使用導管交換器進行經皮擴張氣管切開術

Percutaneous Dilatational Tracheostomy Using Tube Exchanger.

Ronen O1,2, Gurevich A3, Ivry S3, Altman E4, Kukuev E3.
1. From the Department of Otolaryngology, Head and Neck Surgery, Galilee Medical Center, Nahariya, Israel.
2. Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel.
3. Department of Anesthesiology, Galilee Medical Center, Nahariya, Israel.
4. Surgery B, Galilee Medical Center, Nahariya, Israel.

Anesthesia & Analgesia: 2019 129 e45-e47

本文描述了一種使用 15F 導管交換器或 Eschmann 導管的改良經皮擴張氣管切開術。這項對 1180 例使用該技術的回顧性研究顯示，使用改良氣管切開術是有效的，失敗率僅 0.25%（3 例）。此外，該技術提供了額外的保護措施，它能在意外拔管的情況下快速將氣管導管重新插入由交換導管引導的氣管中。該技術不需要額外的特殊設施或裝置（如支氣管鏡）。然而，該專案仍需要前瞻性研究來更好的明確此技術併發症的發生率。

（劉施雯 譯 梁超、潘豔、薛張綱校）

We describe a modified technique for percutaneous dilatational tracheostomy using a 15F tube exchanger or Eschmann catheter. A retrospective review of 1180 procedures using this modified technique demonstrated it to be effective with a failure rate of only 0.25% (3 patients). Moreover, it provides an additional safeguard with the ability to rapidly reintroduce the endotracheal tube into the trachea guided by the exchange catheter in the event of accidental extubation during the procedure. This technique needs no additional special devices or equipment (eg, a bronchoscope). However, a prospective study is needed to better define its complication rate.

凝血因數 X 與活化凝血因數 VII 聯合應用於稀釋性凝血功能障礙

Prohemostatic Activity of Factor X in Combination With Activated Factor VII in Dilutional Coagulopathy.

Takeshita S1, Ogawa S1, Nakayama Y1, Mukai N1, Nakajima Y2, Mizobe T1, Sawa T1, Tanaka KA3.

Anesthesia & Analgesia: 2019 129 339-345

背景在複雜心臟手術中，重組活化因數 VII（rFVIIa）濃縮物可減少同種異體輸血，但可能增加血栓栓塞併發症。活化凝血因數 VII（FVIIa）和因數 X（FX）（FVIIa/FX）(FVIIa:FX = 1:10）的混合物是血友病患者的新型旁路製劑。我們假設FX和FVII因數的組合可以改善如心臟手術中所見的獲得性多因素凝血缺陷中的凝血酶生成（TG），並與其他在體外和體內稀釋性血漿樣本中使用的凝血因數濃縮物平行進行體外FVIIa / FX評估。

方法從 9 名健康志願者和 12 名心臟手術患者收集血漿樣品。我們使用體外 50%稀釋血漿和體外迴圈後體內稀釋血漿，通過血栓彈力測定法（ROTEM）和標準凝血測定法同時測量TG(凝血酶鏡)。評估體外添加FVIIa / FX(0.35,0.7和1.4μg/mL，基於 FVIIa 水準)，rFVIIa（1.4,2.8 和 6.4μg/ mL)，凝血酶原複合物濃縮物（0.3 國際單位）和 20%血漿置換時 TG 的情況。

結果在稀釋血漿中，添加 FVIIa / FX 或 rFVIIa 縮短了時滯並增加了峰值 TG，但是 FVIIa / FX 在 0.35μg/ mL 的效果比 rFVIIa 在 6.4μg/ mL 時的效果更好。凝血酶原複合物濃縮物通過增加凝血酶原水準來增加峰值TG,但未能縮短時滯。在用血漿替換 20%體積後，未觀察到任何 TG 變數的改善。因數濃縮物的添加使凝血酶原時間/國際標準化比率標準化，但不進行血漿置換。在心臟病患者體外迴圈後的樣本中可以觀察到類似的 TG 模式。FVIIa / FX 在血栓彈力測定法上以濃度依賴性方式縮短凝血時間（CT）。血漿置換沒有改善凝血時間，但血漿和 FVIIa / FX（0.35μg/ mL）的組合比單獨的 FVIIa / FX 更有效地縮短了凝血時間。

結論稀釋性凝血病模型中，FVIIa 和 FX 的組合比單獨使用 rFVIIa 或血漿更有效地改善凝血酶生成。FVIIa / FX 中所需的 FVIIa 劑量顯著低於血友病患者旁路治療期間報告的劑量（1.4-2.8μg/ mL)。與單獨使用 FVIIa / FX 相比，與血漿聯合應用可以更有效地恢復凝血。用較少的 FVIIa 發揮促凝血活性在減少全身性血栓栓塞併發症方面可能是有利的。

（高璿 譯 梁超、潘豔、薛張綱校）

BACKGROUND: Recombinant activated factor VII (rFVIIa) concentrate reduces allogeneic blood transfusions, but it may increase thromboembolic complications in complex cardiac surgery. The mixture of activated factor VII (FVIIa) and factor X (FX) (FVIIa/FX) (FVIIa:FX = 1:10) is a novel bypassing agent for hemophilia patients. We hypothesized that the combination of FX and FVIIa could improve thrombin generation (TG) in acquired multifactorial coagulation defects such as seen in cardiac surgery and conducted in vitro evaluation of FVIIa/FX in parallel with other coagulation factor concentrates using in vitro and in vivo diluted plasma samples.

METHODS: Plasma samples were collected from 9 healthy volunteers and 12 cardiac surgical patients. We measured TG (Thrombinoscope) using in vitro 50% dilution plasma and in vivo dilution plasma after cardiopulmonary bypass, in parallel with thromboelastometry (ROTEM) and standard coagulation assays. In vitro additions of FVIIa/FX (0.35, 0.7, and 1.4 μg/mL, based on the FVIIa level), rFVIIa (1.4, 2.8, and 6.4 μg/mL),

prothrombin complex concentrate (0.3 international unit), and 20% plasma replacement were evaluated.
RESULTS: In diluted plasma, the addition of either FVIIa/FX or rFVIIa shortened the lag time and increased the peak TG, but the effect in lag time of FVIIa/FX at 0.35 μg/mL was more extensive than rFVIIa at 6.4 μg/mL. Prothrombin complex concentrate increased peak TG by increasing the prothrombin level but failed to shorten the lag time. No improvement in any of the TG variables was observed after 20% volume replacement with plasma. The addition of factor concentrates normalized prothrombin time/international normalized ratio but not with plasma replacement. In cardiac patients, similar patterns were observed on TG in post-cardiopulmonary bypass samples. FVIIa/FX shortened clotting time (CT) in a concentration-dependent manner on CT on thromboelastometry. Plasma replacement did not improve CT, but a combination of plasma and FVIIa/FX (0.35 μg/mL) more effectively shortened CT than FVIIa/FX alone.
CONCLUSIONS: The combination of FVIIa and FX improved TG more efficiently than rFVIIa alone or plasma in dilutional coagulopathy models. The required FVIIa dose in FVIIa/FX was considerably lower than those reported during bypassing therapy in hemophilia patients (1.4-2.8 μg/mL). The combination of plasma could restore coagulation more efficiently compared to FVIIa/FX alone. Lesser FVIIa requirement to exert procoagulant activity may be favorable in terms of reducing systemic thromboembolic complications.

電子審計和回饋與積極的獎勵提高麻醉供應商遵守基於條碼的藥物安全系統

Electronic Audit and Feedback With Positive Rewards Improve Anesthesia Provider Compliance With a Barcode-Based Drug Safety System

Bowdle TA1, Jelacic S, Nair B, Zucker F, Bussey LS, Togashi K, Yang JT, Lang J.
1From the Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, Washington.
Anesthesia & Analgesia: 2019 129 418-425

背景：我們在所有麻醉場所實施了之前描述的基於條碼的藥物安全系統。在給藥前，醫生被要求使用我們的麻醉資訊管理系統掃描注射器上的條碼，但是醫生的依從率很低。我們研究了一個旨在提高掃描率的實施干預。

方法：我們使用麻醉資訊管理系統和智慧麻醉管理軟體，對麻醉提供者的注射器用藥進行了條碼掃描和非條碼掃描的量化。我們使用麻醉團隊模型，其中主診麻醉師與註冊護士或住院醫師配對。我們的系統確定了與特定藥物管理相關的兩個

提供者，但沒有區分哪些提供者實際管理藥物。因此，每個特定案例的條碼掃描率被平均分配給兩個提供者。基線掃描率是在 17 個月的時間內確定的。然後進行審計和回饋干預，包括每月通過電子郵件發送給各個供應商的業績報告，以及為表現最好的員工頒發的咖啡禮品卡獎勵。咖啡禮品卡只在干預的頭 2 個月發放，而電子郵件的表現報告每月都在繼續。咖啡卡獎被公諸於眾。每月的電子郵件報告了單個麻醉提供者相對於其他提供者的表現排名順序，但在其他方面是匿名的。基線掃描率與干預後 7 個月的掃描率進行比較。

結果：2014 年 11 月至 2017 年 3 月，我們收集了由 88 名麻醉醫師、65 名註冊麻醉護士、148 名住院醫師執行的 60197 個病例。注射器給藥的總數為 653,355。平均注射器條碼掃描表現從 2014 年 11 月至 2016 年 2 月的 8.7%提高到從 2016 年 9 月至 2017 年 3 月的 64.4%(P ＜ .001)。個體之間的表現差異被標記出來，為從 0%到 100%的注射器掃描範圍。一些人的表現表現出明顯的隨時間的振盪。與註冊麻醉護士相比，住院醫生的表現差異更大。

結論：從麻醉資訊系統向提供者回饋單個提供者的表現資料，可以與其他措施一起使用，以改善表現。儘管平均表現有所改善，但個體之間的表現存在顯著差異，有些個體的表現隨著時間的推移出現了明顯的波動。

（劉配配 譯 梁超、潘豔、薛張綱校）

BACKGROUND: We implemented a previously described barcode-based drug safety system in all of our anesthetizing locations. Providers were instructed to scan the barcode on syringes using our Anesthesia Information Management System before drug administration, but the rate of provider adherence was low. We studied an implementation intervention intended to increase the rate of scanning.

