

## 心血管麻醉醫師學會對心臟手術患者圍術期出血及止血管理的臨床實踐的改善

### 建議

#### Society of Cardiovascular Anesthesiologists Clinical Practice Improvement Advisory for Management of Perioperative Bleeding and Hemostasis in Cardiac Surgery Patients

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術後出血是心臟手術常見且嚴重的併發症，可造成多種血液製品的輸注，增加相關併發症的發病率及術後死亡率。儘管已經出臺了大量關於心臟手術患者血液管理的指南及共識，但據調查，醫生們並未嚴格遵守指南，因而患者實際的輸血管理存在明顯差異。此外，在過去十年來，雖然床旁凝血功能監測的應用和濃縮凝血因數等新的圍術期止血治療的實施明顯增加，但這些新方法並不能在所有機構中得到廣泛應用。因此，過去十年間，即使我們付出了不懈的努力，心臟手術患者的血液製品輸注僅有小幅下降，並且高危患者仍 $\geq 50\%$ 。基於上述不足，為積極回應監管和立法機關的新要求，心血管麻醉醫師協會（SCA）成立了心臟手術血液保護工作組，以期組織、總結和傳播心臟手術患者血液管理的最佳實踐知識。通過工作組對現有的心臟手術患者血液管理的相關指南、共識及建議的收集回顧，本文囊括了其對聲明及流程的總結。我們的最終目標是創造一個便利的可教學的動態資源，從而提高治療團隊對現有心臟患者血液管理的最佳循證實踐的依從性。

(許芳霞 譯 李金寶校)

Bleeding after cardiac surgery is a common and serious complication leading to transfusion of multiple blood products and resulting in increased morbidity and mortality. Despite the publication of numerous guidelines and consensus statements for patient blood management in cardiac surgery, research has revealed that adherence to these guidelines is poor, and as a result, a significant variability in patient transfusion practices among practitioners still remains. In addition, although utilization of point-of-care (POC) coagulation monitors and the use of novel therapeutic strategies for perioperative hemostasis, such as the use of coagulation factor concentrates, have increased significantly over the last decade, they are still not widely available in every institution. Therefore, despite continuous efforts, blood transfusion in cardiac surgery has only modestly declined over the last decade, remaining at  $\geq 50\%$  in high-risk patients. Given these limitations, and in response to new regulatory and legislature requirements, the Society of Cardiovascular Anesthesiologists (SCA) has formed the Blood Conservation in Cardiac Surgery Working Group to organize, summarize, and disseminate the available best-practice knowledge in patient blood management in cardiac surgery. The current publication includes the summary statements and algorithms designed by the working group, after collection and review of the existing guidelines, consensus statements, and recommendations for patient blood management practices in cardiac surgery patients. The overall goal is creating a dynamic resource of easily accessible educational material that will help to increase and improve compliance with the existing evidence-based best practices of patient blood management by cardiac surgery care teams.

### 紅肉綜合征和麻醉有何關係？ $\alpha$ -半乳糖綜合征的圍術期管理

#### What Does a Red Meat Allergy Have to Do With Anesthesia? Perioperative Management of Alpha-Gal Syndrome

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在過去的幾十年裡，一種稱為  $\alpha$ -半乳糖過敏或  $\alpha$ -半乳糖綜合征的新型過敏性綜合征越來越被人們所關注，即通常認為的紅肉過敏症。我們通過回顧一系列有關  $\alpha$ -半乳糖綜合征的背景，相關藥物和醫療器械副作用的文章，完成了這篇綜述。 $\alpha$ -半乳糖綜合征與寡糖半乳糖  $\alpha$ -1, 3-半乳糖特異性 IgE 相關，寡糖半乳

糖  $\alpha$ -1,3-半乳糖在非峽鼻猿類動物的肌肉和組織中表達。半乳糖綜合征由孤星蜱蟲叮咬所誘發，並與西妥昔單抗引起的即髮型過敏反應和食用紅肉後引起的遲髮型超敏反應相關。目前一些對於含有  $\alpha$ -半乳糖的藥物和醫療器械過敏的現象也逐漸被認識到，這主要是由於藥物和醫療器械製備過程中的一些凝膠或硬脂酸等非活性物質所引起。這種過敏反應可能會被多種方式所記錄，也可能來自于患者的非專業表述，鑒於其嚴重的影響，麻醉醫生需保持高度警惕，及時發現這種綜合征。 $\alpha$ -半乳糖綜合征給麻醉師帶來了許多獨特的挑戰，包括正確識別這些患者以及為其正確選擇不會引起過敏的麻醉藥物和輔助性藥物。

（許芳霞譯 李金寶校）

Over the past decade, there has been a growing awareness of a new allergic syndrome known as alpha-gal allergy or alpha-gal syndrome, commonly recognized as a red meat allergy. We performed a review of the literature to identify articles that provide both background on this syndrome in general and any reports of reactions to medications or medical devices related to alpha-gal syndrome. Alpha-gal syndrome results from IgE to the oligosaccharide galactose- $\alpha$ -1,3-galactose, expressed in the meat and tissues of noncatarrhine mammals. It is triggered by the bite of the lone star tick and has been implicated in immediate-onset hypersensitivity to the monoclonal antibody cetuximab and delayed-onset hypersensitivity reactions after the consumption of red meat. There is growing recognition of allergic reactions in these patients to other drugs and medical devices that contain alpha-gal. Many of these reactions result from inactive substances that are part of the manufacturing or preparation process such as gelatin or stearic acid. This allergy may be documented in a variety of ways or informally reported by the patient, requiring vigilance on the part of the anesthesiologist to detect this syndrome, given its serious implications. This allergy presents a number of unique challenges to the anesthesiologist, including proper identification of a patient with alpha-gal syndrome and selection of anesthetic and adjunctive medications that will not trigger this allergy.

**術前認知篩查有助於預測體弱人群住院時間的回顧性病例對照研究**

**A Preoperative Cognitive Screening Test Predicts Increased Length of Stay in a Frail Population: A Retrospective Case - Control Study**

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**背景：**患者體弱與圍手術期不良結局相關，如增加主要併發症、死亡率和延長住院時間等。我們試圖闡明術前簡易智力狀態評估在預測高危體弱人群圍手術期不良結局風險中所起的作用。

**方法：**在這項回顧性病例對照研究中，滿足年齡 > 60 歲、臥床、或服用藥物 > 5 種這三項的至少其中之一，且術前做過握力，步行速度和簡易智力狀態評估的人群被納入該研究。然後通過埃默里大學臨床資料庫提取相關資訊及其它圍術期和術後結局的各種資料。

**結果：**有 1132 例接受各種外科手術的患者的資料可用，其中 747 名患者的預期住院時間延長，其預期值 > 1 的機率的增加與其術前簡易智力狀態評分的異常相關（比值比，1.52；95%可信區間，1.05-2.19）；P = .025）。重症監護病房住院時間超過 3 天（P = .182）或出院自我照顧（P = .873）或再入院的風險（P = .104）均與建議智力狀態評分無相關性。基線血紅蛋白水準低與本研究所討論的 4 種結局中其中 2 種的風險增加相關。

**結論：**在高危體弱患者中，術前簡易智力狀態評估可能不夠靈敏，無法檢測出大多數不良結局之間的顯著差異。我們需要做進一步的工作來評估在這種情況下更嚴格的認知篩查是否有價值，並比較可以評估整體體弱狀況的工具。

（許芳霞譯 李金寶校）

**BACKGROUND:** Frailty is associated with adverse perioperative outcomes including major morbidity, mortality, and increased length of stay. We sought to elucidate the role that a preoperatively assessed Mini-Cog can

play in assessing the risk of adverse perioperative outcomes in a population at high risk of frailty.

**METHODS:** In this retrospective case-control study, patients who were >60 years of age, nonambulatory, or had >5 documented medications were preoperatively assessed for handgrip strength, walking speed, and Mini-Cog score. The Emory University Clinical Data Warehouse was then used to extract this information and other perioperative data elements and outcomes data.

**RESULTS:** Data were available for 1132 patients undergoing a wide variety of surgical procedures. For the subset of 747 patients with data for observed-to-expected length of stay, an abnormal Mini-Cog was associated with an increased odds of observed-to-expected >1 (odds ratio, 1.52; 95% CI, 1.05-2.19; P = .025). There was no association of abnormal Mini-Cog with intensive care unit length of stay >3 days (P = .182) discharge to home with self-care (P = .873) or risk of readmission (P = .104). Decreased baseline hemoglobin was associated with increased risk of 2 of the 4 outcomes studied.

**CONCLUSIONS:** In a high-risk pool of patients, Mini-Cog may not be sensitive enough to detect significant differences for most adverse outcomes. Further work is needed to assess whether cognitive screens with greater resolution are of value in this context and to compare tools for assessing overall frailty status.

