**Supplementary Files**

This document has been provided by the authors to give readers additional information about their work.

Supplement to: **Muscular Tissue Oxygen Saturation and Posthysterectomy Nausea and Vomiting: The iMODIPONV Randomized Controlled Trial**

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**Committees**

**Steering Committee:** Lingzhong Meng (chair), Xiangyang Guo, Dong-xin Wang, Mengyuan Zhang, Yanqiu Ai, Ya Liu, Mingjun Xu

**Quality Committee:** Lingzhong Meng, Gang Li, Dong-liang Mu

**Data Safety Monitoring Board:** David McDonagh (Chair, UT Southwestern), Chuanyao Tong (Wake Forest University), Hong Liu (University of California Davis)

**Site Principal Investigators**

|  |  |  |
| --- | --- | --- |
| **Name (First, Last)** | **Email** | **Phone** |
| *Peking University First Hospital, Beijing, China* | | |
| Dong-xin Wang | wangdongxin@hotmail.com | 010-83575138 |
| *Peking University Third Hospital, Beijing, China* | | |
| Xiangyang Guo | puthmzk@bjmu.edu.cn | 15611908488 |
| *Shandong Provincial Hospital, Jinan, Shandong Province, China* | | |
| Mengyuan Zhang | zhangmy717@163.com | 15168886767 |
| *The First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan Province, China* | | |
| Yanqiu Ai | aiyanqiu82@163.com | 13607690334 |
| *The Second Hospital of Hebei Medical University, Shijiazhuang, Hebei Province, China* | | |
| Ya Liu | md2006liuya@aliyun.com | 15803217957 |
| *Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing, China* | | |
| Mingjun Xu | snake650222@163.com | 13701038959 |

**Site Study Coordinators**

|  |  |  |
| --- | --- | --- |
| **Name (First, Last)** | **Email** | **Phone** |
| *Peking University First Hospital, Beijing, China* | | |
| Ju Bao | baoju1985@126.com | 010-83575138 |
| *Peking University Third Hospital, Beijing, China* | | |
| Gang Li | lixinregis@126.com | 13810380824 |
| *Shandong Provincial Hospital, Jinan, Shandong Province, China* | | |
| Xu Wang | [cityhunter54@163.com](mailto:cityhunter54@163.com) | 15168863675 |
| *The First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan Province, China* | | |
| Dandan Tian | ddt0802@163.com | 13939071527 |
| *The Second Hospital of Hebei Medical University, Shijiazhuang, Hebei Province, China* | | |
| Xiaoxian Feng | 1761362430@qq.com | 15081860838 |
| *Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing, China* | | |
| Wenyu Zhang | zwy751105@163.com | 13911864960 |

**Participating Hospitals and Investigators**

|  |  |  |
| --- | --- | --- |
| **Name (First, Last)** | **Email** | **Phone** |
| *Peking University First Hospital, Beijing, China* | | |
| Ju Bao | baoju1985@126.com | 010-83575138 |
| Dong-xin Wang | wangdongxin@hotmail.com | 010-83575138 |
| Dong-liang Mu | mudongliang@icloud.com | 010-83575138 |
| Shuang-jie Cao | caosjie1994@126.com | 010-83575138 |
| Jie-chu Wang | 762167558@qq.com | 010-83575138 |
| Zhan-juan Du | duzhanjuan2644@sina.com | 010-83573218 |
| *Peking University Third Hospital, Beijing, China* | | |
| Gang Li | lixinregis@126.com | 13810380824 |
| Xiangyang Guo | puthmzk@bjmu.edu.cn | 15611908488 |
| Jun Wang | luckyoldhorse@sina.com | 15611908381 |
| Min Li | liminanesth@aliyun.com | 15611908799 |
| Mao Xu | anae@163.com | 18911482830 |
| Cheng Ni | Nicheng83@163.com | 13681569807 |
| Weiping Liu | analwp@163.com | 13466718523 |
| Yishen Qu | 13810934508@163.com | 13810934508 |
| Yang Zhou | exbzy@163.com | 15311414671 |
| Yi Chen | [spschenyi@pku.edu.cn](mailto:spschenyi@pku.edu.cn) | 18811761286 |
| Wenjie Yang | YWJ17865651223@163.com | 17865651223 |
| Yanli Li | Yanlili1995@163.com | 17865651361 |
| *Shandong Provincial Hospital, Jinan, Shandong Province, China* | | |
| Xu Wang | [cityhunter54@163.com](mailto:cityhunter54@163.com) | 15168863675 |
| Mengyuan Zhang | zhangmy717@163.com | 15168886767 |
| Gongmin Wang | tagmwang1971@163.com | 15168863629 |
| Xiaowei Li | siberlia@163.com | 15966324226 |
| Yingxue He | [249540337@qq.com](mailto:249540337@qq.com) | 15866698712 |
| Hao Pan | [panyisheng1988@163.com](mailto:Panyisheng1988@163.com) | 15253126186 |
| Xinlei Chen | 15168866771@163.com | 15168866771 |
| Mengdi Qu | imdrmeng@163.com | 13205339666 |
| Yang Liu | 2012lysdu@sina.com | 18366117258 |
| Yiping Tang | pp1307@126.com | 18366118173 |
| Han Hu | 2546393964@qq.com | 18006369252 |
| Zhun Wang | 15165125395@163.com | 15165125395 |
| Wenqing Yu | 664119795@qq.com | 18853137562 |
| Tiantian Yao | 448368529@qq.com | 18561375885 |
| *The First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan Province, China* | | |
| Dandan Tian | ddt0802@163.com | 13939071527 |
| Yanqiu Ai | aiyanqiu82@163.com | 13607690334 |
| Jianjun Yang | jianjunyang1971@163.com | 13783537619 |
| Yanan Zhang | helloayuan@163.com | 15890688032 |
| Qiong Xue | xueqiong000@163.com | 13837160267 |
| Bingxiao Zhao | ryzhaobingxiao@163.com | 15136287671 |
| Chaofan Zhang | zhangchaofan94@qq.com | 18625523328 |
| Yang Liu | 1179598292@qq.com | 15138931396 |
| Huijuan Li | lhj9101@126.com | 15038178351 |
| Qiqi Fan | 610090791@qq.com | 18860353588 |
| *The Second Hospital of Hebei Medical University, Shijiazhuang, Hebei Province, China* | | |
| Xiaoxian Feng | 1761362430@qq.com | 15081860838 |
| Ya Liu | md2006liuya@aliyun.com | 15803217957 |
| Xiaoying Zhang | 1570691404@qq.com | 18633493229 |
| Rongtian Kang | Kangrongtian@126.com | 15803210585 |
| Liping Ma | maliping1221@163.com | 13933107224 |
| Xiaofeng Duan | doctordxf@126.com | 13731131909 |
| Sufang Jiang | sufangjiang2014@163.com | 13933041534 |
| Yanting Zhai | 191216454@qq.com | 18330105872 |
| Chang Lv | 692319291@qq.com | 13143023023 |
| Jiaojiao Yang | 413505681@qq.com | 18931183565 |
| *Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing, China* | | |
| Wenyu Zhang | zwy751105@163.com | 13911864960 |
| Mingjun Xu | snake650222@163.com | 13701038959 |
| Xiangmin Che | chexming@hotmail.com | 13701109351 |
| *Yale University School of Medicine* | | |
| Lingzhong Meng | lingzhong.meng@yale.edu | (203) 785-2802 |
| Feng Dai | feng.dai@yale.edu | (203) 785-2802 |
| Xu Zhao | xu.zhao@yale.edu | (203) 785-2802 |
| David Yanez | david.yanez@yale.edu | (203) 785-2802 |

**Treatment assignment by hospital**

|  |  |  |  |
| --- | --- | --- | --- |
| **Hospital** | **Site #** | **Intervention**  **(no.)** | **Control**  **(no.)** |
| Peking University First Hospital | 1 | 30 | 30 |
| Peking University Third Hospital | 2 | 122 | 122 |
| Shandong Provincial Hospital | 3 | 68 | 68 |
| Zhengzhou University First Hospital | 4 | 76 | 76 |
| Hebei Medical University Second Hospital | 5 | 64 | 64 |
| Beijing Obstetrics and Gynecology Hospital | 6 | 40 | 40 |

**Randomization errors\***

|  |  |  |  |
| --- | --- | --- | --- |
| **Patient #** | **Planned randomization** | **Actual treatment** | **Reason** |
| 92 | Intervention | Control | Mislabeled envelope |
| 338 | Control | Intervention | Mislabeled envelope |
| 547 | Intervention | Control | Execution error |
| 548 | Control | Intervention | Execution error |
| 623 | Control | Intervention | Mislabeled envelope |
| 792 | Intervention | Control | Execution error |

\* These patients were excluded from the per-protocol population.

