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揭示麻醉藥物與內皮細胞間的相互作用：新進展與新見解

Unraveling Interactions Between Anesthetics and the Endothelium: Update and Novel Insights

Aguirre JA[1], Lucchinetti E, Clanachan AS, Plane F, Zaugg M.

Anesthesia & Analgesia: 2016 122 330-348.

血管內皮細胞是人體最大的器官之一，它由單層高分化細胞構成，具有特定的形態和功能。內皮細胞在調節動脈、靜脈、微血管、淋巴管血管床的血管緊張性中起著重要的作用。此外，內皮細胞還可調節血管生成，控制細胞粘附、調節體液平衡、先天免疫和適應性免疫反應。有基礎研究顯示，在有氧和缺血再灌注的情況下，全身麻醉藥和局部麻醉藥均能顯著調節內皮細胞的生物活性，使內皮細胞成爲麻醉影響心血管系統的重要靶點。儘管鹵化吸入麻醉藥抑制了內皮依賴性的血管舒張，但它有著顯著的抗炎作用，可保護血管

內皮細胞發生缺血再灌注損傷。他們所提供的並不僅是急性，同樣還有長期潛在的、有益的影響。雖然靜脈麻醉藥對血管內皮功能的影響現在仍有爭議，並未被完全研究透徹，但異丙酚和阿片類藥物似乎對血管內皮的保護最爲明顯。一些阿片類藥物和氯胺酮對內皮細胞有立體選擇性。最後，有實驗證據表明，麻醉藥對血管的通透性，包括內皮祖細胞在內的幹細胞的增殖，促進或抑制腫瘤的生長都有著重要影響，這可能與調節血管生成的改變有關。然而，這些研究結果大多數是從體外實驗得到的，還需體內實驗的進一步確認。因此，這些相互作用的臨床意義仍然不確定。

（陸曉斐譯 李士通校）

The vascular endothelium is one of the largest organs in the body and consists of a single layer of highly specialized cells with site-specific morphology and functions. Endothelial cells play a vital role in the regulation of vascular tone in arterial, venous, microvascular, and lymphatic vascular beds. The endothelium also coordinates angiogenesis and controls cell adhesion, fluid homeostasis, and both innate and adaptive immunity. Fundamental research has shown that general and local anesthetics markedly modulate the biological activities of endothelial cells under aerobic and ischemia-reperfusion conditions, making the endothelium an important target of anesthetics in the cardiovascular system. Halogenated volatile anesthetics provide significant anti-inflammatory actions and protect the endothelium against ischemia-reperfusion injury, despite their inhibiting effects on endothelium-dependent vasorelaxation. They provide not only acute but also potential long-term, beneficial effects. Although many effects of IV anesthetics on endothelial function are controversial, or completely unexplored, propofol and opioids appear to have the most favorable profile with respect to the preservation of endothelial function. Some opioids and ketamine have stereoselective effects on the endothelium. Finally, there is experimental evidence to suggest important effects of anesthetics on the regulation of vascular permeability, proliferation of stem cells, including endothelial progenitor cells, and promotion or inhibition of tumor growth, potentially related to alterations in angiogenesis. However, most of these findings are from in vitro experiments and await confirmation in an in vivo setting. Thus, the clinical implications of these interactions remain uncertain.

間歇性缺氧導致成人心肌細胞炎症和損傷

Intermittent Hypoxia Causes Inflammation and Injury to Human Adult Cardiac Myocytes

Wu J[1], Stefaniak J, Hafner C, Schramel JP, Kaun C, Wojta J, Ullrich R, Tretter VE, Markstaller K, Klein KU.

Anesthesia & Analgesia: 2016 122 373–380.

背景：間歇性缺氧可能在一些臨床事件中發生，其中包括心肌缺血或呼吸障礙（如阻塞性睡眠呼吸暫停綜合征）。雖然間歇性缺氧與心腦血管疾病有關，但間歇性缺氧對心臟的影響還不明確。因此，在本研究中，我們比較了在間歇性缺氧、不同程度的持續性缺氧和正常情況下，成人心肌細胞 (HACMs)體外培養的不同細胞反應。

方法：通過使用一種有氣體滲透膜的新型細胞培養生物反應器，使 HACMs 分別暴露於間歇缺氧（0% - 21% O_2）、持續輕度缺氧（10% O2）、持續嚴重缺氧（0% O2）和正常氧（21% O2）的環境下。評估不同實驗條件下細胞增殖，乳酸脫氫酶、血管內皮生長因數

和細胞因數（白細胞介素和巨噬細胞移動抑制因數）釋放的基礎值及暴露 8 小時，24 小時和 72 小時後的改變。通過信號轉導通路查找陣列來確定基因表達的變化。

結果：與持續性正常氧和持續輕度缺氧相比，間歇性缺氧表現的較低的細胞數和較高的乳酸脫氫酶，血管內皮生長因數和促炎性細胞因數（IL-1β，IL-6，IL-8 和巨噬細胞移動抑制因數）的釋放量證明了其細胞損傷程度更爲劇烈，可引起的更早和更強烈的炎症反應。持續嚴重缺氧 HACMs 的晚期影響更爲不利。信號轉導通路分析表明，間歇性缺氧主要改變了氧化應激、Wnt、Notch 和缺氧通路的基因表達。

結論：間歇性缺氧和持續嚴重缺氧可引起 HACMs 的炎症反應和細胞損傷，但持續輕度缺氧和正常氧則不然。間歇性缺氧的細胞損傷發生最早且最爲嚴重。體外研究結果表明，間歇性低氧可能會造成心臟快速和實質性的損害。

（陸曉斐譯 李士通校）

BACKGROUND: Intermittent hypoxia may occur in a number of clinical scenarios, including interruption of myocardial blood flow or breathing disorders such as obstructive sleep apnea. Although intermittent hypoxia has been linked to cardiovascular and cerebrovascular disease, the effect of intermittent hypoxia on the human heart is not fully understood. Therefore, in the present study, we compared the cellular responses of cultured human adult cardiac myocytes (HACMs) exposed to intermittent hypoxia and different conditions of continuous hypoxia and normoxia.

METHODS: HACMs were exposed to intermittent hypoxia (0%-21% O2), constant mild hypoxia (10% O2), constant severe hypoxia (0% O2), or constant normoxia (21% O2), using a novel cell culture bioreactor with gas-permeable membranes. Cell proliferation, lactate dehydrogenase release, vascular endothelial growth factor release, and cytokine (interleukin [IL] and macrophage migration inhibitory factor) release were assessed at baseline and after 8, 24, and 72 hours of exposure. A signal transduction pathway finder array was performed to determine the changes in gene expression.

RESULTS: In comparison with constant normoxia and constant mild hypoxia, intermittent hypoxia induced earlier and greater inflammatory response and extent of cell injury as evidenced by lower cell numbers and higher lactate dehydrogenase, vascular endothelial growth factor, and proinflammatory cytokine (IL-1β, IL-6, IL-8, and macrophage migration inhibitory factor) release. Constant severe hypoxia showed more detrimental effects on HACMs at later time points. Pathway analysis demonstrated that intermittent hypoxia primarily altered gene expression in oxidative stress, Wnt, Notch, and hypoxia pathways.

CONCLUSIONS: Intermittent and constant severe hypoxia, but not constant mild hypoxia or normoxia, induced inflammation and cell injury in HACMs. Cell injury occurred earliest and was greatest after intermittent hypoxia exposure. Our in vitro findings suggest that intermittent hypoxia exposure may produce rapid and substantial damage to the human heart.

昂丹司瓊預防鞘內注射芬太尼及舒芬太尼引起的瘙癢症：一項隨機試驗的薈萃分析

Prophylactic Ondansetron for the Prevention of Intrathecal Fentanyl- or Sufentanil-Mediated Pruritus: A Meta-Analysis of Randomized Trials

Prin M, Guglielminotti J, Moitra V, Li G.

Anesthesia & Analgesia: 2016 122 402–409

背景：瘙癢症是鞘內注射芬太尼及舒芬太尼常見副反應，會降低患者對麻醉的滿意度及延長住院時間。關於預防使用昂丹司瓊降低瘙癢症的有效性的報導仍有爭議。本薈萃分析的目的在於評估預防性給予昂丹司瓊降低鞘內注射芬太尼、舒芬太尼引起的瘙癢症發生率及需要補救治療的概率。

方法：根據系統綜述和薈萃分析優先報告條目指南（PRISMA）,我們系統地檢索了 PubMed, Medline, and the Cochrane Central Register of Controlled Trials 資料庫中從 1994 年 1 月 1 日到 2014 年 1 月 1 日的相關文獻，收集了評價預防性使用昂丹司瓊對與鞘內注射芬太尼和舒芬太尼相關的瘙癢症的效能的隨機對照試驗。主要結果是分析瘙癢症的發生率，次要結果是分析瘙癢症患者對補救治療的需求。敏感性分析評估了包括產科患者、非產科患者、和在鞘內使用阿片類藥物之前或之後使用昂丹司瓊的結果。使用隨機效應模型進行分析。

結果：收集了 6 個隨機對照試驗包括 555 個病人。總的來說，預給昂丹司瓊不能降低瘙癢症發生率，但能降低需要補救治療的概率（危險比 RR, 0.57；95%可信區間,0.35-0.91；I=0%；P=0.02）。進一步分組研究，包括非產科患者組和鞘內注射阿片類藥物前使用昂丹司瓊，也證明有減少補救治療瘙癢症的用藥的趨勢（危險比 RR, 0.47；95% 可信區間, 0.26-0.85； P = 0.01；危險比 RR, 0.62； 95% 可信區間, 0.38-1.00； P = 0.05）。

結論：預防性的靜脈注射 8mg 的昂丹司瓊並不能降低鞘內注射芬太尼和舒芬太尼引起瘙癢症的發生率，但可能減少瘙癢症的用藥，尤其是特定亞組的結果更有說服力。需要更多的隨機對照試驗驗證這些結果。

（黃婷譯 李士通校）

BACKGROUND: Pruritus is a common side effect of intrathecal fentanyl or sufentanil that decreases patient satisfaction and may delay hospital discharge. There are conflicting reports about the efficacy of prophylactic ondansetron in reducing the incidence of pruritus. This meta-analysis aimed to assess the effect of prophylactic ondansetron on the incidence of intrathecal fentanyl- or sufentanil-mediated pruritus and the need for rescue treatment.

METHODS: A systematic search on PubMed, Medline, and the Cochrane Central Register of Controlled Trials from January 1, 1994, to January 1, 2014, was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. Randomized controlled trials evaluating the efficacy of prophylactic ondansetron on pruritus associated with intrathecal fentanyl or sufentanil were included. The primary outcome was the incidence of pruritus, and the secondary outcome was patients' need for rescue therapy. Sensitivity analyses were conducted to assess the outcomes in obstetric and nonobstetric patients and in patients who received ondansetron before or after intrathecal opioid injection. Analyses used random-effect models.

