Article –

SUPPLEMENTAL FILE I for:

Long-term outcomes of breast cancer patients receiving levo-bupivacaine wound infiltration or diclofenac for postoperative pain relief

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**Table S1** – Postoperative pain score through 4 postoperative days in rest and movement measured with Numerical Rating Scale (NRS)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Postoperative day** | **Diclofenac (N=41)** | **p†** | **Levobupivacaine bolus (N=39)** | **p†** | **Levobupivacaine PCA (N=40)** | **p†** |  |
| **NRS1-R** | 1 (0 – 2) | **<0.001** | 1 (0 – 2) | **<0.001** | 0 (0 – 1) | **<0.001** | 0.105 |
| **NRS2-R** | 0 (0 – 0.5) | 0 (0 – 0) | 0 (0 – 0) | 0.138 |
| **NRS3-R** | 0 (0 – 0) | 0 (0 – 0) | 0 (0 – 0) | 0.097 |
| **NRS4-R** | 0 (0 – 0) | 0 (0 – 0) | 0 (0 – 0) | 0.791 |
| **NRS1-M** | 3 (1.5 – 4) | **<0.001** | 3 (2 – 4) | **<0.001** | 3 (2 – 3) | **<0.001** | 0.783 |
| **NRS2-M** | 1 (1 – 3) | 1 (0 – 2) | 1 (1 – 2) | 0.473 |
| **NRS3-M** | 1 (0.5 – 2) | 1 (0 – 1) | 0 (0 – 1.8) | **0.043** |
| **NRS4-M** | 0 (0 – 1) | 0 (0 – 1) | 0 (0 – 1) | 0.630 |

NRS in the postoperative days 1-4 was measured in rest (NRS 1-4R), and in the movement (NRS1-4M), values are presented asmedian (interquartile range); † Friedman’s test; ‡ Kruskal Wallis’s test; p<0.05 was considered statistically significant.

**Table S2** **Significance of differences in domains of health status before and one year after surgery within groups based on Short Form 36 Health Survey (SF-36)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Domains of health status** | **Groups of patients** | | |
| Diclofenac | Levobupivacaine bolus | Levobupivacaine PCA |
| p\* | p\* | **p\*** |
| **Physical health** | Physical functioning | 0.393 | **0.003** | **0.008** |
| Role limitation due to physical problems | 0.180 | 0.082 | 0.692 |
| Bodily pain | 0.087 | **0.042** | 0.325 |
| General health perception | 0.508 | 0.159 | 0.365 |
| **Mental health** | Energy - vitality | 0.100 | 0.084 | 0.298 |
| Social functioning | 0.923 | 0.096 | **0.046** |
| Role limitation due to emotional problems | 0.731 | 0.568 | 0.673 |
| General mental health | 0.657 | 0.721 | 0.793 |

\*Wilcoxon test

**Table S3. Shoulder pain examined with a shoulder disability questionnaire in patients with diclofenac analgesia before and one year after surgery.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Before surgery  N (%)** | | | **One-year follow-up N (%)** | | |  |
|  | NA | No | Yes | NA | No | Yes | P\* |
| I wake up at night because of shoulder pain. | 1 (2.5) | 34 (85) | 5 (12.5) | 1 (4.8) | 14 (66.7) | 6 (28.6) | 0.378 |
| My shoulder hurts when I lie on it. | 1 (2.4) | 32 (78) | 8 (19.5) | 1 (4.8) | 13 (61.9) | 7 (33.3) | 0.295 |
| Because of pain in my shoulder, it is difficult to put on a coat or a sweater | 0 | 36 (87.8) | 5 (12.2) | 0 | 19 (86.4) | 3 (13.6) | 0.260† |
| My shoulder hurts during my usual daily activities | 2 (4.9) | 33 (80.5) | 6 (14.6) | 0 | 17 (77.3) | 5 (22.7) | 0.070 |
| My shoulder hurts when I lean on my elbow or hand | 2 (4.9) | 38 (92.7) | 1 (2.4) | 1 (4.5) | 17 (77.3) | 4 (18.2) | 0.156 |
| My shoulder hurts when I move my arm. | 2 (4.9) | 39 (95.1) | 0 | 1 (4.5) | 20 (90.9) | 1 (4.5) | **0.005** |
| My shoulder hurts when I write or type. | 3 (7.3) | 38 (92.7) | 0 | 0 | 20 (95.2) | 1 (4.8) | 0.143 |
| My shoulder is painful when I hold the driving wheel of my car or handle bars of my bike. | 3 (7.5) | 36 (90) | 1 (2.5) | 4 (20) | 14 (70) | 2 (10) | **<0.001** |
| When I lift and carry something my shoulder hurts. | 2 (4.9) | 30 (73.2) | 9 (22) | 0 | 13 (59.1) | 9 (40.9) | **0.043** |
| During reaching and grasping above shoulder level my shoulder hurts. | 2 (4.9) | 33 (80.5) | 6 (14.6) | 0 | 15 (68.2) | 7 (31.8) | **0.023** |
| My shoulder is painful when I open or close a door. | 2 (4.9) | 36 (87.8) | 3 (7.3) | 1 (4.5) | 20 (90.9) | 1 (4.5) | **<0.001** |
| My shoulder is painful when I bring my hand to the back of my head | 2 (5) | 33 (82.5) | 5 (12.5) | 0 | 16 (76.2) | 5 (23.8) | 0.568 |
| My shoulder is painful when I bring my hand to my buttock | 1 (2.4) | 35 (85.4) | 5 (12.2) | 0 | 18 (81.8) | 4 (18.2) | 0.700 |
| My shoulder is painful when I bring my hand to my low back. | 2 (5) | 34 (85) | 4 (10) | 0 | 16 (72.7) | 6 (27.3) | 0.706 |
| I rub my painful shoulder more than once during the day. | 0 | 38 (92.7) | 3 (7.3) | 0 | 17 (77.3) | 5 (22.7) | 0.227 |
| Because of my shoulder pain I am more irritable and bad tempered with people than usual. | 1 (2.5) | 38 (95) | 1 (2.5) | 0 | 17 (77.3) | 5 (22.7) | 0.151 |

