Pectoral Nerve Blocks for Breast Augmentation Surgery: A Randomized, Double-blind, Dual-centered Controlled Trial

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Moderate levels of pain may be experienced after breast augmentation surgery
- It is unclear whether pectoral nerve blocks add clinically significant benefit to a multimodal analgesic regime after breast augmentation

What This Article Tells Us That Is New

- Patients undergoing breast augmentation who received pectoral nerve blocks in addition to multimodal analgesia experienced less pain in the first 6 h postoperatively and lower maximal pain scores between postoperative days 1 through 5
- The use of pectoral nerve blocks also reduced opioid consumption up to 5 d after surgery

ABSTRACT

Background: Pectoral nerve blocks have been proposed for analgesia during and after breast cancer surgery, but data are conflicted in aesthetic breast surgery. This trial tested the primary hypothesis that adding a preincisional pectoral nerve block is superior to systemic multimodal analgesic regimen alone for pain control after breast augmentation surgery. A second hypothesis is that rescue opioid consumption would be decreased with a long-lasting effect for both outcomes during the following days.

Methods: Seventy-three adult female patients undergoing aesthetic breast augmentation surgery under general anesthesia were randomly allocated to receive a pectoral nerve block *versus* no block. Both groups received standard care with protocolized multimodal analgesia alone including systematic acetaminophen and nonsteroidal anti-inflammatory drugs. The primary outcome measure was the maximal numerical rating scale in the first 6 h after extubation. Secondary outcomes included intraoperative remifentanil consumption and from extubation to day 5: maximal numerical rating scale, postoperative cumulative opioid consumption and postoperative opioid side effects, and patient satisfaction recorded at day 5.

Results: The maximal numerical rating scale score in the first 6 h was lower in the pectoral nerve block group compared with the control group (3.9 ± 2.5 *vs.* 5.2 ± 2.2; difference: –1.2 [95% CI, –2.3 to –0.1]; $P = 0.036$). The pectoral nerve block group had a lower maximal numerical rating scale between days 1 and 5 (2.2 ± 1.9 *vs.* 3.2 ± 1.7; $P = 0.032$). The cumulative amount of overall opioids consumption (oral morphine equivalent) was lower for the pectoral nerve block group from hour 6 to day 1 (0.0 [0.0 to 21.0] *vs.* 21.0 [0.0 to 31.5] mg, $P = 0.006$) and from days 1 to 5 (0.0 [0.0 to 21.0] *vs.* 21.0 [0.0 to 51] mg, $P = 0.002$).

Conclusions: Pectoral nerve block in conjunction with multimodal analgesia provides effective perioperative pain relief after aesthetic breast surgery and is associated with reduced opioid consumption over the first 5 postoperative days.

Breast augmentation is one of the most popular plastic surgery procedures, with 1,862,506 procedures reported worldwide in 2018.[1] Insertion of breast prosthesis causes major postoperative pain due to surgical dissection, damage to the muscles, and expansion of breast tissues.[2] Indeed, it was ranked the 45th most painful surgical act among 179 procedures in a large, observational, multicenter study.[3]

Postoperative pain is associated with an increase of time spent in the postanesthesia care unit (PACU) or in the ambulatory unit, an increased rate of readmission, dissatisfaction, and significant postoperative nausea and vomiting.[4] Postoperative pain is also associated with a higher risk of chronic pain syndrome and impaired quality of life.[5–7] Then adequate pain control is the cornerstone of postoperative management and may have a substantial impact on morbidity and patient satisfaction.[8] Postoperative pain management after breast surgery traditionally involves intravenous and

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oral opioids.[9] Several methods including multimodal analgesia and local anesthetic infiltration have been reported to reduce pain and/or opioid use after breast augmentation.[10,11] However, pain control is not always adequately achieved and may cause unwanted side effects.[12]

Recently, the pectoral nerves blocks (PECtoral nerveS blocks I and II [PECS I and PECS II]) were proposed for analgesia during and after breast surgery. These blocks may be more appropriately compared to other regional anesthetic techniques. Indeed, they are minimally invasive with a rapid-spread use.[13] Since the description by Blanco *et al.*,[14,15] various authors have reported the benefit of isolated or combined PECS I and II blocks for breast cancer surgery, including a recent meta-analysis by Hussain *et al.*[16] that concluded that pectoral nerve block is noninferior to paravertebral block.[17–20] Evidence for the use of pectoral nerve block for pain control after breast augmentation surgery are still scarce.[21–23] Systemic multimodal analgesia remains the most used regimen.[24–27]

We thought that adding a preincisional pectoral nerve block to a systematic nonopioid multimodal analgesic regimen including acetaminophen and nonsteroidal anti-inflammatory drugs will provide superior pain control after breast augmentation surgery than systemic multimodal analgesia alone with a decrease in rescue opioid consumption and a long-lasting effect for both outcomes during the following days. We therefore undertook the current study to assess the analgesic effect of preincisional bilateral pectoral nerve block for aesthetic breast augmentation surgery, in combination with systemic multimodal analgesia.

Materials and Methods

A multicenter, prospective, randomized, double-blind, controlled, superiority clinical trial using two parallel groups PECS I and PECS II in breast augmentation surgery was conducted from February 2016 to October 2019 in Montpellier and Nîmes teaching Hospitals, France. The Nîmes teaching hospital inclusion center was secondarily added after approval of the institutional review board and amended on clinicaltrial.gov due to the cessation of the aesthetic breast surgery at the Montpellier Center (unexpected surgeon departure). In accordance with the Declaration of Helsinki, the trial was approved by the ethics committee (institutional review board contact information: Comité de Protection des Personnes, Sud Méditerranée I, Montpellier-Nîmes, France, June 21, 2015, identification number 2015-A00678-41.) and was prospectively registered in ClinicalTrials.gov (NCT02682186; first registration: February 15, 2016; Principal investigator: Gérald Chanques). All patients provided written informed consent before inclusion.

