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Effect of Epidural Analgesia on Goal-Directed Fluid Therapy with Pleth Variability Index in Patients Who Underwent Laparoscopic Colorectal Surgery

Laparoskopik Kolorektal Cerrahi Geçiren Hastalarda Epidural Analjezinin Pleth Değişkenlik İndeksi ile Hedefe Yönelik Sıvı Tedavisi Üzerine Etkisi

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ABSTRACT

Objective: One of the most critical parameters of the ERAS protocol is perioperative fluid management. Goal-directed fluid therapy has advantages in this respect. We aimed to observe whether the epidural analgesia has an effect on intraoperative fluid replacement and postoperative recovery in patients who underwent major abdominal surgery in this study.

Methods: Forty-six patients who underwent elective laparoscopic colon surgery under general anesthesia, aged 18-75, ASA I-III, were included in the study. The patients were divided into two groups as those who received epidural analgesia and those who did not receive epidural analgesia (intravenous, IV analgesia group). Goal-directed fluid therapy was arranged with Pleth Variability Index (PVI) monitoring in both groups.

Results: There was no difference in the amount of the fluid administered and the hemodynamic parameters between the groups. Intraoperative PVI trend significantly decreased in the epidural group while it was stable in the IV analgesia group. (p=0.03). Body temperature was significantly lower at the end of the surgery compared to the beginning of the epidural analgesia group (p<0.001). But no significant change n body temperature was observed in the IV analgesi group (p=0.182). There was no difference between groups in terms of hospital length of stay, postoperative complications, and clinical recovery time.

Conclusion: The administration of epidural analgesia does not have an advantage in comparison to the IV analgesia group in terms of targeted fluid therapy and the postoperative process and recovery time in laparoscopic colorectal surgery performed under general anesthesia. More detailed evaluations are needed for the effectiveness of PVI in intraoperative fluid therapy optimization.

Keywords: Goal-directed fluid therapy, epidural analgesia, pleth variability index, laparoscopic abdominal surgery

ÖZ

Amaç: ERAS protokolünün en kritik parametrelerinden biri perioperatif sıvı yönetimidir. Hedefe yönelik sıvı tedavisinin bu açıdan pek çok avantajı vardır. Bu çalışmada laparoskopik abdominal cerrahi geçiren hastalarda epidural analjezinin intraoperatif sıvı replasmanı ve postoperatif derlenme üzerine etkisinin olup olmadığını incelemeyi amaçladık.

Yöntem: Genel anestezi altında elektif laparoskopik kolon cerrahisi uygulanan 18-75 yaş arası ASA I-III 46 hasta çalışmaya dahil edildi. Hastalar epidural analjezi uygulananlar ve epidural analjezi uygulanmayanlar (intravenöz, IV analjezi grubu) olarak iki gruba ayrıldı. Her iki grupta da Pleth Değişkenlik İndeksi (PVI) monitorizasyonu ile amaca yönelik sıvı tedavisi düzenlendi.

Bulgular: Verilen sıvı miktarı ve hemodinamik parametreler açısından gruplar arasında fark yoktu. İntraoperatif PVI trendi, IV analjezi grubunda stabilken, epidural analjezi grubunda anlamlı olarak azaldı. (p=0,03). Epidural analjezi grubunda ameliyat sonundaki vücut sıcaklığı, başlangıca göre anlamlı olarak düşüktü (p<0,001). Ancak IV analjezi grubunda vücut sıcaklığında anlamlı değişiklik gözlenmedi (p=0,182). Gruplar arasında hastanede kalış süresi, postoperatif komplikasyonlar ve klinik iyileşme süresi açısından fark yoktu.

Sonuç: Genel anestezi altında yapılan laparoskopik kolorektal cerrahide epidural analjezi uygulamasının IV analjezi grubuna göre hedefe yönelik sıvı tedavisi, postoperatif süreç ve derlenme süresi açısından bir avantajı yoktur. Pleth Değişkenlik İndeksi'nin intraoperatif sıvı tedavisi optimizasyonundaki etkinliği için daha ayrıntılı değerlendirmelere ihtiyaç vardır.

