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A Pilot Study on the Effect of Nasal Continuous Positive Airway Pressure on Arterial Partial Pressure of Carbon Dioxide During Spinal Anesthesia with Intravenous Sedation for Total Knee Arthroplasty
肾素血管紧张素在心血管稳态中作用更新
An Update of the Role of Renin Angiotensin in Cardiovascular Homeostasis
Farag, Ehab MD, FRCA*†; Maheshwari, Kamal MD*†; Morgan, Joseph MD‡; Sakr Esa, Wael Ali MD, PhD*; Doyle, D. John MD, PhD§
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肾素血管紧张素系统（RAS）是人体内主要的血管收缩相关的系统，通过血管紧张素Ⅱ与血管紧张素Ⅰ受体之间的相互作用来发挥生理作用（即经典的 RAS 模型）。尽管如此，随着七肽血管紧张素 1-7 的发现和 RAS 系统的概念的变化，我们所理解的可以降低动脉血压的 RAS 生理系统也发生了巨大的改变。在这篇综述中，我们聚焦在最新发现的 RAS 系统的功能上，特别是这些最新发现的功能的潜在临床意义，尤其是在治疗心血管疾病最新的药理学领域。

背景：氯胺酮常常与改变线粒体功能和氧化应激有关。然而，氯胺酮在体内对线粒体生物能量和氧化还原状态的作用研究甚少。越来越多的证据支持一氧化氮（NO）可能为氯胺酮副作用的调节介质。本文我们研究了 NO 在氯胺酮麻醉中对脑线粒体功能和氧化还原状态的调节机制。

氯胺酮急性损伤大鼠脑内线粒体功能并增强超氧化物歧化酶活性
Acute Ketamine Impairs Mitochondrial Function and Promotes Superoxide Dismutase Activity in the Rat Brain
Venâncio, Carlos DVM, PhD*†; Félix, Luís MSc†; Almeida, Vanessa MSc*; Coutinho, João PhD‡; Antunes, Luis DVM, PhD†; Peixoto, Francisco PhD*; Summavielle, Teresa PhD§
Anesthesia & Analgesia 2015 120 320–328

背景：氯胺酮急性损伤大鼠脑内线粒体功能并增强超氧化物歧化酶活性
方法：成年雄性大鼠分别给予腹腔注射单剂量氯胺酮（50 mg/kg，100 mg/kg，150 mg/kg）或氯胺酮联合 N-硝基-L-精氨酸（3 mg/kg），6 小时后将动物处死。采集脑组织和血标本进行 NO 测定和线粒体分离，并运用多个变量来评价脑线粒体的功能。

结果：氯胺酮可干扰复合物 I 功能，增加耗氧量，使谷氨酸-苹果酸基质氧化磷酸化的效率受损，降低 NADH-泛醌氧化还原酶活性。此外，在给予50 mg/kg 和100 mg/kg 的剂量后，线粒体一氧化氮合酶（mtNOS）活性和血浆 NO 水平有所增加。氯胺酮增加过氧化氢的产生并触发超氧化物歧化酶作用。mtNOS 抑制剂可以通过 N-硝基-L-精氨酸来部分或完全阻止这些效果产生。

结论：氯胺酮急性给药会损害线粒体复合物 I 的作用，增强 mtNOS 活性，增加过氧化氢和 NO 的产生，从而触发超氧化物歧化酶的作用并增强抗氧化活性。本研究结果阐明在氯胺酮麻醉中 NO 的调制作用，为临床作用机制提供依据。

（江凌慧译 薛张纲校）

BACKGROUND: Ketamine is often associated with altered mitochondrial function and oxidative stress. Nevertheless, limited data are still available regarding the in vivo action of ketamine in mitochondrial bioenergetics and redox state. Accumulating evidence supports a role for nitric oxide (NO) as a possible modulator of ketamine’s side effects. In the present study, we investigated the role of NO modulation on ketamine anesthesia at the level of brain mitochondrial function and redox status.

METHODS: Adult male rats received a single dose of ketamine (50, 100, or 150 mg/kg IP) or a combination of ketamine and N-nitro-L-arginine (3 mg/kg IP). Animals were killed 6 hours after treatment. Brain and blood samples were collected for plasma NO determination and mitochondria isolation. Several variables of brain mitochondrial function were evaluated.

RESULTS: Ketamine interfered with complex I function, revealing increased oxygen consumption in state 4, impaired oxidative phosphorylation efficiency of glutamate-malate substrate, and decreased NADH-ubiquinone oxidoreductase activity. In addition, mitochondrial NO synthase (mtNOS) activity and NO plasma levels were increased for the 50 and 100 mg/kg doses. Ketamine administration increased hydrogen peroxide generation and triggered superoxide dismutase activity. All these effects could totally or partially be prevented by mtNOS inhibition through N-nitro-L-arginine.

CONCLUSIONS: Acute ketamine administration impaired the function of mitochondrial complex I leading to increased mtNOS activity, increased generation of hydrogen peroxide and NO, resulting in superoxide dismutase triggering, and improved antioxidant activity. The present findings clarify the role of NO modulation in ketamine anesthesia, providing new data on a relevant clinical mechanism.
Clinically significant gas embolism during laparoscopy is a rare but potentially catastrophic event. Case reports suggest that air, in addition to the insufflation gas, may be present. We studied the effects of equipment design and flushing techniques on the composition of gas present under experimental and routine pediatric surgical conditions. Concentrations of nitrogen (N2), oxygen (O2), and carbon dioxide (CO2) were measured by Raman spectroscopy in gas delivered to and retrieved from a mock peritoneum during simulated laparoscopy. We then analyzed the composition of insufflated and recovered gases during elective laparoscopic procedures conducted with CO2-preflushed and unflushed tubing to determine the presence of significant (10%) quantities of air. In vitro, CO2 was not detected at the distal end of insufflator tubing until after delivery of approximately 0.2 L of gas, and N2 persisted until >0.4 L was delivered, with 40% ± 8% (mean ± SD, range 33%–49%) recovered from the mock peritoneum at the termination of initial insufflation. In clinical studies, preflushing reduced the initial concentration of N2 from 78% ± 0.5% to 23% ± 15%, but >10% air was detected in all subsequent samples, regardless of insufflation technique. Laparoscopic equipment and practice routinely permit delivery of air to the insufflated cavity. Purging the equipment with CO2 reduces but does not eliminate air (N2, O2) within the peritoneal cavity during laparoscopy. Thus, when vascular injury occurs, embolized gases will contain variable quantities of N2, O2, and CO2. As the initial insufflation volume diminishes and approaches the volume of the insufflation tubing, which occurs in infants and young pediatric patients, the concentration of N2 will approximate that of room air in an unflushed system. Small insufflation volumes containing high N2 concentrations can contribute to catastrophic air emboli in neonates and small pediatric patients.

The Effects of Anesthesia, Muscle Paralysis, and Ventilation on the Lung Evaluated by Lung Diffusion for Carbon Monoxide and Pulmonary Surfactant Protein B

Di Marco, Fabiano MD, PhD*; Bonacina, Daniele MD†; Vassena, Emanuele MD†; Arisi, Erik MD†; Apostolo, Anna MD‡; Banfi, Cristina PhD‡; Centanni, Stefano MD, PhD*; Agostoni, Piergiuseppe MD, PhD§∥; Fumagalli, Roberto MD, PhD†¶

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背景：麻醉患者的肺泡-动脉氧分压差通常会增加。本研究旨在评估麻醉，肌松以及短期机械通气对肺功能的影响。

方法：我们选取 45 名接受非胸部手术并且无肺部疾病的病人，测定他们的一氧化碳弥散率（DLCO），包括肺毛细血管血容量（Vc),肺泡-毛细血管屏障的导电性以及肺泡表面活性物质 B 型蛋白（肺泡损伤的标志）
结果：麻醉、肌松以及机械通气都会导致肺泡气体交换受损，伴随着 DM 和 Vc 的下降，麻醉诱导后 DLCO 值也立即下降。然而，DM 的下降是由于肺容量的下降，Vc 的变化并非如此，而是由于 Vc/肺泡容积比值的显著下降。尽管 DLCO 和它的各组成成分在麻醉诱导后立即下降，但在接下来的 1 到 3 小时内它们的数值并没有进一步下降。而表面活性物质 B 型蛋白在麻醉诱导后并没有立立即改变，但在诱导后 1 小时后有所增加，而诱导 3 小时后则进一步增加，肺泡损伤的程度与肺灌注和肺顺应性的下降有关（即潮气量与呼末肺容量之比）。

结论：短时间麻醉及控制通气将会带来：（1）与肺顺应性和肺灌注下降相关的肺泡损伤（2）主要与肺容量下降相关的气体交换障碍，同时也与肺灌注下降有关。

BACKGROUND: An increased alveolar-arterial oxygen tension difference is frequent in anesthetized patients. In this study, we evaluated the effect on the lung of anesthesia, muscle paralysis, and a brief course of mechanical ventilation.

