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Enhanced Recovery After Surgery (ERAS) in Renal
Transplantation Patients

Pelin Karaaslan, Tümay Uludağ Yanaral

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Enhanced Recovery After Surgery (ERAS) in Renal Transplantation Patients

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Abstract

Enhanced recovery after surgery (ERAS) is a set of methods that provide early recovery with a multimodal approach in the perioperative care pathway. ERAS protocols are widely used worldwide in major surgery to improve surgical outcomes and require multidisciplinary collaboration. Using ERAS protocols means better pain management, earlier mobilization, improved oral nutrition, shorter hospital stays, and cost-effectiveness. ERAS protocols were introduced into renal transplant programs quite late. Transplantation patients are challenging and should be well prepared and followed up for ERAS. This review article highlights preoperative, intraoperative, and postoperative important points for preparing patients for renal transplantation for early recovery.

Keywords: Anaesthesia, cost-effectiveness, ERAS, quality, renal transplantation

Main Points

- Enhanced recovery after surgery (ERAS) protocols in renal transplantation by adapting them to the specific dynamics of the transplantation process.
- The ERAS program should be considered a multidisciplinary care approach in kidney transplantation, and its feasibility should be ensured in all clinics that perform kidney transplantation.

Introduction

Enhanced recovery after surgery (ERAS) is a set of methods that provide early recovery with a multimodal approach in the perioperative care pathway.¹ ERAS protocols are widely used worldwide in major surgery to improve surgical outcomes and require multidisciplinary collaboration. ERAS protocols can improve pain management, earlier mobilization, improved oral nutrition, and shorter hospital stays. These results suggest both enhanced quality of care and reduced costs.² The outlined guidelines include preoperative education, preoperative nutrition optimization, opioid-independent pain control, early mobilization, and early postoperative oral nutrition.¹ Even so, the reason for its late introduction into renal transplant programs is that it takes time to be sure of its safety and efficacy in these high-risk patients.³ ERAS for renal transplant patients was only put on the agenda in 2019 when it was realized that there was extremely poor standardization as a result of the study by Morkane et al.⁴ investigating perioperative renal transplantation practice in 23 different centers. The main points here are demonstrating the importance of ERAS in renal transplantation patients and the management facilities providing ERAS to such patients (Table 1).

Preoperative Preparation

A good ERAS protocol should start from the surgical preparation phase. Preparing a patient for transplantation can be challenging.

Patient education and counseling: All patients should be subjected to a preoperative education process about the operation process and its aftermath, possible complications, and how to deal with them. Thus, the patient will be able to reshape his/her expectations about surgery, be psychologically well prepared, and increase his/

her belief in rapid recovery.⁵ When patients are advised to lose weight and quit smoking before surgery, the process will be much more successful. Although the optimal time to quit smoking is not known, *Kidney Disease: Improving Global Outcomes* states that smoking should be stopped at least 4 weeks before surgery, and the risks will decrease in proportion, and the greater the number of weeks of quit, the lower the risks.⁶ With good counseling, the uneasiness of patients with surgical anxiety can be overcome, and this will make things easier, even with pain control.⁵

Medical optimization: If the patient is evaluated well in terms of cardiac, respiratory, and metabolic aspects and is operated on in the best possible condition, the risk of adverse events will decrease. The rate of cardiac disease comorbidity in patients with end-stage renal failure may be 5-30 times higher than that in the normal population.⁷ Patients should be evaluated and treated by a cardiologist who is included in the team and who is familiar with the cardiac management of transplant recipients. Non-invasive coronary tests should be performed in patients deemed necessary, and even the need for percutaneous coronary angiography should be evaluated. Patients with unstable coronary vascular disease, valvular disease, and heart failure should undergo repeated cardiac evaluations because they are on the waiting list and may need to be prepared for emergency surgery.² The optimal screening frequency for cardiac asymptomatic transplant candidates is unknown. Transplant candidates are 2-8 times more likely to be diagnosed with pulmonary hypertension than the normal population because of fistulas used for dialysis, fluid overload, anemia, impaired left ventricular function, and endothelial structure. In particular, patients with a pulmonary pressure >35 mmHg are considered at high risk of morbidity and mortality. The flow and duration of the fistula are also related to the severity of pulmonary hypertension. Pulmonary hypertension should be treated with vasodilator agents in a good preoperative preparation. If patients have substance abuse during preoperative preparation, have heart disease that cardiologists are still treating, have high pulmonary pressures and ongoing problems in lung volumes and capacities, a new stroke, or active peripheral arterial disease; a good ERAS optimization would be to postpone the surgery of these patients until the treatments are completed.⁶

Anemia treatment is also part of medical optimization. It should be remembered that wound infection, pneumonia, sepsis, and mortality are more common in patients who are anemic and require intraoperative blood transfusion. Oral or intravenous iron therapy should be started in the preoperative evaluation of appropriate patients diagnosed with anemia ($Hgb \leq 11$ g dL⁻¹). Anemia in patients with renal failure should be managed if the hemoglobin (Hb) level falls to 11 g L⁻¹ or becomes symptomatic.² Erythropoietin treatment should not be avoided when necessary. Graft life

may be shortened in patients with anemia, and the goal should be a normal Hb level after transplantation. Another important point of care for hematological problems is coagulation problems. Dialysis anticoagulation, medical treatments, and intraoperative heparinization should all be considered and discussed in detail with the patient, and central blocks instead of general anaesthesia should be avoided. Hemodialysis the day before transplantation will optimize fluid status, correct electrolyte imbalance, and prevent metabolic imbalance. Because of the risks of sudden and unintended fluid imbalance, dialysis should not be performed on the day of transplantation unless very high potassium levels and fluid overload are present.

Improving nutritional status and carbohydrate loading: Intense inflammation, loss of appetite, uremia, long fasting periods before the procedure, and high comorbidities can cause poor nutritional status. Because postoperative morbidity will be higher in patients with malnutrition, nutritional correction should be implemented according to ERAS protocols. Oral nutritional supplements and enteral or parenteral nutrition solutions should be started at least seven days before transplantation. Serum albumin levels should be maintained within the normal range. Kidney transplantation patients are usually placed on preoperative dialysis in preparation for transplantation and may remain dehydrated. Clear liquids should be consumed up to the last two hours on the morning of the operation. Preoperative carbohydrate-rich clear liquid food, which accelerates recovery and shortens the fasting period, is an important step for ERAS. Rapid recovery from the surgical catabolic process can be achieved using carbohydrate-rich fluids.¹ Preoperative administration of solutions containing complex carbohydrates, such as maltodextrin, is recommended by ERAS associations and the European Society of Anaesthesia. The advantages of carbohydrate loading include optimizing metabolism, increasing insulin sensitivity, decreasing nausea and vomiting, and decreasing anxiety.⁵ Non-diabetic kidney recipients may benefit from preoperative carbohydrate loading.³ In preoperative transplant recipients who consume carbohydrate beverages, postoperative nausea and vomiting will decrease, insulin resistance will improve, and hospital stay will decrease.²

Anxiolysis: Anxiety may complicate anaesthesia induction, maintenance, and postoperative recovery. There are no studies in the literature showing a relationship between premedication and graft function. Unfortunately, there is not enough information about the best premedication medication for kidney transplant recipients. However, the necessity of adequate preoperative information and psychological support cannot be ruled out. While premedication is recommended for patients with intense anxiety, adequate psychological support is sufficient for others. Premedication with a proton pump inhibitor or H₂

inhibitor in patients with slow gastric emptying can reduce the risk of aspiration.

Intraoperative Care

Standard Anaesthesia Protocol: While propofol or thiopental is safe for induction, ketamine should be avoided, especially in patients with ischemic heart disease associated with renal failure. The selection of muscle relaxants and reversal drugs should be appropriate for renal failure. Thus, atracurium or cisatracurium is the most appropriate option.² Opioid derivatives, except morphine, can be safely used intraoperatively, but it may be more beneficial to avoid them in ERAS protocols for postoperative pain control. Sevoflurane or desflurane inhalation anaesthesia or intravenous infusion anaesthesia with propofol may be appropriate. Norepinephrine is a suitable alternative for patients requiring intraoperative vasopressors.⁸ Prevention of nausea and vomiting at the end of surgery is an important pillar of ERAS protocols. Medical treatment includes ondansetron therapy and avoiding high doses of opioids. Nausea and vomiting delay discharge, decrease patient satisfaction, delay early oral feeding, prolong hospital stay and increase costs. These are important points that need to be addressed in ERAS protocols. Immunosuppressive methylprednisolone may prevent nausea and vomiting, but standard nausea and vomiting prophylaxis may also be helpful in ERAS.

Targeted fluid therapy: Optimized perioperative hemodynamic management can prevent delayed graft function. Current data support the use of targeted fluid therapy during kidney transplantation. It should be recognized that central venous pressure (CVP) measurement is not a precise and reliable method for assessing fluid status in most cases.¹ However, comparing the baseline CVP values with the intraoperative ongoing changes may direct fluid therapy; therefore, central venous catheterization is usually recommended for recipients. The use of transesophageal echocardiography, pulse-volume index, and pulse-pressure index monitoring can prevent cardiovascular complications, fluid overload, and delayed graft function.³ Fluid overload will increase the weight of the kidney transplant patient, cause fluid overload in the lungs, cause intestinal wall edema, and ultimately, cause prolonged ileus and delayed discharge. As a result, the best fluid resuscitation principle should be: "As much as needed, as little as possible".⁹ The proper fluid type remains controversial and open for research, but balanced crystalloid solutions seem to be the best choice.^{1,9} A goal-directed fluid therapy is performed with crystalloid infusion at 3-5 mL kg⁻¹ h⁻¹ supplemented with 5% albumin if needed.¹ Diuresis induced by diuretic agents is recommended, especially immediately after reperfusion, and is particularly important for verifying successful transplantation.

Perioperative hyperglycemia control: Diagnosis of diabetes and the type of steroid used in treatment can complicate glycaemic control. All patients with pre-diabetes and 66% of transplant recipients without a diagnosis of diabetes require insulin treatment after transplantation.¹⁰ In the ERAS application recommendations, blood glucose should be targeted at 140-189 mg dL⁻¹ during the perioperative period.¹¹

Temperature control: Hypothermia can cause perioperative complications, such as wound infection, coagulation disorders, increased transfusion requirements, impaired drug metabolism, and delayed awakening. Each of these would be sufficient to disrupt the proper progression of the ERAS protocol. Patient warming should have started from the ward to the operating room. The temperature should be recorded before sedation and measured every 30 minutes. The central temperature should be targeted at 36.0 °C and above, and the patient should be warmed throughout the surgery. The warming process must be continued in the recovery room.¹²

Postoperative Management

Early mobilization: Poor physical activity is associated with poor quality of life. Early mobilization can reduce both the complication rates and duration of hospital stay. Respiratory and thromboembolic complications associated with prolonged bed rest can be easily prevented with early mobilization.⁵ Lack of physical activity may also trigger muscle atrophy, joint movement limitation, pressure ulcers, and atelectasis.¹³ Patients' quality of life will improve with mobilization. Exercises started in the early period will increase functional capacity, muscle strength, and quality of life.

Early enteral nutrition: According to traditional wisdom, the initiation of postoperative oral nutrition was slow and gradual. In this practice, transparent liquid foods were introduced, followed by a gradual transition to solid foods. However, new evidence suggests that feeding should be started as early as possible after surgery, either orally or through a nasogastric tube. There is no need for a routine nasogastric tube. Patients can tolerate oral fluids quickly. Moreover, they can be rapidly switched to a routine postoperative diet.

Catheter and drain maintenance: Leaving a foley catheter in place for a prolonged period is a high-risk factor for urinary tract infection. The early removal of postoperative catheters is safe for a good ERAS protocol. If a patient has a prophylactic J-stent, it should be removed as early as possible to reduce the risk of postoperative infection and stenosis.

Pain control: In addition to reducing postoperative pain, multimodal pain control in the ERAS guidelines is necessary

to facilitate early oral food intake, early mobilization, and accelerated surgical recovery.¹⁴ The effects of opioid use in postoperative pain control, such as slowing down bowel movements, and side effects, such as dizziness, nausea, vomiting, blurred vision, late mobilization, disruption of the mucosal immune response of host defense mechanisms, and disruption of the microbiota leading to infection of some pathogens, have led to opioid-independent pain control in ERAS steps.¹ Furthermore, unlike ERAS protocols used in other surgeries, nonsteroidal anti-inflammatory drugs have no place in pain control in renal transplantation ERAS protocol because of their nephrotoxicity. Therefore, local anaesthetics, surgical incision infiltration anaesthesia, and plane blocks are the building blocks of the multimodal approach to renal transplant ERAS pain control.¹ Performing a plane block reduces the need for opioids and the associated incidence of nausea and vomiting, prevents slowing of bowel movements, and facilitates early mobilization.²

Table 1. ERAS Protocol for Renal Transplant Patients¹⁵

Preoperative	Perioperative	Post-operative
Oral and written information and patient education	Carbohydrate loading and oral fluid storage until 4 h before surgery	Goal-directed fluid therapy
Smoking cessation	TED stockings	Early mobilization
Average weight and blood pressure	Anxiolysis	Early oral feeding
Cardiac optimization	Proper induction and maintenance anaesthesia agents	Early removal of drains and catheter
Anemia management	Goal-directed fluid therapy using crystalloids	Education about drugs and doses and the outpatient review protocol
		Post-discharge outpatient clinic review
ERAS, Enhanced Recovery After Surgery; TED, thromboembolism deterrent.		