Anahtar sözcükler: Hedefe yönelik sıvı tedavisi, epidural analjezi, pleth değişkenlik indeksi, laparoskopik abdominal cerrahi

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INTRODUCTION

In order to reduce the length of hospital stay and postoperative morbidity in patients who will undergo elective surgery, perioperative care has been emphasized and accelerated surgical techniques have been developed with up to thirty years of experience in surgical clinics (1,2). The accelerated recovery protocol after surgery, known as "Enhanced Recovery After Surgery" (ERAS), is applied with proven methods and a multidisciplinary approach to accelerate the recovery process of the patient in the postoperative period (3). It has been shown in many studies that the ERAS protocol provides faster postoperative recovery and shortens the hospital stay. In addition, it is known that morbidity, mortality, postoperative complications and rehospitalization rates are lower in these patients (4,5).

One of the most important components of the ERAS protocol is perioperative fluid management. Targeted fluid therapy has been proven to reduce length of hospital stay, morbidity, and postoperative complication rate (6). It has been reported that dynamic volume measurement, one of the most frequently used parameters in this regard, allows balanced fluid therapy (7,8). Although it is known that the administration of epidural analgesia in addition to general anesthesia in major abdominal surgical procedures causes hemodynamic changes due to sympathetic blockade and vasoplegia, it is not known to what extent it changes the fluid and vasopressor requirements.

In this study, ERAS compliance was standardized according to the surgical plan of the surgical team, and we aimed to reveal the effect of epidural analgesia on targeted fluid therapy in patients who underwent laparoscopic colorectal surgery by the same surgical team.

MATERIAL and METHODS

The study was planned as a single-center, prospective observational, cross-sectional and was performed in General Surgery Operating Rooms. The informed consent form was approved by ASA I-III patients aged 18-75 years. The study was approved by the Ankara University Faculty of Medicine Ethics Committee (07-428-18, decision numbered 16/04/18). Patients with cognitive dysfunction, cardiac instability, muscle and/or central nervous system disease, infection at the epidural catheter insertion site, suspected drug allergy, kyphoscoliosis, and those who did not want to participate were excluded from the study.

The epidural catheterization procedure was explained to the patients participating in the study. Intravenous (IV) analgesia was planned for patients with absolute or relative contraindications for epidural catheterization. Cases in which the location of the epidural catheter was in doubt or were complicated were excluded from the study.

The patients were divided into two groups as those who received epidural analgesia (EA) and those who received IV analgesia (IVA) (those who did not receive epidural analgesia). Electrocardiography (ECG), oxygen saturation (SpO_2), non-invasive blood pressure, train of four (TOF), pleth variability index (PVI) and body temperature monitoring were performed as standard in patients who were taken to the operating room without premedication. Monitoring of fluid management of all patients was achieved with the PVI parameter using the Masimo Rainbow SET Pulse cooximetry probe (Masimo Corporation, Irvine, USA). Thoracic epidural catheterization was performed at the T9-10 or T10-11 level in patients who were planned to insert an epidural catheter after sedation with IV 0.5 mg kg^{-1} fentanyl. The tip of the catheters was advanced to the T8 level. As a test dose, 2 mL of 2% lidocaine was applied. Sensory block level was aimed to be between T6-T12 dermatomes, 2% lidocaine was titrated until the sensory block reached the T6 dermatome. After reaching the appropriate level of epidural anesthesia, general anesthesia was induced. In the intraoperative period, the hemodynamic response of the patient was evaluated and 0.25% bupivacaine infusion was continued through the epidural catheter at a rate of 5 mL $hour^{-1}$ throughout the operation.

General anesthesia induction was achieved with 1 mg kg^{-1} lidocaine, 0.5 mg kg^{-1} iv remifentanil, 3 mg kg^{-1} propofol, and 1 mg kg^{-1} rocuronium. The patients were ventilated according to the principles of lung protective ventilation. Sevoflurane was administered with 50% O_2 / 50% air for maintenance of anesthesia. The target minimum alveolar concentration was between 1.0-1.2. When the maintenance muscle relaxant requirement was TOFcount 2, 0.15-0.2 mg kg^{-1} rocuronium injection was provided. For intraoperative analgesia, 0.5 mg kg^{-1} IV bolus fentanyl was administered to patients who could not undergo epidural catheterization. Compressed air heating blankets were used in all patients.