METHODS: Lung diffusion for carbon monoxide (DLCO), including pulmonary capillary blood volume (Vc) and conductance of the alveolar-capillary membrane (DM), and pulmonary surfactant protein type B (a marker of alveolar damage) were measured in 45 patients without pulmonary disease undergoing extrathoracic surgery.

RESULTS: Anesthesia, muscle paralysis, and mechanical ventilation led to impairment of gas exchange, with a reduction of DLCO values immediately after anesthetic induction due to a concomitant reduction of both DM and Vc. While changes in DM were due to the reduction of lung volume, changes in Vc were not limited to volume loss, since the Vc/alveolar volume ratio decreased significantly. Although DLCO and its components decreased immediately after induction, none of the values decreased further at 1 and 3 hours. Surfactant protein type B, however, was unchanged immediately after anesthesia but increased at 1 hour after induction and further increased after 3 hours of anesthesia. The level of alveolar damage correlated with the reduction of lung perfusion and lung dynamic strain (i.e., ratio between tidal volume and end-expiratory lung volume).

CONCLUSIONS: A brief course of anesthesia and controlled ventilation leads to: (1) alveolar damage, which is correlated with lung strain and perfusion, and (2) impaired gas exchange mainly due to volume loss but also to reduced aerated lung perfusion.

Excessive Postoperative Bleeding and Outcomes in Neonates Undergoing Cardiopulmonary Bypass

Guzzetta, Nina A. MD, FAAP*; Allen, Nadine N. MD*; Wilson, Elizabeth C. MD*; Foster, Gregory S. BS†; Ehrlich, Alexandra C. MPH‡; Miller, Bruce E. MD*

Anesthesia & Analgesia 2015 120 405–410

背景：进行心脏手术的新生儿特别易于发生与心肺转流（CPB）相关的凝血功能异常，CPB 后出血的风险增高。不成熟的凝血系统，CPB 预充时严重的血液稀释，CPB 时长时间的低体温，过多的缝合增加了新生儿 CPB 后出血的风险以及术后严重并发症的发生。

方法：我们回顾性分析了在 2010 年 1 月至 2011 年 12 月 31 日之间在 CPB 下行复杂先天性心脏病手术的 169 名新生儿的病史资料。收集并分析了围术期患者的资料，通过测定术后 24h 的胸腔引流量（CTO），CPB 术后输血的需要量以及严重的术后并发症，包括肾功能不全、血液透析、血栓、体外膜肺以及住院死亡率，从而重点分析了 CPB 后的出血量。我们使用 Spearman 相关性分析来确定多个围术期的变量和 24hCTO 及术后血制品需
要量之间的关系。此外，我们使用 logistic 回归分析来确定过量出血（定义为 24h CTO 大于第 75 百分位数）及术后重大并发症之间的关系。

结果：24h CTO 和术后输血量与先天性心脏病手术风险评分（RACHS-1），CPB 时间及低体温之间显著相关。Logistic 回归分析发现 CPB 后过量出血使术后出血（相对危险度 [RR] 12.0；可信区间，1.50–54.69；P=0.02）以及 ECMO（RR 9.95；可信区间，3.07–28.47；P=0.0008）的独立预测因素。RACHS-1 评分是住院死亡率的有意义的预测因素（P=0.03）。

结论：新生儿 CPB 术后过量出血与术后不良事件的增加独立相关，尤其是术后血透以及 ECMO 支持。我们在新生儿中研究的结果与近期一致：在儿童 CPB 后增加的输血需求量与术后重大并发症的发生独立相关。我们的研究结果可以帮助临床医生预测新生儿心肺转流术后潜在并发症的发生以及分配资源以处理这些不良事件。

（杜芳译 薛张纲校）

BACKGROUND: Neonates undergoing cardiac surgery are especially prone to the hemostatic alterations of cardiopulmonary bypass (CPB) and are at high risk for post-CPB bleeding. An immature coagulation system, significant hemodilution from the CPB prime, long CPB times at low temperatures, and extensive suture lines increase neonates' susceptibility to bleeding after CPB. In this study, we examined the relationship between excessive bleeding in neonates after CPB and major postoperative adverse events.

METHODS: We retrospectively reviewed the medical records of 169 neonates who underwent complex congenital heart surgery with CPB between January 1, 2010, and December 31, 2011. Perioperative data were collected and analyzed with specific focus on post-CPB bleeding as measured by 24-hour postoperative chest tube output (CTO), post-CPB transfusion requirements, and major postoperative adverse events, including renal dysfunction, dialysis, thrombosis, extracorporeal membrane oxygenation (ECMO), and in-hospital mortality. We used Spearman correlation to determine correlations between multiple perioperative variables and 24-hour CTO and postoperative blood product requirements. Also, we used logistic regression analysis to determine the association between excessive bleeding (defined as 24-hour CTO >75th percentile) and major postoperative adverse events.

RESULTS: Significant correlations were found between 24-hour CTO and postoperative blood product transfusion with weight, Risk Adjustment for Congenital Heart Surgery (RACHS-1) score, CPB time, and lowest temperature. Logistic regression found that excessive bleeding after CPB was an independent predictor of postoperative dialysis (relative risk [RR] 12.0; confidence interval, 1.50–54.69; P = 0.02) and ECMO (RR 9.95; confidence interval, 3.07–28.47; P = 0.0008). RACHS-1 score was a significant predictor of in-hospital mortality (P = 0.03).

CONCLUSIONS: Excessive postoperative bleeding in neonates after CPB is independently associated with increased adverse events, specifically the need for postoperative dialysis and ECMO support. Our findings in neonates are congruent with other recent research that also has found increasing transfusion requirements after pediatric CPB to be independently associated with an increase in major postoperative adverse events. Our results may aid clinicians in anticipating potential adverse events after neonatal bypass and in allocating the resources necessary to manage these events.

超声用于评估儿科患者喉罩放置位置的一项观察性研究

An Ultrasound Evaluation of Laryngeal Mask Airway Position in Pediatric Patients: An Observational Study

Kim, Jeongmin MD*; Kim, Ji Young MD, PhD†; Kim, Won Oak MD*; Kil, Hae Keum MD*

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背景：对于儿科患者，喉罩（LMA）经常在喉咽处移位而需重新定位。当 LMA 的顶端放置在食管入口时，杓状软骨向前侧移位。当 LMA 旋转或倾斜时，杓状软骨的腹侧运动可能导致杓状软骨的不对称，这一现象可被超声检测到。在本研究中，我们试图用超声评估儿科患者 LMA 移位的发生率。主要研究终点是使用超声和支气管镜检查（FOB）评估喉罩移位的发生率。次要终点是测定使用超声和支气管镜用于发现喉罩移位之间关系，并且归纳出超声诊断 LMA 移位的影像表现。

方法：在这项观察研究包括有 100 名儿童。麻醉诱导后，我们分别在喉罩置入前后将超声探头置于患者颈前得到声门处图像用以评估。纤维支气管镜用于评估喉罩位置（纤支镜喉罩分级及喉罩旋转分级）。放置好喉罩后，可以通过超声就杓状软骨的对称性进行评估。基于声门中线来评估杓状软骨的不对称性，并且相对的杓状软骨被分为 0 到 3 级（超声杓状软骨分级）。我们对超声杓状软骨分级、纤支镜喉罩分级及喉罩旋转分级之间相互关系进行分析。

结果：不对称的杓状软骨的发生率为 50%（95% 可信区间 [CI], 40% - 60%）。对于纤支镜，喉罩移位的发生率为 78%（95% 可信区间，69% - 86%），喉罩旋转分级为 43%（95% 可信区间，33% - 53%）。纤支镜检查喉罩移位的发生率较高（P < 0.0001），但旋转的发生率是相似的（P = 0.395）。超声杓状软骨分级与纤支镜喉罩分级无相关性（P = 0.611），但与喉罩旋转分级呈显著相关（P < 0.0001; 95% CI, 60% - 83%）。用于检测喉罩旋转，超声灵敏度为 93%（95% CI, 81% - 98%），特异度为 82%（95% CI, 70% - 91%）。阳性预测值分别为 80%（95% CI, 66% - 90%）和 94%（95% CI, 83% - 99%），准确度为 87%（95% CI, 79% - 93%）。

结论：虽然超声无法检测喉罩放置的最适宜深度，但我们可以认为超声是一种精确检测喉罩旋转移位的工具。

（黄文惠译 薛张纲校）

BACKGROUND: In children, the laryngeal mask airway (LMA) is frequently displaced within the hypopharynx, resulting in repositioning of the device. When the tip of the LMA is placed in the esophageal inlet, the arytenoids are moved ventrally. When the LMA is rotated or deviated, the ventral movement of the arytenoids may result in asymmetric elevation of an arytenoid cartilage, which can be detected with ultrasound (US). In this study, we sought to estimate the incidence of LMA malposition detected with US in pediatric patients. The primary end point was to compare the incidence of LMA malposition between US and fiber optic bronchoscopy (FOB). The secondary end points were to find the interrelationship between US-detected and FOB-detected malposition of the LMA and to locate the diagnostic performance of US in detecting LMA malposition.

