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大鼠暴露在超重环境下 **14** 天增加丙泊酚的作用

Hypergravity Exposure for 14 Days Increases the Effects of Propofol in Rats

Iwata, Chihiro MD*; Abe, Chikara DDS, PhD*; Nakamura, Mitsuhiro PhD†; Morita, Hironobu MD, PhD*

Anesthesia & Analgesia 2014 118 125–131

背景：有人认为太空探索的重力环境改变了麻醉药的效果，然而并没有相关证据发表过。在这篇研究中，我们试图提供直接证据表明 14 天暴露在超重环境中增加了麻醉效果并且验证了可能的原因。

方法：在 3g 环境下饲养 Sprague-Dawley 大鼠 14 天。在进行试验那天，将大鼠从 3g 环境取出，在 1g 环境下休息 1 至 2 小时，然后静脉输注丙泊酚（20mg/kg，输注时间 5 分钟）。对照组的大鼠被持续饲养在 1g 环境下。通过测量诱发脑电图爆发抑制所耗费时间、动脉血压最低点和受到伤害性电刺激后出现翻正反应的耗时来比较饲养在 1g 和 3g 环境下的大鼠之间的丙泊酚效果。也检测了丙泊酚血浆浓度的时相。在有前庭病变的大鼠身上也进行了试验以验证前庭系统是否影响了观察结果。所有参数都用平均数±标准差表示。

结果：在 3g 环境下饲养的大鼠比 1g 环境下饲养的大鼠，诱发出脑电图爆发抑制平均时间更早（195.7 ± 15.1 秒比 267.3 ± 29.4 秒, P = 0.00037），平均动脉血压的最低点更低（75.0 ± 15.5 mmHg 比 100.6 ± 9.1 mm Hg, P = 0.019），出现翻正反应的平均时间更晚（39.0 ± 8.4 分钟比 22.0 ± 3.1 分钟, P < 0.0001）。然而，对比 1g 环境下持续饲养的假处理组大鼠，饲养在 3g 环境下的前庭病变大鼠中诱发出脑电图爆发抑制的平均时间、平均动脉血压最低点和出现翻正反应的平均耗时并没有改变（分别为 275 ± 29.4 秒、108.7 ± 14.6 mmHg 和 20.8 ± 2.8 分钟, P 分别= 0.95、0.73 和 0.98）。丙泊酚血浆浓度的时相评定没有组间差异。

结论：该实验结果为暴露在超重环境下 14 天增加丙泊酚的效果提供了依据。它提示了该结果并不是丙泊酚血浆浓度差异造成的，而是由前庭系统介导的敏感性增加造成的。

（盛嘉君 译， 马皓琳、李士通 审校）

BACKGROUND: It is thought that the gravitational environment of space exploration alters the effects of anesthetics; however, no evidence has as yet been reported. In the present study, we sought to provide direct evidence showing that hypergravity exposure for 14 days increases anesthetic effects and to examine the possible causes.

METHODS: Sprague-Dawley rats were raised in a 3g environment for 14 days. On the day of the experiment, rats were brought out of 3g and rested at 1g for 1 to 2 hours before IV propofol infusion (20 mg/kg, for 5 minutes). Control rats were continuously raised in a 1g environment. The effects of propofol were compared between rats raised in 1g and 3g environment by measuring time taken to induce the burst suppression in an electroencephalogram, nadir of arterial blood pressure, and time taken for the appearance of the righting response to noxious electrical stimulations. The time course of plasma propofol concentrations was also examined. Experiments were also conducted on rats with vestibular lesions to examine whether the vestibular system participated in the observed results. All values were expressed as mean ± SD.

RESULTS: In rats raised in 3g environment, the mean time to induce burst suppression in the electroencephalogram was earlier (195.7 ± 15.1 seconds, P = 0.00037), the nadir of mean arterial blood pressure was lower (75.0 ± 15.5 mm Hg, P = 0.019), and mean time for the righting response to appear was later (39.0 ± 8.4 minutes, P < 0.0001) than in rats raised in 1g environment (267.3 ± 29.4 seconds, 100.6 ± 9.1 mm Hg, and 22.0 ± 3.1 minutes, respectively). However, mean time to induce burst suppression and for the righting response to appear did not change in rats with vestibular lesions raised in 3g environment (275 ± 29.4 seconds, 108.7 ± 14.6 mm Hg, and 20.8 ± 2.8 minutes, P = 0.95, 0.73, and 0.98 vs sham-treated rats continuously

raised in a 1g environment, respectively). There was no difference between groups in the time course assessment of plasma propofol concentrations.

CONCLUSION: The results provide evidence that hypergravity exposure for 14 days increases the effects of propofol. It is suggested that the results were not caused by differences in plasma propofol concentrations but by increased sensitivity, which was mediated via the vestibular system.

腰硬联合麻醉和单次腰麻技术用于病态肥胖患者剖宫产手术的麻醉开始时间：一项随机对照比较研究

A Randomized Controlled Comparison Between Combined Spinal-Epidural and Single-Shot Spinal Techniques in Morbidly Obese Parturients Undergoing Cesarean Delivery: Time for Initiation of Anesthesia

Ross, Vernon H. MD; Dean, Laura S. MD; Thomas, John A. MD; Harris, Lynne C. BSN; Pan, Peter H. MSEE, MD

Anesthesia & Analgesia 2014 118 168–172

背景：虽然已有学者认为腰硬联合麻醉（CSE）比单次腰麻（SSS）更适用于病态肥胖患者，但对该类患者的蛛网膜下腔麻醉的最佳方法至今尚无定论。在本项随机对照研究中，我们比较了 SSS 和 CSE 两种技术用于择期行剖宫产手术的病态肥胖患者蛛网膜下腔麻醉开始所需的时间。

方法：拟行择期剖宫产手术的病态肥胖患者随机接受通过 SSS 或 CSE 技术实施的蛛网膜下腔麻醉。坐位脊椎穿刺过程由一名有经验的住院医师在 10 分钟内完成，如果穿刺失败，则改由产科主治麻醉医师进行操作。主要观察指标是从引导针刺入（SSS 组）或硬膜外针刺入（CSE 组）到鞘内注射药物完毕的时间（操作时间）。

