Randomized Controlled Trial

The Effect of Ultrasound-guided Bilateral Erector Spinae Plane Block With and Without Dexmedetomidine on Intraoperative and Postoperative Pain in Laparoscopic Cholecystectomies: A Randomized, Controlled, Double-blind, Prospective Trial

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Background: Laparoscopic cholecystectomy is the most common surgical procedure performed in the Western world. While it is performed with minimally invasive procedures, patients often complain of moderate to severe postoperative pain, and the role of the anesthesiologist for its effective management remains crucial. Modern anesthesiology practices have embraced trunk blocks which can contribute to perioperative, multimodal analgesia. There is emerging literature about the favorable effect of erector spinae plane block in the reduction of pain after laparoscopic cholecystectomy.

Objective: The aim of this study was to explore the efficacy of preoperative bilateral erector spinae plane block when dexmedetomidine is added in the local anesthetic mixture in patients undergoing elective laparoscopic cholecystectomy.

Study Design: This study is a double-blind, randomized, controlled, prospective study.

Setting: Georgios Papanikolaou General Hospital of Thessaloniki, Greece.

Methods: After Local Ethics Committee approval (No: 1146/7.10.2019, October 2019) and in accordance with the principles outlined in the Declaration of Helsinki, the study was submitted to clinicaltrials.gov with reference number: NCT04587973. Sixty patients were randomized into 3 equal groups. Erector spinae plane block was performed in Group C with normal saline (N/S) 0.9%, in Group DR with ropivacaine 0.375% and dexmedetomidine 1 mcg/kg, and in Group R with ropivacaine 0.375%. The perioperative opioid consumption, pain intensity, time of first mobilization, hospitalization days, and satisfaction score of patients were recorded. Statistical analysis was performed with ANOVA, Kruskal-Wallis and Spearman test, as appropriate.

Results: The perioperative opioid consumption was significantly lower in Groups R and DR as compared to Group C ($P < 0.001$). The median numerical rating scale (NRS) scores of patients at all time points were statistically different between Groups C and DR, as well as between groups C and R. Satisfaction score was significantly higher in Group DR as compared to Group C ($P < 0.001$), and mobilization time was significantly shorter in group DR in comparison to Group C as well as in Group R as compared to Group C ($P = 0.015$ and $P = 0.035$, respectively). Intraoperative remifentanil consumption was lower in Group DR in comparison to Group R ($P < 0.001$). There was no difference in postoperative nausea and vomiting and duration of hospital stay of patients.

Limitations: The limitation of the study is the small sample size of the patients recruited, which may be the reason why no statistically significant differences were found in postoperative morphine consumption and postoperative NRS scores between Groups R and DR and in postoperative nausea and vomiting among the 3 groups.

Conclusion: Erector spinae plane block performed either with ropivacaine or with a combination of ropivacaine and dexmedetomidine is a novel and safe method, which was found to be more effective compared to standard analgesia protocols in patients undergoing laparoscopic cholecystectomy and thus, it can improve the quality of perioperative analgesia.

Key words: Erector spinae plane block, dexmedetomidine, ropivacaine, preemptive analgesia, regional anesthesia, laparoscopic cholecystectomy, multimodal analgesia, adjuvants, general surgery

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Laparoscopic cholecystectomy is the most common surgical procedure performed by general surgeons (1). Although it is performed with minimally invasive techniques, postoperative pain can be moderate to severe, requiring the administration of large doses of opioids perioperatively and a multimodal analgesia approach in order to be relieved. Modern anesthesiology practices tend to limit the administration of opioids not only due to the variety of complications observed after their administration, especially in certain populations (obese, elderly patients) (2) but also due to the opioid crisis recorded in the United States and in many European countries (3). Multimodal analgesia and opioid limitation are cornerstones of modern perioperative pain management (4).

Trunk blocks can play a significant role when managing perioperative pain. Erector spinae plane block (ESPB) is a novel trunk block first described by Forero et al initially used to relieve thoracic neuropathic pain (5). Since then, it has been performed by anesthesiologists for chronic pain, acute post-traumatic pain, and in a wide variety of surgical procedures for postoperative analgesia (6,7). ESPB can also be performed as the sole method of anesthesia and analgesia in high-risk patients undergoing surgery (8).

Although there is emerging literature confirming the efficacy of the performance of ESPB on postoperative analgesia in patients undergoing elective laparoscopic cholecystectomy (9,10), there is no previous literature concerning the addition of dexmedetomidine in the local anesthetic mixture.

