

Minimally Invasive Colectomy Contributes to Decreasing Postoperative Morbidity in Patients With High Naples Prognostic Score

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Abstract

Background/Aim: The Naples prognostic score (NPS), based on nutritional and inflammatory status, may predict postoperative morbidity after colorectal cancer surgery. Minimally invasive colectomy (MIC) may improve short-term outcomes; however, whether MIC lowers morbidity in patients with a high NPS remains unknown. The current study examined the effects of NPS on postoperative morbidity after open colectomy (OC) and MIC.

Patients and Methods: This retrospective analysis included 139 patients who underwent OC and 117 who underwent MIC for colorectal cancer between January 2013 and March 2020. The NPS is a composite score calculated using albumin and cholesterol concentrations, and lymphocyte: monocyte and neutrophil: lymphocyte ratios. Patients were divided into three groups based on NPS. Groups 1-2 were defined as low-NPS and group 3 as the high-NPS group. The OC and MIC groups were further divided into two subgroups according to whether the NPS was high or low.

Results: The high-NPS groups had significantly higher postoperative morbidity after OC [Clavien–Dindo classification (CDc) \geq II; $p=0.022$, CDc \geq IIIb; $p=0.036$]. Multivariate analysis demonstrated that high-NPS was an independent risk factor for postoperative complications (CDc \geq II: hazard ratio=2.40; 95% confidence interval=1.121-5.181; $p=0.024$ and CDc \geq IIIb: hazard ratio=4.19; 95% confidence interval=1.052-20.619; $p=0.042$). Low-NPS did not affect postoperative morbidity after MIC (CDc \geq II; $p=0.12$, CDc \geq IIIb; $p=0.51$).

Conclusion: A high NPS led to postoperative morbidity after OC, but not after MIC. MIC may improve short-term outcomes, even in patients with a low NPS.

Keywords: Colorectal cancer, Naples prognostic score, minimally invasive colectomy.



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Introduction

Colorectal cancer (CRC) is among the most prevalent cancers worldwide and its incidence is rapidly increasing (1). Many risk factors for morbidity after CRC surgery have been reported, including patient background and surgical factors (2, 3).

Recently, a comprehensive prognostic score, the Naples prognostic score (NPS), calculated from serum albumin and total cholesterol concentrations, the lymphocyte-to-monocyte ratio (LMR), and the neutrophil-to-lymphocyte ratio (NLR), has been reported to be a powerful prognostic index for CRC complications (4). A previous study reported that a high NPS was associated with postoperative morbidity after rectal cancer surgery (5). However, the impact on short-term outcomes of surgical strategies was not investigated.

Minimally invasive colectomy (MIC) is less invasive than open colectomy (OC) (6) and may improve short-term outcomes in patients with high NPS. Thus, the current study aimed to retrospectively evaluate the effects of the NPS on postoperative outcomes after OC and MIC.

Patients and Methods

Patients. This retrospective cohort study included 256 consecutive patients who underwent curative surgery for CRC at the Department of Surgery of the Miyazaki Prefectural Nobeoka Hospital between January 2013 and March 2020. The inclusion criteria were as follows: 1) pathologically-confirmed adenocarcinoma, 2) diagnosis of clinical stages I-III colorectal cancer, and 3) curative surgery. The exclusion criteria were as follows: 1) pathological stage IV disease and 2) missing data on clinicopathological characteristics. OC and MIC were performed in 139 and 117 patients, respectively. We further divided each OC and MIC group into two subgroups depending on whether the NPS was high or low. Short-term outcomes between patients with high- and low-NPS were compared in the OC and MIC groups using our institutional database. The ethics committee of our hospital approved the study procedure

Table 1. Calculation of Naples prognostic score (NPS).

Variable	Cut-off value	Points	NPS group
Serum albumin (mg/dl)	≥4	0	Group 1: 0 point
	<4	1	
Total cholesterol (mg/dl)	>180	0	Group 2: 1 or 2 points
	≤180	1	
NLR	≤2.96	0	Group 3: 3 or 4 points
	>2.96	1	
LMR	>4.44	0	
	≤4.44	1	

NLR: Neutrophil-to lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio.

and waived the requirement for written informed consent (Registry Number 20190830-3).