结果：共有 44 名患者纳入并完成本研究，3 名因违反协议而被剔除。剩余的患者中，SSS 组 21 人，CSE 组 20 人。两组人口统计变量和体重指数的均数（标准差）（SSS 组为 48.7 ± 7.6 kg/m2，CSE 组为 49.9 ± 8.6 kg/m2）无差异。SSS 组和 CSE 组操作时间的中位数[四分位距]分别为 210 [116–692]和 180 [75–450]秒(P = 0.36)，差异的 95%可信区间(CI)为−80 到+180 秒。第一位操作者在 10 分钟内完成操作的比例，SSS 组为 71%，CSE 组为 95%(P = 0.09)，差异的 95%CI 为−2% 到+45%。SSS 组成功完成操作过程所需的尝试次数更多(P = 0.007)，差异的 95%CI 为+1 到+6。

结论：我们的结果提示，由有经验的住院医师操作的 CSE 技术比 SSS 技术用于病态肥胖患者蛛网膜下腔麻醉所需时间更短，操作尝试次数更少。

（陈彬彬 译， 马皓琳、李士通 审校）

BACKGROUND: There is no current consensus on the optimal technique for subarachnoid anesthesia in morbidly obese parturients even though some providers prefer the combined spinal-epidural (CSE) over single-shot spinal (SSS) technique. In this randomized controlled study, we compared the time required for initiation of subarachnoid anesthesia between SSS and CSE techniques in morbidly obese parturients undergoing elective cesarean delivery.

METHODS: Morbidly obese parturients presenting for elective cesarean delivery were randomized to receive subarachnoid anesthesia performed either with a SSS or a CSE technique. The spinal procedure in the sitting position was attempted by an experienced resident for up to 10 minutes, and if unsuccessful, the attending obstetric anesthesiologist assumed control of the procedure. The primary outcome was the time it took from the insertion of the introducer needle

(SSS group) or insertion of the epidural needle (CSE group) to the end of intrathecal injection of drugs (procedure time).

RESULTS: Forty-four patients were enrolled and completed the study. Three were excluded due to protocol violations. Of the remaining, 21 patients were in the SSS group and 20 in the CSE group. Demographic variables and mean (SD) body mass index (48.7 ± 7.6 kg/m2 for SSS; 49.9 ± 8.6 kg/m2 for CSE) were not different between groups. The median [interquartile range] for procedure time was 210 [116–692] seconds and 180 [75–450] seconds for SSS and CSE groups, respectively (P = 0.36), while the 95% confidence interval (CI) of the difference was −80 to +180 seconds. The first operator completed the procedure in <10 minutes in 71% of subjects in the SSS group and 95% of those in the CSE group (P = 0.09) and the 95% CI of the difference was −2% to +45%. There were more attempts to successful completion of the procedure in the SSS group (P = 0.007) with its 95% CI of the difference being +1 to +6.

CONCLUSION: Our results suggest that the CSE technique is noninferior to the SS technique in morbidly obese parturients for time of initiation of subarachnoid anesthesia and may be accomplished with fewer attempts than the SSS technique with experienced residents.

对美国学术型麻醉学教职员发表量的考察

Examination of Publications from Academic Anesthesiology Faculty in the United States

Hurley, Robert W. MD, PhD*; Zhao, Kevin MD†; Tighe, Patrick J. MD, MS*; Ko, Phebe S. MD*; Pronovost, Peter J. MD, PhD*; Wu, Christopher L. MD*

Anesthesia & Analgesia 2014 118 192–199

背景：美国麻醉学术协会的领导者发起了一项对麻醉科学历情况的考察，同时也考察了美国国立卫生研究院对美国麻醉医师的基金资助及出版刊物的质量。然而，与学术型麻醉医师（被医学院校定义为学术型）相关的出版物的发表量及人群特征仍未知。我们通过对美国医学院校协会的 2006 年-2008 年的一个两年的数据库的调研，了解相关的出版量及人群特征。

方法：检索 Pubmed 出版物数据库中的每个教职员，并将他们的个人信息，包括工作单位、性别、学历、学位、工作性质(半日制或全职)、任命状态(集体或个人)、部门地位、专业认证状态及研究生培训情况记录进一个新的数据库。

结果：来自任职于 108 项美国麻醉学术项目的 6143 名教职员在 2006 到 2008 年共发表了 8521 篇稿件。37%的教职员发表了稿件，而整体的平均发表率则为 0。至少有 1 篇发表文献的教员在高级职称（教授比讲师的比值比（OR）=6.4；可信区间（CI），4.57–8.49；P < 0.0001）、男性(OR 1.3； CI，0.14–1.47； P < 0.0001)、拥有一个优遇的任用状态(OR 2.1；CI，1.25–3.52；P = 0.0048)、缺少硕士生培养及专业认证(OR（MD 比 MD w/培训+认证）=1.3；CI，1.11–1.60；P = 0.0020)的教员中占有更高比例。只有一个 MD 学位的教员比有 MD/PhD 或 PhD 的教员发表率低（分别是：OR 0.45； CI，0.32–0.65； P < 0.0001； OR 0.27； CI， 0.20–0.37； P < 0.0001）。在至少发表一篇文献的组内，全职教授发表量比讲师多 3.8 倍(CI, 2.99–4.88； P < 0.0001)，缺少研究生培训的教员比培训并且认证过的教员发表量要多 1.4 倍 (CI, 1.16–1.78；P = 0.0009)。PhD 学位 (P = 0.006)、男性 (P = 0.013)及优遇的麻醉任用(P = 0.037) 同样有更高的发表率。

结论：医学院校相关麻醉医师在这个时期的整体发表率较低。以上数据建立起了美国学术型麻醉医师为了将来的竞争发起的“呼吁行动”学术活动的基线。增加结构化住院医师和专业培训医师研究教育项目的利用将同招募更多的 MD/PhD 和 PhD 学位的科学家致力于此领域一起，有助于共同提高麻醉学术部门的出版生产力。

（王赟 译 马皓琳 李士通 校）

BACKGROUND: Leaders in academic anesthesiology in the United States have called for an examination of the state of scholarship within anesthesiology departments. National Institutes of Health funding and publication quality of subsets of U.S anesthesiologists have been examined; however, the publication output of and the demographic characteristics that are associated with academic anesthesiologists, defined as faculty associated with a medical college, are unknown. A database from the American Association of Medical Colleges containing demographic information of all academic anesthesiologists in the United States was used to examine the publication output and demographic characteristics of anesthesiology faculty during a 2-year period from 2006 to 2008.