METHODS: In this observational study, 100 consecutive children were included. After anesthetic induction, US evaluation was performed before and after LMA insertion to obtain the glottic image on the anterior neck. FOB was performed to assess LMA position (FOB LMA grade and LMA rotation grade). With a post-LMA US image, the symmetry of the arytenoid cartilages was evaluated. Asymmetrical elevation of an arytenoid cartilage in reference to the glottic midline and the opposite arytenoid cartilage was graded as 0 to 3 (US arytenoid grade). The interrelationships between US arytenoid grade and FOB LMA grade or LMA rotation grade were assessed.

RESULTS: The incidence of asymmetrical elevation of an arytenoid was 50% (95% confidence interval [CI], 40%–60%). On FOB, the incidence of LMA malposition was 78% (95% CI, 69%–86%), and that of LMA rotation was 43% (95% CI, 33%–53%). The incidence of LMA malposition was higher with FOB (P < 0.0001), but the incidence of rotation was similar (P = 0.395). US arytenoid grade did not correlate with FOB LMA grade (P = 0.611) but showed a significant correlation with LMA rotation grade (P < 0.0001; 95% CI, 60%–83%). To detect a rotated LMA, US had a sensitivity of 93% (95% CI, 81%–98%) and a specificity of 82% (95%
The positive and negative predictive values were 80% (95% CI, 66%–90%) and 94% (95% CI, 83%–99%), respectively. The accuracy was 87% (95% CI, 79%–93%).

CONCLUSIONS: Although US could not detect the suboptimal depth of an LMA, US has promise of being an accurate tool in detecting a rotated LMA.

**Irritant Volatile Anesthetics Induce Neurogenic Inflammation Through TRPA1 and TRPV1 Channels in the Isolated Mouse Trachea**

Kichko, Tatjana I. PhD*; Niedermirtl, Florian MD†; Leffler, Andreas MD, PhD‡; Reeh, Peter W. MD, PhD*

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**BACKGROUND:** Irritating effects of volatile general anesthetics on tracheal nerve endings and resulting spastic reflexes in the airways are not completely understood with respect to molecular mechanisms. Neuropeptide release and neurogenic inflammation play an established role.

**METHODS:** The basal and stimulated calcitonin gene-related peptide (CGRP) release from the isolated superfused mouse trachea was analyzed as an index of sensory neuron activation, applying irritant (desflurane and isoflurane) and nonirritant (sevoflurane) volatile anesthetics as stimuli. Various gas concentrations (0.5-, 1-, or 2-fold minimum alveolar concentration [MAC]) and different O2 atmospheres were used for tracheal stimulation at 38°C. Null mutants of the capsaicin receptor TRPV1 and of the chemoreceptor TRPA1, as well as double knockout mice, were used as tissue donors.

**RESULTS:** Desflurane and, less so, isoflurane caused a concentration-dependent tracheal CGRP release, both saturating at 1 MAC (human), that is, 6% and 1.25%, respectively. With desflurane, the O2 concentration (25% or 94%) did not make a difference. Sevoflurane 1 MAC did not activate tracheal CGRP release. TRPV1 mice showed 75% reduced desflurane responses, and TRPA1 and double-null mutants showed no responses at all.

**CONCLUSIONS:** Our results confirm the clinical experience that desflurane is more irritating than isoflurane at equal anesthetic gas concentration, whereas sevoflurane does not activate.
tracheobronchial sensory nerves to release neuropeptides and induce neurogenic inflammation. Both irritant receptor channels, TRPA1 more than TRPV1, are involved in mediating the adverse effects that may even extend to systemic proinflammatory sequelae.

**Isoflurane Protects the Myocardium Against Ischemic Injury via the Preservation of Mitochondrial Respiration and Its Supramolecular Organization**

Lotz, Christopher MD; Zhang, Jun PhD; Fang, Caiyun PhD; Liem, David MD, PhD; Ping, Peipei PhD, FAHA, FISHR

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**BACKGROUND:** Isoflurane has been demonstrated to limit myocardial ischemic injury. This effect is hypothesized to be mediated in part via effects on mitochondria. We investigated the hypothesis that isoflurane maintains mitochondrial respiratory chain functionality, in turn limiting mitochondrial damage and mitochondrial membrane disintegration during myocardial ischemic injury.

**METHODS:** Mice (9–12 weeks of age) received isoflurane (1.0 minimum alveolar concentration) 36 hours before a 30-minute coronary artery occlusion that was followed by 24 hours of reperfusion. Cardiac mitochondria were isolated at a time point corresponding to 4 hours of reperfusion. 2,3,5-Triphenyltetrazoliumchloride staining was used to determine myocardial infarct size. Mitochondrial respiratory chain functionality was investigated using blue native polyacrylamide gel electrophoresis, as well as specific biochemical assays. Mitochondrial lipid peroxidation was quantified via the formation of malondialdehyde; mitochondrial membrane integrity was assessed by Ca2+-induced swelling. Protein identification was achieved via liquid chromatography mass spectrometry/mass spectrometry.

**RESULTS:** Thirty-one mice were studied. Mice receiving isoflurane displayed a reduced myocardial infarct size (P = 0.0011 versus ischemia/reperfusion [I/R]), accompanied by a preserved activity of respiratory complex III (P = 0.0008 versus I/R). Isoflurane stabilized mitochondrial supercomplexes consisting of oligomers from complex III/IV (P = 0.0086 versus I/R). Alleviation of mitochondrial damage after isoflurane treatment was further demonstrated as
decreased malondialdehyde formation ($P = 0.0019$ versus I/R) as well as a diminished susceptibility to Ca$^{2+}$-induced swelling ($P = 0.0010$ versus I/R).

CONCLUSIONS: Our findings support the hypothesis that isoflurane protects the heart from ischemic injury by maintaining the in vivo functionality of the mitochondrial respiratory chain. These effects may result in part from the preservation of mitochondrial supramolecular organization and minimized oxidative damage, circumventing the loss of mitochondrial membrane integrity.

2-脱氧-D-葡萄糖增强小鼠麻醉作用
2-Deoxy-D-Glucose Enhances Anesthetic Effects in Mice

Wang, Hui MD, PhD*†; Xu, Zhipeng MD, PhD†‡; Wu, Anshi MD, PhD*; Dong, Yuanlin MD, MS*; Zhang, Yiying MD, PhD*; Yue, Yun MD, MS; Xie, Zhongcong MD, PhD†

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BACKGROUND: The mechanisms of general anesthesia by volatile drugs remain largely unknown. Mitochondrial dysfunction and reduction in energy levels have been suggested to be associated with general anesthesia status. 2-Deoxy-D-glucose (2-DG), an analog of glucose, inhibits hexokinase and reduces cellular levels of adenosine triphosphate (ATP). 3-Nitropropionic acid is another compound which can deplete ATP levels. In contrast, idebenone and L-carnitine could rescue deficits of energy. We therefore sought to determine whether 2-DG and/or 3-nitropropionic acid can enhance the anesthetic effects of isoflurane, and whether idebenone and L-carnitine can reverse the actions of 2-DG.

METHODS: C57BL/6J mice (8 months old) received different concentrations of isoflurane with and without the treatments of 2-DG, 3-nitropropionic acid, idebenone, and L-carnitine.
Isoflurane-induced loss of righting reflex (LORR) was determined in the mice. ATP levels in H4 human neuroglioma cells were assessed after these treatments. Finally, 31P-magnetic resonance spectroscopy was used to determine the effects of isoflurane on brain ATP levels in the mice.

RESULTS: 2-DG enhanced isoflurane-induced LORR (P = 0.002, N = 15). 3-Nitropropionic acid also enhanced the anesthetic effects of isoflurane (P = 0.005, N = 15). Idebenone (idebenone + saline versus idebenone + 2-DG: P = 0.165, N = 15), but not L-carnitine (L-carnitine + saline versus L-carnitine + 2-DG: P < 0.0001, N = 15), inhibited the effects of 2-DG on enhancing isoflurane-induced LORR in the mice, as evidenced by 2-DG not enhancing isoflurane-induced LORR in the mice pretreated with idebenone. Idebenone (idebenone + saline versus idebenone + 2-DG: P = 0.177, N = 6), but not L-carnitine (L-carnitine + saline versus L-carnitine + 2-DG: P < 0.0001, N = 15), also mitigated the effects of 2-DG on reducing ATP levels in cells, as evidenced by 2-DG not decreasing ATP levels in the cells pretreated with idebenone. Finally, isoflurane decreased ATP levels in both cultured cells and mouse brains (β-ATP: P = 0.003, N = 10; β-ATP/phosphocreatine: P = 0.006, N = 10; β-ATP/inorganic phosphate: P = 0.001, N = 10).

