Yeni Üroloji Dergisi - *The New Journal of Urology* **2023;18(3):230-239. doi: 10.33719/yud.2023-18-3-1350497**

Original Research / Özgün Araştırma

Does Depth of Anesthesia Effect Clinical Results of Patients Who Underwent Radical Cystectomy in Accordance with Eras Protocols?

Eras Protokollerine Uygun Olarak Radikal Sistektomi Yapılan Hastalarda Anestezi Derinliği Klinik Sonuçları Etkiler Mi?

Nalan Saygı Emir[1], Fatma Çıtak Karacaer[2]

[1] Department of Anesthesiology and Reanimation, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, University of Health Sciences, Istanbul, Turkey

[2] Department of Anesthesiology and Reanimation, Cerkezkoy State Hospital, Tekirdağ, Turkey

Geliş tarihi (Submitted): 2023-08-26
Kabul tarihi (Accepted): 2023-09-27

Yazışma / Correspondence

Nalan Saygı Emir
Address: Bakirkoy Dr. Sadi Konuk Training and Research Hospital, 34180, Bakirkoy, İstanbul, Turkey
E-mail: nasaemir@hotmail.com

ORCID
N.S.E. 0000-0002-7244-5805
F.Ç.K. 0009-0009-5078-1005

Özet

Amaç: Radikal sistektomi ameliyatı geçiren hastalarda cerrahi sonrası hızlandırılmış iyileşme (ERAS [Enhanced Recovery After Surgery]) protokollerine uygun olarak uygulanan, düşük ve yüksek MAC (Minimum Aleveolar Concentration) anestezi düzeyinin anestezi derinliği üzerine etkisinin olup olmadığını araştırmak.

Gereç ve Yöntemler: Hastanemizin yerel etik kurulunun onayı alındıktan sonra 2019-2022 yılları arasında radikal sistektomi uygulanan 41 hastanın retrospektif verileri toplandı, 35 hasta çalışmaya dahil edildi. Anestezisi 0,5 MAC ile sürdürülen hastalar düşük MAC (Grup L), 1 MAC ile sürdürülenler ise yüksek MAC (Grup H) olarak ayrıldı. Tüm hastalara ERAS protokolleri doğrultusunda hazırlanan standart anestezi protokolü uygulandı. Anestezi derinliği hasta durum indeksi (Pneumonia Severity Index [PSI]) ve baskılama oranı (Supression Ratio [SR]), preoperatif ve postoperatif 24. saat Mini Mental Test sonuçları, postoperatif yoğun bakım (post-anesthesia care unit [PACU]) yatış sürelerini ve komplikasyonlarını içeren parametreler karşılaştırıldı.

Bulgular: Hastaların yaş ortalaması (Grup H ve L'de sırasıyla 61 ve 65 yaş) her iki grupta da benzerdi (p=0.234). PSI Grup H'de 60., 120. dakikalarda ve fasya kapanışında anlamlı olarak daha düşük bulundu (sırasıyla p=0.004, p=0.001 ve p=0.000). PSI <25 süresi grup H'de anlamlı

Abstract

Objective: To investigated whether low and high MAC (Minimum Aleveolar Concentration) level of anesthesia have an effect on the depth of anesthesia, clinical results paremeters in patients underwent radical cystectomy in accordance with ERAS (Enhanced Recovery After Surgery) protocols

Material and Methods: Retrospective data of 41 patients underwent radical cystectomy between 2019-2022 were collected, 35 of them were included. The patients were divided in two groups: Group H (1 MAC, n:18) and Group L (0.5 MAC, n:17). All patients were prepared and managed in line with ERAS protocols. Perioperative and early postoperative parameters including depth of anesthesia which was followed by PSI (Pneumonia Severity Index) and SR (Supression Ratio), preoperative and postoperative 24th hours Mini Mental Test results, post-anesthesia care unit (PACU) unit admission and duration and complications were compared.

