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不同膠體導致的稀釋性凝血障礙是否可由纖維蛋白原和凝血因數 XIII 濃縮物來逆轉

Is Dilutional Coagulopathy Induced by Different Colloids Reversible by Replacement of Fibrinogen and Factor XIII Concentrates?

Kind, Stephanie L. MD*; Spahn-Nett, Gabriela H. MD*; Emmert, Maximilian Y. MD†; Eismon, Jennifer MD‡; Seifert, Burkhardt PhD§; Spahn, Donat R. MD, FRCA*; Theusinger, Oliver M. MD*

Anesthesia & Analgesia: 2013 117：1063–1071

背景：本離體試驗評估了使用不同膠體進行 60%血液稀釋後對凝血的影響並研究 XIII 因數(FXIII)、纖維蛋白原及兩者的複合應用對凝血功能的逆轉作用。

方法：取 12 名自願者的血液，分別在血液稀釋前和由 HES 130/0.4 ，明膠或平衡明膠溶液稀釋 60%後測定：血氣分析，凝血因數濃度（I,II,VII,VIII 和 XIII 因數），阻抗法血小板聚集實驗(Multiplate®)，旋轉式血栓彈力圖(ROTEM®)。然後，給予 XIII 因數（1250IU）或纖維蛋白原 6g 或兩者聯合加入樣本，測定 ROTEM® 指標並測定凝血因數濃度。

結果：膠體稀釋後，特別是 HES 能顯著降低纖維蛋白原的聚合作用。所有膠體都會損害血小板功能，其中明膠比 HES 和平衡明膠溶液的損害作用更顯著（曲線下面積，collagen 試驗，P≤0.008）。XIII 因數替代治療僅不改善凝血塊形成。纖維蛋白原替代治療改善由明膠和平衡明膠溶液稀釋後纖維蛋白原的聚合作用（P=0.002），然而它不能糾正 HES 稀釋導致的凝血障礙。聯合應用 XIII 因數和纖維蛋白原比單純使用纖維蛋白原對機體凝血功能有更好的效果。

結論：三種膠體都能損害凝血和血小板功能。然而，在離體試驗中，明膠比 HES 稀釋引起的凝血障礙更具有可逆性。

（邊文玉 譯 陳傑 校）

BACKGROUND: In this in vitro trial, we assessed the effect on blood coagulation of 60% dilution with different colloids and investigated reversibility by replacement of factor XIII (F XIII), fibrinogen, and the combination of fibrinogen and F XIII.

METHODS: Using the blood of 12 volunteers, the following measurements were performed at baseline and after 60% dilution with (hydroxyethyl starch solutions) HES 130/0.42, gelatin, or balanced gelatin solution: blood gas analyses, coagulation factor concentrations (F I, F II, F VII, F VIII, F XIII), impedance aggregometry (Multiplate®), and rotational thromboelastometry (ROTEM®). Then F XIII and fibrinogen as well as a combination of both were added, in concentrations corresponding to 6 g fibrinogen and 1250 IU F XIII in adults. ROTEM® measurements and determination of factor concentrations were again performed.

RESULTS: Colloid dilution led to a significant reduction of fibrinogen polymerization, especially with HES. Platelet function was impaired by all colloids, with gelatin having a significantly greater effect (area under the curve, collagen Test, P ≤ 0.008) than HES and balanced gelatin solution. The substitution of F XIII only did not improve clot formation. Substitution of fibrinogen improved the polymerization of fibrinogen in dilutions with gelatin and balanced gelatin solution (P = 0.002), whereas HES-induced coagulopathy could not be corrected. The combination of fibrinogen and F XIII showed a better effect than the addition of fibrinogen only for certain variables.

CONCLUSION: Coagulation and platelet function are impaired by all 3 colloids. However, in vitro gelatin-induced coagulopathy was significantly more reversible than HES-induced coagulopathy.

一項在志願者行腸鏡檢查時應用多種劑量 Remimazolam (CNS 7056)進行的 Ib 期劑量反應研究

A Phase Ib, Dose-Finding Study of Multiple Doses of Remimazolam (CNS 7056) in Volunteers Undergoing Colonoscopy

Worthington, Mark T. MD*; Antonik, Laurie J. MD†; Goldwater, D. Ronald MD‡; Lees, James P. BSc§; Wilhelm-Ogunbiyi, Karin MD ‖ ; Borkett, Keith M. BSc§; Mitchell, Mack C. MD*

Anesthesia & Analgesia: 2013，117 ：1093–1100

背景：這項 remimazolam 多劑量應用研究目的在於評估此藥物在腸鏡檢查期間維持適當鎮靜作用以及用氟馬西尼逆轉鎮靜作用的可行性。

方法：健康志願者在進行腸鏡檢查時依次給予芬太尼、remimazolam，後者起鎮靜作用。分爲三個劑量組，每組 15 名志願者，每組逐漸增加 remimazolam 的初始劑量，再加上補充劑量以維持 30min 鎮靜。在另一部分的雙盲交叉實驗中，6 名志願者在接收單次高劑量的 remimazolam 鎮靜後使用氟馬西尼或安慰劑進行逆轉。

結果：70%的受試者在腸鏡檢查過程中達到足夠鎮靜深度。在整體中位數爲 10min 內，受試者術後迅速恢復至充分警覺水準。失敗病例是由於無法獲得鎮靜或產生了不良事件，後者爲一例受試者發生了低血壓（血壓 80/40 mmHg）和低血氧飽和度（<90%）。沒有嚴重不良事件報告，也無苯二氮卓類藥和芬太尼聯合使用後的意外事件發生。這項研究還表明 remimazolam 的鎮靜作用可被迅速逆轉（氟馬西尼 1.0min，安慰劑 10.5min），且並不產生再次鎮靜。

結論：remimazolam 是一種鎮靜藥物，與其他藥物的最近研究相比具有相似的成功率。接受腸鏡檢查的 44 例受試者中 33 例，Remimazolam 能提供足夠的鎮靜，並且它的鎮靜效果很容易被氟馬西尼逆轉。

（談婧華 譯 陳傑 校）

BACKGROUND: We performed the first multiple dose study of remimazolam designed to assess both the feasibility of maintaining suitable sedation during colonoscopy and reversing the sedative effects of remimazolam with flumazenil.

METHODS: Healthy volunteers received fentanyl followed by remimazolam for sedation during colonoscopy. Three dose groups of 15 volunteers each received remimazolam in increasing initial doses, plus top-up doses to maintain sedation for a 30-minute period. In a separate double-blind crossover part of the trial, 6 volunteers were sedated with a single high dose of remimazolam, followed by flumazenil or placebo to reverse the sedation.

RESULTS: Successful sedation that was adequate for colonoscopy was achieved in >70% of subjects. After the procedure, subjects rapidly recovered to fully alert, with a median of <10 minutes overall. Failures were due to the inability to sedate or adverse events, with 1 subject failing due to hypotension (arterial blood pressure 80/40) and low SpO2 (<90%). There were no serious adverse events reported, and no events that were unexpected with the combination of a benzodiazepine and fentanyl. The study also showed that sedation was rapidly reversible (1.0 minutes flumazenil vs 10.5 minutes placebo) without resedation.

CONCLUSIONS: Remimazolam has the attributes of a sedative drug, with success rates comparable with recent studies of other drugs. Remimazolam provided adequate sedation in 33 of 44 subjects undergoing colonoscopy, and its sedative effects were easily reversed with flumazenil.

手術期間閉環液體管理與麻醉醫師管理用於血液動力學優化和復蘇的比較：一項在體研究

Closed-Loop Fluid Administration Compared to Anesthesiologist Management for Hemodynamic Optimization and Resuscitation During Surgery: An In Vivo Study

Rinehart, Joseph MD*; Lee, Christine BS*; Canales, Cecilia MPH*; Kong, Allen MD†; Kain, Zeev MD, MBA*; Cannesson, Maxime MD, PhD*

Anesthesia & Analgesia: 2013 117 ：1119–1129

背景：閉環系統已被設計用於說明醫生維持臨床中各項生理參數的穩定。最近完成了一項新的閉合環路液體管理系統的電腦類比測試，此系統被設計用於監測和優化心輸出量和脈壓變異度。本研究的目的是評價此新型系統優化手術期間血流動力學參數的效果。

方法：16 頭約克種豬行 2 期出血處理，並通過記憶靜脈復蘇器閉合環路系統或麻醉醫生進行復蘇。比較兩組間血流動力學參數中值和變異。

結果：在整個實驗過程中，閉合環路組的心臟指數(l/min/m2)和每搏指數(ml/m2)高於麻醉醫生組(心臟指數：3.7 [3.4–4.1] vs 3.5 [3.2–3.9]；95% Wald 可信區間爲−0.5 ~ −0.23；P < 0.0005。每搏指數：40 [34–45] vs 36 [31–38]；95% Wald 可信區間爲 −5.9 ~ −3.1；P <

0.0005)。兩組間總液體輸入量沒有顯著差異(3685 [3230–4418] vs 3253 [2735–3926] ml; 95%可信區間爲−1651~ 431；P = 0.28)。另外，閉合環路組的心臟指數和每搏指數的變異係數較醫生組小(心臟指數：11% [10%–16%] vs 22% [18%–23%]；可信區間爲 0.8%~12.3%；P = 0.02。每搏指數：11% [8%–16%] vs 17% [13%–21%]；可信區間爲 0.2%~11.4%；P = 0.04)。

結論：此在體研究建立於前期電腦類比分析，結果顯示用於此實驗的閉合環路液體管理系統能夠完成輕度和重度出血時的液體復蘇，並能維持高心輸出量和每搏量而降低血流動力學的變化。

（朱浩 譯 陳傑 校）

BACKGROUND: Closed-loop systems have been designed to assist practitioners in maintaining stability of various physiologic variables in the clinical setting. In this context, we recently performed in silico testing of a novel closed-loop fluid management system that is designed for cardiac output and pulse pressure variation monitoring and optimization. The goal of the present study was to assess the effectiveness of this newly developed system in optimizing hemodynamic variables in an in vivo surgical setting.

