

Long-term Results after Laparoscopic Resection for Colorectal Cancer within a Fast-track Regimen in the Elderly: A Prospective Study

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Abstract: *Introduction:* Trials of laparoscopic surgery for colorectal cancer in elderly with co-morbidity are needed. The aim of the present study was to evaluate the oncologic outcome after laparoscopic resection for non-metastatic colorectal cancer within a fast-track regimen comparing patients ≥ 75 years of age to patients < 75 years of age.

Methods: A total of 55 patients were laparoscopically operated upon for non-metastatic colorectal cancer in February 2001- March 2003. Twenty-nine patients were ≥ 75 years old and 26 were younger. All patients had a perioperative fast-track regimen. They were followed up for median 60 months.

Results: The two age groups were comparable with regard to sex distribution, operative procedures and cancer stage. The co-morbidity (ASA score) was higher in the elderly group ($p=0.05$) as well as the perioperative complication rate, 24 vs. 15% ($p=0.3$). The five-year overall survival was 66% in the elderly group vs. 69% in the younger group ($p=0.9$). The disease-free survival was 62 vs. 69%, respectively ($p=0.1$). The recurrence rate was 7 vs. 19%, respectively ($p=0.2$). For all the patients together the recurrence rate was 13% with no significant differences between the stage groups ($p=0.4$).

Conclusion: Laparoscopic surgery and fast-track regimen together seem to have a beneficial effect on long-term oncologic outcome in the elderly.

Keywords: Laparoscopy, fast-track surgery, colorectal cancer, elderly.

INTRODUCTION

The beneficial short-term effect of laparoscopic colorectal cancer surgery in elderly people with regard to reductions in length of hospital stay, morbidity and mortality rates is shown in several studies [1-4]. A recent Cochrane analysis of long-term results of laparoscopic colorectal cancer resection concluded that laparoscopic surgery for colon cancer is a safe procedure with a survival rate equal to survival after open surgery, but trials that also include elderly patients with co-morbidity are needed [5]. In a multivariate analysis of potential risk factors for intra- and postoperative complications in 1316 elective laparoscopic colorectal procedures it was shown that age ≥ 75 years was a significant risk for intra- and postoperative complications [6]. It has also been shown that the presence of postoperative complications not only affects the short-term results of resection of colorectal cancer, but the long-term oncologic outcomes are also adversely affected in open surgery [7]. Thus, in spite of laparoscopic colorectal surgery has a beneficial short term effect with regard to complications compared to open surgery, the complication rate is supposed to increase in older age because of co-morbidity and for that reason a poorer oncologic result could be expected in cancer surgery. However, in a single study of laparoscopic resection for colorectal cancer in 101 selected octogenarians the long-term oncologic outcomes seemed favourable [8]. Furthermore, laparoscopic surgery

combined with a fast-track regimen may further improve the postoperative course for the patients by further reducing the postoperative complications and decreasing the length of stay in hospital without compromising the surgical outcome [9].

The aim of the present study was to evaluate the oncologic long-term results after laparoscopic resection for non-metastatic colon cancer within a fast-track regimen in an unselected cohort of patients comparing the patients ≥ 75 years of age to patients < 75 years of age.

METHODS

In the period from February 2001 to March 2003, 55 patients were laparoscopically operated upon for non-metastatic colon cancer at Department of Colorectal Surgery, Hillerød Hospital. All the operations were performed by the same surgeon. Operative procedures, adjuvant treatment as well as short-term results of the operations have been published earlier [10]. All patients had a perioperative fast-track regimen as first suggested by Kehlet and co-workers [11]. Our setup was the same as described by Hammer *et al.* in their recent article about implementation of such a regimen into daily practice [12]. The regimen contained: no preoperative bowel cleansing, no drains nor tubes, mobilization and normal meal the evening on the day of surgery, epidural analgesia, oral laxatives, and a planned discharge on postoperative day 3.

The characteristics of the patients with regard to age, sex, ASA (American Society of Anesthesiologists) score, operative procedure and stage (according to TNM classification),

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Table 1. Characteristics of Patients with Non-Metastatic Colon Cancer with Regard to Sex, Age, American Society of Anesthesiologists (ASA) Score, Operative Procedure, Stage (According to TNM Classification), Intra- and Postoperative Complications and Postoperative Hospital Stay in Patients ≥ 75 Years and < 75 Years, respectively

