ASTR

ORIGINAL ARTICLE
pISSN 2288-6575 • eISSN 2288-6796
https://doi.org/10.4174/astr.2017.92.4.191
Annals of Surgical Treatment and Research

Differences in the survival rates of older patients with colorectal cancers in 2003 and 2009

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Purpose: The aim of this study was to investigate survival in patients aged ≥70 years who underwent colorectal cancer surgery in 2003 and 2009. In addition, we aimed to identify the factors that could affect survival in these patients.
Methods: In a cross-sectional study, a retrospective review of the data for 878 patients who underwent colorectal cancer surgery with curative intent in the years 2003 and 2009 was performed. The primary outcome was the 5-year overall survival rate (5-OSR), and the clinicopathologic factors that could affect overall survival were analyzed.
Results: The 5-OSR was 77.8% and 84.9% in 2003 and 2009, respectively (P = 0.013). Age, American Society of Anesthesiologists physical status classification, stage, type of surgery, and length of hospital stay possibly affected survival per the univariate and multivariate analyses. In patients aged ≥70 years, the 5-OSR in 2009 was 75.9%, which showed improvement compared to 53.7% in 2003 (P = 0.027). The stage, type of surgery, and hospital stay were the variables that possibly affected survival in patients aged ≥70 years per the univariate analysis, whereas the stage (III; hazard ratio [HR], 2.188; P = 0.005) and length of hospital stay (>12 days; HR, 2.307; P = 0.004), were the variables that showed statistical significance on the multivariate analysis.
Conclusion: We found that early stage and shortening the length of hospital stay could affect survival in older patients with colorectal cancers. Because of limited evidence on the influence of shortening the length of hospital stay on survival in older patients, further investigations are warranted.
[Ann Surg Treat Res 2017;92(4):191-199]

Key Words: Colorectal neoplasms, Surgery, Aged

INTRODUCTION

The rising life expectancy within the older population is expected to increase the prospect of operating on older patients for surgeons. In general, advanced age is a risk factor for surgery, which could be associated with severe postoperative morbidities and mortalities. Increased risk of postoperative morbidities and mortalities could be attributed to the age-related decline in physical function and higher incidence of underlying diseases. Patient age is a risk factor for post-operative morbidity and mortality [1-3]. In addition, Story [4] reported that the risk of 30-day mortality increases by about 10% for every year for patients over the age of 70. These paradoxical facts could increase the difficulty with which a decision for surgery with curative intent is made in older patients.

Jung et al. [5] reported the nationwide cancer statistics in Korea. The 5-year survival rate for colorectal cancer was 66.6% during 2001–2005 and 74.8% during 2008–2012, which indicated a remarkable improvement in survival. In addition, they reported that the incidence of colorectal cancer gradually in-

Received July 19, 2016, **Revised** October 19, 2016,
Accepted October 31, 2016

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The results of this study were presented as a poster at the 49th Annual Congress of the Korean Society of Coloproctology (April 1-3, 2016 Convention Center, Daejeon, Korea).

creased with age, which indicated that older populations could have higher chances of developing colorectal cancer. Therefore, it is imperative to determine the survival rates in older patients and identify the factors that could influence survival. Providing rational explanations could facilitate the decision-making process in older patients regarding surgery, prompting them to consider factors other than the age.

In Korea, the National Cancer Screening Program (NCSP) for colorectal cancer was initiated in 2004 [6]. Cancer screening facilitates early diagnosis, which usually results in better survival outcome. In addition, there have been considerable diagnostic improvements, as well as improvements in the therapeutic, surgical, and perioperative management of colorectal cancer. Such improvements, labeled under the enhanced recovery after surgery category, included the use of short-acting anesthetics, optimized dynamic pain relief (opioid-sparing), and minimally invasive operations (laparoscopy) and proposed changes to peri- and postoperative care principles concerning feeding; mobilization; monitoring; and use of drains, nasogastric tubes, and urinary catheters [7]. These practices could influence patient survival, although supporting evidence is limited.

The aim of this study was to investigate the survival of older patients who underwent colorectal cancer surgery in 2003 and 2009 using a cross-sectional study design, particularly focusing on patients aged ≥70 years to evaluate the factors that could affect survival in older patients.

METHODS

Study design and patient population

Using a cross-sectional study design, we retrospectively analyzed the medical records of patients diagnosed with colorectal adenocarcinoma who underwent curative resection in the years 2003 and 2009. Patients who underwent palliative surgery and patients with carcinoma in situ, familial adenomatous polyposis, or hereditary non-polyposis colorectal cancer were excluded from the study.

