ANTICANCER RESEARCH *41*: 5667-5676 (2021)
doi:10.21873/anticanres.15383

Erector Spinae Plane Block *Versus* Serratus Plane Block in Breast Conserving Surgery: A Randomized Controlled Trial

GIANLUCA VANNI[1], GIORDANA CAIAZZA[2], MARCO MATERAZZO[1], GENEROSO STORTI[2], MARCO PELLICCIARO[1], CHIARA BUONOMO[2], SILVIA NATOLI[2], ELEONORA FABBI[2] and MARIO DAURI[2]

[1]*Breast Unit, Department of Surgical Science, PTV: Policlinico Tor Vergata University, Rome, Italy;*
[2]*Department of Emergency and Admission, Critical Care Medicine, Pain Medicine and Anesthetic Science, Policlinico Tor Vergata University, Rome, Italy*

Abstract. *Background/Aim: Erector spinae plane block (ESP Block) was introduced in 2016 as a surgical post-operative analgesia procedure. The present prospective, randomized trial aimed to compare ESP Block with serratus plane block (SPB) plus pectoral nerve blocks (PECS I) during breast conserving surgery (BCS). Patients and Methods: Between February 2019 and March 2021, 104 patients undergoing BCS were randomized to receive either ESP block (ESP group n=54) or SPB+PECS I (SPB group=49). Assessment of postoperative pain was recorded by the dynamic and static visual analog scale (VAS) and was compared between groups. Results: Between-group two-way ANOVA did not reach a statistically significant difference in static and dynamic VAS (p=0.879; p=0.917, respectively). Despite ESP group requiring for higher value of patient-controlled analgesia (PCA) bolus, no statistically significant difference was found in PCA activation pattern between groups (p=0.109). ESP block was a faster technique when compared to SPB+PECS I (p=0.007) and no complications or opioid side-effects were recorded in all groups examined. Conclusion: ESP Block could represent a safe, faster alternative with a single injection to SPB+PECS I in BCS.*

Breast cancer (BC) is the most common cancer worldwide with over 2.3 million new cases demanding for multidisciplinary treatment which, in the overwhelming majority of cases, require a surgical intervention (1). Although several surgical protocols have been designed to reduce surgical impact (2-5), the number of surgical procedures (6) or even avoid surgery (7), postoperative pain management is still of a pivotal importance (8).

Adequate postoperative pain control is crucial for early mobilization, reduction of postoperative morbidity, hospital length of stay, cross-infections and healthcare expenditure (8). Moreover, adequate perioperative analgesia is imperative for reducing the risk of chronic post-surgical pain (CPSP), which ranges between 25% and 60% after breast conservative surgery (BCS) (9).

Current BCS pain management encompasses regional anesthetic techniques and systemic administration of analgesia with a synergetic effect on pain (10). Regional anesthetic techniques improve perioperative pain control, reduce opioid consumption and side-effects, thus preventing central sensitization and reducing CPSP (11, 12). Furthermore, in surgical oncology, intravenous (IV) opioid administration has been related with immune system impairment, reduction of circulating immune cells (2, 13, 14), and higher risk of cancer recurrence (10, 15). Additionally, a recent study demonstrated that opioid receptors might be involved in promoting BC cells migration, and thus BC recurrence (16). In light of this evidence, regional anesthetic techniques gained popularity in clinical practice as oncological safe procedures (15, 17-19).

Finally, a faster discharge is increasingly called for by patients, who view the Hospital as a potential source of COVID-19 infection (20). In BC, regional techniques encompass thoracic paravertebral block (TPVB), epidural administration, and ultrasound-guided (US-guided) procedures (21). Besides traditional regional anesthetic techniques, novel US-guided blocks such as pectoral nerve blocks (PECS I and II), and serratus plane block (SPB) are currently commonly performed due to their relative simplicity, safety and perceived efficacy (22). Recent studies

Correspondence to: Marco Materazzo, Breast Unit, Department of Surgical Science, PTV: Policlinico Tor Vergata University, Viale Oxford 81, 00133, Rome, Italy. Tel: +39 3395685883, e-mail: mrcmaterazzo@gmail.com

Key Words: Anesthesia, conduction, breast neoplasms, mastectomy, segmental, ultrasonography, pain, postoperative outcome.

have demonstrated how a combination of SPB+PECS I provides excellent analgesic results in breast cancer and Axillary surgery, thanks to their effects on the medial and lateral pectoral nerves (PECS I), and intercostal and thoracodorsal nerves (SPB) (23, 24).

Additionally, in 2016 a further novel promising US-guided block, named Erector Spinae Plane Block (ESP Block), was described by Forero *et al*. (25). ESP Block is performed with a single US-guided shot of local anesthesia (LA) in the interfascial plane, between the transverse vertebral process and the erector spinae muscles (25). ESP Block in breast surgery was reported by several authors as a safe option with a significant analgesic effect and a noteworthy reduction of postoperative opioid consumption (26-29).