## 行復蘇性主動脈球囊阻斷術的創傷患者的麻醉管理

### Anesthetic Management of Patients After Traumatic Injury With Resuscitative Endovascular Balloon Occlusion of the Aorta

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復蘇性血管內球囊閉塞術 (REBOA) 是針對軀體不可壓迫性出血的一種臨時性操作方法。據我們所知，這個單中心的簡報所提供的相關麻醉資料是迄今為止所發表的關於接受 REBOA 的患者中最豐富的。正如預期那樣，這些患者往往病情危重，表現為乳酸性酸中毒、低血壓、高血糖、體溫過低和凝血障礙。他們所有人都會在手術期間接受血液製品輸注，並且吸入的麻醉氣體少於同年齡健康患者的正常需要。本研究是 REBOA 患者的麻醉管理相關的臨床教育和研究的一個重要起點。

(許芳霞譯 李金寶校)

Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a temporizing maneuver for noncompressible torso hemorrhage. To our knowledge, this single-center brief report provides the most extensive anesthetic data published to date on patients who received REBOA. As anticipated, patients were critically ill, exhibiting lactic acidosis, hypotension, hyperglycemia, hypothermia, and coagulopathy. All patients received blood products during their index operations and received less inhaled anesthetic gas than normally required for healthy patients of the same age. This study serves as an important starting point for clinician education and research into anesthetic management of patients undergoing REBOA.

### 產科硬脊膜穿破後頭痛相關主要神經系統併發症的回顧性佇列研究

#### Major Neurologic Complications Associated With Postdural Puncture Headache in Obstetrics: A Retrospective Cohort Study

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產科硬膜外穿刺後頭痛 (PDHP) 的患者出現腦靜脈血栓、硬膜下血腫、細菌性腦膜炎、持續性頭痛或持續性腰痛的風險會增加。此外，急性產後疼痛如 PDHP 也可能導致產後抑鬱症。這項研究想要研究 PDHP 是否與產後主要神經系統及其他併發症的風險顯著增加相關。這項回顧性佇列研究納入了 2005 年 1 月至 2014 年 9 月期間在紐約州醫院採用椎管內麻醉的方法分娩的 1003803 名女性，主要結果為腦靜脈血栓形成和硬膜下血腫，四種次要結果為發生細菌性腦膜炎、抑鬱症、頭痛和腰痛。我們所研究的 PDPH 和併發症是指在分娩住院期間到分娩後 1 年內發現的。採用逆處理概率加權法估計校正比值比 (aORs) 和 95% 可信區間 (CIs)。在被研究的女性中，4808 人 (0.48%；95% CIs, 0.47–0.49) 表現為 PDHP，其中 264 例 (5.2%) 在再入院期間被確診，平均再入院的住院時間為 4 天。患 PDPH 產婦的腦靜脈血栓形成和硬膜下血腫的發生率明顯高於無 PDPH 的婦女 (分別為每 1000 例椎管內麻醉發生數為 3.12，即 1:320 vs 每 1000 例椎管內麻醉發生數

為 0.16，即 1:6250， $P < .001$ )。患 PDPH 產婦的四種次要結果的發生率也明顯高於無 PDPH 的產婦。腦靜脈血栓形成和硬膜下血腫發生率的 aORs 為 19.0 (95%CI，11.2–32.1)，細菌性腦膜炎的 aORs 為 39.7 (95%CI，13.6–115.5)，抑鬱症為 1.9 (95%CI，1.4–2.6)，頭痛為 7.7 (95%CI，6.5–9.0)，腰痛為 4.6 (95%CI，3.3–6.3)。其中 70% 的腦靜脈血栓形成和硬膜下血腫是在再入院時發現的，再入院的平均時間為 5 天。PDPH 與產後大幅度增加的主要神經系統併發症及其他併發症的風險相關，提示我們早期識別和治療產科麻醉相關併發症的重要性。

(許芳霞譯 李金寶校)

Increased risks of cerebral venous thrombosis or subdural hematoma, bacterial meningitis, persistent headache, and persistent low back pain are suggested in obstetric patients with postdural puncture headache (PDPH). Acute postpartum pain such as PDPH may also lead to postpartum depression. This study tested the hypothesis that PDPH in obstetric patients is associated with significantly increased postpartum risks of major neurologic and other maternal complications. This retrospective cohort study consisted of 1,003,803 women who received neuraxial anesthesia for childbirth in New York State hospitals between January 2005 and September 2014. The primary outcome was the composite of cerebral venous thrombosis and subdural hematoma. The 4 secondary outcomes were bacterial meningitis, depression, headache, and low back pain. PDPH and complications were identified during the delivery hospitalization and up to 1 year postdelivery. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were estimated using the inverse probability of treatment weighting approach. Of the women studied, 4808 (0.48%; 95% CI, 0.47–0.49) developed PDPH, including 264 cases (5.2%) identified during a readmission with a median time to readmission of 4 days. The incidence of cerebral venous thrombosis and subdural hematoma was significantly higher in women with PDPH than in women without PDPH (3.12 per 1000 neuraxial or 1:320 vs 0.16 per 1000 or 1:6250, respectively;  $P < .001$ ). The incidence of the 4 secondary outcomes was also significantly higher in women with PDPH than in women without PDPH. The aORs associated with PDPH were 19.0 (95% CI, 11.2–32.1) for the composite of cerebral venous thrombosis and subdural hematoma, 39.7 (95% CI, 13.6–115.5) for bacterial meningitis, 1.9 (95% CI, 1.4–2.6) for depression, 7.7 (95% CI, 6.5–9.0) for headache, and 4.6 (95% CI, 3.3–6.3) for low back pain. Seventy percent of cerebral venous thrombosis and subdural hematoma were identified

during a readmission with a median time to readmission of 5 days. PDPH is associated with substantially increased postpartum risks of major neurologic and other maternal complications, underscoring the importance of early recognition and treatment of anesthesia-related complications in obstetrics.

### **自發運動可恢復大鼠在生命早期異氟烷暴露後導致的空間記憶損傷**

#### **Voluntary Exercise Rescues the Spatial Memory Deficit Associated With Early Life Isoflurane Exposure in Male Rats**

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**背景：**大鼠在生命早期暴露於麻醉藥可導致其長期認知功能損傷。由居住環境、環境刺激和自發運動組成的環境豐富度可改善這一損傷。本研究中我們猜測僅運動這一項足以恢復圍產期麻醉暴露引起的認知損傷。

**方法：**雄性大鼠進行異氟醚 (Iso) 或空氣對照暴露，從出生後 7 天一直到出生後 21 天停止。隨後單獨分籠飼養，每個籠子裡有一個轉動的或固定的輪子。經過 3 周的鍛煉，動物們接受評估空間記憶和認知記憶的行為測試。在不同時間點處死動物，進行溴去氧尿苷 (BrdU) 標記或即時定量聚合酶鏈反應 (qRT-PCR) 檢測腦源性神經營養因數 (BDNF) 信使核糖核酸 (mRNA) 水準。

**結果：**Iso 停止暴露後的自發運動可減輕與圍產期 Iso 暴露相關的長期空間記憶缺陷。與其它組相比，Iso 暴露後非運動組的動物在巴恩斯迷宮探針試驗中未正確識別目標象限，在目標象限所花的時間不多 (單樣本 t 檢驗， $P = .524$ )，而其它組的大鼠均在目標象限的時間多 (單樣本 t 檢驗， $P$  異氟烷暴露後運動組 =  $.033$ ;  $P$  對照 =  $.004$ )。本次實驗中，我們沒有檢測到以前發現的 Iso 暴露後引起的識別記憶缺陷。與空氣暴露的非運動組相比，Iso 暴露後的非運動組大鼠成年海馬內 BrdU 的結合率降低 (Tukey  $P = .005$ )。自發運動可改善這種減少，



與 Iso 暴露後非運動組相比，Iso 暴露後的運動組大鼠成年海馬內 BrdU 的結合率增高 (Tukey  $P < .001$ )。自發運動和 Iso 暴露對海馬和大腦皮層的 BDNF mRNA 均無明顯影響 (皮層: F 運動 [1, 32] = 0.236,  $P = .631$ ; F 異氟烷暴露 [1, 32] = 0.038,  $P = .847$ ; F 相互作用 [1, 32] = 1.543,  $P = .223$ ; 海馬: F 運動 [1, 33] = 1.186,  $P = .284$ ; F 異氟烷 [1, 33] = 1.46,  $P = .236$ ; F 相互作用 [1, 33] = 1.78,  $P = .191$ )。

**結論：**自發運動可以恢復生命早期麻醉暴露所導致的 BrdU 減少，並減輕空間記憶的缺陷。本研究證明了在圍生期的麻醉暴露，僅環境豐富度中的運動這一項就可以恢復其行為表現。

(許芳霞譯 李金寶校)

**BACKGROUND:** Early life anesthesia exposure results in long-term cognitive deficits in rats. Environmental enrichment consisting of social housing, a stimulating environment, and voluntary exercise can rescue this deficit. We hypothesized that exercise alone is sufficient to rescue the cognitive deficit associated with perinatal anesthesia.

**METHODS:** Postnatal day 7 male rats (P7) underwent isoflurane (Iso) or sham exposure and were subsequently weaned at P21. They were then singly housed in a cage with a running wheel or a fixed wheel. After 3 weeks of exercise, animals underwent behavioral testing for spatial and recognition memory assessments. Animals were killed at various time points to accomplish either bromodeoxyuridine (BrdU) labeling or quantitative real-time polymerase chain reaction (qRT-PCR) to quantify brain-derived neurotrophic factor (BDNF) messenger ribonucleic acid (mRNA) levels.

