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A Comparison of Local Infiltration Analgesia and PECS II Block for Analgesia in Mastectomy with Axillary Dissection—A Randomised Equivalence Study

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Abstract

Objective: Various analgesic techniques can be used for a mastectomy with axillary dissection with varying degrees of efficacy. In our institution, local anaesthesia infiltration (LIA) is commonly performed by surgeons. In this study, we hypothesise that the relatively novel PECS II block is equivalent to the analgesic profile of LIA. **Methodology:** In this single center, prospective, randomised control trial, 40 patients undergoing unilateral mastectomy with axillary dissection were randomly assigned to receive either 30 ml 0.5% ropivacaine before skin via LIA by a specialist breast surgeon during surgery or 30 ml 0.5% ropivacaine via PECS II block, before skin incision. Fentanyl was used as rescue analgesia intraoperatively, and all patients received morphine via patient-controlled analgesia (PCA) device postoperatively. The primary outcome was the difference in total morphine consumption in 24 hours between the 2 groups after surgery with equivalency set at ±1 mg. Secondary outcomes included time to rescue analgesia after block administration, post-operative pain score over 24 hours, adverse effects encountered, total intraoperative opioid usage, effect on operative time, block performance time as well as block and surgery related complications. **Results:** Unadjusted mean PCA morphine consumption over 24 hours post-operatively comparing local infiltration analgesia (LIA) to that of PECS II at 95% confidence interval was −1.22 mg (95% CI: −3.77, 1.33). Total IV Fentanyl use comparing LIA to PECS II was 2.53 ± 0.98 mcg/kg and 1.96 ± 0.57 mcg, P = 0.035. There were no other significant differences in the secondary outcome. **Conclusion:** We

conclude there is a lack of equivalence between that of LIA and PECS II block, with the PECS II block providing superior analgesia.

Keywords

PECS-II, Mastectomy, Analgesia, Anaesthesia, Pain, Opioids

1. Introduction

Breast cancer is the most common female cancer worldwide, according to statistics by World Cancer Research Fund in 2018. Consequently, mastectomy is one of the most common oncological surgeries performed in women around the world. Surgical resection is associated with moderate to severe acute post-operative pain [1], and adequate pain relief can help improve the quality of recovery [2] and reduce the risk of chronic postoperative pain [3] [4] [5].

Regional anaesthesia has emerged as an important adjunct in improving patient care and satisfaction [6] [7]. While the thoracic paravertebral block has long been considered the gold standard for analgesia for breast cancer surgery [8], the Pectoralis II (PECS II) [6] [7] [9] [10] [11] block has emerged as a safe and simple regional anaesthetic technique that is superior to systemic analgesia only, and not inferior to a thoracic paravertebral block [12] [13] [14] [15]. Since then, there have been multiple publications comparing PECS block to more traditional regional nerve block techniques such as paravertebral blocks [7] [11] [13] [14] [15]. With the advent of Enhanced Recovery after Surgery (ERAS) program, there is increasing awareness and drive in enhancing analgesia while reducing opioids related adverse events in patients undergoing breast surgeries. Regional anaesthesia is a major adjunct in this new era in improving patient care and satisfaction through ERAS program [16] [17]. The advantage of regional nerve blocks in attenuating chronic pain syndromes associated with mastectomy [18] is another reason why these techniques may be the way forward in breast surgical care.

Local infiltration of analgesia (LIA) is one of the major techniques employed by our surgical colleagues in reducing the need for post-operative opioids and its associated side effects. There is sparse literature comparing the effectiveness of LIA vs the PECS II block in providing analgesia for mastectomy. Both techniques are simple to perform, and with a high safety profile for patients.

Our main objective was to investigate if the PECS II block, performed prior to surgical incision, under general anaesthesia, was as effective, as the LIA techniques employed by our surgical colleagues in reducing opioid requirements postoperatively in the first 24 hours. Equivalence was defined as a mean difference between the 2 groups within +/− 1 mg of IV morphine consumption.

Secondary outcomes such as time to first rescue analgesia, post-operative pain scores over the first 24 hours, and incidence of complications, were also measured as described in **Table 1**.

Table 1. List of Secondary Outcomes.

1) Time to first rescue analgesia after administration of block.
2) Post-operative pain scores over first 24 hours.
3) Incidences of Post-Operative Nausea and Vomiting (PONV).
4) Total intraoperative opioid usage.
5) Duration of Surgery.
6) Block performance time as defined as time from needle insertion until needle exit from skin.
7) Block related complications such pneumothorax, vascular puncture, local anaesthetic toxicity and any other attributable events.
8) Post-operative surgical complications such as bleeding, wound infection, and any other attributable events.
9) Any other post-operative adverse events related to anaesthesia such as hypotension, respiratory depression, pruritis, shivering and urinary retention.