METHODS: Using our Anesthesia Information Management System and Smart Anesthesia Manager software, we quantified syringe drug administrations by anesthesia providers with and without barcode scanning. We use an anesthesia team model in which an attending anesthesiologist is paired

with a certified registered nurse anesthetist (CRNA) or a resident. Our system identified the pair of providers associated with a particular drug administration, but did not distinguish which providers actually administered the drug. Therefore, the rate of barcode scanning for a particular case was assigned to both providers equally. A baseline rate of scanning was established over a period of 17 months. An audit and feedback intervention was then performed that consisted of monthly performance reports sent by email to individual providers along with coffee gift card awards for top performers. The coffee gift cards were awarded in only the first 2 months of the intervention, while the email performance reports continued on a monthly basis. The coffee card awards were made public. The monthly emails reported the individual provider's rank order of performance relative to other providers, but was otherwise anonymous. The baseline rate of scanning was compared to the rate of scanning after the intervention for a period of 7 months.

RESULTS: From November 2014 to March 2017, we accumulated 60,197 cases performed by 88 attending anesthesiologists, 65 CRNAs, and 148 residents. The total number of syringe drug administrations was 653,355. Average scanning performance improved from 8.7% of syringe barcodes scanned during the baseline period from November 2014 to February 2016 to 64.4% scanned during the period September 2016 to March 2017 ($P < .001$). Variation in performance among individuals was marked, ranging from 0% to 100% of syringes scanned. The performance of some individuals showed marked oscillation over time. There was greater variation in performance attributable to residents than in performance attributable to CRNAs.

CONCLUSIONS: Feedback of individual provider performance data from the anesthesia information system to providers can be used in conjunction with other measures to improve performance. Despite improved average performance, there was marked variation in performance between individuals, and some individuals had marked oscillation of their performance over time.

測定 AnaConDa 的體積:在肺模型中評價一種新的小潮氣量麻醉氣體監測器。

.Halving the Volume of AnaConDa: Evaluation of a New Small-Volume Anesthetic Reflector in a Test Lung Model

Bomberg, Hagen MD[*]; Meiser, Franziska MD[*]; Daume, Philipp MS[*]; Bellgardt, Martin MD[†]; Volk, Thomas MD[*]; Sessler, Daniel I. MD[‡]; Groesdonk, Heinrich V. MD[*]; Meiser, Andreas MD[*]

Anesthesia & Analgesia: 2019 129 371-379

背景:揮發性麻醉劑越來越多地應用於重症監護病房的鎮靜。最常見的給藥系統

是 AnaConDa-100 mL (ACD-100; Sedana Medical, Uppsala, Sweden)，這是一

種反映了開放性回路中揮發性麻醉藥物濃度的裝置。AnaConDa-50 mL (ACD-50)是一種具有一半死腔的新裝置。兩種設備都能保留二氧化碳。因此，我們比較了兩種裝置的二氧化碳消除率和異氟醚的檢測敏感度。

方法：將持續注入二氧化碳的試驗肺以 500mL，10 次/分鐘的潮氣量進行通氣。採用熱濕式換熱器(HME, 35ml)、ACD-100、ACD-50 等 3 種不同設備，在環境溫度壓力(ATP)、體溫壓力飽和(BTPS)、BTPS 中添加 0.4 Vol%異氟醚(ISO-0.4)、BTPS 中添加 1.2 Vol%異氟醚等 4 種不同的實驗條件下，測量潮末二氧化碳分壓(EtCO2)。在 3 個時間點(n = 150)記錄每台設備和每種情況下的 50 次呼吸。為了確定設備的死腔量，我們調整了潮氣量以維持每個設備的正常工作狀態(n = 3)。然後，我們通過測量揮發速率從 0.5 到 20ml /h (n = 3)的異氟醚濃度來確定檢測敏感度。

結果：與 ACD-50 和 HME 相比，ACD-100 的 EtCO2 始終大於後者(ISO-0.4，均值±標準差：ACD-100， 52.4 ± 0.8；ACD-50， 44.4 ± 0.8；HME,， 40.1 ± 0.4 mm Hg；EtCO2 均值差異[各自 95%置信區間]：ACD-100 - ACD-50， 8.0 [7.9-8.1] mm Hg， P < .001；ACD-100 - HME，12.3 [12.2-12.4] mm Hg，P < .001；ACD-50 - HME，4.3 [4.2-4.3] mm Hg，P <0.001)。ATP 組最大，BTPS 組最小，ISO-0.4 組和 1.2 Vol%異氟醚組最小。在使用異氟醚時，除了 ACD100mL 或 50 mL 的“檢測死腔”外，添加 ACD-100 的“檢測死腔”為 40 mL，添加 ACD-50 的“檢測死腔”為 25 mL。ATP 作用下異氟醚反射最高。在 CO2 注入和異氟醚濃度為 0.4 Vol%左右的 BTPS 下，ACD-100 的檢測效率為 93%，ACD-50 的檢測效率為 80%

結論：在臨床麻醉濃度下，ACD-50 對異氟醚的檢測敏感度仍然足夠，而對 CO2 的去除得到了改善。ACD-50 應該適用於潮氣量低至 200 毫升的病人，即使是小潮氣量病人也可以進行肺保護通氣。

（何黃威 譯 梁超、潘豔、薛張綱校）

BACKGROUND: Volatile anesthetics are increasingly used for sedation in intensive care units. The most common administration system is AnaConDa-100 mL (ACD-100; Sedana Medical, Uppsala, Sweden), which reflects volatile anesthetics in open ventilation circuits. AnaConDa-50 mL (ACD-50) is a new device with half the volumetric dead space. Carbon dioxide (CO2) can be retained with both devices. We therefore compared the CO2 elimination and isoflurane reflection efficiency of both devices.
METHODS:A test lung constantly insufflated with CO2 was ventilated with a tidal volume of 500 mL at 10 breaths/min. End-tidal CO2 (EtCO2) partial pressure was measured using 3 different devices: a heat-and-moisture exchanger (HME, 35 mL), ACD-100, and ACD-50 under 4 different experimental conditions: ambient temperature pressure (ATP), body temperature pressure saturated (BTPS) conditions, BTPS with 0.4 Vol% isoflurane (ISO-0.4), and BTPS with 1.2 Vol% isoflurane. Fifty breaths were recorded at 3 time points (n = 150) for each device and each condition. To determine device dead space, we adjusted the tidal volume to maintain normocapnia (n = 3), for each device. Thereafter, we determined reflection efficiency by measuring isoflurane concentrations at infusion rates varying from 0.5 to 20 mL/h (n = 3), for each device.
RESULTS: EtCO2 was consistently greater with ACD-100 than with ACD-50 and HME (ISO-0.4, mean ± standard deviations: ACD-100, 52.4 ± 0.8; ACD-50, 44.4 ± 0.8; HME, 40.1 ± 0.4 mm Hg; differences of means of EtCO2 [respective 95% confidence intervals]: ACD-100 - ACD-50, 8.0 [7.9-8.1] mm Hg, $P < .001$; ACD-100 - HME, 12.3 [12.2-12.4] mm Hg, $P < .001$; ACD-50 - HME, 4.3 [4.2-4.3] mm Hg, $P < .001$). It was greatest under ATP, less under BTPS, and least with ISO-0.4 and BTPS with 1.2 Vol% isoflurane. In addition to the 100 or 50 mL "volumetric dead space" of each AnaConDa, "reflective dead space" was 40 mL with ACD-100 and 25 mL with ACD-50 when using isoflurane. Isoflurane reflection was highest under ATP. Under BTPS with CO2 insufflation and isoflurane concentrations around 0.4 Vol%, reflection efficiency was 93% with ACD-100 and 80% with ACD-50.
CONCLUSIONS: Isoflurane reflection remained sufficient with the ACD-50 at clinical anesthetic concentrations, while CO2 elimination was improved. The ACD-50 should be practical for tidal volumes as low as 200 mL, allowing lung-protective ventilation even in small patients.

在大鼠非創傷性出血性休克中，糖萼降解與血管屏障通透性增加無關。

Glycocalyx Degradation Is Independent of Vascular Barrier Permeability Increase in Nontraumatic Hemorrhagic Shock in Rats

Guerci, Philippe MD[*,†,‡]; Ergin, Bulent PhD[*,§]; Uz, Zuhre MD[*]; Ince, Yasin MSc[*]; Westphal, Martin MD, PhD[‖]; Heger, Michal PhD[¶]; Ince, Can PhD[*,§]

Anesthesia & Analgesia: 2019 129 598-607

背景：創傷性出血性休克或敗血症性休克後糖萼缺如，以及不同的復蘇液體，與血管屏障通透性增加有關，將導致組織水腫。在非創傷性出血性休克中，糖萼降解本身是否導致血管屏障通透性的改變仍值得懷疑。液體的組成也可以對糖萼脫落和血管屏障通透性有調節作用。我們假設，在第 n 個生理過程中，糖萼的脫落對血管屏障通透性的影響很小，並且液體的組成可以調節這些影響。

方法：全儀器化的白化大鼠接受壓力控制的非創傷性出血性休克（平均動脈壓 30 mm Hg）60 分鐘。用醋酸鹽林格式液、羥乙基澱粉溶液或 0.9%生理鹽水對動物進行液體復蘇，平均動脈壓為 80 mmHg，並與假手術或非假性非創傷性出血性休克進行比較。在基線和液體復蘇後 60 分鐘測定糖萼脫落產物。用活體顯微鏡觀察骨骼肌微循環。用 3 種螢光染料（40-500kDa 右旋糖酐和 70kDa 白蛋白）的血漿衰減、埃文斯藍染料排斥、活體內螢光顯微鏡檢查和組織水腫（濕/幹重比）測定評估血管屏障通透性的變化。

