Table of Contents

February, 2016

Cardiovascular Anesthesiology

Research Report

二尖瓣返流对彩色多普勒测量的时间动态缩流面积影响的机制

(刘洋译 陈杰校)

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

- Cobey, Frederick C.;
- Ashihkmina, Elena;
- Edrich, Thomas;
- Fox, John;
- Shook, Douglas;
- Bollen, Bruce;
- Breeze, Janis L.;
- Sanouri Ursprung, Wannakuwatte Waduge;
- Shernan, Stanton K.

Anesthesia & Analgesia. 122(2):321-329, February 2016.

Review Article

揭示麻醉药物与内皮细胞间的相互作用：新进展与新见解

(陆晓斐译 李士通校)

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

- Aguirre, José A.;
- Lucchinetti, Eliana;
- Clanachan, Alexander S.;
- Plane, Frances;
- Zaugg, Michael

Anesthesia & Analgesia. 122(2):330-348, February 2016.

Ambulatory Anesthesiology and Perioperative Management

Research Report

开发和验证一个阻塞性睡眠呼吸暂停形态学上的预测评分:DES-OSA 评分

(张雪 译 薛张纲 校)

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

- Deflandre, Eric;
- Degey, Stephanie;
- Brichant, Jean-Francois;
- Poirrier, Robert;
- Bonhomme, Vincent

Anesthesia & Analgesia. 122(2):363-372, February 2016.

间歇性缺氧导致成人心肌细胞炎症和损伤

(陆晓斐译 李士通校)

Intermittent Hypoxia Causes Inflammation and Injury to Human Adult Cardiac Myocytes

- Wu, Jing;
- Stefaniak, Joanna;
- Hafner, Christina;
- Schramel, Johannes Peter;
- Kaun, Christoph;
- Wojta, Johann;
- Ullrich, Roman;
- Tretter, Verena Eva;
- Markstaller, Klaus;
- Klein, Klaus Ulrich

Anesthesia & Analgesia. 122(2):373-380, February 2016.

Anesthetic Pharmacology

Research Report

丙泊酚-瑞芬太尼靶控麻醉下接受标准化刺激后脑电图衍生的催眠和抗伤害作用的比较

(宣伟译 陈杰校)

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

- Shoushtarian, Mehrnaz;
- Sahinovic, Marko M.;
- Absalom, Anthony R.;
- Kalmar, Alain F.;
- Vereecke, Hugo E. M.;
- Liley, David T. J.;
- Struys, Michel M. R. F.

Anesthesia & Analgesia. 122(2):382-392, February 2016.

麻醉选择（七氟醚和地氟醚）和神经肌肉管理对气道反射恢复速度的影响

(邬其玮 译 薛张纲 校)

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

- McKay, Rachel Eshima;
- Hall, Kathryn T.;
- Hills, Nancy

Anesthesia & Analgesia. 122(2):393-401, February 2016.

昂丹司琼预防鞘内注射芬太尼及舒芬太尼引起的瘙痒症：一项随机试验的荟萃分析

(黄婷译 李士通校)

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

- Prin, Meghan;
- Guglielminotti, Jean;
- Moitra, Vivek;
- Li, Guohua

Anesthesia & Analgesia. 122(2):402-409, February 2016.

亚硝酸盐通过抑制连接蛋白-43 的去磷酸化减少大鼠心肌缺血引起的室性心律失常

(袁亚伟译 陈杰校)

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

- Maruyama, Daisuke;

- Hirata, Naoyuki;
- Tokinaga, Yasuyuki;
- Kawaguchi, Ryoichi;
- Yamakage, Michiaki

Anesthesia & Analgesia. 122(2):410-417, February 2016.

在体外使用丹曲林与咖啡因修正布比卡因诱导的肌肉毒性

(施云岑 译 薛张纲 校)

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

- Plank, Christoph;
- Hofmann, Petra;
- Gruber, Michael;
- Bollwein, Gabriele;
- Graf, Bernhard M.;
- Zink, Wolfgang;
- Metterlein, Thomas

Anesthesia & Analgesia. 122(2):418-423, February 2016.

Technology, Computing, and Simulation

Technical Communication

一项关于无线连接重症监护室患者监护仪和麻醉信息管理系统的技术评估

(黄婷译 李士通校)

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

- Simpao, Allan F.;
- Galvez, Jorge A.;
- England, W. Randall;
- Wartman, Elicia C.;
- Scott, James H.;
- Hamid, Michael M. Sr.;
- Rehman, Mohamed A.;
- Epstein, Richard H.

Anesthesia & Analgesia. 122(2):425-429, February 2016.

Research Report

光电容积脉搏波描记法和食管多普勒超声应用于重大非心脏手术中时对心指数评估的比较

(杨渝汀译 陈杰校)

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

- Blanié, Antonia;
- Soued, Mickael;
- Benhamou, Dan;
- Mazoit, Jean Xavier;
- Duranteau, Jacques

Anesthesia & Analgesia. 122(2):430-436, February 2016.

Patient Safety

高保真度分析围术期 QTc 延长

(俞颖 译 薛张纲 校)

High-Fidelity Analysis of Perioperative QTc Prolongation

- Duma, Andreas;
- Pal, Swatilika;
- Helsten, Daniel;
- Stein, Phyllis K.;
- Miller, J. Philip;
- Nagele, Peter

Anesthesia & Analgesia. 122(2):439-448, February 2016.

2002 至 2011 年纽约州门诊手术中心出院记录中恶性高热的发病率

(程鑫宇译 陈杰校)

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

- Lu, Zhen;
- Rosenberg, Henry;
- Brady, Joanne E.;
- Li, Guohua

Anesthesia & Analgesia. 122(2):449-453, February 2016.

Critical Care, Trauma, and Resuscitation

重症监护室非心脏病患者右美托咪定相关的血流动力学不稳定的危险因素

(侯君谊 译 薛张纲 校)

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

- Ice, Calvin J.;
- Personett, Heather A.;
- Frazee, Erin N.;
- Dierkhising, Ross A.;
- Kashyap, Rahul;
- Oeckler, Richard A.

Anesthesia & Analgesia. 122(2):462-469, February 2016.

Obstetric Anesthesiology

Research Report

不同种族和人种剖腹产麻醉方式的差异

(解健译 李士通校)

Racial and Ethnic Disparities in Mode of Anesthesia for Cesarean Delivery

- Butwick, Alexander J.;
- Blumenfeld, Yair J.;
- Brookfield, Kathleen F.;
- Nelson, Lorene M.;
- Weiniger, Carolyn F.

Anesthesia & Analgesia. 122(2):472-479, February 2016.