2. Methodlogy

We designed a prospective, randomised control trial to be conducted in our public health care institution with major surgical capabilities. The study was approved by our local institutional review board in March 2018 and institution research funding was obtained. The study commenced in August 2018 and concluded in March 2019 with conclusion of recruitment of 40 patients.

We recruited 40 patients, who were randomly assigned to either arm of the study to have either a PECS II block performed by the anaesthetist prior to surgical incision, or to local infiltration of analgesia by the surgeon intraoperatively. Suitable patients were identified in surgical clinics following listing for surgery, consent was taken by study team members before day of surgery by study team members.

The 20 patients randomised to the PECS block arm had a PECS II block performed by the anaesthetist, after induction of general anaesthesia and before the start of surgery. The block was performed with aseptic precautions under ultrasound guidance, 10 ml of ropivacaine 0.5% was delivered into the plane between pectoralis major and pectoralis minor, and another 20 ml of ropivacaine 0.5% into the plane between the pectoralis minor and serratus anterior muscles at the level of the third and fourth ribs.

The other 20 patients had local anaesthetic administered by the surgeon under direct vision during the surgery. 10 ml of ropivacaine 0.5% was delivered between the inter-fascial planes of the pectoral muscles. And 20 ml of ropivacaine 0.5% was deposited between the muscle planes of the serratus anterior and pectoralis minor muscles. Both arms received a total local anaesthetic dose of 30 ml of 0.5% ropivacaine (150 mg).

Female patients above the age of 21 years with the ability to give consent and a minimum body weight of 50 kg, who were scheduled for elective unilateral mastectomy with axillary dissection at our institution were invited to take part in the study. Patients who were allergic to local anaesthetics, paracetamol, non-steroidal anti-inflammatory drugs (NSAIDS) or opioids; or with a history of chronic pain, were excluded.

Patients who consented to participate in the study were randomly assigned by a computer-generated randomisation programme to either arm. Sealed envelopes

in numbered sequence with the patient's randomisation status were opened by the anaesthetist prior to induction of anaesthesia. Research coordinators collecting data and patients are blinded to the randomisation.

General anaesthesia was induced in all patients with IV Fentanyl 1 mcg/kg followed by IV Propofol 1.5 - 2 mg/kg until loss of verbal response before administration of IV Atracurium 0.5 mg/kg. A supraglottic airway device was inserted or the patient was intubated at the anaesthetist's discretion. Anaesthesia was subsequently maintained with Desflurane at 1.0 MAC in an oxygen/air mixture. All patients were ventilated with positive pressure ventilation targeting end-tidal carbon dioxide levels between 35 - 45 mmHg.

Perioperative monitoring consisted of continuous electrocardiogram (ECG), regular non-invasive blood pressure (NIBP) monitoring every 3 minutes and continuous peripheral oxygen saturation (SpO_2) monitoring. All subjects received a continuous infusion of Plasmalyte™ at 5 - 8 ml/kg/hr during surgery.

A bolus of IV Fentanyl 1 mcg/kg was given if mean arterial pressure (MAP) exceeded 120% of baseline for two consecutive readings. Hypotension was defined as a MAP of lower than 80% of baseline, and was treated with boluses of Plasmalyte™ and, if required, IV ephedrine 5 - 10 mg or phenylephrine 50 - 100 mcg IV boluses. Bradycardia (rate of fewer than 40 beats/mins) was treated with 0.6 mg of IV atropine. All patients received IV Paracetamol 1 g, IV midazolam 10 - 35 mcg/kg, IV dexamethasone 8 mg and IV ondansetron 4 mg peri-operatively.

LIA, if performed, was administered by the surgeon during the surgery, under direct vision, after the mastectomy was performed.

Post-operatively, all patients received a Patient Controlled Analgesia pump, programmed to deliver morphine at 1mg boluses on demand, with a lockout interval of 5 minutes and with no background infusion, starting on arrival at the Post Anaesthesia Care Unit (PACU). Postoperative pain score was assessed via visual analogue scale from 0 - 10 with 0 indicating a pain free state and 10 indicating the worst imaginable pain.