Results: The mean age of the patients (61 and 65 years, in the Group H and L, respectively) were similar (p=0.234) in both groups. PSI was found to be significantly lower in Group H at the 60th, 120th minutes and fascia closure (p=0.004, p=0.001, and p=0.000 respectively). PSI <25 duration was significantly higher in group H (139.0±186.7 and 17.6±54.8 in group H and L, respectively, p=0.001). The duration of SR>0

This study was reviewed and approved by the Bakırköy Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee 15.11.202/252.
All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants.

olarak daha yüksekti (grup H ve L'de sırasıyla 139.0±186.7 ve 17.6±54.8, p=0.001). SR>0 süresi Grup H'de anlamlı olarak daha yüksekti (p=0.000). Hem anestezi (474 dk) hem de ameliyat (432 dk) süreleri Grup H'de anlamlı olarak daha yüksekti (sırasıyla p=0.013 ve 0.029). Ameliyat sonrası 12. saatte bulantı ve kusma da Grup H'de yaygındı (p=0.008). Mini Mental Test de dahil olmak üzere karşılaştırılan diğer parametreler benzerdi.

Sonuç: MAC değerleri peroperatif ve erken postoperatif sonuçları anlamlı olarak etkilememiştir. Yüksek MAC seviyesi daha derin bir anestezi oluştururken, düşük MAC seviyesi daha düşük bir inhalasyon anestezi ajanı tüketimi sağlayarak etkili bir alternatif gibi görünmektedir.

Anahtar Kelimeler: ERAS, radikal sistektomi, MAC, anestezi

was significantly higher in Group H (p=0.000). Both anesthesia (474 min) and surgery (432 min) times were significantly higher in Group H (p=0.013 and 0.029 respectivelly). Nausea and vomiting at 12 hours postoperatively was also common in Group H (p=0.008). The rest of parameters that compared were similar, including the minimental test.

Conclusion: The MAC values did not significantly affect perioperative and early postoperative outcomes. While high MAC level MAC level generates a deeper anesthesia, low MAC level seems an effective alternative providig a lower inhalation anestesia agent consumption.

Keywords: ERAS, radical cystectomy, MAC, anesthesia

INTRODUCTION

Enhancing Recovery After Surgery (ERAS) protocols are described to improve outcomes and reduce healthcare costs by standardizing medical care with evidence-based protocols. It was first introduced by Dr. Kehlet in 1997 and during early 2000s, and was brought to the agenda by Dr. Gustafsson and Dr. Ljunqvist with more comprehensive studies (1,2). ERAS protocols were developed for colorectal procedures and ERAS programs constitute the best comprehensive and evidence-based care in colorectal surgery. Modified ERAS protocols have also been used in many other specialties, including gynecology, thoracic surgery, vascular surgery, pediatric surgery and orthopedic surgery (3). ERAS protocol has not gained popularity in urologic procedures yet (4). Although radical cystectomy, a urological intervention, shares some similarities with colorectal procedures in terms of principles, it differs significantly due to unique aspects such as the surgical technique, involving small bowel anastomosis, presence of urine in the peritoneal cavity, and the need for both extra and intraperitoneal access (5). Therefore, advanced monitoring techniques can be used for fluid management. (Masimo Radical 7 Pulse CO-Oximeter with pleth variability index [PVI] software [Masimo SET, Masimo Corp., Irvine, CA, USA]) (6).

Although ERAS is recommended in many surgical branches today (7), more data are needed to prove it's effectiveness in major urological procedures.

ERAS protocols recommend to standardize perioperative anesthesia management, to avoid deep anesthesia, and to use the lowest possible doses and possible short-acting anesthetic agents (4). Today, the minimum alveolar concentration (MAC) is widely used as an indicator of the potency of inhalation agents (8). The depth of anesthesia is patient state index (PSI) and suppression ratio (SR) monitored with the SEDLine Brain Function Monitor (Masimo Corp., Irvine, CA, USA) device used to estimate the depth of anesthesia. The PSI is designed to monitor patients' intraoperative sedation levels and drug effects (9). The PSI, a number ranging from 0 to 100, correlates with the clinical states that occur during the administration of an anesthetic agent. Decreasing values of the PSI indicate increasing levels of hypnosis. The range of 100-50 is associated with wakefulness and increasing depth of sedation as the number decreases, while the range of 50-25 indicates general anesthesia, and the range of 25-0 is related to deep anesthesia (10).

In this study, we retrospectively investigated whether low and high MAC concentrations of multimodal anesthesia has an effect on the depth of anesthesia, clinical paremeter of the patient, reaching the postoperative discharge criteria and causes any complication in patients who underwent radical cystectomy in accordance with ERAS protocols.

