




Compliance with the ERAS Protocol and 3-Year Survival After Laparoscopic Surgery for Non-metastatic Colorectal Cancer

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Abstract

Introduction Enhanced recovery after surgery (ERAS) pathways have been proven to enhance postoperative recovery, reduce morbidity, and reduce length of hospital stay after colorectal cancer surgery. However, despite the benefits of the ERAS program on short-term results, little is known about its impact on long-term results.

Objective The aim of the study was to determine the association between adherence to the ERAS protocol and long-term survival after laparoscopic colorectal resection for non-metastatic cancer.

Material and Methodology Between 2013 and 2016, 350 patients underwent laparoscopic colorectal cancer resection in the 2nd Department of General Surgery, Jagiellonian University Medical College, and were enrolled for further analysis. The relationship between the rate of compliance with the ERAS protocol and 3-year survival was analyzed according to the Kaplan–Meier method with log-rank tests. Patients were divided into two groups according to their degree of adherence to the ERAS interventions: Group 1 (109 patients), < 80% adherence, and Group 2 (241 patients), ≥ 80% adherence. The primary outcome was overall 3-year survival. The secondary outcomes were postoperative complications, length of hospital stay, and recovery parameters.

Results The groups were similar in terms of demographics and surgical parameters. The median compliance to ERAS interventions was 85.2%. The Cox proportional model showed that AJCC III (HR 3.28, 95% CI 1.61–6.59, $p = 0.0021$), postoperative complications (HR 2.63, 95% CI 1.19–5.52, $p = 0.0161$), and compliance with ERAS protocol < 80% (HR 3.38, 95% CI 2.23–5.21, $p = 0.0102$) were independent predictors for poor prognosis. Additionally, analysis revealed that adherence to the ERAS protocol in Group 2 with ≥ 80% adherence was associated with a significantly shorter length of hospital stay (6 vs. 4 days, $p < 0.0001$), a lower rate of postoperative complications (44.7% vs. 23.3%, $p < 0.0001$), and improved functional recovery parameters: tolerance of oral diet (53.4% vs. 81.5%, $p < 0.0001$) and mobilization (77.7% vs. 96.1%, $p < 0.0001$) on the first postoperative day.

Conclusions and Relevance This study reports an association between adherence to the ERAS protocol and long-term survival after laparoscopic colorectal resection for non-metastatic cancer. Lower adherence to the protocol, independent from stage of cancer and postoperative complications, was an independent risk factors for poorer survival rates.

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Introduction

Many studies have shown that the enhanced recovery after surgery (ERAS) protocol accelerates convalescence, reduces complications, and shortens hospital stay after colorectal cancer surgery [1–3]. It also reduces the rate of complications and delayed recovery in patients with traditional risk factors (demographic parameters and stage of the disease) [4, 5]. Other research has reported that prolonged hospital stay and complications are associated with a lower level of compliance with some ERAS protocol elements that are mostly under the control of the care giver, such as fluid balance, preoperative carbohydrate loading, or surgical technique [6–9]. The use of catheters, drains, and obviously the development of postoperative complications also prolong hospital stay. Several previous studies have shown that compliance with the ERAS protocol is strongly correlated with short-term outcomes, such as postoperative complications, readmission rate, and shortened length of hospital stay [10–13]. An increase in compliance to the ERAS protocol from high to very high/complete has also been associated with further improvement in short-term outcomes [14]. This is important because large data suggest that postoperative complications may not only have an impact in the short term, but may also affect long-term life expectancy [15]. Two published studies, one in elective orthopedic surgery and another following elective open colorectal cancer surgery, reported that the introduction of ERAS principles was associated with improved long-term survival [11, 16]. The reasons for this association is unknown. The aim of this study was to analyze whether the level of adherence with the ERAS protocol had any impact on long-term survival after laparoscopic colorectal resection for cancer.