**RESULTS:** Postweaning voluntary exercise rescued the long-term spatial memory deficit associated with perinatal Iso exposure. Iso-sedentary animals did not discriminate the goal quadrant, spending no more time than chance during the Barnes maze probe trial (1-sample  $t$  test,  $P = .524$ ) while all other groups did (1-sample  $t$  test,  $P_{\text{Iso-exercise}} = .033$ ;  $P_{\text{control [Con]-sedentary}} = .004$ ). We did not find a deficit in recognition memory tasks after Iso exposure as we observed previously. BrdU incorporation in the adult hippocampus of Iso-sedentary animals was decreased compared to sedentary controls (Tukey  $P = .005$ ). Exercise prevented this decrease, with Iso-exercise animals having more proliferation than Iso-sedentary (Tukey  $P < .001$ ). There was no effect of exercise or Iso on BDNF mRNA in

either the cortex or hippocampus (cortex:  $F_{\text{Exercise}}[1, 32] = 0.236$ ,  $P = .631$ ;  $F_{\text{Iso}}[1, 32] = 0.038$ ,  $P = .847$ ;  $F_{\text{Interaction}}[1, 32] = 1.543$ ,  $P = .223$ ; and hippocampus:  $F_{\text{Exercise}}[1, 33] = 1.186$ ,  $P = .284$ ;  $F_{\text{Iso}}[1, 33] = 1.46$ ,  $P = .236$ ;  $F_{\text{Interaction}}[1, 33] = 1.78$ ,  $P = .191$ ).

**CONCLUSIONS:** Exercise restores BrdU incorporation and rescues a spatial memory deficit after early life anesthesia exposure. This demonstrates sufficiency of exercise alone in the context of environmental enrichment to recover a behavioral phenotype after a perinatal insult.

## 開放性胸腹主動脈修復術中使用亞甲藍後脈搏血氧飽和度快速下降的特徵研究

Characterization of the Rapid Drop in Pulse Oximetry Reading After Intraoperative Administration of Methylene Blue in Open Thoracoabdominal Aortic Repairs

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本研究評估了 103 例接受開放性胸腹主動脈修復手術的患者在靜脈注射亞甲藍後血氧飽和度(SpO<sub>2</sub>)的變化情況。作者發現，在亞甲藍靜脈注射後 1 分鐘內，SpO<sub>2</sub> 下降了 49% (37%-81%，四分位間距[IQR])，並在大約 6 分鐘後完全恢復 (IQR 中位數 270 秒，180 秒-510 秒)。達到 SpO<sub>2</sub> 最低值的時間越短，其 SpO<sub>2</sub> 最低值越高 (Spearman r [95% 置信區間 {CI}], -0.03[-0.50 至 -0.13];  $P=0.001$ )。體表面積 (BSA) 與 SpO<sub>2</sub> 最低值呈正相關 (Spearman r [95% 置信區間，0.36[0.15-0.51];  $P<0.001$ )。

(陳思涵 譯 陳傑 校)

This study evaluates the changes of oxygen saturation

(SpO<sub>2</sub>) after intravenous administration of methylene blue in 103 patients undergoing open repair of thoracoabdominal aortic aneurysms. We found that SpO<sub>2</sub> decreased by a median (interquartile range [IQR]) of 49% (37%-81%) <1 minute after methylene blue administration and recovered completely after approximately 6 minutes-median (IQR) of 270 seconds (180-510). A shorter time to nadir SpO<sub>2</sub> was associated with a higher nadir (Spearman r [95% confidence interval {CI}], -0.32 [-0.50 to -0.13];  $P = .001$ ). Body surface area (BSA) was positively correlated with nadir SpO<sub>2</sub> (Spearman r [95% CI], 0.36 [0.15-0.51];  $P < .001$ ).

## 術後患者輸注 20% 白蛋白後長時血管內滯留的研究

Long Intravascular Persistence of 20% Albumin in Postoperative Patients

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**背景:** 由於外科手術導致的內皮糖萼層的分解 (脫落)，大型手術後患者血管內白蛋白的持續時間比健康志願者更短。

**方法：**在本次隨機臨床試驗中，15 位接受腹部開放手術術後 1 天（平均手術時間 5.9 小時）的患者和 15 位清醒的志願者在 30 分鐘內以恒定速率接受靜脈內輸注 3 mL/kg 的 20% 白蛋白。5 小時期間收集血和尿液標本，根據品質守恆定律計算輸注白蛋白分子的半衰期並根據血液稀釋和血漿白蛋白濃度血漿容量估計血漿容量擴充的半衰期。

**結果：**輸注結束時，外科術後患者和志願者的血漿稀釋增量分別為  $13.3\% \pm 4.9\%$ （平均值 $\pm$ 標準差）、 $14.2\% \pm 4.8\%$ （平均值相差-0.9、95%可信區間，-4.7 至 2.9；單因素方差分析， $P = 0.61$ ），相當於白蛋白輸入量的兩倍。外科手術患者和志願者中，輸注白蛋白分子在血管內的半衰期分別為 9.1(5.7-11.2)小時、6.0(5.1-9.0)小時(Mann-Whitney U 檢驗， $P = 0.26$ ；幾何平均差為 1.2，95%可信區間，0.8-2.0)。手術患者和志願者中的血漿容量擴充半衰期分別為 10.3（5.3-17.6；中位數和四分位數範圍）小時、7.6（3.5-9.0）小時（ $P = 0.10$ ；幾何平均差 1.5%，95%可信區間，0.8-2.8）。所有這些參數都與體重指數呈正相關（相關係數為 0.42-0.47），而年齡和性別均不影響結果。

**結論：**術後患者和健康志願者接受 20% 白蛋白的輸注可導致相似的長時血漿容量擴充效應。

（陳思涵 譯 陳傑 校）

**BACKGROUND:** Albumin may persist intravascularly for a shorter time in patients after major surgery than in healthy volunteers due to a surgery-induced breakdown (shedding) of the endothelial glycocalyx layer.

**METHODS:** In this nonrandomized clinical trial, an IV infusion of 3 mL/kg of 20% albumin was given at a constant rate during 30 minutes to 15 patients on the first day after major open abdominal surgery (mean operating time 5.9 h) and to 15 conscious volunteers. Blood samples and urine were collected during 5 h and mass balance calculations used to estimate the half-lives of the administered albumin molecules and the induced plasma volume expansion, based on measurements of hemodilution and the plasma albumin concentration.

**RESULTS:** At the end of the infusions, albumin had diluted the plasma volume by  $13.3\% \pm 4.9\%$  (mean  $\pm$  SD) in the postoperative patients and by  $14.2\% \pm 4.8\%$  in the volunteers (mean difference  $-0.9$ , 95% CI,  $-4.7$  to  $2.9$ ; 1-way ANOVA  $P = .61$ ), which amounted to twice the infused volume. The intravascular half-life of the infused albumin molecules was  $9.1$  ( $5.7$ - $11.2$ ) h in the surgical patients and  $6.0$  ( $5.1$ - $9.0$ ) h in the volunteers (Mann-Whitney U test,  $P = .26$ ; geometric mean difference  $1.2$ , 95% CI,  $0.8$ - $2.0$ ). The half-life of the plasma volume expansion was  $10.3$  ( $5.3$ - $17.6$ ; median and interquartile range) h in the surgical patients and  $7.6$  ( $3.5$ - $9.0$ ) h in the volunteers ( $P = .10$ ; geometric mean difference  $1.5$ , 95% CI,  $0.8$ - $2.8$ ). All of these parameters correlated positively with the body mass index (correlation coefficients being  $0.42$ - $0.47$ ) while age and sex did not affect the results.

**CONCLUSIONS:** Twenty percent albumin caused a long-lasting plasma volume expansion of similar magnitude in postoperative patients and volunteers.

### 寬頻和離散波長的近紅外光譜檢測細胞色素 aa<sub>3</sub> 降低水準的比較

Comparison of Broadband and Discrete Wavelength Near-Infrared Spectroscopy Algorithms for the Detection of Cytochrome aa<sub>3</sub> Reduction

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**背景：**電子傳遞鏈的末端成分細胞色素 aa<sub>3</sub> 根據其氧化態 (Cytox) 的差異可吸收不同程度的近紅外輻射 (NIR)，據此，理論上可使用近紅外光譜法 (NIRS) 將通過特定波長光的吸收值來測量生色團的濃度。一些 NIRS 演算法使用離散波長，而另一些演算法則分析近紅外波段 (即寬頻 NIRS)。本項研究的目的是測試離散波長和寬頻演算法測量 Cytox 變化 (主要結果) 的能力，並確定在分階段的缺氧氰化物模型中 (缺氧和氰化物對組織飽和有相反的影響，但兩者都會導致細胞色素減少)，離散波長 NIRS 演算法是否可以類似於寬頻 NIRS 演算法來測量細胞中的 Cytox 的含量。

**方法：**20 只 Sprague-Dawley 大鼠接受異氟烷麻醉、氣管插管和儀器監測，同時測量血壓、潮氣末二氧化碳濃度和動脈血氧飽和度。鹵素光源經顱透射近紅外輻射 (NIR)，將來自光源和顱骨的 NIR 傳輸到 2 個冷卻的電荷耦合器件光譜儀。使大鼠進入缺氧狀態 (吸入氧氣的分數，0.0)，直到動脈血氧飽和度降至 70%；恢復後，再靜脈注射氰化鈉 5 mg / kg，重複該迴圈直到大鼠發生心臟驟停。同時使用離散波長和寬頻 NIRS 演算法計算血紅蛋白和細胞色素 aa<sub>3</sub> 的相對濃度。