結果：所有的糖萼脫落產物都因氮合酶而升級。n 組（g=-1668；95%可信區間[CI]=-2336- -1001；p<0.0001）、平衡晶體（g=-964.2；95%可信區間[CI]=-1492- -436.4；p=0.0001）和羥乙基澱粉溶液（g=-1030；95%可信區間[CI]=-1594- -465.8；p=0.0001）的陽性率顯著增加。實驗組與對照組相比，在實驗結束時，非依賴性非創傷性出血性休克（g=-923.1；95%可信區間[CI]=-1216- -630；P=0.0001）和平衡晶體（g=-1039；95%可信區間[CI]=-1332- -745.5；P=0.0001）

或羥乙基澱粉溶液（g=-394.2；95%可信區間[CI]=-670.1- -118.3；P=0.0027）組的透明質酸水準較高。如顯微術觀察到的糖萼脫落導致微循環改變。與對照組相比，生理鹽水組（g=4.092；95%可信區間[CI]=0.6195-7.564；P=0.016）和出血性休克組（g=5.022；95%可信區間[CI]=1.55-8.495；P=0.0024）的總血管密度以及灌注血管密度和平均流量指數均發生了變化。儘管內皮糖球降解，但由 4 種獨立分析確定的血管屏障通透性仍保持完整，並在液體復蘇後繼續如此。

結論：氮合酶誘導糖萼脫落和微循環改變，而不改變血管屏障通透性。液體復蘇部分恢復微循環，但不改變血管通透性。這些結果挑戰了糖萼屏障對血管通透性的重要貢獻這一概念。

（盧旭譯梁超、潘豔、薛張綱校）

BACKGROUND: Glycocalyx shedding after traumatic hemorrhagic or septic shock, as well as different resuscitation fluids, has been causally linked to increased vascular barrier permeability (VBP) resulting in tissue edema. In nontraumatic hemorrhagic shock (NTHS), it remains questionable whether glycocalyx degradation in itself results in an alteration of VBP. The composition of fluids can also have a modulatory effect on glycocalyx shedding and VBP. We hypothesized that the shedding of the glycocalyx during NTHS has little effect on VBP and that the composition of fluids can modulate these effects.
METHODS: Fully instrumented Wistar-albino rats were subjected to a pressure-controlled NTHS (mean arterial pressure of 30 mm Hg) for 60 minutes. Animals were fluid resuscitated with Ringer's acetate, balanced hydroxyethyl starch (HES) solution, or 0.9% normal saline to a mean arterial pressure of 80 mm Hg and compared with shams or nonresuscitated NTHS. Glycocalyx shed products were determined at baseline and 60 minutes after fluid resuscitation. Skeletal muscle microcirculation was visualized using handheld vital microscopy. VBP changes were assessed using plasma decay of 3 fluorescent dyes (40- and 500-kDa dextran and 70-kDa albumin), Evans blue dye exclusion, intravital fluorescence microscopy, and determination of tissue edema (wet/dry weight ratio).
RESULTS: All glycocalyx shedding products were upgraded as a result of NTHS. Syndecan-1 significantly increased in NTHS (mean difference, -1668; 95% confidence interval [CI], -2336 to -1001; P < .0001), balanced crystalloid (mean difference, -964.2; 95% CI, -1492 to -436.4; P = .0001),

and HES (mean difference, -1030; 95% CI, -1594 to -465.8; P = .0001) groups at the end of the experiment compared to baseline. Hyaluronan levels were higher at the end of the experiment in nonresuscitated NTHS (-923.1; 95% CI, -1216 to -630; P = .0001) and balanced crystalloid (-1039; 95% CI, -1332 to -745.5; P = .0001) or HES (-394.2; 95% CI, -670.1 to -118.3; P = .0027) groups compared to controls. Glycocalyx shedding resulted in microcirculation alterations as observed by handheld video microscopy. Total vessel density was altered in the normal saline (mean difference, 4.092; 95% CI, 0.6195-7.564; P = .016) and hemorrhagic shock (mean difference, 5.022; 95% CI, 1.55-8.495; P = .0024) groups compared to the control group, as well as the perfused vessel density and mean flow index. Despite degradation of endothelial glycocalyx, VBP as determined by 4 independent assays remained intact and continued to be so following fluid resuscitation.
CONCLUSIONS: NTHS induced glycocalyx shedding and microcirculation alterations, without altering VBP. Fluid resuscitation partially restored the microcirculation without altering VBP. These results challenge the concept that the glycocalyx barrier is a significant contributor to VBP.

非心臟手術患者緊急超聲心動圖檢查方案的發展

Development of a Rescue Echocardiography Protocol for Noncardiac Surgery Patients

Staudt GE, Shelton K.
Anesthesia & Analgesia. 2019 129 e37-40.

背景:在非心臟手術過程中發生血流動力學改變時,術中經食管超聲心電圖(TEE)是一種有效的診斷工具。然而,這種先進診斷工具的使用可能受到設備和接受培訓的醫生短缺的限制。創建緊急超聲方案是為了提供進行救援 TEE 請求和實施的一項途徑。作者所在機構于 2015 年 5 月制定了一項緊急超聲方案並創建了一個正式的緊急超聲服務(RES),同時還建立了一個認知輔助工具,該工具詳細介紹了緊急超聲方案,包括先前詳細介紹的檢查順序、適應症、禁忌症和排除事件。

方法:收集在 2015 年 5 月 1 日至 2017 年 3 月 31 日的 22 個月期間由 RES 在非心臟手術中執行的所有術中接受 TEE 檢查的患者名單,將病人歸類為接受緊急或監

測檢查的病人。然後，分析接受了緊急檢查的患者的臨床資料，包括醫療記錄、麻醉護理記錄和超聲心動圖報告。收集的資料點包括人口資料（手術時的年齡、性別和 ASA 分類）、外科資訊（外科服務和外科手術的類型）、緊急檢查的適應症、TEE 檢查結果、干預措施和出院的生存情況。通過對麻醉記錄的回顧性審查進行干預措施的收集，實施的干預措施分為“管理上的改變”或“管理上的不改變”。如果符合以下標準之一的話，干預措施符合管理上的改變：1. 藥物使用的改變。2. 液體管理的改變。3. 新的或改變的外科手術程式。4. 監護升級，如入住重症監護病房。

結果：研究物件 ASA 評級差異較大，但大部分都是 III 級（48 中例的 23 例）。手術方式各異，骨科手術和神經外科檢查各占 14.5%（7/48），其次為血管外科，占 12.5%（6/48）。頑固性低血壓是緊急 TEE 最常見的指征（47.9%），其次是心臟驟停（22.9%）和 ST 段改變（10.4%）。TEE 的發現分為 10 類。有些病例顯示 >1 項發現，占總數>48 項，額外發現百分比>100%。47.5%（48 例中的 23 名）病例符合這一最常見的結論。20.8%病例（48 例中的 10 例）顯示左室較小，高動力狀態，舒張期充盈不足且心輸出量低，被診斷為低血容量。緊急 TEE 後，72.9% 的患者管理發生變化，部分患者採取了多種干預措施。

結論：隨著具有特定指導方針、教育目標和人員管理的規範化發展，在非心臟手術血流動力學不穩定的情況下，緊急超聲心動圖可用於指導管理。

（牛芳芳 譯　陳傑 校）

Background: Intraoperative transesophageal echocardiography (TEE) is a helpful diagnostic tool when hemodynamic compromise is encountered during noncardiac surgery. At our institution, a Rescue Echo Protocol was created to provide a structured means for requesting and performing a rescue TEE. At our institution, a Rescue Echo Protocol was created in May 2015 to enable access to TEE services in noncardiac operating rooms. Finally, to

strengthen the educational component of our service, we created a cognitive aid detailing the Rescue Echo Protocol, including the examination sequence detailed earlier, indications, contraindications, and events to exclude.

Methods: Billing data were used to compile a list of all intraoperative TEEs that were performed by RES in noncardiac procedures over a 22-month period from May 1, 2015 to March 31, 2017. Anesthesia care records were reviewed, and patients were classifed as undergoing either a rescue or monitoring examination. Medical records, anesthesia care records, and echocardiographic reports were analyzed. Data points collected included demographic data (age at the time of surgery, sex, and ASA classifcation), surgical information (surgical service and type of surgical procedure), indication for rescue examination, TEE fndings, interventions performed, and survival to hospital discharge. Interventions were collected through retrospective review of anesthesia records. Performed interventions were further grouped into either “change in management” or “no change in management.” An intervention qualifed as a change in management if one of the following criteria was met: 1. Alteration in medication administration. 2. Change in fluid management strategy. 3. New or altered surgical procedure. 4. Escalation in the level of care, such as intensive care unit admission.

Results: There was wide range of ASA classifcations; however, the majority of patients was ASA III (23/48). A wide variety of surgical services were represented. Orthopedic surgery and neurosurgery each accounted for 14.5% (7/48) of examinations, followed by vascular surgery at 12.5% (6/48). The most common indication for rescue TEE was refractory hypotension (47.9%). This was followed by cardiac arrest (22.9%) and ST changes (10.4%). TEE findings were classifed into 10 categories. Some studies revealed >1 finding, with accounts for a count of >48 studies and an additive percentage of >100%. This was the most common conclusion, seen in 23 of 48 studies (47.5%). Hypovolemia was diagnosed by visualizing a small, hyperdynamic ventricle with inadequate diastolic flling and low estimated cardiac output, seen in 10 of 48 examinations (20.8%). The patients (72.9%) had a change in management after rescue TEE, and some had multiple interventions.

Conclusions: With the development of a structured protocol with specifc guidelines, educational goals, and personnel management, rescue echocardiography may be used to guide management during times of hemodynamic instability in noncardiac surgery.

