**SUPPLEMENTAL DIGITAL CONTENT**

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**Supplemental Table 1: Perioperative and Postoperative Characteristics by Randomization Group (As-Treated Analysis)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | General Anesthesia with Masked BIS Values  (n=112) a | Spinal Anesthesia with Targeted Sedation Based on BIS Values  (n=105) a | P-value |
| **Intraoperative** | | | |
| Duration of Surgery (minutes), median (IQR) | 129 (110-163) | 125 (105-154) | 0.352 |
| Number of Levels, median (IQR) | 3 (2-3) | 3 (2-4) | 0.709 |
| Anesthetic Management |  |  |  |
| Spinal Anesthesia Arm | | | |
| Bupivacaine dose (mg), median (IQR) | 12.5 b | 14 (12.5-15) | N/A |
| Maximum propofol infusion (mcg/kg/min), median (IQR) | N/A | 80 (75-100) | N/A |
| General Anesthesia Arm | | | |
| Desflurane, n (%) | 82 (73.2) | 0 | N/A |
| Intrathecal morphine, n (%) | 60 (53.6) | 74 (70.5) | 0.010 |
| Intrathecal morphine (mg), median (IQR) | 0.2 (0.2-0.25) | 0.2 (0.2-0.2) | 0.039 |
| Fentanyl, n (%) | 106 (94.6) | 97 (92.4) | 0.498 |
| Fentanyl (mcg), median (IQR) | 200 (150-250) | 100 (100-100) | <0.001 |
| Hydromorphone, n (%) | 43 (38.4) | 0 (0) | NA |
| Hydromorphone (mg), median (IQR) | 1.5 (1-2) | 0 | NA |
| Midazolam, n (%) | 35 (31.3) | 34 (32.4) | 0.858 |
| Midazolam (mg), median (IQR) | 2 (2-2) | 2 (2-2) | 0.531 |
| Phenylephrine, n (%) | 23 (20.5) | 27 (25.7) | 0.365 |
| Phenylephrine (mcg), median (IQR) | 400 (200-550) | 250 (150-750) | 0.611 |
| Ephedrine, n (%) | 72 (64.3) | 68 (64.8) | 0.942 |
| Ephedrine (mg), median (IQR) | 23 (10-38) | 20 (10-30) | 0.141 |
| Fluids Administered (mL), median (IQR) | 2000 (1500-2650) | 2000 (1850-2875) | 0.032 |
| Estimated Blood Loss (mL), median (IQR) | 300 (200-500) | 300 (200-400) | 0.432 |
| Packed Red Blood Cell Transfusion, n (%) | 1 (0.9) | 3 (2.9) | 0.356 |
| Lowest MAP (mm Hg), median (IQR) | 59 (51-64) | 60 (52-64) | 0.522 |
| Average BIS, median (IQR) | 45 (40-49) | 63 (54-70) | <0.001 |
| Duration of BIS<40 (minutes), median (IQR) | 68 (25-103) | 2 (0-17) | <0.001 |
| Duration of BIS>55 (minutes), median (IQR) | 20 (13-30) | 92 (42-112) | <0.001 |
| Duration of PACU (minutes), median (IQR) | 118 (73-168) | 119 (78-160) | 0.916 |
| Pain score at PACU discharge, median (IQR) | 5 (3-7) | 4 (1-5) | 0.028 |
| **Postoperative** | | | |
| ICU admission, n (%) | 0 (0) | 4 (3.8) | 0.053 |
| Duration of hospitalization (days), median (IQR) | 3 (2-3) | 3 (2-3) | 0.063 |
| Maximum daily pain on postoperative day 1 (0-10), median (IQR) | 8 (7-10) | 8 (7-10) | 0.507 |
| Complications, n (%) |  |  |  |
| Stroke | 0 (0) | 2 (1.9) | 0.233 |
| Atrial Fibrillation | 0 (0) | 1 (1.0) | 0.484 |
| Congestive Heart Failure | 0 (0) | 0 (0) | NA |
| Myocardial Infarction | 0 (0) | 1 (1.0) | 0.484 |
| Sepsis | 0 (0) | 0 (0) | NA |
| Pneumonia | 0 (0) | 2 (1.9) | 0.233 |
| Urinary Tract Infection | 10 (8.9) | 8 (7.6) | 0.727 |
| Pulmonary Embolism or Deep Venous Thrombosis | 1 (0.9) | 1 (1) | 1.000 |
| Acute Kidney Injury | 0 (0) | 1 (1) | 0.484 |
| Fall | 0 (0) | 0 (0) | NA |
| Reoperation | 0 (0) | 1 (1) | 0.484 |
| In-Hospital Death | 1 (0.9) | 0 (0) | 1.000 |
| a All variables were complete except bupivacaine and propofol dose in the spinal anesthesia group (n=101), BIS values (n=192), and postoperative day 1 pain (n=216)  b One patient received bupivacaine via spinal anesthesia, but the analgesia was insufficient, so the patient was converted to general anesthesia | | | |