Female adult patients, scheduled for prosthetic breast augmentation under general anesthesia, were eligible for participation in the study if they were affiliated with the national health insurance system and had an American Society of Anesthesiologists physical status I to III. Patients were not eligible if they were pregnant or breastfeeding, had cognitive impairment with difficulties in pain evaluation (vulnerable people), were protected minor or major patients with consent incapacity, had an allergy to local anesthetics or any contraindication to use the analgesics of our protocol, had severe coagulopathy, were on treatment for chronic pain, were participating in another research, or were scheduled for revision surgery or prosthesis change (table 1). The latter criterion was added in October 2017, and the change was reported in the study protocol in clinicaltrial.gov. No other significant change to the protocol involving the design, outcomes, or treatment was made. Exclusion criteria were consent withdrawal or protocol deviation. During preoperative anesthesia consultation, an independent anesthesiologist evaluated eligibility, obtained informed consent, and enrolled the participants.

Patients were randomly assigned in a 1:1 ratio into either the PECS group or the control group using a computerized process. Group allocation and study number were concealed in sealed envelopes and opened on the day of surgery. The patient, the treating anesthesiologist and nurse ("treating team"), and the investigators performing follow-up visits were blinded to the group allocation. An independent anesthesiologist opened the sequentially numbered envelope containing the randomization assignment and performed the PECS block ("interventional team"). In both centers, the most common surgical technique used is breast augmentation with submuscular implants (retropectoral prosthesis) rather than subglandular (prepectoral prosthesis). However, the surgeon's choice was made on a case-by-case basis according to the known advantages and disadvantages of both techniques.[28]

General Anesthesia

Standardized intraoperative protocol was performed in both groups. General anesthesia was induced with target-controlled infusion of remifentanil (Minto model; effect-site concentration, 4 to 6 ng/ml) and propofol (Schnider model; effect-site concentration, 4 to 6 μg/ml). Glottis local anesthesia with 5% lidocaine was performed for intubation. Immediately after endotracheal tube placement, remifentanil target was lowered to 1 ng/ml, and anesthesia was maintained with sevoflurane in air/oxygen. The remifentanil target was increased to 2 to 3 ng/ml just before surgical incision and then adjusted by 0.3-ng/ml steps to maintain heart rate and arterial blood pressure within 20% of the baseline values, targeting the lowest effective dose. Nitrous oxide, clonidine, dexmedetomidine, and ketamine administration were not allowed. Sevoflurane was maintained between 0.8 and 1.2 of minimum alveolar concentration fraction (measured, age-adjusted, and calculated by the ventilator). All patients were ventilated in volume-controlled mode, received cefazolin (2 g) for infection prophylaxis and 0.1 mg/kg dexamethasone after induction with 1.25 mg

Table 1. Baseline Characteristics of Patients

	Pectoral Nerve Block Group (n = 35)	Control Group (n = 38)	Standardized Mean Difference*
Age, yr	33 (28–39)	32 (28–39)	–0.07
Body mass index, kg/m^2	20.6 (19.3–22.2)	20.2 (19.1–21.6)	–0.06
ASA physical status, n (%)			
ASA I	32 (91.4)	34 (89.5)	0.07
ASA II	3 (8.6)	4 (10.5)	
Ambulatory care, n (%)	13 (37)	14 (37)	–0.21
Apfel score	2 (1–3)	3 (2–3)	0.27
Duration of anesthesia, min	126 (112–169)	144.5 (129–186)	–0.06
Duration of surgery, min	67 (57–90)	85 (63–119)	–0.32
Loss of blood, ml	0 (0–20)	0 (0–50)	–0.30
Prosthesis			
Right prosthesis weight, g	302 (275–335)	295 (265–345)	0.05
Left prosthesis weight, g	302 (275–340)	302 (265–345)	0.06
Retropectoral prosthesis, n (%)	26 (78.8)	34 (91.9)	–0.38

The results are expressed as medians (interquartile ranges) or as number of patients (percentage) as appropriate.

*Standardized mean difference: mean divided by the SD of the difference between the pectoral nerve block group and the control group.

ASA, American Society of Anesthesiologists.

droperidol at the end of surgery for postoperative nausea and vomiting prophylaxis.

PECS Block

Immediately after general anesthesia, the "interventional team" replaced the "treating team" for 15 minutes for both groups to ensure the treating team's blinding. In the PECS group, the blocks were performed with patient in the supine position with the arm abducted. The skin was prepared with 2% chlorhexidine gluconate with 70% isopropyl alcohol (ChloraPrep, Becton Dickinson, USA). A high-frequency linear ultrasound probe (11 to 12 MHz, Vivid Q, GE Healthcare, USA) covered with a sterile sheath was placed longitudinally in the subclavian area, inferior to the clavicle, identifying axillary artery and vein, and then moved caudally and laterally so as to see the second and third ribs. The pectoralis major, pectoralis minor, and serratus anterior muscles were then visualized. Subsequently, the pectoral branch of the thoracoacromial artery was identified between the pectoralis muscles and the lateral pectoral nerve that are typically located closed to the artery. PECS was performed through a single puncture if possible and always *via* in-plane technique. The needle tip was first positioned in the plane between the pectoralis major and minor muscles, and 10 ml of ropivacaine (3.75 mg/ml) was injected. The needle was advanced into the space between the pectoralis minor and serratus anterior muscles, and a further 15 ml of ropivacaine (3.75 mg/ml) was injected. For control group, the PECS was not performed but the ultrasound location of the region of interest was carried out to maintain the blinding of the procedure for the treating team. At the end of the "PECS/control procedure," in both groups, a sterile dressing was applied on the puncture zone. No documentation was reported in the chart for both group. It was only specified in the chart that patients were included in current study to maintain the blind. Then the treating team was allowed to come back and take over anesthesia management.