Naples prognostic score definitions. The NPS was defined based on the following four parameters: serum albumin level, total cholesterol level, LMR, and NLR. As previously reported by Galizia *et al.*, the cutoff values were 4 mg/dl for serum albumin, 180 mg/dl for total cholesterol, 2.96 for NLR, and 4.44 for LMR (4). Patients with serum albumin, total cholesterol or LMR lower than the thresholds got one point; otherwise, they got zero. Patients with an NLR higher than 2.96 got one point, while those with a lower NLR got zero. The sum of the scores for each parameter comprised the NPS score. Patients were categorized into three groups according to the NPS: patients with an NPS of 0 were assigned to group 1, patients with an NPS of 1 or 2 to group 2, and patients with an NPS of 3 or 4 to group 3 (Table I). Patients with NPS 1 and 2 were defined as the low-NPS group and those with NPS score 3 as the high-NPS group.

Treatment strategy. Lower alimentary canal endoscopy and thoracoabdominal computed tomography (CT) were routinely performed to determine the clinical stage before colectomy. The pathological findings were defined according to the tumor, node, metastasis classification (American Joint Committee on Cancer Staging Manual, 8th edition). The treatment strategy and follow-up evaluation were performed according to the 2019

Japanese Society for Cancer of the Colon and Rectum guidelines 2019 (7). Primary resection with lymph node dissection was recommended for stages I-III CRC. MIC was defined as laparoscopic colectomy. Morbidity was defined as a Clavien–Dindo classification (CDc) ≥II (8). Severe morbidity was defined as a CDc ≥IIIb, requiring endoscopic, radiological, or surgical intervention under general anesthesia.

Statistical methods. All data analyses were performed using JMP® software version 13.1 (SAS Institute, Cary, NC, USA). The clinicopathological characteristics and laboratory data of the two groups were compared using the chi-square test for categorical variables and the Mann–Whitney *U*-test for continuous variables. Statistical significance was set at *p*<0.05. Logistic regression analysis was performed to estimate the hazard ratio (HR) with a 95% confidence interval (CI) for postoperative complication (CDc ≥II and IIIb). The following clinical factors were adopted as risk factors for overall survival (OS): age at colectomy (≥70 vs. <70 years), sex (male vs. female), body mass index (≥25 vs. <25 kg/m²), NPS (high-NPS vs. low-NPS), tumor location (right-sided vs. left-sided), American Society of Anesthesiologists physical status (3 vs. 1, 2), pathological stage (stage III vs. stage 0, I, II), and comorbidity with diabetes mellitus (present vs. absent). We selected factors with a *p*-value ≤0.1 for subsequent multivariate analysis, and variables with a *p*-value <0.05 were recognized as independent risk factors.

Results

Clinical features of patients who underwent open colectomy. Table II shows the characteristics of patients who underwent OC, depending on whether the NPS was high or low. No significant differences were observed between high- and low-NPS groups.

Short-term outcomes after open colectomy. Table III demonstrates the short-term outcomes after OC, depending on whether the NPS was high or low. The

Table II. Association between NPS and clinicopathological factors in patients with colorectal cancer (CRC) who underwent open colectomy.

Variable	Low-NPS (n=91)	High-NPS (n=48)	<i>p</i> -Value
Age (mean±SD, years)	73.9±9.9	74.4±9.5	0.79
Sex			0.22
Male	45 (49.5%)	29 (60.4%)	
Female	46 (50.5%)	19 (39.6%)	
BMI (mean±SD, kg/m ²)	22.4±3.4	21.5±3.7	0.12
Tumor location			0.77
Right-sided	30 (33.0%)	17 (35.4%)	
Left-sided	61 (67.0%)	31 (64.6%)	
ASA-PS			0.36
1	12 (13.2%)	4 (8.3%)	
2	69 (75.8%)	35 (72.9%)	
3	10 (11.0%)	9 (18.8%)	
Pathological stage			0.52
Stage 0	5 (5.5%)	1 (2.1%)	
Stage I	11 (12.1%)	4 (8.3%)	
Stage II	43 (47.3%)	21 (43.8%)	
Stage III	32 (35.2%)	22 (45.8%)	
Comorbidity of DM			0.35
Absent	64 (70.3%)	30 (62.5%)	
Present	27 (29.7%)	18 (37.5%)	

NPS: Naples prognostic score; BMI: body mass index; SD: standard deviation; ASA-PS: American Society of Anesthesiologists physical status; DM: diabetes mellitus.