Nausea and vomiting were assessed with four-point numerical scale (0 = no nausea or vomiting, 1 = mild nausea, 2 = severe nausea or vomiting once, and 3 = vomiting more than once). Rescue antiemetic of ondansetron 4 mg was given intravenously if the patient's score was 2 or more.

The patient and the research coordinator carrying out the data collection were blinded to the patient's grouping.

Total morphine consumption over 24 hours post-surgery was recorded.

Data was also collected on time to first rescue analgesia, post-operative pain scores over first 24 hours, incidence of complication and all secondary outcomes were collected by investigating anaesthetic team or clinical research coordinator (**Table 1**).

3. Statistics

Data collected was summarized in frequency (%) for categorical variables, and in mean and standard deviation (SD) for normally distributed data. Other numerical data was presented as median with interquartile range (25^{th} percentile, 75^{th}

percentile) Numerical variables were considered as normally distributed if Shapiro-Wilk test was not statistically significant.

Patient characteristics between the 2 groups were compared using Chi-square test or Fisher's exact test for categorical factors, and Independent T test or Mann-Whitney *U* test for parametric and non-parametric variables, respectively.

$P < 0.05$ was taken to be significant. Baseline characteristics that showed statistically significance differences between the groups were included in the multivariate linear regression model to examine the independent association of total morphine consumption in 24 hours between treatment groups.

The difference in total morphine consumption in 24 hours between two groups was deemed equivalent if the 95% CI of mean difference fell within equivalence region of ±1 mg.

All statistical analyses were performed using IBM SPSS Statistics for Window, version 20 (IBM Corp., Armonk, N.Y., USA)

4. Results

40 patients recruited for the study were randomly assigned to 2 arms (preoperative PECS II block, or intraoperative LIA). We had a single subject drop out in PECS block group due to refusal of participation by the attending anaesthetist.

There were no significant differences between the 2 study groups with regards to age distribution, BMI, presence of type 2 diabetes or hyperlipidaemia and ASA status. There were more patients with hypertension in PECS block arm.

With regards to surgical characteristics, there were no significant differences in the side of operation between groups. Duration of surgery and anaesthesia also did not differ significantly More patients underwent axillary lymph node clearance in the PECS group, while more patients in the LIA group underwent only sampling without clearance of axillary lymph nodes (**Table 2**).

No significant differences were found in terms of the doses of IV paracetamol, IV dexamethasone, IV ondansetron and the type of inhaled anaesthetics used. The amount of IV fluids given were also equivalent between both groups. However, total IV fentanyl use intraoperatively was higher in the LIA group, at 2.53 mcg/kg (±0.98) as compared to the PECS block arm, at 1.96 mcg/kg (±0.57) with a $P = 0.035$ (**Table 3**).

Mean total morphine consumption over the first 24 hours after surgery was 0.58mg in the PECS II block group, vs 1.8 mg in the LIA group.

Equivalence was defined as a mean difference between the 2 groups of within ±1 mg of IV morphine consumption.

Mean difference in 24-hr morphine consumption between the 2 groups was 1.22 mg less in the PECS II block group, with 95% CI of −3.77 to +1.33 mg. When adjusted for hypertension, axillary lymph node dissection/clearance and total IV fentanyl usage, the mean difference was 1.78 mg less in the PECS II block group, with 95% CI between −5.46 and +1.91 (**Table 4**) (**Figure 1**). As such, we concluded that the 2 groups were not equivalent.

Table 2. Subject characteristics between local infiltration and Pecs II block.

	Treatment (n = 39)		P value
	Local infiltration (n = 20)	Pecs II (n = 19)	
Age (years)	60.85 ± 9.98	58.79 ± 9.49	0.513
BMI (kg/m^2)	27.08 ± 4.36	26.98 ± 5.23	0.952
Hypertension			
No	6 (30.0)	12 (63.2)	0.038
Yes	14 (70.0)	7 (36.8)	
Type 2 Diabetes			
No	14 (70.0)	17 (89.5)	0.235
Yes	6 (30.0)	2 (10.5)	
Hyperlipidemia			
No	12 (60.0)	12 (63.2)	0.839
Yes	8 (40.0)	7 (36.8)	
Other co morbidity*			
No	15 (75.0)	5 (26.3)	0.002
Yes	5 (25.0)	14 (73.7)	
ASA			
I	3 (15.0)	1 (5.3)	0.593
II	10 (50.0)	10 (52.6)	
III	7 (35.0)	8 (42.1)	
Unilateral Mastectomy			
Left	10 (50.0)	10 (52.6)	0.869
Right	10 (50.0)	9 (47.4)	
Axillary lymph nodes dissection			
Non-sampling (Clearance/Converted)	5 (25.0)	11 (57.9)	0.037
Sampling	15 (75.0)	8 (42.1)	
Duration of surgery (min)	132.05 ± 25.04	137.74 ± 21.08	0.449
Duration of anaesthesia (min)	156.00 ± 27.79	171.16 ± 27.26	0.094

Value presented in mean ±SD and number (%). Refers to any comorbidities aside from those listed such as Ischemic Heart Diseases, Renal Impairment, etc.