Material and methods

A prospective observation was undertaken with post hoc analysis of consecutive colorectal cancer patients operated between 2013 and 2016. ERAS protocol was introduced in 2013 as a standard protocol for perioperative care in our department. Each patient is initially planned for laparoscopy, and an open-surgery approach is performed mainly in the case of conversion or when an extended multivisceral resection is required. Follow-up was conducted based on oncology visits, imaging studies, and CEA measurements carried out in accordance with recent oncological guidelines. Follow-up controls are carried out every 3–6 months for the first 2 years, and thereafter every 6 months for the next 3 years according to European society for medical oncology (ESMO) guidelines [17]. The

exact date of death of patients who passed away was established using information from the national personal identification number database (PESEL).

Inclusion and exclusion criteria

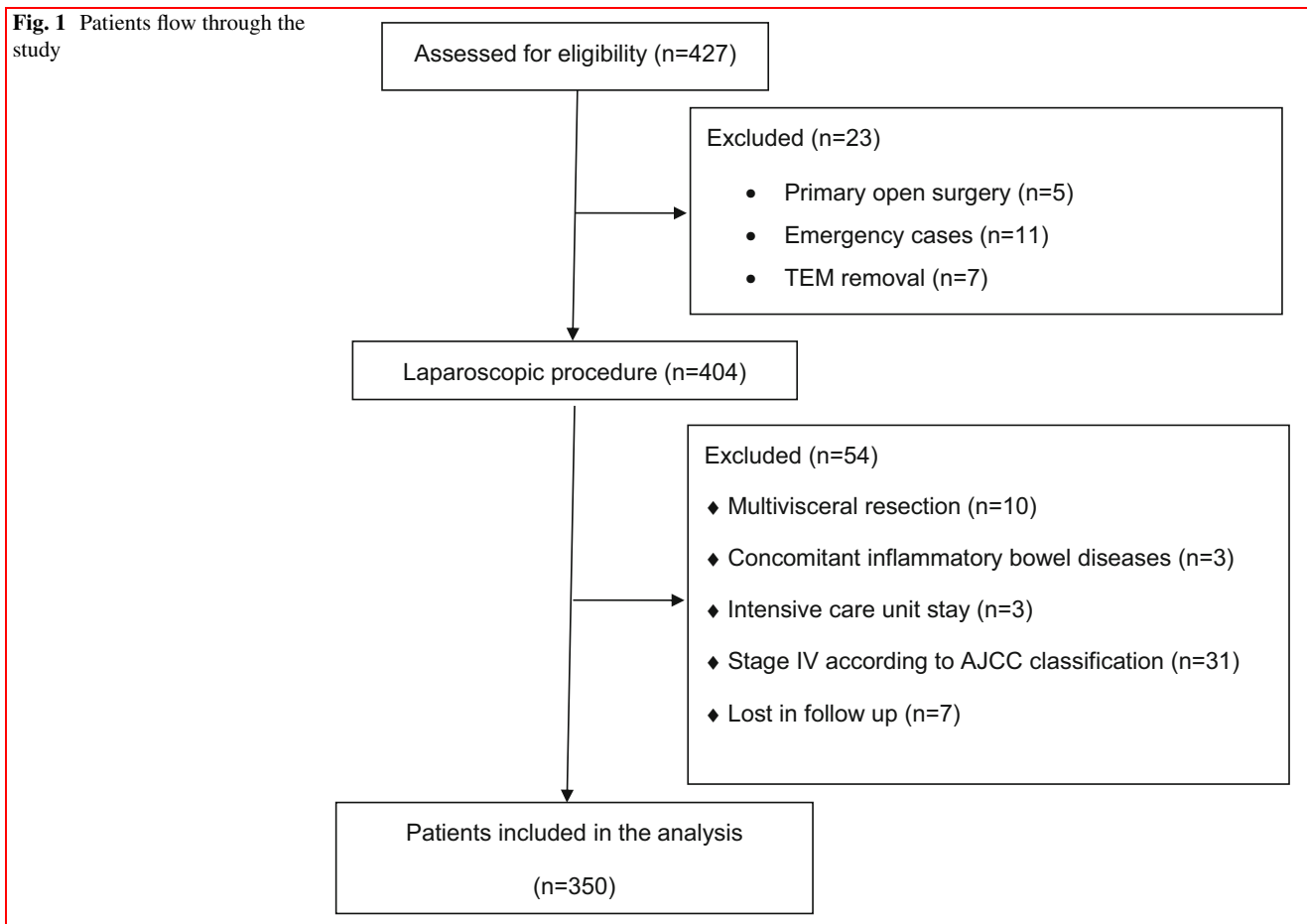
Inclusion criteria were age over 18 years, histopathologically confirmed adenocarcinoma of colon or rectum, initial laparoscopic approach, and patients with at least 12 months of follow-up. Exclusion criteria were emergency or initially open surgery, transanal endoscopic microsurgery (TEM), concomitant inflammatory bowel diseases, and patients with stage IV cancer according to the AJCC classification. Figure 1 shows the patients' flow through the study. In all patients, the 16-item ERAS protocol was applied (Table 1). Mean compliance with ERAS protocol elements in entire group was 85.2%.

