心脏解剖的评估中标准胃肠超声内镜的应用

The Use of Standard Gastrointestinal Endoscopic Ultrasound to Assess Cardiac Anatomy

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在这项在一个学术医疗中心进行的前瞻性观察研究中，我们评估了在基础的经食管超声心动图（TEE）检查中使用内镜超声检查（EUS）技术来确定评估心脏结构的可行性。当在内镜中心发生因低血容量、心室功能低下、主动脉夹层、心包积液或主动脉瓣狭窄引起的血流动力学突发事件，这项技术可能存在潜在的益处。在登记的 20 例患者中，18 例在标准的临床适应征下使用线性超声内镜行内镜超声检查（EUS）和由具有 TEE 执照的心脏麻醉医师的指导下进行心脏评估。20 例病患中有 8 例可以使用线性超声内镜获得 1999 版美国超声心动图协会和心血管麻醉医师协会 TEE 指南所认可的心血管结构的标准影像。以下这些心脏瓣膜结构可以完成可视化：主动脉瓣（100%）、二尖瓣（100%）、三尖瓣（33%）和肺动脉瓣（11%）。左心室收缩功能和右心室收缩功能分别可以在 89%和 67%的病患中进行评估。其他结构诸如升、降主动脉、心包、左心耳和房间隔都可以在 100%的病患中予以识别。依赖多普勒技术的功能不能被评估。鉴于 EUS 的图像不能与 TEE 的图像在这些病患中进行直接的比较，我们不能明确地对这些评估的质量进行评论，在将来的研究中需要进行一个正式的比较。基于这项研究，EUS 技术可以持续评估二尖瓣、主动脉瓣、主动脉、心包和左心室功能。鉴于其局限性，EUS 技术尽管不是一个正式超声心动图检查的替代品，仍可以作为一个有用的早期诊断工具

（俞启蒙 译 薛张纲 校）

In this prospective observational study, conducted at an academic medical center, we evaluated the feasibility of performing a basic transesophageal echocardiography (TEE) examination using endoscopic ultrasound (EUS) technology to determine what cardiac structures could be assessed. This may be potentially beneficial during hemodynamic emergencies in the endoscopy suite resulting from hypovolemia, depressed ventricular function, aortic dissection, pericardial effusions, or aortic stenosis. Of the 20 patients enrolled, 18 underwent EUS with a linear echoendoscope for standard clinical indications followed by a cardiac assessment performed under the guidance of a TEE-certified cardiacanesthesiologist. Eight of the 20 standard views of cardiovascular structures per the 1999 American Society of Echocardiography/Society of Cardiovascular Anesthesiologists guidelines for TEE could be obtained using the linear echoendoscope. The following cardiac valvular structures were visualized: aortic valve (100%), mitral valve (100%), tricuspid valve (33%), and pulmonic valve (11%). Left ventricular and right ventricular systolic function could be assessed in 89% and 67% of patients, respectively. Other structures such as the ascending and descending aorta, pericardium, left atrial appendage, and interatrial septum were identified in 100% of patients. Doppler-dependent functions could not be assessed. Given that the EUS images were not directly compared with TEE in these patients, we cannot comment definitively on the quality of these assessments and further studies would need to be performed to make a formal comparison. Based on this study, EUS technology can consistently assess the mitral valve, aortic valve, aorta, pericardium, and left ventricular function. Given its

limitations, EUS technology, although not a substitute for formal echocardiography, could be a helpful early diagnostic tool in an emergency setting.

用于电休克治疗的琥珀酰胆碱及罗库溴铵的最小有效剂量：一项前瞻性随机交叉研究

Effective Doses of Succinylcholine and Rocuronium During Electroconvulsive Therapy: A Prospective, Randomized, Crossover Trial

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背景：电休克治疗（electroconvulsive therapy，ECT）期间需要应用肌松药以控制过度的肌肉收缩。在一项评估者设盲的前瞻性随机交叉研究中，我们探讨了用于电休克治疗的琥珀酰胆碱及罗库溴铵的最小有效剂量（minimum effective dose, MED）。MED 是指为诱发抽搐过程中控制肌松达可接受程度提供预先的定量评估的最低剂量。

方法：琥珀酰胆碱（0.8mg/kg）或者罗库溴铵（0.4mg/kg）随机用于接受 227 次电休克治疗的 45 名患者。根据两位精神科专家（设盲）对肌肉收缩控制程度（充分、不充分或者过度松弛）的评估结果（可接受或不能接受）逐渐增加或者减少 10%的药物剂量。定量监测神经肌肉传递功能直至肌松完全恢复。

结果：使得 50%的电休克治疗患者产生可接受的肌松程度的琥珀酰胆碱及罗库溴铵的最低有效剂量（$MED50_{ECT}$）分别为 0.85mg/kg(95%置信区间 0.77-0.94)和 0.41mg/kg(95%置信区间 0.36-0.46)，而 90%的患者产生可接受的肌松程度的琥珀酰胆碱及罗库溴铵的最低有效剂量（$MED90_{ECT}$）分别为 1.06mg/kg(95%置信区间 1.0-1.27)和 0.57mg/kg(95%置信区间 0.5-0.6)。使用琥珀酰胆碱和罗库溴铵达到可接受的肌松程度时对应的肌颤搐高度分别为 0%（0-4）和 4%（0-30；$p<0.01$），而肌松恢复时间分别为 9.7±3.5 分钟和 19.5±5.7 分钟。

结果：电休克治疗需要抑制 90%的肌颤搐已到达控制肌肉收缩的目的。琥珀酰胆碱的首次剂量应该根据每一位患者的术前情况而定，0.77-1.27mg/kg 范围内的琥珀酰胆碱可使 50%-90%电休克治疗患者达到可接受的肌松程度。当然，在肌松监测条件下适当剂量的罗库溴铵（0.36-0.6mg/kg）-新斯的明组合也是一个合适的选择。

（王之遥 译 薛张纲 校）

BACKGROUND: Neuromuscular blockade is required to control excessive muscle contractions during electroconvulsive therapy (ECT). In a crossover, assessor-blinded, prospective randomized study, we studied the minimum effective dose (MED) of succinylcholine and rocuronium for ECT. The MED was the lowest dose to provide a predefined qualitative measure of acceptable control of muscle strength during induced convulsions。

METHODS: Succinylcholine (0.8 mg kg) or rocuronium (0.4 mg kg) was randomly administered in 227 ECT sessions to 45 patients. The dose was incrementally increased or decreased by 10% based on 2 psychiatrists' (blinded to treatment) assessment of "acceptable" or "not acceptable" control of evoked muscle contractions (sufficient versus insufficient or excessive paralysis). The neuromuscular transmission was monitored quantitatively until full recovery.

RESULTS: In our study, the MEDs of succinylcholine and rocuronium to produce

acceptable ECT conditions in 50% of patients (MED50ECT) were 0.85 mg kg (95% confidence interval [CI], 0.77-0.94) and 0.41 mg kg (95% CI, 0.36-0.46) and in 90% of patients (MED90ECT) were 1.06 mg kg (95% CI, 1.0-1.27) and 0.57 mg kg (95% CI, 0.5-0.6), respectively. Nadir twitch height for acceptable muscle activity was 0% (0-4) and 4% (0-30; P < 0.001), respectively, and the time to recovery of the neuromuscular transmission was 9.7 ± 3.5 and 19.5 ± 5.7 minutes, respectively.
CONCLUSIONS: A twitch suppression of >90% is needed for control of motor contractions during ECT. The initial ECT dose of succinylcholine should be selected based on each patient's preprocedural condition, ranging between 0.77 and 1.27 mg kg to produce acceptable muscle blockade in 50% to 90% of patients. Rocuronium-neostigmine combination is a safe alternative if appropriately dosed (0.36-0.6 mg kg) and monitored.

利多卡因削弱老年人皮肤成纤维细胞的增殖和生物合成功能

Lidocaine Impairs Proliferative and Biosynthetic Functions of Aged Human Dermal Fibroblasts

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背景：老年人面临着术后伤口愈合并发症发生率增高的风险。因为局部麻醉药经常渗透到外科伤口的真皮层中，我们想证实局部麻醉药是否对成纤维细胞的增殖和生物合成功能有负性作用。胰岛素样生长因子 1(IGF-1)和转化生长因子 β1 (TGF-β1)这类生长因子对伤口愈合有重要调节作用，所以我们还评估了局部麻醉药对其影响。

方法：老年和青年志愿者捐献的人真皮成纤维细胞(HFB)暴露在临床所使用浓度的局部麻醉药中。我们比较了利多卡因、布比卡因、马比弗卡因和罗哌卡因对 HFB 的影响，其中利多卡因对不利影响最大。然后我们评估了利多卡因对生长因子 IGF-1 和 TGF-β1 表达和功能的影响。最后，我们分别将 IGF-1 或 TGF-β1 同时分别暴露在利多卡因中，来评估他们对增殖和真皮胶原纤维的影响。

结果：利多卡因和马比弗卡因抑制了老年人 HFB 的增殖（利多卡因为对照组的 88%，95%CI, 80%–98%, P = .009; 马比弗卡因为对照组的 90%，95% CI, 81%–99%, P = .032），但在年轻人的 HFB 中并没有发现此现象。罗哌卡因和布比卡因对增殖并无抑制作用。因为利多卡因的临床作用与马比弗卡因相似，再此我们仅关注利多卡因。利多卡因对老年人 HFB 的增殖的抑制作用可被 IGF-1 抵消。利多卡因抑制了老年捐献者成纤维细胞中的 IGF-1 复制和胰岛素样生长因子受体(IGF1R) (IGF-1, log2 fold-change −1.25 [为对照组 42%, 95% CI, 19%–92%, P = .035] ; IGF1R, log2 fold-change −1.00 [为对照组 50%, 95% CI, 31%–81%, P = .014])。另一方面，利多卡因并不影响年轻人 HFB 中 GF-1 或 IGF1R 的转录物。暴露于利多卡因之后，无论是老年人还是年轻人 HFB，胶原 III 的转录物都有所下降(老年人 HFB log2 fold-change −1.28 [41% of control, 95% CI, 20%–83%, P = .022]；年轻人 HFB log2 fold-change −1.60 [33% of control, 95% CI, 15%–73%, P = .019])。而胶原 I 的转录物仅在老年人 HFB 中有所下降(log2 fold-change −1.82 [28% of control, 95% CI, 14%–58%, P = .006])。与转录物相似，利多卡因同样同时抑制了年轻人和老年人 HFB 中胶原 III 的蛋白表达(年轻人 HFB log2 fold-change −1.79 [对照组的 29%, 95% CI, 18%–47%, P = .003]；老年人

HFB log2 fold-change −1.76 [对照组的 30%, 95% CI, 9%–93%, P = .043])。在年轻人和老年人 HFB 中，利多卡因对胶原 III 蛋白表达的作用都会被 TGF-β1 消除。**结论：**我们的结果表明利多卡因抑制了老年人 HFB 真皮修复的过程。利多卡因这种负性作用部分是因为与 IGF-1 和 TGF-β1 的相互作用。
（方婕 译 薛张纲 校）