Collection and comparison of clinical data

Demographic data including the age, sex, body mass index (BMI), comorbidities (only subgrouped as hypertension and diabetes mellitus), and the American Society of Anesthesiologists (ASA) physical status classification were assessed. In addition, the pathological status (TNM stage and tumor location (subgrouped as right colon, left colon, and the rectum); diagnostic details (by screening or symptoms); operative details (the number of harvested lymph nodes [LNs]; type of surgery, operation time, estimated blood loss); and postoperative details (days of hospital stay, the first time of flatus after surgery, adjuvant chemotherapy) were assessed. Patients who were subgrouped as 'screening' at diagnostic detail defined as the patient who did not have a subjective symptom, and incidentally diagnosed the disease by the screening test. On the other hand, patients who were subgrouped as 'symptom' defined as the patient who had a preceding subjective symptom before medical evaluations. Staging after surgical resection was performed according to 7th edition of the American Joint Committee on Cancer cancer staging manual guidelines. The cutoff age was determined to be 70 years. There has been no consistent definition of cutoff value for elderly in literature. Present study followed several studies which used 70 as cutoff value [4,8]. The BMI was classified into 2 categories, <25 kg/m^2 and ≥ 25 kg/m^2. If the tumor was located between the cecum and the splenic flexure, it was termed a right colon tumor; if it was located between the splenic flexure and sigmoid colon, it was termed a left colon tumor; and if it was located within 15 cm of the anal verge, it was termed rectum tumor [9,10]. If the surgery was initiated with laparoscopy, it was defined as laparoscopic. If the surgery was initiated with an open technique, it was defined as open. Hospital stay was defined as the period from date of surgery to the date of discharge.

Statistical analysis

The primary endpoint was the 5-year overall survival rate (5-OSR). All statistical analyses were performed using the SPSS ver. 14.0 (SPSS Inc., Chicago, IL, USA). The Pearson chi-square test and Student t-test were used. The survival distributions were estimated using the Kaplan-Meier method and Cox regression analysis. Additional stratification for the year 2003 and 2009 was performed to avoid the potential risk for the confounding bias. P-value <0.05 was considered statistically significant.

Ethical statement

This study protocol was reviewed and approved by the Institutional Review Board of National Cancer Center (NCC2016-0149). Informed consent was waived due to the retrospective nature of the study. All processes were conducted according to the principles expressed in the Declaration of Helsinki.

RESULTS

The difference in survival between all patients who underwent surgery in 2003 and 2009

In total, 878 patients underwent colorectal surgery with curative intent in 2003 and 2009. Of these, 383 patients who underwent surgery in 2003 were grouped into group I, and 495 patients who underwent surgery in 2009 were grouped into group II. The patient demographics are summarized in Table 1. The 2 groups differed in age, BMI, comorbidities (including hypertension and diabetes mellitus), cancer stage, diagnostic details, type of surgery, operation time, number of harvested

