

Long-term survival following elective colon cancer surgery in the aged. A population-based cohort study

S. Niemeläinen* , H. Huhtala†, A. Ehrlich‡, J. Kössi§, E. Jämsen¶**†† and M. Hyöty*

*Department of Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital, Tampere, Finland, †Faculty of Social Sciences, Tampere University, Tampere, Finland, ‡Central Hospital of Central Finland, Jyväskylä, Finland, §Päijät-Häme Central Hospital, Lahti, Finland, ¶Centre of Geriatrics, Tampere University Hospital, Tampere, Finland, **Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland, and ††Gerontology Research Center (GEREC), Tampere, Finland

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Abstract

Aim The number of colorectal cancer patients increases with age. Long-term data support personalized management due to heterogeneity within the older population. This registry- and population-based study aimed to analyse long-term survival, and causes of death, after elective colon cancer surgery in the aged, focusing on patients who survived more than 3 months postoperatively.

Methods The data included patients ≥ 80 years who had elective surgery for Stage I–III colon cancer in four Finnish centres. The prospectively collected data included comorbidities, functional status, postoperative outcomes and long-term survival. Univariate and multivariate Cox regression analysis were conducted to determine factors associated with long-term survival.

Results A total of 386 surgical patients were included, of whom 357 survived over 3 months. Survival rates for all patients at 1, 3 and 5 years were 85%, 66% and 55%, compared to 92%, 71% and 59% for patients alive 3 months postoperatively, respectively. Higher age, American Society of Anesthesiologists (ASA) score ≥ 4 , Charlson Comorbidity Index ≥ 6 , tumour Stage III, open compared to laparoscopic surgery and severe

postoperative complications were independently associated with reduced overall survival. Higher age (hazard ratio 1.97, 1.14–3.40), diabetes (1.56, 1.07–2.27), ASA score ≥ 4 (3.27, 1.53–6.99) and tumour Stage III (2.04, 1.48–2.81) were the patient-related variables affecting survival amongst those surviving more than 3 months postoperatively. Median survival time for patients given adjuvant chemotherapy was 5.4 years, compared to 3.3 years for patients not given postoperative treatment.

Conclusions Fit aged colon cancer patients can achieve good long-term outcomes and survival with radical, minimally invasive surgical treatment, even with additional chemotherapy.

Keywords Colon cancer, surgery, aged patients, long-term outcome

What does this paper add to the literature?

This register-based cohort study shows that aged colon cancer patients who are physically and functionally fit to survive surgery can achieve acceptable long-term outcomes and survival with radical surgical treatment and additional chemotherapy.

Introduction

Colorectal cancer is the second most diagnosed malignancy in Finland, and the third most diagnosed in the world [1,2]. The age-standardized incidence of colorectal cancer has globally increased 9.5%, and in Finland 17.3%, between the years 1990 and 2017. The global burden of colorectal cancer is expected to grow by 60%

by 2030, to more than 2.2 million new cases and 1.1 million deaths [2]. As the population ages, older people are increasingly diagnosed with colorectal cancer [3]. Between 2013 and 2017, 26% of Finnish colorectal cancer patients were aged 80 years or older at the time of diagnosis [1].

Surgery is the cornerstone of treatment for colorectal cancer [4]. The increased number of older people results in more operations for colorectal cancer in this group [5]. Current studies show comparable disease-specific long-term survival rates for all age groups,

Correspondence to: Susanna Niemeläinen, Department of Surgery, Tays Hatanpää, PO Box 2000, 33521 Tampere, Finland.
E-mail: susanna.niemelainen@pshp.fi

which advocates for surgery with curative intent [5–7]. Conversely comorbidities, disability and the occurrence of severe postoperative complications are strongly associated with reduced short-term survival after surgery [8]. Thus, heterogeneity within the older population and differences in physical and cognitive condition make it impossible to base decision-making only on chronological age; some will survive just as younger adults, whereas others experience increased postoperative morbidity and reduced overall survival [9].

If patients survive the first year after surgery, they have reasonably good long-term survival [10]. Patients with more comorbidities have compromised postoperative outcomes [11,12]. Older patients value outcomes with good quality of life [13]. In a recent study from Italy, the authors call for studies focusing on long-term functional outcomes, to provide reliable information to patients on what to expect from cancer surgery [14]. This is important because informing older patients of the risk factors for postoperative morbidity, and diminished long-term outcomes, is essential for shared decision-making regarding surgical and non-surgical treatments [15].

The aim of this study was to analyse the long-term survival and causes of death in a consecutive population-based cohort of aged patients having colon cancer surgery. Because postoperative complications are a major risk factor of short-term mortality [8], the focus in this study was especially on the patients who survived at least 3 months after surgery.

Patients and Materials

Colon cancer patients aged 80 years and older at the time of surgery and operated in four Finnish public hospitals during 2005–2016 were included. Two of the hospitals were tertiary referral centre hospitals and two were small volume secondary care hospitals. These hospitals are responsible for colon cancer surgery in their catchment areas (100 000–250 000 inhabitants, total 750 000 inhabitants). As all colon cancer surgery in Finland is performed in public hospitals independent of social class or insurance status, the materials can be considered representative at population level.

