

## ORIGINAL RESEARCH

## REGIONAL ANESTHESIA

# Efficacy of dexmedetomidine as an adjuvant in erector spinae plane block in breast cancer surgery: a randomized controlled trial

Mohamed E. Hassan, MD, Ahmed S. Abdelgalil, MD

**Authors affiliations:**

1. Mohamed E. Hassan, MD, Department of Anesthesia and Pain Relief, National Cancer Institute, Cairo University, Egypt. E-mail: [msh.hamada76@gmail.com](mailto:msh.hamada76@gmail.com)
2. Ahmed S. Abdelgalil, MD, Department of Anesthesia and Pain Relief, National Cancer Institute, Cairo University, Egypt. E-mail: [ahmed.salah@nci.cu.edu.eg](mailto:ahmed.salah@nci.cu.edu.eg)

**Correspondence:** Mohamed Elsayed Hassan, E-mail: [msh.hamada76@gmail.com](mailto:msh.hamada76@gmail.com); Tel.: +20233360906

## Abstract

**Background:** The erector spinae plane block (ESPB) is a new potential inter-fascial block technique used to decrease pain after breast surgery. Dexmedetomidine (Dex) is used as an adjuvant to local anesthetics and is thought to improve the analgesic profile and duration of different anesthetic techniques. We evaluated the effect of adding Dex in local anesthetic solution for ESPB in breast cancer surgeries regarding the analgesic effect and duration.

**Methodology:** This prospective randomized controlled study included 60 female patients scheduled for breast cancer surgery. All patients were anesthetized in a standard manner, and then were randomized into three equal groups; 1. ESPB group, to receive an ultrasound-guided ESPB with 20 ml bupivacaine 0.5%; 2. Dex group, to receive ESPB with 19 ml bupivacaine 0.5% and 1 ml of normal saline containing 1 µg/kg Dex, and the control group received the standard general anesthesia only. The intraoperative fentanyl and postoperative morphine consumption were noted. Postoperative pain was assessed on numerical pain rating scale (NRS)

**Results:** The duration of analgesia was significantly prolonged in ESPB and Dex groups than in the control group and in the Dex group than in ESPB group ( $P < 0.001$ ). Intraoperative fentanyl and postoperative morphine consumption were significantly lower in ESPB and Dex groups than in the control group. NRS pain scores were comparable in the three groups during the first 24 h.

**Conclusions:** Adding dexmedetomidine 1 µg/kg to bupivacaine 0.5% prolongs the duration of analgesia of the ESPB in breast cancer surgeries.

**Key words:** Analgesia; Breast Cancer; Breast Surgery; Bupivacaine; Dexmedetomidine; Nerve Block

**Citation:** Hassan ME, Abdelgalil AS. Efficacy of dexmedetomidine as an adjuvant in erector spinae plane block in breast cancer surgery: a randomized controlled trial. *Anaesth. pain intensive care* 2022;27(1):16–22; DOI: [10.35975/apic.v27i1.2109](https://doi.org/10.35975/apic.v27i1.2109)

**Received** August 16, 2022; **Reviewed:** November 13, 2022; **Accepted:** December 03, 2022

## 1. Introduction

Breast cancer is the most common female cancer in many parts of the world, accounting for approximately 24.5% of cases.<sup>1</sup> Nearly 60% of women experience severe acute pain after breast cancer surgery.<sup>2</sup> Poorly controlled postoperative pain may lead to chest infection, increased risk of myocardial infarction, and the development of chronic postoperative pain.<sup>3</sup> Several analgesic modalities are used for pain management, but

opioids are usually considered the gold-standard analgesics.<sup>4</sup> However, opioid use is associated with many adverse effects, including respiratory depression, nausea and vomiting, urine retention, and pruritis.<sup>5</sup>

A multimodal analgesic approach has been recommended to enhance pain relief and reduce opioid consumption. Regional anesthetic techniques with the administration of local anesthetics are common components of multimodal analgesia.<sup>6</sup> One of these techniques is the erector spinae plane block (ESPB),

which has been shown to decrease pain after breast surgery.<sup>7</sup> It is an inter-fascial plane block, where the local anesthetic is injected deep to the erector spinae muscle to block ventral and dorsal principal rami and sympathetic fibers.<sup>8</sup> However, the duration of sensory block after one-shot ESPB is relatively short (about 10 h).<sup>8</sup> Adding an adjuvant to the local anesthetic may prolong its analgesic duration. Dexmedetomidine (Dex) can serve as such an adjuvant.

