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Effect of the Enhanced Recovery After Surgery Protocol on Postoperative Cognitive Functions in Colorectal Surgery

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ABSTRACT

Objective: Enhanced Recovery After Surgery (ERAS®) protocols established for colorectal surgery and continuing to develop are multidisciplinary approaches combining several evidence-based interventions to reduce the patient's surgical stress response, to accelerate surgical recovery and to improve the outcome in all perioperative steps. However, it is not yet known how ERAS® protocols affect the cognitive functions in the early and late periods of patients.

Methods: Prospective observational study was performed with 51 cases. Mini Mental Test (MMT) was administered in the patients in the preoperative, postoperative early period (3rd hr,1st day) and postoperative late period (7th day, 30th day).

Results: Changes observed in MMT measurements during the period from the preoperative period to postoperative 30th day were determined to be statistically significant (P < .01). Decrease in postoperative 3rd hr and 24th hr measurements (P < .01), increase in the postoperative 24th hr, 7th day and 30th day measurements (P < .01), compared to the postoperative 3rd hr measurement; increase in the postoperative 7th day and 30th day measurements (P < .01), are statistically significant compared to the postoperative 24th hr measurement. When the differences between the preoperative and postoperative 30th day MMT measurements were considered; an improvement was observed with a rate of 76% (n=38). In the group observed improvement (Group I), ASA scores were lower (P < .01), and mobilization (P < .01), were earlier; lengths of in the intensive care unit stay (P < .01), were shorter.

Conclusion: Cognitive functions improve in the early period with ERAS® protocol and complication rate regresses significantly and it becomes cost efficient due to early discharge.

Keywords: cognitive dysfunction, Colorectal surgery, Enhanced Recovery after Surgery, ERAS protocol, POCD

INTRODUCTION

Enhanced recovery after surgery (ERAS) is an evidence-based perioperative protocol that was implemented for the first time in patients who had undergone colorectal surgery. Different surgical disciplines subsequently improved it, and specific guidelines were established for each surgical branch.[1,2] ERAS protocol provides various regulations for procedures, from the preoperative to the post-recovery period.[1] The data till date have revealed that ERAS protocol increases patients' comfort by providing adequate postoperative pain control, shortens the length of hospital stay, and reduces postoperative morbidity and healthcare costs.[3]

Postoperative cognitive dysfunction (POCD) is a complication that is diagnosed using neuropsychological tests. The International Postoperative Cognitive Dysfunction 1 (ISPOCD 1) study stated that the incidence of POCD was 25.8% one week after surgery and 9.9% three months after surgery.[4] The rate of POCD on the first seven days after general anesthesia in major non-cardiac surgery is 21.2%, especially in elderly patients but reduces to 14.3% three months after surgery.[5] Surgical methods targeting minimally invasive surgery such as ERAS protocol may reduce the likelihood of POCD thanks to minor tissue injury and less postoperative inflammatory response.[6] However, a possible reduction in the incidence and severity of the disease owing to ERAS protocol remains unclear. To our knowledge, there is not enough research to define the relation between ERAS protocol and POCD. Therefore, in this study, we aimed to determine the risk factors related to POCD in patients who underwent colorectal surgery managed by ERAS protocol.

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METHODS

Fifty-one patients who would undergo colorectal surgery and were scheduled for perioperative care and treatment within the frame of ERAS protocol with ethics committee approval (Date: January 17, 2017, Decision no: 2017/587) and written informed consent were included in this prospective observational study.

Study design

The cognitive functions of the patients who decided on an operation were evaluated using MMT (Mini-Mental Test, Appendix 1) during preoperative information and counseling. The same procedure was repeated during the early (postoperative 3rd hour, 1st day) and late (postoperative 7th day and 1 month) postoperative periods. Procedures performed were recorded according to the ERAS guidelines (1).