\* marginal homogeneity test. Statistically significant differences in the shoulder pain during typical movements are bolded.

**Table S4. Shoulder pain examined with a shoulder disability questionnaire in patients with levobupivacaine bolus analgesia before and one year after surgery.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Before surgery  N (%)** | | | **One-year follow-up N (%)** | | | P\* |
|  | NA | No | Yes | NA | No | Yes |
| I wake up at night because of shoulder pain. | 0 | 35 (92.1) | 3 (7.9) | 0 | 21 (80.8) | 5 (19.2) | 0.091 |
| My shoulder hurts when I lie on it. | 2 (5.3) | 30 (78.9) | 6 (15.8) | 2 (8) | 17 (68) | 6 (24) | **0.011** |
| Because of pain in my shoulder, it is difficult to put on a coat or a sweater | 0 | 37 (97.4) | 1 (2.6) | 0 | 22 (84.6) | 4 (15.4) | 0.656 |
| My shoulder hurts during my usual daily activities | 0 | 35 (97.2) | 1 (2.8) | 2 (7.7) | 18 (69.2) | 6 (23.1) | 0.796 |
| My shoulder hurts when I lean on my elbow or hand | 1 (2.6) | 35 (92.1) | 2 (5.3) | 0 | 20 (80) | 5 (20) | 0.600† |
| My shoulder hurts when I move my arm. | 0 | 38 (100) | 0 | 0 | 23 (92) | 2(8) | **-** |
| My shoulder hurts when I write or type. | 0 | 38 (100) | 0 | 0 | 23 (95.8) | 1 (4.2) | - |
| My shoulder is painful when I hold the driving wheel of my car or handle bars of my bike. | 5 (13.2) | 33 (86.8) |  | 5(20.8) | 14 (58.3) | 5 (20.8) | 0.233 |
| When I lift and carry something my shoulder hurts. | 2 (5.4) | 29 (78.4) | 6 (16.2) | 1 (3.8) | 13 (50) | 12 (46.2) | 0.807 |
| During reaching and grasping above shoulder level my shoulder hurts. | 2 (5.3) | 32 (84.2) | 4 (10.5) | 0 | 17 (68) | 8 (32) | 0.779 |
| My shoulder is painful when I open or close a door. | 0 | 37 (97.4) | 1 (2.6) | 0 | 25 (96.2) | 1 (3.8) | 0.835 |
| My shoulder is painful when I bring my hand to the back of my head | 0 | 34 (89.5) | 4 (10.5) | 0 | 19 (73.1) | 7 (26.9) | 0.540 |
| My shoulder is painful when I bring my hand to my buttock | 1 (2.6) | 36 (94.7) | 1 (2.6) | 0 | 21 (80.8) | 5 (19.2) | 0.061 |
| My shoulder is painful when I bring my hand to my low back. | 2 (5.3) | 34 (89.5) | 2 (5.3) | 0 | 19 (73.1) | 7 (26.9) | 0.503 |
| I rub my painful shoulder more than once during the day. | 1 (2.6) | 36 (94.7) | 1 (2.6) | 1 (4) | 17 (68) | 7 (28) | 0.563 |
| Because of my shoulder pain I am more irritable and bad tempered with people than usual. | 0 | 37 (97.4) | 1 (2.6) | 1 (3.8) | 17 (65.4) | 8 (30.8) | 0.331 |

\* marginal homogeneity test. Pain is unchanged in almost all questions of the SDQ, and more present when lying on the shoulder.