METHOD: All the publications found in the PubMed database for each faculty member were retrieved and included in a database containing their demographics including institution, gender, academic degree, academic rank, nature of appointment (part versus full-time), status of appointment (joint versus primary), departmental division, subspecialty certification status, and additional graduate medical education training.

RESULTS: Six thousand one hundred forty-three faculty who held positions at the 108 U.S. academic anesthesiology programs published 8521 manuscripts between 2006 and 2008. Thirty-seven percent of faculty published a manuscript, and the overall median publication rate was 0. The proportion of faculty with at least 1 publication was larger among faculty with higher rank (Odds Ratio [OR] for professors versus instructors = 6.4; confidence interval [CI], 4.57–8.49; P < 0.0001), male gender (OR 1.3; CI, 0.14–1.47; P < 0.0001), possessing a courtesy appointment status (OR 2.1; CI, 1.25–3.52; P = 0.0048) and lacking postgraduate training and subspecialty certification (OR for MD versus MD w/training + certification 1.3; CI, 1.11–1.60; P = 0.0020). Those faculty with an MD had lower probablility of publishing when compared with MD/PhD or PhD faculty (OR 0.45; CI, 0.32–0.65; P < 0.0001; OR 0.27; CI, 0.20–0.37; P < 0.0001, respectively). Within the group of faculty who published at least 1 paper, full professor faculty had 3.8 times more publications than instructors (CI, 2.99–4.88; P < 0.0001), and those who lacked postgraduate training had 1.4 times more publications than those who were trained and certified (CI, 1.16–1.78; P = 0.0009). PhD degree (P = 0.006), male gender (P = 0.013), and courtesy anesthesia appointment (P = 0.037) also were associated with higher publication rates.

CONCLUSIONS: The overall publication rate of anesthesiologists associated with medical schools was low in this time period. These data establish the pre-“call to action” baseline of scholarly activity by U.S. academic anesthesiologists for future comparisons. Increased use of structured resident and fellow research education programs as well as recruiting more MD/PhD and PhD scientists to the field may help to improve the publication productivity of academic anesthesiology departments.

腰椎手术失败与椎管内狭窄的硬膜外粘连松解:与预后相关的因素

Epidural Lysis of Adhesions for Failed Back Surgery and Spinal Stenosis: Factors Associated with Treatment Outcome

Hsu, Eugene MD, MBA*; Atanelov, Levan MD†; Plunkett, Anthony R. MD‡; Chai, Nu MD§; Chen, Yian BS‖ ; Cohen, Steven P. MD¶

Anesthesia & Analgesia 2014 118 215–224

背景:腰椎手术失败综合征是一个具有挑战性的问题。硬膜外粘连松解是被主张用于腰椎手术失败综合征的治疗措施之一。关于硬膜外粘连松解用于腰椎手术失败综合征的研究结果有好有坏，但都因没有找出与结果相关的因素而受到限制。

方法:我们对 2004 年至 2007 年 115 例接受硬膜外粘连松解的患者进行了多中心、回顾性的研究。其中 104 例为腰椎手术失败综合征，11 例为椎管内狭窄。从病历中提取了 27 项人口统计学、临床和手术变量，研究其与预后的相关性。预后定义为≥50%的疼痛缓解持续≥1 个月。进行单变量分析，随后进行多因素 logistic 回归分析。

结果:总体而言，48.7%的患者（95%可信区间为 39.3%–58.1%）达到了良好的预后。单因素分析中，达良好预后的人群包括年长的（平均年龄 64.1 岁，95%可信区间为 59.7–68.6，对比 57.2 岁，95%可信区间为 53.0–61.4，P=0.02），而较高的疼痛评分基础数值与不良预后有关（平均 6.7 年，95%可信区间为 6.0-7.3 对比 7.5 年，95%可信区间为 6.9-8.0，P = 0.07）。使用透明质酸酶并没有在单因素分析中与预后呈现相关性（比值比 1.2， 95%可信区间为 0.6–2.5，P = 0.65）。在多变量分析中，年龄≥81 岁(比值比 7.8，95%可信区间 1.4–53.7), 疼痛评分基础值≤9 (比值比 4.4，95%可信区间 1.4-16.3, P = 0.02), 以及具有或正在寻求残疾或劳工赔偿的患者(比值比 4.4，95%可信区间 1.1-19.5, P = 0.04)显著地更可能经历积极的预后。

结论:考虑到我们不太高的成功率，根据统计学和临床因素来选择进行硬膜外粘连松解手术的患者可有助于更好挑选治疗的候选人。手术操作性因素例如透明质酸酶增加了风险和成本，并没有改善预后。因此将其作为标准疗法前还需要进一步的研究。

（邢怡安 译 马皓琳 李士通 校）

BACKGROUND: Failed back surgery syndrome (FBSS) is a challenging problem. One treatment advocated to treat FBSS is epidural lysis of adhesions (LOA). The results of studies examining LOA for FBSS have been mixed, but are limited because no study has ever sought to identify factors associated with outcomes.

METHODS: We performed this multicenter, retrospective study in 115 patients who underwent LOA for FBSS (n = 104) or spinal stenosis (n = 11) between 2004 and 2007. Twenty-seven demographic, clinical, and procedural variables were extracted from medical records and correlated with the outcome, defined as ≥50% pain relief lasting ≥1 month. Univariable analysis was performed, followed by multivariable logistic regression.

RESULTS: Overall, 48.7% (95% confidence interval [CI], 39.3%–58.1%) of patients experienced a positive outcome. In univariable analysis, those who had a positive outcome were older (mean age 64.1 years; 95% CI, 59.7–68.6 vs 57.2; 95% CI, 53.0–61.4 years; P = 0.02), while higher baseline numerical rating scale pain scores were associated with a negative outcome (mean 6.7 years; 95% CI, 6.0–7.3 vs 7.5; 95% CI, 6.9–8.0; P = 0.07). Use of hyaluronidase did not correlate with outcomes in univariable analysis (odds ratio [OR], 1.2; 95% CI, 0.6–2.5; P = 0.65). In multivariable analysis, age ≥81 years (OR, 7.8; 95% CI, 1.4–53.7), baseline numerical rating scale score ≤9 (OR, 4.4; 95% CI, 1.4-16.3, P = 0.02), and patients on or seeking disability or worker's compensation (OR, 4.4; 95% CI, 1.1-19.5, P = 0.04) were significantly more likely to experience a positive outcome.