All the patients who underwent general anesthesia had an endotracheal intubation procedure, and preoperative medication was avoided. Vital signs such as heart rate (HR), electrocardiogram (ECG), non-invasive blood pressure (NIBP), pulse oxygen saturation (SpO_2), and end-tidal carbon dioxide ($PetCO_2$) were monitored during the surgery. Anesthesia was provided using intravenous injection of remifentanil (0.05–0.3 $\mu g^{-1}kg^{-1}min$), propofol 2% (2 $mg^{-1}kg^{-1}$), and rocuronium bromide (0.6–1 $mg^{-1}kg^{-1}$). Remifentanil (0.04–0.4 $\mu g^{-1}kg^{-1}min$) and propofol (1.5–2.5 $\mu g^{-1}kg^{-1}h$) were continuously infused for maintenance of anesthesia. In addition, intravenous injections of rocuronium bromide were provided intermittently. The effectiveness of anesthesia was adjusted during the procedure, and bispectral index (Aspect-100, BIS) was maintained between 40 and 50. The breathing parameters were adjusted, and the $etCO_2$ was maintained at 35–45 mmHg. Lung protective ventilation strategy was administered as PEEP at 4–6 cmH_20 and tidal volume at 5–7 mL kg^{-1} (low tidal volume) to reduce postoperative pulmonary complications. The nasogastric tube was removed before the anesthesia was completed. Intraoperative hypothermia was prevented, and normothermia was maintained with routinely used actively working suitable warming devices (Mistral-Air Warming, The 37 Company, The Netherlands). Euvolemia was attempted to be maintained with perioperative fluid management. In patients at risk with an excessive amount of blood loss (>7 mL kg^{-1}) and major open surgeries, advanced hemodynamic monitorization was ensured for easy follow-up of individual-specific fluid treatment and provision of optimal oxygen transport during the perioperative period.

MMT was performed at the preoperative informing and counseling and at 3rd postoperative hour and 1st and 7th postoperative days. MMT was repeated by inviting the patients one month after surgery. The groups were divided into two according to the preoperative and postoperative 30th day MMT measurements.

Group I: Cognitive Recovery + (n=38)

Group II: Cognitive Recovery − (n=12)

One patient who died had no MMT measurement, grouping was performed with 50 cases.

In addition, fluids administered in this period, first oral feeding time, glucose monitorization data, whether the patient needed analgesia or not, analgesic administered, time of first mobilization, length of stay in the hospital, length of stay in intensive care, possible postoperative complications, hyperglycemia/hypoglycemia, cardiac/respiratory complications, nausea and vomiting, and mortality were recorded.

Assessment of cognitive function

MMT is the most commonly used cognitive screening instrument. MMT was developed initially to differentiate depression from dementia, and it was suggested that it could be used as a quantitative criterion of the severity of cognitive impairment and change in due course.[7] MMT is a 30-point questionnaire comprising items with a total of 30 points (30 is the best) measuring the following; 10 points of time and space orientation, 6 points of memory including 3 points of record and 3 points of recall, 5 points of attention, 8 points of language, and 1 point of visual-spatial functions. MMT scores between 30 and 24, 23 and 18, and 17 and 0 are considered normal, mild, and severe cognitive impairment, respectively. If the MMT score is less than 23, it indicates cognitive impairment. A decrease of 2 or more in the total MMT score indicates cognitive disorder.[8]

Neuropsychological assessment was performed in a quiet room, where only the patient and the evaluator were present. Delirium was ruled out postoperatively. All the tests were conducted and scored in a standardized manner to minimize possible bias introduced by different evaluators. Project investigators trained in neuropsychological assessment completed all data scoring and interpretations.

Exclusion criteria

- Children under 18 years of age.
- Patients undergoing emergency surgery.
- Patients undergoing procedures related to other organs in addition to elective colorectal surgeries.
- Patients who cannot give informed consent because of mental disorders and other pathologies (Alzheimer's, Parkinson's disease, etc.).

