

Total Risk Points Predict Short- and Long-term Outcomes Following Colorectal Cancer Resection in Older Patients

SHINTARO HASHIMOTO^{1,2}, KAZUO TO¹, HIDEO WADA¹, YUKA SAKAKIBARA¹, KEISUKE OZEKI¹, MICHIIKO KOMAKI¹ and MASAMICHI KONDO¹

¹Department of Surgery, National Hospital Organization Ureshino Medical Center, Ureshino, Japan;

²Department of Surgical Oncology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Abstract. *Background/Aim:* Estimation of physiological ability and surgical stress (E-PASS) is reported to be useful as a predictor of postoperative complications and poor long-term survival after colorectal cancer. The total risk points (TRP) system is a simplified scoring system of E-PASS, and this study evaluated the utility of TRP in colorectal cancer resection in older patients. *Patients and Methods:* The clinicopathological data of 237 patients who underwent curative resection for colorectal cancer from 2015 to 2020 were analyzed retrospectively. The data were compared between a high TRP group ($\geq 1,000$, $n=38$) and a low TRP group ($< 1,000$, $n=199$). We also conducted an analysis to determine risk factors of postoperative complications and poor long-term survival. *Results:* TRP showed statistically significant correlations with the comprehensive risk score (CRS) of E-PASS ($R=0.999$, $p<0.001$). The high TRP group experienced postoperative complications (Clavien-Dindo grade ≥ 2) more frequently (42.1% vs. 11.1%, $p<0.001$). Multivariate analysis showed that high TRP [odds ratio (OR)=5.214; 95% confidence interval (95%CI)=2.338-11.629; $p<0.001$] and age ≥ 80

(OR=2.760; 95%CI=1.308-5.826; $p=0.008$) were independent predictors of postoperative complications. Overall survival (OS) was poor in the high TRP group (5-year OS, 61.2% vs. 82.6%, $p<0.001$) compared with the low TRP group, and in the low prognostic nutritional index (<45) group (5-year OS, 70.9% vs. 86.3%, $p=0.013$) compared with the high prognostic nutritional index (≥ 45) group. Multivariate analysis showed that high TRP [hazard ratio (HR)=3.202; 95%CI=1.324-7.745; $p=0.010$] was an independent prognostic factor for poor OS. *Conclusion:* Patients aged ≥ 80 years should be closely monitored regarding postoperative complications. Reducing TRP to less than 1,000 is important to reduce postoperative complications and improve OS.

The number of older patients with colorectal cancer (CRC) is increasing because of prolonged life expectancy, with physicians treating more patients at the extremes of age (1). Although surgical resection is necessary for the standard treatment of CRC, older patients have more frequent comorbidities, such as cardiovascular disease and respiratory dysfunction (2), and show higher postoperative morbidity and mortality compared with younger patients (3-5).

Previously, various scoring systems were generalized for CRC surgery in older patients. Among them, a scoring system, estimation of physiologic ability and surgical stress (E-PASS) (6) was reported to be a predictor of postoperative complications (3, 7, 8) and long-term outcomes (9) after surgery for CRC in older patients. In E-PASS, the comprehensive risk score (CRS) was calculated from the preoperative risk score (PRS), including perioperative patient condition factors, and the surgical stress score (SSS), including surgical condition factors (7). To simplify the scoring of E-PASS, the total risk points (TRP) system was established (6, 10); requires the same parameters as E-PASS, and is calculated by the addition of the points. Although TRP was reported to be related to the occurrence of anastomotic leakage in digestive surgery and mortality after anastomotic leakage (11), its usefulness as a predictor of postoperative complications and long-term outcomes in older CRC patients was not fully assessed.

Correspondence to: Shintaro Hashimoto, Department of Surgery, National Hospital Organization Ureshino Medical Center, 4561-2 Shimojūkukou, Ureshino machi, Ureshino city, Saga 843-0301, Japan, and Department of Surgical Oncology, Nagasaki University Graduate School of Biomedical Sciences, 1-12-4 Sakamoto, Nagasaki 852-8523, Japan. Tel: +81 954420659, Fax: +81 954422452, e-mail: s.hash12@outlook.jp

Key Words: Colorectal cancer, total risk point, E-PASS, elderly patients.

©2022 International Institute of Anticancer Research
www.iiar-anticancer.org



This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY-NC-ND) 4.0 international license (<https://creativecommons.org/licenses/by-nc-nd/4.0>).

Table I. Estimation of physiologic ability and surgical stress (E-PASS) scoring system.

1. $PRS = -0.0686 + 0.00345 X_1 + 0.323 X_2 + 0.205 X_3 + 0.153 X_4 + 0.148 X_5 + 0.0666 X_6$
 X_1 : age; X_2 : presence (1) or absence (0) of severe heart disease; X_3 : presence (1) or absence (0) of severe pulmonary disease;
 X_4 : presence (1) or absence (0) of diabetes mellitus; X_5 : performance status index (0-4); X_6 : American Society of Anesthesiologists physiological status classification (1-5).
 Severe heart disease is defined as heart failure of New York Heart Association class III or IV, or severe arrhythmia requiring mechanical support. Severe pulmonary disease is defined as any condition with a % vital capacity (%VC) less than 60% and/or a forced expiratory volume in 1 s (FEV1.0%) less than 50%. Diabetes mellitus is defined according to the World Health Organization criteria. Performance status index is defined by the Japanese Society for Cancer Therapy.