成人惡性高熱易感患者與門診手術中心：美國麻醉醫師協會門診麻醉學會和門診手術監護委員會的立場聲明

Malignant Hyperthermia–Susceptible Adult Patient and Ambulatory Surgery Center: Society for Ambulatory Anesthesia and Ambulatory Surgical Care Committee of the American Society of Anesthesiologists Position Statement

Urman, Richard D. MD, MBA*; Rajan, Niraja MD†; Belani, Kumar MBBS, MS‡; Gayer, Steven MD, MBA§; Joshi, Girish P. MBBS, MD, FFARCSI‖

Anesthesia & Analgesia: 2019 129 347-349

背景：在獨立的門診手術中心（ASC）中，對已知的惡性高熱（MH）易感患者進行手術仍存在爭議。本文闡述了成人惡性高熱（MH）易感患者在獨立門診手術中心（ASC）中的安全麻醉監護。

方法：本研究探討了惡性高熱易感患者術前鑒別和預防，術中麻醉管理、術後監測以及惡性高熱危象的處理措施。

結果：MH 易感性狀態的確定應個體化且基於患者病史和體格檢查。對於計畫進行手術的 MH 易感患者，使用丹曲林進行術前預防並非正確。手術過程中應減少或防止 MH 易感患者接觸揮發性麻醉劑。在圍手術期間，必須警惕監測患者的 MH 體征和/或症狀。麻醉後恢復室（PACU）應繼續密切觀察和監測。當發生惡性高熱危象時，應立即使用丹曲林。

結論：假設採取了適當措施預防，識別和管理惡性高熱，MH 易感患者就可以安全地在一個獨立的門診手術中心進行手術。要做到早發現、早治療，並及時轉運至有此類處理經驗的重症監護部門，患者才能在 ASC 環境下安全度過 MH 危象。

（蔣濤 譯 陳傑 校）

Background：Performing surgery in a patient with known susceptibility to malignant hyperthermia (MH) in a free-standing ambulatory surgery center (ASC) remains controversial. This document is concerned with the safe anesthetic care of adult malignant hyperthermia (MH)-susceptible patients in a free-standing ambulatory surgery center (ASC).

Methods：This study investigated preoperative identification and prevention, intraoperative anesthesia management, postoperative

monitoring of MH-susceptible patients and treatment of MH crisis.

Results：Determination of MH susceptibility status should be individualized and based on the history and physical examination. The administration of preoperative prophylaxis with dantrolene is not indicated in MH-susceptible patients scheduled for surgery. MH-susceptible should be reduced or prevented from exposure to volatile anesthetics during surgery.Patients must be vigilantly monitored for signs and/or symptoms of MH during the perioperative period.Close observation and monitoring should continue in the postanesthesia care unit (PACU). Dantrolene should be used immediately when malignant hyperthermia crisis occurs.

Conclusion：MH-susceptible patients can safely undergo procedures in a free-standing ASC assuming that proper precautions for preventing, identifying, and managing MH are taken. Patient survival from an MH crisis in an ASC setting requires early recognition, prompt treatment, and timely transfer to a facility with critical care capabilities.

關於正常氣道患者面罩通氣檢查前後羅庫溴銨早期和晚期給藥的隨機試驗

Randomized Trial Comparing Early and Late Administration of Rocuronium Before and After Checking Mask Ventilation in Patients With Normal Airways

Se-Hee Min, MD,* Hyunjae Im, MD,† Bo Rim Kim, MD,* Susie Yoon, MD,* Jae-Hyon Bahk, MD, PhD,* and Jeong-Hwa Seo, MD, PhD*
Anesthesia & Analgesia: 2019 129 380-386

背景：在全身麻醉誘導期間，通常的做法是在保證提供面罩通氣成功之後才給予肌松藥。然而，這種方法的好處從未得到科學驗證。因此，作者比較了在檢查面罩通氣之前和之後羅庫溴銨的早期和晚期應用來研究面罩通氣的效率和正常氣道患者的氣管插管時間。

方法：114 名患者隨機接受在檢查面罩通氣之前（早期羅庫溴銨組，n = 58）或之後（晚期羅庫溴銨組，n = 56）靜脈輸注羅庫溴銨。在面罩通氣期間呼吸暫停後分別在 10,20,30,40,50 和 60 秒測量呼氣潮氣量（VT）。作者評估了面罩通氣的難易程度，並記錄了從呼吸暫停到氣管插管的時間。主要結果是在呼吸暫停後

10,20,30,40,50 和 60 秒測量的面罩 VT 的平均值。主要的次要結果是從呼吸暫停到氣管插管的時間。統計方法為 STATA。

結果：早期羅庫溴銨組在呼吸暫停後 10,20,30,40,50 和 60 秒測量的面罩 VT 平均值比晚期羅庫溴銨組藥更大（552 ml/呼吸 [165 ml/呼吸]） vs 393 ml/呼吸 [165 ml/呼吸]，平均差異，160 ml/呼吸; 95%CI，98-221 ml/呼吸; p<0.001，非配對 t 檢驗)。因為在呼吸暫停後 10,20,30,40,50 和 60 秒測量的面罩 VT 中，時間和組之間的相互作用是顯著的（p<0.001，線性混合效應模型），在 6 個時間點進行成對比較。在呼吸暫停後 10,20,30,40 和 50 秒兩組間 VT 的差異顯著（p<0.001，STATA 中的對比表述）。早期羅庫溴銨組從呼吸暫停到氣管插管的時間短于晚期羅庫溴銨組（116 秒[42 秒] vs 195 秒[41 秒];平均差異，-79 秒; 95%CI，-96 至 - 64 秒，p <0.001）。

結論:在正常氣道患者中檢查面罩通氣前早期給予羅庫溴銨與在檢查面罩通氣之後晚期給予羅庫溴銨相比，可提供更大的面罩 VT 和更快的氣管插管。

（陳陳 譯　陳傑 校）

Background: During induction of general anesthesia, it is common practice to delay neuromuscular blockade until the ability to deliver mask ventilation has been confirmed. However, the benefits of this approach have never been scientifically validated. We thus compared the early and late administration of rocuronium before and after checking mask ventilation to investigate the efficiency of mask ventilation and the time to tracheal intubation in patients with normal airways.

Methods: Patients (n = 114) were randomized to receive IV rocuronium either before (early rocuronium group, n = 58) or after (late rocuronium group, n = 56) checking mask ventilation. Expiratory tidal volumes (VTs) were measured at 10, 20, 30, 40, 50, and 60 seconds after apnea during mask ventilation. We graded the ease of mask ventilation and measured the time from apnea to tracheal intubation. The primary outcome was the average of mask VTs measured at 10, 20, 30, 40, 50, and 60 seconds after apnea. The main secondary outcome was the time from apnea to tracheal intubation. STATA was used for statistical analysis.

Results: The average of mask VTs measured at 10, 20, 30, 40, 50, and 60 seconds after apnea was larger in the early rocuronium group than in the late rocuronium group (552 mL breath-1 [165 mL breath-1] vs 393 mL breath-1 [165 mL breath-1], mean difference, 160 mL breath-1; 95% CI, 98-221 mL breath-1; P < .001, unpaired t test). Because the interaction between time and group was significant in mask VTs measured at 10, 20, 30, 40, 50, and 60 seconds after apnea (P < .001, linear mixed effects model), pairwise comparisons were performed at the 6 time points. The differences in VTs between the groups were significant at 10, 20, 30, 40, and 50 seconds after apnea (P < .001 each, contrast statements in STATA). The time from apnea to tracheal intubation was shorter in the early rocuronium group than in the late rocuronium group (116 seconds [42 seconds] vs 195 seconds [41 seconds]; mean difference, −79 seconds; 95% CI, −96 to −64 seconds, P < .001).

Conclusions: The early administration of rocuronium before checking mask ventilation resulted in a larger mask VT and earlier tracheal intubation than the late administration of rocuronium after checking mask ventilation in patients with normal airways.

使用單次呼吸檢測法比較 7 種不同感測器在檢測非插管鎮靜志願者的低呼吸頻率方面的影響

Comparison of 7 Different Sensors for Detecting Low Respiratory Rates Using a Single Breath Detection Algorithm in Nonintubated , Sedated Volunteers

Sean Ermer, BS, Lara Brewer, PhD, Joe Orr, PhD, Talmage D. Egan, MD, and Ken Johnson, MD

Anesthesia & Analgesia: 2019 129 399-408

背景：有許多技術可用於監測非氣管插管患者的呼吸頻率，但目前尚無一種技術可成為標準，本研究主要目的是比較一種參照感測器信號(呼吸電感容積描記法）和七種替代感測器信號(經鼻二氧化碳檢測計，鼻壓力感測器，經口鼻熱敏電阻，腹部加速度計，跨肺電阻抗法，圍氣管麥克風檢測法，光電容積描記法）在評估非插管、鎮靜仰臥位志願者中所允許能檢測到的低呼吸頻率次數的一致性評價。每個感測器都採用基於單次呼吸檢測法的統一方法以便比較。作者假設所有的感測器信號都能檢測到參照感測器信號的低呼吸頻率（〈8 次/分～12 次/分〉。

方法：志願者接受瑞芬太尼和丙泊酚預設劑量的靶控輸注來誘導低通氣，採用相同閾值的檢測演算法對每個感測器的信號進行分析來計算呼吸頻率。採用 Bland-Altman 一致性極限和誤差率分析方法，對各感測器的性能和參照感測器進行比較。

結果：使用 Bland-Altman 一致性極限和誤差率分析方法對加速度計和二氧化碳檢測計的信號分析發現，它們是 7 個感測器的呼吸頻率檢測中一致性最高的（在 1.96*標準誤），可檢測的呼吸頻率分別為-2.1 - 2.2 次/分和-2.52.7 次/分。與前兩者相比，其他信號都表現出更寬的檢出範圍，其中最寬的為跨肺電阻抗法，為-7.8—7.4 次/分。腹部加速度計 95%的 Bland-Altman 資料點在-2～2 次/分呼吸頻率範圍內。二氧化碳檢測計有 96%的 Bland-Altman 資料點在-2～2 次/分呼吸頻率範圍內。鼻壓法、熱敏電阻法、麥克風法均有 80%的資料點在-2～2 次/分內，阻抗法和光電容積描記法能檢測到-2～2 次/分呼吸頻率的資料點分別為 58%和 64%。

