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## **Erector Spinae Plane Block. A narrative review**

# Bloqueo del plano del músculo erector de la espina. Revisión narrativa de la literatura

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#### Abstract

The erector spinae plane (ESP) block is an interfascial block described in 2016 by Forero and collaborators, with wide clinical uses and benefits when it comes to analysesic control in different surgeries. This block consists of the application of local anesthetic (LA) in a deep plane over the transverse process, anterior to the erector spinae muscle in the anatomical site where dorsal and ventral branches of the spinal nerve roots are located.

This review will cover its clinical uses according to different surgical models, the existing evidence and complications described to date.

## **Keywords**

Post-cardiac arrest syndrome; In-hospital cardiac arrest; Cardiopulmonary resuscitation; Return of spontaneous cardiac circulation; Ischemia-reperfusion injury.

#### Resumen

El bloqueo del plano del músculo erector de la espina (ESP, por sus siglas en inglés) es un bloqueo interfascial descrito en 2016 por Forero y colaboradores, con amplios usos clínicos y beneficios en relación con el control analgésico de diferentes modelos quirúrgicos. Este consiste en la aplicación de anestésico local (AL) en un plano profundo sobre apófisis transversa anterior al músculo erector de la espina, sitio anatómico donde se encuentra la bifurcación de los ramos dorsal y ventral de las raíces nerviosas espinales. En esta revisión, se expondrán los usos clínicos según diferentes modelos quirúrgicos, la evidencia que existe de ellos y las complicaciones descritas hasta la actualidad.

## Palabras clave

Bloqueo nervioso; Anestesia y analgesia; Fascia; Anestesia regional; Anatomía regional.

#### INTRODUCTION

The erector spinae plane (ESP) block is a regional anesthesia technique first described by Forero et al. (1) as a modified interfascial block initially used for patients with chronic neuropathic thoracic pain to provide wide sensory blockade, including the anterior and posterior regions of the chest.

Reports and case series (2-6) have suggested good results, spurring interest in the scientific community and leading to studies designed to assess anatomic and physiologic considerations, as well as the clinical applications of this technique.

The usefulness and safety of the ESP block have been elucidated in different scenarios (1-3). As an analgesic/anesthetic technique, it appears to offer advantages over other regional options such as neuraxial and paravertebral blocks, which pose a higher risk of dural or pleural punctures and other side effects (3).

Although it needs to be highlighted that there are no learning curves for this block so far, it has positioned itself as an innovative technique described as easy to perform in the practice of anesthesia (1-8).

The purpose of this review is to summarize the main indications for the ESP block in the practice of anesthesia, and to document the complications described to this date. A broad literature search was conducted in PubMed, Google Scholar and the Cochrane Library between July 2018 and November 2020. The inclusion criteria were articles on ESP block identified in the search, including letters to the editor, case reports, case series, cadaveric studies, reviews, meta-analyses and clinical trials in both adult and pediatric populations. The exclusion criteria were articles in languages other than Spanish or English, animal studies or articles unrelated to the ESP block. The terms used were Erector Spinae Plane Block, ESP block, and Erector Spinae block.

The full texts of 80 articles were read and data on the surgical model, anatomic site pain, anesthetic dose and type, numerical pain scale, complications and

other relevant observations were collected. The most relevant findings are described in Tables 1 and 2.

#### **ANATOMY**

The thoracolumbar fascia (TLF) (9) is an important structure in the ESP block since it enables distal spread of the local anesthetic (LA) from the site of administration; it consists of fascia layers and aponeurotic tissue which separate paraspinal muscles from the posterior abdominal wall muscles; it extends cephalad, along the thoracic and cervical spine, up to the skull base, and caudal down to the sacroiliac level posteriorly (9-11).

The erector spinae muscles include the iliocostalis, longissimus and spinalis (multifidus); they arise from a common aponeurosis (the three columns of the broad tendon), form at the level of L5 and attach to the posterior inferior iliac crest, the posterior sacrum, the sacroiliac ligaments and the inferior sacral and lumbar spinous processes. Each muscle has its own cephalic insertion point: ribcage and C4-C6 vertebrae; thoracic and cervical transverse processes, mastoid and temporal bones; and upper lumbar and thoracic spinous processes, respectively (9-12).

The thoracic spinal nerves, known as intercostal nerves (T6 to T11) after they emerge from the intervertebral foramen, divide into posterior and anterior branches, innervating muscle structures, joints, pleura, peritoneum and skin of the dorsal and ventral regions of the thorax. Apart from their intercostal course, they have other divisions that traverse the abdomen to provide motor and sensory innervation to the anterior abdominal wall muscles (13).

The ESP block is classified as a block of the fascial plane of the erector spinae muscle. After it is administered, the local anesthetic spreads through the dorsal fascias described above. In the lumbar fascias and the lumbar interfascial triangle, it allows for anterior, posterior, cephalic

and caudal spread, involving the ventral and dorsal branches of the spinal nerves, as well as the communicating branches of the sympathetic chain which conduct presynaptic and postsynaptic fibers both in the thoracic as well as the lumbar spine, with the potential of providing visceral and somatic analgesia (1,8,9).

## **TECHNIQUE**

The patient can be sitting or in lateral recumbency (1,14) with the side to be blocked facing superiorly. Several ways to orient the transducer in order to localize the target site have been described. Sagittal paramedian (14,15) and transverse placement (2) using a high-frequency linear probe have been proposed.

In the sagittal paramedian axis, the probe is placed at approximately 3 cm from the midline to localize the transverse process (T5 vertebra for thoracic interventions); it is suggested to begin lateral to medial, initially visualizing the ribs which appear markedly convex with a steeper angle (more rounded or U-shaped); when the transverse process is identified, 3 muscles come into view, namely, trapezius, rhomboid major and erector spinae (Figure 1). The rhomboid major is found only at the T5-T6 level (16). Having localized that view, an "in-plane" injection is performed (Figure 2).

The volume of LA varies in the literature. However, in cadaver models, a volume of 20 mL (1,17) to 30 mL (18) has been shown to extend from T2 to T9 when administered on the transverse process of T5 (2) (even from C5 to L3)(5,18), spanning a mean of 9 dermatomes (range 8-11) in the dorsal area, with 2.2 mL (1.81-2.5 mL) of LA per dermatome required (13); and from T2-T3 to T6-T9 in the anterolateral region, with variable extension to the axillary area and the medial aspect of the arm (19). In children, the use of a volume of 0.6 mL/kg has been reported (14).