2. $SSS = -0.342 + 0.0139 X_1 + 0.0392 X_2 + 0.352 X_3$
 X_1 : blood loss/body weight (g/kg); X_2 : operation time (h); X_3 : extent of skin incision (0, minor incision for laparoscopic or thoracoscopic surgery including scope-assisted surgery; 1, laparotomy or thoracotomy alone; 2, both laparotomy and thoracotomy).

3. $CRS = -0.328 + 0.936 (PRS) + 0.976 (SSS)$

Source: Haga *et al.* (10). PRS: Preoperative risk score; SSS: surgical stress score; CRS: comprehensive risk score.

In this study, we aimed to review clinical data of CRC in older patients and to evaluate the risk factors of postoperative complications and poor long-term outcomes after surgery for CRC in older patients, with special reference to TRP.

Patients and Methods

A retrospective review of the medical records of consecutive patients who underwent primary curative tumor resection for CRC from January 2015 to December 2020 at National Hospital Organization Ureshino Medical Center was performed. Patients who underwent emergency surgery, Stage IV patients, and patients who underwent surgery without tumor resection were excluded. Only adenocarcinomas were included. Finally, 237 patients were included in this analysis. This retrospective study was approved by the institutional review board of our hospital, and informed consent was waived. The admission number was 21-09.

We reviewed and recorded the following data: age, sex, body mass index (BMI), The American Society of Anesthesiologists Physical Status (ASA-PS), and Onodera’s prognostic nutritional index (PNI) (12). We evaluated the E-PASS scoring system (6). E-PASS score was calculated on the basis of the preoperative risk score (PRS) (including age, severe heart disease, severe pulmonary disease, diabetes mellitus, performance status index, and ASA-PS), the surgical stress score (SSS) (including the ratio of blood loss to body weight, operation time, and extent of skin incision), and the comprehensive risk score (CRS) determined by PRS and SSS (Table I). TRPs were calculated as previously reported (11) and are shown in Table II. TRP was created to simplify the calculation of CRS and can be calculated by adding the same nine variables as CRS (11). We also reviewed the type of surgery, degree of extensive lymph node dissection, tumor location, operative time, bleeding, pathological T stage, pathological N stage, postoperative complications, length of postoperative hospital stay, and survival time.

Curative resection was defined as macroscopically complete resection without invasion of the surgical margins at histological examination. The tumor stage was classified according to TNM classification (13). Tumor location was classified as colon (cecum to sigmoid colon) and rectum. Postoperative complications were

Table II. Total risk points (TRP).

Factors	
1. Age	×3
2. Presence of severe heart disease	+300
3. Presence of severe pulmonary disease	+190
4. Presence of diabetes mellitus	+140
5. Performance status (0-4)	×140
6. ASA class (1-5)	×60
7. Blood loss (g)/body weight (kg)	×14
8. Operative time (h)	×40
9. Extent of skin excision (0-2)	×340
TRP	Points

TRP is computed by the sum of 1-9 points. Criteria for factors 2, 3, 4, 5, and 9 are the same as those of the E-PASS scoring system (10, 11).

defined as complications that occurred within 30 days of the primary surgery. Patients with Clavien–Dindo grade 2 or higher complications were included in the complication group (14). Postoperative mortality was defined as death within 30 days after the surgery or any later death that was considered to be a direct consequence of a postoperative complication.

We compared the clinicopathological characteristics between patients with and without postoperative complications. The data was also compared between patients with high TRP and low TRP. We performed univariate and multivariate analyses to identify risk factors of postoperative complications and poor survival outcomes. Statistical analysis was performed using Bell Curve for Excel software, version 2.02 (Social Survey Research Information Co., Ltd., Tokyo, Japan). Correlations between different continuous variables were quantified by Pearson’s correlation coefficient (R), the significance of which was determined by Fisher’s z-test. A two-sided *p*-value of <0.05 was considered statistically significant. We used 240 min (15) and 200 ml (16) as cutoffs of operative time and intraoperative blood loss, respectively. We used 1,000 as the cutoff of TRP (11) and 45 for PNI (17) according to previous reports.

Continuous variables were expressed as the median and range. Categorical data were expressed as the number (frequency, %).

Continuous data were compared using Student's *t*-test, and categorical data were compared using Fisher's exact test or the chi-squared test, as appropriate. Overall survival (OS) was evaluated to determine survival outcome. OS was defined as the interval from surgery to death or the last follow-up and calculated according to the Kaplan–Meier method.

The risk factors that determined the complications were investigated by univariate and multivariate analyses. All variables related to the risk of complications with a *p*-value of <0.05 on univariate analysis were included in the multivariate analysis. Multivariate logistic regression models were then constructed to examine the effects of the significant perioperative variables on the odds of each complication. All *p*-values of <0.05 were considered significant.

To identify the independent risk factors for poor OS, multivariate analysis using a Cox hazards model was performed. All variables related to the risk of OS with a *p*-value of <0.05 on univariate analysis were included in the multivariate analysis. All *p*-values of <0.05 were considered statistically significant.

Results

Table III shows the clinicopathological and surgical characteristics of 237 patients. The study population included 151 male (63.7%) and 86 female (37.3%) patients, with a median age of 76 years (range=65-96 years). The median BMI was 21.8 (range=13.3-37.6). Among these patients, 20 patients (8.4%) had a poor performance status (ASA-PS ≥ 3). Most patients had colon cancer ($n=178$, 75.1%). Laparoscopic surgery was performed in 213 patients (89.9%) and open surgery was performed in 24 patients (10.1%). Extensive lymph node dissection was performed in 192 patients (81.0%). Histopathologically, 2 patients (0.8%) were diagnosed as Tis, 38 patients (16.0%) were diagnosed as T1, 35 patients (14.8%) were T2, 130 patients (54.9%) were T3, and 32 patients (13.5%) were T4. Pathological lymph node metastases were positive in 88 patients (37.1%). This cohort experienced 38 (16.0%) complications including 11 cases (4.6%) of anastomotic leakage, 6 cases (2.5%) of prolonged ileus, 5 cases (2.1%) of pneumonia, 4 cases (1.7%) of wound infection, 2 cases (0.8%) of intraabdominal abscess, and 10 cases (4.2%) of other complications. The median length of postoperative hospital stay was 16.0 days (range=7.0-162.0 days). There were no cases of 30-day mortality.