Postoperative Care

No local anesthetic infiltration was performed in the surgical area. Thirty minutes before the end of surgery, 1,000 mg acetaminophen, 100 mg ketoprofen, and 20 mg nefopam were infused. The patients were extubated in the PACU, and extubation time defined the beginning of outcomes recording. We used a numerical rating scale from 0 to 10, with 0 for no pain and 10 for worst possible pain. Analgesia was assessed at rest, every 30 min for 2 h in the PACU, and then every 2 h until hour 6 in the ambulatory or surgical ward.[29] If numerical rating scale was between 4 and 6, IV tramadol (50 to 100 mg) was administered according to patient's body weight (50 mg if the patient weighed less than 60 kg), and IV morphine titration, 2 to 3 mg every 5 min if the numerical rating scale was greater than 6. Postoperative nausea and vomiting were treated with IV ondansetron (4 mg). Maximal numerical rating scale and opioid consumption were recorded by nurses on medical charts in the PACU and in wards until the patient's discharge from the hospital and then self-reported by the patients at home. The data regarding the period after discharge from the hospital were recorded during a surgical consultation at day 1 and during an anesthesiological phone interview at day 5. All caring nurses, surgeons, and anesthesiologists who recorded these data were blinded to the allocation group.

At home for ambulatory care or in the surgical ward then at home after discharge, an oral analgesic management was protocolized including systematic 1,000 mg acetaminophen at 6-h intervals and 100 mg ketoprofen at 12-h intervals. If

the numerical rating scale was greater than 3, a rescue analgesic was allowed, with 50 to 100 mg tramadol according to body weight or 5 to 10 mg oral morphine if the numerical rating scale was greater than 6. The patients were asked to self-evaluate their pain in the same manner as we had done up to discharge (using numerical rating scale pain score) and to record it at every analgesic consumption up to the end of the fifth postoperative day. We retrieved this data at day 1 during the surgeon's consultation (for the "hour 6 to day 1 period") and at day 5 during a phone interview (for the "day 1 to day 5 period"). Overall opioid consumption was measured using oral morphine equivalents. The conversion of tramadol to morphine was calculated as follows: 100 mg tramadol IV or oral equivalent to 30 or 21 mg oral morphine, respectively; 1 mg IV morphine equivalent to 3 mg oral morphine.[30]

Global satisfaction was also assessed at day 5 using a 0 to 10 numerical rating scale with 0 signifying "completely dissatisfied" and 10 signifying "fully satisfied." All patient evaluation was performed by the anesthesiology treating team blinded to the allocated group. Ambulatory care or overnight hospitalization was left to the patient's choice. The distance between hospital and home and whether or not a third person was present at home were the two main criteria for this choice. Full trial protocol is available by request.

Outcome Variables

The primary outcome measure was the maximal numerical rating scale measured in the first 6 h after extubation. *A priori* secondary outcomes were the maximal numerical rating scale from hour 6 to day 1 (surgeon's consultation) and from day 1 to day 5 (phone interview), the intraoperative remifentanil consumption; the postoperative global opioid consumption in oral morphine equivalent, and the incidence of opioid side effects such as postoperative nausea and vomiting, constipation, and pruritus during the first 6 h, from hour 6 to day 1 (surgeon's consultation), and from day 1 to day 5 (phone interview), and global satisfaction at day 5. Any adverse effects, such as hypotension and respiratory depression, were recorded.

Statistical Analysis

The sample size was estimated *a priori* with calculation based on expected maximal numerical rating scale. We used the studies by Bashandy *et al.*[31] and McCarthy *et al.*,[32] which respectively found that patients reported a maximal numerical rating scale in the first 6 h of 4.0 ± 1.1 *vs.* 2.2 ± 0.9 and 4.6 ± 2.1 *vs.* 3.2 ± 1.8 ($P = 0.01$), respectively, for the intervention and control groups. Power calculation for an expected absolute difference of 30% in maximal numerical rating scale between the two groups, with a two-tailed α probability level of 0.05 and a power of 0.80 ($1 - \beta$) yielded a sample size of 36 patients/group. We initially planned to randomize 80 patients to anticipate possible postrandomization exclusions. This number was increased to 92 potentially randomized patients after the addition of Nîmes Center as a precaution to anticipate possible research issues (*i.e.*, loss of follow-up that could preclude any measurement of the primary outcome). Anyway, the total number of patients needed to be analyzed for the primary outcome (n = 72) was not changed. The statistical analysis was carried out with intention to treat. Per-protocol analysis was planned in case of protocol deviation. Descriptive statistics are reported as number and percentage, mean and SD, or median and interquartile range, and the standardized mean difference between groups was calculated. The normality of the distribution of quantitative variables was determined using the Shapiro–Wilk test. Comparisons of quantitative variables between the two study groups were made using independent sample *t* test or the Wilcoxon–Mann–Whitney test according to the variable distribution; comparisons of categorical variables were realized using the chi-square test or Fisher's exact test, as appropriate. The primary outcome (maximal numerical rating scale within 6 h after extubation) was evaluated using the *t* test because of the normal distribution of the variable, as for two other secondary outcomes: the maximal numerical rating scale from hour 6 to day 1 and the maximal numerical rating scale from day 1 to day 5. Other secondary outcomes were evaluated by Wilcoxon–Mann–Whitney test for quantitative variables with nonnormal distribution, by chi-squared test or Fisher test for qualitative variables whenever applicable. The numerical rating scale was recorded every 30 min from extubation to hour 2, and then every 2 h to hour 6 was evaluated by a linear mixed model to take account of repeated measurements in the same patient. The numerical rating scale was the dependent variable. The randomization group and different measurement times were analyzed as fixed effects, and the patient was the random intercept. The slope, the group, and time interaction were tested. $P < 0.05$ was considered statistically significant. The statistical analyses were performed by a senior independent statistician blinded to the allocation group using SAS Enterprise guide, version 7.1 (SAS Institute, USA).

