

Effects of Minimal Invasive Surgery in Elderly Colorectal Cancer Patients

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Effects of Minimal Invasive Surgery in Elderly Colorectal Cancer Patients

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By Yoon Dae Han

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ABSTRACT

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Objective. Colorectal cancer (CRC) is a common disease. Among CRC patients, old aged patients are more likely to suffer from comorbidity than younger patients which increases concern whether to take surgery. However, in recent years, surgical skills have been rapidly evolved and indication of minimal invasive surgery has been increased. Nevertheless, still it has not been clearly established to apply these minimal invasive techniques to elderly CRC patients. This study aimed to compare postoperative and oncologic outcomes between minimal invasive surgery (MIS), including laparoscopic surgery and robotic surgery and open conventional surgery (OCS) in elderly CRC patient age 75 years and over.

Materials and Methods. We retrospectively obtained data of CRC patients who underwent surgery between January 2005 and December 2011 in Gangnam Severance hospital, whose age was 75 years and over. Among 182 patients, 111

patients were diagnosed as colon cancer and 71 patients were diagnosed as rectal cancer, defined as less than 15cm from anal verge. Patients were divided as OCS group and MIS group according to surgical procedure within both cancer groups and analyzed. Patient's characteristics and surgical outcomes, overall survival and disease free survival were evaluated.

Results. There were no statistical differences in sex, age, body mass index, American Society of Anesthesiologists (ASA) class between OCS and MIS group in colon cancer and rectal cancer. Tumor histologic grade and type of operation were significant statistical different factors between OCS and MIS group in colon cancer. ($p=0.044$, $p=0.006$) Postoperative recovery showed time to first flatus ($p=0.009$, $p=0.01$), time to start diet ($p<0.001$, $p<0.001$), length of hospital stay ($p<0.001$, $p=0.003$) as a significant different factors between OCS and MIS group in both colon cancer and rectal cancer. There were no statistical difference with overall survival and disease free survival between OCS and MIS group in both colon cancer ($p=0.861$, $p=0.972$) and rectal cancer. ($p=0.739$, $p=0.277$)

Conclusion. MIS in colorectal cancer surgery could be applied to elderly patients aged over 75 with acceptable morbidity and long-term oncologic outcomes compared to OCS.

Key words: colorectal cancer, elderly patients, minimal invasive surgery

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I. INTRODUCTION

Colorectal cancer (CRC) is a 3rd commonest cancer in men and 2nd commonest in women, with total 1,360,602 new cases seen worldwide every year. (1) In Korea, the incidence rates for colorectal cancers have continued to increase in both sexes, which ranked the 3rd most common type of cancer. (2) Among several risk factors in CRC, age is one of the most critical risk factors. Approximately 70% of CRC cases develop over age of 65, and near 40% of patients in total are 75 years or older. (3) These elderly patients are more likely to suffer from comorbidity than younger patients which increases concern for taking surgery for CRC treatment.

However, in recent years, surgical skills have been rapidly evolved. Indication of laparoscopic surgery has been increased because of improvements in devices and technical advances. (4, 5) In addition, new emerging techniques, so called robotic surgery is also gathering safety evidences to extend its indications on

CRC surgery.

Nevertheless, still it has not been clearly established to apply these minimal invasive techniques to elderly patients with diagnosed as colorectal cancer. As so, we aimed to compare the outcomes between MIS, including laparoscopic surgery and robotic surgery with open conventional surgery in elderly CRC patients age 75 years and over.

II. MATERIALS AND METHODS

1. Patients

Between January 2005 and December 2011, colorectal cancer patients aged 75 and over who underwent surgery in our hospital were selected. The age 75 was chosen as a threshold to emphasize the meaning of advanced age, also as the incidence of colorectal cancer increases dramatically in this age. (6-8) Among 182 patients, 111 patients were diagnosed as colon cancer and 71 patients were diagnosed as rectal cancer, defined as less than 15cm from anal verge. Patients were divided as open conventional surgery group (OCS) and minimally invasive surgery group (MIS) according to surgical procedure. MIS contained laparoscopic surgery and Robotic surgery.