結論：一種統一的方法可以應用於各種感測器信號來估計自主呼吸、非插管、鎮靜志願者的呼吸頻率。然而，檢測臨床相關的低呼吸頻率（<6 次/分）仍是一項技術挑戰。通過作者分析，無一感測器能夠有足夠精度來檢測緩慢的呼吸頻率（參考信號在<±2 次/分）。在評估的感測器中，二氧化碳檢測計和腹部加速度計可能是識別低通氣和呼吸暫停最可靠的感測器。

（陳永輝 譯　陳傑 校）

Background: Numerous technologies are used to monitor respiratory rates in nonintubated patients. No technology has emerged as the standard. The primary aim of this study was to assess the limits of agreement between a reference sensor signal (respiratory inductance plethysmography bands) and 7 alternative sensor signals (nasal capnometer, nasal pressure transducer, oronasal thermistor, abdominal accelerometer,

transpulmonary electrical impedance, peritracheal microphone, and photoplethysmography) for measuring low respiratory rates in sedated, nonintubated, supine volunteers. A unifed approach based on a single breath detection algorithm was applied to each sensor to facilitate comparison. We hypothesized that all of the sensor signals would allow detection of low (<10 breaths per minute) respiratory rates to within ±2 breaths per minute of the reference sensor signal.

Methods: Volunteers received remifentanil and propofol infusions at selected target concentration pairs to induce depression of ventilation. Signals from each sensor were analyzed by an identical threshold-based detection algorithm to compute the breathing rate. Bland-Altman limits of agreement and error rate analyses were used to characterize the performance of each sensor compared to the reference sensor.

Results: The analysis of the accelerometer and capnometer signals, using Bland-Altman and error rate analyses, showed the highest breath rate agreement (1.96 × standard deviation) of the 7 sensors with -2.1 to 2.2 and -2.5 to 2.7 breaths per minute, respectively. All other signals exhibited wider limits of agreement, with impedance being the widest at -7.8 to 7.4 breaths per minute. For the abdomen accelerometer, 95% of Bland-Altman data points were within ±2 breaths per minute. For the capnometer, 96% of data points were within ±2 breaths per minute. Nasal pressure, thermistor, and microphone all had >80% of data points within ±2 breaths per minute. Impedance and photoplethysmograph signals had 58% and 64%, respectively.

Conclusions: A unifed approach can be applied to a variety of sensor signals to estimate respiratory rates in spontaneously breathing, nonintubated, sedated volunteers. However, detecting clinically relevant low respiratory rates (<6 breaths per minute) is a technical challenge. By our analysis, no single sensor was able to detect slow respiratory rates with adequate precision (<±2 breaths per minute of the reference signal). Of the sensors evaluated, capnometers and abdominal accelerometers may be the most reliable sensors for identifying hypopnea and central apnea.

啟動脊髓原肌球蛋白 β 受體減輕大鼠神經病理性疼痛發揮內源性鎮痛機制

Spinal Activation of Tropomyosin Receptor Kinase-B Recovers the Impaired Endogenous Analgesia in Neuropathic Pain Rats

Kato, Daiki MS*; Suto, Takashi MD, PhD*; Obata, Hideaki MD, PhD†; Saito, Shigeru MD, PhD*

Anesthesia & Analgesia: 2019 129 578-586

背景:內源性鎮痛在控制疼痛狀態方面起著重要作用,與健康個體相比,慢性疼痛患者內源性鎮痛機制減弱。傷害性刺激誘導的鎮痛作用（NSIA），作為內源性的

鎮痛指標，在脊神經結紮 6 周後的大鼠（SNL6W）體內是減弱的。最近對去甲腎上腺素能纖維缺失大鼠進行的一項研究表明，去甲腎上腺素能纖維對 NSIA 至關重要。據報導，腦源性神經營養因數增加了脊髓去甲腎上腺素能纖維。因此，本研究檢測了腦源性神經營養因數受體 TrkB 活化對 SNL6W 大鼠受損的 NSIA 的作用。此外還檢測了內源性鎮痛對急性切口疼痛的影響。

方法：每天腹腔注射 7,8-二羥基黃酮（7,8-DHF，TrkB 激動劑，5 mg / kg）5 次後，在前爪中注射辣椒素（250 μg），30min 後測量左側（對側神經結紮）後爪的退縮閾值增量來檢測 NSIA。 K252a（TrkB 拮抗劑，2 μg）鞘內施用 5d。Idazoxan(α2 腎上腺素能受體拮抗劑,30 μg),阿托品(毒蕈堿拮抗劑,30 μg)和普萘洛爾（非選擇性 β 腎上腺素受體拮抗劑，30 μg）在注射辣椒素前 15min 鞘內給藥。採用微透析和免疫組織化學檢測法來檢測脊髓背角的去甲腎上腺素可塑性。在左側（對側神經結紮）進行後爪切口。通過單因素方差分析或雙向重複測量方法分析資料，單因素方差分析，然後使用 Bonferroni 校正進行 Student t 檢驗。

結果:每天 5 次腹腔注射 7,8-DHF 可恢復 SNL6W 大鼠 NSIA 的減弱(n = 7,P = .002; 評估療效[95%CI]：62.9 [27.0-98.7] g），此效應可被 K252a 阻斷（n = 6，P <.001; -57.8 [-78.3 至-37.2] g）。此效應也受到單次鞘內注射的 Idazoxan（n = 8，P <.001; -61.6 [-92.4 至-30.9] g）和阿托品 (n = 8, P = .003; -52.6 [-73.3 to -31.9] g)抑制，但不受普萘洛爾抑制。此外，7,8-DHF 增加脊髓背角中的去甲腎上腺素能纖維和其所釋放的去甲腎上腺素釋放。並且，重複注射 7,8-DHF 可阻止 SNL6W 大鼠切口疼痛恢復延遲。

結論：TrkB 的脊髓啟動可以通過提高腎上腺素能的可塑性來恢復減弱的內源性鎮痛，從而縮短術後疼痛的時間。

（沙婷婷 譯　陳傑 校）

Background: Although endogenous analgesia plays an important role in controlling pain states, chronic pain patients exhibit decreased endogenous analgesia compared to healthy individuals. In rats, noxious stimulus–induced analgesia (NSIA), which is an indicator of endogenous analgesia, diminished 6 weeks after spinal nerve ligation (SNL6W). A recent study in rats with deleted noradrenergic fbers demonstrated that the noradrenergic fbers were essential to NSIA. It has also been reported that brain-derived neurotrophic factor increased spinal noradrenergic fbers. Therefore, this study examined the effect of TrkB activation, which is the receptor for brain-derived neurotrophic factor, on impaired NSIA in SNL6W rats. In addition, we also examined the effect of endogenous analgesia on acute incisional pain.
Methods: After 5 daily intraperitoneal injections of 7,8-dihydroxyflavone (7,8-DHF, TrkB agonist, 5mg/kg), NSIA was examined by measuring the withdrawal threshold increment in the left (contralateral to nerve ligation) hindpaw at 30 minutes after capsaicin injection (250 μg) in the forepaw. K252a (TrkB antagonist, 2 μg) was administrated intrathecally for 5 days. Idazoxan (α2 adrenoceptor antagonist, 30 μg), atropine (muscarinic antagonist, 30 μg), and propranolol (nonselective β antagonist, 30 μg) were administered intrathecally for 15 minutes before capsaicin injection. Microdialysis and immunohistochemistry were performed to examine the noradrenergic plasticity in the spinal dorsal horn. A hindpaw incision was performed on the left (contralateral to nerve ligation) hindpaw. Data were analyzed by 1-way analyses of variance or 2-way repeatedmeasures 1-way analysis of variance followed by a Student t test with Bonferroni correction.
Results: Five daily intraperitoneal injections of 7,8-DHF restored the attenuated NSIA in SNL6W rats (n = 7, P = .002; estimated treatment effect [95% CI]: 62.9 [27.0–98.7] g), with this effect blocked by 5 daily intrathecal coadministrations of K252a (n = 6, P < .001; -57.8 [-78.3 to -37.2] g). This effect was also inhibited by a single intrathecal administration of idazoxan (n = 8, P < .001; -61.6 [–92.4 to -30.9] g) and atropine (n = 8, P = .003; -52.6 [–73.3 to -31.9] g), but not by propranolol. Furthermore, 7,8-DHF increased the noradrenergic fber in the spinal dorsal horn and the noradrenaline release in response to the capsaicin injection in the forepaw in SNL6W rats. In addition, repeated injections of 7,8-DHF prevented delayed recovery from incisional pain in SNL6W rats.

Conclusions: Spinal activation of TrkB may recover the attenuated endogenous analgesia by improving the adrenergic plasticity, thereby leading to prevention of pain prolongation after surgery.