Figure 1 shows a scatter plot of TRP and CRS. We found statistically significant correlations between TRP and CRS ($R=0.999$, $p<0.001$).

Table IV shows the clinical differences between patients with and without postoperative complications. Age ≥ 80 years (60.5% vs. 32.7%, $p=0.002$) and TRP $\geq 1,000$ (42.1% vs. 11.1%, $p<0.001$) were higher in patients who experienced postoperative complications. There were no significant differences in sex, BMI, ASA-PS, PNI, surgical approach, rate of extensive lymph node dissection, tumor location, blood loss, operative time, pathological T status, and pathological N status.

Table III. Clinicopathological characteristics of the patients.

Age	76 (65-96)
Sex, male	151 (63.7%)
BMI (kg/m ²)	21.8 (13.3-37.6)
ASA-PS	
1	17 (7.2%)
2	200 (84.4%)
3	20 (8.4%)
4	0 (0.0%)
PNI	44.6 (19.1-65.0)
TRP	329.5-1,752.9 (689.2)
PRS	0.452 (0.222-1.234)
SSS	-0.167 (-0.300-0.929)
CRS	-0.023 (-0.382-1.022)
Approach	
Open	24 (10.1%)
Laparoscopic	213 (89.9%)
Extent lymph node dissection	192 (81.0%)
Tumor location	
Colon	178 (75.1%)
Rectum	59 (24.9%)
Bleeding (ml)	20 (0-2,640)
Operative time (min)	247 (99-681)
Pathological T stage	
Tis	2 (0.8%)
T1	38 (16.0%)
T2	35 (14.8%)
T3	130 (54.9%)
T4	32 (13.5%)
Pathological N stage	
(+)	88 (37.1%)
(-)	149 (62.9%)
Postoperative complications (CD grade ≥ 2)	38 (16.0%)
Anastomotic leakage	11 (4.6%)
Intraabdominal abscess	2 (0.8%)
Prolonged ileus	6 (2.5%)
Pneumonia	5 (2.1%)
Heart failure	0 (0.0%)
Wound infection	4 (1.7%)
Others	10 (4.2%)
Length postoperative hospital stay (days)	16 (7-162)

BMI: Body mass index; ASA-PS: The American Society of Anesthesiologists Physical Status; PNI: prognostic nutritional index; TRP: total risk points; PRS: preoperative risk score; SSS: surgical stress score; CRS: comprehensive risk score; CD: Clavien–Dindo.

Table V shows the clinical differences between the low (<1,000) and high ($\geq 1,000$) TRP groups. In the high TRP group, age (80.0 years vs. 75.0 years, $p=0.007$) and rate of poor ASA-PS (≥ 3) (21.1% vs. 6.0%, $p=0.006$) were significantly higher and BMI (20.0 vs. 22.1, $p=0.020$) and PNI (37.7 vs. 45.7, $p<0.001$) were significantly lower than in the low TRP group. Open surgery was performed more frequently in the high TRP group (36.8% vs. 5.0%, $p<0.001$). Blood loss was greater (170 ml vs. 10 ml, $p<0.001$) and operative time was longer (324 min vs. 240 min, $p<0.001$) in the high TRP group. The high TRP group

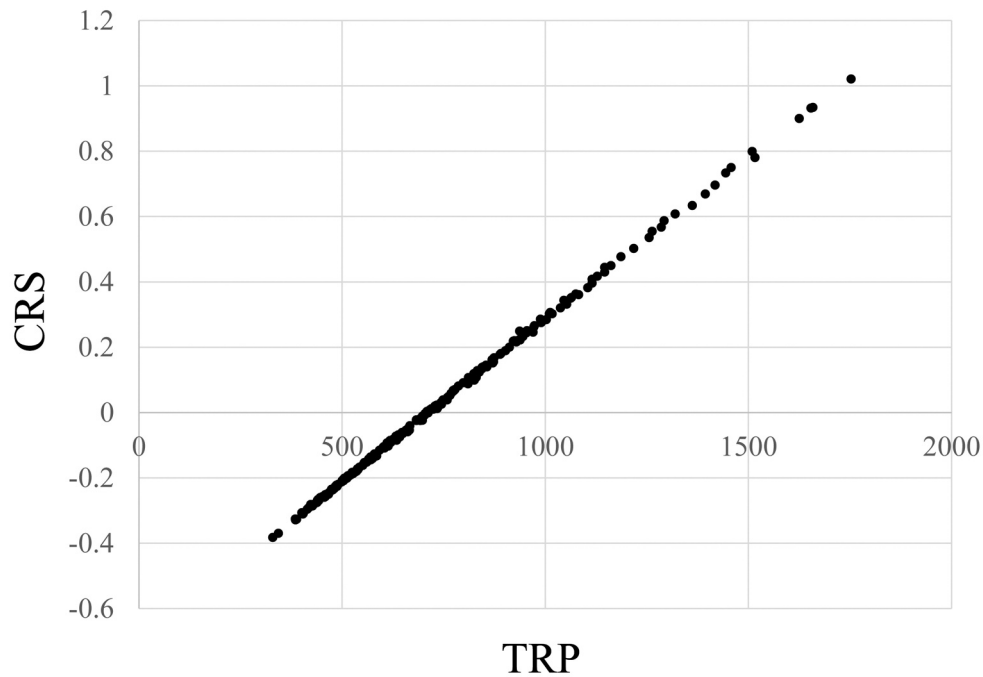


Figure 1. A scatter plot of total risk points (TRP) and the comprehensive risk score (CRS).

