

Postoperative Outcomes of the Awake Colorectal Surgery with Neuraxial Anaesthesia

Ayca Tuba Dumanli Ozcan, Serhat Ocakli, Ezgi Erkilic, Yasemin Yalniz, Sadettin Er and Cengiz Ceylan

Department of Anaesthesiology and Reanimation, Ankara Bilkent City Hospital, Ankara, Turkiye

ABSTRACT

Objective: To determine the outcome of awake surgery with combined spinal epidural in geriatric colon-cancer patients with advanced comorbidity.

Study Design: Quasi-experimental study.

Place and Duration of the Study: Department of Anaesthesiology and Reanimation, Ankara Bilkent City Hospital, Ankara, Turkiye, from April 2022 to 2023.

Methodology: Twenty-four American Society of Anaesthesiologists (ASA) I-II patients, aged 25-65 years and scheduled for colon cancer surgery were included in this research. All patients were observed preoperatively, at the operation room and at the postoperative surgery service. Spinal anaesthesia was planned for Group I and general anaesthesia for Group II. Ketofol (1:1) was administered to the combined spinal-epidural group, with a Ramsay sedation score of 3 after the spinal block. Epidural analgesia was planned for all patients. Patients' age, gender, weight, comorbidities, ASA risk scores, intraoperative haemodynamic parameters, bleeding amounts, colloid, crystalloid, and blood products were collected.

Results: There was no significant difference between the demographic characteristics of both anaesthesia groups ($p > 0.05$). The amount of bleeding was statistically lower in Group I than in the general anaesthesia group ($p = 0.004$). Oral intake, drain withdrawal, mobilisation, discharge times, and costs were similar in all groups ($p > 0.05$).

Conclusion: The regional anaesthesia applications facilitate compliance with routine mobilisation, discharge procedures and prevent complications in abdominal surgery and its positive perioperative effects in patients with poor respiratory parameters, poor general condition, and high comorbidity in advanced age.

Key Words: *Regional anaesthesia, Spinal-epidural, Mobilisation, Pain, Colon cancer.*

How to cite this article: Ozcan ATD, Ocakli S, Erkilic E, Yalniz Y, Er S, Ceylan C. Postoperative Outcomes of the Awake Colorectal Surgery with Neuraxial Anaesthesia. *J Coll Physicians Surg Pak* 2024; **34(09)**:1009-1013.

INTRODUCTION

Colon cancer is a common cancer in elderly adults worldwide and seriously threatens human health owing to its increasing incidence.¹ Age is a major risk factor for the development of colon cancer. It has been shown that the incidence in the general population increases after the age of 40 years, with approximately 70% of colorectal cancers occurring in people over the age of 50 years.¹ Factors such as advanced age, concomitant diseases, decreased physiological capacity, and additional medicines may cause various difficulties in anaesthesia applications. The common changes in lung function in the elderly population are secondary to changes in the respiratory system compliance, resulting in decreased oxygenation efficiency and hence hampering the response to hypoxia. These changes in lung mechanics also affect gas exchange in geriatric patients and predispose them to small-airway collapse and atelectasis.

Hence, several studies have demonstrated that age alone can independently increase the risk of perioperative pulmonary complications.² Compared with general anaesthesia, regional anaesthesia has been assumed to have a positive effect on cancer outcomes.³ Epidural analgesia and anaesthesia reduce the stress response to surgery and prevent suppression of immunity. Thus, it protects the patient from developing postoperative infection and tumour metastases by preventing immunosuppression with surgery and general anaesthesia.³

Thoracic epidural anaesthesia and analgesia are widely used to treat intra- and postoperative pain during open colon cancer surgery. Enhanced recovery after surgery (ERAS) and other groups have shown that intestinal and physiological functions improve with epidural anaesthesia, preoperative bowel cleansing, nasogastric tube, and starting postoperative early enteral nutrition, and they also provide early discharge.⁴

Studies involving the application of high combined-spinal regional anaesthesia in various gastrointestinal surgeries have shown early postoperative recovery, effective analgesia, and decreased rates of mortality and morbidity (20-40%).² It has been found that the duration of hospital stay is shortened in these patients without the need for intubation. It has also been reported to decrease the frequency of respiratory complica-