In this study, our goal was to assess the efficacy of bilateral ESPB in the management of intraoperative and postoperative pain of patients undergoing elective laparoscopic cholecystectomy, when it is performed preoperatively with plain ropivacaine or with a combination of ropivacaine and dexmedetomidine.

Methods

Study Design

This randomized, controlled, double-blinded, prospective study was performed in Georgios Papanikolaou General Hospital of Thessaloniki, Greece, after Local Ethics Committee approval (No: 1146/7.10.2019, October 2019) and in accordance with the principles outlined in the Declaration of Helsinki. Blindness to the treatment groups involved the patients, surgeons, anesthesiologists, and operating theater staff, as well as surgical ward nurses. Recruitment was performed from January 2020 until October 2020. All patients gave written informed consent for inclusion into this study. The study was submitted to clinicaltrials.gov with reference number: NCT04587973.

Inclusion and Exclusion Criteria

The study included 60 patients (men and women), aged between 18 and 70 years old, classified as American Society of Anesthesiologists (ASA) physical status classes I and II, who underwent elective laparoscopic cholecystectomy performed by the same experienced team of general surgeons.

Patients who refused to grant consent, who had coagulation disorders, known allergy to local anesthetics, or other contraindications for regional anesthesia, were excluded from the study. Patients with severe kidney or liver disease and patients with known psychiatric disorders or drug/alcohol abuse were also excluded from this study.

Study Groups

The study consisted of 3 equal groups:

- In Group C (control group), ultrasound-guided, bilateral ESPB was performed in the patients before the induction of general anesthesia with 40 mL of normal saline (N/S) 0.9 % (20 mL at each side).
- In Group R (ropivacaine Group), ultrasound-guided, bilateral ESPB was performed in the patients before the induction of general anesthesia with 40 mL of Ropivacaine 0.375% (20 mL at each side).
- In Group DR (dexmedetomidine + ropivacaine Group), ultrasound-guided, bilateral ESPB was performed in the patients before the induction of general anesthesia with 40 mL of ropivacaine 0.375

% plus dexmedetomidine 1 mcg/kg (20 mL at each side).

The sealed envelope method and computer-generated random numbers were used for allocation and randomization of the patients.

Anesthesia

Preoperatively, all patients were clinically examined by an anesthesiologist, and routine preoperative laboratory exams were performed.

Bilateral ESPB was performed in all patients in the sitting position, before the induction of general anesthesia, under ultrasound guidance with a linear transducer (7-13 MHz). An 80 mm, 22-gauge, short bevel needle was used. After skin disinfection, the transducer was placed in a transverse position on the spinous process of T7, and 3 cm laterally, the transverse process of T7 was identified. The transducer was then turned into a sagittal position, and the landmarks (trapezius muscle, rhomboid muscle, erector spinae muscle, and transverse process) were identified. The needle was inserted in a cephalad to caudad orientation, and an in-plane technique was used in order to identify its correct position. The needle was advanced slowly until its tip reached the fascia between the transverse process and the erector spinae muscle. After negative blood aspiration, 20 mL of the prepared solution was administered to each side (Fig. 1).

Intraoperative monitoring of the patient included oximetry, noninvasive arterial pressure, electrocardiography, and Bispectral Index (BIS) monitor readings. General anesthesia induction was performed with fentanyl 1 mcg/kg, propofol 2 mg/kg, and rocuronium 0.6 mg/kg after pre-oxygenation of the patient for 3 minutes. General anesthesia was maintained with desflurane titration according to BIS readings (target BIS 40-60). Intraoperatively, remifentanil was administered if mean arterial pressure and heart rate were more than 20% of the baseline values recorded prior to induction of general anesthesia. All the patients received paracetamol 1000 mg and tramadol 100 mg 20 minutes before completion of surgery. At the time of placement of the final sutures, a Train of Four (TOF) test was performed in order to assess the depth of neuromuscular blockade, and sugammadex was administered for neuromuscular blockade reversal if needed. Patients were discharged from Post Anesthesia Care Unit (PACU) after achieving a score of > 8 on Aldrete's recovery score. All patients received paracetamol 1000 mg every 6 hours in the surgery ward and were given a Patient Controlled Analgesia (PCA) pump for morphine administration (10

Fig. 1. *Performance of bilateral erector spinae plane block under U/S guidance.* Bilateral ESPB was performed on all patients in the sitting position, before the induction of general anesthesia, under ultrasound guidance with a linear transducer. An 80 mm, 22-gauge, short bevel needle was used. After skin disinfection, the transducer was placed in a transverse position on the spinous process of T7, and 3 cm laterally, the transverse process of T7 was identified. The transducer was then turned into a sagittal position, and the landmarks (trapezius muscle, rhomboid muscle, erector spinae muscle, and transverse process) were identified.

minutes lock-out interval, morphine dose 20 mcg/kg, without continuous infusion).