2. Preoperative evaluation

All patients were basically evaluated with chest radiography. Computed tomography was used for detecting metastatic disease, when appropriate. Preoperative colonoscopy was done and biopsy was performed to confirm the cancer. TNM stage was determined according to the Union International Contre le Cancer classification (UICC).

3. Surgical characteristics

For surgical characteristics, operation time, transfusion during operation, operation type was recorded. The operations were performed by well-skilled three colorectal surgeons. Patients' pathological characteristics were described with histologic grade, lymphovascular invasion, stage, tumor size, number of harvested lymph nodes, distal resection margin and tumor location.

4. Postoperative evaluation

Postoperative complications were defined according to Clavien-Dindo classification. (9) Postoperative complication was categorized into anastomosis leakage, bleeding, ileus or obstruction, urinary dysfunction, wound dehiscence and others. Complications were defined to having an event within postoperative 1 months.

Patients who have undergone preoperative CRT (Chemoradiation therapy)

were excluded as we focused on surgical outcomes. Postoperative adjuvant chemotherapy was offered to all patients who do not have severe comorbid condition after primary surgery, except stage I colorectal cancer. All patients were regularly followed by outpatient clinic.

5. Statistical analysis

All data were analyzed with Statistical Package for the Social Sciences Windows version 20.0 (SPSS 20.0 for Windows; SPSS Inc, Chicago, IL). Categorical variables were analyzed by the two sided Pearson chi-square test or Fisher's exact test, and continuous variables were analyzed by the Student t-test or Mann-Whitney U test. Overall Survival (OS) was defined as the time from primary surgery to death, and Disease free survival (DFS) was defined as the time from primary surgery until the detection of recurrent disease. In survival analysis, OS curve and DFS curve were plotted according to the Kaplan–Meier method. Comparison both survival curve between OCS group and MIS group were performed by the log-rank test. All variables with statistical significance were accepted at p-value < 0.05.

III. RESULTS

1. Baseline patient characteristics

The baseline characteristics of OCS and MIS group in colorectal cancer patients are presented in Table 1. This is schematic table showing baseline patients and tumor characteristics that has no significant difference between OCS and MIS group. However, as there are some differences between colon cancer and rectal cancer, especially approaching operative field and practicing operation, we subdivided colon cancer and rectal cancer to analyze its surgical outcomes precisely.

Table 1. Baseline Patients and Tumor characteristics of Colorectal cancer

		Colorectal Cancer		p-value
		OCS (n=88)	MIS (n=94)	
Sex	Male	52 (59.1%)	64 (68.1%)	0.207
	Female	36 (40.9%)	30 (31.9%)	
Age (year)	Mean ± SD	79.93 ± 4.039	78.95 ± 3.917	0.097
BMI (kg/m ²)		22.82 ± 3.41	22.91 ± 3.09	0.864
ASA	I	37 (42%)	38 (40.4%)	0.823
	II	44 (50%)	46 (51.1%)	
	III	7 (8%)	10 (10.6%)	
OP time (min)	Mean ± SD	216.3 ± 111.5	225.57 ± 100.2	0.656
OP transfusion	Yes	18 (20.5%)	10 (10.6%)	0.067
	No	70 (79.5%)	84 (89.4%)	
Harvested LN	Mean ± SD	19.26 ± 13.42	20.93 ± 16.33	0.455
Pathology	G1	13 (14.8%)	20 (60.6%)	0.475
	G2	72 (81.8%)	72 (76.6%)	
	G3	3 (3.4%)	2 (2.1%)	
Stage	I	10 (11.4%)	19 (20.2%)	0.121
	II	37 (56.1%)	29 (30.9%)	
	III	32 (36.4%)	41 (43.6%)	
	IV	9 (64.3%)	5 (5.3%)	