*Correspondence to: Dr. Ayca Tuba Dumanli Ozcan,
Department of Anaesthesiology and Reanimation, Ankara
Bilkent City Hospital, Ankara, Turkiye
E-mail: draycaozcan@gmail.com*

Received: October 31, 2023; Revised: August 09, 2024;

Accepted: August 19, 2024

DOI: <https://doi.org/10.29271/jcpsp.2024.09.1009>

tions, which are an essential cause of mortality and morbidity in high-risk surgical patients (15.4%).² General anaesthesia is preferred by most anaesthesiologists because it secures the respiratory tract. However, this study was planned to reflect positive observations in awake patients with spinal epidural anaesthesia in the geriatric group with respiratory comorbidities.

The combined spinal-epidural anaesthesia technique reduces the disadvantages of single spinal or epidural anaesthesia methods, such as hypotension, bradycardia, nausea, vomiting, slow onset, and patchy involvement. This study aimed to determine the impact of spinal and epidural anaesthesia on preoperative bleeding, postoperative pain scores, oral intake, mobilisation, drain and catheter withdrawal, discharge times, renal function, and cost in patients scheduled for colon surgery compared to those who received general anaesthesia.

METHODOLOGY

An approval was obtained from the T.C. Ministry of Health, Ankara Bilkent City Hospital's Ethics Committee No. 2. Patients who were planned for colon surgery during April 2022 to 2023 were included in the study after the consent form was signed. The clinical trial number of this study was NCT0533425.

Patients who underwent laparoscopic surgery, had ASA IV and above, liver, and renal failure, bleeding disorder, a history of local anaesthetic allergy, and did not accept the regional technique were excluded from the study. After the patients were taken to the operating room and monitored, an epidural catheter was placed. It was decided to apply spinal or general anaesthesia according to comorbidity and additional diseases. Patients who underwent colorectal surgery during 2022-2023 were included. General anaesthesia was applied to Group II (n:13). Spinal anaesthesia was applied to Group I (n:11); Ketofol (1:1) was administered to the spinal group with a Ramsay sedation score of 3 after the spinal block. Epidural pain catheter was placed in T7/8 intervals before anaesthesia to all patients. After the negative test dose, 7 ml of injection epidural analgesia, 5 ml of bupivacaine 0.5% plus 2 ml of saline from the epidural was administered. Then 4 cc of 0.5% bupivacaine from the epidural was administered intraoperatively at 2-hour intervals, and controlled analgesia was continued until the second postoperative day. A dose of 25 mg of bupivacaine was administered 10 minutes before the surgical incision. Subsequently, induction was performed in Group II by administering 1 mg/kg aritmial, 2 mg/kg propofol, 1 microgram/kg fentanyl, and 0.6 mg/kg rocuronium after preoxygenation. In the maintenance, inhalation anaesthesia with sevoflurane was continued with a minimum alveolar concentration (MAC) value of 2.

Subarachnoid block was performed in the patients in Group I by performing a dural puncture with a spinal needle at the L3-4 level with a 25G Quincke needle and giving 16 mg of bupivacaine and 10 micrograms of fentanyl. Afterwards, iv Ketofol was administered intermittently with a Ramsey sedation score of 3.

Patients' age, gender, weight, comorbidities, ASA risk scores, intraoperative haemodynamic parameters, bleeding amounts, colloid, crystalloid, and blood products were recorded. During general anaesthesia, fluid resuscitation of the patients with general anaesthesia was planned according to pleth variability index (PVI) monitoring that was performed using Masimo Set version V7.1.1.5 pulse oximetry (MasimoCo, Irvine, California). Whenever PVI was higher than 13%, 250 ml bolus crystalloid infusion was performed in this study. In terms of perioperative renal functions, hourly urine follow-ups, preoperative blood urea nitrogen (BUN), and creatinine values were evaluated in Kidney Disease Improving Global Outcomes (KDIGO) criteria.