Dex is a highly selective  $\alpha_2$ -adrenergic receptor agonist with sedative, analgesic, anxiolytic, and sympatholytic properties.<sup>9</sup> Perioperatively, it has been used as a part of the multimodal anesthetic regimen. Dex was shown as a beneficial adjuvant to local anesthetics via epidural, caudal, and paravertebral nerve blocks.<sup>10-12</sup>

We designed this study to assess the assumption that dexmedetomidine can prolong and enhance the analgesic effect of ESPB in breast cancer surgeries.

## 2. Methodology

This prospective randomized controlled open-label study was conducted at National Cancer Institute, Cairo University, from July 2021 to October 2021. It involved 60 female patients aged 18 to 70 y, ASA physical status II, scheduled for breast cancer surgery. All patients provided informed written consent to participate. The study was approved by the institutional Ethical Committee and registered at clinicaltrials.gov (ID: NCT04920669).

Patients with a body mass index more than 35 kg/m<sup>2</sup>, a local infection at the block site, allergy to the study drugs, any coagulation problem, pre-existing neurological diseases, chronic opiate usage, and cardiac dysfunction (ejection fraction less than 45%) were excluded. Pregnant women and those who could not utilize the patient-controlled analgesia (PCA) device were also excluded.

The sample size calculation was performed using G. power 3.1.9.2. The sample size was calculated based on the following considerations: 0.05  $\alpha$  error and 95% power of the study. The mean duration of analgesia without dexmedetomidine was 500.5  $\pm$  548.0 min. and with Dex was 1864.7  $\pm$  1192.1 min. in a previous study.<sup>13</sup> Six cases were added to each group to overcome dropouts and accommodate for secondary outcome measures. Therefore, 20 patients were recruited for each group.

A statistician unrelated to the patient treatment utilized a computer-generated program to randomly allocate the patients into three equal groups using the permuted block technique. The ESPB group received an ultrasound-guided ESPB with 20 ml bupivacaine 0.5%. The Dex group received an ultrasound-guided ESPB with 19 ml

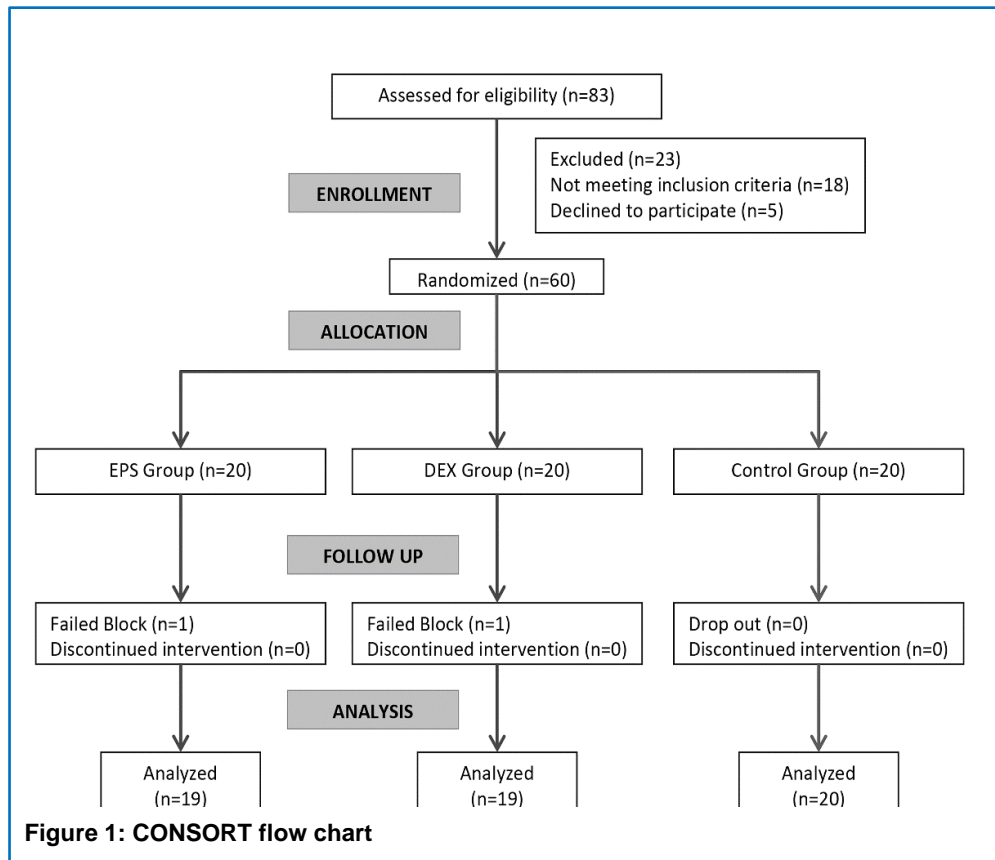
bupivacaine 0.5% plus 1 ml of normal saline containing 1  $\mu$ g/kg Dex. The control group did not receive a regional block before the standard general anesthesia. The random allocation numbers were kept in opaque sealed envelopes, unsealed only at the preoperative assessment visit.

