Cardiovascular Anesthesiology

Comparison of Whole Blood Fibrin-Based Clot Tests in Thrombelastography and Thromboelastometry

- Cristina Solomon,
- Benny Sørensen,
- Gerald Hochleitner,
- Jeffry Kashuk,
- Marco Ranucci,
- and Herbert Schöchl


Anesthetic Pharmacology

The Volatile Anesthetic Isoflurane Prevents Ventilator-Induced Lung Injury via Phosphoinositide 3-Kinase/Akt Signaling in Mice

- Simone Faller,
- Karl M. Strosing,
- Stefan W. Ryter,
- Hartmut Buerkle,
- Torsten Loop,
- Rene Schmidt,
- and Alexander Hoetzel

Increases in Electroencephalogram and Electromyogram Variability Are Associated with an Increased Incidence of Intraoperative Somatic Response

Donald M. Mathews, Laura Clark, Jay Johansen, Emilio Matute, and Chandran V. Seshagiri

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Poor Accuracy of Noninvasive Cardiac Output Monitoring Using Bioimpedance Cardiography [PhysioFlow®] Compared to Magnetic Resonance Imaging in Pediatric Patients

Katherine Taylor, Cedric Manlhiot, Brian McCrindle, Lars Grosse-Wortmann, and Helen Holtby


Is a Neutral Head Position Safer than 45-Degree Neck Rotation During Ultrasound-Guided Internal Jugular Vein Cannulation? Results of a Randomized Controlled Clinical Trial

Massimo Lamperti, Matteo Subert,
Vocalization Assessed by Electrolaryngography Is Unaffected by Topical Lidocaine Anesthesia: A Prospective, Crossover, Randomized, Double-Blind Placebo-Controlled Study

Melanie J. Maxwell, James D. English, Iain K. Moppett, Julian A. McGlashan, and Andrew M. Norris

Determination of Vascular Waterfall Phenomenon by Bedside Measurement of Mean Systemic Filling Pressure and Critical Closing Pressure in the Intensive Care Unit

Jacinta J. Maas, Rob B. de Wilde,
Obstetric Anesthesiology

系统回顾和荟萃分析：地塞米松对预防术后恶心和呕吐与椎管内注射吗啡的相关性
(胡晓清译 薛张纲校)

Dexamethasone for the Prophylaxis of Postoperative Nausea and Vomiting Associated with Neuraxial Morphine Administration: A Systematic Review and Meta-Analysis

Pediatric Anesthesiology

对小儿心脏骤停猪模型的无创自动调节监测
(许辛译 马皓琳 李士通校)

Noninvasive Autoregulation Monitoring in a Swine Model of Pediatric Cardiac Arrest

剖宫产术后静脉注射帕瑞考昔后其主要活性代谢物伐地考昔的母乳转移：单纯集聚数据分析法和非线性混合效应模型法的比较
(俞劼晶译 陈杰校)

Transfer of Parecoxib and Its Primary Active Metabolite Valdecoxib via Transitional Breastmilk Following Intravenous Parecoxib Use After Cesarean Delivery: A Comparison of Naïve Pooled Data Analysis and Nonlinear Mixed-Effects Modeling

Neuroscience in Anesthesiology and Perioperative Medicine

α5γ-氨基丁酸（GABA）A型受体恢复了全麻后认知记忆
(李丽红译 薛张纲校)

Inhibition of α5 γ-Aminobutyric Acid Type A Receptors Restores Recognition Memory After General Anesthesia

利多卡因延期治疗减少脂多糖和干扰素γ刺激后引起的小鼠微神经胶质细胞损伤和细胞因子的产生
(张怡译 马皓琳 李士通校)

Delayed Treatment with Lidocaine Reduces Mouse Microglial Cell Injury and Cytokine Production After Stimulation with Lipopolysaccharide and Interferon γ
General Articles

Special Article: Rationale of Dead Space Measurement by Volumetric Capnography

- Gerardo Tusman,
- Fernando Suarez Sipmann,
- and Stephan H. Bohm

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Analgesia

Pain Mechanisms

The Effects of Electroacupuncture at the ST36 (Zusanli) Acupoint on Cancer Pain and Transient Receptor Potential Vanilloid Subfamily 1 Expression in Walker 256 Tumor-Bearing Rats

- Zhaodi Zhang,
- Changsong Wang,
- Guangying Gu,
- Huiping Li,
- Haifang Zhao,
- Kun Wang,
- Fei Han,
- and Guonian Wang


Regional Anesthesia
The Comparative Effects of Lipid, Epinephrine, and Their Combination in the Reversal of Bupivacaine-Induced Asystole in the Isolated Rat Heart

Le Liu,
Yun Xia,
Ying Chen,
Quanguang Wang,
Tong Shi,
Fangyan Wang,
Robert H. Small,
and Xuzhong Xu


The Effect of Lipid Emulsion Infusion on Postmortem Ropivacaine Concentrations in Swine: Endeavoring to Comprehend a Soldier's Death

Chester C. Buckenmaier III,
John Capacchione,
Arthur R. Mielke,
Saiid Bina,
Cynthia Shields,
Kyung H. Kwon,
Geselle McKnight,
David A. Fish,
and Peter Bedocs


Intravenous Lipid Emulsion Only Minimally Influences Bupivacaine and Mepivacaine Distribution in Plasma and Does Not Enhance Recovery from Intoxication in Pigs

Erik S. Litonius,
Tomohisa Niiya,
Pertti J. Neuvonen,
The Volatile Anesthetic Isoflurane Prevents Ventilator-Induced Lung Injury via Phosphoinositide 3-Kinase/Akt Signaling in Mice

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BACKGROUND: Mechanical ventilation leads to ventilator-induced lung injury in animals, and can contribute to acute lung injury/acute respiratory distress syndrome in humans. Acute lung injury/acute respiratory distress syndrome currently causes an unacceptably high rate of morbidity and mortality among critically ill patients. Volatile anesthetics have been shown to exert anti-inflammatory and organ-protective effects in vivo. We investigated the effects of the volatile anesthetic isoflurane on lung injury during mechanical ventilation.

METHODS: C57BL/6N mice were ventilated with a tidal volume of 12 mL/kg body weight for 6 hours in the absence or presence of isoflurane, and, in a second series, with or without the specific phosphoinositide 3-kinase/Akt inhibitor LY294002. Lung injury was determined by comparative histology, and by the isolation of bronchoalveolar lavage for differential cell counting and analysis of cytokine levels using enzyme-linked immunosorbent assays. Lung homogenates were analyzed for protein expression by Western blotting.

RESULTS: Mechanical ventilation led to increased lung injury, characterized by increased lung injury scores, increased inflammatory cell counts, and increased cytokine levels. The use of isoflurane significantly reduced lung injury, inflammation, and cytokine levels. Conversely, Akt activation was increased during isoflurane ventilation. In vivo, pre-treatment with the specific phosphoinositide 3-kinase/Akt inhibitor LY294002 completely reversed the protective effects of isoflurane.

CONCLUSION: Isoflurane can protect against ventilator-induced lung injury in vivo by inhibiting the pro-inflammatory response. This protection is mediated through the phosphoinositide 3-kinase/Akt signaling pathway.

