STUDY PROTOCOL

EFFICACY OF VASOCONSTRICTOR PERIARTICULAR INFILTRATION (PVI) VERSUS ERECTOR SPINAE PLANE BLOCK (ESP) IN REDUCING BLEEDING AND POSTOPERATIVE PAIN CONTROL IN LUMBAR ARTHRODESIS SURGERY. RANDOMIZED CLINICAL TRIAL

Protocol version	2
Document date	July 18, 2025
Protocol code	**IIBSP-IPV-2024-178**
EU-CT number	**2025-521572-56-00**
Short title	**Efficacy of PVI versus ESP block in reducing bleeding and analgesia in lumbar arthrodesis surgery**
Sponsor	Research Institute of Hospital de la Santa Creu i Sant Pau – IIB Sant Pau c/ Sant Quintí, 77-79 08041 Barcelona, Spain Phone: +34 93 553 78 69
Coordinating investigator	Mireia Rodríguez Prieto, MD Department of Anesthesiology, Resuscitation and Pain Therapy Hospital de la Santa Creu i Sant Pau c/ Sant Antoni Maria Claret, 167 08025 Barcelona, Spain Phone: +34 932919000 (Ext 7541) Email: anestesiologia@santpau.cat

COMPLIANCE WITH GOOD CLINICAL PRACTICE

This trial is designed to comply with ICH E6 (R2) Good Clinical Practice Guidelines, as implemented in the European Union on June 14, 2017 (EMA/CHMP/ICH/135/1995 guideline); Regulation (EU) No. 536/2014 of the European Parliament and of the Council of April 16, 2014 on clinical trials; Royal Decree 1090/2015 on clinical trials with medicinal products, Research Ethics Committees with medicinal products, and the Spanish Clinical Studies Registry; as well as applicable local regulatory requirements.

1. Summary

1.1. Trial identification	EU-CT number: 2025-521572-56-00 ***Protocol code:*** **IIBSP-IPV-2024-178** Protocol version: 2. Document date: july18, 2025
1.2. Clinical trial tittle	EFFICACY OF VASOCONSTRICTOR PERIARTICULAR INFILTRATION (PVI) VERSUS ERECTOR SPINAE PLANE BLOCK (ESP) IN REDUCING BLEEDING AND POSTOPERATIVE PAIN CONTROL IN LUMBAR ARTHRODESIS SURGERY. RANDOMIZED CLINICAL TRIAL
1.3. Sponsor indentification	Research Institute of Hospital de la Santa Creu i Sant Pau – IIB Sant Pau c/ Sant Quintí, 77-79 08041 Barcelona, Spain Phone: +34 93 553 78 69
1.3.1. Monitoring responsable	UICEC Sant Pau Research Institute of Hospital de la Santa Creu i Sant Pau C/ Sant Antoni Maria Claret, 167 08025 Barcelona, Spain Phone: + 34 93 553 76 34 Email: uicec@santpau.cat
1.4. Founding source	No external funding is required, as ESP block and PVI are part of standard clinical practice in spine surgery and trauma procedures at Hospital de la Santa Creu i Sant Pau. Office supplies will be provided by the Department of Anesthesiology. Patient recruitment and follow-up will be conducted by staff from the Departments of Anesthesiology, Resuscitation and Pain Therapy and Traumatology. The cost center will be the Department of Anesthesiology, Resuscitation and Pain Therapy
1.5. Principal investigator	Mireia Rodríguez Prieto, MD Department of Anesthesiology, Resuscitation and Pain Therapy Hospital de la Santa Creu i Sant Pau c/ Sant Antoni Maria Claret, 167

	08025 Barcelona, Spain Phone: +34 677896054 Email: mrodriguezpr@santpau.cat
1.6. Ethics committee	Clinical Research Ethics Committee of Hospital de la Santa Creu i Sant Pau.
1.7. Study sites	Hospital de la Santa Creu i Sant Pau. Hospital Quirón Salud de Murcia.
1.8. Rationale and relevance	Management of bleeding and postoperative pain after lumbar arthrodesis remains a challenge. This surgery involves significant blood loss, which increases with the number of instrumented levels, decompression procedures, and/or osteotomies. Regional blocks are a cornerstone of multimodal analgesia in this procedure, which is associated with severe postoperative pain. The PVI block may reduce intraoperative bleeding during spinal fusion surgery, decreasing the risk of anemia and transfusion requirements, and facilitating early rehabilitation and return to normal activities. Both PVI and ESP block are analgesic strategies that may provide effective postoperative pain control, which is essential for functional recovery. The drug used in both blocks will be ropivacaine, a commonly used local anesthetic approved in Spain for these indications. Epinephrine will be added at a concentration of 1:200,000, a combination commonly used in neuraxial, peripheral, or intra-articular blocks. Commercial preparations of bupivacaine (with a higher cardiotoxic profile than ropivacaine) combined with epinephrine at the same concentration have been widely used in regional anesthesia without complications. There are no studies in the literature comparing these two blocks. The study hypothesis is that the PVI block is superior to the ESP block in reducing bleeding and improving postoperative analgesia.
1.9. Study design. Phase	Prospective, randomized, controlled, parallel-group clinical trial with blinded third-party assessment. National multicenter study. The control group will be active. Outcome assessment will be performed by an investigator blinded to group allocation. Randomization will be performed using the StatsDirect statistical package, ensuring a balanced design with unpaired random allocation to intervention or control groups.

1.10. Primary Objective	To compare the efficacy of PVI versus ESP block in reducing bleeding and improving postoperative pain control in lumbar arthrodesis surgery.
1.11. Investigational and Control Treatments	Ropivacaine with epinephrine (1:200,000) will be used in both blocks. A single dose will be administered prior to surgery, under general anesthesia, with the patient in the prone position. • **PVI block:** administered in the retrolaminar space, thoracolumbar fascia, supraspinous ligament, and subcutaneously at the surgical incision site. • **ESP block:** administered at the level of the transverse processes. Both techniques aim to block the dorsal rami of the spinal nerves. ESP has proven efficacy for postoperative pain but does not affect bleeding. PVI may achieve both analgesia and bleeding reduction.
1.12. Primary Outcome Measure	Intraoperative bleeding, calculated from suctioned fluids and surgical sponges after subtracting irrigation fluids.
1.13. Study Population and sample size	Assuming 80% power (β=0.2) and α=0.05, 31 patients per group are required to detect a minimum 30% reduction in intraoperative bleeding, accounting for 10% dropout. Eligible patients will be those undergoing elective lumbar arthrodesis involving up to 3 instrumented levels. Recruitment will occur during the pre-anesthesia visit.
1.14. Estatistical Analysis	Statistical analysis and randomization will be performed by Sergi Sabaté Tenas. Categorical variables: number and percentage. Continuous variables: mean ± SD or median (IQR). Statistical tests: • Chi-square or Fisher's exact test • Student's t-test or Mann–Whitney U test • Repeated measures ANOVA adjusted for confounders Analysis will follow the intention-to-treat principle.
1.15. Ethical Considerations	The study will follow international ethical standards, the Declaration of Helsinki, and Good Clinical Practice guidelines.

	Participants (or legal representatives) will be informed about: • Study purpose • Procedures • Risks and benefits • Voluntary participation They may withdraw at any time without affecting their care. Regional anesthesia techniques are widely accepted, effective, and associated with low complication rates. This study does not introduce additional risk beyond standard clinical practice.
1.16. Treatment Duration	18 months for recruitment and 3 months for data analysis.
1.17. Safety Assessment	Low-intervention clinical trial.
1.18. Study Timeline	• First patient: after ethics approval • Last patient inclusion: upon reaching sample size • End of study: hospital discharge of last patient • Total duration: ~18 months.

Glosary of Terms

Lumbar arthrodesis surgery:
A procedure involving permanent fusion of two or more lumbar vertebrae to eliminate motion.

Includes:

- Nerve decompression
- Implant placement (screws, rods)
- Bone grafting

Erector Spinae Plane Block at Lumbar Level (ESP)

The erector spinae plane block (ESP) is included among multimodal postoperative analgesia strategies in multiple surgical procedures, such as thoracic and abdominal surgery, since its description by Forero et al. in 2016. More recently, the block has been described at the lumbar level, with good postoperative analgesic results following lumbar spine fixation surgery. The objective of this technique is to block the dorsal ramus of the spinal nerve (DRSN).

After performing aseptic measures at the puncture site, to perform the ESP block at the lumbar level, the ultrasound probe is placed in the interlaminar sagittal plane, identifying the sacrum, and then moved cranially along the laminae of L5 and L4. Subsequently, the transducer is lateralized to identify the different transverse processes. The block will be performed at the levels to be instrumented and one level above the instrumentation. The needle (21G x 11 cm Pajunk) is inserted in-plane, from cranial to caudal direction, until reaching the target transverse processes, injecting the drug between the transverse process and the erector spinae muscle. After negative aspiration, correct spread of the drug will be confirmed. The process is repeated on the contralateral side.

Vasoconstrictor Periarticular Infiltration (PVI)

The vasoconstrictor periarticular infiltration technique has been developed recently. The objective of this technique in lumbar spine surgery is to create chemically induced ischemia and to provide the analgesic benefits derived from blocking the dorsal ramus of the spinal nerve (DRSN), which is involved in postoperative pain in spine surgery.

The PVI block in lumbar spine surgery consists of bilaterally injecting a dilution of local anesthetic and epinephrine into deep periarticular planes (retrolaminar space, thoracolumbar fascia, supraspinous ligament) and superficially into the surgical incision area. After applying aseptic measures, the block is performed bilaterally under ultrasound guidance, using a (21G x 11 cm Pajunk) needle, 15–30 minutes before the surgical incision (see figure).