Despite ESP Block safety, simplicity, and efficacy, to the best of our knowledge, no previous randomized controlled studies comparing ESP Block use for postoperative analgesia with other US-guided regional anesthesia techniques were performed. Our randomized, controlled study aims to compare ESP Block with SPB+PECS I during elective BCS.

Patients and Methods

Study design and patient selection. A single institution, randomized, non-inferiority trial (ESP Block *vs*. SPB+PECS I) (Figure 1) was launched. The local institutional review board (Comitato Etico Indipendente, PTV: Policlinico Tor Vergata, Viale Oxford 81, 00133, Rome) approved the study with the code name of BREAST study and registration number of CEI n° 15/19. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The primary goal of the study was aimed at comparing the analgesic effect of ESP Block with SPB+PECS I during BCS. Pain assessment was performed with dynamic and static visual analog scale (VAS) at the end of the surgical procedure (T0) and at 2, 6, 12, and 24 h after surgery.

Moreover, postoperative opioid consumption (analgesic rescue), opioid side effects (*e.g*., nausea/vomit, itch, constipation, and respiratory depression) and procedure complications (pneumothorax, LA systemic toxicity, peridural or intradural injection, hematoma) were recorded as secondary endpoints and compared. Other secondary endpoints included comparison of mean procedure time and assessment of techniques reproducibility. Procedure time encompasses drug preparation, target US and drug administration. Reproducibility was determined by the number of failed procedures or inability to find the target plane.

Sample size was calculated after preliminary data was obtained from an observational preliminary study with 10 patients allocated in each group (ESP block versus SPB+PECS I groups), recording 12-h postoperative standing pain as VAS to calculate effect size (0.139) and standard error (0.234). After setting an alpha error at 0.05 with power analysis of 90% and enrolment ratio of 1:1, the sample size was established at 98 patients, 49 in each group. Potential dropout was a priori calculated from the abovementioned preliminary study and established at 10%, thus enrolment was set at 110 patients.

Primary inclusion criteria for BREAST study were patients of age between 18 and 70 years old, candidates for BCS with an American Society of Anesthesiology (ASA) score ranging from I to III, and weight between 40 and 80 kg. Patients with a personal history of drug addiction, contraindication for LA US-guided procedure (*e.g*., local infection, allergy to LA), chronic pain under treatment and pregnancy were excluded from the study. According to these prerequisites and requirements, the BREAST study was initiated in February 2019 and terminated in March 2021.

Preoperative assessment. Informed consent was obtained from all individual participants included in the study. Following recruitment, all patients were randomized (1:1) with Excel Database (Redmond, WA, USA) into the two different group: patients undergoing PECS I plus SPB blocks (SPB group), or ESP Block (ESP group).

All anaesthesiologists participating in the study were unaware of the grouping until surgical room admittance, just prior to the US-guided procedure. Grouping allocation was communicated by telephone call in the preoperatory room. Following the US-guided procedure, all patients underwent general anesthesia (GA). Surgeons were not present in the surgical room prior to GA in order to avoid any bias concerning the surgical techniques (blind study). Data collection was performed by physicians not directly involved in any diagnostic or therapeutic procedures regarding the patients.

US-guided block. From surgical room admittance, patients were monitored with continuous electrocardiography (ECG), continuous oxygen saturation (SpO2) and non-invasive blood pressure (NIBP). Subsequently, a single 18-gauge needle was placed in the antecubital vein and patients were administered with Sufentanil 5 mcg. All patients received Cefazolin 2 g IV, or a different antibiotic regimen if allergic, within one hour from incision. Following premedication and telephonic group allocation, patients underwent US-guided block according to group in the preoperatory room under all aseptic precautions.

Both procedures (ESP group or SPB group) utilized the same US machine (SonoSite M-Turbo FUJIFILM SonoSite inc, USA) with a linear array probe (15-6 MHz) and an 80 mm block needle (Stimuplex® Ultra 360, B. Braun Melsungen AG, Melsungen, Germany). All participating anesthesiologists were designated with an alphanumeric code and collected as a categorical variable.

SPB group. Patients in the SPB group underwent PECS I block followed by SPB. For PECS I, patients were placed in supine decubitus with 90° open arm. A linear probe was placed vertically in the deltopectoral groove, under the lateral third of the clavicula. After visualization of the thoracoacromial artery between the pectoralis minor and major muscles, a linear probe was placed to locate the interfascial plane. A block needle was advanced caudally in-plane until the interfascial plane, which was firstly hydrodissected with 2 ml of saline solution, followed by administration of Ropivacaine 0.5% 10 ml (12, 29).