	Patients ≥ 75 years (N=29)	Patients < 75 years (N=26)	P value
Age (yr)			
(median, range)	79 (75-90)	70 (60-74)	<0.0001
Sex*			
(female/male)	17/12 (59/41)	15/11 (58/42)	0.95
ASA score*			0.05
Score 1	0 (0)	2 (8)	
Score 2	15 (52)	17 (65)	
Score 3	14 (48)	7 (27)	
Operative procedure*			0.91
Right hemicolectomy	15 (52)	11 (42)	
Left hemicolectomy	2 (7)	2 (8)	
Sigmoid colectomy	6 (21)	6 (23)	
Rectosigmoid resection	6 (21)	7 (27)	
Stage*			0.31
I	6 (21)	5 (19)	
II	16 (55)	10 (39)	
III	7 (24)	11 (42)	
Intra- and postoperative Complications*	7 (24)	4 (15)	0.32
Postoperative hospital stay (days)(median, range)	5 (2-10)	5 (2-30)	0.20

*Numbers in brackets are percentages.

intra- and postoperative complications and postoperative hospital stay in the two age groups (≥ 75 years and < 75 years, respectively) are shown in Table 1. All patients were followed up according to a pre-established protocol which included medical history, physical examination and laboratory studies including serum carcinoembryonic antigen (CEA) levels 1 and 3 months after surgery and hereafter once a year, where abdominal ultrasonography and chest x-ray or computed tomography of chest and abdomen were performed, as well. The median follow-up was 60 months (range, 6-78).

Statistical Analyses

Non-parametric statistics were used, inclusive χ^2 -test, Mann-Whitney test, Kaplan-Meier analysis and log rank test. Statistical significance was set at $P < 0.05$.

RESULTS

Patient Characteristics

There were no significant differences between the two age groups of patients with regard to sex distribution, operative procedures or stage (Table 1). Not surprisingly, a tendency was found in the elderly group towards a higher ASA score ($p=0.05$). The perioperative complication rate was also higher in the elderly group (24% versus 15%), but the differ-

ence was not statistically different ($p=0.32$) (Table 1). The 30-day mortality was 2% (1 patient in the group < 75 years).

Survival

Five-year oncologic outcomes with regard to overall survival, disease-free survival and recurrence in the two groups are shown in Table 2. The overall survival was nearly similar: 66% in the elderly group and 69% in the younger group ($p=0.9$) (Fig. 1). The disease-free survival was 62% and 69%, respectively ($p=0.1$). For all the patients the overall survival was 69% and the disease-free survival 67%. The recurrence rate for the elderly patients was 7% versus 19% in the younger group, but the difference was not significant. The recurrence rates for all patients together with regard to the different stage groups were 0% for stage I, 15% for stage II and 17% for stage III. The differences were not significant ($p=0.4$). The recurrence rate for all the patients together was 13%.

DISCUSSION AND CONCLUSION

A meta-analysis of four randomized studies (Barcelona, COST, COLOR and CLASICC) with 1536 patients left for analysis showed that laparoscopically assisted colectomy for cancer was oncologically safe compared to the open approach [13]. This was confirmed in a recent Cochrane review

Table 2. Tumor Recurrence and Survival

	Patients > 75 years (N=29)	Patients < 75 years (N=26)	P value
Overall survival (%)	19 (66%)	18 (69%)	0.9
Disease-free survival (%)	18 (62%)	18 (69%)	0.1
Causes of death			
Perioperative mortality	1 (3%)	0 (0%)	0.9
Tumor progression	1 (3%)	5 (19%)	0.1
Others	8 (28%)	3 (12%)	0.1
Tumor recurrence (%)	2 (7%)	5 (19%)	0.2

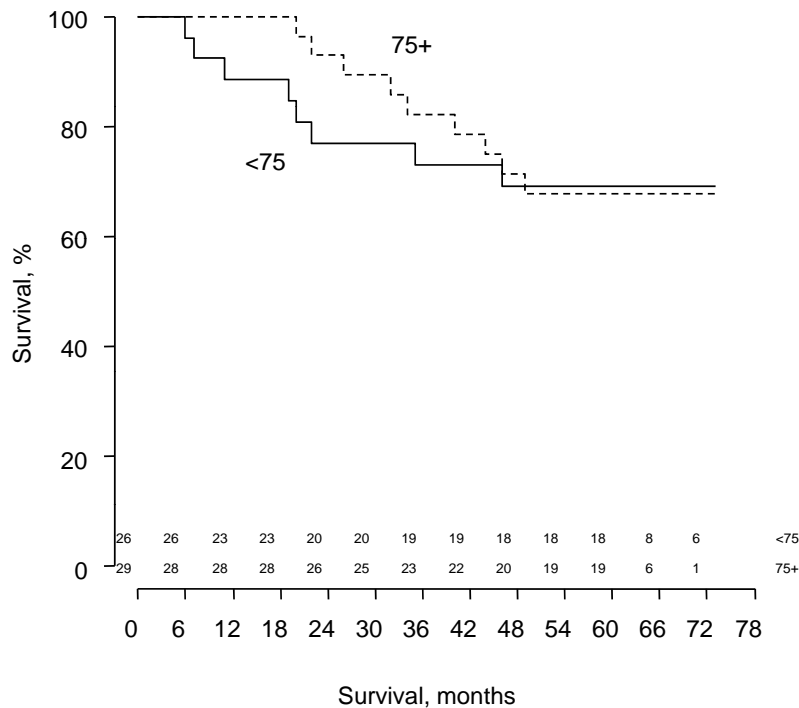


Fig. (1). Overall survival in two groups of patients: ≥ 75 years old and < 75 years old. The number of patients at risk are shown at the bottom.