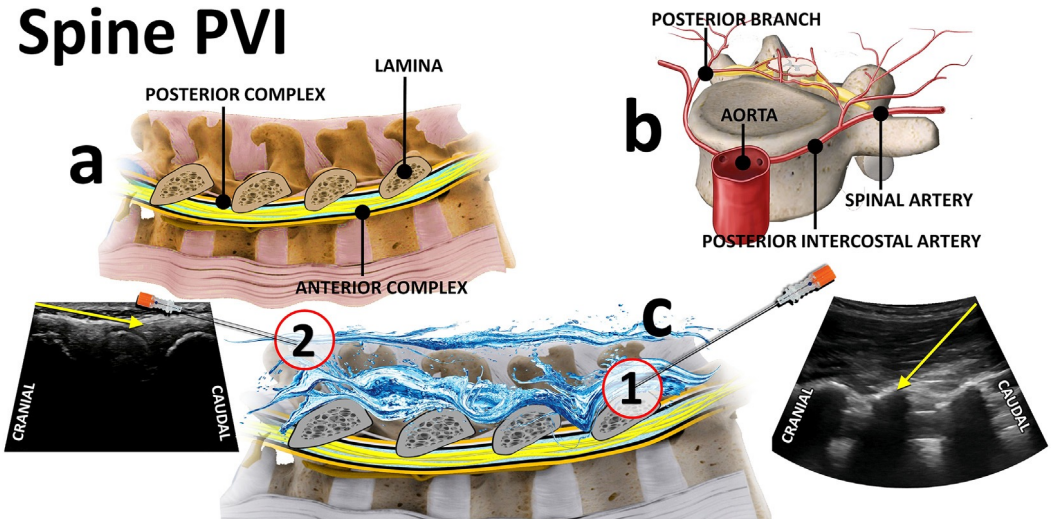
Spine PVI
a
POSTERIOR COMPLEX
LAMINA
ANTERIOR COMPLEX
b
POSTERIOR BRANCH
AORTA
SPINAL ARTERY
POSTERIOR INTERCOSTAL ARTERY
c
1
2
CRANIAL
CAUDAL
CRANIAL
CAUDAL

Table of contents

3. General Information

3.1. Study Title

Efficacy of Vasoconstrictor Periarticular Infiltration (PIV) Versus Erector Spinae Plane Block (ESP) in Reducing Bleeding and Controlling Postoperative Pain in Lumbar Arthrodesis Surgery: A Randomized Clinical Trial

Protocol Code: IIBSP-IPV-2024-178

Protocol Version: 2

Date: July 18, 2025

3.2. Description of Study Products

3.2.1. Experimental Drug

- **International Nonproprietary Name (INN):**
  Periarticular vasoconstrictor infiltration (PVI) with ropivacaine 0.2% and adrenaline 1:200,000
- **Chemical Name:**
  Ropivacaine hydrochloride monohydrate
- **Molecular Formula:**
  C17H26N2O
- **Qualitative and Quantitative Composition:**
  Each mL of solution contains 2 mg of ropivacaine hydrochloride monohydrate and 0.005 mg of epinephrine (adrenaline)
- **Pharmaceutical Form:**
  Injectable solution, clear and colorless
  pH: 3.8–5.8
  Osmolality: 252–308 mOsm/kg
- **Dose and Route of Administration:**
  Two infiltrations (bilateral block) at the retrolaminar level, thoracolumbar fascia, supraspinous ligament, and subcutaneous tissue.
  Volume: 150–200 mL depending on the number of instrumented levels

3.2.2. Control Drug

- **International Nonproprietary Name (INN):**
  Erector spinae plane block (ESP) with ropivacaine 0.2% and adrenaline 1:200,000
- **Chemical Name:**
  Ropivacaine hydrochloride monohydrate
- **Molecular Formula:**
  C17H26N2O

- **Qualitative and Quantitative Composition:**
  Each mL of solution contains 2 mg of ropivacaine hydrochloride monohydrate and 0.005 mg of epinephrine (adrenaline)
- **Pharmaceutical Form:**
  Injectable solution, clear and colorless
  pH: 3.8–5.8
  Osmolality: 252–308 mOsm/kg
- **Dose and Route of Administration:**
  Two infiltrations (bilateral block) at the level of the transverse process
  Volume: 20 mL per side

3.2.3. Supplier of the Medication

Hospital de la Santa Creu i Sant Pau
The drugs used are part of routine clinical practice and are available in all operating rooms

3.3. Sponsor Information

Research Institut of Hospital de la Santa Creu i Sant Pau – IIB Sant Pau
C/ Sant Antoni Maria Claret, 167
08025 Barcelona, Spain
Phone +34 93 553 78 69

3.4. Monitoring Responsible Information

UICEC Sant Pau
Research Institut of Hospital de la Santa Creu i Sant Pau
C/ Sant Antoni Maria Claret, 167
08025 Barcelona, Spain
Phone: +34 93 553 76 34
Email: uicec@santpau.cat

3.5.2. Principal Investigator(s)

Mireia Rodríguez Prieto; MD
Department of Anesthesiology and Resuscitation
Hospital de la Santa Creu i Sant Pau
Barcelona, Spain
Phone: +34 677 896 054
Email: mrodriguezpr@santpau.cat

Vicente Roqués Escobar
Department of Anesthesiology and Resuscitation
Hospital Quirón Salud Murcia
C/ Miguel Hernández, 12
30011 Murcia, Spain

Mobile: +34 639 322 529
Email: virroes@gmail.com

3.5.3. Sub-Investigators

Adrià Font Gual
Laura Parrilla Quiles
Josep María Gil Sánchez
Marisa Moreno Bueno
Irina Millan Moreno
Clara Martínez García
Sergi Núñez Sacristan
Gerard Moreno Giménez
Department of Anesthesiology and Resuscitation
Hospital de la Santa Creu i Sant Pau
Barcelona, Spain

Juan José Velázquez Fragoso
Jesús David Narváez Saldivia
Department of Orthopedic and Trauma Surgery
Hospital de la Santa Creu i Sant Pau
Barcelona, Spain

3.6. Expected Duration of the Study

The estimated recruitment period will be 18 months. The last patient will complete the study 5–7 days after inclusion, coinciding with hospital discharge.

- **First patient inclusion:** Upon approval by the Ethics Committee
- **Last patient inclusion:** Upon completion of the planned sample size
- **End of participation for the last patient:** At hospital discharge following lumbar arthrodesis
- **End of study:** Upon discharge of the last included patient
- **Total study duration:** Approximately 18 months

4. Rationale and Objectives

4.1. Study Rationale

Significant blood loss remains a common surgical risk in major orthopedic procedures, with well-recognized associated costs and complications. Up to 90% of patients undergoing major orthopedic surgery develop postoperative anemia. This risk is higher in procedures where the use of a tourniquet is not feasible, such as spine surgery, hip and shoulder arthroplasty, among others. In lumbar arthrodesis surgery, the main concerns for the anesthesiologist are intraoperative

bleeding and postoperative pain, with regional anesthesia techniques forming the cornerstone of multimodal analgesia in this setting.

Lumbar spinal canal stenosis due to degenerative spondylolisthesis is one of the most common indications for lumbar spinal fusion surgery. This procedure is characterized by significant blood loss due to the rich vascularization and fragile venous plexus of vertebral cancellous bone. Lumbar arthrodesis is among the top ten surgical procedures requiring transfusion, with a transfusion rate of approximately 30%. Blood loss increases with the number of instrumented levels, as well as when decompression (laminectomy) and/or osteotomies are performed. Reported mean blood loss ranges from approximately 500 to 2000 mL, and is higher in instrumented compared to non-instrumented procedures.

To minimize intraoperative blood loss and reduce transfusion-related morbidity, antifibrinolytic agents such as tranexamic acid have become standard practice in orthopedic surgery. Other strategies, such as permissive hypotension, are not recommended due to their association with adverse outcomes, including delirium, renal failure, cardiovascular events, and death when systolic blood pressure falls below 100 mmHg.

In 2020, Mazy et al. published a randomized clinical trial aimed at reducing blood loss in pediatric scoliosis surgery. The study compared large-volume subcutaneous and intramuscular infiltration of local anesthetics (bupivacaine and lidocaine) with adrenaline versus placebo. Results showed a significant reduction in blood loss (38%), transfusion requirements (23%), and operative time (23%), without associated complications and with high surgeon satisfaction due to improved surgical field conditions.

More recently, vasoconstrictor periarticular infiltration (PIV) has been developed based on the principles of tumescent anesthesia and the WALANT (Wide Awake Local Anesthesia No Tourniquet) technique. Tumescent anesthesia consists of the infiltration of large volumes of diluted local anesthetic with epinephrine, providing both adequate anesthesia and significant reduction in perioperative bleeding. WALANT has gained popularity in orthopedic procedures due to its advantages in outpatient settings and cost-effectiveness, with minimal reported risks of local anesthetic systemic toxicity (LAST) or vasoconstrictor-induced ischemia.

In lumbar spine surgery, the PIV technique aims to induce chemical ischemia while also providing analgesia through blockade of the dorsal rami of the spinal nerves, which are involved in postoperative pain. The technique consists of bilateral infiltration of a solution of ropivacaine and epinephrine into deep periarticular planes (retrolaminar space, thoracolumbar fascia, supraspinous ligament) as well as superficial infiltration at the surgical incision site. Approximately 20 mL per vertebral level is administered in deep planes, along with 20–40 mL in subcutaneous tissue, resulting in a total volume of 150–200 mL depending on the number of levels instrumented.