Statistics

The primary outcome of the study was to evaluate the cognitive function data and possible risk factors of patients who underwent colorectal surgery managed with ERAS protocol.-

Statistical analysis

The Number Cruncher Statistical System (NCSS) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. During the evaluation of the study data, descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, and maximum) were used. The conformity of the quantitative data to a normal distribution was tested by using the Shapiro-Wilk test and graphical assessments. Friedman test was used for dependent variables without normal distribution, and Bonferroni-Dunn test was used to evaluate dual comparison of these variables. The Mann-Whitney U test was used for the comparisons of quantitative variables without normal distribution between two groups. The Pearson's chi-squared and Fisher-Freeman-Halton tests were used for comparisons of qualitative data. A $P < .05$ was considered statistically significant.

RESULTS

The study was performed with 51 patients who underwent colorectal surgery and implemented ERAS protocol at the University of Health Sciences, Okmeydanı Training and Research Hospital, Department of Anesthesiology and Reanimation. Of the patients, 30 (58.8%) were male (Table 1). The patients were divided into three age groups, and 66.7% of them (n=34) were between 18 and 65 years old. Most of the patients (n=30, 58.8%) had a normal body mass index (BMI). The number of overweight and obese patients was 15 (29.4%) and six (11.8%), respectively.

Table 1. Preoperative characteristics of patients.

		n (%)
Age (mean ± SD, years)	18-65	34 (66.7)
	66-75	12 (23.5)
	76-85	5 (9.8)
Gender	Male	30 (58.8)
	Female	21 (41.2)
BMI (mean ± SD) (kg/m^2)	Normal (18.5-24.9)	30 (58.8)
	Overweight (25-29.9)	15 (29.4)
	Obese (30-34.9)	6 (11.8)

BMI: Body Mass Index

The median American Society of Anesthesiologists (ASA) score was 2 (1–3) (Table 2). Most of them had an ASA score of 1 or 2. Only seven (13.7%) patients had an ASA score

Table 2. Distribution of clinical features.

		n (%)
ASA Classification	Min-Max (Median)	1-3 (2)
	Mean±SD	2±1
	I	23 (45.1)
	II	21 (41.2)
	III	7 (13.7)
Hematocrit (%)	Min-Max (Median)	29-43 (35)
	Mean±SD	35.33±3.47
Liver function tests	Normal	44 (86.3)
	Abnormal	7 (13.7)
Antiemetic use	Single	26 (51.0)
	Dual	21 (41.2)
	Three or more	4 (7.8)
Perioperative analgesia	IV infusion / PCA	39 (76.5)
	Intermittent epidural injection	5 (9.8)
	Regional block - TAP	7 (13.7)
First oral feeding time (hour)	Min-Max (Median)	4-24 (10)
	Mean±SD	11.00±5.84
First mobilization time (hour)	Min-Max (Median)	6-48 (12)
	Mean±SD	16.12±10.57
Hospital stay (day, mean ± SD)	Min-Max (Median)	4-17 (8)
	Mean±SD	9.14±3.13
ICU stay (day, mean ± SD)	Min-Max (Median)	0-10 (0)
	Mean±SD	0.78±1.64
Postoperative complication	No complication	27 (52.9)
	Cardiac	10 (19.6)
	Nausea	6 (11.8)
	Hyperglycemia	4 (7.8)
	Respiratory	3 (5.9)
	Exitus	1 (2.0)

ASA: American Society of Anesthesiologists, ICU: Intensive Care Unit, TAP: Transversus Abdominis Plane, PCA: Patient Controlled Analgesia, IV: Intravenous.

of 3. The median hematocrit (Htc) was 35 (29–43). Seven (13.7%) patients had impairment of liver function tests. Most of the patients used a single antiemetic therapy; however, 21 (41.2%) and four (7.8%) patients had dual and three or more antiemetic therapies, respectively. Perioperative analgesia was provided with patient-controlled intravenous infusion (IV) in 39 (76.5) patients, intermittent epidural injection in five (9.8%), and regional anesthetic techniques including transversus abdominis plane (TAP) block in seven (13.7%). The median first oral feeding time after surgery was 12 (4–24) hours. The first postoperative mobilization time ranged from six to 48 hours (median, 12 hours). The median hospital and intensive care unit (ICU) stay of the patients was eight (4–17) and zero (0–10) days, respectively. Most of the patients had no perioperative complications (n=27, 52.9%) (Table 2). Cardiac complications occurred in 10 (19.6%) patients, nausea in six (11.8%), hyperglycemia in four (7.8%), and respiratory complications in three (5.9%) patients. One (2.0%) patient died postoperatively.