Results

Among 136 patients scheduled for breast augmentation surgery and assessed for eligibility, 74 patients were enrolled and randomly assigned to one of the two groups. Enrollment ceased when the target sample size of 72 patients who were analyzable for the primary outcome was obtained. One patient withdrew her consent after randomization. No data were recorded, and this patient was excluded according to French law (fig. 1).[31] Finally, 73 patients were included in the final intent-to-treat analysis. We observed four protocol deviations: one patient who was enrolled despite a surgery for prosthesis change, and three patients who received an unplanned subcutaneous infiltration of local anesthetic by

the surgeon at the end of surgery. Thus, intent-to-treat analysis was performed on 73 patents, and per-protocol analysis was performed on 69 patients.

Numerical rating scale scores (primary outcome) were obtained for all patients. Out of 511 planned measurements (73 patients × 7 assessments) for the primary outcome, we have 46 missing data. All patients had at least four pain assessments; all missing data were framed by two 0-to-10 numerical rating scale assessments and occurred after discharge from the PACU. For *a priori* secondary outcomes recorded on day 1 (hour 6 to day 1 period), we had no missing data. According to secondary outcomes recorded at day 5 (day 1 to day 5 period), 12 individuals had missing data (could not be reached by phone).

The maximal numerical rating scale score in the first 6 h after extubation (primary outcome measure) was statistically significant between groups (3.9 [± 2.5] for PECS group *vs.* 5.2 [± 2.2] for control group; $P = 0.036$; absolute difference, −1.2 [−2.3 to −0.1]; table 2). The mean numerical rating scales recorded every 30 min for 2 h and then every 2 h until hour 6 are shown in fig. 2. Comparisons by analysis of repeated measures revealed that pain scores during the first postoperative 6 h were statistically lower in the PECS group ($P = 0.044$). The maximal difference between both groups was found before the first hour after extubation.

Regarding the *a priori* secondary outcomes measured after the surgery, the time before first rescue analgesic and cumulative amount of overall opioids consumption (oral

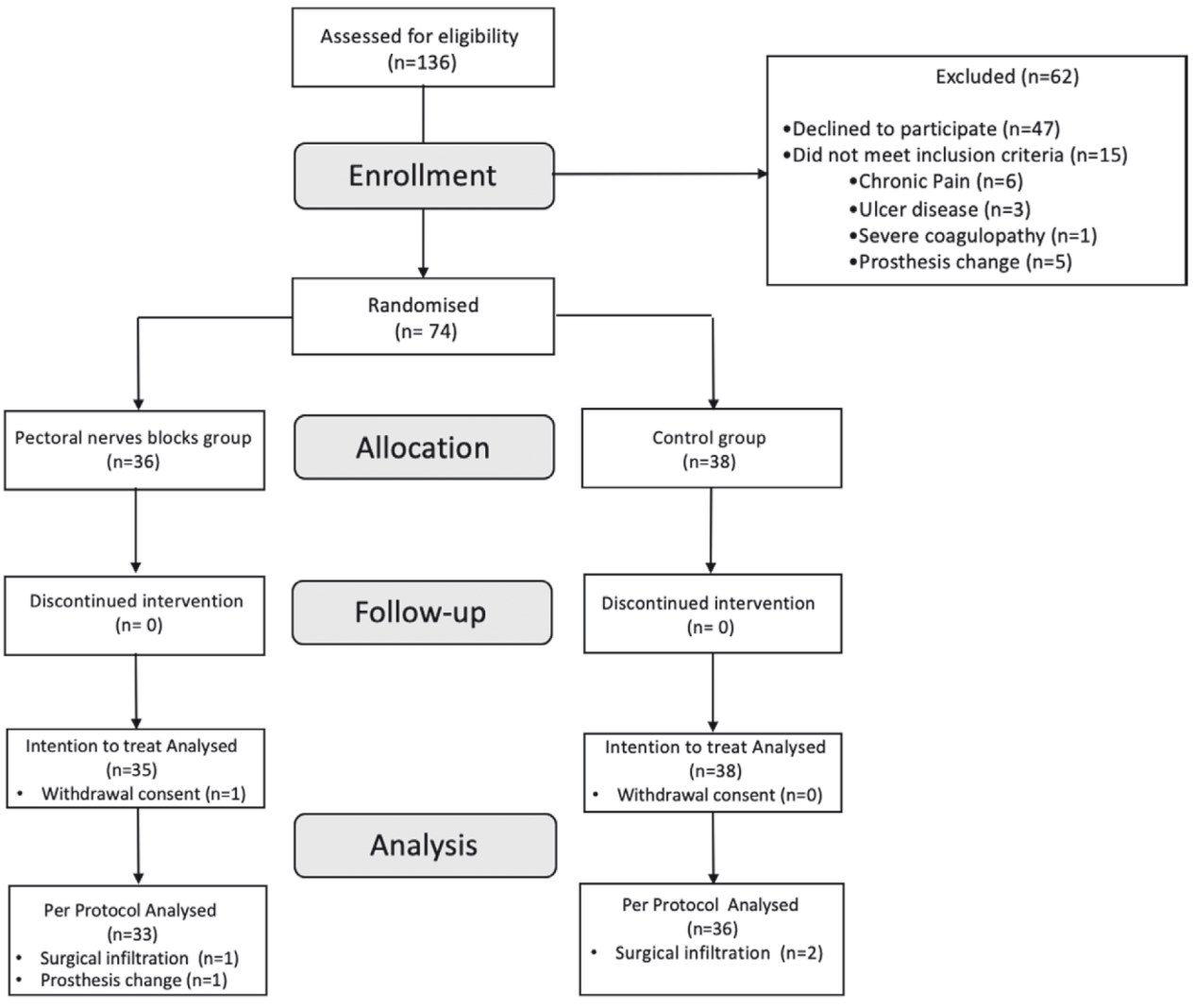

Fig. 1. Consolidated Standards of Reporting Trials diagram showing flow of study participants. n = 136 met eligibility for study, with n = 74 being recruited and randomized. One patient withdrew consent in the pectoral nerve block group after randomization but before anesthesia and surgery.

