中的血管生成素-1 和支氣管肺泡灌洗液中粒細胞巨噬細胞集落刺激因數的表達進行了測量。

**結果：**脂多糖誘導的白細胞浸潤到肺泡中，48 小時後滴入脂多糖滲透幅度達到最大。用腺病毒- GFP – 血管生成素-1 預處理組血管生成素-1 顯著表達，減少白細胞和中性粒細胞浸潤，炎症的持續時間縮短。腺病毒- GFP – 血管生成素-1 預處理組粒細胞巨噬細胞集落刺激因數幅度沒有改變。

**結論：**我們的研究結果表明：血管生成素-1 預處理過的小鼠在內毒素誘導的急性肺損傷模型中通過加速了中性粒細胞和巨噬細胞的凋亡大大促進炎症反應。

(陸麗虹譯 薛張綱校)

**BACKGROUND:** The immune system plays a key role in protecting the organism from infection. Timely resolution of the inflammatory response to infection plays a vital role in returning homeostasis and maintaining normal organ function. Angiotensin1 prevents endothelial activation, part of the inflammatory response to a pathogen, and has an anti-inflammatory effect in acute lung injury. We designed this study to investigate whether increasing serum production of angiotensin1 by IV administration of adenoviral-delivered angiotensin1 could accelerate the resolution of inflammation in endotoxin-induced acute lung injury in mice.

**METHODS:** Lipopolysaccharide was intratracheally instilled to induce acute lung injury in animals pretreated for 24 hours with adenoviral-GFP vector or adenoviral-GFP-angiotensin1, respectively. An additional 6 mice in each pretreatment group were killed before lipopolysaccharide instillation to serve as controls. Indices of resolution of

inflammation were analyzed. Apoptotic polymorphonuclear leukocytes and their phagocytosis by macrophages were determined by fluorescent activated cell sorter. The expression of angiotensin II in tissues and granulocyte macrophage colony-stimulating factor in the bronchoalveolar lavage fluid were measured.

**RESULTS:** Lipopolysaccharide induced leukocyte infiltration into air spaces, with maximal infiltration 48 hours after lipopolysaccharide instillation. Pretreatment with adenovirus-GFP-angiotensin II markedly increased angiotensin II expression, reduced leukocyte, and neutrophil infiltration and shortened the duration of inflammation. Adenovirus-GFP-angiotensin II pretreatment augmented the magnitude without altering the time course of granulocyte macrophage colony-stimulating factor.

**CONCLUSIONS:** Our results suggest that angiotensin II pretreatment promotes resolution of inflammation in endotoxin-induced acute lung injury in mice by accelerating the apoptosis of neutrophils and their phagocytosis by macrophages.

### 在脊麻剖宮產中母體和胎兒 $\beta 2$ 腎上腺素受體和一氧化氮合酶基因型對血管加壓素需求和胎兒酸鹼狀態的影響

#### The Effect of Maternal and Fetal $\beta 2$ -Adrenoceptor and Nitric Oxide Synthase Genotype on Vasopressor Requirement and Fetal Acid-Base Status During Spinal Anesthesia for Cesarean Delivery

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**背景：**先前的研究證實了在剖宮產術中  $\beta 2$  腎上腺素受體基因(ADRB2)的母體單元型影響了麻黃鹼的需要量。與純  $\alpha$  腎上腺素受體激動劑如去氧腎上腺素對比，麻黃鹼的使用與臍動脈(UA)血 pH 降低有關，這被認為繼發於增加的胎兒代謝。沒有資料評估了胎兒或新生兒基因型對母體給予血管加壓素後胎兒代謝反應的影響。我們假設新生兒 ADRB2 基因型會影響新生兒酸血症的程度。我們同時研究了在低血壓時，母體 ADRB2 和內皮細胞氮氧化物合酶基因(NOS3)對麻黃鹼和去氧腎上腺素需求量的影響。