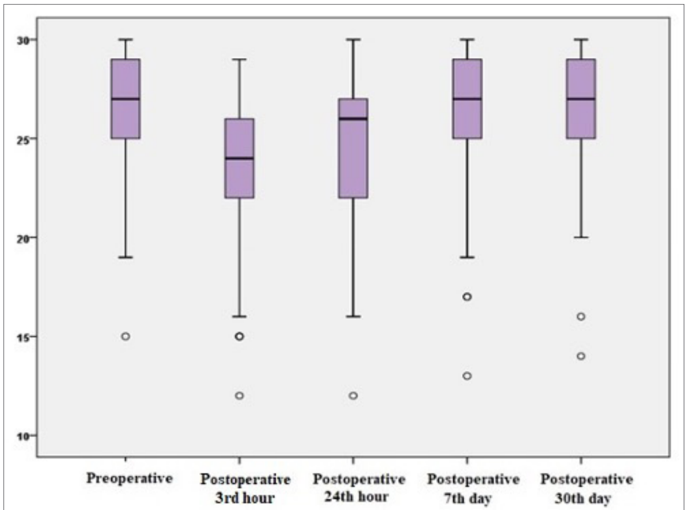

Figure 1. Distribution of MMT scores

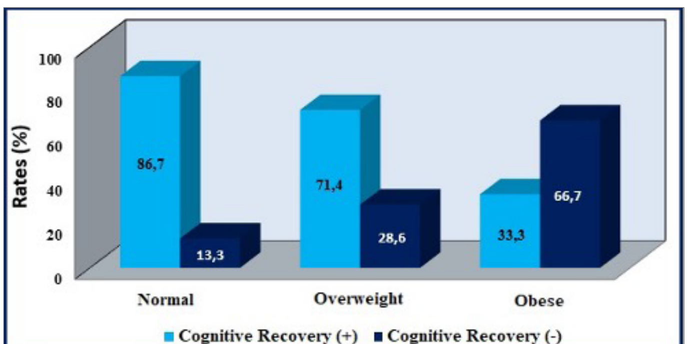

Figure 2. Distribution of cognitive recovery according to BMI rates

Fifty patients were assessed using MMT after the death of one patient (Figure 1). The MMT scores measured at different time periods from preoperative to 30th postoperative day revealed multiple kinds of statistical significance. According to differences in cognitive functions between the preoperative period and the 30th postoperative day, cognitive functions of 38 (76%) patients improved. Compared with those in the preoperative period, cognitive functions decreased in the 3rd and 24th postoperative hours (P = .001 and P = .001, respectively). However, compared with those in the 3rd preoperative hour, cognitive functions increased in the 24th postoperative hour and 7th and 30th postoperative days (P = .001, P = .001, and P = .001, respectively). Cognitive functions recovered significantly in the 7th and 30th postoperative days compared with those in the 24th postoperative hour (P = .004 and P = .001, respectively).

Although age and sex did not indicate any differences for the recovery of cognitive functions, patients with a nor-

Table 3. Evaluation of MMT scores.

	Preop.	Postop. 3rd hour	Postop. 24th hour	Postop. 7th day	Postop. 30th day	P
Mean±SD	26.37±3.12	23.48±3.91	24.74±3.85	25.88±3.76	26.20±3.64	.001* .666 † 1.000 ‡ .004 §
Min-Max (Median)	15-30 (27)	12-29 (24)	12-30 (26)	13-30 (27)	14-30 (27)	.001 ¶

