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SINGLE SESSION PREOPERATIVE BREATHING EXERCISE EDUCATION MAY INFLUENCE POSTOPERATIVE OUTCOMES IN OPEN COLORECTAL CANCER SURGERY

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Summary

Background: Preoperative prehabilitation is a set of interventions leading to better post-treatment outcomes. Prehabilitation protocols in colorectal cancer surgery lack standardization. We retrospectively analyzed the impact of a preoperative breathing exercise session as an additional intervention.

Aim: This study analyzes the potential benefits of breathing exercises for opera singers on patients' outcomes after open colorectal cancer surgery.

Methods: We analyzed a database of colorectal cancer patients from January 2019 until May 2020 at a single cancer center, extracting age, sex, tumor localization, and complications that required medical or surgical interventions in 30 days postoperative period (graded according to the Clavien-Dindo classification), and 365 days post-surgery, and completion of chemotherapy protocol. Then, we compared the existing prehabilitation protocol (nutritional intervention with commercially available pharmaconutrition based on NRS-2002 scores; three times a week aerobic exercise including 30 minutes on a bicycle or targeted walking distance of 5000 or 10000 steps based on individual's capacities starting at least two weeks before surgery), from the experimental protocol (breathing exercises for opera singers with relaxation session with music therapy). Endpoints were short-term and long-term complications, ICU/hospitalization length, and chemotherapy completion.

Results: We included 291 colorectal cancer patients, 173 males, and 118 females, mean age 66 years, of whom 31 (10.7%) completed the experimental protocol breathing exercise for opera singers. Patients of the control and experimental group had comparable demographics and tumor-associated characteristics at baseline. Experimental breathing protocol was associated with a shorter duration of ICU stay (χ 2 =4.132, df=1, p=0.047). However, it did not influence other parameters (length of stay on the ward, short-term and long-term complications, and ability to complete the treatment protocol). The binary regression analysis showed that patients with an NRS-2002 score of 5, with higher BMI and advanced age, would benefit the most from the suggested respiratory prehabilitation protocol.

Conclusion: The addition of breathing exercises might benefit CRC patients by reducing time spent in the ICU and postoperative respiratory complications. Again, this needs to be tested in a larger cohort.

KEYWORDS: *prehabilitation; colorectal cancer; outcomes; prognosis; breathing exercises*

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INTRODUCTION

The risk of colorectal cancer (CRC) has a rising incidence and poses a significant health challenge(1). It is the second leading cause of death from malignant diseases worldwide. The predicted CRC incidence correlates primarily with environmental risk factors, including sedentary lifestyle and westernization of diet, and associated metabolic derangements, such as obesity and type 2 diabetes mellitus, which might also influence patients' prognosis(2,3). Surgery is the only curative option for patients with CRC, but the risk of postoperative complications occurring in about 20% of patients remains high, unfavorably changing patients' morbidity and mortality(4). The number of complications and their severity are related to the patient's comorbidities, preoperative nutritional status, functional capacity, and psychological state. Moreover, the surgery reduces the patients' functional and physiological capacity by up to 40% and might compromise the patient's capacity to fulfill the (neo)adjuvant therapy(5).

Traditionally, various rehabilitation programs are carried out postoperatively to return to daily life activities as quickly as possible and change the lifestyle. Recently, different preoperative interventions (collectively called prehabilitation) have been integrated into cancer patient's care, but with no clear guidelines for specific patient cohorts, timing, and volume(6). Prehabilitation aims to increase patients' physiological reserve and help them better withstand the immediate stress of surgery, avoid postoperative complications, and achieve faster optimal recovery(7). Moreover, the preoperative period might also be the right time to target lifestyle changes that patients would adhere to more postoperatively(8). Programs are usually multimodal and integrate individualized exercise-based interventions, nutrition, lifestyle, and psychological support. In the case of CRC patients, prehabilitation needs to be compressed into a relatively short period of 4 to 5 weeks, the usual timeframe between diagnosis and surgery. There is encouraging data from observational studies on single modalities, while information from RCTs is scarce(9). Moreover, the strength of the evidence is limited by relatively small sample sizes, heterogeneity of type of cancer surgery, and heterogeneity of patient population concerning cancer type and baseline characteristics, as well as potential bias in patient selection due to the inability of some patients to attend the institution-based prehabilitation programs (10,11,12,13). Therefore, the role of specific preoperative exercises for patients undergoing major abdominal surgery still needs to be determined.