Abbreviations: SD: Standard Deviation; BMI: Body Mass Index; ASA: American Society of Anesthesiologist; OP: Operation; LN: Lymph Node, G1: Well differentiated; G2: Moderately differentiated; G3: Poorly differentiated

The subgroup baseline characteristics of OCS and MIS group are presented in Table 2. In colon cancer, mean age was 80.25 years in OCS and 79.54 years in MIS. Male gender was predominated in both groups (56.4% in OCS, 64.3% in MIS). BMI was 23.31 kg/m² in OCS and 22.71 kg/m² in MIS. ASA class I and II were dominant in both groups (96.4% in OCS, 85.7% in MIS). In rectal cancer, mean age was 79.39 years in OCS and 78.08 years in MIS. Male gender was predominated in both groups (63.6% in OCS, 73.7% in MIS). BMI was 22.25 kg/m² in OCS and 23.22 kg/m² in MIS. ASA class I and II were dominant in both groups (84.8% in OCS, 94.7% in MIS).

Table 2. Patients characteristics

		Colon			Rectum		
		OCS (n=55)	MIS (n=56)	P value	OCS (n=33)	MIS (n=38)	P value
Sex	Male	31 (56.4%)	36 (64.3%)	0.673	21 (63.6%)	28 (73.7%)	0.361
	Female	24 (43.6%)	20 (35.7%)		12 (36.4%)	10 (26.3%)	
Age (year)	Mean ±	80.25 ±	79.54 ±	0.381	79.39 ± 3.97	78.08 ±	0.112
	SD	4.08	4.51		2.65		
BMI (kg/m ²)	Mean ±	23.31 ±	22.71 ±	0.390	22.25 ± 2.88	23.22 ±	0.161
	SD	3.71	3.19		2.91		
ASA	I	21 (38.2%)	24 (42.9%)	0.133	16 (48.5%)	14 (36.8%)	0.085
	II	32 (58.2%)	24 (42.9%)		12 (36.3%)	22 (57.9%)	
	III	2 (3.6%)	8 (14.3%)		5 (15.2%)	2 (5.3%)	

Abbreviations: SD: Standard Deviation; BMI: Body Mass Index; ASA: American Society of Anesthesiologist

2. Perioperative surgical and pathologic outcomes

Perioperative surgical factors and pathologic outcomes are described in Table 3. In colon cancer group, tumor histologic grade, and type of operation were significant different factors. Moderate differentiated pathologic type took a majority portion in both OCS and MIS group. Right hemicolectomy (58.2%) was done mostly in OCS group, but Anterior resection (57.1%) was the most frequent surgery taken in MIS group.

Operation time, transfusion status during surgery, lymphovascular invasion, stage, number of harvested lymph nodes have shown no statistical difference between MIS and OCS group in both colon and rectal cancer. There was no statistical difference between MIS and OCS group with distal resection margin length in rectal cancer, also with tumor location in colon cancer.

Table 3. Comparison of perioperative surgical and pathologic outcomes between Open surgery group and MIS group