The block is performed under ultrasound guidance 15–30 minutes prior to surgery to achieve a “chemical tourniquet” effect and reduce perioperative bleeding, while also providing analgesia.

PIV is considered a simple, safe, and reproducible technique. Minor cardiovascular effects such as transient hypertension or tachycardia are infrequent and short-lived, and no major cardiovascular complications have been reported. Epinephrine provides local vasoconstriction lasting 1–2 hours, with peak effect at approximately 30 minutes.

Concerns regarding systemic toxicity appear minimal, as studies on tumescent anesthesia and local infiltration analgesia (LIA) have shown low plasma levels of local anesthetics. The use of multiple injection sites and local vasoconstriction likely reduce systemic absorption. Although infection risk has been discussed in relation to LIA, this is mainly associated with postoperative catheter use, which is not applicable in this study. Contraindications include local infection and caution is advised in patients with compromised peripheral circulation, renal insufficiency, connective tissue diseases, or vasculitis.

PIV is increasingly used in hip, knee, and spine surgery and has been associated with reduced intraoperative and postoperative bleeding. It is considered a cost-effective technique despite requiring multiple injections and additional procedural time. In our institution, its use in lumbar arthrodesis has shown favorable results without complications and with high acceptance among the surgical team.

In addition to bleeding, postoperative pain management remains a major challenge and significantly impacts surgical outcomes. Lumbar fusion surgery is associated with moderate to severe postoperative pain during the first 48 hours. Opioids remain the standard of care, although their use is associated with adverse effects. Pain intensity is influenced by preoperative pain, opioid use, surgical duration, number of levels treated, and individual pain perception.

Effective pain control is essential to reduce opioid consumption, facilitate recovery, and shorten hospital stay. Multimodal analgesia protocols, including regional nerve blocks, are fundamental. The most widely used technique is the erector spinae plane (ESP) block, which provides analgesia through action on the dorsal rami of the spinal nerves.

The ESP block is performed at the level of the transverse process, typically one level above the surgical site, with bilateral administration of 20 mL per side. Higher volumes are avoided due to the risk of spread to the paravertebral space, which may interfere with intraoperative neuromonitoring.

Unlike ESP, the retrolaminar approach used in PIV aligns with the surgical dissection plane, potentially improving hemostatic efficacy. The more lateral ESP approach may be less effective in achieving this effect and carries a risk of affecting neuromonitoring due to local anesthetic spread.

Current evidence comparing ESP and retrolaminar blocks shows similar analgesic outcomes in breast surgery and rib fractures, and potential superiority of the retrolaminar block in lumbar arthrodesis. Additionally, retrolaminar block has shown favorable results in lumbar discectomy within opioid-free anesthesia and ERAS protocols.

In summary, our clinical experience suggests that PIV provides a bloodless surgical field while offering postoperative analgesia comparable to ESP. Given the recent introduction of PIV, there is currently no published evidence directly comparing both techniques in terms of bleeding reduction and analgesic quality, which constitute the objectives of this study.

4.2. Study objectives:

The aim of this study is to compare intraoperative bleeding and postoperative pain between two regional anesthesia techniques commonly used in lumbar arthrodesis surgery, as described in the protocol.

- **PVI Block (Periarticular Vasoconstrictor Infiltration)**

  The PVI block in lumbar spine surgery consists of bilateral infiltration of a solution of local anesthetic and epinephrine at the vertebral levels to be instrumented. The infiltration is performed in deep periarticular planes (retrolaminar space, thoracolumbar fascia, supraspinous ligament) and superficially at the surgical incision site. This technique achieves blockade of the dorsal rami of the spinal nerves, which are involved in postoperative pain following spine surgery. The block is performed bilaterally under ultrasound guidance at the different levels to be treated and requires multiple injections.

- **ESP Block (Erector Spinae Plane Block)**

  The lumbar ESP block consists of injecting a solution of local anesthetic and epinephrine into the deep plane between the transverse process and the erector spinae muscle. It is performed bilaterally under ultrasound guidance. Unlike the PIV block, it generally requires a single injection per side to achieve spread across multiple levels of instrumentation.

4.3. Outcome measures

4.3.1. Primary Outcome Measure

Intraoperative Blood Loss

- **Description:** Total intraoperative blood loss measured from surgical suction canisters and surgical gauze after subtraction of irrigation fluids
- **Time Frame:** During surgery (from incision to wound closure)
- **Measure Type:** Continuous (mL)

4.3.2. Secondary Outcome Measures

Postoperative Pain (Day 1 and Day 2)

- **Description:** Pain intensity assessed using the Numerical Rating Scale (NRS), ranging from 0 (no pain) to 10 (worst imaginable pain)
- **Time Frame:** Postoperative Day 1 and Postoperative Day 2
- **Measure Type:** Continuous (score 0–10)

Opioid Consumption

- **Description:** Total opioid consumption during the first 48 hours after surgery, converted into intravenous morphine equivalents
- **Time Frame:** First 48 hours postoperatively
- **Measure Type:** Continuous (mg of morphine equivalents)

Opioid-Related Adverse Effects

- **Description:** Incidence of nausea and vomiting, and need for antiemetic medication
- **Time Frame:** First 48 hours postoperatively
- **Measure Type:** Categorical (yes/no; incidence rate)

Length of Hospital Stay

- **Description:** Time from surgery to hospital discharge
- **Time Frame:** From surgery until discharge (approximately 5–7 days)
- **Measure Type:** Continuous (days)

Postoperative Blood Loss

- **Description:** Volume of blood collected in surgical drains
- **Time Frame:** First 48 hours postoperatively (or until drain removal if earlier)
- **Measure Type:** Continuous (mL)

5.Study Type and Design

Prospective, randomized, controlled, parallel-group clinical trial with blinded outcome assessment.
National multicenter study.

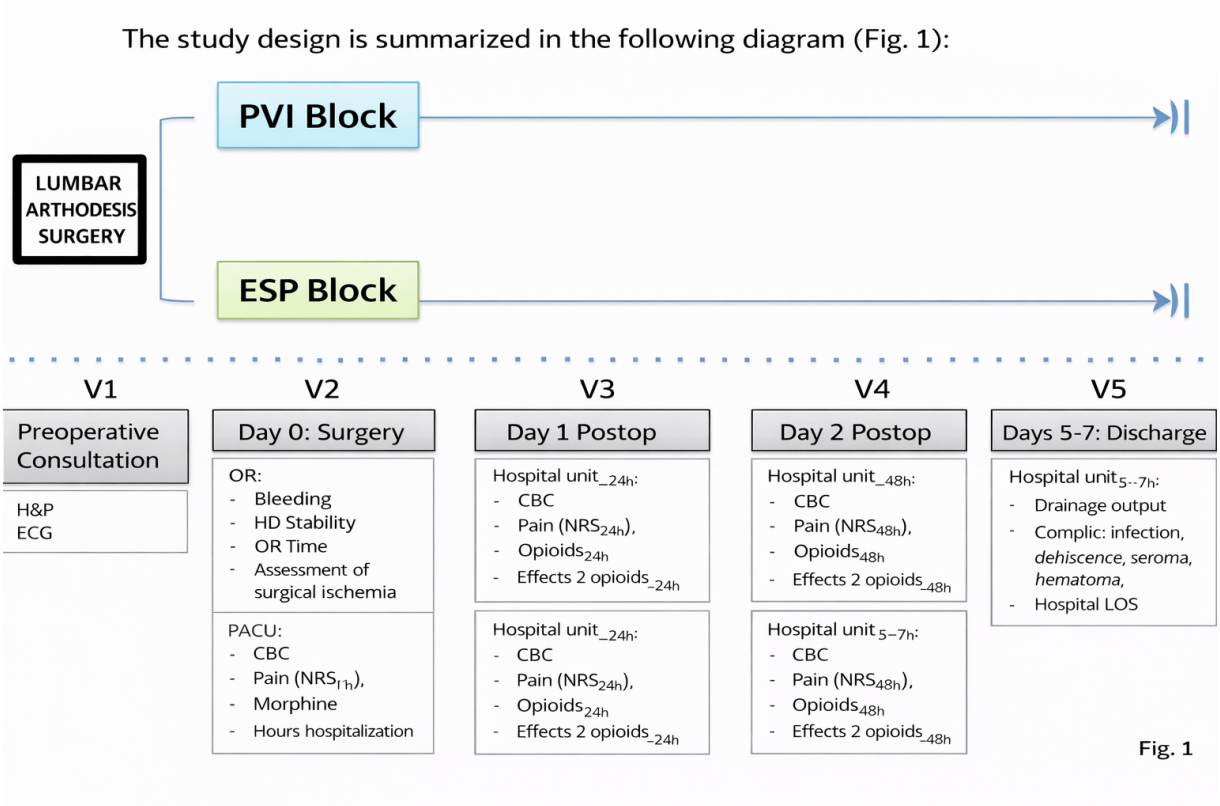

Fig. 1. Parallel-group study design.
HIP: Patient Information Sheet; DCI: Informed Consent Document; HD: Hemodynamics; Qx: Surgical; EVN: Numeric Rating Scale (NRS); MFN: Morphine.

5.2. Randomization

Patient randomization will be generated by Dr. Sergi Sabaté Tenas (Department of Anesthesiology, Intensive Care and Pain Medicine, Hospital de la Santa Creu i Sant Pau).

The randomization list will be created using simple random allocation (unpaired) to either the intervention group or the control group, using the statistical software StatsDirect, ensuring balanced groups.

Allocation will be concealed using consecutively numbered, sealed opaque envelopes stored in the Department of Anesthesiology.