CONCLUSIONS: These results from our pilot studies have established a system and generated a hypothesis that 2-DG enhances anesthetic effects via reducing energy levels. These findings should promote further studies to investigate anesthesia mechanisms.

氧供的有效性和二氧化碳波形的可靠性：4种鼻导管的交叉比较

The Effectiveness of Oxygen Delivery and Reliability of Carbon Dioxide Waveforms: A Crossover Comparison of 4 Nasal Cannulae

Ebert, Thomas J. MD, PhD; Novalija, Jutta MD, PhD; Uhrich, Toni D. MS; Barney, Jill A. MS

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背景：有效氧输送和准确的呼气末 CO2（ETCO2）采样是对呼吸功能受损患者鼻导管（NCs）吸氧基本要求。本实验研究了4种NC设计：分叉鼻塞（NPs）供氧同时在两侧均有CO2传感器（Hudson）,独立的O2/CO2 NPs(Salter),CO2传感器位于NPs上，在NPs外通过多喷口（Oridion）和双喷口（Medline）进行氧供。本研究假设NCs之间设计的差异会影响氧供和ETCO2检测。

方法：45名18至35岁的健康志愿者参与了这项无限制、随机、区组设计试验,每个受试者在一个试验阶段按照他们的意愿控制4种NC的4个交叉研究周期。监测包括心电图,由Hauge气道的后咽O2抽样（Sharn麻醉产品,Tampa,弗罗里达州）和NCETCO2。在11名志愿者中,桡动脉血液采样用于检测O2和CO2分压(PaO2和PaCO2)。在吸入空气和2、4、6Lpm的新鲜氧气（FGFs）期间,依照随机化原则,提供每种NC,收集每2分钟数据（ETCO2,呼后O2,PaO2和PaCO2）。统计分析采用SAS分析软件,9.3版本及JMP统计软件,11版本(SAS Institute Inc., Cary, NC), P<0.05为统计学差异。

结果：血气分析表明每次实验期间PaCO2稳态值与基线值无差异。不同NC间,在基线和2LpmO2时PaO2没有差异。吸氧4Lpm时,独立NPs和分叉NCs的PaO2显著高于多喷口NC。吸氧2,4,6Lpm时,独立NPs的呼后O2显著高于应用多喷口和双喷口NCs。吸氧2Lpm时,分叉NPs的呼后O2显著高于应用多喷口NC；并在吸氧4,6Lpm时显著高于呼后O2。分叉NPs的ETCO2显著低于其他3种NCs,这与在较高FGF时难以追踪CO2相一致。

结论：NCs为肺功能受损患者提供了额外的O2吸入。ETCO2准确测定有利于评估呼吸频率并确定在肺换气不足时是否发生CO2潴留。这些发现表明应用分叉鼻塞（NPs）的鼻导管（NC）在氧供时是最有效的，并且在较高FGFs时提供最可靠且稳定的CO2波形。

（王筱婧 译 陈杰 校）
BACKGROUND: Effective O2 delivery and accurate end-tidal CO2 (ETCO2) sampling are essential features of nasal cannulae (NCs) in patients with compromised respiratory status. We studied 4 NC designs: bifurcated nasal prongs (NPs) with O2 delivery and CO2 sensing in both NPs (Hudson), separate O2/CO2 NPs (Salter), and CO2 sensing in NPs with cloud O2 delivery outside the NPs via multi vents (Oridion) and dual vents (Medline). We hypothesized that design differences between NCs would influence O2 delivery and ETCO2 detection.

METHODS: Forty-five healthy volunteers, 18 to 35 years, participated in an unrestricted, randomized block design, each subject serving as their own control in a 4-period crossover study design of 4 NCs during one session. Monitoring included electrocardiogram, posterior pharynx O2 sampling from a Hauge Airway (Sharn Anesthesia Products, Tampa, FL), and NC ETCO2. In 11 volunteers, radial artery blood was sampled from a catheter for partial pressures of O2 and carbon dioxide (PaO2 and PaCO2) determination. Per randomization, each NC was positioned, and data were collected over 2 minutes (ETCO2, pharyngeal O2, PaO2, and PaCO2) during room air and during O2 fresh gas flows (FGFs) of 2, 4, and 6 Lpm. Statistical analyses were performed with SAS Analytics Pro, Version 9.3, and JMP Statistical Software, Version 11 (SAS Institute Inc., Cary, NC), significance at P < 0.05.

RESULTS: Blood gas analyses indicated PaCO2 during steady state at each experimental time period remained unchanged from physiologic baseline. PaO2 did not differ between NC devices at baseline or 2 Lpm O2. The PaO2 at 4 Lpm from the separate NPs and bifurcated NCs was significantly higher than the multi-vented NC. Pharyngeal O2 with the NC with separate NPs was significantly higher than multivented and dual-vented cloud delivery NCs at 2, 4, and 6 Lpm FGF. Pharyngeal O2 with the NC with bifurcated NPs was significantly higher than the multivented NC at 2 Lpm, and higher than cloud delivery NCs at 4 and 6 Lpm FGF. ETCO2 was significantly lower with the NC with bifurcated NPs compared to the other 3 NCs, consistent with errant CO2 tracings at higher FGF.

CONCLUSIONS: NCs provide supplemental inspired O2 concentrations for patients with impaired pulmonary function. Accurate measures of ETCO2 are helpful in assessing respiratory rate and determining whether CO2 retention is occurring from hypoventilation. These findings suggest the NC with separate NPs was the most effective in delivering O2 and the most consistent at providing reliable CO2 waveforms at higher FGFs.

在国家麻醉临床预后登记中观察到的围术期心脏骤停发生率和危险因素
The Incidence and Risk Factors for Perioperative Cardiac Arrest Observed in the National Anesthesia Clinical Outcomes Registry

Nunnally, Mark E. MD, FCCM*; O’Connor, Michael F. MD, FCCM†; Kordylewski, Hubert PhD‡; Westlake, Benjamin BS†; Dutton, Richard P. MD, MBA*‡

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背景：在手术室和复苏室里，对于经严密监测的手术患者，心脏骤停是一个罕见但重要的事件。近期发表文献报道了后续住院期间而非围术期手术患者心脏骤停的发生率。本文假设在此期间（围术期和复苏期）心脏骤停发生率较报道的住院期间发生率更低。

方法：抽取 2010 年至 2013 年国家麻醉临床预后登记的所有心脏骤停和急性围手术期死亡的数据并且分析麻醉相关危险因素。比较其与发表的术后住院期间心脏骤停发生率差异性。

结果：总体而言，心脏骤停的风险为 5.6／10000 例，低于先前报道的手术患者住院期间总体死亡率，且心脏骤停相关死亡率为 58.4%。心脏骤停的发生率随着年龄和 ASA 分级增加而增加。男性心脏骤停发生率和死亡率更高。
Background: Cardiac arrest is a rare but important event in the operating room and postanesthesia care unit, when surgical patients are most intensively monitored. Several recent publications have reported the rate of cardiac arrest in surgical patients during the subsequent hospital stay but have not uniquely identified the immediate perioperative period. We hypothesized that cardiac arrest during this time (intraprocedure and postanesthesia care) would occur at a lower frequency than that described for inpatient hospital care in the available literature.

Methods: We extracted data from all cardiac arrests and immediate perioperative deaths reported to the National Anesthesia Clinical Outcomes Registry for the period from 2010 to 2013 and analyzed for anesthesia-related risk factors. We compared these data to published rates of in-hospital cardiac arrest after surgery.

Results: Overall, the risk of cardiac arrest was 5.6 per 10,000 cases, which is less than in previous reports of in-hospital arrests in surgical patients overall, with an associated mortality from the arrest of 58.4%. The rate of cardiac arrest increased with age and ASA physical status. The rate of cardiac arrest was significantly higher for males, as was the mortality.

Conclusions: The National Anesthesia Clinical Outcomes Registry is an emerging resource for examination of perioperative and anesthesia-related outcomes. Cardiac arrest is less frequent in the periprocedural setting than later in the hospital course, with most arrests predictably occurring in patients with ASA physical status III–V. The finding of increased risk of mortality in male patients cannot be readily explained and should prompt future research attention.