Laparoscopic cholecystectomies in this study were performed by the same experienced surgical team, and the ESPB was performed in each patient by the same experienced anesthesiologist.

Outcomes and Statistical Analysis

The primary endpoint of this study was to identify the difference in total postoperative morphine consumption among groups. Secondary outcomes included the difference in total intraoperative remifentanil consumption, time spent in PACU, NRS pain scores at arrival and at discharge from PACU and at 3, 6, 12, and 24 hours after surgery, postoperative nausea and vomiting, time until first mobilization of the patient, hospitalization days and satisfaction score of the patients (using a scale from 0 to 6) among groups. The correlation between the body mass index (BMI) of the patients and the ultrasound image quality during ESPB performance was also explored.

The sample size was performed using an electronic calculator (http://powerandsamplesize.com/Calculators/Compare-k-Means/1-Way-ANOVA-Pairwise-1-Sided). There were no data comparing the efficacy of ESPB with N/S 0.9%, ropivacaine 0.375% plus dexmedetomidine 1 mcg/kg, and with plain ropivacaine 0.375% in laparoscopic cholecystectomies. The sample size required to detect a statistically significant difference in total morphine consumption was calculated. Groups C and R were used to calculate the sample size, and considering a 20% patient dropout rate, it was estimated that a sample size of 33 patients (11 in each group) was required for the study to achieve a power of 0.8, significance level 0.05 (one-sided), groups of equal sizes and 3 comparisons per group. We ended up enrolling 60 patients (20 in each group).

The measured variables were checked for the normality of their distribution with the Shapiro-Wilk test. Normally distributed, continuous variables were presented with mean ± standard deviation (mean ± SD), while continuous variables with non-parametric distribution were presented with median and intraquartile range (median, IQR). Qualitative variables, categorical or ordinal, were presented as numbers and percentages. The level of statistical significance was set at $P < 0.05$. The statistical analysis of the results was performed using Jamovi Version 1.2.27.0.

Comparisons were performed among Group C, Group DR, and Group R. ANOVA with Bonferoni correction was performed for independent variables in multiple groups with normal distribution, whereas non-parametric variables were checked with Kruskal-Wallis and the Dwass-Steel-Critchlow-Fligner correction. Two-way ANOVA for repeated measures was utilized to analyze the time-varying data (mean blood pressure, heart rate, SpO_2). The nonparametric Spearman correlation coefficient was used to investigate the possible correlation between the variables BMI (continuous variable) and the image quality of the ultrasound image (ordinal variable).

Results

A total of 68 patients were assessed for appropriateness, and 60 of them were enrolled and completed the study. Four patients refused inclusion in the study, and 4 patients did not meet the inclusion criteria. The inclusion and exclusion of patients in the study are represented in the CONSORT Flow Diagram (Fig. 2).

Patient characteristics were similar among the 3 groups (Table 1).

All patients remained hemodynamically stable throughout their hospitalization, and no complications were recorded.

Regarding the primary endpoint of our study, postoperative morphine consumption (mg), we found an overall statistically significant difference in total postoperative morphine consumption between Groups C and R ($P < 0.001$), between Groups C and DR ($P < 0.001$), but not between Groups R and DR ($P = 0.381$). More specifically, in the first 3 and 6 hours after surgery, morphine consumption was significantly lower in Groups R ($P_3 = 0.006$, $P_6 = 0.002$) and DR ($P_3 < 0.001$, $P_6 < 0.001$) as compared to Group C. However, morphine consumption 12 and 24 hours after surgery remained significantly lower only in Group DR as compared to Group C ($P_{12} = 0.005$ and $P_{24} = 0.008$, respectively); whereas in Group R, no statistical difference was found as compared to Group C ($P_{12} = 0.053$ and $P_{24} = 0.08$ respectively) (Table 2).

The quality of ultrasound image during the performance of ESPB was negatively correlated with the BMI of the patients ($P = 0.001$, spearman rho= - 0.411), and it is represented in Fig. 3.