BACKGROUND: The aged are at increased risk of postoperative wound healing complications. Because local anesthetics are infiltrated commonly into the dermis of surgical wounds, we sought to determine whether local anesthetics adversely affect proliferative and biosynthetic functions of dermal fibroblasts. We also evaluated the effect of local anesthetics on insulin- like growth factor-1 (IGF-1) and transforming growth factor-β1 (TGF-β1), growth factors that are important regulators of wound healing.
METHODS: Human dermal fibroblasts (HFB) from aged and young donors were exposed to local anesthetic agents at clinically relevant concentrations. We screened the effects of lidocaine, bupivacaine, mepivacaine, and ropivacaine on proliferation of HFB. Lidocaine was most detrimental to proliferation in HFB. We then evaluated the effect of lidocaine on expression and function of the growth factors, IGF-1 and TGF-β1. Lastly, concurrent exposure to lidocaine and IGF-1 or TGF-β1 was evaluated for their effects on proliferation and expression of dermal collagens, respectively.
RESULTS: Lidocaine and mepivacaine inhibited proliferation in aged HFB (for lidocaine 88% of control, 95% confidence interval [CI], 80%–98%, P = .009 and for mepivacaine 90% of control, 95% CI, 81%–99%, P = .032) but not in young HFB. Ropivacaine and bupivacaine did not inhibit proliferation. Because of the clinical utility of lidocaine relative to mepivacaine, we focused on lidocaine. Lidocaine decreased proliferation in aged HFB, which was abrogated by IGF-1. Lidocaine inhibited transcripts for IGF-1 and insulin-like growth factor-1 receptor (IGF1R) in fibroblasts from aged donors (IGF-1, log2 fold-change −1.25 [42% of control, 95% CI, 19%–92%, P = .035] and IGF1R, log2 fold-change −1.00 [50% of control, 95% CI, 31%–81%, P = .014]). In contrast, lidocaine did not affect the expression of IGF-1 or IGF1R transcripts in the young HFB. Transcripts for collagen III were decreased after lidocaine exposure in aged and young HFB (log2 fold-change −1.28 [41% of control, 95% CI, 20%–83%, P = .022] in aged HFB and log2 fold-change −1.60 [33% of control, 95% CI, 15%–73%, P = .019] in young HFB). Transcripts for collagen I were decreased in aged HFB (log2 fold-change −1.82 [28% of control, 95% CI, 14%–58%, P = .006]) but not in the young HFB. Similar to the transcripts, lidocaine also inhibited the protein expression of collagen III in young and aged HFB (log2 fold-change −1.79 [29% of control, 95% CI, 18%–47%, P = .003] in young HFB and log2 fold-change −1.76 [30% of control, 95% CI, 9%–93%, P = .043] in aged HFB). The effect of lidocaine on the expression of collagen III protein was obviated by TGF-β1 in both young and aged HFB.
CONCLUSIONS: Our results show that lidocaine inhibits processes relevant to dermal repair in aged HFB. The detrimental responses to lidocaine are due, in part, to interactions with IGF-1 and TGF-β1.

从麻醉住院医生的视角在急救手册的使用期间处理实际关键事件和安全文化的变化:一个试点研究

Emergency Manual Uses During Actual Critical Events and Changes in Safety Culture From the Perspective of Anesthesia Residents: A Pilot Study

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背景：急救手册(EMs),认知帮助或危机列表背景相关的场景,已经在高度危险行业被使用了数十年, 尽管这是一个在医疗卫生方面新生的领域。2012 年秋天,斯坦福大学临床推出急救手册,包括挂在斯坦福手术室(ORs)和用来培训临床医生使用的手术室的体格检查及其理由。虽然模拟研究表明，使用的手术室团队在危机期间使用的环境和类似的工具的有效性，但是完全没有数据表明临床上的实现和使用。在临床使用者的一个子集(麻醉住院医生),这个试点研究的目标是(1)在具有当地性手术室安全文化评估的观点在使用急救手册前前后关于认知援助的改变,虽然住院医生已经在长期的模拟培训背景;和(2) 描述在早期临床关键事件中使用急救手册。

方法：调查收集的定量和定性数据被用来评估在手术室临床使用急救手册。在 2011 年中期调查实施前斯坦福大学麻醉住院医师已经接收到（相关性）邮件,其次是在 2014 年初调查实施后新的一批新住院意思（接受问卷调查）。实现后的调查包括探索性比较是否有调查问题和其他问题对于实现混合方法描述性分析,培训和临床使用过程中关键事件以来实现。

结果：(住院医师)在调查前后反应率对比分别为 52%和 57%。在比较有调查试点研究后,更多住院医师：同意或强烈同意“我工作所在的手术室在我工作时适当的提供咨询急救的援助，”（ 73.8%, n = 31 vs 52.9%, n = 18, P = .0017）和选择更多类型的麻醉专业“在一定程度上利用认知艾滋病，”（的医师）包括训练有素的麻醉医师（z = −2.151, P = .0315）。在 15 个月后临床推行急救手册，19 个受访者（45%）已经使用了急救手册（运用到）一个实际的关键事件，而其中的 15 个人（78.9%）同意或非常同意在（手术室）期间“急救手册帮助团队能够更好照顾病人”。我们目前的定性数据有 16 个来自 19 个急救手册的从在以下领域的自由文本的使用报告：（1）启动紧急手册的使用，（2）阅读使用方法，（3）诊断和治疗，（4）病人护理的影响，和（5）急救手册使用的障碍。

结论：自 2012 年斯坦福大学的临床推行使用急救手册,许多住院医生在临床关键事件中自述成功使用急救手册。虽然这些报告都来自一个单一的机构的一项试验性研究，他们作为一个早期的概念证明了临床使用的可行性。未来需要大型，混合方法的研究来更好理解急救使用者及所面临的困难以确定普遍性。

（童颉 译 薛张纲 校）

BACKGROUND: Emergency manuals (EMs), context-relevant sets of cognitive aids or crisis checklists, have been used in high-hazard industries for decades, although this is a nascent field in health care. In the fall of 2012, Stanford clinically implemented EMs, including hanging physical copies in all Stanford operating rooms (ORs) and training OR clinicians on the use of, and rationale for, EMs. Although simulation studies have shown the effectiveness of EMs and similar tools when used by OR teams during crises, there are little data on clinical implementations and uses. In a subset of clinical users (ie, anesthesia residents), the objectives of this pilot study were to (1) assess perspectives on local OR safety culture regarding cognitive aid use before and after a systematic clinical implementation of EMs, although in the context of long-standing resident simulation trainings; and (2) to describe early clinical uses of EMs during critical events.

METHODS: Surveys collecting both quantitative and qualitative data were used to assess clinical adoption of EMs in the OR. A pre-implementation survey was e-mailed

to Stanford anesthesia residents in mid-2011, followed by a post-implementation survey to a new cohort of residents in early 2014. The post-implementation survey included pre-implementation survey questions for exploratory comparison and additional questions for mixed-methods descriptive analyses regarding EM implementation, training, and clinical use during critical events since implementation.
RESULTS: Response rates were similar for the pre- and post-implementation surveys, 52% and 57%, respectively. Comparing post- versus pre-implementation surveys in this pilot study, more residents: agreed or strongly agreed "the culture in the ORs where I work supports consulting a cognitive aid when appropriate" (73.8%, n = 31 vs 52.9%, n = 18, P = .0017) and chose more types of anesthesia professionals that "should use cognitive aids in some way," including fully trained anesthesiologists (z = −2.151, P = .0315). Fifteen months after clinical implementation of EMs, 19 respondents (45%) had used an EM during an actual critical event and 15 (78.9% of these) agreed or strongly agreed "the EM helped the team deliver better care to the patient" during that event, with the rest neutral. We present qualitative data for 16 of the 19 EM clinical use reports from free-text responses within the following domains: (1) triggering EM use, (2) reader role, (3) diagnosis and treatment, (4) patient care impact, and (5) barriers to EM use.
CONCLUSIONS: Since Stanford's clinical implementation of EMs in 2012, many residents' selfreport successful use of EMs during clinical critical events. Although these reports all come from a pilot study at a single institution, they serve as an early proof of concept for feasibility of clinical EM implementation and use. Larger, mixed-methods studies will be needed to better understand emerging facilitators and barriers and to determine generalizability.

麻醉相关的一氧化碳接触：毒性和潜在的治疗作用

Anesthesia-Related Carbon Monoxide Exposure: Toxicity and Potential Therapy

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通过二氧化碳吸收剂和体内重复呼吸产生的一氧化碳，挥发性麻醉药的降解会导致全身麻醉过程中暴露于一氧化碳。尽管遵守 the Anesthesia Patient Safety Foundation 的指南可以减少一氧化碳中毒的风险，患者在低流量吸入麻醉时仍然可能暴露于亚毒性一氧化碳下。这种结果相对来说比较不为人所知。与广为人知的高浓度一氧化碳的毒性对比，低浓度一氧化碳的生物学活性最近已证明是具有细胞保护作用的。因此，低剂量的一氧化碳正在被探讨作为治疗各种不同的疾病的一种新型方案。我们要在这篇文章复习与麻醉有关的一氧化碳暴露的概念，确定其产生的来源，明确一氧化碳公开毒性的机制，突出低剂量一氧化碳的细胞作用，讨论一氧化碳作为常规麻醉管理部分的潜在

（李桂婷 译 薛张纲 校）

Exposure to carbon monoxide (CO) during general anesthesia can result from volatile anesthetic degradation by carbon dioxide absorbents and rebreathing of endogenously produced CO. Although adherence to the Anesthesia Patient Safety Foundation guidelines reduces the risk of CO poisoning, patients may still experience subtoxic CO exposure during low-flow anesthesia. The consequences of such exposures are relatively unknown. In contrast to the widely recognized toxicity of high CO concentrations, the biologic activity of low concentration CO has recently been shown to be cytoprotective. As such, low-dose CO is being explored as a novel treatment for a variety of different diseases. Here, we review the concept of

anesthesia-related CO exposure, identify the sources of production, detail the mechanisms of overt CO toxicity, highlight the cellular effects of low-dose CO, and discuss the potential therapeutic role for CO as part of routine anesthetic management.

血管加压素和催产素对双灌注、单一的、分离子叶的胎儿胎盘远端干动脉血管阻力的影响

The Effects of Vasopressin and Oxytocin on the Fetoplacental Distal Stem Arteriolar Vascular Resistance of the Dual-Perfused, Single, Isolated, Human Placental Cotyledon

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背景：血管活性药物用于纠正剖腹产时低血压，理论上会加剧低氧胎儿胎盘血管收缩反应，因此，也会对经胎儿胎盘氧供产生负面影响。但是，这方面的药效学资料很少提到，更别说调查了。血管加压素，一种强效的全身血管收缩剂。催产素，剖腹产中常规用的子宫收缩剂，与血管加压素相比，具有显著的舒张全身血管的性质，我们假设其不会影响到远端干绒毛小动脉阻力。
方法：人胎盘灌注模型双灌注、单一的，分离的子叶，被用来研究从健康妇女获得的胎盘中胎儿胎盘循环阻力对催产素和血管加压素的反应。共 17 个研究对象的 12 个被成功的将催产素或血管加压素引入到胎儿储层中，以 10-1M 的增加浓度。胎儿胎盘远端干绒毛动脉灌注压（FAP）被连续测量。催产素或者加压素的胎儿回路浓度以逐步的方式分别从 10-9 到 10−5 M 或 10−11 到 10−6 M。两种储层被药物净化后，1-mL 1.0 mM5-羟色胺(2.5 μM)被引入到胎儿回路中，众所周知，5-羟色胺可以显著增加胎儿胎盘远端干绒毛动脉阻力。暴露于 5-羟色胺，FAP 从基线上的显著增加证实了胎儿胎盘收缩反应保持活性。本实验的主要结果是加压素和催产素剂量增加时 FAP 的变化。
结果：无论是催产素还是加压素，无论哪个药物试验浓度，都没有观察到 FAP 变化。对于每一种药物和每一种浓度，大于±10 mm Hg 的平均压变化在 95%的置信区间都被排除在外。相比之下，5-羟色胺在 12 个成功的试验中能显著增加灌注压。
结论：催产素和加压素不影响人胎儿胎盘远端干绒毛动脉阻力。在此注意到的加压素无影响类似于报道过的对人肺动脉阻力的影响，微不足道。两种药物似乎都不能对低氧血症胎儿胎盘收缩反应代偿产生不利影响。

（李倩倩 译 薛张纲 校）

BACKGROUND: Vasoactive agents administered to counter maternal hypotension at cesarean delivery may theoretically intensify the hypoxemic fetoplacental vasoconstrictor response and, hence, negatively impact transplacental oxygen delivery to the fetus. Yet, this aspect of their pharmacodynamic profiles is seldom mentioned, let alone investigated. We hypothesized that vasopressin, a potent systemic vasoconstrictor, and oxytocin, a uterotonic agent administered routinely at cesarean delivery, which, in contrast to vasopressin, possesses significant systemic vasodilator properties, would not influence distal stem villous arteriolar resistance.

METHODS: The dual-perfused, single, isolated cotyledon, human placental perfusion model was used to examine the resistance response of the fetoplacental circulation to oxytocin and vasopressin in placentae harvested from healthy women.