Pediatric Anesthesiology

Research Report

风险校正后的小儿麻醉相关心脏骤停中麻醉医师和系统相关风险因素

(李悦译 陈杰校)

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

- Zgleszewski, Steven E.;
- Graham, Dionne A.;
- Hickey, Paul R.;
- Brustowicz, Robert M.;

- Odegard, Kirsten C.;
- Koka, Rahul;
- Seefelder, Christian;
- Navedo, Andres T.;
- Randolph, Adrienne G.

Anesthesia & Analgesia. 122(2):482-489, February 2016.

监护对儿童心肺复苏开始的影响：朋友还是敌人?

(王洁 译 薛张纲 校)

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

- Hörner, Elisabeth;
- Schebesta, Karl;
- Hüpfl, Michael;
- Kimberger, Oliver;
- Rössler, Bernhard

Anesthesia & Analgesia. 122(2):490-496, February 2016.

西班牙裔儿童术后疼痛管理：一项描述性队列研究

(冯亚飞 译 李士通 校)

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

- Brown, Rebecca;
- Fortier, Michelle A.;
- Zolghadr, Sheeva;
- Gulur, Padma;
- Jenkins, Brooke N.;
- Kain, Zeev N.

Anesthesia & Analgesia. 122(2):497-502, February 2016.

Neuroscience in Anesthesiology and Perioperative Medicine

Research Report

在复杂的颅底神经外科手术中应用氨甲环酸与减少血制品输入相关性的一项回顾性队列研究

(孙佳昕译 陈杰校)

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

- Mebel, Dmitry;
- Akagami, Ryojo;
- Flexman, Alana M.

Anesthesia & Analgesia. 122(2):503-508, February 2016.

Brief Report

清醒颅骨切开术:一种新的气道管理方法

(杨晓迪 译 薛张纲 校)

Awake Craniotomy: A New Airway Approach

- Sivasankar, Chitra;
- Schlichter, Rolf A.;
- Baranov, Dimitry;
- Kofke, W. Andrew

Anesthesia & Analgesia. 122(2):509-511, February 2016.

Pain and Analgesic Mechanisms

Research Report

NR2B-CREB-CRTC1 信号通路调节慢性压迫性损伤鼠模型的昼夜疼痛

(冯亚飞译 李士通校)

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

- Xia, Tianjiao;
- Cui, Yin;
- Qian, Yue;
- Chu, Shuaishuai;
- Song, Jia;
- Gu, Xiaoping;
- Ma, Zhengliang

Anesthesia & Analgesia. 122(2):542-552, February 2016.

Regional Anesthesia

Research Report

全膝关节置换术后行收肌管阻滞对于股四头肌肌力的影响：一项个体化分析的三盲、随机、对照临床试验

(冯迪译 陈杰校)

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

- Sørensen, Johan Kløvgaard;
- Jæger, Pia;
- Dahl, Jørgen Berg;
- Gottschau, Bo;
- Stephensen, Snorre Læssøe;
- Grevstad, Ulrik

Anesthesia & Analgesia. 122(2):553-558, February 2016.

甲状腺手术中罗哌卡因伤口浸润诱导的镇痛不足：一项随机,双盲,安慰剂对照试验

(殷悦 译 薛张纲 校)

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

- Miu, Mihaela;
- Royer, Catherine;
- Gaillat, Carmen;
- Schaup, Barbara;
- Menegaux, Fabrice;
- Langeron, Olivier;
- Riou, Bruno;
- Aubrun, Frédéric

Anesthesia & Analgesia. 122(2):559-564, February 2016.

揭示麻醉药物与内皮细胞间的相互作用：新进展与新见解

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.

血管内皮细胞是人体最大的器官之一，它由单层高分化细胞构成，具有特定的形态和功能。内皮细胞在调节动脉、静脉、微血管、淋巴管血管床的血管紧张性中起着重要的作用。此外，内皮细胞还可调节血管生成，控制细胞粘附、调节体液平衡、先天免疫和适应性免疫反应。有基础研究显示，在有氧和缺血再灌注的情况下，全身麻醉药和局部麻醉药均能显著调节内皮细胞的生物活性，使内皮细胞成为麻醉影响心血管系统的重要靶点。尽管卤化吸入麻醉药抑制了内皮依赖性的血管舒张，但它有着显著的抗炎作用，可保护血管

内皮细胞发生缺血再灌注损伤。他们所提供的并不仅是急性，同样还有长期潜在的、有益的影响。虽然静脉麻醉药对血管内皮功能的影响现在仍有争议，并未被完全研究透彻，但异丙酚和阿片类药物似乎对血管内皮的保护最为明显。一些阿片类药物和氯胺酮对内皮细胞有立体选择性。最后，有实验证据表明，麻醉药对血管的通透性，包括内皮祖细胞在内的干细胞的增殖，促进或抑制肿瘤的生长都有着重要影响，这可能与调节血管生成的改变有关。然而，这些研究结果大多数是从体外实验得到的，还需体内实验的进一步确认。因此，这些相互作用的临床意义仍然不确定。

（陆晓斐译 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.

间歇性缺氧导致成人心肌细胞炎症和损伤

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：间歇性缺氧可能在一些临床事件中发生，其中包括心肌缺血或呼吸障碍（如阻塞性睡眠呼吸暂停综合征）。虽然间歇性缺氧与心脑血管疾病有关，但间歇性缺氧对心脏的影响还不明确。因此，在本研究中，我们比较了在间歇性缺氧、不同程度的持续性缺氧和正常情况下，成人心肌细胞 (HACMs)体外培养的不同细胞反应。

方法：通过使用一种有气体渗透膜的新型细胞培养生物反应器，使 HACMs 分别暴露于间歇缺氧（0% - 21% O_2）、持续轻度缺氧（10% O2）、持续严重缺氧（0% O2）和正常氧（21% O2）的环境下。评估不同实验条件下细胞增殖，乳酸脱氢酶、血管内皮生长因子

和细胞因子（白细胞介素和巨噬细胞移动抑制因子）释放的基础值及暴露 8 小时，24 小时和 72 小时后的改变。通过信号转导通路查找阵列来确定基因表达的变化。

结果：与持续性正常氧和持续轻度缺氧相比，间歇性缺氧表现的较低的细胞数和较高的乳酸脱氢酶，血管内皮生长因子和促炎性细胞因子（IL-1β，IL-6，IL-8 和巨噬细胞移动抑制因子）的释放量证明了其细胞损伤程度更为剧烈，可引起的更早和更强烈的炎症反应。持续严重缺氧 HACMs 的晚期影响更为不利。信号转导通路分析表明，间歇性缺氧主要改变了氧化应激、Wnt、Notch 和缺氧通路的基因表达。

结论：间歇性缺氧和持续严重缺氧可引起 HACMs 的炎症反应和细胞损伤，但持续轻度缺氧和正常氧则不然。间歇性缺氧的细胞损伤发生最早且最为严重。体外研究结果表明，间歇性低氧可能会造成心脏快速和实质性的损害。

（陆晓斐译 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.

