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Erector spinae plane block for minimally invasive mitral valve surgery: a double-blind, prospective, randomised placebo-controlled trial—a study protocol

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ABSTRACT

Introduction In the context of enhanced recovery after cardiac surgery, surgical techniques for mitral valve surgery have witnessed substantial modifications, from approaching the heart using open approaches with traditional sternotomy to thoracoscopic access via minithoracotomy. After cardiac surgery, acute postoperative pain is frequent and caused by surgical incision and retraction. Perioperative analgesia in cardiac surgery still relies mainly on opioids. Although neuraxial techniques could be a valuable non-opioid-based analgesia regimen, they can be associated with devastating complications in situations with (iatrogenic) coagulation abnormalities. Only two randomised clinical trials describe the erector spinae plane (ESP) block to provide sufficient postoperative analgesia following cardiac surgery with median sternotomy. Regarding postoperative analgesia after cardiac surgery with a minithoracotomy approach, adequately designed trials are still lacking. We, therefore, designed a double-blind, placebo-controlled trial to prove the hypothesis that the ESP block reduces opioid consumption in patients undergoing minimally invasive mitral valve surgery (MIMVS).

Methods and analysis Sixty-four patients undergoing MIMVS will be included in this double-blind, prospective, placebo-controlled trial. Patients will be randomised to receive an ESP block with a catheter with either intermittent ropivacaine 0.5% (ropi group) or normal saline 0.9% (placebo group). Both groups will receive patient-controlled intravenous analgesia with morphine following extubation. Primary endpoint is the 24-hour cumulative morphine consumption after extubation. Multiple secondary endpoints will be evaluated.

Ethics and dissemination The study is approved by the ethics committee of the University Hospitals Leuven, the Clinical Trials Centre of the University Hospitals Leuven and the 'Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten'. Dissemination of the study results will be via scientific papers.

Strengths and limitations of this study

- ► It is a randomised double-blind, placebo-controlled trial to evaluate the clinical impact of an erector spinae plane (ESP) block.
- ► The impact of regional anaesthesia in an enhanced recovery after cardiac surgery programme will be evaluated.
- ► This is the first randomised trial evaluating a unilateral ESP block in cardiac surgery.
- ► The monocentric design is the main limitation of this study.

Trial registration number EudraCT identifier: 2019-001125-27.

INTRODUCTION

Background and rationale

Regional anaesthesia is a fundamental element of virtually every multimodal analgesia concept. With the increasing popularity of enhanced recovery after surgery programmes, the use of regional anaesthesia continues to expand.[1] In cardiac surgery, however, traditional regional anaesthesia techniques such as thoracic epidural anaesthesia or paravertebral thoracic blocks are not routinely implemented in postoperative pain protocols due to the concerns of perioperative heparinisation and the resulting risk of a spinal or epidural haematoma.[2] Furthermore, many cardiac surgery patients are under antiplatelet therapy, which represents another contraindication for these neuraxial anaesthesia techniques.[2] In cardiac surgery, therefore, postoperative pain management is still mainly opioid-based. Unfortunately, opioids may have well-known unwanted and dose-related side effects (eg, nausea,

vomiting, confusion and respiratory depression), which can substantially impair the recovery process.[3]

To overcome these shortcomings, more distal nerve blocks have been (re)discovered and implemented, such as the erector spinae plane (ESP) block and the serratus plane block.[4] These blocks are examples of relatively superficial musculofascial plane blocks. The ESP block is placed into the plane between the erector spinae muscles and the posterior aspect of the transverse processes.[5]

The American Society of Regional Anesthesia (ASRA) 2018 guidelines suggest that performing deep peripheral nerve blockades (ie, a neuraxial or paravertebral block) in an anticoagulated patient is unsafe.[2] The determination of safety for superficial blocks ought to account for compressibility, consequences of bleeding and site vascularity.[2] Based on this principle, it has been suggested that for the ESP block, the complication risk due to bleeding is low and is outweighed by the benefit of superior analgesia and concomitant revalidation possibilities.[6]