**Supplemental Table 2: Effect of the Intervention on Postoperative Delirium (As-Treated Analysis)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | General Anesthesia with Masked BIS Values  (n=112) | Spinal Anesthesia with Targeted Sedation Based on BIS Values  (n=105) | P-value |
| Any Delirium n (%) a | 22 (19.6) | 26 (24.8) | 0.364 |
| Number of Days of Delirium, among Delirious Patients, median (IQR) | 1 (1-2) | 1 (1-2) | 0.105 |
| Delirium by Postoperative Day a |  |  |  |
| Day 1, n (%) | 8 (7.1) | 14 (13.3) | 0.131 |
| Day 2, n (%) | 17 (15.2) | 20 (19) | 0.449 |
| Day 3, n (%) | 11 (9.8) | 14 (13.3) | 0.418 |
| Maximum Delirium Severity Score as Measured by Delirium Rating Scale–Revised-98 b median (IQR) a | 4 (3-7) | 5 (3-8) | 0.218 |
| Maximum Delirium Severity Score as measured by Delirium Rating Scale–Revised-98 a by Postoperative Day a |  |  |  |
| Day 1, median (IQR) | 3 (2-6) | 4 (3-7) | 0.106 |
| Day 2, median (IQR) | 3 (1-5) | 3 (2-5) | 0.250 |
| Day 3, median (IQR) | 3 (1-6) | 3 (2-6) | 0.880 |

a Out of 544 opportunities for delirium assessments for non-discharged patients at assessment, 509 in-person assessments were completed, and 24 assessments were refused by patients. 215 patients had a postoperative assessment with the Confusion Assessment Method and Delirium Rating Scale-Revised-98. (2 patients refused all assessments and were considered to not have delirium). For each postoperative day, the number of patients with a Confusion Assessment Method and Delirium Rating Scale-Revised-98 evaluation among the number of non-discharged patients at assessment was 199/217 (postoperative day 1), 190/198 (postoperative day 2), and 120/129 (postoperative day 3).

b DRS-R-98 severity scores range from 0-39, with higher scores indicating greater severity of delirium.

**Supplemental Table 3: Adjusted Associations of the Intervention with Postoperative Delirium in Multivariable Models**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Odds Ratio | 95% CI | P-value |
| Adjusted for Pre-Specified Variables |  |  |  |
| Spinal anesthesia with targeted sedation based on BIS values | 1.58 | (0.81-3.1) | 0.178 |
| Age (years) | 1.01 | (0.95-1.07) | 0.713 |
| Education (college or greater) | 0.87 | (0.42-1.77) | 0.697 |
| Mini-Mental State Examination | 0.77 | (0.62-0.95) | 0.013 |
| Adjusted for Pre-Specified Variables and Variables Identified in Bivariate Models as Associated with Delirium | | | |
| Spinal anesthesia with targeted sedation based on BIS values | 1.61 | (0.57-4.53) | 0.364 |
| Age (years) | 1.04 | (0.97-1.12) | 0.299 |
| Education (college or greater) | 1.01 | (0.43-2.39) | 0.977 |
| Mini-Mental State Examination | 0.72 | (0.56-0.93) | 0.013 |
| Sex (Female) | 0.47 | (0.19-1.13) | 0.090 |
| Charlson Comorbidity Index > 0 | 1.34 | (0.59-3.03) | 0.479 |
| Selective Serotonin Reuptake Inhibitors, or Serotonin and Norepinephrine Reuptake Inhibitors, or other psychotropic medication | 1.92 | (0.79-4.71) | 0.152 |
| Short-acting opioids | 2.09 | (0.92-4.74) | 0.078 |
| Duration of surgery | 1 | (0.99-1.01) | 0.956 |
| Maximum pain on postoperative day 1 | 1.20 | (0.95-1.52) | 0.118 |
| Mean BIS | 0.98 | (0.94-1.02) | 0.334 |
| Postoperative urinary tract infection | 3.23 | (0.9-11.53) | 0.072 |
| Intrathecal morphine | 2.65 | (1.15-6.12) | 0.022 |