CONCLUSIONS: Considering our modest success rate, selecting patients for epidural LOA based on demographic and clinical factors may help better select treatment candidates. Procedural factors such as the use of hyaluronidase that increase risks and costs did not improve outcomes, so further research is needed before these become standard practice.

局麻药诱导人乳腺肿瘤细胞凋亡

Local Anesthetics Induce Apoptosis In Human Breast Tumor Cells.

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背景：以前的研究已经表明，局麻药可诱导某些细胞凋亡。在这项研究中，我们研究了局麻药对人乳腺肿瘤细胞诱导凋亡的作用。

方法：我们选取了人乳腺癌（MCF -7）细胞株和乳腺上皮细胞（ MCF- 10A）细胞株，用利多卡因和/或布比卡因进行处理，评估了细胞活力， DNA 片段化和膜联蛋白Ⅴ免疫荧光染色。用 Western blot 分析研究对凋亡相关蛋白表达的影响。同时这项研究结果扩展到体内异种移植模型。

结果：经利多卡因和布比卡因处理后的乳腺肿瘤细胞通过诱导细胞凋亡抑制了细胞活力。MCF-7 细胞株比 MCF- 10A 细胞株更加突出。局麻药诱导了 caspase 7 ，8，9 和聚 ADP-核糖聚合酶的裂解。caspase 抑制剂有效封闭了局麻药诱导的 caspase 7 和聚 ADP-核糖聚合酶的裂解物。此外，在 MCF-7 细胞株的异种移植模型中，局麻药诱导后裂解的 caspase 7 表达更高，并增加了原位末端标记法染色的脱氧核苷酸转移酶。

结论：利多卡因和布比卡因在临床相关浓度可诱导乳腺肿瘤细胞的凋亡。我们的研究结果揭示了局部麻醉药先前未确认的益处，并需进一步研究在乳腺癌术中其抑癌作用。

（陈实玉 译 薛张纲校）

BACKGROUND: Previous studies have shown that local anesthetics may induce apoptosis in some cell types. In this study, we investigated the apoptotic effects of local anesthetics in human breast tumor cells.

METHODS: Human breast cancer (MCF-7) and mammary epithelial (MCF-10A) cell lines were treated with lidocaine and/or bupivacaine. Cell viability, DNA fragmentation, and annexin V immunofluorescence staining were assessed. The effects on apoptosis-related protein expression were investigated by Western blot analysis. The findings were extended to studies in an in vivo xenograft model.

RESULTS: Treatment of breast tumor cells with lidocaine and bupivacaine resulted in inhibition of cell viability via induction of apoptosis. The effects were more prominent in MCF-7 cells than in MCF-10A cells. Treatment with local anesthetics induced caspase 7, 8, 9, and poly ADP-ribose polymerase cleavage. The cleavage of caspase 7 and poly ADP-ribose polymerase induced by local anesthetics were effectively blocked by caspase inhibitors. Furthermore, treatment of MCF-7 xenografts with local anesthetics resulted in higher expression of cleaved caspase 7 and an increase in terminal deoxynucleotidyl transferase dUTP nick-end labeling (TUNEL) staining.

CONCLUSION: Lidocaine and bupivacaine induce apoptosis of breast tumor cells at clinically relevant concentrations. Our results reveal previously unrecognized beneficial actions of local anesthetics and call for further studies to assess the oncologic advantages of their use during breast cancer surgery.

系统性回顾：笑气在分娩镇痛中的应用

Nitrous Oxide for the Management of Labor Pain: A Systematic Review

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背景：我们系统性地回顾了笑气对于分娩镇痛的疗效，对笑气应用于产妇分娩镇痛时的满意度及其副作用的等进行了分析。

方法：我们检索了 MEDLINE,EMBASE,护理累积指数，CINAHL 等数据库中的英文文献。研究的对象包括经历阴道分娩的产妇、暴露于笑气的参与分娩过程的及新生儿护理的医护人员。

结果：我们分析了一共 58 篇发表文献，代表了 59 个不同研究人群，2 组研究质量高，11 组较合理，46 组质量不高。笑气吸入麻醉对于减少疼痛的效果较硬膜外麻醉差，关于这方面的文章质量大都比较差。这些参差不齐的结果被用来评估妇女对于她们分娩经历的满意度，而且分娩疼痛管理导致这项综合研究较难实现。很多文献报道的对于母亲的负面效应例如恶心，呕吐，头晕和昏睡都影响了笑气的接受范围。使用笑气镇痛出生的新生儿，相较于其他方式镇痛或未上麻醉的新生儿的 apgar 评分并无明显差异。 对于职业危害以及职业暴露的证据是有限的。

结论：对于笑气应用于分娩镇痛的文献报道较少，且良莠不齐。涵盖镇痛效应，满意度，还有不利影响这些方面的研究还需继续。

（蒋鑫梅译 薛张纲校）

METHODS: We searched the MEDLINE, EMBASE, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases for articles published in English. The study population included pregnant women in labor intending a vaginal birth, birth attendees or health care providers who may be exposed to nitrous oxide during labor, and the fetus/neonate.

BACKGROUND: We systematically reviewed evidence addressing the effectiveness of nitrous oxidefor the management of labor pain, the influence of nitrous oxide on women's satisfaction with their birth experience and labor pain management, and adverse effects associated with nitrous oxide for labor pain management.

RESULTS: We identified a total of 58 publications, representing 59 distinct study populations: 2 studies were of good quality, 11 fair, and 46 poor. Inhalation of nitrous oxide provided less effective pain relief than epidural analgesia, but the quality of studies was predominately poor. The heterogeneous outcomes used to assess women's satisfaction with their birth experience and labor pain management made synthesis of studies difficult. Most maternal adverse effects reported in the literature were unpleasant side effects that affect tolerability, such as nausea, vomiting, dizziness, and drowsiness. Apgar scores in newborns whose mothers used nitrous oxide were not significantly different from those of newborns whose mothers used other labor pain management methods or no analgesia. Evidence about occupational harms and exposure was limited.

CONCLUSIONS: The literature addressing nitrous oxide for the management of labor pain includes few studies of good or fair quality. Further research is needed across all of the areas examined: effectiveness, satisfaction, and adverse effects.