RESULTS: Six randomized controlled trials involving 555 patients were included. In the overall analysis, prophylactic ondansetron did not significantly decrease the incidence of pruritus, but there was a trend toward reduced rescue medication use (risk ratio [RR], 0.57; 95% confidence interval [CI], 0.35-0.91; I = 0%; P = 0.02). Exploratory subgroups, including nonobstetric surgery patients and patients who received ondansetron before spinal opioid administration, also

suggest a trend toward less rescue medication use (RR, 0.47; 95% CI, 0.26-0.85; P = 0.01; and RR, 0.62; 95% CI, 0.38-1.00; P = 0.05).

CONCLUSIONS: IV 8 mg prophylactic ondansetron does not decrease the incidence of fentanyl- or sufentanil-mediated pruritus but may decrease the need for pruritus rescue medication, particularly in specific subgroups. Randomized trials are needed to confirm these results.

一項關於無線連接重症監護室患者監護儀和麻醉資訊管理系統的技術評估

A Technical Evaluation of Wireless Connectivity from Patient Monitors to an Anesthesia Information Management System During Intensive Care Unit Surgery

Simpao AF[1], Galvez JA, England WR, Wartman EC, Scott JH, Hamid MM Sr, Rehman MA, Epstein RH.

Anesthesia & Analgesia: 2016 122 425–429

在費城兒童醫院新生兒重症監護室（NICU）的床邊手術操作是使用紙質麻醉記錄單記錄，相比手術室所有麻醉記錄都是使用麻醉資訊管理系統(AIMS)。這主要是因爲後勤方面的問題，與床旁監護儀和可攜式 AIMS 工作站的連接電纜有關。我們在 NICU 用 AIMS 進行記錄，利用無線路由器把監床旁護設備的資料傳輸到可攜式 AIMS 工作站。檢測無線 AIMS 類比中顯示高頻電刀的使用對資料傳輸沒有干擾。30 例 NICU 手術操作通過無線 AIMS 進行了麻醉記錄。2 例麻醉記錄單有短暫的資料傳輸遺漏；1 例因爲路由器斷電導致麻醉記錄單中資料記錄間隔延長。相比之下，30 例對照組中使用有線連接，麻醉記錄單未出現資料記錄間隔延長。與紙質麻醉記錄單相比，無線 AIMS 爲 NICU 床旁手術操作中麻醉記錄提供了一個簡單的、無干擾的、便攜的選擇。

（黃婷譯 李士通校）

Surgical procedures performed at the bedside in the neonatal intensive care unit (NICU) at The Children's Hospital of Philadelphia were documented using paper anesthesia records in contrast to the operating rooms, where an anesthesia information management system (AIMS) was used for all cases. This was largely because of logistical problems related to connecting cables between the bedside monitors and our portable AIMS workstations. We implemented an AIMS for documentation in the NICU using wireless adapters to transmit data from bedside monitoring equipment to a portable AIMS workstation. Testing of the wireless AIMS during simulation in the presence of an electrosurgical generator showed no evidence of interference with data transmission. Thirty NICU surgical procedures were documented via the wireless AIMS. Two wireless cases exhibited brief periods of data loss; one case had an extended data gap because of adapter power failure. In comparison, in a control group of 30 surgical cases in which wired connections were used, there were no data gaps. The wireless AIMS provided a simple, unobtrusive, portable alternative to paper records for documenting anesthesia records during NICU bedside procedures.

不同種族和人種剖腹產麻醉方式的差異

Racial and Ethnic Disparities in Mode of Anesthesia for Cesarean Delivery

Butwick AJ[1], Blumenfeld YJ, Brookfield KF, Nelson LM, Weiniger CF.
Anesthesia & Analgesia: 2016 122 472–479

背景：目前認爲種族和人種的差異性是構成椎管內分娩鎮痛差異的基礎。這些差異性也可能存在於產科麻醉護理的其他關鍵方面。我們試圖弄清不同種族或人種的差異對剖腹產麻醉方式是否會有影響。

方法：1999 年至 2002 年間，美國 19 所產科中心剖腹產的女性登記完成了母胎醫學單位網路剖腹產的註冊表。種族或人種分類爲：白人，非洲裔美國人，西班牙裔和非西班牙裔人種。麻醉方式分爲：椎管內麻醉（脊麻、硬膜外麻醉和腰硬聯合麻醉）或全身麻醉。爲了說明可能影響產科和非產科麻醉方式的協變數因素，我們使用序列協變數完成多元線性回歸分析。

結果：這個研究佇列包括 50974 例曾行剖腹產麻醉的女性。不同種族或人種之間全麻率分別如下：白種人 5.2%、非洲美裔人 11.3%、西班牙人 5.8%、非西班牙人 6.6%。對產科麻醉和非產科麻醉協變數進行調整之後，非裔美國女性與白種女性相比，非裔美國女性接受全身麻醉的概率最高。（調整後的 OR 值=1.7；95%可信區間，1.5-1.8；P<0.001）.與白種人女性相比，西班牙裔人種和非西班牙人接受全身麻醉的幾率較高，分別爲：西班牙裔人種（調整後的 OR 值爲 1.1；95%可信區間，1.0-1.3；P=0.02）和非西班牙人（調整後的 OR 值爲 1.2；95%可信區間，1.0-1.4；P=0.03）。在靈敏度分析中，爲排除在全身麻醉前進行椎管內麻醉的產婦這種情況，重新建立模型。接受全身麻醉的調整後概率類似於主要分析中得到的結果。即非洲美裔人（調整後的 OR 值爲 1.7; 95% CI, 1.5–1.9; $P < 0.001$）；西班牙裔(調整後的 OR 值爲 1.2; 95%可信區間， 1.1–1.4；$P = 0.006$)以及非西班牙裔(調整後的 OR 值爲 1.2; 95%可信區間， 1.0–1.5; $P = 0.05$)。

結論：根據剖腹產註冊表的資料分析，與白人女性相比，非裔美國女性接受全身麻醉的幾率最高。目前，我們仍不能十分確定這種差異在當前的產科實踐中是否存在。

（解健譯 李士通校）

BACKGROUND: Racial and ethnic disparities have been identified in the provision of neuraxial labor analgesia. These disparities may exist in other key aspects of obstetric anesthesia care. We sought to determine whether racial/ethnic disparities exist in mode of anesthesia for cesarean delivery (CD).

METHODS: Women who underwent CD between 1999 and 2002 at 19 different obstetric centers in the United States were identified from the Maternal-Fetal Medicine Units Network Cesarean Registry. Race/ethnicity was categorized as: Caucasian, African American, Hispanic, and Non-Hispanic Others (NHOs). Mode of anesthesia was classified as neuraxial anesthesia (spinal, epidural, or combined spinal-epidural anesthesia) or general anesthesia. To account for obstetric and non-obstetric covariates that may have influenced mode of anesthesia, multiple logistic regression analyses were performed by using sequential sets of covariates.

RESULTS: The study cohort comprised 50,974 women who underwent CD. Rates of general anesthesia among racial/ethnic groups were as follows: 5.2% for Caucasians, 11.3% for African Americans, 5.8% for Hispanics, and 6.6% for NHOs. After adjustment for obstetric and nonobstetric covariates, African Americans had the highest odds of receiving general anesthesia compared with Caucasians (adjusted odds ratio [aOR] = 1.7; 95% confidence interval [CI], 1.5–

1.8; *P* < 0.001). The odds of receiving general anesthesia were also higher among Hispanics (aOR = 1.1; 95% CI, 1.0–1.3; *P* = 0.02) and NHOs (aOR = 1.2; 95% CI, 1.0–1.4; *P* = 0.03) compared with Caucasians, respectively. In our sensitivity analysis, we reconstructed the models after excluding women who underwent neuraxial anesthesia before general anesthesia. The adjusted odds of receiving general anesthesia were similar to those in the main analysis: African Americans (aOR = 1.7; 95% CI, 1.5–1.9; *P* < 0.001); Hispanics (aOR = 1.2; 95% CI, 1.1–1.4;*P* = 0.006); and NHOs (aOR = 1.2; 95% CI, 1.0–1.5; *P* = 0.05). **CONCLUSIONS:** Based on data from the Cesarean Registry, African American women had the highest odds of undergoing general anesthesia for CD compared with Caucasian women. It is uncertain whether this disparity exists in current obstetric practice.

西班牙裔兒童術後疼痛管理：一項描述性佇列研究

Postoperative Pain Management in Children of Hispanic Origin: A Descriptive Cohort Study

Brown R[1], Fortier MA, Zolghadr S, Gulur P, Jenkins BN, Kain ZN.

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背景：兒童門診手術後的疼痛未能經常得到充分治療已被多次證實。然而很少有試驗從種族差異人群的角度研究這種現象。

方法：這項研究包括 105 個年齡在 2 歲至 15 歲之間，接受門診扁桃體切除術和腺樣體切除術的低收入的西班牙家庭的孩子。參與的家長完成基礎資訊和統計學資訊。以家庭訪問的形式記錄術後一周內疼痛評分及鎮痛藥在家中的使用情況。

結果：儘管術後 24 小時內顯著疼痛的發病率很高（70%；99%可信區間，82% -57%），32%（95%可信區間，45%-20%）的兒童僅接受 0 到 1 個劑量的鎮痛藥治療。總的來看，21%（99%可信區間，11%-35% ）的兒童在手術後整個周內接受了 4 個或更少劑量的止痛藥。手術後一周內，只有 44%（99%可信區間，40%-47%）的兒童總鎮痛藥劑量在可接受範圍內。

結論：儘管有顯著的術後疼痛，這項研究中的西班牙裔兒童卻在家中接受著未達標準的鎮痛治療。

（馮亞飛 譯 李士通 校）

BACKGROUND: It has been established that pain is frequently undertreated in children following outpatient surgery. Very few studies, however, have investigated this phenomenon in ethnically diverse populations.

METHODS: This study included 105 families of children aged 2 to 15 years of Hispanic origin and low income undergoing outpatient tonsillectomy and adenoidectomy surgery. Participating parents completed baseline and demographic packets. Recorded postoperative pain ratings and administration of analgesics at home for 1 week were collected during home visits.

RESULTS: Despite the high (70%; 99% confidence interval [CI], 57%-82%) incidence of significant pain in the first 24 hours home, 32% (95% CI, 20%-45%) of the children received 0 to 1 dose of analgesia. Overall, 21% children (99% CI, 11%-35%) received 4 or less total doses

of pain medication over the entire week after surgery. Of the total analgesic doses administered to children in the week after surgery, only 44% (99% CI, 40%-47%) were in accepted ranges.

CONCLUSIONS: Despite experiencing significant postoperative pain, Hispanic children assessed in this study received suboptimal analgesic therapy at home.

NR2B-CREB-CRTC1 信號通路調節慢性壓迫性損傷鼠模型的晝夜疼痛

Regulation of the NR2B-CREB-CRTC1 Signaling Pathway Contributes to Circadian Pain in Murine Model of Chronic Constriction Injury

Xia T[1], Cui Y, Qian Y, Chu S, Song J, Gu X, Ma Z.