		Colon			Rectum		
		OCS (n=55)	MIS (n=56)	P value	OCS (n=33)	MIS (n=38)	P value
OP time (min)	Mean	± 216.30	± 225.57	0.656	± 263.66	± 270.45	0.775
	SD	111.50	100.15		103.39	94.13	
OP Transfusion	No	46 (83.6%)	50 (89.3%)	0.384	24 (72.7%)	34 (89.5%)	0.069
	Yes	9 (16.4%)	6 (10.7%)		9 (27.3%)	4 (10.5%)	
Histologic grade	G1	4 (7.3%)	12 (21.4%)	0.044	9 (27.3%)	8 (21.1%)	0.766
	G2	49 (89.1%)	44 (78.6%)		23 (69.7%)	28 (73.7%)	
	G3	2 (3.6%)	0 (0.0%)		1 (3.0%)	2 (5.3%)	
LVI	No	37 (67.3%)	40 (71.4%)	0.197	21 (63.6%)	25 (65.8%)	0.514
	Yes	11 (20.0%)	14 (25.0%)		7 (21.2%)	12 (31.6%)	
	Missing	7 (12.7%)	2 (3.6%)		5 (15.2%)	1 (2.6%)	
Stage	I	5 (9.1%)	8 (14.3%)	0.217	4 (12.1%)	12 (31.6%)	0.135
	II	23 (41.8%)	19 (33.9%)		15 (45.5%)	9 (23.7%)	
	III	22 (40.0%)	28 (50.0%)		10 (30.3%)	13 (34.2%)	
	IV	5 (9.1%)	1 (1.8%)		4 (12.1%)	4 (10.5%)	
Tumor size (cm)	≥ 5cm	29 (52.7%)	24 (42.9%)	0.298	16 (48.5%)	13 (34.2%)	0.222
	<5 cm	26 (47.3%)	32 (57.1%)		17 (51.5%)	25 (65.8%)	
No. of harvest LNs	Mean	± 21.53	± 23.95	0.429	± 15.48	± 16.47	0.736
	SD	15.02	17.00		9.25	14.36	
Operation type	RHC	32 (58.2%)	20 (35.7%)	0.006			
	LHC	8 (14.5%)	4 (7.1%)				
	AR	15 (27.3%)	32 (57.1%)				
DRM (cm)	Mean	±			± 2.88	± 2.96	0.860
	SD				1.97	2.05	
Tumor location	Low (<10cm)				24 (72.7%)	19 (50.0%)	0.051
	High (≥10cm)				9 (27.3%)	19 (50.0%)	

Abbreviations: OP: Operation; SD: Standard Deviation; G1: Well differentiated; G2: Moderately differentiated; G3: Poorly differentiated; LVI: Lymphovascular invasion; LN: Lymph node; RHC: Right hemicolectomy; LHC : Left hemicolectomy; AR: Anterior resection; DRM: Distal Resection Margin;

3. Postoperative characteristics

Postoperative complication and recovery are summarized in Table 4. There were no statistical difference with postoperative complication between OCS and MIS. In postoperative recovery, time to first flatus (4.19 vs 3.12 days in colon cancer, 3.91 vs 2.57 days in rectal cancer, $P=0.009$, $P=0.01$), time of starting diet (8.44 vs 5.41 days in colon cancer, 5.57 vs 2.53 days in rectal cancer, $P<0.001$ each), length of hospital stay (20.25 vs 11.38 days in colon cancer, 22.55 vs 12.84 days in rectal cancer, $P=<0.001$, $P=0.003$) were significantly shorter in MIS group than in OCS group.

Table 4. Postoperative complications and recovery

		Colon			Rectum			
		OCS (n=55)	MIS (n=56)	P value	OCS (n=33)	MIS (n=38)	P value	
Postoperative complications	Overall	14 (25.5%)	10 (17.9%)	0.331	16 (48.5%)	13 (34.2%)	0.222	
	Anastomotic leakage	0	0		2	2		
	Bleeding	0	0		0	2		
	Ileus & Obstruction	3	1		6	1		
	Urinary dysfunction	3	6		3	5		
	Wound dehiscence	3	0		4	1		
	Others	5	3		1	2		
	Time to first flatus (day)	Mean ± SD	4.19 ± 1.42	3.12 ± 1.45	0.009	3.91 ± 1.6	2.57 ± 1.09	0.01
	Time to start diet (day)	Mean ± SD	8.44 ± 2.80	5.41 ± 2.76	<0.001	5.57 ± 1.83	2.53 ± 0.8	<0.001
Length of hospital stay (day)	Mean ± SD	20.25 ± 15.09	11.38 ± 5.61	<0.001	22.55 ± 14.34	12.84 ± 12.32	0.003	
	Recur							
	Total	8 (14.5%)	4 (7.1%)	0.209	7 (21.2%)	7 (18.4%)	0.768	
	Systemic	8	4		6	7		
	Local	0	0		1	0		