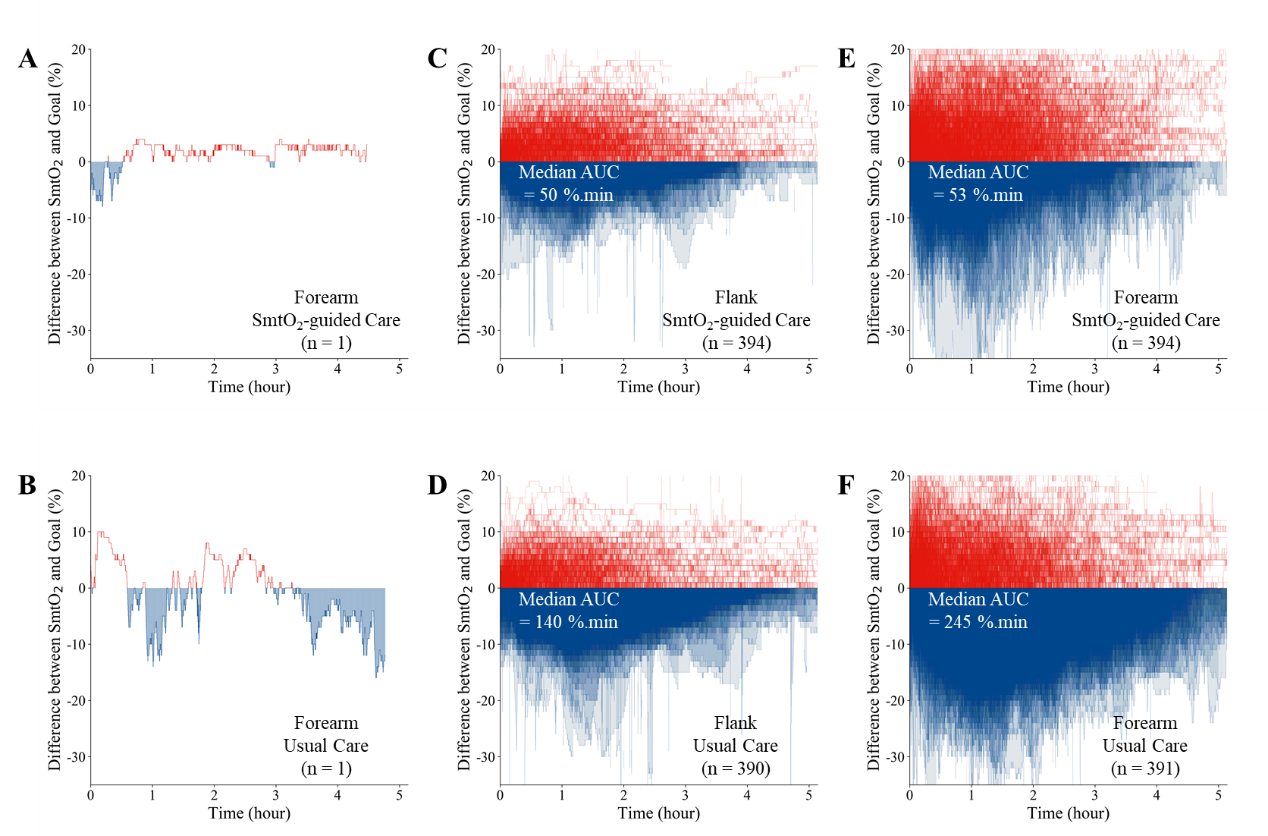
**Protocol violation**

|  |  |  |  |
| --- | --- | --- | --- |
| **Patient #** | **Group** | **Reason** | **Exclusion\*** |
| *The following based on intraoperative and postoperative information* | | | |
| 196 | Intervention | Converted to open | Yes |
| 218 | Intervention | Procedure aborted | Yes |
| 514 | Intervention | Procedure aborted | Yes |
| 603 | Intervention | Converted to open | Yes |
| 709 | Intervention | Converted to open | Yes |
| 730 | Intervention | Converted to open | Yes |
| 745 | Intervention | Remain intubated | Yes |
| 41 | Control | Bowel resection | Yes |
| 91 | Control | Procedure aborted | Yes |
| 100 | Control | Converted to open | Yes |
| 125 | Control | Converted to open | Yes |
| 148 | Control | Bowel resection | Yes |
| 177 | Control | Procedure aborted | Yes |
| 324 | Control | Converted to open | Yes |
| 389 | Control | Converted to open | Yes |
| 433 | Control | Converted to open | Yes |
| 444 | Control | Procedure aborted | Yes |
| 653 | Control | Procedure aborted | Yes |
| 701 | Control | Bowel resection | Yes |
| 763 | Control | Converted to open | Yes |
| *The following based on CASMED tissue oxygenation monitoring* | | | |
| 374 | Intervention | Protocol not followed | Yes |
| 380 | Intervention | Data missing | Yes |
| 538 | Intervention | Data missing | Yes |
| 643 | Intervention | Data missing | Yes |
| 717 | Intervention | Protocol not followed | Yes |
| 21 | Control | Data missing | No |
| 336 | Control | Monitor malfunctioning | No |
| 390 | Control | Data missing | No |
| 536 | Control | Data missing | No |
| 537 | Control | Data missing | No |
| 579 | Control | Monitor malfunctioning | No |
| 638 | Control | Monitor malfunctioning | No |
| 723 | Control | Monitor malfunctioning | No |
| 777 | Control | Monitor malfunctioning | No |
| *The following based on LiDCO hemodynamic monitoring* | | | |
| 34 | Intervention | Monitor malfunctioning | Yes |
| 72 | Intervention | Monitor malfunctioning | Yes |
| 129 | Intervention | Data missing | Yes |
| 182 | Intervention | Data missing | Yes |
| 212 | Intervention | Monitor malfunctioning | Yes |
| 300 | Intervention | Data missing | Yes |
| 373 | Intervention | Data missing | Yes |
| 379 | Intervention | Data missing | Yes |
| 391 | Intervention | Protocol not followed | Yes |
| 407 | Intervention | Monitor malfunctioning | Yes |
| 442 | Intervention | Monitor malfunctioning | Yes |
| 546 | Intervention | Data missing | Yes |
| 550 | Intervention | Protocol not followed | Yes |
| 645 | Intervention | Protocol not followed | Yes |
| 721 | Intervention | Monitor malfunctioning | Yes |
| 2 | Control | Monitor malfunctioning | No |
| 44 | Control | Monitor malfunctioning | No |
| 53 | Control | Data missing | No |
| 121 | Control | Monitor malfunctioning | No |
| 130 | Control | Data missing | No |
| 176 | Control | Monitor malfunctioning | No |
| 186 | Control | Data missing | No |
| 208 | Control | Monitor malfunctioning | No |
| 209 | Control | Monitor malfunctioning | No |
| 211 | Control | Monitor malfunctioning | No |
| 213 | Control | Monitor malfunctioning | No |
| 265 | Control | Data missing | No |
| 304 | Control | Data missing | No |
| 361 | Control | Monitor malfunctioning | No |
| 376 | Control | Data missing | No |
| 525 | Control | Monitor malfunctioning | No |
| 535 | Control | Data missing | No |
| 558 | Control | Monitor malfunctioning | No |
| 640 | Control | Monitor malfunctioning | No |
| 719 | Control | Data missing | No |
| 728 | Control | Data missing | No |
| 787 | Control | Monitor malfunctioning | No |

\* “Yes” indicates that patients were excluded from the per-protocol population, while “No” indicates that patients were not excluded from the per-protocol population. Patients from the control group were not excluded from the per-protocol population for malfunctioning research monitors or missing monitoring data because the intraoperative care was not guided by these monitors.

* Converted to open = the procedure was converted from laparoscopic to open approach;
* Procedure aborted = the planned hysterectomy was not performed;
* Remained intubated = the patient remained intubated for 2 hours or longer after surgery;
* Bowel resection = unplanned bowel resection was performed;
* Protocol not followed = the monitoring duration of either the flank or the forearm SmtO2 was less than 20 min in the SmtO2-guided care group;
* Data missing = the monitoring data of either tissue oxygenation or hemodynamics were lost;
* Monitor malfunctioning = at least 50% monitoring data of either tissue oxygenation or hemodynamics were missing or artifacts, or the monitoring duration of either tissue oxygenation or hemodynamics was less than 20 minutes in the usual care group.

**Figure S1. Therapeutic efficacy based on below-goal SmtO2 AUC**

****

The therapeutic efficacy of SmtO2-guided intraoperative care was assessed using the below-goal AUC. The abscissa and ordinate are the surgical duration and the difference between SmtO2 and the prespecified goal, respectively. The zero point on the ordinate indicates the therapeutic goal for SmtO2, i.e., the baseline or 70%, whichever is higher. Continuous tracings of forearm SmtO2 from a patient from the SmtO2-guided care group (A) and a patient from the usual care group (B) are illustrated. SmtO2 measurements higher than the goal are shown in red, while those equal to or less than the goal are shown in blue. The below-goal AUC is depicted in blue. Continuous flank (C and D) and forearm (E and F) SmtO2 tracings from patients in the SmtO2-guided care group (C and E) and the usual care group (D and F) are plotted on the same axes, making the AUCs from different patients overlapping onto each other. The median SmtO2 AUCs measured at different locations and for different treatment groups are indicated. SmtO2 denotes muscular tissue oxygen saturation; AUC denotes area under the curve.

**Figure S2. Risk ratios for postoperative nausea and vomiting in patients with a body mass index ≥ 25 in different hospitals**

****

SmtO2 = muscular tissue oxygen saturation; CI = confidence interval

Body mass index is defined as body mass in kilograms divided by the square of height in meters.

\* P = 0.005 after adjustment of multiple testing (number of hypothesis tests = 8).

† P = 0.126 after adjustment of multiple testing (number of hypothesis tests = 8).

‡ P = 0.233 after adjustment of multiple testing (number of hypothesis tests = 8).