Table 2. Comparison of Numerical Rating Scale for Pain Evaluation

	Pectoral Nerve Block Group (n = 35)	Control Group (n = 38)	Group Difference* (95% CI)	*P* Value
Maximal numerical rating scale during the first 6 h after extubation	3.9 ± 2.5	5.2 ± 2.2	–1.2 (–2.3 to –0.1)	0.036
Maximal numerical rating scale from hour 6 to day 1	4.5 ± 2.1	5.3 ± 2.2	–0.7 (–1.7 to 0.3)	0.159
Maximal numerical rating scale from day 1 to day 5	2.2 ± 1.9	3.2 ± 1.7	–0.9 (–1.8 to –0.1)	0.033

The results are expressed as means ± SD.

*Group difference refers to the pectoral nerve block group value minus the control group value: absolute mean difference.

morphine equivalent) during these 6 h were not different (37 min [15 to 61] *vs.* 31 min [26 to 60]; $P = 0.644$; absolute difference, 6.0 [–4.0 to 11.0]) and 9.0 mg [0.0 to 15.0] *vs.* 12.0 mg [0.0 to 30.0]; $P = 0.201$; absolute difference, –3.0 [–12.0 to 0.0]), respectively, in the PECS group and in the control group (fig. 3). During the "hour 6 to day 1" period (6 h after extubation to surgeon's consultation), the maximal numerical rating scale was not statistically significant (4.5 [± 2.1] *vs.* 5.3 [± 2.2]; $P = 0.159$; absolute difference, –0.7 [–1.7 to 0.3]; table 2), but the PECS group had statistically lower opioid consumption (0.0 mg [0.0 to 21.0] *vs.* 21.0 mg [0.0 to 31.5]; $P = 0.006$; absolute difference, –10.5 [–21 to 0.0]; fig. 3). During the "day 1 to day 5" period (from surgeon's consultation to phone interview), the maximal numerical rating scale and opioid consumption were lower in the PECS group (2.2 [± 1.9] *vs.* 3.2 [± 1.7]; $P = 0.032$; absolute difference, –0.9 [–1.8 to –0.2] and 0.0 mg [0.0 to 21.0] *vs.* 21.0 mg [0.0 to 51.0]; $P = 0.002$; absolute difference, –21 [–30 to –15.0]), respectively, when compared with the control group (table 2; fig. 3). Regarding opioid-related side effects, there was no statistically significant difference between the groups for postoperative nausea and vomiting, pruritus, or constipation at all time points (table 3).

Patient satisfaction was very good in both groups (8.5 [8.0 to 9.0] for the PECS group *vs.* 8.0 [7.0 to 8.0] for the control group; $P = 0.052$). The proportion of patients with

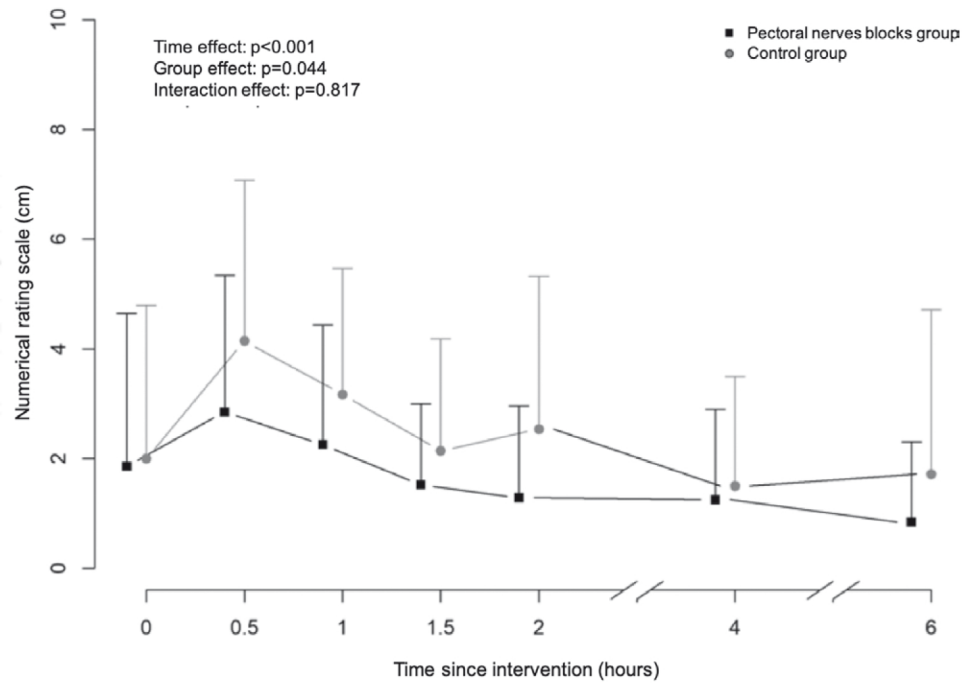

Fig. 2. Line graph with mean (SD) of numerical rating scale for pain at rest on the *y axis* over time (h) on the *x axis*. The means (SDs) of the pectoral nerve block and control groups are represented. The mixed model shows that, regardless of the group, the numerical rating scale changes significantly over time ($P < 0.001$). Likewise, considering all times overall, the two groups have significantly different numerical rating scale values ($P = 0.044$), with the graph showing lower values for pectoral nerve block patients. On the other hand, the evolution of the numerical rating scale over time is not different between the two groups (the interaction term is not significant, $P = 0.817$).