Twelve of a total of 17 individual experiments were conducted successfully during which either oxytocin (n = 6) or vasopressin (n = 6) was introduced into the fetal reservoir in concentration increments of 10^{-1} M. Fetoplacental distal stem villous arteriolar perfusion pressure (FAP) was measured continuously. The fetal circuit concentration of either oxytocin or vasopressin was raised in a stepwise fashion from 10^{9} to 10^{-5} M or 10^{-11} to 10^{-6} M, respectively. Both reservoirs were then purged of drug, after which 1-mL 1.0 mM 5-hydroxytryptamine (2.5 μM), an agent well known to manifestly increase fetoplacental distal stem villous arteriolar resistance, was introduced into the fetal circuit. A significant increase in FAP from baseline in response to exposure to 5-hydroxytryptamine confirmed that the fetoplacental vasoconstrictor response remained reactive. The primary outcome of this study was changes in FAP after incremental dosing of vasopressin and oxytocin.

RESULTS: No changes in FAP were observed with either oxytocin or vasopressin regardless of the drug concentration tested. For each drug and concentration, a mean pressure change greater than ±10 mm Hg was excluded with 95% confidence. In contrast, 5-hydroxytryptamine significantly increased perfusion pressure in all 12 successful experiments.

CONCLUSIONS: Oxytocin and vasopressin do not influence human fetoplacental distal stem villous arteriolar resistance. The neutral impact of vasopressin noted here is thus analogous to the reported negligible influence of the drug on human pulmonary arteriolar resistance. Neither drug seems likely to adversely influence the compensatory hypoxemic fetoplacental vasoconstrictor response.

未经修复的法洛四联症相关病理生理学改变减少了患儿对依托醚酯的系统清除率

Unrepaired Tetralogy of Fallot-related Pathophysiologic Changes Reduce Systemic Clearance of Etomidate in Children

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背景：先天性心脏病儿童的病理生理学改变可能通过影响药代动力学（PK）而改变药物的效果。考虑到描述儿科患者药代动力学的文献很有限，尤其是那些有法洛四联症（TOF）的患者，我们的目标是描绘依托醚酯的药代动力学，并且探索 TOF 对其的影响。

方法：29 名在全麻下行择期外科手术的儿科患者（15 名 TOF 患儿，14 名正常心脏解剖患儿）被纳入本次研究。在麻醉诱导期间所有患儿静脉使用了 60μg/kg/min 的依托醚酯，直到 BIS 值≤50 持续 5 秒。动脉血标本被抽取并且分析了。我们用了 NONMEM 软件来进行人口学分析以定义 PK 特征。

结果：从平均年龄为 236 天（从 86-360 天）的 29 名儿童中收取了 244 个标本数据，包括平均年龄为 221 天（从 86-360 天）的 TOF 组及平均年龄 221 天（从 86-360 天）的心脏解剖结构正常组。我们发现用三室分布模型来描述依托醚酯的 PK 是最合适的。TOF 的引入作为一个系统清除率（Cl1）的协变量优化了这个模型并且导致了目标函数的显著缩减（Δ 目标函数= -7.33; P = .0068），这意味着 TOF 是 Cl1 的一个重要协变量，TOF 儿童的依托醚酯 Cl1 值(1.67 × (体重[WT]/70 kg) L/min) 低于心脏解剖结构正常的患者的 Cl1 值（2.28 × (WT/70 kg)

L/min）。其他 PK 参数值如下：V1 = 8.05 × (WT/70 kg) L; V2 = 13.7 × (WT/70 kg) L; V3 = 41.3 × (WT/70 kg) L; Cl2 = 3.35 × (WT/70 kg) L/min; Cl3 = 0.563 × (WT/70 kg) L/min。

总结：TOF 患儿的依托醚酯清除率的减少导致了比起正常儿童，只需更低的注射速度以及更短的注射时间便可达到相同的血浆浓度并且维持一个平衡的目标浓度，或者在单次剂量或持续注射后有更长的镇静时间以及恢复时间。

（黄慧芸 译 薛张纲 校）

BACKGROUND： Pathophysiologic changes in children with congenital heart disease may alter the effect of drugs by influencing the pharmacokinetics (PK). Considering the limited literature that describes the PK of etomidate in pediatric patients, especially in those with tetralogy of Fallot (TOF), our aim was to characterize the PK of etomidate and explore the effects of TOF.

METHODS: Twenty-nine pediatric patients (15 with TOF and 14 with normal cardiac anatomy) scheduled to undergo elective surgery under general anesthesia were recruited in the study. All children received etomidate 60 μg/kg/min intravenously until a bispectral index of ≤50 was reached for 5 seconds during anesthesia induction. Arterial blood samples were drawn and analyzed. Population analysis was performed by using NONMEM to define PK characteristics. The estimates were standardized to a 70-kg adult using a per-kilogram model.

RESULTS: Data consisting of 244 samples from 29 children with a mean age of 236 days (range, 86-360 days) were used, including a TOF group with a mean age of 250 days (range, 165-360 days) and a normal cardiac anatomy group with a mean age of 221 days (range, 86-360 days). A 3-compartment disposition model was best fitted to describe the PK of etomidate. The introduction of TOF as a covariate for systemic clearance (Cl1) improved the model and resulted in a significant reduction of objective function (Δobjective function = -7.33; P = .0068), which means that TOF was a significant covariate of Cl1, and the etomidate Cl1 in children with TOF (1.67 × (weight [WT]/70 kg) L/min) was lower than those with normal cardiac anatomy (2.28 × (WT/70 kg) L/min). Other PK parameter values were as follows: V1 = 8.05 × (WT/70 kg) L; V2 = 13.7 × (WT/70 kg) L; V3 = 41.3 × (WT/70 kg) L; Cl2 = 3.35 × (WT/70 kg) L/min; Cl3 = 0.563 × (WT/70 kg) L/min.

CONCLUSIONS: A decreased systemic clearance for etomidate in children with TOF resulted in a lower required infusion rate and variation with time to achieve the same plasma concentration and maintain an equivalent target concentration or have longer sedation and recovery times after bolus or continuous infusion than normal children.

在神经病理性疼痛模型中，奈福泮的抗痛觉超敏作用可被三磷酸腺苷敏感的钾离子通道调停

The Antiallodynic Effects of Nefopam Are Mediated by the Adenosine Triphosphate–Sensitive Potassium Channel in a Neuropathic Pain Model

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背景：在神经病理性疼痛模型中，奈福泮在镇痛和抗痛觉超敏作用上起着核心作用。以往的研究已经证实，三磷酸腺苷敏感的钙离子通道的激活可以起到抗神经病理性疼痛中痛觉超敏的作用。在这项研究中，我们探索了钾离子通道和

奈福泮的关系，来证实在神经病理性疼痛模型中，是否钾离子通道可以调停奈福泮的抗痛觉超敏作用。

方法：机械性痛觉超敏可以在脊神经结扎的鼠中被诱发出来。所有鼠的缩足反应阈值通过冯弗雷纤维刺激来评估。在实验鼠脊神经结扎前后分别腹腔内给予奈福泮。我们评估了奈福泮和鞘内注射 KCa^{2+} 通道抑制剂—蜂毒明肽、卡律蝎毒素，和 KATP 通道阻滞剂格列本脲来评估它们逆转奈福泮抗痛觉超敏的能力。除此之外，我们还要评估是否 KATP 通道开放剂吡那地尔有抗痛觉超敏作用和促进奈福泮的抗痛觉超敏的作用。

结果：在实验鼠脊神经结扎前后给予奈福泮可引出显著的抗痛觉超敏的作用 ($P < .01$)，在给予格列本脲也出现了显著的抗痛觉超敏作用 ($P < .01$)。吡那地尔可提高奈福泮的抗痛觉超敏作用 ($P < .01$)。然而蜂毒明肽、卡律蝎毒素对奈福泮的抗痛觉超敏几乎无作用。

结论： KATP 通道激动剂可使奈福泮的抗痛觉超敏作用增加，而 KATP 通道抑制剂可逆转奈福泮的抗痛觉超敏作用。这些数据都说明了在神经病理性疼痛模型中，KATP 通道参与了奈福泮的抗痛觉超敏作用。

（李祥婷 译 薛张纲 校）

BACKGROUND: Nefopam hydrochloride is a centrally acting compound that induces antinociceptive and antihyperalgesic properties in neuropathic pain models. Previous reports have shown that activation of adenosine triphosphate (ATP)-sensitive and calcium-activated potassium (K_{ATP} and K_{Ca2+}) channels has antiallodynic effects in neuropathic pain. In the present study, we evaluated the relationship between potassium channels and nefopam to determine whether the antiallodynic effects of nefopam are mediated by potassium channels in a neuropathic pain model.

METHODS: Mechanical allodynia was induced by spinal nerve ligation (SNL) in rats, and the paw withdrawal threshold (PWT) was evaluated by the use of von Frey filaments. Nefopam was administered intraperitoneally before or after SNL. We assessed the relationship between nefopam and intrathecal injection of the K_{Ca2+} channel antagonists apamin and charybdotoxin, and the K_{ATP} channel blocker glibenclamide to assess their abilities to reverse the antiallodynic effects of nefopam. In addition, we evaluated whether the K_{ATP}channel opener pinacidil had antiallodynic effects and promoted the antiallodynic effects of nefopam.

RESULTS: Administration of nefopam before and after SNL induced significant antiallodynic effects ($P < .01$, respectively), which were significantly reduced by glibenclamide ($P < .01$). Pinacidil improved the antiallodynic effects of nefopam ($P < .01$); however, apamin and charybdotoxin had little effects on the antiallodynic properties of nefopam.

CONCLUSIONS: The antiallodynic effects of nefopam are increased by a K_{ATP} channel agonist and reversed by a K_{ATP} channel antagonist. These data suggest that the K_{ATP}channel is involved in the antiallodynic effects of nefopam in a neuropathic pain model.

走向平衡的一步：凝血因子联合抗凝血酶补充能够促进凝血酶生成

A Step Toward Balance: Thrombin Generation Improvement via Procoagulant Factor and Antithrombin Supplementation

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背景：在创伤及手术引起的凝血功能障碍情况下应用凝血酶原复合物可能伴发血栓栓塞的不良事件。本次试验通过建立血浆稀释模型，在其中单独或联合加入 3-4 种因子的凝血酶原复合物、抗凝血酶或重组凝血因子Ⅶ，以研究其在促进血栓形成（TG）中的作用，同时构建计算机模型并检验其能否预测在治疗稀释性凝血障碍患者时的 TG 情况。
方法：研究者运用自动校正凝血酶曲线法分别对 10 名健康志愿者的未稀释血浆，3 倍生理盐水稀释血浆，稀释血浆中加入重组凝血因子 VII（rFVIIa 组），加入凝血因子 II,IX,X 和抗凝血酶（CCF-AT 组），加入凝血因子 II,VII,IX,X（CCF-FVII 组）进行凝血酶试验。同时本次研究根据现有凝血酶生成计算机模型，在其中加入影响自动校正凝血酶曲线法结果的因素，并利用不同凝血酶试验数据进行建模和模型检验。
结果：rFVIIa 组较其稀释前水平，明显缩短凝血酶形成的峰值和延迟时间（P<0.001），但无法恢复正常凝血酶峰值（P<0.001）。CCF-FVII 组在较其稀释前水平，明显缩短凝血酶形成的峰值时间(P < 0.001)和延迟时间(P = 0.034)，同时增加凝血酶峰值和内源性凝血酶潜能。CCF-AT 组能够促进凝血酶生成，同时不影响凝血因子 VII 和 CCF-FVII 的作用。CCF-AT 组与加入 rFVIIa 的 CCF-FVII 组相比，分别在延迟时间（(P < 0.001 和 P = 0.005)，凝血酶形成的峰值时间（P < 0.001 和 P = 0.004），速率（P < 0.001 和 P = 0.019），凝血酶峰值（两组均 P < 0.001）和内源性凝血酶潜能（P = 0.034 和 P = 0.019）上存在差异。本研究构建的模型能够个体差异性地进行预测和描述治疗后的凝血酶生成的促进效果。
结论：在稀释血浆中，与单独使用重组凝血因子 VII 和凝血因子 II,VII,IX,X 复合物相比，凝血因子 II,IX,X 和抗凝血酶复合物能够更好促进凝血酶生成。同时本研究中构建的预测模型能够指导进一步的血浆稀释/因子补充实验。
（吴玮　译　陈杰　校）
BACKGROUND: The use of prothrombin complex concentrates in trauma- and surgery-induced coagulopathy is complicated by the possibility of thromboembolic events. To explore the effects of these agents on thrombin generation(TG), we investigated combinations of coagulation factors equivalent to 3- and 4-factor prothrombin complex concentrates with and without added antithrombin (AT), as well as recombinant factor VIIa (rFVIIa), in a dilutional model. These data were then used to develop a computational model to test whether such a model could predict the TG profiles of these agents used to treat dilutional coagulopathy.
METHODS: We measured TG in plasma collected from 10 healthy volunteers using Calibrated Automated Thrombogram. TG measurements were performed in undiluted plasma, 3-fold saline-diluted plasma, and diluted plasma supplemented with the following factors: rFVIIa (group rFVIIa); factors (F)II, FIX, FX, and AT (group "combination of coagulation factors" [CCF]-AT); or FII, FVII, FIX, and FX (group CCF-FVII). We extended an existing computational model of TG to include additional reactions that impact the Calibrated Automated Thrombogram readout. We developed and applied a computational strategy to train the model using only a subset of the obtained TG data and used the remaining data for model validation.
RESULTS: rFVIIa decreased lag time and the time to thrombin peak generation