SPB was performed in the same decubitus and the linear probe was placed vertically in the middle axillary line, at the level of the 5th rib and serratus muscle. A block needle was advanced in-plane until the 5th rib to reach the plane under the serratus muscle. The target plane was hydrodissected with 2 ml of saline solution, followed by injection of Ropivacaine 0.5% 20 ml plus Dexamethasone 4 mg (30-32).

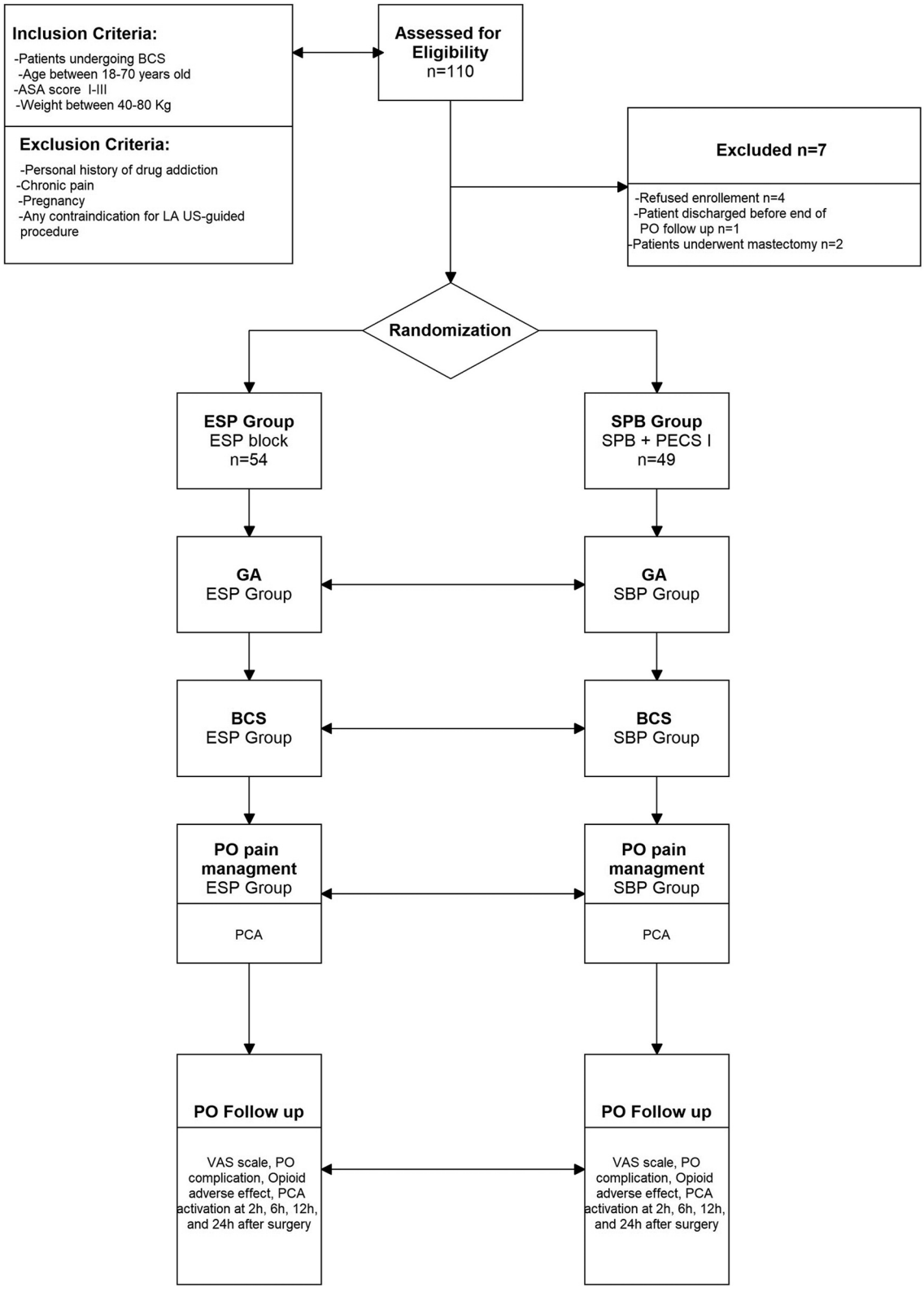

Figure 1. *Study flowchart. BCS: Breast conserving surgery; ASA score: American Society of Anesthesiologists score. LA: local anesthesia; US-guided: ultrasound-guided; PO: postoperative; ESP: erector spine plane block; SPB: serratus plane block; PECS I: pectoralis nerve block I; GA: general anesthesia; PCA: patient controlled analgesia.*

ESP group. During ESP Block procedure, patients were placed in lateral decubitus, contralateral to the surgical field. A linear probe was placed in a parasagittal manner 3 cm from the spinous process of T5 to locate T5 transverse process and erector spinae muscle. Block needle was advanced in-plane until reaching the transverse process of T5, beneath the erector spinae muscle. The target plane (under the erector spinae muscle) was hydrodissected with 2 ml of saline solution, and Ropivacaine 0.5% 25 ml plus Dexamethasone 4 mg were injected (25, 30, 33, 34).