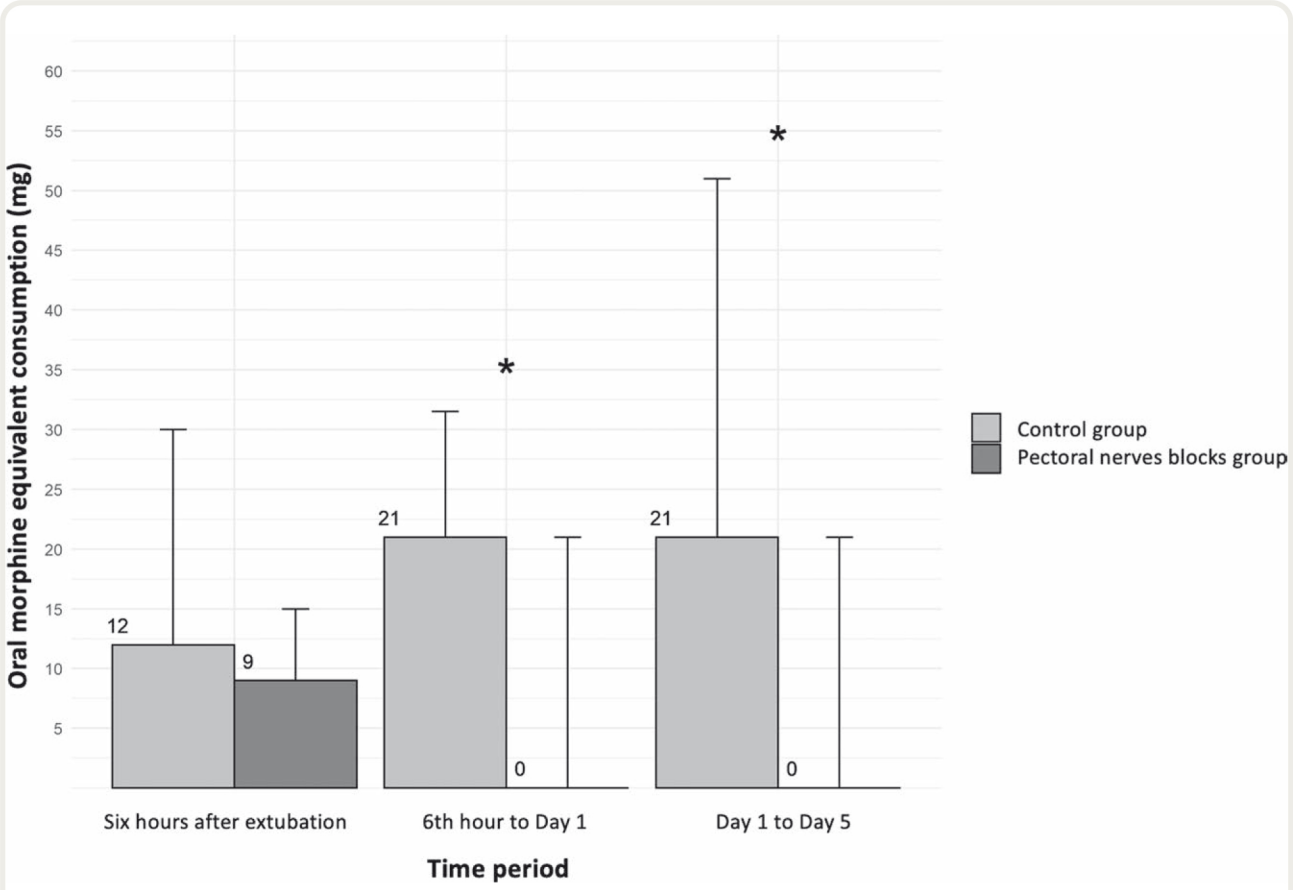

Fig. 3. Equivalent morphine consumption (mg) on the *y axis* over time (h) on the *x axis*. The medians are represented by *boxes*, and the upper 75th percentile is represented by the *upper bar*. The difference between groups was significant for the periods from hour 6 to day 1 and from day 1 to day 5. *Statistically significant, $P < 0.05$.

at least good satisfaction (numerical scale of more than 7 of 10) was statistically higher in the PECS group ($P = 0.044$; table 3).

Regarding other *a priori* outcomes related to anesthesia and surgery, remifentanil effect-site target concentration during surgery was statistically lower in the PECS group (2.5 ng/ml [2.0 to 2.9] *vs.* 3.0 ng/ml [2.5 to 3.5], $P < 0.004$; absolute difference, –0.5 [–0.9 to –0.2]). There was no statistically significant difference between the groups with respect to heart rate, systolic or mean arterial pressure, and use of vasopressors (ephedrine and neosynephrine; table 3). No PECS block-related complications, such as pneumothorax, vascular puncture, or local anesthetic toxicity, were recorded. One patient in the PECS group had a surgery-related postoperative hematoma requiring surgical intervention at the first hour after extubation.