In cardiac surgery, the ESP block has been described to adequately provide perioperative analgesia in only two randomised controlled trials and several case reports and case series.[6–11] Based on these clinical reports, analgesia is believed to be achieved by paravertebral and craniocaudal spread of local anaesthetics with only a single injection.[5] This presumed paravertebral spread can anaesthetise not only the ventral and dorsal rami of the spinal nerve roots but also the autonomical fibres of the sympathetic ganglia.[5] Data from cadaveric studies confirmed the extensive craniocaudal spread of dye. However, there is still debate about whether the local anaesthetic administered also reaches the paravertebral space.[12–14] To achieve an extensive spread, the ESP block requires the injection of relatively large volumes of local anaesthetic (approximately 20–30 mL) due to the distance between the injection site and the target area.[15] Duration of analgesia after an ESP block remains a matter of controversy, depending on the used mixture and systemic absorption of the local anaesthetics,[8 9] but can be prolonged with the placement of a catheter.[16] Although limited data is available, the consensus among experts is that the use of intermittent bolus administration of local anaesthetics results in a better spread and analgesia as compared to continuous infusion.[17]

Ropivacaine, a long-acting amide local anaesthetic, is routinely used in musculofascial plane blocks with a proven safety profile.[18] Pre-clinical pharmacological studies show anti-inflammatory effects of ropivacaine; this still needs validation in the clinical setting.[19]

Minimally invasive procedures, such as minimally invasive mitral valve surgery (MIMVS), are often part of an enhanced recovery after cardiac surgery (ERACS) programme, aiming to improve postoperative outcome and reduce the postoperative complication rate.[20] In contrast to conventional sternotomy, thoracotomy can result in an increased incidence of moderate to severe postoperative pain.[21] In these surgeries, musculofascial plane blocks appear to be a valid option to improve postoperative pain and reduce opioid consumption.[22] In our centre, MIMVS is performed via a right-sided minithoracotomy, between the third or fourth intercostal space, with a 4–5 cm periareolar or submammarian incision.

Based on the perceived advantage of a paravertebral spread of the local anaesthetic following an ESP block and the encouraging results of previous ESP studies as mentioned above, we hypothesise that an ESP block with ropivacaine (ropi group) after MIMVS will result in a significant reduction in total postoperative opioid consumption compared with an ESP block with normal saline 0.9% (placebo group). To our knowledge, this study is the first double-blind, placebo-controlled trial to evaluate the clinical impact of a unilateral ESP block in minimally invasive cardiac surgery.

Primary objective

This trial will evaluate the efficacy of an ESP block with intermittent boluses of ropivacaine on postoperative pain and recovery compared with normal saline following MIMVS.

METHODS AND ANALYSIS

Trial design

This single-centre, double-blind, prospective, randomised controlled trial will be performed at the University Hospitals Leuven. The investigator will perform the anaesthesia and perform the ESP block. Following extubation, the investigator will evaluate postoperative pain scores and check the ESP catheter position after 18 hours. Both the investigator and the patient are blinded to the group affiliation. This protocol follows the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines and fulfills the SPIRIT checklist (online supplemental file 1); a SPIRIT checklist is provided in figure 1.

Randomisation

All patients will be randomised through a computer-generated permuted block randomisation sequence (variable block size with 1:1 allocation). Enclosing assignments in opaque, sequentially numbered, sealed envelopes will ensure allocation concealment. Envelopes will only be opened at the end of surgery after confirmation of ERACS programme, including postanaesthesia care unit (PACU) admittance. Research personnel will then prepare the trial medications (ropi group: ropivacaine 0.5% or placebo group: normal saline 0.9%). Of note, the trial medications have the same volume, 30 mL for the first dose and 20 mL for the following three doses, and are identically looking. Syringes will be labelled with the mark 'trial medication' so that the investigator will remain blinded.