METHODS: Sixteen Yorkshire pigs underwent a 2-phase hemorrhage protocol and were resuscitated by either the Learning Intravenous Resuscitator closed-loop system or an anesthesiologist. Median hemodynamic values and variation of hemodynamics were compared between groups.

RESULTS: Cardiac index (in liters per minute per square meter) and stroke volume index (in milliliters per square meter) were higher in the closed-loop group compared with the anesthesiologist group over the protocol (3.7 [3.4–4.1] vs 3.5 [3.2–3.9]; 95% Wald confidence interval, −0.5 to −0.23; P < 0.0005 and 40 [34–45] vs 36 [31–38]; 95% Wald confidence interval, −5.9 to −3.1; P < 0.0005, respectively). There was no significant difference in total fluid administration between the closed-loop and anesthesiologist groups (3685 [3230–4418] vs 3253 [2735–3926] mL; 95% confidence interval, −1651 to 431; P = 0.28). Closed-loop group animals also had lower coefficients of variance of cardiac index and stroke volume index during the protocol (11% [10%–16%] vs 22% [18%–23%]; confidence interval, 0.8%–12.3%; P = 0.02 and 11% [8%–16%] vs 17% [13%–21%]; confidence interval, 0.2%–11.4%; P = 0.04, respectively).

CONCLUSION: This in vivo study building on previous simulation work demonstrates that the closed-loop fluid management system used in this experiment can perform fluid resuscitation during mild and severe hemorrhages and is able to maintain high cardiac output and stroke volume while reducing hemodynamic variability.

應急手冊的實施：認知輔助在突發事件期間是否可幫助將最佳實踐應用于患者監護

Implementing Emergency Manuals: Can Cognitive Aids Help Translate Best Practices for Patient Care During Acute Events?

Goldhaber-Fiebert, Sara N. MD*; Howard, Steven K. MD†*

Anesthesia & Analgesia: 2013 ，117 ：1149 – 1161

本文闡明應急手冊是否對於幫助麻醉醫生、圍手術期團隊處理緊急重大事件，是一種已知的有效手段。本文回顧了過去相關健康護理中的認知輔助，以及其他高風險行業中的事例，解釋爲何應急手冊在類似事件中能促進病人的監護工作。本文採用圍手術期的具體實例，提出四個重要因素：創建、熟悉、使用和整合，這些對於醫療應急手冊的傳播、發展和實施很重要。每個因素的細節均來自於醫學文件，或是有著長達 30 餘年總結經驗的麻醉醫生模擬和實際重大事件管理觀察組。作者強調應急手冊在內容、地點以及方式上訓練

臨床醫生的重要性。最後，作者討論了對於改變所需的文化方面的準備，展示了一套成功整合的系統實例，著重提出對於應急手冊實施方面進一步研究的重要性。

（賀加貝 譯 陳傑 校）

In this article, we address whether emergency manuals are an effective means of helping anesthesiologists and perioperative teams apply known best practices for critical events. We review the relevant history of such cognitive aids in health care, as well as examples from other high stakes industries, and describe why emergency manuals have a role in improving patient care during certain events. We propose 4 vital elements: create, familiarize, use, and integrate, necessary for the widespread, successful development, and implementation of medical emergency manuals, using the specific example of the perioperative setting. The details of each element are presented, drawing from the medical literature as well as from our combined experience of more than 30 years of observing teams of anesthesiologists managing simulated and real critical events. We emphasize the importance of training clinicians in the use of emergency manuals for education on content, format, and location. Finally, we discuss cultural readiness for change, present a system example of successful integration, and highlight the importance of further research on the implementation of emergency manuals.

內質網應激對於吸入麻醉藥引起的神經毒性的影響

The Effect of Endoplasmic Reticulum Stress on Neurotoxicity Caused by Inhaled Anesthetics

Komita, Mari MD; Jin, Hisayo; Aoe, Tomohiko MD, PhD

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背景：吸入麻醉藥引起神經毒性的機制尚未闡明。暴露於吸入麻醉藥可引起 Ca2+從細胞質內質網（ER）釋放入胞質。異常的 Ca2 +動員可改變 ER 中的蛋白質折疊環境，引起 ER 應激。結合免疫球蛋白（BIP）是一種 ER 伴侶，對 ER 功能維持是至關重要的。由於 ER 應激導致細胞功能障礙和細胞凋亡，從而引起不同的人類疾病，如神經退行性疾病，作者推測 ER 應激可能在吸入麻醉藥引起的神經毒性方面起一定作用。

方法：本研究通過表達突變 BIP 的基因敲除小鼠和神經元培養細胞調查 ER 應激與吸入麻醉藥引起的神經退行性疾病之間的關係。神經元培養細胞和突變 BIP 懷孕小鼠暴露於 3％七氟醚。 通過對神經元細胞和剖腹產胎鼠大腦進行 Western blot 分析來評估 BIP 和 C / EBP 同源蛋白（CHOP）水準，後者是一種 ER 應激期間細胞死亡相關的轉錄因數。使用 TUNEL 染色來評估胎鼠大腦的細胞死亡。採用非配對 t 核對總和方差分析，之後多重比較來評估是否有統計學意義。

結果：七氟烷暴露增強神經元培養細胞的 BIP 和 CHOP 表達。一種輔助 ER 功能的化學伴侶可減少七氟醚暴露所誘導的 CHOP 表達。在一項在體研究中發現，與野生型相比，突變 BIP 純合子胎鼠大腦中 CHOP 表達加強，細胞凋亡更顯著。七氟醚暴露後，來自突變 BIP 小鼠的胚胎成纖維細胞也表現出 CHOP 和裂解 caspase-3 水準的增強。

結論:七氟醚暴露可引起 ER 應激, 野生型細胞在一定程度上可以耐受。而如存在突變 BIP 的細胞，若無法耐受此種應激，七氟醚暴露導致大腦的細胞死亡，暗示內質網應激可能部分介導了吸入麻醉藥引起的神經毒性。此項研究表明一定條件下，如缺血、低氧、發育中大腦、或神經退行性疾病可能對吸入麻醉藥較敏感。

（李峰日 譯 陳傑 校）

BACKGROUND: The mechanisms by which inhaled anesthetics cause neurotoxicity are not well clarified. Exposure to inhaled anesthetics induces a release of Ca2+ from the endoplasmic reticulum (ER) into the cytosol. Aberrant Ca2+ mobilization may alter the protein-folding environment in the ER, causing ER stress. Binding immunoglobulin protein (BiP) is an ER

chaperone that is critical to ER functions. Because ER stress leads to cellular dysfunction and apoptotic cell death, leading to diverse human disorders such as neurodegenerative diseases, we hypothesized ER stress may play a role in neurotoxicity caused by inhaled anesthetics.

METHODS: We investigated the relationship between ER stress and neurodegeneration caused by inhaled anesthetics by using knock-in mice expressing a mutant BiP and neuronal culture cells. Neuronal culture cells and mutant BiP pregnant mice were exposed to 3% sevoflurane. The levels of BiP and C/EBP homologous protein (CHOP), a transcription factor related to cell death during ER stress, were evaluated by Western blot in neuronal cells and fetal brains delivered by cesarean delivery. Cell death in the fetal brains was evaluated with TUNEL staining. Statistical significance was assessed using unpaired t test and analysis of variance followed by multiple comparison tests.

RESULTS: Sevoflurane exposure enhanced the expression of BiP and CHOP significantly in neuronal culture cells. A chemical chaperone that assisted ER functions reduced the expression of CHOP induced by sevoflurane exposure. In an in vivo study, we observed that an enhanced expression of CHOP and significantly more apoptotic cells in the brains of homozygous mutant BiP fetuses compared with the wild type. Mouse embryonic fibroblasts derived from the mutant BiP mice also exhibited enhanced levels of CHOP and cleaved caspase-3 after sevoflurane exposure.

CONCLUSIONS: Sevoflurane exposure may cause ER stress, which is tolerated to some extent in wild-type cells. When this tolerance is limited, like in cells with mutant BiP, the exposure leads to cell death in the brain, suggesting that ER stress may partially mediate neurotoxicity caused by inhaled anesthetics. This study suggests that patients with certain conditions sensitive to ER stress such as ischemia, hypoxia, developing brain, or neurodegenerative diseases may be vulnerable to inhaled anesthetics.

來自 Charles T. Jackson 包含已知最早的莫頓醚吸入器圖示的信件

Correspondence by Charles T. Jackson Containing the Earliest Known Illustrations of a Morton Ether Inhaler

Haridas, Rajesh P. MBChB, FANZCA; Bause, George S. MD, MPH*†

Anesthesia & Analgesia: 2013 117 ： 1236–1240

一份日期爲 1846 年 12 月 1 日，來自 Charles T. Jackson 博士給 Josiah D. Whitney 的回信中包含了以前未報導過的描述莫頓乙醚吸入器和唯一已知的同期這種類型乙醚吸入器的手繪插圖。這份回信和另外兩份已知的關於乙醚麻醉的回信可能來自麻塞諸塞州的波士頓通過明輪船（阿卡迪亞）發往英國利物浦，該船同樣載有還有來自 Jacob Bigelow 博士發給 Francis Boott 博士的著名信件。

（林甲票 譯 陳傑 校）

A letter, dated December 1, 1846, from Charles T. Jackson, MD, to Josiah D. Whitney contains a previously unreported description of a Morton ether inhaler and the only known contemporaneous hand-drawn illustrations of this type of ether inhaler. This letter and 2 other known letters on ether anesthesia were probably carried from Boston, MA, to Liverpool, United Kingdom, on the same paddle steamer (Acadia) that carried the well-known letter from Jacob Bigelow, MD, to Francis Boott, MD.