In conclusion, even though ERAS protocols have entered practice later than other surgeries, it is possible to implement ERAS protocols in renal transplantation by adapting them to the specific dynamics of the transplantation process. The ERAS program should be considered a multidisciplinary care approach in kidney transplantation, and its feasibility should be ensured in all clinics that perform kidney transplantation.

Footnotes

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The Erector Spinae Plane Block with 20 or 30 mL of 0.25% Bupivacaine Provides Equivalent Postoperative Analgesia after Mastectomy: A Prospective Randomized Trial

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Abstract

Objective: Analgesia management following breast surgery is a critical concern. The erector spinae plane block (ESPB) is a regional anaesthesia technique that is frequently used for analgesia after breast surgery. However, there is no consensus on the volume. Therefore, the aim of this study was to compare ESPB performed using 20 mL vs. 30 mL.

Methods: The study included 43 female patients with American Society of Anesthesiologist class I-II physical status. Participants were randomized into two groups: 20 mL ESPB and 30 mL ESPB. Ibuprofen (400 mg) 3x1 was ordered, and a fentanyl patient-controlled analgesia device was attached intravenously to the participants. If the pain score was ≥ 4 , meperidine (0.5 mg kg⁻¹) was administered.

Results: Postoperative fentanyl use was similar between the groups. There was no difference in the amount of rescue analgesic use between the groups. The static and dynamic numerical rating scores were similar between the groups. No statistical difference was noted in terms of nausea, vomiting, or itching between the groups.

Conclusion: A similar analgesic effect is achieved by performing ESPB using 20 or 30 mL of local anaesthetic at the same concentration.

Keywords: Breast, erector spinae plane block, mastectomy, pain management, volume

Main Points

- Erector spinae plane block (ESPB) is a regional anaesthesia method frequently used for analgesia management after breast surgery.
- However, different spread patterns have been reported in radiological and cadaver studies of this block.
- The amount of volume to be applied is also a matter of debate.
- In this study, we observed that 20 and 30 mL ESPB had equal analgesic efficacy.

Introduction

Pain control is a significant challenge that affects patient comfort after mastectomy and axillary lymph node dissection, which are common surgeries nowadays. In the postoperative period, approximately 50% of patients experience severe acute pain that may lead to the development of chronic pain.¹ This pain can hinder postoperative recovery by causing difficulties in breathing and delayed mobilization,^{1,2} and regional anaesthesia methods, such as the erector spinae plane block (ESPB), are employed to manage postoperative pain following breast surgery.

When applied at the T4-T5 level, ESPB provides thoracic analgesia by targeting the posterior and anterior branches of the spinal nerves through the administration of a local anaesthetic between the transverse process (TP) of the thoracic vertebra and the anterior fascia of the erector spinae muscles (ESM).³ Because the block's application site is distant from the pleura and neuraxial tissues, it has a reduced risk of complications related to injury to these structures. Performing the block under ultrasound guidance allows visualization of the anatomy and spread of the local anaesthetic.³⁻⁵

Randomized controlled studies have reported that ESPB provides effective postoperative analgesia after breast surgery.⁶⁻¹⁸ However, the optimal volume of local anaesthetic to be administered remains unclear. Radiological imaging and cadaver studies have demonstrated different spread patterns with varying local anaesthetic volumes.¹¹⁻¹⁴ Therefore, in our study, we performed ESPB with different volumes of local anaesthetic (20 mL and 30 mL) to evaluate the effectiveness of pain relief in participants who underwent mastectomy and axillary lymph node dissection. Our primary goal was to compare opioid consumption after surgery, with secondary goals of assessing and comparing postoperative pain levels [numerical rating score (NRS)], the amount of rescue analgesic use, and the adverse consequences of opioid use, including emesis, nausea, and allergic responses.

Methods

Study Design

This prospective, randomized study was approved by the İstanbul Medipol University Non-Interventional Clinical Research Ethics Committee (approval no.: 997, dated: September 30, 2021). After receiving ethics committee approval, the study was registered at clinicaltrials.gov (NCT05232084). The study included 43 female patients aged 18-65 years who were classified into the American Society of Anesthesiologist (ASA) I-II group and underwent elective, unilateral mastectomy and axillary lymph node dissection under general anaesthesia at Medipol Mega University Hospital between January 2022 and June 2023.

Patients with a thoracic region deformity or bleeding diathesis, those receiving anticoagulant treatment, those with infection in the block area, and those allergic to opioids and local anaesthetics were excluded from the study.

Grouping and Randomization

Prior to their arrival in the operating room, the patients were randomly divided into 2 groups (Group 20 mL ESPB = Group 20; Group 30 mL ESPB = Group 30) using a computerized randomization program. Patients were

informed about ESPB and the use of the patient-controlled analgesia (PCA) device, and they provided written informed consent.

General Anaesthesia

Following patient transfer to the operating room, electrocardiography, peripheral oxygen saturation (SpO₂), and non-invasive arterial blood pressure were continuously monitored. Intubation was then performed using an appropriately sized endotracheal tube. Anaesthesia was maintained by infusion of 0.01-0.1 µg kg⁻¹ min⁻¹ remifentanyl and inhalation of 1-2% sevoflurane in a 50% oxygen/air mixture. The mechanical ventilator settings were adjusted to a tidal volume of 6-8 mL kg⁻¹ and an end-tidal CO₂ of 30-35 mmHg. All surgical procedures, including breast-conserving surgery and axillary lymph node dissection, were performed by the same team following the same protocol. For multimodal analgesia, all patients received 400 mg intravenous (IV) ibuprofen and 100 mg IV tramadol 30 minutes before the conclusion of the surgery. Additionally, ondansetron was intravenously administered to prevent postoperative nausea and vomiting. Participants who exhibited sufficient spontaneous breathing were extubated.

ESPB Procedure

Following the surgical procedure, ESPB was performed under general anaesthesia before extubation. During the ESPB, the patient was placed in the lateral decubitus position with the surgical side up during the ESPB (Figure 1).

A high-frequency linear transducer (11-12 MHz) and an 80-mm block needle (Braun 360°) were used. The transducer was located longitudinally over the TP of the T4 vertebrae. The muscles are seen on the hyperechoic TP, from top to bottom: the ESM, rhomboid major in the middle, and trapezius at the top. Using the in-plane technique, the block needle was moved forward in the craniocaudal direction, and five milliliters of regular isotonic injection were used to confirm the block position deep into the ESM. Following confirmation, Group 20 was given 20 mL of 0.25% bupivacaine, while Group 30 was given 30 mL of the same substance (Figure 2).

Protocol for the Postoperative Management and Evaluation of Outcomes

Following surgery, patients were administered 400 mg of ibuprofen every 8 hours. Patients in all groups were connected to an IV PCA containing 10 µg mL⁻¹ fentanyl, a 10 µg bolus without an infusion dose, and a 10-min lock-time protocol. An anaesthesiologist who was not involved in the study conducted a postoperative patient evaluation. NRS was used for postoperative pain evaluation (From 0/no discomfort to 10/the greatest amount of pain felt). Resting and dynamic NRS scores were evaluated and recorded at

the 1st, 2nd, 4th, 8th, 16th, and 24th hours. If the NRS score was ≥ 4 , 0.5 mg kg⁻¹ IV meperidine was administered as a rescue analgesic. The amount of rescue analgesic administered, the amount of PCA used, and any side effects, such as itchiness, nausea, and emesis, were recorded.

Quantity of Samples and Statistical Evaluations

The G*Power tool (V.3.1.9) was used to determine the study sample size. Comparison of postoperative opioid usage was the main goal. A preliminary study involving eight patients included in each group (16 patients in total) revealed postoperative opioid consumption of 20 µg in Group 20 and 30 µg in Group 30. The standard deviations were determined as 13 µg and 11 µg, respectively. Based on 0.05 alpha (α) error and 0.20 β error, the minimum number of patients needed to be included in each group was 19 with 80% power.

The Shapiro-Wilk test was used to assess the normality of the data and distribution patterns of the variables. When test results showed that the data were normally distributed, the data were described using mean ± standard deviation and subjected to an Independent Samples t-test to evaluate group-wise differences in outcome parameters. Group differences were examined using the Mann-Whitney U test, and continuous data with a non-parametric distribution were characterized using the median and interquartile range. A

value of p<0.05 was considered statistically significant. We used SPSS V.25 (SPSS, Chicago, IL, USA) for all statistical analyses.

Results

A CONSORT flow diagram was used for patient enrollment in the study (Figure 3). Each patient’s age, ASA score, height, weight, surgical duration, and anaesthesia duration are presented in Table 1. There were no discernible changes in demographic information, surgical duration, or anaesthetic duration in the groups.

Fentanyl use from the PCA device was evaluated at postoperative 0-8, 8-16, and 16-24 hours, and as total consumption in 24 hours. Postoperative fentanyl use showed no discernible variation between the groups. Nine patients in Group 20 and eight in group 30 required rescue analgesics. The extent of rescue analgesic use was similar between the groups (Table 2).

NRS scores were recorded in both groups at the 1st, 2nd, 4th, 8th, 16th, and 24th hours. The static and dynamic NRS scores were similar between the groups (Table 3). No statistical difference was noted in terms of nausea, vomiting, or itching between the groups (Table 4).

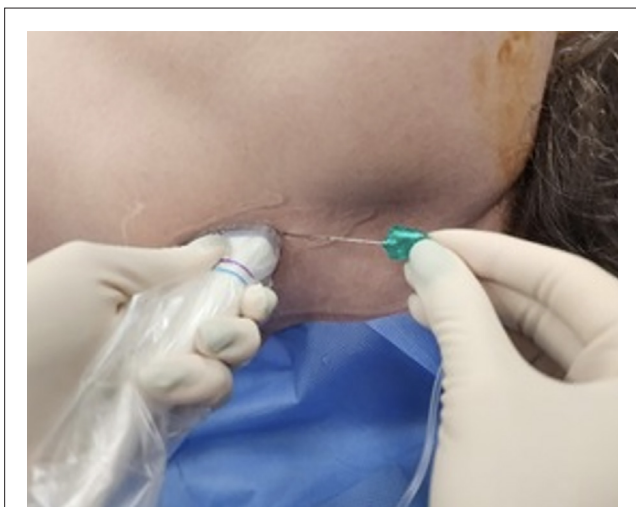


Figure 1. Patient, probe, and needle positions during block



Figure 2. Sonographic images of the ESPB at the T4 vertebral level and local anaesthetic spread.

ESM; erector spinae muscle; TP, transverse process, LA; local anaesthetic

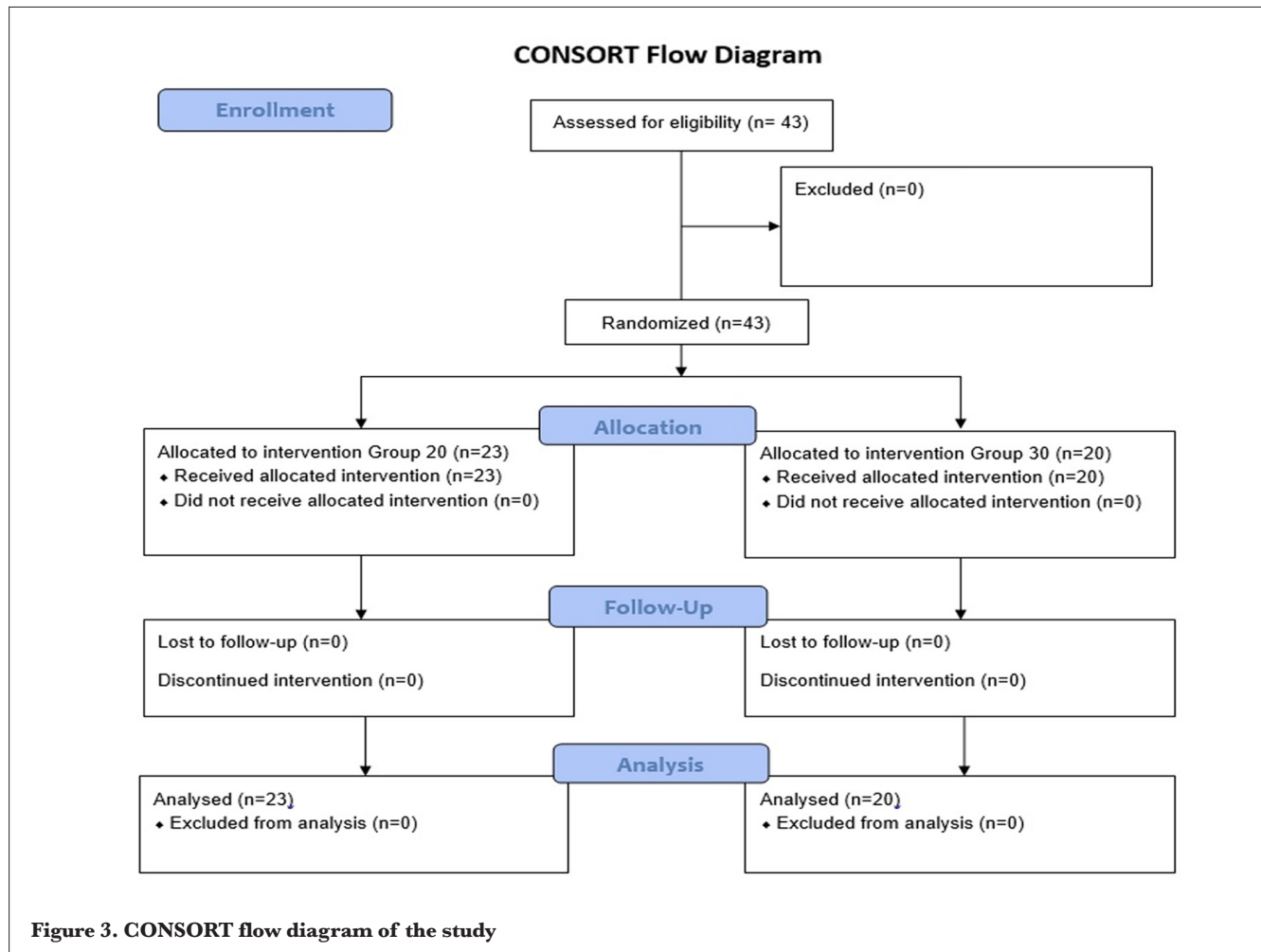


Table 1. Comparison of Demographic Data, Surgery and Anaesthesia Times Between Groups

	Group 20 (n=23)	Group 30 (n=20)	P value
Age	51 (41-59)	60 (45-63)	0.247*
ASA (I/II)	11/12	7/13	0.395†
Height (cm)	165 (161-170)	157 (154-160)	0.565*
Weight (kg)	71 (65-80)	66 (58-79)	0.201*
Duration of surgery (min)	110 (93-129)	106 (97-127)	0.981*
Duration of anaesthesia (min)	85 (68-105)	80 (65-100)	0.687*

Values are expressed as mean ± standard deviation or numbers.
 *P value was obtained by Mann-Whitney U test median (percentiles 25-75).
 †P value was obtained by Pearson's χ^2 test (n).
 ASA, American Society of Anesthesiologist.