**Supplemental Table 4: Subgroup Analyses with Number of Events**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Strata | Number of Patients | General Anesthesia with Masked BIS Values | Spinal Anesthesia with Targeted Sedation Based on BIS Values | Relative Risk (95% CI) | Interaction P value |
| Intention to Treat | | | | | |
| Age (years) |  |  |  |  |  |
| <75 | 126 | 10/63 (15.9) | 15/63 (23.8) | 1.31 (0.85-2.56) | 0.651 |
| ≥75 | 91 | 10/43 (23.3) | 13/48 (27.1) | 1.12 (0.69-2.15) |  |
| Sex |  |  |  |  |  |
| Female | 134 | 14/71 (19.7) | 10/63 (15.9) | 0.89 (0.62-1.4) | 0.060 |
| Male | 83 | 6/35 (17.1) | 18/48 (37.5) | 1.97 (1.05-5.75) |  |
| Education |  |  |  |  |  |
| <College | 113 | 15/57 (26.3) | 14/56 (25.0) | 0.97 (0.65-1.56) | 0.100 |
| College or more | 104 | 5/49 (10.2) | 14/55 (25.5) | 1.97 (1.01-7.05) |  |
| Charlson Comorbidity Index |  |  |  |  |  |
| 0 | 106 | 7/60 (11.7) | 10/46 (21.7) | 1.45 (0.86-3.48) | 0.262 |
| >0 | 111 | 13/46 (28.3) | 18/65 (27.7) | 0.98 (0.61-1.73) |  |
| Mini-Mental State Examination |  |  |  |  |  |
| <27 | 40 | 10/23 (43.5) | 3/17 (17.7) | 0.63 (0.36-1.04) | 0.009 |
| 27-30 | 177 | 10/83 (12.1) | 25/94 (26.6) | 1.8 (1.12-3.78) |  |
| Preoperative Rapid Release Opioids |  |  |  |  |  |
| No | 109 | 8/60 (13.3) | 8/49 (16.3) | 1.12 (0.71-2.26) | 0.865 |
| Yes | 106 | 11/44 (25) | 20/62 (32.3) | 1.24 (0.74-2.39) |  |
| Intrathecal Morphine |  |  |  |  |  |
| No | 83 | 10/49 (20.4) | 3/34 (8.8) | 0.72 (0.65-1.37) | 0.029 |
| Yes | 134 | 10/57 (17.5) | 25/77 (32.5) | 1.66 (0.86-4.93) |  |
| As-Treated | | | | | |
| Age (years) |  |  |  |  |  |
| <75 | 126 | 11/68 (16.2) | 14/58 (24.1) | 1.28 (0.85-2.35) | 0.475 |
| ≥75 | 91 | 11/44 (25.0) | 12/47 (25.5) | 1.02 (0.64-1.86) |  |
| Sex |  |  |  |  |  |
| Female | 134 | 15/76 (19.7) | 9/58 (15.5) | 0.89 (0.63-1.35) | 0.100 |
| Male | 83 | 7/36 (19.4) | 17/47 (36.2) | 1.69 (0.94-4.3) |  |
| Education |  |  |  |  |  |
| <College | 113 | 15/59 (25.4) | 14/54 (25.9) | 1.01 (0.69-1.63) | 0.317 |
| College or more | 104 | 7/53 (13.2) | 12/51 (23.5) | 1.47 (0.86-3.73) |  |
| Charlson Comorbidity Index |  |  |  |  |  |
| 0 | 106 | 9/65 (13.9) | 8/41 (19.5) | 1.19 (0.77-2.28) | 0.571 |
| >0 | 111 | 13/47 (27.7) | 18/64 (28.1) | 1.01 (0.63-1.79) |  |
| Mini-Mental State Examination |  |  |  |  |  |
| <27 | 40 | 11/25 (44.0) | 2/15 (13.3) | 0.61 (0.37-0.94) | 0.007 |
| 27-30 | 177 | 11/87 (12.6) | 24/90 (26.7) | 1.7 (1.09-3.31) |  |
| Preoperative Rapid Release Opioids |  |  |  |  |  |
| No | 109 | 9/63 (14.3) | 7/46 (15.2) | 1.03 (0.69-1.92) | 0.718 |
| Yes | 106 | 12/47 (25.5) | 19/59 (32.2) | 1.21 (0.74-2.21) |  |
| Intrathecal Morphine |  |  |  |  |  |
| No | 83 | 10/52 (19.2) | 3/31 (9.7) | 0.78 (0.65-1.29) | 0.088 |
| Yes | 134 | 12/60 (20.0) | 23/74 (31.1) | 1.41 (0.8-3.91) |  |