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背景：許多臨床調查顯示慢性疼痛有晝夜節律性變化，臨床上大多數慢性疼痛的峰值在夜間。然而疼痛節律是否存在於齧齒類動物及其可能的特定機制尚未被研究。我們研究了鼠慢性壓迫性損傷（CCI）模型痛覺過敏的節律性變化並探討了 N-甲基-D-天門冬氨酸（NMDA）2B 受體(NR2B)—cAMP 反應元件結合蛋白（CREB）— CREB 轉錄共啓動因數 1 (CRTC1)信號通路在這種疼痛節律的作用。

方法：用慢性壓迫性損傷手術模擬臨床慢性疼痛。應用機械刺激縮足反應閾值和熱刺激縮足反應潛伏期測試鼠的疼痛行爲。用 von Frey 纖維觸痛儀連續 14 天在晝夜時點 ZT4、ZT10、ZT16、ZT22 這幾個時間點測試機械性痛覺過敏。用即時聚合酶鏈反應和 Western blot 法分別測定視交叉上核和脊髓背角處 NR2B、CRTC1 、CREB 的 mRNA 和蛋白的表達。 分別在兩個時間點（ZT12 和 ZT0）鞘內注射 CRTC1 和 CREB 干擾腺病毒載體，進一步探討疼痛治療的適當時間點。

結果：在慢性疼痛狀態期間，慢性壓迫性損傷動物的疼痛反應表現爲晝夜節律，並且在每天的 ZT4 和 ZT10 達到峰值。活動期和休息期的疼痛閾值有顯著差異。脊髓水準的 NR2B、CRTC1、CREB 的表達與疼痛節律一致。慢性壓迫性損傷手術後第 7 天到 9 天鞘內注射 CRTC1 和 CREB 的干擾腺病毒明顯改善疼痛反應。然而，與 ZT12 相比，當 ZT0 給予 CRTC1 和 CREB 的干擾腺病毒治療時，其緩解峰值疼痛更爲有效。

結論：慢性壓迫性損傷後慢性疼痛患者的疼痛反應表現爲晝夜節律，並與疼痛相關受體的晝夜節律性分泌有關。NR2B-CREB-CRTC1 信號通路可能在這種節律性裡起著至關重要的作用。此外，我們的研究結果表明，緩解疼痛的措施，應在疼痛達到高峰前即採取。

（馮亞飛譯 李士通校）

BACKGROUND: Numerous clinical investigations have revealed the circadian rhythm changes in the perception of chronic pain, and most clinical chronic pain types peak in the night. However, it is still undiscovered whether circadian rhythm of pain exists in rodents and the specific mechanism that may underlie it. Our study was conducted to investigate the rhythmic changes of hyperalgesia behavior in a chronic constrictive injury (CCI) model of rodents and to explore the role of the N-methyl-d-aspartate receptor 2B (NR2B)-cAMP response element binding protein (CREB)-CREB-regulated transcription coactivator 1 (CRTC1) signaling pathway in this pain rhythm.

METHODS: A CCI operation was performed to mimic clinical chronic pain. Paw mechanical withdrawal threshold and paw withdrawal thermal latency were used to test pain behavior in rats; a von Frey cilia test was used to test mechanical hyperalgesia in mice at Zeitgeber time (ZT) 4, ZT10, ZT16, and ZT22 for 14 contiguous days. The relative mRNA and protein expression of NR2B, CREB and CRTC1 in the suprachiasmatic nuclei and the dorsal horn were measured by real-time polymerase chain reaction and Western blot. CRTC1 and CREB interference adenovirus vectors were injected intrathecally at 2 time points, respectively (ZT12 and ZT0), to further explore the proper time point for pain treatment.

RESULTS: During the period of chronic pain state, the pain behavior of CCI rodents showed a circadian rhythm with the peak at ZT4 or ZT10 daily. The pain thresholds were significantly different between the activity period and the rest period. The expressions of NR2B, CRTC1, and CREB at the spinal level were consistent with the pain rhythm. The intrathecal treatment with CRTC1 or CREB interference adenovirus from day 7 to day 9 after CCI surgery markedly improved pain behaviors. Nevertheless, when given at ZT0, they were both more effective at relieving peak pain than drugs given at ZT12.

CONCLUSIONS: Pain behavior in the chronic pain of CCI displayed circadian rhythm and was associated with circadian secretion of pain-related receptors. The NR2B-CREB-CRTC1 signaling pathway may play a crucial role in this rhythm. Moreover, our results suggest that measures to relieve pain should be taken before pain reaches its peak.

二尖瓣返流對彩色多普勒測量的時間動態縮流面積影響的機制

The Mechanism of Mitral Regurgitation Influences the Temporal Dynamics of the Vena Contracta Area as Measured with Color Flow Doppler

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背景：對於二尖瓣返流(MR)患者，可以通過測量縮流面積(VCA)來評估反流口面積。推測 VCA 的時間動態特徵與功能性二尖瓣反流（FMR）或退行性二尖瓣瓣膜病(DMVD)的存在不同機制。

方法： 對 42 例心臟外科手術患者進行三維經食道超聲心動圖(TEE) 檢查，通過彩色血流多普勒的近端噴流面積獲得 VCA 資料, 共包括 22 個 FMR 和 20 個 DMVD。得到每個患者整個收縮期的連續 VCA 資料用來評價有效反流口面積的變化。採用重複測量方差分析對 FMR 和 DMVD 兩組的百分數平均值進行組內和組間比較。通過 Bonferroni 法校正兩兩測試的比較次數。

結果：FMR 組病人的標準化平均 VCA 值顯示爲兩相模式；而 DMVD 組病人爲單相模式。在 FMR 組內，標準化平均 VCA 值在收縮早期（1.10±0.32 cm^2）和末期（1.11±0.33 cm^2）相似，都顯著高於收縮中期(0.79 ± 0.22 cm^2，P = 0.0144；P = 0.0106)。在 DMVD 組內，收縮中期的標準化平均 VCA 值(1.37 ± 0.15 cm^2)較收縮早期 (0.53 ± 0.14 cm^2) 和晚期 (1.09 ± 0.18 cm^2; P < 0.0001)顯著增高。對標準化平均 VCA 值分析得出收縮早期(1.10 ±

0.32 cm^2 vs 0.53 ± 0.14 cm^2)和中期(0.79 ± 0.22 cm^2 vs 1.37 ± 0.15 cm^2; P < 0.0001)時 FMR 和 DMVD 兩組存在顯著差異。

結論： MR 機制導致了 VCA 的動態變化。同時觀察到 VCA 動態變化在 FMR 患者中呈現雙相時間模式而 DMVD 患者呈現單相時間模式。

（劉洋譯 陳傑校）

BACKGROUND: In patients with mitral regurgitation (MR), the effective regurgitant orifice area can be estimated by measuring the vena contracta area (VCA). We hypothesize that the VCA has characteristic temporal dynamics related to the underlying mechanism of functional mitral regurgitation (FMR) versus degenerative mitral valve disease (DMVD).

METHODS: VCA measurements obtained by planimetry of the proximal jet from 3D transesophageal echocardiographic (TEE) color flow Doppler data sets were acquired in 42 cardiac surgical patients, including 22 with FMR and 20 with DMVD. Serial VCAs were measured throughout systole for each patient to evaluate variation in the effective regurgitant orifice area. Tercile averages were compared within and between the FMR and DMVD groups using repeated measures analysis of variance. Pairwise tests were Bonferroni-corrected for the number of comparisons。

RESULTS: Normalized average VCA values in patients with FMR revealed a biphasic pattern compared with a monophasic pattern in patients with DMVD. Among FMR patients, normalized average VCA values in early (1.10 ± 0.32 cm2) and late systole (1.11 ± 0.33 cm2) were similar but were both significantly greater compared with mid-systole (0.79 ± 0.22 cm2; P = 0.0144 and P = 0.0106, respectively). Among DMVD patients, normalized average VCA values in mid-systole (1.37 ± 0.15 cm2) were significantly greater than those in early (0.53 ± 0.14 cm2) and late systole (1.09 ± 0.18 cm2; P < 0.0001 for both). An analysis of normalized average VCAs also revealed significant differences between the FMR and the DMVD groups during early (1.10 ± 0.32 cm2 vs 0.53 ± 0.14 cm2) and mid-systole (0.79 ± 0.22 cm2 vs 1.37 ± 0.15 cm2; P < 0.0001 for both).

CONCLUSIONS: VCA dynamics are governed by the mechanism of MR and are observed in FMR patients primarily as a biphasic temporal pattern compared with a monophasic temporal pattern in patients with DMVD.

丙泊酚-瑞芬太尼靶控麻醉下接受標準化刺激後腦電圖衍生的催眠和抗傷害作用的比較

Comparisons of Electroencephalographically Derived Measures of Hypnosis and Antinociception in Response to Standardized Stimuli During Target-Controlled Propofol-Remifentanil Anesthesia

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背景: 目前腦電圖（EEG）衍生測量能提供大腦皮層活動和催眠深度的資訊，但是對皮層下的活動監測還不夠精確，而一般認爲後者是隨著抗傷害效應程度而變化。最近，以神經

生理爲基礎的皮層腦電輸入（CI）和皮層所處狀態（CS）的 EEG 監測分別被認爲是麻醉/抗傷害效應以及催眠深度的可靠指標。本研究將腦電雙頻指數（BIS）和另一個最新研究出的指示抗傷害效應的複合變異指數(CVI)，與 CI 和 CS 的一種替代測量—複合皮層狀態（CCS）進行比較。CVI 是綜合量化 BIS 和預估肌電活動的一種 EEG 衍生參數。通過評估這些指標與催眠深度間的等效關係（用 BIS 定量）以及痛/不痛的平衡關係（用瑞芬太尼預計效應室濃度決定），評價催眠和鎮痛聯合監測對有害刺激的體動反應的預測作用是否優於單獨監測。

方法: 重新分析了先前發表的一項實驗中 BIS 和 CVI 指數以及原始腦電圖資料的時間序列。在本研究中，80 名患者隨機分爲靶催眠深度組（BIS50-70）和靶瑞芬太尼濃度組（瑞芬 0、2、4、6ng/ml）。運用觀察評估警覺/鎮靜量表，在一系列強直刺激後，計算或定量 CCS, CI, BIS, 及 CVI 的基礎值，以及每個時間間隔後的數值。定量分析瑞芬太尼效應室濃度時的鎮痛作用的指標 CI 和 CVI，以及它們和催眠指標 CCS 和 BIS 的關係。最後，運用統計學聚類方法評價鎮痛和催眠雙指標是否能更好的監測和預測對刺激的反應。

結果: 在刺激前，CI 和 CVI 均能區分接受 0 ng/ml 瑞芬輸注與其他劑量組患者(CI: Cohen's d = 0.65, 95% 可信區間，0.48–0.83; CVI: Cohen's d = 0.72, 95% 可信區間， 0.56–0.88)。BIS 和 CCS 間有很強的關聯(不同時間: 0.55 < R2 < 0.68, P < 0.001)。觀察評估警覺/鎮靜刺激與 CI 和 CCS 的變化相關，然而刺激後所有指標均有變化。CI 和 CCS 成對運用比 CVI 和 BIS 聯合應用更敏感地監測了刺激反應(敏感度 [99% 可信區間], 75.8% [52.7%–98.8%] vs 42% [15.4%–68.5%], P = 0.006), 特異 CI 和 CCS 所達顯著性(52% [34.7%–69.3%] vs 24% [9.1%–38.9%], P = 0.0159).