beyond their predilution levels (P < 0.001) but did not restore normal thrombin peak height (P < 0.001). CCF-FVII supplementation decreased lag time (P = 0.034) and thrombin peak time (P < 0.001) and increased both peak height (P < 0.001) and endogenous thrombin potential (P = 0.055) beyond their predilution levels. CCF-AT supplementation in diluted plasma resulted in an improvement in TG without causing the exaggerated effects of rFVIIa and CCF-FVII supplementation. The differences between the effects of CCF-AT and supplementation with rFVIIa and CCF-FVII were significant for lag time (P < 0.001 and P = 0.005, respectively), time to thrombin peak (P < 0.001 and P = 0.004, respectively), velocity index (P < 0.001 and P = 0.019, respectively), thrombin peak height (P < 0.001 for both comparisons), and endogenous thrombin potential (P = 0.034 and P = 0.019, respectively). The computational model generated subject-specific predictions andidentified typical patterns of TG improvement.
CONCLUSIONS: In this study of the effects of hemodilution, CCF-AT supplementation improved the dilution-impaired plasma TG potential in a more balanced way than either rFVIIa alone or CCF-FVII supplementation. Predictive computational modeling can guide plasma dilution/supplementation experiments.

心脏外科手术病人体外循环复温时与脱机后血栓弹力图纤维蛋白原水平比较
Comparison of Thrombelastography-Derived Fibrinogen Values at Rewarming and Following Cardiopulmonary Bypass in Cardiac Surgery Patients
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背景：围术期过度输血的高成本与不良反应使得临床工作者探究针对性凝血因子替代疗法，其中备受关注的凝血因子之一是凝血因子 I（纤维蛋白原）。低纤维蛋白原血症可由标准实验室检测手段进行诊断，但相对费时。血小板抑制的全血血栓弹力图（TEG）可检测功能性纤维蛋白原水平（FLEV）并计算出纤维蛋白原含量，显著缩短了检测时间。若体外循环（CPB）复温过程中与 CPB 停止后即刻 FLEV 值相似，则 CPB 复温过程中的 FLEV 值可作为血制品输注的预先评判指标。
方法：51 例心脏手术病人被纳入此项前瞻性非随机研究，采用 TEG FLEV 方法测定比较 CPB 复温过程与 CPB 后纤维蛋白原水平。所有病人的基线、复温过程与 CPB 后纤维蛋白原值通过传统实验室检测（Clauss 法）和 FLEV 测得。运用混合效应回归模型检测 TEG FLEV 值的变化。Bland-Altman 法分析标准实验室检查与 FLEV 法之间的偏移和一致性范围（LOA）。
结果：49 例患者被纳入统计分析。复温 FLEV 平均值为 333.9mg/dL，给予鱼精蛋白后 FLEV 平均值为 332.8mg/dL，两者差异-1.1mg/dL（95％可信区间［CI］，-25.8～23.6，P=0.917）。给予鱼精蛋白后 FLEV 测值前平均 47 分钟获得复温 FLEV 值。Bland-Altman 分析提示 FLEV 与标准测法存在较大差异，基线值平均相差 92.5mg/dL（95% CI，71.1～114.9），最低 LOA -56.5mg/dL（95% CI，-94.4～-18.6），最高 LOA 242.4mg/dL（95% CI，204.5～280.3）。两种检测方法的差别在 CPB 结束后更显著并持续到给予鱼精蛋白后。
结论：本研究提示 FLEV 值在复温过程与 CPB 后无明显变化，CI 区间变化无临床意义。这些结果表明在 CPB 脱机前可采用复温样本来指导纤维蛋白原特异性治疗。平均 FLEV 值在各时间点均高于传统实验室检查测定值。另外，病例之

间存在显著异质性，提示在同一个病人运用不同检测方法存在较大差异。
（谢律　译　陈杰　校）

BACKGROUND: The inflated costs and documented deleterious effects of excess perioperative transfusion have led to the investigation of targeted coagulation factor replacement strategies. One particular coagulation factor of interest is factor I (fibrinogen). Hypofibrinogenemia is typically tested for using time-consuming standard laboratory assays. The thrombelastography (TEG)-based functional fibrinogen level (FLEV) provides an assessment of whole blood clot under platelet inhibition to report calculated fibrinogen levels in significantly less time. If FLEV valuesobtained on cardiopulmonary bypass (CPB) during rewarming are similar to values obtained immediately after the discontinuation of CPB, thenrewarming values could be used for preemptive ordering of appropriate blood product therapy.
METHODS: Fifty-one cardiac surgery patients were enrolled into this prospective nonrandomized study to compare rewarming fibrinogen valueswithpostbypass values using TEG FLEV assays. Baseline, rewarming, and postbypass fibrinogen values were recorded for all patients using both standard laboratory assay (Clauss method) and FLEV. Mixed-effects regression models were used to examine the change in TEG FLEV valuesover time. Bland-Altman analysis was used to examine bias and the limits of agreement (LOA) between the standard laboratory assay and FLEVs.
RESULTS: Forty-nine patients were included in the analysis. The mean FLEV value during rewarming was 333.9 mg/dL compared with 332.8 mg/dL after protamine, corresponding to an estimated difference of -1.1 mg/dL (95% confidence interval [CI], -25.8 to 23.6; P = 0.917). Rewarmingvalues were available on average 47 minutes before postprotamine values. Bland-Altman analysis showed poor agreement between FLEV and standard assays: mean difference at baseline was 92.5 mg/dL (95% CI, 71.1 to 114.9), with a lower LOA of -56.5 mg/dL (95% CI, -94.4 to -18.6) and upper LOA of 242.4 mg/dL (95% CI, 204.5 to 280.3). The difference between assays increased after CPB and persisted after protamine administration.
CONCLUSIONS: Our results revealed negligible change in FLEV values from the rewarming to postbypass periods, with a CI that does not include clinically meaningful differences. These findings suggest that rewarming samples could be utilized for ordering fibrinogen-specific therapies before discontinuation of CPB. Mean FLEV values were consistently higher than the reference standard at each time point. Moreover, bias was highly heterogeneous among samples, implying a large range of potential differences between assays for any 1 patient.

比较静脉注射和口服方式摄入扑热息痛后药物在血浆和脑脊液中的药代动力学情况

Comparative Plasma and Cerebrospinal Fluid Pharmacokinetics of Paracetamol After Intravenous and Oral Administration

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背景：本研究比较了静脉注射(IV)和口服方式摄入扑热息痛后，药物在血浆和

脑脊液中的药代动力学情况，目的为调整用药以获得最适脑脊液浓度。
方法：21 位成年患者随机分三组：静脉注药 1g，口服给药 1g，口服给药 1.5g。分别留置静脉导管和鞘内导管，给药后 6h 内采集静脉血和脑脊液标本。通过非房室模型技术分析血浆和脑脊液的最大药物浓度（Cmax），达到最大药物浓度的时间（Tmax），血浆和脑脊液的药物浓度-时间曲线下面积（AUCs）。当 P < .0167 时有统计学意义（用 Bonferroni 法校正 3 次比较对应的参数值）。用 Bonferroni 校正 95%置信区间（CIs）（0.5 的置信区间是无效假设）来计算概率（X<Y）(P'')。统计结果用中位数或 P''（置信区间）来表示。分别比较静脉注药 1g-口服给药 1g，静脉注药 1g-口服给药 1.5g，口服给药 1g-口服给药 1.5g，三组两两比较求出 P 值。
结果：扑热息痛浓度在不同组中有较大差异，尤其是口服药物组。静脉注药 1g 组的血浆 Cmax 中位数明显高于口服给药 1g 组。相反，两组的脑脊液 Cmax 中位数无差异。静脉注药 1g 组的血浆 Tmax 中位数是 105min，比口服药物 1g 和 1.5g 组提前 75min。而两组的脑脊液 Tmax 中位数无明显差异。血浆 AUC（总）中位数在两组间无明显差异；然而用药第一个小时，静脉注药 1g 组血浆 AUC 中位数明显高于口服给药组。第二个小时两组无差异。两组的脑脊液 AUC（总）中位数无明显差异；然而用药第一个小时，静脉注药 1g 组脑脊液 AUC 中位数明显高于口服药组。第二个小时两组无差异。由于样本量太小，研究分析 Cmax、Tmax 和 AUC 中位数值缺乏精确性。
结论：静脉注药与口服药物相比可达到更大的血浆浓度峰值，达峰时间更快。由于研究样本量小，不同给药方式对脑脊液的 Cmax 和 Tmax 影响并未显示差异性。
（戴依利　译　陈杰　校）
BACKGROUND: We compared plasma and cerebrospinal fluid (CSF) pharmacokinetics of paracetamol after intravenous (IV) and oral administration to determine dosing regimens that optimize CSF concentrations.
METHODS: Twenty-one adult patients were assigned randomly to 1 g IV, 1 g oral or 1.5 g oral paracetamol. An IV cannula and lumbar intrathecal catheter were used to sample venous blood and CSF, respectively, over 6 hours. The plasma and CSF maximum concentrations (C max), times to maximum concentrations (T max), and area under the plasma and CSF concentration-time curves (AUCs) were calculated using noncompartmental techniques. Significance was defined by P < .0167 (Bonferroni correction for 3 comparisons for each parameter). Probability (X < Y) (P″) with Bonferroni corrected 95% confidence intervals (CIs) were calculated (CIs including 0.5 meet the null hypothesis). Results are presented as median (range) or P″ (CI). P values are listed as 1 g IV vs 1 g orally, 1 g IV vs 1.5 g orally and 1 g orally vs 1.5 g orally, respectively.
RESULTS: Wide variation in measured paracetamol concentrations was observed, especially in the oral groups. The median plasma C max in the 1 g IV group was significantly greater than the oral groups. In contrast, the median CSF C maxwas not different between groups. The median plasma T max in the 1 g IV group was 105 and 75 minutes earlier than in the 1 and 1.5 g oral groups. The median CSF T max was not significantly different between groups. The median plasma AUC (total) was not significantly different between groups; however, in the first hour, the median plasma AUC was significantly greater in the IV group than in the oral groups. In the second hour, there was no difference between groups. The median CSF AUC (total) did not significantly differ between groups; however, in the first hour, the median CSF AUC

was significantly greater in the IV compared with the orally groups. In the second hour, there was no difference between groups. Our analysis indicated that the median C max, T max, and AUC values lacked precision because of small sample sizes.
CONCLUSIONS: Peak plasma concentrations were greater and reached earlier after IV than oral dosing. Evidence for differences in CSF C max and T max was lacking because of the small size of this study.