All patients were infused with 500 mL of balanced electrolyte solution from the epidural test dose to the beginning of surgery, followed by a maintenance infusion at a rate of 4 mL kg^{-1} hr^{-1}. Intraoperative fluid therapy was arranged according to the algorithm shown in Figure 1. Demographic data of patients, preoperative vital signs, amount of fluid intake in the intraoperative period, amount of urine output, PVI and blood pressure values, time to start oral intake. Postoperative period, mobilization, gas and stool output, discharge times and developing complications were recorded.

Data were evaluated with Statistical Package for the Social Science (SPSS) for Windows 22.0 (SPSS Inc, Chicago, IL)". The conformity of the variables to the normal distribution was examined by visual (histogram and probability graphs) and analytical methods (Shapiro-Wilk Test). Descriptive sta-

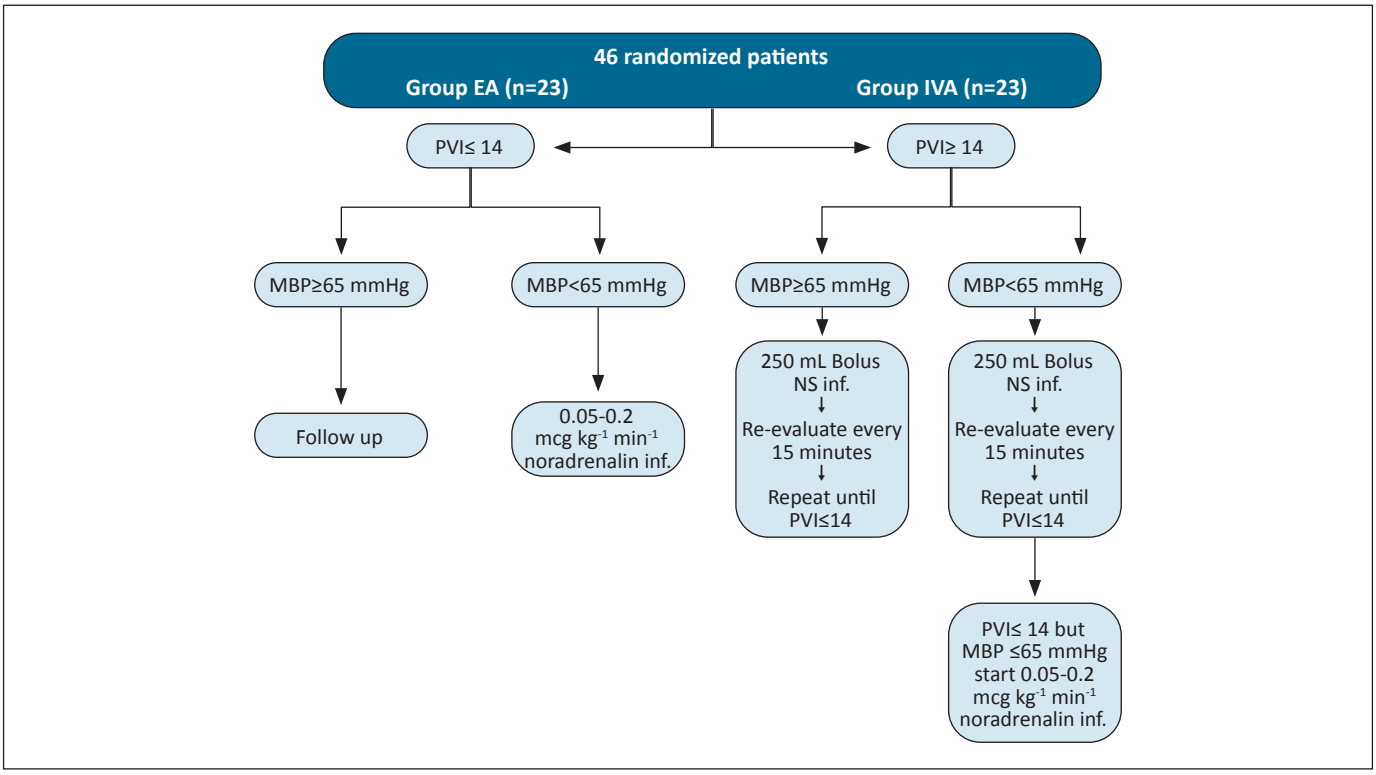

Figure 1: Intraoperative fluid management algorithm. **EA:** Epidural analgesia, **IVA:** Intravenous analgesia, **PVI:** Pleth variability index, **MBP:** Mean blood pressure, **NS:** Normal saline.

tistics were presented as mean ± standard deviation (minimum-maximum), frequency distribution, and percentage. Pearson Chi-Square Test and Fisher's Exact Test were used to evaluate categorical variables. Student's T-test and Paired Sample T-test were applied for the variables found to have normal distribution. The Mann-Whitney U Test was used as a statistical method between two independent groups for non-normally distributed variables. Statistical significance level was accepted as $p<0.05$.

RESULTS

A total of 46 patients, 23 patients in both groups, were evaluated. There was no statistically significant difference between the groups in terms of age, gender, height, body weight, body mass index (BMI) and American Society of Anesthesiologists (ASA) classification (Table I). In both groups, there was no statistically significant difference between the amount of fluid intake, total crystalloid bolus count, and the number of patients receiving noradrenaline infusion in the intraoperative period ($p > 0.05$) (Table II). There was no statistically significant difference between the study groups in terms of length of stay in the intensive care unit, length of hospital stay and postoperative complication development (Table III). While