MATERIAL AND METHODS

After obtaining the approval of the local ethics committee of our hospital with the decision number 2022-15-11, the data of the patients who underwent radical cystectomy between 2019-2022 were reviewed retrospectively. Data of the patients collected from hospital's electronic Database (Probel, Izmir, Turkey), anesthesia follow-up slips and pain follow-up charts. This study was retrospective, cross-sectional, and single-centered. The data of 41 patients in total were collected, and 6 patients were exclude (4 because different levels of depth of anesthesia was different the rest of the groups, 2 because epidural catheter could not inserted). The patients were divided in two groups; Group H, whose anesthesia was maintained with 1 MAC and Group L, those with 0.5 MAC. All patients prepared and managed in line with ERAS protocols with standart anesthesia protocol. All patients were seen the day before, be informed about anesthesia, and Mini Mental Tests were performed. In operating room, in addition to ASA standard monitorisation, patient state index (PSI) for depth of anesthesia, suppression ratio (SR), SEDLine Brain Function Monitor (Masimo Corp., Irvine, CA, USA) (Masimo Root, California, USA), pleth variability index (PVI) Masimo Radical 7 Pulse CO-Oximeter with PVI software (Masimo SET, Masimo Corp., Irvine, CA, USA) monitoring for invasive arterial pressure and fluid management were performed.

Preventive pain treatment was started with preoperative non-opioid paracetamol (Paracerol, Polifarma). Prophylactic anti-emetic therapy was given. An epidural catheter was inserted. Radial artery cannulation and intra-arterial pressure monitoring (IABM) were done. MAC values that calculated automatically by the device were followed and recorded.

Crystalloid infusion was started at a rate of 3-5 ml/kg/h. PVI was aimed to be less than 15 by using PVI monitoring in fluid management. If it exceeded 15, 250 cc bolus crystalloid was given. In the follow-up of the depth of anesthesia, the dose of remifentanil was titrated to a PSI of 25-50 and an SR of 0. The vaporizer was turned off as the fascia began to close. At the end of the case, the duration of surgery and anesthesia, and whether the patient was transferred were recorded. Patient-controlled analgesia was used through an epidural catheter for postoperative pain control. Their 24-hour follow-up was done by the pain team and recorded. The Mini Mental Test was repeated at the postoperative 24th hour in all patients.

All the data were recorded at the specified times (1-start of ventilation, 2-30. min, 3-60. min, 4-120. min, 5-fascia closing, 6-after extubation).

Statistical Analysis

Statistical comparison of hemodynamic data (mean arterial pressure [MAP] and peak heart rate [HR]) at the same time will be made. Demographic data of the patients, BMI's (Body Mass Index), ASA scores (American Society of Anesthesiology), whether the surgery is robotic or open, anesthesia and surgery times, the amount of fluid given as perioperative bolus and infusion, the amount of blood and blood products used, the number of patients admitted to the post-anesthesia care unit (PACU) unit, and duration of stay in PACU, any surgical complications, need for analgesics within 12 hours, nausea and vomiting, and discharge times were also recorded.

Statistical Analysis: The Statistical Package for Social Sciences (version 28.0) program was used for statistical analysis. Mean, standard deviation, median minimum, maximum, frequency and ratio values were used in descriptive statistics of the data. The distribution of variables was measured with the Kolmogorov Simirnov test. Independent sample t test and Mann-Whitney U test were used to analyze quantitative independent data. Chi-square test was used in the analysis of qualitative independent data, and Fischer test was used when chi-square test conditions were not met.

RESULTS

A total of 35 patient data, 18 high MAC (Group H) and 17 low MAC (Group L) were analyzed. The mean age of the patients in the Group H was 61

years, 65 years in the Group L. Male gender was dominant between the groups. There was no statistical differences between groups regarding patients ages and BMI (p=0.234) (Table 1).

