|                                      | All Patients<br>(n=1,058)      | Propofol<br>(n=294)              | Sevoflurane<br>(n=371)         | Desflurane<br>(n=393)          | p-value |  |
|--------------------------------------|--------------------------------|----------------------------------|--------------------------------|--------------------------------|---------|--|
| Age (years)                          | 69.8 <u>+</u> 6.3              | 69.2 <u>+</u> 5.8                | 70.3 <u>+</u> 6.5              | 69.7 <u>+</u> 6.5              | n.s.    |  |
| Gender male / female (%)             | 54 % / 46%                     | 34% / 66%                        | 67 % / 33%                     | 55.5% / 44.5%                  | <0.001  |  |
| ВМІ                                  | 27.1 <u>+</u> 5.1              | 27.2 <u>+</u> 5.2                | 27.8 <u>+</u> 5.4              | 26.4 <u>+</u> 4.7              | <0.001  |  |
| ASA status 1 / 2 / 3 / 4 (%)         | 3.1% / 49.1% / 45.8% /<br>1.9% | 3.4% / 54.4.% / 40.8 % /<br>1.4% | 2.7% / 45.6% / 49.6% /<br>2.2% | 3.3% / 48.6% / 46.1% /<br>2.0% | n.s.    |  |
| MMSE preoperative**                  | 28.9 <u>+</u> 1.4              | 29 <u>+</u> 1.4                  | 28.9 <u>+</u> 1.4              | 28.9 <u>+</u> 1.5              | n.s.    |  |
| Midazolam Premedication yes / no (%) | 5% / 95%                       | 4% / 96%                         | 5% / 95%                       | 6% / 94%                       | n.s.    |  |
| Surgery duration (min)               | 171 <u>+</u> 102               | 151 <u>+</u> 89                  | 162 <u>+</u> 97                | 195 <u>+</u> 110               | 0.000   |  |
| Surgical specialty (%)               |                                |                                  |                                |                                | <0.001  |  |
| General surgery                      | 49,1%                          | 20%                              | 26%                            | 54%                            |         |  |
| Orthopedics                          | 29.7%                          | 31%                              | 48%                            | 21%                            |         |  |
| Urology                              | 8.1%                           | 60%                              | 11%                            | 29%                            |         |  |
| Gynecology                           | 10.6%                          | 34%                              | 63%                            | 3%                             |         |  |
| other                                | 2.5%                           | 15%                              | 23%                            | 62%                            |         |  |
| Outcome parameter                    |                                |                                  |                                |                                |         |  |
| Discharge (%)                        |                                |                                  |                                |                                | 0.021   |  |
| Home                                 | 88.9%                          | 92.8%                            | 87%                            | 87.8%                          |         |  |
| Other hospital or nursing home       | 8.9%                           | 6.9%                             | 10.8%                          | 8.6%                           |         |  |
| death                                | 2.2%                           | 0.3%                             | 2.2%                           | 3.6%                           |         |  |

| Burst suppression duration | 22.6 <u>+</u> 17.4 | 32.5 <u>+</u> 20.3 | 17.1 <u>+</u> 12.6 | 20.2 <u>+</u> 16.0 | 0.000 |
|----------------------------|--------------------|--------------------|--------------------|--------------------|-------|
| (min)                      |                    |                    |                    |                    |       |
| Burst suppression ratio    | 0.19 <u>+</u> 0.10 | 0.25 <u>+</u> 0.08 | 0.16 <u>+</u> 0.09 | 0.18 <u>+</u> 0.12 | 0.000 |
|                            |                    |                    |                    |                    |       |
| Postoperative delirium     | 81% / 19%          | 87% / 13%          | 84% /16%           | 75% / 25%          | 0.000 |
| NoPOD / POD (%)            |                    |                    |                    |                    |       |
|                            |                    |                    |                    |                    |       |

Table S1: Patients' characteristics for all and for each one of the three anesthetic agent groups propofol, sevoflurane and desflurane. Differences calculated between the different anesthetic agents are seen in sex, were female patients more likely received a *total intravenous anesthesia with propofol*. Patients with *desflurane anesthesia* had a lower BMI, surgery duration was prolonged and patients underwent more frequently a general surgery, *sevoflurane anesthesia* was most frequently given in gynecological surgeries and *propofol anesthesia* was most frequently seen in urological surgery. We found no significant differences in age, ASA status, preoperative MMSE score and premedication with midazolam between the patients groups. Differences in age, BMI, MMSE, surgery duration were calculated by Kruskal-Wallis test, differences in sex, ASA status, MMSE score, surgery specialty, POD and discharge were calculated by chi-square test.