昂丹司琼预防鞘内注射芬太尼及舒芬太尼引起的瘙痒症：一项随机试验的荟萃分析

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：瘙痒症是鞘内注射芬太尼及舒芬太尼常见副反应，会降低患者对麻醉的满意度及延长住院时间。关于预防使用昂丹司琼降低瘙痒症的有效性的报道仍有争议。本荟萃分析的目的在于评估预防性给予昂丹司琼降低鞘内注射芬太尼、舒芬太尼引起的瘙痒症发生率及需要补救治疗的概率。

方法：根据系统综述和荟萃分析优先报告条目指南（PRISMA）,我们系统地检索了 PubMed, Medline, and the Cochrane Central Register of Controlled Trials 数据库中从 1994 年 1 月 1 日到 2014 年 1 月 1 日的相关文献，收集了评价预防性使用昂丹司琼对与鞘内注射芬太尼和舒芬太尼相关的瘙痒症的效能的随机对照试验。主要结果是分析瘙痒症的发生率，次要结果是分析瘙痒症患者对补救治疗的需求。敏感性分析评估了包括产科患者、非产科患者、和在鞘内使用阿片类药物之前或之后使用昂丹司琼的结果。使用随机效应模型进行分析。

结果：收集了 6 个随机对照试验包括 555 个病人。总的来说，预给昂丹司琼不能降低瘙痒症发生率，但能降低需要补救治疗的概率（危险比 RR, 0.57；95%可信区间,0.35-0.91；I=0%；P=0.02）。进一步分组研究，包括非产科患者组和鞘内注射阿片类药物前使用昂丹司琼，也证明有减少补救治疗瘙痒症的用药的趋势（危险比 RR, 0.47；95% 可信区间, 0.26-0.85； P = 0.01；危险比 RR, 0.62； 95% 可信区间, 0.38-1.00； P = 0.05）。

结论：预防性的静脉注射 8mg 的昂丹司琼并不能降低鞘内注射芬太尼和舒芬太尼引起瘙痒症的发生率，但可能减少瘙痒症的用药，尤其是特定亚组的结果更有说服力。需要更多的随机对照试验验证这些结果。

（黄婷译 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.

一项关于无线连接重症监护室患者监护仪和麻醉信息管理系统的技术评估

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

在费城儿童医院新生儿重症监护室（NICU）的床边手术操作是使用纸质麻醉记录单记录，相比手术室所有麻醉记录都是使用麻醉信息管理系统(AIMS)。这主要是因为后勤方面的问题，与床旁监护仪和便携式 AIMS 工作站的连接电缆有关。我们在 NICU 用 AIMS 进行记录，利用无线路由器把监床旁护设备的数据传输到便携式 AIMS 工作站。检测无线 AIMS 模拟中显示高频电刀的使用对数据传输没有干扰。30 例 NICU 手术操作通过无线 AIMS 进行了麻醉记录。2 例麻醉记录单有短暂的数据传输遗漏；1 例因为路由器断电导致麻醉记录单中数据记录间隔延长。相比之下，30 例对照组中使用有线连接，麻醉记录单未出现数据记录间隔延长。与纸质麻醉记录单相比，无线 AIMS 为 NICU 床旁手术操作中麻醉记录提供了一个简单的、无干扰的、便携的选择。

（黄婷译 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.

不同种族和人种剖腹产麻醉方式的差异

Racial and Ethnic Disparities in Mode of Anesthesia for Cesarean Delivery

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Anesthesia & Analgesia: 2016 122 472–479

背景：目前认为种族和人种的差异性是构成椎管内分娩镇痛差异的基础。这些差异性也可能存在于产科麻醉护理的其他关键方面。我们试图弄清不同种族或人种的差异对剖腹产麻醉方式是否会有影响。

方法：1999 年至 2002 年间，美国 19 所产科中心剖腹产的女性登记完成了母胎医学单位网络剖腹产的注册表。种族或人种分类为：白人，非洲裔美国人，西班牙裔和非西班牙裔人种。麻醉方式分为：椎管内麻醉（脊麻、硬膜外麻醉和腰硬联合麻醉）或全身麻醉。为了说明可能影响产科和非产科麻醉方式的协变量因素，我们使用序列协变量完成多元线性回归分析。

结果：这个研究队列包括 50974 例曾行剖腹产麻醉的女性。不同种族或人种之间全麻率分别如下：白种人 5.2%、非洲美裔人 11.3%、西班牙人 5.8%、非西班牙人 6.6%。对产科麻醉和非产科麻醉协变量进行调整之后，非裔美国女性与白种女性相比，非裔美国女性接受全身麻醉的概率最高。（调整后的 OR 值=1.7；95%可信区间，1.5-1.8；P<0.001）.与白种人女性相比，西班牙裔人种和非西班牙人接受全身麻醉的几率较高，分别为：西班牙裔人种（调整后的 OR 值为 1.1；95%可信区间，1.0-1.3；P=0.02）和非西班牙人（调整后的 OR 值为 1.2；95%可信区间，1.0-1.4；P=0.03）。在灵敏度分析中，为排除在全身麻醉前进行椎管内麻醉的产妇这种情况，重新建立模型。接受全身麻醉的调整后概率类似于主要分析中得到的结果。即非洲美裔人（调整后的 OR 值为 1.7; 95% CI, 1.5–1.9; *P* < 0.001）；西班牙裔(调整后的 OR 值为 1.2; 95%可信区间， 1.1–1.4；*P* = 0.006)以及非西班牙裔(调整后的 OR 值为 1.2; 95%可信区间， 1.0–1.5; *P* = 0.05)。

结论：根据剖腹产注册表的数据分析，与白人女性相比，非裔美国女性接受全身麻醉的几率最高。目前，我们仍不能十分确定这种差异在当前的产科实践中是否存在。

（解健译 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.

西班牙裔儿童术后疼痛管理：一项描述性队列研究

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.