Table 1. Patient demographics according to the year of surgery for all patients

Characteristic	2003 (n = 383)	2009 (n = 495)	P-value
Age (yr)	56.87 ± 11.40	61.67 ± 11.00	<0.001
<70	329 (85.9)	365 (73.7)	<0.001
≥70	54 (14.1)	130 (26.3)	
Sex			0.972
Men	234 (61.1)	303 (61.2)	
Women	149 (38.9)	192 (38.8)	
Body mass index (kg/m^2)	23.67 ± 3.33	24.33 ± 3.31	0.005
<25	236 (70.4)	314 (63.4)	0.036
≥25	99 (29.6)	181 (36.6)	
ASA PS classification			0.705
I, II	304 (93.8)	449 (93.2)	
≥III	20 (6.2)	33 (6.8)	
Comorbidities			0.002
(–)	189 (49.3)	192 (38.8)	
(+)	194 (50.7)	303 (61.2)	
Hypertension			<0.001
(–)	304 (79.4)	315 (63.6)	
(+)	79 (20.6)	180 (36.4)	
Diabetes mellitus			0.017
(–)	347 (90.6)	422 (85.3)	
(+)	36 (9.4)	73 (14.7)	
Stage			0.044
0/I/II	207 (54.0)	301 (60.8)	
III	176 (46.0)	194 (39.2)	
Location			0.088
Right colon	70 (18.3)	99 (20.0)	
Left colon	145 (37.9)	215 (43.4)	
Rectum	168 (43.9)	181 (36.6)	
CRT (–)	31 (8.1)	54 (10.9)	
CRT (+)	137 (35.8)	127 (25.7)	
Diagnostic details			<0.001
Screening	22 (5.7)	96 (19.4)	
Symptoms	361 (94.3)	399 (80.6)	
Type of surgery			<0.001
Laparoscopic	14 (3.7)	393 (79.4)	
Open	369 (96.3)	102 (20.6)	
Operation time (min)	162.77 ± 82.44	227.21 ± 89.86	<0.001
Estimated blood loss	226.11 ± 250.69	225.27 ± 391.84	0.205
No. of harvested LNs	21.15 ± 11.30	25.80 ± 14.53	<0.001
≥12	310 (80.9)	444 (89.7)	<0.001
<12	73 (19.1)	51 (10.3)	
Length of hospital stay (day)	13.84 ± 16.35	11.15 ± 6.61	0.001
≤12	263 (68.7)	387 (78.2)	0.001
>12	120 (31.3)	108 (21.8)	
First flatus after surgery	3.54 ± 1.22	3.13 (4.81)	0.102
Adjuvant chemotherapy			<0.001
(–)	55 (14.4)	158 (31.9)	
(+)	328 (85.6)	337 (68.1)	

Values are presented as mean ± standard deviation or number (%).
ASA PS, American Society of Anesthesiologists physical status; CRT, chemoradiotherapy.

LNs, length of hospital stay, and adjuvant chemotherapy. The mean age of group II (61.57 ± 11.00 years) was significantly higher than that of group I (56.87 ± 11.40 years). Moreover, group II had significantly more patients aged ≥70 years (130 [26.3%]) than did group I (54 [14.1%]). Group II potentially had more patients with comorbidities than group I. In addition,

cancer stage differed significantly between the 2 groups. Group II had significantly more patients with stage 0/I/II cancers (301 [60.8%]) than group I (207 [54.0%]). Compared to group I, more patients were diagnosed by screening in group II. We evaluated the association between stage and screening through whole data. There were 508 patients with stage 0/I/II.

Table 2. Univariate and multivariate analyses of prognostic factors for predicting the 5-year overall survival rate in all patients

Variable	Univariate analysis		Multivariate analysis		
	5-OSR (%)	P-value	HR[a]	95% CI	P-value
Age		<0.001			<0.001
<70	85.0		1.000		
≥70	68.5		2.466	1.740–3.496	
Sex		0.153			
Men	81.2				
Women	82.9				
Body mass index		0.134			
<25	81.3				
≥25	83.0				
ASA PS classification		0.011			0.044
I, II	82.2		1.000		
≥III	75.0		1.713	1.015–2.892	
Comorbidities		0.083			
(–)	83.8				
(+)	80.5				
Hypertension		0.633			
(–)	80.8				
(+)	84.8				
Diabetes mellitus		0.474			
(–)	81.2				
(+)	87.0				
Stage		<0.001			<0.001
0/I/II	91.3		1.000		
III	69.5		3.449	2.446–4.863	
Location		0.240			
Right colon	83.4				
Left colon	82.3				
Rectum	80.8				
CRT (–)					
CRT (+)					
Diagnostic details		<0.001			0.041
Screening	95.7		1.000		
Symptoms	79.7		2.233	1.033–4.826	
Type of surgery		<0.001			0.153
Laparoscopic	87.1		1.000		
Open	77.2		1.456	0.869–2.438	
No. of harvested LNs		0.181			
≥12	77.9				
<12	82.5				
Length of hospital stay		<0.001			<0.001
≤12	86.6		1.000		
>12	68.3		1.997	1.435–2.780	
Adjuvant chemotherapy		0.810			
(–)	83.8				
(+)	82.1				

5-OSR, 5-year overall survival rate; HR, hazard ratio; CI, confidence interval; ASA PS, American Society of Anesthesiologists physical status; LN, lymph node.
[a]Stratified for the year (2003/2009) of curative resection.