Operative technique

Following anesthesia, patients were placed in the low lithotomy position. After creating pneumoperitoneum (12 mm Hg), 4–6 trocars (5–12 mm) were inserted depending on the type of resection. A standard 10-mm 30° laparoscope camera was used together with a set of Olympus laparoscopic hand instruments. The procedure consisted of medial-to-lateral laparoscopic mobilization of the segment of the colon followed by dissection of the bowel together with blood vessels and the accompanying mesocolon and lymph nodes. In the case of rectal carcinoma, concomitant total mesorectal excision and defunctioning loop ileostomy were performed. For vessel sealing, we used either Ethicon Harmonic ACE®, Olympus THUNDERBEAT® or Covidien LigaSure® (according to the surgeon's preference). Greater vessels were clipped with titanium clips. The specimen was extracted via transverse minilaparotomy, which was protected with Applied Medical Alexis Wound Protector®. The continuity of the bowel was restored using a circular stapler (left hemicolectomy, sigmoid resection, rectal resection) or with extracorporeal or intracorporeal side-to-side anastomosis (right hemicolectomy). Neither nasogastric tubes nor drains were used routinely. Finally, bilateral *transversus abdominis* plane block (TAP block) under ultrasound guidance was used at the end of the surgery (20 mL of 0.25% bupivacaine solution on each side).

Outcome measures

The patients were divided into two groups depending on the level of compliance with ERAS protocol (above or below 80% compliance). Compliance was assessed similarly to Gustafsson et al. [11], including elements that were primarily decided by the staff and delivered before and

Fig. 1 Patients flow through the study**Table 1** ERAS protocol used in our department

1. Preoperative counselling and patient's education
2. No bowel preparation (oral bowel preparation in the case of low rectal resection with TME and defunctioning loop ileostomy) plus oral neomycin 3 × 4 g and Metronidazole 3 × 500 mg on the day before surgery)
3. Preoperative carbohydrate loading (400 ml of Nutricia preOp[®] 2 h prior surgery)
4. Antithrombotic prophylaxis (Clexane[®] 40 mg sc. starting in the evening prior surgery)
5. Antibiotic prophylaxis (preoperative cefuroxime 1,5 g + metronidazole 0,5 g iv 30–60 min. prior surgery)
6. Laparoscopic surgery
7. Balanced intravenous fluid therapy (< 2500 mL intravenous fluids during the day of surgery, less than 150 mmol sodium)
8. No nasogastric tubes postoperatively
9. No drains left routinely for colonic resections, one drain placed for < 24 h in case of TME
10. TAP block and standard anesthesia protocol
11. Urinary catheter removal on the first postoperative day
12. Prevention of postoperative nausea and vomiting (PONV) (dexamethasone 8 mg iv., ondansetron 8 mg iv., metoclopramide 10 mg iv.)
13. Postoperative oxygenation therapy (4–6 l/min.)
14. Early oral feeding (oral nutritional supplement 4 h postoperatively—Nutricia Nutridrink[®] or Nestlé Impact[®], light hospital diet and oral nutritional supplements on the first postoperative day, full hospital diet in the second postoperative day)
15. Avoiding opioids, multimodal analgesia (oral when possible—paracetamol 4 × 1 g, ibuprofen 2 × 200 mg, metamizole 2 × 500 mg, or ketoprofen 2 × 100 mg)
16. Full mobilization on the first postoperative day (getting out of bed, going to toilette, walking along the corridor, at least 4 h out of bed)