Anesthesia & Analgesia: 2016 122 497–502

背景：儿童门诊手术后的疼痛未能经常得到充分治疗已被多次证实。然而很少有试验从种族差异人群的角度研究这种现象。

方法：这项研究包括 105 个年龄在 2 岁至 15 岁之间，接受门诊扁桃体切除术和腺样体切除术的低收入的西班牙家庭的孩子。参与的家长完成基础信息和统计学信息。以家庭访问的形式记录术后一周内疼痛评分及镇痛药在家中的使用情况。

结果：尽管术后 24 小时内显著疼痛的发病率很高（70%；99%可信区间，82% -57%），32%（95%可信区间，45%-20%）的儿童仅接受 0 到 1 个剂量的镇痛药治疗。总的来看，21%（99%可信区间，11%-35% ）的儿童在手术后整个周内接受了 4 个或更少剂量的止痛药。手术后一周内，只有 44%（99%可信区间，40%-47%）的儿童总镇痛药剂量在可接受范围内。

结论：尽管有显著的术后疼痛，这项研究中的西班牙裔儿童却在家中接受着未达标准的镇痛治疗。

（冯亚飞 译 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 信号通路调节慢性压迫性损伤鼠模型的昼夜疼痛

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

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Anesthesia & Analgesia: 2016 122 542–552

背景：许多临床调查显示慢性疼痛有昼夜节律性变化，临床上大多数慢性疼痛的峰值在夜间。然而疼痛节律是否存在于啮齿类动物及其可能的特定机制尚未被研究。我们研究了鼠慢性压迫性损伤（CCI）模型痛觉过敏的节律性变化并探讨了 N-甲基-D-天门冬氨酸（NMDA）2B 受体(NR2B)—cAMP 反应元件结合蛋白（CREB）— CREB 转录共激活因子 1 (CRTC1)信号通路在这种疼痛节律的作用。

方法：用慢性压迫性损伤手术模拟临床慢性疼痛。应用机械刺激缩足反应阈值和热刺激缩足反应潜伏期测试鼠的疼痛行为。用 von Frey 纤维触痛仪连续 14 天在昼夜时点 ZT4、ZT10、ZT16、ZT22 这几个时间点测试机械性痛觉过敏。用实时聚合酶链反应和 Western blot 法分别测定视交叉上核和脊髓背角处 NR2B、CRTC1 、CREB 的 mRNA 和蛋白的表达。 分别在两个时间点（ZT12 和 ZT0）鞘内注射 CRTC1 和 CREB 干扰腺病毒载体，进一步探讨疼痛治疗的适当时间点。

结果：在慢性疼痛状态期间，慢性压迫性损伤动物的疼痛反应表现为昼夜节律，并且在每天的 ZT4 和 ZT10 达到峰值。活动期和休息期的疼痛阈值有显著差异。脊髓水平的 NR2B、CRTC1、CREB 的表达与疼痛节律一致。慢性压迫性损伤手术后第 7 天到 9 天鞘内注射 CRTC1 和 CREB 的干扰腺病毒明显改善疼痛反应。然而，与 ZT12 相比，当 ZT0 给予 CRTC1 和 CREB 的干扰腺病毒治疗时，其缓解峰值疼痛更为有效。

结论：慢性压迫性损伤后慢性疼痛患者的疼痛反应表现为昼夜节律，并与疼痛相关受体的昼夜节律性分泌有关。NR2B-CREB-CRTC1 信号通路可能在这种节律性里起着至关重要的作用。此外，我们的研究结果表明，缓解疼痛的措施，应在疼痛达到高峰前即采取。

（冯亚飞译 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.

二尖瓣返流对彩色多普勒测量的时间动态缩流面积影响的机制

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：对于二尖瓣返流(MR)患者，可以通过测量缩流面积(VCA)来评估反流口面积。推测 VCA 的时间动态特征与功能性二尖瓣反流（FMR）或退行性二尖瓣瓣膜病(DMVD)的存在不同机制。

方法： 对 42 例心脏外科手术患者进行三维经食道超声心动图(TEE) 检查，通过彩色血流多普勒的近端喷流面积获得 VCA 数据, 共包括 22 个 FMR 和 20 个 DMVD。得到每个患者整个收缩期的连续 VCA 数据用来评价有效反流口面积的变化。采用重复测量方差分析对 FMR 和 DMVD 两组的百分数平均值进行组内和组间比较。通过 Bonferroni 法校正两两测试的比较次数。

结果：FMR 组病人的标准化平均 VCA 值显示为两相模式；而 DMVD 组病人为单相模式。在 FMR 组内，标准化平均 VCA 值在收缩早期（1.10±0.32 cm^2）和末期（1.11±0.33 cm^2）相似，都显著高于收缩中期(0.79 ± 0.22 cm^2，P = 0.0144；P = 0.0106)。在 DMVD 组内，收缩中期的标准化平均 VCA 值(1.37 ± 0.15 cm^2)较收缩早期 (0.53 ± 0.14 cm^2) 和晚期 (1.09 ± 0.18 cm^2; P < 0.0001)显著增高。对标准化平均 VCA 值分析得出收缩早期(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)时 FMR 和 DMVD 两组存在显著差异。

结论： MR 机制导致了 VCA 的动态变化。同时观察到 VCA 动态变化在 FMR 患者中呈现双相时间模式而 DMVD 患者呈现单相时间模式。

（刘洋译 陈杰校）

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标准化刺激后脑电图衍生的催眠和抗伤害作用的比较

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: 目前脑电图（EEG）衍生测量能提供大脑皮层活动和催眠深度的信息，但是对皮层下的活动监测还不够精确，而一般认为后者是随着抗伤害效应程度而变化。最近，以神经

生理为基础的皮层脑电输入（CI）和皮层所处状态（CS）的 EEG 监测分别被认为是麻醉/抗伤害效应以及催眠深度的可靠指标。本研究将脑电双频指数（BIS）和另一个最新研究出的指示抗伤害效应的复合变异指数(CVI)，与 CI 和 CS 的一种替代测量—复合皮层状态（CCS）进行比较。CVI 是综合量化 BIS 和预估肌电活动的一种 EEG 衍生参数。通过评估这些指标与催眠深度间的等效关系（用 BIS 定量）以及痛/不痛的平衡关系（用瑞芬太尼预计效应室浓度决定），评价催眠和镇痛联合监测对有害刺激的体动反应的预测作用是否优于单独监测。

方法: 重新分析了先前发表的一项实验中 BIS 和 CVI 指数以及原始脑电图资料的时间序列。在本研究中，80 名患者随机分为靶催眠深度组（BIS50-70）和靶瑞芬太尼浓度组（瑞芬 0、2、4、6ng/ml）。运用观察评估警觉/镇静量表，在一系列强直刺激后，计算或定量 CCS, CI, BIS, 及 CVI 的基础值，以及每个时间间隔后的数值。定量分析瑞芬太尼效应室浓度时的镇痛作用的指标 CI 和 CVI，以及它们和催眠指标 CCS 和 BIS 的关系。最后，运用统计学聚类方法评价镇痛和催眠双指标是否能更好的监测和预测对刺激的反应。

