Chronic Pain in Patients Undergoing Mastectomy: The Difference Between Pectoral Nerve Block (PECS I-II) and Erector Spinae Plane (ESP) Block

APRIL 2024

STUDY PROTOCOL

1. Project Title:
Chronic Pain in Patients Undergoing Mastectomy: The Difference Between Pectoral Nerve Block (PECS I-II) and Erector Spinae Plane (ESP) Block

2. Rationale of the Project:
Breast cancer is the most commonly diagnosed cancer among women and remains a leading cause of cancer-related mortality. Globally, it ranks second only to lung cancer in incidence, with both accounting for approximately 11.6% of all diagnosed cancer cases (1). In the United States, the lifetime risk for a woman to develop breast cancer is estimated at 13%, indicating that one in eight women will be affected during their lifetime (2).

Over the past two decades, significant advances in breast cancer research have markedly improved our understanding of the disease, enabling the development of more effective and less toxic treatments. Enhanced public awareness and improved screening methods have facilitated early detection at stages amenable to surgical resection and curative therapy. Consequently, survival rates—especially among younger women—have substantially improved (3).

Surgical treatment of breast cancer includes both conservative and non-conservative approaches. Conservative surgeries account for approximately 40% of all procedures, with quadrantectomy being the most commonly performed among them (4). However, surgical treatment may lead to various complications, including chronic postoperative pain (5).

Post-mastectomy pain syndrome (PMPS) is typically defined as chronic pain in the breast or chest wall persisting for at least three months following cancer treatment. It arises after surgical interventions for breast cancer and is believed to result from primary nerve injury or dysfunction of the nervous system (6,7). Clinically, it presents with features of neuropathic pain such as burning, tingling, stabbing, or shooting sensations, and hyperesthesia (8). Although no standardized diagnostic criteria exist, the estimated incidence ranges from 40% to 50% (7,9), with about half of affected women reporting moderate to severe pain (10).

Younger age (<40 years) has been identified as a major risk factor, though age does not appear to correlate with the intensity of reported pain (10). Severe acute postoperative pain is also considered a predictive factor for the development of chronic pain. Furthermore, radiotherapy to the breast and/or axillary region has been associated with an increased risk of chronic pain when compared to patients who did not receive radiation therapy (11). Among surgical contributors to PMPS, extensive axillary lymph node dissection is significant due to the increased risk of intercostobrachial nerve injury, which may lead to neuropathic pain (12,13).

Strategies aimed at reducing the risk of PMPS emphasize optimizing perioperative pain management. Techniques such as paravertebral, erector spinae plane (ESP), and pectoral

nerve blocks are routinely applied in appropriate surgical cases to reduce postoperative pain and minimize the risk of chronic pain development in many centers, including ours (14). Both ESP and PECS I-II blocks have demonstrated efficacy and are associated with low complication rates (14,15,16).

In our study, we aim to observe the incidence of chronic pain following mastectomy in patients who have received either a pectoral nerve block (PECS I-II) or an erector spinae plane (ESP) block as part of their pain management strategy. These blocks will be administered by the attending anesthesiologist after general anesthesia induction and prior to the initiation of surgery. The choice and timing of the block will be determined independently by the anesthesiologist and not influenced by the study team. The primary outcome of this study is to compare the incidence of chronic postoperative pain between the two groups. The secondary outcome is to assess the impact of these blocks on acute postoperative pain levels and opioid requirements.

3. Materials and Methods of the Study

3.1 Study Setting

Department of Anesthesiology and Reanimation, Hacettepe University.

3.2 Study Timeline

April 15, 2024 – August 15, 2024.

3.3 Study Population, Sample Size, and Study Groups

Following approval by the Hacettepe University Ethical Committee, patients aged 18 to 65 years, classified as ASA physical status I–II, and scheduled to undergo elective modified radical mastectomy or simple mastectomy with sentinel/axillary lymph node dissection under general anesthesia at Hacettepe University Hospitals between April 15 and May 15, 2024, will be included. Patients must have already been scheduled to receive either an ESP or PECS I-II block for postoperative pain management independently of the study. A total of 40 patients will be enrolled, with 20 in each group at least. Patients with coagulation disorders, allergies to local anesthetics, obesity (BMI > 35 kg/m^2), infection at the injection site, pre-existing neurological deficits, or unwillingness to participate, as well as those with failed blocks, will be excluded. The decision to perform blocks is made by the responsible anesthesiologist and will not be influenced by the study team.

3.4 Study Type

Prospective Cohort Study

3.5. Research Method and Data Collection Tools:

Upon admission to the operating room, non-invasive arterial blood pressure, electrocardiogram, and peripheral oxygen saturation monitoring will be conducted before

the induction of general anesthesia. This is the routine monitoring protocol applied prior to anesthesia. All patients will receive standard general anesthesia and standard ventilation modes. The research team will not intervene in the anesthesia procedure.

According to the standard anesthesia practice in these cases, anesthesia induction is performed with propofol (1.5–2.5 mg/kg), rocuronium (0.4–0.6 mg/kg), and fentanyl (1–2 mcg/kg), with a 50% oxygen-air mixture. Standard ventilator settings are applied. Anesthesia maintenance consists of 2% sevoflurane with 50% oxygen-air mixture. These practices are routine in our operating theater and are not specifically designed for this study. In the event of any non-routine requirement, decisions will be made by the responsible anesthesiologist, without any intervention from the research team. The study will commence after anesthesia induction and block application.