机械通气对锁骨下静脉穿刺置管术中气胸发生率的影响：一个前瞻性随机的非劣效性试验

Influence of Mechanical Ventilation on the Incidence of Pneumothorax During InfraclavicularSubclavian Vein Catheterization: A Prospective Randomized Noninferiority Trial

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背景：目前仍不清楚在锁骨下静脉穿刺置管术期间是否需要中断机械通气。在实践中，由临床医生自己决定是否进行肺萎陷。本研究目的是评估机械通气对锁骨下静脉穿刺置管术中气胸发生率的影响。
方法：一共 332 名需要进行锁骨下静脉穿刺置管术的病人被随机分配至：锁骨下静脉穿刺置管期间维持机械通气（机械通气组，n=165）或中断机械通气（肺萎陷组，n=167）。比较两组气胸和其他并发症如误入动脉、血胸或导管移位以及穿刺置管成功率的差异。
结果：机械通气组气胸发生率为 0%（0/165），肺萎陷组 0.6%（1/167）。肺萎陷组气胸发生率比机械通气组高 0.6%，差异的双侧 90%可信区间为（-1.29%~3.44%），由于可信区间下限-1.29%比预先设定的非劣效性界限-3%高，在 0.05 显著性水准下，机械通气组比肺萎陷组更劣的假设被拒绝。两组其他并发症发生率和穿刺置管成功率相似。肺萎陷组 9 名患者氧饱和度下降低于 95%，而机械通气组则没有发生（P=0.007）。
结论：不管是否进行机械通气，锁骨下静脉穿刺置管术的成功率和并发症发生率相似。在置管术期间，中断机械通气对预防气胸似乎并非必要。
（殷智宇 译 陈杰 校）
BACKGROUND: It remains unclear whether we have to interrupt mechanical ventilation during infraclavicular subclavian venous catheterization. In practice, the clinicians' choice about lung deflation depends on their own discretion. The purpose of this study was to assess the influence ofmechanical ventilation on the incidence of pneumothorax during infraclavicular subclavian venous catheterization.
METHODS: A total of 332 patients, who needed subclavian venous catheterization, were randomly assigned to 1 of the 2 groups: catheterizations were performed with the patients' lungs under mechanical ventilation (ventilation group, n = 165) or without mechanical ventilation (deflation group, n = 167). The incidences of pneumothorax and other complications such as arterial puncture, hemothorax, or catheter misplacements and the success rate of catheterization were compared.
RESULTS: The incidences of pneumothorax were 0% (0/165) in the ventilation group and 0.6% (1/167) in the deflation group. The incidence of pneumothorax in the deflation group was 0.6% higher than that in the ventilation group and the 2-sided 90% confidence interval for the difference was (-1.29% to 3.44%). Because the lower

bound for the 2-sided 90% confidence interval, -1.29%, was higher than the predefined noninferiority margin of -3%, the inferiority of the ventilation group over the deflation group was rejected at the .05 level of significance. Other complication rates and success rates of catheterization were comparable between 2 groups. The oxygen saturation dropped below 95% in 9 patients in the deflation group, while none in the ventilation group (P =0.007).
CONCLUSIONS: The success and complication rates were similar regardless of mechanical ventilation. During infraclavicular subclavian venous catheterization, interruption of mechanical ventilation does not seem to be necessary for the prevention of pneumothorax.

完全液体通气诱发的短暂性低体温减少主动脉阻断诱发的靶器官损伤及多器官功能衰竭

A Brief Period of Hypothermia Induced by Total Liquid Ventilation Decreases End-Organ Damage and Multiorgan Failure Induced by Aortic Cross-Clamping

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背景：在动物模型中，心跳骤停和其他低灌注状态发生后全身降温可减少靶器官损伤。但是，可能由于长时间低体温的不利影响可抵消任何潜在的好处，在人体中进行低体温处理的获益是不确定的。完全液体通气（TLV）可同时提供超快降温和复温。先前报道，用 TLV 超快降温可有效地降低心脏骤停后动物模型的神经损伤。本研究假设通过 TLV 快速降温和复温可以减轻主动脉阻断引起的缺血再灌注后多器官功能衰竭（MOF）。
方法：对麻醉后家兔先行腹腔干上腹主动脉阻断 30min，随后进行 300min 再灌注。分别在阻断前，阻断时和阻断后进行常规通气（对照组）或低温 TLV（33℃）（分别为夹闭前组，夹闭组和夹闭后组）。所有 TLV 组，低温持续 75min 后并在恢复常规机械通气前切换到复温模式。研究终点包括再灌注后 300min 检测的心血管、肾脏、肝脏及炎症参数。
结果：在常温（对照）组，缺血再灌注损伤引发 MOF 的证据包括严重血管麻痹、低心输出量、急性肾损伤和肝功能衰竭。观察到与对照组相比，TLV 组的心输出量在夹闭后组、夹闭组和夹闭前组渐次改善（再灌注 300min 后分别为 53±8，64±12 和 90±24vs36±23 mL/min/kg）。预夹闭组和夹闭组的肝脏生物标志物水平较对照组更低。然而，预夹闭组可预防急性肾损伤发生，预夹闭可将其控制在一定程度，但夹闭后组不可预防急性肾损伤。例如，预夹闭组和对照组在随访末肌酐清除率分别为 4.8±3.1 和 0.5±0.6 mL/kg/min（p =0.0004）。比较 TLV 组和对照组的心脏、肾脏、肝脏和空肠的组织学检查也证实 TLV 可降低损伤。
结论：TLV 短暂超快降温继而快速复温可以减弱主动脉阻断后多器官功能衰竭生化和病理指标。即使再灌注后实施短暂低温 TLV，也可减轻心血管和肝功能障碍。相反，只有再灌注前进行降温才能限制急性肾损伤。需要进一步研究以确定该实验结果的临床意义，并确定 TLV 诱导低温对低灌注状态终末器官保护的最佳持续时间和时机。

(陈依 译 陈杰　校)

BACKGROUND: In animal models, whole-body cooling reduces end-organ injury after cardiac arrest and other hypoperfusion states. The benefits of cooling in humans, however, are uncertain, possibly because detrimental effects of prolonged cooling may offset any potential benefit. Total liquid ventilation (TLV) provides both ultrafast cooling and rewarming. In previous reports, ultrafast cooling with TLV potently reduced neurological injury after experimental cardiac arrest in animals. We hypothesized that a brief period of rapid cooling and rewarming via TLV could also mitigate multiorgan failure (MOF) after ischemia-reperfusion induced by aortic cross-clamping.

METHODS: Anesthetized rabbits were submitted to 30 minutes of supraceliac aortic cross-clamping followed by 300 minutes of reperfusion. They were allocated either to a normothermic procedure with conventional ventilation (control group) or to hypothermic TLV (33°C) before, during, and after cross-clamping (pre-clamp, per-clamp, and post-clamp groups, respectively). In all TLV groups, hypothermia was maintained for 75 minutes and switched to a rewarming mode before resumption to conventional mechanical ventilation. End points included cardiovascular, renal, liver, and inflammatory parameters measured 300 minutes after reperfusion.

RESULTS: In the normothermic (control) group, ischemia-reperfusion injury produced evidence of MOF including severe vasoplegia, low cardiac output, acute kidney injury, and liver failure. In the TLV group, we observed gradual improvements in cardiac output in post-clamp, per-clamp, and pre-clamp groups versus control (53 ± 8, 64 ± 12, and 90 ± 24 vs 36 ± 23 mL/min/kg after 300 minutes of reperfusion, respectively). Liver biomarker levels were also lower in pre-clamp and per-clamp groups versus control. However, acute kidney injury was prevented in pre-clamp, and to a limited extent in per-clamp groups, but not in the post-clamp group. For instance, creatinine clearance was 4.8 ± 3.1 and 0.5 ± 0.6 mL/kg/min at the end of the follow-up in pre-clamp versus control animals (P = .0004). Histological examinations of the heart, kidney, liver, and jejunum in TLV and control groups also demonstrated reduced injury with TLV.

CONCLUSIONS: A brief period of ultrafast cooling with TLV followed by rapid rewarming attenuated biochemical and histological markers of MOF after aortic cross-clamping. Cardiovascular and liver dysfunctions were limited by a brief period of hypothermic TLV, even when started after reperfusion. Conversely, acute kidney injury was limited only when hypothermia was started before reperfusion. Further work is needed to determine the clinical significance of our results and to identify the optimal duration and timing of TLV-induced hypothermia for end-organ protection in hypoperfusion states.

鞘内注射氢吗啡酮和吗啡的剖宫产术后镇痛：使用顺序分配偏倚钱币法确定 ED90

Intrathecal Hydromorphone and Morphine for Postcesarean Delivery Analgesia: Determination of the ED90 Using a Sequential Allocation Biased-Coin Method

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背景：鞘内注射（IT）吗啡被认为是腰麻下剖宫产后的“金标准”镇痛，最常用的剂量在 100 至 200 μg。鞘内注射氢吗啡酮用于剖宫产术后镇痛经验不足，最

佳镇痛剂量相关的研究信息有限。此项研究目的为确定对择期剖宫产后接受 IT 氢吗啡酮镇痛 90%患者对应的有效镇痛剂量（ED90）和其与 IT 吗啡的效价比。

方法：在这个剂量探索试验中，80 名患者接受脊髓麻醉的剖腹产。参与者被随机分配接受 IT 吗啡或 IT 氢吗啡，使用带有偏置硬币设计上下顺序分配的方法确定的剂量以确定 ED90。所有患者除了 IT 阿片类药物接受规范的多模式术后镇痛。有效剂量定义为脊髓注射后 12 小时的对疼痛的数字响应得分≤3（比例 0-10）。

结果：IT 氢吗啡酮、IT 吗啡 ED90 分别是 75μg（95％可信区间[CI]，46-93μg）和 150μg（95％CI，145-185μg）。在这些剂量下，氢吗啡酮、吗啡有效镇痛百分比（数字评定量表≤3）的 95％CI 分别是 64％至 100％、68％至 100％。探索性实验结果表明，IT 吗啡酮或 IT 吗啡在常用剂量下恶心和瘙痒的发生率相似（分别为：P= 0.44 和 P =0.74；P= 0.67 和 P =0.38）。当使用 ED90 或更高剂量的 IT 阿片类药物时， IT 氢吗啡酮和 IT 吗啡患者的镇痛满意率分别为 100％（21/21）和 95％（37/39）。

结论：IT 吗啡对 IT 氢吗啡酮产生剖宫产术后有效镇痛比为 2：1。患者对两者的满意度都较高。

(董璐 译 陈杰 校)

BACKGROUND: Intrathecal (IT) morphine is considered the "gold standard" for analgesia after cesarean delivery under spinal anesthesia, most commonly administered at a dose of 100 to 200 μg. There is less experience with IT hydromorphone for postcesarean analgesia and limited information on its optimal analgesic dose. We conducted this study to determine the effective analgesic dose for 90% patients (ED90) of IT hydromorphone that provides effective analgesia for women undergoing elective cesarean delivery and its potency ratio to IT morphine.

METHODS: In this dose-finding trial, 80 patients received spinal anesthesia for cesarean delivery. Participants were randomized to receive IT morphine or IT hydromorphone at a dose determined using up-down sequential allocation with a biased-coin design to determine ED90. All patients received standardized multimodal analgesia postoperatively in addition to IT opioid. An effective dose was defined as a numeric response score for pain of ≤3 (scale 0-10) 12 hours after spinal injection.

RESULTS: The ED90 was 75 μg (95% confidence interval [CI], 46-93 μg) for IT hydromorphone and 150 μg (95% CI, 145-185 μg) for IT morphine. At these doses, the 95% CI for the percentage of patients with effective analgesia (numeric rating scale ≤3) was 64% to 100% for hydromorphone and 68% to 100% for morphine. Exploratory findings showed that the incidence of nausea and pruritus was not different among the most commonly used doses of IT hydromorphone (P = 0.44 and P = 0.74) or IT morphine (P = 0.67 and P = 0.38, respectively). When administering IT opioids at ED90 doses or higher, 100% (21/21) of IT hydromorphone and 95% (37/39) of IT morphine patients were satisfied with their analgesia.

CONCLUSIONS: The ratio of IT morphine to IT hydromorphone for effective postcesarean analgesia is 2:1. Patient satisfaction was high with both medications.