Others:

colon OCS – pneumonia 2, ICU psychosis 1, peripancreatic abscess 1, chyle 1,

colon MIS – Rt. MCA infarction 1, pneumonia 1, small bowel hernia 1

rectum OCS - pneumonia 1

rectum MIS – anastomosis stenosis 1, pneumonia 1

4. Survival analysis

Figure 1 and 2 shows OS and DFS in rectal cancer and colon cancer, between OCS and MIS. Median follow up period was 30 months in rectal cancer patients and 32 months in colon cancer patients. There were 60.5% (n=43) rectal cancer patients and 45% (n=50) colon cancer patients who have received adjuvant chemotherapy after surgery. Total 14 patients have recurred in rectal cancer. 13 patients were systemic recur cases, and only 1 patient was local recur case. In colon cancer, total 12 patients recurred and all of them were systemic recur cases. However, there were no statistical differences in both OS and DFS. Rectal cancer OS rate was 75.6% in OCS and 72.8% in MIS. Colon cancer OS was 83.8% in OCS and 80.9% in MIS. Meanwhile, DFS in rectal cancer was 72% in OCS and 73.4% in MIS. DFS in colon cancer was 85.2% in OCS and 90.9% in MIS.

In rectal cancer, 7 patients in OCS group and 8 patients in MIS group expired. In colon cancer, 12 patients in OCS group and 10 patients in MIS group expired. There were no statistical differences between two groups.

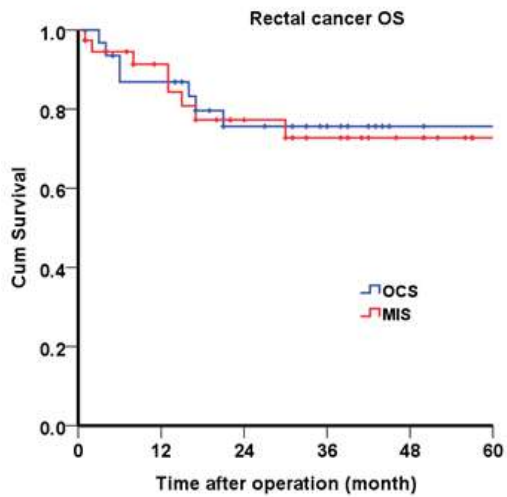


Fig 1A. Overall survival of rectal cancer. 3-year overall survival rates were 75.6% in OCS and 72.8% in MIS. ($P = 0.861$)

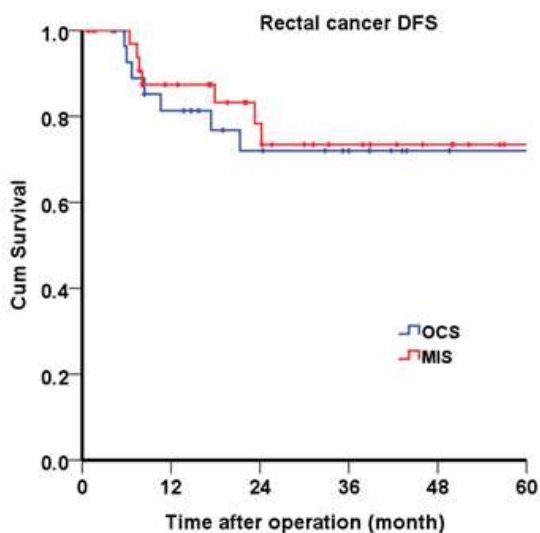


Fig 1B. Disease free survival of rectal cancer. 3-year disease free survival survival rates were 72% in OCS and 73.4% in MIS. ($P = 0.739$)