Following the induction of general anesthesia, the responsible anesthesiologist will independently administer either the PECS I-II or ESP block prior to surgical incision. The choice of block will not be influenced by the study and will be determined solely by the anesthesiologist, regardless of group distribution. The research team will not interfere in the selection or method of block administration.

PECS I-II Block Protocol:

With the patient in the supine position and the upper limb abducted 90°, the ultrasound (USG) probe is placed under the lateral third of the clavicle. After identifying the axillary artery and vein, the probe is aligned with the second rib. It is then moved inferolaterally to visualize the third rib and the pectoralis major, pectoralis minor, and serratus anterior muscles. A 10 cm block needle is advanced between the pectoralis major and minor muscles under ultrasound guidance. After confirming the site with 2–3 mL isotonic saline (hydrodissection), 10 mL of 0.25% bupivacaine is administered (PECS I). The probe is then moved toward the axilla, and when the serratus anterior muscle over the fourth and fifth ribs is visualized, another 20 mL of 0.25% bupivacaine is injected between the pectoralis minor and serratus anterior muscles (PECS II).

ESP Block Protocol:

The patient is placed in lateral decubitus position with the surgical side up. The ultrasound probe is placed longitudinally at the level of the T4–5 spinous processes and then moved laterally toward the surgical side. The transverse process and overlying trapezius, rhomboid, and erector spinae muscles are visualized. Under aseptic conditions, the block needle is inserted at a 30–40° cranio-caudal angle, passing through the trapezius, rhomboid, and erector spinae muscles. After confirming placement with 2–3 mL isotonic saline, 20–30 mL of 0.25% bupivacaine is injected between the erector spinae muscle and transverse process.

Both PECS I-II and ESP blocks will be performed under ultrasound guidance, and the needle position will be verified through anatomical visualization and hydrodissection. Blocks will

be considered successful if applied by the responsible anesthesiologist under these conditions.

At the end of surgery, maintenance agents will be discontinued, and intravenous sugammadex will be administered to reverse muscle relaxation, dosed according to patient weight. About 30 minutes prior to the end of surgery, 1000 mg intravenous paracetamol will be routinely administered for analgesia. Extubation will occur after the patient regains spontaneous breathing and emerges from anesthesia. This is standard procedure and will not be modified for the study. No interference will occur with decisions regarding anesthesia drugs, ventilation methods, or intubation technique.

Postoperative Pain Control:

In addition to routine 3×1000 mg IV paracetamol, rescue analgesia with IV tramadol (0.5 mg/kg) will be administered as needed. These practices are part of our standard multimodal analgesia protocol and not specific to the study. After discharge, patients will be transitioned to oral paracetamol, with a recommendation of 3×500 mg daily for one month if necessary

Postoperative follow-up interviews will be conducted by a study assistant. Time of initial pain, and whether rescue analgesia was needed within the first 24 hours, will be recorded. Pain levels will be assessed at 20 minutes, 6 hours, and 1 day postoperatively using the Numerical Rating Scale (NRS). If NRS >0, the DN4 (Douleur Neuropathique 4) questionnaire will be administered. At the 3-month follow-up, patients will be contacted via phone and evaluated with the DN2 and SF-12 questionnaires. No blood samples or invasive procedures will be performed for research purposes.

The NRS is a simple and widely used 0–10 scale to assess pain severity, from "0 = no pain" to "10 = worst imaginable pain." It is considered valid and reliable. The DN4 questionnaire, administered by clinicians, includes 10 items to evaluate neuropathic pain, with a sensitivity of 83% and specificity of 90%. A score ≥4 indicates neuropathic pain. The SF-12 Quality of Life questionnaire, validated in Turkish, consists of 12 items and is used to assess overall health status and quality of life.

3.6. Data Collection

Following ethics committee approval, eligible patients aged 18–65 years scheduled for elective modified radical mastectomy between April 15 and May 15, 2024, at Hacettepe University Hospital, who had already been assigned ESP or PECS I-II blocks for postoperative pain control independent of the study, will be enrolled. The study is observational, and no interventions will be made regarding clinical treatment decisions. Patient demographic data (ASA score, age, sex, weight, height, BMI, comorbidities) and intraoperative details will be recorded

Postoperative data within the first 24 hours will be collected via face-to-face interviews and entered into the follow-up and DN4 forms. At 3 months, DN2 and SF-12 questionnaires will be administered via telephone interviews

3.7. Data Analysis

Normality of numeric data will be assessed using the Shapiro-Wilk test. Data following a normal distribution will be compared between two independent groups using the Student's t-test. Non-normally distributed data will be analyzed using the Mann-Whitney U test. For three-group comparisons, one-way ANOVA will be used if parametric assumptions are met; otherwise, the Kruskal-Wallis H test will be applied. Descriptive statistics will include mean ± standard deviation for normally distributed data, or median (minimum–maximum) for non-normal data. Categorical variables will be summarized as counts (percentages), and group comparisons will be performed using chi-square or Fisher's exact test as appropriate. A p-value <0.05 will be considered statistically significant in all analyses.

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