**方法：**共有 104 名在脊麻下行剖宮產術的中國婦女入選了這項雙盲隨機臨床試驗，評估了麻黃鹼和去氧腎上腺素輸注對母體和新生兒的影響。血樣採自於臍動脈、臍靜脈和母體橈動脈，試驗測量了血氣值、乳酸、麻黃鹼和去氧腎上腺素濃度，並在 ADRB2 密碼子 16(rs1042713)和 27 (rs1042714)以及 NOS 密碼子 298 (rs1799983)用非同義單核苷酸多態性確定母體和新生兒基因型。臨床變數(臍動脈血 pH、乳酸和血管加壓素的劑量)在不同基因型中對照，回歸分析被創建來評價基因型對血管加壓素劑量和胎兒酸鹼狀態的影響。

**結果：**母體 ADRB2 基因型不影響麻黃碱用量。新生兒基因型密碼子 16 影響了胎兒酸鹼狀態。臍動脈血 pH 在精氨酸 16 純合子新生兒中升高( $7.31 \pm 0.03$  在 p.16Arg/Arg 對比  $7.25 \pm 0.11$  在 p.16 Arg/Gly 和 p.16 Gly/Gly;  $P < 0.001$ , 差異的 95% 置信區間(CI)為  $0.03 \sim 0.09$ )，臍動脈血乳酸值降低( $2.67 \text{ mmol/L} \pm 0.99$  in p.16Arg/Arg 對比  $4.28 \text{ mmol/L} \pm 2.79$  在 p.16 Arg/Gly 和 p.16 Gly/Gly;  $P < 0.001$ , 差異的 95% 置信區間(CI)為  $-2.40 \sim -0.82$ )。在母親接受麻黃碱的新生兒中，基因型間的差異程度更大(pH  $7.30 \pm 0.02$  在 p.16Arg/Arg 對比  $7.19 \pm 0.10$  在 p.16 Arg/Gly 和 p.16 Gly/Gly;  $P < 0.001$ , 差異的 95% 置信區間(CI)為  $0.07 \sim 0.14$ )，臍動脈血乳酸含量更低( $3.66 \text{ mmol/L} \pm 1.30$  在 p.16Arg/Arg 對比  $5.79 \text{ mmol/L} \pm 2.88$  在 p.16 Arg/Gly 和 p.16 Gly/Gly;  $P = 0.003$ , 差異的 95% 置信區間(CI)為  $-3.48 \sim -0.80$ )。在多元線性回歸模型中( $R^2 = 63.6\%$ ;  $P = 0.03$ )，新生兒 ADRB2 基因型(p.16Arg/Arg 和 p.27Gln/Glu)和更低的新生兒出生體重預示了更低的臍動脈血乳酸濃度。去氧腎上腺素劑量不為母體 ADRB2 或 NOS3 基因型所改變，胎兒型 NOS3 基因型不影響臍動脈血 pH 和乳酸值。

**結論：**與之前北美人群研究對比，在中國人群行擇期剖宮產手術中，母體型 ADRB2 基因型不影響麻黃碱需求。儘管如此，我們的研究顯示新生兒 ADRB2 p.Arg16 純合子基因型對麻黃碱誘導的胎兒酸血症有保護作用。

(任雲譯 薛張綱校)

**BACKGROUND:** Previous work demonstrated that maternal haplotypes of the  $\beta(2)$ -adrenoceptor gene (ADRB2) influence ephedrine requirements during cesarean delivery. The use of ephedrine versus a pure  $\alpha$ -adrenergic agonist such as phenylephrine has been associated with lower umbilical artery (UA) pH, thought to be secondary to increased fetal metabolism. There are no data evaluating the effect of fetal/neonatal genotypes on the metabolic response to maternally administered vasopressors. We hypothesized that neonatal ADRB2 genotype would affect the extent of neonatal acidemia. We also examined the effect of maternal ADRB2 and the endothelial nitric oxide synthase gene (NOS3) on ephedrine and phenylephrine requirements for treatment of maternal hypotension.