The percentage of robotic surgery was 50% in Group H, and 24% in Group L. Anesthesia times were 474.6±112.8 / 389.1±103.5 minutes and surgery times were 432.5±115.6 / 356.8±102.2 minutes in Group H and Group L respectively and these differences were found statiscically significant (p=0.013 and p=0.029). The total amount of fluid was 3389 ml in Group H and 2917 ml in Group L and there was no significant difference between groups (p>0.05, Table 2). ES (Erythrocyte Suspension) and FFP (Fresh Frozen Plasma) usage rates did not differ significantly between the groups (p>0.05). Of the group H patients, 1 ES was given to one of the 3 open surgery cases, and 2 ES to the other two. Of the group L patients, 3 ES were given to 4 open surgery cases and 2 ES to 1 robotic case. FFP was given to 6 patients in Group H and 5 patients in Group L. There was no statistical difference between the minimental test results of the patients in both groups at the preoperative and postoperative 24th hour (p>0.05, Table 2). Table 2 shows the surgical methods, anesthesia and surgery durations, as well as the perioperative data of the patients.

PSI, at the 60th, 120th minutes and fascia closure were 25.9±5.3, 25.9±6.3, 25.4±2.5 (respectively) in Group H and 30.6±7.4, 32.5±6.6, 34.2±7.8 (respectively) in Group L and these differences were significantly lower in Group H (p=0.004, p=0.001, and p=0.000, respectivel). The duration of SR>0 was 86.8±123.5 (mean 24.5) in Group H and 1.0±2.0 (mean 0.0) in group L, and was significantly higher in Group H (p=0.000). PSI <25 times were 139.0±186.7 and 17.6±54.8 in group H and L respectively, and was significant higher in group H (p=0.001, Table 3). Hemodynamic data was measured at time periods simultaneous with evaluation of depth of anesthesia did not differ between the two groups (p>0.05, Table 4). The hemodynamic data of both groups are shown in Table 4. Presence of nausean and vomiting at postoperative 12th hour was positive in 16 of group H patients (88.9%) and in 8 of group L patients (47.1%) and this difference was significanly higher in group H. No significant difference was found between the two groups in the evaluation of the post-operative processes of the patients (Table 5).

Table 1. Demographic Values

		Group H				Group L				p	
		Mean.±ss/n-%			Median	Mean.±ss/n-%			Median		
Age		61.6	±	7.3	63.0	65.2	±	7.7	66.0	0.234	m
Gender	Female	2		11%		1		6%		1.000	X^2
	Male	16		89%		16		94%			
BMI		24.8	±	3.7	25.0	26.1	±	3.3	25.1	0.509	m
ASA	II	9		50%		8		47%		0.862	X^2
	III	9		50%		9		53%			

X^2 Ki-Kare test / m Mann-Whitney u test

MAC: minimum alveolar concentration, BMI: Body mass index, ASA: American Society of Anesthesiolgy

Table 2. Perioperative Datas

		Group H				Group L				p	
		Mean±ss/n-%			Median	Mean±ss/n-%			Median		
Surgical technique											
Open		9		50%		13		76%		***0.105***	X^2
Robotic		9		50%		4		24%			
Minimental Test											
Preop		23.1	±	4.4	23.0	24.1	±	4.3	26.0	0.497	m
Postop		23.3	±	3.3	22.0	24.0	±	3.5	25.0	0.583	m
Cristalloid fluid											
Infusion		1536	±	432	1650	1303	±	456	1250	0.091	m
Bolus		1631	±	708	1600	1497	±	1208	1100	0.457	m
Colloid fluid		222.2	±	255.7	0.0	117.6	±	218.6	0.0	0.199	m
ES	(-)	15		83.3%		12		71%		0.657	X^2
	(+)	3		16.7%		5		29.4%			
I		*1*		*5.6%*		*3*		*18%*			
II		*2*		*11.1%*		*2*		*12%*			
FFP	(-)	12		66.7%		12		70.6%		0.657	X^2
	(+)	6		33.3%		5		29.4%			
I		*2*		*11.1%*		*3*		*17.6%*			
II		*4*		*22.2%*		*2*		*11.8%*			
Anesthesia time		474.6	±	112.8	490.0	389.1	±	103.5	390.0	***0.013***	m
Surgery time		432.5	±	115.6	440.0	356.8	±	102.2	370.0	***0.029***	m