Our research aimed to analyze the potential benefits of breathing exercises for opera singers and music relaxation for patients undergoing CRC curative surgery. Mentioned exercises have previously been investigated in different settings of oncological patients(14).

PATIENTS AND METHODS

We conducted a single-center data analysis from a prospective study of CRC patients from January 2019 to May 2020 in the Department of Surgical Oncology, University Hospital for Tumors, Sestre milosrdnice University Hospital Center, Zagreb, Croatia. The local Ethics Committee approved the study conducted by principles of good clinical practice and the Declaration of Helsinki. Participants signed informed consent before recruitment.

We extracted the data from EMRs (electronic medical Records), including age, sex, tumor localization, and complications that required medical or surgical interventions in 30 days postoperative period (graded according to the Clavien-Dindo classification), 365 days post-surgery, and completion of chemotherapy protocol. Then, we separated the existing prehabilitation protocol (nutritional intervention with commercially available pharmaconutrition based on NRS-2002 scores; three times a week aerobic exercise including 30 minutes on a bicycle or targeted walking distance of 5000 or 10000 steps based on individual's capacities starting at least two weeks before surgery), from the experimental protocol (breathing exercises for opera singers with relaxation session with music therapy). Endpoints of interest were short-term and long-term complications, ICU/ hospitalization length, and chemotherapy completion.

The Ethical Committee of Sestre Milosrdnice University Hospital Centre of Zagreb, Croatia, approved the study.

Study participants

We included 291 consecutive patients, mean age 66 years, 173 males and 118 females, who re-

ceived curative operative treatment for CRC at our institution. Detailed patient data is presented in Table 1. Overall, 31 patients completed the experimental breathing protocol.

All patients were adults who were awaiting elective open colorectal cancer surgery. That required general anesthesia and a 5 cm or longer incision. We excluded patients with metastatic cancer or premorbid conditions (i.e. cardiorespiratory, musculoskeletal, and/or neurological) that were contraindications for exercises and fitness assessment, patients awaiting laparoscopic surgery. Written informed consent was obtained before intervention.

Intervention and procedure

All participants, as per standard care listed for colorectal cancer surgery, are required to attend a hospital multidisciplinary team for pre-surgical evaluation. Patients were seen by a surgeon, anaesthesiologist, nurse, and stoma therapist before surgery. All participants (rehabilitation and control group) had nutritional support preoperatively, if needed, provided by a nurse/stomal therapist. Also, all participants had early mobilization after surgery.

After admission to the hospital, participants in the interventional group received an additional breathing exercise for opera singers, progressive muscle relaxation, and guided imagery with a music therapist. The program was introduced in a group setting, lasting 45 - 60 minutes. The size of the group was usually 4 - 6 patients. The patients participated only once preoperatively (fig 1). The session started with 5 - 10 minutes of deep breathing exercises without music. The therapist demonstrated the activity, followed by the participant's active involvement. The deep diaphragmatic breathing exercise was supported by silent ambient music with slow-paced and gentle melody line movement, which induced relaxation. The duration of progressive muscle relaxation was 15 - 20 minutes. Exercises based on contracting different muscle groups and their intentional relaxation were conducted using the previously acquired proper diaphragmatic breathing technique, where the voluntary contraction of muscle was followed by breathing in, and the relaxation of the contracted muscle was followed by breathing out. The last activity of the session included guided imagery and music, which lasted 10 minutes. The essence of the exercise was that music encourages emotional response. While actively listening to music and focusing on the emotions evoked by the music, participants are instructed in guided imagery, which involves the creation of mental images. It can be, for example, imagining happy event from the future that they were eagerly anticipating or a happy memory from the past that left a strong impression on them.