Postoperative VAS scores, discharge, mobilisation, and initiation of oral intake, nasogastric and drain withdrawal times, and total costs were evaluated.

All analysis was performed in SPSS v23 (SPSS Inc., Chicago, IL, USA). Compliance control of numerical data with normal distribution was done with the Shapiro-Wilk's test. It was seen that none of the variables met the assumption of normal distribution. Continuous numerical variables were analysed with the Mann-Whitney U test, and the mean, standard deviation, median, minimum, and maximum values of these variables were given.

Chi-square analysis was performed for categorical variables. The frequency and percentage values of these variables were given. A p-value <0.05 was considered statistically significant.

RESULTS

It was observed that there was no difference between the groups in terms of demographic characteristics. Statistically, there was no difference between the distribution of patients in terms of additional diseases. There was no difference between the two groups in terms of postoperative complications (Table I).

All patients in Group II were kept in the grey zone according to PVI (9-13) range. In terms of fluid resuscitation, there was no difference between the amounts of colloid and crystalloid given in both groups. The amount of bleeding was statistically significantly lower in Group I than in the general anaesthesia patients ($p = 0.004$). The median value for the amount of bleeding in Group I was 300 ml, while in Group II it was 500 ml.

It was observed that there was a statistical difference between the preoperative saturation values of the patients ($p = 0.007$). The clinics of these patients were also found suitable for regional anaesthesia.

There was no difference between the groups in terms of the amount of bupivacaine administered perioperatively and the pain scores at all times ($p > 0.05$). Oral intake, drain withdrawal, mobilisation, discharge times, and costs were similar in all groups ($p > 0.05$, Table II).

The kidney functions of the patients in both groups were preserved. The initial urea and creatinine values were similar in both groups, and there was no statistical difference between creatinine values in terms of postoperative increase ($p > 0.05$).

According to the KDIGO criteria, the patients progressed to Stage 1 at most. The risk of developing acute renal failure was low. Although the increase in urea values is within normal limits, it is statistically higher in the spinal epidural group in terms of the amount of increase ($p = 0.012$).

Table I: Analysis of categorical data between groups by type of anaesthesia.

Variable		Group I N (%)	Group II N (%)	Total N (%)	p-value
Gender	Male	3 (27.3%)	8 (72.7%)	11 (45.8%)	0.093
	Female	8 (61.5%)	5 (38.5%)	13 (54.2%)	
Allergy	Absence	10 (45.5%)	12 (54.5%)	22 (91.7%)	0.717
	Presence	1 (50%)	1 (50%)	2 (8.3%)	
ASA ^a	1	0 (0%)	4 (100%)	4 (16.6%)	0.063
	2-3	11 (100%)	5 (55.6%)	20 (83.4%)	
Clavien-Dindo	1	7 (38.9%)	11 (61.1%)	18 (75%)	0.17
	2	4 (80%)	1 (20%)	5 (20.8%)	
	3a	0 (0%)	1 (100%)	1 (4.2%)	
Anaesthesia History	Absence	9 (42.9%)	12 (57.1%)	21 (87.5%)	0.576
	Presence	2 (66.7%)	1 (33.3%)	3 (12.5%)	
COPD ^b	Absence	9 (40.9%)	13 (59.1%)	22 (91.7%)	0.199
	Presence	2 (100%)	0 (0%)	2 (8.3%)	
CAD ^c	Absence	5 (33.3%)	10 (66.7%)	15 (62.5%)	0.206
	Presence	6 (66.7%)	3 (33.3%)	9 (37.5%)	
DM ^d	Absence	7 (41.2%)	10 (58.8%)	17 (87.5%)	0.659
	Presence	4 (57.1%)	3 (42.9%)	7 (12.5%)	
HT ^e	Absence	3 (37.5%)	5 (62.5%)	8 (33.3%)	0.679
	Presence	8 (50%)	8 (50%)	16 (66.7%)	

^aASA = American Society of Anaesthesiologists, ^bCOPD = Chronic obstructive pulmonary disease, ^cCAD = Coronary artery disease, ^dDiabetes mellitus, ^eHT = Hypertension, Fisher's exact test was considered significant at $p < 0.05$.