**TABLE 1.** ESP block randomized clinical trials.

| Surgical<br>area | Author/<br>Year                | Study<br>type | Pain | Surgical model/<br>intervention   | Comparison   | Sample | Level          | Single<br>dose vs.<br>continuous | Laterality | Local<br>anesthetic<br>and dose  | Mean NRS*<br>afterwards   | Conclusion   | Complica-<br>tion                                     | Primary outcome statistical value   |
|------------------|--------------------------------|---------------|------|---|--|--------|----------------|----------------------------------|------------|--|---|--|---|---|
|                  | Barrios,<br>2020 <u>(13)</u>   | СО            | А    | Rib fractures.<br>herpes zoster<br>neuritis. tho-<br>racostomy and<br>myofascial pain<br>syndrome |  | 18     | T5-<br>T7      | SD                               | U          | 0.5% B<br>20 mL  | < 2   | 16 patients with<br>pain modulation,<br>mean blocked<br>dermatome<br>extension of 9<br>(range 8-11)  | None  |   |
|                  | Ciftci,<br>2019 <u>(28)</u>    | RCT           | А    | Videothoracos-<br>copy  | ESP vs.<br>multi-<br>modal<br>analgesia                | 60     | T5             | SD                               | U          | 0.25% B<br>20 mL   | ESP1 vs.<br>No ESP 5  | ESP less POP<br>pain and less res-<br>cue opioids. No<br>adverse effects   | None  | Opioid use in ESP<br>10.00 ug±14.62 ug<br>vs. no ESP 47.33 ug±<br>16.17 ug, p<0.001   |
| Thorax           | Gaballah,<br>2019 <u>(29)</u>  | RCT           | Α    | Videothoracos-<br>copy  | ESP vs. PVB  | 60     | T5             | SD                               | U          | 0.25% B<br>20 mL   | ESP 1.13<br>vs. No<br>ESP 5.13  | ESP less POP<br>pain, longer time<br>to first rescue<br>dose of analgesic,<br>lower opioid use   | None  | POP in first 4 h lower<br>in ESP group 1.87 ±<br>0.35 vs. 2.0 ± 0.01, p<br>= 0.04, POP pain at 6<br>h lower in ESP group<br>3.33 ± 0.48 vs. 3.73 ±<br>0.45, p = 0.002.Time<br>to first analgesia<br>longer in ESP group<br>379.07 ± 7.78 vs. 296.04<br>± 6.62 minutes, p <<br>0.001 |
|                  | Chen,<br>2020<br>(30)          | RCT           | А    | Videothoracos-<br>copy  | ESP vs. PVB<br>vs. ICNB                                | 75     | T <sub>5</sub> | SD                               | U          | 0.375% R<br>20 mL  | Three<br>groups<br>< 4  | PPV less POP<br>pain. Greater<br>need for rescue<br>analgesia in ESP.<br>Higher morphine<br>use at 24 h in ESP   | Hematoma<br>in 4 PVB<br>patients,<br>5 ICNB, 0<br>ESP | Morphine use in PVB 10.5 (9-15) mg; ICNB 18 (13.5-22.1) mg; ESP, 22 (15-25.1) mg; p = 0.000   |
|                  | Nagaraja,<br>2018 <u>(34)</u>  | RCT           | А    | Median sterno-<br>tomy  | Bilateral<br>ESP vs.<br>epidural<br>catheter           | 50     | T <sub>5</sub> | СС                               | BL         | 0.25% B<br>15 mL in<br>each side<br>and CC<br>(0.125%<br>B 0.1 mL/<br>kg/h)          | First 12<br>hours<br>ESP 1.68<br>/10 vs.<br>Epid<br>1.92/10 ///<br>24 hours<br>ESP 1.44<br>/10 vs.<br>Epid<br>2.08/10 | ESP less POP at<br>24 hours, with<br>no difference in<br>NSR in first 12<br>hours, opioid use,<br>spirometry, ICU<br>length of stay. No<br>adverse effects | None  | NSR Epid 1.56 ±1.08<br>vs. ESP 1.04 ± 0.98<br>P < 0.08 first 12 h<br>// NRS Epid 2 ±1.32<br>vs. ESP 0.8±0.64 p<br>< 0.0002 after 24<br>hours  |
| Cardio           | Borys,<br>2020<br>( <u>36)</u> | со            | А    | Minimally<br>invasive<br>thoracotomy<br>(mitral valve<br>replacement)                             | ESP vs. IV<br>analgesia                                | 44     | T4             | SD                               | U          | 0.375% R<br>0.2 mL/<br>kg  | 3.72 out<br>of 10   | Shorter mecha-<br>nical ventilation<br>time and shorter<br>ICU stay  | None  | Oxycodone use in ESP<br>group was 18.26 (95%<br>Cl: 15.55-20.98) mg   |
|                  | Krishna,<br>2019 <u>(37)</u>   | RCT           | А    | Median sterno-<br>tomy  | Bilateral<br>ESP vs.<br>tramadol +<br>paraceta-<br>mol | 106    | Т6             | SD                               | BL         | R 0.375 %<br>3 mg/kg<br>(1.5 mg/<br>kg each<br>side,<br>20-25 mL<br>in each<br>side) | < 4 out of<br>10 first<br>8 hours   | More prolonged<br>pain modulation<br>in ESP group  | None  | NRS < 4/10 postextu-<br>bation p = 0.0001 in<br>favor of ESP  |