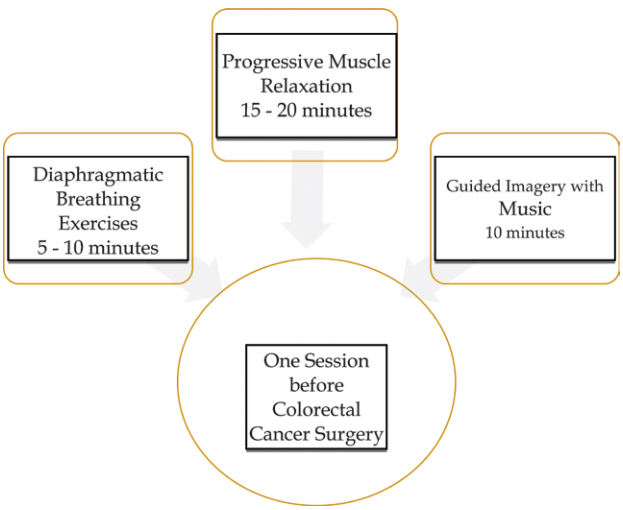

Fig 1. The breathing exercise protocol

Postoperative recovery protocol

Hospital for Tumors of Sestre milosrdnice University Hospital Center is an elective cancer hospital with an onco-anesthesia practice. Our intensive care unit (ICU) is, in fact, ICU and post-intensive care in one space. The idea is to have more focused pain management in the first 72 hours postoperative, plus nutritional support and early mobilization in one area. After that, patients were transferred to the Department of Oncologic Surgery, where they stayed 4 - 6 days before discharge. The patients were transferred to the Department of Oncologic Surgery if they were hemodynamically stable and had peristalsis.

Outcome measurement

The primary outcome measurement was the total length of hospital stay (LOS) and LOS in the ICU. The secondary endpoint was the incidence of postoperative complications 30 days and one year after surgery. Data on readmission to the emer-

Table 1.

Baseline characteristics

		Breathing exercises			
		no breathing exercises (control group)		breathing exercises (experimental group)	
		n	(%)	n	(%)
Sex	men	150	(57.7)	23	(74.2)
	women	110	(42.3)	8	(25.8)
Age groups	<60	76	(29.2)	11	(35.5)
	61-70	90	(34.6)	12	(38.7)
	70+	94	(36.2)	8	(25.8)
NSR2002	3	125	(57.6)	20	(76.9)
	4	86	(39.6)	5	(19.2)
	5	6	(2.8)	1	(3.8)
Clavien-Dindo classification of 30 days complication	I	39	(56.5)	8	(80)
	II	18	(26.1)	1	(10)
	IIIa	1	(1.5)	0	0
	IIIb	17	(24.6)	1	(10)
	IVa	1	(1.5)	0	0
	IVb	0	0	0	0
	V	3	(4.3)	0	0
Calvien-Dindo classification of 365 days complication	I	64	(60.4)	14	(93.3)
	II	19	(17.9)	0	0
	IIIa	0	0	0	0
	IIIb	19	(17.9)	1	(6.7)
	IVa	0	0	0	O
	IVb	0	0	0	0
	V	4	(3.8)	0	0
BMI (kg/m2)	underweight (<=18.50)	5	(2.3)	1	(3.8)
	normal (18.51-24.99)	79	(36.4)	10	(38.5)
	overweight (25.00-29.99)	87	(40.1)	11	(42.3)
	obese (>=30.00)	46	(21.2)	4	(15.4)
Tumor localization	Right colon	54	(20.8)	2	(6.5)
	Left colon	69	(26.5)	7	(22.6)
	Rectum	137	(52.7)	22	(71.0)
Operative procedure	Right hemicolectomy	54	(20.8)	1	(3.2)
	Left hemicolectomy	17	(6.6)	4	(12.9)
	Low anterior resection of rectum	119	(45.9)	13	(41.9)
	Transanal excision	5	(1.9)	3	(9.7)
	Segmental resection	45	(17.4)	5	(16.1)
	Abdominoperineal extirpation of the rectum	12	(4.6)	4	(12.9)
	Subtotal colectomy	3	(1.2)	1	(3.2)
	Hartmann	3	(1.2)		
	Other	1	(.4)		
Tumor size	T1	20	(8.2)	3	(10.0)
	T2	53	(21.7)	9	(30.0)
	T3	159	(65.2)	15	(50.0)
	T4	12	(4.9)	3	(10.0)
Lymphovascular invasion	no	189	(75.0)	25	(83.3)
	yes	63	(25.0)	5	(16.7)
Perineural invasion	0	200	(80.0)	25	(83.3)
	1	49	(19.6)	5	(16.7)
	2	1	(.4)		

gency department 30 days after surgery was obtained from participants' electronic medical records.