脑电活动遵循 Benford 法则

Brain Electrical Activity Obeys Benford's Law

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背景：监测和自动在线分析脑电活动经常用于诊断脑部疾病和评估手术中麻醉深度。然而错误的诊断会给病人带来例如术中知晓等灾难性后果。这主要是由信号分析过程中不规则所导致。这里我们主要探讨 Benford 法则是否可用于检测神经生物信号有意或无意的调制。该法则认为许多数据库的首批数字资料，例如原子量和河流长度，都是对数分布且不均等的。我们特意检测了在使用或不使用麻醉药物的情况下，来自病人代表全脑生物电活动的记录信号，以及器官型切片代表单纯皮质活动的信号是否遵循 Benford 法则。

方法： 在使用七氟醚前后分别描记来自病以及局部皮质电位。数据资料中第一批数字分布与 Benford 分布进行对比。

结果：所有数据显示 Benford 样分布。然而在离体及人体实验采集的生物电信号，均显示不同麻醉深度条件下，分布也不同。在七氟醚麻醉状态下，离体实验中第一数字分布曲线冯家陡峭，而活体脑电图资料较为平坦。在高频噪声存在条件下，Benford 分布消失。

结论：离体实验和 EEG 资料都显示 Benford 样分布。该分布可被七氟醚麻醉所改变，也可被人工模拟产生的噪音消除。这些发现表明基于 Benford 法则的运算可以成功用于检测七氟醚介导的电生理记录的信号调制。

（李春译 薛张纲校）

BACKGROUND: Monitoring and automated online analysis of brain electrical activity are frequently used for verifying brain diseases and for estimating anesthetic depth in subjects undergoing surgery. However, false diagnosis with potentially catastrophic consequences for patients such as intraoperative awareness may result from unnoticed irregularities in the process of signal analysis. Here we ask whether Benford's Law can be applied to detect accidental or intended modulation of neurophysiologic signals. This law states that the first digits of many datasets such as atomic weights or river lengths are distributed logarithmically and not equally. In particular, we tested whether data obtained from electrophysiological recordings of human patients representing global activity and organotypic slice cultures representing pure cortical activity follow the predictions of Benford's Law in the absence and in the presence of an anesthetic drug.

METHODS: Electroencephalographic (EEG) recordings from human subjects and local field potential recordings from cultured cortical brain slices were obtained before and after administration of sevoflurane. The first digit distribution of the datasets was compared with the Benford distribution.

RESULTS: All datasets showed a Benford-like distribution. Nevertheless, distributions belonging to different anesthetic levels could be distinguished in vitro and in human EEGs. With sevoflurane, the first digit distribution of the in vitro data becomes steeper, while it flattens for EEG data. In the presence of high frequency noise, the Benford distribution falls apart.

CONCLUSIONS: In vitro and EEG data show a Benford-like distribution which is altered by sevoflurane or destroyed by noise used to simulate artefacts. These findings suggest that algorithms based on Benford's Law can be successfully used to detect sevoflurane-induced signal modulations in electrophysiological recordings.

基于麻醉信息管理系统的接近实时决策支持用于管理术中低血压和高血压

Anesthesia Information Management System-Based Near Real-Time Decision Support To Manage Intraoperative Hypotension And Hypertension.

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背景：术中低血压和高血压都与不良的临床结果和发病率有关。通过麻醉信息管理系统（AIMS）干预的临床决策支持已被证明能够提高医疗质量。我们假设一个以 AIMS 为基础的临床决策支持系统可以用来改善术中低血压和高血压的管理。

方法：一个以 AIMS 为基础接近实时的决策支持模块，智能麻醉管理器（SAM）被用于检测事先选定的造成低血压和高血压的情景。分别使用低血压（收缩压<80 毫米汞柱）与高浓度吸入麻醉药（>1.25 最低肺泡有效浓度[MAC]）、高血压（收缩压>160 毫米汞柱）与输注去氧肾上腺素进行场景匹配来用于检测。麻醉工作人员通过电脑屏幕上的“弹出”信息获得通知。 对 AIMS 的资料进行回顾性分析，以评估 SAM 的通知消息对低血压和高血压事件发生情况的影响。

结果：收集和比较了建立 SAM 信息系统前 12 个月（N = 16913）及后 12 个月（N = 17132）的麻醉病例资料，使用信息系统通知后低血压合并高 MAC 的中位持续时间明显缩短（曼惠特尼秩和检验，P = 0.031）。然而，高血压事件合并输注苯肾上腺素的中位持续时间并无显著性减少（P = 0.47）。持续时间超过 6 分钟（SAM 的采样周期）的低血压发生频率（δ= -0.26 ％ [可信区间，-0.38 ％至-0.11 ％]，P <0.001）或高血压发生频率（δ= -0.92 ％ [可信区间，-1.79 ％至-0.04 ％] ，P = 0.035），以每 100 例手术（或百分比发生）发生的该类事件数量来表达，在使用信息系统通知后都显著减少。对于低血压事件，在接到通知信息后 81%的情况下麻醉工作人员会将吸入麻醉药浓度降至 1.25 MAC 以下，无通知时则只有 59%（P = 0.003）。对于高血压发作，虽然麻醉人员在接到通知信息后，降低或中止注射苯肾上腺素的情况从 22%提高到 37%（P = 0.030），但整体反应较对低血压发作的反应不太一致。

结论：在具有自动采集动脉血压和吸入麻醉药浓度变量的麻醉信息管理系统时，接近实时的通知信息可以有效减少低血压合并>1.25 MAC 吸入麻醉药事件的持续时间和频率。然而，由于苯肾上腺素是手动记录在 AIMS 中的，通知消息对减少高血压合并注射苯肾上腺素的事件发生作用不太明显。自动数据采集和 AIMS 较高频率的数据采集可以提高术中临床决策支持系统的有效性。

（凌晓敏译 薛张纲校）

BACKGROUND: Intraoperative hypotension and hypertension are associated with adverse clinical outcomes and morbidity. Clinical decision support mediated through an anesthesia information management system (AIMS) has been shown to improve quality of care. We hypothesized that an AIMS-based clinical decision support system could be used to improve management of intraoperative hypotension and hypertension.

METHODS:A near real-time AIMS-based decision support module, Smart Anesthesia Manager (SAM), was used to detect selected scenarios contributing to hypotension and hypertension. Specifically, hypotension (systolic blood pressure <80 mm Hg) with a concurrent high concentration (>1.25 minimum alveolar concentration [MAC]) of inhaled drug and hypertension(systolic blood pressure >160 mm Hg) with concurrent phenylephrine infusion were

detected, and anesthesia providers were notified via "pop-up" computer screen messages. AIMS data were retrospectively analyzed to evaluate the effect of SAM notification messages on hypotensive and hypertensive episodes.