對心臟手術的患者，FIBTEM PLUS 可提供一種更好的血栓彈力測試來評價纖維蛋白凝塊品質

FIBTEM PLUS Provides an Improved Thromboelastometry Test for Measurement of Fibrin-Based Clot Quality in Cardiac Surgery Patients.

Solomon C, Baryshnikova E, Schlimp CJ, Schöchl H, Asmis LM, Ranucci M.

From the *Department of Anesthesiology and Intensive Care, Salzburger Landeskliniken SALK, Salzburg, Austria; †CSL Behring, Marburg, Germany; ‡Department of Cardiothoracic and Vascular Anesthesia and Intensive Care, IRCCS Policlinico San Donato, Milan, Italy; §Haemostasis Research, Ludwig Boltzmann Institute for Experimental and Clinical Traumatology and AUVA Research Centre, Vienna, Austria; ‖ Department of Anesthesiology and Intensive Care, AUVA Trauma Hospital of Salzburg, Salzburg, Austria; and ¶Laboratory Medicine, Unilabs Coagulation Laboratory, Zurich, Switzerland.

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背景：粘彈性功能纖維蛋白原（FF）和 FIBTEM 分析法可用於測量纖維蛋白對血凝塊強度的影響。這些試驗都要先經過抑制血小板功能的預處理。我們研究了一種新的測試法，即 FIBTEM PLUS，在心外科手術中與 FF 法和 FIBTEM 法比較。

方法：這是一項前瞻性，觀察性研究，入組了 30 例心外科手術需要體外迴圈的患者。分別在手術開始（體外迴圈前），停體外迴圈前 20 分鐘，魚精蛋白中和肝素後 5 分鐘，共 3 個時間點提取血樣本。所有的血樣本分別用 FF、FIBTEM 和 FIBTEM PLUS 法測定 2 次，同時記錄其他一些凝血參數，包括血小板計數，血漿纖維蛋白原水準，凝血因數 XIIIa 和肝素濃度。

結果：在所有時間點裡，FIBTEM PLUS 測得平均 MCF（maximum clot firmness）最小，儘管 FIBTEM 和 FIBTEM PLUS 的測量只有在基線上有統計學差異（平均值 22 vs 19mm，P = 0.01；FF 測得平均 27.7mm）。體外迴圈前、迴圈中和中和肝素後 FF 法測得的 MA（maximum amplitude）相較於 FIBTEM 法測的 MCF 和 FIBTEM PLUS 法測的 MCF 明顯升高。FIBTEM 法和 FIBTEM PLUS 法測得的 MCF 的差異與血小板計數有關（r = 0.46;P < 0.001），而 FF 法測得的 MA 和 FIBTEM 法、FIBTEM PLUS 法測得的 MCF 是沒有這種相關性(分別爲 r = -0.07, P = 0.51；r = 0.16, P = 0.12)。各方法測得值的差異與肝素水準無關。停體外迴圈前使用魚精蛋白使肝素水準顯著下降（抗凝血因數 IIa 從 2.1 降至 0.1 U/mL，抗凝血因數 Xa 從 2.8 降至 0.2U/mL）。用 FIBTEM PLUS 法重複測量的值與 FIBTEM 一致，FF 法測得偏低。MCF 或 MA 和纖維蛋白原濃度顯著正相關（所有 P< 0.001）；最高相關性是 FIBTEM PLUS 測得的 MCF(r = 0.70)。

結論：用 FIBTEM PLUS 法重複測量的值與 FIBTEM 一致，FF 法測得偏低。MCF 或 MA 和纖維蛋白原濃度顯著正相關（所有 P< 0.001）；最高相關性是 FIBTEM PLUS 測得的 MCF(r = 0.70)。

（陳實玉譯 薛張綱校）

BACKGROUND: The viscoelastic functional fibrinogen (FF) and FIBTEM assays measure the contribution of fibrin to clot strength. Inhibition of platelet function is a necessary precondition for these tests to work. We investigated a novel test for measuring fibrin-based clotting, FIBTEM PLUS, in cardiac surgery and compared it with FF and FIBTEM.

METHODS: A prospective, observational study was performed which included 30 patients undergoing cardiac surgery with cardiopulmonary bypass (CPB). Blood samples were drawn at the beginning of surgery (pre-CPB), approximately 20 minutes before weaning from CPB and 5 minutes after heparin neutralization. FF, FIBTEM, and FIBTEM PLUS tests were performed in duplicate for all blood samples. Additional coagulation parameters, including platelet count, plasma fibrinogen levels, factor XIII activity, and heparin concentration, were also recorded for each sample.

RESULTS: At all time points, the lowest mean maximum clot firmness (MCF) was observed with FIBTEM PLUS, although a statistically significant difference between FIBTEM and

FIBTEM PLUS was observed only at baseline (mean values 22 vs 19 mm, P = 0.01; FF value for comparison: 27.7 mm). FF maximum amplitude (MA) values were significantly higher than FIBTEM MCF and FIBTEM PLUS MCF pre-CPB, during CPB and after heparin neutralization ($P \leq 0.001$ for FF MA versus FIBTEM MCF and for FF MA versus FIBTEM PLUS MCF at all time points). The difference between FIBTEM MCF and FIBTEM PLUS MCF correlated with platelet count ($r = 0.46$;$P < 0.001$), whereas differences between FF MA and FIBTEM MCF, or FF MA and FIBTEM PLUS MCF did not ($r = -0.07$, $P = 0.51$; $r = 0.16$, $P = 0.12$, respectively). Differences between the assays were unrelated to heparin levels, which decreased considerably after protamine administration compared with heparin levels recorded before weaning from CPB (decrease from 2.1 to 0.1 U/mL and from 2.8 to 0.2 U/mL for anti-factor IIa and anti-factor Xa, respectively). Agreement between duplicate measurements was similar with FIBTEM and FIBTEM PLUS assays and lower with FF. Significant positive correlations were found between MCF or MA and fibrinogen concentration (all $P < 0.001$); the highest correlation was with FIBTEM PLUS MCF ($r = 0.70$).

CONCLUSION: The FIBTEM PLUS assay produces precise results. At baseline, it provides greater inhibition of platelets than FIBTEM, but there is no meaningful difference between FIBTEM PLUS and FIBTEM in patients with low platelet counts.

系統綜述：肥胖患者如何選擇門診手術

Selection of obese patients undergoing ambulatory surgery: a systematic review of the literature.

Joshi GP, Ahmad S, Riad W, Eckert S, Chung F.

From the *Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center, Dallas, Texas; †Department of Anesthesiology, Northwestern University Feinberg School of Medicine, Chicago, Illinois; ‡Department of Anesthesia, Toronto Western Hospital, University Health Network, University of Toronto, Toronto, Ontario, Canada; §Ambulatory Surgery Division, Hospital Corporation of America, Austin, Texas; and ‖Department of Anesthesia, Toronto Western Hospital, University Health Network, University of Toronto, Toronto, Ontario, Canada

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背景：肥胖症的發病率在過去的二十年中有所增加。近年來，一些研究致力於評估接受門診手術的肥胖患者在圍手術期的預後。然而，這些研究結論並未進行系統審查和評估。

方法：研究者對 1948 年至 2012 年 5 月發表的研究進行了系統回顧並評估接受門診手術的成年肥胖患者的圍手術期預後。所有的研究均符合納入標準，即使其圍手術期發生併發症包括意外的入院以及再入院。

結果：文獻檢索一共搜得 23 項研究（13 項前瞻性研究以及 10 項回顧性研究）和一項針對腹腔鏡減肥手術的系統回顧。共有 106119 名患者被納入分析，其中前瞻性試驗有 62476 名患者，回顧性試驗有 43643 名患者（不包括腹腔鏡減肥手術的系統回顧）。其中，有 39548 名患者接受了減肥手術。超級肥胖（體脂指數 BMI）50 公斤/米）的患者出現併發症的風險較高。接受非減肥手術的患者的肥胖程度較低（BMI 約 30 公斤/米）。接受減肥手術的病態肥胖（BMI 大於 40 公斤/米）的患者有較高的合併症風險。然而，該患者群體意外住院率的上升可能與缺乏全面的術前評估以及忽視了患者的合併症相關。

討論：文獻缺乏足夠的資訊作爲有力的證據指標提示肥胖患者是否適合選擇做門診手術。文獻顯示，超級肥胖（BMI 大於 50 公斤/米）的患者圍手術期發生併發症的風險增加，而 BMI 較低的患者在術前發生併發症或者合併症的可能性非常小。本綜述填補了該項知識空白並對將來的研究引導了方向，即需要引導肥胖患者如何做出門診手術的最佳選擇。

（陳婉南譯 薛張綱校）

BACKGROUND: The incidence of obesity has increased over the past 2 decades. In recent years, several studies have assessed perioperative outcomes in obese patients undergoing ambulatory surgery. However, this evidence has not been reviewed and evaluated systematically.

METHODS: We conducted a systematic review of studies published between 1948 and May 2012, assessing perioperative outcome in adult obese patients undergoing ambulatory surgery. All studies were eligible for inclusion if they reported perioperative complications including unplanned hospital admission and readmission.

RESULTS: A literature search revealed 23 studies (13 prospective and 10 retrospective), and 1 systematic review assessing laparoscopic bariatric surgery. A total of 106,119 patients were included in the analysis with 62,476 patients included in the prospective trials and 43,643 patients included in the retrospective trials (not including the systematic review of laparoscopic bariatric surgery). Of these, 39,548 patients underwent bariatric surgery. The super obese (body mass index [BMI] >50 kg/m) appear to be at higher risk of complications. Patients undergoing nonbariatric surgery had a lower degree of obesity (BMI approximately 30 kg/m). Patients undergoing bariatric surgery were morbidly obese (BMI >40 kg/m), which is associated with a higher comorbidity burden. However, the lack of increase in unanticipated admission rate in this patient population may be related to thorough preoperative assessment and avoidance of patients with comorbid conditions.