of long-term results of laparoscopic colorectal cancer resection involving 3346 patients [5]. The Cochrane analysis concluded that trials also including elderly patients with comorbidity were needed, since the study population then would resemble the general population more closely. In the Barcelona study of Lacy *et al.* [14] the median age of the patients was 68 and 71 years in the laparoscopic and open group, respectively ($p=0.02$). Co-morbidity was not mentioned. In the COST study the median age was 70 and 69 years in the two groups, respectively, and 86% of the patients were in the ASA groups 1 or 2. In the COLOR trial the median age was 71 years and patients in ASA groups 1 and 2 were approximately 80% in both the laparoscopic and open group. Finally, in the CLASICC trial the mean age was 69 years and the WHO performance status was in the categories 0 or 1 in nearly 90% of the patients. Thus, the patients from these studies to a certain extent seem selected excluding the elderly patients with a high co-morbidity. In the present study the median age in the elderly patients was 79 years and only 52% was in ASA groups 1 or 2 opposite to the younger

group of patients which was more similar to the patients from the above mentioned randomized trials with a median age of 70 years and ASA score 1 or 2 in 73% of the patients. The overall mortality in the Danish population in the age group of 70-80 years old inhabitants is the double of the 60-70 years old (16% versus 7%) in a five years period [15]. Therefore, it is remarkable that the outcome with regard to overall mortality is almost similar in the two groups and comparable to the outcomes from the randomized studies, also. Thus, the overall mortality in the Barcelona study [14] was 36% compared to 34% in the elderly group in the present study, while the cancer-related mortality in the present study in the elderly was 6% against 16% in the Barcelona study. The distribution of stages and interventions was fairly identical in the two studies.

In the Barcelona study [14] a survival benefit of laparoscopic surgery was seen in patients with stage III tumors. Correspondently, in the present study no difference was found in the recurrence rate between stage II and III patients

and the overall recurrence rate was equal to or even better than the rate in the laparoscopic group in the Barcelona study (13 versus 18%). A possible explanation for this could be the lesser suppression of the immune system in laparoscopic surgery [16,17]. Surgery itself is believed to increase the risk of recurrence by releasing tumor cells into circulation, decreasing antiangiogenic factors, increasing growth factors, and causing immunosuppression. These risk factors are transitory, and the fate of residual disease is probably decided within days; therefore the immediate postsurgical period appears to play a disproportional role in determining long-term recurrence [17]. In a systematic review of enhanced recovery programmes in colonic surgery it was shown that the morbidity was significantly lower than for conventional regimens [18]. It has also been shown that the presence of perioperative complications adversely affects the long-term oncologic outcome [7]. Thus, the beneficial oncologic result in the present study could be a combined effect of laparoscopic surgery and the enhanced recovery programme. In this context it should be mentioned that the median postoperative hospital stay in the present study was 5 days and not 3 days as planned, maybe due the relatively high comorbidity of the patients. A similar difference between planned and real discharge is seen in other studies, as well, but the important factor is probably that the principles for the fast-track regimen has been followed [9,12].

Patients with major co-morbidities including elderly often are denied laparoscopic colorectal resections because they are thought to be at too "high risk". Nevertheless, several studies as mentioned earlier have shown a beneficial short-term effect of laparoscopic colorectal cancer surgery in elderly people [1-4]. A recent paper dealing with redefining contraindications to laparoscopic colorectal resection for high-risk patients has concluded that in experienced hands, laparoscopic colorectal surgery can be performed safely for these patients and argued against using parameters of increased age, morbid obesity, high ASA class, or preoperative radiation alone as contraindications to even complex laparoscopic colorectal procedures [19].

The present study has some limitations in the small number of partly selected patients not being randomized to its two groups, but in conclusion it seems that laparoscopic surgery and fast-track regimen together have a beneficial effect on long-term oncologic results in colorectal cancer surgery in the elderly. However, further studies of the laparoscopic approach in elderly patients with co-morbidity are needed, as well as studies of the oncologic effect of enhanced recovery programmes, which for the time being are totally lacking.

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