Total intraoperative remifentanil consumption (mcg) was found to be statistically different among the 3 groups ($P < 0.001$). We found an overall statistically significant difference in total intraoperative remifentanil consumption between Groups C and R ($P < 0.001$), between Groups C and DR ($P < 0.001$), as well as between Groups R and DR ($P < 0.001$). More specifically,

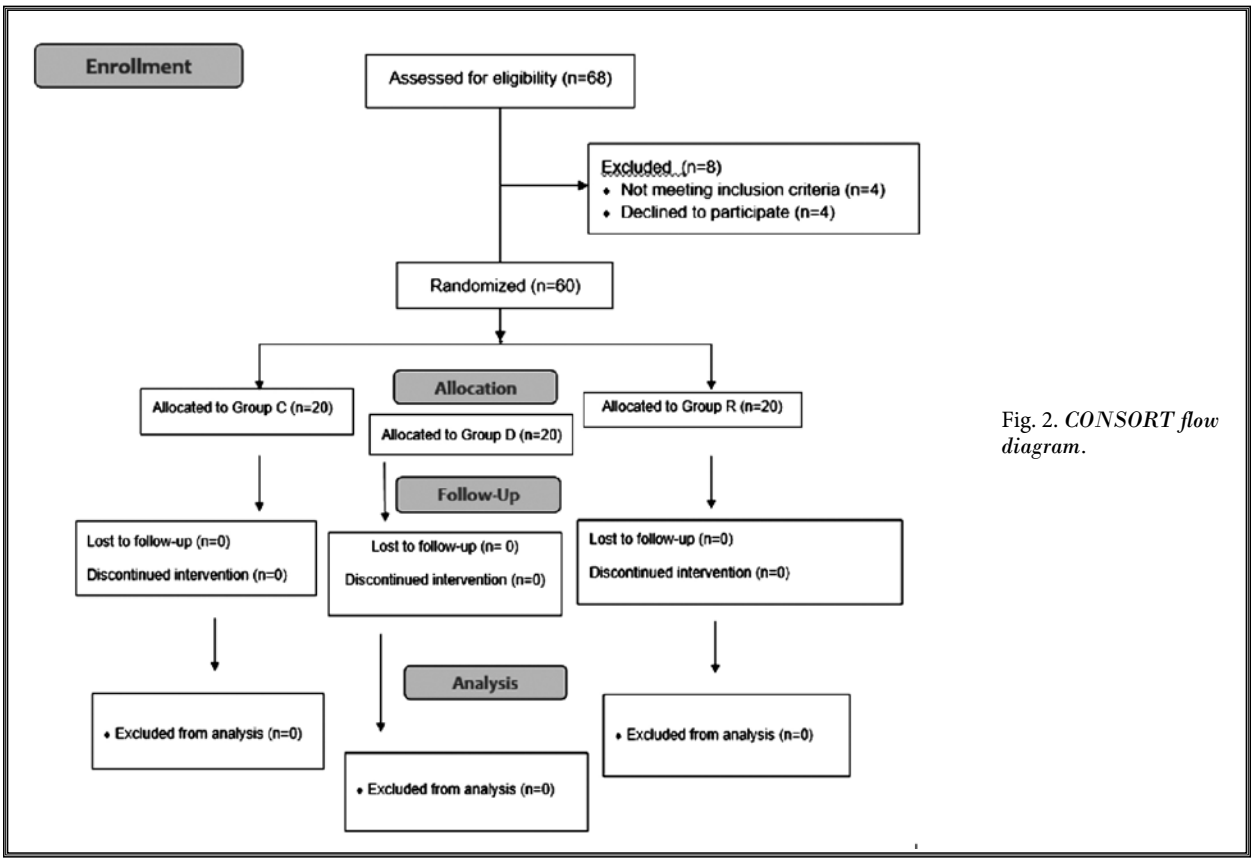

Fig. 2. *CONSORT flow diagram.*

the median total intraoperative remifentanil consumption in Group C was 374.5 mcg, in Group R 100 mcg, and in Group DR 0 mcg (Table 3).

The median time until extubation (time from the end of surgical procedure until the extubation of the patient) was found to be significantly lower in Group R ($P < 0.001$) and DR ($P = 0.016$) as compared to Group C, however, we found no statistically significant difference regarding this variable between Groups R and DR ($P = 0.772$) (Table 1).