MMT: Mini Mental Test; Preop.: preoperative; postop.: postoperative
* Comparison of preoperative and postoperative 3rd hour; preoperative and postoperative 24th hour; postoperative 3rd hour and postoperative 24th hour; postoperative 3rd hour and postoperative 7th day; postoperative 3rd hour and postoperative 30th day, postoperative 24th hour and postoperative 30th day, by using Bonferroni-Dunn Test.
† Comparison of preoperative and postoperative 7th day by using Bonferroni-Dunn Test.
‡ Comparison of preoperative and postoperative 30th day; postoperative 7th day and postoperative 30th day by using Bonferroni-Dunn Test.
§ Comparsion of postoperative 24th hour and postoperative 7th day by using Bonferroni-Dunn Test.
¶ Comparison of median MMT test results by using Friedman Test.

mal BMI had significantly higher rates of cognitive recovery than those who were overweight (26 [86.7%] vs. 10 [71.4%], *P* = .021) (Table 4). The rate of cognitive recovery in patients with normal weight was found to be higher than in those who were obese. Moreover, ASA scores revealed statistical significance between patients with and without cognitive recovery (Table 5). Patients with an ASA score I were significantly high in Group I (*P* = .043). The

Table 4. Evaluation of cognitive recovery according to patient characteristics.

		Group I (Recovery +) (n=38)	Group II (Recovery -) (n=12)	*P*
Age (years)	18-65	27 (81.8)	6 (18.2)	c.311
	66-75	8 (66.7)	4 (33.3)	
	76-85	3 (60.0)	2 (40.0)	
Gender	Male	23 (79.3)	6 (20.7)	d.520
	Female	15 (71.4)	6 (28.6)	
BMI (kg/m^2)	Normal (18.5-24.9)	26 (86.7)	4 (13.3)	c.021*
	Overweight (25-29.9)	10 (71.4)	4 (28.6)	
	Obese (30 or 34.9)	2 (33.3)	4 (66.7)	

cFisherFreemanHalton Test
dPearsonChi-Square Test
**P* < .05
BMI: Body Mass Index

Table 5. Evaluation of cognitive recovery according to clinical features.

		Group I (Recovery +) (n=38)	Group II (Recovery -) (n=12)	e*P*
ASA score	Min-Max (Median)	1-3 (1.5)	1-3 (2)	.043*
	Mean±SD	1.58±0.64	2.08±0.79	
	I	19 (86.4)	3 (13.6)	
	II	16 (76.2)	5 (23.8)	
	III	3 (42.9)	4 (57.1)	
First oral feeding time (hour)	Min-Max (Median)	4-24 (8)	10-24 (18)	.001**
	Mean±SD	8.89±3.62	17.67±6.65	
First mobilization time (hour)	Min-Max (Median)	6-48 (12)	8-48 (24)	.009**
	Mean±SD	13.79±8.56	23.50±13.16	
Hospital stay (day)	Min-Max (Median)	4-17 (8)	6-14 (9.5)	.498
	Mean±SD	8.97±3.29	9.58±2.78	
ICU stay (day)	Min-Max (Median)	0-3 (0)	0-2 (2)	.002**
	Mean±SD	0.37±0.88	1.33±0.98	

eMannWhitney U Test
**P* < .05*
**P* < .01

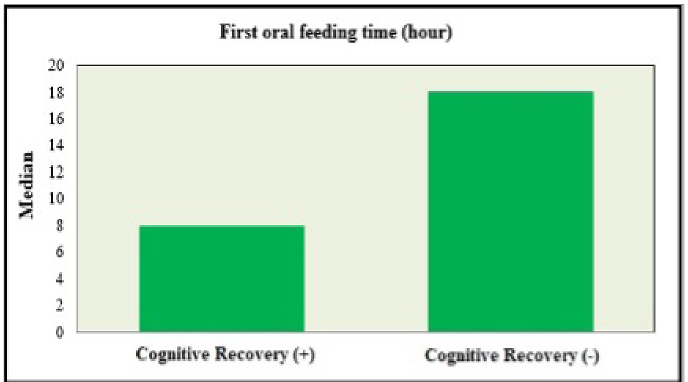

Figure 3. Distribution of first oral feeding times according to cognitive recovery