**METHODS:** The study was performed on 104 Chinese women scheduled for cesarean delivery under spinal anesthesia who were participating in a double-blind randomized clinical trial evaluating the maternal and neonatal effects of ephedrine versus phenylephrine infusions. Blood samples were drawn from the UA, umbilical vein, and maternal radial artery to measure blood gas values and lactate, ephedrine, and phenylephrine concentrations, and to determine maternal and neonatal genotype at nonsynonymous single nucleotide polymorphisms at codons 16 (rs1042713) and 27 (rs1042714) of ADRB2 and codon 298 (rs1799983) of NOS. Clinical variables (UA pH, UA lactate, and dose of vasopressors) among genotypes were compared, and regression models were created to assess the effect of genotype on vasopressor dose and fetal acid-base status.

**RESULTS:** Maternal ADRB2 genotype did not affect the ephedrine dose. Neonatal genotype at codon 16 influenced fetal acid-base status. UA pH was higher in Arg16 homozygous neonates ( $7.31 \pm 0.03$  in p.16Arg/Arg vs.  $7.25 \pm 0.11$  in p.16 Arg/Gly and p.16 Gly/Gly;  $P < 0.001$ , 95% confidence interval (CI) of difference  $0.03 \sim 0.09$ ) and UA lactate was lower ( $2.67 \text{ mmol/L} \pm 0.99$  in p.16Arg/Arg vs  $4.28 \text{ mmol/L} \pm 2.79$  in p.16

Arg/Gly and p.16 Gly/Gly;  $P < 0.001$ , 95% CI of difference  $-2.40 \sim -0.82$ ). In neonates born to mothers receiving ephedrine, the magnitude of the difference among genotypes was even greater (pH  $7.30 \pm 0.02$  in p.16Arg/Arg vs.  $7.19 \pm 0.10$  in p.16 Arg/Gly and p.16 Gly/Gly;  $P < 0.001$ , 95% CI of difference  $0.07 \sim 0.14$ ) and UA lactate was lower ( $3.66 \text{ mmol/L} \pm 1.30$  in p.16Arg/Arg vs.  $5.79 \text{ mmol/L} \pm 2.88$  in p.16 Arg/Gly and p.16 Gly/Gly;  $P = 0.003$ , 95% CI of difference  $-3.48 \sim -0.80$ ). In a multiple linear regression model ( $R(2) = 63.6\%$ ;  $P = 0.03$ ), neonatal ADRB2 genotypes (p.16Arg/Arg and p.27Gln/Glu) and lower neonatal birth weight predicted lower UA lactate concentrations. Phenylephrine dose was not affected by maternal ADRB2 or NOS3 genotypes, and neonatal NOS3 genotype did not affect UA pH or UA lactate.

**CONCLUSION:** In contrast to previous findings in a North American cohort, maternal ADRB2 genotype did not affect ephedrine requirements during elective cesarean delivery in a Chinese cohort. However, our findings suggest that neonatal ADRB2 p.Arg16 homozygosity confers a protective effect against developing ephedrine-induced fetal acidemia.

在頸動脈內膜剝脫術中降壓藥對術中升壓藥需求的影響。

### The Effect of Antihypertensive Class on Intraoperative Pressor Requirements During Carotid Endarterectomy

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**背景：**有某種類型的降壓藥與術中低血壓有關，通常還與病人同時使用多種類型的降壓藥有關。我們試圖去尋找在全麻下頸動脈內膜剝脫術中，是否一種降壓藥單獨或者聯合其他幾種降壓藥同時使用會增加術中低血壓的發生率。我們通過術中監測血壓，使用加壓藥的劑量來決定低血壓的發生率。

**方法：**有 252 名患者擇期在全麻下行頸動脈的內膜剝脫術，他們都參加了認知功能不良的評估。這些患者都服用一種或者幾種降壓藥。麻醉方案是事先制訂的，使用苯腎上腺素（新福林）來滴定維持平頸動脈血壓在頸動脈夾閉前維持在基線水準，在頸動脈夾閉期間維持在基線的 20% 以上。通過電腦記錄麻醉資料，記錄血流動力學的波動，並保證術中用藥。