DISCUSSION: The literature lacks adequate information to make strong recommendations regarding appropriate selection of the obese patients scheduled for ambulatory surgery. The literature does indicate that the super obese (BMI >50 kg/ m) do present an increased risk for perioperative complications, while patient with lower BMIs do not seem to present any increased risk as long as any comorbidities are minimal or optimized before surgery. This review also identifies knowledge gaps and recommends future research required to guide optimal selection of obese patients scheduled for ambulatory surgery.

閉環式液體復蘇：對於體重及心肌收縮性變化時的穩定性

Closed-loop fluid resuscitation: robustness against weight and cardiac contractility variations.

Rinehart J, Lee C, Cannesson M, Dumont G.

From the *Department of Anesthesiology and Perioperative Care, University of California Irvine, Orange, California; and †Department of Electrical and Computer Engineering, University of British Columbia, Vancouver, British Columbia, Canada.

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背景：不同外科手術病人的體型及血容量有著較大範圍的變化，在基礎容量狀態及心功能上有著較大的不同。所有的閉環式液體循環管理系統對面這些變數時必須保持穩定。目前的研究中，我們用了系統工程方法論測試了閉環式液體循環管理系統對面這些變數時的穩定性。

方法：應用獨立先前公佈的包括血液容量及心功能的血液迴圈類比模型，類比 monte-carlo 系列，包括起始血容量、體重（phase 1，體重 35-100kg），起始血容量、心功能（phase 2，心功能從 1500[嚴重心衰]到 6000[高動力性]）。在復蘇控制組中設置的目標靶點以評估血容量的毫升數作爲最佳值的偏差，小於 250ml 的偏差定義爲成功。

結果：這項研究中兩個階段分別進行了 1000 例的模擬。階段 1 示血容量最佳值的偏差± SD 是 25± 59ml. 階段二示血容量最佳值的偏差± SD 是-60 ± 89 mL.復蘇時低於 95%的

clopper-pearson 二項置信度干擾，在最佳血容量偏差在 250ml 內時階段 1 及階段 2 分別爲 99.6%和 97.1%。

結論：這項研究的結果示控制組在調控最佳血容量及休克血容量時，可忽略體重、心功能及起始血容量

（蔣鑫梅譯 薛張綱校）

BACKGROUND: Surgical patients present with a wide variety of body sizes and blood volumes, have large differences in baseline volume status, and may exhibit significant differences in cardiac function. Any closed-loop fluid administration system must be robust against these differences. In the current study, we tested the stability and robustness of the closed-loop fluid administration system against the confounders of body size, starting volume status, and cardiac contractility using control engineering methodology.

METHODS: Using an independently developed previously published hemodynamic simulation model that includes blood volumes and cardiac contractility, we ran a Monte-Carlo simulation series with variation in starting blood volume and body weight (phase 1, weight 35-100 kg), and starting blood volume and cardiac contractility (phase 2, contractility from 1500 [severe heart failure] to 6000 [hyperdynamic]). The performance of the controller in resuscitating to the target set point was evaluated in terms of milliliters of blood volume error from optimal, with <250 mL of error defined as "successful."

RESULTS: One thousand simulations were run for each of the 2 phases of the study. The phase 1 mean blood volume error ± SD from optimal was 25 ± 59 mL. The phase 2 mean blood volume error from optimal was -60 ± 89 mL. The lower 95% Clopper-Pearson binomial confidence interval for resuscitation to within 250 mL of optimal blood volume for phase 1 and 2 was 99.6% and 97.1%, respectively.

CONCLUSION: The results indicate that the controller is highly effective in targeting optimal blood and stroke volumes, regardless of weight, contractility or starting blood volume.

麻醉閉環控制系統:麻醉學家的入門基礎

Closed-loop control of anesthesia: a primer for anesthesiologists.

Dumont GA, Ansermino JM.

Departments of *Electrical & Computer Engineering and Anesthesiology, Pharmacology & Therapeutics, University of British Columbia; and Department of Anesthesia, BC Children's Hospital, Vancouver, British Columbia, Canada.

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回饋控制系統普遍存在於自然界和工程學中,使得包括太空旅行到汽車業的廣大領域的安全性發生變革。在麻醉學界，儘管由於病人個體差異存在，自動回饋控制系統的效果受到制約，但它優化了麻醉醫生的工作負荷，增加了花費於更佳臨床狀態所需時間，最終改善了臨床麻醉的安全性和品質。控制系統的優點沒有被健康服務機構及其工作夥伴意識到，更談不上獲得廣泛支援。本綜述提供了日常麻醉醫生所制定使用的控制系統的介紹。我們介紹了重要的概念比如回饋和解決問題的特定數學模型，並展望了確保安全性和可行性的回饋控制系統的設計需要。我們的討論聚焦於麻醉藥物使用的優化。

（李春譯 薛張綱校）

Feedback control is ubiquitous in nature and engineering and has revolutionized safety in fields from space travel to the automobile. In anesthesia, automated feedback control holds the promise of limiting the effects on performance of individual patient variability, optimizing the workload of the anesthesiologist, increasing the time spent in a more desirable clinical state, and ultimately

improving the safety and quality of anesthesia care. The benefits of control systems will not be realized without widespread support from the health care team in close collaboration with industrial partners. In this review, we provide an introduction to the established field of control systems research for the everyday anesthesiologist. We introduce important concepts such as feedback and modeling specific to control problems and provide insight into design requirements for guaranteeing the safety and performance of feedback control systems. We focus our discussion on the optimization of anesthetic drug administration.

預防氣道著火：不要忽視呼出的氧氣濃度

Prevention of airway fires: do not overlook the expired oxygen concentration.

Remz M, Luria I, Gravenstein M, Rice SD, Morey TE, Gravenstein N, Rice MJ.

From the Department of Anesthesiology, University of Florida College of Medicine, Gainesville, Florida.

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背景：一般認爲，當使用明火源時，呼吸通道中的吸氧濃度（FIO2）應低於 30%，從而幫助防止氣道著火。關於將呼吸回路中的吸氧濃度降低到 30%以下所需的時間和條件，尚未有系統的研究。

方法：我們評估了 Aestiva Avance S/5 麻醉機在（減少 FIO2 濃度到 21%後）初始 FIO2 濃度爲 100%和 60%，吸入和呼出通道到達濃度小於 30%氧濃度回應時間。我們將該通道連接至一個病患模擬器上，該模擬器的功能殘氣量爲 2 升，肺總容量爲 2.8 升，耗氧量爲 200 毫升/分鐘，呼吸商爲 0.8。我們選用 2 升/分鐘和 5 升/分鐘的新鮮氣體流量（FGF），來表現臨床上一系列典型的新鮮氣體流量（FGF）值。每分通氣量設定爲 4L/分鐘。確定呼吸通道中達到 O2 濃度<30%所需的中位時間，是本研究的首要目標。

結果：在擴展的通道結構中， 5L FGF 初始爲 60%時， 吸入和呼出的氧氣濃度<30%所需的中位時間（1%-99%的置信區間）分別爲 35 （32-36）以及 104（88-122）秒。用 2L 的 FGF，中位時間各自提高至 303（291-313）和 255（232-278）秒。試驗中注意到，縮短的通道結構（P=0.006）和更高的 FGF 流速（P<0.0001）則是縮短達到氧濃度爲<30%的中位時間的因素。

結論：吸入和呼出通道的氧氣濃度可能都需要幾分鐘減少到<30%，這取決於呼吸回路的長度、FGF 流速和呼吸回路中的初始氧氣濃度。在 FIO2 減少的時候，FIO2 處於“安全”範圍之後有一段相當長的時間，呼出氧氣濃度可能大於 30%。呼出氧氣濃度的增加也應視作氣道著火的風險增加的因素，而且患者的護理記錄或許需要根據進一步的修訂。

（劉毅譯 薛張綱校）

BACKGROUND: It is generally accepted that when an ignition source is used the inspired oxygen concentration (FIO2) should be <30% in the breathing circuit to help prevent airway fires. The time and conditions required to reduce a high O2% in the breathing circuit to <30% has not yet been systematically studied.

METHODS: We evaluated the inspired and expired circuit oxygen concentration response times of an Aestiva Avance S/5 anesthesia machine to reach an FIO2 of <30% from a starting FIO2 of 100% and 60% after reducing the FIO2 to 21%. The circuit was connected to a human patient simulator which has a functional residual capacity of 2 L, total lung capacity of 2.8 L, an oxygen consumption of 200 mL/min, and respiratory quotient of 0.8. Fresh gas flow (FGF) inputs of 2 L/min and 5 L/min were chosen to represent a spectrum of typical clinical FGF rates. Minute ventilation was set at 4 L/min. Determining the requisite median time to reach an O2 concentration of <30% in the breathing circuit was the primary aim of the study.

RESULTS: The median times (1st-99th percent confidence interval) required to achieve inspiratory and expiratory oxygen concentrations of <30% with the extended circuit configuration when starting at 60% for 5 L FGFs were 35 (32-36) and 104 (88-122) seconds, respectively. With 2 L FGF, these median times increased to 303 (291-313) and 255 (232-278) seconds, respectively. A shortened circuit configuration (P = 0.006) and higher FGF flow rate (P < 0.0001) were noted to be factors decreasing the median time required to achieve an oxygen concentration of <30%.

CONCLUSIONS: Both inspired and expired circuit oxygen concentration may take minutes to decrease to <30% depending on circuit length, FGF rate, and starting circuit oxygen concentration. During the reduction in FIO2, the expiratory oxygen concentration may be >30% for a considerable time after the FIO2 is in a "safe" range. An increased expired oxygen concentration should also be considered an airway fire risk, and patient care protocols may need to be modified based on future studies.

鐮狀細胞貧血患兒行外科手術的類型及預後

Surgical Procedures and Outcomes Among Children with Sickle Cell Disease

Hyder O, Yaster M, Bateman BT, Firth PG.