RESULTS: For anesthetic cases 12 months before (N = 16913) and after (N = 17132) institution of SAM messages, the median duration of hypotensive episodes with concurrent high MAC decreased with notifications (Mann Whitney rank sum test, P = 0.031). However, the reduction in the median duration of hypertensive episodes with concurrent phenylephrine infusion was not significant (P = 0.47). The frequency of prolonged episodes that lasted >6 minutes (sampling period of SAM), represented in terms of the number of cases with episodes per 100 surgical cases (or percentage occurrence), declined with notifications for both hypotension with >1.25 MAC inhaled drug episodes (δ = -0.26% [confidence interval, -0.38% to -0.11%], P < 0.001) and hypertension with phenylephrine infusion episodes (δ = -0.92% [confidence interval, -1.79% to -0.04%], P = 0.035). For hypotensive events, the anesthesia providers reduced the inhaled drug concentrations to <1.25 MAC 81% of the time with notifications compared with 59% without notifications (P = 0.003). For hypertensive episodes, although the anesthesia providers' reduction or discontinuation of the phenylephrine infusion increased from 22% to 37% (P = 0.030) with notification messages, the overall response was less consistent than the response to hypotensive episodes.

CONCLUSIONS: With automatic acquisition of arterial blood pressure and inhaled drug concentration variables in an AIMS, near real-time notification was effective in reducing the duration and frequency of hypotension with concurrent >1.25 MAC inhaled drug episodes. However, since phenylephrine infusion is manually documented in an AIMS, the impact of notification messages was less pronounced in reducing episodes of hypertension with concurrent phenylephrine infusion. Automated data capture and a higher frequency of data acquisition in an AIMS can improve the effectiveness of an intraoperative clinical decision support system.

术后恶心呕吐管理的共识指南

Consensus Guidelines for the Management of Postoperative Nausea and Vomiting

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摘要：现有指南包含关于术后恶心呕吐的最新数据，以及对 2003 年和 2007 年版指南的更新。这些指南是在非住院患者麻醉学会的主持下，由各 PONV 专家组成的一个多学科国际工作组编撰而成。工作组成员系统地对现有的 PONV 医学文献进行评价，以便对那些接收手术并有 PONV 高危风险的成人和儿童如何进行管理提出循证医学的参考工具。这些指南确认有 PONV 风险的成年和儿童患者，推荐减少发生 PONV 风险的方法，确认包括非药物方法在内的最有效的止吐单一治疗和预防 PONV 的联合治疗方案; 推荐 PONV 发生时的治疗策略，为管理有 PONV 高危风险的个体以及确保预防和治疗 PONV 应用于临床的步骤提出一种算法。

（谈婧华 译 陈杰 校）

The present guidelines are the most recent data on postoperative nausea and vomiting (PONV) and an update on the 2 previous sets of guidelines published in 2003 and 2007. These guidelines were compiled by a multidisciplinary international panel of individuals with interest and expertise in PONV under the auspices of the Society for Ambulatory Anesthesia. The panel members critically and systematically evaluated the current medical literature on PONV to provide an evidence-based reference tool for the management of adults and children who are undergoing surgery and are at increased risk for PONV. These guidelines identify patients at risk for PONV in adults and children; recommend approaches for reducing baseline risks for PONV; identify the most effective antiemetic single therapy and combination therapy regimens for PONV prophylaxis, including nonpharmacologic approaches; recommend strategies for treatment of PONV when it occurs; provide an algorithm for the management of individuals at increased risk for PONV as well as steps to ensure PONV prevention and treatment are implemented in the clinical setting.

病态肥胖病人肺复张的无创监测：脉搏血氧饱和度仪和容积二氧化碳图的作用

Noninvasive Monitoring of Lung Recruitment Maneuvers in Morbidly Obese Patients: The Role of Pulse Oximetry and Volumetric Capnography

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背景：此研究目的是探讨脉搏血氧饱和度监测和容积二氧化碳图(VCap)能否测定麻醉状态下病态肥胖患者肺开放和关闭压。

方法：研究 20 位行气腹下腹腔镜减肥手术的病态肥胖患者。控制通气压力的肺复张手法如下：（1）在升支测量肺的开放压。呼气末正压(PEEP)从 8 cm H2O 增至 16cmH2O 后，吸入氧浓度(FIO2)开始下降直到脉搏血氧饱和度(SpO2)小于 92%。然后，吸气末压力以 2 cm H2O 递增，可从 36 cm H2O 增加到 50 cm H2O 高限。当 SpO2 超过 97%时达到开放压。（2）在随后的降支，确认肺的关闭压。PEEP 以 2cm H2O 为单位从 22 cm H2O 递降至 10 cm H2O。关闭压定义为呼吸顺应性从其最大值开始下降的 PEEP 值。持续的记录肺力学参数、SpO2 和 VCap。

结果：肺的开放压为 44(4) cm H2O（中位数和四分位间距），关闭压为 14（2）cm H2O。因此，维持肺不塌陷的 PEEP 水平为 16（3）cm H2O。利用呼吸顺应性作参考，受试者工作特征分析表明 SpO2（曲线下面积[AUC] 0.80 [SE 0.07]，敏感性 0.65，特异性 0.94)；每次呼吸的 CO2 清除(AUC 0.91 [SE 0.05], 敏感性 0.85, 特异性 0.98)；Bohr 死腔(AUC 0.83 [SE 0.06], 敏感性 0.70, 特异性 0.95)。在复张手法的下降支，这些数据对于探测肺塌陷相对准确。

结论：通过结合脉搏血氧饱和度测定和 Vcap 的无创方法，对病态肥胖患者的肺复张可进行有效监测。SpO2、CO2 清除和 Bohr 死腔可判定个体的开放压和关闭压。

（朱浩 译 陈杰 校）

BACKGROUND: We conducted this study to determine whether pulse oximetry and volumetric capnography (VCap) can determine the opening and closing pressures of lungs of anesthetized morbidly obese patients.

METHODS: Twenty morbidly obese patients undergoing laparoscopic bariatric surgery with capnoperitoneum were studied. A lung recruitment maneuver was performed in pressure control ventilation as follows: (1) During an ascending limb, the lungs' opening pressure was detected.