**Table S1. Demographic and perioperative characteristics of the patients at baseline – analysis based on the per-protocol population**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Characteristic** | **SmtO2-Guided Care**  **(N = 370)** | **Usual Care**  **(N = 383)** | **Mean, Median or Proportion Difference (95% CI)\*** | ***P* Value** |
| Mean age ± SD, yr | 50 ± 8 | 50 ± 7 | 0.1 (-0.9–1.1) | 0.870 |
| Median height (IQR), cm | 160 (157–164) | 160 (157–163) | 0.0 (0.0–1.0) | 0.498 |
| Median body weight (IQR), kg | 64 (58–70) | 63 (57–69) | 1.0 (0.0–2.0) | 0.100 |
| Mean body mass index ± SD | 25 ± 4 | 25 ± 3 | 0.4 (-0.1–0.9) | 0.130 |
| ASA physical status, no. (%)† | | | | |
| * I | 108 (29.2) | 124 (32.4) | -3.2 (-10.0–3.7) | 0.591 |
| * II | 259 (70.0) | 255 (66.6) | 3.4 (-3.5–10.3) |
| * III | 3 (0.8) | 4 (1.0) | -0.2 (-1.8–1.4) |
| Marital status, no. (%) | | | | |
| * Married | 356 (96.2) | 365 (95.3) | 0.9 (-2.2–4.1) | 0.533 |
| * Other (never married, divorced, or widow) | 14 (3.8) | 18 (4.7) | -0.9 (-4.1–2.2) |
| Education, no. (%) | | | | |
| * No school | 12 (3.2) | 22 (5.7) | -2.5 (-5.7–0.7) | 0.731 |
| * Elementary school | 55 (14.9) | 51 (13.3) | 1.5 (-3.7–6.8) |
| * Middle school | 116 (31.4) | 128 (33.4) | -2.1 (-9.0–4.9) |
| * High school | 90 (24.3) | 88 (23.0) | 1.3 (-5.0–7.7) |
| * College | 88 (23.8) | 86 (22.5) | 1.3 (-5.0–7.6) |
| * Master degree | 6 (1.6) | 5 (1.3) | 0.3 (-1.7–2.3) |
| * Doctor degree | 3 (0.8) | 3 (0.8) | 0.0 (-1.3–1.3) |
| Median education (IQR), yr | 10 (9–15) | 9 (9–12) | 0.0 (0.0–0.0) | 0.440 |
| Surgical diagnosis, no. (%) | | | | |
| * Dysfunctional uterine bleeding | 13 (3.5) | 17 (4.4) | -0.9 (-4.0–2.1) | 0.319 |
| * Uterine pain, bleeding, and enlargement | 9 (2.4) | 14 (3.7) | -1.2 (-3.9–1.5) |
| * Uterine descensus and prolapse | 22 (5.9) | 10 (2.6) | 3.3 (0.2–6.5) |
| * Uterine leiomyomas | 135 (36.5) | 137 (35.8) | 0.7 (-6.4–7.8) |
| * Pelvic inflammatory disease | 1 (0.3) | 0 (0.0) | 0.3 (-0.5–1.1) |
| * Pelvic endometriosis | 11 (3.0) | 12 (3.1) | -0.2 (-2.8–2.5) |
| * Cervical stenosis with recurring pyometra following unsuccessful attempts to keep the cervix open | 0 (0.0) | 1 (0.3) | -0.3 (-1.0–0.5) |
| * Cervical intraepithelial carcinomas | 39 (10.5) | 60 (15.7) | -5.1 (-10.2– -0.1) |
| * Early invasive cervical cancer | 45 (12.2) | 41 (10.7) | 1.5 (-3.4–6.3) |
| * Endometrial adenocarcinoma and sarcoma | 73 (19.7) | 72 (18.8) | 0.9 (-5.0–6.8) |
| * Trophoblastic disease | 1 (0.3) | 0 (0.0) | 0.3 (-0.5–1.1) |
| * Ovarian and fallopian tube neoplasms | 19 (5.1) | 17 (4.4) | 0.7 (-2.6–4.0) |
| * Malignant disease of other adjacent organs | 2 (0.5) | 2 (0.5) | 0.0 (-1.0–1.1) |
| Coexisting medical condition, no. (%) | | | | |
| * Psychiatric disease | 0 (0.0) | 3 (0.8) | -0.8 (-1.9–0.4) | 0.088 |
| * Neurological disease | 9 (2.4) | 5 (1.3) | 1.1 (-1.1–3.3) | 0.252 |
| * Hypertension | 88 (23.8) | 75 (19.6) | 4.2 (-1.9–10.4) | 0.162 |
| * Cardiovascular disease | 10 (2.7) | 17 (4.4) | -1.7 (-4.6–1.2) | 0.200 |
| * Pulmonary disease | 6 (1.6) | 4 (1.0) | 0.6 (-1.3–2.5) | 0.489 |
| * Endocrinological disease | 34 (9.2) | 41 (10.7) | -1.5 (-6.1–3.0) | 0.487 |
| * Renal insufficiency | 1 (0.3) | 1 (0.3) | 0.0 (-0.7–0.8) | 0.980 |
| * Digestive disease | 12 (3.2) | 9 (2.3) | 0.9 (-1.7–3.5) | 0.457 |
| History of alcoholism, no. (%) | | | | |
| * Never | 352 (95.1) | 360 (94.0) | 1.1 (-2.4–4.6) | 0.776 |
| * Occasional drinker | 17 (4.6) | 22 (5.7) | -0.5 (-3.9–2.8) |
| * ≥ 3 drinks per week | 1 (0.3) | 1 (0.3) | 0.0 (-0.7–0.8) |
| History of anesthesia, no. (%) | | | | |
| * Never | 145 (39.2) | 142 (37.1) | 2.1 (-5.1–9.3) | 0.551 |
| * General anesthesia | 116 (31.4) | 125 (32.6) | -1.3 (-8.2–5.6) | 0.706 |
| * Spinal anesthesia | 94 (25.4) | 95 (24.8) | 0.6 (-5.9–7.1) | 0.849 |
| * Nerve block | 0 (0.0) | 2 (0.5) | -0.5 (-1.5–0.5) | 0.164 |
| * Local anesthesia | 30 (8.1) | 31 (8.1) | 0.0 (-3.9–3.9) | 0.994 |
| History of PONV, no. (%) | | | | |
| * Never had surgery | 140 (37.8) | 140 (36.6) | 1.3 (-5.9–8.5) | 0.453 |
| * Surgery without PONV | 207 (55.9) | 210 (54.8) | 1.1 (-6.3–8.5) |
| * Surgery with PONV | 23 (6.2) | 33 (8.6) | -2.4 (-6.4–1.6) |
| History of motion sickness, no. (%) | 83 (22.4) | 77 (20.1) | 2.3 (-3.8–8.4) | 0.435 |
| Preoperative lab results and bowel preparation | | | | |
| * Median hemoglobin (IQR), g/l | 129 (116–138) | 127 (111–135) | 3.0 (0.0–5.0) | **0.029** |
| * Median creatinine (IQR), μmol/l‡ | 57 (50–65) | 57 (51–64) | 0.0 (-1.8–1.0) | 0.770 |
| Bowel preparation before surgery, no. (%) | 349 (94.3) | 359 (93.7) | 0.6 (-3.1–4.2) | 0.732 |
| Patients recruited at each hospital, no. (%) | | | | |
| * Peking University First Hospital | 29 (7.8) | 30 (7.8) | 0.0 (-3.9–3.8) | 0.994 |
| * Peking University Third Hospital | 118 (31.9) | 118 (30.8) | 1.1 (-5.8–8.0) |
| * Shandong Provincial Hospital | 63 (17.0) | 64 (16.7) | 0.3 (-5.3–5.9) |
| * Zhengzhou University First Hospital | 72 (19.5) | 73 (19.1) | 0.4 (-5.5–6.3) |
| * Hebei Medical University Second Hospital | 52 (14.1) | 60 (15.7) | -1.6 (-7.0–3.7) |
| * Beijing Obstetrics Gynecology Hospital | 36 (9.7) | 38 (9.9) | -0.2 (-4.6–4.3) |

SmtO2 = muscular tissue oxygen saturation; SD = standard deviation; IQR = interquartile range; ASA = American Society of Anesthesiologists; PONV = postoperative nausea and vomiting.

\* The between-median or between-proportion difference and 95% CI were calculated using Hodges-Lehmann estimates and Newcombe’s method with continuity correction, respectively.

† The ASA criteria for physical status include a classification for normal health (I), mild systemic disease (II), and severe systemic disease (III).

‡ Data regarding the preoperative creatinine were missing for one patient in the SmtO2-guided care group.

**Table S2. Perioperative interventions and measurements – analysis based on the per-protocol population**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Variable** | **SmtO2-Guided Care**  **(N = 370)** | **Usual Care**  **(N = 383)** | **Median or Proportion Difference (95% CI)\*** | ***P* Value** | ***P* Value (Adjusted)†** |
| Median duration of anesthesia (IQR), min | 158 (115–205) | 149 (116–207) | 1.0 (-8.0–10.0) | 0.838 | > 0.999 |
| Median duration of surgery (IQR), min | 120 (83–168) | 115 (85–162) | 1.0 (-7.0–9.0) | 0.860 | > 0.999 |
| Medication administered during surgery | | | | | |
| * Median propofol (IQR), mg | 880 (620–1160) | 820 (615–1125) | 36.0 (-19.0–90.0) | 0.176 | > 0.999 |
| * Median remifentanil (IQR), mg | 1.0 (0.7–1.7) | 1.0 (0.7–1.5) | 0.0 (0.0–0.1) | 0.336 | > 0.999 |
| * Median sufentanil (IQR), mcg | 30 (20–40) | 30 (20–40) | 0.0 (0.0–5.0) | 0.062 | > 0.999 |
| * Dexamethasone, no. (%) | 370 (100.0) | 383 (100.0) | 0.0 (0.0–0.0) | NA | NA |
| * 5-HT3 antagonist, no. (%) | 368 (99.5) | 381 (99.5) | 0.0 (-1.1–1.0) | 0.972 | > 0.999 |
| * Cisatracurium, no. (%) | 181 (48.9) | 197 (51.4) | -2.5 (-9.9–4.9) | 0.490 | > 0.999 |
| * Rocuronium, no. (%) | 180 (48.6) | 175 (45.7) | 3.0 (-4.4–10.4) | 0.417 | > 0.999 |
| * Cisatracurium and rocuronium, no. (%) | 9 (2.4) | 11 (2.9) | -0.4 (-3.0–2.1) | 0.708 | > 0.999 |
| Input and output during surgery | | | | | |
| * Median crystalloid (IQR), ml | 1600 (1250–2000) | 1250 (1000–1600) | 300.0 (250.0–400.0) | **< 0.001** | **< 0.001** |
| * Colloid, no. (%) | 104 (28.1) | 85 (22.2) | 5.9 (-0.5–12.4) | 0.061 | > 0.999 |
| * Packed red blood cell, no. (%) | 5 (1.4) | 9 (2.3) | -1.0 (-3.2–1.2) | 0.311 | > 0.999 |
| * Median estimated blood loss (IQR), ml | 50 (20–100) | 50 (20–100) | 0.0 (0.0–0.0) | 0.157 | > 0.999 |
| * Median urine output (IQR), ml | 329 (200–500) | 200 (150–400) | 100.0 (50.0–100.0) | **< 0.001** | **< 0.001** |
| Baseline tissue oxygenation, median measurement (IQR), % | | | | | |
| * Flank SmtO2 | 76 (73–79) | 76 (73–79) | 0.0 (-1.0–1.0) | 0.733 | > 0.999 |
| * Forearm SmtO2 | 81 (76–86) | 81 (76–87) | 0.0 (-1.0–1.0) | 0.687 | > 0.999 |
| Intraoperative tissue oxygenation, median AUC (IQR), % ⋅ min‡ | | | | | |
| * Flank SmtO2 AUC < baseline§ | 41 (3–179) | 114 (14–392) | -39.0 (-65.0– -19.5) | **< 0.001** | **< 0.001** |
| * Flank SmtO2 AUC < 70%¶ | 0 (0–2) | 0 (0–31) | 0.0 (0.0–0.0) | **< 0.001** | **< 0.001** |
| * Flank SmtO2 AUC < goal (baseline or 70%, whichever is higher)§ | 47 (3–185) | 137 (15–422) | -49.2 (-73.5– -26.0) | **< 0.001** | **< 0.001** |
| * Forearm SmtO2 AUC < baseline|| | 46 (5–215) | 238 (19–931) | -118.0 (-182.5– -61.0) | **< 0.001** | **< 0.001** |
| * Forearm SmtO2 AUC < 70%\*\* | 0 (0–3) | 0 (0–42) | 0.0 (0.0–0.0) | **< 0.001** | **< 0.001** |
| * Forearm SmtO2 AUC < goal (baseline or 70%, whichever is higher)|| | 52 (5–236) | 249 (23–954) | 0.0 (0.0–0.0) | **< 0.001** | **< 0.001** |
| Baseline hemodynamics, median measurement (IQR) | | | | | |
| * Cardiac index, ml min-1 m-2†† | 3.4 (2.8–4.0) | 3.3 (2.7–3.9) | 0.1 (0.0–0.2) | 0.203 | > 0.999 |
| * Stroke volume, ml†† | 75 (63–90) | 75 (60–88) | 1.3 (-1.0–4.0) | 0.293 | > 0.999 |
| * Heart rate, beats/min | 74 (67–82) | 73 (67–81) | 0.0 (-1.0–2.0) | 0.543 | > 0.999 |
| * Systemic vascular resistance, mmHg ⋅ min/ml†† | 1313 (1100–1626) | 1384 (1150–1660) | -47.0 (-102.0–7.0) | 0.087 | > 0.999 |
| * Systolic blood pressure, mmHg | 132 (119–143) | 132 (120–145) | 0.0 (-3.0–2.0) | 0.753 | > 0.999 |
| * Diastolic blood pressure, mmHg | 77 (70–85) | 79 (71–85) | -1.0 (-3.0–1.0) | 0.221 | > 0.999 |
| * Mean blood pressure, mmHg | 95 (86–103) | 95 (86–104) | 0.0 (-2.0–1.0) | 0.654 | > 0.999 |
| Intraoperative hemodynamics, median AUC < baseline (IQR)‡ | | | | | |
| * Cardiac index, ml/m2‡‡ | 70 (36–135) | 91 (43–170) | -15.4 (-26.5– -4.9) | **0.004** | 0.124 |
| * Stroke volume, ml ⋅ min§§ | 1036 (497–2292) | 1301 (556–2469) | -130.3 (-296.3–18.4) | 0.090 | > 0.999 |
| * Heart rate, beats¶¶ | 849 (328–1578) | 1177 (629–2021) | -282.3 (-418.9– -151.4) | **< 0.001** | **< 0.001** |
| * Systemic vascular resistance, mmHg ⋅ min2/ml§§ | 9514 (2324–26175) | 8068 (2197–23040) | 752.8 (-270.3–2005.5) | 0.145 | > 0.999 |
| * Systolic blood pressure, mmHg ⋅ min¶¶ | 1630 (806–3059) | 1963 (961–3574) | -247.3 (-475.7– -32.5) | **0.024** | 0.720 |
| * Diastolic blood pressure, mmHg ⋅ min¶¶ | 1090 (529–2010) | 1357 (672–2280) | -160.8 (-318.3– -14.0) | **0.031** | 0.899 |
| * Mean blood pressure, mmHg ⋅ min¶¶ | 897 (399–1929) | 1102 (427–2203) | -118.3 (-262.8–10.3) | 0.074 | > 0.999 |
| Postoperative PONV prophylaxis | | | | | |
| * 5-HT3 antagonist, no. (%) | 87 (23.5) | 83 (21.7) | 1.8 (-4.4–8.1) | 0.545 | > 0.999 |
| * Droperidol, no. (%) | 2 (0.5) | 4 (1.0) | -0.5 (-2.0–1.0) | 0.437 | > 0.999 |
| Postoperative PONV treatment | | | | | |
| * 5-HT3 antagonist, no. (%) | 21 (5.7) | 29 (7.6) | -1.9 (-5.7–1.9) | 0.296 | > 0.999 |
| * Metoclopramide, no. (%) | 21 (5.7) | 18 (4.7) | 1.0 (-2.5–4.4) | 0.546 | > 0.999 |