(俞芳 译 陈杰 校)
RESULTS: Mechanical ventilation caused increases in alveolar wall thickening, cellular infiltration, and an elevated ventilator-induced lung injury score. Neutrophil influx and cytokine (i.e., interleukin-1β, and macrophage inflammatory protein-2) release were enhanced in the bronchoalveolar lavage of ventilated mice. The expression levels of the stress proteins hemeoxygenase-1 and heat shock protein-70 were elevated in lung tissue homogenates. Isoflurane ventilation significantly reduced lung damage, inflammation, and stress protein expression. In contrast, phosphorylation of Akt protein was substantially increased during mechanical ventilation with isoflurane. Inhibition of phosphoinositide 3-kinase/Akt signaling before mechanical ventilation completely reversed the lung-protective effects of isoflurane treatment in vivo.

CONCLUSIONS: Inhalation of isoflurane during mechanical ventilation protects against lung injury by preventing proinflammatory responses. This protection is mediated via phosphoinositide 3-kinase/Akt signaling.

超声引导的颈内静脉置管期间颈正中位的安全性高于颈部旋转45°吗？一项临床随机对照试验结果

Is a Neutral Head Position Safer than 45-Degree Neck Rotation During Ultrasound-Guided Internal Jugular Vein Cannulation? Results of a Randomized Controlled Clinical Trial

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背景：理想的颈内静脉（internal jugular vein，IJV）置管时采取的最佳颈部旋转角度仍不清楚，因为先前研究使用超声，但未及刺破静脉的情况。本文旨在比较超声引导下的颈内静脉置管过程中颈正中位（neutral position，NP，0度）与旋转45度的安全性。首要评估指标是这两种体位对超声引导下的颈内静脉置管主要并发症的影响，另外还评估了整体并发症、穿刺时间和穿刺过程中的困难。

方法：在一家神经外科医院进行此项前瞻性随机对照非盲研究，将接受择期神经外科手术并需要中心静脉置管的患者随机分为两组，进行平面外技术超声引导下的颈内静脉置管。

结果：总共对1424名患者进行了评估，其中92名患者被排除，颈部旋转位组有670人，正中位组有662人。置管成功率均为100%，除了颈内静脉的位置两组样本的人口学数据相似。出现的严重并发症只有10例：其中6例出现在0度NP组，4例出现在45度旋转组。并发症的发生率两组无明显差异。整体并发症发生率是13%，女性、ASA≥II、静脉直径小、静脉在外侧较深或前外侧的患者的发生率更高。穿刺时间的延长与并发症发生率的增加一致。两组在穿刺时感觉到困难的差异并无统计学意义。

结论：由于主要及次要并发症、穿刺时间方面的相似性，采取正中位进行颈内静脉置管和旋转45°体位置管相比安全性并无明显差异。超声引导可以帮助我们选择颈内静脉置管时的最佳旋转角度。

（夏苏云 译 陈杰 校）
BACKGROUND: The optimal degree of neck rotation during internal jugular vein (IJV) cannulation remains undetermined because previous studies suggested using sonography, but without puncturing the vein. We assessed whether a neutral position (NP) of the head (0 degrees) during ultrasound-guided cannulation of the IJV was safer than rotating the neck to 45 degrees head turned. The effect of these 2 positions during ultrasound-guided cannulation on major complications was the primary outcome. Overall complications, venous access time, and perception of difficulty during the procedure were also evaluated.

METHODS: A prospective, randomized, controlled, nonblinded study was conducted in a tertiary neurosurgical hospital. Patients undergoing major elective neurosurgical procedures requiring a central venous line were randomly allocated to 2 groups; ultrasound-guided cannulation of the IJV was then performed using an out-of-plane orientation.

RESULTS: One thousand four hundred twenty-four patients were evaluated, but 92 were excluded; 670 were allocated to the head turned group and 662 to the NP group. Cannulation was 100% successful. Demographic data were similar in the 2 groups except for IJV positions. There were only 10 major complications: 6 in the 0-degree NP group and 4 in the 45-degree head turned group. The frequency of these complications was not different between the 2 groups. The overall complication rate was 13%, and was higher in women, in patients with ASA physical status ≥II, and in patients with a smaller diameter vein, or when the vein was located deeper and lateral or in the anterolateral position. An increased venous access time was associated with an increased rate of overall complications. The perception of difficulty performing the procedure with the head placed in the 2 positions was not statistically different in either group.

CONCLUSION: A head NP was as safe as a 45-degree neck rotation during ultrasound-guided IJV cannulation with regard to both major and minor complications, and venous access time was similar. Ultrasound guidance helps determine optimal head rotation for IJV cannulation.

ICU中床边监测平均灌注压（Pmsf）和临界闭合压（Pcc）确定血管瀑布现象

Determination of Vascular Waterfall Phenomenon by Bedside Measurement of Mean Systemic Filling Pressure and Critical Closing Pressure in the Intensive Care Unit

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背景：平均灌注压（Pmsf）数据可以在床边通过在屏气过程中测量中心静脉压（Pcv）和心输出量（CO）得到。临界闭合压（Pcc）的数据也可以通过同样的方法测得动脉压（Pa）和CO得出。当Pcc 大于Pmsf，就会出现血管瀑布现象。此项研究通过床边测量Pmsf和Pcc来评定血流瀑布现象的存在以及与其相关的血管阻力的计算。

方法：10例心脏术后机械通气的患者中，通过屏气短暂增加Pcv和降低Pa和CO到4个不同的稳定状态。对于每个患者，Pcv和CO的值被绘制成静脉回流曲线从而得出Pmsf。同样，Pa和CO也可绘制成心室输出曲线而得出Pcc。在每个病人扩容前以及用0.5L胶体扩容后分别进行以上测量，同时计算血管阻力。
BACKGROUND: Mean systemic filling pressure (Pmsf) can be determined at the bedside by measuring central venous pressure (Pcv) and cardiac output (CO) during inspiratory hold maneuvers. Critical closing pressure (Pcc) can be determined using the same method measuring arterial pressure (Pa) and CO. If Pcc > Pmsf, there is then a vascular waterfall. In this study, we assessed the existence of a waterfall and its implications for the calculation of vascular resistances by determining Pmsf and Pcc at the bedside.

METHODS: In 10 mechanically ventilated postcardiac surgery patients, inspiratory hold maneuvers were performed, transiently increasing Pcv and decreasing Pa and CO to 4 different steady-state levels. For each patient, values of Pcv and CO were plotted in a venous return curve to determine Pmsf. Similarly, Pcc was determined with a ventricular output curve plotted for Pa and CO. Measurements were performed in each patient before and after volume expansion with 0.5 L colloid, and vascular resistances were calculated.

RESULTS: For every patient, the relationship between the 4 measurements of Pcv and CO and of Pa and CO was linear. Baseline Pmsf was 18.7 ± 4.0 mm Hg (mean ± SD) and differed significantly from Pcc 45.5 ± 11.1 mm Hg (P < 0.0001). The difference of Pcc and Pmsf was 26.8 ± 10.7 mm Hg, indicating the presence of a systemic vascular waterfall. Volume expansion increased Pmsf (26.3 ± 3.2 mm Hg), Pcc (51.5 ± 9.0 mm Hg), and CO (5.5 ± 1.8 to 6.8 ± 1.8 L/min). Arterial (upstream of Pcc) and venous (downstream of Pmsf) vascular resistance were 8.27 ± 4.45 and 2.75 ± 1.23 mm Hg·min·L⁻¹, respectively, and the sum of both (11.01 mm Hg·min·L⁻¹) was significantly different from total systemic vascular resistance (16.56 ± 8.57 mm Hg·min·L⁻¹; P = 0.005). Arterial resistance was related to total resistance.