Table 2. Comparison of Postoperative Opioid Consumption and Rescue Analgesia Use Between Groups

	Group 20 (n=23)	Group 30 (n=20)	P value
PCA 0-8 th hour (µg)	0 (0-10)	0 (0-20)	0.537
PCA 8-16 th hour (µg)	0 (0-0)	0 (0-10)	0.504
PCA 16-24 th hour (µg)	0 (0-0)	0 (0-0)	0.351
PCA total (µg)	0 (0-15)	0 (0-40)	0.647
Rescue analgesia (number of patients)	9	8	0.95†
Dosage of rescue analgesia (mg)	100 (100-100)	100 (62-100)	0.271

Data are expressed as median.
 P value was obtained by Mann-Whitney U test median (percentiles 25-75).
 †P value was obtained by Pearson's χ^2 test (n).
 PCA, patient-controlled analgesia.

Table 3. Comparison of Static and Dynamic NRS Assessment Between Groups

	Group 20 (n=23)	Group 30 (n=20)	P value
Static NRS			
1 st hour	0 (0-1)	0 (0-0)	0.221
2 nd hour	0 (0-2)	0 (0-3)	0.369
4 th hour	0 (0-1)	0 (0-2)	0.105
8 th hour	0 (0-1)	0 (0-0)	0.497
16 th hour	0 (0-0)	0 (0-0)	0.615
24 th hour	0 (0-0)	0 (0-0)	0.218
Dynamic NRS			
1 st hour	0 (0-2)	0 (0-0)	0.147
2 nd hour	0 (0-2)	1 (0-4)	0.529
4 th hour	0 (0-1)	0 (0-2)	0.142
8 th hour	0 (0-2)	0 (0-1)	0.295
16 th hour	0 (0-1)	0 (0-1)	0.975
24 th hour	0 (0-0)	0 (0-0)	0.120
Data are expressed as median (25-75 th percentile). NRS, numerical rating score.			

Table 4. Comparison of Side Effects Between Groups

	Group 20 (n=23)	Group 30 (n=20)	P value
Nausea	6	6	0.775
Vomiting	2	2	1
Itching	4	6	0.473
P value was obtained by Pearson χ^2 (n) test.			

Discussion

This study compared the effectiveness of ESPB administered at different volumes (20 mL vs. 30 mL) for postoperative analgesia management after mastectomy and axillary lymph node dissection. Our results indicated no difference in postoperative analgesia management between 20 mL and 30 mL ESPB in participants undergoing breast surgery and axillary dissection. According to our results; there was no difference between groups in terms of fentanyl use from the PCA device, static/dynamic NRS, need for rescue analgesia, and adverse effects. After breast surgery, patients often experience significant pain due to extensive tissue manipulation and potential nerve damage. Effective pain management is crucial to facilitate recovery and improve quality of life,^{1,2} particularly because postsurgical pain in these patients can lead to complications, such as delayed mobilization, prolonged hospital stays, and decreased patient comfort. Methods for analgesia include a combination of pharmacological and regional anaesthesia

approaches. Pharmacologically, opioids, non-steroidal anti-inflammatory drugs, and acetaminophen are commonly used to manage acute postoperative pain, whereas regional anaesthesia techniques provide targeted pain relief and reduce the need for systemic medications. Although the most commonly used analgesic method for this purpose is opioids, these drugs have adverse effects. For this reason, regional anaesthesia methods have begun to take on prominence. Several regional anaesthesia techniques are used for the breast and axillary regions. A multimodal pain management strategy tailored to the individual patient's needs is often the most effective approach for controlling pain following breast surgery.¹

ESPB is an innovative plane-blocking technique used to manage pain, particularly in thoracic and abdominal surgeries, including breast surgery. This block involves the injection of a local anaesthetic into the plane at the depth of the ESM adjacent to the TP of the thoracic vertebrae.³⁻⁵ The mechanism of the ESPB hinges on the diffusion of the anaesthetic along the fascial planes and the subsequent spread of the drug to the dorsal and ventral rami of the spinal nerves. This diffusion effectively numbs the nerves responsible for transmitting pain signals from the surgical site. By blocking these nerves, the ESPB provides substantial pain relief and reduces the need for systemic analgesics, such as opioids, which can have significant side effects. This technique is valued for its simplicity, safety, and ability to cover a wide area of innervation, making it a versatile option for managing postoperative pain. In recent years, many studies on the ESPB mechanism have been published. In their article, Bailey and Uppal¹¹ asked whether the ESPB is a silver bullet or overhyped. They stated that the possible mechanism of ESPB is an anaesthesia's dissemination to the paravertebral and epidural spaces. Coppens et al.¹² raised the question of whether ESPB is "Stranger Things" or a "paranormal block". In their article, they explained the mechanism of action of ESPB as a "triple mechanism" involving dorsal, anterior, and paravertebral spread. The available literature indicates that all these mechanisms and diffusion/spread theories are volume-dependent. Tulgar et al.¹³ asked whether ESPB is "a miracle or self-persuasion," and emphasized that the mechanism of action of ESPB actually changes when the needle touches different points of the TP and when the volume differs. Gadsden et al.¹⁴ compared the spread of different volumes of ESPB in a cadaver study. They reported that the spread increased with the applied volume, and they concluded that the ideal volume for ESPB was 30 mL. Ciftci et al.¹⁵ compared 20 mL and 30 mL ESPB in their cadaver study and stated that the spread was greater with 30 mL, but they reported no axillary spread with either volume. While cadaver studies have suggested that higher volumes may be more effective, our clinical study found that 30 mL and 20 mL volumes had comparable effects. We attribute this difference to factors

such as tissue perfusion in living subjects versus cadavers and the influence of respiratory movement on local anaesthetic spread. Although cadaver studies are invaluable for regional anaesthesia techniques, the solution distribution in blood-perfused living tissue may follow distinct patterns. Additionally, the similar efficacy between volumes in our study may be related to the individual anatomical characteristics of the patients. Abdella et al.¹⁶ evaluated the effect of different volumes (20 mL vs. 40 mL) of ESPB on the pain scores, craniocaudal spread, paravertebral spread, epidural spread, and clinical dermatomal spread in patients who underwent mastectomy. They reported no difference in pain scores, spread to the paravertebral area, epidural area, or exit point of the spinal nerve roots. However, in the high-volume applied group, the craniocaudal spread area was wider. In our study, there was no difference between the groups in terms of pain scores or opioid consumption. Zengin et al.¹⁷ conducted a clinical trial that compared 20 mL vs. 30 mL ESPB in patients who underwent thoracotomy. They concluded that 30 mL of ESPB provided more effective analgesia. Solmaz Demirel et al.⁷ compared 20 mL vs. 30 mL volumes of ESPB in patients who underwent breast surgery. They used 0.375% bupivacaine and reported no differences between the groups. Similarly, in our study, we found no difference between the effectiveness of 20 mL or 30 mL volumes of bupivacaine at a 0.25% concentration. On the other hand, the concentration is as important as the volume for the effectiveness of the block. Altuparmak et al.¹⁸ compared different concentrations of ESPB (0.375% vs 0.25% bupivacaine) and reported that higher is more effective than lower concentrations. In our study, different volumes with the same concentrations were compared.

Study Limitations

Our study has some limitations. Our sample size was relatively small; therefore, different results may be obtained with studies involving a larger number of patients. Different results may also be obtained for volumes other than 20 mL and 30 mL. We were also unable to perform dermatome analysis; thus, further valuable results could be obtained by performing this analysis.

Conclusion

According to our results, a similar analgesic effect was achieved by performing ESPB using 20 or 30 mL of local anaesthetic at the same concentration. NRS scores, opioid consumption, and incidence of adverse effects were similar between the groups.

Ethics

Ethics Committee Approval: This prospective, randomized study was approved by the İstanbul Medipol University Non-Interventional Clinical Research Ethics Committee (approval no.: 997, dated: September 30, 2021).

Informed Consent: Patients were informed about ESPB and the use of the patient-controlled analgesia (PCA) device, and they provided written informed consent.

Footnotes

Author Contributions: Surgical and Medical Practices - M.B., B.Ç., P.B., Y.O.A.; Concept - M.B., B.Ç., P.B., B.E.G., Y.O.A.; Design - M.B., B.Ç., P.B., B.E.G., Y.O.A.; Data Collection and/or Processing - M.B., B.Ç., P.B., Y.O.A.; Analysis and/or Interpretation - B.Ç., B.E.G.; Literature Review - M.B., B.Ç., Y.O.A.; Writing - M.B., B.Ç., Y.O.A.

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Bilateral Modified Thoracoabdominal Nerve Block Through a Perichondrial Approach in Patients Undergoing Major Abdominal Surgery: A Randomized Single-Blind Controlled Trial

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Abstract

Objective: Modified thoracoabdominal nerve block with a perichondrial approach (M-TAPA) provides effective analgesia in the anterior and lateral thoracoabdominal regions. Previous studies have shown the efficacy of M-TAPA in laparoscopic surgery. The primary aim of this study was to investigate the efficacy of M-TAPA block in patients undergoing open major abdominal surgery.

Methods: This study was designed as a prospective, randomized, single-blind, controlled study. A total of 43 patients were included in the study. In group M-TAPA, the block was performed bilaterally at the end of the surgery. Local wound infiltration was performed on the control group. Postoperative analgesia was provided with patient-controlled intravenous morphine. When numeric rating scale (NRS) pain scores exceeded 4, rescue analgesia with tramadol was administered. The primary outcome of this study was to compare the 24-hour total morphine consumption. The secondary outcomes included comparing pain scores, rescue analgesia requirements, and patient satisfaction.

Results: Regarding our primary outcome, median morphine consumption during the first 24 hours was lower in the M-TAPA group [16 (14-18)] than in the control group [24.5 (19.5-27)] ($P < 0.01$, 95% confidence interval: -9, 42 and -3.01). Additionally, NRS scores were significantly lower and patient satisfaction was significantly higher in the M-TAPA group. The need for rescue analgesics in the first 24 hours was comparable among the study groups.

Conclusion: The M-TAPA block is an effective abdominal wall block that can be considered part of multimodal analgesia in open major abdominal surgery.

Keywords: Analgesia, major abdominal surgery, plane block, pain management, postoperative pain, ultrasonography

Main Points

- Major abdominal surgery is associated with severe postoperative pain.
- The use of multimodal analgesic therapy is essential for postoperative pain management in major abdominal surgery.
- The Modified thoracoabdominal nerve block with a perichondrial approach (M-TAPA) block has the potential to offer extensive analgesia across a wide area of the anterior abdomen with a single puncture per side, indicating promise for effective pain relief.
- Bilateral M-TAPA block can be used as part of multimodal analgesia in open major abdominal surgery with a midline incision.

Introduction

Intense postoperative pain and distress are linked to increased morbidity, prolonged recovery time, and decreased patient satisfaction. Inadequate pain management is a risk factor for ongoing opioid use and persistent postoperative pain.¹ While traditional opioid-based regimens are effective, they have adverse effects that can hinder recovery and prolong hospital stays. In open abdominal surgeries, enhanced recovery protocols emphasize limiting opioid use through multimodal analgesia, including central and peripheral nerve blocks.^{2,3} Despite being effective, central blocks are less frequently used due to technical challenges and systemic side effects. Peripheral blocks, which are easier to administer, offer targeted pain relief with fewer systemic effects, thereby reducing opioid consumption and related side effects.^{4,5}

Major abdominal surgery encompasses a wide range of procedures across diverse patient groups, resulting in varying levels of pain and analgesia needs. Fascial plane blocks offer effective analgesia for abdominal surgeries, thereby avoiding the sympathetic block and hypotension associated with central blocks, as well as the risk of epidural hematoma in patients with coagulopathy. Recent studies have demonstrated the efficacy of quadratus lumborum blocks, erector spinae plane blocks, transversus abdominis plane, and rectus sheath blocks in providing postoperative analgesia and assisting in functional recovery in major abdominal surgery.⁶⁻¹⁰ Consequently, interest in local anaesthetic abdominal wall blocks as a component of multimodal analgesia has increased.