X^2 Chi-Square test / ^{t} Independent Sample t test / ^{m} Mann-Whitney u test

Table 3. Perioperative Anesthesia Depth Status

	Group H				Group L				p	
	Mean.±ss/n-%			Median	Mean±ss/n-%			Median		
PSI										
Beginnig of ventilation	30.9	±	4.9	30.5	29.6	±	6.0	28.0	0.518	m
30. minute	25.9	±	5.1	25.0	29.1	±	7.0	26.0	0.154	m
60.minute	25.9	±	5.3	24.5	30.6	±	7.4	28.0	***0.004***	m
120. minute	25.9	±	6.3	24.0	32.5	±	6.6	33.0	***0.001***	m
Fascia closure	25.4	±	2.5	25.0	34.2	±	7.8	32.0	***0.000***	m
Extubation	87.9	±	3.9	88.0	87.6	±	3.7	88.0	0.932	m
SR > 0 time	86.8	±	123.5	24.5	1.0	±	2.0	0.0	***0.000***	m
PSI < 25 time	139.0	±	186.7	45.0	17.6	±	54.8	5.0	***0.001***	m
PSI> 50 time	0.0	±	0.0	0.0	0.0	±	0.0	0.0	1.000	m

^{m} Mann-Whitney U test, PSI: Patient State İndex

Table 4. Perioperative Hemodynamic values

	Group H				Group L				p	
	Ort.±ss/n-%			Median	Ort.±ss/n-%			Median		
Mean BP (mm/Hg)										
İnitiation of ventilation	76.3	±	12.6	76.0	77.9	±	12.1	73.0	0.843	m
30. minute	65.9	±	9.3	66.5	66.8	±	12.0	63.0	0.987	m
60. minute	69.1	±	13.0	63.5	73.4	±	13.2	69.0	0.306	m
120. minute	79.4	±	11.7	77.5	80.3	±	13.3	80.0	0.792	m
Fascial closure	73.1	±	15.2	72.0	82.4	±	16.2	82.0	0.083	m
Extubation	88.4	±	17.8	83.0	87.6	±	12.0	87.0	0.766	m
HB										
İnitiation of ventilation	79.3	±	15.3	77.5	71.1	±	9.7	73.0	0.099	m
30. minute	69.6	±	11.4	66.0	63.8	±	10.6	63.0	0.160	m
60. minute	69.7	±	14.6	64.0	64.6	±	11.5	67.0	0.391	m
120. minute	70.7	±	15.2	66.5	65.0	±	9.9	64.0	0.409	m
Fascial closure	74.6	±	17.0	73.5	72.1	±	14.4	73.0	0.856	m
Extubation	92.0	±	15.0	90.5	84.5	±	11.5	85.0	0.228	m

[m] Mann-Whitney U test

Table 5. Postoperative parameters

		Group H				Group L				p	
		Mean.±ss/n-%			Median	Mean±ss/n-%			Median		
PACU admission	(-)	13		72%		8		47%		0.105	X^2
	(+)	5		28%		9		53%			
PACU period (day)		0.33	±	0.59	0.00	0.76	±	1.03	1.00	0.133	m
Surgical complications	(-)	16		89%		15		88%		0.129	X^2
	(+)	2		11%		2		12%			
Postop 12h analgesic requirement	(-)	12		66.7%		15		88.2%		0.129	X^2
	(+)	6		33.3%		2		11.8%			
PONV 12h	(-)	2		11.1%		9		52.9%		0.008	X^2
	(+)	16		88.9%		8		47.1%			
Anesthesia time		474.6	±	112.8	490.0	389.1	±	103.5	390.0	0.013	m
Surgical time		432.5	±	115.6	440.0	356.8	±	102.2	370.0	0.029	m
Hospital stay		13.6	±	8.7	10.5	15.9	±	11.0	13.0	0.497	m

[X^2] Chi-Square test / [t] Independent Sample t test / [m] Mann-Whitney u test

PACU: post-anesthesia care unit, PONV: Postoperative nausea and vomiting

DISCUSSION

In this retrospective clinical study, we investigated whether low and high MAC concentrations of multimodal anesthesia has an effect on the depth of anesthesia and if MAC level effect clinical parameters in patients who underwent radical cystectomy surgery in accordance with ERAS protocols.

PSI, showing the depth of general anesthesia at the 60th, 120th minutes and fascia closure were recorded significantly lower in Group H. The duration of SR>0 (suppression ratio) and PSI <25 times were statistically significantly higher in Group H. Nausea and vomiting at 12 hours postoperatively was also common in Group H. We did not found any statistical significant difference between the groups that compared, including perioperative and postoperative clinical parameters and minimental test results.