結論: 聯合應用腦電監測衍生的催眠和鎮痛量化指標可能更好地預測患者對強直刺激的反應。

（宣偉譯 陳傑校）

BACKGROUND: Current electroencephalogram (EEG)-derived measures provide information on cortical activity and hypnosis but are less accurate regarding subcortical activity, which is expected to vary with the degree of antinociception. Recently, the neurophysiologically based EEG measures of cortical input (CI) and cortical state (CS) have been shown to be prospective indicators of analgesia/antinociception and hypnosis, respectively. In this study, we compared CI and an alternate measure of CS, the composite cortical state (CCS), with the Bispectral Index (BIS) and another recently developed measure of antinociception, the composite variability index (CVI). CVI is an EEG-derived measure based on a weighted combination of BIS and estimated electromyographic activity. By assessing the relationship between these indices for equivalent levels of hypnosis (as quantified using the BIS) and the nociceptive-antinociceptive balance (as determined by the predicted effect-site concentration of remifentanil), we sought to evaluate whether combining hypnotic and analgesic measures could better predict movement in response to a noxious stimulus than when used alone.

METHODS: Time series of BIS and CVI indices and the raw EEG from a previously published study were reanalyzed. In our current study, the data from 80 patients, each randomly allocated to a target hypnotic level (BIS 50 or BIS 70) and a target remifentanil level (Remi-0, -2, -4 or -6 ng/mL), were included in the analysis. CCS, CI, BIS, and CVI were calculated or quantified at baseline and at a number of intervals after the application of the Observer's Assessment of Alertness/Sedation scale and a subsequent tetanic stimulus. The dependency of the putative

measures of antinociception CI and CVI on effect-site concentration of remifentanil was then quantified, together with their relationship to the hypnotic measures CCS and BIS. Finally, statistical clustering methods were used to evaluate the extent to which simple combinations of antinociceptive and hypnotic measures could better detect and predict response to stimulation.

RESULTS: Before stimulation, both CI and CVI differentiated patients who received remifentanil from those who were randomly allocated to the Remi-0 group (CI: Cohen's d = 0.65, 95% confidence interval, 0.48–0.83; CVI: Cohen's d = 0.72, 95% confidence interval, 0.56–0.88). Strong correlations between BIS and CCS were found (at different periods: 0.55 < R2 < 0.68, P < 0.001). Application of the Observer's Assessment of Alertness/Sedation stimulus was associated with changes in CI and CCS, whereas, subsequent to the application of both stimuli, changes in all measures were seen. Pairwise combinations of CI and CCS showed higher sensitivity in detecting response to stimulation than CVI and BIS combined (sensitivity [99% confidence interval], 75.8% [52.7%–98.8%] vs 42% [15.4%–68.5%], P = 0.006), with specificity for CI and CCS approaching significance (52% [34.7%–69.3%] vs 24% [9.1%–38.9%], P = 0.0159).

CONCLUSIONS: Combining electroencephalographically derived hypnotic and analgesic quantifiers may enable better prediction of patients who are likely to respond to tetanic stimulation.

亞硝酸鹽通過抑制連接蛋白-43 的去磷酸化減少大鼠心肌缺血引起的室性心律失常

Nitrite Reduces Ischemia-Induced Ventricular Arrhythmias by Attenuating Connexin 43 Dephosphorylation in Rats

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背景：缺血性心臟病引起的室性心律失常是心源性猝死的主要原因。缺血通過調節連接蛋白 43（Cx43，一種重要的心肌細胞間隙連接通道蛋白）導致危及生命的心律失常。本研究探索在大鼠模型中亞硝酸鹽是否可以抑制缺血引起的室性心律失常和 Cx43 的去磷酸化水準。

方法：按接受藥物不同將實驗動物分爲以下幾組：生理鹽水組（對照組，n= 10），亞硝酸鹽組（0.015、0.15、1.5 mg/kg，每組 9 或 10 只），以及 0.15mg/kg 亞硝酸鹽複合一氧化氮清除物（2-(4-carboxyphenyl)-4, 4, 5, 5-tetramethylimidazoline-1-oxyl-3-oxide，cPTIO; n= 9）組和 0.15mg/kg 亞硝酸鹽複合別嘌呤醇（黃嘌呤氧化還原酶抑制劑，n = 9）組。根據心律失常評分標準確定室性心律失常的嚴重程度並測定 Cx43 的磷酸化水準。

結果：亞硝酸鹽 0.15 mg/kg 模型鼠心律失常評分中位數 (4 [interquartile range {IQR}, 4–5]) 要低於對照組模型鼠的 (4 [interquartile range {IQR}, 4–5])。對照組與亞硝酸鹽 0.015mg/kg 組及亞硝酸鹽 1.5mg/kg 組之間沒有差異。而亞硝酸鹽複合 cPTIO 組和複合別嘌呤醇組的心律失常評分均要高於 0.15 mg/kg 亞硝酸鹽組(分別爲 6 [IQR, 5–8]; P = 0.030；7 [IQR, 5–8]; P = 0.005)。免疫組化實驗顯示，亞硝酸鹽 0.15 mg/kg 組的磷酸化連接蛋白 43 水準與對照組的（P= 0.007）相比顯著升高，而其他治療組則無顯著差異。

結論：亞硝酸鹽可能抑制了大鼠急性心肌缺血引起的室性心律失常並抑制 Cx43 的去磷酸化。一氧化氮由亞硝酸鹽經黃嘌呤氧化還原酶還原產生，本研究提示其在抗心律失常方面發揮重要的作用。

（袁亞偉譯 陳傑校）

BACKGROUND: Ventricular arrhythmias induced by ischemic heart disease are the main cause of sudden cardiac death. Ischemia can cause life-threatening arrhythmias by modulating connexin 43 (Cx43), a principal cardiac gap junction channel protein. The present study investigates whether nitrite can attenuate ischemia-induced ventricular arrhythmias and dephosphorylation of Cx43 in a rat model.

METHODS: Rats were medicated with normal saline (control, n = 10), nitrite (0.015, 0.15, and 1.5 mg/kg, n = 9 or 10 each), and 0.15 mg/kg nitrite with either the nitric oxide scavenger 2-(4-carboxyphenyl)-4, 4, 5, 5-tetramethylimidazoline-1-oxyl-3-oxide, sodium salt (cPTIO; n = 9) or allopurinol (xanthine oxidoreductase inhibitor, n = 9). We determined the severity of ventricular arrhythmias based on arrhythmia scores and levels of phosphorylated Cx43.

RESULTS: The median arrhythmia score may have been lower in the group given 0.15 mg/kg nitrite (4 [interquartile range {IQR}, 4–5]) than that in the control group (7.5 [IQR, 5.25–8]; P = 0.013). There was no difference among the control, the given 0.015 mg/kg nitrite (7 [IQR, 5–8]), and 1.5 mg/kg nitrite (7 [IQR, 5.5–7.75]; P = 0.95). The arrhythmia scores in the cPTIO (6 [IQR, 5–8]; P = 0.030) and allopurinol (7 [IQR, 5–8]; P = 0.005) groups may have been higher than that in 0.15 mg/kg nitrite group. Immunoblotting revealed that the level of phosphorylated Cx43 in the group given 0.15 mg/kg nitrite, but not in the other treated groups, was significantly higher compared with the control group (P = 0.007).

CONCLUSIONS: Nitrite may have attenuated acute ischemia-induced ventricular arrhythmias and Cx43 dephosphorylation in rats. Nitric oxide, which might be generated by xanthine oxidoreductase via nitrite reduction, appears to play a crucial role in this antiarrhythmic effect.

光電容積脈搏波描記法和食管多普勒超聲應用於重大非心臟手術中時對心指數評估的比較

A Comparison of Photoplethysmography Versus Esophageal Doppler for the Assessment of Cardiac Index During Major Noncardiac Surgery

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背景：在本次前瞻性觀察研究中，比較重大非心臟手術患者在液體負荷後使用光電容積脈搏波描記法（CIPPG）和食管多普勒超聲（CIED）描記心臟指數（CI）變化的區別。

方法：在麻醉主治醫生開始進行液體負荷後獲得測量值。採用線性回歸，B-A 法和協方差分析相關性。採用兩種不同的方法即四象限圖和極座標圖進行趨勢分析。

結果：對 43 例患者進行總共 111 次輸液方案。CIPPG 和 CIED 之間有顯著的線性關係(r2 = 0.34; P < 0.001)，ED 和 PPG 間對於 CI 測量的偏差爲-0.114 L/min/m2(95%可信區間

[CI95], −1.9 to 1.7)，平均百分比誤差爲 55%。同一種輸液方式中的 CI 變化具有顯著的相關性（r2 = 0.25; P = 0.002），CIPPG 和 CIED 的總體資料中變化趨勢（升高或降低）在的一致性爲 67% (CI95, 57–75)，而將排除域設定爲 15%前提下一致性爲 85%(CI95, 70–94)。將 ED 值視爲參考值，PPG 評估額外的液體需求量的敏感性和特異性增加 35%（(CI95, 19–55) 和 90%（CI95, 81–96），陽性預測值爲 58%（CI95，33-80），陰性預測值爲 78%（CI95，68-86）。

結論：在重大非心臟手術的患者中，使用 PPG 對 CI 的評估與 ED 對其評估並不對等。如果將 ED 評估 CI 值作爲金標準，那麼採用 PPG 評估額外的液體需求量則並不恰當。這些結果明確表明 PPG 用於評估 CI 的變化時與 ED 相比具有局限性。

（楊渝汀譯 陳傑校）

BACKGROUND: In this prospective observational study, we compared changes in cardiac index (CI) during fluid challenge using photoplethysmography (PPG; Nexfin™) (CIPPG) versus esophageal Doppler (ED) (CIED) in major noncardiac surgery patients.

METHODS: Measurements were obtained when the attending anesthesiologist decided to perform a fluid challenge. Correlations with linear regression, Bland-Altman analysis, and analysis of covariance were performed. Trending ability was studied using 2 different methods: a 4-quadrant plot and a polar plot.

RESULTS: Forty-three patients were analyzed with a total of 111 fluid challenges. There was a significant linear relationship between CIPPG and CIED (r2 = 0.34; P < 0.001). The bias between the ED and the PPG measurements of CI was −0.114 (95% confidence interval [CI95], −1.9 to 1.7) L/min/m2, with a mean percentage error of 55%. The correlation between the changes in CI during a fluid challenge was significant (r2 = 0.25; P = 0.002). The concordance rate of directional changes (increase or decrease) of CIPPG and CIED during fluid challenge was 67% (CI95, 57–75) for the whole data set and 85% (CI95, 70–94) with an exclusion zone of 15%. When considering ED as a reference, the sensitivity and specificity to give an additional bolus with PPG (increase in CIPPG ≥15%) were 35% (CI95, 19–55) and 90% (CI95, 81–96), respectively, with a positive predictive value of 58% (CI95, 33–80) and a negative predictive value of 78% (CI95, 68–86).