Table II: The local anaesthetic dose used, postoperative pain scores, and postoperative service follow-ups.

Variable	Group I Median (min-max)	Group II Median (min-max)	p-value
Local anaesthetic amount, mL	50 (30-75)	50 (50-75)	0.082
VAS ^a			
2 hour	2 (2-3)	3 (1-4)	0.361
4 hour	2 (1-3)	3 (1-3)	0.082
8 hour	2 (1-4)	2 (1-4)	0.459
12 hour	2 (1-4)	2 (1-3)	0.608
16 hour	2 (1-3)	2 (1-4)	0.776
24 hour	1 (1-3)	2 (1-4)	0.119
Oral intake, hour	24 (6-72)	16 (6-72)	0.82
Drain withdrawal, hour	96 (48-312)	96 (0-168)	0.459
Mobilisation, hour	8 (6-16)	8 (6-16)	0.649
Cost, TL	7881 (3393-11534)	7565 (714-14263)	0.608
Discharge, day	7 (4-14)	6 (2-12)	0.494

^aVAS= Visual Analogue Scale, Mann-Whitney U test results were considered significant at $p < 0.05$.

DISCUSSION

In this study, when general anaesthesia was compared with combined spinal-epidural anaesthesia and sedation *via* Ketofol, no difference was found between the groups in postoperative VAS scores, discharge, mobilisation, and initiation of oral intake, nasogastric, drain withdrawal times, and total costs.

Regional anaesthesia techniques are used to minimise intraoperative and postoperative opioid consumption. ERAS protocols also recommend regional analgesia for postoperative pain. It has been shown that thoracic epidural analgesia (TEA) reduces the use of anaesthetic drugs, systemic opioids, neuromuscular blocking agents, and the catabolic response to stress.⁵

With epidural analgesia, pulmonary complications decrease, intestinal function improves, and patient mobilisation increases. Although the results of the MASTER trial did not show a benefit of combining general anaesthesia with epidural anaesthesia, in a recent report, Vester-Andersen *et al.* presented

findings that indicated an adjusted association between TEA and reduced 30-day (OR 0.75, 95% CI 0.62-0.90) and 90-day (OR 0.80, 95% CI 0.67-0.94) mortality rates.^{6,7}

Sedation application, together with regional anaesthesia, prevents the adverse effects of staying in the same position for a long time and noise coming from the environment. However, conditions that increase morbidities, such as prolonged recovery, airway obstruction, hypoxia, and hypotension, are associated with sedation.⁸ However ketamine sedation would be effective to control the hypotension because of spinal anaesthesia.⁹ Moreover, in the literature, it has been reported that the patients who are spontaneously breathing and receiving propofol sedation, at the same time, the use of ketamine increased inspiratory flow and reduced inspiratory work of breathing. This effect was related to the activated electroencephalographic pattern.¹⁰

Ketamine, as an adjuvant to nearby anaesthesia, can extend the length of analgesia with an out-of-ketamine-associated destructive effect.¹¹ In this study, consistent with the literature, ketofol sedation did not prolong postoperative recovery.

In the literature, it was remarked that the fluid overload may result in harmful third-space weight gain, associated with higher rates of pulmonary complications, postoperative ileus, altered mental status, and oedema-related anastomotic complications, thus impeding postoperative recovery.¹² Perioperative fluid management strategies have traditionally suggested a restrictive rather than liberal approach in clinical practice. Colonic blood flow is poorly auto-regulated, and perfusion of the colon is mainly dependent on mean arterial pressure more than cardiac output.¹³ No statistically significant difference was detected between the haemodynamic parameters of the groups. Perioperative fluid management with PVI was applied in the general anaesthesia group which has been the most preferred fluid therapy in the last years.¹⁴ The regional group was not intubated, making it unsuitable following with PVI, and the conventional fluid management method was used. PVI, a non-invasive parameter, is a recently widespread monitoring system that continuously, automatically, and non-invasively measures plethysmographic changes during the respiratory cycle. Changes in ventricular filling can be observed during the respiratory cycle. When preload / volume is low, these changes in ventricular filling cause more variability in stroke volume. PVI can be used as a non-invasive dynamic indicator of fluid responsiveness in certain populations of mechanically ventilated adult patients.¹⁴ There was no difference in the total amount of fluid infused between the groups. However, patients with PVI had lower crystalloid infusion rates than those in the spinal group, in accordance with the literature. There was no significant difference between the two groups regarding kidney function, which has been attributed to adequate fluid resuscitation and close monitoring of fluid deficits. Goal-directed fluid management with PVI kept BUN and creatinine levels during general anaesthesia. An increase in BUN values was observed in patients who did not undergo PVI follow-up. Less bleeding had a positive