Although ERAS protocols offer preoperative, perioperative and post-operative recommendations, the main purpose is to improve the post-operative process. To reach that goal a well-coordinated multidisciplinary study group which consist of patients, surgeons, anesthesiologists, pain specialists, and nurses is essential (10)(11).

This retrospective study was carried on the radical cystectomy cases who had been managed according to the ERAS protocols. Because ERAS protocols favor less inhalation anesthesia agent consumption, we have focused on perioperative MAC levels of our patient. At this point we constituted group H, composes of the patients with MAC level 1. Among all patients' data we also collected lower MAC level patients' data and constituted group L composed of the patients with MAC level 0,5 so that we were able to compare the results, to achieve our goal.

While conducting an interdisciplinary consensus study, a group of researchers reviewed meta-analyses, randomized controlled trials, and large prospective cohort studies and published a consensus statement for each item of the perioperative treatment pathway and stated that anesthetists control several preoperative, intraoperative, and postoperative ERAS elements (12). In the early 2000s, there were no prospective single-intervention studies evaluating the value of a standardized anesthesia protocol for cystectomy (13). By 2022, when the groups with and without ERAS protocols were compared, It was found that the hospitalization period was 13 days and 15 days in the ERAS group and in without ERAS group, respectively. It was also emphasized that the two groups differed significantly in terms of intraoperative data, and the significant difference that changed the results over time was increased minimally invasive surgical intervention ratio and differences with anesthesia protocols (14). In radical cystectomies, less intraoperative blood loss and less intraoperative fluid infusion were seen in patients treated according to the ERAS protocol and also average length of stay decreased from 12 days to 9 days in (15).

In our study groups all patients were followed and managed according ERAS protocol. In this main group we selected and compared the patients who received deep (Group H) and superficial (Group L) standard anesthesia. Therefore, we were able to see if the depth of the anesthesia effects the results. The average hospital stay was 13 days in Group L and 15 days in Group H in our patients. Although this difference was no statistically significant, we believe that a mean 2-days hospitalization difference is clinically significant. At this point robotic surgery ratio which is higher in group H may be an important parameter that effects lenght of hospitalisation. In a meta-analysis, covering the years 2005-2021, the evidence for the effectiveness of ERAS protocols on postoperative complication rates, length of hospital stay, investigated and it was found that length of hospital stay was shorter when ERAS protocol applied but postoperative complication rate did not show any significant difference (16). Galich et al. investigated the use of robotic radical cystectomy with extracorporeal urinary diversion in 13 consecutive patients and compared the results with a homogeneous group of 24 patients who underwent standard open radical cystectomy. They found a lower length of hospital stay and less blood loss in the robotic group, while the operative time was significantly longer (17). We

attribute the significantly higher duration of surgery and therefore anesthesia time in our study Group H to the higher percentage of robotic surgery in these group of patients.

There are studies suggesting that not all ERAS elements are equally weighted in terms of the effect on postoperative complications and healing (18). Each of the intraoperative strategies deserves to be investigated separately. We think the depth level of anesthesia is one of them. End-tidal inhalation anesthetic concentration (ETAC), raw or processed electroencephalography (EEG), or other specialized monitors are often used to estimate anesthetic depth. None of the available inhalation or IV anesthetic agents are ideal for all patients, and they all have potential adverse side effects. In a meta-analysis including 40,317 patients, an association between increased depth of anesthesia (measured by processed EEG, such as a Bispectral Index [BIS] monitor) and decreased postoperative survival has been noted in some observational studies (19). We avoid excessive depth of anesthesia and significant hypotension, especially in elderly patients, patients at risk of developing perioperative neurocognitive impairment. However, there is insufficient evidence to recommend the use of EEG monitoring to prevent postoperative delirium or other neurocognitive disorders (20).

We use PSI monitoring to reach the lowest possible anesthesia depth level without creating awareness. In our study, the PSI values of our patients in both groups were between 25-50, which corresponds to general anesthesia. In Group H, suppression rates ranging from 0-100%, which measure how much the electrical activity of the brain's frontal and prefrontal cortex are suppressed as a percentage of time, were found to be significantly lower at the 60th, 120th minutes and fascia closure. In our study grops we also found a statistically significan higher duration of SR>0 and PSI <25 duration in group H. All these data support that higher MAC level causes deeper anesthesia as expected. However, the depth level of anestesia did not seem to have a significant negative effect on any of the results of the patients, including the postoperative minimental test results.