## Correlations

|                |                                                            |                         | POD outcome | age (years) | ASA status | preoperative<br>MMSE score | Surgery<br>Speciality | surgery<br>duration (min) | Anesthetic<br>agent<br>(propofol,<br>sevoflurane,<br>desflurane) | average BIS<br>(mean<br>intraoperative<br>) | minimum BIS<br>(mean<br>intraoperative<br>) | burst<br>suppression<br>ratio | burst<br>suppression<br>duration (min) |
|----------------|------------------------------------------------------------|-------------------------|-------------|-------------|------------|----------------------------|-----------------------|---------------------------|------------------------------------------------------------------|---------------------------------------------|---------------------------------------------|-------------------------------|----------------------------------------|
| Spearman's rho | POD outcome                                                | Correlation Coefficient | 1,000       | ,178        | ,140       | -,090**                    | -,125                 | ,279"                     | ,133**                                                           | -,016                                       | -,031                                       | ,006                          | ,113                                   |
|                |                                                            | Sig. (2-tailed)         | - 4         | ,000        | ,000       | ,004                       | ,000                  | ,000                      | ,000                                                             | ,657                                        | ,357                                        | ,839                          | ,000                                   |
|                |                                                            | N                       | 1058        | 1058        | 1058       | 1001                       | 1054                  | 1058                      | 1058                                                             | 785                                         | 895                                         | 1058                          | 1058                                   |
|                | age (years)                                                | Correlation Coefficient | .178        | 1,000       | ,143       | -,096**                    | -,033                 | -,023                     | ,006                                                             | -,027                                       | ,014                                        | ,062                          | ,038                                   |
|                |                                                            | Sig. (2-tailed)         | ,000        | -           | ,000       | ,002                       | ,282                  | ,464                      | ,857                                                             | ,454                                        | ,681                                        | ,042                          | ,222                                   |
|                |                                                            | N                       | 1058        | 1058        | 1058       | 1001                       | 1054                  | 1058                      | 1058                                                             | 785                                         | 895                                         | 1058                          | 1058                                   |
|                | ASA status                                                 | Correlation Coefficient | .140        | ,143        | 1,000      | -,127**                    | -,204**               | ,073                      | ,039                                                             | ,050                                        | ,038                                        | -,002                         | ,042                                   |
|                |                                                            | Sig. (2-tailed)         | ,000        | ,000        |            | ,000                       | ,000                  | ,017                      | ,208                                                             | ,160                                        | ,253                                        | ,935                          | ,173                                   |
|                |                                                            | N                       | 1058        | 1058        | 1058       | 1001                       | 1054                  | 1058                      | 1058                                                             | 785                                         | 895                                         | 1058                          | 1058                                   |
|                | preoperative MMSE score                                    | Correlation Coefficient | -,090       | -,096       | -,127**    | 1,000                      | ,033                  | -,004                     | -,045                                                            | -,010                                       | ,032                                        | ,000                          | ,026                                   |
|                |                                                            | Sig. (2-tailed)         | ,004        | ,002        | ,000       |                            | ,300                  | ,906                      | ,157                                                             | ,796                                        | ,356                                        | ,989                          | ,403                                   |
|                |                                                            | N                       | 1001        | 1001        | 1001       | 1001                       | 997                   | 1001                      | 1001                                                             | 740                                         | 846                                         | 1001                          | 1001                                   |
|                | Surgery Speciality                                         | Correlation Coefficient | -,125       | -,033       | -,204      | ,033                       | 1,000                 | -,131**                   | -,307**                                                          | -,024                                       | -,017                                       | ,070                          | ,066                                   |
|                |                                                            | Sig. (2-tailed)         | ,000        | ,282        | ,000       | ,300                       | 14                    | ,000                      | ,000                                                             | ,499                                        | ,605                                        | ,023                          | ,033                                   |
|                |                                                            | N                       | 1054        | 1054        | 1054       | 997                        | 1054                  | 1054                      | 1054                                                             | 783                                         | 891                                         | 1054                          | 1054                                   |
|                | surgery duration (min)                                     | Correlation Coefficient | ,279**      | -,023       | ,073*      | -,004                      | -,131"                | 1,000                     | ,179**                                                           | -,028                                       | -,020                                       | -,193                         | ,283**                                 |
|                |                                                            | Sig. (2-tailed)         | ,000        | ,464        | ,017       | ,906                       | ,000                  |                           | ,000                                                             | ,433                                        | ,558                                        | ,000                          | ,000                                   |
|                |                                                            | N                       | 1058        | 1058        | 1058       | 1001                       | 1054                  | 1058                      | 1058                                                             | 785                                         | 895                                         | 1058                          | 1058                                   |
|                | Anesthetic agent<br>(propofol, sevoflurane,<br>desflurane) | Correlation Coefficient | ,133**      | ,006        | ,039       | -,045                      | -,307**               | ,179**                    | 1,000                                                            | ,029                                        | -,006                                       | -,306**                       | -,253"                                 |
|                |                                                            | Sig. (2-tailed)         | ,000        | ,857        | ,208       | ,157                       | ,000                  | ,000                      | +                                                                | ,413                                        | ,850                                        | ,000                          | ,000                                   |
|                |                                                            | N                       | 1058        | 1058        | 1058       | 1001                       | 1054                  | 1058                      | 1058                                                             | 785                                         | 895                                         | 1058                          | 1058                                   |
|                | average BIS (mean                                          | Correlation Coefficient | -,016       | -,027       | ,050       | -,010                      | -,024                 | -,028                     | ,029                                                             | 1,000                                       | ,990**                                      | ,054                          | ,033                                   |
|                | intraoperative)                                            | Sig. (2-tailed)         | ,657        | ,454        | ,160       | ,796                       | ,499                  | ,433                      | ,413                                                             |                                             | ,000                                        | ,129                          | ,357                                   |
|                |                                                            | N                       | 785         | 785         | 785        | 740                        | 783                   | 785                       | 785                                                              | 785                                         | 785                                         | 785                           | 785                                    |
|                | minimum BIS (mean                                          | Correlation Coefficient | -,031       | ,014        | ,038       | ,032                       | -,017                 | -,020                     | -,006                                                            | ,990                                        | 1,000                                       | ,051                          | ,033                                   |
|                | intraoperative)                                            | Sig. (2-tailed)         | ,357        | ,681        | ,253       | ,356                       | ,605                  | ,558                      | ,850                                                             | ,000                                        |                                             | ,129                          | ,330                                   |
|                |                                                            | N                       | 895         | 895         | 895        | 846                        | 891                   | 895                       | 895                                                              | 785                                         | 895                                         | 895                           | 895                                    |
|                | burst suppression ratio                                    | Correlation Coefficient | ,006        | .062        | -,002      | ,000                       | ,070                  | -,193**                   | -,306"                                                           | ,054                                        | ,051                                        | 1,000                         | ,555                                   |
|                |                                                            | Sig. (2-tailed)         | ,839        | ,042        | ,935       | ,989                       | ,023                  | ,000                      | ,000                                                             | ,129                                        | ,129                                        |                               | ,000                                   |
|                |                                                            | N                       | 1058        | 1058        | 1058       | 1001                       | 1054                  | 1058                      | 1058                                                             | 785                                         | 895                                         | 1058                          | 1058                                   |
|                | burst suppression                                          | Correlation Coefficient | ,113        | ,038        | ,042       | ,026                       | ,066                  | ,283**                    | -,253"                                                           | ,033                                        | ,033                                        | ,555                          | 1,000                                  |
|                | duration (min)                                             | Sig. (2-tailed)         | ,000        | ,222        | ,173       | ,403                       | ,033                  | ,000                      | ,000                                                             | ,357                                        | ,330                                        | ,000                          |                                        |
|                |                                                            | N                       | 1058        | 1058        | 1058       | 1001                       | 1054                  | 1058                      | 1058                                                             | 785                                         | 895                                         | 1058                          | 1058                                   |