结果: 在刺激前，CI 和 CVI 均能区分接受 0 ng/ml 瑞芬输注与其他剂量组患者(CI: Cohen's d = 0.65, 95% 可信区间，0.48–0.83; CVI: Cohen's d = 0.72, 95% 可信区间， 0.56–0.88)。BIS 和 CCS 间有很强的关联(不同时间: 0.55 < R2 < 0.68, P < 0.001)。观察评估警觉/镇静刺激与 CI 和 CCS 的变化相关，然而刺激后所有指标均有变化。CI 和 CCS 成对运用比 CVI 和 BIS 联合应用更敏感地监测了刺激反应(敏感度 [99% 可信区间], 75.8% [52.7%–98.8%] vs 42% [15.4%–68.5%], P = 0.006), 特异 CI 和 CCS 所达显著性(52% [34.7%–69.3%] vs 24% [9.1%–38.9%], P = 0.0159).

结论: 联合应用脑电监测衍生的催眠和镇痛量化指标可能更好地预测患者对强直刺激的反应。

（宣伟译 陈杰校）

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.

亚硝酸盐通过抑制连接蛋白-43 的去磷酸化减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：缺血性心脏病引起的室性心律失常是心源性猝死的主要原因。缺血通过调节连接蛋白 43（Cx43，一种重要的心肌细胞间隙连接通道蛋白）导致危及生命的心律失常。本研究探索在大鼠模型中亚硝酸盐是否可以抑制缺血引起的室性心律失常和 Cx43 的去磷酸化水平。

方法：按接受药物不同将实验动物分为以下几组：生理盐水组（对照组，n= 10），亚硝酸盐组（0.015、0.15、1.5 mg/kg，每组 9 或 10 只），以及 0.15mg/kg 亚硝酸盐复合一氧化氮清除物（2-(4-carboxyphenyl)-4, 4, 5, 5-tetramethylimidazoline-1-oxyl-3-oxide，cPTIO; n= 9）组和 0.15mg/kg 亚硝酸盐复合别嘌呤醇（黄嘌呤氧化还原酶抑制剂，n = 9）组。根据心律失常评分标准确定室性心律失常的严重程度并测定 Cx43 的磷酸化水平。

结果：亚硝酸盐 0.15 mg/kg 模型鼠心律失常评分中位数 (4 [interquartile range {IQR}, 4–5]) 要低于对照组模型鼠的 (4 [interquartile range {IQR}, 4–5])。对照组与亚硝酸盐 0.015mg/kg 组及亚硝酸盐 1.5mg/kg 组之间没有差异。而亚硝酸盐复合 cPTIO 组和复合别嘌呤醇组的心律失常评分均要高于 0.15 mg/kg 亚硝酸盐组(分别为 6 [IQR, 5–8]; P = 0.030；7 [IQR, 5–8]; P = 0.005)。免疫组化实验显示，亚硝酸盐 0.15 mg/kg 组的磷酸化连接蛋白 43 水平与对照组的（P= 0.007）相比显著升高，而其他治疗组则无显著差异。

结论：亚硝酸盐可能抑制了大鼠急性心肌缺血引起的室性心律失常并抑制 Cx43 的去磷酸化。一氧化氮由亚硝酸盐经黄嘌呤氧化还原酶还原产生，本研究提示其在抗心律失常方面发挥重要的作用。

（袁亚伟译 陈杰校）

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.

光电容积脉搏波描记法和食管多普勒超声应用于重大非心脏手术中时对心指数评估的比较

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

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背景：在本次前瞻性观察研究中，比较重大非心脏手术患者在液体负荷后使用光电容积脉搏波描记法（CIPPG）和食管多普勒超声（CIED）描记心脏指数（CI）变化的区别。

方法：在麻醉主治医生开始进行液体负荷后获得测量值。采用线性回归，B-A 法和协方差分析相关性。采用两种不同的方法即四象限图和极坐标图进行趋势分析。

结果：对 43 例患者进行总共 111 次输液方案。CIPPG 和 CIED 之间有显著的线性关系(r2 = 0.34; P < 0.001)，ED 和 PPG 间对于 CI 测量的偏差为-0.114 L/min/m2(95%可信区间

[CI95], −1.9 to 1.7)，平均百分比误差为 55%。同一种输液方式中的 CI 变化具有显著的相关性（r2 = 0.25; P = 0.002），CIPPG 和 CIED 的总体数据中变化趋势（升高或降低）在的一致性为 67% (CI95, 57–75)，而将排除域设定为 15%前提下一致性为 85%(CI95, 70–94)。将 ED 值视为参考值，PPG 评估额外的液体需求量的敏感性和特异性增加 35%（(CI95, 19–55) 和 90%（CI95, 81–96），阳性预测值为 58%（CI95，33-80），阴性预测值为 78%（CI95，68-86）。

结论：在重大非心脏手术的患者中，使用 PPG 对 CI 的评估与 ED 对其评估并不对等。如果将 ED 评估 CI 值作为金标准，那么采用 PPG 评估额外的液体需求量则并不恰当。这些结果明确表明 PPG 用于评估 CI 的变化时与 ED 相比具有局限性。

（杨渝汀译 陈杰校）

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 年纽约州门诊手术中心出院记录中恶性高热的发病率

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

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背景：恶性高热（Malignant hyperthermia，MH）是由接触吸入麻醉药和去极化肌松药琥珀酰胆碱引发的一种罕见但可能致命的药物遗传学疾病。关于 MH 的流行病学研究主要限于住院病人。本研究检测记录在门诊手术中心（ambulatory surgery centers, ASCs）出院病人中的 MH 发病率。

方法：检索 2002 年至 2011 年纽约州门诊手术数据库，根据诊断标准参考第九版国际疾病分类法（临床修订码 995.86）筛选出了所有出院诊断为与麻醉相关的 MH 的病人。并按照不同人群特点、临床信息和 ASC 手术信息对 MH 患病率进行了具体分析。

结果：在研究期间，17092765 个 ASC 的出院病人中，31 人有 MH 的诊断记录，发病率为 0.18/100000（95%CI，0.12-0.25）。MH 的发病率在不同患者年龄组和手术类型中有显著差异。所有诊断为 MH 的患者在 ASC 出院时均无死亡记录。

结论：ASC 患者出院诊断为 MH 的比率约为 1/500,000，与外科手术类别显著相关。

（程鑫宇译 陈杰校）

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.