| Surgical<br>area | Author/<br>Year             | Study<br>type | Pain | Surgical model/<br>intervention                             | Comparison                                     | Sample | Level           | Single<br>dose vs.<br>continuous | Laterality | Local<br>anesthetic<br>and dose                                 | Mean NRS*<br>afterwards  | Conclusion  | Complication                             | Primary outcome statistical value  |
|------------------|-----------------------------|---------------|------|---|--|--------|-----------------|----------------------------------|------------|---|--|---|--|--|
|                  | Yayik,<br>2020<br>(40)      | RCT           | А    | Lumbar spine<br>decompression                               | ESP vs.<br>control<br>(PCA<br>tramadol)        | 60     | L3              | SD                               | BL         | 0.25% B<br>20 mL in<br>each side                                | ESP<br>group <<br>2.4 at rest<br>and < 2.6<br>dynamic<br>in the<br>first 24<br>hours                           | ESP less<br>dynamic and<br>static pain, less<br>tramadol use  | None                                     | Higher tramadol use for control group (370.33 ±73.27 mg and 268.33 ±71.44 mg, p < 0.001). Static pain ESP 1.93 ± 0.87 vs. 3.83 ±1.18 and dynamic pain e.30 ± 0.60 vs. 4.63 ±1.10 p < 0.001   |
| Columna          | Singh,<br>2020<br>(41)      | RCT           | А    | Major lumbar<br>spine surgery                               | ESP vs.<br>control                             | 40     | T10             | SD                               | BL         | 0.5% B<br>20 mL in<br>each side                                 | ESP<br>group<br><3 vs.<br>control<br>group<br><4   | ESP less morphi-<br>ne use and lower<br>pain scores than<br>control group   | None                                     | Lower morphine<br>consumption (1.4 ±<br>1.5 vs. 7.2 ± 2.0 mg p<br>< 0.001) ESP   |
|                  | Qiu, 2020<br>(42)           | М             | А    | Lumbar spine<br>surgery                                     |  | 171    | T8 -<br>L4      | SD+C                             | BL         | B, R, L   |  | Effectiveness<br>and safety<br>of ESP for<br>lumbar spine<br>surgery still<br>controversial   |  |  |
|                  | Aksu,<br>2019 <u>(43)</u>   | RCT           | A    | Breast surgery  | ESP + PCA<br>vs. control<br>(PCA)              | 50     | T2<br>and<br>T4 | SD                               | U          | 0.25%<br>B 20 mL<br>(10 mL<br>for T2<br>and 10<br>mL for<br>T4) | Both<br>groups<br>< 2  | Morphine use<br>significantly lower<br>in ESP group at 6,<br>12 and 24 hours<br>POP   | None                                     | Morphine use at 24<br>h lower in ESP 3.02<br>± 2.06 mg vs.13.2 ±<br>4.98 mg in control<br>group, p < 0.001   |
|                  | Swisher,<br>2020<br>(44)    | RCT           | A    | Breast surgery<br>without uni<br>or bilateral<br>mastectomy | ESP vs. PVB                                    | 100    | T3<br>or<br>T4  | SD                               | UoBL       | 0.5% R CE 20 mL unila- teral or 16 mL/ side for bilateral       | ESP<br>group 3<br>vs. PVB<br>group 0   | Higher pain sco-<br>res and opioid<br>use in ESP<br>group. Lower<br>POP morphine<br>use for PVB<br>group  | None                                     | Pain scores -3.0 a 0<br>(p = 0.0011)   |
| Mama             | Gürkan,<br>2020<br>(45)     | RCT           | А    | Breast cancer<br>surgery                                    | ESP vs. PVB<br>vs. control<br>(opioid<br>only) | 75     | T4              | SD                               | U          | o.25% B<br>20 mL vs.<br>20 mL vs.<br>opioid<br>analge-<br>sia   | ESP and<br>PVB<br>groups <<br>2 first 12<br>h < 5 first<br>24 h  | Opioid use (no<br>difference in<br>ESP and PVB).<br>VAS 1 and 6<br>hours POP (be-<br>tter in PVB than<br>control, but<br>no difference<br>between ESP<br>and control) | None                                     | Morphine use at 24<br>hours 5.6 ± 3.43 mg<br>in ESP group, 5.64 ±<br>4.15 mg PVB group<br>and 14.92 ± 7.44 mg<br>in control group, p<br>= 0.001  |
|                  | Gürkan,<br>2018 <u>(46)</u> | RCT           | А    | Breast cancer<br>surgery                                    | ESP vs.<br>control<br>(opioid<br>only)         | 50     | T4              | SD                               | U          | 0.25% B<br>20 mL  | < 2 in<br>first 24 h<br>for both<br>groups   | Pain modulation<br>no different than<br>control, 65%<br>lower morphine<br>use than in<br>control group  | None                                     | Morphine use at<br>1, 6, 12, 24 hours<br>lower in ESP 5.76<br>± 3.8 mg vs. 16.6 ±<br>6.92 mg in control<br>group, p < 0.05   |
|                  | Leong,<br>2020<br>(47)      | RS M          | Α    | Breast surgery  | ESP vs.<br>no block<br>vs. other<br>blocks     | 861    | T4              | SD                               | U          | 0.25% B<br>20 mL  | EPS group lower pain scores vs. no block group. ESP group hi- gher pain scores vs. PNB group in first 12 hours | ESP less pain at<br>2, 6, 12, 24 h POP.<br>Lower need for<br>morphine and<br>better recovery<br>quality   | Pneumo-<br>thorax<br>2.6% PVB,<br>0% ESP | POP pain at 2 hours<br>(-2.97 to -0.29, p<br>= 0.02), at 6 hours<br>(-1.49 to -0.30 p =<br>0.003), at 12 hours<br>(-0.67 to -0.25 p<br><0.0001), and at 24<br>h (-0.70 to -0.30 p<br><0.0001). Lower<br>morphine require-<br>ments for ESP group<br>(-32.57 to -10.52) p<br>= 0.00 |