Compliance was calculated from elements 1–13 (items of which implementation was depending on the medical staff). Elements 14–16 are convalescence parameters

during the day of surgery. It was calculated as the number of interventions fulfilled/13*100% (total number of pre-operative, intra and early postoperative interventions). These elements were chosen because their use was mainly dependent on the medical staff. Postoperative compliance is also influenced by the previous treatments and can, to a large extent, be regarded as outcomes. For this reason, they were not included in the calculation.

The primary outcome was overall 3-year survival. The secondary outcomes were postoperative complications, length of hospital stay and recovery parameters.

Statistical analysis

All data were analyzed with Statsoft STATISTICA v.13 (StatSoft Inc., Tulsa, OK, USA). The results are presented as mean \pm standard deviation (SD), median and interquartile range (IQR), and hazard ratio (HR) with 95% confidence intervals (CI) when appropriate. The study of categorical variables used the Chi-square test of independence. The Shapiro–Wilk test was used to check for normal distribution of data, and Student's *t* test was used for normally distributed quantitative data. For non-normally distributed quantitative variables, the Mann–Whitney *U* test was used. For the purposes of further analysis, the entire group of patients was divided into subgroups depending on compliance with the ERAS protocol ($< 80\%$ and $\geq 80\%$). This was the target compliance with the ERAS protocol in our department [18]. Survival data were analyzed according to the Kaplan–Meier method. The log-rank test was used to detect differences between groups. Univariate and multivariate analysis was performed using Cox proportional hazards. The variables from $p < 0.05$ have been included in the model. Results were considered statistically significant when the *p* value was found to be less than 0.05.

Ethical approval

The study was approved by the local ethics review committee (approval number 1072.6120.225.2017). All procedures have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Results

Characteristics of the study group

During the study period, 427 patients with colorectal cancer were treated in our department. Figure 1 shows the patients' flow through the study and the reasons for

exclusion. In total, 350 patients were enrolled for further analysis (181 males, 169 females). The mean age was 64.4 years (19–94 years). The demographic analysis of the group is shown in Table 2.

Group 1 included 109 patients and Group 2 included 241 patients. There were no statistically significant differences between groups for the demographic parameters sex, age, BMI, ASA scale, and comorbidities. The groups were also comparable in terms of location and characteristics of their tumor/s (Table 2).

A subgroup analysis demonstrated that $> 80\%$ compliance with ERAS protocol was associated with better survival among patients with colorectal cancer (Fig. 2). The median time of follow-up was 35 months (mean 35.6 months, range 12–60 months). Three patients died within 30 days after surgery in ICU care, because of respiratory failure in two cases (as a result of pneumonia) and anastomotic leakage in one case.

A univariate analysis of overall survival (Table 3) showed that age ≥ 65 years (HR 3.33, 95% CI 1.32–8.23, $p = 0.0037$), ASA scale III–IV (HR 3.92, 95% CI 1.91–7.74, $p = 0.0006$), cardiovascular disease (HR 3.28, 95% CI 1.52–7.44, $p = 0.0009$), renal disease (HR 2.96, 95% CI 1.13–7.74, $p = 0.0269$), AJCC stage III (HR 2.86, 95% CI 1.44–5.81, $p = 0.0031$), postoperative complications (HR 2.46, 95% CI 1.22–4.76, $p = 0.0133$), and $< 80\%$ compliance with the ERAS protocol (HR 4.51, 95% CI 3.29–21.21, $p = 0.0018$) were predictors for poor prognosis.

The Cox proportional model showed that only AJCC III (HR 3.28, 95% CI 1.61–6.59, $p = 0.0021$), postoperative complications (HR 2.63, 95% CI 1.19–5.52, $p = 0.0161$), and $< 80\%$ compliance with ERAS protocol (HR 3.38, 95% CI 2.23–5.21, $p = 0.0102$) were independent predictors for poor prognosis and shorter survival.