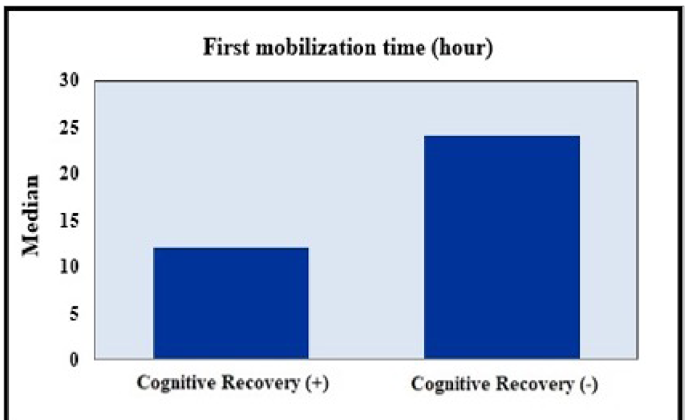

Figure 4. Distribution of first mobilization times according to cognitive recovery

first oral feeding was significantly earlier in the Group 1 than in Group 2 (median 8 [4–24] vs. 18 [10–24] hours, *P* = .001) (Figure 3). Patients in Group 1 had significantly earlier postoperative mobilization time (median 12, [6–48] vs. median 24 [8–48] hours, *P* = .001) (Figure 4). Hospital stays of the patients did not indicate any differences between the groups, but the length of ICU stay was significantly low in patients with cognitive recovery than the others (median, 0 [0–3] vs. median 2 [0–2] days, *P* = .002) (Table 5).

DISCUSSION

In this prospective observational study, we determined that preservation of cognitive function and minimization of complication development have occurred in parallel in patients who underwent colorectal surgery under the management of ERAS protocol.

In the study performed to detect the change in cognitive functions during early postoperative period of patients undergoing colorectal surgery and managed with ERAS protocol, it was determined that cognitive functions were preserved together with minimization of development of complications. Although neuropsychological tests are used for evaluation of cognitive functions, it is debatable whether there is a gold standard for this. In this study, we used MMT, the most commonly used test in international literature and in our country, to evaluate cognitive functions.

Colorectal surgery is the basis for the development of ERAS protocol. In this protocol, new evidence-based approaches are recommended instead of traditional approaches used in surgery and anesthesia. The primary purpose is to support organ functions to return to normal as soon as possible and enable patients to return to their daily routine quickly by minimizing the metabolic stress response to surgical trauma.[1] A multidisciplinary team consisting of a surgeon, an anesthesiologist, a nurse, a dietician, and a physiotherapist takes part in implementing the ERAS protocol beginning from patient optimization for surgical procedures to recovering at home. It has been shown that the ERAS protocol shortened the length of hospital stay by nearly 2–3 days, decreased complications by almost 50%, and provided cost saving of around USD 2,800 to 5,900 per patient.[9,10]

The diagnostic criteria of the cognitive dysfunction in the postoperative period have not been defined yet with a consensus as in other neurological complications such as delirium. POCD is a multifactorial condition that may affect patients in all age groups.[11] It has been reported that POCD was associated with the degeneration of the central nervous system, oxidative stress, inflammation, endocrinopathies, and immune dysfunction. There are some risk factors for developing POCD, including advanced age, coexisting comorbidity, prolonged surgery procedure, and lengthy intensive care unit stay.[12] The rate of POCD is 56% in patients discharged after coronary artery surgery and 23% three months after discharge. In addition, cognitive dysfunction is diagnosed preoperatively in patients with colorectal cancer 15% more frequently than healthy volunteers in the same age range. Its frequency was higher in women than men (52% vs. 40%). Processing speed, attention/working memory, and verbal learning were the most affected functions. These conditions indicate a dysfunction primarily in fronto-subcortical brain systems rather than being associated with inflammatory cytokines.[13] Age is the single risk factor generally accepted for prolonged or irreversible POCD. The high incidence of POCD in elderly individuals is not unusual and could be owing to possible interactions between anesthetic agents and amyloid beta-peptide, which is also associated with Alzheimer's disease.[14] The impairment of cognitive functions occurs also in the postoperative period, especially in elderly patients. Plas et al.[15] in their study demonstrated that the rate of cognitive dysfunction in elderly patients undergoing colorectal surgery was 12% in the third postoperative month, and cognitive recovery was observed in only 53% of the patients. The incidence of cognitive impairment was 37% preoperatively in patients with a Mini-Mental State Examination (MMSE) score ≤26 and 18% in patients undergoing major surgery. In this study, the improvement of cognitive functions began at 24th postoperative hour compared to that in our study in the third postoperative hour owing to the implementation of ERAS protocol and reached the preoperative level on the 30th postoperative day in 76% of the patients. Tuman et al.[16] reported that there was a positive correlation between POCD and increased age in patients undergoing coronary artery bypass graft surgery. The researchers also showed POCD incidence with the rates of 0.9%, 3.6%, and 8.9% in patients aged <65, 65 to 74, and >75 years, respectively.