| Surgical<br>area | Author/<br>Year                      | Study<br>type | Pain | Surgical model/<br>intervention  | Comparison                             | Sample | Level | Single<br>dose vs.<br>continuous | Laterality | Local<br>anesthetic<br>and dose   | Mean NRS*<br>afterwards  | Conclusion   | Complication  | Primary outcome statistical value  |
|------------------|--------------------------------------|---------------|------|--|--|--------|-------|----------------------------------|------------|---|--|--|---|--|
|                  | Altıpar-<br>mak,<br>2019 <u>(48)</u> | RCT           | Α    | Breast cancer<br>surgery (radical<br>mastectomy)                                       | ESP vs.<br>PEC2                        | 38     | Т4    | SD                               | U          | 0.25% B ESP 20 mL vs. PEC2 (20 mL between pectora- lis minor and serratus +10 mL between pectora- lis major and pec- toralis minor) | Similar pain sco- res (<1.5) between both groups at 15 and 30 minutes. Lower scores in PECS group after 60 min | Pain modulation<br>greater in PEC2<br>group, lower<br>tramadol use in<br>PEC2 group  |   | POP tramadol<br>use lower in PEC2<br>group (132.78 ±<br>22.44) than in ESP<br>group (196 ± 27.03)<br>p=0.001 |
|                  | Gad, 2019<br>(49)                    | RCT           | Α    | Radical mastec-<br>tomy  | ESP vs.<br>PEC2                        | 50     | T4    | SD                               | U          | 0.25% L<br>20 mL  | Scores<br>below<br>20/100<br>in both<br>groups   | Lower opioid<br>use in PECS,<br>better pain<br>modulation<br>and lower POP<br>morphine use   | None  | Opioid use higher<br>in ESP group (16.7 ±<br>7.21) vs. (10.7 ± 3.12)<br>p = 0.001                            |
|                  | Sinha,<br>2019 <u>(50)</u>           | RCT           | А    | Modified radical mastectomy  | ESP vs.<br>PEC2                        | 64     | T4    | SD                               | U          | 0.2% R<br>20 mL   | PECS2<br>group 2<br>vs. ESP<br>group<br>2.6  | POP morphine<br>use lower in<br>PEC2 group   |   | Morphine use lower<br>in PEC2 (4.40 ± 0.94<br>mg) vs. ESP group<br>(6.59 ± 1.35 mg; p =<br>0.000)            |
| Mama             | El Cha<br>mry, 2019<br>(51)          | RCT           | Α    | Radical mastec-<br>tomy  | ESP vs. PVB                            | 70     | T5    | SD                               | U          | 0.25% B<br>20 mL  | ESP<br>group <<br>3 first 6<br>h, PVB<br>group < 4<br>first 6 h  | POP morphine use during first 24 hours and time to first analgesia requirement similar between both groups. No difference in the VAS, PONV or intraoperative fentanyl use between the two groups. POP morphine use during 24 hours was similar | 4 patients<br>in the PVB<br>group<br>developed<br>pneumo-<br>thorax, O<br>in the ESP<br>group | POP morphine use<br>in ESP group (26.7<br>± 2.1) vs. (27.3 ± 2.9)<br>(p = 0.32)                              |
|                  | Moustafa,<br>2020 <u>(52)</u>        | RCT           | Α    | Radical mastec-<br>tomy  | ESP vs. PVB                            | 102    | Т4    | SD                               | U          | 0.25% B<br>20 mL  | Not<br>assessed  | 100% success<br>rate in ESP vs.<br>77.8% in PVB.<br>POP morphine<br>use similar<br>between both<br>groups  | None  | 100% success rate<br>in ESP vs. 77.8% in<br>PVB (\(\chi_2=9.11\) p =<br>0.002\)                              |
|                  | Sharma,<br>2020<br>(53)              | RCT           | А    | Breast cancer<br>surgery (radical<br>mastectomy +<br>axillary lymph<br>node resection) | ESP vs.<br>control<br>(opioid<br>only) | 60     | T5    | SD                               | U          | 0.5% R<br>0.4 mL/<br>kg   | ESP<br>group <<br>1, control<br>group<br>< 4   | Pain modulation<br>similar in both<br>groups, lower<br>morphine use in<br>ESP 43%  | None  | Morphine use in<br>first 24 hours lower<br>in ESP mean diffe-<br>rences 2.1 (2.0–2.2),<br>p 0.01             |
|                  | Singh,<br>2019 <u>(54)</u>           | RCT           | A    | Modified radical<br>mastectomy   | ESP vs.<br>control<br>(opioid<br>only) | 40     | Т5    | SD                               | U          | 0.5% B<br>20 mL   | ESP<br>group 2.7<br>vs control<br>group<br>4.2   | Pain modula-<br>tion higher and<br>opioid use lower<br>in ESP group  | None  | Morphine use in<br>ESP (1.95 ± 2.01 mg)<br>vs. control group<br>(9.3 ± 2.36 mg) p<br>= 0.01                  |

| Surgical<br>area | Author/<br>Year                      | Study<br>type | Pain | Surgical model/<br>intervention              | Comparison   | Sample | Level | Single<br>dose vs.<br>continuous | Laterality | Local<br>anesthetic<br>and dose  | Mean NRS*<br>afterwards   | Conclusion   | Complication | Primary outcome<br>statistical value  |
|------------------|--------------------------------------|---------------|------|--|--|--------|-------|----------------------------------|------------|--|---|--|--------------|---|
|                  | Yao, 20<br>20 <u>(55)</u>            | RCT           | А    | Radical mastec-<br>tomy                      | ESP vs. pla-<br>cebo (0.9%<br>NSS)                     | 82     | T4    | SD                               | U          | 0.5% R<br>25 mL  | ESP group with better overall scores on the QoR-15 24 hours POP, less static and dynamic pain | ESP group<br>better recovery<br>quality and pain<br>modulation   | None         | Better recovery<br>quality (95% CI: 9<br>to 12, p < 0.001)  |
| Mama             | Altipar-<br>mak,<br>2019 <u>(56)</u> | RCT           | А    | Unilateral<br>modified radical<br>mastectomy | ESP with 0.375% B vs. ESP with 0.25% B                 | 42     | T4    | SD                               | U          | 0.375%<br>B vs. 0.25<br>% 20<br>mL   | ESP group with 0.375% B less than 2 vs. ESP group with 0.25% B less than 3.5 in first 12 h    | POP tramadol<br>use lower in<br>ESP group with<br>0.375% B   | None         | POP trama-<br>dol use in ESP<br>with 0.375% B<br>(149.52±25.39 mg)<br>vs. ESP group<br>with 0.25% B<br>(199.52±32.78 mg)<br>(p=0.001)   |
|                  | Oksuz,<br>2019 <u>(57)</u>           | RCT           | А    | Reduction mam-<br>moplasty                   | ESP vs.<br>tumescent<br>anesthesia                     | 44     | T4    | SD                               | BL         | 0.25%<br>B 40 mL<br>(20 mL<br>in each<br>side)   | ESP<br>group<br>4.1 ± 1.4,<br>control<br>group 5.6<br>±1.0                                    | Pain modula-<br>tion, opioid use<br>and patient sa-<br>tisfaction better<br>in ESP group   | None         | Tramadol use 24<br>hours lower in ESP<br>than tumescent, p<br>< 0.001   |
| Abdo-<br>men     | Altıpar-<br>mak,<br>2019 <u>(59)</u> | RCT           | А    | Laparoscopic<br>cholecystectomy              | ESP vs.<br>OSTAP                                       | 68     | Т7    | SD                               | BL         | 0.375%<br>B 20 mL<br>each side<br>in both<br>groups  | ESP<br>group<br>1.5 vs.<br>OSTAP<br>group<br>2.2  | Pain modulation<br>and tramadol<br>requirement<br>lower in ESP<br>group  | None         | Tramadol use lower<br>in ESP (-72.40 to -<br>48.19 p < 0.001)   |
|                  | Tulgar,<br>2019 <u>(60)</u>          | RCT           | A    | Laparoscopic<br>cholecystectomy              | ESP vs.<br>OSTAP vs.<br>control<br>group (no<br>block) | 60     | Т9    | SD                               | BL         | 0.5 % B<br>20 mL,<br>L2 10 mL<br>0.9 %<br>NSS<br>10 mL,<br>20 mL<br>applied<br>in each<br>side in<br>the block<br>groups | ESP<br>group<br>1.4 vs.<br>OSTAP<br>group<br>1.7 vs.<br>control<br>group<br>2.4               | Pain modula-<br>tion, need for<br>tramadol and<br>paracetamol<br>analgesia lower<br>in both block<br>groups than in<br>control group | None         | NRS in ESP group<br>1±1.10. OSTAP 1.27<br>±1.41, and control<br>group 2.95±1.81, p<br><0.001  |
|                  | Tulgar,<br>2018,<br><u>(61)</u>      | RCT           | A    | Laparoscopic<br>cholecystectomy              | ESP vs.<br>control<br>(opioid<br>only)                 | 30     | Т9    | SD                               | BL         | 0.375%<br>B 20 mL<br>(0.375%<br>in each<br>side)   | ESP<br>group<br>1.4 vs.<br>OSTAP<br>group<br>2.3  | Pain modula-<br>tion, need for<br>tramadol and<br>paracetamol<br>analgesia lower<br>in ESP than in<br>control group                  | None         | NRS at 0-3 h ESP<br>group 1.00 ± 1.13 vs.<br>control group 2.88<br>±1.79, p < 0.01  |
|                  | Kwon,<br>2020<br>(62)                | RCT           | А    | Laparoscopic<br>cholecystectomy              | ESP + RSB<br>vs. RSB                                   | 53     | Т7    | SD                               | BL         | 0.20% R<br>20 mL in<br>each side   | ESP<br>group +<br>RSB 2 vs.<br>RSB 3  | Lower opioid<br>use, pain scores<br>and remifenta-<br>nil use in ESP<br>group + RSB  | None         | Use of analgesic<br>at 6 h POP 41.9 µg<br>(165.1±67.7 µg) in<br>ESP group + RSB<br>vs. 207±45.5 µg in<br>RSB, p=0.012, at<br>24 h POP, 77.2 µg<br>(206.5±82.8 µg) in<br>ESP group + RSB vs.<br>283.7±102.4 µg in<br>RSB p=0.004 |