CONCLUSIONS: Vascular pressure gradients in cardiac surgery patients suggest the presence of a vascular waterfall phenomenon, which is not affected by CO. Thus, measures of total systemic vascular resistance may be irrelevant in assessing systemic vasomotor tone.
从*医学与药理学学院，西澳大学，珀斯，澳大利亚；†医学与药理学学院，西澳大学，珀斯，澳大利亚；‡临床药理学与毒理学实验室，西澳大学，珀斯，澳大利亚；§麻醉与疼痛医学部，金爱德华妇产医院，珀斯，澳大利亚（当前归属于：布里斯托皇家医院，布里斯托，英国）。

背景：剖宫产术后数日通常运用多模式镇痛，包括非阿片类镇痛药的使用。由于母乳喂养小孩在此期间接受母乳，所以有必要了解究竟有多少母体的麻醉药被婴儿接受。为此本试验目的为评估在母体剖宫产术后单次静脉注射帕瑞考昔，婴儿对帕瑞考昔及其活性代谢物伐地考昔的暴露程度。

方法：40名妇女及其婴儿参与研究，在婴儿出生平均41小时后，母体静注帕瑞考昔（40mg）。在之后的24小时收集母乳（4个样本）和血浆（1个样本），用液相色谱-串联质谱分析法测定药物含量。婴儿的数据收集在帕瑞考昔注射后的第二天。使用单纯集聚数据的标准方法评估母乳的帕瑞考昔和伐地考昔的绝对（AID）和相对婴儿剂量（RID），这样也可以计算出母乳/血浆（M/P）浓度比。非线性混合效应模型也被用来将伐地考昔的母乳和血浆的数据集与房室模型配对，并预测M/P，AID和RID。

结果：帕瑞考昔和伐地考昔的M/P比（中位数[四分位范围，IQR]）分别为0.5（0.15至1.15）和0.14（0.11至0.18）。运用单纯集聚数据分析，帕瑞考昔的AID（母乳中的药物浓度×每天的乳汁摄入量/公斤）为0.24（0.05至1.85）微克/公斤/天，伐地考昔的AID为1.82（1.12至2.73）微克/公斤/天。帕瑞考昔的RID是0.04（0.01至0.43）%的产妇体重调整剂量（24小时内一次剂量），伐地考昔的为0.47（0.29至0.69）%（与帕瑞考昔等值）。伐地考昔的房室模型单独生产的平均（个体差异）M/P为0.149（26%），中位数（IQR）AID为1.47（0.96至2.03）微克/公斤/天，中位数（IQR）RID为0.39（0.28至0.47）%。新生儿神经和适应能力评分（平均=34，95%CI为33%至35%）为正常的预期得35分一致。

结论：单纯集聚数据分析法和非线性混合效应模型法都给出了相似的结论，帕瑞考昔和伐地考昔的RID很低。本研究结论显示：给予剖宫产术后哺乳的妇女静注40毫克一次剂量的COX-2抑制剂帕瑞考昔，不会对母乳喂养的婴儿造成不良影响。

背景：Multimodal analgesia, including nonopioid analgesics, is usually used for several days after cesarean delivery. Because the breastfed infant receives transitional milk during this same period, it is important to know how much of a maternal analgesic drug is received by the infant. We designed this study to estimate infant exposure to parecoxib and its active metabolite valdecoxib (a cyclooxygenase-2 inhibitor) after a single IV maternal dose of parecoxib after cesarean delivery.

方法：Forty women and their infants participated in the study. Parecoxib (40 mg) was administered IV at a mean of 41 hours after birth. Milk (4 samples) and plasma (1 sample) were
collected from the women over the subsequent 24 hours and drug content was measured by liquid chromatography-tandem mass spectrometry. The infants were assessed the day after parecoxib dosing. Absolute (AID) and relative infant doses (RID) of both parecoxib and valdecoxib through milk were estimated by standard methods using the naïve pooled datasets, and where possible milk/plasma (M/P) concentration ratios were calculated. Nonlinear mixed-effects modeling was also used to fit the valdecoxib milk and plasma datasets to a compartmental model and to predict M/P, AID, and RID.

RESULTS: M/P ratios (median [interquartile range; IQR]) were 0.5 (0.15 to 1.15) for parecoxib and 0.14 (0.11 to 0.18) for valdecoxib. Using the naïve pooled datasets, AID (drug concentration in milk×daily milk intake/kg) was 0.24 (0.05 to 1.85) μg/kg/day for parecoxib, and 1.82 (1.12 to 2.73) μg/kg/day, for valdecoxib. RID was 0.04 (0.01 to 0.43) % of the weight-adjusted maternal dose (one dose in 24 hours) for parecoxib and 0.47 (0.29 to 0.69) % for valdecoxib (as parecoxib equivalents). Compartmental modeling of valdecoxib alone produced a mean (interindividual variability) M/P of 0.149 (26%), median (IQR) AID of 1.47 (0.96 to 2.03) μg/kg/day, and median (IQR) RID of 0.39 (0.28 to 0.47) %. Neonatal neurologic and adaptive capacity scores (mean=34, 95% CI 33 to 35) were consistent with a normal expected score of 35.

CONCLUSIONS: Both the naïve pooling of data and the modeling analyses gave similar results. The RID of both parecoxib and valdecoxib was low. We conclude that a single 40 mg IV dose of the cyclooxygenase-2 inhibitor parecoxib administered to lactating women after cesarean delivery is unlikely to cause adverse effects in breastfed infants.

Special Article: Rationale of Dead Space Measurement by Volumetric Capnography
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死腔是潮气量的一部分，因其没有接触到流经肺毛细血管的血液而不参与气体交换。通常使用容积二氧化碳图，即一种相对潮气量作出呼出气CO2的曲线来计算，它是一种评估特定通气参数无效的床边监测方式。如今，可通过一个完全无创性和每拍呼吸的方式，比如平均肺泡二氧化碳分压（PACO2），来测量Bohr死腔，而其中PACO2现在可以从二氧化碳描记图直接确定。Enghoff对玻尔公式修改的值（使用动脉血二氧化碳分压而不是肺泡CO2）因为它是受各种肺通气/灌注不匹配原因（从真死腔到分流）的影响。因此，玻尔和Enghoff公式取得的结果有不同的生理意义，临床医生在分析病人的数据时必须意识到这种差异。本文描述了容积二氧化碳图测量死腔的原理并讨论其临床意义以及对其的误解。

（龚寅 译 陈杰 校）

Dead space is the portion of a tidal volume that does not participate in gas exchange because it does not get in contact with blood flowing through the pulmonary capillaries. It is commonly calculated using volumetric capnography, the plot of expired carbon dioxide (CO2) versus tidal volume, which is an easy bedside assessment of the inefficiency of a particular ventilatory setting. Today, Bohr's original dead space can be calculated in an entirely noninvasive and
breath-by-breath manner as the mean alveolar partial pressure of CO₂ (PACO₂) which can now be determined directly from the capnogram. The value derived from Enghoff’s modification of Bohr's formula (using PaCO₂ instead of PACO₂) is a global index of the inefficiency of gas exchange rather than a true “dead space” because it is influenced by all causes of ventilation/perfusion mismatching, from real dead space to shunt. Therefore, the results obtained by Bohr's and Enghoff's formulas have different physiological meanings and clinicians must be conscious of such differences when interpreting patient data. In this article, we describe the rationale of dead space measurements by volumetric capnography and discuss its main clinical implications and the misconceptions surrounding it.