If, for any cause, a patient is withdrawn from the ERACS programme (eg, due to perioperative complications or for logistic reasons), this will be classified as screening failure. Code break will only be permitted if the patient

	STUDY PERIOD							
	Enrolment	Allocation	Post-allocation					Close-out
Timepoint	*0*	B_0	*T_0 +0-2h*	*B_0 +6h*	*B_0 +12h*	*B_0 +18h*	*T_0 +24h*	*B_0 +30d*
ENROLMENT:								
Eligibility screen	X							
Informed consent	X							
Allocation		X						
INTERVENTIONS:								
Ropivacaine-group			◆—	—	—	—◆		
Placebo-group			◆—	—	—	—◆		
ASSESSMENTS:								
Baseline dataset	X	X						
Extubation time			X					
Morphine consumption							X	
NRS for pain			X	X	X	X	X	
Sensory block			X			X		
Catheter position						X		
Adverse events							X	X
Safety endpoints (VARC-2)							X	X

Figure 1 Standard Protocol Items: Recommendations for Interventional Trials. B_0, block placement; d, days; h, hours; NRS, 11-point Numerical Rating Scale; T_0, time of extubation; VARC-2, Valve Academic Research Consortium-2.

shows life-threatening symptoms of local anaesthetic systemic toxicity (LAST) to allow appropriate treatment.

Anaesthesia and interventional plan

Our institutional ERACS programme will be used in all patients to standardise perioperative treatment in both groups. This protocol includes (1) avoidance of prolonged fasting (by stimulating the intake of a carbohydrate drink up to 2 hours preoperatively), (2) no premedication, (3) postoperative nausea and vomiting (PONV) and antibiotic prophylaxis, (4) early postoperative removal of drains and catheters (if possible on postoperative day 1), (5) early restart of oral nutrition (at the day of surgery) and (6) early mobilisation of the patient. The study visits are summarised in figure 2.

Induction and maintenance of anaesthesia

In general, patient management will be performed according to the below-mentioned institutional standards. However, it is possible that the attending anaesthesiologist changes this management plan to optimise the patients' care.

Prior to anaesthesia, all patients must be in a fasting state for 6 hours and no premedication is given. After applying a five-lead ECG and pulse oximetry, a peripheral intravenous line (16-gauge cannula) and radial arterial catheter (20-gauge cannula) will be placed. After preoxygenation (fraction of inspired oxygen=1.0), general anaesthesia will be induced with intravenous remifentanil (0.5 µg/kg/min) followed by a bolus of propofol 0.5–1 mg/kg. Tracheal intubation will be facilitated by a bolus administration of rocuronium 1.0 mg/kg. For one-lung ventilation, a left-sided double-lumen endotracheal tube or bronchus blocker will be inserted. Positioning will be checked with fibre-optic bronchoscopy. Standard American Society of Anesthesiologists monitoring will be completed with temperature and capnography measurements. Besides, respiratory and haemodynamic monitoring will be used to facilitate haemodynamic management based on our