effect on fluid resuscitation in the regional anaesthesia group, although there was no PVI monitoring. In line with this, Cros *et al.* reported in the literature that PVI monitoring was related to earlier blood transfusion.¹⁵ In terms of complications, no difference was found between the Clavien-Dindo scores in either group. Solakhan *et al.* did not observe a significant difference between the spinal and general groups in terms of the amount of bleeding.¹⁶ On the other hand, hypotensive epidural anaesthesia resulted in arterial hypotension requiring low-dose epinephrine infusion and reduced blood loss by maintaining central venous pressure, heart rate, and cardiac output.^{17,18} In this study, the amount of bleeding was found to be lower in patients under regional anaesthesia.

As a study, intrathecal hydrophilic opioid use in major abdominal surgeries has recently been reported.¹⁹ However, the side effect of respiratory depression has been put forward as a risk.²⁰ In a meta-analysis, it was revealed that epidural decreased the amount of opioid consumption in abdominal colorectal surgery but had six times more hypotension effect than transversus abdominis plane blocks.²¹ In this study, long-acting local anaesthesia such as bupivacaine was preferred instead of intrathecal opioids and postoperative respiratory complications and hypotension were prevented with postoperative epidural analgesia.

Colon surgery with awake anaesthesia was reported in the literature as a case series by Romanzi *et al.* during the COVID-19 pandemic. They reported five cases of awake laparotomy within a year.²² The same study team also reported eight patients with spinal or spinal epidural.²³ Publications are in the form of case reports. It presented a total of 70 cases during COVID pandemic, of which, only 20% needed ICU and 5.7% returned to general anaesthesia.²⁴ These reports made during the pandemic were mostly presented as an approach to solving the problem of insufficient or unavailability of the intensive care beds.

Marrone *et al.* also reported a case; open low-anterior rectal resection with spinal epidural anaesthesia and suggested that postoperative outcomes improved with successful postoperative pain control and rapid perioperative recovery in selected cases.²⁵ In this study, the reason for the use of the regional technique was the pulmonary risks and comorbidity of the patients. However, in this study surgery was performed with spinal epidural anaesthesia in all of the study patients and the intensive care unit was not required.

Although it was observed in the clinic that awake colon cancer surgery enhanced the postoperative recovery and discharge of the patients with low saturation values and high-risk scores in the respiratory system examination, the lack of statistical difference was attributed to the insufficient number of patients. The rarity of the suitable patients to the awake colon surgery limited the number of patients. That is the limitation of this study. If general anaesthesia were applied to these patients, postoperative recovery and discharge would be longer. The significant differences can be obtained in a controlled randomised study

with high comorbidity patients. Simultaneously, routine mobilisation and discharge procedures were performed at certain times by the surgical clinic. This clinical routine could be blocked by revealing clinical differences between the two groups.

CONCLUSION

Regional anaesthesia with Ketafol sedation can be preferred to prevent complications and facilitate routine mobilisation and discharge in patients with poor respiratory parameters, poor general condition, and high comorbidity in advanced age.

ETHICAL APPROVAL:

This study was approved by the T.C. Ministry of Health, Ankara Bilkent City Hospital's Ethics Committee No. 2 (Approval no. NCT0533425).