The Effect of Lipid Emulsion Infusion on Postmortem Ropivacaine Concentrations in Swine: Endeavoring to Comprehend a Soldier's Death

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背景：现在主张脂肪乳可用于局麻药中毒时的抢救药。但至今还没有一项研究测量脂肪乳对死后局麻药血清浓度的影响。

方法：本实验中使用的是约克夏猪（n=11），进行常规监护。给实验猪按1.5mg/kg/min注射罗派卡因直至死亡（心脏停搏）。输注前及输注中每隔5分钟采集血液样本，用于血气分析，并通过高效液相色谱检测血浆游离、结合以及总的罗派卡因浓度。在平均动脉压达到50mmHg时，5只实验猪仅给予罗派卡因，而另外6只猪给予罗派卡因和单剂量20%脂肪乳（1mg/kg）的混合液。直至心脏停搏后停止输注罗派卡因，不予任何心肺复苏。记录总的罗派卡因浓度以及实验开始至死亡的时间。给予实验猪降温（平均体温，死后6小时25.5℃±0.8℃）从而反映停尸房的环境条件。分别在心脏停搏时、停搏后1小时、3小时、6小时采集血样。另外，在以上各时间点上行开颅和开腹手术以获取1.5-3g大脑、肺、肝脏、肾脏和肌肉组织用于分析。

结果：将对照组和脂肪乳治疗组的实验猪死后血浆罗派卡因浓度进行分析，发现脂肪乳治疗组的总罗派卡因浓度（结合和未结合白蛋白的罗派卡因）以及游离罗派卡因浓度（未结合白蛋白）均显著高于对照组（分别是P = 0.0094 and P = 0.0063)。此外，时间对增加死后游离血浆罗派卡因浓度也有显著作用（P=0.0095）。脂肪乳组与对照组相比，更早发生心脏停搏（P=0.0274）。组织学分析发现，脂肪乳组的实验猪死后肺、肾脏和大脑组织中的罗派卡因的浓度明显下降（分别是P = 0.0168, P = 0.0073, and P = 0.0018）。对照组其组织中的药物浓度没有改变。

结论：本实验的数据显示，有过局麻药心脏毒性且给予脂肪乳治疗的实验猪，其死后的血标本的检测可能无法直接反映死后的药物浓度。

（张婷 译 陈杰 校）
**BACKGROUND:** Lipid emulsion (20%) is advocated as a rescue drug for local anesthetic toxicity. No study has measured the impact of lipid emulsion therapy on postmortem local anesthetic serum levels.

**METHODS:** We anesthetized Yorkshire swine (n = 11) and standard monitors were placed. The swine received 1.5 mg/kg/min IV ropivacaine until death (asystole). Blood samples were drawn before infusion (baseline) and at 5-minute intervals during the infusion for measurement of blood gases and free, bound, and total serum ropivacaine concentrations via high-performance liquid chromatography. Five swine received ropivacaine only, and 6 swine received ropivacaine plus a single bolus dose of 20% lipid emulsion (1 mg/kg) when the mean arterial blood pressure reached 50 mm Hg. Ropivacaine infusions were terminated at asystole and no resuscitation was initiated. Total ropivacaine dose and time to death were recorded. The swine were cooled (mean temperature, 25.5°C ± 0.8°C at 6 hours postmortem) to reflect morgue conditions. Serum samples were drawn at asystole, 1, 3, and 6 hours postmortem for analysis. Additionally, a craniotomy and laparotomy were performed at those times to remove 1.5 to 3 g each of brain, lung, liver, kidney, and muscle for analysis.

**RESULTS:** Analysis of the postmortem serum ropivacaine concentrations in the control and the lipid-treated animals indicated that both the total (bound and not bound to proteins) and free (not bound to proteins) ropivacaine concentrations were significantly higher in the lipid-treated animals ($P = 0.0094$ and $P = 0.0063$, respectively). Furthermore, time had a significant effect on increasing the postmortem free ropivacaine concentrations ($P = 0.0095$). The lipid group had a statistically significant earlier onset of death (asystole) compared with the control group ($P = 0.0274$). Tissue analysis indicated that the ropivacaine concentration significantly decreased postmortem in the lung, kidney, and brain tissues of the lipid-treated animals ($P = 0.0168$, $P = 0.0073$, and $P = 0.0018$, respectively). Tissue drug concentrations in the control animals remained unchanged after death.

**CONCLUSIONS:** Our data show that postmortem blood samples in swine that experience local anesthetic cardiovascular collapse and are treated with lipid emulsions will result in measurements that cannot be directly extrapolated to premortem drug concentrations.

**脑电图和肌电图变化率的增加与术中躯体反应发生率增加的关系**

**Increases in electroencephalogram and electromyogram variability are associated with an increased incidence of intraoperative somatic response.**

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**背景：**BIS-脑电双频指数，EMG-体表肌电变化率，以及CVI-复合变化指数是脑电和肌电变化率监测的三个新指标。我们研究增加这些指数的变化是否与术中躯体反应有关。
方法：这一多中心研究包括来自4个不同的中心经过筛选后的120名非心脏手术患者。全麻术中维持，2个中心用丙泊酚和瑞芬，另外2个中心用七氟醚和瑞芬，通过调整丙泊酚和七氟醚维持BIS在45-60。临床医生一直以来不了解CVI(v2.0)，瑞芬的输注全凭个人经验。这次术中所有的躯体反应（包括体动，怪相，睁眼等）都被记录。每个事件都被划分为连续不重叠10分钟为一段的事件。每一片段都包括体动事件或者未发生事件。对于每个阶段，BIS，EMG、CVI、HR、ART都要监测。为有效量化区别每个在体动事件和非体动事件中的变量，我们通过计算了每个变量受试者特性曲线(ROC)的曲线下面积。最终，我们观察到每个体动事件发生前的BIS，EMG，CVI和HR波动的时间进程，以及每个变量能区分体动和特殊非体动事件的最早特征。

结果：分析结果包括来自105例手术的33个体动事件和829个非体动事件。ROC曲线曲线下面积计算结果BIS为0.84±0.04，EMG为0.92±0.02，CVI为0.89±0.03，HR为0.77±0.03，ART为0.68±0.05。CVI、BIS、EMG对体动发生的敏感性高。心率只在体动发生前的几秒钟稍有变化。

结论：BIS、EMG、CVI监测增加术中体动发生的预知，在10分钟的体动和非体动实验中，相比HR和ART，前三者变化更明显。进一步讲，在体动发生前，相比心率的增加，CVI增加更早，可更早提示镇痛不足。

（韩旭译 薛张纲校）

BACKGROUND: sBIS, the variability of the Bispectral Index (BIS), sEMG, the variability of facial electromyogram power (EMG), and the Composite Variability Index (CVI) are 3 new measures of electroencephalogram and EMG variability. CVI is a single measure of the combined variability in BIS and EMG. We investigated whether increases in these variables are associated with intraoperative somatic responses.

METHODS: This multicenter study included 120 patients undergoing elective, noncardiac surgery from 4 different sites. General anesthesia was maintained using propofol and remifentanil at 2 of the sites and sevoflurane and remifentanil at the 2 other sites. Propofol or sevoflurane was adjusted to maintain BIS between 45 and 60. Clinicians were blinded to CVI (v2.0) at all times, and remifentanil infusions were adjusted at the discretion of the clinician. The times of all intraoperative somatic events, defined as movement, grimacing, or eye opening, were recorded. Offline, the maintenance phase of each case was divided into consecutive, nonoverlapping, 10-minute segments. Segments were identified as containing a somatic event or containing no events. For each segment, mean sBIS, sEMG, and CVI and the heart rate (HR) range and mean arterial blood pressure range were calculated. To quantify how effectively each variable discriminated between somatic event segments and nonevent segments, we computed the area under the receiver operating characteristic (ROC) curve for each variable. Finally, we observed the time course of sBIS, sEMG, CVI, and the HR range before each somatic event and characterized the earliest time before the somatic event at which each variable was able to discriminate between the somatic events and a specified set of nonevents.