We also analyzed our hemodynamic data at the same measurement times. There was no significant difference between the groups. Mean arterial pressure was in the range of 65-88 mm/Hg, indicates that the patients were not hypotensive. In the first 12 hours postoperatively, nausea and vomiting were significantly less in group L (p:0,008) where open technique surgery was more common. We attributed this to the fact that the need for analgesia (IV analgesics) was less even though the surgery was open technique.

Different ERAS protocols for radical cystectomy have been published. A meta-analysis of 860 studies was performed through databases; hospitalization times were in favor of the protocols in terms of complications. Early mobilization focused on the implementation of optimized fluid management. The meta-analysis concluded that these protocols are useful to be applied in clinical practice (21). This meta-analysis emphasizes the importance of per operative fluid management. Compared to colorectal surgery, fluid monitoring is more challenging in cystectomy patients as urine output can be unreliable. We used plet variability index (PVI) monitoring to plan our intraoperative fluid management in our patients as it is an important component of ERAS protocols. Both groups of patients received restrictive fluid therapy and PVI was kept below 15 to avoid hypervolemia (6).

In ERAS protocols, inhalation anesthesia or total intravenous anesthesia (TIVA) technique can be used for intraoperative anesthesia maintenance. For both techniques, it is wise to use short-acting agents at the lowest possible doses, as they may delay healing or cause other adverse effects. In a 2022 meta-analysis (23 studies; 1611 participants) in which the intravenous maintenance technique and inhalation technique in anesthesia maintenance were compared, it was found that mean inflammatory biomarker levels measured after various types of surgery were not effected (22).

Our study showed that MAC values did not significantly affect perioperative and early postoperative outcomes in patients who underwent radical cystectomy, but the higher MAC level

generates a deeper anesthesia. In accordance with ERAS protocols, perioperative low MAC level seems an effective alternative providig a lower inhalation anestesia agent consumption, but this should to be supported by larger, prospective studies.

Conflict of Interest: No potential conflict of interest relevant to this article was reported.

Funding: This article has no funding.

Ethics Committee: Bakırköy Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee 15.11.202/252.

Authors Contributions: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Nalan Saygı Emir and Fatma Citak Karacaer. The first draft of the manuscript was written by Nalan Saygı Emir and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

REFERENCES

1. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth. 1997;78(5):606-17. https://doi.org/10.1093/bja/78.5.606.
2. Fearon KC, Ljungqvist O, Von Meyenfeldt et al. Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. Clin Nutr. 2005;24(3):466-77. https://doi.org/10.1016/j.clnu.2005.02.002.
3. Ansari D, Gianotti L, Schröder J et al. Fast-track surgery: procedure-specific aspects and future direction. Langenbecks Arch Surg. 2013;398(1):29-37. https://doi.org/10.1007/s00423-012-1006-9.
4. Cerantola Y, Valerio M, Persson B et al. Guidelines for perioperative care after radical cystectomy for bladder cancer: Enhanced Recovery After Surgery (ERAS(®)) society recommendations. Clin Nutr. 2013;32(6):879-87. https://doi.org/10.1016/j.clnu.2013.09.014.
5. Nygren J, Thacker J, Carli F et al; Enhanced Recovery After Surgery (ERAS) Society, for Perioperative Care; European Society for Clinical Nutrition and Metabolism (ESPEN); International Association for Surgical Metabolism and Nutrition (IASMEN). Guidelines for perioperative care in elective rectal/pelvic surgery: Enhanced Recovery After Surgery (ERAS(®)) Society recommendations. World J Surg. 2013;37(2):285-305. https://doi.org/10.1007/s00268-012-1787-6
6. Cannesson M, Desebbe O, Rosamel P et al. Pleth variability index to monitor the respiratory variations in the pulse oximeter plethysmographic waveform amplitude and predict fluid responsiveness in the operating theatre. Br J Anaesth. 2008;101(2):200-6. https://doi.org/10.1093/bja/aen133.
7. Debono B, Wainwright TW, Wang MY et al. Consensus statement for perioperative care in lumbar spinal fusion: Enhanced Recovery After Surgery (ERAS®) Society recommendations. Spine J. 2021;21(5):729-752. https://doi.org/10.1016/j.spinee.2021.01.001
8. Kanazawa S, Oda Y, Maeda C et al. Electroencephalographic effect of age-adjusted 1 MAC desflurane and sevoflurane in young, middle-aged, and elderly patients. J Anesth. 2017;31(5):744-750. https://doi.org/10.1007/s00540-017-2391-6.
9. Prichep LS, Gugino LD, John ER et al. The Patient State Index as an indicator of the level of hypnosis under general anaesthesia. Br J Anaesth. 2004;92(3):393-9. https://doi.org/10.1093/bja/aeh082.
10. Kehlet H, Wilmore DW. Evidence-based surgical care and the evolution of fast-track surgery. Ann Surg. 2008;248(2):189-98. https://doi.org/10.1097/