Patients will not be informed of their assigned study arm, although both treatment options will be explained prior to signing the informed consent form.

5.3. Study Procedures

All patients scheduled for lumbar arthrodesis surgery (maximum of 3 instrumented levels) at Hospital de la Santa Creu i Sant Pau will be screened.

Patients meeting inclusion criteria and none of the exclusion criteria will receive study information and be provided with the Patient Information Sheet and Informed Consent Form.

Patients who agree to participate will be assigned to either the PIV or ESP group according to the randomization list.

Blinding of the anesthesiologist performing the block is not feasible due to the nature of the interventions. However, outcome assessors will be blinded to group allocation.

Patients who decline participation will receive either technique as part of standard clinical practice.

PERIOPERATIVE PROTOCOL

- Upon arrival in the operating room, a peripheral intravenous line will be placed
- Standard antibiotic prophylaxis will be administered (gentamicin 5 mg/kg and cefazolin 2 g)
- Tranexamic acid will be administered (15 mg/kg bolus followed by 1 g infusion over 8 hours)
- General anesthesia will be induced, followed by prone positioning
- The assigned regional block will then be performed under ultrasound guidance (Sonosite system) by three experienced anesthesiologists trained in both techniques
- Equipment: low-frequency convex probe (2–5 MHz) and SonoTAP needle (21G × 110 mm, Pajunk, Germany)

Block Techniques

A. PVI Group:

- Ultrasound probe in sagittal plane to identify sacrum and laminae
- Block performed at surgical levels and one level above
- Injection sites: retrolaminar space, thoracolumbar fascia, supraspinous ligament, and subcutaneous tissue
- After negative aspiration, ~20 mL per vertebral level in deep planes and 20–40 mL subcutaneously
- Total volume: 150–200 mL depending on levels
- Multiple punctures required
- Bilateral block

B. ESP Group:

- Ultrasound probe in sagittal plane, moved laterally to identify transverse processes

- Needle inserted cranial-to-caudal direction with tip on transverse process
- Injection between transverse process and erector spinae muscle
- Correct interfascial spread confirmed
- Multiple punctures may be required for adequate spread
- Bilateral block
- Total volume: 20 mL per side

The study medication (ropivacaine + epinephrine) will be administered once, prior to surgical incision, according to standard practice.

Intraoperative Management

- Multimodal intravenous analgesia before incision:
  - Dexamethasone 0.2 mg/kg
  - Paracetamol 1 g
  - Dexketoprofen 50 mg or metamizole 2 g (if renal impairment or age >80)
  - Ketamine bolus 0.5 mg/kg + infusion 0.2 mg/kg/h
  - Magnesium sulfate 40 mg/kg
- Anesthesia: TIVA (propofol + remifentanil)
- Morphine rescue: 0.1 mg/kg (30 minutes before end of surgery)
- Intraoperative blood loss will be recorded (suction + gauze, excluding irrigation fluids)

Postoperative Management

- Extubation in operating room
- Transfer to Post-Anesthesia Care Unit (PACU) for 2–3 hours
- If stable, transfer to ward

Postoperative analgesia:

- Paracetamol 1 g every 8 hours
- Dexketoprofen 50 mg every 8 hours or metamizole 2 g
- Morphine rescue: 4 mg every 4 hours

Thromboprophylaxis:

- Enoxaparin 40 mg SC daily or tinzaparin (if renal impairment) starting 24 hours post-operative
- Pneumatic compression devices during first 24 hours

Follow-up Assessments

Postoperative care unit (PACU):

- Hemoglobin measurement
- Time to discharge
- Pain assessment (NRS) and rescue morphine

Ward:

- **At 24 hours:**
  - Hemoglobin
  - NRS
  - Opioid consumption (Morphine 24h)
  - Nausea/vomiting (PONV 24h)
  - Antiemetic use
- **At 48 hours:**
  - NRS
  - Opioid consumption (Morphine 48h)
  - PONV
  - Antiemetic use
- **At hospital discharge:**
  - Total drain output
  - Patient satisfaction (5-point Likert scale: 1 = very dissatisfied to 5 = very satisfied)
  - Length of hospital stay

Patients will complete the study at hospital discharge (typically 5–7 days). The study will end upon discharge of the last enrolled patient.

5.4. Data Handling and Statistical Analysis

Randomization will be generated using StatsDirect software and stored in sealed envelopes.

Screening, consent, and randomization will be performed by the study team.

Statistical analysis:

- Categorical variables: frequency (n) and percentage (%)
- Continuous variables: mean ± SD or median (IQR), depending on distribution

Comparisons:

- Categorical variables: Chi-square test or Fisher's exact test
- Continuous variables: Student's t-test or Mann–Whitney U test
- Repeated measures ANOVA adjusted for confounders will be performed

Sample size:

- Total: 62 patients (31 per group)
- 32 patients: Hospital de la Santa Creu i Sant Pau
- 30 patients: Hospital Quirón Salud Murcia

Analysis population:

- Intention-to-treat
- Includes all patients who received the assigned block

Data management:

- Database and data entry: Mireia Rodríguez Prieto
- Data stored in the Department of Anesthesiology
- Includes CRFs and informed consent forms

Study duration:

- Recruitment: 18 months
- Data analysis: 3 months
- Participation per subject: 5–7 days

5.5. End of Study

The study will be considered completed upon hospital discharge of the last enrolled patient.

6. Subject Selection and Withdrawal

6.1. Subject Selection

The study population will consist of patients scheduled for lumbar arthrodesis surgery by the Orthopedic Surgery and Traumatology (OST) team at Hospital de la Santa Creu i Sant Pau. Subjects will be selected on the day of the pre-anesthetic consultation, during which the study will be explained to them, the Patient Information Sheet will be provided, and written informed consent will be obtained for participation in the study.

6.1.1. Inclusion Criteria

- Men and women scheduled to undergo lumbar arthrodesis surgery (maximum of 3 instrumented levels).
- Age > 18 years.
- Signed informed consent document.

6.1.2. Exclusion Criteria

- Allergy to local anesthetics.
- Previous lumbar spine surgery (reintervention).
- Patients with local infection.
- Patients with connective tissue diseases or vasculitis.
- Chronic pain treated with opioids (Oral Morphine Equivalent Dose > 50 mg/day).

6.2. Sample Size Determination

Assuming a statistical power of 80% ($\beta = 0.2$) and an α error of 0.05, a sample size of 31 patients per group was calculated. This is sufficient to detect a minimum difference of 30% in the reduction of intraoperative bleeding, considering an anticipated dropout rate of 10%, based on previous publications and our average blood loss during the skeletalization phase.

6.3. Withdrawal Criteria and Planned Analysis of Withdrawals and Dropouts

All patients included in the study will receive the block assigned to them. Patient follow-up will be conducted according to standard postoperative care in the recovery unit and hospital ward (assessment of bleeding and analgesia). No additional visits, either in-person or by telephone, are required, as the study concludes once the patient is discharged from the hospital.

Therefore, given the characteristics of the study, a low withdrawal rate is expected. Specifically, patients who, due to technical difficulties or poor visualization of the target structures, cannot receive the assigned block, or for whom data on the primary variables (perioperative bleeding and postoperative pain assessment) are unavailable or inaccurate, will be withdrawn from the study and excluded from the analysis.

7. Description of Treatment

7.1. Dose, Posology, Route of Administration, and Pharmaceutical Form

7.1.1. Experimental Treatment

Name: Periarticular vasoconstrictor infiltration (PVI) with 0.2% ropivacaine with epinephrine 1:200,000
Posology: 150–200 mL, depending on the number of instrumented levels

Route of administration: Two infiltrations (bilateral block) at the retrolaminar level, thoracolumbar fascia, supraspinous ligament, and subcutaneous level
Pharmaceutical form: Injectable solution, clear and colorless. pH 3.8–5.8. Osmolarity: 252–308 mOsm/kg
Duration of treatment: Single-dose block

7.1.2. Control Treatment

Name: Erector spinae plane (ESP) block with 0.2% ropivacaine with epinephrine 1:200,000
Posology: 20 mL bilaterally
Route of administration: Two infiltrations (bilateral block) at the level of the transverse process
Pharmaceutical form: Injectable solution, clear and colorless. pH 3.8–5.8. Osmolarity: 252–308 mOsm/kg
Duration of treatment: Single-dose block

7.1.3. Blinding Procedures

Blinding of the treatment administration is not feasible, as the investigator performing the intervention must be aware of the study group assignment in order to apply the corresponding block. The drug administered is the same in both groups. However, the investigator assessing the outcomes will be blinded to the treatment received by the patient.

7.1.4. Rescue Medication

No rescue anesthetic regimen is planned.
In the postoperative period, standard analgesic protocols will be followed, including the use of morphine on demand.

7.2. Concomitant Treatments

Usual treatments taken by the patient for comorbidities will be permitted before, during, and after the trial. As in routine surgical practice, medications such as anticoagulants or antiplatelet agents will be discontinued when indicated, following standard preoperative clinical practice guidelines.

During the trial, analgesic treatment will follow the hospital protocol for surgeries associated with moderate-to-severe postoperative pain.

7.3. Special Precautions for Handling and Storage

Ropivacaine 0.2% cartridges do not require any special storage conditions.

7.4. Assessment of Compliance

Treatment compliance will be 100%, as the investigator will administer the assigned block and drug. During the postoperative period, in both the recovery unit and hospital ward, analgesic medication will be administered according to standard protocol, which will not differ between the two treatment groups.

8. Evaluation of Outcomes

8.1. Efficacy Assessment

The clinical trial aims to evaluate the efficacy of the PIV block compared to the ESP block in reducing intraoperative bleeding and improving postoperative pain control in lumbar arthrodesis surgery.