Patients with metastatic or recurrent disease and palliative or emergency surgery were excluded. Data were extracted from prospective local colorectal databases and completed from hospital records. The dates and causes of death were obtained from the Death Certificate Register of Statistics Finland, which registers all deaths in Finland [16]. The duration of survival was calculated from the date of surgery to the date of death or to the closure of follow-up on 31 December 2018.

Recorded variables included age, living and functional status, comorbidities, modified Charlson Comorbidity Index (CCI) [17], surgical and postoperative outcomes, colon cancer recurrences or metastasis, overall survival and, for those who survived > 3 months after surgery, date and cause of death. Details of the patients' baseline characteristics and operative variables included in the study have been presented previously [8]. The diagnosis of colon cancer, operative treatment and postoperative surveillance were performed according to the standards of the study hospitals and national guidelines [18]. The postoperative complications were graded with Clavien–Dindo classification [19]. Clinical follow-up was continued for 5 years after surgery, or until death. Personal follow-up was arranged for patients considered too unfit or frail to attend a routine follow-up programme.

The data analysis focused on those patients who survived more than 3 months after the primary cancer operation, intended to exclude the effect of early postoperative mortality. The primary outcome measure was overall survival, reported separately for all patients and for those who survived over 3 months after the primary treatment.

Associations between the categorical variables were tested with the chi-squared test or the Fisher exact test, as appropriate. Survival and recurrence rates were calculated from the time of primary surgery using the Kaplan–Meier method. Log minus log plots were used to validate the proportional hazard assumption. Univariate and multivariate analyses of the factors influencing overall survival were carried out using binary logistic regression. All variables that were statistically significant in the univariate model were included in the multivariate model. Statistical analyses were performed using SPSS version 23 (IBM, Armonk, NY, USA).

The study was approved by the ethics committee of Pirkanmaa Hospital District, Tampere, Finland (R18188).

Results

A total of 386 patients fulfilled the inclusion criteria. Their median age was 83 years (range 80–96 years) and 56.2% were women. Most of the surgeries were right-sided hemicolectomy ($n = 261$, 67.6%), and two-thirds of the surgeries were laparoscopic ($n = 252$, 65.3%). 154 patients (40%) had postoperative complications with 92 (24%) patients having surgical and 62 (16%) non-surgical complications. According to the Clavien–Dindo classification, 69 (18%) patients had severe complications (Grades III–V). Reoperation was needed in 39 patients (10%), most commonly due to anastomotic

leakage ($n = 19$). Three per cent of patients who lived at home before surgery were discharged to nursing homes. Postoperative adjuvant chemotherapy was given to 80 patients (21%), the majority of whom ($n = 67$, 84%) had Stage III disease. Of patients with Stage II tumour, 7.3% (13/176) received adjuvant treatment mainly due to a pT4 tumour. The detailed data of patients' baseline and clinical characteristics as well as complications and early postoperative outcomes have been described elsewhere [8]. Of the study population, 29 patients died within 3 months after surgery, mainly due to cardiovascular causes or surgical complications. The baseline and clinical characteristics of the 357 patients who survived over 3 months after surgery are shown in Table 1.

Follow-up and survival

Of the whole cohort, a total of 232 patients (60.1%) died during the follow-up period (median follow-up 6.3 years, ranging from 1 day to 14 years). Therefore, the overall survival rate was 39.9%. The 1-year survival rate was 85% (327/386), and the 3- and 5-year rates were 66% (255/386) and 55% (211/386), respectively. The median overall survival time was 5.4 years (95% CI 4.72–6.08). For patients who survived the first 3 months after surgery ($n = 357$), the 1-, 3- and 5-year survival rates were 92%, 71% and 59%, respectively. The median survival time for these patients was 5.9 years (95% CI 5.31–6.48). Age-related survival for patients who survived over 3 months after surgery is presented in Fig. 1. The overall median survival time for patients with no complications was 5.9 years (95% CL 5.30–6.50), with mild complications 5.2 years (3.87–6.49) and with severe complications 1.8 years (0.18–3.34). The survival analysis of complications in patients who survived over 3 months after operation is shown in Fig. 2, and the respective survival proportions at 1, 3 and 5 years are shown in Table 2.

Recurrences and adjuvant chemotherapy

The recurrence rate for the whole study population was 17.6% (68 patients). Distant recurrence rate was 15%, involving liver (27 patients), lung (12 patients), peritoneum (17 patients) and pelvis (two patients). Local recurrence rate was 2.6% (10 patients). According to the Union for International Cancer Control stages, recurrences developed in 8.2%, 8.4% and 32.9% of Stage I, Stage II and Stage III tumours, respectively. The recurrence rate was 8.5% (33 patients) at 1 year, 14.7% (57 patients) at 3 years and 16.1% (62 patients) at 5 years. The median survival times with tumour Stages I, II and

III in the whole study cohort were 5.9 (95% CI 4.16–7.58), 6.5 (4.67–8.37) and 3.5 years (2.04–5.01), respectively. The comparable figures for patients who survived over 3 months postoperatively were 5.9 years (95% CI 4.65–7.15) for Stage I, 7.5 years (5.89–9.19) for Stage II and 4.4 years (3.03–5.75) for Stage III.