From the Departments of *Surgery and †Anesthesiology and Critical Care Medicine, Johns Hopkins School of Medicine, Baltimore, MD; ‡Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital; and §Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, Boston, MA.

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背景：雖然鐮狀細胞貧血的兒童經常接受手術，關於這類患者的流行病學資料很有限的。我們對一個資料庫進行分析，用來評估這類人群的特徵，外科手術及圍手術期的結局。

方法：我們查詢國家住院病人樣本資料庫，這個資料庫收集了 2000 至 2010 年的診斷爲鐮狀細胞貧血病的 18 歲以下患者，並且接受了一次以上的外科手術。我們使用臨床分類軟體程式碼和 ICD-9-CM 的程式碼概括手術方式。我們描述了做常見的 6 類手術患兒的特徵。

結果：2000 年至 2010 年期間，3.6%（SE0.12）該病患兒進行手術。最常見的手術爲膽囊切除術（1.47%[0.08]），扁桃體/腺樣體切除術（0.81%[0.06]），脾切除術（0.62%[0.06]），疝修補術（0.19%[0.02]），和闌尾手術（ 0.17%[0.02]）。擇期手術患者急性肺部併發症發生率是 3.08%（0.60）。中風的發病率是 0.20%（0.11），死亡病例<11 例（<0.20%）。

結論：鐮狀細胞貧血患兒行諸如膽囊切除術、扁桃體切除術、脾切除術、疝修補術或闌尾手術總數不多，但所占比例不低。急性肺部併發症是擇期手術中最常見的併發症，而中風和死亡是罕見的。

（徐升譯 薛張綱校）

BACKGROUND: Although children with sickle cell disease often undergo surgery, there are limited current epidemiological data for this pediatric population. We performed a database analysis to estimate population characteristics, surgical procedures, and perioperative outcomes in this population.

METHODS: We queried the Nationwide Inpatient Sample Database from 2000 to 2010 for discharges pertaining to patients <18 years of age having a diagnosis of sickle cell disease who underwent 1 or more surgical procedures during that admission. We abstracted surgical

procedures using the Clinical Classifications Software procedure codes and the ICD-9-CM procedure codes. We described characteristics of patients undergoing the 6 most common procedures.

RESULTS: During 2000 to 2010, 3.6 % (SE 0.12) of individual hospital discharges were of children with sickle cell disease who had undergone surgical procedures. The most frequent surgical procedures were cholecystectomy (1.47% [0.08]), tonsillectomy/adenoidectomy (0.81% [0.06]), splenectomy (0.62% [0.06]), repair of umbilical hernia (0.19% [0.02]), and appendectomy (0.17% [0.02]). Acute chest syndrome was recorded among 3.08% (0.60) of patients undergoing elective surgery. The incidence of stroke was 0.20% (0.11); death was reported in <11 patients (<0.20%).

CONCLUSION: Surgical procedures such as cholecystectomy, tonsillectomy, splenectomy, hernia repair, and appendectomy account for a small but significant proportion of hospital admissions in children with sickle cell disease. Acute chest syndrome is among the most common complications of elective surgery, while stroke and death are rare.

關於波士頓麻塞諸塞州總醫院的莫爾頓醚吸入器的研究

Researches regarding the morton ether inhaler at massachusetts general hospital, Boston.

Haridas RP, Mifflin JA.

From the *Archives and Special Collections Program, Massachusetts General Hospital, Boston, Massachusetts.

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波士頓的麻塞諸塞州總醫院擁有莫爾頓醚吸入器的歷史可以最早的照片發表追溯到 1906 年。作者認爲吸入器是由威廉.莫爾頓，醫學博士在 1847 年 1 月贈與麥森.沃倫，醫學博士的。吸入器是由沃倫解剖學博物館在一個未知的日期獲得，在 1946 年 10 月租借給麻塞諸塞州總醫院，並在 1948 年 4 月長期租借給麻塞諸塞州總醫院。關於吸入器的許多檔都消失了，能確定的只有在 2009，吸入器可能屬於 J. 麥森.沃倫，醫學博士，但這個吸入器並不認爲是 1846 年 10 月 16 日在麻塞諸塞州總醫院的那個。它是已知的唯一的擁有閥門的莫爾頓醚吸入器（不包括複製品及再生產的吸入器）和類似的設計，於 1846 年 10 月 16 日被莫爾頓使用的吸入器。

（徐崢譯 薛張綱校）

The Morton ether inhaler in the possession of Massachusetts General Hospital, Boston, MA, was traced back to 1906 when the earliest known photograph of it was published. The authors believe that the inhaler was given by William T. G. Morton, MD, to J. Mason Warren, MD, in January 1847. The inhaler was acquired by the Warren Anatomical Museum at an unknown date, loaned to Massachusetts General Hospital in October 1946, and placed on permanent loan to Massachusetts General Hospital in April 1948. Many documents relating to the inhaler have disappeared, and it was only identified in 2009 as the inhaler that probably belonged to J. Mason Warren, MD. The inhaler is not believed to be the one that Morton used on October 16, 1846, at Massachusetts General Hospital. It is the only known example of a Morton ether inhaler with valves (excluding replicas or reproduction inhalers) and is probably of similar design to the inhaler that Morton used on October 16, 1846.

外周神經阻滯單次注射脂質體布比卡的劑量反應研究

Liposomal Bupivacaine as a Single-Injection Peripheral Nerve Block: A Dose-Response Study

Ilfeld BM, Malhotra N, Furnish TJ, Donohue MC, Madison SJ.

From the Department of Anesthesiology, University of California San Diego, San Diego, California.

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背景：使用目前常用的局部麻醉藥物實施單次注射外周神經阻滯後，其最長阻滯持續時間不超過 24 小時。最近，FDA 批准了一種脂質體布比卡因製劑（EXPAREL®，Pacira 製藥公司，聖達戈，加利福尼亞州），該劑型可在至少 96 小時內緩慢釋放布比卡因，但目前 FDA 批准其僅限於外傷後浸潤麻醉使用，而尚未批准其可應用于外周神經阻滯。

方法：對受試的健康志願者（n=14）採用單次注射進行雙側股神經阻滯。阻滯所使用的藥液爲脂質體布比卡因 0-80mg 溶於生理鹽水中，並配製成總容量 30ml 的研究液。採用隨機雙盲的方法對每位受試者進行神經阻滯，於雙側股神經分別給予兩種不同劑量的研究液。研究觀察終點包括股四頭肌的最大自主等長收縮（MVIC）及股神經支配區域皮膚的電流刺激耐受性。測量記錄基礎資料，並收集資料直至雙側股四頭肌 MVIC 恢復至基線水準的 80%。

結果：MVIC 及皮膚電流耐受性雖具有顯著的劑量相關性，但卻與預期結果相反：劑量越大所觀察到的阻滯效果越弱（統計學結果分別爲 MVIC 0.09%/mg, 標準誤=0.03, 95%可信區間 0.04–0.14, P = 0.002；皮膚電流耐受性 -0.03 mA/mg, 標準誤=0.01, 95%可信區間 -0.04 to -0.02, P < 0.001）。得出這一反比關係的結論在生物學上難以解釋，很有可能是由於樣本量太小和測量儀器的主觀性質所致。儘管用藥後 75%的受試者（95%可信區間 43%-93%）在 24 小時內達到阻滯峰效應，但阻滯持續時間通常更長：布比卡因劑量>40mg 組 100%的病例（95%可信區間 56%-100%）在阻滯後 24 小時內皮膚電流耐受性未恢復至基線的 20%以上；與此一致的是，90%的病例（95%可信區間 54%-100%）在阻滯後 24 小時內 MVIC 未恢復至基線的 20%。運動阻滯持續時間與布比卡因劑量沒有相關性（0.06 小時/mg, 標準誤=0.14, 95%可信區間 -0.27-0.39, P = 0.707）。

結論：本研究結果提示，在股神經周圍應用脂質體布比卡因製劑後，以本研究中所應用最大劑量可產生 24 小時以上的部分感覺和運動神經阻滯效應。然而不同個體間阻滯程度的巨大差異及所得的劑量效應反比關係進一步說明需要具有更大樣本容量的 III 期臨床試驗，也說明本研究應被視作啓示性的研究，並需要進一步的研究工作來驗證。

(朱怡琦譯 薛張綱校)

BACKGROUND: Currently available local anesthetics approved for single-injection peripheral nerve blocks have a maximum duration of <24 hours. A liposomal bupivacaine formulation (EXPAREL® , Pacira Pharmaceuticals, Inc., San Diego, CA), releasing bupivacaine over 96 hours, recently gained Food and Drug Administration approval exclusively for wound infiltration but not peripheral nerve blocks.

METHODS: Bilateral single-injection femoral nerve blocks were administered in healthy volunteers (n = 14). For each block, liposomal bupivacaine (0–80 mg) was mixed with normal saline to produce 30 mL of study fluid. Each subject received 2 different doses, 1 on each side, applied randomly in a double-masked fashion. The end points included the maximum voluntary isometric contraction (MVIC) of the quadriceps femoris muscle and tolerance to cutaneous electrical current in the femoral nerve distribution. Measurements were performed from baseline until quadriceps MVIC returned to 80% of baseline bilaterally.

RESULTS: There were statistically significant dose responses in MVIC (0.09%/mg, SE = 0.03, 95% confidence interval [CI], 0.04–0.14, P = 0.002) and tolerance to cutaneous current (-0.03 mA/mg, SE = 0.01, 95% CI, -0.04 to -0.02, P < 0.001), however, in the opposite direction than expected (the higher the dose, the lower the observed effect). This inverse relationship is biologically implausible and most likely due to the limited sample size and the subjective nature of the measurement instruments. While peak effects occurred within 24 hours after block

administration in 75% of cases (95% CI, 43%–93%), block duration usually lasted much longer: for bupivacaine doses >40 mg, tolerance to cutaneous current did not return to within 20% above baseline until after 24 hours in 100% of subjects (95% CI, 56%–100%). MVIC did not consistently return to within 20% of baseline until after 24 hours in 90% of subjects (95% CI, 54%–100%). Motor block duration was not correlated with bupivacaine dose (0.06 hour/mg, SE = 0.14, 95% CI, -0.27 to 0.39, P = 0.707).