Finally, a per-protocol analysis was performed including 69 patients among 73. Similar results were found for the primary outcome (maximal numerical rating scale in the first 6 h after extubation): (4.0 [± 2.5] *vs.* 5.3 [± 2.2]; $P = 0.034$; absolute difference, –1.2 [–2.4 to –0.1]). Similar results were also found for the mean numerical rating scale recorded every 30 min for 2 h and then every 2 h until hour 6 ($P = 0.023$). The maximal numerical rating scales from hour 6 to day 1 and from day 1 to day 5 were lower in the PECS group, but the difference was not significant (4.6 [± 2.1] *vs.* 5.4 [± 2.2]; $P = 0.121$; absolute difference, –0.8 [–1.9 to 0.2]) and (2.4 [± 1.8] *vs.* 3.1 [± 1.8]; $P = 0.086$; absolute difference, –0.7 [–1.6 to 0.2]), respectively. Maximal remifentanil site effect (2.5 ng/ml [2.0 to 2.9] *vs.* 3.0 ng/ml [2.5 to 3.5]; $P = 0.004$; absolute difference, –0.5 [–0.9 to –0.2]) and opioid consumption in oral morphine equivalent from hour 6 to day 1 (0.0 [0.0 to 21.0] *vs.* 21.0 [5.25 to 35.25]; $P = 0.004$; absolute difference, –10.5 [–21.0 to 0.0]) and from day 1 to day 5 (0.0 [0.0 to 21.0] *vs.* 21.0 [10.5 to 51.0]; $P = 0.002$; absolute difference, –21.0 [–31.5 to 0.0]) were all statistically significantly lower in the PECS group, whereas opioid consumption in the first 6 h was not (9.0 [0.0 to 15.0] *vs.* 12.0 [0.0 to 30.0]; $P = 0.086$; absolute difference, –3.0 [–12.0 to 0.0]), as for the intention-to-treat analysis.

Table 3. Adverse Events and Patient Satisfaction Scores

	Pectoral Nerve Block Group (n = 35)	Control Group (n = 38)	*P* Value
Maximal heart rate variation, %	6.4 (0.0–11.6)	8.6 (0.0–29.0)	0.304
Maximal systolic arterial pressure, mmHg	111 ± 13	115 ± 12	0.194
Minimal systolic arterial pressure, mmHg	86 ± 7	84 ± 6	0.196
Worst mean arterial pressure, mmHg	56 ± 7	55 ± 7	0.482
Hypotension, %	26 (74.3)	28 (73.7)	0.953
Total ephedrine use, mg	9.0 (0.0–18.0)	12.0 (0.0–21.0)	0.429
Total neosynephrine use, µg	15.0 ± 49.0	18.0 ± 61.0	0.991
Stay in postanesthesia care unit, min	88 (66–103)	95 (82–115)	0.194
Opioid side effects, n (%)			
Postoperative nausea and vomiting during the 6 h after extubation	4 (11.4)	9 (23.7)	0.172
Postoperative nausea and vomiting from hour 6 to day 1	4 (12.1)	7 (18.9)	0.435
Postoperative nausea and vomiting from day 1 to day 5	2 (6.3)	3 (8.8)	1.000
Constipation during the 6 h after extubation	0	0	—
Constipation from hour 6 to day 1	0	0	—
Constipation from day 1 to day 5	0	0	—
Pruritus during the 6 h after extubation	0	0	—
Pruritus from hour 6 to day 1	0	0	—
Pruritus from day 1 to day 5	0	0	—
Patient satisfaction score (0 to 10), n (%)*	8.5 (8.0–9.0)	8.0 (7.0–8.0)	0.052
Patients with satisfaction score higher than 7 out of 10, n (%)*	20 (77)	16 (52)	0.048

Results are expressed as medians (interquartile range) or as the number of patients (percentage) as appropriate. Hypotension is defined as mean arterial pressure under 65 mmHg.
*The patient satisfaction score was recorded for 57 patients (26 in the pectoral nerve block group and 31 in the control group).

Discussion

This prospective study shows that preoperative combined PECS blocks I and II associated with a systematic multimodal analgesia regimen reduced maximal pain intensity assessed by numerical rating scale during the first postoperative 6 h in patients scheduled for breast augmentation surgery. The PECS group had a statistically significant lower pain from day 1 to day 5. The cumulative amount of overall opioid consumption was also statistically lower for the PECS group from hour 6 after extubation to day 1 and from days 1 to 5.

Analgesia for aesthetic breast surgery receives less attention compared with cancer surgery. However, pain generated by breast augmentation surgery is quite similar to pain after modified radical mastectomy.[13] Indeed, the dissection required for the implant involves the disruption of the pectoralis major muscle and its attachments to the ribs. In some cases, the muscle fibers are split to access the plane between pectoral muscles, and the stretch of the pectoralis major muscle can be substantial. The major source of pain from submuscular breast augmentation is myofascial and transmitted by the pectoral nerves. The skin incision may be periareolar, inframammary, or transaxillary. Nerves involved in pain related to skin incision are, respectively, the anterior and lateral branches of intercostal nerves from T2 to T4, from T5 to T6, or the long thoracic nerves, and sometimes some branches from supraclavicular nerves, depending on implant size.[13]

PECS is a relatively new fascial plane block that aims to provide analgesia to the upper anterior chest wall.[15] PEC I targets the medial and lateral pectoral nerves to anesthesize the pectoralis muscles. PEC II targets several divisions of the intercostal nerves and the long thoracic nerve. These nerves need to be blocked to provide effective analgesia during breast surgery.[13,33]

PECS is associated with less complications than other described techniques for breast surgery, like paravertebral blocks. Indeed, they are minimally invasive with a rapid spread use.[34] These blocks have been used for analgesia during and after breast cancer surgery with relevant analgesic effect.[35] There is still a paucity of high-quality evidence supporting the analgesic benefit of these approaches in aesthetic breast surgery. Small recent randomized controlled trials assessed PECS for breast augmentation surgery, with heterogeneous results.