Patients with Stage III disease who received postoperative adjuvant chemotherapy had a median survival time of 5.4 years, compared to 2.3 years for those who did not receive postoperative chemotherapy ($P = 0.001$, log-rank). The respective figures for patients who survived over 3 months after surgery were 5.4 and 3.3 years ($P = 0.025$, log-rank). The survival analysis for patients who survived over 3 months with different tumour stages (I–III) is shown in Fig. 3.

Causes for death

The most frequent causes of death within 3 months after surgery ($n = 29$) were cardiopulmonary (55%) and surgery-related (24%) factors. Of the deaths that occurred after 3 months of surgery ($n = 203$), 30% were due to colon cancer, 44% due to cardiopulmonary reasons and 10% due to dementia. The causes of death within and after 3 months of surgery are shown in Fig. 4.

Factors influencing survival

Univariate Cox regression analysis showed that higher age, living in a nursing home, diabetes, coronary disease, congestive heart failure, chronic renal insufficiency, American Society of Anesthesiologists (ASA) score ≥ 3 , CCI score ≥ 6 , open compared to laparoscopic operation, tumour stage and severe postoperative complications were associated with poor survival after surgery. Multivariate Cox regression survival analysis showed that higher age [hazard ratio (HR) 1.08, 95% CI 1.04–1.13, $P < 0.001$], living in a nursing home (HR 1.54, 1.03–2.30, $P = 0.034$), ASA score ≥ 4 (HR 2.62, 1.32–5.21, $P = 0.006$), CCI score ≥ 6 (HR 1.47, 1.07–2.01, $P = 0.018$), tumour Stage III (HR 1.88, 1.40–2.52, $P < 0.001$), open compared to laparoscopic surgery (HR 1.41, 1.05–1.88, $P = 0.020$) and severe postoperative complications (HR 2.11, 1.49–2.99, $P < 0.001$) were independently associated with diminished overall survival in the whole cohort. For patients who survived over 3 months after surgery these same patient-related variables, except chronic renal insufficiency and type of surgery, were significant in univariate Cox regression analysis. In multivariate Cox regression analysis age ≥ 90 years, living in a nursing home, diabetes, ASA score ≥ 4 and tumour Stage III were independently associated with diminished survival. Detailed

Table 1 Baseline and clinical characteristics of patients who survived at least 3 months after surgery.

| | <i>n</i> , median | % (range) |
|----------------------------------|-------------------|-----------|
| Gender ratio (female/male) | 205/152 | 57/43 |
| Age (years) | 83.0 | (80–96) |
| 80–84 | 233 | 65 |
| 85–89 | 96 | 27 |
| ≥ 90 | 28 | 8 |
| Type of living | | |
| Home | 313 | 87.7 |
| Nursing home | 31 | 8.7 |
| Not known | 13 | 3.6 |
| Aid at home | | |
| No | 145 | 40.6 |
| Yes | 109 | 30.5 |
| Not known | 103 | 28.9 |
| BMI (kg/m ²) | 25.0 | 15.4–40.6 |
| < 25 | 150 | 42.0 |
| 25–29.9 | 102 | 28.6 |
| 30– | 45 | 12.6 |
| Not available | 60 | 16.8 |
| ASA score | | |
| 2 | 34 | 9.5 |
| 3 | 248 | 69.5 |
| 4 | 70 | 19.6 |
| Not known | 5 | 1.4 |
| CCI (modified) | | |
| 4–5 | 227 | 63.6 |
| 7–12 | 130 | 36.4 |
| Procedure | | |
| Right-sided colectomy | 250 | 70.0 |
| Left-sided colectomy | 93 | 26.0 |
| Other colonic resection | 14 | 4.0 |
| Type of surgery | | |
| Open | 120 | 33.6 |
| Laparoscopy | 204 | 57.1 |
| Conversion | 33 | 9.2 |
| Postoperative complications | | |
| None | 229 | 64.1 |
| Minor complications (CD I–II) | 83 | 23.2 |
| Major complications (CD III–V) | 45 | 12.6 |
| Length of hospitalization (days) | 7 | 2–58 |
| Reoperation | 32 | 9.0 |
| Readmission | 23 | 6.4 |
| TNM stage | | |
| 1 | 46 | 12.9 |
| 2 | 176 | 49.3 |
| 3 | 135 | 37.8 |
| Number of lymph nodes | 15 | 0–71 |
| Postoperative adjuvant therapy | 80 | 22.4 |
| Stage III (<i>n</i> = 135) | 67 | 43.3 |

ASA, American Society of Anesthesiologists; BMI, body mass index; CCI, Charlson Comorbidity Index; CD, Clavien–Dindo classification.

analysis data of patients who survived over 3 months are shown in Table 3.