**結果：**缺氧可導致去氧血紅蛋白增加 ( $0.20$  任意單位[AUs]; 95%的置信區間[CI]， $0.17$ - $0.22$ ;  $P < 0.0001$ )，氧合血紅蛋白降低 ( $-0.16$  AUs; 95%CI,  $-0.19$  至  $-0.14$ ;  $P < 0.0001$ )，以及 Cytox 降低 ( $-0.057$  AUs; 95%CI,  $-0.073$  至  $0.0040$ ;  $P < 0.001$ )。氰化物可導致去氧血紅蛋白減少 ( $-0.037$  AUs; 95%CI,  $0.046$  至  $-0.029$ ;  $P < .001$ )，氧基血紅素增加 ( $0.053$  AUs; 95%CI,  $0.040$ - $0.065$ ;  $P < 0.001$ )，以及 Cytox 降低 ( $-0.056$  AUs; 95%CI,  $-0.064$  至  $-0.048$ ;  $P < 0.001$ )。“離散”波長演算法 (使用 4、6、8 和 10 個波長) 與寬頻測量演算法計算 Cytox 濃度之間的相關性分別為  $0.54$  (95%CI,  $0.52$ - $0.56$ )， $0.87$  ( $0.87$ - $0.88$ )， $0.88$  ( $0.88$ - $0.89$ ) 和  $0.95$  ( $0.95$ - $0.95$ )。

**結論：**使用寬頻和 10 個波長演算法均能在所有實驗中準確測量 Cytox 的變化。  
(陳思涵 譯 陳傑 校)

**BACKGROUND:** Cytochrome aa3, the terminal component of the electron transport chain, absorbs near-infrared radiation (NIR) differentially depending on its oxidation state (Cytox), which can in theory be measured using near-infrared spectroscopy (NIRS) by relating light absorption at specific wavelengths to chromophore concentrations. Some NIRS algorithms use discrete wavelengths, while others analyze a band of NIR (broadband NIRS). The purpose of this study was to test the ability of discrete wavelength and broadband algorithms to measure changes in Cytox (primary outcome), and to determine whether or not a discrete wavelength NIRS algorithm could perform similarly to a broadband NIRS algorithm for the measurement of Cytox in a staged hypoxia-cyanide model (hypoxia and cyanide have oppositional effects on tissue saturation, but both cause cytochrome reduction).

**METHODS:** Twenty Sprague-Dawley rats were anesthetized with isoflurane, intubated, and instrumented. Blood pressure, end-tidal carbon dioxide, and arterial oxygen saturation were measured. A halogen light source transmitted NIR transcranially. NIR from the light source and the skull was transmitted to 2 cooled charge-coupled device spectrometers. Rats were subjected to anoxia (fraction of inspired oxygen, 0.0) until arterial oxygen saturation decreased to 70%. After recovery, 5 mg/kg sodium cyanide was injected intravenously. The cycle was repeated until cardiac arrest occurred. Relative concentrations of hemoglobin and cytochrome aa3 were calculated using discrete wavelength and broadband NIRS algorithms.

**RESULTS:** Hypoxia led to an increase in calculated deoxyhemoglobin (0.20 arbitrary units [AUs]; 95% confidence interval [CI], 0.17-0.22;  $P < .0001$ ), a decrease in calculated oxyhemoglobin (-0.16 AUs; 95% CI, -0.19 to -0.14;  $P < .0001$ ), and a decrease in calculated Cytox (-0.057 AUs; 95% CI, -0.073 to 0.0040;  $P < .001$ ). Cyanide led to a decrease in calculated deoxyhemoglobin (-0.037 AUs; 95% CI, 0.046 to -0.029;  $P < .001$ ), an increase in calculated oxyhemoglobin (0.053 AUs; 95% CI, 0.040-0.065;  $P < .001$ ), and a decrease in calculated Cytox (-0.056 AUs; 95% CI, -0.064 to -0.048;  $P < .001$ ). The correlations between "discrete" wavelength algorithms (using 4, 6, 8, and 10 wavelengths) and the broadband algorithm for the measurement of calculated Cytox were 0.54 (95% CI, 0.52-0.56), 0.87 (0.87-0.88), 0.88 (0.88-0.89), and 0.95 (0.95-0.95), respectively.

**CONCLUSIONS:** The broadband and 10 wavelength algorithm were able to accurately track changes in Cytox for all experiments.

### 培養陰性和培養陽性膿毒症：特徵和結果的比較

Culture-Negative and Culture-Positive Sepsis: A Comparison of Characteristics and Outcomes

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**背景：**本研究的主要目的是比較培養陽性和陰性膿毒症患者的不同特徵。作者還分別確定了培養狀況是否與死亡率相關，以及不同培養狀況患者的死亡率是否與獨特變數相關。

**方法：**在一所大型學術醫療中心的重症監護病房、急診科和普通病房的患者病歷中篩選並納入 2007 年 1 月 1 日至 2014 年 5 月 31 日期間，疑似感染且  $\geq 2$  項全身炎症反應綜合征標準的成年患者。作者比較了培養陽性和培養陰性患者的特徵，並使用二元邏輯回歸分析來確定

與培養狀況和死亡率獨立相關的變數。同時對符合膿毒症序貫器官衰竭評估 (SOFA) 和快速序貫器官衰竭評估 (qSOFA) 標準的患者進行敏感性分析。

**結果：**納入 9288 名培養陰性患者 (占 89%) 和 1105 名培養陽性患者 (占 11%)。培養陰性的患者在診斷前 48 小時內接受了更多的抗生素，但在其他方面表現出與培養陽性的患者相似的特徵。在對疾病嚴重程度進行校正後，陽性培養與死亡率沒有獨立相關性 (優勢比 = 1.01 [95% CI, 0.81-1.26]; P = .945)。預測培養陰性和培養陽性患者死亡率的模型分別顯示出良好、優異的區分度 (C 統計量 ± SD, 0.87 ± 0.01 和 0.92 ± 0.01)。在使用符合 SOFA 和 qSOFA 標準的膿毒症患者進行敏感性分析中，在對疾病嚴重程度校正後，陽性培養仍與死亡率無關 (優勢比 = 1.13 [95% CI, 0.86-1.43]; P = .303; 優勢比 = 1.05 [95% CI, 0.83-1.33]; P = .665)。在所有模型中，生理紊亂都與死亡率有關。

**結論：**培養狀態對於抗生素的選擇很重要，而培養陰性和培養陽性膿毒症患者表現出相似特徵，且對疾病嚴重程度進行校正後，也得到同樣結果。與陰性培養有關的最重要因素是在前 48 小時內接受了抗生素。疑似感染患者的死亡風險與疾病嚴重程度最相關。這與使用 SOFA 評分的膿毒症 3.0 定義相符，以便於更好地識別那些最可能有不良預後的疑似感染者。

(婁曉梅 譯 陳傑 校)

**BACKGROUND** The primary objective of this study was to compare the characteristics of culture-positive and culture-negative status in septic patients. We also determined whether culture status is associated with mortality and whether unique variables are associated with mortality in culture-positive and culture-negative patients separately.

**METHODS:** Utilizing patient records from intensive care units, emergency department, and general care wards in a large academic medical center, we identified adult patients with suspected infection and  $\geq 2$  systemic inflammatory response syndrome criteria between January 1, 2007, and May 31, 2014. We compared the characteristics between culture-positive and culture-negative patients and used binary logistic regression to identify variables independently associated with culture status and mortality. We also did sensitivity analyses using patients with Sequential Organ Failure Assessment and quick Sequential Organ Failure Assessment criteria for sepsis.

**RESULTS** The study population included 9288 culture-negative patients (89%) and 1105 culture-positive patients (11%). Culture-negative patients received more antibiotics during the 48 hours preceding diagnosis but otherwise demonstrated similar characteristics as culture-positive patients. After adjusting for illness severity, a positive culture was not independently associated with mortality (odds ratio = 1.01 [95% CI, 0.81-1.26]; P = .945). The models predicting mortality separately in culture-negative and culture-positive patients demonstrated very good and excellent discrimination (C-statistic ± SD, 0.87 ± 0.01 and 0.92 ± 0.01), respectively. In the sensitivity analyses using patients with sepsis by Sequential Organ Failure Assessment and quick Sequential Organ Failure Assessment criteria, after adjustments for illness severity, positive cultures were still not associated with mortality (odds ratio = 1.13 [95% CI, 0.86-1.43]; P = .303; and odds ratio = 1.05 [95% CI, 0.83-1.33]; P = .665), respectively. In all models, physiological derangements were associated with mortality.

**CONCLUSIONS** While culture status is important for tailoring antibiotics, culture-negative and culture-positive patients with sepsis demonstrate similar characteristics and, after adjusting for severity of illness, similar mortality. The most important factor associated with negative cultures is receipt of antibiotics during the preceding 48 hours. The risk of death in patients suspected of having an infection is most associated with severity of illness. This is aligned with the Sepsis-3

definition using Sequential Organ Failure Assessment score to better identify those suspected of infection at highest risk of a poor outcome.