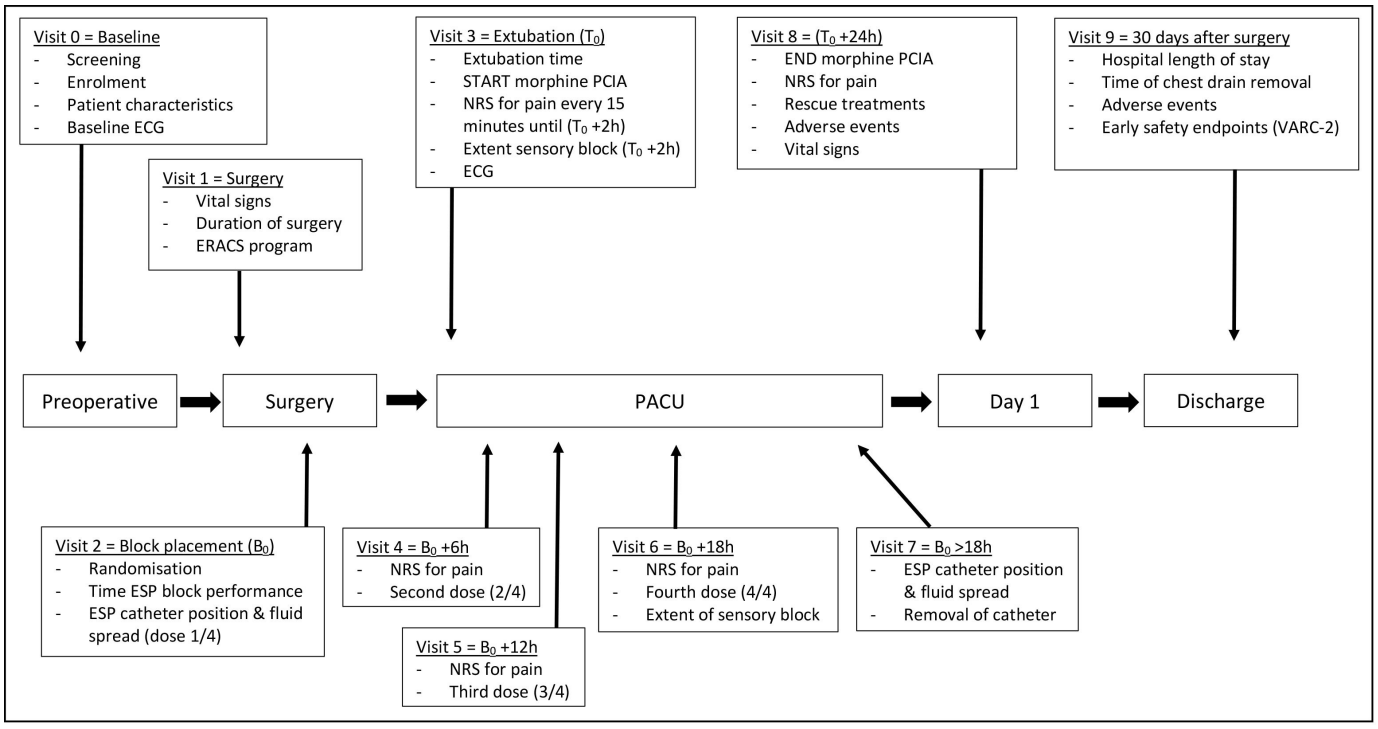

Figure 2 Schematics illustration of the study visits. B_0, block placement; ECG, electrocardiogram; ERACS, enhanced recovery after cardiac surgery; ESP, erector spinae plane; IV, intravenous; PACU, postanaesthesia care unit ; PCIA, patient-controlled intravenous analgesia; NRS, 11-point Numerical Rating Scale; T_0, time of extubation; VARC-2, Valve Academic Research Consortium-2.

institutional routine, including the placement of an invasive arterial and central venous line, and transesophageal echocardiography. Moreover, the Bispectral Index (BIS) will guide the depth of anaesthesia in both groups.

PONV prophylaxis will be achieved with 5 mg intravenous dexamethasone and 4 mg intravenous ondansetron.

General anaesthesia will be maintained with inspiratory sevoflurane concentrations of 1.5%–2.0%, titrated to achieve a BIS of 40–60. Moreover, patients will receive a continuous infusion of dexmedetomidine 0.5 µg/kg/hour. Analgesia is achieved with a continuous infusion of remifentanil (0.1–0.3 µg/kg/min) and adjusted depending on patient's responses such as spontaneous movements, sweating, eyelash reflex, pupillary size, a sudden increase in heart rate or arterial blood pressure.

The surgical procedure is performed on cardiopulmonary bypass (CPB). Before the initiation of CPB, heparin is administered to achieve an activated clotting time (ACT) of >400 s. Prior to the release of the aortic clamp, magnesium sulfate 3 g intravenously will be administered. After separating the patient from CPB, protamine is administered for the reversal of heparin in order to achieve the normalisation of the ACT.

Interventional treatment

After completion of the surgery, the patient will be placed in a left lateral decubitus position (on the non-operated hemithorax). A high-frequency linear ultrasound transducer will be positioned 3 cm lateral to the T5 spinous process tip in a longitudinal orientation. After identifying three landmark muscles (trapezius, rhomboid major and erector spinae) and the T5 transverse process's tip, a 75 mm Sonolong Sono NanoLine needle (Pajunk, Germany) will be inserted in a cephalad-to-caudal direction as shown in figure 3.

The needle will be positioned on the tip of the T5 transverse process.[5] The needle's correct position will be confirmed by a linear pattern of fluid spread (20 mL) of trial medication deep to the erector spinae muscle. Subsequently, a catheter will be advanced 5 cm beyond the needle's tip into the interfascial plane below the erector spinae muscle.[5] Following visual confirmation (on ultrasound) of the correct catheter position, the remaining 10 mL of trial medication will be injected through the catheter; this will be defined as block time 0 (B_0). After securing the catheter with transparent sterile dressings, the patient will be turned on his back. Further administration of the trial medication will be performed through the catheter every 6 hours, with the last dose being administered 18 hours after the first injection.