After increasing positive end-expiratory pressure (PEEP) from 8 to 16 cm H2O, fraction of inspired oxygen (FIO2) was decreased until pulse oximetric arterial saturation (SpO2) was <92%. Thereafter, end-inspiratory pressure was increased in steps of 2 cm H2O, from 36 to a maximum of 50 cm H2O. The opening pressure was attained when SpO2 exceeded 97%. (2) During a subsequent decreasing limb, the lungs' closing pressure was identified. PEEP was decreased from 22 to 10 cm H2O in steps of 2 cm H2O. The closing pressure was determined as the PEEP value at which respiratory compliance decreased from its maximum value. We continuously recorded lung mechanics, SpO2, and VCap.

RESULTS: The lungs' opening pressures were detected at 44 (4) cm H2O (median and interquartile range) and the closing pressure at 14 (2) cm H2O. Therefore, the level of PEEP that kept the lungs without collapse was found to be 16 (3) cm H2O. Using respiratory compliance as a reference, receiver operating characteristic analysis showed that SpO2 (area under the curve [AUC] 0.80 [SE 0.07], sensitivity 0.65, and specificity 0.94), the elimination of CO2 per breath (AUC 0.91 [SE 0.05], sensitivity 0.85, and specificity 0.98), and Bohr's dead space (AUC 0.83 [SE 0.06], sensitivity 0.70, and specificity 0.95] were relatively accurate for detecting lung collapse during the decreasing limb of a recruitment maneuver.

CONCLUSIONS: Lung recruitment in morbidly obese patients could be effectively monitored by combining noninvasive pulse oximetry and VCap. SpO2, the elimination of CO2, and Bohr's dead space detected the individual's opening and closing pressures.

先天性心脏病患者进行心导管术时心跳骤停的发生率

The Frequency of Cardiac Arrests in Patients with Congenital Heart Disease Undergoing Cardiac Catheterization

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背景：因为导管技术的发展，心导管术对于有先天性心脏病的患者已经从诊断法转变成主要用于介入治疗。接受治疗性心导管术的儿童可能会有更高的不良事件发生风险，本研究目的是确定在一个大型的三级儿童转诊中心，先天性心脏病患者接受心导管术时心跳骤停（CA）的发生率。

方法：回顾从 2004 年 1 月至 2009 年 12 月所有在心导管实验室中发生的 CA。心跳骤停定义为需要进行胸外按压的循环停止。调查手术、患者、医生和系统相关的因素。

结果：研究期间共行 7289 例导管手术，70 例手术与心跳骤停相关(0.96 [99% 可信区间, 0.7–1.3]每 100 例手术)；48 例（69%）成功复苏至灌注节律，18 例（26%）需要行体外膜肺氧合，4 例（6%）导致复苏失败。38 例（54%）继发于突然产生的心律失常。在 CA 发生后 71%的复苏时间≤11 min（71%）。心跳骤停的发生与介入治疗和更小的年龄(P < 0.001)相关(P < 0.001)。病例规划和沟通系统的改变有效降低了心跳骤停的发生率(1.5% vs 0.7%; P = 0.002)。

结论：与非儿科心脏手术相比，接受心导管术儿童的 CA 发生率更高。在此群体中，程序和系统性因素也与心跳骤停的发生相关。这些问题强调密切沟通、预见和准备的必要性。

（李峰日 译 陈杰 校）

BACKGROUND: Cardiac catheterization for patients with congenital heart disease has shifted from diagnostic to predominantly interventional procedures because of advances in catheter-based technologies. Children undergoing therapeutic catheterization may be at higher risk of adverse events, and the purpose of our study was to determine the incidence of cardiac arrest

(CA) in patients with congenital heart disease undergoing cardiac catheterization at a large pediatric tertiary referral center.

METHODS: All CAs from January 2004 through December 2009 occurring in the cardiac catheterization laboratory were reviewed. A CA was defined as an event in which cessation of circulation required chest compressions. Procedure, patient, practitioner, and system-related factors were examined.

RESULTS: Over the study period, during 7289 catheterization procedures, 70 procedures were associated with a CA (0.96 [99% confidence interval, 0.7–1.3] per 100 procedures); 48 events (69%) were successfully resuscitated to a perfusing rhythm, 18 events (26%) resulted in need for extracorporeal membrane oxygenation, and 4 events (6%) resulted in unsuccessful resuscitation. Sudden onset of cardiac arrhythmia led to CA during 38 events (54%). The duration of resuscitation after CA was ≤11 minutes in 71%. Occurrence of CA was associated with interventional procedures ($P < 0.001$) and younger age ($P < 0.001$). A change in systems for scheduling and communication of cases was associated with a significant reduction in the incidence of CA (1.5% vs 0.7%; $P = 0.002$).

CONCLUSIONS: The incidence of CA in children undergoing cardiac catheterization is high compared with pediatric noncardiac surgery. Procedural and system factors were associated with occurrence of CA in this cohort. These issues highlight the need for close communication, anticipation, and preparation.

毕业后医学教育评鉴委员会（ACGME）授权的外科及麻醉住院医师项目中负责人的学术生产力研究

Academic Productivity of Directors of ACGME-Accredited Residency Programs in Surgery and Anesthesiology

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背景：毕业后医学教育评鉴委员会（ACGME）授权的住院医师训练计划中，要求项目负责人参与学术活动。由于相对外科项目而言，麻醉科住院医师计划往往被提及在学术生产力方面相对不足。猜测这一定程度上反映了麻醉与外科培训计划的负责人之间参与学术活动的不同。为验证此猜想，本研究以 PubMed 引用和国家卫生研究院（NIH）的资助作为学术活动的标准，检查了同一个机构内，目前经过 ACGME 授权的麻醉、外科住院医师计划负责人的执业记录。

方法：在 2011 年 11 月 1 日至 12 月 31 日之间，从完全公开的网站上收集了来自 127 个机构中的，拥有 ACGME 授权的麻醉学、外科学项目负责人数据。针对个人信息的收集包括证书登录年份、被任命为负责人的年份、学衔、NIH 承认的资金支持记录以及 PubMed 的引用数。同时计算了随机抽选的 25 位对应机构的负责人组成的子集中的 h 指数。

结果：各组之间负责人的证书登录年份（P=0.42）、学衔（P=0.38）以及作为项目负责人的年限（P=0.22）之间没有统计学差异。然而，麻醉学的项目负责人在过去或现在获得的 NIH 资助上较少（P=0.002）。在总体或与教学相关的 PubMed 引用上也较少（P 均＜0.001）。在 h 指数上也相对于外科学的负责人们要少（P=0.001）。多变量分析显示，在其他变量保持不变时，麻醉学负责人的发表率是相对应的外科学负责人的 43%（95%置信区间，0.31-0.58）。