风险校正后的小儿麻醉相关心脏骤停中麻醉医师和系统相关风险因素

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

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背景：小儿麻醉相关的心脏骤停（ARCA）是一种罕见但潜在可预防的不良事件。婴儿和患有严重潜在疾病的儿童的风险是最高的。本次研究的目的是识别 ARCA 的系统和麻醉医师相关风险因素。

方法：对大型三级儿科医院 2000 至 2011 年实施儿童麻醉相关的前瞻性队列数据进行分析。术前全身性疾病的分级由 ASA 身体状态（ASA-PS）来描述。两位评价者独立回顾了心脏骤停事件，并按其麻醉相关性分类。在单变量分析中与 ARCA 相关的因素在行年龄和 ASA-PS 校正后重新评估。

结果：在 276209 例麻醉中出现 142 例心脏骤停事件（发生率 5.1/10,000），其中 72 例（2.6/10,000）被列为与麻醉相关。在单变量分析中，心脏病患者，由年麻醉例数较少或年工作日较少的麻醉医师实施麻醉导致 ARCA 风险更高（所有的 $P < 0.001$）。具有最高学术地位和多年经验的麻醉医师也有更高的 ARCA 发生概率 （$P = 0.02$）。在对 ASA-PS ≥III 级和年龄≤6 个月的进行风险调整后，与年工作日较少的麻醉医师实施麻醉的关联性继续保持（$P = 0.03$），但其它因素不再显著。

结论：在作者单位，结合病例能够解释儿科 ARCA 的更高风险与一些麻醉医师相关因素之间的关联，而麻醉医师年工作日较少这一因素是始终关联的。本研究强调了在麻醉患者安全性研究中对患者风险因素严密校正的需要性。

（李悦译 陈杰校）

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.

在复杂的颅底神经外科手术中应用氨甲环酸与减少血制品输入相关性的一项回顾性队列研究

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：与其他外科手术相比，复杂性颅底神经外科手术中仍有将大量术中失血降至更低的可能性。抗纤维蛋白溶解药——氨甲环酸在择期神经外科手术中的安全性和疗效尚未明了。本研究首要目标是确定本单位氨甲环酸的使用和血制品输入的关系。次要目标是了解应用氨甲环酸后不良事件的发生率。

方法：在这个回顾性队列研究中纳入本单位 2001 到 2013 年所有接受复杂性颅底神经外科手术的患者。氨甲环酸在 2006 年开始应用于患者。从病史中收集病人和手术参数、输血数据和围手术期不良事件信息。比较是否应用氨甲环酸的两组患者输血量及不良事件发生率的差异。通过多变量回归分析确认围手术期输血的影响因素。

结果：比较研究周期中 245 例使用氨甲环酸及 274 例未使用的患者。两组患者条件相近，但应用氨甲环酸的患者有更大的肿瘤（3.5 vs 2.9 cm; P < 0.001）和更长的手术时间（7.2 vs 6.2h, P < 0.001）。使用氨甲环酸的患者在围手术期输血率低（7% vs 13%, P = 0.04）。在校正了术前血红蛋白水平、肿瘤直径和手术方式后，是否使用氨甲环酸是围术期输血量的独立预测因素（校正后优势比 0.32，95%置信区间 0.15–0.65, P = 0.002）。两组发生癫痫和血栓栓塞事件概率相似。

结论：本研究结果表明，在作者单位研究的人群中，应用氨甲环酸可以减少术中的输血率，而癫痫和血栓栓塞发生率并不增加。数据支持需要进一步进行复杂颅底神外手术中应用氨甲环酸的随机临床试验，以评价其疗效和安全性。

（孙佳昕译 陈杰校）

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.

全膝关节置换术后行收肌管阻滞对于股四头肌肌力的影响：一项个体化分析的三盲、随机、对照临床试验

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：全膝关节置换(TKA)术后实施周围神经阻滞，且不影响运动功能具有挑战性的。本研究假设收肌管阻滞(ACB)的镇痛效果能增加 TKA 术后股四头肌最大随意等长收缩(MVIC)。

方法：纳入了 64 例术后第一天的病人。A 组患者接受收肌管阻滞（ACB）：在 t_0 时间给予 0.75%罗哌卡因 30ml，60min 后给予 30ml 生理盐水（t_{60}）。B 组治疗顺序与 A 组相反。主要研究终点为两组之间在 t_{60} 时 MVIC 的差异，用术后的阻滞前值的百分数表达。依此区分 ACB 作用与手术造成的肌力影响。次要终点是两组间活动度和疼痛评分的差异。本研究根据在膝关节屈曲时的阻滞前疼痛评分差异设计了一项亚组分析。

结果：在 t_{60}，A 组的 MVIC 阻滞前值中位数为 170%（95%可信区间，147-231）明显高于 B 组（95%可信区间，82-98）($P < 0.0001$)。站起-行走实验（TUG）无统计学差异。A 组中 3 个病人失去执行 TUG 实验的能力。在 t_{60}, A 组的疼痛视觉模拟评分良好, 静息时为 12mm(95% CI,6 - 18), 在膝盖屈曲时为 14mm(95% CI,5-22), TUG 测试时为 18mm(95% CI,10-26)。

结论：ACB 改善了股四头肌肌力，但这是否意味着增强活动度未有定论。

（冯迪译 陈杰校）

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.

开发和验证一个阻塞性睡眠呼吸暂停形态学上的预测评分:DES-OSA 评分

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

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背景：阻塞性睡眠呼吸暂停（OSA）是一种常见但容易忽略的疾病，容易增加围手术期的患病率。几个解剖特点使患者易患 OSA 综合征。我们开发了一个新的临床评分, 根据病人的形态学特征来检测 OSA 综合征。

方法：研究纳入了拟行整夜多导睡眠图的患者（n = 149）。比较他们的形态学指标，并将这些指标进行组合测试其预测至少轻度、中重度、或严重 OSA 综合征的能力,以低通气指数（AHI）> 5，>15 或>30 次/ h 来定义三种程度。使用科恩 κ 系数和预测概率来计算这种能力。

结果：以下 5 个变量被认为是预测能力最好的（DES-OSA 分数）：Mallampati 评分,甲状腺和下颌之间的距离,身体质量指数,颈围以及性别。这些变量以 1、2、或 3 分加权。DES-OSA 得分> 5、6、7 都分别与 AHI > 5，> 15 或> 30 次/ h 的概率增加有关，并且这些阈值有很好的科恩 κ 系数, 敏感性和特异性。ROC 曲线分析显示，DES-OSA 预测 AHI> 5，> 15，和> 30 次/ h 曲线下的面积分别是 0.832（95%可信区间（CI）,0.762 - -0.902）,0.805（95%可信区间,0.734 - -0.876），和 0.834（95% CI,0.757 - -0.911）。上述阈值相应的敏

感性（95% CI）分别为 82.7%（74.5 - -88.7）、77.1%（66.9 - -84.9）和 75%（61.0 - -85.1）和特异性（95% CI）72.4%（54.0 - -85.4）、73.2%（60.3 - -83.1）和 76.9%（67.2 - -84.4）。在独立样本验证 DES-OSA 的能力得到了非常相似的结果。

结论：DES-OSA 是一个简单的检测 OSA 综合征病人的评分。它主要依靠患者的自然解剖学形态。源自欧洲的人口,它在术前可能是有用的,但它仍应与其他在一般手术和种族的人口中得到的筛查工具进行比较。

（张雪 译 薛张纲 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.