Median time spent in PACU was found to be significantly lower in Group DR as compared to Group C ($P = 0.024$) (Table 4). NRS pain scores of the patients at the arrival and at the discharge of the patient from PACU and at 3, 6, 12, and 24 hours after completion of surgery were found to be significantly lower in Group R as compared to Group C ($P_{arrival} < 0.001$, $P_{discharge} = 0.002$, $P_3 = 0.002$, $P_6 = 0.017$, $P_{12} = 0.023$, $P_{24} = 0.01$), significantly lower in Group DR as compared to Group C ($P_{arrival} < 0.001$, $P_{discharge} < 0.001$, $P_3 < 0.001$, $P_6 = 0.002$, $P_{12} = 0.002$, $P_{24} < 0.001$), but there was no significant difference between Groups R and DR ($P_{arrival} = 0.920$, $P_{discharge} = 0.568$, $P_3 = 0.175$, $P_6 = 0.394$, $P_{12} = 0.08$, $P_{24} = 0.536$) (Table 5).

Table 1. *Patients' descriptive characteristics and operation times.*

Variables		Group C (n_1=20)	Group DR (n_2=20)	Group R (n_3=20)	*P* value
Gender (n%)	Women	15/20 (75%)	11/20 (55%)	11/20 (55%)	0.330
	Men	5/20 (25%)	9/20 (45%)	9/20 (45%)	
Age (y), m ± SD		49.1 ± 13.4	50.8 ± 14.1	54.0 ± 11.6	0.466
BMI (kg/m^2), m ± SD		27.5 ± 4.2	28.2 ± 4.72	30.8 ± 6.74	0.212
ASA (n%)	I	3/20 (15%)	2/20 (10%)	1/20 (5%)	0.579
	II	17/20 (85%)	18/20 (90%)	19/20 (95%)	
Surgical time (min), median (IQR)		55.5 (28.25)	53.5 (28.75)	71 (27.75)	0.056
Duration of Anesthesia (min), median (IQR)		87.5 (23.5)	72.5 (25.25)	91.5 (34)	0.399
Extubation time (min), median (IQR)		9 (9.25)	3 (5.25)	2 (3.25)	< 0.001

BMI = Body Mass Index, ASA = American Society of Anesthesiologists Physical Status Classification

Table 2. *Postoperative morphine consumption and patients' satisfaction.*

Morphine Consumption	**Group C (n_1=20)**	**Group DR (n_2=20)**	**Group R (n_3=20)**	***P* value**
3 hours postoperatively (mg), median (IQR)	4 (4.5)	0 (1.25)	0.5 (3)	< 0.001
6 hours postoperatively (mg), median (IQR)	3 (1)	0 (1)	0 (2)	< 0.001
12 hours postoperatively (mg), median (IQR)	2.5 (4.25)	0 (1)	0 (2)	0.004
24 hours postoperatively (mg), median (IQR)	2 (5.25)	0 (0)	0 (1.25)	0.005
Total Morphine Consumption (mg), median (IQR)	13.5 (12.25)	0.5 (5)	4 (6)	< 0.001
Patients' Satisfaction Score, median (IQR)	5 (1)	6 (1)	5 (1)	< 0.001
Morphine Consumption / Groups	**C vs. R (*P* value)**	**C vs. DR (*P* value)**	**DR vs. R (*P* value)**	
3 hours postoperatively, mg	0.006	< 0.001	0.302	
6 hours postoperatively, mg	0.002	< 0.001	0.947	
12 hours postoperatively, mg	0.053	0.005	0.730	
24 hours postoperatively, mg	0.080	0.008	0.293	
Total Morphine Consumption, mg	< 0.001	< 0.001	0.381	
Patients' Satisfaction Score	0.099	< 0.001	0.095	

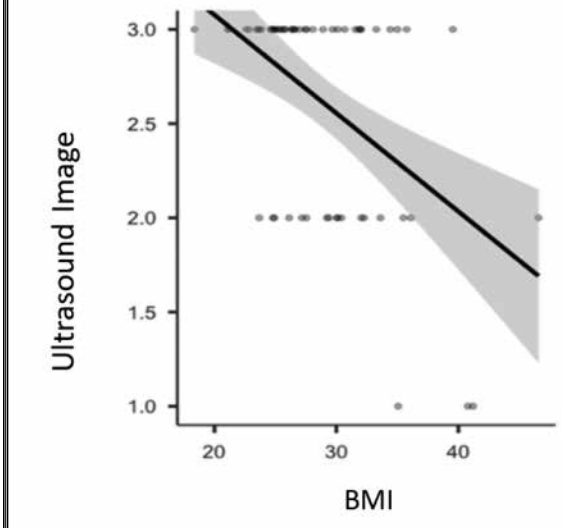

Fig. 3. *Correlation of the quality of ultrasound image and BMI of the patients.*
The quality of ultrasound image during the performance of ESPB was correlated with the BMI of the patients (P = 0.001, spearman rho = -0.411).