先天性心脏病儿童围术期右美托咪定的应用：一项来自 CCAS 和 STS 的先心病数据分析

The Perioperative Use of Dexmedetomidine in Pediatric Patients with Congenital Heart Disease: An Analysis from the Congenital Cardiac Anesthesia Society-Society of Thoracic Surgeons Congenital Heart Disease Database

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背景：右美托咪定是一种选择性 α-2 受体激动剂，其镇静作用及心肺影响特点使该药在先心（CHD）儿童手术麻醉的应用方面有很大的吸引力。然而只有一些小的单中心研究提示右美在儿童先心患者围术期的应用上越来受欢迎，但缺乏多中心的数据，并且对于不同年龄范围、手术难度和医疗中心情况下如何调整用药还并不清楚。本研究旨在分析患者疾病因素和中心水平对先心儿童围术期应用右美托咪定的影响。
方法：为了研究 CHD 患者手术中右美托咪定的应用，本研究分析了 2010-2013 年 CCAS-STS 数据库中所有关于体外循环手术的数据。比较围术期右美托咪定应用与未应用患者的病情和手术特征的差异。也对右美托咪定应用相关的选择性预后进行描述。
结果：在 12142 项手术中，有 3600（29.6%）项围术期用了右美托咪定（DEX），8542 个未应用（NoDEX）。两组患者临床特点不同：右美托咪定组患者病情较轻，手术风险较小。应用右美托咪定患者与未应用患者相比有更低的 STS 死亡率。与其总的低风险特征相一致。且右美托咪定应用者较未应用者相比，有更好的预后。
结论：研究发现在儿童先心手术的麻醉中右美托咪定使用越来越多，尤其倾向于行非复杂性先心手术的大龄儿童。本研究所纳入数据量在对于 CHD 患者的单一麻醉药研究领域中首屈一指；也是首次同时对 CCAS 和 STS 先心疾病数据库的麻醉数据进行分析。
(戴依利　译　陈杰　校)
BACKGROUND: Dexmedetomidine is a selective α-2 receptor agonist with a sedative and cardiopulmonary profile that makes it an attractive anesthetic for pediatric patients with congenital heart disease (CHD). Although several smaller, single-center studies suggest thatdexmedetomidine use is gaining traction in the perioperative setting in children with CHD, there are limited multicenter data, with little understanding of the variation in use across age ranges, procedural complexity, and centers. The aim of this study was to use the CongenitalCardiac Anesthesia Society-Society of Thoracic Surgeons (CCAS-STS) registry to describe patient- and center-level variability in the use of dexmedetomidine in the perioperative setting in children with heart disease.
METHODS: To describe the use of dexmedetomidine in patients for CHD surgery, we analyzed all index cardiopulmonary bypass operations entered in the CCAS-STS database from 2010 to 2013. Patient and operative characteristics were compared between those who received intraoperative dexmedetomidine and those who did not. Selective outcomes associated with dexmedetomidine use were also described.
RESULTS: Of the 12,142 operations studied, 3600 (29.6%) received perioperative dexmedetomidine (DEX) and 8542 did not receive the drug (NoDEX). Patient characteristics were different between the 2 groups with the DEX group generally exhibiting both lower patient and procedural risk factors. Patients who received dexmedetomidine were more likely to have a lower level of Society of Thoracic Surgeons mortality complexity than patient who did not receive it. Consistent with their overall lower risk profile, children in the DEX group also demonstrated improved outcomes compared with patients who did not receive dexmedetomidine.

CONCLUSIONS: We described the growing use of dexmedetomidine in children anesthetized for surgical repair of CHD. Dexmedetomidineappears to be preferentially given to older and larger children who are undergoing less complex CHD surgery. We believe that the data provided in this study are the largest investigating the use of an anesthetic drug in CHD patients. It is also the first analysis of the anesthesia data in the CCAS-STS Congenital Heart Disease database.

肌间沟神经阻滞在全肩关节置换术中的应用模式

The Patterns of Utilization of Interscalene Nerve Blocks for Total Shoulder Arthroplasty

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肌间沟阻滞 (interscalene block, ISB)是全肩关节置换术(total shoulder arthroplasty, TSA)中全身麻醉的一项辅助方法。本研究目的提供目前国内实施肌间沟阻滞的全肩关节置换术病人的相关统计资料。对全国麻醉临床效果注册中心 2010 年至 2015 年的数据进行了回顾性分析。在 28810 例病例中，42.1%的病人接受一次肌间沟阻滞。只有 0.83%将区域神经阻滞作为主要的麻醉方式。2010 年至 2014 年之间，肌间沟阻滞在外科手术中的利用率有所增加(OR 比值，1.21；95%置信区间，1.19 -1.23；P < .0001)。此外报告了美国国内神经阻滞实施的人口分布情况。明确了全肩关节置换术中区域神经阻滞的实施模式，为将来研究提供参考。

(傅丹云　译　陈杰　校)

The interscalene block (ISB) is a common adjunct to general anesthesia for total shoulder arthroplasty (TSA). The aim of the study was to report the current national demographics of the patients who are receiving ISB for TSAs. We performed a retrospective analysis of data from the National Anesthesia Clinical Outcomes Registry from 2010 to 2015. Of 28,810 cases, 42.1% received an ISB. Only 0.83% of cases received regional anesthesia as the primary anesthetic. From 2010 to 2014, there has been an increase in ISB utilization for this surgery (odds ratio, 1.21; 95% confidence interval, 1.19-1.23; P < .0001). Furthermore, we report a geographic distribution of block utilization in the United States. We have identified national patterns for the utilization of regional anesthesia for TSAs that may provide insight into future design of research studies.

先天性心脏病的心脏胚胎学和分子机制：麻醉医生的引物

Cardiac Embryology and Molecular Mechanisms of Congenital Heart Disease: A Primer for Anesthesiologists

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新生儿患有先天性心脏病的概率是在 0.4%到 5%，这对儿科麻醉医生来说是特有的挑战。此外,外科的进步提高了这些患者的生存率,并且有很多负责成人的麻醉医师开始照顾一些曾经做过先天性心脏病手术的青年以及成年患者。在分子和基因层面上了解关于异常心脏发育的知识扩展并增强了麻醉医生对先天性心脏病的理解。在本文中,我们的目标是回顾当前有关的基因突变的知识以及与先天性心脏病的形成有关的细胞学的影响。鉴于目前先天性心脏病只能偶尔追

溯到单个基因突变,我们高度重视研究人员在试图确定心脏损伤的致病过程的具体步骤时所面临的一些困难。
（董欣怡 译 李士通 校）

Congenital heart disease is diagnosed in 0.4% to 5% of live births and presents unique challenges to the pediatric anesthesiologist. Furthermore, advances in surgical management have led to improved survival of those patients, and many adult anesthesiologists now frequently take care of adolescents and adults who have previously undergone surgery to correct or palliate congenital heart lesions. Knowledge of abnormal heart development on the molecular and genetic level extends and improves the anesthesiologist's understanding of congenital heart disease. In this article, we aim to review current knowledge pertaining to genetic alterations and their cellular effects that are involved in the formation of congenital heart defects. Given that congenital heart disease can currently only occasionally be traced to a single genetic mutation, we highlight some of the difficulties that researchers face when trying to identify specific steps in the pathogenetic development of heart lesions.

术中氧储备指数与动脉血氧分压的关系

The Relationship Between Oxygen Reserve Index and Arterial Partial Pressure of Oxygen During Surgery

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背景：在术中应用脉搏血氧饱和度（SpO_2）监测使我们能更及时地发现缺氧，因此减少了围术期缺氧事件的发生。然而当动脉血氧分压（PaO_2）低至70mmHg时可能脉搏血氧饱和度仍然显示98%。因此，除非动脉血氧分压接近这一水平，否则脉搏血氧饱和度并不能更及时地对动脉血氧含量进行预警。多波长脉冲氧饱和度能提供一个氧合指数的预测值，该预测值可能可以填补脉搏血氧饱和度 SpO_2>98%以上这段数据信息。本研究评估了在术中多波长脉冲氧饱和度（ORI）与动脉血氧分压（PaO_2）之间的关系。

方法：本试验的研究对象为进行了动脉置管拟行术中动脉血气分析的择期手术患者。每名患者术中均持续进行多波长脉冲氧饱和度监测，监测数据存储于试验专用电脑中。应用回归分析对ORI值与每次动脉血气分析时的 PaO_2 值进行比较，并且通过连续的测量对二者的变化趋势进行比较。通过对术中不同时间点重复测量受试者 PaO_2 和ORI，应用重复测量的线性混合效应回归模型描述二者相互关系。应用 PaO_2 值为100和150mmHg时对应的ORI值对回归曲线进行检验。应用特定主题随机拦截的混合效应模型对ORI值与 PaO_2 进行比较。

结果：本研究收集了106名患者术中的ORI值和 PaO_2 测量值。回归分析显示ORI与 PaO_2 的相关性在 PaO_2 小于240mmHg这一区间内（r^2=0.536）要强于PaO2大于240mmHg这一区间（r^2=0.0016）。当 PaO_2 测量值≥100mmHg时所有样本的ORI值均大于0.24。当 PaO_2 测量值≥150mmHg时96.6%的样本的ORI值均大于0.55。重复测量的随机拦截方差分量线性混合效应模型分析表明 PaO_2 与ORI显著相关（β[95%可信区间]=0.002[0.0019-0.0022]；P<0.0001）。相似性分析表明 PaO_2 的变化趋势与ORI的变化趋势显著相关（β[95%可信区间]=0.0044[0.0040-0.0048]；P<0.0001）。

结论：这些研究结果提示当 SpO_2 在98%以上时，ORI>0.24可以作为识别 PaO_2≥100mmHg的标志。同理ORI>0.55也可以作为 PaO_2≥150mmHg的临界

点。这些数值的实用性还需要进一步的研究进行评估。当 SpO_2>98%时，ORI 值下降至 0.24 附近可能进一步提示 PaO_2 已经跌至 100mmHg 附近。ORI 对临床干预的实用性是建立在持续监测的基础上的，需要进一步研究支持。
（陈峰 译 李士通 校）

BACKGROUND: The use of intraoperative pulse oximetry (SpO_2) enhances hypoxia detection and is associated with fewer perioperative hypoxic events. However, SpO2 may be reported as 98% when arterial partial pressure of oxygen (PaO_2) is as low as 70 mm Hg. Therefore, SpO_2 may not provide advance warning of falling arterial oxygenation until PaO_2 approaches this level. Multiwave pulse co-oximetry can provide a calculatedoxygen reserve index (ORI) that may add to information from pulse oximetry when SpO_2 is >98%. This study evaluates the ORI to PaO_2 relationship during surgery.

METHODS: We studied patients undergoing scheduled surgery in which arterial catheterization and intraoperative arterial blood gas analysis were planned. Data from multiple pulse co-oximetry sensors on each patient were continuously collected and stored on a research computer. Regression analysis was used to compare ORI with PaO_2 obtained from each arterial blood gas measurement and changes in ORI with changes in PaO_2 from sequential measurements. Linear mixed-effects regression models for repeated measures were then used to account for within-subject correlation across the repeatedly measured PaO_2 and ORI and for the unequal time intervals of PaO_2 determination over elapsed surgical time. Regression plots were inspected for ORI values corresponding to PaO_2 of 100 and 150 mm Hg. ORI and PaO_2 were compared using mixed-effects models with a subject-specific random intercept.

RESULTS: ORI values and PaO_2 measurements were obtained from intraoperative data collected from 106 patients. Regression analysis showed that the ORI to PaO_2 relationship was stronger for PaO2 to 240 mm Hg (r = 0.536) than for PaO_2 over 240 mm Hg (r = 0.0016). Measured PaO_2 was ≥100 mm Hg for all ORI over 0.24. Measured PaO_2 was ≥150 mm Hg in 96.6% of samples when ORI was over 0.55. A random intercept variance component linear mixed-effects model for repeated measures indicated that PaO_2 was significantly related to ORI (β[95% confidence interval] = 0.002 [0.0019-0.0022]; P < 0.0001). A similar analysis indicated a significant relationship between change in PaO_2 and change in ORI (β [95% confidence interval] = 0.0044 [0.0040-0.0048]; P < 0.0001).