**Supplemental Table 5: Baseline Patient Characteristics by Delirium**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Delirium  (n=48) a | No Delirium  (n=169) a | P-value |
| Age (years), median (IQR) | 74 (69-78) | 72 (69-77) | 0.483 |
| Male, n (%) | 24 (50.0) | 59 (34.9) | 0.058 |
| Race, n (%) |  |  | 0.145 |
| Caucasian | 41 (85.4) | 156 (92.3) |  |
| African-American | 7 (14.6) | 13 (7.7) |  |
| Education college or higher, n (%) | 19 (39.6) | 85 (50.3) | 0.190 |
| Living arrangement (% at home) | 44 (91.7) | 159 (95.2) | 0.346 |
| Mini-Mental State Examination, b median (IQR) | 28 (26-29) | 29 (27-29) | 0.003 |
| Instrumental Activities of Daily Living, c median (IQR) | 13 (12-14) | 14 (12-14) | 0.054 |
| Comorbidities, n (%) |  |  |  |
| Prior Stroke | 0 (0) | 3 (1.8) | 1.000 |
| Hypertension | 39 (81.3) | 118 (69.8) | 0.118 |
| Atrial Fibrillation | 3 (6.3) | 9 (5.3) | 0.73 |
| Congestive Heart Failure | 0 (0) | 1 (0.6) | 1.000 |
| Myocardial Infarction | 9 (18.8) | 11 (6.5) | 0.01 |
| Peripheral Vascular Disease | 1 (2.1) | 8 (4.7) | 0.687 |
| Chronic Obstructive Pulmonary Disease | 11 (22.9) | 11 (6.5) | 0.001 |
| Tobacco (prior) | 19 (39.6) | 54 (32) | 0.323 |
| Diabetes | 16 (33.3) | 38 (22.5) | 0.125 |
| Chronic Kidney Disease | 15 (31.3) | 23 (13.6) | 0.005 |
| ASA Classification, d median (IQR) | 3 (2-3) | 2 (2-3) | 0.017 |
| Charlson Comorbidity Index, e median (IQR) | 1 (0-2) | 0 (0-1) | 0.003 |
| Hemoglobin (g/dL), mean (SD) | 13.6 (1.3) | 13.5 (1.3) | 0.623 |
| Baseline Medications |  |  |  |
| Aspirin, n (%) | 6 (12.8) | 15 (8.9) | 0.433 |
| Beta Blockers, n (%) | 15 (31.9) | 41 (24.4) | 0.300 |
| Calcium Channel Blockers, n (%) | 14 (29.8) | 37 (22) | 0.269 |
| Angiotensin Converting Enzyme-Inhibitors, n (%) | 7 (14.9) | 36 (21.4) | 0.322 |
| Angiotensin II-Receptor Blockers, n (%) | 10 (21.3) | 39 (23.2) | 0.780 |
| Statin, n (%) | 24 (51.1) | 85 (50.6) | 0.955 |
| Selective Serotonin Reuptake Inhibitors or Serotonin and Norepinephrine Reuptake Inhibitors, n (%) | 12 (25.5) | 27 (16.1) | 0.137 |
| Other psychotropic medication, n (%) | 8 (17) | 15 (8.9) | 0.113 |
| Short-acting opioids, n (%) | 31 (66) | 75 (44.6) | 0.010 |
| Current Pain, f median (IQR) | 3.5 (1-7) | 3 (0.5-6) | 0.480 |
| Average Pain, f median (IQR) | 7.5 (5.5-8) | 7 (5-8) | 0.992 |
| a All variables were complete (n=217) except the following: Instrument Activities of Daily Living, ASA score (n=211), current and average pain (n=212), living status, all baseline medications (n=215), hemoglobin (n=216) b Mini-Mental State Examination scores range from 0-30, with higher scores indicating better performance. c Instrumental Activities of Daily Living scores range from 0-14 with higher scores indicating better functional status. d For non-brain dead surgical patients, ASA scores range from 1-5 with higher scores indicating greater co-morbidities. e The Charlson Comorbidity Index ranges from 0-33, with higher scores indicating greater risk of long-term mortality. f Pain is rated on a scale of 0-10, with higher scores indicating more pain. | | |  |