麻醉选择（七氟醚和地氟醚）和神经肌肉管理对气道反射恢复速度的影响

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与使用地氟醚的患者相比保护性气道反射恢复较慢。我们问这种差异是否在使用罗库溴铵的气管插管患者仍然显著，或者是否神经肌肉恢复的变量在其中占主导地位而减少了两种麻醉药物之间的差别。

方法：在签署知情同意书后,病人被随机分配到七氟醚组（n = 41）或地氟醚组（n = 40）。神经肌肉功能监测采用加速度仪定量 TOF 指数。使用 1mg/kg 的罗库溴铵来帮助插管。产生神经肌肉阻滞，以维持 10%至 15%的基线水平为目标。手术后给予新斯的明 70μg/kg 及格隆溴铵 14μg /kg。当 TOF 比率达到≥0.7 时，停用吸入麻醉药，并把新鲜气体流量提高到 15 L / min。记录对指令有第一次反应的时间，之后患者分别在 2min，6min，14min，22 min，30min 和 60min 饮用 20ml 水行吞咽测试。以下平均时间间隔在 2 组之间进行比较：终止使用麻醉药物到患者对指令第一次有反应的时间（T1）； 对指令第一次有反应到首次成功的吞咽测试的时间（T2）；停用麻醉药到首次吞咽试验成功的时间（T3）。我们也测定两组中对指令出现第一次反应后 2min 时吞咽试验的成功率。在 2min 时无法进行吞咽试验的患者被认为失败，同时也除外了因嗜睡以外的原因不能完成试验的 10 名患者（n=10）。

结果：使用地氟醚的患者在对指令第一次有反应后通过吞咽试验的时间间隔短于使用七氟醚的患者（Wilcoxon-Mann-Whitney 指数= 1.60；95%可信区间（CI），1.01 - -2.69;P = 0.054）。对指令第一次有反应 2min 后, 在所有 81 名病人中, 与七氟醚麻醉相比, 地氟醚麻醉的患者吞咽测试成功率明显增加（相对危险度= 1.6；95%可信区间,1.0 - -2.5；P = 0.04）。在 71 名患者中（如上所述），我们观察到患者对指令第一次有反应 2min 后使用地氟醚的患者（25/33）吞咽试验的成功率高于使用七氟醚的患者（16/38）（相对危险度 = 1.8；95%可信区间，1.2 - -2.7;P = 0.006）。在接受地氟醚（25/33）与接收七氟醚（16/38）的 81 名患者中 18 人和 71 名患者中的 16 人，神经肌肉监测和逆转并未实施（新斯的明剂量不足, 在 TOF < 0.7 时拔管,或依赖触觉而不是定量测定的 TOF）。在整个队列人群和 71 人的亚组中，多变量逻辑回归分析（分别为 P = 0.02，P = 0.02）表明神经肌肉管理成为独立于麻醉药物使用的增加吞咽测试成功率的因素，表明其为独立于麻醉剂选择的显著影响气道反射恢复的因素。

结论：与七氟烷相比,地氟醚麻醉气管插管的患者气道反射恢复更快。神经肌肉阻滞的临床管理,包括完全的逆转和 TOF 的测定可影响气道反射的恢复——一个和强效吸入麻醉药物选择一样有意义的影响因素。

（邬其玮 译 薛张纲 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.

在体外使用丹曲林与咖啡因修正布比卡因诱导的肌肉毒性

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

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背景:局部麻醉剂,尤其是布比卡因，在临床使用的浓度下具有肌肉毒性。这些影响的详细机制尚未可知，但增加细胞内钙含量可能是最重要的触发因素。丹曲林和咖啡因可以修正细胞内钙离子从肌浆网的释放。我们的研究的目的是在体外研究丹曲林和咖啡因对布比卡因诱导的肌肉毒性的作用。

方法: 建立 BALB/cAnNCrl 小鼠的原代肌细胞培养模型。细胞与浓度增加的布比卡因，丹曲林及咖啡因同时孵育。坏死细胞的比例在碘化丙啶染色和流式细胞术分析后计算得出。计算每个浓度的布比卡因最大半数抑制浓度。组间差异采用单向方差分析和 post hoc 1-way Dunnett t 检验计算。

结果:丹曲林和咖啡因本身没有影响肌细胞的生存。布比卡因浓度增加会增加细胞死亡。丹曲林以剂量依赖的方式降低了坏死细胞的比例，而咖啡因剂量依赖性增加了坏死细胞的比例。

结论:丹曲林减少，咖啡因增强布比卡因诱导的细胞毒性,可能通过修改肌质钙释放。这表明细胞内钙释放是局麻药诱导细胞死亡的重要因素。

（施云岑 译 薛张纲 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.

高保真度分析围术期 QTc 延长

High-Fidelity Analysis of Perioperative QTc Prolongation

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背景: QTc 间期延长表示异常心脏复极化。最近的一项研究表明, 术后 QTc 间期延长是常见的。然而, QTc 间期延长是否为一个术后独立的现象，或规律的发生在手术过程中，以及麻醉的类型是否影响其发生率。

方法:要回答这个问题,我们进行了一项前瞻性队列研究（n = 300），使用 12 导联动态心电图连续监测术前 30 分钟及术后 60 分钟的 QTc 间期。QTc 间期延长于在全身麻醉（n = 101），椎管内麻醉（n = 99） 或局部麻醉（n = 100）下行整形手术的,至少有一个心脏危险因素的成人中进行行。主要结果是术中 QTc 间期的增加（ΔQTc 定义为术中及术前 QTc 间期的差）。长 QTc 间期发作的发病率 （QTc ＞500 毫秒，持续至少 15 分钟）也被确定。

结果: QTc 间期显著延长 （中位数,四分位范围（IQR）发生在全身麻醉（ΔQTc + 33ms；IQR，22 – 46ms）和椎管内麻醉（ΔQTc + 22ms；IQR，12 – 29ms）中,在局部麻醉中并未发现 QTc 间期延长（活检,n = 53:ΔQTc,+ 4ms；IQR,−4 + 7ms；冠状动脉造影时，n = 47：ΔQTc,+ 6ms； IQR，−5 + 16ms）。长 QTc 间期发作的发病率在全身麻醉（n = 6/63，9.5%）,椎管内麻醉（n = 1/56，1.8%）,局部麻醉的活检（n = 0/46，0%）和冠状动脉造影（n = 0/19，0%;P = 0.045）中显著不同。

结论:延长这些结果表明 QTc 间期延长不是一个孤立的术后现象，并且在全身麻醉和椎管内麻醉下手术中很常见。

（俞颖 译 薛张纲 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.