CONCLUSIONS: These findings suggest that ORI >0.24 can distinguish PaO_2 ≥100 mm Hg when SpO2 is over 98%. Similarly, ORI > 0.55 appears to be a threshold to distinguish PaO_2 ≥150 mm Hg. The usefulness of these values should be evaluated prospectively. Decreases in ORI to near 0.24 may provide advance indication of falling PaO_2 approaching 100 mm Hg when SpO2 is >98%. The clinical utility of interventions based on continuous ORI monitoring should be studied prospectively.

精氨酸酶抑制剂在转基因镰状细胞小鼠模型中可逆转血管内皮功能障碍，肺动脉高压和血管硬化

Arginase Inhibition Reverses Endothelial Dysfunction, Pulmonary Hypertension, and Vascular Stiffness in Transgenic Sickle Cell Mice

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背景：镰状细胞病（SCD）所致的溶血可引起精氨酸酶的释放和激活，而精氨酸酶则可与一氧化氮（NO）的合成与产生互相调节。然而，单纯补充两者的共同底物 L-精氨酸并不能提高 NO 的生物利用度。在本次研究中，我们对于精氨酸酶抑制剂可提高 NO 的生物利用度，从而降低 SCD 转基因小鼠的全身和肺血管内皮功能障碍这一假设进行了验证。
方法：本次研究中，我们选择 5 个月大的转基因镰状细胞小鼠作为实验组（SC 组），而与其年龄匹配的野生型作为对照组（WT 组）。其中，SC 组小鼠又分为经精氨酸酶抑制剂处理组（即使用 2(S)氨基-6-溴己酸（ABH），约 400μg/日，处理 4 周）和未经精氨酸酶抑制剂处理组。
结果：未接受精氨酸酶抑制剂处理的 SC 组小鼠，其血管精氨酸酶活性显著高于 WT 组（SC 未处理组：346±69.3 pmol 尿素/mg 蛋白/分钟，WT 组 69±17.3 pmol 尿素/mg 蛋白/分钟；P = 0.0043；n = 4–5（每组动物数））。使用 ABH 治疗可显著降低精氨酸酶活性，使其接近于 WT 组水平（SC + ABH 组：125.2±17.3 pmol 尿素/mg 蛋白/分钟；P = 0.0213）。与 WT 组相比，SC 未处理组小鼠的主动脉中 NO 显著减少，活性氧（ROS）生成显著增加（SC 未处理组 NO 荧光率 0.76±0.14 RFU/s，WT 组 NO 荧光率 1.34±0.17 RFU/s；P = 0.0005；SC 未处理组 ROS 荧光率：3.96±1.70 RFU/s，WT 组 ROS 荧光率 1.63±1.20 RFU/s，P = 0.0039；n = 3（每组动物数））。接受 ABH 处理 4 周的 SC 组小鼠，其 NO 水平（荧光率：1.16±0.16 RFU/s）和活性氧水平（荧光率：2.02±0.45 RFU/s）与年龄匹配的 WT 组基本持平（n = 3 （每组动物数））。SC 组小鼠主动脉对于乙酰胆碱的内皮依赖性血管舒张反应显著弱于 WT 组小鼠（SC 组：57.7%±8.4% ，WT 组：80.3%±11%；P = 0.02；n = 6（每组动物数））。组间比较内皮依赖性反应无显著差异。SC 组小鼠右室输出指数和收缩末期弹性无显著差异（4.60±0.51 vs 2.9±0.85 ml/min/ 100 g 和 0.89±0.48 vs 0.58±0.11 mmHg/μL），但 SC 组小鼠肺血管阻力和右心室收缩末期压力更大（2.9±0.28 vs 5.5±2.0 mmHg×min/μL / 100 g 和 18.9±1.1 vs 23.1±4 mmHg；N =8（每组动物数））。SC 组小鼠的脉搏速度（用于测量动脉僵硬度）显著高于 WT 组（3.74±0.54 vs 3.25±0.21m/s；N = 20（每组动物数）），经精氨酸酶抑制剂处理 4 周可显著降低 SC 组小鼠的血管硬化，使其与 WT 组接近（P = 0.0009）。
结论：精氨酸酶抑制剂可提高 NO 的生物利用度，进而减少 SCD 转基因小鼠的全身和肺血管内皮功能障碍。因此，精氨酸酶是 SCD 心血管功能障碍的一个潜在治疗靶点。
（陆晓斐 译 李士通 校）
BACKGROUND: In sickle cell disease (SCD), hemolysis results in the release and activation of arginase, an enzyme that reciprocally regulates nitric oxide (NO) synthase activity and thus, NO production. Simply supplementing the common substrate L-arginine, however, fails to improve NO bioavailability. In this study, we tested the hypothesis that arginase inhibition would improve NO bioavailability and thereby attenuate systemic and pulmonary vascular endothelial dysfunction in transgenic mice with SCD.
METHODS: We studied 5-month-old transgenic sickle cell (SC) mice and age matched wild-type (WT) controls. SC mice were treated with the arginase inhibitor, 2(S)-amino-6-boronohexanoic acid (ABH; approximately 400 μg/d) for 4 weeks or left untreated.
RESULTS: Vascular arginase activity was significantly higher at baseline in

untreated SC mice compared to WT controls (SC versus WT, 346 ± 69.3 vs 69 ± 17.3 pmol urea/mg protein/minute; P = 0.0043; n = 4–5 animals per group). Treatment with ABH may significantly decrease arginase activity to levels near WT controls (SC + ABH 125.2 ± 17.3 pmol urea/mg protein/minute; P = 0.0213). Aortic strips from untreated SC mice showed decreased NO and increased reactive oxygen species (ROS) production (NO: fluorescence rate 0.76 ± 0.14 vs 1.34 ± 0.17 RFU/s; P = 0.0005 and ROS: fluorescence rate 3.96 ± 1.70 vs 1.63 ± 1.20 RFU/s, P = 0.0039; n = 3– animals per group). SC animals treated with ABH for 4 weeks demonstrated NO (fluorescence rate: 1.16 ± 0.16) and ROS (fluorescence rate: 2.02 ± 0.45) levels comparable with age-matched WT controls (n = 3– animals per group). The maximal endothelial-dependent vasorelaxation response to acetylcholine was impaired in aortic rings from SC mice compared with WT (57.7% ± 8.4% vs 80.3% ± 11.0%; P = 0.02; n = 6 animals per group). The endothelial-independent response was not different between groups. In SC mice, the right ventricular cardiac output index and end-systolic elastance were similar (4.60 ± 0.51 vs 2.9 ± 0.85 mL/min/100 g and 0.89 ± 0.48 vs 0.58 ± 0.11 mm Hg/μL), whereas the pulmonary vascular resistance index and right ventricular end-systolic pressure were greater (2.9 ± 0.28 vs 5.5 ± 2.0 mm Hg × min/μL/100 g and 18.9 ± 1.1 vs 23.1 ± 4.0 mm Hg; n = 8 animals per group). Pulse wave velocity (a measure of arterial stiffness) was greater in SC mice compared with WT (3.74 ± 0.54 vs 3.25 ± 0.21 m/s; n = 20 animals per group), arginase inhibition for 4 weeks significantly reduced the vascular SC phenotype to one similar to WT animals (P = 0.0009).
CONCLUSIONS: Arginase inhibition improves NO bioavailability and thereby attenuates systemic and pulmonary vascular endothelial dysfunction in transgenic mice with SCD. Therefore, arginase is a potential therapeutic target in the treatment of cardiovascular dysfunction in SCD.

在腰硬联合阻滞分娩镇痛中行硬膜外容量扩充不会升高感觉阻滞平面

Epidural Volume Extension During Combined Spinal-Epidural Labor Analgesia Does Not Increase Sensory Block

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背景：腰硬联合麻醉（CSE）广泛用于分娩镇痛。硬膜外容量扩充（EVE）是在硬膜外腔注入溶液压迫硬脊膜，促使脑脊液向头端扩散。我们假设，在 CSE 中用　生理盐水作 EVE，15 分钟后感觉阻滞平面升高。我们预计 CSE 中行 EVE 比未行 EVE（NEVE）的疼痛评分降低，减少镇痛起效时间、运动阻滞。
方法：我们随机分配 60 例子宫颈口扩张小于 5 厘米的足月分娩产妇行 CSE 在导管置入前通过 TUOHY 针注入 10 mL 生理盐水或行 CSE NEVE。鞘内注射镇痛由 2 mg 纯布比卡因和 10 芬太尼（总量 1 mL）组成。应用盲法由研究人员评估感觉阻滞平面、痛觉阻滞平面和 30 分钟运动阻滞。主要测量指标是 15 分钟最高感觉阻滞平面的中位数。
结果：对 54 名产妇进行了分析。15 分钟（平均差，1 节段；95%置信区间的中位数差异，0 到 2；P = 0.22）和 30 分钟（平均差，0 节段；95%置信区间，2 到 2；P = 0.76）最高感觉阻滞平面的中位数无显著差异。在最高感觉阻滞平面、最低疼痛评分和最快镇痛起效时间的组间比较无显著差异。

结论：我们发现感觉阻滞平面和疼痛分数在 EVE 和 NEVE 组间无显著差异。我们的研究表明，在对产妇应用 CSE 分娩镇痛中加行 EVE 并没有优化镇痛技术。（周延青 译 李士通 校 ）

BACKGROUND: Combined spinal-epidural (CSE) analgesia is widely used for delivering labor analgesia. Epidural volume extension (EVE) involves the injection of fluid into the epidural space compressing the dural sac, causing cephalad shift of the cerebral spinal fluid. Our hypothesis was that EVE with 10 mL normal saline during CSE would increase the sensory block height at 15 minutes after intrathecal injection. We expected EVE to decrease pain scores, decrease analgesia onset time, and decrease motor block compared with performing CSE without EVE (NEVE).
METHODS: We randomly assigned 60 healthy term laboring nulliparous parturients with cervical dilation <5 cm to receive CSE either with EVE of 10 mL normal saline through the Tuohy needle before catheter insertion or CSE NEVE. Intrathecal analgesia consisted of 2 mg plain bupivacaine and 10 μg fentanyl (1 mL total). A blinded researcher assessed sensory dermatome level, analgesia, and motor blockade at regular intervals for 30 minutes. The primary outcome measure was the median peak sensory dermatome level at 15 minutes.
RESULTS: Fifty-four parturients were analyzed. There was no significant difference in peak sensory dermatome levels at 15 minutes (median difference, 1 dermatome level; 95% confidence interval of median difference, 0 to 2; P = 0.22) and 30 minutes (median difference, 0 dermatome level; 95% confidence interval, -2 to 2; P = 0.76). There was no difference in the time to peak dermatome, minimum pain score, or the time to minimum pain score between groups.
CONCLUSIONS: We found no significant difference between groups with regard to sensory dermatome level or pain scores when using EVE compared with NEVE. Our study demonstrates that addition of EVE does not offer superior analgesia when using a CSE technique for parturients requesting labor analgesia.