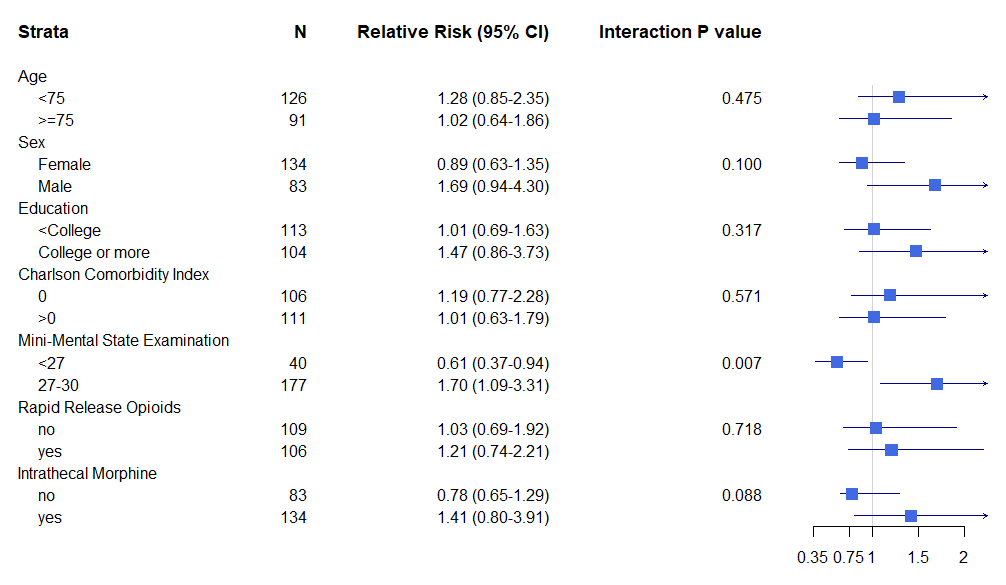
**Supplemental Table 6: Perioperative and Postoperative Characteristics by Delirium**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Delirium  (n=48) a | No Delirium  (n=169) a | P-value |
| **Intraoperative** | | | |
| Duration of Surgery (minutes), median (IQR) | 144 (115-174) | 123 (105-153) | 0.066 |
| Number of Levels median (IQR) | 3 (2-3) | 2 (2-3) | 0.016 |
| Anesthetic Management |  |  |  |
| Intrathecal morphine, n (%) | 35 (72.9) | 99 (58.6) | 0.071 |
| Intrathecal morphine (mg), median (IQR) | 0.2 (0.2-0.3) | 0.2 (0.2-0.2) | 0.119 |
| Fentanyl, n (%) | 46 (95.8) | 157 (92.9) | 0.740 |
| Fentanyl (mcg) | 100 (100-200) | 150 (100-250) | 0.301 |
| Hydromorphone, n (%) | 11 (22.9) | 32 (18.9) | 0.541 |
| Hydromorphone (mg) | 1 (0.5-2) | 2 (1-2) | 0.043 |
| Midazolam, n (%) | 16 (33.3) | 53 (31.4) | 0.796 |
| Midazolam (mg) | 2 (2-2) | 2 (2-2) | 0.040 |
| Phenylephrine, n (%) | 15 (31.3) | 35 (20.7) | 0.126 |
| Phenylephrine (mcg) | 200 (100-750) | 300 (100-450) | 0.941 |
| Ephedrine, n (%) | 31 (64.6) | 109 (64.5) | 0.991 |
| Ephedrine (mg) | 20 (10-35) | 20 (10-30) | 0.479 |
| Fluids Administered (mL) | 2000 (1900-2913) | 2000 (1600-2700) | 0.187 |
| Estimated Blood Loss (mL) | 300 (200-500) | 300 (200-450) | 0.350 |
| PRBC Transfusion, n (%) | 0 (0) | 4 (2.4) | 0.578 |
| Lowest MAP (mm Hg) | 59 (50-64) | 59.5 (52-64) | 0.673 |
| Average BIS, median (IQR) | 51 (44-65) | 51 (44-63) | 0.700 |
| Duration of BIS<40 (minutes), median (IQR) | 19 (1-69) | 26 (1-79) | 0.538 |
| Duration of BIS>55 (minutes), median (IQR) | 32 (17-99) | 31 (16-92) | 0.962 |
| Duration of PACU (minutes), median (IQR) | 118 (75-155) | 119 (77-165) | 0.517 |
| Pain score at PACU discharge, median (IQR) | 5 (2-5) | 5 (2-6) | 0.968 |