Table III. Short-term outcomes of patients with colorectal cancer (CRC) who underwent open colectomy.

Variable	Low-NPS (n=91)	High-NPS (n=48)	<i>p</i> -Value
Operative time (mean±SD, min)	175.6±65.9	180.7±69.9	0.67
Bleeding (mean±SD, g)	323.5±707.5	538.1±1128.5	0.17
Any morbidity of CDc ≥II	21 (23.1%)	20 (41.7%)	0.022*
Severe morbidity of CDc ≥IIIb	3 (3.3%)	6 (12.5%)	0.036*
Surgical site infection	14 (15.4%)	12 (25.0%)	0.17
Anastomotic leakage	3 (3.3%)	2 (4.2%)	0.79
Bowel obstruction	7 (7.7%)	3 (6.3%)	0.75
Reoperation	0 (0.0%)	4 (8.3%)	0.0052*

NPS: Naples prognostic score; SD: standard deviation ; CDc : Clavien-Dindo classification. **p*<0.05.

high-NPS groups had significantly higher incidences of postoperative morbidities compared with the low-NPS groups after OC (Clavien-Dindo classification (CDc) ≥II; *p*=0.022, CDc ≥IIIb; *p*=0.036). Furthermore, patients

Table IV. Univariate and multivariate analysis for factors associated with postoperative complication (CDc \geq II) in patients with colorectal cancer (CRC) who underwent open colectomy.

Factors	Objective variable	Control	Univariate analysis			Multivariate analysis		
			HR	95% CI	p-Value	HR	95% CI	p-Value
Age	\geq 70 years	<70 years	2.06	(0.913-5.037)	0.083	2.09	(0.909-5.165)	0.084
Sex	Male	Female	1.02	(0.493-2.140)	0.95			
BMI	\geq 25 kg/m ²	<25 kg/m ²	0.87	(0.348-2.022)	0.75			
NPS	High-NPS	Low-NPS	2.38	(1.122-5.090)	0.024*	2.40	(1.121-5.181)	0.024*
Tumor location	Right-sided	Left-sided	1.19	(0.547-2.537)	0.66			
ASA-PS	3	1, 2	1.92	(0.688-5.164)	0.21			
Pathological stage	Stage III	Stage 0, I, II	1.01	(0.473-2.124)	0.98			
Comorbidity of DM	Present	Absent	1.31	(0.600-2.802)	0.50			

CDc: Clavien-Dindo classification; CRC: colorectal cancer; BMI: body mass index; NPS: Naples prognostic score; ASA-PS: American Society of Anesthesiologists physical status; LN: lymph node; DM: diabetes mellitus; HR: hazard ratio; CI: confidence interval. * p <0.05.

Table V. Univariate and multivariate analysis for factors associated with severe postoperative complication (CDc \geq IIIb) in patients with colorectal cancer (CRC) who underwent open colectomy.

Factors	Objective variable	Control	Univariate analysis			Multivariate analysis		
			HR	95% CI	p-Value	HR	95% CI	p-Value
Age	\geq 70 years	<70 years	1.73	(0.398-11.939)	0.49			
Sex	Male	Female	3.29	(0.761-22.644)	0.12			
BMI	\geq 25 kg/m ²	<25 kg/m ²	0.91	(0.131-4.012)	0.91			
NPS	High-NPS	Low-NPS	4.19	(1.052-20.619)	0.042*	4.19	(1.052-20.619)	0.042*
Tumor location	Right-sided	Left-sided	0.98	(0.200-3.891)	0.98			
ASA-PS	3	1, 2	3.56	(0.699-14.991)	0.12			
Pathological stage	Stage III	Stage 0, I, II	0.77	(0.158-3.074)	0.77			
Comorbidity of DM	Present	Absent	1.74	(0.411-6.893)	0.43			

CDc: Clavien-Dindo classification; CRC: colorectal cancer; BMI: body mass index; NPS: Naples prognostic score; ASA-PS: American Society of Anesthesiologists physical status; LN: lymph node; DM: diabetes mellitus; HR: hazard ratio; CI: confidence interval. * p <0.05.

with high NPS experienced significantly more frequent reoperations after OC ($p=0.0052$).