According to the Kaplan–Meier curves, 3-year overall survival was 88% in Group 2 and 76% in Group 1. The risk of death 3 years after surgery was lowered by 56%, HR 0.44 (0.21–0.91) in Group 2 compared to Group 1.

There were statistically significant differences in short-term outcomes between groups. There were more complications in Group 1 compared to Group 2 (44% vs. 23.2%, $p < 0.0001$), without a difference in severity according to the Clavien–Dindo classification ($p = 0.6277$). Median length of stay (LOS) was significantly lower in Group 2 (6 vs. 4 days, $p < 0.0001$). Readmission rate was comparable in both groups (9.2% vs. 9.1%, $p = 0.9999$), respectively. Functional recovery was also improved with better compliance. Both tolerance of an oral diet on the first postoperative day (53.2% vs. 81.3%, $p < 0.0001$) and mobilization of a patient on the day of surgery (78% vs. 96.3%, $p < 0.0001$) was better in Group 2. The percentage of patients who did not require administration of opioid

Table 2 Demographic analysis of patient groups

| Parameter | Group 1 < 80% | Group 2 ≥ 80% | <i>p</i> value |
|--|---------------|---------------|----------------|
| Number of patients, <i>n</i> | 109 | 241 | – |
| Females, <i>n</i> (%) | 54 (49.5%) | 113 (46.9%) | 0.6454 |
| Males, <i>n</i> (%) | 55 (50.5%) | 128 (53.1%) | |
| Mean age, years ± SD | 64.9 ± 14.3 | 63.8 ± 13.9 | 0.3291 |
| BMI, kg/m ² ± SD | 26.1 ± 4.2 | 26.7 ± 5.2 | 0.3405 |
| ASA 1, <i>n</i> (%) | 6 (5.5%) | 9 (3.7%) | 0.5739 |
| ASA 2, <i>n</i> (%) | 61 (56%) | 153 (63.6%) | |
| ASA 3, <i>n</i> (%) | 39 (35.8%) | 74 (30.7%) | |
| ASA 4, <i>n</i> (%) | 3 (2.7%) | 5 (2%) | |
| Any comorbidity, <i>n</i> (%) | 75 (68.8%) | 158 (65.6%) | 0.5510 |
| Cardiovascular, <i>n</i> (%) | 40 (36.7%) | 81 (33.6%) | 0.5739 |
| Hypertension, <i>n</i> (%) | 53 (48.6%) | 119 (49.4%) | 0.8961 |
| Diabetes, <i>n</i> (%) | 23 (21.1%) | 38 (15.8%) | 0.2232 |
| Pulmonary disease, <i>n</i> (%) | 11 (10.1%) | 20 (8.3%) | 0.5846 |
| Renal disease, <i>n</i> (%) | 8 (7.3%) | 14 (5.8%) | 0.5849 |
| Formation of stoma | 23 (21.1%) | 66 (27.4%) | 0.2112 |
| Median operative time, min. (IQR) | 180 (140–240) | 190 (160–230) | 0.7148 |
| Median intraoperative blood loss, mL (IQR) | 100 (50–100) | 100 (50–150) | 0.7797 |
| Conversion, <i>n</i> (%) | 5 (4.6%) | 7 (2.9%) | 0.4231 |
| Need for blood transfusion, <i>n</i> (%) | 9 (8.3%) | 21 (8.7%) | 0.8876 |
| Colon, <i>n</i> (%) | 71 (65.1%) | 155 (64.3%) | 0.8816 |
| Rectum, <i>n</i> (%) | 38 (34.9%) | 86 (35.7%) | |
| Neoadjuvant treatment, <i>n</i> (%) | 19 (17.4%) | 59 (24.5%) | 0.1422 |
| Adjuvant chemotherapy, <i>n</i> (%) | 37 (33.9%) | 62 (25.7%) | 0.1139 |
| AJCC stage I, <i>n</i> (%) | 40 (36.7%) | 101 (41.9%) | 0.6425 |
| AJCC stage II, <i>n</i> (%) | 36 (33.0%) | 75 (31.1%) | |
| AJCC stage III, <i>n</i> (%) | 33 (30.3%) | 65 (27.0%) | |
| Tumor grade G1, <i>n</i> (%) | 11 (16.0%) | 27 (17.1%) | 0.5287 |
| Tumor grade G2, <i>n</i> (%) | 49 (71.0%) | 118 (74.7%) | |
| Tumor grade G3, <i>n</i> (%) | 9 (13.0%) | 13 (8.2%) | |

drugs was not statistically significant between groups (51.4% vs. 40.2%, $p = 0.052$). Short-term outcomes are presented in Table 4.