| **Postoperative** | | | |
| ICU admission, n (%) | 3 (6.3) | 1 (0.6) | 0.035 |
| Duration of hospitalization (days) | 3 (3-4) | 3 (2-3) | <0.001 |
| Maximum daily pain on postoperative day 1 (0-10) | 10 (7-10) | 8 (7-9) | 0.002 |
| IV Pain Medication Postoperative Day 1 | 46 (95.8) | 145 (85.8) | 0.076 |
| Complications b |  |  |  |
| Stroke | 2 (4.2) | 0 (0) | 0.048 |
| Atrial Fibrillation | 0 (0) | 1 (0.6) | 1.000 |
| Congestive Heart Failure | 0 (0) | 0 (0) | NA |
| Myocardial Infarction | 1 (2.1) | 0 (0) | 0.221 |
| Sepsis | 0 (0) | 0 (0) | NA |
| Pneumonia | 2 (4.2) | 0 (0) | 0.048 |
| Urinary Tract Infection | 6 (12.5) | 12 (7.1) | 0.231 |
| Pulmonary Embolism or Deep Venous Thrombosis | 0 (0) | 2 (1.2) | 1.000 |
| Acute Kidney Injury | 0 (0) | 1 (0.6) | 1.000 |
| Fall | 0 (0) | 0 (0) | NA |
| Reoperation | 0 (0) | 1 (0.6) | 1.000 |
| In-Hospital Death | 0 (0) | 1 (0.6) | 1.000 |

a All variables were complete except bupivacaine and propofol dose in the spinal anesthesia group (n=101), BIS values (n=192), and postoperative day 1 pain (n=216)

b Some patients experienced multiple complications, apart from urinary tract infections. One patient in the general anesthesia group had both a pulmonary embolism and died. One patient in the spinal anesthesia group had a stroke, myocardial infarction, and pneumonia.

**Supplemental Figure 1: Subgroup Analyses of the Primary Outcome of Incident Delirium (As-Treated)**

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**Legend:** Subgroup analyses based on as-treated analyses with the primary outcome of incident delirium. Rapid release opioids refer to baseline opioids. Relative Risk <1 favors spinal anesthesia with targeted sedation based on BIS values. Relative Risk >1 favors general anesthesia with masked BIS values.