A: acute; B: bupivacaine; BL: bilateral; C: continuous; CC: continuous catheter; CI: Confidence interval; CO: cohort; Epid: Epidural; ICNB: intercostal nerve block; ICU: Intensive care unit; IV: intravenous; L: lidocaine; M: meta-analysis; NRS: numerical rating scale; OSTAP: oblique subcostal transverse abdominis plane; PCA: patient-controlled analgesia; PECS: pectoralis plane block; PEC2: pectoralis 2 block; PONV: postoperative nausea and vomiting; POP: postoperative; PVB: paravertebral block; QoR-15: quality of recovery; R: ropivacaine; RCT: randomized clinical trial; RSB: rectus sheath block; SD: single dose; SPB: serratus plane block; SR: systematic review; U: unilateral; VAS: visual analog scale; 0.9% NSS: 0.9% saline solution.

**Source:** Authors.

**TABLE 2.** ESP block case series and reports.

| Comprised natomical site | Author/Year                       | Pain | Surgical model/Intervention                                     | Sample | Level          | SD vs. CC | Laterality | Dose and anesthetic  |
|--------------------------|-----------------------------------|------|---|--------|----------------|-----------|------------|--|
|                          | Forero, 2016 (1)                  | A/C  | Oncologic pain/costal fractures/VATS                            | 4      | T5             | SD+C      | U          | 0.25% B 20 mL/0.5% R 20 mL/<br>1:1 L 2% + 0.5% R 20 mL /0.5%<br>R 20 mL  |
|                          | Muñoz, 2017 (3)                   | Α    | Thoracotomy for costal tumor resection (T11)                    | 3      | Т8             | SD        | U          | 0.5% B with epinephrine 5 μg/<br>mL14 mL   |
|                          | Adhikary, 2018 <u>(5)</u>         | Α    | VATS  | 1      | T5             | SD+C      | U          | 0.5% R 20 mL + 0.2% R infu-<br>sion 8 mL/h   |
|                          | De la Cuadra,<br>2018 <u>(14)</u> | Α    | Thoracotomy for correction of dia-<br>phragmatic paresis        | 1      | T9             | С         | U          | LB 8 mL initial bolus, 0.1% infusion 3 mL/h  |
|                          | Forero, 2017 (16)                 | Α    | Thoracotomy for lobectomy                                       | 1      | T5             | С         | U          | 0.5% R 25 mL + infusion 8<br>mL/h 0.2% R   |
|                          | Wilson, 2018 <u>(25)</u>          | Α    | VATS (metastasis for T11 paraspinal thymoma)                    | 1      | T <sub>5</sub> | SD        | U          | 0.5% R 30 mL   |
|                          | Hu, 2019 <u>(26)</u>              | Α    | VATS (bullectomy)   | 1      | T5             | SD        | U          | 0.375% R 20 mL   |
|                          | Navarro, 2018 ( <u>27)</u> A      |      | VATS (lung metastases/cystic carcino-<br>ma/lobectomy)          | 4      | T5             | С         | U          | 0.5% B 20 mL + continuous<br>infusion of 0.15% R 12 mL/h<br>(first and second patients),<br>0.15% R at 7-12 mL/h (third<br>patient) and 0.15% R at 12<br>mL/h (fourth patient)                   |
|                          | Raft, 2019 <u>(32)</u> A          |      | Thoracotomy   | 1      | T <sub>5</sub> | SD+C      | U          | 0.5% R 20 mL + 0.2% R infu-<br>sion 8 mL/h   |
| Thorax                   | Kelava, 2018 <u>(33)</u>          | А    | Thoracotomy for lung transplant                                 | 1      | Т5             | С         | U          | 0.25% B 15 mL + 0.2% R<br>infusion 10 mL/h, 10 mL bo-<br>luses every 4 hours while the<br>patient remained intubated<br>and, following extubation, 8<br>mL/h infusions with boluses<br>of 12 cm3 |
|                          | Leyva, 2020 <u>(35)</u>           | Α    | Minimally invasive thoracotomy (mi-<br>tral valve replacement)  | 1      | T <sub>7</sub> | С         | U          | 0.125% bupivacaine at 7 mL/h   |
|                          | Gaio, 2018 <u>(65)</u>            | А    | Thoracotomy for paracardiac teratoma resection                  | 1      | T5             | С         | U          | 0.2% R 5 mL (0.45 mL/kg) plus<br>continuous infusion of 0.1% R<br>at 2 mL/hour   |
|                          | Nardiello, 2018<br>(66)           | Α    | Sternal reconstruction (pectum excava-<br>tum/pectum carinatum) | 2      | T <sub>5</sub> | SD        | BL         | 0.25% B 20 mL on each side   |
|                          | Forero, 2017 (22)                 | С    | Post-thoracotomy chronic pain                                   | 7      | T5-T6          | SD        | U          | R. Doses varied between 0.25<br>and 0.50%, and 20-30 mL<br>volume  |
|                          | Hamilton, 2017<br>(17)            | Α    | Costal fractures  | 1      | T <sub>5</sub> | С         | U          | 0.125% B 10 mL/h   |
|                          | Ahiskalioglu,<br>2020 <u>(23)</u> | С    | Chronic thoracic oncologic pain                                 | 1      | T5             | С         | U          | 0.25% B 20 mL plus 0.250%<br>B infusion 8 mL/h and 5 mL/h<br>boluses   |
|                          | Ueshima, 2018<br>(21)             | Α    | Acute pain management after posther-<br>petic neuralgia         | 1      | T6             | SD        | U          | 0.25% LB 10 mL   |
|                          | Bonvicini, 2017 <u>(6)</u>        | Α    | Siliconoma excision + breast implant                            | 1      | T5             | SD        | U          | R 75 mg + M 20 mg 25 mL  |
| Breast                   | Nair, 2018 <u>(15)</u>            | А    | Modified radical mastectomy + lymph node resection              | 5      | T4             | SD        | U          | 0.25% B 30 mL  |
|                          | Ueshima, 2018<br>(73)             | Α    | Radical mastectomy  | 1      | T4             | SD        | U          | 0.25% L10 mL   |