On the 7th postoperative day, POCD was detected in 26% of patients who underwent colorectal surgery. Zhang et al.[17] observed that age, ASA score, and diabetes mellitus were the risk factors for POCD. Radtke et al.[18] revealed that cognitive impairment occurred in patients with severe systemic diseases at a rate of 37.4% seven days after surgery, and the authors verified that increased morbidity was a risk factor related to the POCD. In our study, patients with lower ASA scores had better preserved cognitive functions than the patients with a higher ASA score, and age was not a risk factor for the POCD contrary to expected. In addition, advanced age, lower preoperative MMSE score, and major surgery were the risk factors for the POCD in the third postoperative month after surgery. Therefore, the risk factors defined above should be considered in the clinical decision-making progress, and patients with these risk factors should be closely followed up.

Studies targeting development of interventions for improving the quality of life should focus on the subpopulations at high risk.[15] In a previous study, including POCD patients (24.7% of 80 patients) who underwent colorectal surgery under general anesthesia, researchers determined that diabetes mellitus, length of the postoperative fasting time greater than three days, and a systemic inflammatory response syndrome score ≥ 3 two days after surgery were independent risk factors for early POCD.[12] According to ERAS protocol, oral feeding was started as soon as possible. The first oral feeding time ranged from four to 24 hours, and only 7.8% (n=4) of the patients had a complication of hyperglycemia. There was a high rate of POCD in the early postoperative period; however, cognitive functions improved over time in the late period. The main reason for the high rate of POCD in the early period might be the timing of the MMT. Similarly, in a previous study on weight loss and changes in cognitive functions in patients who underwent bariatric surgery, Spitznagel et al.[19] determined that cognitive impairment in the early period improved within 12 weeks after surgery. Furthermore, researchers revealed that cognitive functions were better preserved in patients with a lower BMI.

Early mobilization, one of the targets of the ERAS protocol, is also related to reduced rates of postoperative delirium in elderly patients.[20] In our study, mobilization time ranged between six and 48 hours, and it contributed positively to the improvement of cognitive functions. In our study, there was a correlation between early oral feeding and cognitive recovery. Although coexisting comorbidities can be optimized, prolonging hospital and ICU stay because of various postoperative complications may cause delirium-like cognitive impairment. Regional anesthesia or analgesia may reduce mortality in the early postoperative period, and the POCD rate may reduce in 80% of patients.[5,21,22] There was no correlation between the hospital stay and POCD, but cognitive functions were better preserved in patients with a short ICU stay. These consequences might be an argument for the efficiency of the ERAS protocol.

This study has some limitations, including the fact that it was performed in a single center with a limited number of patients. A large number of patients are necessary for a more accurate analysis; however, this is the first study on this topic. Therefore, the results should be reconfirmed with new randomized controlled studies.