CONCLUSIONS: In major noncardiac surgery patients, the evaluation of CI using PPG is not interchangeable with the evaluation of CI using ED. When considering the ED as an accurate device to assess changes in CI, PPG is not appropriate to assess the need for additional fluid administration. These results clearly indicate the limitations of PPG as an accurate device to track changes in CI compared with ED.

2002 至 2011 年紐約州門診手術中心出院記錄中惡性高熱的發病率

Prevalence of Malignant Hyperthermia Diagnosis in New York State Ambulatory Surgery Center Discharge Records 2002 to 2011

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背景：惡性高熱（Malignant hyperthermia，MH）是由接觸吸入麻醉藥和去極化肌松藥琥珀醯膽鹼引發的一種罕見但可能致命的藥物遺傳學疾病。關於 MH 的流行病學研究主要限於住院病人。本研究檢測記錄在門診手術中心（ambulatory surgery centers, ASCs）出院病人中的 MH 發病率。

方法：檢索 2002 年至 2011 年紐約州門診手術資料庫，根據診斷標準參考第九版國際疾病分類法（臨床修訂碼 995.86）篩選出了所有出院診斷爲與麻醉相關的 MH 的病人。並按照不同人群特點、臨床資訊和 ASC 手術資訊對 MH 患病率進行了具體分析。

結果：在研究期間，17092765 個 ASC 的出院病人中，31 人有 MH 的診斷記錄，發病率爲 0.18/100000（95%CI，0.12-0.25）。MH 的發病率在不同患者年齡組和手術類型中有顯著差異。所有診斷爲 MH 的患者在 ASC 出院時均無死亡記錄。

結論：ASC 患者出院診斷爲 MH 的比率約爲 1/500,000，與外科手術類別顯著相關。

（程鑫宇譯 陳傑校）

BACKGROUND: Malignant hyperthermia (MH) is a rare yet potentially fatal pharmacogenetic disorder triggered by exposure to inhaled anesthetics and the depolarizing neuromuscular blocking drug succinylcholine. Epidemiologic research on MH is largely limited to inpatients. In this study, we examined the prevalence of recorded MH diagnosis in patients discharged from ambulatory surgery centers (ASCs).

METHODS: We analyzed the New York State Ambulatory Surgery Dataset for the years 2002 to 2011 and identified patients with a discharge diagnosis of MH due to anesthesia by using the International Classification of Disease, Ninth Revision, Clinical Modification code 995.86. MH prevalence was assessed by demographic, clinical, and ASC characteristics.

RESULTS: During the study period, 31 of 17,092,765 discharges from ASCs had a recorded diagnosis of MH, yielding a prevalence of 0.18 per 100,000 discharges (95% confidence interval, 0.12–0.25). The prevalence of recorded MH diagnosis per discharge differed significantly across age groups and surgical procedure categories. All patients with a recorded diagnosis of MH were from hospital-based ASCs and were discharged alive from ASCs.

CONCLUSIONS: The prevalence of recorded MH diagnosis in ASC patients is approximately 1 per 500,000 and varies considerably with surgical procedures.

風險校正後的小兒麻醉相關心臟驟停中麻醉醫師和系統相關風險因素

Anesthesiologist- and System-Related Risk Factors for Risk-Adjusted Pediatric Anesthesia-Related Cardiac Arrest

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背景：小兒麻醉相關的心臟驟停（ARCA）是一種罕見但潛在可預防的不良事件。嬰兒和患有嚴重潛在疾病的兒童的風險是最高的。本次研究的目的是識別 ARCA 的系統和麻醉醫師相關風險因素。

方法：對大型三級兒科醫院 2000 至 2011 年實施兒童麻醉相關的前瞻性佇列資料進行分析。術前全身性疾病的分級由 ASA 身體狀態（ASA-PS）來描述。兩位評價者獨立回顧了心臟驟停事件，並按其麻醉相關性分類。在單變數分析中與 ARCA 相關的因素在行年齡和 ASA-PS 校正後重新評估。

結果：在 276209 例麻醉中出現 142 例心臟驟停事件（發生率 5.1/10,000），其中 72 例（2.6/10,000）被列爲與麻醉相關。在單變數分析中，心臟病患者，由年麻醉例數較少或年工作日較少的麻醉醫師實施麻醉導致 ARCA 風險更高（所有的 $P < 0.001$）。具有最高學術地位和多年經驗的麻醉醫師也有更高的 ARCA 發生概率 （$P = 0.02$）。在對 ASA-PS ≥III 級和年齡≤6 個月的進行風險調整後，與年工作日較少的麻醉醫師實施麻醉的關聯性繼續保持（$P = 0.03$），但其它因素不再顯著。

結論：在作者單位，結合病例能夠解釋兒科 ARCA 的更高風險與一些麻醉醫師相關因素之間的關聯，而麻醉醫師年工作日較少這一因素是始終關聯的。本研究強調了在麻醉患者安全性研究中對患者風險因素嚴密校正的需要性。

（李悅譯 陳傑校）

BACKGROUND: Pediatric anesthesia-related cardiac arrest (ARCA) is an uncommon but potentially preventable adverse event. Infants and children with more severe underlying disease are at highest risk. We aimed to identify system- and anesthesiologist-related risk factors for ARCA.

METHODS: We analyzed a prospectively collected patient cohort data set of anesthetics administered from 2000 to 2011 to children at a large tertiary pediatric hospital. Pre-procedure systemic disease level was characterized by ASA physical status (ASA-PS). Two reviewers independently reviewed cardiac arrests and categorized their anesthesia relatedness. Factors associated with ARCA in the univariate analyses were identified for reevaluation after adjustment for patient age and ASA-PS.

RESULTS: Cardiac arrest occurred in 142 of 276,209 anesthetics (incidence 5.1/10,000 anesthetics); 72 (2.6/10,000 anesthetics) were classified as anesthesia-related. In the univariate analyses, risk of ARCA was much higher in cardiac patients and for anesthesiologists with lower annual caseload and/or fewer annual days delivering anesthetics (all $P < 0.001$). Anesthesiologists with the highest academic rank and years of experience also had higher odds of ARCA ($P = 0.02$). After risk adjustment for ASA-PS ≥III and age ≤6 months, however, the association with lower annual days delivering anesthetics remained ($P = 0.03$), but the other factors were no longer significant.

CONCLUSIONS: Case-mix explained most associations between higher risk of pediatric ARCA and anesthesiologist-related variables at our institution, but the association with fewer annual days delivering anesthetics remained. Our findings highlight the need for rigorous adjustment for patient risk factors in anesthesia patient safety studies.

在複雜的顱底神經外科手術中應用氨甲環酸與減少血製品輸入相關性的一項回顧性佇列研究

Use of Tranexamic Acid Is Associated with Reduced Blood Product Transfusion in Complex Skull Base Neurosurgical Procedures: A Retrospective Cohort Study

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背景：與其他外科手術相比，複雜性顱底神經外科手術中仍有將大量術中失血降至更低的可能性。抗纖維蛋白溶解藥——氨甲環酸在擇期神經外科手術中的安全性和療效尚未明瞭。本研究首要目標是確定本單位氨甲環酸的使用和血製品輸入的關係。次要目標是瞭解應用氨甲環酸後不良事件的發生率。

方法：在這個回顧性佇列研究中納入本單位 2001 到 2013 年所有接受複雜性顱底神經外科手術的患者。氨甲環酸在 2006 年開始應用于患者。從病史中收集病人和手術參數、輸血資料和圍手術期不良事件資訊。比較是否應用氨甲環酸的兩組患者輸血量及不良事件發生率的差異。通過多變數回歸分析確認圍手術期輸血的影響因素。

結果：比較研究週期中 245 例使用氨甲環酸及 274 例未使用的患者。兩組患者條件相近，但應用氨甲環酸的患者有更大的腫瘤（3.5 vs 2.9 cm; P < 0.001）和更長的手術時間（7.2 vs 6.2h, P < 0.001）。使用氨甲環酸的患者在圍手術期輸血率低（7% vs 13%, P = 0.04）。在校正了術前血紅蛋白水準、腫瘤直徑和手術方式後，是否使用氨甲環酸是圍術期輸血量的獨立預測因素（校正後優勢比 0.32，95%置信區間 0.15–0.65, P = 0.002）。兩組發生癲癇和血栓栓塞事件概率相似。

結論：本研究結果表明，在作者單位研究的人群中，應用氨甲環酸可以減少術中的輸血率，而癲癇和血栓栓塞發生率並不增加。資料支援需要進一步進行複雜顱底神外手術中應用氨甲環酸的隨機臨床試驗，以評價其療效和安全性。

（孫佳昕譯 陳傑校）

BACKGROUND: Compared with other procedures, complex skull base neurosurgery has the potential for increased intraoperative blood loss yet coagulation near eloquent cranial structures should be minimized. The safety and efficacy of the antifibrinolytic, tranexamic acid in elective neurosurgical procedures is not known. Our primary objective was to determine the relationship between the use of tranexamic acid and transfusion at our institution. Our secondary objective was to determine the incidence of adverse events associated with the use of tranexamic acid.

METHODS: In this retrospective cohort study, we included all patients who underwent complex skull base neurosurgical procedures at our institution between 2001 and 2013. Tranexamic acid was introduced during these procedures in 2006. Patient and surgical variables, transfusion data, and adverse events in the perioperative period were abstracted from the medical record. The rates of transfusion and adverse events were compared between patients who did and did not receive tranexamic acid. Multivariate regression was used to identify independent predictors of perioperative transfusion.

RESULTS: We compared 245 patients who received tranexamic acid with 274 patients who did not receive the drug during the study period. The 2 groups were similar, with the exception that patients who received tranexamic acid had larger tumors (mean, 3.5 vs 2.9 cm; $P < 0.001$) and longer procedures (mean, 7.2 vs 6.2 hours, $P < 0.001$). The rate of perioperative transfusion in patients who received tranexamic acid was lower (7% vs 13%, $P = 0.04$). After adjusting for preoperative hemoglobin, tumor diameter, and surgical procedure category, the use of tranexamic acid was independently predictive of perioperative transfusion (adjusted odds ratio, 0.32; 95% confidence interval, 0.15–0.65, $P = 0.002$). The rates of thromboembolic events and seizure were similar between the 2 groups.

CONCLUSIONS: Our results demonstrate that tranexamic acid use is associated with reduced transfusion rates in our study population, with no apparent increase in seizure or thrombotic complications. Our data support the need for further randomized clinical trials to evaluate the efficacy and safety of tranexamic acid on perioperative blood loss during complex skull base neurosurgery.