Among these patients, 85 patients were diagnosed the disease by screening, and they account for 72.0% of whole screening group. On the other hand, 423 patients were diagnosed the disease by symptom presentation, and they account for 55.7% of whole symptom presentation group (P = 0.001). The mean duration of hospital stay for group II was 11.15 ± 6.61 days, and that for group I was 13.84 ± 16.35 days. Therefore, we divided the patients into 2 groups based on a cutoff value of 12 days. Compared to group I, group II had significantly more patients who underwent laparoscopic surgery. Compared to group I,

Table 3. Patient demographics according to the year of surgery in patients aged ≥70 years

Characteristic	2003 (n = 54)	2009 (n = 130)	P-value
Sex			0.430
Men	29 (53.7)	78 (60.0)	
Women	25 (46.3)	52 (40.0)	
Body mass index (kg/m^2)	23.15 ± 3.71	24.47 ± 3.68	0.034
<25	36 (73.5)	80 (61.5)	0.136
≥25	13 (26.5)	50 (38.5)	
ASA PS classification			0.602
I, II	43 (89.6)	116 (92.1)	
≥III	5 (10.4)	10 (7.9)	
Comorbidities			0.735
(–)	12 (22.2)	26 (20.0)	
(+)	42 (77.8)	104 (80.0)	
Hypertension			0.715
(–)	36 (66.7)	83 (63.8)	
(+)	18 (33.3)	47 (36.2)	
Diabetes mellitus			0.485
(–)	50 (92.6)	116 (89.2)	
(+)	4 (7.4)	14 (10.8)	
Stage			0.157
0/I/II	28 (51.9)	82 (63.1)	
III	26 (48.1)	48 (36.9)	
Location			0.725
Right colon	14 (25.9)	35 (26.9)	
Left colon	19 (35.2)	48 (36.9)	
Rectum	21 (38.9)	47 (36.2)	
CRT (–)	9 (16.7)	25 (19.2)	
CRT (+)	12 (22.2)	22 (16.9)	
Diagnostic details			0.198
Screening	2 (3.7)	12 (9.2)	
Symptoms	52 (96.3)	118 (90.8)	
Type of surgery			<0.001
Laparoscopic	0 (0)	98 (75.4)	
Open	54 (100)	32 (24.6)	
Operation time (min)	176.44 ± 85.67	231.30 ± 80.79	<0.001
Estimated blood loss	258.70 ± 281.37	239.62 ± 203.91	0.608
No. of harvested LNs	19.39 ± 11.45	24.56 ± 14.08	0.018
≥12	40 (74.1)	115 (88.5)	0.015
<12	14 (25.9)	15 (11.5)	
Length of hospital stay (day)	16.37 ± 1.69	11.68 ± 6.92	0.001
≤12	27 (50.0)	97 (74.6)	0.001
>12	27 (50.0)	33 (25.4)	
First flatus after surgery	4.28 ± 1.70	4.30 ± 8.84	0.985
Adjuvant chemotherapy			0.001
(–)	10 (18.5)	58 (44.6)	
(+)	44 (81.5)	72 (55.4)	

Values are presented as mean ± standard deviation or number (%).
ASA PS, American Society of Anesthesiologists physical status; CRT, chemoradiotherapy.

group II had a significantly longer operation duration. Group II had fewer patients who underwent adjuvant chemotherapy than did group I.

The 2 groups significantly differed in their overall survival rates. The 5-OSR was 77.8% for group I, and 84.9% for group II (P = 0.013). The prognostic factors of overall survival identified by univariate and multivariate analyses are summarized in Table 2. The age, ASA physical status classification, cancer stage, diagnostic details, and the length of hospital stay were factors that were identified by univariate analysis to be significantly associated with 5-OSR. The prognostic significance of these factors in predicting the 5-OSR was confirmed by multivariate analysis.

The difference in survival between older patients who underwent surgery in 2003 and 2009

Demographics for patients aged ≥70 years are summarized in the Table 3. Variables that statistically differed between the 2 groups were the BMI, type of surgery, operation time, number of harvested LNs, length of hospital stay, and adjuvant chemotherapy. Group II had more patients with BMIs ≥25 kg/m^2 than did group I. Moreover, group II had significantly longer OP duration and significantly shorter hospital stay than group I. More patients in group II underwent laparoscopic surgery than group I, and fewer patients underwent adjuvant chemotherapy in group II than in group I.

Survival significantly improved for group II patients aged ≥70 years (Fig. 1). The 5-OSR was 75.9% in 2009, and 53.7% in 2003, indicating a statistically significant improvement (P = 0.027). In order to identify the prognostic factors for survival, the analyses of variables for patients aged ≥70 years are summarized in Table 4. Cancer stage, type of surgery, and the length of hospital stay were variables that were identified via the univariate analysis to be statistically significant prognostic factors for predicting overall survival. However, multivariate analysis only identified cancer stage and length of hospital stay as statistically significant prognostic factors for predicting overall survival.