RESULTS: The analysis included 33 somatic event segments and 829 nonevent segments from 105 surgical cases. The areas under the ROC curve (±SE) for sBIS, sEMG, and CVI were 0.83 ± 0.04, 0.92 ± 0.02, and 0.89 ± 0.03, respectively. The areas under the ROC curve for HR range and mean arterial blood pressure range were 0.77 ± 0.03 and 0.68 ± 0.05, respectively. CVI, sBIS, and sEMG all demonstrated higher average values before upcoming somatic events when
compared with nonevents. HR range only showed a difference within a few seconds before the somatic event.

**CONCLUSION:** sBIS, sEMG, and CVI, measures of electroencephalogram and EMG variability, increased when intraoperative somatic events occurred. sBIS, sEMG, and CVI discriminated between 10-minute segments that contained a somatic event and those segments that did not contain an event better than changes in HR and mean arterial blood pressure. Furthermore, CVI increases before somatic events began earlier than HR changes and may provide caregivers with an early warning of potentially inadequate antinociception.

**Vocalization assessed by electrolaryngography is unaffected by topical lidocaine anesthesia: a prospective, crossover, randomized, double-blind placebo-controlled study.**
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**BACKGROUND:** Topical anesthesia of the upper airway is often recommended when difficulty in airway management is anticipated. There are published reports, however, of administration of topical anesthesia resulting in complete loss of airway control. Adverse effects are mostly attributed to interference with involuntary protective airway reflexes, while gross motor function itself generally is thought to be preserved. We hypothesized that if motor control is affected, measurable quantitative changes in vocalization should follow the use of topical anesthesia.

**METHODS:** A prospective, crossover, randomized, double-blind study was conducted, in which 24 healthy volunteers each performed 2 vocal exercises, while having their glottic appearance recorded digitally via fiberoptic nasendoscopy. Subjects gargled with 3 test solutions on separate occasions (placebo, 2% lidocaine, and 4% lidocaine) and repeated the vocal exercises and nasendoscopy. The angle between the vocal cords was measured using MB-Ruler®, and the Laryngograph Speech Studio® software was used for vocal parameter analysis.
RESULTS: The only significant changes in voice quality occurred between the control and test groups (P = 0.014). No difference could be found between the placebo and lidocaine groups.

CONCLUSIONS: Although gargling with local anesthetic affected vocalization, no pharmacological effect attributable to local anesthetic was observed.

系综回顾和荟萃分析：地塞米松对预防术后恶心和呕吐与椎管内注射吗啡的相关性
Dexamethasone for the Prophylaxis of Postoperative Nausea and Vomiting Associated with Neuraxial Morphine Administration: A Systematic Review and Meta-Analysis
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BACKGROUND: We performed a systematic review to assess the efficacy of dexamethasone in reducing postoperative nausea, vomiting (PONV), pruritus, and enhancing postoperative analgesia in patients receiving neuraxial anesthesia with neuraxial morphine.

METHODS: We searched Medline (1966-2011), the Cochrane Central Register of Controlled Trials, EMBASE, and Web of Science for all randomized controlled trials comparing dexamethasone with placebo for the prevention of PONV and/or pruritus in patients receiving neuraxial morphine as part of a neuraxial anesthetic technique. Data were extracted independently by the authors on the incidence of PONV, pruritus, pain scores at 4 and 24 hours, and use of rescue antiemetics, antipruritics, and analgesics.
RESULTS: Eight randomized controlled trials (4 cesarean deliveries, 4 total abdominal hysterectomies) were included. From these trials, 768 patients were analyzed with 473 receiving dexamethasone and 295 receiving placebo. The doses of dexamethasone investigated ranged from 2.5 to 10 mg. Dexamethasone reduced the incidence of postoperative nausea (relative risk, RR [95% confidence interval, CI] = 0.57 [0.45, 0.72]), vomiting (RR [95% CI] = 0.56 [0.43, 0.72]), and the use of rescue antiemetic therapy (RR [95% CI] = 0.47 [0.36, 0.61]) compared with placebo. There was no evidence of dose responsiveness with respect to its antiemetic effect. Dexamethasone also reduced 24-hour visual analog pain scores (measured on an 11-point scale [0-10]) (mean difference [95% CI] = -0.30 [-0.46, -0.13]) and the use of rescue analgesics (RR [95% CI] = 0.72 [0.52, 0.98]). Dexamethasone did not reduce the incidence of pruritus (RR [95% CI] = 0.98 [0.84, 1.15]). Examination of the funnel plots and Egger's test revealed evidence of publication bias in the primary outcomes.

CONCLUSION: Dexamethasone is an effective antiemetic for patients receiving neuraxial morphine for cesarean delivery and abdominal hysterectomy. In addition, the doses used for antiemetic prophylaxis enhanced postoperative analgesia compared with placebo. However, dexamethasone was not effective for the prophylaxis against neuraxial morphine-induced pruritus.

α5γ酪氨酸（GABA）A型受体恢复了全麻后认知记忆

Inhibition of α5 γ-Aminobutyric Acid Type A Receptors Restores Recognition Memory After General Anesthesia.

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背景：全麻所致认知障碍持续时间比依照其药理学特性所预期的长得多。这些麻醉后认知障碍的细胞学机制仍然不清楚。GABA A型受体是大多麻醉药的主要作用靶点。尤其是α5亚型GABA受体参与了麻醉后急性记忆阻断及术后早期记忆缺失的形成。本研究中，首先我们探索了工作记忆及短期认知记忆在应用异氟醚后是否可以修复；其次研究了异氟醚使用后引起的记忆缺失能否通过抑制α5亚型GABA受体而得到翻转；同时我们也研究了α5亚型GABA受体表达对使用异氟醚处理后记忆缺失的形成是否是必要的。

方法：野生型及GABA受体α5亚型敲除小鼠用异氟醚（1.3%，1 mac）或七氟醚（2.3%，1mac）或对照气体处理一小时。记忆评估用一种新型的目标识别任务。小鼠在吸入异氟醚麻醉结束后24小时或72小时进行识别任务训练。工作记忆和短时记忆在训练后1分钟和1小时分别进行检测。为了测定抑制α5亚型GABA受体是否可翻转记忆缺失，我们对经异氟醚处理后23.5及小时或行为训练前30分钟用L-655, 708对小鼠进行预处理。

结果：野生型小鼠在异氟醚处理后24小时，其分辨率下降，证明其短时记忆功能修复。相反地，工作记忆在异氟醚处理后不能修复。短时记忆在经L-655, 708处理后可完全被翻转。72小时候后，短时记忆缺失可自行修复。Gabra5/-
小鼠在异氟醚处理后不表现出短时记忆缺损。七氟醚麻醉后24小时也可导致记忆缺损，表现为分辨率下降。

结论：吸入麻醉药会导致顺时认知记忆的缺失，通过这种“证明-概念式”的研究发现α5亚型GABA受体对麻醉后认知记忆缺失的形成是必须的，同时，这些受体也是气体消除后恢复认知记忆的作用靶点。

(李丽红译 薛张纲校)

BACKGROUND: General anesthetics cause cognitive deficits that persist much longer than would be expected on the basis of their pharmacokinetics. The cellular mechanisms underlying these postanesthetic cognitive deficits remain unknown. γ-Aminobutyric acid type A (GABA(A)) receptors are principal targets for most anesthetics. In particular, the C receptor subtype has been implicated in acute memory blockade during anesthesia and memory deficits in the early postoperative period. We first sought to determine whether working memory and short-term recognition memory are impaired after isoflurane anesthesia. The second aim of the study was to determine whether memory deficits after isoflurane can be reversed by inhibiting α5GABA(A) receptors. We also sought to determine whether the expression of α5GABA(A) receptors is necessary for the development of memory dysfunction after isoflurane. Lastly, the effect of sevoflurane on memory was studied.