Intraoperative management. Following the US-guided block, all patients underwent GA. Continuous monitoring was performed with ECG, SpO2, heart rate (HR), NIBP and Bispectral Index (BIS, Medtronic, Dublin, Republic of Ireland). GA was induced with injection of 2 mg/kg Propofol IV followed by 4.5/5 mg/ml Propofol IV in a target-controlled infusion (TCI) to the effector site. Airway management was carried out with I-Gel (Intersurgical, Wokingham, UK) and a mechanical ventilator under pressure control ventilation (PCV). Anesthesia was maintained with propofol in TCI to the effector site in order to maintain BIS value between 40 and 50. Operative time was defined as incision to skin suture surgical time and reported in minutes. All patients received a continuous infusion of normal saline at a rate of 5-8 mg/kg/h during surgery. If mean NIBP or HR exceeded 20% of baseline for two consecutive readings, a 5 mcg IV Sufentanil bolus was administered. All patients received 0.1 mg/kg ondansetron IV for antiemetic prophylaxis, 40 mg pantoprazole and paracetamol 1 gr before completion of surgery.

Postoperative management. Patients were monitored in the postoperative room until achieving a score equal to or greater than 12 on the White and Song scale, and then were transferred to the surgical ward. In the postoperative room, Patient Controlled Analgesia (PCA) was administered through an infusion pump. PCA protocol consisted of a 1 mg/ml morphine bolus with a minimum interval of 10 min and a maximum of 16 mg of morphine every 4 h. Following the transfer to the surgical ward, patients were reevaluated at 2, 6, 12 and 24 h after surgery by a physician not directly involved in any diagnostic or therapeutic procedures. During each reevaluation, postoperative pain as dynamic and static VAS scale, any opioid, or procedure side effects were collected. At the end of the observation, the PCA infusion pump was removed and analgesic rescue pattern, according to the time frame (0-2; 2-6; 6-12; 12-24 h after surgery), were recorded and included in the analysis.

Statistical analysis. All data were submitted into the EXCEL datasheet (Microsoft, Washington, DC, USA). All continuous variables are expressed as medians and interquartile ranges (IQR), and categorical data are presented as frequency (percentage). For continuous variables, Mann-Whitney *U*-test was used to compare the data of the two groups that did not conform to normal distribution, otherwise Student's *t*-test was applied. Chi-square or Fisher's Exact test were used to compare dichotomous categorical variables and Monte Carlo methods was applied for non-dichotomous variables. Longitudinal repeated measures of dynamic VAS, static VAS and PCA activations pattern were collected, and a two-way analysis of variance test (two-way-ANOVA) was applied to determine between-groups *p*-values. Prior analysis, Mauchly's Sphericity Test, was performed and when *p*-value was <0.05, Greenhouse-Geisser correction was applied. The statistically significant cut-off value was defined as $p<0.05$. Variables with assigned *p*-values <0.05 were considered statistically significant. All the statistical analysis was performed in SPSS statistical package version 23.0 (SPSS Inc., Chicago, IL, USA).

Results

Baseline data. A total of 110 patients were considered for enrolment, as described in the study design. Following recruitment, 4 patients withdrew (no reason given). After allocation, 3 patients were excluded from the study; one was discharged before the end of the follow-up, following patient's request, and 2 patients underwent mastectomy. Consequently, the final study population considered for the study consisted of 103 patients divided into two groups (ESP group, n=54; SPB group, n=49). Patient characteristics and procedures variables are listed in Table I with no statistically significant difference found when compared between the groups. Age and body mass index (BMI) analysis reported casual distribution between ESP and SPB groups ($p=0.578$, $p=0.243$; respectively). Moreover, neither sorting of ESP and SPB groups according to ASA classification nor according to the physician performing the US-guided block reached statistically significant differences ($p=0.264$, $p=0.066$; respectively). Finally, neither mean intraoperative Sufentanil consumption (ESP Group 5.000 *vs*. SPB Group 3.947; $p=0.603$) nor median Operative time exhibited any statistically significant difference between the groups ($p=0.967$).