Modified thoracoabdominal nerve block through the pericondrial approach (M-TAPA), is a novel plane block technique that provides analgesic effects through the injection of local anaesthetic at the lower aspect of the chondrium, at the costochondral corner.¹¹ Studies have demonstrated the analgesic effects of the M-TAPA block in the T7-11, T5-10, and T3-12 dermatomes.¹¹⁻¹³ Cadaveric evaluations have shown that dye spreads in T 8-11.¹⁴ The M-TAPA block has the potential to offer extensive analgesia across a wide area of the anterior abdomen with a single puncture per side, indicating promise for effective pain relief. However, further investigation is needed, particularly in laparotomies.

Therefore, this prospective randomized study aimed to evaluate the efficacy of ultrasound-guided bilateral M-TAPA block for pain management compared with surgical site infiltration in patients who underwent open major abdominal surgery. We hypothesized that bilateral M-TAPA would provide superior analgesia compared with surgical site infiltration. The primary outcome of this study was the comparison of 24-hour total morphine consumption. The secondary outcomes included postoperative pain scores, the need for rescue analgesia, and patient satisfaction.

Methods

Study Design

This single-center, prospective, and randomized study was reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines and was approved by the Marmara University Faculty of Medicine Clinical Research Ethics Committee (protocol code: 03.3.2023/371, date: 03.03.2023). It was conducted in compliance with the Ethical Principles for Medical Research Involving Human Subjects, as outlined in the Helsinki Declaration, and was registered prior to patient enrollment at ClinicalTrials.gov (NCT06384677).

Eligibility Criteria

Between April 2023 and February 2024, patients older than 18 years who were scheduled for elective primary open abdominal surgery under general anaesthesia (GA) and who provided informed consent were included in the study. Exclusion criteria were allergy to local anaesthetics, infection at the block site, refusal of the procedure, prior gabapentin use, revision or emergency surgery, planned or unexpected postoperative admission to the intensive care unit (ICU), and inability to use the patient-controlled analgesia (PCA) device due to cognitive impairment like postoperative delirium.

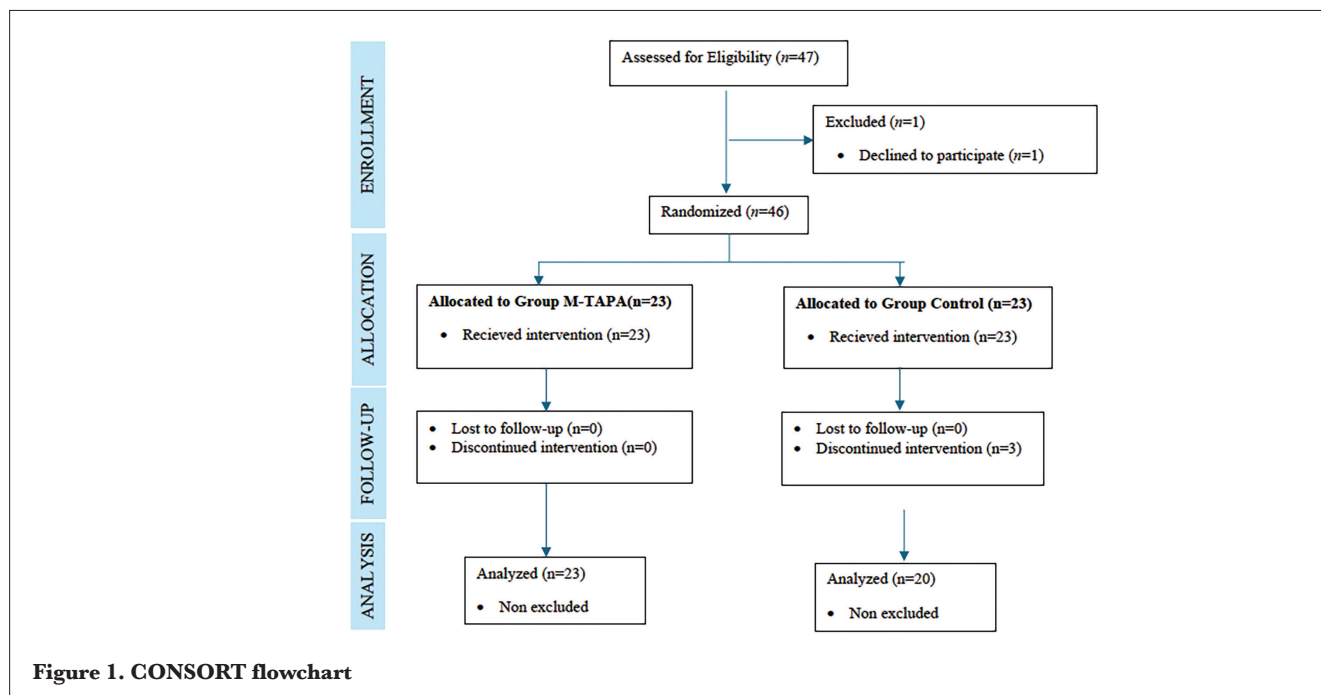
Randomization

A simple randomization method was utilized, with allocation concealment achieved by randomly drawing from sealed opaque envelopes containing assignments the day before surgery. These envelopes were attached to the preanaesthetic assessment form by the investigator. The attending anaesthetist opened the envelope after the patient was under GA, ensuring patient blinding. If surgery was cancelled, or the patient could not use PCA postoperatively, the envelope was returned to the pool. A CONSORT diagram illustrates the participant flow (Figure 1).

Intervention

All surgeries were performed by the same surgical team using a midline incision above and below the umbilicus. Standard monitoring, including electrocardiography, invasive blood pressure measurements, and peripheral oxygen saturation, was initiated. After the patients were placed under GA and maintained with intravenous remifentanyl infusion and sevoflurane inhalation, the envelopes were opened. At the end of the surgery, the treatment group received a block performed by designated anaesthetists, who had extensive experience, using a linear (12-4 MHz) ultrasound probe (Sparq Ultrasound; Philips, USA) with the patients in the supine position. In the control group, the surgeons administered local infiltration to the surgical site.

For the M-TAPA block, the 10th costal cartilage was identified by locating the notch between the 9th and 10th



costal cartilages. The transducer was then placed on the chondrium in the sagittal plane at the level of the 9th-10th ribs. The probe was angled deeply to visualize the lower aspect of the costochondrium. A 100 mm, 21 G needle (Sonoplex® Pajunk Medizintechnologie, Germany) was inserted. After confirming negative aspiration, 20 mL of 0.25% bupivacaine was injected per side between the transversus abdominis muscle and the lower aspect of the costal cartilage. In the control group, the surgeon performed local infiltration with 40 mL of 0.25% bupivacaine around the incisions.

At the end of surgery, the routine analgesia protocol in both groups included intravenous morphine (0.1 mg kg⁻¹) and intravenous paracetamol (1 g). Postoperative analgesia was managed via PCA with intravenous morphine administered at no basal rate, with a 1 mg bolus and a 10-minute lockout period, hourly limit were set at 6 mg h⁻¹, which continued for 48 hours after surgery. Additionally, all patients received 1000 mg of intravenous paracetamol every six hours. Demographic and baseline characteristics, as well as surgical details, were documented. Postoperative pain was assessed using the numerical rating scale (NRS)-from 0 (no pain) to 10 (worst pain imaginable)-at the 0, 2nd, 6th, 12th, 24th, 36th, and 48th hours. If the NRS score was ≥4, intravenous tramadol (1 mg kg⁻¹) was administered as rescue analgesia. An anaesthesiologist conducted pinprick tests to assess the sensory block in the M-TAPA group after the first hour of surgery, to ensure block success, without the involvement of the anaesthesiologist who performed the M-TAPA block. A postoperative pain team, blinded to the study conditions, recorded all relevant data, including

total morphine consumption, pain scores, rescue analgesic requests, and adverse effects such as nausea, vomiting, and itching. Hemodynamic data were also collected. Patient satisfaction status was classified as complaining, dissatisfied, satisfied, very satisfied on a scale from 1 to 4.

Statistical Analysis

The data were collected by the investigator and analyzed with Number Cruncher Statistical System (NCSS) 2020 statistical software (NCSS LLC, Kaysville, Utah, USA). For the evaluation of the study data, quantitative variables, including the mean, standard deviation, median, minimum, and maximum values, were presented via descriptive statistical methods. Qualitative variables are displayed as frequencies and percentages. The Shapiro-Wilks test and box plot graphics were employed to assess the normality of the data distribution. Student's t-test was used for normally distributed quantitative comparisons between two groups, whereas the Mann-Whitney U test was applied for non-normally distributed variables. For non-normally distributed group comparisons, the Friedman test and Wilcoxon-corrected pairwise comparisons were used. The chi-square test and Fisher's exact test were used for qualitative data comparisons. The results were considered significant at a 95% confidence interval, with $P < 0.05$.

Sample Size Estimation

The sample size was estimated based on a preliminary study from our center with ten patients (unpublished). In this initial study, the mean morphine consumption in the first 24 hours after surgery was 17.4 mg (±8.5) for the M-TAPA group and 28.3 mg (±16.9) for the surgical site infiltration group. The

effect size was calculated as 0.814. Using G*Power 3.1, we determined that at least 20 patients per group were needed to achieve a power of 0.80, an alpha level of 0.05, and an effect size of 0.85. To account for a 15% drop-out rate, the study planned to include 23 patients in each group.

Results

A total of 47 patients were initially assessed for eligibility. One patient refused to participate, leaving 46 patients who were included in the randomization. M-TAPA was successfully performed on 23 patients in the M-TAPA group without any complications. Three patients' follow-ups were discontinued due to ICU admission for two patients and

the development of postoperative delirium for one patient. The CONSORT flow chart of the study is provided in Figure 1.¹⁵

The demographic characteristics of the patients, including sex, body mass index, American Society of Anesthesiology status, comorbidities, and type of surgery, were comparable between the two groups. The mean age of the patients was 59.23±11.92 years. The most common surgical operation was the Whipple procedure (53.5%). The study groups were comparable in terms of intravenous fluids and blood products, as well as the durations of surgery and anaesthesia (Table 1). In the M-TAPA group, all patients maintained bilateral sensory block in the T8-11

Table 1. Demographic and Peroperative Informations of the Patients

		Analgesia group		P
		M-TAPA (n=23)	Control (n=20)	
Age (year)		56.91±12.15	61.9±11.37	0.209 ^a
Sex	Female	8 (35)	10 (50)	0.313 ^b
	Male	15 (65)	10 (50)	
BMI (kg/m ²⁻¹)		24.1±9.4	26.06±10.8	0.078 ^a
ASA	II	11 (48)	14 (70)	0.146 ^a
	III	12 (52)	6 (30)	
Comorbidity	DM	4 (17)	4 (20)	1.000 ^c
	Asthma/COPD	1 (4)	0 (0)	1.000 ^c
	Hipertension	5 (21.7)	4 (20)	1.000 ^c
Duration of Anaesthesia (h)		3.74±1.02	3.63±1.15	0.666 ^a
Duration of Surgery (h)		3.3±0.94	3.09±1.1	0.513 ^a
Volume of cristalloid (mL)		3543.48±928.26	3125±792.65	0.152 ^a
Blood Products (packet)	ES	5 (21.7)	3 (15.0)	0.704 ^c
	FFP	1 (4.3)	0 (0.0)	1.000 ^c
Volume of colloid (mL)		413.04±245.51	400.00±261.57	0.852 ^a
Rescue analgesic in PACU		0 (0)	0 (0)	NA
				n (%)
Type of surgery		Distal pancreatectomy		1 (2.3)
		Gastrectomy		3 (7)
		Cystectomy		2 (4.7)
		Metastasectomy		2 (4.7)
		Right hemicolectomy		4 (9.3)
		Left hemicolectomy		5 (11.6)
		Subtotal pancreatectomy		1 (2.3)
		Total colectomy		2 (4.7)
		Whipple		23 (53.4)

^aMann-Whitney U test, ^bPearson chi-square test, ^cFisher's exact test

Summary statistics are reported as medians (interquartile ranges), means ± standard deviations or numbers (%).M-TAPA, modified thoracoabdominal nerve block through the pericondrial approach; SSI, surgical site infiltration; BMI, body mass index; ASA, American Society of Anesthesiology; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; ES, erythrocyte suspension; FFP, fresh frozen plasma; PACU: post anaesthesia care unit; NA: not applicable.

dermatomal distribution.

In terms of our primary outcome, median morphine consumption during the first 24 hours was lower in the M-TAPA group [16 (14-18)] than in the control group [24.5 (19.5-27)] [$P < 0.01$, 95% confidence interval (CI): -9.42 and -3.01]. The M-TAPA group consumed significantly less morphine at all time intervals except for the 2nd-6th second to sixth hour (Table 2).

The median NRS score was 4 in the control group at the 6th and 12th hours, which was significantly higher than that in the M-TAPA group ($P=0.002$, 95% CI: -1.54 -0.48; $P < 0.001$, 95% CI: -2.12-0.93, respectively). The median NRS score remained below 4 for both study groups at all time intervals, except the 6th and 12th hours. NRS scores were significantly

lower in the M-TAPA group than in the control group at all time intervals except at the 0th and 48th hour (Table 3).

In the first 2 hours after surgery, 8% of the patients in the M-TAPA group and 30% of those in the control group required rescue analgesia. This ratio was 17% versus 45% between the 2nd and 6th hours, and 4% versus 20% between the 6th and 12th hours. No patient in the M-TAPA group required rescue analgesia between the 12th and 48th hours. The need for rescue analgesics in the first 24 hours was proportionally lower in the M-TAPA group. However, these differences were comparable between the groups over the entire period (Table 4). Patient satisfaction data for the groups are presented in Table 5. Patient satisfaction was significantly greater in the M-TAPA group than in the other groups at all time points.