| Comprised anatomical site | Author/Year                   | Pain | Surgical model/Intervention  | Sample | Level          | SD vs. CC | Laterality | Dose and anesthetic  |
|---------------------------|-------------------------------|------|--|--------|----------------|-----------|------------|--|
| Spine                     | Ueshima, 2017<br>(38)         | Α    | Thoracic vertebral surgery (lumbar stenosis and spinal cord tumor resection) | 2      | T <sub>5</sub> | SD        | BL         | 0.375% L 40 mL (20 mL each side)   |
|                           | Canturk, 2019 <u>(39)</u>     | Α    | Spondylolisthesis correction   | 1      | L1             | SD        | BL         | 0.25% B 10 mL, 1% P 10 mL  |
|                           | Hannig, 2018 <u>(7)</u>       | Α    | Laparoscopic cholecystectomy   | 3      | T7             | SD        | BL         | 0.5% R 20 mL   |
|                           | Chin, 2017 <u>(2)</u>         | А    | Laparoscopic bariatric surgery   | 3      | Т7             | SD/SD/C   | BL         | 1% R 5 mL + 2% L 5 mL + 0.9%<br>NSS 10 mL / 0.5% R 20 mL /<br>0.5% R 20 mL   |
|                           | Tulgar, 2018 <u>(58)</u>      | Α    | Laparoscopic abdominal surgery   | 3      | Т8             | SD        | BL         | 0.5% B 10 cm3, 2% L 5 cm3,<br>0.9% NSS 5 cm3   |
|                           | Restrepo, 2017<br>(64)        | А    | Major abdominal surgery (open radical cystoprostatectomy)                    | 1      | Т8             | С         | BL         | 2% L3 mL + 0.25% B10 mL + continuous infusion of 0.1% B at 6 mL/h  |
|                           | Aksu, 2019 <u>(67)</u>        | Α    | Laparoscopic cholecystectomy   | 3      | T7             | SD        | U          | 0.25% B at 0.5 mL/kg   |
| Abdomen and pelvis        | Hernández, 2018<br>(68)       | Α    | Inguinal hernia repair (anesthetic)  | 1      | T6             | SD        | U          | o.4 mL/kg (1:1 solution of<br>o.25% B and 1% L)  |
|                           | Chin, 2017 (18) A             |      | Ventral hernia repair  | 4      | T <sub>7</sub> | SD        | BL         | 0.5% R + adrenaline 5 μg/ mL<br>20 mL/ 0.5% R + dexametha-<br>sone 4 mg 30 mL / 0.5% R +<br>dexamethasone 4 mg 20 mL/<br>R 0,5 % + dexamethasone 4<br>mg 20 mL |
|                           | Selvi, 2018 <u>(75)</u>       | Α    | Cesarean section   | 1      | T11            | SD        | BL         | 0.5% B 15 mL + 2% L 5 mL+<br>0.9% NSS 5 mL   |
|                           | Altinpulluk, 2018<br>(63)     | Α    | Cesarean section   | 1      | T9             | SD        | BL         | 0.25% B 20 mL  |
|                           | Forero, 2017 <u>(24)</u>      | С    | Chronic shoulder pain  | 1      | T2             | SD        | U          | 0.5% B 20 mL   |
|                           | Tulgar, 2018 <u>(69)</u>      | Α    | Hip arthroplasty   | 1      | L4             | SD        | U          | 0.5% B 15 mL, 2% L 5 mL, 0.9%<br>NSS 10 mL   |
| Limbs                     | Bugada, 2018 <u>(70)</u>      | А    | Hip replacement/surgical revision of recurrent hip dislocation               | 2      | L4             | С         | U          | 0.75% R 25 mL, PCA infusion<br>0.5 mL/h + 20 mL bolus every<br>3 h   |
| Limbs                     | Darling, 2018 <u>(71)</u>     | Α    | Surgical hip dislocation and femur osteotomy                                 | 1      | T12            | С         | U          | 0.2% R 10 mL   |
|                           | Balaban, 2019<br>(72)         | Α    | Total knee arthroplasty  | 1      | L4             | С         | U          | 0.375% B 30 mL   |
|                           | Am J Emerg Med.,<br>2019 (74) | С    | Regional complex syndrome in right ankle and foot                            | 1      | L4             | SD        | U          | 0.5% B + 2% L 30 mL  |

A: acute; B: bupivacaine; BL: bilateral; C: chronic; CC: continuous catheter; L: lidocaine; LB: levobupivacaine; NSS: 0.9% saline solution; PCA: patient-controlled analgesia; R: ropivacaine; 0.9%; SD: single dose; U: unilateral; VATS: video-assisted thoracoscopic surgery.