Discussion

Treatment decisions for colon cancer in the aged population have become extremely important as the number of these patients rises due to increased life expectancy. The results of this register- and population-based cohort study of 386 electively operated, non-metastatic colon cancer patients aged ≥ 80 years suggest that, for physically and cognitively fit patients, surgical treatment with curative intent can lead to similar long-term survival as for younger patients. This is especially true when the patients survive the critical first 3 months after surgery.

The study hospitals had standardized protocols for treatment and follow-up based on national evidence based medicine guidelines [18], and the nationwide registers ensured comprehensive death records. There were no statistical differences in patients' baseline characteristics, operative outcomes and tumour characteristics between the four operating hospitals. Considering the older population, it was valuable that we could identify preoperative morbidity and living arrangements, although functional ability could not be clarified in detail. Supporting earlier observations [20,21], postoperative complications were common (40%) and almost half of them (45%) were severe (Grade III–V according to the Clavien–Dindo classification). As complications are a major predictor of short-term mortality [8], we intended to analyse their continued effect among the patients who survived the early postoperative period, through longer-term follow-up. Among all patients with severe complications (Clavien–Dindo III–V), 1-year and overall survival were 45% and 27.5%. However, those who survived the first three postoperative months had survival rates comparable to those with no or mild complications. Thus, preventing complications through preoperative health evaluation is essential, especially for high-risk patients [8].

In 2018, the median life expectancy for Finns aged 80 years and over was 9.9 years for women and 8.2 years for men [22]. In our study (with an average age of 83 years), the overall median survival time was 5.4 years, increasing to 5.9 years when early postoperative deaths were excluded. The 5-year survival rates (54.7% in the whole cohort and 59.1% in patients who survived over 3 months after surgery) are comparable or slightly higher than the figures reported in the EURO-CARE-5 study (49% for colon cancer patients aged 75 years or older and 57% for all ages) [23]. The large SEER database study from the USA shows similar

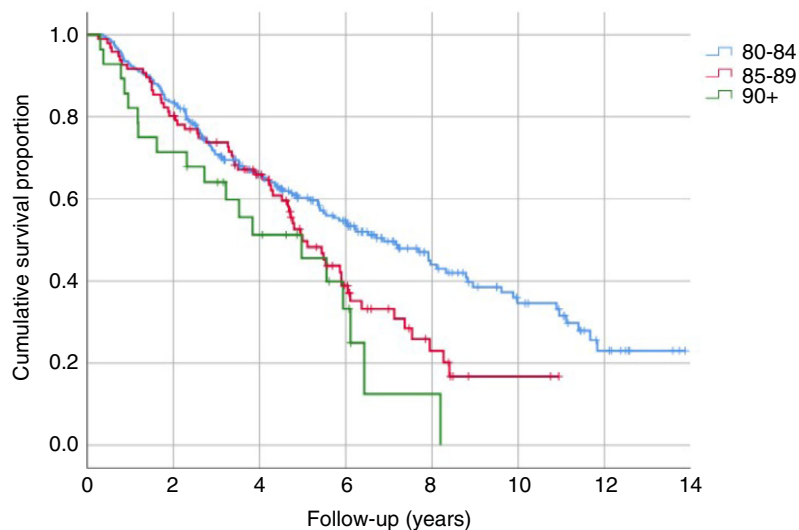


Figure 1 Kaplan–Meier analysis of age-related overall survival in patients who survived at least 3 months after surgery ($P = 0.005$, log-rank).

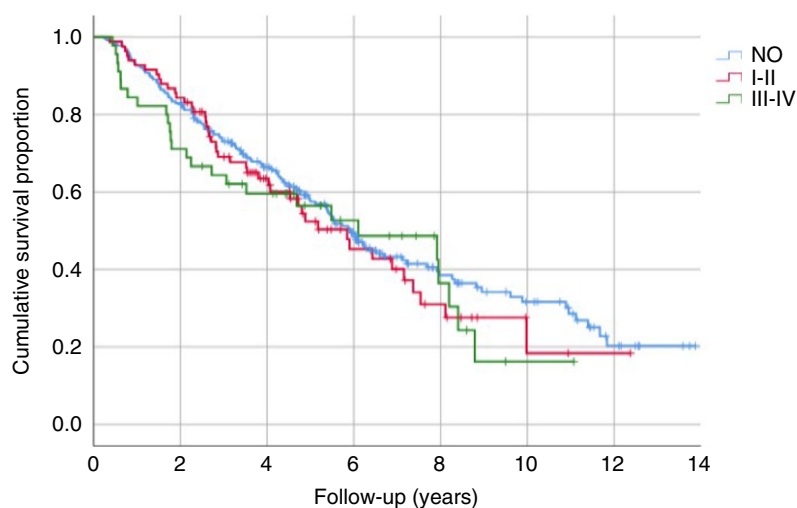


Figure 2 Kaplan–Meier analysis of overall survival in patients who survived at least 3 months after surgery with and without complications graded with Clavien–Dindo classification ($P = 0.575$, log-rank).

survival rates for Stage II rectal cancers for patients aged 80 years or over treated with resection and neoadjuvant therapy as for younger patients [24], and patients treated non-operatively had lower survival than those who underwent surgery. In an English study, which included non-operatively treated Stage I–III colorectal cancer patients over 80 years, the average life expectancy following diagnosis was 1.5 years, and only 20% of patients survived over 3 years [25]. The non-operative outcomes are as essential as surgical outcomes to patients. The authors thus suggested that cancer surgery is not beneficial for frail aged patients and has higher risks for postoperative morbidity and reduced survival

than for physically and mentally fit patients. Conversely, in a recent case series study from the UK, elective surgical management of carefully selected nonagenarian (over 90 years) patients enabled the majority to return to the same functional level of care following discharge [26].