## 使用連續即時壓力傳感技術的客觀硬膜外腔識別：與螢光檢查和傳統阻力消失法的隨機對照比較

Objective Epidural Space Identification Using Continuous Real-Time Pressure Sensing

Technology: A Randomized Controlled Comparison With Fluoroscopy and Traditional Loss of Resistance

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**背景：**硬膜外麻醉和鎮痛的效果取決於硬膜外腔（ES）的成功識別。儘管多項研究描述了確認 ES 的一些客觀和替代方法，但傳統的阻力消失法（LOR）和螢光檢查（FC）目前分別是分娩（L&D）和慢性疼痛（CP）管理的治療標準。儘管 FC 成功率較高，但它使患者暴露於放射線下，並需要適當的放射設備。LOR 簡單卻很主觀，因此失敗率更高。此項研究目的是比較使用新型電腦控制的 ES 識別技術下的連續、定量、即時針尖壓力傳感與 FC 和 LOR 在腰 ES 識別方面的差異。

**方法：**本前瞻、隨機、對照、非劣效性試驗共納入 400 名患者。CP 人群，有 240 名計畫接受腰椎硬膜外類固醇注射的患者通過 FC 或針尖壓力測量來確定 ES 位置。L&D 人群，將 160 名接受腰椎硬膜外導管置入的女性患者隨機分配至 LOR 組或針尖壓力測量組。盲法觀察員判斷 CP 和 L&D 方面 ES 的成功確認情況。實施了改良的意向性處理方案，排除了由於干預前的原因而無法進行手術的患者。當優勢比（OR）的 97.27% 可信區間（CI）下限超過 0.5 時（即 ES 確認可能性小於 50%），根據成功 ES 確認概率的針尖壓力測量是非劣的。非劣效性的 P 值 < 0.023。

**結果：**通過標準化差異評估時，除了性別方面存在輕度失衡，其他組間的人口統計學參數具有可比性。在疼痛治療患者通過兩種方法對於 ES 確認成功率均為 100% 的情況下，與 FC 相比，針尖壓力測量具有非劣效性（OR，1.1；97.27% CI，0.52-8.74；非劣質性 P 值為 .021）。在 L&D 患者中，當先驗非劣效性臨界值為 0.50 時，新技術具有非劣的成功率（97.1% vs 91%；OR，3.3；97.27% CI，0.62-21.54；P = .019）。

**結論：**使用連續、定量、即時的針尖壓力測量結合 CompuFlo 硬膜外電腦控制麻醉系統進行客觀的腰椎 ES 確認，分別在 CP 治療人群和 L&D 人群中與 FC 和 LOR 方法相比，成功率不低。這項新技術的好處可能包括使患者免于輻射和造影劑暴露，從而降低醫療治療成本。（婁曉梅 譯 陳傑 校）

**BACKGROUND** Performance of epidural anesthesia and analgesia depends on successful identification of the epidural space (ES). While multiple investigations have described objective and alternative methodologies to identify the ES, traditional loss of resistance (LOR) and fluoroscopy (FC) are currently standard of care in labor and delivery (L&D) and chronic pain (CP) management, respectively. While FC is associated with high success, it exposes patients to radiation and requires appropriate radiological equipment. LOR is simple but subjective and consequently associated with higher failure rates. The purpose of this investigation was to compare continuous, quantitative, real-time, needle-tip pressure sensing using a novel computer-controlled ES identification technology to FC and LOR for lumbar ES identification.

**METHODS** A total of 400 patients were enrolled in this prospective randomized controlled noninferiority trial. In the CP management arm, 240 patients scheduled to receive a lumbar epidural steroid injection had their ES identified either with FC or with needle-tip pressure measurement. In the L&D arm, 160 female patients undergoing lumbar epidural catheter placements were randomized to either LOR or needle-tip pressure measurement. Blinded observers determined successful ES identification in both arms. A modified intention-to-treat protocol was implemented, with patients not having the procedure for reasons preceding the intervention excluded. Noninferiority of needle-tip pressure measurement regarding the incidence of successful ES identification was claimed when the lower limit of the 97.27% confidence interval (CI) for the odds ratio (OR) was above 0.50 (50% less likely to identify the ES) and P value for noninferiority <.023.

**RESULTS** Demographics were similar between procedure groups, with a mild imbalance in relation to gender when evaluated through a standardized difference. Noninferiority of needle-tip pressure measurement was demonstrated in relation to FC where pain management patients presented a 100% success rate of ES identification with both methodologies (OR, 1.1; 97.27% CI, 0.52-8.74; P = .021 for noninferiority), and L&D patients experienced a noninferior success rate with the novel technology (97.1% vs 91%; OR, 3.3; 97.27% CI, 0.62-21.54; P = .019) using a priori noninferiority delta of 0.50.

**CONCLUSIONS** Objective lumbar ES identification using continuous, quantitative, real-time, needle-tip pressure measurement with the CompuFlo Epidural Computer Controlled Anesthesia System resulted in noninferior success rates when compared to FC and LOR for CP management and L&D, respectively. Benefits of this novel technology may include nonexposure of patients to radiation and contrast medium and consequently reduced health care costs.

### 除了麻醉毒性之外：減少新生兒神經系統損傷風險的麻醉考慮

Beyond Anesthesia Toxicity: Anesthetic Considerations to Lessen the Risk of Neonatal Neurological Injury

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在生命的最初幾個月內接受外科手術的嬰兒，死亡或繼發神經發育異常的風險更高。儘管這些結局的發病機制是多因素的，但瞭解這些嬰兒腦損傷的性質和發病機制可能有助於麻醉醫師思考他們的日常實踐以最大程度地降低此類風險。這篇綜述將總結早產和足月嬰兒腦損傷的主要類型及其主要致病途徑。此外，本綜述還將探討可避免的關鍵潛在致病途徑，包括術中低血壓，低碳酸血症，高氧血症或低氧血症，低血糖症和體溫過高。這些情況中的每一種都可能增加圍術期神經系統損傷的風險，但其長期影響尚不清楚。

(婁曉梅 譯 陳傑 校)

Infants who undergo surgical procedures in the first few months of life are at a higher risk of death or subsequent neurodevelopmental abnormalities. Although the pathogenesis of these outcomes is multifactorial, an understanding of the nature and pathogenesis of brain injury in these infants may assist the anesthesiologist in consideration of their day-to-day practice to minimize such risks.

This review will summarize the main types of brain injury in preterm and term infants and their key pathways. In addition, the review will address key potential pathogenic pathways that may be modifiable including intraoperative hypotension, hypocapnia, hyperoxia or hypoxia,



hypoglycemia, and hyperthermia. Each of these conditions may increase the risk of perioperative neurological injury, but their long-term ramifications are unclear.

### 術後認知功能障礙患者中腦脊液單核細胞的流式細胞特徵：一項初步研究

Flow Cytometry Characterization of Cerebrospinal Fluid Monocytes in Patients With Postoperative Cognitive Dysfunction: A Pilot Study

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動物模型顯示術後認知功能障礙可能是由腦部單核細胞彙集引起。為了研究人體中的類似機制，作者收集了 5 例 60 歲以上大型非心臟手術術後發生認知功能障礙的病人術前和術後的腦脊液，以及與之匹配的 5 例未發生術後認知功能障礙的對照組標本，建立流式細胞通道來測定以上腦脊液（CSF）樣品。在 10 毫升腦脊液樣品中檢測到了 12,654±4895 個細胞（均值±標準差）。術後認知功能障礙的病人腦脊液分析示單核細胞/淋巴細胞比例升高和術後 24 小時腦脊液單核細胞趨化蛋白 1 受體下調。這些初步研究的資料表明腦脊液流式細胞檢測能用於術後神經認知功能障礙的機制研究。

（鄒沅芫 譯 陳傑 校）

Animal models suggest postoperative cognitive dysfunction may be caused by brain monocyte influx. To study this in humans, we developed a flow cytometry panel to profile cerebrospinal fluid (CSF) samples collected before and after major noncardiac surgery in 5 patients  $\geq 60$  years of age who developed postoperative cognitive dysfunction and 5 matched controls who did not. We detected 12,654  $\pm$  4895 cells/10 mL of CSF sample (mean  $\pm$  SD). Patients who developed postoperative cognitive dysfunction showed an increased CSF monocyte/lymphocyte ratio and monocyte chemoattractant protein 1 receptor downregulation on CSF monocytes 24 hours after surgery. These pilot data demonstrate that CSF flow cytometry can be used to study mechanisms of postoperative neurocognitive dysfunction.