**結果：**服用利尿劑的患者比單獨服用其他降壓藥的患者術中需要更多的新福林（1.6 倍）。這種使用新福林的差異只在頸動脈夾閉前發生，即從誘導到夾閉頸動脈來維持術中血壓穩定。然而，和這個結果相反的是，在頸動脈夾閉期間使用新福林來維持血壓高於基線的 20%，各降壓藥組均沒有差異。

**結論：**在全麻下行頸動脈內膜剝脫術，在頸動脈內膜夾閉前，平時服用利尿劑來降壓的患者術中需要更多的升壓藥來維持血壓的穩定。

（翁梅琳譯 薛張綱校）

**Background:** Certain classes of antihypertensive drugs have been associated with intraoperative hypotension, and frequently, patients are receiving multiple classes of

antihypertensive medications. We sought to determine whether one class of antihypertensive medication either alone, or in combination with other classes of antihypertensive medications, increased the probability of intraoperative hypotension, determined by the amount of vasopressor required during carotid endarterectomy (CEA) performed under general anesthesia with specific arterial blood pressure management.

**Methods:** This is a post hoc analysis of 252 patients scheduled for elective CEA under general anesthesia, all of whom participated in a prospective evaluation of cognitive dysfunction. Patients were characterized by class and number of preoperative antihypertensive medications taken. A predetermined anesthetic regimen was administered to all patients, with a phenylephrine infusion titrated to maintain mean arterial blood pressure at baseline before clamping the carotid artery, and approximately 20% above baseline during clamping. Computerized anesthesia records were used to record hemodynamics and to quantify medication administered intraoperatively.

**Results:** Patients taking diuretics as part of their antihypertensive regimen required significantly more (1.6 times) total intraoperative phenylephrine than those not taking diuretics, independently of the number of other antihypertensive medications. This difference in the phenylephrine requirement occurs only during the preclamp period, i.e., from induction to application of carotid artery clamping for the maintenance of preoperative blood pressure. However, in contrast to this result, there is no difference in pressor requirement comparing classes of antihypertensive medications to increase the mean arterial blood pressure 20% above baseline during the period when the carotid artery is clamped.

**Conclusion:** Diuretics are associated with increased vasopressor requirements in patients having a CEA under general anesthesia in the preclamp period, which is likely true for any patient having a general anesthetic.

### 低劑量 $\alpha_2$ 受體拮抗劑反常性提高大鼠去甲腎上腺素和可樂定的鎮痛效能

#### Low Dose Alpha-2 Antagonist Paradoxically Enhances Rat Norepinephrine and Clonidine Analgesia

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超低劑量阿片類拮抗劑延長了阿片類的鎮痛作用並且阻斷耐受。

本研究中我們探討了低劑量  $\alpha_2$  受體阻斷劑，阿替美啞是否同樣具有  $\alpha_2$  受體介導的鎮痛作用和耐受作用。在大鼠鞘內注射去甲腎上腺素或者可樂定聯合阿替美啞，用夾尾試驗進行測試。連續注射後可介導對去甲腎上腺素的急性耐受。低劑量阿替美啞顯著延長了去甲腎上腺素和可樂定介導的鎮痛作用。阿替美啞和  $\alpha_2$  受體激動劑的聯合注射也能預防急性耐受模型中激動劑效能的喪失。該試驗顯示了低劑量  $\alpha_2$  受體拮抗劑對於  $\alpha_2$  受體激動劑介導的鎮痛作用的反常擴大效應。

(姚敏敏譯，薛張綱校)

Ultralow-dose opioid antagonists prolong opioid antinociception and block tolerance. In this study we determined whether low doses of the  $\alpha_2$  adrenergic receptor (A2-R)

antagonist, atipamezole, similarly influenced A2-R-induced antinociception and tolerance. In rats, intrathecal norepinephrine (NE) or clonidine in combination with atipamezole was tested using tail-flick and paw pressure tests. Acute tolerance to NE was induced by serial injections. Low-dose atipamezole significantly prolonged NE and clonidine-induced antinociception. Coadministration of atipamezole with A2-R agonists also prevented loss of agonist potency in the acute tolerance model. This study demonstrates paradoxical effects of low-dose A2-R antagonists augmenting A2-R agonist-induced analgesia.