Risk factors for any postoperative morbidities (CDc \geq II) after open colectomy. Table IV shows the results of the univariate and multivariate analyses of risk factors for postoperative morbidities (CDc \geq II) after OC. Multivariate analysis demonstrated that high-NPS was an independent risk factor for postoperative morbidities (CDc \geq II) after OC (HR=2.40; 95%CI=1.121-5.181; $p=0.024$).

Risk factors for severe postoperative morbidities (CDc \geq IIIb) after open colectomy. Table V shows the results of

the univariate and multivariate analyses of risk factors for severe postoperative morbidities (CDc \geq IIIb) after OC. Multivariate analysis demonstrated that high-NPS was an independent risk factor for severe postoperative morbidities (CDc \geq IIIb) after OC (HR=4.19; 95%CI=1.052-20.619; $p=0.042$).

Clinical features of patients who underwent minimally invasive colectomy. Table VI shows the characteristics of patients who underwent MIC, depending on whether the NPS was high or low. High-NPS was significantly correlated with older age than those in the low-NPS groups. In addition, the high NPS group showed a

trend toward a lower body mass index, which was not statistically significant.

Short-term outcomes after minimally invasive colectomy.

Table VII shows the short-term outcomes after MIC depending on whether the NPS score was high or low. No significant differences were observed in operative time, bleeding, or postoperative morbidities after MIC.

Discussion

In this study, we demonstrated that a high NPS was an independent risk factor for postoperative morbidity after OC, but not after MIC.

The NPS is an inflammation-based prognostic score developed as a marker for CRC by Galizia *et al.* (4). The NPS includes factors that reflect nutritional status (albumin and total cholesterol) and inflammation (NLR and LMR), and has emerged as a novel prognostic marker for various types of cancer, such as colorectal (4, 9, 10), lung (11), esophageal (12), and hepatocellular (13). Recently, a high NPS was a risk factor for oncological postoperative morbidity. Hosoda *et al.* reported that high-NPS was associated with postoperative morbidity (CDc ≥III) after liver resection for hepatocellular carcinoma (14). Galizia *et al.* reported that a high NPS significantly correlated with postoperative morbidity after gastrectomy for gastric cancer (15). Recently, high-NPS was reported to lead to postoperative morbidity (CDc ≥III) after colectomy for rectal cancer (5). However, to the best of our knowledge, no study has elucidated the superiority of MIC over OC for postoperative morbidity in patients with CRC with a high NPS.

OC is generally considered to be more invasive than MIC. Serum interleukin (IL)-6 and IL-10 levels after OC, which are commonly used to assess surgical stress, were significantly higher than those after MIC (6, 16). In addition, C-reactive protein levels (CRP) after OC were also significantly higher than those after MIC (6, 17, 18). McSorley *et al.* demonstrated that the magnitude of the postoperative systemic inflammatory response, as evidenced by CRP levels, was significantly associated with

Table VI. Association between NPS and clinicopathological factors in patients with colorectal cancer (CRC) who underwent minimally invasive colectomy.

Variable	Low-NPS (n=82)	High-NPS (n=35)	p-Value
Age (mean±SD, years)	69.5±8.6	77.1±9.6	<0.0001*
Sex			0.46
Male	55 (67.1%)	21 (60.0%)	
Female	27 (32.9%)	14 (40.0%)	
BMI (mean±SD, kg/m ²)	23.2±3.3	21.9±4.2	0.084
Tumor location			0.63
Right-sided	20 (24.4%)	10 (28.6%)	
Left-sided	62 (75.6%)	25 (71.4%)	
ASA-PS			0.46
1	13 (15.9%)	3 (8.6%)	
2	65 (79.3%)	29 (82.9%)	
3	4 (4.9%)	3 (8.6%)	
Pathological stage			0.89
Stage 0	6 (7.3%)	3 (8.6%)	
Stage I	29 (35.4%)	11 (31.4%)	
Stage II	25 (30.5%)	13 (37.1%)	
Stage III	22 (26.8%)	8 (22.9%)	
Comorbidity of DM			0.16
Absent	64 (78.1%)	23 (65.7%)	
Present	18 (21.9%)	12 (34.3%)	

NPS: Naples prognostic score; BMI: body mass index; SD: standard deviation; ASA-PS: American Society of Anesthesiologists physical status; DM: diabetes mellitus. *p<0.05.