CONCLUSIONS: The results of this investigation suggest that deposition of a liposomal bupivacaine formulation adjacent to the femoral nerve results in a partial sensory and motor block of >24 hours for the highest doses examined. However, the high variability of block magnitude among subjects and inverse relationship of dose and response magnitude attests to the need for a phase 3 study with a far larger sample size, and that these results should be viewed as suggestive, requiring confirmation in a future trial.

瑞芬太尼對豚鼠心臟竇房結的起搏點活動具有輕微的直接作用

Remifentanil Has a Minimal Direct Effect on Sinoatrial Node Pacemaker Activity in the Guinea Pig Heart

Kojima, Akiko MD, PhD*; Ito, Yuki MD*; Kitagawa, Hirotoshi MD, PhD*; Matsuura, Hiroshi MD, PhD†; Nosaka, Shuichi MD, PhD*

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背景：雖然瑞芬太尼引起嚴重心動過緩，但是其負性變時作用是由對心臟竇房結起搏點活動的直接作用導致還是由增加迷走神經活動的間接作用導致，目前尚無定論。

方法：本研究採用兩性黴素 B 多孔細胞膜片鉗技術，在 5、10、100 和 1000 nM 的濃度驗證瑞芬太尼和芬太尼對豚鼠竇房結細胞自發性動作電位的影響。離體豚鼠心臟分別以 5、10、100 和 1000 nM 濃度的瑞芬太尼進行離體心臟灌流。

結果：在對照情況下，竇房結動作電位的自主發放頻率和舒張期去極化速度（DDR）分別爲 189.1 ± 14.8 /min 和 74.1 ± 2.9 mV/s (n = 8)，且不受濃度爲 5 nM（自主發放頻率和 DDR 均 P = 1.0; n = 6）、10 nM (自主發放頻率 P = 0.62，DDR P = 0.99; n = 6)或 100 nM (自主發放頻率 P = 0.23，DDR P = 0.38; n = 6)瑞芬太尼的顯著影響。然而，濃度爲 1000 nM 的瑞芬太尼輕度但顯著降低了自主發放頻率(P = 0.0087)和 DDR (P = 0.0072, n = 6)。瑞芬太尼在濃度爲 5 nM (P = 0.98)、10 nM (P = 0.35),或 100 nM (P = 0.24)時對離體灌流的豚鼠心臟的心率無影響，但在 1000 nM 時顯著降低心率(P < 0.0001)。芬太尼在濃度爲 5 nM (自主發放頻率和 DDRP = 1.0)和 10 nM (自主發放頻率 P = 0.62，DDR P = 0.79)對自主發放頻率和 DDR 無影響，但在 100 nM (自主發放頻率 P = 0.00038，DDR P = 0.0080)和 1000 nM (自主發放頻率和 DDR P 都< 0.0001)時顯著降低自主發放頻率和 DDR。

結論：臨床相關濃度的瑞芬太尼（nM 級濃度）對內在的心臟自主節律性無顯著的直接影響。因此，研究提示臨床上由瑞芬太尼引起的心動過緩不依賴於直接的心臟作用。

（陳彬彬 譯， 馬皓琳、李士通 審校）

BACKGROUND: Whereas remifentanil administration is associated with severe bradycardia, it has yet to be fully investigated whether the negative chronotropic action of remifentanil is mediated by its direct action on sinoatrial (SA) node pacemaker activity in the heart versus indirect results of enhanced vagal activity.

METHODS: We examined the effects of remifentanil and fentanyl on the spontaneous action potentials of guinea pig SA node cells at concentrations of 5, 10, 100, and 1000 nM using the amphotericin B-perforated whole-cell patch-clamp technique. Isolated guinea pig hearts were perfused in a Langendorff mode with 5, 10, 100, and 1000 nM remifentanil.

RESULTS: The spontaneous firing rate and diastolic depolarization rate (DDR) of the SA node action potentials were 189.1 ± 14.8 /min and 74.1 ± 2.9 mV/s (n = 8), respectively, under control conditions, and were not significantly affected by exposure to 5 nM (P = 1.0 for both spontaneous firing rate and DDR; n = 6), 10 nM (P = 0.62 for spontaneous firing rate, P = 0.99 for DDR; n = 6), or 100 nM (P = 0.23 for spontaneous firing rate, P = 0.38 for DDR; n = 6) remifentanil. However, 1000 nM remifentanil modestly but significantly decreased the spontaneous firing rate (P = 0.0087) and DDR (P = 0.0072, n = 6). Remifentanil did not affect the heart rate of isolated Langendorff-perfused guinea pig hearts at concentrations of 5 nM (P = 0.98), 10 nM (P = 0.35), or 100 nM (P = 0.24) but significantly reduced the heart rate at 1000 nM (P < 0.0001). Fentanyl did not affect the spontaneous firing rate and DDR at concentrations of 5 nM (P = 1.0 for both spontaneous firing rate and DDR) and 10 nM (P = 0.62 for spontaneous firing rate, P = 0.79 for DDR), but it significantly reduced both at 100 nM (P = 0.00038 for spontaneous firing rate, P = 0.0080 for DDR) and 1000 nM (P < 0.0001 for both spontaneous firing rate and DDR).

CONCLUSIONS: Clinically relevant concentrations (nanomolar order concentrations) of remifentanil do not produce significant direct effects on intrinsic cardiac automaticity; thus, suggesting that remifentanil-induced bradycardia in the clinical setting is independent of its direct cardiac effects.

用於“脂肪復蘇”的脂肪乳劑對開放及布比卡因引發的心臟鈉通道 Nav1.5 抑制的特殊功效

The Distinct Effects of Lipid Emulsions Used for “Lipid Resuscitation” on Gating and Bupivacaine-Induced Inhibition of the Cardiac Sodium Channel Nav1.5

Nadrowitz, Felix*; Stoetzer, Carsten MD*; Foadi, Nilufar MD*; Ahrens, Jörg MD*; Wegner, Florian MD†; Lampert, Angelika MD‡; Koppert, Wolfgang MD*; de la Roche, Jeanne PhD*; Leffler, Andreas MD*

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背景：脂肪乳劑的全身應用是已經確定了的用於局部麻醉藥中毒的治療方法。然而，它發揮這項作用的具體機制尚未清楚。親脂性局部麻醉藥布比卡因的高心臟毒性可能是由於其對心臟 Na+通道 Nav1.5 的長時間抑制造成的。在此項研究中，我們探究脂肪乳劑是否功能性地影響 Nav1.5 或者抵消布比卡因對其的抑制作用。

方法：用全細胞膜片鉗的方法研究人胚胎腎細胞表達的人類 Nav1.5。研究英脫利匹特® 和力保肪寧® 對功能性特性及對布比卡因誘導引發的通道抑制作用的影響。

結果：英脫利匹特和力保肪寧並不影響通道電壓依賴的啓動作用，但可以誘導產生穩定快速失活的小的超極化轉化，並破壞通道從快速失活的狀態恢復。 力保肪寧，誘導產生濃度依賴性的而非電壓依賴性的增強阻滯（42%±4%，3%力保肪甯），英脫利匹特不具有此特點。當同時使用脂質時，布比卡因發揮增強阻滯作用的半數最大抑制濃度（IC50）值（50 ± 4 μM）顯著增高（5%英脫利匹脫：196±22 μM 和 5%力保肪寧：103 ± 8 μM）。在 10Hz 時，布比卡因的使用依賴性阻滯作用也可以被這兩個脂肪乳劑所減輕。此外，在脂質存在的情況下，離子通道從布比卡因誘導阻滯失活狀態中恢復的速度加快。

結論：我們的資料證明了脂肪乳劑可以減少而不是增加 Nav1.5 的可利用率。然而，不論是英脫利匹特還是力保肪寧都只能部分緩解布比卡因對 Nav1.5 的阻滯作用。這些作用的產生不但涉及到脂質對 Nav1.5 的直接作用，還可能涉及到脂肪乳劑對布比卡因的吸收，進而減少布比卡因的濃度效應。

（董靜 譯 馬皓琳 李士通 校）

BACKGROUND: Systemic administration of lipid emulsions is an established treatment for local anesthetic intoxication. However, it is unclear by which mechanisms lipids achieve this function. The high cardiac toxicity of the lipophilic local anesthetic bupivacaine probably results from a long-lasting inhibition of the cardiac Na+ channel Nav1.5. In this study, we sought to determine whether lipid emulsions functionally interact with Nav1.5 or counteract inhibition by bupivacaine.

METHODS: Human embryonic kidney cells expressing human Nav1.5 were investigated by whole-cell patch clamp. The effects of Intralipid® and Lipofundin® were explored on functional properties and on bupivacaine-induced inhibition.

RESULTS: Intralipid and Lipofundin did not affect the voltage dependency of activation, but induced a small hyperpolarizing shift of the steady-state fast inactivation and impaired the recovery from fast inactivation. Lipofundin, but not Intralipid, induced a concentration-dependent but voltage-independent tonic block (42% ± 4% by 3% Lipofundin). The half-maximal inhibitory concentration (IC50) values for tonic block by bupivacaine (50 ± 4 μM) were significantly increased when lipids were coapplied (5% Intralipid: 196 ± 22 μM and 5% Lipofundin: 103 ± 8 μM). Use-dependent block by bupivacaine at 10 Hz was also reduced by both lipid emulsions. Moreover, the recovery of inactivated channels from bupivacaine-induced block was faster in the presence of lipids.