the mean body temperature of the patients in the IVA group did not show a significant change compared to the beginning of the operation, the body temperature of the patients in the EA group decreased statistically significantly ($p<0.001$). There was no statistically significant difference between the groups in terms of mean body temperature (Table IV). In the patients in the IVA group, the PVI value at the end of the operation did not differ significantly from the beginning of the operation ($p=0.753$). In the patients in the EA group, the PVI value at the end of the operation was significantly lower than at the beginning of the operation ($p=0.033$) (Table V). No statistically significant difference was found between the study groups in terms of postoperative mobilization, initiation of oral intake and duration of gas and stool removal (Table VI).

DISCUSSION

According to the results of our study, when IV analgesia administration and epidural analgesia administration were compared in patients undergoing laparoscopic colorectal surgery, there was no difference in the amount of fluid given and the amount of bolus administered with targeted fluid therapy using PVI monitoring in both analgesia methods. At the end of the surgery, the body temperature was found to be significantly lower in the patients in the epidural analgesia group.

Different anesthesia and analgesia procedures applied may affect the hemodynamics of the patients in the intraoperative period, thus the amount of fluid given and their vasopressor requirements. In addition, administering an appropriate

Table I: Demographic Data

	Epidural (n=23)	IV (n=23)	p
Age (year)	55.3 ± 15.3 (21-75)	59.5 ± 13.2 (31-75)	0.3[a]
Gender			
Female	7 (30.4)	10 (43.5)	0.3[b]
Male	16 (69.6)	13 (56.5)	
Height (cm)	168.4 ± 7.4 (153-182)	166.2 ± 12.4 (140-188)	0.9[a]
Body weight (kg)	75.2 ± 11.8 (55-101)	75.7 ± 19.9 (40-116)	0.4[a]
BMI (kg m^{-2})	26.6 ± 4.3 (17.8-35.0)	27.1 ± 4.8 (20.4-38.6)	0.7[a]
ASA Classification			
I	4 (17.4)	5 (21.7)	
II	16 (69.6)	16 (69.6)	0.8[b]
III	3 (13.0)	2 (8.7)	

Continuous variables are presented as "mean ± standard deviation (minimum-maximum)" and categorical variables as "number (percent of column)" **n:** Number of patients, **BMI:** Body mass index, **a:** Student's t- test, **b:** Chi-square test, **IV:** Intravenous, **ASA:** American Society of Anesthesiologists.