Table VII. Short-term outcomes of patients with colorectal cancer (CRC) who underwent minimally invasive colectomy.

Variable	Low-NPS (n=82)	High-NPS (n=35)	p-Value
Operative time (mean±SD, min)	222.4±67.2	209.2±55.9	0.31
Bleeding (mean±SD, g)	133.9±179.1	123.8±144.6	0.77
Any morbidity of CDc ≥II	19 (23.2%)	13 (37.1%)	0.12
Severe morbidity of CDc ≥IIIb	1 (1.2%)	0 (0.0%)	0.51
Surgical site infection	11 (13.4%)	2 (5.7%)	0.22
Anastomotic leakage	5 (6.1%)	0 (0.0%)	0.14
Bowel obstruction	7 (8.5%)	3 (8.6%)	1.00
Reoperation	1 (1.2%)	0 (0.0%)	0.51

NPS: Naples prognostic score; SD: standard deviation; CDc: Clavien-Dindo classification.

complications after CRC surgery (19). NPS is valuable in predicting postoperative complications because it serves as an indicator of inflammation, malnutrition, and immunosuppression (14). The higher invasiveness

of OC compared to MIC might increase postoperative complications in patients with CRC with a high NPS.

Previous studies reported that high-NPS was correlated with severe postoperative morbidity (CDc \geq III) after hepatectomy for hepatocellular carcinoma (14) and colectomy for rectal cancer (5). Furthermore, a large cohort study showed that a high NPS was significantly associated with mortality and reoperation in patients undergoing colectomy for diverticulitis (20). It also suggested a correlation between the NPS and severity of complications after colectomy for diverticulitis (20). In the present study, high-NPS was significantly associated with severe postoperative morbidity (CDc \geq IIIb) and reoperation after OC. Four cases of reoperation after OC (none after MIC) were noted, and the reasons were two anastomotic leakages, one abdominal dehiscence, and one postoperative bleeding. High NPS may lead to more severe complications after surgery because of increased inflammation, malnutrition, and immunosuppression.

The lower invasiveness of MIC could yield various advantages during colectomy. A large cohort study demonstrated that MIC contributed to fewer postoperative complications than OC, specifically surgical site infections, urinary tract infections, and pneumonia (21). A recent retrospective study investigating 69,418 colectomies from the Japanese Diagnosis Procedure Combination database suggested that MIC could contribute to decreasing the postoperative mortality rate, surgical morbidity rate, and postoperative length of stay (22). In addition, a randomized controlled trial showed that MIC was associated with a lower incidence of long-term complications and a better quality of life in the first 12 months after surgery than OC (23). Furthermore, a multi-center cohort analysis revealed that the postoperative complication rate was lower in the MIC group compared to the OC group (24). In the current study, a novel advantage was suggested: MIC may not increase postoperative morbidity, even in patients with a high NPS.

Study limitations. First, this was a single-center, retrospective study. Second, this study did not include robotic surgeries.

Conclusion

A high NPS was associated with postoperative complications after OC, but not after MIC. The reduced invasiveness of MIC may contribute to lower postoperative morbidity in patients with a high NPS.

Conflicts of Interest

The Authors declare that they have no conflicts of interest in relation to this study.

Authors' Contributions

T Yamane wrote the manuscript. K Doi developed the study concept and design. T Kaida, Y Suzuki, F Kitamjura and H Ishiodori collected the clinical data. S. Honda conducted critical revision of manuscript. M Iwatsuki coordinated the study, oversaw collection and analysis of the results. All Authors discussed the data and commented on the manuscript.

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Artificial Intelligence (AI) Disclosure

No artificial intelligence (AI) tools, including large language models or machine learning software, were used in the preparation, analysis, or presentation of this manuscript.

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