experienced postoperative complications ($CD \geq 2$) more frequently (42.1% vs. 11.1%, $p < 0.001$). Regarding specific complications, anastomotic leakage (18.4% vs. 2.0%, $p < 0.001$), pneumonia (7.9% vs. 2.0%, $p = 0.030$), and wound infection (2.6% vs. 1.5%, $p = 0.030$) were more frequent in the high TRP group. Length of postoperative hospital stay was longer in high TRP patients (36 days vs. 15 days, $p = 0.001$). Clinical factors, including sex, tumor location, rate of extent of lymph node dissection, rate of pathological T3 and T4, and rate of pathological lymph node metastases were not significantly different between the groups.

Table VI shows the results of univariate and multivariate analyses of risk factors for postoperative complications. High TRP ($p < 0.001$) and age ≥ 80 years ($p = 0.002$) were significantly associated with complications on univariate analysis. Multivariate analysis showed that high TRP (OR=5.214; 95%CI=2.338-11.629; $p < 0.001$) and age ≥ 80 years (OR=2.760; 95%CI=1.308-5.826; $p = 0.008$) were independent prognostic factors for postoperative complications in older patients with CRC.

Among the 237 patients, the median follow-up period was 30.3 months (range=0.6-72.2 months). The 1-, 3-, and 5-year cumulative OS rates were 94.9%, 90.5%, and 79.2%, respectively. OS was poor in the high TRP group (5-year cumulative OS, 61.2% vs. 82.6%, $p < 0.001$; Figure 2) and low PNI (<45) group (5-year cumulative OS, 70.9% vs. 86.3%, $p = 0.013$; Figure 3). Table VII shows the results of

univariate and multivariate analyses of risk factors for poor OS. Multivariate analysis showed that high TRP (HR=3.202; 95%CI=1.324-7.745; $p = 0.010$) was an independent prognostic factor for poor OS.

Discussion

The results from our retrospective study showed that high TRP was associated with increased postoperative complications and poor survival prognosis after curative resection for CRC in older patients.

Typically, older patients often have comorbidities including cardiovascular disease, respiratory disease, renal dysfunction, and liver dysfunction, which lead to higher risk for surgery (3-5). Previous studies showed the frequency of postoperative complications in older patients (3). Furthermore, postoperative complications are associated with poor oncological outcomes and survival after CRC resection in older patients (18, 19). To predict the occurrence of postoperative complications and long-term outcome in older CRC patients, various scoring parameters including PNI (20-22), neutrophile-lymphocyte ratio (NLR) (23), and Glasgow prognostic score (mGPS) (24, 25) were analyzed. The E-PASS system was also reported to be a predictor of postoperative complications (3, 7, 8) and poor survival outcome (9) after surgery in older CRC patients.

Table IV. Comparison of clinical characteristics between colorectal cancer patients with and without postoperative complications.

	Clavien–Dindo grade ≥2 (n=38)	Clavien–Dindo grade <2 (n=199)	p-Value
Age			0.002
≥80	23 (60.5%)	65 (32.7%)	
<80	15 (39.5%)	134 (67.3%)	
Sex			0.360
Male	27 (71.1%)	124 (62.3%)	
Female	11 (28.9%)	75 (37.7%)	
BMI (kg/m ²)			0.264
≥18.5	28 (73.7%)	163 (81.9%)	
<18.5	10 (26.3%)	36 (18.1%)	
ASA-PS			0.538
<3	34 (89.5%)	183 (92.0%)	
≥3	4 (10.5%)	16 (8.0%)	
PNI			0.111
<45	25 (65.8%)	101 (50.8%)	
≥45	13 (34.2%)	98 (49.2%)	
TRP			<0.001
≥1,000	16 (42.1%)	22 (11.1%)	
<1,000	22 (57.9%)	177 (88.9%)	
Approach			0.238
Open	6 (15.8%)	18 (9.0%)	
Laparoscopic	32 (84.2%)	181 (91.0%)	
Extent lymph node dissection			0.659
Yes	32 (84.2%)	160 (80.0%)	
No	6 (15.8%)	39 (20.0%)	
Tumor location			>0.999
Colon	29 (76.3%)	149 (74.9%)	
Rectum	9 (23.7%)	50 (25.1%)	
Blood loss (ml)			0.109
≥200	8 (21.1%)	22 (11.1%)	
<200	30 (78.9%)	177 (88.9%)	
Operative time (min)			0.212
≥240	25 (65.8%)	106 (53.3%)	
<240	13 (34.2%)	93 (46.7%)	
Pathological T status			0.851
T1-2	13 (34.2%)	64 (32.2%)	
T3-4	25 (65.8%)	135 (67.8%)	
Pathological N status			0.855
(+)	15 (39.5%)	73 (36.7%)	
(-)	23 (60.5%)	126 (63.3%)	

BMI: Body mass index; ASA-PS: The American Society of Anesthesiologists Physical Status; PNI: prognostic nutritional index; TRP: total risk points.