Before removing the ESP catheter, visual confirmation, by ultrasound, for correct catheter position and spread will be performed after administering the last trial medication (B_0 +18 hours). The correct catheter position is defined as a visualisation of the catheter tip within the interfascial plane below the erector spinae muscle and a linear pattern of fluid spread into this plane.

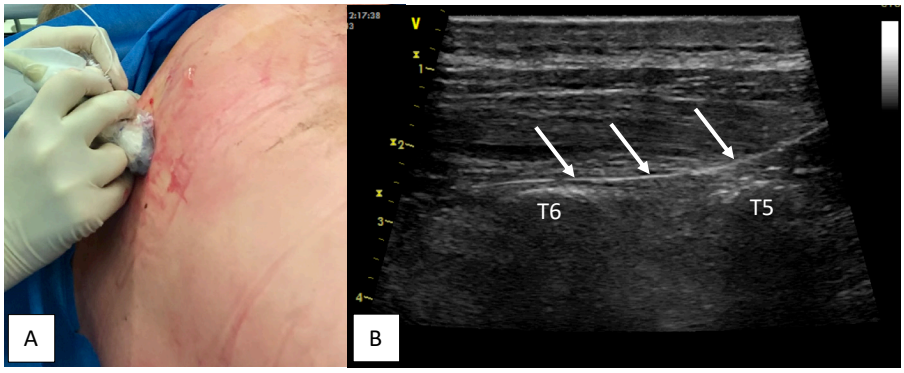

Figure 3 Placement of erector spinae plane catheter. (A) Patient in left lateral decubitus with the needle inserted in a cephalad-to-caudal direction. (B) Ultrasound image with the catheter (arrow) positioned below the erector spinae muscle above the tip of T5 and T6 transverse process.

Postoperative analgesia

Irrespective of group allocation, postoperative analgesia will be provided with a bolus of intravenous morphine (0.1 mg/kg) at the end of surgery and acetaminophen intravenously (15 mg/kg, four times a day). Patients are transferred intubated to the PACU under sedation with dexmedetomidine (0.5 µg/kg/hour) and remifentanil (0.1 µg/kg/min). These infusions will be stopped once the patient is clinically deemed ready for extubation, usually 30–120 min after admission to the PACU. Following extubation (T_0), patients will receive a patient-controlled intravenous analgesia (PCIA) pump with morphine, which will be programmed in an on-demand-only mode (morphine bolus of 1.5 mg every 7 min with a maximum of 30 mg every 4 hours). Administration of the trial medication through the ESP catheter at the PACU will be done every 6 hours after the first dose (B_0 +6 hours, B_0 +12 hours and B_0 +18 hours), three times in total.

Following extubation, the severity of pain will be assessed at rest and during coughing using an 11-point Numerical Rating Scale (NRS) for pain (0=no pain, 1–3=presence of pain but no additional treatment necessary, 4–7=moderate to severe pain requiring additional treatment with morphine PCIA and 7–10=severe to worst imaginable pain requiring rescue treatment). In case of severe postoperative pain (NRS for pain ≥7), a clinical bolus (1–2 mg) of morphine will be given to the patient. If the pain is localised at the drain incision site and does not respond to morphine PCIA treatment, an infiltration of 10 mL of ropivacaine 0.5% can be considered. The latter will be classified as treatment failure of the ESP block. Moreover, morphine PCIA is not sufficient to treat 'pericarditis pain'. The latter is expressed as sharp, stabbing chest pain and is mainly diagnosed based on clinical suspicion AND the documentation of new widespread ST segment elevations or PR depression on the ECG.[23] These patients will be treated with acetylsalicylic acid 500 mg intravenously every 8 hours and colchicine 1 mg orally two times per day.[23]

Twenty-four hours postextubation, morphine PCIA will be stopped and data will be extracted from the pump. Further analgesic treatment depends on the protocol used on the ward with acetaminophen (15 mg/kg every 6 hours) and intermittent subcutaneous morphine (0.1 mg/kg).

Patient and public involvement

Patient or members of the public were not involved in the development, recruitment or conduction of this study. After completion of the study, an information letter about the results will be provided for study participants.