结论：根据同行评议的发表数以及联邦研究基金，麻醉学住院医师计划项目的负责人相对于外科学项目的负责人而言，其学术活动明显较少。如此，本研究亦显示了在麻醉研究的学术结构中存在系统性弱点的进一步证据。

（贺加贝 译 陈杰 校）

BACKGROUND: Scholarly activity is expected of program directors of Accreditation Council for Graduate Medical Education (ACGME)-accredited residency training programs. Anesthesiology residency programs are cited more often than surgical programs for deficiencies in academic productivity. We hypothesized that this may in part reflect differences in scholarly activity between program directors of anesthesiology and surgical trainings programs. To test the hypothesis, we examined the career track record of current program directors of ACGME-accredited anesthesiology and surgical residency programs at the same institutions using PubMed citations and funding from the National Institutes of Health (NIH) as metrics of scholarly activity.

METHODS: Between November 1, 2011 and December 31, 2011, we obtained data from publicly available Web sites on program directors at 127 institutions that had ACGME-accredited programs in both anesthesiology and surgery. Information gathered on each individual included year of board certification, year first appointed program director, academic rank, history of NIH grant funding, and number of PubMed citations. We also calculated the h-index for a randomly selected subset of 25 institution-matched program directors.

RESULTS: There were no differences between the groups in number of years since board certification (P = 0.42), academic rank (P = 0.38), or years as a program director (P = 0.22). However, program directors in anesthesiology had less prior or current NIH funding (P = 0.002), fewer total and education-related PubMed citations (both P < 0.001), and a lower h-index (P = 0.001) than surgery program directors. Multivariate analysis revealed that the publication rate for anesthesiology program directors was 43% (95% confidence interval, 0.31–0.58) that of the corresponding program directors of surgical residency programs, holding other variables constant.

CONCLUSIONS: Program directors of anesthesiology residency programs have considerably less scholarly activity in terms of peer-reviewed publications and federal research funding than directors of surgical residency programs. As such, this study provides further evidence for a systemic weakness in the scholarly fabric of academic anesthesiology.

连续外周神经阻滞患者的血清游离罗哌卡因浓度：长期输注是否安全？

Serum Free Ropivacaine Concentrations Among Patients Receiving Continuous Peripheral Nerve Block Catheters: Is It Safe for Long-Term Infusions?

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背景：罗哌卡因是一种用于持续外周神经阻滞导管输注的长效药物。导管可以长期原位留置。在本研究中，入组患者给予持续外周神经置管并测定游离血清罗哌卡因浓度。

方法：放置外周神经导管用于创伤患者的术后疼痛管理，对其输注 0.2%的罗哌卡因或单次次给予 0.5%的剂量。取每个患者术后当天（预输注）、第 3、5、7、10 和随后每隔两天直至导管拔除的血液标本。使用高效液相色谱法测定游离血清罗哌卡因浓度并用 wilcoxon 符号秩检验对样本进行统计分析。

结果：对 35 位患者的 133 个血液样本进行了分析：开始输注后所有血清游离罗哌卡因的浓度（35 位患者中的 99 个样本）均低于 0.34 mg/L（先前设定的中毒阈值）。血液样本

中最高浓度为 0.19 mg/L；所有其他样本值都小于 0.09 mg/L。研究中药物使用量在 1146~22320mg 范围内（中位数为 3722mg）。导管留置的平均时间为 7 天（范围：3~23 天）。从术后当天到第 3 天（预输注），77%的患者血清游离罗哌卡因浓度有所增加。第 3 天的平均浓度为 0.025 mg/L（95%均值的置信上限为: 0.05, 范围：<0.01–0.19；与预输注水平相比，P < 0.001）。从术后第 3 天到第 5 天，68%的患者血清游离罗哌卡因浓度下降(平均水平为 0.016 mg/L[95%均值的置信上限为: 0.021]，术后第 5 天与第 3 天相比，P = 0.007)。

结论：在本研究中，尽管战伤患者大剂量使用罗哌卡因，但该药物血清游离浓度一直低于中毒剂量。长时间持续罗哌卡因输注以及联合多种药物单次剂量给药，并不产生中毒或接近中毒的血清药物浓度。

（边文玉 译 陈杰 校）

BACKGROUND: Ropivacaine is a long-acting local anesthetic used for continuous peripheral nerve catheter infusions. Catheters may remain in situ for prolonged time periods. In the present study, patients were enrolled to receive continuous peripheral nerve catheters with measurement of free serum ropivacaine concentrations.

METHODS: Peripheral nerve catheters were placed for postoperative pain management in trauma patients and infused with ropivacaine 0.2% or bolused with 0.5%. Blood samples were obtained from each subject on days 0 (preinfusion), 3, 5, 7, 10, and every third day until catheter removal. Serum free ropivacaine concentrations were measured via high-performance liquid chromatography and were compared using the Wilcoxon signed rank test.

RESULTS: One hundred thirty-three blood samples were analyzed in 35 patients; all serum free ropivacaine concentrations after infusion initiation (99 samples from 35 subjects) were below 0.34 mg/L (previously determined toxic threshold). The highest concentration achieved in a blood sample was 0.19 mg/L; all other values were <0.09 mg/L. The total amount of drug received during the study ranged from 1146 to 22,320 mg (median of 3722 mg). Catheters remained in situ for a median of 7 days (range: 3–23). From day 0 to 3 (preinfusion), 77% of the study participants had an increase in the serum free-fraction ropivacaine concentrations. The median concentration on day 3 was 0.025 mg/L (95% upper confidence limit for mean: 0.05, range: <0.01–0.19); P < 0.001 compared with preinfusion levels). From day 3 to 5, 68% of the participants had a decrease in the serum free ropivacaine concentrations (median level 0.016 mg/L [95% upper confidence limit for mean: 0.021] P = 0.007 for day 5 compared with day 3).

CONCLUSIONS: In this study, free serum ropivacaine concentrations remained well below toxic values despite large amounts of drug administration in combat-wounded patients. The administration of continuous ropivacaine infusions over prolonged time periods, coupled with multiple drug boluses, did not produce toxic or near-toxic serum concentrations.