静脉内过滤器在儿科患者低流量输液泵给药中的使用

Syringe Pump Performance Maintained with IV Filter Use During Low Flow Rate Delivery for Pediatric Patients

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背景：复杂外科手术和危重患儿静脉药物的精确输注依赖注射器输液泵。低流量和内置过滤器的使用可能影响药物输注。为了评价内置过滤器在消除低流量注射器输液泵使用时的空气和/或污染物的效果，我们比较了在设定流量下使用和不使用内置过滤器时的实际测得流量。
方法：分别使用和不使用过滤器制作静脉输注设备（过滤器组和对照组）连接到一个 10ml 注射器，再装上一个输液泵，连接到 16cm 的单腔导管。导管悬浮在生理盐水液柱中用来模拟中心静脉循环的压力。采用重量法在预定的时间间隔测量注射量和计算流量。实验设定对照组和过滤器组依次采用 1、0.8、0.6 和 0.4ml/h 的初始流量进行。在每一个试验中，流量改为双倍初始流量，然后再回到初始流量，用于分析给药过程中通常要求的反应输注泵性能的滴定率。这些条件（初始流量、双倍初始流量、回到初始流量）分别进行了独立的稳态流量和到达稳定状态的时间分析，而他们的平均值用来进行百分偏差分析。对照组和过滤器组之间的差异采用 t 检验与多样性调整 （使用 n = 3 重复每组）。

结果：两组从 0 到初始流量（启动延迟）的平均时间均小于 1 分钟差异无统计学意义（P = 1.0）。两组在任意流量或任意阶段（初始流量、双倍初始流量、回到初始流量），开始输注和流量改变时达到稳态流量的平均时间没有统计学差异（范围 0.8-5.5 分钟），尽管实验不足以发现微小的时间差异。总的来说，每个实验的平均稳态流量低于设定的流量，为负的平均百分偏差。在 1.0ml/h 初始流量试验中，过滤器组较对照组初始流量获得稳态流量低（P = 0.04），双倍初始流量获得稳态流量低（P = 0.04），回到初始流量获得稳态流量也低（P = 0.06），虽然与对照组相比，在 0.8ml/h 、0.6ml/h 或其他组实验中没有观察到相同结果。

结论：随着低流量输液泵在复杂外科和儿科危重病人中的应用，使用内置过滤器并不能显著改善输液泵给药过程中的启动延迟，流量变化，和达到稳态流量的时间。不论是否使用过滤器，整体流量均低于设定流量。

（章健萍 译 李士通 校）

BACKGROUND: Complex surgical and critically ill pediatric patients rely on syringe infusion pumps for precise delivery of IV medications. Low flow rates and in-line IV filter use may affect drug delivery. To determine the effects of an in-line filter to remove air and/or contaminants on syringe pump performance at low flow rates, we compared the measured rates with the programmed flow rates with and without in-line IV filters.

METHODS: Standardized IV infusion assemblies with and without IV filters (filter and control groups) attached to a 10-mL syringe were primed and then loaded onto a syringe pump and connected to a 16-gauge, 16-cm single-lumen catheter. The catheter was suspended in a normal saline fluid column to simulate the back pressure from central venous circulation. The delivered infusate was measured by gravimetric methods at predetermined time intervals, and flow rate was calculated. Experimental trials for initial programmed rates of 1.0, 0.8, 0.6, and 0.4 mL/h were performed in control and filter groups. For each trial, the flow rate was changed to double the initial flow rate and was then returned to the initial flow rate to analyze pump performance for titration of rates often required during medication administration. These conditions (initial rate, doubling of initial rate, and return to initial rate) were analyzed separately for steady-state flow rate and time to steady state, whereas their average was used for percent deviation analysis. Differences between control and filter groups were assessed using Student t tests with adjustment for multiplicity (using n = 3 replications per group).

RESULTS: Mean time from 0 to initial flow (startup delay) was <1 minute in both groups with no statistical difference between groups (P = 1.0). The average time to reach steady-state flow after infusion startup or rate changes was not statistically different between the groups (range, 0.8-5.5 minutes), for any flow rate or part of the trial (initial rate, doubling of initial rate, and return to initial rate), although the study was underpowered to detect small time differences. Overall, the mean steady-state flow rate for each trial was below the programmed flow rate with negative mean percent deviations for each trial. In the 1.0-mL/h initial rate trial, the steady-state flow rate attained was lower in the filter than the control group for the initial rate (P = 0.04) and doubling of initial rate (P = 0.04) with a trend during the return to initial rate (P = 0.06), although this same effect was not observed when doubling the initial rate trials of 0.8 or 0.6 mL/h or any other rate trials compared with the control group.

CONCLUSIONS: With low flow rates used in complex surgical and pediatric critically ill patients, the addition of IV filters did not confer statistically significant

changes in startup delay, flow variability, or time to reach steady-state flow of medications administered by syringe infusion pumps. The overall flow rate was lower than programmed flow rate with or without a filter.

可乐定不降低非心脏手术后的疼痛或阿片类药物的用量

Clonidine Does Not Reduce Pain or Opioid Consumption After Noncardiac Surgery

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背景：可乐定是一种具有镇痛作用的 α2 肾上腺素受体激动剂。然而，围手术期可乐定的镇痛效果尚不清楚。因此，我们验证了非心脏手术后的最初 72 小时内可乐定降低了疼痛评分和阿片类药物累积用量这一假说。

方法：624 例全身麻醉和脊髓麻醉的择期非心脏手术的病人被纳入围术期缺血评估-2 试验的子研究中。术前 2-4 小时将患者随机分组，分别为口服可乐定 0.2mg 组或口服安慰剂组，接着给予 0.2mg/天透皮可乐定贴片或安慰剂，并维持至术后 72 小时，再对术后 72 小时疼痛评分和阿片类药物的用量进行了评估。

结果：与安慰剂相比，可乐定在减少阿片类药物用量上没有作用，估计均值比为 0.98（95%置信区间，0.70-1.38）；P = 0.92。可乐定组阿片类药物用量的中位数（Q1、Q3）为 63（30，154）mg 吗啡当量，这与安慰剂组 60（30，128）mg 吗啡当量相似。此外，用 11 点量表评估疼痛评分，发现对两组的疼痛评分无明显影响，估计平均差值为 0.12（95%置信区间，-0.02 -0.26）；P = 0.10。可乐定组的患者平均疼痛评分为 3.6±1.8，安慰剂组患者平均疼痛评分 3.6±1.8。

结论：可乐定不降低患者非心脏手术恢复过程中阿片类药物的用量或疼痛评分。

（吕良策 译 李士通 校）

BACKGROUND: Clonidine is an α2-adrenoceptor agonist, which has analgesic properties. However, the analgesic efficacy of perioperative clonidine remains unclear. We, therefore, tested the hypothesis that clonidine reduces both pain scores and cumulative opioid consumption during the initial 72 hours after noncardiac surgery.

METHODS: Six hundred twenty-four patients undergoing elective noncardiac surgery under general and spinal anesthesia were included in this substudy of the PeriOperative ISchemia Evaluation-2 trial. Patients were randomly assigned to 0.2 mg oral clonidine or placebo 2 to 4 hours before surgery, followed by 0.2 mg/d transdermal clonidine patch or placebo patch, which was maintained until 72 hours after surgery. Postoperative pain scores and opioid consumption were assessed for 72 hours after surgery.

RESULTS: Clonidine had no effect on opioid consumption compared with placebo, with an estimated ratio of means of 0.98 (95% confidence interval, 0.70-1.38); P = 0.92. Median (Q1, Q3) opioid consumption was 63 (30, 154) mg morphine equivalents in the clonidine group, which was similar to 60 (30, 128) mg morphine equivalents in the placebo group. Furthermore, there was no significant effect on pain scores, with an estimated difference in means of 0.12 (95% confidence interval, -0.02

to 0.26); 11-point scale; P = 0.10. Mean pain scores per patient were 3.6 ± 1.8 for clonidine patients and 3.6 ± 1.8 for placebo patients.
CONCLUSIONS: Clonidine does not reduce opioid consumption or pain scores in patients recovering from noncardiac surgery.

在瑞芬太尼诱发的痛觉超敏中，PICK1 调节氨甲基膦酸(AMPA)受体的表达和转运

PICK1 Regulates the Expression and Trafficking of AMPA Receptors in Remifentanil-Induced Hyperalgesia

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背景：瑞芬太尼因为比其他阿片类止痛药诱导更快速，从而被广泛应用于临床麻醉，但其也更容易发生痛觉超敏。激活的门冬氨酸受体（NMDA 受体）是诱发瑞芬太尼痛觉超敏的关键部分。和 NMDA 受体一样，AMPARs（α-氨基-3-羟基-5-甲基-4-异唑丙酸受体），在突触后膜是离子型兴奋性谷氨酸受体，参与急性和慢性疼痛的传递。PICK1，C 激酶 1 蛋白相互作用蛋白，在 NMDA 受体介导的含 GluR2（谷氨酸受体 2）亚单位的 AMPARs 受体的内化中扮演一个重要的角色，并作用于炎症性疼痛的发生和持续。本研究的目的是，验证 PICK1 能通过调节 AMPAR 在脊髓中的表达和转运，从而在瑞芬太尼诱发的痛觉过敏中起作用这一假说。
方法：使用大鼠模型进行瑞芬太尼静脉灌注来诱发痛觉过敏。我们首先测量瑞芬太尼灌注前 24 小时和注入后 2、6、24、48 小时的机械和热痛觉过敏变化。在脊髓中 PICK1 的 mRNA 和蛋白质的表达、AMPAR 亚基的表达和转运分别由反转录定量 PCR、免疫组化和免疫印迹测得。此外，我们通过鞘内注射 PICK1 反义寡脱氧核苷酸来沉默 PICK1 的表达，研究 PICK1 缺乏对瑞芬太尼诱发的痛觉过敏和 AMPARs 表达和转运的影响。
结果：在疼痛阈值中发现了一个明显的时间-组别相关性(缩足反应的阈值和缩足反应的潜伏期；差异有统计学意义， P<.0001)。瑞芬太尼灌注在不同时间点引起不同的痛觉过敏 (P<.0001)，且部分因 PICK1 的沉默而逆转 (P<.007)。此外，在脊髓背角神经元，瑞芬太尼的注入增加了 PICK1 的 mRNA 和蛋白的表达 (P<.0001)和细胞膜上谷氨酸 1、2 受体的内化 (P<.0011)。更重要的是，PICK1 缺乏可以在脊髓背角处减弱瑞芬太尼诱导的 GluR2 内化 (P<.01)，但不影响瑞芬太尼诱导的细胞膜上的 GluR1 表达(P≥.985)。
结论：这些结果表明，PICK1 缺乏可能会通过调节含 GluR2 亚单位的 AMPAR 在脊髓背角的表达和转运从而逆转瑞芬太尼诱发的痛觉过敏。
（俞泳 译 李士通 校）

BACKGROUND: Remifentanil is used widely in clinical anesthesia because it induces more rapid and more common hyperalgesia than other opioid analgesics. Activation of N-methyl-D-aspartate (NMDA) receptors takes a pivotal part in remifentanil-induced hyperalgesia. Like NMDA receptors, the α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors (AMPARs) are excitatory ion glutamate receptors in postsynaptic membrane, which are involved in the transmission of both acute and chronic pain. Protein interacting with C kinase 1 (PICK1) plays an important role in NMDA receptor-mediated internalization of glutamate receptor 2

(GluR2)-containing AMPARs and contributes to the induction and maintenance of inflammation-induced pain. This study aimed to test the hypothesis that PICK1 contributes to remifentanil-induced hyperalgesia by regulating AMPAR expression and trafficking in the spinal cord.
METHODS: Using a rat model of remifentanil-induced hyperalgesia by intravenous infusion of remifentanil, we first measured changes in mechanical and thermal hyperalgesia at 24 hours before remifentanil infusion and 2, 6, 24, and 48 hours after infusion. PICK1 mRNA and protein expression and AMPAR subunit expression and trafficking in the spinal cord were then detected by reverse transcription-qualitative polymerase chain reaction, immunohistochemistry, and Western blot. In addition, we knocked down PICK1 expression by intrathecal administration of PICK1 antisense oligodeoxynucleotide to investigate the effects of PICK1 deficiency on remifentanil-induced hyperalgesia and the expression and trafficking of AMPARs.
RESULTS: A significant time-group interaction was found for nociceptive thresholds (paw withdrawal threshold and paw withdrawal latency; all $P < .0001$). Remifentanil infusion induced distinct hyperalgesia at different time points ($P < .0001$), which was partly reversed by PICK1 knockdown ($P < .007$). Besides, remifentanil infusion increased the expression of PICK1 mRNA and protein ($P < .0001$) and the membrane GluR1 and GluR2 internalization in spinal dorsal horn neurons ($P < .0011$). More importantly, PICK1 deficiency could attenuate remifentanil-induced GluR2 internalization in the spinal cord dorsal horn ($P < .01$) but had no effect on remifentanil-induced membrane GluR1 expression ($P \geq .985$).
CONCLUSIONS: These results indicate that PICK1 deficiency might reverse remifentanil-induced hyperalgesia through regulating GluR2-containing AMPAR expression and trafficking in the spinal cord dorsal horn.