**Source:** Authors.

# CLINICAL APPLICATIONS OF THE ERECTOR SPINAE BLOCK

The technique is apparently safe and easy to implement (4,8); however, there are no studies with large numbers of patients supporting its application in certain conditions. We describe its use in the setting

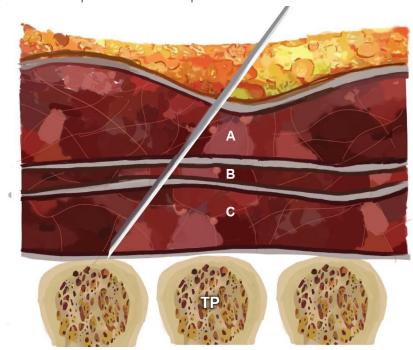
of chronic pain (1-4,18) and cardiac, thoracic, abdominal, breast and limb surgery, with evidence from randomized clinical trials (RCT) in some of these areas (20).

In the original report (1) and in other similar reports (21), the ESP block was performed in adult patients with chronic neuropathic pain (postherpetic neuralgia

and chronic neuropathic pain secondary to rib fractures). Later, Forero described a case series in post-thoracotomy chronic neuropathic pain (22), followed by new publications showing favorable results (23), including chronic shoulder pain (24).

In video-assisted thoracic surgery (VATS) for lobectomy, adequate pain

**FIGURE 1.** Schematic representation of needle position for the ESP block.



A: trapezius; B: rhomboid major; C: erector spinae plane. TP: transverse process. **Source:** Authors.

**FIGURE 2.** Ultrasound technique and view of the transverse process and the three paraspinal muscles superficial to it, identified from superficial to deep.



A: trapezius; B: rhomboid major; C: Erector spinae at the level of the transverse process of T6. **Source:** Authors.

modulation has been documented (1). Reports have described the use of this block in cases where epidural analgesia or any other regional technique is more risky (25,26), is contraindicated or is more technically challenging (27). One RCT compared ultrasound-guided ESP block plus intravenous analgesia in 60 patients undergoing VATS. It was found that the use of opioids at 1, 2, 4, 8, 16 and 24 hours, and dynamic and static pain scores at those time points, were statistically lower in the ESP block group (5 patients out of 30) than in the control group (22 patients out of 30) (28). In the latter, the rates of nausea and pruritus were higher and there were no differences between the groups in terms of other adverse effects.

When the serratus plane and the ESP were compared for VATS in 60 adult patients, a significantly lower score for static pain as well as a lower dynamic pain score were found in the ESP group when compared to the serratus plane group 4-6 hours after the intervention. Similarly, the time to first analgesic requirement was longer in the ESP group, with no relevant side effects (29).

Despite its good results, when compared to the paravertebral block (PVB), the ESP block is not as favorable. An RCT published in 2020 (30) compared ESP vs. PVB vs. intercostal nerve block (ICNB) in 75 patients undergoing VATS and showed better postoperative pain (POP) control in the PVB group and a higher need for rescue analgesia in the ESP group, with no differences in the comparison between ESP and ICNB. However, pain scores were similar at different POP time points in the three groups.

## Thoracotomy for lobectomy

The successful use of this technique as rescue has been reported in cases of failed thoracic peridural analgesia (16). According to some publications, the failure rate of the peridural neuraxial technique ranges between 11.2% (31) and 32% (32);

for this reason, the continuous ESP block is an option that offers excellent results in this group of patients. Likewise, the use of this block in two thoracic levels has been described (32), but RCTs showing superiority when compared with single-level injection are needed. Case reports have been described in POP analgesia after thoracotomy for lung transplant (33). In summary, in thoracic surgery, there is support for the use of the ESP block in VATS, thoracotomy for lobectomy, lung transplantation, and as rescue in cases of failed peridural analgesia.

#### **Cardiac surgery**

A prospective, randomized study assigned 50 patients to two groups: continuous epidural thoracic analgesia and continuous bilateral ESP block for the management of perioperative pain. Dynamic and static pain scores were similar in both groups at different time points during the first 12 hours; however, after 24 hours and up until 48 hours, pain was lower and statistically significant in the ESP block group when compared to epidural analgesia. There were no differences in ICU length of stay or the need for invasive mechanical ventilation (MV) (34). The ESP block used as part of multimodal analgesia in patients undergoing mitral and/or tricuspid valve repair through right minithoracotomy was analyzed in a case report (35) and also in a cohort study, which found that the time on MV as well as the ICU length of stay were shorter in the ESP block group (36).

An RCT published in 2019 compared bilateral ESP block vs. conventional analgesia in 106 patients undergoing cardiac surgery with by-pass circulation. In the ESP group, ultrasound-guided block at the level of T6 was performed before anesthetic induction. The results showed lower scores on the numerical pain scale (NPS) and longer analgesia duration in the bilateral ESP block group (37).

## **Spinal surgery**

Current evidence is insufficient to support the generalized use of the ESP block; however, cases of its use have been described in spinal cord tumor resection surgery, laminoplasty for spinal canal stenosis (38) and correction of spondylolisthesis, with good results, opioid sparing and no complications (39). To this date, two RCTs (40,41) have been conducted, showing promising analgesic results in lumbar spine surgery, with no adverse effects. Notwithstanding the above, a systematic review carried out in 2020 concluded that the effectiveness and safety of this block for lumbar spine surgery are controversial (42).

#### **Breast surgery**

The ESP block has been gaining importance in breast surgery as a result of adequate analgesic response (6) and opioid sparing effect. RCTs comparing the ESP block with other techniques such as PVB (44) or intravenous techniques have been performed in recent years, showing superiority for fascial blocks when compared with intravenous strategies, as well as similar results in terms of pain control and opioid use (45,46).

In radical mastectomy, some RCTs comparing pectoralis nerve block (PECS) vs. ESP block have shown better POP results in the PECS group (47-50). Although no differences have been reported (51) when comparing the ESP and paravertebral blocks in terms of POP opioid use at 24 hours, pain scores, or PONV, shorter localization time by anesthetists with (44) or without (52) experience in regional techniques has been described in the case of the ESP block. Moreover, a comparison between the ESP block and intravenous analgesia (53) showed significantly lower POP morphine use and lower scores on the numerical pain scales in the first 4 hours in patients receiving the ESP block (54).