SmtO2 = muscular tissue oxygen saturation; CI = confidence interval; IQR = interquartile range; NA = not applicable; AUC = area under the curve; PONV = postoperative nausea & vomiting.

\* The between-median or between-proportion differences and 95% CIs calculated using Hodges-Lehmann estimates and Newcombe’s method with continuity correction, respectively, were used to characterize the between-group difference.

† The *P* value was adjusted for multiple comparisons based on the Holm-Bonferroni method. All 41 hypotheses in this table were regarded as a family during calculation.

‡ Patients with more than 50% missing data or less-than-20-minutes data recording time were excluded from analysis.

§ Data regarding the flank SmtO2 AUC < baseline and goal (baseline or 70%) were missing for 9 patients in the usual care group.

¶ Data regarding the flank SmtO2 AUC < 70% were missing for 9 patients in the usual care group. 116/370 (31%) patients in the SmtO2-guided care group and 165/374 (44%) patients in the usual care group had an AUC that was > 0.

|| Data regarding the forearm SmtO2 AUC < baseline and goal (baseline or 70%) were missing for 8 patients in the usual care group.

\*\* Data regarding the forearm SmtO2 AUC < 70% were missing for 8 patients in the usual care group. 120/370 (32%) patients in the SmtO2-guided care group and 180/375 (48%) patients in the usual care group had an AUC that was > 0.

†† Data regarding the baseline cardiac index, stroke volume, and systemic vascular resistance were missing for 2 patients in the usual care group.

‡‡ Data regarding the cardiac index AUC < baseline were missing for 31 patients in the usual care group.

§§ Data regarding the stroke volume and systemic vascular resistance AUC < baseline were missing for 30 patients in the usual care group.

¶¶ Data regarding the heart rate, systolic, diastolic, and mean blood pressure AUC < baseline were missing for 29 patients in the usual care group.

**Table S3. Primary and secondary outcomes – analysis based on the per-protocol population**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Outcome** | **SmtO2-Guided Care**  **(N = 370)** | **Usual Care**  **(N = 383)** | **Risk Ratio or Median Difference**  **(95% CI)\*** | ***P* Value** | ***P* Value (Adjusted)†** |
| **Primary outcome** | | | | | |
| Incidence of PONV within postoperative 24 h, no. (%) | 112 (30.3) | 139 (36.3) | 0.83 (0.68–1.02) | 0.080 | > 0.999 |
| **Secondary outcomes** | | | | | |
| *Incidence of PONV at different stages* | | | | | |
| * Postoperative 0-2 h (very early), no. (%) | 46 (12.4) | 67 (17.5) | 0.71 (0.50–1.01) | 0.052 | > 0.999 |
| * Postoperative 2-6 h (early), no. (%) | 56 (15.1) | 74 (19.4) | 0.78 (0.57–1.07) | 0.125 | > 0.999 |
| * Postoperative 6-24 h (late), no. (%) | 73 (19.7) | 97 (25.4) | 0.78 (0.60–1.02) | 0.063 | > 0.999 |
| *Incidence of moderate-to-severe nausea at different stages‡* | | | | | |
| * Postoperative 0-2 h (very early), no. (%) | 17 (4.6) | 36 (9.4) | 0.49 (0.28–0.85) | **0.010** | 0.380 |
| * Postoperative 2-6 h (early), no. (%) | 24 (6.5) | 34 (8.9) | 0.73 (0.44–1.21) | 0.219 | > 0.999 |
| * Postoperative 6-24 h (late), no. (%) | 29 (7.8) | 46 (12.0) | 0.65 (0.42–1.02) | 0.056 | > 0.999 |
| * Postoperative 0-24 h (overall), no. (%) | 50 (13.5) | 82 (21.4) | 0.63 (0.46–0.87) | **0.004** | 0.160 |
| *Incidence of moderate-to-severe pain at different stages‡* | | | | | |
| * Postoperative 0-2 h (very early), no. (%) | 66 (17.8) | 62 (16.2) | 1.10 (0.80–1.51) | 0.547 | > 0.999 |
| * Postoperative 2-6 h (early), no. (%) | 48 (13.0) | 62 (16.2) | 0.80 (0.57–1.14) | 0.206 | > 0.999 |
| * Postoperative 6-24 h (late), no. (%) | 33 (8.9) | 49 (12.8) | 0.70 (0.46–1.06) | 0.088 | > 0.999 |
| * Postoperative 0-24 h (overall), no. (%) | 93 (25.1) | 107 (27.9) | 0.90 (0.71–1.14) | 0.384 | > 0.999 |
| *Median quality of recovery (QoR-15) (IQR)* | | | | | |
| Part A: How have you been feeling in the last 24 hours? (0 to 10, where 0 = none of the time [poor] and 10 = all of the time [excellent]) | | | | | |
| * Able to breathe easily | 10 (9–10) | 10 (9–10) | 0.0 (0.0–0.0) | 0.834 | > 0.999 |
| * Been able to enjoy food | 8 (7–10) | 8 (6–10) | 0.0 (0.0–1.0) | **0.038** | > 0.999 |
| * Feeling rested | 8 (7–9) | 7 (6–8) | 0.0 (0.0–1.0) | **0.002** | 0.082 |
| * Have had a good sleep | 7 (5–8) | 7 (5–8) | 0.0 (0.0–1.0) | 0.086 | > 0.999 |
| * Able to look after personal toilet and hygiene unaided | 7 (1–10) | 6 (1–10) | 0.0 (0.0–1.0) | 0.102 | > 0.999 |
| * Able to communicate with family or friends | 10 (10–10) | 10 (10–10) | 0.0 (0.0–0.0) | 0.425 | > 0.999 |
| * Getting support from hospital doctors and nurses | 10 (10–10) | 10 (10–10) | 0.0 (0.0–0.0) | 0.376 | > 0.999 |
| * Able to return to work or usual home activities | 8 (5–10) | 7 (4–9) | 0.0 (0.0–1.0) | 0.109 | > 0.999 |
| * Feeling comfortable and in control | 8 (6–10) | 8 (5–9) | 0.0 (0.0–1.0) | **0.027** | 0.972 |
| * Having a feeling of general well-being | 8 (6–9) | 7 (6–9) | 0.0 (0.0–1.0) | **0.013** | 0.481 |
| * Part A score | 80 (69–92) | 76 (65–88) | 3.0 (1.0–5.0) | **0.007** | 0.273 |
| Part B: Have you had any of the following in the last 24 hours? (10 to 0, where 10 = none of the time [excellent] and 0 = all of the time [poor]) | | | | | |
| * Moderate pain | 9 (8–10) | 9 (8–10) | 0.0 (0.0–0.0) | 0.272 | > 0.999 |
| * Severe pain | 10 (10–10) | 10 (10–10) | 0.0 (0.0–0.0) | 0.150 | > 0.999 |
| * Nausea or vomiting | 10 (9–10) | 10 (8–10) | 0.0 (0.0–0.0) | 0.346 | > 0.999 |
| * Feeling worried or anxious | 10 (8–10) | 10 (8–10) | 0.0 (0.0–0.0) | 0.587 | > 0.999 |
| * Feeling sad or depressed | 10 (8–10) | 10 (8–10) | 0.0 (0.0–0.0) | 0.454 | > 0.999 |
| * Part B score | 47 (43–50) | 46 (42–50) | 0.0 (0.0–1.0) | 0.103 | > 0.999 |
| *Sleep, ambulance and p.o. tolerance* | | | | | |
| * Median quality of the first night sleep (IQR)§ | 7 (4–8) | 6 (4–8) | 0.0 (0.0–1.0) | 0.062 | > 0.999 |
| * Able to get out of bed at postoperative 48 h, no. (%) | 350 (94.6) | 372 (97.1) | 0.97 (0.95–1.00) | 0.080 | > 0.999 |
| * Median time to get out of bed for the first time (IQR), hr¶ | 22 (18–29) | 21 (17–29) | 0.0 (-1.0–2.0) | 0.626 | > 0.999 |
| * Able to tolerate p.o. at postoperative 48 h, no. (%) | 356 (96.2) | 372 (97.1) | 0.99 (0.96–1.02) | 0.485 | > 0.999 |
| * Median time to tolerate the first p.o. (IQR), hr|| | 19 (11–25) | 19 (12–26) | 0.0 (-1.0–1.0) | 0.931 | > 0.999 |
| *30-day complications* | | | | | |
| * Mortality, no. (%) | 0 (0.0) | 0 (0.0) | NA | NA | NA |
| * Neurological, no. (%) | 0 (0.0) | 0 (0.0) | NA | NA | NA |
| * Cardiovascular, no. (%) | 0 (0.0) | 0 (0.0) | NA | NA | NA |
| * Pulmonary, no. (%) | 0 (0.0) | 0 (0.0) | NA | NA | NA |
| * Renal, no. (%) | 0 (0.0) | 0 (0.0) | NA | NA | NA |
| * Gastrointestinal, no. (%)\*\* | 0 (0.0) | 1 (0.3) | NA | 0.325 | > 0.999 |
| * Hematologic, no. (%)†† | 1 (0.3) | 2 (0.5) | 0.51 (0.05–5.68) | 0.583 | > 0.999 |
| * Surgery-related, no. (%)‡‡ | 1 (0.3) | 0 (0.0) | NA | 0.309 | > 0.999 |
| * Infectious, no. (%)§§ | 1 (0.3) | 3 (0.8) | 0.35 (0.04–3.30) | 0.333 | > 0.999 |
| *Other outcomes* | | | | | |
| Median length of hospital stay (IQR), hr | 116 (72–144) | 117 (89–144) | -2.0 (-8.0–1.0) | 0.300 | > 0.999 |
| ICU admission, no. (%) | 4 (1.1) | 1 (0.3) | 4.14 (0.46–36.87) | 0.166 | > 0.999 |
| Readmission within 30 days after surgery, no. (%) | 25 (6.8) | 30 (7.8) | 0.86 (0.52–1.44) | 0.570 | > 0.999 |

SmtO2 = muscular tissue oxygen saturation; CI = confidence interval; PONV = postoperative nausea & vomiting; QoR = quality of recovery; IQR = interquartile range; NA = not applicable.