Altogether, our data and previous reports show that elderly patients who are fit enough to survive the early perioperative period have similar overall survival times to younger patients. On the other hand, severe ill-health, living in a nursing home and the occurrence of complications considerably impair long-term survival. Generally, chronic conditions and multiple morbidities increase mortality and prolonged hospitalizations in the

Table 2 Survival proportion at 1, 3 and 5 years of patients who survived at least 3 months after surgery.

| | Survival proportion (%) | | | | | | | |
|---|-------------------------|------|--------|----------------|---------|----------------|---------|----------------|
| | <i>n</i> | % | 1 year | <i>P</i> value | 3 years | <i>P</i> value | 5 years | <i>P</i> value |
| Gender | | | | | | | | |
| Male | 152 | 42.6 | 93.4 | 0.337 | 69.7 | 0.556 | 59.2 | 1.000 |
| Female | 205 | 57.4 | 90.2 | | 72.7 | | 59.0 | |
| Age | | | | | | | | |
| 80–84 | 233 | 65.3 | 92.7 | 0.163 | 71.2 | 0.605 | 62.2 | 0.238 |
| 85–89 | 96 | 26.9 | 91.7 | | 74.0 | | 54.2 | |
| ≥ 90 | 28 | 7.8 | 82.1 | | 64.3 | | 50.0 | |
| BMI (kg/m²) | | | | | | | | |
| < 25 | 150 | 42.0 | 91.3 | 0.966 | 70.7 | 0.972 | 55.3 | 0.516 |
| 25–29.9 | 102 | 28.6 | 92.2 | | 70.6 | | 61.8 | |
| ≥ 30 | 45 | 12.6 | 91.1 | | 68.9 | | 62.2 | |
| Type of living | | | | | | | | |
| Home | 313 | 87.7 | 92.0 | 0.729 | 72.2 | 0.098 | 60.1 | 0.051 |
| Nursing home | 31 | 8.7 | 90.3 | | 58.1 | | 41.9 | |
| Aid at home | | | | | | | | |
| None | 145 | 40.6 | 93.8 | 0.751 | 84.1 | < 0.001 | 73.1 | < 0.001 |
| Relatives | 58 | 16.2 | 91.4 | | 58.6 | | 44.8 | |
| Other | 51 | 14.3 | 92.2 | | 58.8 | | 41.2 | |
| Hospital admissions | | | | | | | | |
| < 6 months | | | | | | | | |
| No | 266 | 74.5 | 91.4 | 0.643 | 70.3 | 0.499 | 58.6 | 0.977 |
| One or more | 85 | 23.8 | 92.9 | | 74.1 | | 58.8 | |
| ASA score | | | | | | | | |
| 2 | 34 | 9.5 | 97.1 | 0.463 | 76.5 | 0.001 | 76.5 | 0.002 |
| 3 | 248 | 69.5 | 90.7 | | 76.2 | | 61.7 | |
| 4 | 70 | 19.6 | 91.4 | | 54.3 | | 42.9 | |
| CCI (modified) | | | | | | | | |
| 4–6 | 302 | 84.6 | 92.1 | 0.434 | 73.8 | 0.023 | 61.9 | 0.016 |
| 7–12 | 55 | 15.4 | 89.1 | | 58.2 | | 43.6 | |
| Type of operation | | | | | | | | |
| Laparoscopy | 204 | 57.2 | 94.1 | 0.140 | 74.5 | 0.312 | 61.8 | 0.282 |
| Conversion | 33 | 9.2 | 87.9 | | 69.7 | | 63.6 | |
| Open | 120 | 33.6 | 88.3 | | 66.7 | | 53.3 | |
| Postoperative complications | | | | | | | | |
| None | 229 | 64.1 | 92.6 | 0.180 | 73.4 | 0.451 | 59.8 | 0.933 |
| CD I–II | 83 | 23.2 | 92.8 | | 69.9 | | 57.8 | |
| CD III–V | 45 | 12.6 | 84.4 | | 64.4 | | 57.8 | |
| Tumour stage | | | | | | | | |
| I | 45 | 12.9 | 95.7 | 0.031 | 78.3 | < 0.001 | 58.7 | 0.003 |
| II | 176 | 49.3 | 94.3 | | 79.0 | | 67.6 | |
| III | 135 | 37.8 | 86.7 | | 59.3 | | 48.1 | |
| Postoperative adjuvant therapy (Stage III) | | | | | | | | |
| No | 68 | 50.4 | 83.8 | 0.449 | 51.5 | 0.080 | 39.7 | 0.059 |
| Yes | 67 | 49.6 | 89.6 | | 67.2 | | 56.7 | |