Outcomes, measurement and data collection

Primary endpoint

The cumulative 24-hour morphine consumption, after patient's extubation, will be considered as the primary outcome parameter.

Secondary endpoints

Secondary endpoints include pain intensity evaluated by the NRS for pain, requested dosage of morphine PCIA, additional analgesic requirements (non-opioids), the extent of sensory block (assessed at T_0 +2 hours and T_0 +18 hours), time to chest drain removal, hospital length of stay and the incidence of adverse events (AE) related to the intervention or surgical procedure. Also, the incidence of other (serious) AE such as the incidence of atrial fibrillation, pleural effusion, pericarditis, LAST and PONV will be recorded. To detect a difference in the inflammatory response, blood samples will be collected at three different time points: at baseline (placement of arterial line), at the end of the surgery and at postoperative day 1 following the last dose through the ESP catheter. From these blood samples, inflammatory parameters (C reactive protein, interleukin (IL)-6 and IL-10) will be examined.

Safety issues

The interventional treatment will be performed under haemodynamic monitoring in a fully equipped operating theatre. The risk of accidental intravenous or intramuscular injection will be minimised by ultrasound guidance and needle aspiration before injection. Patients are

admitted to the PACU following surgery and block placement. A dedicated nurse will follow the patients' vital signs, and a computer-generated early warning system is continuously monitoring these vital signs.

The ESP block has been shown to be safe in numerous reports, with only two publications reporting a pneumothorax linked to the ESP block.[24] Large doses of local anaesthetics carry the potential risk of LAST and can affect the cardiovascular system (causing arrhythmias and hypotension) and the central nervous system (causing confusion, drowsiness and seizures). However, the doses administered in our study have been repeatedly used in recent studies without any side effects.[25 26] As a safety measure, patients will be continuously monitored in the PACU with pulse oximetry, ECG and invasive blood pressure until at least 1 hour after the last administration of the trial medication according to the guidelines of the ASRA.[2] In case of symptoms suggesting LAST, code break is allowed to start adequate treatment according to international guidelines.[27]

Also, the inclusion of each patient into the trial is entered in the electronic hospital information system. Hence, this is visible to all physicians and nurses involved in the patients' care. All AE will be reported immediately to the research coordinator and principal investigator. The latter will report suspected unexpected serious AE to the federal health authorities. Although safety will be evaluated, due to the small sample size, we will not be able to provide firm evidence on the safety of the ESP block in these patients.

Safety endpoints

Early safety endpoints at 30 days as defined by Valve Academic Research Consortium-2 (all-cause mortality, stroke, life-threatening bleeding, acute kidney injury (stage 2 or 3), major vascular complication or valve-related dysfunction) will be evaluated.[28]

Statistical analysis and sample size calculation

Sample size estimation

The present study aims to confirm the efficacy of the proposed treatment defined as an ESP block with ropivacaine 0.5% compared with placebo (normal saline 0.9%).

To have 80% power to show a 25% reduction in the 24-hour morphine consumption in the ropi group versus the placebo group using a two-sided test for a ratio of means (with an alpha=5%), 30 patients per group are needed assuming a coefficient of variation (CV) (SD divided by the mean) equals to 0.40. The assumed CV is a conservative estimate obtained from preliminary own, non-published data on MIMVS. To anticipate the loss of study power due to the possibility of dropouts, two extra patients in each group will be included, yielding 32 patients per group.

The CV will be checked in a blinded interim analysis after the inclusion of 32 patients in total. If the CV appears higher than assumed in the sample size calculation, we will increase the number of patients accordingly.[29] If the CV is lower than assumed, the sample size will remain the same.

Statistical data analysis

For the primary outcome, a two-sided t-test for the ratio of means on log-transformed data will be used to compare the 24-hour cumulative morphine intake between both groups. A 95% CI for the ratio of the geometrical means will be reported. A Mann-Whitney U test will test the robustness of the conclusion if the log-transformed data shows a departure from normality based on the Shapiro-Wilk W test statistic. A p value smaller than 0.05 will be considered significant.