In the E-PASS system, the CRS is calculated from the PRS that includes perioperative patient condition factors with the consideration of comorbidities, and the SSS that includes surgical condition factors (7). For older patients, the E-PASS system has advantages in the assessment of the presence of comorbidities and in the evaluation of surgical stress, which are extremely important in these patients (9), compared with other simply calculated scoring systems such as PNI, NLR, and mGPS.

Meanwhile, despite its utility, the E-PASS system requires calculators, as shown Table I. The TRP system was derived from the CRS of E-PASS to simplify the E-PASS system, and is calculated by addition of the points (6, 10). Compared with E-PASS, TRP is considered to be more convenient in clinical practice (10, 26). TRP requires 10 variables including the same preoperative comorbidities and surgical factors as those of E-PASS calculated just after surgery, and showed a high correlation with the CRS of E-PASS in our cohort (R=0.999, $p<0.001$), consistent with a previous report (10). Haga *et al.* reported the usefulness of TRP in predicting short-term outcomes after gastrointestinal surgery, including surgery for esophageal cancer, gastric cancer, cancer of the periampullary duodenum and biliary tract, pancreatic cancer, colorectal cancer, and others. The incidences of anastomotic leakage increased when TRP increased. Furthermore, an in-hospital mortality rate at TRP <1,000 was significantly lower than that at TRP of ≥1,000 (1.1 vs. 15.9%, $p<0.001$) (11). We set the cut-off point of TRP as 1,000 as previously reported (11), and TRP ≥1,000 and age ≥80 years were independent risk factors of postoperative complications in multivariate analysis. Regarding specific complications, pneumonia and wound infections were more frequent in patients with high TRP. Furthermore, as previously reported (11), anastomotic leakage was higher in high TRP patients.

Regarding long-term outcomes, in older patients with cancer, the outcomes were determined by not only tumor-related factors but by patient-related factors, such as inflammation, nutrition, and immune status (9). Yamamoto *et al.* reported that the CRS of E-PASS was significantly associated with poor OS and disease-specific survival (9) after surgery for CRC in older patients. Similarly, in this study, high TRP was related to poor OS despite a comparable pathological tumor stage. The high TRP group included more older patients with a poor ASA-PS (≥3). In surgical parameters, blood loss was greater, operative time was longer, and the rate of open surgery was higher in the high TRP group. These frailty and surgical stress factors could have influenced poor OS.

Although no nutritional status was directly included in the parameters calculated in TRP, BMI and PNI were significantly lower in the high TRP group. Our results showed that low PNI was also significantly associated with poor OS. Tominaga *et al.* reported similar poor survival outcomes in oldest-old CRC patients with low PNI (22). Possible explanations were hypoalbuminemia partially reflecting an immunosuppressed condition and weak systemic defense. Furthermore, the systemic inflammation response is an important regulator of tumor growth, invasion, and metastasis (22, 27).

Although postoperative complications were not a predictor of poor OS, high TRP patients experienced postoperative complications more frequently in this study. In older CRC patients, postoperative complications were reported to be a

Table V. Comparison of clinical characteristics between patients with TRP ($\geq 1,000$) and TRP $< 1,000$.

	TRP $\geq 1,000$ (n=38)	TRP $< 1,000$ (n=199)	p-Value
Age	80 (66-95)	75 (65-96)	0.007
Sex			0.855
Male	25 (65.8%)	126 (63.3%)	
Female	13 (34.2%)	73 (36.7%)	
BMI (kg/m ²)	20.0 (13.3-26.2)	22.1 (13.8-37.6)	0.020
ASA-PS			0.006
< 3	30 (78.9%)	187 (94.0%)	
≥ 3	8 (21.1%)	12 (6.0%)	
PNI	37.7 (19.1-53.9)	45.7 (24.5-65.0)	< 0.001
Approach			< 0.001
Open	14 (36.8%)	10 (5.0%)	
Laparoscopic	24 (63.2%)	189 (95.0%)	
Tumor location			0.156
Colon	25 (65.8%)	153 (76.9%)	
Rectum	13 (34.2%)	46 (23.1%)	
Extent lymph node dissection	27 (71.1%)	165 (82.9%)	0.112
Blood loss (ml)	170 (0-2,640)	10 (0-611)	< 0.001
Operative time (min)	324 (121-681)	240 (99-668)	< 0.001
Pathological T status			0.851
T1-2	11 (28.9%)	66 (33.2%)	
T3-4	27 (71.1%)	133 (66.8%)	
Pathological N status			0.855
(+)	18 (47.4%)	70 (35.2%)	
(-)	20 (52.6%)	129 (64.8%)	
Postoperative complication \geq CD2	16 (42.1%)	22 (11.1%)	< 0.001
Anastomotic leakage	7 (18.4%)	4 (2.0%)	< 0.001
Intraabdominal abscess	0 (0.0%)	2 (1.0%)	> 0.999
Prolonged ileus	2 (5.3%)	4 (4.0%)	0.247
Pneumonia	3 (7.9%)	2 (2.0%)	0.030
Heart failure	0 (0.0%)	0 (0.0%)	> 0.999
Wound infection	1 (2.6%)	3 (1.5%)	0.030
Others	3 (7.9%)	7 (3.5%)	0.150
Length postoperative hospital stay (days)	36 (11-165)	15 (7-125)	0.001

TRP: Total risk points; BMI: body mass index; ASA-PS: The American Society of Anesthesiologists Physical Status; PNI: prognostic nutritional index; CD: Clavien–Dindo.

predictor of poor OS (28), and prevention of postoperative complications is important for survival after surgery (18). From our result, decreasing TRP to less than 1,000 is important for reducing postoperative complications and improving OS. Other than patients' condition factors, choosing laparoscopic surgery, reducing blood loss, and shortening operative time can lead to a lower TRP. Meanwhile, surgeons should perform laparoscopic surgery considering the limitation that TRP includes no technical factors, especially when they do not possess extensive experience in their laparoscopic procedures (11).