8.1.1. Primary Outcome Measure

The primary outcome will be the total amount of intraoperative blood loss, expressed in milliliters (mL), in both study groups.

Blood loss will be determined as the sum of the following components:

- The volume recorded in the surgical suction canister, from which the volume of irrigation fluids used during the procedure will always be subtracted.
- The volume absorbed by surgical gauzes and sponges, quantified using the gravimetric method: all gauzes and sponges will be weighed before and after surgery. The difference between wet weight (after the procedure) and dry weight (before surgery) will be used to calculate the volume of absorbed blood, applying the standard equivalence of 1 gram = 1 milliliter of blood.

The total intraoperative blood loss will be calculated as the sum of the suction volume (after subtracting irrigation fluids) and the volume obtained from the gravimetric measurement of surgical materials.

Data will be collected by the research team from the anesthesia records.

8.1.2. Secondary Outcome Measures

Secondary outcomes will include:

- **Surgical field bleeding assessment**, evaluated by the surgeon using the Fromme's scale (no units), graded as follows:
    - 5: Massive uncontrollable bleeding. Continuous suction required. Surgery impossible.
    - 4: Severe but controllable bleeding. Rapid suction required. Interferes with dissection.
    - 3: Moderate bleeding. Frequent suction required. Moderately interferes with dissection.
    - 2: Moderate bleeding. Occasional suction required. Does not interfere with dissection.
    - 1: Mild bleeding. No suction required. Does not interfere.
    - 0: No bleeding. Bloodless field.
- **Pain assessment**, measured using the Numeric Rating Scale (NRS, 0–10), where 0 = no pain and 10 = worst imaginable pain. Pain will be assessed at discharge from the post-anesthesia care unit (PACU), and at 24 and 48 hours postoperatively. Data will be collected by the research team in the PACU and hospital ward. Pain intensity will be categorized as:
    - Mild: NRS 0–3
    - Moderate: NRS 4–6
    - Severe: NRS 7–10
- **Opioid consumption during the first 24 hours postoperatively (Morphine24h):** total opioid dose administered during the first postoperative day, expressed in mg of morphine equivalents.
- **Opioid consumption during the second 24 hours postoperatively (Morphine48h):** total opioid dose administered during the second postoperative day, expressed in mg of morphine equivalents.
- **Duration of surgery (t IQ):** surgical time in minutes (skin-to-skin), obtained from anesthesia records.
- **Length of stay in the post-anesthesia care unit (t PACU):** duration in minutes, obtained from recovery room records.
- **Opioid-related adverse effects:** incidence of postoperative nausea and vomiting during the first and second postoperative days (PONV24h and PONV48h).
- **Rescue antiemetic use (Antiemetics24h and Antiemetics48h):** requirement for antiemetic medication during the first and second postoperative days, collected from nursing records and electronic medical records.
- **Postoperative complications:** including surgical wound infection, dehiscence, seroma, or hematoma.
- **Postoperative drain output:** total postoperative bleeding collected from surgical drains, recorded at hospital discharge from clinical records.
- **Patient satisfaction:** assessed prior to discharge using a 5-point Likert scale:
    - 1 = Very dissatisfied

  - 2 = Dissatisfied
  - 3 = Neither satisfied nor dissatisfied
  - 4 = Satisfied
  - 5 = Very satisfied
- **Time to hospital discharge:** measured in days from the day of surgery to discharge. Days of prolonged hospitalization due to non-medical reasons (e.g., waiting for rehabilitation or social care placement) will not be counted. Data will be collected from medical records.

8.2. Safety Assessment

No clinically relevant adverse events are expected with the administration of ropivacaine with epinephrine.

During the intraoperative period, the following parameters will be recorded:

- Hypertension and tachycardia
- Occurrence of arrhythmias
- Need for vasodilator treatment within the first two hours after performing the nerve block (PIV or ESP)

These data will be documented in the intraoperative anesthesia record and evaluated by an investigator blinded to the treatment allocation, together with the rest of the study variables.

Other complications, potentially related to surgery rather than the nerve block (e.g., surgical wound infection, dehiscence, seroma, or hematoma), will also be recorded and analyzed.

Patients will be monitored for complications throughout their hospital stay.

9. Statistical Analysis

For descriptive statistical analysis, categorical variables will be expressed as absolute numbers (n) and percentages (%), while continuous variables will be expressed as mean and standard deviation (SD), or median and interquartile range (IQR), depending on the normality of data distribution.

Statistical analyses will be performed using the StatsDirect 25 software (version 4.0.3), with a significance level (alpha) set at 0.05.

Comparisons of categorical variables will be performed using Pearson's chi-square (χ^2) test and/or Fisher's exact test. Comparisons of continuous variables will be performed using the Student's t-test and/or the Mann–Whitney U test, as appropriate.

A repeated-measures analysis of variance (ANOVA) will be conducted, adjusted for potential confounding variables identified during the study.

A total of 31 patients per group will be included, for a total sample size of 62 patients. Of these, 32 patients will be recruited at Hospital de la Santa Creu i Sant Pau and 30 at Hospital Quirónsalud Murcia.

Data analysis will be conducted according to the intention-to-treat principle. Subjects included in the analysis will be those who have received the assigned block (PIV or ESP).

The person responsible for database creation and data entry will be Mireia Rodríguez Prieto (Department of Anesthesiology, Resuscitation and Pain Management, Hospital de la Santa Creu i Sant Pau). The database used for data collection and management will be Clinapsis.

Patient data, case report forms, and informed consent documents will be stored in the Department of Anesthesiology.

A low rate of missing data is anticipated due to the nature of the study. In any case, missing or erroneous data will be verified against the medical records. If missing data correspond to key variables (perioperative blood loss or postoperative pain assessment), the case will be excluded from the analysis.

10. Adverse Events

10.1. Definitions

Adverse Event (AE)
Any untoward medical occurrence in a patient or clinical trial subject administered a medicinal product, which does not necessarily have a causal relationship with the treatment.
An AE may therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational medicinal product, whether or not related to it.

Adverse Reaction (AR)
An AR is any noxious and unintended response to an investigational medicinal product, regardless of the dose administered.
Unlike an AE, an adverse reaction implies a suspected causal relationship between the medicinal product and the event.

10.2. Description

Intensity
According to intensity, AEs and ARs are classified as:

- Mild: no limitation of usual activities
- Moderate: some limitation of usual activities

- Severe: inability to perform usual activities

Severity
According to severity, AEs and ARs are classified as:

Serious: Any adverse event or adverse reaction that, at any dose:

- Results in death
- Is life-threatening
- Requires hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Results in a congenital anomaly or birth defect

For reporting purposes, events considered medically important will also be treated as serious, even if they do not meet the above criteria, including those requiring intervention to prevent one of the outcomes listed above. Any suspected transmission of an infectious agent via a medicinal product will also be considered serious.

Non-serious: Any adverse event not meeting the above criteria.

Causality Assessment

Causality between an AE and the investigational medicinal product will be classified as follows:

- **Certain:** Clear temporal relationship, not explained by other conditions or treatments, with a plausible response to withdrawal and, if applicable, confirmed by re-exposure.
- **Probable:** Reasonable temporal relationship, unlikely to be explained by other factors, with a clinically plausible response to withdrawal.
- **Possible:** Reasonable temporal relationship, but could also be explained by other factors.
- **Unlikely:** Temporal relationship makes causality improbable; other explanations are more likely.
- **Conditional/Unclassified:** More data are needed for proper assessment.
- **Unassessable/Unclassifiable:** Insufficient or contradictory information that cannot be clarified.

For regulatory reporting purposes, causality will be simplified as:

- **Related/Suspected:** A causal relationship is possible and cannot be explained by other factors.
- **Not related/Not suspected:** A causal relationship is unlikely or better explained by other factors.

Unexpected Adverse Reaction (UAR)

An adverse reaction whose nature, severity, or outcome is not consistent with the reference safety information for the medicinal product.

Serious Unexpected Adverse Reaction (SUAR)

A serious adverse reaction whose nature, severity, or outcome is not consistent with the reference safety information.

10.3. Adverse Event Recording

All adverse events occurring during the study, whether voluntarily reported by the subject or observed by the investigator, must be recorded in the adverse events section of the case report form (CRF), regardless of the investigator's opinion on causality.

The investigator will assess the relationship between the AE and the investigational treatment and record this in the CRF.

Methods of Collection and Assessment

Each AE must be documented in the designated CRF section, including:

- Onset
- Duration and, where applicable, resolution
- Description of the event
- Potential causal factors
- Concomitant medication
- Investigator assessment of intensity, seriousness, causality, and expectedness

10.4. Reporting

Any serious adverse event (SAE) must be reported to the monitor and sponsor by telephone or fax within 24 hours of awareness, unless otherwise specified in the protocol.

The investigator will complete the SAE form in the CRF and Annex D (modified version), and send it to the monitor and sponsor by fax or email within 24 hours, even if all information is not yet available. Missing information must be completed within 10 days.

Follow-up reports will be submitted until the event resolves or stabilizes. Additional information will be provided as necessary.

Subjects will be identified only by their trial identification code in all communications.

In case of death, the investigator will provide all additional requested information to the sponsor and Ethics Committee.

The pharmacovigilance officer will determine whether the event is related and expected based on the reference safety information (Summary of Product Characteristics).

If a **suspected SUAR** occurs, the sponsor will report it to the Spanish Agency of Medicines and Medical Devices (AEMPS) and the relevant regional pharmacovigilance authority within the following timelines:

- Fatal or life-threatening: as soon as possible, no later than 7 days
- Non-life-threatening: within 15 days
- Reclassified events: within 7 days of recognition

An initial incomplete report may be submitted and completed within 8 days.