Discussion

The novel finding in this study is that compliance with the ERAS protocol was an independent predictor of improved 3-year survival after laparoscopic colorectal resections. The 3-year risk of death was more than three times higher in patients with compliance < 80%. In addition, other well-known predictors of poorer survival rates also influenced survival, including postoperative complications and stage III of colorectal cancer. There were no differences in study groups in terms of baseline demographic

characteristics, ASA score and stage of cancer, nor for the use adjuvant chemotherapy.

ERAS protocols in elective colorectal surgery have been widely accepted, and the evidence behind the benefits and safety of ERAS has repeatedly been shown [11, 18, 19]. The adoption of ERAS principles is increasing due to significantly better short-term outcomes, but less is known about what ERAS can bring to long-term outcomes. Large database studies have shown an association between postoperative complications and reduced long-term survival after major surgery [15]. Similar findings were recently reported for open colorectal cancer surgery in ERAS-managed care [11, 15]: Improved compliance with the ERAS protocol was associated with the improved short-term benefits of fewer postoperative complications, which in turn was associated with a 42% reduction in 5-year

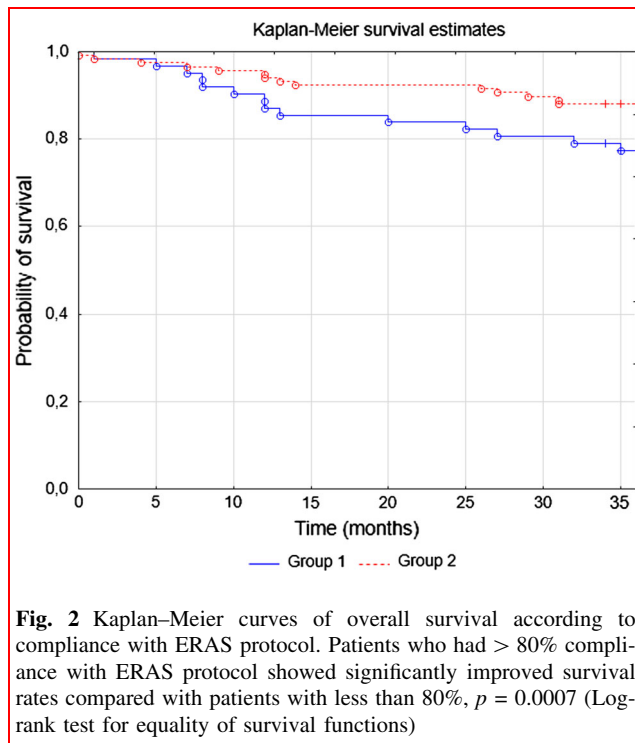


Fig. 2 Kaplan–Meier curves of overall survival according to compliance with ERAS protocol. Patients who had > 80% compliance with ERAS protocol showed significantly improved survival rates compared with patients with less than 80%, $p = 0.0007$ (Log-rank test for equality of survival functions)

mortality. Our study is one of the first focusing on patients operated only with laparoscopic technique. This allowed us to achieve a homogenous group of patients.