Table II: Distribution of Fluid Volume, Total Urine Output, Total Bolus Count and Noradrenaline Infusion Initiation

	Epidural (n=23)	IV (n=23)	p
Fluid intake (mL)	2667.4 ± 984.8 (1000-4500)	2466.5 ± 1217.5 (780-5400)	0.5[a]
Number of patients who have noradrenaline infusion	6 (26.1)	3 (13.0)	0.4[c]
Urine output (mL)	550 (85-800)	980 (40-1850)	0.8[b]
Number of times bolus infusion	7 (0-11)	5 (0-14)	0.6[b]

Continuous variables are presented as "mean ± standard deviation (minimum-maximum)" or "median (min-max)" and categorical variables as "number (percent of column)". **n:** Number of patients, **SD:** Standard deviation, **IV:** Intravenous, **a:** Student's t-test, **b:** Mann-Whitney U test, **c:** Fisher's test.

Tablo III: Total Length of Stay in the Intensive Care Unit and Hospital, Postoperative Surgical Complications

	Epidural (n=23)	IV (n=23)	p	Total (n=46)
Hospitalisation in ICU (days)	1.8 ± 1.2 (1-6)	1.4 ± 1.0 (0-5)	0.112[a]	1.6 ± 1.1 (0-6)
Length of hospital stay (days)	9.6 ± 5.0 (3-28)	9.6 ± 3.7 (4-18)	0.964[a]	9.6 ± 4.3 (3-28)
Postoperative Complication				
Number of patients	5 (21.7)	3 (13.0)	0.699[b]	8 (17.4)
Complications (n=8)				
Anastomotic leak-reoperated	1 (20.0)	0		1 (12.5)
Infection	0	2 (66.7)		2 (25.0)
Intraoperative anal stump-coloanal anastomosis	1 (20.0)	0		1 (12.5)
Re-admission with rectal bleeding	1 (20.0)	0		1 (12.5)
Bleeding in the stoma	1 (20.0)	0		1 (12.5)
Wound infection	0	1 (33.3)		1 (12.5)
Hematoma at the operation area	1 (20.0)	0		1 (12.5)

Continuous variables are presented as "mean ± standard deviation (minimum-maximum)" and categorical variables as "number (percent of column)". **n:** Number of patients, **SD:** Standard deviation, **ICU:** Intensive Care Unit, **IV:** Intravenous, **a:** Student's t-test, **b:** Mann-Whitney U test, **c:** Fisher's test.

Table IV: Distribution of Body Temperature Values at the Beginning and End of Surgery

		Epidural (n=23)	IV (n=23)	p[a]	Total (n=46)
Body temperature (°C)	Beginning of operation	36.2 ± 0.4 (35.4-36.9)	36.3 ± 0.4 (35.5-37.0)	0.434	36.3 ± 0.4 (35.4-37.0)
	End of operation	35.7 ± 0.6 (34.5-36.6)	36.0 ± 0.7 (34.4-37.5)	0.212	35.9 ± 0.7 (34.4-37.5)
	p[b]	**<0.001**	0.182		

Continuous variables are presented as "mean ± standard deviation (minimum-maximum)". **n:** Number of patients, **SD:** Standard deviation, **IV:** Intravenous, **a:** Student's t-test, **b:** Paired-Samples T Test.

Table V: Distribution of Pleth Variability Index (PVI) Values at the Beginning and End of Surgery Among the Study Groups

		Epidural (n=23)	IV (n=23)	p[a]
PVI	Beginning of the operation	11.3 ± 2.7 (4-17)	10.7 ± 5.3 (4-25)	0.653
	End of the operation	9.2 ± 3.7 (4-20)	10.3 ± 3.2 (4-17)	0.271
	p[b]	**0.033**	0.753	

Continuous variables are presented as "mean ± standard deviation (minimum-maximum)". **n:** Number of patients, **SD:** Standard deviation, **a:** Student's t-test, **b:** Paired-Samples T test, **IV:** Intravenous, **PVI:** Pleth variability index**.**

Table VI: Distribution of Postoperative Clinical Characteristics Among Study Groups