Postoperative pain. Static and dynamic postoperative pain values between the ESP group and SPB group are listed in Table II. Higher static VAS value in SPB group and ESP group were 4 and 6 at baseline, respectively. Despite reports of higher static VAS score at 0 h and 2 h in ESP group, no statistically significant difference was found when compared with SPB group, as displayed in Figure 2. Conversely, static VAS score in the SPB group resulted in a peak between 2 h and 6 h. Notwithstanding the different trends, a between-group two-way ANOVA confirmed the absence of a statistically significant difference ($p=0.879$). Regarding dynamic VAS score, higher values were 6 and 5 at baseline in ESP and SPB group, respectively. Both ESP and SPB groups experienced similar trends with a peak at 6 h, as displayed in Figure 3. Although a slightly higher dynamic VAS score was seen throughout the observation in the ESP group, no statistically significant difference was found at either time point (Table II), nor the between-group two-way ANOVA ($p=0.917$) resulted in a statistically significant value.

PCA infusion pump analysis revealed different PCA activation patterns among the groups. As reported in Figure 4, the ESP group required a higher number of boluses during the postoperative course, especially at 6h (mean value ESP Group 0.450 *vs*. SPB Group 0.160; $p=0.264$). Despite the different trends, no statistically significant difference was found in between-group two-way ANOVA ($p=0.109$).

Table I. *Patient baseline characteristics and procedure variables*.

Variable	ESP Group (n=54)	SPB Group (n=49)	*p*-Value
Age (IQR) yr	55.87 (48.02-68.05)	58.02 (48.59-70	0.578
BMI (IQR) kg/m^2	20.90 (20.30-24.45)		0.243
Mean operative time (IQR) min	86.02 (65.03-99.85)	85.81 (63.04-105.75)	0.976
Intraoperatory Sufentanyil (IQR) min	0 (0;10)	5 (0;10)	0.603
ASA			
I	10 (18.52%)	16 (32.65%)	0.264
II	42 (77.78%)	31 (63.26%)	
III	2 (3.70)	2 (40.9%)	
Physician			
A	12 (22.22%)	23 (46.94%)	0.066
B	33 (61.11%)	20 (40.82%)	
C	5 (9.56%)	3 (6.12%)	
D	4 (7.40%)	3 (6.12%)	
Median procedures' time (IQR) min	9.52 (7.56-11.12)	14.16 (11.07-17.74)	0.007*
Opioids side-effects	0/54 (0%)	0/49 (0%)	1.000

All continuous variables are reported as median and interquartile range (IQR) within brackets; categorical data are reported as frequency and percentage within brackets. *p*-Values are calculated with Fisher's exact test for categorical variables and Mann-Whitney *U*-test for continuous variables. *Statistically significant values ($p<0.05$). ESP: Erector spine block; SPB: serratus plane block; BMI: body mass index; ASA: American Society of Anesthesiologists physical status classification system.

Table II. *Patient static and dynamic VAS*.

Time	ESP Group (n=54)	SPB Group (n=49)	*p*-Value	Between-group ANOVA *p*-Value
Mean static VAS				
Baseline	0.58 (0;1)	0.53 (0;1)	0.887	0.879
2 h	0.90 (0;2)	0.63 (0;1)	0.515	
6 h	0.81 (0;2)	0.84 (0;2)	0.924	
12 h	0.74 (0;2)	0.68 (0;2)	0.872	
24 h	0.48 (0;1)	0.37 (0;1)	0.669	
Mean dynamic VAS				
Baseline	0.52 (0;1)	0.53 (0;1)	0.978	0.917
2 h	1.42 (0;2)	1.21 (0;3)	0.687	
6 h	1.65 (0;3)	1.47 (0;3)	0.745	
12 h	1.26 (0;2)	0.89 (0;2)	0.456	
24 h	0.61 (0;1)	0.58 (0;1)	0.925	

All continuous variables are reported as median and interquartile range (IQR) within brackets. *p*-Values are calculated with the Mann-Whitney *U*-test for continuous variables and with two-way ANOVA. ESP: Erector spine block; SPB: serratus plane block; VAS: visual analogue scale.

Discussion

Despite evidence supporting conventional regional anesthetic techniques in surgical oncology (35, 36), the exact role of different techniques is still debated in the literature (37, 38). For instance, TPVB and neuraxial anesthetic administration are contraindicated in case of coagulation disorders. Moreover, conventional regional anesthetic techniques require a long learning curve and include limitations and serious complications such as pneumothorax, accidental dural puncture, spinal anesthesia, and epidural hematoma (21, 23).

In recent years, an increasing interest arose in the development of alternatives to the conventional regional anesthetic techniques. US-guided wall blocks are gaining popularity in postoperative pain management thanks to their effectiveness, feasibility and low rate of complications when compared to conventional regional anesthetic techniques. PECS I, PECS II and SPB blocks are routinely applied in breast surgery (21, 39). However, as during oncoplastic surgery, tumor multifocality and being overweight could represent a contraindication to PECS and SPB blocks (40).