\* The risk ratio and 95% CI were used to characterize the effectiveness of SmtO2-guided care for categorical variables. The median difference and 95% CI based on the Hodges–Lehmann estimator were used to characterize the effectiveness of SmtO2-guided care for continuous variables.

† The *P* value was adjusted for multiple comparisons based on the Holm-Bonferroni method. All 46 hypotheses in this table were regarded as a family during calculation.

‡ The severity of nausea and pain was assessed using a Numeric Rating Scale (NRS), an 11‐point scale where 0 indicates no nausea or pain and 10 indicates the worst nausea or pain. A score ≥ 5 indicates moderate-to-severe nausea or pain.

§ The quality of the first night sleep was assessed based on a 0 to 10 scale, where 0 = none of the time [poor] and 10 = all of the time [excellent]. Data regarding the quality of the first night sleep were missing for 1 patient in the SmtO2-guided care group.

¶ Data regarding the time to get out of bed for the first time were missing for 2 patients in the SmtO2-guided care group.

|| Data regarding the time to tolerate the first p.o. were missing for 3 patients in the usual care group.

\*\* Ileus occurred in 1 patient in the usual care group.

†† Deep vein thrombosis occurred in 1 patient in the SmtO2-guided care group and 2 patients in the usual care group.

‡‡ Wound dehiscence occurred in 1 patient in the SmtO2-guided care group.

§§ Urinary tract infection occurred in 1 patient in the SmtO2-guided care group; surgical site infection occurred in 3 patients in the usual care group.

**Table S4. Additional analysis – multivariable logistic regression based on the modified intention-to-treat population**

|  |  |  |
| --- | --- | --- |
| **Factor** | **Risk Ratio (95% CI)\*†** | ***P* Value** |
| Randomization (usual care) | Ref | Ref |
| Randomization (SmtO2-guided care) | 0.89 (0.71–1.10) | 0.284 |
| Peking University First Hospital | Ref | Ref |
| Peking University Third Hospital | 1.24 (0.80–1.78) | 0.333 |
| Shandong Provincial Hospital | 2.32 (1.90–2.63) | **< 0.001** |
| Zhengzhou University First Hospital | 1.07 (0.64–1.63) | 0.784 |
| Hebei Medical University Second Hospital | 1.62 (1.10–2.14) | **0.021** |
| Beijing Obstetrics and Gynecology Hospital | 1.48 (0.94–2.06) | 0.093 |

|  |  |  |
| --- | --- | --- |
| **Factor** | **Risk Ratio (95% CI)\*‡** | **P Value** |
| Randomization (usual care) | Ref | Ref |
| Randomization (SmtO2-guided care) | 0.94 (0.74–1.16) | 0.553 |
| Peking University First Hospital | Ref | Ref |
| Peking University Third Hospital | 1.56 (1.04–2.10) | **0.043** |
| Shandong Provincial Hospital | 2.64 (2.22–2.84) | **< 0.001** |
| Zhengzhou University First Hospital | 1.45 (0.79–2.15) | 0.213 |
| Hebei Medical University Second Hospital | 1.88 (1.22–2.43) | **0.010** |
| Beijing Obstetrics and Gynecology Hospital | 1.61 (1.03–2.18) | **0.043** |
| Age (18-39) | Ref | Ref |
| Age (40-49) | 0.94 (0.61–1.37) | 0.766 |
| Age (50-65) | 0.91 (0.58–1.33) | 0.645 |
| BMI (< 25) | Ref | Ref |
| BMI (≥ 25) | 0.85 (0.66–1.06) | 0.156 |
| Baseline hemoglobin (< 126 g/L) | Ref | Ref |
| Baseline hemoglobin (≥ 126 g/L) | 0.84 (0.65–1.06) | 0.154 |
| Baseline SVR (< 1380 mmHg ⋅ min/ml) | Ref | Ref |
| Baseline SVR (≥ 1380 mmHg ⋅ min/ml) | 1.20 (0.97–1.44) | 0.093 |
| Duration of anesthesia (< 120 min) | Ref | Ref |
| Duration of anesthesia (≥ 120 min) | 0.72 (0.53–0.95) | **0.019** |
| Urine output (< 500 mL) | Ref | Ref |
| Urine output (≥ 500 mL) | 0.92 (0.70–1.18) | 0.551 |
| Intraoperative sufentanil (< 30 ug) | Ref | Ref |
| Intraoperative sufentanil (≥ 30 ug) | 0.89 (0.53–1.34) | 0.608 |
| History of motion sickness (no) | Ref | Ref |
| History of motion sickness (yes) | 1.26 (0.99–1.54) | 0.059 |
| History of PONV (never had surgery) | Ref | Ref |
| History of PONV (surgery without PONV) | 1.09 (0.86–1.35) | 0.464 |
| History of PONV (surgery with PONV) | 1.77 (1.31–2.19) | **< 0.001** |

SmtO2 = muscular tissue oxygen saturation; CI = confidence interval; BMI = body mass index; SVR = systemic vascular resistance; Ref = reference; PONV = postoperative nausea and vomiting.

\* The risk ratio is for the subgroups as compared with the reference subgroup within the same strata (e.g., hospital, age, etc.).

† A multiple logistic regression model for the 24-hour PONV rate was fit where hospital was adjusted for to assess the impact of between-hospital heterogeneity on risk estimates.

‡ A multiple logistic regression model for the 24-hour PONV rate was fit with additional adjustments for the stratification variables including site, age, any variables exhibiting substantial between-group imbalance at baseline (*P* < 0.10), any variables exhibiting statistical significance during subgroup analysis (*P* < 0.05), and recognized risk factors for PONV.

**Table S5. Additional analysis – multivariable logistic regression based on the per-protocol population**

|  |  |  |
| --- | --- | --- |
| **Factor** | **Risk Ratio (95% CI)\*†** | ***P* Value** |
| Randomization (usual care) | Ref | Ref |
| Randomization (SmtO2-guided care) | 0.82 (0.64–1.02) | 0.082 |
| Peking University First Hospital | Ref | Ref |
| Peking University Third Hospital | 1.33 (0.85–1.89) | 0.211 |
| Shandong Provincial Hospital | 2.41 (1.99–2.71) | **< 0.001** |
| Zhengzhou University First Hospital | 1.15 (0.68–1.74) | 0.584 |
| Hebei Medical University Second Hospital | 1.64 (1.10–2.19) | **0.023** |
| Beijing Obstetrics and Gynecology Hospital | 1.46 (0.89–2.07) | 0.132 |

|  |  |  |
| --- | --- | --- |
| **Factor** | **Risk Ratio (95% CI)\*‡** | ***P* value** |
| Randomization (usual care) | Ref | Ref |
| Randomization (SmtO2-guided care) | 0.85 (0.66–1.08) | 0.189 |
| Peking University First Hospital | Ref | Ref |
| Peking University Third Hospital | 1.62 (1.08–2.18) | **0.030** |
| Shandong Provincial Hospital | 2.75 (2.37–2.92) | **< 0.001** |
| Zhengzhou University First Hospital | 1.69 (0.94–2.39) | 0.083 |
| Hebei Medical University Second Hospital | 2.03 (1.32–2.57) | **0.005** |
| Beijing Obstetrics and Gynecology Hospital | 1.57 (0.96–2.18) | 0.074 |
| Age (18-39) | Ref | Ref |
| Age (40-49) | 0.86 (0.53–1.3) | 0.505 |
| Age (50-65) | 0.86 (0.53–1.29) | 0.480 |
| BMI (< 25) | Ref | Ref |
| BMI (≥ 25) | 0.85 (0.65–1.07) | 0.179 |
| Baseline hemoglobin (< 126 g/L) | Ref | Ref |
| Baseline hemoglobin (≥ 126 g/L) | 0.90 (0.70–1.14) | 0.405 |
| Baseline SVR (< 1380 mmHg ⋅ min/ml) | Ref | Ref |
| Baseline SVR (≥ 1380 mmHg ⋅ min/ml) | 1.13 (0.90–1.38) | 0.284 |
| Duration of anesthesia (< 120 min) | Ref | Ref |
| Duration of anesthesia (≥ 120 min) | 0.71 (0.51–0.95) | **0.020** |
| Urine output (< 500 mL) | Ref | Ref |
| Urine output (≥ 500 mL) | 0.98 (0.74–1.25) | 0.877 |
| Intraoperative sufentanil (< 30 ug) | Ref | Ref |
| Intraoperative sufentanil (≥ 30 ug) | 0.77 (0.41–1.26) | 0.336 |
| History of motion sickness (no) | Ref | Ref |
| History of motion sickness (yes) | 1.19 (0.91–1.49) | 0.187 |
| History of PONV (never had surgery) | Ref | Ref |
| History of PONV (surgery without PONV) | 1.13 (0.88–1.40) | 0.322 |
| History of PONV (surgery with PONV) | 1.81 (1.32–2.24) | **< 0.001** |

SmtO2 = muscular tissue oxygen saturation; CI = confidence interval; BMI = body mass index; SVR = systemic vascular resistance; Ref = reference; PONV = postoperative nausea and vomiting.

\* The risk ratio is for the subgroups as compared with the reference subgroup within the same strata (e.g., hospital, age, etc.).

† A multiple logistic regression model for the 24-hour PONV rate was fit where hospital was adjusted for to assess the impact of between-hospital heterogeneity on risk estimates.