	Epidural (n=23)	IV (n=23)	p	Total (n=46)
Mobilization, min	57,6 ± 302,4	129,6 ± 417,6	0.555[a]	100 ± 360
Day 0	22 (95.7)	21 (91.3)	1.000[b]	43 (93.5)
Day 1	1 (4.3)	2 (8.7)		3 (6.5)
Initiation of oral intake, day	1.6 ± 0.5 (1-2)	1.7 ± 0.9 (1-4)	0.942[a]	
Day 0	10 (43.5)	12 (52.3)	0.112[c]	22 (47.8)
Day 1	13 (56.5)	7 (30.4)		20 (43.5)
Day 2	0	3 (13.0)		3 (6.5)
Day 3	0	1 (4.3)		1 (2.2)
Duration of gas and stool removal, day	1.5 ± 0.7 (0-3)	2.0 ± 0.9 (0-3)	0.070[a]	
Day 0	1 (4.3)	1 (4.3)	0.236[c]	2 (4.3)
Day 1	11 (47.8)	6 (26.1)		17 (37.0)
Day 2	9 (39.1)	9 (39.1)		18 (39.1)
Day 3	2 (8.7)	7 (30.4)		9 (19.6)

Continuous variables are presented as "mean ± standard deviation (minimum-maximum)" and categorical variables as "number (percent of column)". **IV:** Intravenous, **Min:** Minute, **a:** Mann-Whitney U Test; **b:** Fisher's Definitive Test; **c:** Chi-Square Test.

amount of fluid with a small dose of vasopressor may preserve the patient's vascular tone and prevent complications due to fluid overload. In a study by Hong et al., three different concentrations of local anesthetic were administered for epidural analgesia to patients undergoing abdominal surgery, and their hemodynamic parameters were monitored. It has been mentioned that the decrease in systemic vascular resistance and mean arterial blood pressure in the patient group in which a higher concentration of local anesthetic was administered for epidural analgesia was more pronounced and significant compared to the other groups (9). Monnet et al. reported that the dose of noradrenaline can affect the accuracy of PVI, even if it is low, and therefore, it is inevitable that the response to fluid will be affected (10). The reason why there was no difference between the groups in the amount of fluid administered in our study may be due to the low concentration of local anesthetic applied to the epidural group. In addition, the relatively low hourly epidural local anesthetic infusion rate applied in our study may be another reason for the absence of significant hemodynamic changes.

Vasodilation due to sympathetic block causes rapid heat loss in neuraxial blocks. The block also suppresses the patient's body temperature by shivering. This situation continues until the effect of the block wears off. Hypothermia is even more profound in general anesthesia combined with neuraxial block (11). In addition, pneumoperitoneum performed during laparoscopic surgery has the potential to cause a decrease in body temperature (12,13). In our study, post-operative body temperature was found to be significantly lower in the epidural analgesia group than at the beginning of the operation. This situation made us think that standard warming methods may be insufficient in patients undergoing epidural analgesia and studies on extra warming methods should be continued.

The PVI parameter can predict the relative hypovolemia caused by vasoplegia after epidural block. In our study, it was observed that the mean PVI value at the beginning of surgery was higher in the epidural group than in the IV group. This PVI elevation can be evaluated as a result of vasoplegia. The PVI value at the end of surgery in patients who received epidural analgesia was significantly lower than at the beginning of surgery. The PVI value at the end of surgery in patients who received IV analgesia did not show a significant change compared to the beginning of surgery. This significant decrease in PVI in the epidural group indicates that volume optimization is sufficient in the preoperative and intraoperative periods of the patients.

Unlike other invasive dynamic indices, the PVI parameter we used in our study offers clinicians a noninvasive, automatic and continuously obtained numerical value (14-16). In patients undergoing general anesthesia, targeted fluid management with PVI has been shown to reduce intraoperative and postoperative lactate levels as well as intraoperative fluid overload (17,18). It has been shown that pneumoperitoneum applied during laparoscopic surgical interventions increases the PVI, which is a plethysmographic variable, but does not change the dynamic variables (SVV, PPV) obtained from the arterial pressure waveform (19). On the other hand, a lower probability of fluid replacement compared to conventional methods can be considered as the success of PVI follow-up (20). On the other hand, it has been shown that noradrenaline infusion can significantly reduce the value of dynamic variables and mask a true intravascular volume deficit (21). Although it has been stated that even small doses of noradrenaline may affect the accuracy of PVI and thus the assessment of fluid response, it has also been stated that infusion of appropriate dose of noradrenaline can protect vascular vessels and prevent the development of complications due to excessive fluid administrations (18). Other researchers emphasized that factors that may affect PVI should be excluded when using PVI to objectively evaluate fluid response after epidural block performed under general anesthesia (22).