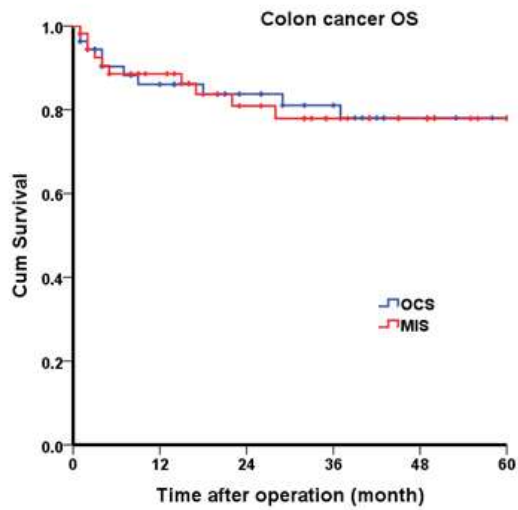


Fig 2A. Overall survival of colon cancer. 3-year overall survival rates were 83.8% in OCS and 80.9% in MIS. ($P = 0.972$)

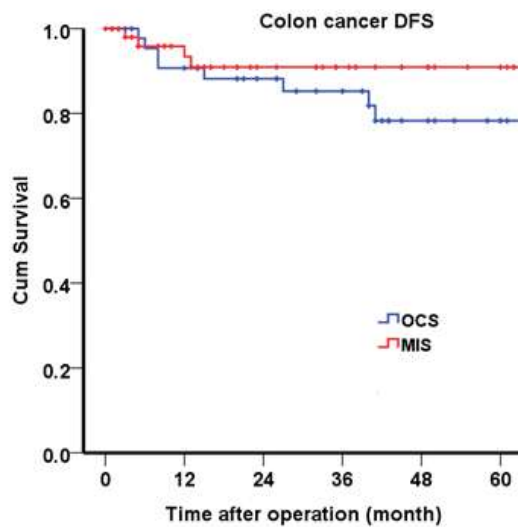


Fig 2B. Disease free survival of colon cancer. 3-year disease free survival survival rates were 85.2% in OCS and 90.9% in MIS. ($P = 0.739$)

IV. DISCUSSION

This study shows that minimally invasive surgery in colorectal cancer surgery could be applied to elderly patients aged over 75 with acceptable morbidity and long-term oncologic outcomes compared to open conventional surgery. Many literatures provide comparable oncologic and perioperative result of MIS to OCS and the feasibility of MIS (10-12). Moreover, studies including old age patients report comparable rate of postoperative complication in colorectal surgery. (13). Fujii et al reported favorable short-term surgical results of MIS as lower complication, ileus, amount of blood loss, and duration of surgery compared to OCS in elderly CRC patients (14). Chautard et al. also reported 178 patients matched case-control study of laparoscopic colorectal surgery between elderly (≥ 70 years) and younger (< 70 years). Overall postoperative complications and hospital stay was comparable between two groups, but cardiopulmonary comorbidities were significantly more frequent in elderly patients (80% versus 33%, $p < 0.001$). (15) In our study, similar results have shown, as postoperative complications revealed no statistical difference between MIS group and OCS group in colon cancer and rectal cancer. However, results show the trend of more wound problem, ileus and obstruction in OCS group. Longer incision and greater exposure of peritoneum in OCS compared to MIS might have affected the result. There are some concerns about safety of laparoscopic surgery associated with carbon oxide pneumoperitoneum and steep

head down positioning, which is related to cardiopulmonary complications, but those complications also showed no significant differences, which is recorded as “others”.

With early postoperative outcomes, such as shorter hospital stay and tolerable early feeding was possible in MIS group. This result is also provided in other studies as well (16-18). Our result suggests that elective MIS in elderly patients can be also performed safely compared to OCS.