No statistically significant difference was recorded regarding postoperative nausea and vomiting of patients 3, 6, 12, and 24 hours after completion of surgery among the 3 groups (P_3 = 0.567, P_6 = 0.837, P_{12} = 0.117, P_{24} = 0.349) (Table 6).

Regarding the time of first mobilization of the patients after completion of surgery, there was a statistically significant difference between Groups C and R (P = 0.035) and Groups C and DR (P = 0.015) but not between Groups R and DR (P = 0.891) (Table 7).

Patients' satisfaction score regarding their postoperative analgesia was found to be significantly higher in Group DR as compared to Group C (P < 0.001), but there was no significant difference between Groups C and R and Groups DR and R (P = 0.099 and 0.095, respectively) (Table 2).

All patients were discharged from the hospital 24 hours after completion of surgery.

Discussion

According to the results of this randomized trial, ultrasound-guided bilateral ESPB with or without the addition of dexmedetomidine significantly improved acute postoperative pain management in comparison to control in patients undergoing elective laparoscopic cholecystectomy. More specifically, in Groups R and DR, total postoperative morphine consumption, total intraoperative remifentanil consumption, time until extubation, postoperative pain scores at several time points after surgery, and time of first mobilization after surgery were found to be significantly lower as compared to Group C. Moreover, the satisfaction score of the patients regarding their postoperative analgesia was found to be higher in patients of Group DR as compared to patients of Group C.

Postoperative pain is one of the most important factors affecting patients' quality of recovery. It can delay patients' mobilization after surgery, increase their hospital stay and the cost of their hospitalization, while it can untowardly affect patients' satisfaction after surgery. Providing adequate intraoperative

Table 3. *Intraoperative remifentanil consumption.*

Variables	**Group C (n_1=20)**	**Group DR (n_2=20)**	**Group R (n_3=20)**	***P* value**
Total Remifentanil Consumption (mcg), median (IQR)	374.5 (387.75)	0 (0)	100 (55)	< 0.001
Variables/Groups	**C vs. R (*P* value)**	**C vs. DR (*P* value)**	**DR vs. R (*P* value)**	
Total Remifentanil Consumption, mcg	< 0.001	< 0.001	< 0.001	

Table 4. *Time spent at PACU.*

Variables	**Group C (n_1 = 20)**	**Group DR (n_2 = 20)**	**Group R (n_3 = 20)**	***P* value**
PACU time (min), median (IQR)	17.5 (7.5)	12.5 (5)	15 (6.25)	0.023
Variables/Groups	**C vs. R (*P* value)**	**C vs. DR (*P* value)**	**DR vs. R (*P* value)**	
PACU time, min	0.268	0.024	0.340	

Table 5. *Postoperative pain.*

Variables	**Group C (n^1=20)**	**Group DR (n_2=20)**	**Group R (n_3=20)**	***P* value**
NRS PACU arrival, median (IQR)	2.5 (3)	0 (0)	0 (0)	< 0.001
NRS PACU discharge, median (IQR)	2 (1)	0 (1.25)	0.5 (2)	< 0.001
NRS 3 hours postoperatively, median (IQR)	5 (4)	1 (1.25)	2 (1)	< 0.001
NRS 6 hours postoperatively, median (IQR)	4 (3)	1 (1)	2 (1.25)	0.001
NRS 12 hours postoperatively, median (IQR)	4 (3)	1 (1.25)	2 (2)	< 0.001
NRS 24 hours postoperatively, median (IQR)	3 (3)	1 (1)	1 (2)	< 0.001
Variables/Groups	**C vs. R (*P* value)**	**C vs. DR (*P* value)**	**DR vs. R (*P* value)**	
NRS PACU arrival	< 0.001	< 0.001	0.920	
NRS PACU discharge	0.002	< 0.001	0.568	
NRS 3 hours postoperatively	0.002	< 0.001	0.175	
NRS 6 hours postoperatively	0.017	0.002	0.394	
NRS 12 hours postoperatively	0.023	0.002	0.080	
NRS 24 hours postoperatively	0.010	< 0.001	0.536	