Non-serious or expected events will be reported in tabulated form in the final study report.

An **annual safety report** will be submitted to AEMPS and the Ethics Committee. Additionally, ad hoc safety reports will be prepared if relevant safety concerns arise.

10.5. Specific Safety Considerations

Nerve blocks will be performed under ultrasound guidance, increasing procedural safety.

Both ESP and retrolaminar (PIV) blocks are associated with a low complication rate, as no major structures (vessels, pleura, or spinal cord) are at risk. These techniques are simple, reliable, and reproducible, with continuous visualization of the needle.

No clinically relevant adverse events are expected with the administration of ropivacaine with epinephrine.

Although large volumes of local anesthetic are used in PIV blocks, evidence from tumescent anesthesia and local infiltration analgesia (LIA) suggests low systemic absorption due to multi-site injection and local vasoconstriction.

Minor cardiovascular effects (e.g., hypertension, tachycardia) are rare and transient. Epinephrine has a short plasma half-life (2–3 minutes) and a peak ischemic effect at approximately 30 minutes.

Local infection is a contraindication for PIV block. Caution is advised in patients with compromised peripheral circulation, renal insufficiency, connective tissue diseases, or vasculitis.

The investigator will closely monitor all AEs and implement appropriate clinical measures to ensure patient safety.

11. Ethical Considerations

Participation in this study is voluntary and does not involve financial compensation.

11.1. General Considerations

The study will be conducted in accordance with:

- The Declaration of Helsinki
- Spanish regulations on clinical trials
- ICH Good Clinical Practice (GCP) guidelines

Approval from an Ethics Committee (CEIm) and AEMPS will be obtained prior to subject inclusion.

Any protocol amendments will be submitted for approval.

11.2. Patient Information and Informed Consent

The investigator is responsible for obtaining informed consent before any study procedures.

Participants (or legal representatives) will be informed about:

- Study objectives, methods, risks, and benefits
- Voluntary participation and right to withdraw
- Confidentiality of data
- Alternative treatments

Consent must be documented by signature. Oral consent in the presence of a witness may be accepted if necessary.

11.3. Risk–Benefit Assessment

Participants may benefit from improved pain control and reduced bleeding, although this is not guaranteed.

The study may contribute to improving analgesic techniques in lumbar arthrodesis.

11.4. Data Confidentiality

Data processing will comply with:

- Regulation (EU) 2016/679 (GDPR)
- Spanish Organic Law 3/2018

Data will be coded and anonymized. Only authorized personnel will have access.

Participants may exercise their rights of access, rectification, erasure, restriction, and data portability.

Data will be retained for at least 25 years.

11.5. Insurance

This trial is considered a **low-intervention clinical trial** under Spanish Royal Decree 1090/2015.

As investigational medicinal products are used according to their marketing authorization, additional insurance coverage is not required if covered by institutional professional liability insurance.

12. Practical Considerations

A major limitation of this study is the heterogeneity of the sample regarding the number of instrumented levels (ranging from 1 to 3), as well as the need for laminectomy and/or arthrotomies. These factors may influence both intraoperative bleeding and postoperative pain.

Another relevant limitation is the lack of prior scientific evidence regarding this block, which makes it difficult to compare our results with previously published studies.

Additionally, it should be considered that in some patients the block may not be feasible due to difficulties in adequately visualizing the required anatomical structures. This could result in failed blocks and consequently affect both the effective sample size and the validity of the study results.

12.1. Responsibilities of Trial Participants

Investigators
The principal investigator will be responsible for conducting the trial in accordance with current clinical trial regulations in Spain and will have overall responsibility for trial execution. The principal investigator and collaborators commit to performing all procedures and assessments specified in the protocol for all included subjects.

Auxiliary staff involved in the study must be informed by the principal investigator of their responsibilities toward study participants.

Responsibilities of Auxiliary Staff
Auxiliary staff involved in the study will comply with general trial procedures and follow the instructions of the investigator at all times.

12.2. Data Archiving and Corrections

Data obtained will be recorded in the Case Report Form (CRF), which will constitute the valid source for subsequent efficacy and safety analyses.

Corrections to CRF data must be made by crossing out the incorrect entry, adding the correct value, and ensuring that all changes are dated and signed by the investigator or authorized personnel.

The Trial Master File (TMF) will comply with Articles 57 and 58 of Regulation (EU) No. 536/2014. The sponsor and investigator will retain the TMF for at least 25 years after trial completion.

Data must be readily available for inspection by competent authorities.

Patient medical records will be maintained in accordance with applicable legislation and institutional policies.

Any transfer of ownership of the TMF will be documented, and the new owner will assume all related responsibilities.

12.3. Monitoring, Audits, and Inspections

a) Monitoring
The study will be monitored by a sponsor-appointed monitor. Monitoring will include on-site visits and remote communication to ensure compliance with the protocol, Good Clinical Practice (GCP), and regulatory requirements.

Monitoring activities will include review of:

- Informed consent procedures
- Investigator site file documentation
- A sample of CRF data against source documents
- Inclusion/exclusion criteria
- Adverse events

Findings will be reported to the sponsor, and follow-up letters will be sent to the investigator.

A final monitoring report will summarize data quality, reliability, and protocol adherence.

CRFs will be submitted to the sponsor or designated entity for archiving at study completion.

b) Audits
The trial will be included in the IR-HSCSP Quality Assurance Program, with audits conducted based on trial criticality.

c) Inspections
The investigator and sponsor will allow direct access to source data for monitoring, auditing, ethics review, and regulatory inspections.

12.4. Protocol Amendments

Any changes to the protocol will be documented as written amendments or addenda.

All amendments must be approved by the responsible parties who signed the protocol. Substantial amendments require approval from the Ethics Committee and regulatory authorities.

12.5. Protocol Deviations

Protocol deviations are not permitted, particularly regarding unplanned treatments, dosages, administration routes, or treatment durations.

Serious breaches will be reported by the sponsor to the Spanish Agency of Medicines and Medical Devices (AEMPS) and the Ethics Committee within seven calendar days.

A serious breach is defined as one that significantly affects subject safety, rights, or data reliability.

12.6. Drug Accountability

Drug receipt and inventory records will be maintained by the hospital pharmacy.

- Study medication will be stored securely and accessible only to authorized personnel.
- The pharmacist will maintain detailed inventory records, including administration details and remaining stock.
- A final inventory of unused medication will be performed at study completion.
- The investigator will not provide study medication to unauthorized individuals.

12.7. Sample Identification and Labeling

Study labels will be prepared using the ETIK system prior to final preparation.

Medication will be labeled according to the randomization list.

Label information will include:

- Product name
- Volume or concentration
- Preparation date
- Expiry date
- Product code
- Study code
- Patient identification number
- Storage conditions
- “For clinical trial use only”

12.8. Treatment Allocation

The randomization list will be generated by the Methodology and Statistics Unit of the IR-HSCSP.

Both treatments will have equal probability of assignment.

Patients will be consecutively enrolled. Each subject will be assigned a sequential identification code based on inclusion order.

Randomization codes will be assigned sequentially.

A screening log of included and non-included patients is recommended to minimize selection bias.

If randomized treatment is discontinued, alternative treatment may be prescribed. The patient will not contribute further to the exposure phase but will remain in follow-up.

12.9. Trial Discontinuation

The trial may be discontinued by the investigator or sponsor in the following cases:

- Lack of treatment efficacy
- Emergence of unexpected or unacceptable adverse events
- Insufficient recruitment

12.10. Publication Policy

Study results will be reviewed jointly by the investigators and sponsor prior to publication.

Data will not be disclosed to third parties without sponsor agreement, except that investigators may include the study title in their CVs (without sponsor identification).

12.11. Final Report

A final report will be prepared in collaboration with the sponsor after study completion.

The report will include statistical analysis and medical interpretation of results, based on the study objectives defined in the protocol.

References

1. Lei F, Li Z, et al. Hidden blood loss and risk factors after posterior lumbar fusion surgery: a retrospective study. *Medicine (Baltimore).* 2020;99(19):e20103.
2. Kang T, Park SY, et al. Patient blood management during lumbar spinal fusion surgery. *World Neurosurgery.*2019;30:e566–e572.
3. Hu SS. Blood loss in adult spine surgery. *European Spine Journal.* 2004;13(Suppl 1):S3–S5. doi:10.1007/s00586-004-0753-x
4. Luan H, Liu K, et al. Efficacy and safety of tranexamic acid in posterior lumbar interbody fusion: a meta-analysis of randomized controlled trials. *Journal of Orthopaedic Surgery and Research.* 2023;14.
5. Haratian A, Shelby T, et al. Utilization of tranexamic acid in surgical orthopaedic practice: indications and current considerations. *Orthopedic Research and Reviews.* 2021;13:187–199.
6. Sessler DI, Bloomstone JA, Aronson S, et al. Perioperative Quality Initiative consensus statement on intraoperative blood pressure, risk and outcomes for elective surgery. *British Journal of Anaesthesia.* 2019;122(5):563–574. doi:10.1016/j.bja.2019.01.013
7. Mazy A, Elmaadawy AEA, Serry M, Kassem M. High-volume, multilevel local anesthetic–epinephrine infiltration in kyphoscoliosis surgery: blood conservation. *Anesthesia Essays and Researches.* 2019;13(3):405–410. doi:10.4103/aer.AER_89_19
8. Roques Escolar V, Oliver-Fornies P, Fajardo Perez M. Periarticular vasoconstrictor infiltration: a novel technique for chemical vasoconstriction in major orthopaedic surgery. *British Journal of Anaesthesia.* 2022. doi:10.1016/j.bja.2022.07.001