**Table S5. Shoulder pain examined with a shoulder disability questionnaire (SDQ) in patients with continuous levobupivacaine analgesia before and one year after surgery.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Before surgery  N (%)** | | | **One-year follow-up N (%)** | | | P\* |
|  | NA | No | Yes | NA | No | Yes |
| I wake up at night because of shoulder pain. | 0 | 33 (84.6) | 6 (15.4) | 1 (4.2) | 18 (75) | 5 (20.8) | 0.291 |
| My shoulder hurts when I lie on it. | 1 (2.6) | 33 (84.6) | 5 (12.8) | 0 | 18 (78.3) | 5 (21.7) | 0.839 |
| Because of pain in my shoulder, it is difficult to put on a coat or a sweater | 1 (2.6) | 37 (94.9) | 1 (2.6) | 0 | 22 (91.7) | 2 (8.3) | 0.901 |
| My shoulder hurts during my usual daily activities | 0 | 33 (84.6) | 6 (15.4) | 0 | 20 (83.3) | 4 (16.7) | 0.453 |
| My shoulder hurts when I lean on my elbow or hand | 0 | 35 (89.7) | 4 (10.3) | 0 | 21 (87.5) | 3 (12.5) | 0.648 |
| My shoulder hurts when I move my arm. | 0 | 36 (92.3) | 3 (7.7) | 0 | 24 (100) | 0 | **-** |
| My shoulder hurts when I write or type. | 0 | 38 (97.4) | 1 (2.6) | 0 | 22 (91.7) | 2 (8.3) | - |
| My shoulder is painful when I hold the driving wheel of my car or handle bars of my bike. | 1 (2.6) | 36 (92.3) | 2 (5.1) | 6 (25) | 15 (62.5) | 3 (12.5) | 0.109 |
| When I lift and carry something my shoulder hurts. | 0 | 31 (79.5) | 8 (20.5) | 2 (8.3) | 17 (70.8) | 5 (20.8) | 0.153 |
| During reaching and grasping above shoulder level my shoulder hurts. | 0 | 32 (82.1) | 7 (17.9) | 0 | 20 (87) | 3 (13) | 0.260 |
| My shoulder is painful when I open or close a door. | 0 | 37 (94.9) | 2 (5.1) | 0 | 24 (100) | 0 | - |
| My shoulder is painful when I bring my hand to the back of my head | 0 | 32 (82.1) | 7 (17.9) | 1 (4.3) | 21 (91.3) | 1 (4.3) | 0.629 |
| My shoulder is painful when I bring my hand to my buttock | 0 | 35 (89.7) | 4 (10.3) | 1 (4.2) | 22 (91.7) | 1 (4.2) | 0.752 |
| My shoulder is painful when I bring my hand to my low back. | 0 | 34 (87.2) | 5 (12.8) | 1 (4.2) | 23 (95.8) | 0 | - |
| I rub my painful shoulder more than once during the day. | 0 | 35 (89.7) | 4 (10.3) | 0 | 21 (87.5) | 3 (12.5) | 0.567 |
| Because of my shoulder pain I am more irritable and bad tempered with people than usual. | 0 | 35 (89.7) | 4 (10.3) | 0 | 22 (95.7) | 1 (4.3) | 0.746 |

\* marginal homogeneity test. No statistically significant differences were found between the groups.

**Table S6 – Hand grip strength before surgery, 4 days, and one year after surgery.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Hand grip strength on operated side | Diclofenac (N=41) | p† | Levobupivacaine bolus (N=39) | p† | Levobupivacaine PCA (N=40) | p† | p‡ |
| before surgery | 0.38  (0.34 – 0.44) | 0.125 | 0.37  (0.31 – 0.44) | 0.263 | 0.40  (0.34 – 0.47) | **0.022** | 0.452 |
| 4 days after | 0.37  (0.30 – 0.43) | 0.35  (0.27 – 0.46) | 0.38  (0.30 – 0.41) | 0.778 |
| 1 year after | 0.32  (0.25 – 0.43) | 0.34  (0.30 – 0.40) | 0.39  (0.32 – 0.51) | 0.161 |
| **Hand grip strength – non-operated side** | | | | | | | |
| before surgery | 0.37  (0.32 – 0.46) | 0.269 | 0.38  (0.30 – 0.43) | 0.734 | 0.39  (0.33 – 0.46) | 0.145 | 0.686 |
| 4 days after | 0.37  (0.32 – 0.48) | 0.40  (0.32 – 0.44) | 0.40  (0.32 – 0.45) | 0.888 |
| 1 year after | 0.35  (0.27 – 0.44) | 0.38  (0.29 – 0.42) | 0.40  (0.32 – 0.49) | 0.457 |