Moreover, in 2016 a novel US-guided superficial block, named ESP, was designed by Forero *et al*. for acute and

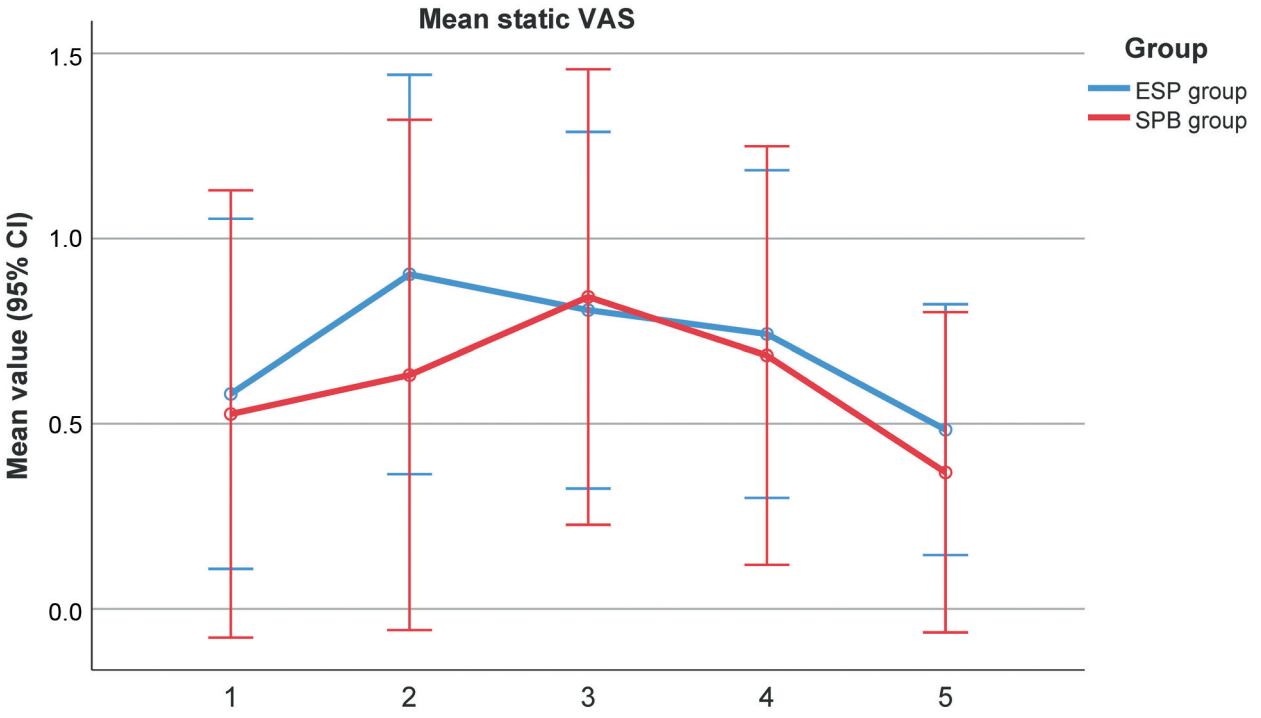

Figure 2. *Mean static VAS in ESP vs. SPB Group. VAS: Visual analogue scale; 95% CI: 95% confidence interval; ESP: erector spine block; SPB: serratus plane block. 1: Baseline; 2: follow-up at 2 h; 3: follow up at 6 h; 4: follow-up at 12 h; 5: follow up at 24h.*