NRS = Numerical Rating Scale; PACU = Post Anesthesia Care Unit

Table 6. *Postoperative nausea and vomiting.*

Variables		**Group C (n_1=20)**	**Group DR (n_2=20)**	**Group R (n_3=20)**	***P* value**
PONV 3 (n%)	YES	2/20 (10%)	2/20 (10%)	4/20 (20%)	0.567
PONV 6 (n%)	YES	3/20 (15%)	2/20 (10%)	3/20 (15%)	0.837
PONV 12 (n%)	YES	2/20 (10%)	0/20 (0%)	4/20 (20%)	0.117
PONV 24 (n%)	YES	2/20 (10%)	0/20 (0%)	1/20 (5%)	0.349

PONV 3, 6, 12, 24 = Postoperative nausea and vomiting 3, 6, 12, and 24 hours after completion of surgery, respectively

Table 7. Mobilization time.

Variables	**Group C (n_1=20)**	**Group DR (n_2=20)**	**Group R (n_3=20)**	***P* value**
Mobilization Time (h), median (IQR)	8 (6)	6 (2)	6 (2)	0.009
Variables/ Groups	**C vs. R (*P* value)**	**C vs. DR (*P* value)**	**DR vs. R (*P* value)**	
Mobilization Time, h	0.035	0.015	0.891	

and postoperative analgesia to patients is one of the cornerstones of modern anesthesia practice, and it can be accomplished by combining different categories of analgesics and adjuvants as well as performing regional anesthetic techniques.

Pain after laparoscopic cholecystectomy is multifactorial and can be visceral, somatic, or referred (e.g., pain identified at the right shoulder of the patient when the peritoneum is irritated by CO_2 insufflation in laparoscopic techniques) (11).

ESPB is a novel analgesic technique, and its mechanism of action remains to be clarified. According to literature, when performing ESPB, the local anesthetic

is diffused through fascias and acts on the ventral and dorsal rami of spinal nerves. Local anesthetic is believed to diffuse also in intercostal, paravertebral, and epidural spaces. Consequently, ESPB can provide a combination of somatic and visceral analgesia (12). It can be performed safely and simply with ultrasound guidance or with a landmark-guided technique at different transverse processes, depending on the surgical procedure (13,14). The volume of local anesthetic injected varies from 15 to 30 mL, and different local anesthetics have been used. The ideal concentration of local anesthetic and the efficacy of adding adjuvants to the solution have not been specified yet. As far as the complications of the block are concerned, local anesthetic systemic toxicity (LAST) has been reported, as well as muscle weakness and pneumothorax (15).

In our study, we performed ultrasound-guided bilateral ESPB at T7 level, preoperatively, in all patients, using 40 mL of N/S 0.9% (Group C), ropivacaine 0.375% (Group R), or a combination of ropivacaine 0.375% and dexmedetomidine 1 mcg/kg (Group DR). When performing ESPB before the induction of general anesthesia, the anesthesiologist can assess the successfulness of the block or complications arising from block performance. Moreover, when ESPB is performed preoperatively, it can contribute to the minimization of not only postoperative but also intraoperative opioid administration. The majority of the studies in current literature explore the efficacy of preoperative, bilateral ESPB in laparoscopic cholecystectomies before or after the induction of general anesthesia (16-21). Additionally, there is only one study that explores the efficacy of bilateral versus unilateral ESPB for postoperative analgesia in patients undergoing elective laparoscopic cholecystectomy (22).

In the majority of the studies in current literature, ESPB is performed with the administration of bupivacaine. Limited studies used ropivacaine as the local anesthetic (20,23). There is only one study in the literature that explores the efficacy of the combination of local anesthetic and an adjuvant (dexamethasone) when ESPB is performed (24). In our study, we preferred to use ropivacaine, as it has less cardiotoxic effects when compared to bupivacaine (25), and to add dexmedetomidine in the local anesthetic mixture to Group DR, which, as an adjuvant, has been shown to ameliorate the quality of peripheral blocks and to prolong their analgesic duration (26). This is the first study that explores the efficacy of the addition of dexmedetomidine to the local anesthetic mixture when performing ESPB in patients undergoing elective laparoscopic cholecystectomy.

Regarding ESPB, it is stated that every dermatome needs an average of 3.4 mL of local anesthetic in order to be efficiently blocked (15). In accordance with the majority of the studies that already exist in current literature, in our study the ESPB was performed at T7 level with the administration of 20 mL of local anesthetic mixture on each side (16,18-19,23,27,28).