異丙酚通過鈣調蛋白依賴性蛋白激酶 II/AMPK/ATF5 信號軸調控神經幹細胞的增殖和分化。

Propofol Regulates Neural Stem Cell Proliferation and Differentiation via Calmodulin-Dependent Protein Kinase II/AMPK/ATF5 Signaling Axis

Liang, Chao PhD; Du, Fang MD; Wang, Jiaxing PhD; Cang, Jing MD; Xue, Zhanggang MD

Anesthesia & Analgesia: 2019 129 608-617

背景:異丙酚可以引起發育中腦細胞退變,從而導致相關的長期學習或記憶損害。然而,異丙酚抑制神經幹細胞在胚胎發育早期發育的分子機制尚且不明。本研究旨在明確異丙酚在抑制神經幹細胞發育的作用,進一步探索其機制。

方法:首先,向懷孕大鼠腹腔內單次注射異丙酚,注射後 6h 抽取海馬體 RNA 和胚胎大腦蛋白並檢測神經元特異標誌物的表達。其次,從老鼠胚胎腦的海馬體中分離出原始神經幹細胞,使用異丙酚處理,進行細胞活性、免疫染色和 transwell 試驗。除此之外採用 RNA 測序,利用 q-逆轉錄聚合酶鏈式反應明確異丙酚對基因表達的調控。同時使用免疫印跡、小片段干擾 RNA(SiRNA)和螢光素酶測定來研究異丙酚在鈣調蛋白依賴性蛋白激酶 II(CaMkII)、腺苷酸活化蛋白激酶(AMPK)、啟動轉錄因數 5(ATF5)信號通路中的作用。

結果:研究結果表明,異丙酚治療可以抑制神經幹細胞的增殖、遷移和分化。RNA 測序顯示異丙酚促使一組 Ca^{2+} 依賴基因的下游調節。後續的機制研究顯示,異丙酚通過 CaMkII、氨基酸 485 位點的絲氨酸磷酸化(pS485)、AMPK、ATF5 信號通路調節神經幹細胞的增殖、分化和遷移。

結論:本研究結果提示,異丙酚抑制神經幹細胞的增殖,分化和遷移,而這些效應部分由 CaMkII、pS485、AMPK、ATF5 信號通路調節。

（劉碧瑩 譯　陳傑 校）

Background: Propofol can cause degeneration of developing brain cells and subsequent long-term learning or memory impairment. However, at the early stage of embryonic development, the molecular mechanism of propofol-induced inhibition in neural stem cells (NSCs) neurogenesis is still unclear. The aim of this study was to determine the role of propofol in NSCs neurogenesis and, more importantly, to explore the underlying mechanism.
Methods: First, a single intraperitoneal injection of propofol was performed in pregnant mice, and 6 hours after administration of propofol, the hippocampus RNA and the protein of the embryos' brains was extracted to analyze the expression of neuron-specifc markers. Second, the primary NSCs were isolated from the hippocampus of mouse embryonic brain and then treated with propofol for cell viability, immunostaining, and transwell assays; more importantly, we performed RNA sequencing (RNA-seq) and q-reverse transcription polymerase chain reaction assays to identify genes regulated by propofol; the Western blot, small interfering RNA (SiRNA), and luciferase reporter assays were used to study the effects of propofol on calmodulin-dependent protein kinase (CaMk) II/5' adenosine monophosphate-activated protein kinase (AMPK)/activating transcription factor 5 (ATF5) signaling pathway.
Results: Our results indicated that propofol treatment could inhibit the proliferation, migration, and differentiation of NSCs. The results of RNA-seq assays showed that propofol treatment resulted in downregulation of a group of Ca2+-dependent genes. The following mechanism studies showed that propofol regulates the proliferation, differentiation, and migration of NSCs through the CaMkII/phosphorylation of serine at amino acid position 485 (pS485)/AMPK/ATF5 signaling pathway.
Conclusions: The results from study demonstrated that propofol inhibits the proliferation, differentiation, and migration of NSCs, and these effects are partially mediated by CaMkII/pS485/AMPK/ATF5 signaling pathway.

體外迴圈過程中的抗凝治療與肝素抵抗：心血管麻醉醫師協會會員調查 Anticoagulation Management and Heparin Resistance During Cardiopulmonary Bypass: A Survey of Society of Cardiovascular Anesthesiologists Members

Sniecinski, Roman M. MD, MSc*; Bennett-Guerrero, Elliott MD†; Shore-Lesserson, Linda MD‡

Anesthesia & Analgesia: 2019 129 e41-e44

我們調查了心血管麻醉醫師協會成員關於體外迴圈中的抗凝及對肝素抵抗的態度。在550 名受試者（占應答率的 18.5%）中，74.9%（95%可信區間為 71.3%-78.5%）根據經驗按

公斤體重使用了肝素劑量，70.7%（95%可信區間為 66.9%-74.5%）以啟動凝血時間（ACT）400 或 480 秒作為開始體外迴圈的抗凝目標。值得注意的是，17.1%（95%可信區間為 13.9%-20.2%）的受訪者報告啟動凝血時間目標低於 2018 年胸外科醫師學會/心血管麻醉醫師學會/美國體外技術學會指南建議的目標，或根本未能監測肝素的有效性。當遇到肝素抵抗時，54.2%的受試者(95%可信區間為 50.0%-58.4%)將抗凝血酶複合物作為一線治療手段。
We surveyed Society of Cardiovascular Anesthesiologists members regarding anticoagulation practices for cardiopulmonary bypass and attitudes on heparin resistance. Of 550 respondents (18.5% response rate), 74.9% (95% CI, 71.3%-78.5%) used empiric weight-based dosing of heparin, and 70.7% (95% CI, 66.9%-74.5%) targeted an activated clotting time of either 400 or 480 seconds to initiate cardiopulmonary bypass. Of note, 17.1% (95% CI, 13.9%-20.2%) of respondents reported activated clotting time targets lower than those recommended by recent 2018 Society of Thoracic Surgeons/Society of Cardiovascular Anesthesiologists/American Society of Extracorporeal Technology guidelines or failed to monitor heparin effects at all. When heparin resistance was encountered, 54.2% of respondents (95% CI, 50.0%-58.4%) administered antithrombin concentrates as a first-line therapy.
（吳潔譯 李士通校）

在獨立的門診手術機構中接受癌症手術的阻塞性睡眠呼吸暫停患者的預後和安全性
Outcomes and Safety Among Patients With Obstructive Sleep Apnea Undergoing Cancer Surgery Procedures in a Freestanding Ambulatory Surgical Facility
Szeto, Betsy MPH*; Vertosick, Emily A. MPH†; Ruiz, Karin RT*; Tokita, Hanae MD*; Vickers, Andrew PhD†; Assel, Melissa MS†; Simon, Brett A. MD, PhD*; Twersky, Rebecca S. MD, MPH*
Anesthesia & Analgesia: 2019 129 360-368

背景：患有阻塞性睡眠呼吸暫停（OSA）的患者圍手術期嚴重併發症的風險可能會增加。對於患有 OSA 的患者進行的門診手術的適用性仍然存在爭議，一些國家指導方針要求更多的證據來評估臨床顯著的結果。在本研究中，我們調查了 OSA 狀態（STOP-BANG 量表風險，或早前已診斷的患者）與在獨立門診手術室接受癌症手術的患者的短期結果和安全性之間的關係。
方法：我們對所有在 Josie Robertson 手術中心進行手術的患者進行了回顧性分析，該中心是 Sloan Kettering 癌症紀念中心的獨立式門診手術中心。手術包括較複雜的通常患者需要延長恢復時間至過夜的門診手術，如乳房切除術、甲狀腺切除術、微創子宮切除術、前列腺切除術和腎切除術，以及其他典型的日間手術。單變數和多變數分析均用於評估 OSA 風險與手術後 30 天內轉運到總院、急診中心就診和醫院再入院（主要結果）以及住院時間和出院時間（次要結果）之間的關係。多變數模型根據年齡、美國麻醉師學會評分（ASA 評分）、機器人手術和麻醉方式（全身麻醉或監護性麻醉）進行了調整，並根據住院時間和出院時間的結果對手術開始時間進行了調整。採用 χ 檢驗評估 OSA 風險與呼吸事件和使用器械保證通氣之間的關係。
結果：在分析中的 5721 例患者中，526 例（9.2%）被診斷為 OSA，或有中度或高度 OSA 風險。在比較高風險或已確診為 OSA 的患者與低或中度 OSA 風險的患者時，無論他們接受日間手術（P=0.2）還是門診手術（P=0.3），我們並未發現其住院時長存在差異的證據。儘管高危或確診 OSA 患者術後呼吸事件發生率高於中度風險患者（P=0.004），但兩組之間的轉院率並無

顯著差異（風險差異為 0.78%；95%CI 為-0.43%-2%；P=0.2）。在多變數分析中，沒有證據表明在比較高危患者或確診為高危患者時，急診中心就診率（調整後的風險差異為 1.4%；95%CI 為-0.68%-3.4%；P=0.15）或 30 天內再入院率（調整後的風險差異為 1.2%；95%CI 為-0.40%-2.8%；P=0.077）增加。根據上述一系列可信區間（CI），轉院、再入院和就診急診中心的臨床相關事件不可能增加。

結論：我們的研究結果有助於證明中度風險、高危或診斷為 OSA 的患者可以安全地接受日間和門診腫瘤手術並不會增加住院時長或住院醫療負擔，並同樣可以避免不良的術後併發症。我們的研究結果支援幾個國家 OSA 指南，重點關注術前識別 OSA 患者，以及用於圍手術期管理和術後監測的臨床路徑。

（吳潔譯 李士通校）

BACKGROUND: Patients with obstructive sleep apnea (OSA) may be at increased risk for serious perioperative complications. The suitability of ambulatory surgery for patients with OSA remains controversial, and several national guidelines call for more evidence that assesses clinically significant outcomes. In this study, we investigate the association between OSA status (STOP-BANG risk, or previously diagnosed) and short-term outcomes and safety for patients undergoing cancer surgery at a freestanding ambulatory surgery facility.

METHODS: We conducted a retrospective analysis of all patients having surgery at the Josie Robertson Surgery Center, a freestanding ambulatory surgery facility of the Memorial Sloan Kettering Cancer Center. Surgeries included more complex ambulatory extended recovery procedures for which patients typically stay overnight, such as mastectomy, thyroidectomy, and minimally invasive hysterectomy, prostatectomy, and nephrectomy, as well as typical outpatient surgeries. Both univariate and multivariable analyses were used to assess the association between OSA risk and transfer to the main hospital, urgent care center visit, and hospital readmission within 30 days postoperatively (primary outcomes) and length of stay and discharge time (secondary outcomes). Multivariable models were adjusted for age, American Society of Anesthesiologists score, robotic surgery, and type of anesthesia (general or monitored anesthesia care) and also adjusted for surgery start time for length of stay and discharge time outcomes. χ tests were used to assess the association between OSA risk and respiratory events and device use.