PATIENTS' CONSENT:

Since it was a retrospective study, the data were collected from the hospital's archive following the approval of the Ethics Committee. Informed consent was obtained from all the patients before the procedure.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

ATDO, SO: Study conception, design, and preparation of the manuscript.

SE: Data collection.

CC: Analysis and interpretation of the results.

EE, YY: Drafting of the work, discussion, and literature review.

All authors approved the final version of the manuscript to be published.

REFERENCES

1. Ali G, Shaukat A, Masood S, Akram B, Ghaffar A, Gondal KM. A profile of colorectal tumors presenting as emergency. *J Coll Physicians Surg Pak* 2021; **31(1)**:74-8. doi: 10.29271/jcpcsp.2021.01.74.
2. Chong RC, Ong MW, Tan KY. Managing elderly with colorectal cancer. *J Gastrointest Oncol* 2019; **10(6)**: 1266-73. doi: 10.21037/jgo.2019.09.04.
3. Moraca RJ, Sheldon DG, Thirlby RC. The role of epidural anesthesia and analgesia in surgical practice. *Ann Surg* 2003; **238(5)**:663-73. doi: 10.1097/01.sla.0000094300.36689.ad.
4. Gustafsson UO, Scott MJ, Hubner M, Nygren J, Demartines N, Francis N, *et al.* Guidelines for perioperative care in elective colorectal surgery: Enhanced recovery after surgery (ERAS®) society recommendations: 2018. *World J Surg* 2019; **43(3)**: 659-95. doi: 10.1007/s00268-018-4844-y.
5. Hewson DW, Tedore TR, Hardman JG. Impact of spinal or epidural anaesthesia on perioperative outcomes in adult noncardiac surgery: A narrative review of recent evidence. *Br J Anaesth* 2024; **133(2)**:380-99. doi: 10.1016/j.bja.2024.04.044.
6. Rigg JR, Jamrozik K, Myles PS, Silbert BS, Peyton PJ, Parsons RW, *et al.* Epidural anaesthesia and analgesia and outcome of major surgery: A randomised trial. *Lancet* 2002; **359(9314)**:1276-82. doi: 10.1016/S0140-6736(02)08266-1.