Table 2. Postoperative Morphine Consumption

		Analgesia group		95% CI of the difference	P ^a
		M-TAPA (n=23)	Control (n=20)		
0th-2nd hour	Median (Q1-Q3)	2 (2-3)	4 (4-5)	-2.72 -0.93	<0.001*
2nd-6th hour	Median (Q1-Q3)	5 (4-7)	6 (4.5-7.5)	-1.55 2.26	0.572
6th-12th hour	Median (Q1-Q3)	5 (4-6)	7 (5-8)	-2.99 -0.32	0.007*
12th-24th hour	Median (Q1-Q3)	4 (2-5.5)	7 (5.5-9.5)	-4.95 -1.15	0.001*
24th-48th hour	Median (Q1 - Q3)	6 (5-8)	25 (19.5-30)	-23.01 -12.78	<0.001*
24th hour total	Median (Q1 - Q3)	16 (14-18)	24.5 (19.5-27)	-9.42 -3.01	<0.001*

^aMann-Whitney U test (Bonferroni correction applied, $P=0.01$)

Summary statistics are reported as medians (interquartile ranges). CI, confidence interval; M-TAPA, modified thoracoabdominal nerve block through the perichondrial approach; SSI, surgical site infiltration; NRS, numeric rating scale.

Table 3. Numerical Rating Scale (NRS) Scores

		Analgesia group		95% CI of the difference	P ^a
		M-TAPA (n=23)	Control (n=20)		
0th hour	Median (Q1-Q3)	3 (2-4)	3 (3-4)	-0.99 0.15	0.205
2th hour	Median (Q1-Q3)	2 (2-2)	3 (2-4)	-1.63 -0.54	<0.001*
6th hour	Median (Q1-Q3)	3 (2-4)	4 (3-4)	-1.54 -0.48	0.002*
12th hour	Median (Q1-Q3)	2 (1-3)	4 (3.5-4)	-2.12 -0.93	<0.001*
12th hour	Median (Q1-Q3)	1 (0-2)	2 (2-3)	-2.05 -0.85	0.001*
24th hour	Median (Q1-Q3)	0 (0-1)	1 (0-1)	-0.78 0.58	0.116

^aMann-Whitney U test (Bonferroni correction applied, $P=0.01$)

* $P < 0.05$

Summary statistics are reported as medians (interquartile ranges).

CI, confidence interval; M-TAPA, Modified thoracoabdominal nerve block through the perichondrial approach; SSI, Surgical site infiltration.

		Analgesia group		<i>P</i> ^b
		M-TAPA (n=23)	Control (n=20)	
2th hour	Absent	21 (92)	14 (70)	0.073
	Present	2 (8)	6 (30)	
6th hour	Absent	19 (83)	11(55)	0.056
	Present	4 (17)	9 (45)	
12th hour	Absent	22 (96)	16 (80)	0.110
	Present	1 (4)	4 (20)	
24th hour	Absent	23 (100)	18 (90)	0.120
	Present	0 (0)	2 (10)	
48th hour	Absent	23 (100)	20 (100)	NA
	Present	0 (0)	0 (0)	

^bCochran's Q test. Summary statistics are reported as numbers (percentiles).

		Analgesia group		<i>P</i> ^c
		M-TAPA (n=23)	Control (n=20)	
2th hour	Median (Min.-Max.)	2 (0-3)	2 (0-3)	0.002*
6th hour	Median (Min.-Max.)	3 (0-3)	2 (0-3)	0.003*
12th hour	Median (Min.-Max.)	3 (2-3)	2 (1-3)	0.003*
24th hour	Median (Min.-Max.)	3 (2-3)	2 (1-3)	0.012*
48th hour	Median (Min.-Max.)	3 (2-3)	2 (1-3)	0.001*

^cMann-Whitney U test. Summary statistics are reported as the median (minimum-maximum).
**P* < 0.05
M-TAPA, Modified thoracoabdominal nerve block with a perichondrial approach; Min.-Max., minimum-maximum.

Discussion

This prospective, randomized controlled study evaluated the analgesic efficacy of the M-TAPA block in major abdominal surgery. We demonstrated that the bilateral M-TAPA block, performed under ultrasound guidance, significantly reduced morphine consumption and resulted in lower NRS scores at all time points than did the control group. Additionally, the M-TAPA block positively impacted patient satisfaction.

Since the block was first described in 2019, several studies have demonstrated the analgesic effect of M-TAPA and compared it with different plane blocks, mostly in laparoscopic surgeries such as cholecystectomy or hernia repair.^{16,18} This is the first randomized controlled study on the analgesic efficacy of the M-TAPA block in open major abdominal surgery involving a midline incision above and below the umbilicus.

In this study, M-TAPA block significantly reduced postoperative morphine consumption after surgery. In a study demonstrating the analgesic efficacy of the M-TAPA block, in laparoscopic cholecystectomy, postoperative total

tramadol consumption was recorded. This randomized controlled study found that a bilateral M-TAPA block reduced total opioid consumption for up to 24 hours.¹⁸ Another study comparing oblique subcostal TAP block with M-TAPA block for postoperative analgesia in patients undergoing laparoscopic cholecystectomy reported that opioid consumption in the first 24 hours was lower in the M-TAPA group.¹⁹ Several other studies, including patients who had undergone laparoscopic surgeries, reported effective postoperative pain control with M-TAPA block.^{12,13,16,20}

While M-TAPA is known to provide effective pain relief in laparoscopic surgery, there is limited evidence regarding its effectiveness in relieving pain during open abdominal surgery. At the time of this trial, only one study in the literature reported the application of the M-TAPA block in open abdominal surgery. In that prospective, observational pilot study, 10 patients who underwent open radical hysterectomy via a vertical incision or laparotomy using a midline incision from under the xiphoid process to the symphysis pubis were

included. This case series showed that the analgesic effect lasted up to 24 hours; however, the incisions in the surgeries within the case series were not the same.¹⁴ In our study, all patients underwent a midline surgical incision above and below the umbilicus.

Although 24-hour total morphine consumption was lower in the M-TAPA group, this difference was not observed between 2nd-6th hours. We believe that the absence of variation in morphine consumption between the 2nd and 6th hours may be related to the consumption of rescue analgesics. Although the difference in rescue analgesic requirement is not statistically significant, the control group has a higher percentage of rescue analgesic requirements compared to the M-TAPA group.

Ohgoshi et al.²¹ investigated the efficacy of continuous M-TAPA block in major abdominal surgery in a case series of two patients. Both patients underwent emergency surgery to remove the adhesion. After induction of GA, M-TAPA block, and catheterization were performed. Neither of the patients required additional analgesics other than PCA in the postoperative period.

In this study, we evaluated NRS scores and patient satisfaction to assess the effectiveness of pain control. The median NRS score was always less than 4 in the M-TAPA group. In the control group, the median NRS scores at the 6th and 12th hours were 4 and 4, respectively. Patients who received the M-TAPA block were more satisfied than patients who did not receive the block. In a randomized controlled study by Bilge et al.¹⁷ on laparoscopic cholecystectomy, the M-TAPA group had significantly lower NRS scores than did the control group. Alver et al.¹⁶ reported similar results in patients who underwent laparoscopic hernia repair. A study comparing M-TAPA block with local wound infiltration for postoperative analgesia in patients undergoing laparoscopic cholecystectomy showed that NRS scores were significantly lower in the M-TAPA group during the postoperative hours 1-4 and 5-16, first 4, 20, 16 postoperative hours 20. In a case series of M-TAPA block in patients undergoing open gynecologic surgery, 80% of patients did not require additional analgesics, and patient satisfaction was rated as 8.5 out of 10 (range 8-10)¹⁴. In a randomized controlled study demonstrating the efficacy of the M-TAPA block during laparoscopic cholecystectomy, patient satisfaction was evaluated with a Likert scale. The Likert score was significantly higher in the M-TAPA group than in the control group.

The need for rescue analgesia is comparable between groups over the entire period. These findings may be due to the effect of multimodal analgesia and the relatively small sample size.

The strengths of our study are as follows. In our institution,

the regional anaesthesia team and the pain team are made up of different doctors; as a result, pain intensity and patient satisfaction data are free of bias.

Study Limitations

This study has several limitations. First, the single-center design may affect the generalizability of the findings. Additionally, while the pinprick test was essential for evaluating the block's efficacy, it may have compromised patient blinding. We collected NRS scores only when the patient was at rest, not during movement or coughing. Movement-based assessments were excluded from data collection because of their variation based on the surgical differences among patients. Instead of using a validated scoring system for patient satisfaction, we chose to use a simple satisfaction scale based on clinical experience, which was more subjective. Also, the small sample size limits the generalizability of our findings.

Our patient groups that underwent abdominal surgery were highly diverse. More specific patient populations could be used in future studies. In addition, prolonging the duration of the block by placing a catheter may be considered. From a future perspective, multicenter, double-blind, randomized studies comparing M-TAPA with sham blocks could be planned.

Conclusion

This study demonstrated that M-TAPA block reduces postoperative morphine consumption and NRS scores in patients undergoing open abdominal surgery, with a midline incision above and below the umbilicus. M-TAPA block is an effective abdominal wall block and can be considered part of multimodal analgesia in open major abdominal surgery.

Ethics

Ethics Committee Approval: This study approved by the Marmara University Faculty of Medicine Clinical Research Ethics Committee (protocol code: 03.3.2023/371, date: 03.03.2023).

Informed Consent: Written informed consent was obtained from each patient.

Footnotes

Author Contributions: Surgical and Medical Practices - E.G.Ö., G.T.Ç., G.C.T., M.E.; Concept - E.G.Ö., G.T.Ç., G.C.T., M.E.; Design - E.G.Ö., G.T.Ç., G.C.T., M.E.; Data Collection and/or/Processing - E.G.Ö., G.T.Ç., G.C.T., M.E.; Analysis and/or/Interpretation - E.G.Ö., G.T.Ç., G.C.T., M.E.; Literature Review - E.G.Ö., G.T.Ç., G.C.T., M.E.; Writing - E.G.Ö., G.T.Ç., G.C.T., M.E.

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Assessment of the Incidence of Hemi-Diaphragmatic Paralysis Following Infraclavicular and Supraclavicular Approaches for Brachial Plexus Block: A Randomized Controlled Study

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Abstract

Objective: With the regional anaesthetic technique used for brachial plexus block, the phrenic nerve (C3-C5) can be blocked due to its anatomical proximity to the brachial plexus and the effect of a significant volume of local anaesthetic deposited near the nerve roots. The goal of this study was to compare the incidence of hemi-diaphragmatic paralysis (HDP) following infraclavicular and supraclavicular approaches for brachial plexus block, using a low-volume local anaesthetic.

Methods: A total of 60 patients were enrolled in this study: 30 patients were assigned to the supraclavicular brachial plexus block group, and 30 patients were assigned to the infraclavicular brachial plexus block group. Under aseptic precautions and ultrasound guidance, both groups received 20 mL of 0.5% bupivacaine. The diaphragmatic excursion was measured using ultrasound before the block and 2 hours afterward in the postoperative care unit. A reduction in excursion of more than 75% compared with pre-block values was considered complete paralysis, whereas a reduction of 25-75% was considered partial paralysis.

Results: Infraclavicular brachial plexus block (3.33%) had a lower incidence of HDP compared with supraclavicular brachial plexus block (36.66%). The complications in both groups were not significant, and there was no need to use general anaesthesia.

Conclusion: The incidence of phrenic nerve palsy in the supraclavicular and infraclavicular brachial plexus groups was low, with a lower incidence of HDP in the infraclavicular group.

Keywords: Hemi-diaphragmatic paralysis, infraclavicular brachial plexus block, phrenic nerve palsy, supraclavicular brachial plexus block

Main Points

- Phrenic nerve palsy (PNP) leading to hemi-diaphragmatic paralysis is a well-known consequence of brachial plexus block, with varied incidence depending on whether the block is performed using an anatomical landmark technique without guidance or guided by a nerve stimulator.
- Ultrasound-guided blocks allow for precise administration of local anaesthetic, potentially reducing the volume or dose of the drug needed in clinical practice.
- The ultrasound-guided infraclavicular approach to the brachial plexus block may be safer against PNP compared with the supraclavicular approach.



Introduction

Regional anaesthetic techniques for upper limb surgeries offer several advantages over general anaesthesia, including the ability for patients to remain conscious, minimize polypharmacy, improve cardiovascular stability, and provide adequate postoperative pain relief.^{1,2} Due to its rapid onset and higher success rate, the supraclavicular approach to brachial plexus block has been favored by anaesthesiologists for upper limb surgeries over the infraclavicular approach, which is considered more complex.³ However, the primary drawbacks of supraclavicular blocks include an increased risk of complications such as unintentional intravascular injections, pneumothorax, phrenic nerve palsy, and Horner's syndrome. The advent of ultrasound in anaesthesiology has become a valuable adjunct in brachial plexus blocks, leading to renewed interest in the infraclavicular approach.⁴

Phrenic nerve palsy (PNP) leading to hemi-diaphragmatic paralysis (HDP) is a well-known consequence of brachial plexus block, with varied incidence rates. The rates of phrenic nerve paralysis vary widely depending on the approach and technique (multiple injections vs. single injection; "corner pocket" vs. neural cluster; ultrasound-guided vs. nerve-stimulation-guided),^{5,6} as well as the volume and concentration of the local anaesthetic used.⁷ The incidence of diaphragmatic paralysis following a supraclavicular block has been reported to range from 0% to 67%,⁵⁻¹⁰ whereas for the infraclavicular approach, the range is 0-26%.¹¹⁻¹³

Transient HDP, although generally well tolerated in healthy individuals, can lead to respiratory complications in patients with pre-existing respiratory compromise or significant abdominal obesity.¹⁴⁻¹⁷ Traditionally, the diagnosis of PNP is confirmed through real-time fluoroscopy, pulmonary function testing, or chest radiography. In recent times, M-mode ultrasonography has emerged as an innovative imaging technique that measures diaphragmatic excursion by demonstrating paradoxical movement of the diaphragm indicative of paralysis.¹⁸ Thus, M-mode ultrasonography is an easy, reliable, non-invasive alternative imaging technique, available at the bedside, for assessing diaphragmatic function.^{19,20}

The advantages of using ultrasound to investigate PNP include its speed, ease of use, and accuracy in evaluation while avoiding radiation exposure. It offers high specificity and sensitivity in analyzing diaphragmatic excursion.²¹⁻²⁵

This study primarily aims to determine the incidence of HDP due to PNP in contemporary ultrasound-guided supraclavicular brachial plexus block versus infraclavicular brachial plexus block with equal low volumes of local anaesthetic administration. The occurrence of PNP is assessed by measuring diaphragmatic movements using M-mode ultrasonography.