Crystalloids Versus Colloids: Exploring Differences in Fluid Requirements by Systematic Review and Meta-Regression

Orbegozo Cortés, Diego MD; Gamarano Barros, Teresa MD; Njimi, Hassane MSc, PhD; Vincent, Jean-Louis MD, PhD

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Background: Fluid balance and outcome. The clinical relevance of the comparative fluid outcome is related to the clinical parameters. Smaller molecules stayed in the circulation longer than the crystalloid, but the colloid fluid may achieve similar hemodynamic goals with less fluid. However, recent clinical data challenge this physiological concept, as studies have reported lower-than-expected crystalloid-to-colloid ratios in different patient populations. The aim of this systematic review was to compare the crystalloid-to-colloid ratio in various patient populations and to identify factors that influence this ratio by meta-regression analysis.

Methods: In this study, we searched MEDLINE, EMBASE, and CENTRAL to identify studies that compared crystalloid and colloid fluid administration in various patient populations. The crystalloid-to-colloid ratio was calculated for each study, and the meta-analysis was performed using a random-effects model. The crystalloid-to-colloid ratio was then compared across different patient populations and between studies with different fluid management strategies using meta-regression analysis.

Results: A total of 976 studies were identified, and 48 studies were included in the meta-analysis. The crystalloid-to-colloid ratio was significantly lower in studies with higher crystalloid-to-colloid ratio (P = 0.001). The crystalloid-to-colloid ratio was also significantly lower in studies with higher plasma volume expansion (P = 0.001). The crystalloid-to-colloid ratio was not significantly different between studies with different fluid management strategies (P = 0.05).

Conclusion: The crystalloid-to-colloid ratio is significantly lower in studies with higher crystalloid-to-colloid ratio, and the crystalloid-to-colloid ratio is also significantly lower in studies with higher plasma volume expansion. Further studies are needed to identify the factors that influence the crystalloid-to-colloid ratio.
**BACKGROUND:** Positive fluid balance has been associated with worse outcomes, and knowledge of differences in the amounts of different types of fluid needed to achieve the same end points may have important clinical implications. Large molecules persist longer in the blood vessels than smaller molecules, such that less IV colloid may be needed to achieve similar hemodynamic end points compared with crystalloid. Recent clinical data have, however, challenged this physiological concept, with investigators reporting lower-than-expected crystalloid/colloid ratios in various populations.

**METHODS:** We performed a systematic search in MEDLINE, EMBASE, and CENTRAL up to December 18, 2013, to retrieve all studies comparing (any) crystalloid with (any) colloid in all types of patients. The crystalloid/colloid ratio was calculated for each study. Descriptive analysis was performed for all studies, and a meta-analysis was performed in those studies reporting full data (in terms of means and standard deviations) of infused fluid volumes. Studies were grouped according to study and population characteristics. A meta-regression analysis was then performed to evaluate some of the possible reasons for differences in crystalloid/colloid ratios across studies.

**RESULTS:** From 976 studies, 48 were retained for the final analysis; 24 of the studies had sufficient data for meta-analysis. The crystalloid/colloid ratio across all the studies included in the meta-analysis was 1.5 (95% confidence interval, 1.36–1.65) with marked heterogeneity among studies (I² = 94%). From the meta-regression analysis, decade of publication across all publications (P = 0.001) and concentration (tonicity) in the subgroup of albumin studies (P = 0.001) were associated with the administered crystalloid/colloid ratio. The reduction in heterogeneity among studies for all publications in the meta-regression was minimal, with the maximal decrease obtained when decade of publication was considered (R² = 12%).

**CONCLUSIONS:** Greater fluid volumes are required to meet the same targets with crystalloids than with colloids, with an estimated ratio of 1.5 (1.36–1.65), but there is marked heterogeneity among studies. The crystalloid/colloid ratio seems to have decreased over the years, and differences in ratios are correlated with the concentration of albumin solutions; however, the main reasons behind the high heterogeneity among studies remain unclear.

**靶向治疗对儿科肺动脉高压患者围术期发病率和死亡率影响**

**The Impact of Targeted Therapies for Pulmonary Hypertension on Pediatric Intraoperative Morbidity or Mortality**

Taylor, Katherine BMed (Hons), BA, FANZCA; Moulton, Dagmar MD; Zhao, Xiu Yan MSc; Laussen, Peter MBBS, FCICM

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**背景:** 肺动脉高压（PHT）是麻醉期间主要不良事件的重要风险因素，据报道其发生率为5%至7%，并可继发急性肺动脉高压危象或右心室缺血。PHT新型治疗方法已可减少死亡率。在此次单中心研究中，研究者统计了在当前治疗PHT的策略下麻醉期间主要和次要事件发生率。

**方法:** 研究者回顾了2008年到2012年间PHT患儿进行非心肺转流手术的记录。研究者记录了麻醉前的临床主要症状，体征和研究数据，并收集了围术期并发症和死亡（至术后7天）的发生率及类型。
BACKGROUND: Pulmonary hypertension (PHT) is a significant risk factor for major adverse events during anesthesia, with a reported incidence of 5% to 7%, secondary to acute pulmonary hypertensive crises or right ventricular ischemia. Newer therapies for treating PHT have reduced mortality. In this single-center study, we investigated the frequency of major and minor events during anesthesia under the current strategies to manage PHT.

METHODS: We reviewed the records of children with PHT who underwent noncardiopulmonary bypass procedures from 2008 to 2012. Clinically important symptoms, physical signs, and results of investigations present before anesthesia were recorded. The incidence and type of intraoperative complications and death (up to 7 days) were collected.

RESULTS: Data were collected for 122 patients undergoing 284 procedures. Minor (3.9%) and major (3.2%) complication rates were unchanged from previous publications. The etiology of PHT was not significant for complications (P = 0.14). Disease-modifying agents were not associated with reduced complications: 4.1% in treated versus 8.6% untreated (all P > 0.14). Patients receiving home oxygen had more complications (P = 0.02). Multiple logistic regression identified age and degree of PHT as significant predictors of complications (all P ≤ 0.03).

CONCLUSIONS: The risk for adverse events during anesthesia in patients with PHT remains high, despite newer disease-modifying treatments. Risk factors for complications include age and severity of PHT.
结果：鞘内注射安非他酮产生剂量依赖性抗痛觉过敏效应 (3、10、30 和 100 μg, P < 0.001)。使用安非他酮注射前15分钟α2-肾上腺素受体拮抗剂咪唑克生(3、10和30 μg, P < 0.001)和D2受体拮抗剂舒必利(3、10和30 μg, P < 0.001)进行鞘内预处理可剂量依赖性地逆转此效应(30μg组)。微量透析表明在鞘内注射安非他酮(30 μg)后脊髓背角去甲肾上腺素和多巴胺浓度增加(分别 P < 0.001, P = 0.001)。此外脊髓背角的去甲肾上腺素和多巴胺含量在SNL 2周后增加(分别 P < 0.001, P = 0.044),然后逐渐下降。

结论：这些研究结果表明：下行抑制通路，如去甲肾上腺素和多巴胺系统，其适应性与神经病理性疼痛的维持相关，脊髓去甲肾上腺素和多巴胺在神经病理性疼痛中起到抑制作用。

(秦懿译 陈杰校)

BACKGROUND: Antidepressants are often used for the treatment of neuropathic pain, and their analgesic effects rely on increased noradrenaline and serotonin levels in the spinal cord. Clinical studies have also shown that bupropion, a dopamine and noradrenaline reuptake inhibitor, has strong efficacy in neuropathic pain; however, the role of spinal cord dopamine in neuropathic pain is unknown. We hypothesized that bupropion inhibits neuropathic pain by increasing noradrenaline and dopamine in the spinal cord. In the present study, we determined the efficacy and underlying mechanisms of intrathecal administration of bupropion in a rat model of neuropathic pain.

METHODS: Male Sprague-Dawley rats were anesthetized, and right L5 spinal nerve ligation (SNL) was performed to produce mechanical hyperalgesia of the hindpaw. Withdrawal threshold to a paw pressure test was measured before and after intrathecal administration of bupropion, without or with intrathecal antagonists for α2-adrenoceptors and dopamine D2 receptors. In vivo microdialysis was performed in the dorsal horn of the lumbar spinal cord to measure noradrenaline and dopamine concentrations after intrathecal injection of bupropion. We also measured the noradrenaline and dopamine contents in the ipsilateral dorsal lumbar spinal cord in normal rats and in rats 2, 3, and 4 weeks after SNL.