<sup>\*\*.</sup> Correlation is significant at the 0.01 level (2-tailed).

<sup>\*.</sup> Correlation is significant at the 0.05 level (2-tailed).

**Table S2: Spearman Rho correlation** for POD and different known risk factors. We found a high correlation of POD with age, ASA status, MMSE score, surgery duration, surgery specialization, burst suppression duration and anesthetic agent given for maintenance, but no correlation for average BIS level, minimum BIS level and burst suppression ratio.

|                                  | All Patients<br>(n=1,058) |                       |         | Propofol<br>(n=294)   |                       |         | Sevoflurane<br>(n=371) |                       |         | Desflurane<br>(n=393) |                       |         |
|----------------------------------|---------------------------|-----------------------|---------|-----------------------|-----------------------|---------|------------------------|-----------------------|---------|-----------------------|-----------------------|---------|
|                                  | No-POD<br>(n=860)         | POD<br>(n=198)        | p-value | No-POD<br>(n=256)     | POD<br>(n=38)         | p-value | No-POD<br>(n=311)      | POD<br>(n=60)         | p-value | No-POD<br>(n=293)     | POD<br>(n=100)        | p-value |
| Burst suppression duration (min) | 21.4 <u>+</u><br>16.2     | 27.5 <u>+</u><br>21.3 | 0.000   | 30.8 <u>+</u><br>18.9 | 44.1 <u>+</u><br>25.0 | 0.000   | 15.8 <u>+</u><br>11.5  | 23.9 <u>+</u><br>15.4 | 0.000   | 19.1 <u>+</u><br>14.2 | 23.5 <u>+</u><br>20.0 | 0.025   |
| Burst suppression ratio          | 0.19 <u>+</u><br>0.1      | 0.2 <u>+</u><br>0.11  | n.s.    | 0.24 <u>+</u><br>0.08 | 0.26 <u>+</u><br>0.1  | n.s.    | 0.16 <u>+</u><br>0.09  | 0.17 <u>+</u><br>0.06 | n.s.    | 0.18 <u>+</u><br>0.11 | 0.19 <u>+</u><br>0.12 | n.s.    |
| Surgery duration                 | 157 <u>+</u> 92           | 175 <u>+</u><br>127   | 0.000   | 143 <u>+</u> 83       | 205 <u>+</u><br>106   | 0.000   | 153 <u>+</u> 90        | 208 <u>+</u><br>117   | 0.000   | 172 <u>+</u> 98       | 264 <u>+</u><br>116   | 0.000   |

**Table S3:** Burst Suppression parameters for the single anesthetic agent groups for NoPOD and POD patients.