CONCLUSIONS: Our data indicate that lipid emulsions reduce rather than increase availability of Nav1.5. However, both Intralipid and Lipofundin partly relieve Nav1.5 from block by bupivacaine. These effects are likely to involve not only a direct interaction of lipids with Nav1.5 but also the ability of lipid emulsions to absorb bupivacaine and thus reduce its effective concentration.

類比研究顯示自動、即時新鮮氣體流量指導改變麻醉維持階段的異氟醚消耗

Automated, Real-Time Fresh Gas Flow Recommendations Alter Isoflurane Consumption During the Maintenance Phase of Anesthesia in a Simulator-Based Study

Luria, Isaac MS*; Lampotang, Samsun PhD*; Schwab, Wilhelm PhD†‡; Cooper, Lou Ann PhD§; Lizdas, David BSME*; Gravenstein, Nikolaus MD*

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背景：低流量嚮導(LFW)在吸入全麻期間爲使用者提供最佳新鮮氣體流量(FGF)設置的即時指導。LFW 可以持續告知使用者它測得的他們的 FGF 是否太小、剛好或太大，並且它對使用者執行 FGF 的變化以彩色標記指導意見即時回饋。我們的研究目的是判斷在不影響患者監護的前提下，LFW 作爲 Dräger Apollo 工作站的一項裝置是否會改變 FGF 的選擇並因此影響吸入麻醉藥的消耗。

方法：爲了減少可能的混雜變數，我們使用了一種可以消耗並呼出揮發性麻醉藥的病人模擬器。麻醉初始階段對患者實施標準監護，麻醉誘導後增加有創動脈血壓監測。在此項組內研究中，入組的 17 位參與者均由自己完成操作。每位參與者被要求使用一台 Dräger Apollo 工作站對同一位模擬患者實施兩次麻醉，第一次不使用 LFW 性能，第二次使用 LFW 性能。揮發性麻醉藥使用異氟醚。兩次模擬過程的麻醉不同階段，如誘導、切皮和維持均被設置爲相似的時間。未模擬急診手術麻醉。在每次類比過程前後使用電子稱對異氟醚揮發罐稱重來計算揮發性麻醉藥的總消耗量。另一方面，用 FGF（由 Apollo 顯示）與異氟醚容積濃度（由用於 Apollo 的 FGF 軟管上的多氣體分析儀取樣）的乘積結合時間行積分運算來獲得異氟醚的消耗率（使用中麻醉藥消耗率測量法）。

結果：行 LFW 顯示的麻醉維持階段異氟醚消耗率和 FGF 較未使用 LFW 顯示時明顯降低 (P = 0.005)。FGF 平均降低 53.6% (95% 可信區間, 39.2%–67.9%)。肺泡中異氟醚濃度無明顯差異(差異<0.1%的 P = 0.13)。計算法與稱重法測得異氟醚消耗量相當。

結論：我們在一個模擬的全麻藥中的資料顯示使用由 LFW 指導的 FGF 顯示平均可以降低 53.2%的揮發性麻醉藥消耗率。由於中位數的 95%可信區間下限是 39.4%，這項發現或許可以轉換爲費用的節約和臨床裝置中產生的和排放到大氣中的麻醉廢氣降低。

（張怡 譯 馬皓琳 李士通 校）

BACKGROUND: The Low Flow Wizard (LFW) provides real-time guidance for user optimization of fresh gas flow (FGF) settings during general inhaled anesthesia. The LFW can continuously inform users whether it determines their FGF to be too little, efficient, or too much, and its color-coded recommendations respond in real time to changes in FGF performed by users. Our study objective was to determine whether the LFW feature, as implemented in the Dräger Apollo workstation, alters FGF selection and thereby volatile anesthetic consumption without affecting patient care.

METHODS: To reduce potentially confounding variables, we used a human patient simulator that consumes and exhales volatile anesthetics. Standard monitoring was provided for the patient initially with invasive arterial blood pressure added after anesthetic induction. In this within-group study, each of 17 participants acted as his or her own control. Each participant was asked to anesthetize an identical simulated patient twice using a Dräger Apollo workstation, first with the LFW feature disabled and subsequently enabled. The volatile anesthetic was isoflurane. Both simulation runs were set up to have similar time durations for the different phases of anesthesia: induction, incision, and maintenance. Emergence was not simulated. The isoflurane vaporizer was weighed before and after each simulation run on a digital scale to verify total computed volatile liquid anesthetic consumption. In addition, the product of FGF (reported by the Apollo) times the isoflurane volumetric concentration (sampled by a multigas analyzer at the equivalent of the FGF hose for the Apollo) was integrated over time to obtain isoflurane consumption rate (on-the-fly anesthetic consumption rate measurement).

RESULTS: The maintenance isoflurane consumption rate and FGF were significantly lower with the LFW display enabled than without (P = 0.005). The mean reduction in FGF was 53.6% (95% confidence interval, 39.2%–67.9%). There was no significant difference in alveolar isoflurane concentration (P = 0.13 for differences <0.1%). The isoflurane consumption measurement closely matched the consumption measured via the digital scale.

CONCLUSIONS: Our data in a simulated anesthetic suggest that enabling the display of FGF efficiency data by the LFW results in a median percent reduction in volatile liquid anesthetic consumption rate of 53.2%. Since the lower limit of the 95% confidence interval for the median is 39.4%, this finding is likely to translate into cost savings and less waste anesthetic gas generated in the clinical setting and released into the atmosphere.

認知助手在麻醉緊急事件中的應用--文獻回顧

The Use of Cognitive Aids During Emergencies in Anesthesia: A Review of the Literature

Marshall, Stuart MB, ChB, MHumanFact

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認知助手是設計用來幫助使用者完成一項或一系列任務的提示。它呈現的方式可以是海報、流程圖、清單或者甚至是記憶法。既往已有研究顯示，使用認知助手可改善在麻醉緊急事件中的表現和病人的預後，然而仍缺乏一系統的證據評估。本文獻綜述的目的在於明確以下幾個問題：（1）認識助手是否可以改善個人及團隊的表現；（2）是否可提出對未來的認知助手的設計、測試及實現的建議。本文使用廣泛標準搜索醫學、護理及心理學的相關資料庫來尋找關於麻醉緊急情況下使用認知助手的已報導文獻。亦對選用於綜述的文獻的參考文獻進行篩選來明確額外的研究。對選取的描述用於麻醉緊急情況下的認識助手的評價的文獻進行綜述，以確定如何派生助手的內容、如何評價設計及助手在改善技術和

團隊表現的成功率。這樣的檢索發現了已在 23 個研究中被評估的開發來在麻醉緊急事件中支援臨床醫生的 22 個認知助手。用模擬的 10 個研究表明，在一些麻醉緊急事件，例如惡性高熱、心肺復蘇及氣道管理中，使用認知助手可提高技術表現。然而在基於模擬的評估的 3 個研究中，參與者在診斷和處理中沒有提高表現或者花費更長時間，甚至做出錯誤診斷。4 個研究調查了助手對於團隊的影響，得出了不同的結論。1 個研究表明助手可提高參與者的合作模式，另 1 個則發現助手可提高其決策得分，但另外兩個則提示沒有提高，甚至提供了在類比情況下使用認知助手會降低團隊交流水準的證據。認知助手的設計很少被考慮到。教育可彌補設計不好的助手，但只在助手可提供較少甚至無指導的情況下使正確行爲根深蒂固。認知助手應該在有指南存在的領域根據已建立的臨床指南持續發展。它們也將在使用前從更多的基於模擬的廣泛使用測試中獲益。需要進一步的證據來探討在麻醉緊急狀態下使用認知助手的影響、它們如何影響團隊功能及它們的設計考慮。

（王贇譯 馬皓琳 李士通校）

Cognitive aids are prompts designed to help users complete a task or series of tasks. They may take the form of posters, flowcharts, checklists, or even mnemonics. It has been suggested that the use of cognitive aids improves performance and patient outcomes during anesthetic emergencies; however, a systematic assessment of the evidence is lacking. The aim of this literature review was to determine (1) whether cognitive aids improve performance of individuals and teams and (2) whether recommendations can be made for future cognitive aid design, testing, and implementation. Medical, nursing, and psychology databases were searched using broad criteria to find cognitive aids that have been reported in the literature for use in anesthetic emergencies. The reference lists of the articles selected for review were also screened to identify additional studies. Selected articles that described the evaluation of cognitive aids used in anesthetic emergencies were reviewed to determine how the content of the aid was derived, how the design was evaluated, and the success of the aid in improving technical and team performance. The search yielded 22 cognitive aids developed to support clinicians during anesthetic emergencies that had been evaluated in 23 studies. Ten studies using simulation suggested that technical performance improves with the use of cognitive aids in some anesthetic emergencies such as malignant hyperthermia, cardiopulmonary resuscitation, and airway management. However, in 3 of the simulator-based evaluations, participants had either no improvement or took longer to diagnose and treat and made more incorrect diagnoses. Four studies investigated the effect of the aids on teamwork with differing conclusions. One study suggested improved participants' coordination patterns and one found aids improved their decision-making scores, but 2 other studies indicated that there was no improvement and even provided evidence of reduced levels of team communication when teams used a cognitive aid in simulated conditions. The designs of cognitive aids were rarely considered. Education may compensate for a poorly designed aid, but only by ingraining correct actions for situations in which the aid provides little or no guidance. Cognitive aids should continue to be developed from established clinical guidelines where guidelines exist. They would also benefit from more extensive simulation-based usability testing before use. Further evidence is required to explore the effects of cognitive aids in anesthetic emergencies, how they affect team function, and their design considerations.