RESULTS: Intrathecal injection of bupropion produced a dose-dependent antihyperalgesic effect (3, 10, 30, and 100 μg, P < 0.001). The effect (30 μg) was dose-dependently reversed by intrathecal pretreatment (15 minutes before bupropion injection) with the α2-adrenoceptor antagonist idazoxan (3, 10, and 30 μg, P < 0.001) and D2 receptor antagonist sulpiride (3, 10, and 30 μg, P < 0.001). Microdialysis revealed that noradrenaline and dopamine concentrations in the spinal dorsal horn were increased after intrathecal injection of bupropion (30 μg, P < 0.001 and P = 0.001, respectively). Furthermore, the noradrenaline and dopamine contents in the spinal dorsal horn were increased 2 weeks after SNL (P < 0.001 and P = 0.044, respectively) and then decreased gradually.

CONCLUSIONS: These findings suggest that plasticity of descending inhibitory pathways such as the noradrenaline and dopamine systems contributes to the maintenance of neuropathic pain and that spinal cord noradrenaline and dopamine both play an inhibitory role in neuropathic pain.

A Pilot Study on the Effect of Nasal Continuous Positive Airway Pressure on Arterial Partial Pressure of Carbon Dioxide During Spinal Anesthesia with Intravenous Sedation for Total Knee Arthroplasty

Smith, Stephen B. MD*; Carr, Shawn CRNA*; Psikula, Stacey CRNA*; Das, Anita PhD1; Grichnik, Katherine MD, MS

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BACKGROUND: Deep sedation of surgical patients may be associated with hypoventilation, airway collapse, and hypercarbia, although the extent of hypercarbia is rarely quantified. In this prospective, randomized, controlled clinical pilot study, we assessed the efficacy of nasal continuous positive airway pressure (nCPAP) for reducing arterial partial pressure of carbon dioxide (PaCO2) among deeply sedated, spontaneously ventilated patients undergoing total knee arthroplasty (TKA) under subarachnoid block (SAB), versus standard airway management in a control group.

METHODS: Forty ASA status I–III patients underwent deep sedation with propofol to level 2 on the Modified Observers Assessment of Alertness/Sedation Scale during TKA performed under SAB. Nasal or oral airways were placed at the discretion of the anesthesia team, but they were not used in conjunction with nCPAP. Baseline arterial blood gas analysis (ABG-1) was performed after Modified Observers Assessment of Alertness/Sedation Scale level 2 was reached. Patients were then randomized to receive nCPAP (nCPAP group, N = 20) or standard oxygen mask management (control group, N = 20). A second ABG (ABG-2) was performed 30 minutes later to assess the effect of nCPAP on PaCO2. The primary efficacy end point was change in PaCO2 from baseline to the 30-minute time point.

RESULTS: Baseline (ABG-1) PaCO2 values were similar between nCPAP and control groups with median values of 54.5 and 56.1 mmHg, respectively. There was a significant decline in PaCO2 in the nCPAP group (median of −4.6 mm Hg [10th–90th quantile, −14.55 to 3.85]) as compared with the control group (median of 0.95 mm Hg [−4.75 to 9.85]; P = 0.015; 95% confidence interval [CI] for location shift = −9.5 to −1.3). Within the control group, PaCO2 was similar from ABG-1 to ABG-2 (median [10th–90th quantile] = 56.1 mm Hg [47.2–67.0] vs 56.6 mm Hg [46–68.8]; P = 0.52; 95% CI for the median = −3.4 to 3.4). Forty percent of all patients received an airway before ABG-1. The baseline PaCO2 value of patients receiving an airway was not different from that of patients without an airway (median [10th–90th quantile] = 56.0 mm Hg [46.0–68.4] vs 54.1 mm Hg [45.6–65.6], respectively; P = 0.33; 95% CI for location shift = −2.30 to 7.20).
CONCLUSIONS: Deep sedation of TKA patients during SAB resulted in moderate hypercarbia (mean and median PaCO2 = 55). There was a trend showing that nCPAP treatment reduced PaCO2 versus treatment for control group patients receiving standard airway management; however, estimated treatment difference varied widely, from 1.4 to 12.6 mm Hg. Among control group patients, the initial PaCO2 during deep sedation was similar to the PaCO2 when measured after a 30-minute period of continued deep sedation. Finally, baseline PaCO2 among deeply sedated patients who received an airway was not different from that of patients who did not receive an airway.

呼气末正压通气在外科领域条件下对功能性内窥镜鼻窦手术的影响

The influence of positive end-expiratory pressure on surgical field conditions during functional endoscopic sinus surgery.

DeMaria S¹, Govindaraj S, Huang A, Hyman J, McCormick P, Lin HM, Levine A. Anesthesia & Analgesia 2015 120 305–310

背景：功能性内窥镜鼻窦手术（FESS）是鼻腔鼻窦疾病外科治疗中的中流砥柱。这个手术也有一定的风险。大部分风险与手术的质量有关。因此，研究这种能提高手术质量的机制很重要。我们试图确定呼气末正压通气（PEEP）是否对急诊手术患者的手术质量产生有害的影响。

方法：407例患者随机采用5 cm H2O PEEP或零 PEEP通气策略。手术野的质量每15分钟用一个有效的手术评分方法进行测量。

结果：PEEP 的加入没有对术后质量发生任何可衡量的效果（比值比 OR（95%置信区间 CI）= 1.06，P = 0.895（0.44-2.58）侧面 1；或（95% CI）= 0.56，P = 0.356（0.16-1.93）侧面 2）。吸气峰压确实影响手术成绩。每增加 1 cm H2O 的压力，超过 15 cm H2O 的总压力将贡献于增加更高的手术得分率。每增加 1 cm H2O 的吸气压，将有超过15 cm H2O 用于增加手术得分。

结论：在鼻内镜手术中通过增加平均吸气压力低于 15 cm H2O 的 PEEP，可以避免手术野的模糊程度。

（王晓莉译 李士通审校）

BACKGROUND: Functional endoscopic sinus surgery (FESS) is the mainstay of surgical treatment for sinonasal disease. This surgery carries certain risks. Most of these risks relate to the quality of the surgical field. Thus, mechanisms by which the surgical field can be improved are important to study. We sought to determine whether positive end-expiratory pressure (PEEP) had a deleterious effect on the quality of the surgical field in patients undergoing primary FESS.

METHODS: Forty-seven patients were randomized to a ventilation strategy using either 5 cm H2O of PEEP or zero added PEEP. The quality of the surgical field was measured every 15 minutes using a validated surgical scoring method.

RESULTS: The addition of PEEP did not have any measurable effect on the surgical field scores after onset of surgery (odds ratio [OR] (95% confidence interval [CI]) = 1.06 (0.44-2.58), P = 0.895 for side 1; OR (95% CI) = 0.56 (0.16-1.93), P = 0.356 for side 2). The peak inspiratory pressure did have an effect on surgical grades. Every cm H2O of added pressure over 15 cm H2O total pressure contributing to increased odds of higher surgical field score. For each cm H2O increase in inspiratory pressure above 15 cm H2O increased the surgical field score (OR [95% CI] 1.13 [1.04-1.22], P = 0.002).
CONCLUSIONS: During FESS surgery if PEEP is added, it is important to keep the mean inspiratory pressure below 15cm H2O to avoid worsening surgical field conditions.

Propofol (Diprivan®) and Intralipid® Exacerbate Insulin Resistance in Type-2 Diabetic Hearts by Impairing GLUT4 Trafficking.

Lou PH¹, Lucchinetti E, Zhang L, Affolter A, Gandhi M, Zhakupova A, Hersberger M, Hornemann T, Clanachan AS, Zaugg M.

Anesthesia & Analgesia 2015 120 329–340

BACKGROUND: The IV anesthetic, propofol, when administered as fat emulsion-based formulation (Diprivan) promotes insulin resistance, but the direct effects of propofol and its solvent, Intralipid, on cardiac insulin resistance are unknown.

METHODS: Hearts of healthy and type-2 diabetic rats (generated by fructose feeding) were aerobically perfused for 60 minutes with 10 μM propofol in the formulation of Diprivan or an equivalent concentration of its solvent Intralipid (25 μM) ± insulin (100 mU•L). Glucose uptake, glycolysis, and glycogen metabolism were measured using [H]glucose. Activation of Akt, GSK3β, AMPK, ERK1/2, p38MAPK, S6K1, JNK, protein kinase C0 (PKC0), and protein kinase CβII (PKCβII) was determined using immunoblotting. GLUT4 trafficking and phosphorylations of insulin receptor substrate-1 (IRS-1) at Ser307 (H312), Ser1100 (H1101), and Tyr608 (hTyr612) were measured. Mass spectrometry was used to determine acylcarnitines, phospholipids, and sphingolipids.