ASA, American Society of Anesthesiologists; BMI, body mass index; CCI, Charlson Comorbidity Index; CD, Clavien–Dindo classification.

elderly [27], and severe complications are more common in patients who have preoperative hospitalizations and who live in nursing homes [28]. Complications and

older age [29] are associated with lower health-related quality of life after cancer surgery. Thus, careful preoperative assessment of physical and cognitive fitness, and

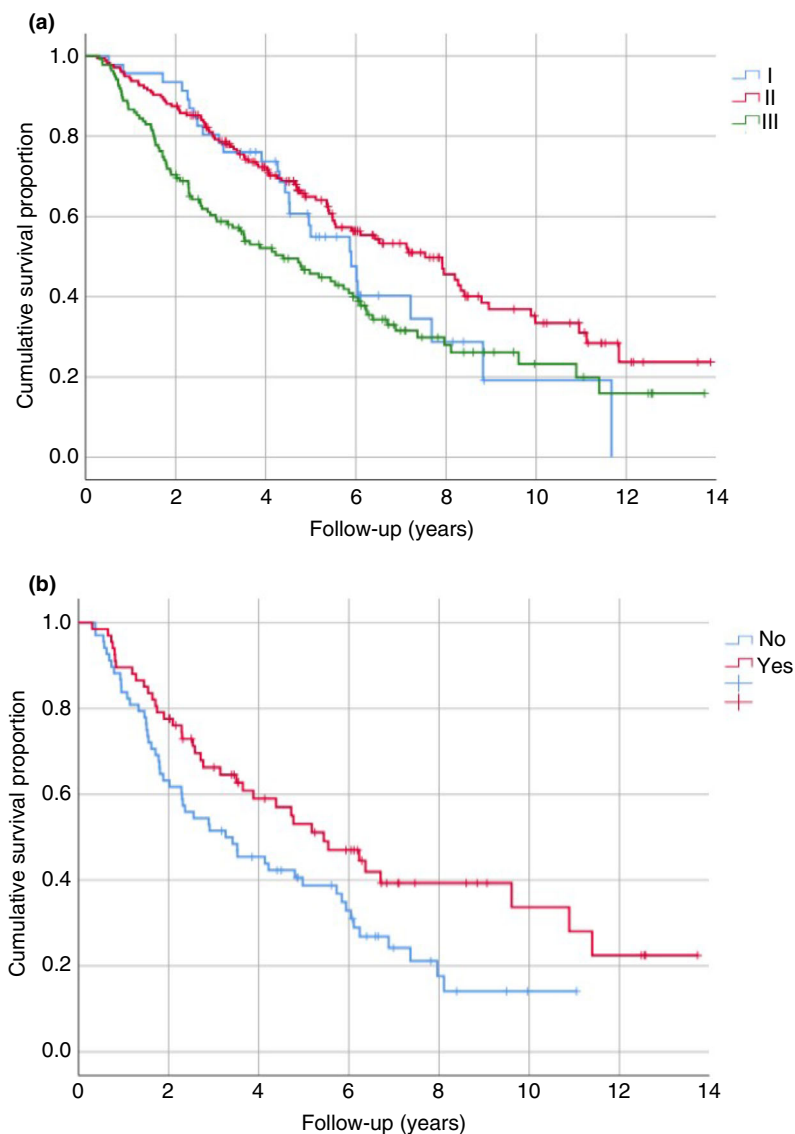


Figure 3 Kaplan–Meier analysis of overall survival in patients who survived at least 3 months after surgery, according to (a) tumour stage ($P = 0.002$, log-rank) and (b) adjuvant therapy ($P = 0.025$, log-rank).

the provision of accurate and clear information about treatment options, allows patients to participate in management decisions and contributes to good outcomes and long-term patient satisfaction and quality of life.

The leading causes of death in our cohort were cardiovascular (31%), colon cancer (28%), pulmonary (14%) and dementia (8.6%). Noticeably, colon cancer is not the most frequent cause of death in these older cancer patients. Diabetes, coronary artery disease and congestive heart failure were important predictors of mortality in very old age in a large Finnish follow-up study [27]. The same factors were significantly associated with reduced survival in our data. In the total study population, only 3.9% of patient deaths were

directly related to surgery, although patients with severe surgical complications had greatly reduced median survival (3.7 months) compared to patients with cardiopulmonary causes (2.9 years) [8]. However, those patients with severe surgical complications who survived more than 3 months had similar long-term outcomes to those without or with minor complications. In contrast, a Dutch study reported that severe postoperative complications were most predictive of diminished long-term survival [30].