All patients had guidance regarding the use of the PCA device and reporting pain severity on an 11-point numerical rating scale (NRS), where 0 = no pain and 10 = worst imaginable pain. A preoperative assessment was completed to confirm fitness for general anesthesia.

An IV line was set for all patients on arrival to the operating room and routine monitoring (electrocardiography, pulse oximetry, and non-invasive blood pressure measurements) started. The patient was sedated with midazolam 0.04 mg/kg. A linear multi-frequency 13-16 MHz probe (Fujifilm Sonosite™, inc Bothell, WA 98021, USA) was utilized to conduct ESPB on participants assigned to the ESPB and Dex groups preoperatively by the same anesthesiologist.

With the patient in the sitting position, the ESPB was performed under sterile conditions. The spinous process of the T5 vertebra was identified. Then, at the place of needle entry, 3 cm lateral to the 5th thoracic spinous process, 5 ml of 2% lidocaine was injected subcutaneously. The three muscles (trapezius, rhomboid major, and erector spinae) were detected by the ultrasound probe in the sagittal paramedian plane lying over the transverse process from superficial to deep. An 18-gauge Tuohy needle (Portex®, Smiths Group, London, UK) was inserted in-plane until its tip was seen deep to the erector spinae muscle and superficial to the 5th thoracic transverse process. On visualizing the separation of the erector spinae muscle from the transverse process, two ml of saline was injected to check the precise placement of the needle point. Following negative aspiration, the drug was injected according to group allocation to be distributed cranially and caudally. A pinprick test was done to determine the block success by a blind observer uninvolved in data collection. After 30 min, pain on pinprick in T1-T8 dermatomes on the blocked side indicated a failed block, and the patient was excluded from the trial.

After preoxygenation with 100% oxygen, fentanyl 1  $\mu$ g/kg and propofol 2 mg/kg were used to induce general anesthesia for all patients. Rocuronium 0.6 mg/kg was used to facilitate tracheal intubation. Sevoflurane and oxygen with 2.5% were used to maintain anesthesia. Additional doses of rocuronium 0.1 mg/kg were given to maintain muscle relaxation as determined by a peripheral nerve stimulator. The end-tidal CO<sub>2</sub> was kept between 30 and 35 mmHg by adjusting the mechanical ventilation settings. Fentanyl 0.5  $\mu$ g/kg was provided as a supplement to prevent mean arterial blood pressure and



heart rate from rising > 20% above baseline. At the end of the surgery, 4 mg ondansetron was given. The neuromuscular block was reversed with neostigmine 0.05 mg/kg and atropine 0.02 mg/kg. Extubation was performed following full consciousness recovery. After transferring the patients to the post-anesthesia care unit (PACU), NRS was assessed.

The primary outcome was the duration of analgesia, defined as the interval between recovery from general anesthesia and the time of the first request of rescue analgesia (when NRS was  $\geq 4$ ). On requesting analgesia, the patient received morphine 3 mg. The IV route was connected to a PCA device (B. Braun Melsungen AG, Germany) containing a morphine solution (1 mg/ml) set to deliver a demand dose of 1 mg morphine, with a lockout interval of 10 min without a continuous background infusion. The main secondary outcome was the total amount of PCA morphine used in the first 24 h after surgery. Other outcomes were the total intraoperative fentanyl consumption and pain intensity at rest and with shoulder movement measured by NRS after 30 min and at 2, 4, 8, 12, and 24 h postoperatively. Opioid side effects such as PONV, pruritis, and respiratory depression were recorded and managed accordingly.

### Statistical analysis

Statistical analysis was performed by SPSS version 25 (IBM Inc., Chicago, IL, USA). Shapiro-Wilks test was used to test the distribution of quantitative variables. Normally distributed variables were expressed as mean and standard deviation (SD) and compared using ANOVA, followed by the post hoc (Tukey) test. Non-normally distributed variables were expressed as median and range and were analyzed using Kruskal-Wallis test followed by the proper post hoc test.