When all these data are evaluated together with our study, although PVI monitoring is a non-invasive, highly sensitive, and frequently used continuous method in targeted fluid therapy; Since there are many factors that can affect the PVI value such as vasopressor use, pneumoperitoneum, and epidural analgesia, the reliability of this study and whether PVI can make an objective assessment in this patient group can be questioned.

Enhanced Recovery After Surgery is a protocol that aims to reduce patients' clinical recovery time, postoperative complication rate and hospital stay. In studies and reviews on the role of epidural analgesia in surgeries where the ERAS protocol is applied, it has been reported that pain control is better in patients treated with epidural analgesia compared to other analgesia techniques, but there is no reduction in hospital stay and complication rate (23,24). In our study, there was no significant difference between the groups in terms of postoperative complication rate, length of stay in the intensive care unit, length of hospital stay, duration of mobilization, initiation of oral intake, and duration of first flatulence in the postoperative period.

Numerically, the complication rate in the EA group (21.7%) was higher than in the IVA group (13%). In addition, we observed that the complications in the EA group were mostly due to bleeding and anastomosis problems, although they were not statistically significant, and the complications in the IVA group were in favor of infection.

Levy et al. compared spinal, epidural and iv. analgesia methods in patients undergoing laparoscopic colorectal surgery. Although there was no statistically significant difference, it was observed that the number of patients who developed complications in the epidural analgesia group was higher than the other groups. In addition, although there was no statistically significant difference, it was observed that complications related to anastomosis were more common in patients who received spinal and epidural analgesia compared to the IV analgesia group (25). In our study, even if there is no statistical difference, we believe that the increase in clinically significant complications in the epidural analgesia group can reach statistical significance in studies with larger patient groups. For this reason, it can be said that it would be a better choice not to apply epidural catheterization, which is an invasive procedure, in minimally invasive surgeries.

Limitations of the study

The primary aim of our study was whether there would be a difference between the two groups in terms of the amount of intraoperative fluid volume, and we determined that 46 patients were needed for this purpose. However, when the results were examined, the numerical difference in the num-

ber of patients who were started on vasopressors, postoperative complications and recovery parameters was not statistically significant. When other studies were also examined, we thought that the sample size was small. Another limitation was that we did not record the total amount of local anesthetic given to the patients and the total dose of noradrenaline. If we record these details, a more detailed comment can be made about how much it affects the PVI parameter.

CONCLUSION

It was observed that there was no significant difference between the amount of fluid given according to PVI monitoring in epidural or IV analgesia protocols in patients who underwent laparoscopic colorectal surgery in accordance with the ERAS protocol. Although PVI monitoring guides conventional fluid therapy, it should be used with caution in the presence of conditions that may affect measurements and/or in high-risk patients whose monitoring results may change. In addition, the high tendency to hypothermia in patients who received epidural analgesia indicates that active warming strategies should be applied in this patient group. Although there was no difference between the two groups in terms of initiation of oral intake, mobilization, first flatulence and hospital stay, and postoperative complication rate, it should not be forgotten that epidural catheterization is an invasive procedure and is open to complications. Although the combination of general anesthesia and epidural anesthesia/analgesia in laparoscopic colorectal surgery is not recommended in the ERAS guidelines, it should be noted that the potential benefits are still likely to be demonstrated by better planned and larger studies.

AUTHOR CONTRIBUTIONS

Conception or design of the work: ACD, NU
Data collection: ACD, CA
Data analysis and interpretation: OB, NU, CA
Drafting the article: OB, ACD
Critical revision of the article: NU, OB
The author (ACD, OB, CA, NU) reviewed the results and approved the final version of the manuscript.

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