全膝關節置換術後行收肌管阻滯對於股四頭肌肌力的影響：一項個體化分析的三盲、隨機、對照臨床試驗

The Isolated Effect of Adductor Canal Block on Quadriceps Femoris Muscle Strength After Total Knee Arthroplasty: A Triple-Blinded, Randomized, Placebo-Controlled Trial with Individual Patient Analysis

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背景：全膝關節置換(TKA)術後實施周圍神經阻滯，且不影響運動功能具有挑戰性的。本研究假設收肌管阻滯(ACB)的鎮痛效果能增加 TKA 術後股四頭肌最大隨意等長收縮(MVIC)。

方法：納入了 64 例術後第一天的病人。A 組患者接受收肌管阻滯（ACB）：在 t_0 時間給予 0.75%羅呱卡因 30ml，60min 後給予 30ml 生理鹽水（t_{60}）。B 組治療順序與 A 組相反。主要研究終點爲兩組之間在 t_{60} 時 MVIC 的差異，用術後的阻滯前值的百分數表達。依此區分 ACB 作用與手術造成的肌力影響。次要終點是兩組間活動度和疼痛評分的差異。本研究根據在膝關節屈曲時的阻滯前疼痛評分差異設計了一項亞組分析。

結果：在 t_{60}，A 組的 MVIC 阻滯前值中位數爲 170%（95%可信區間，147-231）明顯高於 B 組（95%可信區間，82-98）($P < 0.0001$)。站起-行走實驗（TUG）無統計學差異。A 組中 3 個病人失去執行 TUG 實驗的能力。在 t_{60}, A 組的疼痛視覺類比評分良好, 靜息時爲 12mm(95% CI,6 - 18), 在膝蓋屈曲時爲 14mm(95% CI,5-22), TUG 測試時爲 18mm(95% CI,10-26)。

結論：ACB 改善了股四頭肌肌力，但這是否意味著增強活動度未有定論。

（馮迪譯 陳傑校）

BACKGROUND: Using peripheral nerve block after total knee arthroplasty (TKA), without impeding mobility, is challenging. We hypothesized that the analgesic effect of adductor canal block (ACB) could increase the maximum voluntary isometric contraction (MVIC) of the quadriceps femoris muscle after TKA.

METHODS: We included 64 patients on the first postoperative day. Group A received an ACB with 30 mL ropivacaine 0.75% at t0 and with 30 mL saline 60 minutes later (t60). Group B received the treatment in the opposite order. The primary end point was the difference between groups in MVIC at t60, expressed as a percentage of postoperative preblock values. In this manner, the effect of the ACB could be isolated from the detrimental effect on muscle strength caused by the surgery. Secondary end points were differences between groups in mobility and pain scores. We planned a subgroup analysis dividing patients according to preblock pain scores during knee flexion.

RESULTS: At t60, MVIC was higher in group A, with a median of 170% (95% confidence interval [CI], 147–231) of preblock values compared with 93% (95% CI, 82–98) in group B ($P < 0.0001$). No statistically significant differences were found in the Timed Up and Go (TUG) test. Three patients lost the ability to perform the TUG test in group A. At t60, differences in visual analog scale pain were in favor of group A; 12 mm (95% CI, 6–18) at rest, 14 mm (95% CI, 5–22) during knee flexion, and 18 mm (95% CI, 10–26) during the TUG test.

CONCLUSIONS: ACB improves quadriceps femoris muscle strength, but whether this translates into enhanced mobility is not clearly supported by this study.

開發和驗證一個阻塞性睡眠呼吸暫停形態學上的預測評分:DES-OSA 評分

Development and Validation of a Morphologic Obstructive Sleep Apnea Prediction Score: The DES-OSA Score

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背景：阻塞性睡眠呼吸暫停（OSA）是一種常見但容易忽略的疾病，容易增加圍手術期的患病率。幾個解剖特點使患者易患 OSA 綜合征。我們開發了一個新的臨床評分, 根據病人的形態學特徵來檢測 OSA 綜合征。

方法：研究納入了擬行整夜多導睡眠圖的患者（n = 149）。比較他們的形態學指標，並將這些指標進行組合測試其預測至少輕度、中重度、或嚴重 OSA 綜合征的能力,以低通氣指數（AHI）> 5，>15 或>30 次/ h 來定義三種程度。使用科恩 κ 係數和預測概率來計算這種能力。

結果：以下 5 個變數被認爲是預測能力最好的（DES-OSA 分數）：Mallampati 評分,甲狀腺和下頜之間的距離,身體品質指數,頸圍以及性別。這些變數以 1、2、或 3 分加權。DES-OSA 得分> 5、6、7 都分別與 AHI > 5，> 15 或> 30 次/ h 的概率增加有關，並且這些閾值有很好的科恩 κ 係數, 敏感性和特異性。ROC 曲線分析顯示，DES-OSA 預測 AHI> 5，> 15，和> 30 次/ h 曲線下的面積分別是 0.832（95%可信區間（CI）,0.762 - -0.902）,0.805（95%可信區間,0.734 - -0.876），和 0.834（95% CI,0.757 - -0.911）。上述閾值相應的敏

感性（95% CI）分別爲 82.7%（74.5 - -88.7）、77.1%（66.9 - -84.9）和 75%（61.0 - -85.1）和特異性（95% CI）72.4%（54.0 - -85.4）、73.2%（60.3 - -83.1）和 76.9%（67.2 - -84.4）。在獨立樣本驗證 DES-OSA 的能力得到了非常相似的結果。

結論：DES-OSA 是一個簡單的檢測 OSA 綜合征病人的評分。它主要依靠患者的自然解剖學形態。源自歐洲的人口,它在術前可能是有用的,但它仍應與其他在一般手術和種族的人口中得到的篩查工具進行比較。

（張雪 譯 薛張綱 校）

BACKGROUND: Obstructive sleep apnea （OSA） is a common and underdiagnosed entity that favors perioperative morbidity. Several anatomical characteristics predispose to OSA. We developed a new clinical score that would detect OSA based on the patient's morphologic characteristics only.

METHODS: Patients （n = 149） scheduled for an overnight polysomnography were included. Their morphologic metrics were compared, and combinations of them were tested for their ability to predict at least mild, moderate-to-severe, or severe OSA, as defined by an apnea-hypopnea index （AHI） >5, >15, or >30 events/h. This ability was calculated using Cohen κ coefficient and prediction probability.

RESULTS: The score with best prediction abilities （DES-OSA score） considered 5 variables: Mallampati score, distance between the thyroid and the chin, body mass index, neck circumference, and sex. Those variables were weighted by 1, 2, or 3 points. DES-OSA score >5, 6, and 7 were associated with increased probability of an AHI >5, >15, or >30 events/h, respectively, and those thresholds had the best Cohen κ coefficient, sensitivities, and specificities. Receiver operating characteristic curve analysis revealed that the area under the curve was 0.832 （95% confidence interval [CI], 0.762-0.902）, 0.805 （95% CI, 0.734-0.876）, and 0.834 （95% CI, 0.757-0.911） for DES-OSA at predicting an AHI >5, >15, and >30 events/h, respectively. With the aforementioned thresholds, corresponding sensitivities （95% CI） were 82.7% （74.5-88.7）, 77.1% （66.9-84.9）, and 75% （61.0-85.1）, and specificities （95% CI） were 72.4% （54.0-85.4）, 73.2% （60.3-83.1）, and 76.9% （67.2-84.4）. Validation of DES-OSA performance in an independent sample yielded highly similar results.

CONCLUSIONS: DES-OSA is a simple score for detecting OSA patients. Its originality relies on its morphologic nature. Derived from a European population, it may prove useful in a preoperative setting, but it has still to be compared with other screening tools in a general surgical population and in other ethnic groups.

麻醉選擇（七氟醚和地氟醚）和神經肌肉管理對氣道反射恢復速度的影響

The Effect of Anesthetic Choice （Sevoflurane Versus Desflurane） and Neuromuscular Management on Speed of Airway Reflex Recovery

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背景：使用七氟醚的未插管患者與使用地氟醚的患者相比保護性氣道反射恢復較慢。我們問這種差異是否在使用羅庫溴銨的氣管插管患者仍然顯著，或者是否神經肌肉恢復的變數在其中占主導地位而減少了兩種麻醉藥物之間的差別。

方法：在簽署知情同意書後,病人被隨機分配到七氟醚組（n = 41）或地氟醚組（n = 40）。神經肌肉功能監測採用加速度儀定量 TOF 指數。使用 1mg/kg 的羅庫溴銨來幫助插管。產生神經肌肉阻滯，以維持 10%至 15%的基線水準爲目標。手術後給予新斯的明 70μg/kg 及格隆溴銨 14μg /kg。當 TOF 比率達到≥0.7 時，停用吸入麻醉藥，並把新鮮氣體流量提高到 15 L / min。記錄對指令有第一次反應的時間，之後患者分別在 2min，6min，14min，22 min，30min 和 60min 飲用 20ml 水行吞咽測試。以下平均時間間隔在 2 組之間進行比較：終止使用麻醉藥物到患者對指令第一次有反應的時間（T1）； 對指令第一次有反應到首次成功的吞咽測試的時間（T2）；停用麻醉藥到首次吞咽試驗成功的時間（T3）。我們也測定兩組中對指令出現第一次反應後 2min 時吞咽試驗的成功率。在 2min 時無法進行吞咽試驗的患者被認爲失敗，同時也除外了因嗜睡以外的原因不能完成試驗的 10 名患者（n=10）。

結果：使用地氟醚的患者在對指令第一次有反應後通過吞咽試驗的時間間隔短於使用七氟醚的患者（Wilcoxon-Mann-Whitney 指數= 1.60；95%可信區間（CI），1.01 - -2.69;P = 0.054）。對指令第一次有反應 2min 後, 在所有 81 名病人中, 與七氟醚麻醉相比, 地氟醚麻醉的患者吞咽測試成功率明顯增加（相對危險度= 1.6；95%可信區間,1.0 - -2.5；P = 0.04）。在 71 名患者中（如上所述），我們觀察到患者對指令第一次有反應 2min 後使用地氟醚的患者（25/33）吞咽試驗的成功率高於使用七氟醚的患者（16/38）（相對危險度 = 1.8；95%可信區間，1.2 - -2.7;P = 0.006）。在接受地氟醚（25/33）與接收七氟醚（16/38）的 81 名患者中 18 人和 71 名患者中的 16 人，神經肌肉監測和逆轉並未實施（新斯的明劑量不足, 在 TOF < 0.7 時拔管,或依賴觸覺而不是定量測定的 TOF）。在整個佇列人群和 71 人的亞組中，多變數邏輯回歸分析（分別爲 P = 0.02，P = 0.02）表明神經肌肉管理成爲獨立於麻醉藥物使用的增加吞咽測試成功率的因素，表明其爲獨立於麻醉劑選擇的顯著影響氣道反射恢復的因素。

結論：與七氟烷相比,地氟醚麻醉氣管插管的患者氣道反射恢復更快。神經肌肉阻滯的臨床管理,包括完全的逆轉和 TOF 的測定可影響氣道反射的恢復——一個和強效吸入麻醉藥物選擇一樣有意義的影響因素。

（鄔其瑋 譯 薛張綱 校）

BACKGROUND: Nonintubated patients receiving sevoflurane have slower protective airway reflex recovery after anesthesia compared with patients receiving desflurane. We asked whether this difference would remain significant among intubated patients receiving rocuronium or whether the impact of variable neuromuscular recovery would predominate and thus minimize differences between anesthetics.