苯腎上腺素和去甲腎上腺素間歇靜脈注射預防和治療剖宮產術中脊髓誘發性低血壓的比較：隨機對照試驗

**Comparison of Intermittent Intravenous Boluses of Phenylephrine and Norepinephrine to Prevent and Treat Spinal-Induced Hypotension in Cesarean Deliveries: Randomized Controlled Trial**

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**背景：**苯腎上腺素（PE）是目前預防和治療剖宮產（CD）時脊髓誘發的低血壓的首選血管活性藥物。但是，它的使用常導致反射性心動過緩。去甲腎上腺素（NE）已被提出作為 CD 期間的替代性升壓藥，因為它具有在治療低血壓的同時維持心律（HR）能力。最近的研究集中於與 PE 相比選擇輸注 NE 具有良好的效果。尚無研究比較 CD 中 PE 和 NE 的等效推注劑量。我們假設當以等效劑量作為預防和治療脊髓誘發的低血壓的間歇推注方案時，NE 與 PE 相比可降低心動過緩的發生率。

**方法：**這是一項針對在椎管內麻醉下接受選擇性 CD 的女性的雙盲、隨機臨床試驗。當收縮壓（SBP）低於基線時，受試者被隨機分配注射 PE 100 μg 或 NE 6 μg。除隨機治療方案外，當兩組中連續兩次 SBP 低於基線且 HR <60 次/分或 SBP < 基線的 80%，則兩組受試者均予靜脈注射麻黃碱。主要觀察的結果為分娩前簡短出現心動過緩（HR <50 次/分）。次要觀察的結果包括低血壓（SBP < 基線的 80%），高血壓（SBP > 基線的 120%），心動過速（HR > 基線的 120%），≥2 次心動過緩，噁心，嘔吐，臍動脈和靜脈血氣和 Apgar 得分。

**結果：**112 例患者被隨機分組。NE 組的心動過緩發生率比 PE 組低（10.7% vs 37.5%；P < .001；差值 [95% 置信區間 {CI}]，-26.8% [-41.8%—11.7%]），意味著發生率相對減少約 71%（95% CI，35%—88%）。兩組之間心動過緩發作次數

的分佈也不同 ( $P = .007$ )。進一步的測試表明，與 NE 組相比，PE 組的患者發生多次心動過緩 ( $\geq 2$  次) 的風險更高 (PE 組為 19.6%，NE 組為 3.6%； $P = 0.008$ )。與 PE 組相比，NE 組中需要麻黃碱補救推注的患者比例更低 (NE 組為 7.2%，PE 組為 21.4%； $P < .03$ ；差值[95%CI]，-14.3%[-27.0%—1.6%])。兩組之間其他次要結果的發生率未見差異。

**結論：**當採用間歇推注方案預防和治療 CD 期間椎管內誘發的低血壓時，與 PE 等當量推注方案相比，使用 NE 顯著降低心動過緩的發生率。因此我們得出結論，由於對心率和可能對心輸出量造成較少的影響，在 CD 期間 NE 對血流動力學的影響優於 PE。

(吳兆藝 譯 潘豔、薛張綱校)

**BACKGROUND:** Phenylephrine (PE) is currently the vasopressor of choice to prevent and treat spinal-induced hypotension at cesarean delivery (CD). However, its use is often associated with reflex bradycardia. Norepinephrine (NE) has been put forward as an alternative vasopressor during CD due to its ability to treat hypotension while maintaining heart rate (HR). Recent studies have focused on the role of NE used as an infusion with favorable results compared to PE. No studies have compared equipotent bolus doses of PE and NE at CD. We hypothesized that when used in equipotent doses as an intermittent bolus regimen to prevent and treat spinal-induced hypotension, NE would result in a reduction in the incidence of bradycardia compared to PE.

**METHODS:** This was a double-blind, randomized clinical trial of women undergoing elective CD under spinal anesthesia. Women were randomized to receive either PE 100  $\mu\text{g}$  or NE 6  $\mu\text{g}$  when the systolic blood pressure (SBP) was below baseline. In addition to the randomized treatment, ephedrine was given intravenously to both groups if the SBP was below baseline and the HR  $< 60$  bpm or if the SBP was  $< 80\%$  of baseline for 2 consecutive readings. The primary outcome was bradycardia (HR  $< 50$  bpm) in the predelivery period. Secondary outcomes included hypotension (SBP  $< 80\%$  of baseline), hypertension (SBP  $> 120\%$  of baseline), tachycardia (HR  $> 120\%$  of baseline),  $\geq 2$  episodes of bradycardia, nausea, vomiting, umbilical artery and vein blood gases, and Apgar scores.

**RESULTS:** One hundred twelve patients were randomized. The incidence of bradycardia was lower in the NE group compared to the PE group (10.7% vs 37.5%;  $P < .001$ ; difference [95% confidence interval {CI}], -26.8% [-41.8% to -11.7%]), implying an estimated 71% relative reduction (95% CI, 35%–88%). The distribution

of the number of bradycardia episodes was also different between the 2 groups ( $P = .007$ ). Further testing showed that the patients in the PE group had a higher risk of multiple bradycardia episodes ( $\geq 2$  episodes) compared to the NE group (19.6% for PE versus 3.6% for NE;  $P = .008$ ). The proportion of patients requiring rescue boluses of ephedrine was lower in the NE group compared to the PE group (7.2% for NE versus 21.4% for PE;  $P < .03$ ; difference [95% CI], -14.3% [-27.0% to -1.6%]). No differences were observed between the 2 groups in the incidence of other secondary outcomes.

**CONCLUSIONS:** When used as an intermittent bolus regimen to prevent and treat spinal-induced hypotension during CD, NE resulted in a significant reduction in the incidence of bradycardia as compared to an equipotent bolus regimen of PE. We conclude that the hemodynamic profile offered by NE during CD is superior to that of PE due to less fluctuations in HR and possibly cardiac output.

### 血管內冷卻裝置與食管熱交換器用於輕度治療性低溫的比較

#### **Intravascular Cooling Device Versus Esophageal Heat Exchanger for Mild Therapeutic Hypothermia in an Experimental Setting**

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**背景：**目標導向的體溫管理是無意識心臟驟停患者的一種標準治療。現如今，有多種冷卻裝置可供採用，如有創血管內冷卻裝置（IVDs），在臨床中已被廣泛使用。近期，食道熱交換器（EHEs）也已被開發出來，這是一種通過位於主動脈弓和下腔靜脈附近的食道提供的一種冷卻裝置。本研究的目的是比較目標溫度維持及復溫期間有創血管內冷卻裝置（IVD）和食道熱交換器（EHE）的平均製冷速度及兩者間的差別。

**方法：**此研究物件為 16 只母豬。在隨機化分為有創血管內冷卻裝置（IVD）組和食道熱交換器（EHE）組（每組各 8 只母豬）後，將母豬的核心體溫降至 33 °C 並維持 24 小時以後，使用每小時升高 0.25 °C 的目標導向復溫設備復溫 10 小時。

所有動物在冷卻期間都使用頸內靜脈和冷切器之間的閉合回饋系統控制。在處死動物之前，留取動物喉和食管的組織進行組織病理學檢驗。

**結果：**在平均冷卻速度上，有創血管內冷卻裝置（IVD）組為  $4^{\circ}\text{C}/\text{h}\pm 0.4^{\circ}\text{C}/\text{h}$ ，食道熱交換器（EHE）組為  $2.4^{\circ}\text{C}/\text{h}\pm 0.3^{\circ}\text{C}/\text{h}$ （ $P<0.0008$ ），達到目標溫度所需時間有創血管內冷卻裝置（IVD）組為  $85.1\pm 9.2\text{min}$ ，食道熱交換器（EHE）組為  $142.0\pm 21.2\text{min}$ （ $P=0.0008$ ），兩者間有顯著差別。在目標溫度維持期間，兩者的體溫波動幅度有創血管內冷卻裝置（IVD）組為  $0.07^{\circ}\text{C}\pm 0.05^{\circ}\text{C}$ ，食道熱交換器（EHE）組為  $0.08^{\circ}\text{C}/\text{h}\pm 0.10^{\circ}\text{C}$ （ $P=0.496$ ），在平均複溫速度上有創血管內冷卻裝置（IVD）組為  $0.2^{\circ}\text{C}/\text{h}\pm 0.1^{\circ}\text{C}/\text{h}$ ，食道熱交換器（EHE）組為  $0.3^{\circ}\text{C}/\text{h}\pm 0.2^{\circ}\text{C}/\text{h}$ （ $P=0.226$ ），兩者基本相似。實驗中相關的喉部和食管損傷未被發現。兩者在不良副反應（如心動過緩和心動過速，低鉀血症和高鉀血症，低血壓，低體溫，寒戰等）方面無顯著差異。

**結論：**與食道熱交換器（EHE）相比，有創血管內冷卻裝置（IVD）能更快的達到目標溫度。根據重症監護室的指南，這兩個設備在目標溫度的維持和積極複溫操作中的性能效果是沒有明顯差異的。

（石平 譯 潘豔、薛張綱校）

**BACKGROUND:** Targeted temperature management is a standard therapy for unconscious survivors of cardiac arrest. To date, multiple cooling methods are available including invasive intravascular cooling devices (IVDs), which are widely used in the clinical setting. Recently, esophageal heat exchangers (EHEs) have been developed providing cooling via the esophagus that is located close to the aorta and inferior vena cava. The objective was to compare mean cooling rates, as well as differences, to target temperature during maintenance and the rewarming period of IVD and EHE.

**METHODS:** The study was conducted in 16 female domestic pigs. After randomization to either IVD or EHE ( $n = 8/\text{group}$ ), core body temperature was reduced to  $33^{\circ}\text{C}$ . After 24 hours of maintenance ( $33^{\circ}\text{C}$ ), animals were rewarmed using a target rate of  $0.25^{\circ}\text{C}/\text{h}$  for 10 hours. All cooling phases were steered by a

closed-loop feedback system between the internal jugular vein and the chiller. After euthanasia, laryngeal and esophageal tissue was harvested for histopathological examination.