Statistical methods

Data were analyzed using SPSS software (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Descriptive statistics were used to describe the basic features of the sample in a study (proportions for categorical data, M and SD for continuous variables). Binary or categorical outcome variables were analyzed with the Chi-square test or Fisher's exact test (alternative to the chi-square for 2x2 contingency tables). Univariate and multivariate binary logistic regression was used to determine independent outcome predictors (prolonged ICU and hospital ward stay, complications, and whether patients finished their chemotherapy protocol).

RESULTS

Data were collected for a total of 291 patients. We included 31 patients in the rehabilitation group with breathing exercises for opera singers and 260 patients in the control group. Patients' baseline characteristics are presented in Table 1. We perform the data extraction in January and February 2022.

The two groups (control and experimental) did not differ in the initial demographic or tumor-related characteristics (all p>0.05; Table 1, respectively. In Fig 2, we presented data of prolonged ICU stay for rehabilitation and the control group.

Binary logistic regression was calculated for BMI, age, sex, and NSR as predictors of outcomes.

For patients enrolled in experimental breathing protocol, a statistically significant predictor for prolonged ICU stay was NSR-i.e., patients with NSR 5 had 12 times higher chances for prolonged ICU stay (OR=12.236, p=0.030, CI:1.283-116.722). In addition, a lower BMI for 1 unit shortens the ward stay by 9% (OR=0.912, p=0.010, CI:0.850-0.978), and the patient's age adds to the risk of complications by 4.2% within a year of surgery (OR=1.042, p=0.019, CI:1.007-0.079).

For the control group, a lower BMI by 1 unit also contributed to shorter ward stays by 9% (OR=0.917, p=0.010, CI:0.852-0.998). In addition, patients' age adversely affected outcomes within a year of surgery by 4.3% (OR=1.043, p=0.019, CI:1.005-0.081) for both patients of the experimental and control group male sex was a predictor of potential to fulfill the treatment protocol by 4.2% (OR=4.259, p=0.014, CI:1.337-13.566) and 4.5% (OR=4.473, p=0.014, CI:1.331-15.025) respectively.

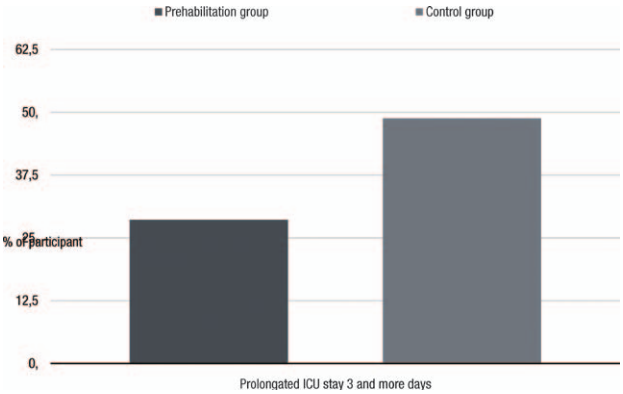

Fig 2. Data of prolongated ICU stay for rehabilitation and control group

DISCUSSION

In this clinical trial, opera singers' breathing exercises reduce prolonged ICU stay (χ 2 =4.132, df=1, p=0.047). There was no effect on prolonged ward stay and complications 30 and 365 days after surgery. Also, patients with lower BMI had shorter ward stays of 9% (p=0.010, CI:1.005-0.081). The binary regression analysis showed that patients with an NRS-2002 score of 5, with higher BMI and advanced age, would benefit most from the suggested respiratory prehabilitation protocol.

Surgery can significantly reduce patients' physiological and functional capacity and eligibility for adjuvant chemotherapy. The postoperative complications, occurring in up to 50% of patients, may prolong the ICU and hospital stay, increasing the morbidity and mortality rates and adding burden to already high healthcare costs. Therefore, a targeted prehabilitation program, standardized according to specific patients' needs, should be introduced into the treatment protocol(6,15). Medical nutrition, psychological support, and different exercise programs intending to strengthen functional capacity before surgery have gained particular attention for CRC patients(16). A multicentric randomized control trial including 441 patients recruited for upper abdominal surgery suggested

the remarkable effectiveness of breathing exercises in reducing postoperative pulmonary complications by 52%(17). Our data suggest CRC patients benefit from breathing exercises for opera singers as a prehabilitation modality, even with only one educational session, which increases the probability of compliance.