METHODS: After obtaining written informed consent, patients were randomly assigned to receive sevoflurane （n = 41） or desflurane （n = 40）, with neuromuscular monitoring by quantitative train-of-four （TOF） method using accelerometry. Intubation was facilitated by administration of 1 mg/kg rocuronium. Neuromuscular block was produced, with the goal of maintaining 10% to 15% of baseline function. After surgery, neostigmine 70 μg/kg +

glycopyrrolate 14 μg/kg was administered. When TOF ratio reached ≥0.7, anesthetic was discontinued and fresh gas flow was raised to 15 L/m. The time of first response to command was noted, after which patients were given a 20-mL water swallowing test at 2, 6, 14, 22, 30, and 60 minutes. The following average time intervals were compared between the 2 intervention groups: anesthetic discontinuation to first response to command （T1）; first response to command to first successful passing of swallow test （T2）; and anesthetic discontinuation to first successful passing of swallow test （T3）. We also compared the rates of successful swallow tests at 2 minutes after first response to command in the 2 groups, first categorizing as failures all those who were unable to take the test at 2 minutes, and then excluding 10 patients unable to take the test at this time for reasons other than somnolence （n = 10）.

RESULTS: Patients receiving desflurane passed the swallowing test at shorter time intervals after first response to command than did patients receiving sevoflurane （Wilcoxon-Mann-Whitney odds = 1.60; 95% confidence interval [CI], 1.01–2.69; P = 0.054）. Two minutes after the first response to command, among all 81 patients, the chance of passing the swallowing test was higher after desflurane compared with sevoflurane anesthesia （relative risk = 1.6; 95% CI, 1.0–2.5; P = 0.04）. Of the 71 patients （as above）, we observed a significantly higher chance of passing at 2 minutes after first response to command （relative risk = 1.8; 95% CI, 1.2–2.7; P = 0.006） in patients receiving desflurane （25/33） compared with those receiving sevoflurane （16/38）. In 18 of 81 and 16 of 71 patients, the neuromuscular monitoring and reversal protocols were not followed （neostigmine underdosed, extubation at TOF <0.7, or reliance on tactile as opposed to quantitative TOF measurement）. In both the total cohort and the subset of 71, neuromuscular protocol adherence increased the chance of passing the swallow test, independent of anesthetic assignment in multivariable logistic regression （P = 0.02 and P = 0.006, respectively）, demonstrating significant effect on airway reflex recovery independent of chosen anesthetic.

CONCLUSIONS: Compared with sevoflurane, desflurane allowed faster recovery of airway reflexes after anesthesia in intubated patients. Clinical management of neuromuscular block, including full reversal and the use of quantitative TOF, affects airway reflex recovery—an effect that may be at least as profound as the choice of potent inhaled anesthetic.

在體外使用丹曲林與咖啡因修正布比卡因誘導的肌肉毒性

Modification of Bupivacaine-Induced Myotoxicity with Dantrolene and Caffeine In Vitro

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背景:局部麻醉劑,尤其是布比卡因，在臨床使用的濃度下具有肌肉毒性。這些影響的詳細機制尚未可知，但增加細胞內鈣含量可能是最重要的觸發因素。丹曲林和咖啡因可以修正細胞內鈣離子從肌漿網的釋放。我們的研究的目的是在體外研究丹曲林和咖啡因對布比卡因誘導的肌肉毒性的作用。

方法: 建立 BALB/cAnNCrl 小鼠的原代肌細胞培養模型。細胞與濃度增加的布比卡因，丹曲林及咖啡因同時孵育。壞死細胞的比例在碘化丙啶染色和流式細胞術分析後計算得出。計算每個濃度的布比卡因最大半數抑制濃度。組間差異採用單向方差分析和 post hoc 1-way Dunnett t 檢驗計算。

結果:丹曲林和咖啡因本身沒有影響肌細胞的生存。布比卡因濃度增加會增加細胞死亡。丹曲林以劑量依賴的方式降低了壞死細胞的比例，而咖啡因劑量依賴性增加了壞死細胞的比例。

結論:丹曲林減少，咖啡因增強布比卡因誘導的細胞毒性,可能通過修改肌質鈣釋放。這表明細胞內鈣釋放是局麻藥誘導細胞死亡的重要因素。

（施雲岑 譯 薛張綱 校）

BACKGROUND: Local anesthetics, especially bupivacaine, have myotoxic effects in clinically used concentrations and context. Detailed mechanisms of these effects are unknown, but an increase in intracellular calcium levels is suspected to be the most important trigger. Dantrolene and caffeine modify cellular calcium release from the sarcoplasmic reticulum. The aim of our study was to investigate the effect of dantrolene and caffeine on bupivacaine-induced myotoxicity in vitro.

METHODS: A cell culture model of primary muscle cells of BALB/c AnNCrl mice was established. Cells were incubated simultaneously with increasing concentrations of bupivacaine, dantrolene, and caffeine. The fraction of dead cells was calculated after staining with propidium iodide and analysis by flow cytometry. The half-maximal inhibitory concentration of bupivacaine was calculated for each concentration. Group differences were determined by using 1-way analysis of variances with subsequent post hoc 1-way Dunnett t test.

RESULTS: Both dantrolene and caffeine alone had no effect on muscle cell survival. Increasing concentrations of bupivacaine caused increasing cell death. Dantrolene dose-dependently reduced the fraction of necrotic cells, whereas caffeine dose-dependently increased the fraction of dead cells.

CONCLUSIONS: Dantrolene attenuated, and caffeine enhanced, bupivacaine-induced myotoxicity, presumably by modifying sarcoplasmic calcium release. This indicates that intracellular calcium release is an important factor for local anesthetic–induced cell death.

高保真度分析圍術期 QTc 延長

High-Fidelity Analysis of Perioperative QTc Prolongation

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背景: QTc 間期延長表示異常心臟複極化。最近的一項研究表明, 術後 QTc 間期延長是常見的。然而, QTc 間期延長是否爲一個術後獨立的現象，或規律的發生在手術過程中，以及麻醉的類型是否影響其發生率。

方法:要回答這個問題,我們進行了一項前瞻性佇列研究（n = 300），使用 12 導聯動態心電圖連續監測術前 30 分鐘及術後 60 分鐘的 QTc 間期。QTc 間期延長於在全身麻醉（n = 101），椎管內麻醉（n = 99） 或局部麻醉（n = 100）下行整形手術的,至少有一個心臟危險因素的成人中進行行。主要結果是術中 QTc 間期的增加（ΔQTc 定義爲術中及術前 QTc 間期的差）。長 QTc 間期發作的發病率 （QTc ＞500 毫秒，持續至少 15 分鐘）也被確定。

結果: QTc 間期顯著延長 （中位數,四分位範圍（IQR）發生在全身麻醉（ΔQTc + 33ms；IQR，22 – 46ms）和椎管內麻醉（ΔQTc + 22ms；IQR，12 – 29ms）中,在局部麻醉中並未發現 QTc 間期延長（活檢,n = 53:ΔQTc,+ 4ms；IQR,−4 + 7ms；冠狀動脈造影時，n = 47：ΔQTc,+ 6ms； IQR，−5 + 16ms）。長 QTc 間期發作的發病率在全身麻醉（n = 6/63，9.5%）,椎管內麻醉（n = 1/56，1.8%）,局部麻醉的活檢（n = 0/46，0%）和冠狀動脈造影（n = 0/19，0%;P = 0.045）中顯著不同。

結論:延長這些結果表明 QTc 間期延長不是一個孤立的術後現象，並且在全身麻醉和椎管內麻醉下手術中很常見。

（俞穎 譯 薛張綱 校）

BACKGROUND: Prolongation of the QTc interval indicates abnormal cardiac repolarization. A recent study has shown that postoperative QTc prolongation is common. However, it is unknown whether QTc prolongation is an isolated postoperative phenomenon or occurs regularly during surgery, or whether the type of anesthesia influences its incidence.

METHODS: To answer this question, we conducted a prospective cohort study （n = 300）, where QTc duration was continuously recorded by 12-lead Holter electrocardiogram from 30 minutes preoperatively to up to 60 minutes postoperatively. QTc prolongation was compared between adult patients with at least 1 cardiac risk factor undergoing general （n = 101） or spinal anesthesia （n = 99） for orthopedic surgery, or local anesthesia （n = 100）. Primary outcome was intraoperative QTc increase （ ΔQTc, as defined by the intraoperative-to-preoperative QTc duration difference）. The incidence of long QTc episodes （QTc > 500 milliseconds for at least 15 minutes） was also determined.

RESULTS: Significant QTc prolongation （ median; interquartile range [IQR]） occurred during general anesthesia （ΔQTc, +33 milliseconds; IQR, +22 to 46 milliseconds） and spinal anesthesia （ ΔQTc, +22 milliseconds; IQR, +12 to 29 milliseconds ）, whereas no QTc prolongation was observed during local anesthesia （biopsy, n = 53: ΔQTc, +4 milliseconds; IQR, −4 to +7 milliseconds; coronary angiography, n = 47: ΔQTc, +6 milliseconds; IQR, −5 to +16 milliseconds）. The incidence of long QTc episodes was significantly different between general anesthesia （n = 6/63, 9.5%）, spinal anesthesia （n = 1/56, 1.8%）, local anesthesia for biopsy （n = 0/46, 0%）, and coronary angiography （n = 0/19, 0%; P = 0.045）.

CONCLUSIONS: These results indicate that QTc prolongation is not an isolated postoperative phenomenon and is common during surgery under general and spinal anesthesia.

重症監護室非心臟病患者右美托咪定相關的血流動力學不穩定的危險因素

Risk Factors for Dexmedetomidine-Associated Hemodynamic Instability in Noncardiac Intensive Care Unit Patients

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背景: 接受右美托咪定鎮靜的患者中報導的低血壓和心動過緩的發病率通常超過 50%。在這項研究中,我們描述右美托咪定相關的血流動力學不穩定的發生率,患者治療的危險因素和臨床意義。

方法:這項回顧性佇列研究納入了明尼蘇達州羅徹斯特的梅奧醫院一年期間接受右美托咪定鎮靜的危重患者。主要的研究終點是血流動力學不穩定：在右美托咪定治療期間，結合低血壓和/或心動過緩，低血壓定義爲收縮壓小於 80 mm Hg,舒張壓< 50 mm Hg,或心率<每分鐘 50 次。Cox 比例風險模型被構建來確定血流動力學不穩定的危險因素的風險比率（HRs）以及 95%置信區間（CIs）。

結果:分析接受右美托咪定治療的 300 例患者中發生血流動力學不穩定的有 197 人，通過 kaplan meier 估計，結果在 24 小時內累積發病率爲 71%。除了右美托咪定，單變數分析發現年齡、血管加壓的使用,低基礎動脈血壓,和同時使用的鎮靜劑與血流動力學不穩定的風險增加有關。多變數分析表明年齡（HR,每 10 年 1.23，95% CI，1.10 - -1.38）， 低基礎血壓（HR 2.42 起始使用右美托咪定，95% CI，1.68 - -3.49） 和血流動力學不穩定的發生風險之間有關聯。在被分析的樣本中，同時服用心臟藥物，或鎮靜治療，以及右美托咪定的輸注速率> 0.7 μg/kg/h 等變數不能預測血流動力學不穩定的發生。

結論: 在接受右美托咪定治療的危重成人患者中，常見血流動力學不穩定，在本佇列中，通常在使用藥物 24 小時內，有超過三分之二的患者出現低血壓和/或心動過緩。年齡增加，低基礎動脈血壓與血流動力學不穩定的發生有關。這些結果提示，臨床醫生應該意識到在高齡患者或低基礎動脈血壓患者中使用右美托咪定時血流動力學不穩定發生的潛在風險。

（侯君誼 譯 薛張綱 校）

BACKGROUND: The reported incidence of hypotension and bradycardia in patients receiving dexmedetomidine for sedation commonly exceeds 50%. In this study, we describe the incidence of, patient- and treatment-specific risk factors for, and clinical significance of dexmedetomidine-associated hemodynamic instability.