Methods

Sri Ramachandra Institute of Higher Education and Research Institutional Ethical Committee clearance was obtained (approval no.: IEC/21/JUN/163/23, date: November 14, 2022), and clinical trial registration (CTRI Trial 2022/11/047720) was completed before the study commenced. This prospective, randomized, single-blinded study was conducted in the operating rooms of "Sri Ramachandra Institute of Higher Education and Research" between October 2021 and October 2022.

Patients scheduled to undergo right upper extremity surgery under brachial plexus block were enrolled in this study after providing written informed consent. The inclusion criteria were American Society of Anesthesiologists (ASA) Physical Status I and II elective surgical patients aged 20-60 years who were undergoing upper extremity surgeries and had a body mass index less than 35 kg m⁻².

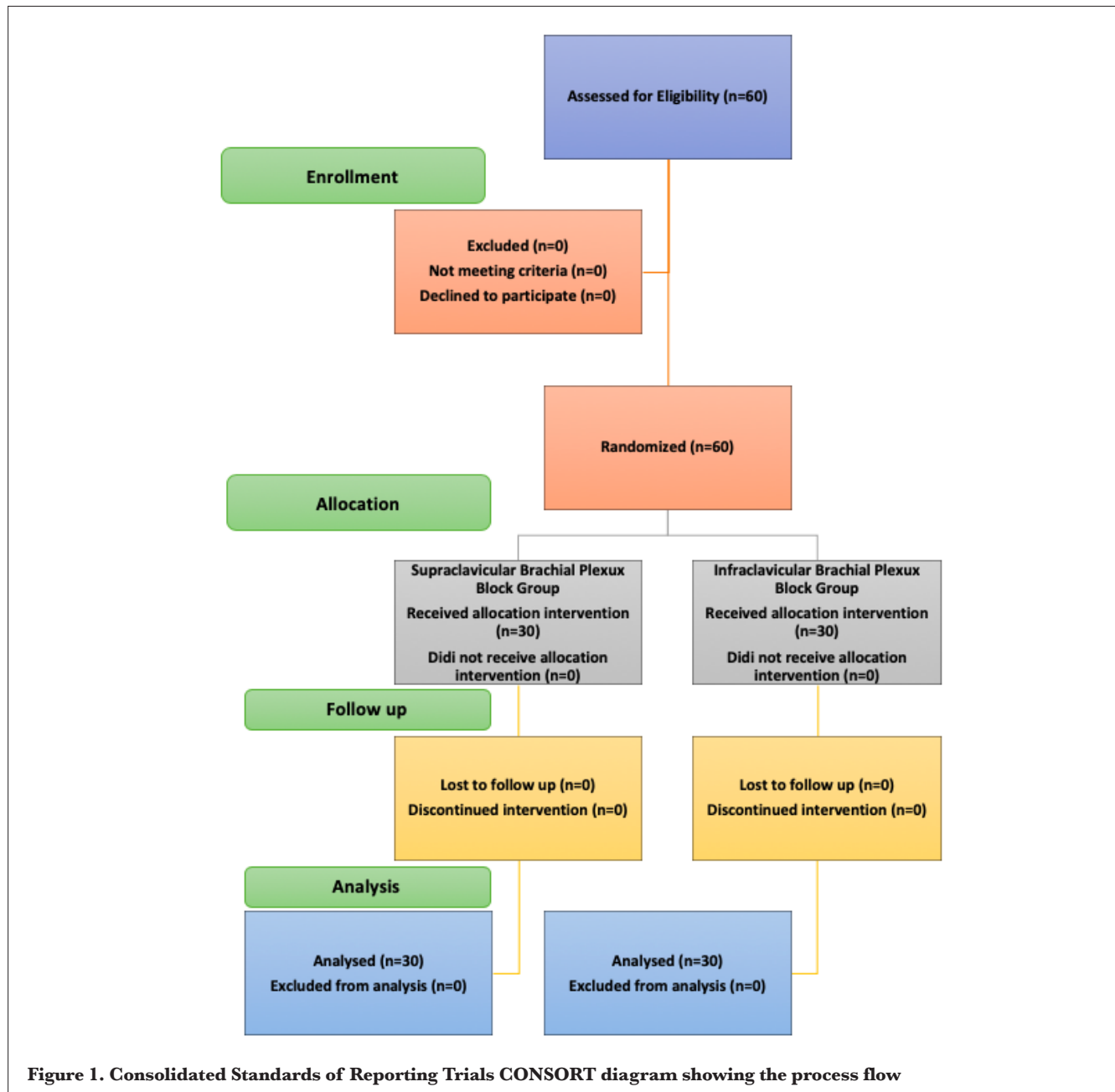
The exclusion criteria were as follows: patients who refused to participate; those who were pregnant; individuals with acute or chronic pulmonary disease, neuromuscular disease, or allergies to local anaesthetics; and patients who experienced a failed block and required conversion to general anaesthesia.

The principal investigator collected detailed patient histories and performed clinical examinations. The patients were then randomly assigned to one of two groups using computer-generated randomization. Anonymity was maintained by using sealed opaque envelopes numbered sequentially from 1 to 60 (Figure 1). Each envelope was opened and viewed only by the anaesthesiologist performing the block, who was familiar with both supraclavicular and infraclavicular brachial plexus blocks. The patients were unaware of the block group to which they had been assigned. Outcomes were assessed by a different, blinded anaesthesiologist who performed the M-mode ultrasound examination.

All patients were instructed to refrain from oral intake for 8 hours before surgery. Before administering the block, patients were sent to the holding area, where their vital signs were recorded. Baseline measurements of diaphragmatic excursion were taken by the primary investigator, who was blinded to group allocation.

After positioning the patients supine, a low-frequency curved array transducer was used in B-mode to measure diaphragmatic excursion. The liver served as an acoustic landmark to guide the probe medially, cephalad, and dorsally, positioning it between the right mid-clavicular and mid-axillary lines, beneath the right costal border, and focusing on the posterior third of the right hemidiaphragm.

Once optimal images were obtained, the ultrasound machine was switched to M-mode, where the diaphragm appeared as



a crisp white, hyperechoic line moving with the respiratory cycle in a slow, smooth up-and-down motion. Under normal resting conditions, during inspiration, the diaphragm moved toward the transducer, resulting in an upward deflection in the M-mode trace. During expiration, the diaphragm moved away from the transducer, producing a downward deflection in the M-mode trace. When the patient was asked to take a deep breath, the distance traveled from the baseline to the point of maximal inspiration was measured in centimeters using digital calipers on the ultrasound machine interface. Three readings were recorded, and the average value was noted.

Afterward, the patient was moved to the operating room, where standard monitors were connected and baseline vital signs were recorded. According to the randomization, either a supraclavicular or infraclavicular brachial plexus block was administered using 20 mL of 0.5% bupivacaine under aseptic conditions and with ultrasound guidance by an independent anaesthesiologist who was not involved in outcome measurement. A supraclavicular block was given after positioning a high frequency linear transducer ultrasound probe at the mid-clavicle, to obtain a short axis view at the junction of the first rib and subclavian artery. The needle was advanced using the “in plane technique”

towards the “corner pocket” to inject 10 mL of the local anaesthetic after the appropriate motor response of the hand to neurostimulation, and the additional 10 mL was given in the heart of the plexus. Infraclavicular block was performed after placing the transducer medial to the coracoid process and inferior to the clavicle to visualize the axillary artery. The needle was inserted using the “in plane technique” towards the posterior part of the axillary artery, where 10 mL of local anaesthetic was deposited, and the remaining 10 mL was given lateral to the axillary artery to achieve a U-shaped spread around it after appropriate motor response of the hand to neurostimulation. Following the completion of the surgery, the diaphragmatic excursion was re-evaluated after 2 hours in the postoperative care area by the same primary investigator who conducted the preoperative assessment.

The primary outcome measured was complete HDP, defined as a greater than 75% reduction in mean diaphragmatic excursion compared with pre-block values.²⁶ Partial paralysis was defined as a 25-75% reduction in mean diaphragmatic excursion compared with pre-block values.²⁶ A mean diaphragmatic excursion of less than 25% was considered an absence of significant diaphragmatic excursion.²⁶ The incidence of hemi-diaphragmatic palsy, secondary to ipsilateral PNP, included both complete and partial paralysis cases.

Vital signs, including heart rate, blood pressure, and oxygen saturation, were measured and documented pre- and post-block. Complications such as inadvertent vascular puncture, hematoma, nerve injury, pneumothorax, local anaesthetic toxicity, dyspnea, Horner’s syndrome, and block failure (requiring conversion to general anaesthesia) were also documented. Additionally, the need for light sedation and supplementary local anaesthetic infiltration by the surgeon was recorded.

According to the study by Petrar et al.,¹² the incidence of complete hemi-diaphragmatic palsy following supraclavicular brachial plexus block was 34%, compared with 3% for infraclavicular brachial plexus block. Based on these findings and assuming a 30% risk difference in the incidence of hemi-diaphragmatic palsy between the groups,

a minimum sample size of 26 per group was required to achieve a power of 80% with an α error of 0.05. Four additional patients were included in each group to account for potential dropouts or changes in surgical plans.

Quantitative variables between the two groups were analyzed by comparing the means and standard deviations. Categorical variables were analyzed by frequency and proportion. Mean differences along with their 95% confidence intervals were calculated. The independent samples t-test was used to assess the statistical significance of quantitative variables. Categorical variables were compared between groups using cross-tabulation and percentage comparison. The chi-squared test or Fisher’s exact test was employed to test statistical significance for categorical data. A value of $P < 0.05$ was considered statistically significant. NMaster software version 2.0 was used for statistical analysis.

Results

A total of 60 patients were recruited and enrolled in this study. They were then randomized and assigned to either the supraclavicular brachial plexus block group or the infraclavicular brachial plexus block group. All 60 patients achieved adequate sensory and motor blockade post-block, without delay in onset and completed the study without conversion to general anaesthesia. None of the patients in either group required sedation or supplementary local anaesthetic infiltration by the surgeon. 20 mL of bupivacaine was sufficient to provide an adequate brachial plexus block with either technique. The demographic data, including age, sex, weight, ASA Physical Classification, and site of surgery, were comparable between the two groups (Table 1).

The incidence of HDP after brachial plexus block (Figure 2) was significantly lower in the infraclavicular group (3.33%) compared with the supraclavicular group (36.66%) ($P=0.0047$).

A significant difference in the mean diaphragmatic excursion (Table 2) was observed when comparing values before and after the block values between the supraclavicular group ($P=0.0002$) and the infraclavicular group ($P=0.0000$), indicating impaired mean diaphragmatic

S. No	Demographic parameter	Supraclavicular brachial plexus block	Infraclavicular brachial plexus block
1.	Sex (Man/Woman)	12/18	15/15
2.	Mean age (years)	42.13±11.15	38.33±9.61
3.	Mean weight (kg)	72.30±12.09	72.87±9.19
4.	American Society of Anesthesiologists Physical Classification (ASA I/ASA II)	11/19	14/16
5.	Site of surgical procedure (Elbow/Forearm/Wrist/Hand)	2/11/15/2	3/13/13/1

The data was represented as frequency or mean (SD).
SD, standard deviation.

excursion post-block in both groups. However, when comparing post-block values between the groups, the mean diaphragmatic excursion (Table 2), was more impaired in the supraclavicular group compared with the infraclavicular group ($P=0.0233$).

There was a statistically significant difference in the number of patients with complete paralysis of the diaphragm (4 patients) or partial paralysis (11 patients) in the supraclavicular brachial plexus block compared with the infraclavicular brachial plexus block, which had 1 patient

with partial paralysis and 0 patients with complete paralysis ($P=0.000$) (Figure 3, Table 3).

The infraclavicular group had one complication of accidental vascular puncture. However, no other complications related to the brachial plexus block technique, such as nerve injury, pneumothorax, hematoma, breathing difficulty, or Horner's syndrome, were observed in either group. Additionally, no signs or symptoms suggestive of local anaesthetic toxicity were noted in any of the patients during the study.