**RESULTS:** Mean cooling rates ( $4.0^{\circ}\text{C}/\text{h} \pm 0.4^{\circ}\text{C}/\text{h}$  for IVD and  $2.4^{\circ}\text{C}/\text{h} \pm 0.3^{\circ}\text{C}/\text{h}$  for EHE;  $P < .0008$ ) and time to target temperature ( $85.1 \pm 9.2$  minutes for IVD and  $142.0 \pm 21.2$  minutes for EHE;  $P = .0008$ ) were different. Mean difference to target temperature during maintenance ( $0.07^{\circ}\text{C} \pm 0.05^{\circ}\text{C}$  for IVD and  $0.08^{\circ}\text{C} \pm 0.10^{\circ}\text{C}$  for EHE;  $P = .496$ ) and mean rewarming rates ( $0.2^{\circ}\text{C}/\text{h} \pm 0.1^{\circ}\text{C}/\text{h}$  for IVD and  $0.3^{\circ}\text{C}/\text{h} \pm 0.2^{\circ}\text{C}/\text{h}$  for EHE;  $P = .226$ ) were similar. Relevant laryngeal or esophageal tissue damage could not be detected. There were no significant differences in undesired side effects (eg, bradycardia or tachycardia, hypokalemia or hyperkalemia, hypoglycemia or hyperglycemia, hypotension, overcooling, or shivering).

**CONCLUSIONS:** After insertion, target temperatures could be reached faster by IVD compared to EHE. Cooling performance of IVD and EHE did not significantly differ in maintaining target temperature during a targeted temperature management process and in active rewarming protocols according to intensive care unit guidelines in this experimental setting. (Anesth Analg 2019;129:1224–31)

系統綜述和薈萃分析：兒科學領域中虛擬實境（VR）技術在減輕疼痛和焦慮方面的效果

### **Systematic Review and Meta-analysis of Virtual Reality in Pediatrics: Effects on Pain and Anxiety**

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**背景：**醫療操作往往會引起兒童患者的疼痛和焦慮。VR 作為一項相對新穎的技術，可以用於在醫療操作準備前或操作中分散病人的注意力。本文是第一篇收集了相關證據的薈萃研究，研究關於 VR 技術在醫療操作過程中減輕兒科病人的疼痛和焦慮的效用。

**方法：**在 2018 年 4 月 35 日，我們在 EMBASE、MEDLINE、CENTRAL、PubMed、Web of Science、PsycINFO 等資料庫中以“VR”、“兒童”和“成年人”為關鍵字進行

了相關搜索。我們納入了在患者背景下將 VR 技術用於 21 歲以下參與者的研究。VR 被定義為通過頭戴式設備，將自身置於立體視野的完全沉浸式的三維環境。我們分別評估了在 VR 條件下和標準環境中兒童患者的疼痛和焦慮情況。

**結果：**我們查找到 2889 篇文獻，其中 17 篇滿足我們的納入標準。在 16 篇文獻中，VR 技術在靜脈采血、拔牙、治療燒傷或腫瘤照顧等情況下被應用以分散病人的注意力；而另一篇則應用於擇期手術的全身麻醉前，通過將患者置於虛擬實境的環境中。VR 技術的效果在燒傷病人中進行了最多的研究（共有 6 篇文獻）。總體加權標準化均數差（SMD）在疼痛方面（基於 14 篇文獻）是 1.3（95%CI，0.68-1.91），在焦慮方面（基於 7 篇文獻）是 1.32（95%CI，0.21-2.44）。VR 技術在減輕兒童疼痛方面的效果是顯著的，無論是基於照顧者的觀察（SMD=2.08，95%CI：0.55-3.61）還是專業人員的觀察（SMD=3.02，95%CI：0.79-2.25）。在減輕焦慮方面，只有較為有限的觀察者資料是有價值的。

**結論：**VR 在兒科學中的研究主要專注於分散注意力方面。大量的有效資料表明 VR 技術是一種有效的分散兒童注意力的干預措施，在他們接受醫療操作的過程中可以減輕他們的疼痛和焦慮。然而，將 VR 暴露作為醫療操作前的準備步驟的研究較少，需要更多的研究。

（王沛 譯 潘豔、薛張綱校）

**BACKGROUND:** Medical procedures often evoke pain and anxiety in pediatric patients. Virtual reality (VR) is a relatively new intervention that can be used to provide distraction during, or to prepare patients for, medical procedures. This meta-analysis is the first to collate evidence on the effectiveness of VR on reducing pain and anxiety in pediatric patients undergoing medical procedures.

**METHODS:** On April 25, 2018, we searched EMBASE, MEDLINE, CENTRAL, PubMed, Web of Science, and PsycINFO with the keywords “VR,” “children,” and “adolescents.” Studies that

applied VR in a somatic setting with participants  $\leq 21$  years of age were included. VR was defined as a fully immersive 3-dimensional environment displayed in surround stereoscopic vision on a head-mounted display (HMD). We evaluated pain and anxiety outcomes during medical procedures in VR and standard care conditions.

**RESULTS:** We identified 2889 citations, of which 17 met our inclusion criteria. VR was applied as distraction ( $n = 16$ ) during venous access, dental, burn, or oncological care or as exposure ( $n = 1$ ) before elective surgery under general anesthesia. The effect of VR was mostly studied in patients receiving burn care ( $n = 6$ ). The overall weighted standardized mean difference (SMD) for VR was 1.30 (95% CI, 0.68–1.91) on patient-reported pain (based on 14 studies) and 1.32 (95% CI, 0.21–2.44) on patient-reported anxiety (based on 7 studies). The effect of VR on pediatric pain was also significant when observed by caregivers (SMD = 2.08; 95% CI, 0.55–3.61) or professionals (SMD = 3.02; 95% CI, 0.79–2.25). For anxiety, limited observer data were available.

**CONCLUSIONS:** VR research in pediatrics has mainly focused on distraction. Large effect sizes indicate that VR is an effective distraction intervention to reduce pain and anxiety in pediatric patients undergoing a wide variety of medical procedures. However, further research on the effect of VR exposure as a preparation tool for medical procedures is needed because of the paucity of research into this field.

回顧術中知曉：一項基於調查的描述性佇列研究

### **Intraoperative Awareness With Recall: A Descriptive, Survey-Based, Cohort Study.**

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**背景：**意外的術中知曉與是全身麻醉的潛在併發症。患者通常報告以下情況的

回憶：（1）聽到聲音或交談，（2）無法呼吸或移動，（3）感到疼痛，和/或（4）

遭受情緒困擾。本研究的目的是通過對一大批未選定的成人手術佇列進行術後調查，確定並進一步表明術中知曉的體驗。

**方法：**這是一項前瞻性註冊研究的子研究，該研究對患者的手術後健康狀況進行了調查。分析了針對術中知曉的4個問題的回答。通過電話聯繫了疼痛，癱瘓和/或困擾的患者，以獲取有關其術中知曉經歷的更多資訊。將接受全身麻醉的患者的訪談結果發送給3位麻醉師，他們對報告的術中知曉進行裁決。



結果：發送的 48,151 項調查中，我們收到了 17,875 例患者的答覆。在這些受訪者中，有 622 人報告了從入睡到覺察到的全身麻醉之間的特定記憶，其中 282 人報告了相關的疼痛，麻痺和/或困擾。我們試圖聯繫這 282 位患者，其中 149 位元參加了電話調查。在 149 位參與者中，有 87 位贊同了他們先前的術中知曉報告。但是，這些患者中只有 22 例接受了全身麻醉，而 51 例僅接受了鎮靜，而 14 例接受了局部麻醉。三名麻醉師分別對 22 例全身麻醉病例的調查結果進行了裁決，並分別將 6 例確定為術中知曉，8 例確定為可能 AWR，8 例確定為非術中知曉。在接受區域或鎮靜麻醉後認為自己術中知曉的 65 位患者中，有 37 位（鎮靜患者 31 位元，局部麻醉 6 位元）其實是在手術期間無意識。

**結論：**在全身麻醉期間，術中知曉還在繼續發生。許多關於術中知曉發作的報導發生在接受鎮靜或區域麻醉的患者中，這些患者對麻醉技術和意識體驗有不匹配的期望，這也是潛在的干預。

（王碩 譯潘豔、薛張綱校）

**BACKGROUND:** Unintended *intraoperative awareness with recall* (AWR) is a potential complication of general anesthesia. Patients typically report recollections of (1) hearing sounds or conversations, (2) being unable to breathe or move, (3), feeling pain, and/or (4) experiencing emotional distress. The purpose of the current *study* was to identify and further characterize AWR experiences identified through postoperative surveys of a large unselected adult surgical cohort.

**METHODS:** This is a substudy of a prospective registry *study*, which surveys patients on their health and well-being after surgery. Responses to 4 questions focusing on AWR were analyzed. Patients who reported AWR *with* pain, paralysis, and/or distress were contacted by telephone to obtain more information about their AWR experience. The interview results for patients who received general anesthesia were sent to 3 anesthesiologists, who adjudicated the reported AWR episodes.

**RESULTS:** Of 48,151 surveys sent, 17,875 patient responses were received. Of these respondents, 622 reported a specific memory from the period between going to sleep and waking up from perceived general anesthesia and 282 of these reported related pain, paralysis, and/or distress. An attempt was made to contact these 282 patients, and 149 participated in a telephone survey. Among the 149 participants, 87 endorsed their prior report of AWR. However, only 22 of these patients had received general

anesthesia, while 51 received only sedation and 14 received regional anesthesia. Three anesthesiologists independently adjudicated the survey results of the 22 general anesthesia cases and assigned 6 as definite AWR, 8 as possible AWR, and 8 as not AWR episodes. Of the 65 patients who confirmed their report of AWR after regional or sedation anesthesia, 37 (31 *with* sedation and 6 *with* regional anesthesia) had not expected to be conscious during surgery.