RESULTS: Of the 5721 patients included in the analysis, 526 (9.2%) were diagnosed or at moderate or high risk for OSA. We found no evidence of a difference in length of stay when comparing high-risk or diagnosed patients with OSA to low- or moderate-risk patients whether they underwent outpatient (P = .2) or ambulatory extended recovery procedures (P = .3). Though a greater frequency of postoperative respiratory events were reported in high-risk or diagnosed patients with OSA compared to moderate risk (P = .004), the rate of hospital transfer was not significantly different between the groups (risk difference, 0.78%; 95% CI, -0.43% to 2%; P = .2). On multivariable analysis, there was no evidence of increased rate of urgent care center visits (adjusted risk

difference, 1.4%; 95% CI, -0.68% to 3.4%; P = .15) or readmissions within 30 days (adjusted risk difference, 1.2%; 95% CI, -0.40% to 2.8%; P = .077) when comparing high-risk or diagnosed OSA to low- or moderate-risk patients. Based on the upper bounds of the CIs, a clinically relevant increase in transfers, readmissions, and urgent care center visits is unlikely.

CONCLUSIONS: Our results contribute to the body of evidence supporting that patients with moderate-risk, high-risk, or diagnosed OSA can safely undergo outpatient and advanced ambulatory oncology surgery without increased health care burden of extended stay or hospital admission and avoiding adverse postoperative outcomes. Our results support the adoption of several national OSA guidelines focusing on preoperative identification of patients with OSA and clinical pathways for perioperative management and postoperative monitoring

羅呱卡因在 2 個脂質體修飾體系中的臨床前評價

Preclinical Evaluation of Ropivacaine in 2 Liposomal Modified Systems

Rennó, Carolina C. MSc*; Papini, Juliana Z. B. PhD*; Cereda, Cintia Maria Saia PhD†; Martinez, Elizabeth PhD†; Montalli, Victor Angelo PhD†; de Paula, Eneida PhD‡; Pedrazzoli Júnior, José PhD*; Calafatti, Silvana Aparecida PhD*; Tofoli, Giovana Radomille PhD†

Anesthesia & Analgesia: 2019 129 387-396

背景：我們的研究小組最近開發了離子梯度脂質體，並以內含 2%或 0.75%的羅呱卡因（RVC）的聯合供體和受體的囊泡方式存在。為了尋找這種新型 RVC 藥物在術後鎮痛中的應用，我們評估了其產生的麻醉持續時間、藥代動力學和以及其引起的組織反應。

方法：本研究中使用的製劑是 PH5.5 的含有醋酸鈉緩衝液的大的多泡囊（LMVV），或以 LMVV 作為供體，以大的單泡囊（LUVs）作為受體，外部 PH 為 7.4 的聯合體。Wistar 大鼠分為 6 組（n=6），分別給予 6 種不同配方的 RVC（LMVV RVC 0.75%，LMVV/LUVRVC 0.75%，LMVV RVC 2%，LMVV/LUVRVC2%，0.75%RVC，2%RVC_）0.4ml 行坐骨神經阻滯。為了驗證麻醉效果，動物接受了疼痛壓力測試，並監測了運動阻滯情況 。阻滯後 2 天和 7 天，對坐骨神經周圍組織的組織病理學進行評估。將大鼠（n=6）後爪切口周邊注射 6 種不同配方製劑後使用 von frey 動物測痛儀通過退縮反應測量機械性傷害高敏反應情況。最後，紐西蘭白兔（n=6）使用 6 種不同配方 RVC 製劑中的 1 種接受坐骨神經阻滯(3ml)。注射前(0 分鐘)和注射後 15、30、45、60、90、120、180、240、300、360、420、480 和 540 分鐘分別採集血樣。採用三節四極質譜儀測定 RVC 血漿水準。

結果：與普通 RVC 溶液相比，所有脂質體配方的感覺阻滯持續時間和強度更長（$p<0.05$）。組織病理學顯示陽性對照組（10%利多卡因）的毒性高於所有 RVC 配方（$p<0.05$）。後爪切口後，所有動物均表現出切口後超敏反應，脂質體製劑表現出更長的鎮痛時間（$p<0.05$）。LMVV RVC0.75%比剩餘的 RVC 0.75%的製劑達到最大濃度所需和平均停留時間的時間更長($p<0.05$)，因此，由於該脂質體系統的緩慢釋放，LMVV 能夠降低 RVC 的全身暴露量。

結論：由於脂質體緩慢釋放 RVC，所有含有 0.75%RVC 的新型脂質體配方製劑都能夠改變藥代動力學並延長麻醉作用時間，而不會對局部組織產生明顯的毒性作用。

（吳潔譯 李士通校）

BACKGROUND: Our research group has recently developed liposomes with ionic gradient and in a combined manner as donor and acceptor vesicles

containing ropivacaine (RVC; at 2% or 0.75%). Looking for applications of such novel formulations for postoperative pain control, we evaluated the duration of anesthesia, pharmacokinetics, and tissue reaction evoked by these new RVC formulations.

METHODS: The formulations used in this study were large multivesicular vesicle (LMVV) containing sodium acetate buffer at pH 5.5 or in a combined manner with LMVV as donor and large unilamellar vesicles (LUVs) as acceptor vesicles with an external pH of 7.4. Wistar rats were divided into 6 groups (n = 6) and received sciatic nerve block (0.4 mL) with 6 formulations of RVC (LMVVRVC0.75%, LMVV/LUVRVC0.75%, LMVVRVC2%, LMVV/LUVRVC2%, RVC 0.75%, and RVC 2%). To verify the anesthetic effect, the animals were submitted to the pain pressure test and the motor block was also monitored. Histopathology of the tissues surrounding the sciatic nerve region was also assessed 2 and 7 days after treatment. Rats (n = 6) were submitted to a hind paw incision, and mechanical hypersensitivity was measured via the withdrawal response using von Frey filaments after injection of the 6 formulations. Finally, New Zealand white rabbits (n = 6) received sciatic nerve block (3 mL) with 1 of the 6 formulations of RVC. Blood samples were collected predose (0 minutes) and at 15, 30, 45, 60, 90, 120, 180, 240, 300, 360, 420, 480, and 540 minutes after injection. RVC plasma levels were determined using a triple-stage quadrupole mass spectrometer.

RESULTS: Duration and intensity of the sensory block were longer with all liposomal formulations, when compared to the plain RVC solution ($P < .05$). Histopathological evaluation showed greater toxicity for the positive control (lidocaine 10%), when compared to all formulations ($P < .05$). After the hind paw incision, all animals presented postincisional hypersensitivity and liposomalformulations showed longer analgesia ($P < .05$). LMVVRVC0.75% presented higher time to reach maximum concentration and mean residence time than the remaining formulations with RVC 0.75% ($P < .05$), so LMVV was able to reduce systemic exposure of RVC due to slow release from this liposomal system.

CONCLUSIONS: All new liposomal formulations containing 0.75% RVC were able to change the pharmacokinetics and enhance anesthesia duration due to slow release of RVC from liposomes without inducing significant toxic effects to local tissues.

氧儲備指數：新變數的驗證

Oxygen Reserve Index: Validation of a New Variable

Vos, Jaap Jan MD, PhD*; Willems, Cornelis H. MD*; van Amsterdam, Kai MSc*; van den Berg, Johannes P. MD*; Spanjersberg, Rob*; Struys, Michel M. R. F. MD, PhD, FRCA*,†; Scheeren, Thomas W. L. MD, PhD*

Anesthesia & Analgesia: 2019 129 409-415

背景：在正常和高氧狀態下，脈搏血氧飽和度通常大於 97%，限制了其臨床應用。新的氧儲備指數（ORI），是一個在 100-200 mm Hg 壓力範圍內溶解於動脈血中氧分壓（PaO2）的相對指標，可能實現獲得對氧狀態的額外監測。

方法：在這項前瞻性驗證干預研究中，20 名健康志願者通過密閉面罩呼吸標準化的範圍從輕度缺氧（吸入氧分數為 0.14）到高氧（吸入氧分數為 1.0）濃度的氧氣。用 2 個手指感測

器，採用多波長脈衝共血氧法無創測量 ORI。將這些 ORI 值（無單位值，範圍為 0.00-1.00）與測量的 PaO_2 值進行比較。重複測量相關分析用於評估 ORI/PaO_2 關係。採用四象限圖評估 ORI 的趨勢。計算受試者操作特性曲線下的面積，以評估對缺氧的預測（缺氧定義為低 PaO2，<100 mm Hg）。

結果：在ORI敏感範圍內，兩個感測器的ORI和PaO2均呈強正相關（r=0.78和0.83；p<0.0001）。在這一範圍內，PaO_2 的 ORI 趨勢良好（一致率為 94%）。PaO_2<100 mmHg 的預測也很好，受試者工作特性曲線下面積為 0.91%，敏感性為 99%，特異性為 82%。

結論：在這項前瞻性志願者驗證研究中，發現 PaO_2 和 ORI 之間存在強且正向的相關性，並且具有良好的趨勢分析能力。基於這些資料，將來將 ORI 作為一種連續無創監測工具，可能是可靠的用於評估接受吸氧治療患者的氧合狀態的工具。

（吳潔譯 李士通校）

BACKGROUND: Pulse oximetry-derived oxygen saturation is typically >97% in normoxia and hyperoxia, limiting its clinical use. The new Oxygen Reserve Index (ORi), a relative indicator of the partial pressure of oxygen dissolved in arterial blood (PaO2) in the range of 100-200 mm Hg, may allow additional monitoring of oxygen status.

METHODS: In this prospective validation intervention study, 20 healthy volunteers were breathing standardized oxygen concentrations ranging from mild hypoxia (fraction of inspired oxygen = 0.14) to hyperoxia (fraction of inspired oxygen = 1.0) via a tight-fitting face mask. ORi was measured noninvasively by multiwavelength pulse co-oximetry using 2 finger sensors. These ORi values (unitless scale, 0.00-1.00) were compared with measured PaO2 values. Repeated-measurements correlation analysis was performed to assess the ORi/PaO2 relationship. ORi trending ability was assessed using a 4-quadrant plot. The area under the receiver operating characteristics curve was calculated to assess the prediction of hypoxia (low-ranged PaO2, <100 mm Hg).