Studies from Spain and Italy show that laparoscopy is safe in the older population with increased comorbidity and leads to better short-term outcomes than open procedures and equivalent long-term oncological

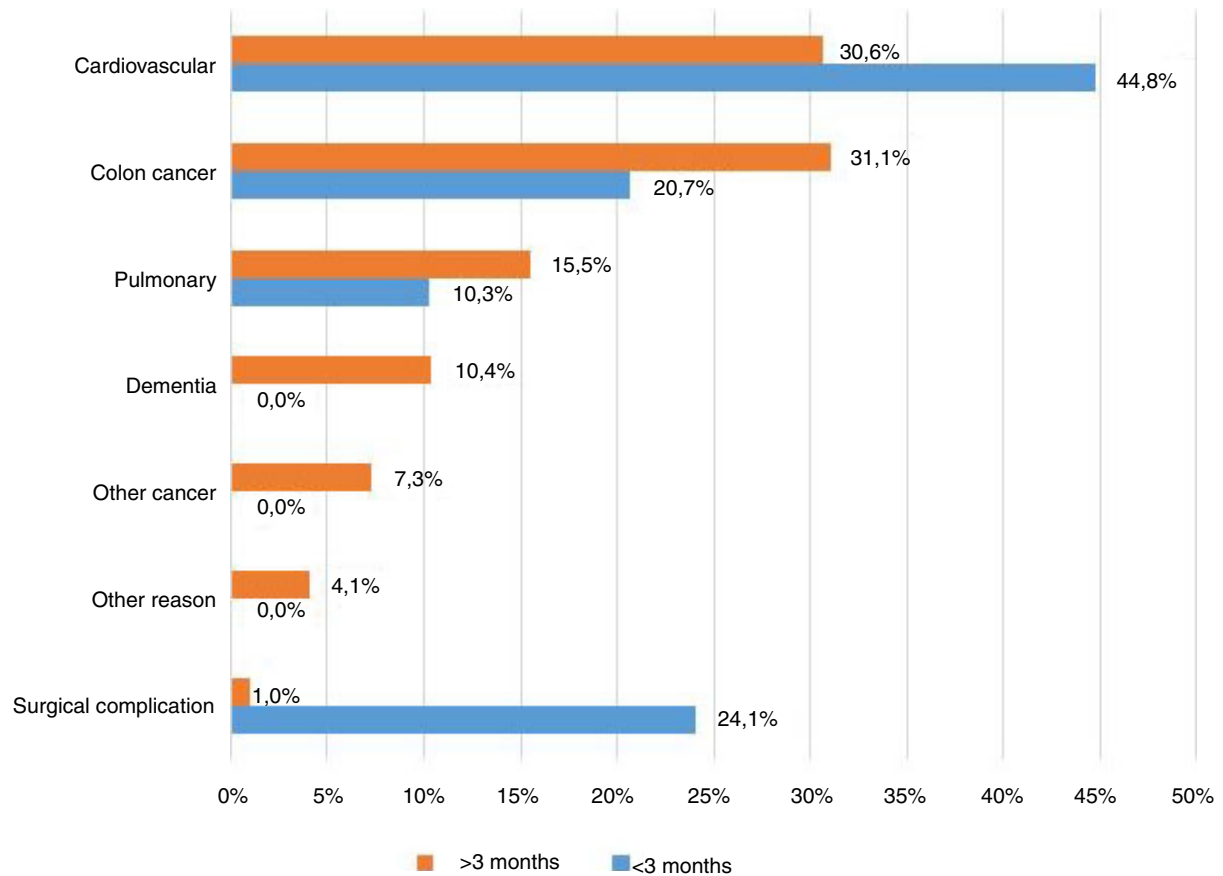


Figure 4 Causes of death within and after 3 months of surgery ($n = 29$ and $n = 193$).

outcomes [31,32]. A review article from the UK shows that age is not a risk factor or a limitation for laparoscopic colorectal surgery, and even very old patients may benefit from a minimally invasive approach [33]. In our study the overall median survival time for patients operated with a laparoscopic approach (5.8 years) was significantly better than survival after an open operation (4.4 years). The knowledge of the benefits of minimally invasive surgery has changed our study hospitals' practices, and laparoscopy is now considered the best approach for colon cancer surgery for aged patients.

Besides age, high comorbidity burden and complications, the only significant factor affecting survival was tumour stage. Long-term survival and recurrent disease depend on the stage of tumour [30]. Stage III disease is associated with diminished survival [4,30,34]. The recurrence rate was 17.6%, with Stage I 8.2%, Stage II 8.4% and Stage III 32.9%. The high proportion of Stage I recurrences may reflect the quality of individual pathology reports (lymph nodes counted 10–18 in four Stage I patients) or tumour biology. Otherwise the numbers correspond to recent studies from Sweden and

Denmark [35,36]. However, the real rate of recurrences in our series may have been higher, as further investigations and treatment may have been stopped by an unwilling patient or by a physician who considered a patient too frail or unfit. Some of the patients may have died from non-cancer-related causes while having recurrences. In contrast, patients with Stage III disease receiving adjuvant chemotherapy had significantly better overall survival rate compared to patients not having postoperative therapy, comparable to recent studies [37,38]. That finding suggests that, for patients fit enough to survive radical surgery, adjuvant chemotherapy is advisable.