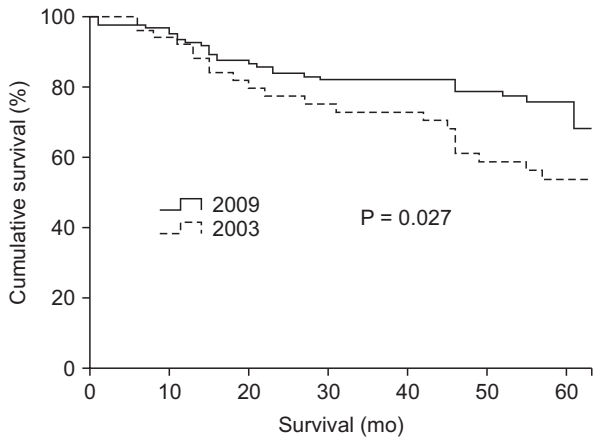

Fig. 1. The 5-year overall survival in patients aged ≥70 years for the years 2003 and 2009.

DISCUSSION

In the present study, we found that in comparison to that observed in 2003, the 5-OSR significantly improved in 2009 even though there were more patients aged ≥70 years, with BMIs ≥25 kg/m^2 and with comorbidities. Although the present study was a cross-sectional study that could only provide a hypothesis for case-control studies, we found that patients aged ≥70 years showed improved overall survival in 2009. Cancer stage (HR, 2.188; 95% confidence interval [CI], 1.260–3.800) and length of hospital stay (HR, 2.307; 95% CI, 1.308–4.070) were factors that significantly influenced the survival of older patients.

The numbers of patients who were diagnosed through screening, who underwent laparoscopic surgery, and stayed at the hospital for 12 days in 2009, were higher compared to those in 2003. Compared to 2003, the operation time was significantly longer in 2009, which indicated that laparoscopic surgery could take longer than open surgery, and was associated with a shorter hospital stay [11]. The definition for old age has been controversial. The cutoff age in the present study was determined to be 70 years, because several studies showed that the risk of mortality increased after surgery in patients aged ≥70 years compared to that in patients <70 years [2,4,12]. The incidence of colorectal cancer is known to gradually increase with age, which indicates that the likelihood of developing colorectal cancer could be higher in older patients [5]. Possible rational reasons other than the age should be considered for older patients before reaching a final decision concerning surgery.

Cancer screening results in the early detection of cancer, which usually results in better survival outcome. A microsimulation model, MISCAN-Colon [13] suggested that screening can account for a 53% reduction in colorectal cancer-related mortality. In Korea, the NCSP for colorectal cancer was initiated in 2004. NCSP recommends that adults aged >50 years should undergo fecal occult blood testing every year. Adults with positive results are recommended to undergo further examination via colonoscopy or double-contrast barium enema. Suh et al. [6] reported that between 2004 and 2013, screening rates showed an annual increase of 5.0% for colorectal cancer. In addition, they showed that the rate of screening after recommendation increased annually by 3.0% for colorectal cancer, from 25.3% in 2004 to 48.1% in 2009. Screening rates have been increasing gradually; however, it appears that stronger recommendations for screening are required. In

Table 4. Univariate and multivariate analyses of prognostic factors for predicting 5-year overall survival in patients aged ≥70 years

Variable	Univariate analysis		Multivariate analysis		
	5-OSR	P-value	HR[a)]	95% CI	P-value
Sex		0.560			
Men	66.2				
Women	72.4				
Body mass index		0.810			
<25	68.0				
≥25	72.6				
ASA PS classification		0.874			
I, II	71.6				
≥III	72.2				
Comorbidities		0.515			
(–)	66.6				
(+)	69.4				
Hypertension		0.565			
(–)	70.8				
(+)	68.0				
Diabetes mellitus		0.808			
(–)	71.0				
(+)	70.3				
Stage		0.001			0.005
0/I/II	79.8		1.000		
III	50.3		2.188	1.260–3.800	
Location		0.595			
Right colon	66.2				
Left colon	66.6				
Rectum	71.6				
CRT (–)					
CRT (+)					
Diagnostic details		0.056			
Screening	92.9				
Symptoms	66.0				
Type of surgery		0.010			0.282
Laparoscopic	79.9		1.000		
Open	57.1		1.545	0.699–3.417	
No. of harvested LNs		0.167			
≥12	85.3				
<12	65.0				
Length of hospital stay		<0.001			0.004
≤12	78.9		1.000		
>12	46.9		2.307	1.308–4.070	
Adjuvant chemotherapy		0.193			
(–)	62.0				
(+)	72.3				