CONCLUSION

We determined that cognitive functions were preserved within parallel of minimization of complication development in patients who had the ERAS protocol implemented. In addition, cognitive impairment was related to ASA score, BMI, and length of ICU stay. The complication rate regressed significantly in patients with the implementation of the ERAS protocol. POCD can be significantly reduced with persistent multidisciplinary implementation of the ERAS protocol.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Okmeydanı Training and Research Hospital local ethic committee. (Date: January 17, 2017, Decision no: 2017/587)

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - P.Ü., M.H.; Design: P.Ü., K.A., M.H.; Supervision – M.H.; Resources – P.Ü., K.A., Y.N.Ö., F.T., Ş.A., B.K.Ç.; Materials – P.Ü., K.A., Y.N.Ö., F.T., Ş.A., B.K.Ç.; Data Collection and/or Processing – P.Ü., K.A., Y.N.Ö., F.T., Ş.A., B.K.Ç.; Analysis and/or Interpretation – P.Ü., B.K.Ç., M.H.; Literature Search – P.Ü., M.H.; Writing Manuscript – P.Ü., M.H.; Critical Review - M.H.

Declaration of Interests: The authors have no conflicts of interest to declare.

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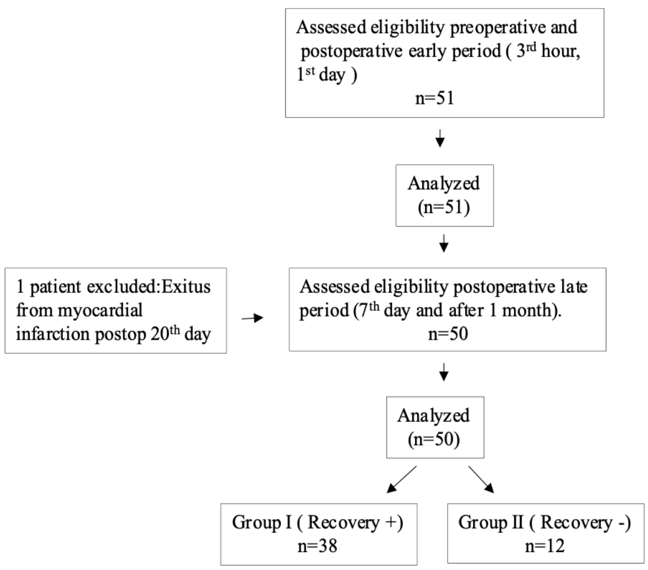

APPENDIX 1. STANDARDIZED MINI MENTAL TEST

ORIENTATION (Total 10 points)
What is the year..( )
What season is it?..( )
What is the month? ....( )
What is today's date? ....( )
What is the day of the week today? ....( )
What country we are in?..( )
What city we are in? ....( )
What locality we are in?...( )
What building we are in?...( )
What floor of the building are we in?............................( )

RECALL MEMORY (Total 3 points)
Now please listen carefully. I will say three words and you will repeat them after I have said them (Table, Flag, Cloth)(Allow time for a response, at least 20 seconds)
Score 1 point for each correct reply ....( )

ATTENTION and CALCULATE (Total 5 points)
I would like you to substract backward from 100 by 7. Continue until when I say you to stop. Score 1 point for each correct transaction on the account. (100, 93, 86, 79, 72, 65)..( )

VERBAL RECALL (Total 3 points)
Do you remember the words we repeated above? Say what you remember
Table, flag, cloth ....( )

LANGUAGE (Total 9 points)
a) What are the names of these objects you see? (watch, pencil) (2 points) (Allow time for a response, at least 20 seconds) ....()

b) Now please listen to the sentence I will say carefully and repeat it after me. "No ifs, ands or buts"................( )

c) Now I'm going to ask you to perform a task, please listen to me carefully and do what I say. "Please take the paper on the table with your right/left hand, then fold it in half once with both your hand, and put it on the floor" (Total 3 points, time 30 seconds). Score 1 point for each correct action...( )

d) Now I will give you a sentence. Please read it and do what is written in the paper. (1 point)"CLOSE YOUR EYES" ....( )

e) Now write the first sentence that comes to your mind on the piece of paper that I will give (1 point) ....( )

f) Please copy the design that I will show you (1 point)..( )