SLA.0b013e31817f2c1a

11. Ljungqvist O, Scott M, Fearon KC. Enhanced Recovery After Surgery: A Review. JAMA Surg. 2017(1);152(3):292-298. https://doi.org/10.1001/jamasurg.2016.4952
12. Feldheiser A, Aziz O, Baldini G et al. Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice. Acta Anaesthesiol Scand. 2016;60(3):289-334. https://doi.org/10.1111/aas.1265
13. Maffezzini M, Campodonico F, Capponi G et al. Fast-track surgery and technical nuances to reduce complications after radical cystectomy and intestinal urinary diversion with the modified Indiana pouch. Surg Oncol. 2012;21(3):191-5. https://doi.org/10.1016/j.suronc.2012.02.001
14. Lannes F, Walz J, Maubon T et al. Enhanced Recovery after Surgery for Radical Cystectomy Decreases Postoperative Complications at Different Times. Urol Int. 2022;106(2):171-179. https://doi.org/0.1159/000518163
15. Brusasco C, Di Domenico A, Ennas M, Benelli A, Dotta F, Tosi M, Manfredi M, Calcagno T, Campodonico F, Germinale F, Montevecchi A et al. Application of a protocol for enhanced recovery after radical cystectomy: a before-and-after cohort study. World J Urol. 2023;41(8):2273-2280. do https://doi.org/10.1007/s00345-023-04468-y
16. Peerbocus M, Wang ZJ. Enhanced Recovery After Surgery and Radical Cystectomy: A Systematic Review and Meta-Analysis. Res Rep Urol. 2021 Jul 29;13:535-547. https://doi.org/10.2147/RRU.S307385
17. Galich A, Sterrett S, Nazemi T et al. Comparative analysis of early perioperative outcomes following radical cystectomy by either the robotic or open method. JSLS. 2006 Apr-Jun;10(2):145-50.
18. Joshi GP, Kehlet H. Enhanced Recovery Pathways: Looking Into the Future. Anesth Analg. 2019;128(1):5-7. https://doi.org/10.1213/ANE.0000000000003746
19. Zorrilla-Vaca A, Healy RJ, Wu CL et al. Relation between bispectral index measurements of anesthetic depth and postoperative mortality: a meta-analysis of observational studies. Can J Anaesth. 2017;64(6):597-607. https://doi.org/10.1007/s12630-017-0872-6
20. Chan MTV, Hedrick TL, Egan TD et al; Perioperative Quality Initiative (POQI) 6 Workgroup. American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on the Role of Neuromonitoring in Perioperative Outcomes: Electroencephalography. Anesth Analg. 2020;130(5):1278-1291. https://doi.org/10.1213/ANE.0000000000004502
21. Wessels F, Lenhart M, Kowalewski KF et al. Early recovery after surgery for radical cystectomy: comprehensive assessment and meta-analysis of existing protocols. World J Urol. 2020;38(12):3139-3153. https://doi.org/10.1007/s00345-020-03133-y
22. O'Bryan LJ, Atkins KJ, Lipszyc A et al. Inflammatory Biomarker Levels After Propofol or Sevoflurane Anesthesia: A Meta-analysis. Anesth Analg. 2022 Jan 1;134(1):69-81. https://doi.org/10.1213/ANE.0000000000005671