METHODS: Wild-type and α5GABA(A) receptor null-mutant (Gabra5/-) mice were treated with isoflurane (1.3%; 1 minimum alveolar concentration [MAC]) or sevoflurane (2.3%; 1 MAC) or vehicle gas for 1 hour. Memory performance was assessed with a novel object recognition task. Mice were trained on the recognition task either 24 hours or 72 hours after isoflurane anesthesia. Working memory and short-term memory were tested 1 minute and 1 hour after training, respectively. To determine whether inhibition of α5GABA(A) receptors reverses memory deficits, we treated a subset of mice with L-655,708 (0.35 mg/kg or 0.7 mg/kg) 23.5 hours after isoflurane and 30 minutes before behavioral training.

RESULTS: Short-term memory was impaired in wild-type mice 24 hours after isoflurane as evidenced by a decrease in the discrimination ratio (control 0.66 ± 0.03 vs isoflurane 0.51 ± 0.03, P = 0.0005). In contrast, working memory was not impaired by isoflurane (control 0.68 ± 0.05 vs isoflurane 0.67 ± 0.04, F(2,102) = 3.59, P = 0.032). The deficit in short-term memory was fully reversed by L-655,708 (effect of isoflurane × L-655,708, F(2,102) = 3.59, P = 0.032; isoflurane 0.51 ± 0.03 vs isoflurane + L-655,708 at 0.35 mg/kg 0.67 ± 0.03, P < 0.05). By 72 hours, the deficits in short-term memory resolved spontaneously (control 0.65 ± 0.05 vs isoflurane 0.60 ± 0.04, P = 0.441). Gabra5/- mice showed no short-term memory deficits 24 hours after isoflurane (effect of isoflurane F(1,47) = 0.375, P = 0.544). Sevoflurane also caused memory deficits 24 hours after anesthesia, as evidenced by a reduction in the discrimination ratio (control 0.63 ± 0.02 vs sevoflurane 0.53 ± 0.03, P = 0.039).

CONCLUSIONS: Inhalational anesthetics cause deficits in anterograde recognition memory. This proof-of-concept study shows that α5GABA(A) receptors are necessary for the development of postanesthetic deficits in recognition memory and that these receptors can be targeted to restore memory even after the anesthetic has been eliminated.

沃克256细胞癌时针对足三里穴位的电针刺疗法对癌症疼痛的作用和瞬态感受器阳离子电压通道的解释
The Effects of Electroacupuncture at the ST36 (Zusanli) Acupoint on Cancer Pain and Transient Receptor Potential Vanilloid Subfamily 1 Expression in Walker 256 Tumor-Bearing Rats.

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BACKGROUND: Several studies have addressed the expression of transient receptor potential vanilloid subfamily 1 (TRPV1) playing an important role in the generation of cancer pain. Electroacupuncture (EA) is an effective method of acupuncture shown to attenuate different kinds of pain such as inflammatory, neuropathic, and cancer. In this study, we investigated the effect of EA on cancer pain caused by intraplantar injection of Walker 256 carcinoma cells and cancer-driven TRPV1 expression in the dorsal root ganglia (DRGs).

METHODS: Rats were randomly divided into 4 groups: the nontumor cell inoculation group (normal control, n = 8); Walker 256 carcinoma cell inoculation group (tumor control, n = 8); sham point electrical stimulation treatment with Walker 256 carcinoma cell inoculation group (SES, n = 8); EA treatment with Walker 256 carcinoma cell inoculation group (EA, n = 8). The time courses of thermal, mechanical sensitivity, and spontaneous nocifensive behavior were determined. In addition, TRPV1 expression in DRGs was observed by quantitative real-time polymerase chain reaction and Western blotting.

RESULTS: Injection of cancer cells decreased the paw withdrawal threshold, increased spontaneous nocifensive behavior, and induced significant thermal hyperalgesia that was attenuated by EA at the ST36 acupoint (2 Hz, 0.3 ms, ≤1 mA). TRPV1 mRNA and protein in
DRGs were upregulated in the cancer pain model, and EA at ST36 acupoint counteracted the cancer-driven upregulation of TRPV1 expression in the corresponding DRGs.

**CONCLUSIONS:** EA at ST36 could attenuate cancer-induced pain, at least in part, through suppressing TRPV1 mRNA and protein upregulation in the DRGs.

静脉注射脂肪乳只是最低限度的影响血浆中布比卡因和甲哌卡因的分布，并不会提高猪中毒的复苏

**Intravenous lipid emulsion only minimally influences bupivacaine and mepivacaine distribution in plasma and does not enhance recovery from intoxication in pigs.**

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**BACKGROUND:** The reported successful use of IV lipid emulsions in local anesthetic intoxications is thought to be due to lipid sequestration of local anesthetics. However, controlled efficacy studies were lacking, and other mechanisms of action have also been suggested. We investigated the effect of lipid infusion on plasma concentrations and cardiovascular effects of 2 local anesthetics differing in lipophilicity, bupivacaine, and mepivacaine.

**METHODS:** Bupivacaine (n = 20) or mepivacaine (n = 20) was infused into a central vein of anesthetized (isoflurane 1%, Fio(2) 0.21) pigs until mean arterial blood pressure decreased to 50% from baseline. Isoflurane was discontinued and Fio(2) was increased to 1.0. Ten pigs in each local anesthetic group were treated with 20% lipid emulsion (ClinOleic®), and 10 pigs with
Ringer’s solution: 1.5 mL/kg in 1 minute followed by an infusion of 0.25 mL · kg(-1) · min(-1) for 29 minutes. Five additional pigs were infused bupivacaine and Intralipid®. Total and nonlipid-bound local anesthetic concentrations were determined from repeated blood samples.

**RESULTS:** There were no overall differences in total or nonlipid-bound plasma local anesthetic concentrations between the lipid and Ringer’s groups. However, plasma median total bupivacaine concentration was 21% and 23% higher at 20 and 30 minutes, respectively, in the lipid group (P = 0.016 without Holm-Bonferroni correction). There was also no overall difference between lipid and Ringer’s groups in the rate of recovery of hemodynamic and electrocardiographic variables. Median mean arterial blood pressure in the lipid group with bupivacaine intoxication was 16 mm Hg and 15 mm Hg higher than in the corresponding Ringer’s group at 10 and 15 minutes, respectively (P = 0.016 and P = 0.021, respectively, without Holm-Bonferroni correction). Intralipid® also caused no difference between total plasma and nonlipid-bound concentrations of bupivacaine with no apparent enhancement of recovery.

**CONCLUSIONS:** Lipid emulsion neither had any measurable effect on the disposition of the studied local anesthetics in plasma, nor did it improve the rate of recovery from intoxication by either local anesthetic as measured by hemodynamic variables.