7. Vester-Andersen M, Lundstrom LH, Moller MH. The association between epidural analgesia and mortality in emergency abdominal surgery: A population-based cohort study. *Acta Anaesthesiol Scand* 2020; **64(1)**:104-11. doi: 10.1111/aas.13461.
8. Park JW, Bae SI, Ryu J, Chung SH, Do SH. Effects of earmuffs and eye masks on propofol sedation during spinal anaesthesia for orthopedic surgery: A randomized controlled trial. *J Clin Med* 2023; **12(3)**:899. doi: 10.3390/jcm12030899.
9. Zhang X, Wang J, An XH, Chao YC, Bian Y, Xu Z, et al. Optimum dose of spinal ropivacaine with or without single intravenous bolus of S-ketamine during elective cesarean delivery: A randomized, double-blind, sequential dose-finding study. *BMC Pregnancy Childbirth* 2021; **21(1)**:746. doi: 10.1186/s12884-021-04229-y.
10. Suleiman A, Santer P, Munoz-Acuna R, Hammer M, Schaefer MS, Wachtendorf LJ et al. Effects of ketamine infusion on breathing and encephalography in spontaneously breathing ICU patients. *J Intensive Care Med* 2023; **38(3)**:299-306. doi: 10.1177/08850666221119716.
11. Xiang J, Cao C, Chen J, Kong F, Nian S, Li Z, et al. Efficacy and safety of ketamine as an adjuvant to regional anesthesia: A systematic review and meta-analysis of randomized controlled trials. *J Clin Anesth* 2024; **94**: 111415. doi: 10.1016/j.jclinane.2024.111415.
12. Huisman DE, Bootsma BT, Ingwersen EW, Reudink M, Slooter GD, Stens J, et al. Fluid management and vasopressor use during colorectal surgery: The search for the optimal balance. *Surg Endosc* 2023; **37(8)**:6062-70. doi: 10.1007/s00464-023-09980-1.
13. Deslarzes P, Jurt J, Larson DW, Blanc C, Hubner M, Grass F. Perioperative fluid management in colorectal surgery: Institutional approach to standardized practice. *J Clin Med* 2024; **13(3)**:801. doi: 10.3390/jcm13030801.
14. Hokenek UD, Gurler HK, Saracoglu A, Kale A, Saracoglu KT. Pleth variability index guided volume optimisation in major gynaecologic surgery. *J Coll Physicians Surg Pak* 2022; **32(8)**:980-6. doi: 10.29271/jcpsp.2022.08.980.
15. Cros J, Dalmay F, Yonnet S, Charpentier M, Tran-Van-Ho J, Renaudeau F, et al. Continuous hemoglobin and plethysmography variability index monitoring can modify blood transfusion practice and is associated with lower mortality. *J Clin Monit Comput* 2020; **34(4)**:683-91. doi: 10.1007/s10877-019-00367-z.
16. Solakhan M, Bulut E, Erturhan MS. Comparison of two different anaesthesia methods in patients undergoing percutaneous nephrolithotomy. *Urol J* 2019; **16(3)**:246-50. doi: 10.22037/uj.v0i0.4291.
17. Hahm KD, Jin SJ, Cho SS, Park J, Park H, Kim DH, et al. Relationship of epidural patient-controlled analgesia with postoperative bleeding after unilateral total knee arthroplasty: A propensity score-matching analysis. *Sci Rep* 2021; **11(1)**:11284. doi: 10.1038/s41598-021-90946-5.
18. Wang TK, Wang YY, Ku MC, Huang KC, Tong KM, Wu CC, et al. A retrospective comparison of clinical efficacy between multimodal analgesia and patient-controlled epidural analgesia in patients undergoing total knee arthroplasty. *Medicina (Kaunas)* 2023; **59(12)**:2137. doi: 10.3390/medicina59122137.
19. Koning MV, Klimek M, Rijs K, Stolker RJ, Heesen MA. Intrathecal hydrophilic opioids for abdominal surgery: A meta-analysis, meta-regression, and trial sequential analysis. *Br J Anaesth* 2020; **125(3)**:358-72. doi: 10.1016/j.bja.2020.05.061.
20. American Society of Anaesthesiologists. Practice Guidelines for the prevention, detection, and management of respiratory depression associated with neuraxial opioid administration: An updated report by the American Society of Anesthesiologists task force on neuraxial opioids and the American society of regional anesthesia and pain medicine. *Anesthesiology* 2016; **124(3)**:535-52. doi: 10.1097/ALN.0000000000000975.
21. Desai N, El-Boghdady K, Albrecht E. Epidural vs. transversus abdominis plane block for abdominal surgery - A systematic review, meta-analysis and trial sequential analysis. *Anaesthesia* 2021; **76(1)**:101-17. doi: 10.1111/anae.15068.
22. Romanzi A, Gallo G, De Rango S, Vignati B, Vannelli A. Pain distraction during awake major colorectal surgery: Supporting patients beyond the COVID-19 era. Preliminary findings. *Front Surg* 2021; **8**:754059. doi: 10.3389/fsurg.2021.754059.
23. Romanzi A, Boleso N, Di Palma G, La Regina D, Mongelli F, Milanesi M, et al. Awake major abdominal surgeries in the COVID-19 era. *Pain Res Manag* 2021; **2021**:8763429. doi: 10.1155/2021/8763429.
24. Romanzi A, Dragani TA, Adorni A, Colombo M, Farro A, Maspero M, et al. Neuraxial anesthesia for abdominal surgery, beyond the pandemic: A feasibility pilot study of 70 patients in a suburban hospital. *Updates Surg* 2023; **75(6)**:1691-7. doi: 10.1007/s13304-023-01554-z.
25. Marrone F, Fusco P, Lepre L, Giulii Capponi M, Villani A, Paventi S, et al. Neuraxial anesthesia for an open low anterior rectal resection: Tip the scales in patient's favor. *Cureus* 2024; **16(3)**:e57094. doi: 10.7759/cureus.57094.