**CONCLUSIONS:** The complication of AWR continues to occur during intended general anesthesia. Many reports of AWR episodes occur in patients receiving sedation or regional anesthesia and relate to incorrect expectations regarding anesthetic techniques and conscious experiences, representing a potential target for intervention.

靜脈注射利多卡因預防咳嗽：隨機對照試驗的系統回顧和薈萃分析

### **Intravenous Lidocaine for the Prevention of Cough: Systematic Review and Meta-analysis of Randomized Controlled Trials**

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**背景：**目前尚不清楚靜脈注射利多卡因在多大程度上預防咳嗽，以及是否存在劑量反應性和危害風險。

**方法：**我們檢索了截至 2017 年 1 月 1 日的電子資料庫，以進行比較靜脈注射利多卡因和安慰劑預防外科患者咳嗽的隨機試驗。主要結果是咳嗽的發生率。資料採用隨機效應模型進行分析，以 95% 可信區間表示為風險比 (RR) 和治療所需次數 (NNT)。

**結果：**在 20 項成人試驗 (n=3062) 和 5 項兒童試驗 (n=445)，靜脈注射利多卡因 0.5-2mg·kg<sup>-1</sup> 用於預防插管、拔管或阿片類藥物引起的咳嗽，其中 22 項試驗僅包括美國麻醉師學會 I 或 II 級患者；3 項試驗 (n=99) 也包括美國麻醉師學會 III 級患者。與安慰劑相比，利多卡因在成人和兒童中的咳嗽發生率較低，與劑量和咳嗽病因無關。來自成人的資料表明劑量反應性：0.5 mg·kg<sup>-1</sup>，RR 為 0.66 (0.50–0.88)，NNT 為 8 (5.4–14.3)；1 mg·kg<sup>-1</sup>，RR 為 0.58 (0.49–0.69) NNT

為 7(4.6–8.9); 1.5 mg·kg<sup>-1</sup>, RR 為 0.44(0.33–0.58), NNT 為 5(3.3–5.2); 2 mg·kg<sup>-1</sup>, RR 為 0.39(0.24–0.62), NNT 為 3(2.0–3.4)。不良反應報告很少。

**結論：**在 0.5-2 mg·kg<sup>-1</sup> 範圍內，靜脈注射利多卡因預防成人和兒童的插管、拔管和阿片誘導的咳嗽 NNTs 範圍在 8-3。高危患者的傷害風險仍然未知。

(魏婉婷 譯 潘豔、薛張綱校)

**BACKGROUND:** It remains unclear to what extent intravenous lidocaine prevents cough and whether there is dose-responsiveness and risk of harm.

**METHODS:** We searched electronic databases to January 1, 2017 for randomized trials comparing intravenous lidocaine with placebo for the prevention of cough in surgical patients. Primary outcome was the incidence of cough. Data were analyzed using a random-effects model and were expressed as risk ratio (RR) and number needed to treat (NNT) with 95% confidence interval.

**RESULTS:** In 20 trials in adults (n = 3062) and 5 trials in children (n = 445), intravenous lidocaine 0.5–2 mg·kg<sup>-1</sup> was tested for the prevention of intubation-, extubation-, or opioid-induced cough. Twenty-two trials included only American Society of Anesthesiologists I or II patients; 3 trials (n = 99) also included American Society of Anesthesiologists III patients. Lidocaine was associated with a lower incidence of cough compared to placebo in adults and children, irrespective of dosage and cough etiology. Data from adults suggested dose-responsiveness; with 0.5 mg·kg<sup>-1</sup>, RR was 0.66 (0.50–0.88) and NNT was 8 (5.4–14.3); with 1 mg·kg<sup>-1</sup>, RR was 0.58 (0.49–0.69) and NNT was 7 (4.6–8.9); with 1.5 mg·kg<sup>-1</sup>, RR was 0.44 (0.33–0.58) and NNT was 5 (3.3–5.2); and with 2 mg·kg<sup>-1</sup>, RR was 0.39 (0.24–0.62) and NNT was 3 (2.0–3.4). Adverse effect reporting was sparse.

**CONCLUSIONS:** Within a range of 0.5–2 mg·kg<sup>-1</sup>, intravenous lidocaine dose dependently prevents intubation-, extubation-, and opioid-induced cough in adults and children with NNTs ranging from 8 to 3. The risk of harm in high-risk patients remains unknown.

發作性睡病、麻醉和鎮靜：發作性睡病患者圍手術期情況的調查

### **Narcolepsy, Anesthesia, and Sedation: A Survey of the Perioperative Experience of Patients With Narcolepsy.**

Hershner S1, Kakkar R2,3, Chung F4, Singh M4,5, Wong J4, Auckley D6.  
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**背景:**由於麻醉、發作性睡病和發作性睡病藥物之間的相互作用，發作性睡病患者的圍手術期風險可能增加。本研究試圖確定發作性睡病患者麻醉或鎮靜狀態的圍手術期經驗、圍手術期諮詢的頻率和自我報告的手術併發症。

**方法:**以專家共識為基礎，通過發作性睡病網路進行了包含 22 個問題的調查。入組是通過發作性睡病網路的清單服務和 Facebook 上的調查連結進行的。120 名調查物件被報告診斷為發作性睡病，並在麻醉或鎮靜狀態下進行了 1 次或 1 次以上的手術。文章採用了描述性、比較統計學和邏輯回歸分析來分析資料。

**結果:**調查對象多為女性(79.5%)和白人(84.9%)，平均年齡  $45 \pm 16$  歲。大多數調查對象沒有諮詢麻醉後嗜睡(70%)、猝倒(90%)或疲勞駕駛(59%)等問題。超過一半的調查對象報告了不良事件(藥物戒斷症狀、疼痛未完全緩解、猝倒次數增加)。合併猝倒的患者更常報告手術併發症(70% vs 31%;  $P = 0.03$ )和藥物戒斷症狀(激動劑:優勢比 3.0 [95% CI, 1.9-3.06];  $P > 0.001$  和抗抑鬱藥物:優勢比 6.5 [95% CI, 2.1-19.5];  $P = 0.001$ )。在所有調查物件中，18% 報告出現手術併發症。經歷 5 次或 5 次以上獨立手術或程式的患者自我報告併發症(優勢比，2.2 [95% CI, 1.3-3.4];  $P = 0.001$ )，蘇醒困難(優勢比，2.1 [95% CI, 1.45-3.06];  $P = 0.001$ )，以及疼痛未完全緩解(優勢比 1.77 [95% CI, 1.01-3.13];  $P < 0.05$ )可高達 2 倍。

**結論:**大多數發作性睡病患者報告說，他們沒有接受有關麻醉後嗜睡症狀可能惡化或疲勞駕駛風險增加的諮詢。加強對圍手術期麻醉提供者的教育，讓他們瞭解發作性睡病患者潛在的問題是至關重要的。調查物件在圍手術期經常自我報告不良事件。未來的研究應明確與發作性睡病相關的圍手術期風險，以優化對發作性睡病患者的護理和安全管理。

(王甲利潘豔、薛張綱校譯)

**BACKGROUND:** Patients with narcolepsy may be at increased perioperative risk due to the interactions among anesthesia, narcolepsy, and narcolepsy medications. This study sought to determine the perioperative experience of narcoleptic patients undergoing anesthesia or sedation, the frequency of perioperative counseling, and self-reported surgical complications.

**METHODS:** A 22-question survey was developed by expert consensus and distributed by the Narcolepsy Network. Recruitment was via the Narcolepsy Network's list-serve and a Facebook link to the survey. One thousand and twenty respondents reported a diagnosis of narcolepsy and 1 or more procedures under anesthesia or sedation. Descriptive, comparative statistics and logistic regression were utilized.

**RESULTS:** Respondents were mostly women (79.5%) and Caucasian (84.9%), with a mean age of  $45 \pm 16$  years. Most respondents did not receive counseling regarding the possibility of increased sleepiness (70%), cataplexy (90%), or drowsy driving (59%) postanesthesia. More than half of respondents reported adverse events (medication withdrawal symptoms, inadequate pain relief, increased cataplexy). Subjects with cataplexy more frequently reported surgical complications (70% vs 31%;  $P = .03$ ) and medication withdrawal symptoms (stimulant medications: odds ratio, 3.0 [95% CI, 1.9, 3.06];  $P > .001$  and antidepressant medications: odds ratio, 6.5 [95% CI, 2.1-19.5];  $P = .001$ ). Of the total sample, 18% indicated surgical complications. Undergoing 5 or more separate surgeries or procedures was associated with a 2-fold increase in self-reported complications (odds ratio, 2.2 [95% CI, 1.3-3.4];  $P = .001$ ), difficulty waking (odds ratio, 2.1 [95% CI, 1.45-3.06];  $P = .001$ ), and inadequate pain relief (odds ratio, 1.77 [95% CI, 1.01-3.13];  $P < .05$ ).

**CONCLUSIONS:** Most narcoleptic patients report not receiving counseling regarding potential worsening of narcolepsy symptoms postanesthesia or an increased risk of drowsy driving. Enhanced education of perioperative providers about potential narcolepsy-related issues is essential. Respondents frequently self-report adverse events in the perioperative period. Future studies should clarify the perioperative risk associated with narcolepsy to optimize the care and safety of narcoleptic patients.