There are several potential explanations why better compliance with ERAS protocols contributed to improved survival. Firstly, it has been shown that improved adherence to the protocol leads to not only shorter recovery but

also lowers postoperative complication rates [14]. This was also the case in the present study, as were return of key functions which resulted in shorter length of postoperative stay. Previous studies have confirmed that the occurrence of postoperative complications has a great impact on long-term outcomes [15, 20]. This could be the result of either delayed adjuvant treatment or no adjuvant treatment at all in complicated cases. An analysis of Merkow et al. showed that only 70% of uncomplicated stage III cancer patients receive postoperative chemotherapy, and this rate drops dramatically when major postoperative complications occur [21]. This factor, together with prolonged length of stay and readmission, has been also confirmed by Malietzis in a meta-analysis of 15 studies [22]. Moreover, Tevis et al. observed that even though adjuvant treatment is administered within the window of opportunity, patients suffering from postoperative complications still had a poorer prognosis [23]. Other factors than the delay in starting postoperative chemotherapy may also contribute to postoperative survival. Less stress during uncomplicated surgery may improve the function of the immune system, and this in turn may enhance the resistance to relapsing cancer and manage any remaining cancer cells [24]. In the present study, both adherence to ERAS protocol and development complications were independent risk factors for the multivariate analyses, which suggest they both contribute to the outcomes. Our results are in line with Gustafsson et al. who confirmed the association between increased adherence to the ERAS protocol and improved colorectal cancer-specific 5-year survival. It seems that our

Table 3 Univariate analysis of overall survival

| Parameter | HR (95% CI) | <i>p</i> value |
|---|-------------------|----------------|
| Sex (female vs. male) | 0.87 (0.42–1.81) | 0.7411 |
| Age (< 65 vs. ≥ 65 years) | 3.33 (1.32–8.23) | 0.0037 |
| BMI (< 25 vs. ≥ 25 kg/2) | 1.44 (0.69–2.99) | 0.3264 |
| ASA scale (I–II vs. III–IV) | 3.92 (1.91–7.74) | 0.0006 |
| Neoadjuvant treatment (yes vs. no) | 0.32 (0.07–1.33) | 0.1184 |
| Cardiovascular disease (no vs. yes) | 3.28 (1.52–7.44) | 0.0009 |
| Hypertension (no vs. yes) | 1.16 (0.56–2.39) | 0.6826 |
| Diabetes (no vs. yes) | 1.55 (0.69–3.47) | 0.2907 |
| Pulmonary disease (no vs. yes) | 2.09 (0.86–5.13) | 0.1045 |
| Renal disease (no vs. yes) | 2.96 (1.13–7.74) | 0.0269 |
| Tumor location (rectum vs. colon) | 0.61 (0.13–2.91) | 0.5122 |
| AJCC (I–II vs. III) | 2.86 (1.44–5.81) | 0.0031 |
| Time of the surgery (< 200 vs. > 200 min.) | 2.02 (0.97–4.99) | 0.0501 |
| Intraoperative blood loss (< 200 vs. > 200 mL) | 1.11 (0.42–2.687) | 0.8491 |
| Postoperative complications (no vs. yes) | 2.46 (1.22–4.76) | 0.0133 |
| Compliance with ERAS protocol (≥ 80% vs. < 80%) | 4.51 (3.29–21.21) | 0.0018 |

Table 4 Short-term outcomes in analyzed groups

| Parameter | Group 1 < 80% | Group 2 ≥ 80% | <i>p</i> value |
|---|---------------|---------------|----------------|
| Tolerating oral diet on the first postoperative day, <i>n</i> (%) | 58 (53.2%) | 196 (81.3%) | < 0.0001 |
| Mobilization on the first postoperative day, <i>n</i> (%) | 85 (78.0%) | 232 (96.3%) | < 0.0001 |
| No postoperative use of opioids, <i>n</i> (%) | 56 (51.4%) | 97 (40.2%) | 0.0520 |
| Time to first flatus, days ± SD | 2.32 ± 1.53 | 1.90 ± 2.05 | 0.0040 |
| Patients without complications, <i>n</i> (%) | 61 (56.0%) | 185 (76.8%) | < 0.0001 |
| Patients with complications, <i>n</i> (%) | 48 (44.0%) | 56 (23.2%) | |
| Clavien–Dindo 1, <i>n</i> (%) | 22 (45.8%) | 25 (44.6%) | 0.6277 |
| Clavien–Dindo 2, <i>n</i> (%) | 9 (18.8%) | 16 (28.6%) | |
| Clavien–Dindo 3, <i>n</i> (%) | 12 (25.0%) | 11 (19.6%) | |
| Clavien–Dindo 4, <i>n</i> (%) | 4 (8.3%) | 2 (3.6%) | |
| Clavien–Dindo 5, <i>n</i> (%) | 1 (2.1%) | 2 (3.6%) | |
| Mean length of hospital stay, days ± SD | 8.11 ± 8.23 | 5.48 ± 6.76 | < 0.0001 |
| Median length of hospital stay, days (IQR) | 6 (4–8) | 4 (3–6) | |
| Readmission, <i>n</i> (%) | 10 (9.2%) | 22 (9.1%) | 0.9999 |