RESULTS: Diprivan and Intralipid reduced insulin-induced glucose uptake and redirected glucose to glycogen stores in diabetic hearts. Reduced glucose uptake was accompanied by lower GLUT4 trafficking to the sarcolemma. Diprivan and Intralipid inactivated GSK3β but activated AMPK and ERK1/2 in diabetic hearts. Only Diprivan increased phosphorylation of Akt(Ser473/Thr308) and translocated PKC0 and PKCβII to the sarcolemma in healthy hearts, whereas it activated S6K1 and p38MAPK and translocated PKCβII in diabetic hearts.
Furthermore, only Diprivan phosphorylated IRS-1 at Ser1100(h1101) in healthy and diabetic hearts. JNK expression, phosphorylation of Ser307(h312) of IRS-1, and PKCθ expression and translocation were increased, whereas GLUT4 expression was reduced in insulin-treated diabetic hearts. Phosphatidylglycerol, phosphatidylethanolamine, and C18-sphingolipids accumulated in Diprivan-perfused and Intralipid-perfused diabetic hearts.

CONCLUSIONS: Propofol and Intralipid promote insulin resistance predominantly in type-2 diabetic hearts.

BACKGROUND: Many airway management guidelines include the use of airway exchange catheters (AECs). There are reports, however, of harm from their use, from both malpositioning and in particular from the administration of oxygen via an AEC leading to barotrauma.

METHODS: We used an in vitro pig lung model to investigate the safety of administering oxygen at 4 different flow rates from a high-pressure source via 2 different AECs: a standard catheter and a soft-tipped catheter. Experiments were performed with the catheters positioned either above the carina or below it at the first point of resistance to advancement (hold-up). The experiments were then repeated to produce a series of 32 cases.

RESULTS: With an AEC positioned above the carina, we did not observe macroscopic lung damage after the administration of oxygen. The administration of oxygen through an AEC positioned below the carina resulted in macroscopic barotrauma regardless of the rate of oxygen delivery. Increasing speed of oxygen flow led to faster and more extensive damage. Use of an “injector” at 2.5 or 4 bar led to instantaneous macroscopic lung damage and advancement of the AEC through the lung tissue. Our observations were the same when both types of AECs were used.

在一系列体外的实验中发现硬质和软质气管交换导管所造成的明显的肺损伤

Macroscopic Barotrauma Caused by Stiff and Soft-Tipped Airway Exchange Catheters: An In Vitro Case Series

Axe, Robert FRCA*; Middleditch, Alex FRCA*; Kelly, Fiona E. MRCP, FRCA, DICM*; Batchelor, Tim J. FRCS (CTh); Cook, Tim M. FRCA*

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CONCLUSIONS: Our results are consistent with reports of harm during the use of AECs and demonstrate the risk of administering oxygen through these devices when they are positioned below the carina. An indicator, ideally made on an AEC at the time of manufacture and designed to lie at the same level as the teeth, may be useful in preventing the insertion of that AEC beyond the level of the carina and improve the safety of using such devices.

The Effects of Exogenous Surfactant Treatment in a Murine Model of Two-Hit Lung Injury

Zambelli, Vanessa PhD*; Bellani, Giacomo MD, PhD†; Amigoni, Maria MD‡; Grassi, Alice MD*; Scanziani, Margherita MD†; Farina, Francesca PhD*; Latini, Roberto MD†; Pesenti, Antonio MD†‡
Anesthesia & Analgesia 2015 120 381–388

BACKGROUND: Because pulmonary endogenous surfactant is altered during acute respiratory distress syndrome, surfactant replacement may improve clinical outcomes. However, trials of surfactant use have had mixed results. We designed this animal model of unilateral (right) lung injury to explore the effect of exogenous surfactant administered to the injured lung on inflammation in the injured and noninjured lung.

METHODS: Mice underwent hydrochloric acid instillation (1.5 mL/kg) into the right bronchus and prolonged (7 hours) mechanical ventilation (25 mL/kg). After 3 hours, mice were treated with 1 mL/kg exogenous surfactant (Curosurf®) (surf group) or sterile saline (NaCl 0.9%) (vehicle group) in the injured (right) lung or did not receive any treatment (hydrochloric acid, ventilator-induced lung injury). Gas exchange, lung compliance, and bronchoalveolar
inflammation (cells, albumin, and cytokines) were evaluated. After a significant analysis of variance (ANOVA) test, Tukey post hoc test was used for statistical analysis.

RESULTS: At least 8 to 10 mice in each group were analyzed for each evaluated variable. Surfactant treatment significantly increased both the arterial oxygen tension to fraction of inspired oxygen ratio and respiratory system static compliance ($P = 0.027$ and $P = 0.007$, respectively, for surf group versus vehicle). Surfactant therapy increased indices of inflammation in the acid-injured lung compared with vehicle: inflammatory cells ($685 [602–773] \times 1000 \text{mL}$ and $216 [125–305] \times 1000 \text{mL}$, respectively; $P < 0.001$) and albumin in bronchoalveolar lavage (BAL) ($1442 ± 588$ and $743 ± 647 \text{μg/mL}$, respectively; $P = 0.027$). These differences were not found ($P = 0.96$ and $P = 0.54$) in the contralateral (uninjured) lung (inflammatory cells $131 [78–195]$ and $119 [87–149] \times 1000 \text{mL}$ and albumin $135 ± 100$ and $173 ± 115 \text{μg/mL}$).

CONCLUSIONS: Exogenous surfactant administration to an acid-injured right lung improved gas exchange and whole respiratory system compliance. However, markers of inflammation increased in the right (injured) lung, although this result was not found in the left (uninjured) lung. These data suggest that the mechanism by which surfactant improves lung function may involve both uninjured and injured alveoli.

**由于小儿围手术期呼吸事件产生的医院额外费用和住院时间**

Excess Costs and Length of Hospital Stay Attributable to Perioperative Respiratory Events in Children

Oofuvong, Maliwan MD*; Geater, Alan Frederick PhD†; Chongsuvivatwong, Virasakdi MD, PhD‡; Chanchayanon, Thavat MD; Sriyanaluk, Bussarin; Saefung, Boonthida; Nuanjun, Kanjana

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**背景**：由于围手术期呼吸事件导致多余的住院费用和住院时间的认知在医院规划是有用的。在该项研究中我们在泰国南部的一家三级医院，比较小儿有围手术期呼吸事件和没有该事件成本（多余的住院费用和间接费用）和住院长度。

**方法**：对 2012 十一月到 2013 十二月在 songklanagarind 儿童医院年龄<15 岁患者，全麻儿童进行前瞻性队列研究。孩子们没有任何事前匹配（1:1）使用一个随机选择的程序对门诊/住院，手术类型，手术费（泰铢），ASA 分级，年龄<9 岁，和不同的手术<6 个月的时间进行分组。主要终点是手术后的住院费用和住院天数。手术后住院天数、多余的住院费用和间接费用、组与组之间的父母的收入损失进行比较采用 Wilcoxon 符号秩检验。术后住院天数比较采用 McNemar 检测；障碍模型被用来预测术后住院天数和住院天数。多个混合效应线性回归被用来确定预测的调整多余的住院费用和间接费用

**结论**：研究共包括 430 名儿童（215 配对）。更多的呼吸事件的孩子需要术后住院（81% vs 72%，$P = 0.004$），并且有较长的住院天数术后（中位数[四分位数]：1 [1] 1 [0 VS 3.5–2 ]：$P < 0.001$）和产生较高的超额成本（$P < 0.001$）而不是间接成本（$P = 0.23$）。在多重分析中，围手术期呼吸事件是重要的预测因子，预测手术后住院时长（优势比，2.56；95%置信区间，）成本（成本比 1.30 [1.12, 1.53 ]）和间接成本（成本比 1.58 [ 1.20, 2.08 ]），可以调整病人的麻醉特点。普遍覆盖（74%）与 35% 和 64% 更高的超额成本与审计总署相比较（17%）和自付（7%），分别为（$P = 0.003$）。

（田园译 李士通审校）

BACKGROUND: Knowledge of the excess hospital costs and prolonged length of stay attributable to perioperative respiratory event (PRE) in pediatric anesthesia is useful for hospital planning. In this study, we compared costs (excess hospital costs and indirect costs) and length
METHODS: A prospective matched cohort study was conducted in children aged <15 years who underwent general anesthesia between November 2012 and December 2013 at Songklanagarind Hospital. PRE children were matched with no PRE children (1:1) using a random selection procedure on outpatients/inpatients, type of surgery, surgical charge (baht), ASA physical status, age difference <9 years, and difference in time of surgery <6 months. Primary end points were excess hospital costs and number of days hospitalized after surgery. Number of days hospitalized after surgery, excess hospital costs and indirect costs regarding transportation, and income loss of parents between groups were compared using Wilcoxon signed rank test. Any hospital stay after surgery between groups was compared using McNemar \( \chi^2 \) test. A hurdle model was used to predict any hospital stay and number of days hospitalized after surgery. Multiple mixed-effects linear regression was used to identify predictors of adjusted excess hospital costs and indirect costs.