**血栓弹性描记器和血栓弹性检测器全血纤维蛋白凝块试验的比较**

Comparison of Whole Blood Fibrin-Based Clot Tests in Thrombelastography and Thromboelastometry

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**背景：**基于纤维蛋白的血凝块硬度测量，功能性纤维蛋白原（FF）血栓弹性描记法测量的是最大振幅（MA），FIBTEM血栓弹性检测法测量的是凝块的最大硬度（MCF）。方法仪器的不同可能有临床意义。我们的目的是通过标准（血栓弹性描记器[TEG®]测量FF;血栓弹性检测器[ROTEM®]测量FIBTEM）和交叉 (ROTEM®测量FF; TEG®测量FIBTEM)比较凝块硬度参数。

**方法：**对采集健康志愿者的全血样本进行血栓弹性描记器和血栓弹力检测仪的分析。分别检测不经过处理的样本，以及使用氯化钠溶液逐步稀释过的样本（稀释20%、40%和60%）。并且还评估了在体外加入药物（肝素、鱼精蛋白、氨甲环酸）后和使用羟乙基淀粉、明胶、氯化钠和白蛋白稀释50%后的样本。
BACKGROUND: Fibrin-based clot firmness is measured as maximum amplitude (MA) in the functional fibrinogen (FF) thrombelastographic assay and maximum clot firmness (MCF) in the FIBTEM thromboelastometric assay. Differences between the assays/devices may be clinically significant. Our objective was to compare clot firmness parameters through standard (FF on a thrombelastography device [TEG®]; FIBTEM on a thromboelastometry device [ROTEM®]) and crossover (FF on ROTEM®; FIBTEM on TEG®) analyses.

METHODS: Whole-blood samples from healthy volunteers were subjected to thrombelastography and thromboelastometry analyses. Samples were investigated native and following stepwise dilution with sodium chloride solution (20%, 40%, and 60% dilution). Samples were also assessed after in vitro addition of medications (heparin, protamine, tranexamic acid) and 50% dilution with hydroxyethyl starch, gelatin, sodium chloride, and albumin.

RESULTS: FF produced higher values than FIBTEM, regardless of the device, and TEG® produced higher values than ROTEM®, regardless of the assay. With all added medications except heparin 400 U/kg bodyweight, FF MA remained significantly higher ($P < 0.05$) than FIBTEM MCF, which was largely unchanged. FF MA was significantly reduced ($P = 0.04$) by high-dose heparin and partially restored with protamine. Fifty percent dilution with hydroxyethyl starch, albumin, and gelatin decreased FIBTEM MCF and FF MA by >50%.

CONCLUSIONS: These results demonstrate differences when measuring fibrin-based clotting via the FF and FIBTEM assays on the TEG® and ROTEM® devices. Point-of-care targeted correction of fibrin-based clotting may be influenced by the assay and device used. For the FF assay, data are lacking.
BACKGROUND: Identification of low cardiac output (CO) states in anesthesia is important because preoperative hemodynamic optimization may improve outcome in surgery. Accurate real-time CO measurement would be useful in optimizing “goal-directed” therapy. We sought to evaluate the reliability and accuracy of CO measurement using bioimpedance cardiography (PhysioFlow®, NeuMeDx, Bristol, PA) in pediatric patients with and without cardiac disease undergoing anesthesia for magnetic resonance imaging (MRI).

METHODS: All consenting patients undergoing anesthesia for cardiac MRI were enrolled. After equilibration of anesthesia for ≥10 minutes, 6 PhysioFlow electrodes were applied to the patient’s chest for continuous real-time monitoring for 10 minutes. Data were stored in 15-second epochs and later averaged offline to obtain CO. Phase contrast MRI measurements of flow volumes in the superior vena cava and ascending and descending aorta were made from a single imaging plane through all 3 vessels at the level of the right pulmonary artery. Both CO measurements were indexed to body surface area. The anesthetic technique was the same for both measurements. Agreement was assessed using Bland-Altman analysis.

RESULTS: Thirty-one patients were enrolled and 23 were analyzed. The median age at study was 2.8 years (range, 0.02–8.02 years) and median body surface area was 0.54 m² (range, 0.21–1.00 m²). Eleven of 23 patients (48%) were males. Patients were grouped into those with univentricular physiology, 6 of 23 (26%); biventricular physiology with shunt, 3 of 23 (13%); biventricular without shunt, 10 of 23 (43%); and no structural heart disease, 4 of 23 (17%). The mean bias was $-0.34 \pm 1.50$ L/min/m² ($P = 0.29$). The 95% limits of agreement were $-3.21$ to $+2.69$ L/min/m². Only 8 of 23 measurements (35%) were within 20% and 14 of 23 measurements (61%) were within 30% of each other.

CONCLUSION: PhysioFlow performance was not sufficiently accurate in this population. Modifications of the algorithm and further testing are required before this device can be recommended for routine clinical use in pediatric patients.
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The Anesthesia Patient Safety Foundation (APSF) was created in 1985. Its founders coined the term “patient safety” in its modern public usage and created the very first patient safety organization, igniting a movement that is now universal in all of health care. Driven by the vision “that no patient shall be harmed by anesthesia,” the APSF has worked tirelessly for more than a quarter century to promote safety education and communication through its widely read Newsletter, its programs, and its presentations. The APSF’s extensive research grant program has supported a great many projects leading to key safety improvements and, in particular, was central in the development of high-fidelity mannequin simulation as a research and teaching tool. With its pioneering collaboration, the APSF is unique in incorporating the talents and resources of anesthesia professionals of all types, safety scientists, pharmaceutical and equipment manufacturers, regulators, liability insurance companies, and also surgeons. Specific alerts, campaigns, discussions, and projects have targeted a host of safety issues and dangers over the years, starting with minimal intraoperative monitoring in 1986 and all the way up to beach-chair position cerebral perfusion pressure, operating room medication errors, and the extremely popular DVD on operating room fire safety in 2010; the list is long and expansive. The APSF has served as a model and inspiration for subsequent patient safety organizations and has been recognized nationally as having a dramatic positive impact on the safety of anesthesia care. Recognizing that the work is not over, that systems, organizations, and equipment still at times fail, that basic preventable human errors still do sometimes occur, and that “production pressure” in anesthesia practice threatens past safety gains, the APSF is firmly committed and continues to work hard both on established tenets and new patient safety principles.
Noninvasive Autoregulation Monitoring in a Swine Model of Pediatric Cardiac Arrest

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BACKGROUND: Cerebrovascular autoregulation after resuscitation has not been well studied in an experimental model of pediatric cardiac arrest. Furthermore, developing noninvasive methods of monitoring autoregulation using near-infrared spectroscopy (NIRS) would be
clinically useful in guiding neuroprotective hemodynamic management after pediatric cardiac arrest. We tested the hypotheses that the lower limit of autoregulation (LLA) would shift to a higher arterial blood pressure between 1 and 2 days of recovery after cardiac arrest and that the LLA would be detected by NIRS-derived indices of autoregulation in a swine model of pediatric cardiac arrest. We also tested the hypothesis that autoregulation with hypertension would be impaired after cardiac arrest.

METHODS: Data on LLA were obtained from neonatal piglets that had undergone hypoxic–asphyxic cardiac arrest and recovery for 1 day \((n = 8)\) or 2 days \((n = 8)\), or that had undergone sham surgery with 2 days of recovery \((n = 8)\). Autoregulation with hypertension was examined in a separate cohort of piglets that underwent hypoxic–asphyxic cardiac arrest \((n = 5)\) or sham surgery \((n = 5)\) with 2 days of recovery. After the recovery period, piglets were reanesthetized, and autoregulation was monitored by standard laser-Doppler flowmetry and autoregulation indices derived from NIRS (the cerebral oximetry \([\text{COx}]\) and hemoglobin volume \([\text{HVx}]\) indices). The LLA was determined by decreasing blood pressure through inflation of a balloon catheter in the inferior vena cava. Autoregulation during hypertension was evaluated by inflation of an aortic balloon catheter.