Categorical variables were expressed as

frequency and percentage and analyzed by the Chi-square test or Fisher's exact test. A two-tailed  $P < 0.05$  was considered statistically significant.

## 3. Results

In this study, 83 patients were assessed for eligibility. After screening, 18 patients did not meet inclusion criteria, and five refused participation. Sixty patients were allocated into three equal groups. Failed blocks occurred in one patient of the ESPB group and the Dex group and were excluded (Figure 1). All groups were comparable regarding the baseline characteristics, as shown in Table 1.

Table 2 shows that patients in the Dex group had the more prolonged analgesia compared to the ESPB and the control groups ( $P < 0.001$  for both). Also, the ESPB group showed a significantly longer analgesia duration than the control group ( $P < 0.001$ ). The postoperative morphine consumption in the control group was significantly higher than Dex group ( $P = 0.001$ ), but not the ESPB group ( $P = 0.374$ ). The ESPB and Dex groups

**Table 1: Baseline characteristics of the three studied groups**

Variable	ESP group (n = 19)	DEX group (n = 19)	Control group (n = 20)	P value
Age (y)	49.5 ± 11.9	45.4 ± 12.7	48.0 ± 12.8	0.596
Weight (kg)	81.3 ± 11.2	78.2 ± 10.4	77.9 ± 10.9	0.555
Height (cm)	159 ± 5	161 ± 6	159 ± 5	0.346
BMI (kg/m <sup>2</sup> )	32.0 ± 4.0	30.1 ± 4.4	30.7 ± 4.1	0.382
Duration of surgery (min)	96.8 ± 19.5	98.4 ± 17.1	102.5 ± 21.2	0.643
<b>Types of surgery</b>				
Segmentectomy	5 (26.3)	4 (21.1)	8 (40.0)	0.557
Lobectomy	4 (21.1)	6 (31.6)	6 (30.0)	
Mastectomy	10 (52.6)	9 (47.4)	6 (30.0)	

Data presented as mean ± SD or Number (%); BMI: body mass index

**Table 2: Duration of analgesia, intraoperative fentanyl consumption, and postoperative morphine consumption in the three studied groups**

	ESP group (n = 19)	DEX group (n = 19)	Control group (n = 20)	P value	Post-hoc Test
<b>Duration of analgesia (min)</b>	270.0 (80.0–450.0)	460.0 (200.0–700.0)	47.5 (25.0–90.0)	< 0.001	P1 < 0.001 P2 < 0.001 P3 < 0.001
<b>Intraoperative fentanyl consumption (µg)</b>	120.0 (60.0–200.0)	110 (60.0–210.0)	205.0 (100.0–350.0)	< 0.001	P1 0.856 P2 0.001 P3 < 0.001
<b>Total postoperative morphine consumption (mg)</b>	13.0 (6.0–32.0)	11.0 (4.0–22.0)	24.5 (8.0–40.0)	0.002	P1 0.154 P2 0.374 P3 0.001

Data presented as median (range); P1: ESP vs. DEX, P2: ESP vs. Control, P3: DEX vs. Control

**Table 3: Postoperative numerical rating scale scores of pain at rest in the three studied groups**

Time to measure NRS score at rest	ESP group (n = 19)	DEX group (n = 19)	Control group (n = 20)	P value
After 30 min.	2 (1–3)	2 (1–3)	2 (1–4)	0.509
After 2 h	2 (0–3)	2 (0–3)	2 (0–3)	0.590
After 4 h	2 (0–3)	2 (0–3)	2 (0–3)	0.883
After 8 h	2 (0–3)	2 (0–3)	2 (0–3)	0.816
After 12 h	2 (0–3)	2 (0–3)	2 (0–3)	0.570
After 24 h	2 (0–3)	1 (0–3)	2 (0–3)	0.322

Data presented as median (range)

had comparable morphine consumption (P = 0.154). Intraoperative fentanyl consumption was significantly higher in the control group than ESPB and Dex groups

(P = 0.001, P < 0.001, respectively). The ESPB and Dex groups had comparable fentanyl consumption (P = 0.856).