‡ A multiple logistic regression model for the 24-hour PONV rate was fit with additional adjustments for the stratification variables including site, age, any variables exhibiting substantial between-group imbalance at baseline (*P* < 0.10), any variables exhibiting statistical significance during subgroup analysis (*P* < 0.05), and recognized risk factors for PONV.

**Table S6. Demographic and perioperative characteristics of the patients at baseline – analysis based on patients with a body mass index ≥ 25**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Characteristic** | **SmtO2-Guided Care**  **(N = 183)** | **Usual Care**  **(N = 160)** | **Mean, Median or Proportion Difference (95% CI)\*** | ***P* Value** |
| Mean age ± SD, yr | 51 ± 7 | 51 ± 7 | -0.4 (-1.9–1.1) | 0.580 |
| Median height (IQR), cm | 160 (157–163) | 160 (157–163) | 0.0 (0.0–1.0) | 0.617 |
| Median body weight (IQR), kg | 70 (66–75) | 70 (67–75) | 0.0 (-1.0–2.0) | 0.651 |
| Median body mass index (IQR) | 28 (26–29) | 27 (26–29) | 0.0 (-0.4–0.4) | 0.898 |
| ASA physical status, no. (%)† | | |  |  |
| * I | 35 (19.1) | 29 (18.1) | 1.0 (-7.8–9.8) | 0.817 |
| * II | 146 (79.8) | 128 (80.0) | -0.2 (-8.9–8.5) |
| * III | 2 (1.1) | 3 (1.9) | -0.8 (-4.0–2.4) |
| Marital status, no. (%) | | |  |  |
| * Married | 179 (97.8) | 155 (96.9) | 0.9 (-3.1–5.0) | 0.587 |
| * Other (never married, divorced, or widow) | 4 (2.2) | 5 (3.1) | -0.9 (-5.0–3.1) |
| Education, no. (%) | | |  |  |
| * No school | 8 (4.4) | 12 (7.5) | -3.1 (-8.8–2.5) | 0.767 |
| * Elementary school | 33 (18.0) | 25 (15.6) | 2.4 (-6.1–10.9) |
| * Middle school | 58 (31.7) | 58 (36.2) | -4.6 (-15.2–6.1) |
| * High school | 45 (24.6) | 31 (19.4) | 5.2 (-4.1–14.5) |
| * College | 36 (19.7) | 31 (19.4) | 0.3 (-8.4–9.0) |
| * Master’s degree | 2 (1.1) | 2 (1.2) | -0.2 (-2.6–2.3) |
| * Doctor’s degree | 1 (0.5) | 1 (0.6) | -0.1 (-1.8–1.6) |
| Median education (IQR), yr | 9 (8–12) | 9 (8–12) | 0.0 (0.0–1.0) | 0.397 |
| Surgical diagnosis, no. (%) | | |  |  |
| * Dysfunctional uterine bleeding | 8 (4.4) | 3 (1.9) | 2.5 (-1.7–6.7) | 0.878 |
| * Uterine pain, bleeding, and enlargement | 5 (2.7) | 6 (3.8) | -1.0 (-5.4–3.3) |
| * Uterine descensus and prolapse | 9 (4.9) | 7 (4.4) | 0.5 (-4.5–5.5) |
| * Uterine leiomyomas | 68 (37.2) | 60 (37.5) | -0.3 (-10.9–10.3) |
| * Pelvic inflammatory disease | 0 (0.0) | 1 (0.6) | -0.6 (-2.4–1.2) |
| * Pelvic endometriosis | 4 (2.2) | 6 (3.8) | -1.6 (-5.8–2.6) |
| * Cervical stenosis with recurring pyometra following unsuccessful attempts to keep the cervix open | 0 (0.0) | 1 (0.6) | -0.6 (-2.4–1.2) |
| * Cervical intraepithelial carcinomas | 17 (9.3) | 19 (11.9) | -2.6 (-9.7–4.5) |
| * Early invasive cervical cancer | 12 (6.6) | 9 (5.6) | 0.9 (-4.7–6.6) |
| * Endometrial adenocarcinoma and sarcoma | 51 (27.9) | 40 (25.0) | 2.9 (-7.1–12.8) |
| * Trophoblastic disease | 8 (4.4) | 7 (4.4) | 0.0 (-4.3–4.3) |
| * Ovarian and fallopian tube neoplasms | 1 (0.5) | 1 (0.6) | -0.1 (-1.8–1.6) |
| * Malignant disease of other adjacent organs | 12 (6.6) | 9 (5.6) | 0.9 (-4.7–6.6) |
| Coexisting medical condition, no. (%) | | |  |  |
| * Psychiatric disease | 0 (0.0) | 3 (1.9) | -1.9 (-4.6–0.8) | 0.063 |
| * Neurological disease | 7 (3.8) | 4 (2.5) | 1.3 (-2.9–5.6) | 0.487 |
| * Hypertension | 65 (35.5) | 51 (31.9) | 3.6 (-7.0–14.2) | 0.477 |
| * Cardiovascular disease | 3 (1.6) | 15 (9.4) | -7.7 (-13.2– -2.3) | **0.001** |
| * Pulmonary disease | 4 (2.2) | 1 (0.6) | 1.6 (-1.5–4.6) | 0.229 |
| * Endocrinological disease | 21 (11.5) | 21 (13.1) | -1.6 (-9.2–5.9) | 0.642 |
| * Renal insufficiency | 1 (0.5) | 0 (0.0) | 0.5 (-1.1–2.2) | 0.349 |
| * Digestive disease | 6 (3.3) | 2 (1.2) | 2.0 (-1.7–5.7) | 0.214 |
| History of alcoholism, no. (%) | | |  |  |
| * Never | 171 (93.4) | 155 (96.9) | -3.4 (-8.5–1.6) | 0.119 |
| * Occasional drinker | 12 (6.6) | 4 (2.5) | 4.1 (-0.9–9.0) |
| * ≥ 3 drinks per week | 0 (0.0) | 1 (0.6) | -0.6 (-2.4–1.2) |
| History of anesthesia, no. (%) | | |  |  |
| * Never | 82 (44.8) | 61 (38.1) | 6.7 (-4.3–17.7) | 0.210 |
| * General anesthesia | 51 (27.9) | 51 (31.9) | -4.0 (-14.3–6.3) | 0.418 |
| * Spinal anesthesia | 41 (22.4) | 38 (23.8) | -1.3 (-10.9–8.2) | 0.768 |
| * Nerve block | 0 (0.0) | 0 (0.0) | NA | NA |
| * Local anesthesia | 15 (8.2) | 16 (10.0) | -1.8 (-8.5–4.9) | 0.561 |
| History of PONV, no. (%) | | |  |  |
| * Never had surgery | 77 (42.1) | 60 (37.5) | 4.6 (-6.4–15.5) | 0.686 |
| * Surgery without PONV | 95 (51.9) | 90 (56.2) | -4.3 (-15.5–6.8) |
| * Surgery with PONV | 11 (6.0) | 10 (6.2) | -0.2 (-5.6–5.1) |
| History of motion sickness, no. (%) | 36 (19.7) | 36 (22.5) | -2.8 (-12.1–6.4) | 0.521 |
| Preoperative lab results and bowel preparation | | |  |  |
| * Median hemoglobin (IQR), g/l | 130 (119–139) | 128 (114–137) | 2.0 (-2.0–5.0) | 0.304 |
| * Median creatinine (IQR), μmol/l | 57 (49–65) | 56 (51–63) | 0.8 (-1.5–2.9) | 0.523 |
| Bowel preparation before surgery, no. (%) | 173 (94.5) | 152 (95.0) | -0.5 (-5.6–4.7) | 0.847 |
| Patients recruited at each hospital, no. (%) | | |  |  |
| * Peking University First Hospital | 10 (5.5) | 9 (5.6) | -0.2 (-5.2–4.9) | 0.551 |
| * Peking University Third Hospital | 56 (30.6) | 40 (25.0) | 5.6 (-4.5–15.7) |
| * Shandong Provincial Hospital | 36 (19.7) | 38 (23.8) | -4.1 (-13.4–5.3) |
| * Zhengzhou University First Hospital | 35 (19.1) | 23 (14.4) | 4.8 (-3.7–13.2) |
| * Hebei Medical University Second Hospital | 29 (15.8) | 33 (20.6) | -4.8 (-13.6–4.0) |
| * Beijing Obstetrics Gynecology Hospital | 17 (9.3) | 17 (10.6) | -1.3 (-8.3–5.6) |

SmtO2 = muscular tissue oxygen saturation; SD = standard deviation; IQR = interquartile range; ASA = American Society of Anesthesiologists; NA not applicable; PONV = postoperative nausea and vomiting.

\* The between-median or between-proportion difference and 95% CI were calculated using Hodges-Lehmann estimates and Newcombe’s method with continuity correction, respectively.

† The ASA criteria for physical status include a classification for normal health (I), mild systemic disease (II), and severe systemic disease (III).