重症监护室非心脏病患者右美托咪定相关的血流动力学不稳定的危险因素

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

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背景: 接受右美托咪定镇静的患者中报道的低血压和心动过缓的发病率通常超过 50%。在这项研究中,我们描述右美托咪定相关的血流动力学不稳定的发生率,患者治疗的危险因素和临床意义。

方法:这项回顾性队列研究纳入了明尼苏达州罗彻斯特的梅奥医院一年期间接受右美托咪定镇静的危重患者。主要的研究终点是血流动力学不稳定：在右美托咪定治疗期间，结合低血压和/或心动过缓，低血压定义为收缩压小于 80 mm Hg,舒张压< 50 mm Hg,或心率<每分钟 50 次。Cox 比例风险模型被构建来确定血流动力学不稳定的危险因素的风险比率（HRs）以及 95%置信区间（CIs）。

结果:分析接受右美托咪定治疗的 300 例患者中发生血流动力学不稳定的有 197 人，通过 kaplan meier 估计，结果在 24 小时内累积发病率为 71%。除了右美托咪定，单变量分析发现年龄、血管加压的使用,低基础动脉血压,和同时使用的镇静剂与血流动力学不稳定的风险增加有关。多变量分析表明年龄（HR,每 10 年 1.23，95% CI，1.10 - -1.38）， 低基础血压（HR 2.42 起始使用右美托咪定，95% CI，1.68 - -3.49） 和血流动力学不稳定的发生风险之间有关联。在被分析的样本中，同时服用心脏药物，或镇静治疗，以及右美托咪定的输注速率> 0.7 μg/kg/h 等变量不能预测血流动力学不稳定的发生。

结论: 在接受右美托咪定治疗的危重成人患者中，常见血流动力学不稳定，在本队列中，通常在使用药物 24 小时内，有超过三分之二的患者出现低血压和/或心动过缓。年龄增加，低基础动脉血压与血流动力学不稳定的发生有关。这些结果提示，临床医生应该意识到在高龄患者或低基础动脉血压患者中使用右美托咪定时血流动力学不稳定发生的潜在风险。

（侯君谊 译 薛张纲 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.

监护对儿童心肺复苏开始的影响：朋友还是敌人?

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

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背景:立即启动和高质量的基本生命支持（BLS）是改善心脏骤停后病人预后的关键。尽管心脏呼吸监护可以缩短识别心脏骤停发生的时间,对监控和监测数据的误解可能影响 BLS 的启动。在这项研究中,我们评估了在模拟有监护和无监护心脏骤停的儿童中，BLS 的启动速度和质量。

方法: 经常参与照顾重病的儿童的 60 位居民被随机分配到干预组（监护）或对照组（非监护）。发生以下 2 种临床一致的未察觉的模拟心脏骤停的场景时，两组参与者均实施 BLS。尽管在场景 1 中使用心脏呼吸监护（比如，心电图），另一个场景反映了无监护的心脏骤停。第一个开始胸按压的时间作为研究主要的结果变量。坚持复苏指南和主观判断速度是次要研究结果变量。

结果:监护组的参与者开始胸外按压明显晚于无监护组（91±36 vs 71±26 秒，风险比，0.26;95%可信区间，0.14 - -0.49，P < 0.001）。六个监护小组的成员开始胸外按压的时间大于 5 分钟。在非监护组能更好地坚持指南。曾参加过 BLS 培训的参与者曾并没有更好的表现。

结论:在模拟心脏骤停的情境下，心脏呼吸监护显著延迟甚至阻止胸外按压的开始并影响心肺复苏的质量。基于这些数据,应对相关人员进行特殊培训。

（王洁 译 薛张纲 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.

清醒颅骨切开术:一种新的气道管理方法

Awake Craniotomy: A New Airway Approach

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自 2004 年以来，清醒开颅手术在宾夕法尼亚大学常规实施。在这个手术中，探索了不同的气道管理方法 ,包括气管内插管，使用喉罩通气、简单的面罩,或鼻咽通气道。在此病例系列中,我们描述了在 90 位行清醒开颅手术的患者中双腔鼻咽通气道的成功使用（即：不需要因气体交换不足而气管插管）。使用鼻咽通气道可以开颅手术中清醒和麻醉阶段的切换变得简单，而不需要刺激气道。我们的目的是描述我们的经验并报告与此技术相关的不良事件。

（杨晓迪 译 薛张纲 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.

甲状腺手术中罗哌卡因伤口浸润诱导的镇痛不足：一项随机,双盲,安慰剂对照试验

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:手术部位局部麻醉药浸润可减少各种类型的手术中镇痛药物的使用。因为甲状腺手术可能会引起严重的术后疼痛，我们测试假设罗哌卡因在手术部位浸润会显著减少甲状腺手术患者术后吗啡的使用量。

方法:我们进行了双盲,安慰剂对照试验来评估在成人甲状腺手术结束时罗哌卡因（10ml，75mg）手术部位镇痛的效果。主要研究终点是患者在苏醒室中不需要使用静脉吗啡治疗的比例。

结果：163 名患者完成了研究，安慰剂组包括 85 名患者和罗哌卡因组包括 88 名患者。患者在苏醒室中需要使用静脉吗啡的比例为 55% vs 53%，P = 0.80，静脉注射吗啡的剂量比例为 5.6±6.1 vs 5.5±6.0mg，P = 0.90。两组之间第一个 24 小时内使用阿片类药物的总剂量（以口服吗啡等效剂量表示：64±27 vs 69±29mg，P = 0.20）,视觉模拟疼痛量表评分无显著差异。不良事件的发生率（36% vs 39%，P = 0.88）,吗啡相关不良事件（19% vs 17%，P = 0.84）,严重不良事件（0% vs %，P = 0.50）,和患者满意度（9±1 vs 9±1，P = 0.70），在两组之间无显著差异。

结论: 甲状腺手术结束时罗哌卡因手术部位镇痛在患者镇痛中无显著获益。

（殷悦 译 薛张纲 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.