As for the secondary endpoints, a linear model for longitudinal measurements (with the selection of the covariance structure based on the Akaike information criterion) will be used for variables that were measured over time (NRS for pain). The number of times morphine PCIA is requested will be analysed using a model for count data (Poisson or negative binomial model, depending on the presence of overdispersion). The incidence of LAST will be compared between the groups using Fisher's exact test. A Mann-Whitney U test will be used for the maximum number of dermatomes, separately at two time points (after the first and the last dose).

The postoperative evolution of the incidence of nausea and vomiting will be evaluated with a logistic regression model with generalised estimating equations. Fisher's exact test will be used for the comparison of the presence of 'ever PONV' during the postoperative follow-up, as well as for each of the early safety endpoints at 30 days (all-cause mortality, stroke (disabling and non-disabling), life-threatening bleeding, acute kidney injury—stage 2 or 3 (including renal replacement therapy), coronary artery obstruction requiring intervention and major vascular complication). A linear model for longitudinal measurements will be used with an unstructured covariance matrix to analyse the inflammatory response. For each serum marker, a separate analysis will be performed. If needed, a transformation of the response will be applied to obtain a normal distribution.

The (co-)investigator or study nurse will review completed case record forms for completeness and correctness before digitalisation and statistical analysis. Case record forms will be completed from data drawn from the source documents and the electronic hospital information system. Data will be coded and analysed in line with the intention-to-treat principle.

Ethics and dissemination

The trial will be carried out in compliance with the principles of the Declaration of Helsinki, the principles of Good Clinical Practice and following all regulatory requirements. The study, version DH 005—31 May 2019, is approved by the ethics committee of