**Table 4: Postoperative numerical rating scale scores of pain on movement in the three studied groups**

Time to measure NRS score on movement	ESP group (n = 19)	DEX group (n = 19)	Control group (n = 20)	P value
After 30 min	3 (1-4)	3 (2-6)	4 (2-7)	0.147
After 2 h	4 (2-6)	3 (1-5)	4 (2-5)	0.119
After 4 h	3 (2-4)	3 (1-5)	3 (1-6)	0.825
After 8 h	3 (2-6)	3 (1-6)	4 (2-5)	0.402
After 12 h	3 (2-6)	3 (1-6)	4 (2-6)	0.550
After 24 h	2 (1-4)	2 (1-4)	3 (1-4)	0.325

*Data presented as median (range)*

On the other hand, NRS scores of pain at rest and with movement were comparable throughout the postoperative period in the three groups (Tables 3 and 4).

Two, three, and five patients complained of postoperative nausea and vomiting (PONV) in Dex, ESPB, and control groups, respectively. No patients in this study developed pruritis or respiratory depression.

No block-related complications were recorded as local anesthetic toxicity and infection.

## 4. Discussion

This study demonstrated that adding Dex to the local anesthetic during single-shot ultrasound-guided ESPB prolongs the duration of analgesia after breast cancer surgery. Adding Dex to bupivacaine did not reduce postoperative morphine consumption compared to ESPB with bupivacaine only. However, morphine consumption was significantly reduced compared to the control group. There was no noticeable effect of ESPB with or without Dex on pain intensity, probably due to the use of PCA. On the other hand, intraoperative fentanyl consumption was significantly reduced during ESPB with or without Dex.

Most authors acknowledge ESPB as a relatively safe and easy to perform regional analgesic technique compared to conventional procedures performed close to the neuroaxis.<sup>14</sup> Paravertebral block (PVB) has been used for many years in breast analgesia.<sup>15</sup> However, it is not devoid of complications such as pleural and vascular puncture, pneumothorax, nerve injury, and organ damage. In addition, it has a relatively high failure rate depending on the experience of the operator.<sup>16</sup> Many inter-fascial plane block techniques have been suggested to avoid these complications, ESPB is one of these.

In ESPB, the local anesthetic is deposited in the fascial plane deeper to the erector spinae muscle at the tip of the transverse vertebral process. The LA is distributed cranially and caudally.<sup>17</sup> It also diffuses anteriorly to the

paravertebral and epidural spaces and laterally to the intercostal spaces.<sup>18</sup> The erector spinae plane is safe and free of any vitally complicated structures that needles could injure. Therefore, the risk of inadvertent hematoma and nerve injury is reduced. ESPB is a safe approach that employs the transverse process as an anteromedial barrier to keep the injecting needle from contacting the pleura, reducing the incidence of pleural damage.<sup>19</sup>

This study confirms the analgesic role of the ESPB as the duration of analgesia was longer than the control group, even with the injection of a local anesthetic only. The maximum duration of analgesia was only 90 min in the absence of regional block, but it reached up to 5 h using ESPB. Perhaps, this is the main drawback of ESPB, the relatively short analgesic duration. This was the main motive for performing the current study to see if the addition of Dex can prolong analgesia instead of the technically demanding continuous ESPB.

Many studies showed that adding Dex to local anesthetics enhanced the effectiveness of central and peripheral nerve blocks. Dex has been reported to significantly extend the analgesia time when used as an adjuvant in epidural block,<sup>20</sup> PVB,<sup>13,21</sup> subarachnoid block,<sup>22</sup> and brachial plexus block analgesia.<sup>23</sup> A systematic review of 12 RCTs found that epidural Dex was associated with prolonged duration of analgesia, short onset of sensory block, decreased need for rescue analgesia, and higher sedation scores compared to control treatment.<sup>24</sup>

Few studies investigated the value of Dex as an adjuvant to local anesthetic in ESPB. Gao et al.<sup>25</sup> used Dex as an adjuvant to ropivacaine-based ESPB in video-assisted thoracoscopic lobectomy surgery (VATLS). Dex achieved prolonged sensory block duration and reduced the need for rescue analgesia. More recently, adding 1 µg/kg Dex to 0.5% ropivacaine in ESPB improved analgesia and prolonged sensory block duration

compared to ropivacaine alone in patients undergoing VATLS.<sup>26</sup>

Wang et al. found that Dex was effective as an adjuvant to ESPB in pain relief and reducing opioid consumption during modified radical mastectomy.<sup>27</sup> They added Dex in a 1 µg/kg dose to 30 mL of 0.33% ropivacaine. Dex was associated with decreased postoperative VAS scores and opioid use in the first 48 postoperative hours. They also reported reduced intraoperative opioid use in patients who received the combined Dex and ropivacaine in ESPB. The discrepancy between these results and ours can probably be attributed to the different volumes and concentrations of LA used by Wang. The higher concentration provided a denser block with a more analgesic effect masking the difference in intraoperative requirement of opioids found in their study.