\*Median (interquartile range); † Friedman's test; ‡ Kruskal Wallis test

**Table S7. Survival of patients operated on for breast cancer after 10 years related to body mass index, ASA status, and type of postoperative analgesia.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Number (%) of deceased | Number (%) of survivors | Total | Survival | The arithmetic mean of months (95% CI) | Logrank test (P) |
| The survival rate after 10 years | 18 (15) | 102 (85) | 120 | 85 % | 110 (104 – 115) | - |
| The survival rate after 10 years | | |  |  |  |  |
| BMI (< 20) | 1 (25) | 3 (75) | 4 | 75 % | 120 (120 – 120) | 0.72 |
| BMI (20 – 35) | 15 (14) | 91 (86) | 106 | 86 % | 110 (105 – 116) |
| BMI (> 35) | 2 (22) | 7 (78) | 9 | 78 % | 103 (79 – 126) |
| The survival rate after 10 years | | |  |  |  |  |
| ASA 1 | 1 (10) | 9 (90) | 10 | 90 % | 120 (120 – 120) | 0.45 |
| ASA 2 | 12 (13) | 77 (87) | 89 | 86 % | 110 (104 – 115) |
| ASA 3 | 5 (24) | 16 (76) | 21 | 76 % | 107 (92 – 122) |
| The survival rate after 10 years | | |  |  |  |  |
| Diclofenac | 6 (15) | 35 (85) | 41 | 85 % | 107 (96 – 117) | 0.36 |
| Levobupivacaine bolus | 3 (8) | 36 (92) | 39 | 92 % | 117 (113 – 121) |
| Levobupivacaine PCA | 9 (23) | 31 (77) | 40 | 77 % | 107 (97 – 117) |
| The survival rate after 10 years | | |  |  |  |  |
| Diclofenac | 6 (15) | 35 (85) | 41 | 85 % | 106 (96 – 117) | 0.99 |
| Any levobupivacaine group | 12 (15) | 67 (85) | 79 | 85 % | 112 (107 – 117) |

BMI body mass index, ASA American Society of Anesthesiologists.

**Table S8 A survival rate of patients operated on for breast cancer until analysis related to body mass index, ASA status and type of postoperative analgesia.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Number (%) of  deceased | Number (%) of survivors | Total | Survival | The arithmetic mean of months (95% CI) | Logrank test (P) |
| Overall survival until analysis | 23 (19) | 97 (81) | 120 | 80 % | 159 (150 – 168) |  |
| Overall survival until analysis & | | |  |  |  |  |
| BMI (< 20) | 1 (25) | 3 (75) | 4 | 75 % | 156 (136 – 176) | 0.94 |
| BMI (20 – 35) | 20 (19) | 86 (81) | 106 | 81 % | 159 (150 – 168) |
| BMI (> 35) | 2 (22) | 7 (78) | 9 | 78 % | 140 (105 – 175) |
| Overall survival until analysis & | | |  |  |  |  |
| ASA 1 | 1 (10) | 9 (90) | 10 | 90 % | 163 (154 – 172) | 0.43 |
| ASA 2 | 16 (18) | 73 (82) | 89 | 82 % | 159 (149 – 169) |
| ASA 3 | 6 (29) | 15 (71) | 21 | 67 % | 144 (122 – 167) |
| Overall survival until analysis & | | |  |  |  |  |
| Diclofenac | 9 (22) | 32 (78) | 41 | 78 % | 154 (137 – 171) | 0.22 |
| Levobupivacaine bolus | 4 (10) | 35 (90) | 39 | 85 % | 162 (154 – 170) |
| Levobupivacaine PCA | 10 (25) | 30 (75) | 40 | 75 % | 141 (126 – 157) |
| Overall survival until analysis & | | |  |  |  |  |
| Diclofenac | 9 (22) | 32 (78) | 41 | 78 % | 154 (137 – 171) | 0.52 |
| Any levobupivacaine group | 14 (18) | 65 (82) | 79 | 81 % | 151 (142 – 161) |

BMI body mass index, ASA American Society of Anesthesiologists.