Our study is the first to examine the relationship between short-and long-term outcomes and TRP in older CRC patients. However, our study has several limitations. First, this was a retrospective, single-center study. Second, there is no standard definition of older age. While we defined older patients as those aged ≥ 65 years in this study, a similar analysis should be

performed in more aged cohort because of the increasing life expectancy. Third, the selection of patients and surgical procedures depended on the patients, families, and surgeons.

In conclusion, high TRP ($\geq 1,000$) and age of 80 years and older were independent risk factors for postoperative complications after curative resection for CRC in older patients. High TRP is an independent prognostic factor for poor OS. TRP will be useful for surgical decision-making and pre- and postoperative informed consent. Reducing TRP to less than 1,000 is important to reduce postoperative complications and improve OS. Older patients with high TRP should be carefully monitored after surgery for CRC in short- and long-term follow-up periods.

Conflicts of Interest

The Authors have no conflicts of interest related to this study.

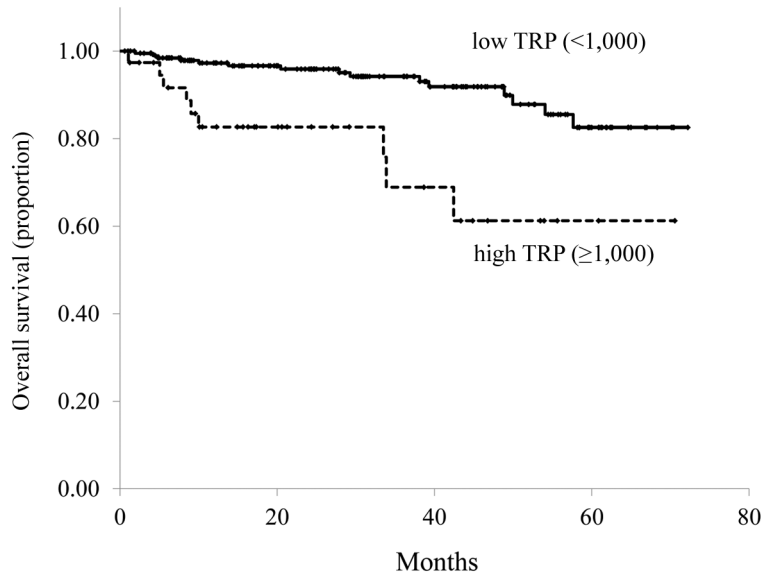


Figure 2. Comparison between the overall survival (OS) of patients with low total risk points (TRP) (TRP<1,000) and high TRP (TRP≥1,000).

Table VI. Univariate and multivariate analyses of short-term morbidity of the patients.

	Univariate analysis			Multivariate analysis		
	Odds ratio	95%CI	p-Value	Odds ratio	95%CI	p-Value
Male	1.484	0.696-3.166	0.306			
Age≥80	5.851	1.548-6.460	0.002	2.760	1.308-5.826	0.008
BMI<18.5	1.167	0.721-3.625	0.244			
ASA-PS≥3	1.346	0.424-4.272	0.615			
PNI<45	1.866	0.903-3.855	0.092			
TRP≥1,000	5.851	2.678-12.786	<0.001	5.214	2.338-11.629	<0.001
Surgical approach, open (vs. laparoscopic surgery)	1.885	0.695-5.112	0.213			
Tumor location, colon (vs. rectum)	1.018	0.479-2.439	0.851			
Blood loss (ml)≥200	2.146	0.875-5.261	0.095			
Operative time (min)≥240	1.687	0.817-3.486	0.158			
pT1-2	1.097	0.527-2.284	0.805			
pN(+)	1.126	0.553-2.293	0.744			

BMI: Body mass index; ASA-PS: The American Society of Anesthesiologists Physical Status; PNI: prognostic nutritional index; TRP: total risk points.

Authors’ Contributions

Shintaro Hashimoto was responsible for the study concept. Shintaro Hashimoto, Kazuo To, Hideo Wada, Yuka Sakakibara and Keisuke Ozeki performed the operation. Michihiko Komaki and Masamichi Kondo collaborated in the patient’s medical care. All Authors reviewed and approved the final article.

Acknowledgements

The Authors thank H. Nikki March, PhD, from Edanz (<https://jp.edanz.com/ac>) for editing a draft of this manuscript.

References

- Chan TY, Foo CC, Law WL and Lo O: Outcomes of colorectal cancer surgery in the nonagenarians: 20-year result from a tertiary center. *BMC Surg* 19(1): 155, 2019. PMID: 31660937. DOI: 10.1186/s12893-019-0623-4
- Sasaki M, Miyoshi N, Fujino S, Ogino T, Takahashi H, Uemura M, Matsuda C, Yamamoto H, Mizushima T, Mori M and Doki Y: The Geriatric Nutritional Risk Index predicts postoperative complications and prognosis in elderly patients with colorectal cancer after curative surgery. *Sci Rep* 10(1): 10744, 2020. PMID: 32612136. DOI: 10.1038/s41598-020-67285-y