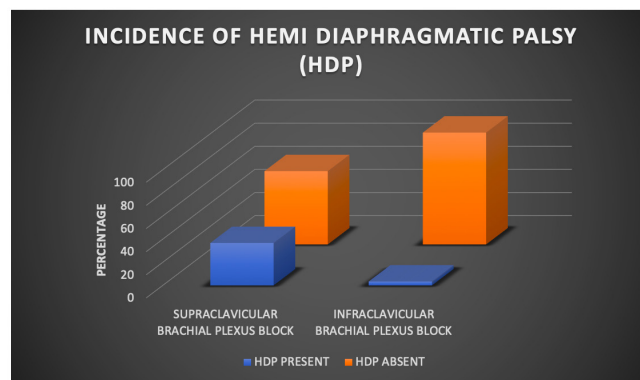


Figure 2. Incidence of hemi-diaphragmatic palsy

Table 2. Mean Diaphragmatic Excursion

Mean diaphragmatic excursion (cm)	Supraclavicular brachial plexus block	Infraclavicular brachial plexus block	P value
Pre-block	4.9 (1.8)	4.8 (1.9)	0.8341
Post-block	3.2 (1.5)	3.9 (1.3)	0.0233*
P value	0.0002**	0.000**	

The data were represented as the mean (SD).

*P values less than 0.05 were considered significant.

**P values less than 0.01 were considered highly significant.

SD, standard deviation.

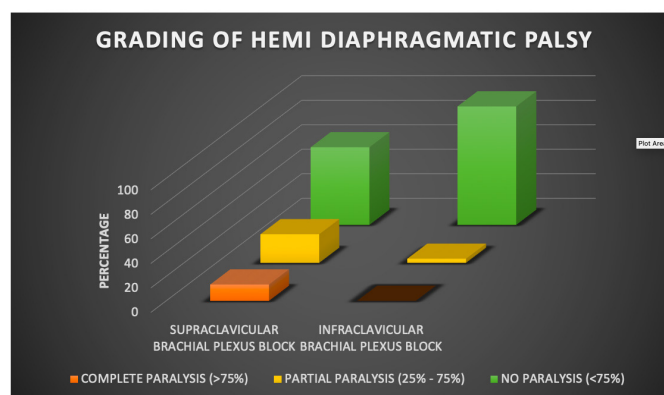


Figure 3. Grading of hemi-diaphragmatic palsy

Table 3. Incidence and Grading of Hemi-Diaphragmatic Paralysis (HDP)

Incidence of hemi-diaphragmatic paralysis (HDP)			
Incidence of HDP	Supraclavicular brachial plexus block	Infraclavicular brachial plexus block	P value
HDP present	11 (36.66%)	1 (3.33%)	0.0047**
HDP absent	19 (63.33%)	29 (96.66%)	
Grading of hemi-diaphragmatic paralysis			
Proportion of cases with HDP	Supraclavicular brachial plexus block	Infraclavicular brachial plexus block	P value
Complete paralysis (>75%)	4 (13.33%)	0	0.000**
Partial paralysis (25-75%)	7 (23.33%)	1 (3.33%)	
No paralysis (<25%)	19 (63.33%)	29 (96.66%)	
The data were represented as frequency (percentage). P values less than 0.05 were considered significant. **P values less than 0.01 were considered highly significant.			

Discussion

Hemi-diaphragmatic paralysis is a common complication following brachial plexus block, particularly with more proximal approaches;^{5,10,12,27} the use of higher volumes of local anaesthetic,²⁸ and injections administered within the satellite neural clusters of the brachial plexus.^{5,27} Although this condition is usually well tolerated in healthy patients, it can be critical in those with poor pulmonary reserve.

Ultrasound-guided regional anaesthesia allows for more precise delivery of the local anaesthetic while reducing the volume and dose required to achieve the desired clinical effect. Therefore, we conducted this prospective, randomized trial to determine the incidence of HDP during ultrasound-guided supraclavicular vs. infraclavicular brachial plexus blocks, using a lower volume of local anaesthetic.

The 20 mL of 0.5% bupivacaine was chosen based on previous studies by Renes et al.⁶ and Duggan et al.,²⁹ which demonstrated that using a low volume of local anaesthetic did not result in HDP during ultrasound-guided supraclavicular brachial plexus block while achieving 100% block success.

In our study, the incidence of hemi-diaphragmatic palsy was higher in the supraclavicular group (36.33%) compared with the infraclavicular group (3.33%), with this difference being statistically significant ($P=0.0047$). These results are similar to those of Petrar et al.,¹² who reported a higher incidence of hemi-diaphragmatic palsy on M-mode ultrasonography with a supraclavicular block (34%) compared with an infraclavicular block (3%). However, a notable difference was that none of our patients with hemi-diaphragmatic palsy experienced breathing difficulties or desaturation, whereas Petrar et al.,¹² found that patients developed subjective breathing difficulties post-block (43% in the supraclavicular group vs. 75% in the infraclavicular group).

One possible explanation for hemi-diaphragmatic palsy after these brachial plexus blocks is the reverse diffusion of local anaesthetic from the injection site to the level of the cervical nerve roots in the interscalene groove. The local anaesthetic could spread to the phrenic nerve due to anatomical variations or the presence of an accessory phrenic nerve.

Due to the lower volume of local anaesthetic used in our study, none of our patients who developed hemi-diaphragmatic palsy in either group experienced breathing difficulty or desaturation, probably due to the lower concentration of local anaesthetic reverse diffusion from the injection site.

Another study by Johnson and Daniel²⁶ concluded that a higher volume of local anaesthetic increased the incidence of hemi-diaphragmatic palsy during ultrasound-guided supraclavicular block. Our findings align with previous research, where the use of a lower volume of local anaesthetic, specifically 20 mL, resulted in a reduced incidence of hemi-diaphragmatic palsy, as assessed by M-mode ultrasonography. However, unlike our study, the researchers employed spirometry-guided FVC and FEV1 measurements to identify the true incidence of ventilatory dysfunction associated with hemi-diaphragmatic palsy. We did not use spirometry measurements because this sequela was not significant in our patients, who were otherwise healthy. Their respiratory rate and oxygen saturation remained stable, likely due to contributions from the opposite diaphragm and accessory muscles.

From the studies mentioned above, it is evident that using ultrasound for brachial plexus blocks, compared with landmark or nerve stimulator-based techniques, does not completely eliminate the risk of phrenic nerve paralysis, whether using the supraclavicular or infraclavicular approach.

A study by Oh et al.³⁰ compared ultrasound-guided supraclavicular blocks with costoclavicular blocks (a modification of the traditional infraclavicular approach). PNP was assessed with chest radiography, a less sensitive tool. The incidence of PNP was 2.5% for the costoclavicular block and 3% for the infraclavicular block. However, the costoclavicular block demonstrated better performance in terms of duration and quality of analgesia, and it had less impact on pulmonary function. Therefore, it can be considered an alternative technique for the supraclavicular brachial plexus block.

Diaphragmatic paralysis has traditionally been investigated using chest radiography, fluoroscopic sniff testing, computed tomography, and magnetic resonance imaging.³⁰ In this study, we employed a simple, cost-effective, and readily available real-time M-mode ultrasound to measure diaphragmatic excursion; as a paradoxical movement of the diaphragm indicates paralysis. This novel imaging approach can be used to rule out or confirm suspected hemi-diaphragmatic palsy in patients experiencing difficulty breathing or desaturation following a brachial plexus block.

In contrast, the study by Bao et al.⁷ utilized electrophysiological characteristics of the diaphragm to identify HDP. This was based on the amplitude and latency of diaphragmatic compound muscle action potentials, determined by comparing pulmonary function before and after the block. Paralysis was defined as a reduction in the amplitude of the diaphragm CMAP by <50%. Their study also found that a higher volume of local anaesthetic in the supraclavicular block was associated with a higher incidence of diaphragmatic paralysis. We did not use this technique because of the technical challenges associated with electromyography of the hemi-diaphragm. Due to inaccurate placement of subcutaneous needles during diaphragmatic needle electromyography recordings, unreliable measurements of diaphragm CMAP occurred. Additionally, the procedure was uncomfortable for patients. Consequently, in our study, we used only ultrasound, which provided good temporal resolution for detecting and recording rapid movements and was a cost-effective method for observing diaphragm movements at the bedside.

Study Limitations

Our study has several limitations. First, it did not include patients with pre-existing pulmonary diseases, which could compound the risk of respiratory problems during the perioperative period. Second, further studies are needed to explore the incidence of ventilatory dysfunction associated with hemi-diaphragmatic palsy in obese individuals. Third, the liver's acoustic window facilitated M-mode ultrasound of the right diaphragm, whereas the splenic acoustic window for the left diaphragm proved less optimal. Thus, the applicability of this approach for left-side brachial

plexus blocks requires further investigation. Fourth, patients who underwent continuous peripheral nerve blocks with indwelling catheters were not included in our study. Finally, we did not assess the precise duration of PNP post-brachial plexus block or its recovery in patients with evidence of HDP.

Conclusion

When a lower volume of local anaesthetic was used, the incidence of HDP due to the involvement of the phrenic nerve was found to be lower in the ultrasound-guided infraclavicular brachial plexus block group (3.33%). Complete paralysis was not observed in any patient who underwent the brachial plexus block via the infraclavicular approach.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Sri Ramachandra Institute of Higher Education and Research Institutional Ethical Committee (approval no.: IEC/21/JUN/163/23, date: November 14, 2022).

Informed Consent: Written informed consent was obtained from the patients.

Footnotes

Author Contributions: Surgical and Medical Practices - A.P., A.P.P., K.U.; Concept - A.P., A.P.P., K.U.; Design - A.P., A.P.P., K.U.; Data Collection and/or Processing - A.P., A.P.P., K.U.; Analysis and/or Interpretation - A.P., A.P.P.; Literature Review - A.P., A.P.P.; Writing - A.P., A.P.P.

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Anaesthesia Management of a Pregnant Woman with Glutaric Aciduria Type 1 Undergoing Cesarean Section

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Abstract

Glutaric aciduria type 1 (GA-1) presents unique challenges for anaesthetists. This case report discusses anaesthesia management in a pregnant woman with GA-1 undergoing cesarean delivery. Based on a cautious consideration of potential complications, combined spinal-epidural anaesthesia was preferred in this case. Maintenance of normoglycemia, normothermia, low-protein diet, carnitine supplementation, and proper hydration were prioritized. A healthy baby was delivered without complications. This case underscores the importance of comprehensive preoperative assessment and individualized anaesthesia strategies for achieving optimal outcomes in pregnant patients with GA-1. The cautious management of anaesthesia-related risks is important to ensure patient safety and decrease stress responses. Neuraxial anaesthesia and analgesia may be advantageous in specific cases.

Keywords: Cesarean section, glutaric aciduria type 1, neuraxial anaesthesia, pregnancy

Main Points

- Glutaric aciduria type 1 is a rare metabolic disorder that poses unique challenges, particularly during the perioperative period.
- Cautious preoperative evaluation and preparation are important for reducing catabolic stress.
- As physiological changes during pregnancy pose unique challenges for anaesthesiologists, appropriate anaesthesia techniques and complication management techniques should be selected.
- Combined spinal-epidural anaesthesia can be used in selected pregnant patients to provide effective pain management while avoiding general anaesthesia and reducing catabolic stress.

Introduction

Glutaric aciduria type 1 (GA-1) is a significant metabolic disorder caused by genetic deficiency in glutaryl-CoA dehydrogenase. Patients with GA-1 may exhibit diverse clinical features, particularly neurological disorders attributed to the accumulation of amino acids and other metabolites. Symptoms can manifest from childhood to adulthood.^{1,2}

Formation of non-toxic glutarylcarnitine via conjugation of glutaryl-CoA with carnitine is a physiological detoxification mechanism for glutaryl excretion and intracellular CoA regeneration. Nevertheless, this process can lead to secondary plasma carnitine deficiency, potentially contributing to complications such as cardiomyopathy, muscle weakness, and fatigue. Special attention must be given to patients with fever, infection, surgery, and pregnancy because they can present with acute encephalopathic crises and metabolic acidosis.¹⁻³



Herein, we present the anaesthesia management of a pregnant woman diagnosed with GA-1 who underwent cesarean delivery.

Case Presentation

A 30-year-old woman, with a height of 166 cm and weight of 82 kg, at 39 weeks of gestation and a history of GA-1 was admitted to the hospital. She had previously delivered via emergency cesarean section with regional anaesthesia, and the procedure had gone smoothly. The patient's second pregnancy planned as elective cesarean section was reviewed preoperatively. Risks and anaesthesia methods were determined.

Preoperative echocardiography revealed normal functions. Further, the patient's neurological examination result was normal, and previous magnetic resonance imaging revealed intracranial demyelinating plaques. After consultation with neurology, no contraindications for regional anaesthesia were identified. Additionally, a dietician was referred to prevent the catabolic process.

Combined spinal-epidural (CSE) anaesthesia and preparations for possible conversion to general anaesthesia were reviewed. Considering the risk of malignant hyperthermia, dantrolene was kept on standby. In the preoperative period, oral and intravenous carnitine treatments were switched. The risk of metabolic acidosis and ketonuria was evaluated by arterial blood gas analysis and complete urinalysis. Dextrose fluids and balanced solutions were preferred for perioperative fluid replacement. To avoid prolonged fasting, she was scheduled as the first case of the day.

CSE was performed at the lumbar 3rd-4th interspace using a needle-through-needle technique with an 18-G Tuohy needle and a 27-G pencil-point spinal needle (Espocan® CSE set). After obtaining cerebrospinal fluid, 2 mL of 0.5% heavy bupivacaine was injected. The dosage was determined based on a regimen adjusted for height and weight, as used in our department. After the withdrawal of the spinal needle, the epidural catheter was advanced 5 cm into the epidural space. The patient was then positioned supine. A T4-level sensory block, confirmed using the pinprick method, was achieved within 8 min. The surgical duration was 90 minutes. During the perioperative period, the vital signs were as follows: heart rate, 65-105 beats min⁻¹; mean blood pressure, 72-88 mmHg; and oxygen saturation level, 98-100%. Forced air warmers were used with frequent tympanic temperature measurements to achieve normothermia.