**Table S7. Perioperative interventions and measurements – analysis based on patients with a body mass index ≥ 25**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Variable** | **SmtO2-Guided Care**  **(N = 183)** | **Usual Care**  **(N = 160)** | **Median or Proportion Difference (95% CI)\*** | ***P* Value** | ***P* Value (Adjusted)†** |
| Median duration of anesthesia (IQR), min | 160 (119–210) | 159 (122–219) | -3.0 (-17.0–11.0) | 0.708 | > 0.999 |
| Median duration of surgery (IQR), min | 125 (85–169) | 120 (91–175) | -3.0 (-15.0–9.0) | 0.567 | > 0.999 |
| Medication administered during surgery | | | | | |
| * Median propofol (IQR), mg | 900 (670–1235) | 855 (648–1183) | 30.0 (-50.0–113.0) | 0.448 | > 0.999 |
| * Median remifentanil (IQR), mg | 1.1 (0.8–1.9) | 1.0 (0.8–1.5) | 0.0 (-0.1–0.2) | 0.517 | > 0.999 |
| * Median sufentanil (IQR), mcg | 35 (20–45) | 31 (20–45) | 0.0 (-3.0–5.0) | 0.884 | > 0.999 |
| * Dexamethasone, no. (%) | 183 (100.0) | 160 (100.0) | 0.0 (0.0–0.0) | NA | NA |
| * 5-HT3 antagonist, no. (%) | 182 (99.5) | 159 (99.4) | 0.1 (-1.6–1.8) | 0.924 | > 0.999 |
| * Cisatracurium, no. (%) | 98 (53.6) | 94 (58.8) | -5.2 (-16.3–5.9) | 0.334 | > 0.999 |
| * Rocuronium, no. (%) | 82 (44.8) | 62 (38.8) | 6.1 (-5.0–17.1) | 0.257 | > 0.999 |
| * Cisatracurium and rocuronium, no. (%) | 3 (1.6) | 4 (2.5) | -0.9 (-4.5–2.8) | 0.574 | > 0.999 |
| Input and output during surgery | | | | | |
| * Median crystalloid (IQR), ml | 1600 (1225–2000) | 1300 (1000–1600) | 0.0 (0.0–0.0) | **< 0.001** | **< 0.001** |
| * Colloid, no. (%) | 49 (26.8) | 35 (21.9) | 4.9 (-4.8–14.6) | 0.292 | > 0.999 |
| * Packed red blood cell, no. (%) | 3 (1.6) | 6 (3.8) | -2.1 (-6.2–1.9) | 0.222 | > 0.999 |
| * Median estimated blood loss (IQR), ml | 50 (30–100) | 50 (30–100) | 0.0 (0.0–0.0) | 0.921 | > 0.999 |
| * Median urine output (IQR), ml | 300 (200–525) | 275 (150–450) | 80.0 (0.0–100.0) | **0.003** | 0.096 |
| Baseline tissue oxygenation, median measurement (IQR), % | | | | | |
| * Flank SmtO2 | 74 (72–77) | 74 (71–76) | 1.0 (0.0–2.0) | 0.114 | > 0.999 |
| * Forearm SmtO2 | 81 (77–87) | 82 (77–86) | 0.0 (-0.0–2.0) | 0.690 | > 0.999 |
| Intraoperative tissue oxygenation, median AUC (IQR), min ⋅ %‡ | | | | | |
| * Flank SmtO2 AUC < baseline§ | 50 (2–172) | 104 (10–363) | -28.0 (-65.0– -5.5) | **< 0.001** | **0.024** |
| * Flank SmtO2 AUC < 70%¶ | 0 (0–14) | 4 (0–105) | 0.0 (-3.0–0.0) | **< 0.001** | **0.012** |
| * Flank SmtO2 AUC < goal (baseline or 70%, whichever is higher)§ | 51 (4–183) | 152 (14–407) | -45.5 (-95.0– -13.0) | **< 0.001** | **0.002** |
| * Forearm SmtO2 AUC < baseline|| | 33 (5–147) | 283 (38–1054) | -177.5 (-284.5– -83.0) | **< 0.001** | **< 0.001** |
| * Forearm SmtO2 AUC < 70%\*\* | 0 (0–0) | 0 (0–45) | 0.0 (-1.5–0.0) | **< 0.001** | **< 0.001** |
| * Forearm SmtO2 AUC < goal (baseline or 70%, whichever is higher)|| | 35 (5–147) | 296 (44–1054) | -196.5 (-294.0– -109.0) | **< 0.001** | **< 0.001** |
| Baseline hemodynamics, median measurement (IQR) | | | | | |
| * Cardiac index, ml min-1 m-2†† | 3.5 (2.9–4.1) | 3.4 (2.8–4.1) | 0.1 (0.0–0.3) | 0.154 | > 0.999 |
| * Stroke volume, ml†† | 83 (70–99) | 82 (68–93) | 2.0 (-2.0–7.0) | 0.272 | > 0.999 |
| * Heart rate, beats/min | 74 (67–81) | 73 (67–80) | 0.0 (-2.0–2.0) | 0.892 | > 0.999 |
| * Systemic vascular resistance, mmHg ⋅ min/ml†† | 1240 (1075–1511) | 1321 (1129–1558) | -67.0 (-137.0–5.0) | 0.070 | > 0.999 |
| * Systolic blood pressure, mmHg | 136 (124–148) | 134 (122–148) | 1.0 (-3.0–5.0) | 0.529 | > 0.999 |
| * Diastolic blood pressure, mmHg | 80 (72–86) | 80 (74–86) | -1.0 (-3.0–2.0) | 0.536 | > 0.999 |
| * Mean blood pressure, mmHg | 98 (92–107) | 98 (89–106) | 0.0 (-2.0–3.0) | 0.765 | > 0.999 |
| Intraoperative hemodynamics, median AUC < baseline (IQR)‡ | | | | | |
| * Cardiac index, ml/m2‡‡ | 77 (41–149) | 99 (49–193) | -16.5 (-34.8– -0.3) | **0.046** | > 0.999 |
| * Stroke volume, ml ⋅ min§§ | 1067 (631–2560) | 1523 (571–3261) | -153.2 (-450.0–105.9) | 0.245 | > 0.999 |
| * Heart rate, beats¶¶ | 926 (336–1568) | 1219 (670–1989) | -311.0 (-521.6– -103.0) | **0.002** | 0.066 |
| * Systemic vascular resistance, mmHg⋅min2/ml§§ | 10011 (3569–24892) | 7836 (1771–23574) | 1468.3 (-222.8–3893.0) | 0.090 | > 0.999 |
| * Systolic blood pressure, mmHg ⋅ min¶¶ | 1832 (939–3494) | 1992 (1140–3601) | -167.8 (-523.3–179.2) | 0.332 | > 0.999 |
| * Diastolic blood pressure, mmHg ⋅ min¶¶ | 1174 (561–2344) | 1447 (673–2384) | -108.0 (-359.0–140.3) | 0.373 | > 0.999 |
| * Mean blood pressure, mmHg ⋅ min¶¶ | 1068 (618–2043) | 1136 (509–2277) | -74.7 (-292.5–136.5) | 0.456 | > 0.999 |
| Postoperative PONV prophylaxis | | | | | |
| * 5-HT3 antagonist, no. (%) | 41 (22.4) | 31 (19.4) | 3.0 (-6.2–12.2) | 0.492 | > 0.999 |
| * Droperidol, no. (%) | 0 (0.0) | 1 (0.6) | -0.6 (-2.4–1.2) | 0.284 | > 0.999 |
| Postoperative PONV treatment | | | | | |
| * 5-HT3 antagonist, no. (%) | 13 (7.1) | 9 (5.6) | 1.5 (-4.3–7.2) | 0.577 | > 0.999 |
| * Metoclopramide, no. (%) | 11 (6.0) | 9 (5.6) | 0.4 (-5.0–5.7) | 0.879 | > 0.999 |

SmtO2 = muscular tissue oxygen saturation; CI = confidence interval; IQR = interquartile range; NA = not applicable; AUC = area under the curve; PONV = postoperative nausea & vomiting.

\* The between-median or between-proportion difference and 95% CIs calculated using Hodges-Lehmann estimates and Newcombe’s method with continuity correction, respectively, were used to characterize the between-group difference.

† The *P* value was adjusted for multiple comparisons based on the Holm-Bonferroni method. All 41 hypotheses in this table were regarded as a family during calculation.

‡ Patients with more than 50% missing data or less-than-20-minutes data recording time were excluded from analysis.

§ Data regarding the flank SmtO2 AUC < baseline and goal (baseline or 70%) were missing for 2 patients in the SmtO2-guided care group and 3 patients in the usual care group.

¶ Data regarding the flank SmtO2 AUC < 70% were missing for 2 patients in the SmtO2-guided care group and 3 patients in the usual care group. 74/181 (41%) patients in the SmtO2-guided care group and 88/157 (56%) patients in the usual care group had an AUC that was > 0.

|| Data regarding the forearm SmtO2 AUC < baseline and goal (baseline or 70%) were missing for 2 patients in the SmtO2-guided care group and 3 patients in the usual care group.

\*\* Data regarding the forearm SmtO2 AUC < 70% were missing for 2 patients in the SmtO2-guided care group and 3 patients in the usual care group. 40/181 (22%) patients in the SmtO2-guided care group and 78/157 (50%) patients in the usual care group had an AUC that was > 0.

†† Data regarding the baseline cardiac index, stroke volume, and systemic vascular resistance were missing for 2 patients in the usual care group.

‡‡ Data regarding the cardiac index AUC < baseline were missing for 8 patients in the SmtO2-guided care group and 12 patients in the usual care group.

§§ Data regarding the stroke volume and systemic vascular resistance AUC < baseline were missing for 8 patients in the SmtO2-guided care group and 12 patients in the usual care group.

¶¶ Data regarding the heart rate, systolic, diastolic, and mean blood pressure AUC < baseline were missing for 8 patients in the SmtO2-guided care group and 11 patients in the usual care group.