RESULTS: A total 430 children were included (215 matched pairs). More PRE children required hospital stay after surgery (81% vs 72%, \( P = 0.004 \)), and PRE children had a longer number of days hospitalized after surgery (median [interquartile ranges]: 1 [1–3.5] vs 1 [0–2];\( P < 0.001 \)) and incurred higher excess costs (\( P < 0.001 \)) but not indirect costs (\( P = 0.23 \)). In multivariate analysis, PRE was a significant predictor for hospital stay after surgery (odds ratio, 2.56; 95% confidence interval, 1.23–5.31), longer hospitalization (count ratio, 2.10 [1.31–3.35]), higher excess costs (cost ratio, 1.30 [1.12–1.53]), and indirect cost (cost ratio, 1.58 [1.20–2.08]) after adjusting for patient and anesthesia characteristics. Universal coverage (74%) was associated with 35% and 64% higher excess cost compared with the Comptroller General’s Department (17%) and self-pay (7%), respectively (\( P = 0.003 \)).

CONCLUSIONS: The effects of PRE in pediatric anesthesia were hospital stay after surgery, 2 times longer hospitalization, 30% higher excess hospital costs, and 58% higher indirect cost among outpatients. Hospital policy to efficiently manage hospital beds and compensatory budget should be developed.

**Propofol-Induced Electroencephalographic Seizures in Neonatal Rats: The Role of Corticosteroids and \( \gamma \)-Aminobutyric Acid Type A Receptor-Mediated Excitation**

Willis, Jesse BS*; Zhu, Wanti ng BS*; Perez-Downes, Julio BS†; Tan, Sijie PhD*; Xu, Changqin MD, PhD*; Seubert, Christoph MD, PhD*; Gravenstein, Nikolaus MD*‡; Martynyuk, Anatoly PhD, DSc*‡

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**背景**：中枢神经系统兴奋和抑制之间的不平衡可能会导致病理结果。我们研究麻醉剂异丙酚通过内分泌活性物质和 \( \gamma \)-氨基丁酸 A 型受体（GABAAR）介导的选择性激发 GABAAR 对新生大鼠脑电图癫痫发作作用机理

**方法**：出生 4 天的 SD 大鼠 6，接受小手术植入电极，腹腔注射异丙酚（40 毫克公斤 \( \uparrow \)1）前 1 小时和 1 小时后观察脑电活动（40 毫克公斤 \( \uparrow \)1）。各种治疗前给予丙泊酚 15 分钟。

**结论**：异丙酚麻醉时发生的脑电图癫痫发作样持续低幅度尖峰。血清多种皮质酮增加（\( T (10) = -5.062; P = 0.0005 \)）醛固酮（\( T (10) = -5.069; P = 0.0005 \）增加，在动物身上进行的实验操作相同，见于研究脑电活动丙泊酚给药后 1 小时。预处理与布美他尼，Na+ K+—2Cl–共转运体抑制剂，从而减少 GABAAR 介导的激励，消除异丙酚引起发作尖峰脑电活动。盐皮质激素和糖皮质激素受体拮抗剂 RU486，RU 28318 和抑郁症脑电图癫痫发
BACKGROUND: An imbalance between excitation and inhibition in the developing central nervous system may result in a pathophysiological outcome. We investigated the mechanistic roles of endocrine activity and γ-aminobutyric acid type A receptor (GABAAR)-mediated excitation in electroencephalographic seizures caused by the GABAAR-selective anesthetic propofol in neonatal rats.

METHODS: Postnatal day 4–6 Sprague Dawley rats underwent a minor surgical procedure to implant electrodes to measure electroencephalographic activity for 1 hour before and 1 hour after intraperitoneal administration of propofol (40 mg·kg⁻¹). Various treatments were administered 15 minutes before administration of propofol.

RESULTS: Episodes of electroencephalographic seizures and persistent low-amplitude spikes occurred during propofol anesthesia. Multifold increases in serum levels of corticosterone (t(10) = −5.062; P = 0.0005) and aldosterone (t(10) = −5.069; P = 0.0005) were detected 1 hour after propofol administration in animals that underwent experimental manipulations identical to those used to study electroencephalographic activity. Pretreatment with bumetanide, the Na⁺-K⁺-2Cl⁻ cotransporter inhibitor, which diminishes GABAAR-mediated excitation, eliminated both seizure and spike electroencephalographic activities caused by propofol. Mineralocorticoid and glucocorticoid receptor antagonists, RU 28318 and RU486, depressed electroencephalographic seizures but did not affect the spike electroencephalographic effects of propofol. Etomidate, at a dose sufficient to induce loss of righting reflex, was weak at increasing serum corticosteroid levels and eliciting electroencephalographic seizures. Etomidate given to corticosterone-pretreated rat pups further increased the total duration of electroencephalographic seizures caused by administration of exogenous corticosterone (t(21) = −2.512, P = 0.0203).

CONCLUSIONS: Propofol increases systemic corticosteroid levels in neonatal rats, which along with GABAAR-mediated excitation appear to be required for propofol-induced neonatal electroencephalographic seizures. Enhancement of GABAAR activity alone may not be sufficient to elicit neonatal electroencephalographic seizures.

Spontaneous Pain-Like Behaviors Are More Sensitive to Morphine and Buprenorphine Than Mechanically Evoked Behaviors in a Rat Model of Acute Postoperative Pain

Background: nonevoked 自发性疼痛是术后最棘手的问题。医师通常利用人类视觉模拟评分或口头的数字评定量表评估这种形式的疼痛。最近的研究提出，自发抬足（SFL）的行为是一种动物脊髓神经损伤后表达自发性疼痛的行为。在目前的研究中，我们系统的描述了大鼠急性术后疼痛行为，其中包括比较镇痛治疗诱发的行为

Method: 对四系手动 5 分钟的时间用 10 分钟的时间间隔记录每个测试结果。随后用电子 Von Frey 计测定缩爪阈值。年龄的影响进行评估，大鼠在不同年龄组的测试：2，7，和大于 26 个月。丁丙诺啡和吗啡的作用在单独的一组动物进行了测试，测试前腹腔注射生理盐水，吗啡（0.01, 0.1, 1, 或 2 毫克/公斤），或丁丙诺啡（0.001, 0.01, 0.1 毫克/公斤）
Background: Nonevoked spontaneous pain is most problematic for postoperative patients. Physicians assess this form of pain using the human visual analog scale or verbal numeric rating scale. Recent studies have proposed that spontaneous foot-lifting (SFL) behaviors are an expression of spontaneous pain in animals after spinal nerve injury or adjuvant-induced inflammation. In the current study, we characterize SFL behaviors in a rat model of acute postoperative pain, which includes comparisons with evoked behaviors to analgesic treatments.

Methods: SFL was manually recorded over four 5-minute periods with 10-minute intervals between each testing session. Paw-withdrawal thresholds were subsequently measured with an electronic von Freyesthesiometer. To evaluate the effects of age, rats were tested in different age groups: 2, 7, and >26 months. The effects of buprenorphine and morphine were tested in a separate group of animals, which received intraperitoneal injections of saline, morphine (0.01, 0.1, 1, or 2 mg/kg), or buprenorphine (0.001, 0.01, or 0.1 mg/kg) before testing.

Results: SFL behaviors peaked at 3 hours after incision and significantly recovered by the 3rd or 4th postoperative day (P < 0.0001). The presentation of these behaviors did not significantly vary with animal age (2, 7, and >26 months old; P = 0.30). SFL behaviors, with the exception of rapid SFL at 3 hours after incision, did not show significant correlation with paw-withdrawal threshold behaviors. The median effective dose of buprenorphine for reversal of mechanical hyperalgesia (0.0452 mg/kg; 95% CI, 0.0259–0.0787) was significantly larger than for reversing rapid (0.0027 mg/kg; 95% CI, 0.0009–0.0083; P < 0.0001) and prolonged (0.0004 mg/kg, 95% CI, 0.0000, 0.0035; P = 0.001) SFL at 3 hours after incision. Similarly, the median effective dose of morphine for reversal of mechanical hypersensitivity behaviors (2.901 mg/kg; 95% CI, 1.132–7.436) was larger than for SFL count (0.4044 mg/kg; 95% CI, 0.1048–1.561; P = 0.0103) and SFL duration (0.0309 mg/kg; 95% CI, 0.0095–0.0998; P < 0.0001) at 3 hours after incision.

Conclusions: The present study demonstrates that a hindpaw plantar incision induces SFL behaviors in rats and that these behaviors have higher bioassay sensitivity to analgesic interventions with morphine and buprenorphine compared with mechanically evoked behaviors.