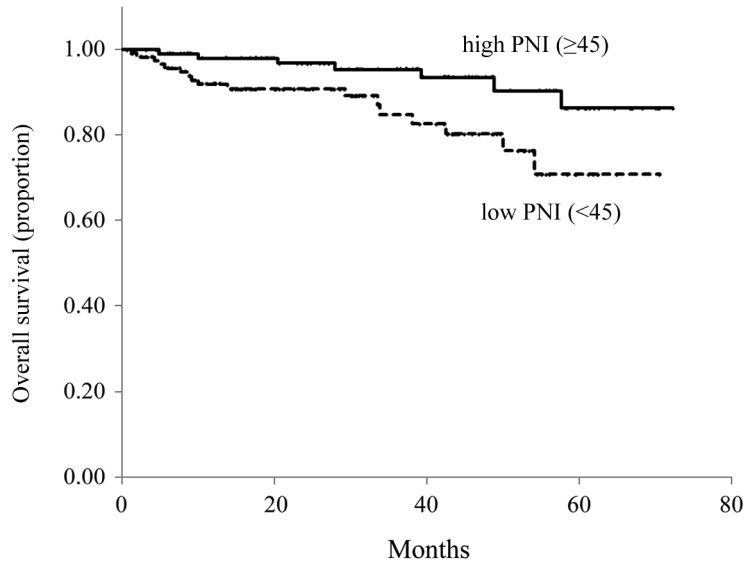


Figure 3. Comparison between the overall survival (OS) of the patients with low prognostic nutritional index (PNI) ($PNI < 45$) and high PNI ($PNI \geq 45$).

Table VII. Clinical factors predicting overall survival after curative resection for patients.

	Univariate analysis	Multivariate analysis		
	p-Value	HR	95%CI	p-Value
Male	0.878			
Age ≥ 80	0.879			
BMI < 18.5	0.159			
ASA-PS ≥ 3	0.825			
PNI < 45	0.013	2.151	0.838-5.512	0.111
TRP $\geq 1,000$	< 0.001	3.202	1.324-7.745	0.002
Surgical approach, open (vs. laparoscopic surgery)	0.236			
Tumor location, rectum (vs. colon)	0.458			
Blood loss (ml) ≥ 200	0.214			
Operative time (min) ≥ 240	0.335			
pT3-4	0.087			
pN(+)	0.320			
Postoperative complications (CD ≥ 2)	0.204			

BMI: Body mass index; ASA-PS: The American Society of Anesthesiologists Physical Status; PNI: prognostic nutritional index; TRP: total risk points; CD: Clavien–Dindo.

3 Inoue K, Ueno T, Akishige N, Soeta T, Tsuchiya T, Nakayama S, Shima K, Goto S, Takahashi M, Naitoh T and Naito H: What is the optimal risk scoring for predicting complications after colorectal surgery in elderly patients? *International Journal of Surgery Open 21*: 52-57, 2019. DOI: 10.1016/j.ijso.2019.11.007

4 Ahiko Y, Shida D, Horie T, Tanabe T, Takamizawa Y, Sakamoto R, Moritani K, Tsukamoto S and Kanemitsu Y: Controlling nutritional status (CONUT) score as a preoperative risk assessment index for older patients with colorectal cancer. *BMC Cancer 19(1)*: 946, 2019. PMID: 31690275. DOI: 10.1186/s12885-019-6218-8

5 Itatani Y, Kawada K and Sakai Y: Treatment of elderly patients with colorectal cancer. *Biomed Res Int 2018*: 2176056, 2018. PMID: 29713641. DOI: 10.1155/2018/2176056

6 Haga Y, Ikei S and Ogawa M: Estimation of Physiologic Ability and Surgical Stress (E-PASS) as a new prediction scoring system for postoperative morbidity and mortality following elective gastrointestinal surgery. *Surg Today 29(3)*: 219-225, 1999. PMID: 10192731. DOI: 10.1007/BF02483010