Prevention of postoperative pulmonary complications is relevant because they are strongly associated with increased morbidity and mortality and decreased quality of life. The most common postoperative pulmonary complications are pneumonia, atelectasis, embolization, acute respiratory distress syndrome, respiratory fatigue, and dysfunction in the chest wall or diaphragm(18). Also, standard preoperative medications like anesthetics, sedatives, opioids, neuromuscular blocking agents, and postoperative, even supine positions, affect the respiratory muscle subgroup(19). Postoperative pulmonary complications are reflected in the length of hospital stay and treatment costs (20). During surgery, general anesthesia, intraoperative mechanical ventilation and position, neuromuscular blockers, and surgical approach directly contribute to the pathophysiological effects on the respiratory system. These factors almost completely paralyze respiratory muscles with alert chest wall compliance and subsequently lower functional residual capacity(21). In the first week after abdominal surgery, lung volumes are significantly reduced(22). Also, the respiratory muscle demonstrated a significantly diminished capacity to generate force with maximal inspiratory pressure, and peak cough flows were reduced by 20 - 50% from preoperative measures(23). Respiratory muscle weakness is worst on the first postoperative day(24). The strength of these muscles improves slowly with small daily incremental strength grains. At discharge from the hospital, there is still a considerable weakness in the respiratory muscles compared to the preoperative status. Moreover, it normalizes approximately within a month after surgery(25,26).

A Swedish trial evaluated prophylactic chest physiotherapy's physiologic effects and clinical benefits in open major abdominal surgery. They included a total of 368 participants in the trial. The experimental group received chest physiotherapy, including breathing with pursed lips, huffing and coughing, and education about the importance of early mobilization. In conclusion, chest physiotherapy reduced postoperative pulmonary complications by 78% and improved oxygen saturation and mobilization after surgery. However, the low-risk population reduces the impact of this trial as well as the non-blinded accessor(27). A Pakistan trial evaluated the effect of preoperative counseling regarding postoperative mobilization and its impact on the reduction of postoperative pulmonary complications. The trial included 232 participants. There was no significant difference between age, duration of surgery, and pain after surgery. A significant difference was identified in the transfer from bed to chair and mobilization, which lasted less than 10 minutes(28). An Australian trial assessed a single preoperative physiotherapy session to reduce postoperative pulmonary complications after upper abdominal surgery. Four hundred forty-one patients were included in this trial. The intervention included 30 minutes of breathing exercises and education focused on postoperative pulmonary complication and their prevention through early ambulation and self-directed breathing exercises. The single 30-minute face-to-face treatment halved the incidence of postoperative pulmonary complications, including hospital-acquired pneumonia(29).

Our results are significant considering the existing evidence of reducing the length of intensive care unit stay for colorectal cancer patients who had preoperative respiratory muscle training *prehabilitation* by breathing exercises for opera singers provided by music therapists. Our study is the first to offer breathing exercises to opera singers and CRC patients undergoing curative surgery. Also, we included most types of colorectal cancers via the traditional full-length open incision approach. Given this, our retrospective study is representative of the heterogeneous population having elective colorectal cancer surgery.

Considering the standardization of postoperative length of hospital stays, the length of intensive care unit stay reduction might be partly due to the breathing exercise for opera singers as taught preoperatively. We cannot provide spirometry data to corroborate this as we did not measure breathing exercises' preoperative and postoperative cohort performance. We considered that measuring such performance would not reflect the pragmatic nature of the intervention.

We recommended a real-world evidence study with breathing exercises for opera singers,

which would be one of the possible modules for tailored patient prehabilitation. In such a protocol, each module should be standardized in content but adaptable to the patient's preferences and abilities. Another option is considering the effect gradients according to the experience levels of the therapist and the reproducibility of this intervention. Also, the applicability of preoperative education needs to be validated in other elective surgery settings, such as cardiac surgery or neurosurgery.

This trial's main limitation is the small number of patients in the prehabilitation program with breathing exercises for opera singers. Only 31 patients were included in our study, of 291 patients. The retrospective analysis is also a limiting factor, but similar baseline characteristics of the experimental and control groups add strength to statistical analysis and obtained results.

CONCLUSION

Our retrospective study provides evidence that single preoperative breathing exercises for opera singers reduce the length of intensive care unit stay. Our format of preoperative breathing exercise was a single 45-minute intervention with minimal or no potential harm.

These results may warrant the exploration of this module in most patients listed for elective major cancer abdominal surgery worldwide. It could be considered for all patients awaiting colorectal cancer surgery since there are no contraindications.