Table 3. Comparison of intravenous medication between local infiltration analgesia vs Pecs II block.

	Treatment (n = 39)		P value
	Local infiltration (n = 20)	Pecs II (n = 19)	
Paracetamol 1 g			
No	0 (0.0)	1 (5.3)	0.487
Yes	20 (100.0)	18 (94.7)	

Continued

Dexamethasone 8 mg			
No	1 (5.0)	1 (5.3)	1.000
Yes	19 (95.0)	18 (94.7)	
Ondansetron 4 mg			
No	5 (25.0)	2 (10.5)	0.407
Yes	15 (75.0)	17 (89.5)	
Inhaled Anaesthetics			
Sevoflurane	0 (0.0)	0 (0.0)	NA
Desflurane	20 (0.0)	19 (100.0)	
Total use of IV Fentanyl (mcg/kg)	2.53 ± 0.98	1.96 ± 0.57	0.035
Total IV fluids given	1.5 (1.0, 1.5)	1.2 (1.0, 1.5)	0.749

Value presented in mean ± SD, number (%) and median (IQR).

Table 4. Total morphine consumption within 24 hours between local infiltration analgesia vs Pecs II block.

	Unadjusted Model β (95% CI)	Adjusted Model β (95% CI)
Local infiltration analgesia	REF	REF
PECS II	−1.22 (−3.77, 1.33)	−1.78 (−5.46, 1.91)

Adjusted model included hypertension, other co-morbidity, axillary lymph nodes dissection and total use of IV Fentanyl (mcg/kg).

Patients experienced minimal pain at rest and during movement during the first 24 hours in both arms of study, with reported pain scores generally less than 1. No significant difference was found in pain scores over 24 hrs between the 2 groups (**Figure 2**, **Figure 3**).

Post-operative nausea and vomiting were almost universally reported despite the prophylactic use of IV dexamethasone and ondansetron, but there was no significant difference between the groups.

There was also no significant difference between total surgical time and anaesthetic time, nor was there a difference in surgical complication rate with or without a PECS II block.

A single serious adverse event was reported during the study when a patient from the LIA arm developed pneumothorax after discharge. The patient was admitted and managed as per institutional practice and was discharged well with no long-term sequelae. Pneumothorax is a potential complication in any thoracic level nerve block, and patient had been given appropriate advice on what signs or symptoms to look out for as well as how to seek help during the consenting process. No other adverse events were observed during the study (**Table 5**).

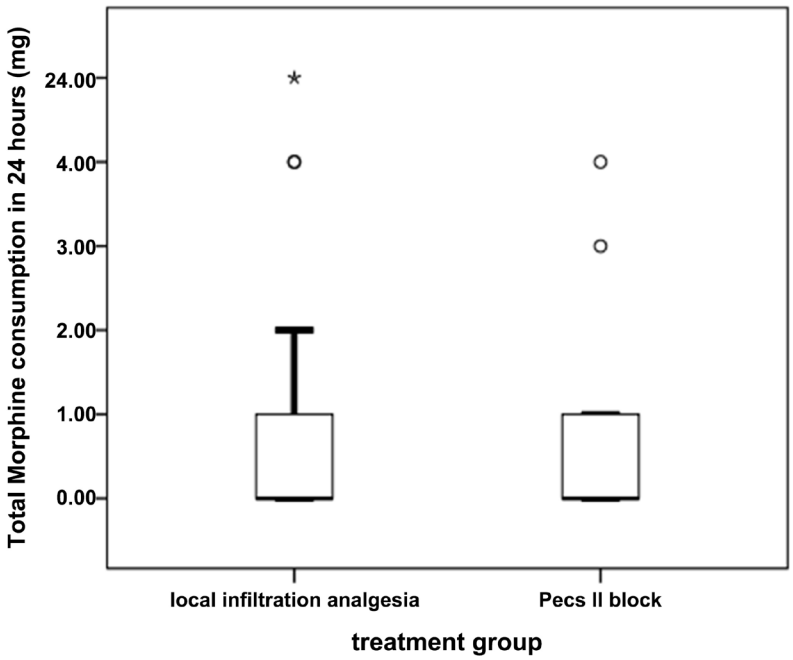

Figure 1. Total morphine consumption in 24 hours between infiltration analgesia vs Pecs II block.