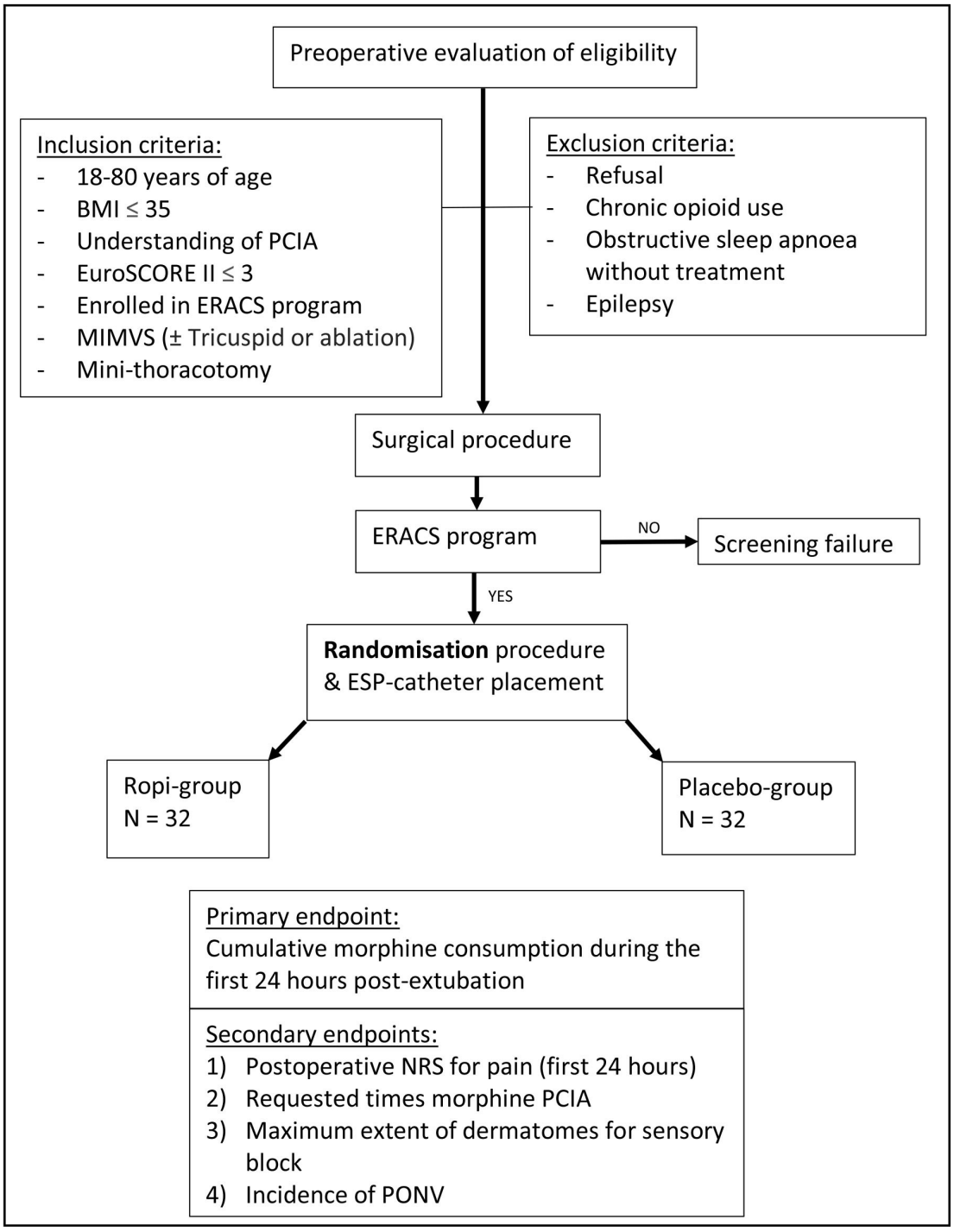

Figure 4 Schematic diagram of the study protocol and sampling process. BMI, body mass index; ERACS, enhanced recovery after cardiac surgery; ESP, erector spinae plane; MIMVS, minimally invasive mitral valve surgery; NRS, 11-point Numerical Rating Scale; PCIA, patient-controlled intravenous analgesia; PONV, postoperative nausea and vomiting.

the University Hospitals Leuven, the Clinical Trials Centre of the University Hospitals Leuven (S62638) and the 'Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten'. The study is registered in the European Clinical Trials Database of the European Medicines Agency. The trial design is summarised in figure 4. With regard to dissemination, the results of this trial will be published in an international journal.

Recruitment

The principal investigator or co-investigator will recruit all consecutive patients planned for elective MIMVS and being candidates according to the inclusion and exclusion criteria of this study (figure 4). Detailed background information will be given about the study and any issue brought forward by the patient will be answered. Besides, patients will be informed about the possible risk of the

study. Each eligible patient willing to participate in the present trial will have to give written informed consent before any particular study procedure.

Advantages for the participating patients

There is no guarantee that the use of ESP block with local anaesthetic ropivacaine will provide a benefit to the participating patient.

DISCUSSION

The primary goal of the current trial is to test whether an ESP block significantly reduces postoperative opioid consumption in patients undergoing MIMVS.

Strengths and limitations

Several publications have shown the benefits of ESP block in recent years.[6 8–11] Reduced opioid consumption, pain scores and even faster postoperative recovery after cardiac surgery have been reported.[9] To our knowledge, the current trial is the first placebo-controlled, double-blind, randomised controlled trial for a unilateral ESP block in an ERACS programme. We will evaluate the effect of adding an ESP block to a standard postoperative analgesic regimen on postoperative morphine consumption. Furthermore, we will evaluate the presence of a sensory block with a loss of cold sensation.

There are several limitations to our protocol. First, due to the novelty of the ESP block, little is known about optimal dosing regimens. The dosing of ropivacaine used in our trial has been chosen to balance the risk of LAST against the benefit of this regional anaesthetic technique. One could argue to reduce the concentration of ropivacaine from 0.5% to 0.25% or even lesser to increase the volume and/or reduce the dosing interval. We opted to use ropivacaine 0.5% to provide a dense block with adequate analgesic effect. Second, the interval between the boluses could theoretically be reduced. Based on our clinical practice in peripheral nerve blocks and published analgesic duration, we decided to set the interval between each bolus to 6 hours.[9] We will evaluate the timing of analgesic request from the PCIA pump and NRS for pain to detect whether the interval between the boluses is adequate.

Trial status

The final protocol version of the current study is DH 005, with the date of this version being 31 May 2019. Patient recruitment was started in July 2019. Enrolment is planned for a period of 24 months. An additional period of 4 months is intended for statistical analysis, manuscript preparation and publication of the study results in an international journal.

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Disclaimer The funders had no role in the design of the study. Nor will they have any role with data collection, analysis, reporting, dissemination plans of the study and publication.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Obtained.

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