RESULTS: Within the ORi-sensitive range, a strong positive correlation was found between ORi and PaO2 for both sensors (R = 0.78 and 0.83; P < .0001). ORi trending of PaO2 was good within this range (concordance rate = 94%). The prediction of PaO2 <100 mm Hg was also good, with an area under the receiver operating characteristics curve of 0.91 and 99% sensitivity and 82% specificity.

CONCLUSIONS: In this prospective volunteer validation study, a strong and positive correlation between PaO2 and ORi was found, together with a good trending ability. Based on these data, the future use of ORi as a continuous noninvasive monitoring tool for assessing oxygenation status in patients receiving supplemental oxygen might be supported.

不依賴于外周抗傷害性作用，抑制脂肪酸醯胺水解酶可改善神經病理性疼痛大鼠模型的抑鬱樣行為。

Inhibition of Fatty Acid Amide Hydrolase Improves Depressive-Like Behaviors Independent of Its Peripheral Antinociceptive Effects in a Rat Model of Neuropathic Pain

Jiang, Hai-xia MD[*,†]; Ke, Bo-wen PhD[*,‡]; Liu, Jin MD[*,‡]; Ma, Gang MD[§]; Hai, Ke-rong MD[‖]; Gong, De-ying PhD[‡]; Yang, Zheng PhD[¶]; Zhou, Cheng PhD[*,‡]

Anesthesia & Analgesia: 2019 129 587-597

背景：神經病理性疼痛常與抑鬱症有關。通過脂肪酸醯胺水解酶（FAAH）抑制劑增強內源性大麻素可減輕動物模型中的神經病理性疼痛和由其應激誘導的抑鬱樣行為。然而，尚不清楚FAAH抑制劑是否能通過其抗強迫症的作用減輕神經病理性疼痛引起的抑鬱。

方法：使用全身性FAAH抑制劑URB597（腹腔內注射5.8 mg/kg/d）或使用外周作用的FAAH抑制劑URB937（腹腔內注射1.6 mg/kg/d）(n=11-12)治療成年雄性Wistar大鼠坐骨神經慢性收縮性損傷（CCI）。治療從手術後第15天開始，持續15天。手術前和CCI後28天，通過Von Frey試驗(Von Frey纖毛機械刺激針測痛儀)檢查機械性退縮閾值。經15天治療後，通過強迫游泳試驗（FST）和新奇抑制攝食實驗（NSF）評估抑鬱樣行為。採用液相色譜法和質譜法測定了海馬中阿南達胺和 2-花生醯甘油酯的含量。採用免疫組化方法對新生細胞的增殖、分化和存活等海馬神經發生進行了評價。

結果：CCI 損傷後，大鼠出現明顯的傷害性和抑鬱性行為症狀，表現為 Von Frey 試驗中的持續性機械超敏反應，FST中的靜止時間顯著延長（對照組：84.2±13.4秒，CCI組:137.9±18.8 秒；P<0.001），並且持續時間延長。NSF 實驗的進食時間延遲（對照組：133.4±19.4秒，CCI組：234.9±33.5秒；P<0.001）。對於接受治療的CCI大鼠，與安慰劑對照組相比，痛閾值增加了urb597（3.1±1.0 vs 11.2±1.2 g；p<0.001）和urb937（3.1±1.0 vs 12.1±1.3 g；p<0.001）。FST的固定時間減少了urb597（135.8±16.6 vs 85.3±17.2秒；p<0.001），而不是urb937（135.8±16.6 vs 129.6±17.8秒；p=0.78）。URB597使NSF實驗的攝食潛伏期縮短（235.9±30.5 vs 131.8±19.8秒；p<0.001），而URB937並無此效應（235.9±30.5 vs 232.2±33.2秒；p=0.72）。同時，CCI降低了海馬中增殖細胞的數量，減少了新成熟神經元的存活率。URB597而不是URB937治療改善了這些細胞缺陷。

結論：FAAH 的抑制作用可以改善由其周圍抗傷害作用的神經病變獨立作用所引起的抑鬱樣行為。海馬體的神經發生增強可能得益於URB597的抗抑鬱作用。

（吳潔譯 李士通校）

BACKGROUND: Neuropathic pain is often associated with depression. Enhancing endocannabinoids by fatty acid amide hydrolase (FAAH) inhibitors relieves neuropathic pain and stress-induced depressive-like behaviors in animal models. However, it is unclear whether FAAH inhibitor can relieve neuropathic pain-induced depression by or not by its antinociceptive effects.

METHODS: Adult male Wistar rats with chronic constriction injury (CCI) to the sciatic nerve were treated with the systemic FAAH inhibitor URB597 (5.8 mg·kg·day, intraperitoneally) or peripherally acting FAAH inhibitor URB937 (1.6 mg·kg·d, intraperitoneally; n = 11-12). The treatment was applied from the 15th day after surgery and continued for 15 days. Mechanical withdrawal threshold was examined by Von Frey test before surgery and on the 28th day after CCI. Depressive-like behaviors were evaluated by forced swimming test (FST) and novelty-suppressed feeding (NSF) after 15-day treatment. The levels of anandamide and 2-arachidonoylglycerol in hippocampus were examined by liquid chromatography and mass spectrometry. Hippocampal neurogenesis including proliferation, differentiation, and survival of newborn cells was assessed by immunohistochemistry.

RESULTS: After CCI injury, the rats developed significantly nociceptive

and depressive-like behaviors, indicated by persistent mechanical hypersensitivity in Von Frey test, significantly prolonged immobility time in FST (sham: 84.2 ± 13.4 seconds versus CCI: 137.9 ± 18.8 seconds; P < .001), and protracted latency to feed in NSF (sham: 133.4 ± 19.4 seconds versus CCI: 234.9 ± 33.5 seconds; P < .001). For the CCI rats receiving treatment, compared to vehicle placebo group, pain threshold was increased by both URB597 (3.1 ± 1.0 vs 11.2 ± 1.2 g; P < .001) and URB937 (3.1 ± 1.0 vs 12.1 ± 1.3 g; P < .001). Immobility time of FST was reduced by URB597 (135.8 ± 16.6 vs 85.3 ± 17.2 seconds; P < .001) but not by URB937 (135.8 ± 16.6 vs 129.6 ± 17.8 seconds; P = .78). Latency to feed in NSF was also reduced by URB597 (235.9 ± 30.5 vs 131.8 ± 19.8 seconds; P < .001) but not by URB937 (235.9 ± 30.5 vs 232.2 ± 33.2 seconds; P = .72). Meanwhile, CCI decreased the number of proliferating cells and reduced survival of new mature neurons in hippocampus. URB597 but not URB937 treatment improved these cellular deficits.

CONCLUSIONS: Inhibition of FAAH can improve depressive-like behaviors induced by neuropathicpain independent of its peripheral antinociceptive action. Enhanced neurogenesis in hippocampus might contribute to the antidepressive effects of URB597.

分段回歸和差異方法：評估醫療保健系統變化的影響

Segmented Regression and Difference-in-Difference Methods: Assessing the Impact of Systemic Changes in Health Care

Mascha, Edward J. PhD[*,†]; Sessler, Daniel I. MD[†]

Anesthesia & Analgesia: 2019 129 618-633

圍術期的研究者和專業人員越來越多地試圖評估系統性實踐改變的實施是否比以往的常規做法更能改善預後。集群隨機試驗是評估系統實踐變化的最佳實驗設計，但往往不切實際難以；因此，研究者通常選擇前後設計。在這個統計大循環中，我們首先討論了前後設計固有的偏差，包括由於時間完全分開的週期造成的混淆、均值回歸、霍桑效應及其他情況。其中許多偏差至少可以通過我們討論的恰當的設計和分析得到部分解決。我們的重點是不需要同期對照組的中斷時間序列的分段回歸；我們還提出了包括差分、階梯楔形和聚類隨機化等備選設計方案。良好的分段回歸需要在每個週期內有足夠數量的時間點，以及一組潛在的混雜變數。該方法比較了干預前和干預後隨時間的變化、干預開始時的結果差異以及干預觀察到的趨勢與無干預預測的趨勢。不同方法之間的差異增加了一個並行控制，使得推理更加有力。如果做得好，儘管仍然需要假設和存在局限性，但所討論的方法可以對干預的效果進行有力的推斷。該方法通過一項中斷時間序列研究來證明，在本項研究中，內科醫師組成的成人醫療急救小組由麻醉醫生負責，以期改善預後。

（吳潔譯 李士通校）

Perioperative investigators and professionals increasingly seek to evaluate whether implementing systematic practice changes improves outcomes compared to a previous routine. Cluster randomized trials are the optimal design to assess a systematic practice change but are often impractical; investigators, therefore, often select a before-after design. In this Statistical Grand Rounds, we first

discuss biases inherent in a before-after design, including confounding due to periods being completely separated by time, regression to the mean, the Hawthorne effect, and others. Many of these biases can be at least partially addressed by using appropriate designs and analyses, which we discuss. Our focus is on segmented regression of an interrupted time series, which does not require a concurrent control group; we also present alternative designs including difference-in-difference, stepped wedge, and cluster randomization. Conducting segmented regression well requires a sufficient number of time points within each period, along with a robust set of potentially confounding variables. This method compares preintervention and postintervention changes over time, divergences in the outcome when an intervention begins, and trends observed with the intervention compared to trends projected without it. Difference-in-difference methods add a concurrent control, enabling yet stronger inference. When done well, the discussed methods permit robust inference on the effect of an intervention, albeit still requiring assumptions and having limitations. Methods are demonstrated using an interrupted time series study in which anesthesiologists took responsibility for an adult medical emergency team from internal medicine physicians in an attempt to improve outcomes.