**Table S8. Primary and secondary outcomes – analysis based on patients with a body mass index ≥ 25**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Outcome** | **SmtO2-Guided Care**  **(N = 183)** | **Usual Care**  **(N = 160)** | **Risk Ratio or Median Difference**  **(95% CI)\*** | ***P* Value** | ***P* Value (Adjusted)†** |
| **Primary outcome** | | | | | |
| Incidence of PONV within postoperative 24 h, no. (%) | 44 (24.0) | 66 (41.2) | 0.58 (0.42–0.80) | **< 0.001** | **0.026** |
| **Secondary outcomes** | | | | | |
| *Incidence of PONV at different stages* | | | | | |
| * Postoperative 0-2 h (very early), no. (%) | 17 (9.3) | 31 (19.4) | 0.48 (0.28–0.83) | **0.007** | 0.245 |
| * Postoperative 2-6 h (early), no. (%) | 27 (14.8) | 33 (20.6) | 0.72 (0.45–1.14) | 0.156 | > 0.999 |
| * Postoperative 6-24 h (late), no. (%) | 29 (15.8) | 42 (26.2) | 0.60 (0.40–0.92) | **0.018** | 0.558 |
| *Incidence of moderate-to-severe nausea at different stages‡* | | | | | |
| * Postoperative 0-2 h (very early), no. (%) | 8 (4.4) | 17 (10.6) | 0.41 (0.18–0.93) | **0.026** | 0.728 |
| * Postoperative 2-6 h (early), no. (%) | 12 (6.6) | 17 (10.6) | 0.62 (0.30–1.25) | 0.177 | > 0.999 |
| * Postoperative 6-24 h (late), no. (%) | 11 (6.0) | 18 (11.2) | 0.53 (0.26–1.10) | 0.082 | > 0.999 |
| * Postoperative 0-24 h (overall), no. (%) | 23 (12.6) | 38 (23.8) | 0.53 (0.33–0.85) | **0.007** | 0.245 |
| *Incidence of moderate-to-severe pain at different stages‡* | | | | | |
| * Postoperative 0-2 h (very early), no. (%) | 28 (15.3) | 28 (17.5) | 0.87 (0.54–1.41) | 0.582 | > 0.999 |
| * Postoperative 2-6 h (early), no. (%) | 23 (12.6) | 27 (17.0) | 0.74 (0.45–1.25) | 0.249 | > 0.999 |
| * Postoperative 6-24 h (late), no. (%) | 15 (8.2) | 23 (14.4) | 0.57 (0.31–1.05) | 0.069 | > 0.999 |
| * Postoperative 0-24 h (overall), no. (%) | 45 (24.6) | 49 (30.6) | 0.80 (0.57–1.13) | 0.211 | > 0.999 |
| *Median quality of recovery (QoR-15) (IQR)§* | | | | | |
| Part A: How have you been feeling in the last 24 hours? (0 to 10, where 0 = none of the time [poor] and 10 = all of the time [excellent]) | | | | | |
| * Able to breathe easily | 10 (10–10) | 10 (9–10) | 0.0 (0.0–0.0) | 0.353 | > 0.999 |
| * Been able to enjoy food | 8 (7–10) | 8 (6–9) | 1.0 (0.0–1.0) | **0.004** | 0.144 |
| * Feeling rested | 8 (7–9) | 7 (6–8) | 1.0 (0.0–1.0) | **< 0.001** | **0.030** |
| * Have had a good sleep | 7 (5–8) | 7 (4–8) | 1.0 (0.0–1.0) | **0.036** | 0.972 |
| * Able to look after personal toilet and hygiene unaided | 7 (1–10) | 5 (0–9) | 0.0 (0.0–1.0) | **0.025** | 0.725 |
| * Able to communicate with family or friends | 10 (10–10) | 10 (10–10) | 0.0 (0.0–0.0) | 0.122 | > 0.999 |
| * Getting support from hospital doctors and nurses | 10 (10–10) | 10 (10–10) | 0.0 (0.0–0.0) | 0.406 | > 0.999 |
| * Able to return to work or usual home activities | 8 (5–10) | 7 (5–9) | 0.0 (0.0–1.0) | 0.262 | > 0.999 |
| * Feeling comfortable and in control | 8 (6–10) | 7 (5–9) | 1.0 (0.0–1.0) | **0.016** | 0.528 |
| * Having a feeling of general well-being | 8 (6–9) | 7 (6–9) | 0.0 (0.0–1.0) | **0.019** | 0.570 |
| * Part A score | 80 (69–92) | 74 (65–85) | 5.0 (2.0–8.0) | **0.002** | 0.074 |
| Part B: Have you had any of the following in the last 24 hours? (10 to 0, where 10 = none of the time [excellent] and 0 = all of the time [poor]) | | | | | |
| * Moderate pain | 9 (8–10) | 9 (8–10) | 0.0 (0.0–0.0) | 0.990 | > 0.999 |
| * Severe pain | 10 (10–10) | 10 (10–10) | 0.0 (0.0–0.0) | 0.076 | > 0.999 |
| * Nausea or vomiting | 10 (9–10) | 10 (8–10) | 0.0 (0.0–0.0) | **0.016** | 0.528 |
| * Feeling worried or anxious | 10 (8–10) | 10 (7–10) | 0.0 (0.0–0.0) | 0.506 | > 0.999 |
| * Feeling sad or depressed | 10 (8–10) | 10 (8–10) | 0.0 (0.0–0.0) | 0.584 | > 0.999 |
| * Part B score | 47 (43–50) | 46 (42–49) | 0.0 (0.0–1.0) | 0.077 | > 0.999 |
| *Sleep, ambulance and p.o. tolerance* | | | | | |
| * Median quality of the first night sleep (IQR)¶ | 7 (4–8) | 6 (4–8) | 0.0 (0.0–1.0) | 0.138 | > 0.999 |
| * Able to get out of bed at postoperative 48 h, no. (%) | 174 (95.1) | 154 (96.2) | 0.99 (0.94–1.03) | 0.598 | > 0.999 |
| * Median time to get out of bed for the first time (IQR), hr|| | 23 (18–29) | 21 (18–30) | 1.0 (-1.0–3.0) | 0.457 | > 0.999 |
| * Able to tolerate p.o. at postoperative 48 h, no. (%) | 175 (95.6) | 155 (96.9) | 0.99 (0.95–1.03) | 0.546 | > 0.999 |
| * Median time to tolerate the first p.o. (IQR), hr\*\* | 20 (12–26) | 19 (10–26) | 0.0 (-1.0–3.0) | 0.631 | > 0.999 |
| *30-day complications* | | | | | |
| * Mortality, no. (%) | 0 (0.0) | 0 (0.0) | NA | NA | NA |
| * Neurological, no. (%) | 0 (0.0) | 0 (0.0) | NA | NA | NA |
| * Cardiovascular, no. (%) | 0 (0.0) | 0 (0.0) | NA | NA | NA |
| * Pulmonary, no. (%) | 0 (0.0) | 0 (0.0) | NA | NA | NA |
| * Renal, no. (%) | 0 (0.0) | 0 (0.0) | NA | NA | NA |
| * Gastrointestinal, no. (%) | 0 (0.0) | 0 (0.0) | NA | NA | NA |
| * Hematologic, no. (%)†† | 1 (0.5) | 1 (0.6) | 0.87 (0.06–13.86) | 0.924 | > 0.999 |
| * Surgery-related, no. (%) | 0 (0.0) | 0 (0.0) | NA | NA | NA |
| * Infectious, no. (%)‡‡ | 1 (0.5) | 2 (1.2) | 0.44 (0.04–4.78) | 0.485 | > 0.999 |
| *Other outcomes* | | | | | |
| Median length of hospital stay (IQR), hr | 118 (72–144) | 120 (93–149) | -3.0 (-21.0–1.0) | 0.203 | > 0.999 |
| ICU admission, no. (%) | 4 (2.2) | 1 (0.6) | 3.50 (0.39–30.97) | 0.229 | > 0.999 |
| Readmission within 30 days after surgery, no. (%) | 11 (6.0) | 13 (8.1) | 0.74 (0.34–1.60) | 0.444 | > 0.999 |

SmtO2 = muscular tissue oxygen saturation; CI = confidence interval; PONV = postoperative nausea & vomiting; QoR = quality of recovery; IQR = interquartile range; NA = not applicable.

\* The risk ratio and 95% CI were used to characterize the effectiveness of SmtO2-guided care for categorical variables. The between-median difference and 95% CI based on the Hodges–Lehmann estimator were used to characterize the effectiveness of SmtO2-guided care for continuous variables.

† The *P* value was adjusted for multiple comparisons based on the Holm-Bonferroni method. All 46 hypotheses in this table were regarded as a family during calculation.

‡ The severity of nausea and pain was assessed using a Numeric Rating Scale (NRS), an 11‐point scale where 0 indicates no nausea or pain and 10 indicates the worst nausea or pain. A score ≥ 5 indicates moderate-to-severe nausea or pain.

§ Data regarding QoR-15 were missing for 1 patient in the SmtO2-guided care group.

¶ The quality of the first night sleep was assessed based on a 0 to 10 scale, where 0 = none of the time [poor] and 10 = all of the time [excellent]. Data regarding the quality of the first night sleep were missing for 1 patient in the SmtO2-guided care group.

|| Data regarding the time to get out of bed for the first time were missing for 1 patient in the SmtO2-guided care group and 1 patient in the usual care group.

\*\* Data regarding the time to tolerate the first p.o. were missing for 1 patient in the control group.

†† Deep vein thrombosis occurred in 1 patient in the SmtO2-guided care group and 1 patient in the usual care group.

‡‡ Surgical site infection occurred in 1 patient in the SmtO2-guided care group and 2 patients in the usual care group.

**Table S9. Additional analysis – multivariable logistic regression based on patients with a body mass index ≥ 25**

|  |  |  |
| --- | --- | --- |
| **Factor** | **Risk Ratio (95% CI)\*†** | ***P* Value** |
| Randomization (usual care) | Ref | Ref |
| Randomization (SmtO2-guided care) | 0.57 (0.37–0.83) | **0.003** |
| Peking University First Hospital | Ref | Ref |
| Peking University Third Hospital | 1.00 (0.40–2.02) | 0.999 |
| Shandong Provincial Hospital | 2.20 (1.35–2.82) | **0.009** |
| Zhengzhou University First Hospital | 0.95 (0.35–2.00) | 0.911 |
| Hebei Medical University Second Hospital | 1.58 (0.75–2.50) | 0.220 |
| Beijing Obstetrics and Gynecology Hospital | 1.32 (0.52–2.36) | 0.523 |

|  |  |  |
| --- | --- | --- |
| **Factor** | **Risk Ratio (95% CI)\*‡** | ***P* value** |
| Randomization (usual care) | Ref | Ref |
| Randomization (SmtO2-guided care) | 0.58 (0.37–0.86) | **0.006** |
| Peking University First Hospital | Ref | Ref |
| Peking University Third Hospital | 1.24 (0.50–2.29) | 0.609 |
| Shandong Provincial Hospital | 2.45 (1.34–2.98) | **0.014** |
| Zhengzhou University First Hospital | 1.14 (0.32–2.39) | 0.807 |
| Hebei Medical University Second Hospital | 1.71 (0.68–2.68) | 0.228 |
| Beijing Obstetrics and Gynecology Hospital | 1.40 (0.55–2.44) | 0.437 |
| Age (18-39) | Ref | Ref |
| Age (40-49) | 1.59 (0.76–2.48) | 0.204 |
| Age (50-65) | 1.86 (1.00–2.64) | 0.064 |
| Baseline hemoglobin (< 126 g/L) | Ref | Ref |
| Baseline hemoglobin (≥ 126 g/L) | 0.79 (0.51–1.15) | 0.234 |
| Baseline SVR (< 1380 mmHg ⋅ min/ml) | Ref | Ref |
| Baseline SVR (≥ 1380 mmHg ⋅ min/ml) | 1.05 (0.72–1.45) | 0.774 |
| Duration of anesthesia (< 120 min) | Ref | Ref |
| Duration of anesthesia (≥ 120 min) | 0.67 (0.38–1.09) | 0.108 |
| Urine output (< 500 mL) | Ref | Ref |
| Urine output (≥ 500 mL) | 1.20 (0.81–1.64) | 0.347 |
| Intraoperative sufentanil (< 30 ug) | Ref | Ref |
| Intraoperative sufentanil (≥ 30 ug) | 1.00 (0.42–1.82) | 0.995 |
| History of motion sickness (no) | Ref | Ref |
| History of motion sickness (yes) | 1.18 (0.77–1.65) | 0.409 |
| History of PONV (never had surgery) | Ref | Ref |
| History of PONV (surgery without PONV) | 1.11 (0.74–1.54) | 0.597 |
| History of PONV (surgery with PONV) | 1.61 (0.85–2.36) | 0.127 |
| History of cardiovascular disease (no) | Ref | Ref |
| History of cardiovascular disease (yes) | 1.23 (0.56–2.04) | 0.556 |

SmtO2 = muscular tissue oxygen saturation; CI = confidence interval; BMI = body mass index; SVR = systemic vascular resistance; Ref = reference; PONV = postoperative nausea and vomiting.

\* The risk ratio is for the subgroups as compared with the reference subgroup within the same strata (e.g., hospital, age, etc.).

† A multiple logistic regression model for the 24-hour PONV rate was fit where hospital was adjusted for to assess the impact of between-hospital heterogeneity on risk estimates.

‡ A multiple logistic regression model for the 24-hour PONV rate was fit with additional adjustments for the stratification variables including site, age, any variables exhibiting substantial between-group imbalance at baseline (*P* < 0.10), any variables exhibiting statistical significance during subgroup analysis (*P* < 0.05), and recognized risk factors for PONV.

**References**

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