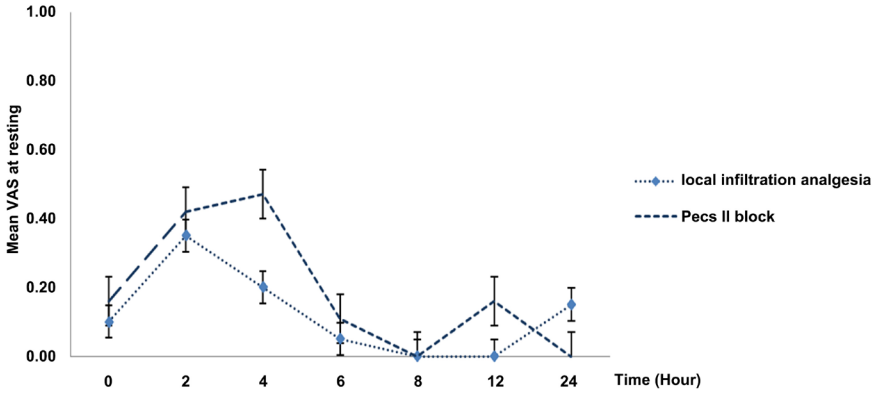

Figure 2. Pain score at resting between local infiltration analgesia vs Pecs II block.

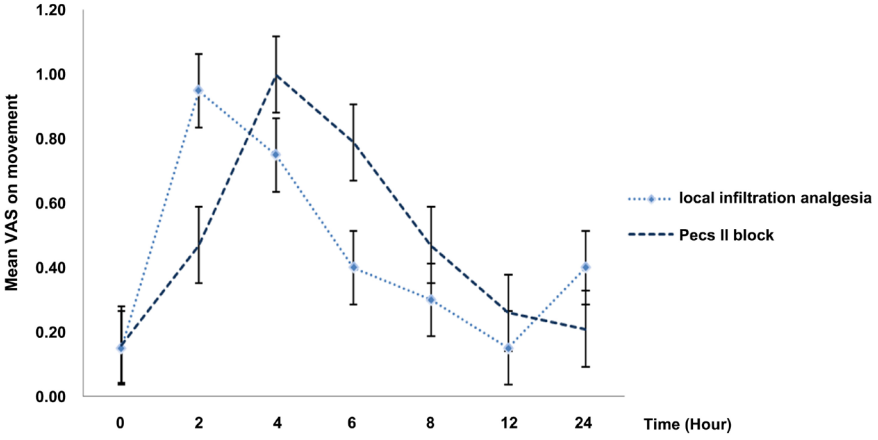

Figure 3. Pain score on movement between local infiltration analgesia vs Pecs II block.

Table 5. Adverse event and complication between local infiltration analgesia vs Pecs II block.

	Treatment (n = 39)		P value
	Local infiltration (n = 20)	Pecs II (n = 19)	
Adverse Event			
No	20 (100.0)	19 (100.0)	NA
Yes	0 (0.0)	0 (0.0)	
Block Related Complicated			
No	19 (95.0)	19 (100.0)	1.000
Yes	1 (5.0)	0 (0.0)	
Post-operative nausea and vomiting			
No	19 (95.0)	18 (94.7)	1.000
Yes	1 (5.0)	1 (5.3)	
Post-operative Bleeding			
No	20 (100.0)	19 (100.0)	NA
Yes	0 (0.0)	0 (0.0)	
Post-operative Wound infection			
No	18 (90.0)	19 (100.0)	0.487
Yes	2 (10.0)	0 (0.0)	
Post-operative Complication within 1 month after surgery			
No	20 (100.0)	18 (94.7)	0.487
Yes	0 (0.0)	1 (5.3)	

Value presented in number (%).

5. Discussion

Our study showed that post mastectomy morphine consumption was not equivalent following a PECS II block vs LIA. This could have been the result of the less complete analgesia intraoperatively afforded by fentanyl prior to administration of LIA, when compared with a well-placed PECS II block performed before incision.

The performance of the block did not appear to significantly increase overall surgical (LIA mean 132 min vs PECS II block 137 min, $p = 0.45$) or anaesthetic time (LIA mean 156 min vs PECS II block 171 min, $p = 0.094$). Neither did the block appear to increase the risk of surgical complications in our study.