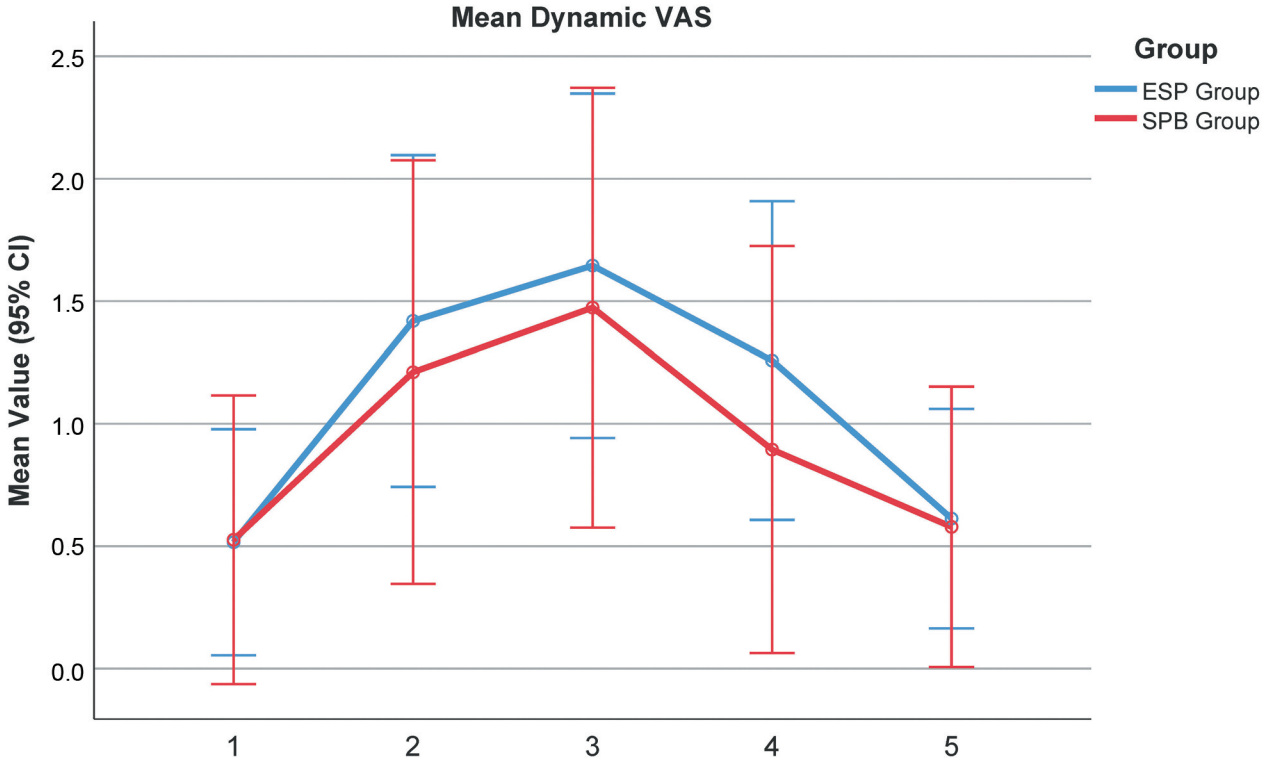

Figure 3. *Mean dynamic VAS in ESP vs. SPB Group. VAS: Visual analogue scale; 95% CI: 95% confidence interval; ESP: erector spine block; SPB: serratus plane block. 1: Baseline; 2: follow up at 2 h; 3: follow up at 6 h; 4: follow up at 12 h; 5: follow up at 24h.*