results are comparable when looking at their Kaplan–Meier survival estimates, although we set different cutoff values of adherence (70% vs. 80%).

We also confirmed that better compliance to the ERAS protocol results in better short-term results. This not only shortens LOS and enhances convalescence, but also reduces the morbidity rates. This has been previously studied elsewhere [6, 11, 14, 18]. Subsequently, an extensive systematic review by Messenger et al. of 34 studies containing 10,861 laparoscopic resections identified protocol compliance as the most frequently reported and most influential predictive factor for outcomes of ERAS perioperative care following laparoscopic colorectal resection [25].

A key mechanism of ERAS protocols improving postoperative outcomes is stress minimization and the reduction in insulin resistance [26–28]. ERAS impacts immune function by minimizing the inflammatory responses, and this may affect long-term survival after cancer surgery. A better-preserved immune competence, which includes specific HLA-DR immune response, might protect against potential consequences of dissemination of cancer cells and in consequence distant metastases [29–31]. Minimally invasive techniques also reduce this aspect of the stress response [32–34]. Moreover, the philosophy of ERAS involved many aspects of perioperative care. It is believed and often shown that its success lays rather in the aggregation of marginal gains and multimodal approach rather than in one particular element [14, 35].

There are limitations of our study. To assess survival, we used the national personal identification number database (PESEL) which allows for determination of the date of death but does not provide information on cancer-specific death. The compliance of ERAS protocol in our group was not equal throughout the whole study and was

lower at the early stages [10, 14]. Additionally, we lack detailed data of the adjuvant treatment because a significant proportion of patients were treated outside our oncology department, and therefore, we were not able to confirm which chemotherapy had been administered. We also decided to include 13 elements rather than all 16 for compliance analysis. The way we studied compliance was to investigate the adherence to items that are subject to staff decisions (pre- and intraoperatively), leaving aside postoperative elements that depend on compliance levels in the earlier phases as was shown in our results and reported elsewhere (11, should also be available in most other short-term studies).. This way of compliance calculations has been previously used in other studies[11]. All our patients are actively encouraged to get out of bed, start eating and drinking (meaning that in terms of implementation of these items we would get 100% compliance to these items). However, not all of them are getting out of bed and tolerating oral diet in part due to poor compliance in the earlier phases.

Conclusions

This study reports an association between adherence to the ERAS[®] Society Guidelines and long-term survival after laparoscopic colorectal resection for non-metastatic cancer. Lower adherence to the protocol, together with stage of cancer and postoperative complications, was an independent risk factor for poorer 3-year survival rates. Due to the lack of data about disease-specific survival and type of adjuvant treatment, our study requires confirmation via other similar analyses. Nevertheless, the findings suggest

that ERAS brings benefits in oncologic surgery beyond the early postoperative period.

Author contribution MP contributed to study conception and design, acquisition of data, analysis and interpretation of data, statistical analyses, drafting of manuscript, and critical revision of manuscript. GT and NG contributed to acquisition of data, analysis and interpretation of data, statistical analyses, and drafting of manuscript. MR, PM, and MW contributed to acquisition of data and analysis and interpretation of data. AB helped in study conception and design and critical revision of manuscript. OL analyzed and interpreted the data and critically revised the manuscript. MP contributed to study conception and design, and drafting and critical revision of the manuscript.

Compliance with ethical standards

Conflict of interest OL is the co-founder and acting Executive Chairman of the ERAS Society (www.erassociety.org). The remaining authors declare no conflict of interest.

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