使用混合手術組套進行剖腹產：對於高風險產科手術的一項新的前景很好的應用

Cesarean Delivery in the Hybrid Operating Suite: A Promising New Location for High-Risk Obstetric Procedures

Clark, Allison MD; Farber, Michaela K. MD; Sviggum, Hans MD; Camann, William MD

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背景：日益增長的剖腹產率和伴隨的胎盤植入異常，加上產科人群全身的醫療複雜性，已經驅動改革來使分娩過程中的高風險產婦的護理更優化。法律和多學科的應用和定位可能增強了選擇的可能性。

方法：我們回顧了從 2007 年 12 月到 2013 年 3 月期間在應用混合手術組套進行剖腹產且描述爲高風險剖腹產的所有 11 個病人的記錄。

結果：使用混合手術組套最常見的指征是出血風險的增加，最常歸因於異常的胎盤植入。其他的指征包括心血管疾病和顱內病變。

結論：這種混合手術組套可以是剖腹產術的一個位置選擇，我們的經驗表明這種環境可以爲有合併症的病人提供優勢。

（王曉莉 譯 馬皓琳 李士通 校）

BACKGROUND: The increasing cesarean delivery rate and attendant placental implantation abnormalities, coupled with increasing general medical complexity in the obstetric population, has driven innovation to optimize the care of high-risk parturients during delivery. Novel and multidisciplinary approaches and locations may enhance the options available for care.

METHODS: We reviewed the records of all 11 patients who underwent cesarean delivery in our hybrid operating suite between December 2007 and March 2013 and describe the high-risk cesarean deliveries.

RESULTS: The most common indication for the use of the hybrid operating suite was an increased risk of hemorrhage, most commonly due to abnormal placental implantation. Other indications included cardiovascular disease and intracranial pathology.

CONCLUSION: The hybrid operating suite may be an alternative location for obstetric delivery, and our experience suggests that this environment may prove advantageous for patients with a variety of comorbid conditions.

有助於顱內動脈瘤夾閉結紮的腺苷誘導的止流並不會使神經系統預後惡化

Adenosine-Induced Flow Arrest to Facilitate Intracranial Aneurysm Clip Ligation Does Not Worsen Neurologic Outcome

Bebawy, John F. MD; Zeeni, Carine MD; Sharma, Sonal MBBS, MD; Kim, Edina S. MD; DeWood, Mark S. BS; Hemmer, Laura B. MD; Ramaiah, Vijay K. MBBS, MD; Bendok, Bernard R. MD; Koht, Antoun MD; Gupta, Dhanesh K. MD

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背景：當究其解剖原因暫時性阻塞上一級動脈有難度時，或者在術中解剖時發生不慎血管瘤破裂時，給予腺苷可用來產生止流和短暫的、有深度的全身低血壓，這樣有助於顱內動脈瘤夾閉結紮。但是我們關注的是，相較於其他的技術來幫助動脈瘤的夾閉結紮。但是值得關注的是，與便於動脈瘤夾閉結紮的其他方法相比較，由腺苷產生的止流和深度低血壓，即使很短暫，也可能會引起腦缺血並因此而惡化神經系統預後。因此，我們進行了一個回顧性的病例對照研究來確定腺苷誘導的止流對於我們的患者神經系統的預後是否有不良效應。

方法：我們回顧了自 2006-08-01 至 2012-07-15 期間所有行顱內動脈瘤手術的患者預後資料的圍術期記錄。主要的觀察指標爲是否存在術後 48 小時的神經系統預後欠佳。改良 Rankin 量表得分大於 2 分即可被定義爲神經系統預後欠佳。在出院時的神經系統預後是一項次要指標。與心臟疾病有關的次要指標包括需要處理的房性或室性心律失常和符合缺血的心臟生物標記物升高。

結果：在研究期間，在行顱內動脈瘤夾閉結紮術的 413 名患者當中的 27 名（17.4%）使用了腺苷誘導的止流。腺苷誘導組和非腺苷誘導組的神經系統預後欠佳的發生率的差異，在術後 48 小時時不大於 15.7%（P=0.524），在出院時爲不大於-12.7%(P=0.741)。另外，在術後 48 小時內心臟疾病的發生率的差別是頑固性心律失常不大於-16.0%（P=0.155），心肌缺血的生物標記物爲不大於-9.4%（P=0.898）.

結論：當用來便於顱內動脈瘤夾閉結紮時，腺苷誘導的止流使神經系統預後欠佳的發病率在術後 48 小時時增加不超過 15.7%，在出院的時候減少不超過 12.7%。此外，腺苷使用和圍術期心臟發病率（即，持久的心律失常或心肌缺血的生物標記物）沒有相關性。

（趙曉 譯 馬皓琳 李士通 校）

BACKGROUND: When temporary arterial occlusion of the parent artery is difficult for anatomical reasons, or when inadvertent aneurysmal rupture occurs during surgical dissection, adenosine administration can be used to produce flow arrest and brief, profound systemic hypotension that can facilitate intracranial aneurysm clip ligation. There is a concern, however, that the flow arrest and profound hypotension produced by adenosine, although brief, may cause cerebral ischemia and therefore worsen neurologic outcome compared with other techniques to facilitate aneurysm clip ligation. Therefore, we performed a retrospective, case-control study to determine whether adenosine-induced flow arrest had negative effects on the neurologic outcome of our patients.

METHODS: We reviewed the perioperative records of all patients in our intracranial aneurysm surgery outcomes database between August 1, 2006, and June 15, 2012. The primary outcome was the presence or absence of a poor neurologic outcome 48 hours after surgery, with a modified Rankin scale score >2 being defined as a poor neurologic outcome. The neurologic outcome at the time of hospital discharge was a secondary outcome. Secondary outcomes related to cardiac morbidity included atrial or ventricular arrhythmia requiring treatment and elevated cardiac biomarkers consistent with ischemia (i.e., Troponin-I).

RESULTS: During the study period, adenosine-induced flow arrest was used in 72 of the 413 patients (17.4%) who underwent intracranial aneurysm clip ligation. The difference in the incidence of poor neurological outcome, with or without the use of adenosine, was no larger than 15.7% at 48 hours after surgery (P =0.524) or −12.7% at discharge (P = 0.741). In addition, the difference in the incidence of cardiac morbidity was no larger than −16.0% for persistent arrhythmia (P = 0.155) or −9.4% for biomarkers of myocardial ischemia (P = 0.898) in the initial 48 hours after surgery.

CONCLUSION: When used to facilitate intracranial aneurysm clip ligation, adenosine-induced flow arrest was associated with no more than a 15.7% increase or a 12.7% decrease in the incidence of a poor neurologic outcome at either 48 hours or at the time of hospital discharge. In addition, adenosine use was not associated with cardiac morbidity in the perioperative period (i.e., persistent arrhythmia or biomarkers of cardiac ischemia).

Quincke 針型與 Whitacre 針型在 S1 經孔硬膜外類固醇注射中血管內吸收的風險比較：一個 1376 個病例的隨機試驗

A Comparison of Quincke and Whitacre Needles with Respect to Risk of Intravascular Uptake in S1 Transforaminal Epidural Steroid Injections: A Randomized Trial of 1376 Cases

Shin, Jaehyuck MD*; Kim, Yong Chul MD, PhD†; Lee, Sang Chul MD, PhD†; Kim, Jae Hun MD‡

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背景：經孔硬膜外注射類固醇(TFESI)是很有效的一種鎮痛方法。TFESI 的大部分併發症是小而暫時的。但也有發生嚴重併發症的風險，比如神經損傷、脊髓梗死或截癱。有些風險與直接損傷血管或是血管內注入類固醇微粒有關。我們預測假設：在 TFESI 時，Whitacre 針型血管內注射的幾率低於 Quincke 針型。

方法：本研究是 1376 例在 S1 水準的 TFESI 的隨機試驗。我們收集的病人資料有：年齡、性別、身高、體重、偏側（左或右）、腰骶脊柱手術史、停用抗凝藥的適當的間隔時間以及基礎疾病史。在 S1 水準做 TFESI 期間，我們觀察了骶內骨的接觸、血液回抽試驗及用造影劑對血管內注射的即時 X 線透視。

結果：年齡、性別、身高、體重、是否有高血壓、糖尿病病史、偏側、腰骶脊柱手術史以及合適的停用抗凝藥間隔時間與血管內注射的發生率沒有明顯的相關性。血管內注射的顯著相關因素爲：血的抽吸試驗($P < 0.001$)、針頭型號($P = 0.002$)、骶內骨接觸($P < 0.001$）及內科醫生(部分 $P < 0.05$）。Quincke 針型和骶內骨接觸增加了血管內注射的機率。

結論：爲了減少血管內注射的風險，更安全且更有效的方法是使用 Whitacre 針型以及避免骶內骨接觸。

（王慧娟 譯 馬皓琳 李士通 校）

BACKGROUND: Transforaminal epidural steroid injection (TFESI) is a useful treatment modality for pain management. Most complications of TFESI are minor and transient. However, there is a risk of serious complications such as nerve injury, spinal cord infarct, or paraplegia. Some of the risks are related to direct injury to the vessel or intravascular injection of the particulate steroid. We prospectively tested the hypothesis that the intravascular injection rate of the Whitacre needle is lower than that of the Quincke needle during TFESI.

METHODS: This study was a randomized trial of 1376 TFESIs at the S1 level. We collected data of age, gender, height, weight, laterality (right/left), history of lumbosacral spine operation, history of appropriate interval discontinuation of anticoagulation medicines, and underlying disease. During the S1 TFESI, intrasacral bone contact, a blood aspiration test, and real-time fluoroscopy of the intravascular injection using contrast media were investigated.

RESULTS: There were no significant differences in the intravascular injection rate with respect to age, gender, height, weight, hypertension, diabetes mellitus, laterality, history of lumbosacral spine operation, or history of appropriate interval discontinuation of anticoagulation medicines. Intravascular injection was significantly associated with a blood aspiration test ($P < 0.001$), needle tip type ($P = 0.002$), intrasacral bone contact ($P < 0.001$), and physicians (some $P < 0.05$). The use of Quincke needles and intrasacral bone contact increased the rate of intravascular injection.

CONCLUSIONS: To reduce the risk of intravascular injection, the use of Whitacre needles without intrasacral bone contact may be a safer and more effective approach.