Title : Remifentanil-Sparing E_ect of Pectoral Nerve Block Type II in Breast Surgery under Surgical Pleth Index-Guided Analgesia during Total Intravenous Anesthesia

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The ethics committee of Gachon University Gil Hospital approved this study. The study was registered at www.ClinicalTrials.gov (NCT03210220) prior to patient recruitment. Written informed consent was provided by all participants.

The inclusion criteria for this study were the following: women, aged between 20 and 65 years, with an American Society of Anesthesiologists physical status of 1 or 2, who were scheduled for BCS with SLNB for the treatment of breast cancer. The exclusion criteria were as follows: patients receiving anticoagulant therapy, those with bleeding disorders, hypersensitivity to local anesthetics, body mass index greater than 35 kg/m2, the presence of spine or chest wall deformities, and pregnancy. Patients either received the Pecs II block (Pecs group) or did not receive it (control group). One anesthesiologist (JJC) performed all blocks in the Pecs group enrolled patients. After the intervention, the participants and the investigator responsible for the study outcome assessment were blinded.

Premedication was not given. Electrocardiography, non-invasive blood pressure monitoring and the bispectral index (BIS vista monitor revision 3.0; Aspect Medical Systems, Norwood, MA, USA) were applied in the operating room. SPI (S5 monitor; GE Healthcare, Helsinki, Finland) was monitored using a pulse oximeter sensor attached to the index finger contralateral to the operative site. For anesthesia induction and maintenance, lidocaine (1 mg/kg), propofol, and remifentanil were administered. The effect-site concentrations of propofol and remifentanil were automatically calculated by Schnider's [15] and Minto's [16] pharmacokinetic models, respectively, using a target-controlled infusion (TCI) pump (Orchestra; Fresenius Kabi, Bad Homburg, Germany). To facilitate orotracheal intubation, rocuronium (0.8 mg/kg) was administered after loss of consciousness.

For the patients in the Pecs group, a linear ultrasound probe was placed on the lateral third of the clavicle with bilateral abduction in the supine position. After identifying the axillary vein and artery, the ultrasound probe was positioned inferio-laterally, between the 3rd and 4th ribs, and then the pectoralis major and minor, and serratus anterior muscles were confirmed. The needle was advanced in a medio-lateral direction in-plane view of the ultrasound. For the Pecs II block, a total 30 mL of 0.5% ropivacaine was injected. First, the needle tip was advanced into the fascia between the pectoralis major and minor muscles and 10 mL of 0.5% ropivacaine was injected. Thereafter, the needle tip was advanced into the tissue plane between the pectoralis minor and serratus anterior muscles, and 20 mL of 0.5% ropivacaine was injected in a similar manner.

Fifteen minutes after the Pecs II block, a skin incision was made for the scheduled surgery. During

the surgery, the remifentanil dose was adjusted to a target SPI of 20–50 and the propofol dose was adjusted to a target BIS of 40–60, using a TCI pump. When the SPI was >50 or <20, the remifentanile effect-site concentration was adjusted to a step of 0.5 ng/kg with intervals of 1 min or more. When the BIS value was >60 or <40, the propofol effect-site concentration was adjusted to a step of 0.5 g/kg with intervals of 1 min or more. When the systolic blood pressure dropped below 90 mm Hg or below 80% of the baseline value, ephedrine 5 mg was administered intravenously at 2-min intervals. If the heart rate (HR) dropped below 50 beats/min, atropine 0.5 mg was administered intravenously.

Patient-controlled analgesia (PCA) (Accufuser plus®, Wooyoung medical, Seoul, Korea) was provided for 48 h with ketorolac 120 mg and sufentanil 50 g in normal saline 100 mL, (basal infusion rate 2 mL/h, 0.5 mL intermittent bolus with a 15 min lock-out interval). For preventing PONV, ramosetron 0.3 mg was administered intravenously before the end of the surgery.

In the postanesthetic care unit (PACU), the postoperative pain was evaluated using an 11-point numerical rating scale (NRS) (0–10) and was accessed immediately after arrival at the PACU, 1 h postoperatively, 16–24 h postoperatively, and 24–48 h postoperatively. Fentanyl 50 g bolus was administered as a rescue analgesic agent when the NRS was greater than 5 points.

The primary outcome was the intraoperative remifentanil consumption, and the secondary outcomes were the postoperative pain score and rescue analgesic requirement. The sample size was calculated based on the previous study of breast cancer surgery under TIVA. The intraoperative remifentanil consumption was 10.9 2.9 g/kg/h and 7.3 3.3 g/kg/h in the control and Pecs groups, respectively. With type 1 error of 0.05 and a power of 0.9, the study required 14 patients in each group. Considering the possible drop-out, 20 patients were included in each group. Patients were randomly assigned to the Pecs group (n = 20) or the control group (n = 20), based on a randomized list generated with Excel 2013 (Microsoft office, Redmond, WA, USA), without stratification.

Data were analyzed using SPSS 19.0 (SPSS, Chicago, IL, USA). Values were presented as number of patients, medians (interquartile ranges; IQR) or mean standard deviation (SD). The Kolmogorov-Smirnov test was performed for the normality test of continuous variables. The normally distributed data were presented as mean SD and the skewed data were presented as median (IQR). An independent t-test was used for normally distributed variables (intraoperative dosages of remifentanil and propofol), and the Mann–Whitney U Test was used for variables with a non-normal distribution (postoperative pain scores). The chi-squared test or Fisher's exact test was

used to analyze the categorical data (the use of atropine, ephedrine and rescue analgesics), where appropriate. Repeated, measured ANOVA was used for accessing the intergroup differences of MBP, HR, SPI, and BIS over time. Statistical significance was accepted for p value < 0.05.

Primary completion date : December 30, 2018