The patient delivered a baby boy weighing 2,300 g, with a normal physical examination. Following delivery, patient-controlled analgesia (PCA) was initiated using a mixture of bupivacaine and fentanyl after administering a test dose

of 40 mg of lidocaine. The PCA mixture was prepared with a concentration of 2 µg mL⁻¹ fentanyl and 1 mg mL⁻¹ bupivacaine. The solution was administered at a bolus dose of 5 mL with a lockout interval of 15 min. The patient did not present with any pain during or after surgery. The surgical procedure was uneventful, and the patient was subsequently transferred to the intensive care unit. Urinalysis, arterial blood gas, lactate, and electrolytes were normal. The patient was closely monitored in the intensive care unit for 24 hours and was discharged without complications after 2 days.

Discussion

GA-1 is a mitochondrial metabolic disorder in which minimizing catabolic stress is essential. Infections, stress, fever, pregnancy, or surgery can trigger encephalopathic crises, causing central nervous system (CNS) damage.^{1,2}

This case highlights the importance of comprehensive preoperative assessment and preparation. This includes evaluating respiratory and cardiac function and neurological status and reviewing previous medical records to identify potential anaesthesia risks.

There are no specific radiological findings in patients with GA-1, but CNS imaging may reveal suggestive clinical features, including hydrocephalus, brain atrophy, structural changes of the basal ganglia, and demyelination. However, non-traumatic subdural hematoma was also reported.⁴ Hence, conducting a comprehensive neurological examination prior to any anaesthetic procedure, seeking neurological consultation, and reviewing radiological images are important as they may help identify contraindications to regional anaesthesia.

Because the CNS is primarily affected, patients frequently experience dystonic movements and seizures. Thus, anticonvulsants should be readily available as per the neurologist's recommendations, and routine anticonvulsants should be administered until the morning of surgery. Valproate can significantly disrupt the mitochondrial acetyl-CoA/CoA ratio and should be avoided.²

Patients with GA-1 are typically managed with a low-protein diet and carnitine and riboflavin supplementation. Considering the physiological changes caused by pregnancy, patients should be evaluated by a dietician immediately after hospital admission. Anaesthetists must ensure that intravenous dextrose fluids are administered preoperatively because fasting can cause protein degradation, leading to increased amino acid levels and clinical symptom onset. Switching from oral to intravenous carnitine supplementation can prevent secondary carnitine deficiency. In addition, decreasing fasting times and scheduling the surgery as the first surgery performed on the day reduces the risk of metabolic decompensation.^{2,3}

A rapid rise in plasma lactate levels has been observed after administering Ringer's lactate to patients with mitochondrial disorders.⁵ This phenomenon is likely due to impaired lactate metabolism, suggesting that intravenous fluids containing lactate should generally be avoided.⁶ Similarly, we avoided Ringer's lactate in our patient to prevent lactate accumulation.

General anaesthesia might be challenging because of concerns about neuromuscular blockers, inhalational anaesthesia, and propofol-related complications. Although low-dose propofol has been reported in the literature, long-term and high-dose propofol can inhibit mitochondrial electron transport.⁷ Patients may also have increased sensitivity and a prolonged response to neuromuscular blockers as neurological involvement in this disease.⁸ Another concern is the relationship between mitochondrial disease and malignant hyperthermia.⁹ Therefore, regional anaesthesia was preferred in our patient given that our evaluation did not show any contraindications.

To the best of our knowledge, this is the first report of CSE in a patient with GA-1. Studies have indicated that epidural anaesthesia alone does not provide sufficient analgesia for pregnant women undergoing surgical procedures, particularly in the sacral region.¹⁰ This can result in inadequate pain control during the perioperative period. Additionally, the slower onset of blockade with epidural anaesthesia compared with spinal anaesthesia poses a significant drawback in emergencies requiring rapid intervention.¹¹ The CSE anaesthesia technique effectively addresses these challenges by combining rapid-onset spinal anaesthesia with the prolonged analgesic effects of epidural anaesthesia. This method not only ensures effective anaesthesia during surgery but also enables postoperative pain control via the epidural catheter. Furthermore, some studies have indicated that CSE anaesthesia enhances maternal hemodynamic stability and reduces the risk of hypotension.¹² In our case, CSE anaesthesia provided a painless and comfortable experience during and after the procedure, minimizing the stress response. This approach also allowed for safe anaesthesia management by avoiding the potential adverse effects associated with intravenous or inhaled anaesthesia.

In patients with GA-1, in addition to pain management, treatment primarily aims to maintain normoglycemia and normothermia, implement a low-protein diet, prevent secondary depletion via carnitine supplementation, and ensure adequate hydration, electrolyte balance, and normal pH levels.

Conclusion

In pregnant women with GA-1, preventing stress response via cautious anaesthesia management is important. Neuraxial anaesthesia and analgesia can achieve optimal outcomes in selected patients.

Ethic

Informed Consent: The patient provided consent for the clinical information pertaining to the case to be published in a medical journal

Footnotes

Author Contributions: Surgical and Medical Practices - Y.D., S.K.; Concept - Y.D., S.K., C.K., S.O.; Design - Y.D., S.K., C.K., S.O., H.Ş.T.; Data Collection and/or Processing - Y.D., S.K., C.K., S.O., H.Ş.T.; Analysis and/or Interpretation - Y.D., S.K., C.K., S.O., H.Ş.T.; Literature Review - Y.D., S.K., C.K.; Writing - Y.D., S.K., C.K.

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Living Liver Donor Paired Exchange: Can Anaesthesia Management Challenge?

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Dear editor,

Living-donor liver paired exchange (LPE) is an effective strategy to increase the availability of organs for liver transplantation in patients with end-stage liver disease. Reasons for LPE include ABO incompatibility, inadequate hepatic mass, poor graft quality, anatomical considerations of the liver, and low residual liver volume in the donor.

It was reported that the first five-way [involving five living-donor hepatectomies and five living-donor liver transplants (LDLT)], paired exchange transplantation was performed simultaneously. The anesthetic challenges of this choice were also discussed.

We have shown that LPE can be performed at high-volume transplant institutes like ours, and is a useful strategy for ABO incompatibility and size incompatibility. Performing multiple LPEs simultaneously may present challenges in anesthesia management, and require a high-capacity center.

LPE offers a promising strategy to increase the organ supply for liver transplantation.¹ This report describes the first-ever simultaneous five-way LPE transplantation (involving five living-donor hepatectomies and five LDLT). The anesthetic challenges associated with this complex process are also discussed.

Following thorough psychosocial evaluation, by psychiatrists to ensure suitability, written informed consent was obtained from all participating donors and recipients for the paired exchange program. The Liver Transplant Institute of İnönü University's established matching algorithm facilitated the pairing process.² Standard anesthesia monitoring protocols were employed for all donors, including a 3-lead electrocardiogram, oxygen saturation, non-invasive blood pressure, and bispectral index, before induction. Induction typically involved propofol (2.5 mg kg⁻¹), fentanyl (1-2 µg kg⁻¹), and rocuronium for muscle relaxation. Following intubation, vital signs (blood pressure and urine output), body temperature, and bleeding were closely monitored. Anesthesia was maintained with a combination of 1 MAC sevoflurane and remifentanyl infusions. Restrictive fluid management was implemented until graft removal. After successful liver retrieval, aggressive fluid resuscitation was administered to restore the donor's normovolemic state.

Multimodal postoperative analgesia was administered to donors including a transversus abdominis plane block and/or local anesthesia at the wound site, combined with intravenous morphine and dexketoprofen. Standard monitoring of the recipients included electrocardiography, pulse oximetry, capnography, temperature, urine output, coagulation profile, invasive arterial pressure, and central venous pressure (measured from the right internal jugular vein). The

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anesthesia management protocol for all recipients involved induction with propofol (1-2 mg kg⁻¹) and fentanyl (1-2 µg kg⁻¹), muscle relaxation with rocuronium (0.6-1 mg kg⁻¹), and maintenance with sevoflurane (0.8-1 MAC), remifentanyl, and rocuronium (as needed). Goal-directed fluid therapy with balanced saline solution and albumin supplementation was provided as needed. PVi (pleth variability index), Perfusion Index and Plethysmograph waveform analysis (Radical 7 Pulse CO-Oximeter™, Masimo) was used for goal-directed fluid therapy and cardiac output monitoring technique. The team minimized fluid administration to avoid dilutional coagulopathy. Red blood cell transfusions were administered if hemoglobin dropped below 8 g dL⁻¹. Vasopressors were used for hypotension unresponsive to fluid resuscitation. Coagulation management was guided by Rotem.

In our institute, the annual case number of adult LDLT is 204, and the number of pediatric LDLT is 37. Our institute boasts eight experienced surgeons dedicated to donor procedures and another eight for recipient surgeries. Each senior surgeon was assisted by two fellow trainees. The anesthesia team comprised five senior anesthesiologists, each responsible for one donor-recipient pair. Additionally, two junior fellows worked under the supervision of senior anesthesiologists, assisting in either the donor or recipient operating room. Importantly, both surgical procedures and anesthesia management for all donors and recipients proceeded uneventfully, with no major complications observed.

Pair-1 faced ABO incompatibility while the remaining pairs were incompatible in size. For Pair-5, the donor's right liver lobe was considered too small due to a graft-to-recipient weight ratio of only 0.66%. In Pair-3, a right lobe hepatectomy was not feasible due to the recipient's

low residual liver volume (27%), and the left lobe was also deemed unsuitable due to its small size. Similarly, for the pediatric recipients in Pair-2 and Pair-4, the donor grafts were too large, and left lobe hepatectomy was not an option due to the presence of three arteries less than 1 mm in diameter in each patient. Figure 1 illustrates the details of this five-way LPE.

LPE offers a solution for situations where conventional LDLT is limited by factors such as small graft size, unsuitable recipient anatomy, specific donor anatomical features, and ABO incompatibility. LPE expands the pool of potential donors, benefiting patients who would otherwise have no chance of receiving a suitable deceased donor liver graft. Hepatic size incompatibility alone excludes 4-14% of potential LDLT donors. Gunabushanam et al.³ highlighted the effectiveness of LPE in expanding the donor pool and reducing waitlist mortality for liver transplant recipients. In our specific case, both ABO and size incompatibility necessitated LPE. Without this approach, none of these recipients would have been able to undergo transplantation.

The timing of pairing in LPE is crucial. While some centers perform donor and recipient surgeries simultaneously, others schedule them sequentially. To avoid complications associated with simultaneous LPE surgeries, stringent criteria are often established for donor and recipient selection.⁴ Given these considerations, we opted to perform the surgeries in this five-way LPE simultaneously.

Previous studies have documented the logistical complexities associated with performing LPE surgeries simultaneously. These challenges encompass the matching program, multi-site coordination of large teams (including senior surgeons, anesthesiologists, technicians, and nurses), and ensuring sufficient blood and blood product supplies.^{1,5} To overcome

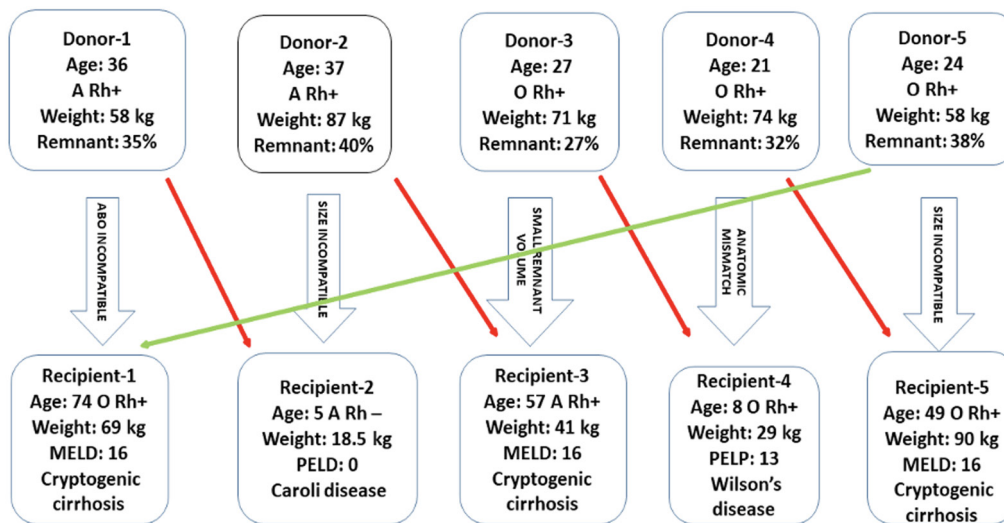


Figure 1. Diagrammatic representation of liver paired exchange

these hurdles, we established ten distinct teams. Each team comprised experienced anesthesiologists, surgeons, and anesthesia technicians (all with over 20 years of LDLT experience) and was allocated a significant portion of hospital and operating room resources.

All donor operations and anesthesia inductions were initiated simultaneously to mitigate the risk of donor withdrawal. Any complications arising during anesthesia management, such as airway issues or invasive procedures, could lead to the cancellation of the entire LPE sequence, placing immense stress on the anesthesiologists.

Our experience demonstrates the feasibility of performing high-volume LPE at our transplant institute, highlighting its effectiveness in addressing ABO and size incompatibility issues. However, it is important to acknowledge that conducting multiple LPE surgeries simultaneously can pose significant challenges for anesthesia management and necessitates a high-capacity medical center. In addition, the main requirements for the anesthesiology team during the perioperative period are adequate infrastructure, experience, and close coordination with the surgeon and other stakeholders (blood center, nurse, technician).

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