Several possible mechanisms can explain the action of Dex to improve blockade efficacy. Dex exerts its effect by suppressing C fibers and inducing hyperpolarization of posterior horn neurons leading to analgesia.<sup>28</sup> It is supposed to reduce the release of inflammatory mediators and inhibit potassium channel-mediated discharge of C-fibers.<sup>29</sup> It acts on the pre- and postsynaptic sympathetic nerve terminal, decreasing the sympathetic outflow and norepinephrine release. These actions are the source of its sedative, antianxiety, and hemodynamic effects.<sup>30</sup> Dexmedetomidine has a central action, activating α-2 adrenoreceptors in the locus ceruleus and lowering substance P release at dorsal horn neurons, leading to suppressing the nociceptive pathway.<sup>13</sup>

## 5. Limitations

Our study had several limitations, including short postoperative assessment duration and missing to measure the impact of Dex on the incidence of postmastectomy chronic pain.

## 6. Conclusion

Adding dexmedetomidine 1 µg/kg to bupivacaine 0.5% can significantly prolong the analgesic duration of the erector spinae plane block in breast cancer surgeries. It is also associated with reduced perioperative opioid consumption relative to the control group.

## 7. Data availability

The numerical data generated during this research is available with the authors.

## 8. Acknowledgement

We gratefully thank Faculty of Medicine, Universitas Indonesia for the PUTI grant (NKB-

2247/UN2.RST/HKP.05.00/2020) which helped fund this project.

## 9. Conflict of interest

The study utilized a grant by Faculty of Medicine, Universitas Indonesia, and no external or industry funding was involved.

## 10. Authors' contribution

MH: Concept; conduction of the study work; manuscript editing and final revision

AA: Concept; conduction of the study work and manuscript editing

Both authors approved the final draft.

## 11. References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin.* 2021;71(3):209–49. [PubMed] DOI: [10.3322/caac.21660](https://doi.org/10.3322/caac.21660)
2. Fecho K, Miller NR, Merritt SA, Klauber-Demore N, Hultman CS, Blau WS. Acute and persistent postoperative pain after breast surgery. *Pain Med.* 2009 Jun;10(4):708–15. [PubMed] DOI: [10.1111/j.1526-4637.2009.00611.x](https://doi.org/10.1111/j.1526-4637.2009.00611.x)
3. American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology.* 2012 Feb;116(2):248–73. [PubMed] DOI: [10.1097/ALN.0b013e31823c1030](https://doi.org/10.1097/ALN.0b013e31823c1030)
4. Abraham A. Gold standards and anaesthesia. *Indian J Anaesth.* 2013;57(2):207–9. [PubMed] DOI: [10.4103/0019-5049.111876](https://doi.org/10.4103/0019-5049.111876)
5. Cu villon P, Alonso S, L'Hermite J, Reubrecht V, Zoric L, Vialles N, et al. Post-operative opioid-related adverse events with intravenous oxycodone compared to morphine: A randomized controlled trial. *Acta Anaesthesiol Scand.* 2021;65(1):40–6. [PubMed] DOI: [10.1111/aas.13685](https://doi.org/10.1111/aas.13685)
6. Jacobs A, Lemoine A, Joshi GP, Van de Velde M, Bonnet F; PROSPECT Working Group collaborators#. PROSPECT guideline for oncological breast surgery: a systematic review and procedure-specific postoperative pain management recommendations. *Anaesthesia.* 2020 May;75(5):664–673. [PubMed] DOI: [10.1111/anae.14964](https://doi.org/10.1111/anae.14964)
7. Kot P, Rodriguez P, Granell M, Cano B, Rovira L, Morales J, et al. The erector spinae plane block: a narrative review. *Korean J Anesthesiol.* 2019 Jun;72(3):209–20. [PubMed] DOI: [10.4097/kja.d.19.00012](https://doi.org/10.4097/kja.d.19.00012)
8. Zhang J, He Y, Wang S, Chen Z, Zhang Y, Gao Y, et al. The erector spinae plane block causes only cutaneous sensory loss on ipsilateral posterior thorax: a prospective observational volunteer study. *BMC Anesthesiol.* 2020 Apr 20;20(1):88. [PubMed] DOI: [10.1186/s12871-020-01002-0](https://doi.org/10.1186/s12871-020-01002-0)
9. Aksay SS, Bumb JM, Remennik D, Thiel M, Kranaster L, Sartorius A, et al. Dexmedetomidine for the management of postictal agitation after electroconvulsive therapy with S-