Article information

Author contribution: Brigita Vilč, Ljiljana Mayer and Iva Kirac – methodology; Tanja Režić Palaversa, Ljiljana Mayer and Maja Cigrovski Berković – formal analysis; Tanja Režić Palaversa and Milica Šostarić – investigation; Nikolina Šantek and Brigita Vilč – resources; Maja Cigrovski Berković - data curation; Nikolina Šantek and Anna Mrzljak – writing, original draft; Nikolina Šantek and Anna Mrzljak – writing, review and editing; Iva Kirac – visualisation; Maja Cigrovski Berković – supervision.

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Institutional board review statement: The study was approved by the Ethical comet of Sestre milosrdnice University Hospital Center, Zagreb, Croatia, study approval number: SP-9247/19-7.

Informed consent statement: Participants signed informed consent prior to recruitment.

Data availability statement:

Data sharing not applicable

No new data were created or analyzed in this study. Data sharing is not applicable to this article.

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Sažetak

JEDNOKRATNO PREOPERATIVNO VJEŽBANJA DISANJA MOŽE UTJECATI NA POSTOPERATIVNE ISHODE KOD OTVORENIH OPERACIJA RAKA DEBELOG CRIJEVA

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Uvod: Preoperativna prehabilitacija definirana je kao skup intervencija koje dovode do boljih ishoda liječenja. Prehabilitacijskim protokolima u kirurgiji karcinoma debelog crijeva nedostaje standardizacija. Retrospektivno smo analizirali učinak preoperativne vježbe disanja kao dodatne intervencije.

Cilj: Cilj je ovog istraživanja analizirati potencijalne prednosti vježbi disanja za operne pjevače na ishode liječenja nakon otvorene operacije kolorektalnog karcinoma.

Metode: Analizirali smo bazu podataka oboljelih od kolorektalnog karcinoma od siječnja 2019. do svibnja 2020. u centru za maligne bolesti, izdvajajući dob, spol, lokalizaciju tumora i komplikacije koje su zahtijevale medicinske ili kirurške intervencije u 30 dana postoperativnog razdoblja (stupnjevano prema Clavien-Dindo klasifikacija), te 365 dana nakon operacije i završetka kemoterapijskog protokola. Zatim smo odvojili postojeći prehabilitacijski protokol (prehrambena intervencija s komercijalno dostupnom farmakonutricijom na temelju rezultata NRS-2002; tri puta tjedno aerobne vježbe uključujući 30 minuta vožnje biciklom ili ciljanu udaljenost hodanja od 5000 ili 10000 koraka na temelju individualnih kapaciteta počevši od najmanje dva tjedna prije operacije), iz eksperimentalnog protokola (vježbe disanja za operne pjevače sa sesijom opuštanja uz glazbenu terapiju). Krajnje točke bile su kratkoročne i dugoročne komplikacije, trajanje boravka u jedinici intenzivnog liječenja te hospitalizacije i završetak kemoterapije.

Rezultati: Uključili smo 291 bolesnika s kolorektalnim karcinomom, 173 muškarca i 118 žena, prosječne dobi 66 godina; od kojih je 31 (10,7%) završilo eksperimentalnu protokolarnu vježbu disanja za operne pjevače. Pacijenti kontrolne i eksperimentalne skupine imali su usporedive demografske karakteristike i karakteristike povezane s tumorom na početku. Eksperimentalni protokol disanja bio je povezan s kraćim trajanjem boravka u JIL-u (χ 2 =4,132, df=1, p=0,047). Međutim, to nije utjecalo na ostale parametre (duljina boravka na odjelu, kratkoročne i dugotrajne komplikacije te sposobnost ispunjavanja protokola liječenja). Binarna regresijska analiza pokazala je da bi pacijenti s NRS-2002 rezultatom 5, s višim BMI i starijom dobi, imali najviše koristi od predloženog protokola respiratorne prehabilitacije.

Zaključak: Dodatak vježbi disanja mogao bi biti od koristi pacijentima s kolorektalnim karcinomom u vidu smanjenjem vremena provedenog u JIL-u i postoperativnih respiratornih komplikacija. Opet, ovo treba testirati u većoj kohorti.

KLJUČNE RIJEČI: *prehabilitacija; karcinom debelog crijeva; ishodi; prognoza; vježbe disanja*