5-OSR, 5-year overall survival rate; HR, hazard ratio; CI, confidence interval; ASA PS, American Society of Anesthesiologists physical status; LN, lymph node.
[a)]Stratified for the year (2003/2009) of curative resection.

the present study, although screening was not identified via univariate and multivariate analyses as a significant prognostic factor that predicted survival in older patients (P = 0.056) (Table 4), it was identified as a statistically significant predictor of overall survival for all patients (Table 2). Cancer stage, a well-known predictor of overall survival, was also identified as a statistically significant predictor of overall survival in the present study (Tables 2, 4). Considering the results, the importance of screening in the management of colorectal cancer cannot be denied. However, the appropriate time to

discontinue screening for older adults remains controversial.

In the present study, the length of hospital stay was a strong predictor of overall survival. In a study similar to the present one, Hendren et al. [14] studied early discharge and hospital readmission after colectomy. They set the cutoff value to 5 days, which was the median length of stay. They concluded that early discharge (with median length of stay within 5 days after surgery) did not increase the risk for readmission. In the present study, we used the cutoff value of 12 days, which was the median length of hospital stay. The average length of stay after colorectal surgery has been reported as 10–15 days [15,16], which is consistent with the present study. "Fast-track" therapy, also known as enhanced recovery, started developing in the late 1990s to improve patient outcome and to accelerate recovery after surgery [17]. However, no study has considered overall survival as the endpoint. "Fast-track" was a movement to accelerate recovery after surgery. Although we did not employ fast track therapy in the present study, our results showing the short hospital stay in 2009 could be influenced by the improvement of postoperative management in 2009 compared with that in 2003. And also it could have affected the improvement of survival in this study. Scharfenberg et al. [18] reported that in patients aged ≥70 years, general morbidity was lower and recovery was faster, resulting in the early discharge of patients after a median stay of 5 days compared to that observed with traditional care, where fast track rehabilitation was employed after colonic surgery. They concluded that employing fast track therapy in the treatment of older patients was not only feasible, but might also reduce the number of general complications and the duration of hospital stay. Moreover, there are several studies showing that postoperative complication could decrease survival [19,20]. Carefully considering from these results, movements to accelerate recovery after surgery could be a factor that might affect survival.

The key concepts behind fast track therapy include minimally invasive procedures, optimal pain management, and aggressive postoperative rehabilitation, such as early enteral nutrition and ambulation [17]. However, these concepts are not as simple as they appear. They include preoperative counseling and education, preoperative oral carbohydrate nutrition, preanesthesia medication, laxative use, nasogastric tube feeding, anesthesia management, laparoscopic approach, early removal of urinary catheter, and immediate mobilization [21,22]. As a result, current fast track therapy protocols involve multiple components that would naturally have variable success rates. Because of this complexity, Day et al. [23] reported that the current standard of enhanced recovery protocols is frequently insufficient. In the present study, although we found that shortening hospital stay could improve survival, this could indicate that shortening the length of hospital stay could be an important factor that facilitates the fast track pathway and improves survival.

The present study had several limitations. First, it was a cross-sectional study, which could only provide hypotheses for case-control studies. There could be a selection bias of patients who underwent laparoscopic surgery. Because of the retrospective nature of the study, we could not accurately evaluate the intraoperative events and postoperative complications. The length of hospital stay could vary according to the complications. Thus, further prospective investigations are required.

In conclusion, in the present study, the factors that could predict survival in older patients included early diagnosis, and length of hospital stay. NCSP for colorectal cancer, which was initiated in 2004, could have a role in the early diagnosis of lesions in older patients. However, the screening rate by recommendation for Korean colorectal cancer patients aged ≥70 years was only 55.0% in 2013 [6]. Although screening rates have been gradually increasing, stronger recommendation for screening is still required. As mentioned above, the concept of fast track therapy could be beneficial to patients, and we suggest with caution that shortening the length of hospital stay could be important in facilitating the fast track pathway. Further investigations to confirm our results and hypotheses are required.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGEMENTS

This work was supported by a grant from the National Cancer Center (NCC-1510150).

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