- ketamine anesthesia. *Neuropsychiatr Dis Treat*. 2017 May 23;13:1389–94. [PubMed] DOI: [10.2147/NDT.S134751](https://doi.org/10.2147/NDT.S134751)
10. Gao W, Wang J, Zhang Z, He H, Li H, Hou R, et al. Opioid-free labor analgesia: dexmedetomidine as an adjuvant combined with ropivacaine. *J Healthc Eng*. 2022;2022:2235025. [PubMed] DOI: [10.1155/2022/2235025](https://doi.org/10.1155/2022/2235025)
  11. Wang K, Wang LJ, Yang TJ, Mao QX, Wang Z, Chen LY. Dexmedetomidine combined with local anesthetics in thoracic paravertebral block: A systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)*. 2018 Nov;97(46):e13164. [PubMed] DOI: [10.1097/MD.00000000000013164](https://doi.org/10.1097/MD.00000000000013164)
  12. Iyer LS, Bhat SS, Nethra HN, Vijayakumar HN, Sudheesh K, Ramachandriah. A Comparative Study of Effect of 0.25% Levobupivacaine with Dexmedetomidine versus 0.25% Levobupivacaine in Ultrasound-Guided Supraclavicular Brachial Plexus Block. *Anesth Essays Res*. 2021 Oct-Dec;15(4):443-447. [PubMed] DOI: [10.4103/aer.aer\\_145\\_21](https://doi.org/10.4103/aer.aer_145_21)
  13. Mohta M, Kalra B, Sethi AK, Kaur N. Efficacy of dexmedetomidine as an adjuvant in paravertebral block in breast cancer surgery. *J Anesth*. 2016 Apr;30(2):252–60. [PubMed] DOI: [10.1007/s00540-015-2123-8](https://doi.org/10.1007/s00540-015-2123-8)
  14. Kot P, Rodriguez P, Granell M, Cano B, Rovira L, Morales J, et al. The erector spinae plane block: a narrative review. *Korean J Anesthesiol*. 2019 Jun;72(3):209–20. [PubMed] DOI: [10.4097/kja.d.19.00012](https://doi.org/10.4097/kja.d.19.00012)
  15. Tahiri Y, Tran DQH, Bouteaud J, Xu L, Lalonde D, Luc M, et al. General anaesthesia versus thoracic paravertebral block for breast surgery: a meta-analysis. *J Plast Reconstr Aesthet Surg*. 2011 Oct;64(10):1261–9. [PubMed] DOI: [10.1016/j.bjps.2011.03.025](https://doi.org/10.1016/j.bjps.2011.03.025)
  16. Pace MM, Sharma B, Anderson-Dam J, Fleischmann K, Warren L, Stefanovich P. Ultrasound-guided thoracic paravertebral blockade: a retrospective study of the incidence of complications. *Anesth Analg*. 2016 Apr;122(4):1186–91. [PubMed] DOI: [10.1213/ANE.0000000000001117](https://doi.org/10.1213/ANE.0000000000001117)
  17. De Cassai A, Tonetti T. Local anesthetic spread during erector spinae plane block. *J Clin Anesth*. 2018 Aug;48:60–1. [PubMed] DOI: [10.1016/j.jclinane.2022.110834](https://doi.org/10.1016/j.jclinane.2022.110834)
  18. Vidal E, Giménez H, Forero M, Fajardo M. Erector spinae plane block: A cadaver study to determine its mechanism of action. *Rev Esp Anestesiol Reanim (Engl Ed)*. 2018 Nov;65(9):514–519. [PubMed] DOI: [10.1016/j.redar.2018.07.004](https://doi.org/10.1016/j.redar.2018.07.004)
  19. Fang B, Wang Z, Huang X. Ultrasound-guided preoperative single-dose erector spinae plane block provides comparable analgesia to thoracic paravertebral block following thoracotomy: a single center randomized controlled double-blind study. *Ann Transl Med*. 2019 Apr;7(8):174. [PubMed] DOI: [10.21037/atm.2019.03.53](https://doi.org/10.21037/atm.2019.03.53)
  20. Qureshi F, Meena SC, Kumar V, Jain K, Chauhan R, Luthra A. Influence of epidural ropivacaine with or without dexmedetomidine on postoperative analgesia and patient satisfaction after thoraco-lumbar spine instrumentation: a randomized, comparative, and double-blind study. *Asian Spine J*. 2021 Jun;15(3):324–32. [PubMed] DOI: [10.31616/asj.2020.0072](https://doi.org/10.31616/asj.2020.0072)