Regarding the novelty of this study which lies in the addition of dexmedetomidine to the local anesthetic mixture, we found that during the first 6 hours after surgery, morphine consumption was significantly lower in both Groups R and DR as compared to Group C. However, morphine consumption 12 and 24 hours after surgery remained significantly lower as compared to the control group only when dexmedetomidine was added to the local anesthetic mixture, whereas when plain ropivacaine was administered, no statistical difference was found as compared to Group C. This finding can be justified, as the duration of action of plain ropivacaine when administered for regional anesthesia techniques is 10 hours (30). When an adjuvant such as dexmedetomidine is added, the analgesic duration of the regional anesthetic technique is significantly prolonged.

The NRS scores of the patients at the arrival and at the discharge from the PACU and at 3, 6, 12, and 24 hours after surgery were significantly lower in patients of Group R and DR when compared with Group C. The results of this study are in accordance with the clinical trials that already exist in the literature, which prove that when ESPB is added to the multimodal analgesia approach of patients undergoing laparoscopic cholecystectomy, the consumption of postoperative opioids is reduced (16,18,23,28,29). We did not find a statistically significant difference in postoperative morphine consumption and NRS scores postoperatively between Groups R and DR, which may be due to the small sample of our study.

In our study, ESPB was also found to contribute to the reduction of intraoperative opioid administration. More specifically, in Group DR, the median total intraoperative remifentanil administration was 0 mcg, whereas in Group R, it was also significantly lower compared to Group C. This finding is in accordance with current literature that explores the contribution of ESPB to the reduction of intraoperative opioid consumption (16,18-20,23). Of note, dexmedetomidine appears to offer an additional benefit in intraoperative opioid consumption since there was a significant difference between Groups

R and DR as to this specific outcome.

Postoperative nausea and vomiting are inextricably linked to perioperative opioid administration. However, in our study, we found no statistically significant difference regarding this variable among the 3 groups, probably due to the overall moderate postoperative opioid consumption.

Time spent in PACU was found to be shorter in patients of Group DR when compared to Group C. Moreover, the satisfaction score of the patients regarding their postoperative analgesia was significantly higher in patients of Group DR compared to the patients of Group C. These facts further highlight additional benefits of the action of dexmedetomidine as an adjunct in the local anesthetic mixture. There is only one clinical trial in the current literature which investigates and confirms that the quality of recovery of patients after laparoscopic cholecystectomy is improved when ESPB is performed (31).

In our study, ESPB was successfully performed in all patients, and the anatomical structures were depicted efficiently with the ultrasound in the majority of patients. However, there was a negative correlation between the BMI of the patients and the ultrasound image quality. More specifically, in patients with higher BMI, there was a lower quality of the ultrasound image during the performance of the block. No complications associated with the performance of the block were recorded.

The limitation of our study is the small sample size of the patients recruited. The sample size was calculated in order to find a statistically significant difference in total postoperative morphine consumption, using Groups C and R for the calculation of the sample size. Maybe this is the reason why we did not find statistically significant differences in postoperative morphine consumption and postoperative NRS scores between Groups R and DR and in postoperative nausea and vomiting among the 3 groups.

Regarding the strong points of our study, all laparoscopic cholecystectomies in this study were performed by the same experienced surgical team, and the ESPB was performed in each patient by the same experienced anesthesiologist. Moreover, blindness to the treatment groups involved the patients, surgeons, anesthesiologists, and operating theater staff, as well as surgical ward nurses. We performed ESPB preoperatively in order to investigate its efficacy in the management of perioperative pain in patients undergoing elective laparoscopic cholecystectomy. Lastly, to the best of our knowledge, the addition of dexmedetomidine to the local anesthetic mixture has not been investigated in this context, which prompted us to undertake the current study. According to the results of our study, it appears that the addition of dexmedetomidine has a definitive advantage in the intraoperative opioid requirement and also seems to decrease the duration of stay in the PACU and to improve postoperative satisfaction scores in comparison to placebo to a greater extent than when ropivacaine is administered alone.

Conclusions

Performing EPSB in patients scheduled for laparoscopic cholecystectomy is a novel, safe and simple method that can contribute to the reduction of perioperative opioid administration, enhance patients' recovery and satisfaction scores, lower the total cost of hospitalization, improve perioperative analgesia, and thus achieve pre-emptive and multimodal analgesia.

The results of this study and the literature that exists concerning the performance of EPSB in patients undergoing elective laparoscopic cholecystectomy are encouraging. Certainly, these results should be further validated with more randomized controlled trials exploring various local anesthetic mixtures and adjuvants that could further enhance the quality of the block.

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