One RCT (55) compared the quality of POP recovery in patients taken to

modified radial mastectomy using LA vs. placebo, with better quality of recovery in the group assigned to the LA technique according to the QoR-15 questionnaire. A systematic review and meta-analysis (47) found that, in this surgical model, the ESP block offers superior analgesia and lower POP oral morphine use when compared to no use of regional techniques, as well as similar analgesic effects as those of the PVB, with absent risk of pneumothorax and other complications. The dose and useful anesthetic concentration are not clear yet; however, a recent RCT (56) compared two anesthetic concentrations in the ESP block, showing that 0.375% bupivacaine concentrations offer better analgesic results than 0.25% concentrations.

In other surgical models such as reduction mastectomy, a double-blind RCT (57) of 44 women comparing tumescent anesthesia vs. ESP block in terms of POP analgesia requirement, pain scores and patient satisfaction showed that the use of tramadol was significantly lower in the ESP block group as was also the case with pain scores at several time points during the first 24 hours and the need for additional analgesia, with improved patient satisfaction.

Considering that the erector spinae muscle extends towards the inferior spinal region, the ESP block at the level of T7-T8 allows the spread of the anesthetic mix to the inferior thoracoabdominal nerves that provide abdominal innervation. Moreover, the mechanism of action includes penetration of the LA into the paravertebral space, with action on the ventral and dorsal branches as well as the communicating branches containing sympathetic nerve fibers, thus providing sensory, somatic and visceral blockade in abdominal surgery (2). Against this backdrop, a report of 3 patients taken to laparoscopic bariatric surgery with adequate analgesic response to the ESP block has been described (2). Lower opioid requirements have been reported in case series (7,58) using this technique in patients undergoing laparoscopic ventral hernia repair (2) and in different laparoscopic surgery models.

## Laparoscopic cholecystectomy

Three RCTs have been found: the first (59) with 76 patients, comparing the ESP block vs. transversus abdominis plane (TAP) block, showed that the POP use of tramadol and pain scores were significantly lower in the ESP group. The second study compared the same regional techniques in 72 patients in terms of the NRS score, paracetamol and tramadol consumption and the need for rescue analgesia (60) and it showed that pain intensity was similar between the two groups in the first 3 hours, while the consumption of additional analgesics was comparable. A third RCT (61) with 36 patients compared the ESP block vs. multimodal analgesia and showed that pain on the NRS was lower in the ESP block group during the first 3 hours, with no differences after that time; in turn, tramadol consumption and additional analgesic requirements were lower in the ESP group. These conclusions were also supported by a meta-analysis (62).

## Lower abdominal surgery

In lower abdominal surgery, particularly in gynecological surgery for cesarean section, one case of bilateral ESP block for effective and lasting POP analgesia in a patient taken to an emergent procedure under general anesthesia (63) was found. Another case described a male patient taken to major abdominal surgery (open radical cystoprostatectomy) who received continuous analgesia with bilateral ESP block with very good analgesic results (64).

## **Pediatric patients**

In these patients, the ESP block appears to be a safe and effective analgesic option, especially in thoracotomy (3,14,65). In other thoracic surgery models, the use of the ESP block has been described in pediatric patients undergoing pectum excavatum and pectum carinatum correction with

scores on the visual analog scale lower than 4 and absence of intraoperative and longterm postoperative opioid requirement (66). Likewise, case series (67) of pediatric patients described laparoscopic cholecystectomy with regional analgesia provided by the ESP block, showing adequate POP pain control and patient satisfaction. Also, a case report (68) described the use of a single-dose ESP block as anesthetic method for inguinal hernia repair in a two-month-old patient (born at 29 weeks of gestation) weighing 2.5 kg, with hemodynamic stability during the 35 minutes of the procedure, or al intake tolerance over the following 6 hours and a pain score of o on the FLACC (Face, Legs, Activity, Cry, Consolability) scale over the next 24 hours.

#### **Lower extremities**

Finally, in surgery involving the lower limbs, some published case reports show potential analgesic effectiveness of the ESP block, considering LA spread to the lumbar plexus, in surgical models such as hip arthroplasty (69) and knee arthroplasty (72); however, studies of better methodological quality are needed in order to arrive at a conclusion regarding the role of the ESP block in these procedures.

## **COMPLICATIONS**

The ESP block appears to avoid the types of complications that can arise with the use of other regional techniques, including hypotension, permanent spinal cord injury and urinary retention with epidural analgesia, epidural spread, vascular puncture in PVB, and pneumothorax in intercostal nerve blocks and PVB (8,47). However, cases of pneumothorax (73) and priapism (74) have been reported in two patients subjected to the ESP block.

One case of motor blockade was recently described as an unexpected side effect of the ESP block in a patient undergoing cesarean section who refused neuraxial techniques (75). During her stay

in the postanesthetic care unit (PACU), bilateral motor weakness and sensory deficit between the T9 and L3 dermatomes were documented. Motor strength began to return after 13 hours, with complete resolution at 16 hours. The authors of this case propose LA infiltration into the lumber plexus as the first explanation, or spread through the epidural space, considering that, on neurological examination, the patient showed weakness of the psoas, iliac and quadriceps muscles, confirming compromise of the spinal nerves at L1, L2 and L3, and of the femoral nerve.

The absence of important blood vessels and neural structures in immediate proximity minimizes concerns regarding the development of clinically significant hematomas. However, until more clinical data are available, caution is recommended in patients with coagulation disorders or who are receiving perioperative anticoagulation (76).

Although complications have been described generally with the in-plane ultrasound-guided approach, the use of the ESP with the out-of-plane approach using the convex transducer for hip (69), shoulder, thoracic, breast and abdominal surgery has shown a similar rate of efficacy and complications (77).

## CONCLUSION

The ESP block is presented as an effective analgesic management option in anesthesia and should be considered as part of the multimodal analgesia strategies on the basis of its good analgesic results, low incidence of complications and less side effects when compared with epidural analgesia, and its wide applications in different surgical models. Therefore it may be considered as a safe, simple and optimal analgesic alternative (1,3,8).

Larger studies and more in-depth research are required in order to gain more insight into the mechanism of action, side effects and duration of the effects of this intervention.

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#### **Authors' contributions**

**LPCE:** Conception of the original project, planning of the study, interpretation of the results, drafting and approval of the final manuscript.

**GGD** and **ZBM**: Planning of the study, interpretation of the results, drafting and approval of the final manuscript.

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#### **Conflict of interest**

None declared.

#### **Presentations**

None declared.

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