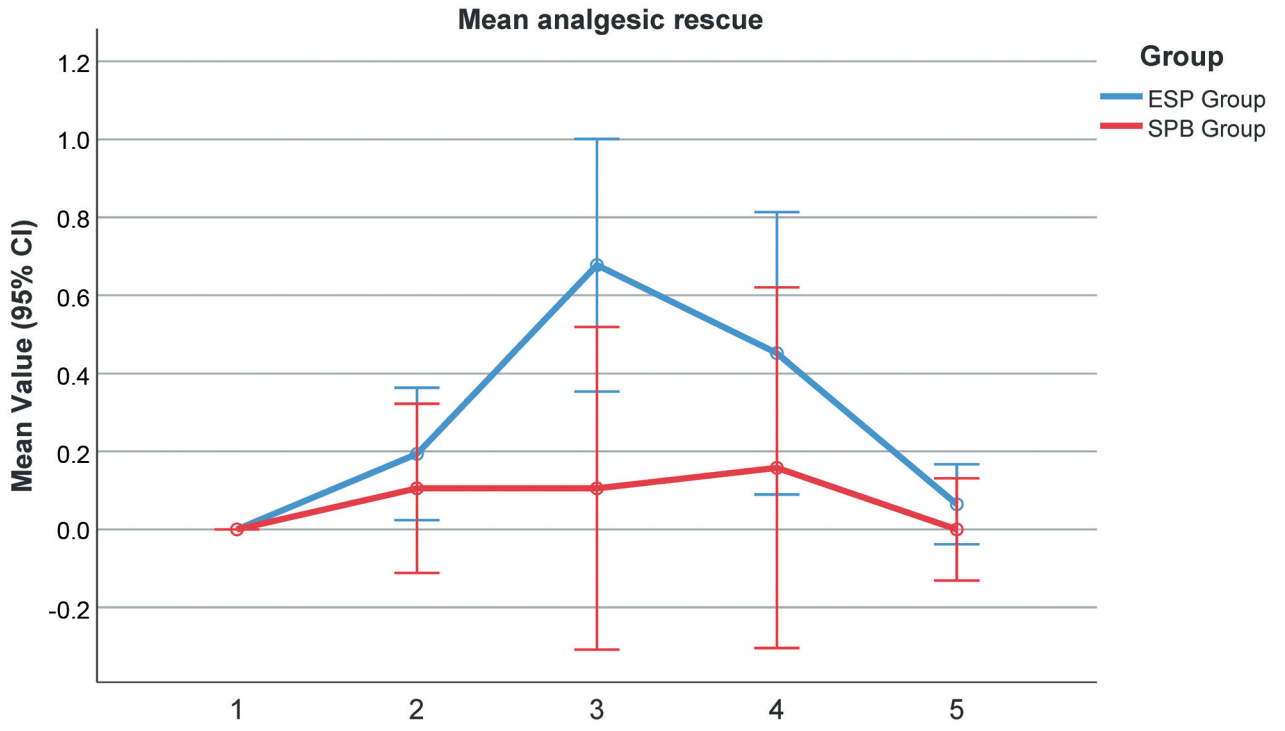

Figure 4. *Mean analgesic rescue in ESP vs. SPB Group. VAS: Visual analogue scale; 95% CI: 95% confidence interval; ESP: erector spine block; SPB: serratus plane block. 1: Baseline; 2: follow up at 2 h; 3: follow up at 6 h; 4: follow up at 12 h; 5: follow up at 24h.*

chronic thoracic pain (25). ESP Block anatomical and radiological studies demonstrate how LA spread along the plane, deep to the erector spinae muscles, within the intercostal spaces for ventral ramus involvement and within the intervertebral foramen for dorsal root ganglion involvement (33). According to this mechanism, when LA is administered at T5 transverse process, ESP Block could theoretically guarantee an adequate analgesic coverage during breast surgery with a single injection through direct action on the Brachial plexus and intercostal (T2-T9) nerves (33, 39). Over the past two years, several studies have been published describing ESP Block as an easy and safe technique with low complications rate and a good alternative when traditional techniques are contraindicated (27, 29, 41, 42).

Unfortunately, due to the retrospective design of these studies, evidence on ESP Block for acute and chronic pain following breast surgery is insufficient to provide high-grade recommendations (38). Kot *et al*., in a recent review, advocates the need of randomized prospective studies to evaluate the efficacy, feasibility and safety of ESP Block compared with other techniques in order to provide correct indications (41-43).

Our randomized prospective control study aimed to compare ESP Block with PECS I plus SPB blocks. Static and dynamic postoperative pain did not show any statistically significant differences between ESP group and SPB group during postoperative follow-up, nor a statistically significant difference was found regarding sufentanil administration during the surgical procedure. Despite higher PCA activation rates in ESP group, no opioid side-effects were reported in both groups and patients expressed a high degree of satisfaction.

Additionally, regarding feasibility and safety, ESP was a faster technique (ESP block mean time 9.51 *vs*. SPB+PECS I mean time 14.51 min), safe, without complications, easy to perform and without any failure. Moreover, ESP Block was better tolerated by patients, even when compared to PECS I plus SPB, due to the single injection. However, ESP block absolute contraindications are represented by infection at the site of injection in the paraspinal region or patient refusal, while anticoagulation may be a relative contraindication to ESP block (28).

Our research has some known limitations. First, the small sample size, could have affected the power of our study. However, we achieved two well-matched study groups and the sample size was calculated prior to recruitment to assure a statistically acceptable power in detecting intergroup differences. The second limitation of the current analysis is the sole quantitative assessment without information regarding quality of life (QoL), tolerance of patients and long-term effect such as CPSP. Nonetheless, our study was

designed specifically to compare the analgesic effects of ESP Block with PECS I plus PSB blocks while QoL, tolerance, and CPSP were not formally investigated. Regardless of the high satisfaction and optimal analgesic profile of both groups, further studies are required to assess these aspects.

Conclusion

In conclusion, although many other factors could have altered our results, the well-matched baseline data led us to postulate that ESP Block could be considered as an effective alternative when traditional regional anesthetic techniques or other US-guided blocks, such as PECS I or SPB, are contraindicated.

ESP Block advantages include all the pros of US-guided block with a lower dose of anesthetic and a single injection. Furthermore, owing to the injection site, ESP Block can be performed in a distinct site from the surgical field in cases of congenital or acquired thoracic abnormality (*e.g.*, locally advanced BC, recent surgery), contaminated surgical field, or when a fast, safe, and reliable technique is called for at the end of the surgery.

Conflicts of Interest

The Authors declare that they have no potential conflicts of interest.

Authors' Contributions

Conceptualization: Mario Dauri, Eleonora Fabbi, Giordana Caiazza; Methodology: Eleonora Fabbi, Generoso Storti; Formal analysis and investigation: Marco Materazzo, Chiara Buonomo, Writing - original draft preparation Marco Materazzo; Writing - review and editing: Giordana Caiazza, Gianluca Vanni, Marco Pellicciaro; Supervision: Mario Dauri.

Acknowledgements

The Authors acknowledge Jonathan Caspi for proofreading activity. The Authors sincerely acknowledge all the health care workers involved in the COVID-19 pandemic.

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Received September 11, 2021
Revised September 24, 2021
Accepted October 5, 2021