9. Roques Escolar V, Molina-Garrigo P. The periarticular vasoconstrictor infiltration technique (PVI) for total knee and hip arthroplasty: a brief description of a new technique complemented by audiovisual presentations. *Journal of Clinical Anesthesia.* 2024;92:111284.
10. Klein A. The tumescent technique for liposuction surgery. *American Journal of Cosmetic Surgery.* 1987;4:263–267. doi:10.1177/074880688700400403
11. Lalonde DH. "Hole-in-one" local anesthesia for wide-awake carpal tunnel surgery. *Plastic and Reconstructive Surgery.* 2010;126:1642–1644.
12. Lalonde D. Minimally invasive anesthesia in wide-awake hand surgery. *Hand Clinics.* 2014;30:1–6.
13. Lalonde DH. Conceptual origins, current practice, and views of wide-awake hand surgery. *Journal of Hand Surgery (European Volume).* 2017;42:886–895.
14. Khudr J, Hughes L, Younis F. The what, why and when of wide-awake local anaesthesia no tourniquet surgery. *British Journal of Hospital Medicine.* 2022;83:1–10.
15. Fenten MG, Bakker SM, Touw DJ, et al. Pharmacokinetics of 400 mg ropivacaine after periarticular local infiltration analgesia for total knee arthroplasty. *Acta Anaesthesiologica Scandinavica.* 2017;61(3):338–345. doi:10.1111/aas.12849
16. Nordström H, Stange K. Plasma lidocaine levels and risks after liposuction with tumescent anaesthesia. *Acta Anaesthesiologica Scandinavica.* 2005;49(10):1487–1490. doi:10.1111/j.1399-6576.2005.00885.x
17. Jiang W, Fu M, Dong W, et al. Use of a multifunctional cocktail for postoperative bleeding and pain control in spinal fusion: a randomized, double-blind, controlled trial. *Spine (Phila Pa 1976).* 2022;47(18):1328–1335. doi:10.1097/BRS.0000000000004249
18. Geisler A, Zachodnik J, Køppen K, Chakari R, Bech-Azeddine R. Postoperative pain treatment after spinal fusion surgery: a systematic review with meta-analyses and trial sequential analyses.
19. Liu H, Zhu J, Wen J, Fu Q. Ultrasound-guided erector spinae plane block for postoperative short-term outcomes in lumbar spine surgery: a meta-analysis and systematic review. *Medicine (Baltimore).* 2023;102(7):e32981. doi:10.1097/MD.0000000000032981
20. Viderman D, Aubakirova M, Umbetzhanov Y, et al. Ultrasound-guided erector spinae plane block in thoracolumbar spinal surgery: a systematic review and meta-analysis. *Frontiers in Medicine.* 2022;9:932101. doi:10.3389/fmed.2022.932101
21. Sotome S, Sawada A, Wada A, et al. Erector spinae plane block versus retrolaminar block for postoperative analgesia after breast surgery: a randomized controlled trial. *Journal of Anesthesia.* 2021;35(1):27–34. doi:10.1007/s00540-020-02855-y
22. Zhao Y, Tao Y, Zheng S, et al. Effects of erector spinae plane block and retrolaminar block on analgesia for multiple rib fractures: a randomized, double-blinded clinical trial. *Brazilian Journal of Anesthesiology.* 2022;72(1):115–121. doi:10.1016/j.bjane.2021.04.004
23. Tao T, Zhou Q. Efficacy of erector spinae block versus retrolaminar block for postoperative analgesia following posterior lumbar surgery. *Nan Fang Yi Ke Da Xue Xue Bao.* 2019;39(6):736–739.
24. Kamel AAF, Fahmy AM, Medhat MM, et al. Retrolaminar block for opioid-free anaesthesia and enhanced recovery after posterior lumbar discectomy: a randomized

controlled study. *Indian Journal of Anaesthesia.* 2024;68(3):261–266. doi:10.4103/ija.ija_773_23

25. Buchan I. StatsDirect statistical software. Available at: http://www.statsdirect.com. England: StatsDirect Ltd; 2024.

3.1. ANNEXES

- **Annex 1:** Schedule of Study Assessments
- **Annex 2:** Patient Information Sheet and Informed Consent Form
- **Annex 3:** Basic information on the medicinal products used in the study

Annex 1: Schedule of Study Assessments

STUDY ASSESSMENT SCHEDULE

Visit / Procedure	V1 Preoperative	V2 Surgery	V3 Post-op Day 1	V4 Post-op Day 2	V5 Discharge Day
Informed consent signature	X				
Sociodemographic data	**				
Inclusion/Exclusion criteria	X				
Clinical status assessment	**				
Tests					
Electrocardiogram	**				
Blood test: Hemogram	**	**	**		
Blood test: Biochemistry	**				
Blood test: Coagulation	**				
Bleeding	**				**
Pain (NRS)		**	**	**	

- "X" = procedure performed at that visit
- "**" = performed as part of routine clinical practice / collected from medical records

Annex 2: Patient Information Sheet and Informed Consent Form

PATIENT INFORMATION SHEET

STUDY TITLE:

Efficacy of Periarticular Vasoconstrictive Infiltration (PVI) versus Erector Spinae Plane (ESP) Block in Reducing Blood Loss and Postoperative Pain Control in Lumbar Spinal Fusion Surgery. A Randomized Clinical Trial

STUDY CODE: IIBSP-IPV-2024-178

SPONSOR: Research Institut of Hospital de la Santa Creu i Sant Pau – IIB Sant Pau

PRINCIPAL INVESTIGATOR: MIREIA RODRÍGUEZ PRIETO

STUDY CENTER: Hospital de la Santa Creu i Sant Pau

INTRODUCTION

We are inviting you to participate in a research study. This study has been approved by an Ethics Committee for Clinical Research with Medicinal Products and by the Spanish Agency of Medicines and Medical Devices (AEMPS), in accordance with current legislation: Royal Decree 1090/2015 of 4 December and Regulation (EU) No. 536/2014 of 16 April governing clinical trials with medicinal products.

Our aim is to provide you with clear and sufficient information so that you can decide whether or not to participate. Please read this information carefully. We will answer any questions you may have. You may also discuss your participation with anyone you consider appropriate.

VOLUNTARY PARTICIPATION

You are invited to participate because you will undergo lumbar spinal fusion surgery.

Participation is completely voluntary. You may decide not to participate or withdraw your consent at any time without affecting your medical care or relationship with your physician.

STUDY OBJECTIVE

The aim of this study is to compare the efficacy of two regional anaesthetic techniques (PVI versus ESP block) in reducing intraoperative blood loss and improving postoperative pain control in lumbar spinal fusion surgery.

We aim to determine whether the PVI technique is more effective than the ESP block in reducing bleeding and postoperative pain.

STUDY DESCRIPTION

A total of 62 patients are expected to be included.

Participants will be randomly assigned (50% probability) to one of two groups:

- Erector Spinae Plane (ESP) block
- Periarticular Vasoconstrictive Infiltration (PVI)

Both techniques involve administration of a local anaesthetic with adrenaline (ropivacaine), which is routinely used in regional anaesthesia.

STUDY PROCEDURES

Your participation will last approximately 5–7 days, from hospital admission for surgery until discharge.

The recruitment period is expected to last 18 months.

No additional visits, tests (blood tests, imaging, etc.), or non-standard medications will be required.

You will receive the same postoperative care as patients not participating in the study.

RISKS AND DISCOMFORTS

The drug used in both techniques is the same: ropivacaine, a licensed local anaesthetic combined with a vasoconstrictor (epinephrine 1:200,000), commonly used in regional anaesthesia.

Regional nerve blocks are routinely performed and are considered safe and effective for postoperative pain control.

The block will be performed under general anaesthesia, so you will not feel any discomfort.

Potential complications are rare and include:

- Infection at the injection site
- Local anaesthetic toxicity or allergic reaction
- Block failure

Because the injection sites (PVI and ESP) are distant from major vessels, the spinal cord, pleura, and major nerves, the risk of serious complications is very low.

POTENTIAL BENEFITS

Possible benefits include:

- Reduced intraoperative and postoperative blood loss
- Reduced need for blood transfusion
- Improved postoperative pain control
- Reduced need for opioid analgesics and related side effects (nausea, vomiting, itching)

However, there is no guarantee that you will personally benefit from participation.

PREGNANCY WARNING

Pregnant patients will not be included in this study. Pregnancy is a contraindication for surgery due to the need for radiological imaging and because the procedure is elective.

ALTERNATIVE TREATMENTS

If you choose not to participate, both techniques (PVI or ESP block) remain available as standard clinical practice at our hospital.

INSURANCE

According to Royal Decree 1090/2015, this is a low-intervention clinical trial. As such, any potential harm is covered by the hospital's existing professional liability insurance, as no procedures beyond standard clinical practice are performed.

DATA PROTECTION

Your personal data will be processed in accordance with:

- EU Regulation 2016/679 (GDPR)
- Spanish Organic Law 3/2018 on Data Protection

Your data will be coded and anonymised. Only authorised study personnel will be able to link the data to your identity.

Your data may be accessed by:

- Study investigators
- Regulatory authorities (AEMPS and others)
- Ethics committees
- Auditors/monitors

You may exercise your rights of access, rectification, objection, restriction, and data portability by contacting:

- Principal Investigator
- Data Protection Officer: dpd@santpau.cat

Data may be stored for at least 25 years after study completion.

COSTS AND COMPENSATION

You will not receive financial compensation for participation.