  21. Alimian M, Imani F, Rahimzadeh P, Faiz SHR, Bahari-Sejahrood L, Hertling A. Adding Dexmedetomidine to Bupivacaine in Ultrasound-guided Thoracic Paravertebral Block for Pain Management after Upper Abdominal Surgery: A Double-blind Randomized Controlled Trial. *Anesth Pain Med*. 2021 Dec 8;11(6):e120787. [PubMed] DOI: [10.5812/aapm.120787](https://doi.org/10.5812/aapm.120787)
  22. Khosravi F, Sharifi M, Jarineshin H. Comparative Study of Fentanyl vs Dexmedetomidine as Adjuvants to Intrathecal Bupivacaine in Cesarean Section: A Randomized, Double-Blind Clinical Trial. *J Pain Res*. 2020;13:2475–82. [PubMed] DOI: [10.2147/JPR.S265161](https://doi.org/10.2147/JPR.S265161)
  23. Hussain N, Grzywacz VP, Ferreri CA, Atrey A, Banfield L, Shaparin N, et al. Investigating the Efficacy of Dexmedetomidine as an Adjuvant to Local Anesthesia in Brachial Plexus Block: A Systematic Review and Meta-Analysis of 18 Randomized Controlled Trials. *Reg Anesth Pain Med*. 2017 Apr;42(2):184–96. [PubMed] DOI: [10.1097/AAP.0000000000000564](https://doi.org/10.1097/AAP.0000000000000564)
  24. Zhang X, Wang D, Shi M, Luo Y. Efficacy and Safety of Dexmedetomidine as an Adjuvant in Epidural Analgesia and Anesthesia: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Clin Drug Investig*. 2017 Apr;37(4):343–54. [PubMed] DOI: [10.1007/s40261-016-0477-9](https://doi.org/10.1007/s40261-016-0477-9)
  25. Gao Z, Xiao Y, Wang Q, Li Y. Comparison of dexmedetomidine and dexamethasone as adjuvant for ropivacaine in ultrasound-guided erector spinae plane block for video-assisted thoracoscopic lobectomy surgery: a randomized, double-blind, placebo-controlled trial. *Ann Transl Med*. 2019 Nov;7(22):668. [PubMed] DOI: [10.21037/atm.2019.10.74](https://doi.org/10.21037/atm.2019.10.74)
  26. Rao J, Gao Z, Qiu G, Gao P, Wang Q, Zhong W, et al. Nalbuphine and dexmedetomidine as adjuvants to ropivacaine in ultrasound-guided erector spinae plane block for video-assisted thoracoscopic lobectomy surgery. *Medicine (Baltimore)*. 2021 Aug 13;100(32):e26962. [PubMed] DOI: [10.1097/MD.00000000000026962](https://doi.org/10.1097/MD.00000000000026962)
  27. Wang X, Ran G, Chen X, Xie C, Wang J, Liu X, et al. The Effect of Ultrasound-Guided Erector Spinae Plane Block Combined with Dexmedetomidine on Postoperative Analgesia in Patients Undergoing Modified Radical Mastectomy: A Randomized Controlled Trial. *Pain Ther*. 2021 Jun;10(1):475–84. [PubMed] DOI: [10.1007/s40122-020-00234-9](https://doi.org/10.1007/s40122-020-00234-9)
  28. Guo TZ, Jiang JY, Buttermann AE, Maze M. Dexmedetomidine injection into the locus ceruleus produces antinociception. *Anesthesiology*. 1996 Apr;84(4):873–81. [PubMed] DOI: [10.1097/0000542-199604000-00015](https://doi.org/10.1097/0000542-199604000-00015)
  29. Choi S, Rodseth R, McCartney CJL. Effects of dexamethasone as a local anaesthetic adjuvant for brachial plexus block: a systematic review and meta-analysis of randomized trials. *Br J Anaesth*. 2014 Mar;112(3):427–39. [PubMed] DOI: [10.1093/bja/aet417](https://doi.org/10.1093/bja/aet417)
  30. Maze M, Scarfini C, Cavaliere F. New agents for sedation in the intensive care unit. *Crit Care Clin*. 2001 Oct;17(4):881–97. [PubMed] DOI: [10.1016/s0749-0704\(05\)70185-8](https://doi.org/10.1016/s0749-0704(05)70185-8)