7 Tominaga T, Takeshita H, Takagi K, Kunizaki M, To K, Abo T, Hidaka S, Nanashima A, Nagayasu T and Sawai T: E-PASS

- score as a useful predictor of postoperative complications and mortality after colorectal surgery in elderly patients. *Int J Colorectal Dis* 31(2): 217-225, 2016. PMID: 26607908. DOI: 10.1007/s00384-015-2456-7
- 8 Kondo H, Hirano Y, Ishii T, Hara K, Obara N, Wang L, Asari M, Kato T and Yamaguchi S: E-PASS scoring system may be useful for prediction of postoperative complications in super elderly colorectal cancer surgery patients. *J Anus Rectum Colon* 4(3): 137-144, 2020. PMID: 32743116. DOI: 10.23922/jarc.2020-017
 - 9 Yamamoto M, Saito H, Uejima C, Tanio A, Tada Y, Matsunaga T, Sakamoto T, Honjo S, Ashida K and Fujiwara Y: Estimation of physiological ability and surgical stress score is a useful prognostic indicator for elderly patients with colorectal cancer. *Dig Surg* 37(2): 145-153, 2020. PMID: 30844817. DOI: 10.1159/000497455
 - 10 Haga Y, Wada Y, Takeuchi H, Kimura O, Furuya T, Sameshima H and Ishikawa M: Estimation of physiologic ability and surgical stress (E-PASS) for a surgical audit in elective digestive surgery. *Surgery* 135(6): 586-594, 2004. PMID: 15179364. DOI: 10.1016/j.surg.2003.11.012
 - 11 Haga Y, Wada Y, Takeuchi H, Ikejiri K and Ikenaga M: Prediction of anastomotic leak and its prognosis in digestive surgery. *World J Surg* 35(4): 716-722, 2011. PMID: 21184072. DOI: 10.1007/s00268-010-0922-5
 - 12 Onodera T, Goseki N and Kosaki G: [Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients]. *Nihon Geka Gakkai Zasshi* 85(9): 1001-1005, 1984. PMID: 6438478.
 - 13 Brierley JD and Gospodarowicz MK: TNM classification of malignant tumours. New York, John Wiley & Sons, 2017.
 - 14 Dindo D, Demartines N and Clavien PA: Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 240(2): 205-213, 2004. PMID: 15273542. DOI: 10.1097/01.sla.0000133083.54934.ae
 - 15 Chiappa A, Zbar AP, Bertani E, Biella F, Audisio RA and Staudacher C: Surgical outcomes for colorectal cancer patients including the elderly. *Hepatogastroenterology* 48(38): 440-444, 2001. PMID: 11379328.
 - 16 Okamura R, Hida K, Hasegawa S, Sakai Y, Hamada M, Yasui M, Hinoi T, Watanabe M and Japan Society of Laparoscopic Colorectal Surgery: Impact of intraoperative blood loss on morbidity and survival after radical surgery for colorectal cancer patients aged 80 years or older. *Int J Colorectal Dis* 31(2): 327-334, 2016. PMID: 26412248. DOI: 10.1007/s00384-015-2405-5
 - 17 Jian-Hui C, Iskandar EA, Cai ShI, Chen CQ, Wu H, Xu JB and He YL: Significance of Onodera's prognostic nutritional index in patients with colorectal cancer: a large cohort study in a single Chinese institution. *Tumour Biol* 37(3): 3277-3283, 2016. PMID: 26438061. DOI: 10.1007/s13277-015-4008-8
 - 18 Dekker JW, van den Broek CB, Bastiaannet E, van de Geest LG, Tollenaar RA and Liefers GJ: Importance of the first postoperative year in the prognosis of elderly colorectal cancer patients. *Ann Surg Oncol* 18(6): 1533-1539, 2011. PMID: 21445672. DOI: 10.1245/s10434-011-1671-x
 - 19 Duraes LC, Stocchi L, Steele SR, Kalady MF, Church JM, Gorgun E, Liska D, Kessler H, Lavryk OA and Delaney CP: The relationship between Clavien-Dindo morbidity classification and oncologic outcomes after colorectal cancer resection. *Ann Surg Oncol* 25(1): 188-196, 2018. PMID: 29116488. DOI: 10.1245/s10434-017-6142-6
 - 20 Mohri Y, Inoue Y, Tanaka K, Hiro J, Uchida K and Kusunoki M: Prognostic nutritional index predicts postoperative outcome in colorectal cancer. *World J Surg* 37(11): 2688-2692, 2013. PMID: 23884382. DOI: 10.1007/s00268-013-2156-9
 - 21 Tokunaga R, Sakamoto Y, Nakagawa S, Miyamoto Y, Yoshida N, Oki E, Watanabe M and Baba H: Prognostic Nutritional Index predicts severe complications, recurrence, and poor prognosis in patients with colorectal cancer undergoing primary tumor resection. *Dis Colon Rectum* 58(11): 1048-1057, 2015. PMID: 26445177. DOI: 10.1097/DCR.0000000000000458
 - 22 Tominaga T, Nonaka T, Hisanaga M, Fukuda A, Tanoue Y, Yoshimoto T, Hidaka S, Sawai T and Nagayasu T: Prognostic value of the preoperative prognostic nutritional index in oldest-old patients with colorectal cancer. *Surg Today* 50(5): 449-459, 2020. PMID: 31720800. DOI: 10.1007/s00595-019-01910-w
 - 23 Cook EJ, Walsh SR, Farooq N, Alberts JC, Justin TA and Keeling NJ: Post-operative neutrophil-lymphocyte ratio predicts complications following colorectal surgery. *Int J Surg* 5(1): 27-30, 2007. PMID: 17386911. DOI: 10.1016/j.ijsu.2006.05.013
 - 24 Moyes LH, Leitch EF, McKee RF, Anderson JH, Horgan PG and McMillan DC: Preoperative systemic inflammation predicts postoperative infectious complications in patients undergoing curative resection for colorectal cancer. *Br J Cancer* 100(8): 1236-1239, 2009. PMID: 19319134. DOI: 10.1038/sj.bjc.6604997
 - 25 Lu X, Guo W, Xu W, Zhang X, Shi Z, Zheng L and Zhao W: Prognostic value of the Glasgow prognostic score in colorectal cancer: a meta-analysis of 9,839 patients. *Cancer Manag Res* 11: 229-249, 2018. PMID: 30636896. DOI: 10.2147/CMAR.S185350
 - 26 Coelen RJ, Olthof PB, van Dieren S, Besselink MG, Busch OR and van Gulik TM: External validation of the estimation of physiologic ability and surgical stress (E-PASS) risk model to predict operative risk in perihilar cholangiocarcinoma. *JAMA Surg* 151(12): 1132-1138, 2016. PMID: 27579510. DOI: 10.1001/jamasurg.2016.2305
 - 27 Condeelis J and Pollard JW: Macrophages: obligate partners for tumor cell migration, invasion, and metastasis. *Cell* 124(2): 263-266, 2006. PMID: 16439202. DOI: 10.1016/j.cell.2006.01.007
 - 28 Weerink LBM, Gant CM, van Leeuwen BL, de Bock GH, Kouwenhoven EA and Faneyte IF: Long-term survival in octogenarians after surgical treatment for colorectal cancer: prevention of postoperative complications is key. *Ann Surg Oncol* 25(13): 3874-3882, 2018. PMID: 30244418. DOI: 10.1245/s10434-018-6766-1

Received January 14, 2022

Revised February 7, 2022

Accepted February 8, 2022