The strength of our study was that the trial conditions were very tightly controlled to reduce to risk of confounding factors affecting the trial. A standardised block performance method was used to reduce confusion of differing block techniques with particular care taken to avoid a serratus plane blockade. However, we recognised that this was a single centre study with limited sample size. We were unable to blind all anaesthetists involved in the trial as we cannot prevent

them from observing the surgical process of LIA being given, however we believe this confounding factor is adequately addressed by strict protocol governing when to give IV fentanyl intraoperatively and morphine consumption post operation is governed by patients who are blinded to the study group they fall under. We found it challenging recruiting patients of appropriate weight to accommodate the amount and volume of local anaesthetics (LA) in our local study.

However, given the safety profile of both techniques and the fact that our study demonstrated a trend towards better analgesia with the PECS II block, without impacting total anaesthetic and surgical time significantly, or increasing surgical complications, we believe that the PECS II block performed prior to surgery is a viable alternative to intraoperative LIA.

In this study, we conclude that between LIA and PECS II block being performed for analgesia for patients undergoing unilateral mastectomy with axillary dissection, there was a lack of equivalence between LIA and PECS II in terms of total morphine consumption over the first 24 hours post-surgery. Total morphine consumed was less in the PECS block arm when compared to the LIA arm with our pre-study end point of equivalence set at a difference of less than 1mg between the two groups. However, we are aware of an extreme outlier in the LIA group who consumed 24 mg of morphine via PCA modality. In our small set of patients, this may have skewed the statistics. To address this, we conducted additional post-hoc analysis excluding the outliers using the same statistical methods. These results showed the difference is −0.55 mg with 95% CI is −1.65 to 0.55 when comparing morphine usage of PECS group vs LIA group. This result although does not support the conclusion of non-equivalence between the 2 techniques, shows a trend toward less morphine consumption in the PECS II block group.

In general, overall demand for morphine via PCA was low with most patients using less than 4 mg of morphine in the first 24 hours. This illustrates that PECS II nerve block is at least equivalent if not superior to LIA in providing post-operative analgesia in post mastectomy patients with axillary dissection. This also supports the current evidence that pectoral nerve blockade can be an effective technique in controlling pain for breast surgeries [17] [19]-[27].

Another significant finding was that more IV fentanyl was used intraoperatively in the LIA arm as compared to the PECS block arm although this did not lead to significantly more opioid related adverse events. Higher fentanyl usage in the LIA group can be explained by the fact that in our study, patients did not have any strong analgesia on board after induction of anaesthesia for surgery until the pectoral muscle layers are identified after surgical dissection and LIA performed. This was one of the possible advantages of pre-incision PECS II block as a working block can negate the need for opioids in all phases of the surgery with a lasting effect though the 24 hours.

With anaesthesia practice leaning towards opioid sparing techniques in view of the multitude side effects of opioids which can lead to increase morbidity of patients, prolong the duration of hospitalisation, and increase healthcare costs as

well as the concern about the role of opioid in immunomodulation which may increase risk of cancer recurrence and progression [28] [29] [30]. It is generally accepted that any sensible reduction in opioids consumption by patients may beneficial as long as the quality of analgesia and care is not compromised.

There are many other modalities of regional nerve blocks such as serratus plane, epidural, paravertebral and erector spinae nerve block described as alternative for PECS block in providing opioid sparing anaesthesia for breast surgeries and PECS block is not without its own issues such as motor blockade and block failure [7] [11] [31] [32] [33].

The techniques employed in our study is easily replicable in many clinical settings with access to ultrasound, it is our hope that this report at to the scientific evidence accumulated in improving patient care for patients undergoing breast surgery, especially mastectomy. In centers where nerve blocks under ultrasound may not be possible, LIA technique remains a crucial and important role in improving quality of life for mastectomy and other breast surgery patients. Future studies can potentially focus on comparing long term efficacy of catheter placement in PECS block versus more conventional nerve blocks as well as efficacy of PECS block in reducing incidences of chronic pain in post mastectomy patients.

6. Conclusion

Our study shows that LIA and PECS II block are not equivalent, with the PECS II block performed before incision providing superior analgesia both intraoperatively and postoperatively. With the proliferation of ultrasound-guided local anaesthetic blocks and the excellent safety profile of this block, it appears to be a good alternative to LIA for breast surgery. Our study adds more data to the field of research in providing superior analgesia via regional techniques for breast surgeries [34].

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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