METHODS: This retrospective cohort study was conducted in critically ill adults receiving dexmedetomidine for sedation at Mayo Clinic Hospital in Rochester, MN, during a 1-year period. The primary end point was hemodynamic instability: a composite of hypotension and/or bradycardia, defined as systolic blood pressure <80 mm Hg, diastolic blood pressure <50 mm Hg, or heart rate <50 beats per minute during dexmedetomidine therapy. Cox proportional hazards models were constructed to determine hazard ratios （HRs） and 95% confidence intervals （CIs） for the risk factors of hemodynamic instability.

RESULTS: Hemodynamic instability occurred in 197 of the analyzed 300 patients receiving dexmedetomidine, resulting in a cumulative incidence of 71% at 24 hours via Kaplan-Meier

estimation. In addition to dexmedetomidine, univariate analysis identified age, vasopressor use, low baseline arterial blood pressure, and concomitant sedatives as associated with increased risk of hemodynamic instability. Multivariable analysis demonstrated associations between age （HR, 1.23 per 10 years, 95% CI, 1.10–1.38） and low baseline blood pressure （HR, 2.42 at dexmedetomidine initiation, 95% CI, 1.68–3.49） and risk of hemodynamic instability. Variables such as concomitantly administered cardiac medications or sedative therapies and dexmedetomidine infusion rates >0.7 μg/kg/h were not found to be predictors of hemodynamic instability among the analyzed sample.

CONCLUSIONS: Hemodynamic instability commonly occurs in critically ill adults receiving dexmedetomidine, with more than two thirds of this cohort experiencing hypotension and/or bradycardia within 24 hours of initiation. Increasing age and low baseline arterial blood pressure were associated with the development of hemodynamic instability. These findings suggest that clinicians should be aware of the potential risk of hemodynamic instability when using dexmedetomidine in patients with advanced age or low baseline arterial blood pressure.

監護對兒童心肺復蘇開始的影響：朋友還是敵人?

The Impact of Monitoring on the Initiation of Cardiopulmonary Resuscitation in Children: Friend or Foe?

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背景:立即啓動和高品質的基本生命支持（BLS）是改善心臟驟停後病人預後的關鍵。儘管心臟呼吸監護可以縮短識別心臟驟停發生的時間,對監控和監測資料的誤解可能影響 BLS 的啓動。在這項研究中,我們評估了在模擬有監護和無監護心臟驟停的兒童中，BLS 的啓動速度和品質。

方法: 經常參與照顧重病的兒童的 60 位居民被隨機分配到干預組（監護）或對照組（非監護）。發生以下 2 種臨床一致的未察覺的模擬心臟驟停的場景時，兩組參與者均實施 BLS。儘管在場景 1 中使用心臟呼吸監護（比如，心電圖），另一個場景反映了無監護的心臟驟停。第一個開始胸按壓的時間作爲研究主要的結果變數。堅持復蘇指南和主觀判斷速度是次要研究結果變數。

結果:監護組的參與者開始胸外按壓明顯晚於無監護組（91±36 vs 71±26 秒，風險比，0.26;95%可信區間，0.14 - -0.49，P < 0.001）。六個監護小組的成員開始胸外按壓的時間大於 5 分鐘。在非監護組能更好地堅持指南。曾參加過 BLS 培訓的參與者曾並沒有更好的表現。

結論:在模擬心臟驟停的情境下，心臟呼吸監護顯著延遲甚至阻止胸外按壓的開始並影響心肺復蘇的品質。基於這些資料,應對相關人員進行特殊培訓。

（王潔 譯 薛張綱 校）

BACKGROUND: The immediate initiation and high quality of basic life support （BLS） are pivotal to improving patient outcome after cardiac arrest. Although cardiorespiratory monitoring could shorten the time to recognize the onset of cardiac arrest, little is known about how monitoring and the misinterpretation of monitor readings could impair the initiation of BLS. In this study, we assessed the speed of initiation and quality of BLS in simulated monitored and nonmonitored pediatric cardiac arrest.

METHODS: Sixty residents frequently involved in the care of critically ill children were randomly assigned to either the intervention （ monitoring ） group or the control （ nonmonitoring ） group. Participants of both groups performed BLS in 1 of 2 clinically identical, unwitnessed simulated cardiac arrest scenarios. Although in 1 scenario cardiorespiratory monitoring （ i.e., electrocardiogram ） was attached, the other scenario reflected a nonmonitored cardiac arrest. Time to first chest compression was chosen as the primary outcome variable. Adherence to resuscitation guidelines and subjective performance ratings were secondary outcome variables.

RESULTS: Participants in the monitoring group initiated chest compressions significantly later than those in the nonmonitoring group （91 ± 36 vs 71±26 seconds, hazard ratio, 0.26; 95% confidence interval, 0.14–0.49, P < 0.001）. Six members of the monitoring group did not start chest compression within 5 minutes. Furthermore, adherence to the guidelines was better in the nonmonitoring group. Participants who were previously involved in BLS training did not show better performance.

CONCLUSIONS: The presence of cardiorespiratory monitoring significantly delayed or even prevented the initiation of chest compressions and impaired the quality of BLS in simulated pediatric cardiac arrest. Based on these data, specific training should be conducted for exposed personnel.

清醒顱骨切開術:一種新的氣道管理方法

Awake Craniotomy: A New Airway Approach

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自 2004 年以來，清醒開顱手術在賓夕法尼亞大學常規實施。在這個手術中，探索了不同的氣道管理方法 ,包括氣管內插管，使用喉罩通氣、簡單的面罩,或鼻咽通氣道。在此病例系列中,我們描述了在 90 位行清醒開顱手術的患者中雙腔鼻咽通氣道的成功使用（即：不需要因氣體交換不足而氣管插管）。使用鼻咽通氣道可以開顱手術中清醒和麻醉階段的切換變得簡單，而不需要刺激氣道。我們的目的是描述我們的經驗並報告與此技術相關的不良事件。

（楊曉迪 譯 薛張綱 校）

Awake craniotomies have been performed regularly at the University of Pennsylvania since 2004. Varying approaches to airway management are described for this procedure, including intubation with an endotracheal tube and use of a laryngeal mask airway, simple facemask, or nasal cannula.

In this case series, we describe the successful use （i.e., no need for endotracheal intubation related to inadequate gas exchange） of bilateral nasopharyngeal airways in 90 patients undergoing awake craniotomies. The use of nasopharyngeal airways can ease the transition between the asleep and awake phases of the craniotomy without the need to stimulate the airway. Our purpose was to describe our experience and report adverse events related to this technique.

甲狀腺手術中羅哌卡因傷口浸潤誘導的鎮痛不足：一項隨機,雙盲,安慰劑對照試驗

Lack of Analgesic Effect Induced by Ropivacaine Wound Infiltration in Thyroid Surgery: A Randomized, Double-Blind, Placebo-Controlled Trial

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背景:手術部位局部麻醉藥浸潤可減少各種類型的手術中鎮痛藥物的使用。因爲甲狀腺手術可能會引起嚴重的術後疼痛，我們測試假設羅哌卡因在手術部位浸潤會顯著減少甲狀腺手術患者術後嗎啡的使用量。

方法:我們進行了雙盲,安慰劑對照試驗來評估在成人甲狀腺手術結束時羅哌卡因（10ml，75mg）手術部位鎮痛的效果。主要研究終點是患者在蘇醒室中不需要使用靜脈嗎啡治療的比例。

結果：163 名患者完成了研究，安慰劑組包括 85 名患者和羅哌卡因組包括 88 名患者。患者在蘇醒室中需要使用靜脈嗎啡的比例爲 55% vs 53%，P = 0.80，靜脈注射嗎啡的劑量比例爲 5.6±6.1 vs 5.5±6.0mg，P = 0.90。兩組之間第一個 24 小時內使用阿片類藥物的總劑量（以口服嗎啡等效劑量表示：64±27 vs 69±29mg，P = 0.20）,視覺類比疼痛量表評分無顯著差異。不良事件的發生率（36% vs 39%，P = 0.88）,嗎啡相關不良事件（19% vs 17%，P = 0.84）,嚴重不良事件（0% vs %，P = 0.50）,和患者滿意度（9±1 vs 9±1，P = 0.70），在兩組之間無顯著差異。

結論: 甲狀腺手術結束時羅哌卡因手術部位鎮痛在患者鎮痛中無顯著獲益。

（殷悅 譯 薛張綱 校）

BACKGROUND: Surgical site infiltration with local anesthetic reduces analgesic requests in various types of surgeries. Because thyroid surgery may induce severe postoperative pain, we tested the hypothesis that ropivacaine surgical site infiltration would significantly decrease postoperative administration of morphine in patients undergoing thyroid surgery.

METHODS: We performed a double-blind, placebo-controlled superiority trial to assess the efficacy of surgical site analgesia with ropivacaine （10 mL, 75 mg） performed at the end of thyroid surgery in adult patients. The primary end point was the proportion of patients not requiring IV morphine in the postanesthesia care unit.

RESULTS: One hundred sixty-three patients completed the study, 85 in the placebo group and 88 in the ropivacaine group. The proportion of patients requiring morphine administration in the

postanesthesia care unit （55% vs 53%, P = 0.80）, the dose of IV morphine administered （5.6 ± 6.1 vs 5.5 ± 6.0 mg, P = 0.90）, the total dose of opioids administered （expressed as oral morphine equivalent dose: 64 ± 27 vs 69 ± 29 mg, P = 0.20）, and the visual analog pain scale over the first 24 hours were not significantly different between groups. The incidence of adverse events （36% vs 39%, P = 0.88）, morphine-related adverse events （19% vs 17%, P = 0.84）, serious adverse events （0% vs 2%, P = 0.50）, and the patient satisfaction scores （9 ± 1 vs 9 ± 1, P = 0.70） was not significantly different between the 2 groups.

CONCLUSIONS: Surgical site analgesia with ropivacaine at the end of thyroid surgery is not associated with any significant analgesic benefit.