Ekinci *et al.*[21] compared postoperative analgesic effect of PEC 1 alone with no block (30 patients in each group) and reported a difference in fentanyl consumption in their primary outcome (25.7 *vs.* 18.2 mg IV morphine equivalent respectively at day 1 [$P = 0.008$]). Using a PECS and serratus plane block compared with a sham block with no additional systemic analgesic in postoperative care (15 patients in each group), Schuitemaker *et al.*[22] failed to demonstrate a significant difference in their first goal, a decrease in intraoperative hemodynamic variability, but reported a 40% numerical rating scale decrease in the PACU (5.3 ± 2.3, *vs.* 2.9 ± 2.7 [$P = 0.014$]) without any difference in morphine consumption. Karaca *et al.*[23] compared postoperative PECS block with no block and a nonopioid analgesia regimen without acetaminophen (27 patients in each group). In

their primary outcome, the 24-h IV morphine consumption was nearly 4-fold lower with PECS (mean SD, 11.6 *vs.* 37.9 mg; $P < 0.001$). The numerical rating scale was also significantly lower with PECS. Our study presents substantial differences. This is the first study in which PECS block was realized immediately after general anesthesia, leading analgesia of area of interest during all surgeries. Preincisional regional anesthesia techniques offer better pain relief and decreased intraoperative opioid consumption and may decrease postoperative opioid use.[36] Therefore, a systematic nonopioid and multimodal analgesic regimen was applied for all patients, associating acetaminophen and nonsteroidal anti-inflammatory drugs before rescue opioids with respect of current international guidelines.[8,24–27] A systematic double prophylaxis for postoperative nausea and vomiting according to guidelines and Apfel scores was also applied for all patients.[37] Consequently, we report similar pain scores with two- or threefold lower morphine equivalent consumption and lower postoperative nausea and vomiting rate than previous works in both the PECS and control groups. Thus, this study is a demonstration of how patients may benefit from associating several analgesics (systemic or regional analgesia), acting on different receptors, to improve postoperative pain outcomes.[8]

In the pathway of enhanced recovery after surgery, regional anesthesia is a major component of perioperative pain management.[38] Searching for optimal analgesia with less invasive techniques made interfascial plane blocks increasingly popular.[39] Fascial plane blocks such as PECS blocks, are based on the dissection of intermuscular spaces to target the nerve branches progressing within these spaces. However, no surgeon reported any change in their landmarks and dissection planes in this in the study. In our experience, as in previous studies, no additional operative difficulties related to the realization of these blocks have been reported. Several interfascial plane blocks have been indeed assessed for analgesia after breast surgery.[13] Thoracic paravertebral blockade is suggested for major breast surgery but not in aesthetic breast augmentation surgery. Indeed, it may be not sufficient with an incomplete anesthesia, because supraclavicular branches from the superficial cervical plexus, pectoral nerves, long thoracic and thoracodorsal nerves are not blocked with thoracic paravertebral blockade.[13,17] On the other hand, thoracic paravertebral blockade involves the risk of pneumothorax, spinal cord trauma, sympathetic block, and hypotension. More rarely, thoracic paravertebral blockade may become an epidural block or may result in total spinal anesthesia. Thus, it may be not suitable for a day-case surgery, considering the possible side effects.[17,40] Recently, Hussain *et al.*[16] undertook this systematic review and meta-analysis to identify the potential clinical role of PECS. They found no differences in pain scores or opioid consumption between the two groups for the first 24 h after breast cancer surgery, and both were superior to systemic analgesia alone.[18]

Erector spinae plane block has been proposed as an alternative to PECS block in patients scheduled for major breast surgery. In two recent studies, the authors failed to demonstrate the superiority of the erector spinae plane block, with statistically significantly lower opioid consumption and pain scores in the PECS group.[41,42]

There are several limitations with this study. The main limitation was not using a placebo in the control group. PECS as an interfascial plane block, need large volumes of local anesthetic.[39] We thought that injection of 10 and 15 ml of saline solution may generate a pain by itself. Concerning the potential imprecision of any results due to unreliability of outcome measurements, misdiagnosis, or misclassification of events, the primary outcome was self-measured by the patients themselves. Although subjective by nature, this precluded the potential bias of a measurement made by observers. In addition, a very strict blinding procedure was performed using different anesthesia teams for the research (procedure of PECS) and the general management (patient management and data recording). Formal dermatomal cold-sensation testing was not undertaken. It would have caused a loss of the blind. The absence of this testing means a lack of confirmation of correct block efficiency. However, cold stimulation may be poorly correlated with the spread and efficiency of regional analgesia for postoperative pain.[43] Postoperative hyperalgesia was also not assessed. Regional anesthesia is effective to prevent from hyperalgesia.[44] That may explain the opioid consumption difference during the last 4 days of follow-up.[44] All surgical procedures were not the same. Indeed, prostheses may be prepectoral or subpectoral, which may lead to different postoperative pain.[39–45] Finally, 136 patients were screened for eligibility, and only 74 were randomized. Some patients refused the randomization, wanting the certain realization of PECS block, and the main plastic surgeon quit one center unexpectedly, which explains the slowdown in the rate of inclusions. Finally, several sources of bias could substantially impact interpretation of the trial. However, the randomized double-blind design should provide reassurance.

Conclusions

Preincisional PECS block associated with recommended multimodal analgesia is an effective and safe technique that provides better postoperative analgesia immediately and over 5 days of follow-up; moreover, it is associated with lower opioid consumption. Further studies are required to assess the clinical effect of PECS for preventing chronic postsurgical pain after breast augmentation.

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Competing Interests

The authors declare no competing interests.

Reproducible Science

Full protocol available at: y-aarab@chu-montpellier.fr. Raw data available at: y-aarab@chu-montpellier.fr.

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