RESULTS: The LLAs were similar between sham-operated piglets and piglets that recovered for 1 or 2 days after arrest. The NIRS-derived indices accurately detected the LLA determined by laser-Doppler flowmetry. The area under the curve of the receiver operator characteristic curve for cerebral oximetry index was 0.91 at 1 day and 0.92 at 2 days after arrest. The area under the curve for hemoglobin volume index was 0.92 and 0.89 at the respective time points. During induced hypertension, the static rate of autoregulation, defined as the percentage change in cerebrovascular resistance divided by the percentage change in cerebral perfusion pressure, was not different between postarrest and sham-operated piglets. At 2 days recovery from arrest, piglets exhibited neurobehavioral deficits and histologic neuronal injury.

CONCLUSIONS: In a swine model of pediatric hypoxic–asphyxic cardiac arrest with confirmed brain damage, the LLA did not differ 1 and 2 days after resuscitation. The NIRS-derived indices accurately detected the LLA in comparison with laser-Doppler flow measurements at those time points. Autoregulation remained functional during hypertension.
BACKGROUND: Neuroinflammation is an important pathological process for almost all acquired neurological diseases. Microglial cells play a critical role in neuroinflammation. We determined whether lidocaine, a local anesthetic with anti-inflammatory property, protected microglial cells and attenuated cytokine production from activated microglial cells.

METHODS: Mouse microglial cultures were incubated with or without 1 μg/mL lipopolysaccharide and 10 U/mL interferon γ (IFNγ) for 24 hours in the presence or absence of lidocaine for 1 hour started at 2, 3, or 4 hours after the onset of lipopolysaccharide and IFNγ stimulation. Lactate dehydrogenase release and cytokine production were determined after the cells were stimulated by lipopolysaccharide and IFNγ for 24 hours.

RESULTS: Lidocaine dose-dependently reduced lipopolysaccharide and IFNγ-induced microglial cell injury as measured by lactate dehydrogenase release. This effect was apparent with lidocaine at 2 μg/mL (30.3% ± 5.8% and 23.1% ± 9.7%, respectively, for stimulation alone and the stimulation in the presence of lidocaine, n = 18, P = 0.025). Lidocaine applied at 2, 3, or 4 hours after the onset of lipopolysaccharide and IFNγ stimulation reduced the cell injury. This lidocaine effect was not affected by the mitochondrial K_{ATP} channel inhibitor 5-hydroxydecanoate. Similar to lidocaine, QX314, a permanently charged lidocaine analog that usually does not permeate through the plasma membrane, reduced lipopolysaccharide and IFNγ-induced microglial cell injury. QX314 also attenuated the stimulation-induced interleukin-1β production.

CONCLUSIONS: Delayed treatment with lidocaine protects microglial cells and reduces cytokine production from these cells. These effects may involve action site(s) on the cell surface.
背景：治疗布比卡因引起的心脏毒性作用时，脂质与肾上腺素合用的效果究竟优于还是劣于其中任一药物单独应用，至今仍不清楚。我们比较了脂质、肾上腺素以及两种药物联合应用在离体大鼠心脏模型中逆转布比卡因引起的心脏停搏的作用，并且测定了这三种治疗方案对心肌组织中布比卡因含量的影响。

方法：切取雄性Sprague-Dawley大鼠的心脏，并在非再循环的Langendorff灌流装置中逆向灌流。灌注100μmol/L布比卡因直到心脏停搏后3分钟。随后，脂质组灌注2%脂质和30μmol/L布比卡因混合物；肾上腺素组灌注0.15μg/mL肾上腺素和30μmol/L布比卡因混合物；联合组灌注2%脂质、0.15μg/mL肾上腺素和30μmol/L布比卡因混合物；对照组单独灌注30μmol/L布比卡因。心搏恢复定义为形成自主规律的节律，且心率血压乘积（RPP）大于基础值的10%，持续一分钟以上。我们比较各组从100μmol/L布比卡因灌注结束到心搏恢复的时间（T_recovery）。记录心搏恢复后40分钟内的心功能相关指标。实验结束后，取每个心脏标本的心尖，通过液相色谱-串联质谱法测定布比卡因含量。

结果：脂质组和联合组的心搏恢复的时间（T_recovery）明显短于肾上腺素组和对照组（P < 0.001），且肾上腺素组T_recovery短于对照组（P < 0.05）。心搏恢复后40分钟内平均RPP由高到低依次为：联合组>脂质组和肾上腺素组>对照组（P < 0.01）。恢复期间RPP最大值（RPP_{maximum}）和RPP_{maximum}与基础值之比（RPP_{maximum}/RPP_{baseline}）由高到低依次为：联合组>脂质组和肾上腺素组>对照组（P < 0.01）。RPP、RPP_{maximum}和RPP_{maximum}/RPP_{baseline}在脂质组和肾上腺素组之间均无显著性差异。肾上腺素组和对照组的心肌组织布比卡因含量高于脂质组和联合组（P < 0.001）。

结论：在离体大鼠心脏模型中逆转布比卡因引起的心脏停搏的作用，脂质与肾上腺素联合应用对心功能的恢复作用优于其中任一药物单独应用。

（陈彬彬译 马皓琳 李士通校）

BACKGROUND: It remains unclear whether lipid combined with epinephrine is superior or inferior to either drug alone in treating bupivacaine cardiotoxicity. We compared the effects of lipid, epinephrine, and the combination of the two in reversing bupivacaine-induced asystole in the isolated rat heart model. We also measured the effects of lipid, epinephrine, and the combination of the two on bupivacaine content in cardiac tissue.

METHODS: Hearts from male Sprague–Dawley rats were excised and retrograde-perfused in a nonrecirculating Langendorff preparation. Bupivacaine 100 μmol/L was perfused until 3 minutes after asystole. Two percent lipid and 30 μmol/L bupivacaine mixture was then perfused in the lipid group; 0.15 μg/mL epinephrine and 30 μmol/L bupivacaine mixture in the epinephrine group; 2% lipid combined with 0.15 μg/mL epinephrine and 30 μmol/L bupivacaine in the combination group; and 30 μmol/L bupivacaine alone in the control group. Recovery of heartbeat was defined as unassisted regular rhythm with a rate-pressure product (RPP) >10% of
baseline for >1 minute. We compared the time from the end of 100 μmol/L bupivacaine infusion to recovery of heartbeat (T\text{recovery}) for each group. The variables of cardiac function were recorded for 40 minutes after recovery of heartbeat. The cardiac apex of each heart was taken for measurement of the bupivacaine content by liquid chromatography–tandem mass spectrometry at the end of the experiment.

**RESULTS:** Time to recovery (T\text{recovery}) in the lipid and combination groups was significantly shorter than that in the epinephrine and control groups (P < 0.001), and T\text{recovery} in the epinephrine group was shorter than that in the control group (P < 0.05). The rank order of the mean RPP during the 40 minutes after recovery of heartbeat from highest to lowest was the combination group > the lipid and epinephrine groups > the control group (P < 0.01). The rank order of the highest RPP value during recovery (RPP_{maximum}) and the ratio of RPP_{maximum} to baseline value (RPP_{maximum}/RPP_{baseline}) from highest to lowest was the combination group > the lipid and epinephrine groups > the control group (P < 0.01). There was no significant difference between the lipid and epinephrine groups for RPP, RPP_{maximum}, and RPP_{maximum}/RPP_{baseline}.

Cardiac tissue bupivacaine content in the epinephrine and control groups was higher than that in the lipid and combination groups (P < 0.001).

**CONCLUSIONS:** Lipid combined with epinephrine resulted in better recovery of cardiac function than either drug alone in reversal of bupivacaine-induced asystole in the isolated rat heart model.