There will be no additional costs to you. The study does not involve extra procedures beyond standard care.

POST-STUDY TREATMENT

You will receive standard postoperative analgesia according to hospital protocol. No experimental treatments will be administered outside the study block technique.

BIOLOGICAL SAMPLES

No additional biological samples will be collected beyond routine postoperative blood tests.

OTHER INFORMATION

Study details will be publicly available at: http://reec.aemps.es

Participation may be discontinued by investigators for safety or clinical reasons.

Data collected may be used in future related research if you provide consent.

CONTACT INFORMATION

If you have any questions, please contact:

Mireia Rodríguez Prieto, MD
Department of Anaesthesiology, Resuscitation and Pain Management

Hospital de la Santa Creu i Sant Pau
Phone: +34 932 919 000 (ext. 7541)

INFORMED CONSENT FORM

STUDY TITLE:

Efficacy of Periarticular Vasoconstrictive Infiltration (PVI) versus Erector Spinae Plane (ESP) Block in Reducing Blood Loss and Postoperative Pain Control in Lumbar Spinal Fusion Surgery. A Randomized Clinical Trial

I, _____ (participant's full name)

- Have read the information sheet provided
- Have had the opportunity to ask questions
- Have received sufficient information
- Have spoken with _____ (investigator's name)

I understand that:

- Participation is voluntary
- I may withdraw at any time without explanation
- Withdrawal will not affect my medical care

I freely agree to participate in the study and consent to the use of my data as described.

☐ YES ☐ NO (future use of data in related studies)

I will receive a signed copy of this document.

Signature of participant: _____
Signature of investigator: _____
Date: _____

CONSENT FORM (NON-READING PARTICIPANTS / WITNESS VERSION)

I, _____ (witness name), confirm that:

The participant _____ has been informed about the study and has had the information read and explained. They have had the opportunity to ask questions.

The participant understands:

- Participation is voluntary
- They may withdraw at any time without consequences
- Medical care will not be affected

The participant freely agrees to participate and consents to data use as described.

☐ YES ☐ NO (future use of data in related studies)

Signature of witness: _____
Signature of investigator: _____
Date: _____

Annex 3: Classification, dosing guidelines and precautions of drugs used in lumbar arthrodesis surgery

ADRENERGIC AGENTS

Adrenaline

- **Presentation:** 1 mg/ml, 1 ml ampoule
- **Route of administration:** interfascial, intra-articular
- **Dose and administration:** 1 mg added to ropivacaine 2 mg/ml (0.2%) solution

Contraindications:

- Heart failure / coronary disease, cardiac arrhythmias
- Hyperthyroidism, severe hypertension, pheochromocytoma
- Organic brain lesions (cerebral arteriosclerosis), narrow-angle glaucoma

Precautions:

- Cerebrovascular insufficiency, heart disease with angina, COPD
- Prostatic hypertrophy with urinary retention
- Concomitant use of corticosteroids, diuretics, theophylline, digoxin
- Diabetic and elderly patients
- Rotate injection sites due to risk of necrosis

MILD ANALGESICS

Paracetamol (Acetaminophen)

- **Presentation:** IV 10 mg/ml 100 ml ampoule; tablets 500 mg; effervescent tablets 500 mg; oral solution 10 mg/ml
- **Route:** IV / oral
- **Dose:** 500–1000 mg every 8 h
- **Max dose:** 4 g/day (2 g/day in chronic alcohol users)
- **IV administration:** slow infusion ≥15 min

Contraindications:

- Severe hepatic failure (Child-Pugh C)

Precautions:

- Chronic alcohol use: do not exceed 2 g/day

Dexketoprofen

- **Presentation:** 50 mg/2 ml ampoule
- **Route:** IM, IV
- **Dose:** 50 mg every 8–12 h (max 150 mg/day)
- **Administration:** dilute in 50 ml saline, infuse over 10–30 min

Contraindications:

- Hypersensitivity (asthma, urticaria)
- History of gastric ulcer, active inflammatory bowel disease
- Severe heart failure, renal or hepatic failure
- Coagulation disorders

Precautions:

- Hypertension (fluid retention risk)
- Avoid with other gastrotoxic drugs
- Concomitant anticoagulants

Ibuprofen

- **Presentation:** 400 mg, 600 mg tablets; 20 mg/ml suspension
- **Route:** oral
- **Dose:** 400–600 mg every 8 h
- **Max dose:** 2400 mg/day

Metamizole (Dipyrone)

- **Presentation:** 400 mg/ml ampoule (5 ml); 575 mg capsules
- **Route:** IV, IM, oral
- **Dose:** 1000 mg every 6–8 h
- **Max dose:** 4000 mg/day (oral max 3450 mg/day)
- **IV administration:** dilute in 50 ml saline, infuse over 20–60 min

Contraindications:

- Allergy to pyrazolones/pyrazolidines
- History of agranulocytosis
- Analgesic-induced asthma or urticaria
- Acute hepatic porphyria
- G6PD deficiency

Precautions:

- Cardiac conduction disorders, epilepsy, thyroid dysfunction
- Elderly patients (risk of hypotension, confusion, agitation)
- Treatment should not exceed 1 week unless strictly monitored

LOCAL ANESTHETICS

Ropivacaine

- **Presentation:** 2 mg/ml (200 ml bag)
- **Route:** interfascial
- **Dose:** 0.2% ropivacaine + adrenaline 5 µg/ml

Contraindications:

- Allergy to amide local anesthetics
- IV regional anesthesia
- Obstetric paracervical anesthesia
- Hypovolemia

Precautions:

- Peripheral nerve blocks (head and neck)
- Poor general condition
- Antiarrhythmics class III or CYP1A2 inhibitors
- Hepatic/renal impairment
- Acute porphyria

ANTIFIBRINOLYTICS

Tranexamic Acid

- **Presentation:** 100 mg/ml, 5 ml ampoule
- **Route:** IV
- **Dose:** 15 mg/kg IV slow injection (1 ml/min) OR 1 g infusion over 8 h

Contraindications:

- Active arterial/venous thrombosis
- Severe renal impairment (GFR <30 ml/min)
- Seizure history
- Intrathecal/intraventricular/intracerebral injection

Precautions:

- Slow IV administration required
- Not to be administered intramuscularly

Enoxaparin

- **Presentation:** 40 mg/0.4 ml prefilled syringe
- **Route:** subcutaneous
- **Dose:** 40 mg once daily

Contraindications:

- Heparin-induced thrombocytopenia (HIT)
- Active bleeding or high bleeding risk

Precautions:

- Avoid IM injections
- Severe renal impairment (GFR <30 ml/min)
- Hyperkalemia risk (diabetes, acidosis, potassium-sparing drugs)

Tinzaparin

- **Presentation:** 3500 IU prefilled syringe
- **Route:** subcutaneous
- **Dose:** 3500 IU once daily

Contraindications:

- HIT type II
- Active major bleeding
- Septic endocarditis

ANTIEMETICS

Granisetron

- **Presentation:** 1 mg/ml ampoule; 1 mg tablets
- **Route:** IV / oral
- **Dose:** 1 mg IV single dose or 1–2 mg/day oral

Precautions:

- Intestinal obstruction
- QT prolongation / arrhythmias
- Serotonin syndrome risk

CORTICOSTEROIDS

Dexamethasone

- **Presentation:** 4 mg/ml ampoule; 40 mg/ml vial
- **Route:** IV
- **Dose:** 0.2 mg/kg IV slow injection (1–3 min), 30 min pre-surgery

Contraindications:

- Systemic infection (unless treated)
- Gastric/duodenal ulcer
- Live vaccines during high-dose therapy

Precautions:

- Pregnancy, diabetes, osteoporosis
- Hypertension
- Psychosis risk
- Hypoalbuminemia

PROTON PUMP INHIBITORS

Omeprazole

- **Presentation:** 40 mg vial; 20 mg capsules
- **Route:** IV / oral
- **Dose:** 20 mg once daily
- **IV administration:** dilute in 100 ml saline, infuse over 20–30 min

Contraindications:

- Concomitant nelfinavir use

Precautions:

- Vitamin B12 deficiency
- CYP2C19 interactions
- Hypomagnesemia
- Increased fracture risk in elderly

OPIOIDS

Morphine

- **Presentation:** 10 mg/ml ampoule; 20 mg/ml ampoule
- **Route:** IV, SC, IM
- **Dose:** 2.5–20 mg every 4 h IV slow infusion (4–5 min)

Contraindications:

- Shock, severe hypoxia
- Respiratory depression, severe asthma
- Concurrent MAOI use (or within 10 days)

Precautions:

- COPD, cardiovascular disease
- Hypotension, CNS depressants
- Urinary retention (prostate disease)
- Increased intracranial pressure
- Hypothyroidism

MAGNESIUM SULFATE

- **Presentation:** 150 mg/ml, 10 ml ampoule
- **Route:** IV
- **Dose:** 40 mg/kg diluted in 50 ml saline

Contraindications:

- Severe renal failure
- Liver failure
- Heart block
- Hypermagnesemia

Precautions:

- Renal impairment
- Conduction disorders
- Myasthenia gravis

KETAMINE

- **Presentation:** 50 mg/ml, 10 ml ampoule
- **Route:** IV
- **Dose:** 0.5 mg/kg bolus + 0.2 mg/kg/h infusion

Contraindications:

- Uncontrolled severe hypertension
- Cardiovascular disease, heart failure
- Increased intracranial/intraocular pressure
- Pregnancy

- Active psychosis
- Acute intermittent porphyria

Precautions:

- Psychomimetic effects
- Liver disease
- Seizure risk
- Laryngospasm risk
- Hyperthyroidism