Oncologic outcome showed no significant difference between MIS group and OCS group in both rectal and colon cancer. Total recur rate showed two times higher between MIS (7.1%) and OCS (14.5%) in colon cancer. However, as the sample size was small, this difference has shown no significant statistical difference. Ker-Kan Tan et al reported significant higher morbidity and mortality rates in octogenarian colorectal cancer patients, but most of them (92%, n= 187) were treated with open surgery and 40.7% of patients (n=83) underwent surgery in emergency status (19). Hamaker ME et al reported that utilization of laparoscopic approach reduced mortality rates, particularly in elderly, within 2.1 % for 1 year mortality. (20) Antonious SA et al presented meta-analysis of 66,483 colorectal patients with age over 65 treated with laparoscopic surgery and provided data of decreased mortality, overall morbidity and respiratory complications. (21) These results support that performing elective MIS colorectal surgery is feasible and safe in both short term and long term outcomes compared with OCS.

There are some limitations in this study. First, this study is retrospective study in single institution. Second, this study was not performed in case-controlled comparison between MIS and OCS. However, patient's characteristics were similar which helped to overcome the selection bias.

V. CONCLUSION

Applying MIS to elderly CRC patients is comparable to OCS. It is an effective procedure for elderly patients within short term complications, also with OS and DFS.

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ABSTRACT(IN KOREAN)

고령의 대장암 및 직장암 환자에서
미세침습수술 방법의 효용성

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한운대

대장암 및 직장암은 이제는 흔한 질병으로 근치적 수술이 치료에 반드시 필요하다. 그러나 점차 고령환자가 늘어남에 따라 젊은 환자에 비해 수술적 치료에 의한 합병증 등의 위험성을 고려하지 않을 수 없게 되었다. 최근에는 로봇 수술이나 복강경 수술 같은 미세침습수술이 늘어나게 되면서 이러한 수술방법이 고령환자에게 적용 시 기존의 개복수술과 비교하여 어떠한 차이가 있는지 알아보려고 하였다. 강남 세브란스 병원에서 2005년 1월부터 2011년 12월까지 대장암 혹은 직장암으로 수술을 받은 75세 이상의 고령환자들을 대상으로 조사를 하였고, 임상병리적 변수들과 외과적 치료 성적을 후향적으로 분석하였다. 환자군은 총 182명으로, 대장암 환자는 111명, 직장암 환자는 71명이었으며 이들을 각각 개복수술군과 미세침습수술군으로 나누어 분석하였다. 대장암과 직장암 모두에서 개복수술군과 미세침습수술군 간의 성별, 나이, 신체질량지수, 마취 전 평가 등에서는 통계학적 유의성이 없었다. 수술 관련 인자와 병리학적 결과에서는 수술 시간, 수술 중 수혈 여부, 림프관 침윤, 병기, 암의 크기, 적출된

림프절 수에서 두 군간의 통계학적 차이가 없었다. 또한 직장암에서 따로 측정된 말단절제연과 직장암의 위치 또한 통계학적 차이가 없었다. 대장암에서만 병리학적 분화도와 수술 방법의 차이가 개복수술군과 미세침습수술군 간의 유의한 차이를 보였다. ($p=0.044$, $p=0.006$) 수술 후 합병증은 대장암과 직장암 모두에서 미세침습수술군과 개복수술군 간의 유의한 차이가 없었으며 회복 시 수술 후 첫 가스 배출, 첫 식사 시작, 총 재원일수에서 미세침습수술군이 통계학적으로 유의하게 빨랐다.(대장암: $p=0.009$, $p<0.001$, $p<0.001$, 직장암: $p=0.01$, $p<0.001$, $p=0.003$) 재발 정도 또한 대장암과 직장암 모두에서 두 군간의 통계학적 차이가 없었다. 전체생존율과 무병생존율에서 또한 대장암과 직장암 모두에서 두 군간의 통계학적 차이가 없었다. 이처럼 복강경 수술과 로봇 수술 같은 최신 수술방법은 수술 후 단기적 합병증 및 장기적 암 치료 성적에 있어서도 기존 개복수술에 비해 떨어지지 않으므로, 75세 이상의 고령환자에게도 충분히 적용시킬 수 있는 수술방법으로 생각된다.

핵심되는 말 : 대장암, 직장암, 고령환자, 미세침습수술