There are some limitations to our study. Due to its retrospective nature, detailed information on daily physical and cognitive functional activity as well as the severity of the comorbidities could not be documented. Thus, patients with better health status were likely to be selected for operative treatment. Exact long-term data of cancer recurrences was not complete, as invasive investigations may not have been performed for physically and cognitively unfit patients. However, our

Table 3 Factors influencing survival with patients who survived at least 3 months after surgery (Cox regression analysis).

| | Univariate | | | Multivariate | | |
|-----------------------------------|------------|-----------|----------------|--------------|-----------|----------------|
| | HR | 95% CI | <i>P</i> value | HR | 95% CI | <i>P</i> value |
| Age (years) | | | | | | |
| 80–84 | 1 | | | | | |
| 85–89 | 1.45 | 1.06–1.99 | 0.020 | 1.29 | 0.91–1.83 | 0.148 |
| > 90 | 1.96 | 1.20–3.20 | 0.007 | 1.97 | 1.14–3.40 | 0.015 |
| Gender | | | | | | |
| Female | 1 | | | | | |
| Male | 1.12 | 0.84–1.48 | 0.450 | | | |
| Type of living | | | | | | |
| Home | 1 | | | 1 | | |
| Nursing home | 1.76 | 1.17–2.65 | 0.006 | 1.56 | 1.01–2.43 | 0.047 |
| Hospital admissions ≤ 6 months | | | | | | |
| No | 1 | | | | | |
| Yes | 1.06 | 0.76–1.46 | 0.746 | | | |
| BMI (kg/m ²) | | | | | | |
| < 25 | 1 | | | | | |
| 25–29.9 | 0.89 | 0.63–1.25 | 0.506 | | | |
| > 30 | 0.89 | 0.57–1.40 | 0.616 | | | |
| Diabetes | | | | | | |
| No | 1 | | | 1 | | |
| Yes | 1.45 | 1.05–2.01 | 0.026 | 1.56 | 1.07–2.27 | 0.022 |
| Hypertension | | | | | | |
| No | 1 | | | | | |
| Yes | 1.06 | 0.80–1.41 | 0.672 | | | |
| Coronary heart disease | | | | | | |
| No | 1 | | | 1 | | |
| Yes | 1.50 | 1.11–2.01 | 0.008 | 0.98 | 0.69–1.38 | 0.890 |
| Congestive heart failure | | | | | | |
| No | 1 | | | 1 | | |
| Yes | 1.65 | 1.04–2.63 | 0.033 | 1.24 | 0.69–2.21 | 0.470 |
| Arteriosclerosis obliterans (ASO) | | | | | | |
| No | 1 | | | | | |
| Yes | 0.710 | 0.22–2.27 | 0.563 | | | |
| Renal failure | | | | | | |
| No | 1 | | | | | |
| Yes | 1.61 | 0.97–2.69 | 0.067 | | | |
| Cerebral stroke | | | | | | |
| No | 1 | | | | | |
| Yes | 1.49 | 0.99–2.26 | 0.057 | | | |
| Atrial fibrillation | | | | | | |
| No | 1 | | | | | |
| Yes | 1.28 | 0.93–1.76 | 0.130 | | | |
| Chronic pulmonary disease | | | | | | |
| No | 1 | | | | | |
| Yes | 1.38 | 0.61–3.11 | 0.442 | | | |
| Rheumatic diseases | | | | | | |
| No | 1 | | | | | |
| Yes | 1.24 | 0.61–2.51 | 0.554 | | | |
| Dementia | | | | | | |
| No | 1 | | | | | |
| Yes | 1.22 | 0.79–1.89 | 0.378 | | | |

Table 3 (Continued).

| | Univariate | | | Multivariate | | |
|-----------------------------|------------|-----------|----------------|--------------|-----------|----------------|
| | HR | 95% CI | <i>P</i> value | HR | 95% CI | <i>P</i> value |
| Other cancer | | | | | | |
| No | 1 | | | | | |
| Prostate | 1.35 | 0.77–2.39 | 0.297 | | | |
| Breast | 1.02 | 0.45–2.32 | 0.957 | | | |
| Colorectal | 1.35 | 0.66–2.76 | 0.404 | | | |
| Urinary tract | 0.68 | 0.17–2.73 | 0.583 | | | |
| Gynaecology | 0.77 | 0.25–2.41 | 0.652 | | | |
| Other cancer | 1.68 | 1.02–2.77 | 0.043 | 0.94 | 0.51–1.75 | 0.849 |
| ASA score | | | | | | |
| 2 | 1 | | | 1 | | |
| 3 | 2.22 | 1.23–4.02 | 0.008 | 1.93 | 0.99–3.75 | 0.053 |
| 4 | 3.92 | 2.05–7.48 | < 0.001 | 3.27 | 1.53–6.99 | 0.002 |
| CCI (modified) | | | | | | |
| 4–5 | 1 | | | 1 | | |
| 6–12 | 1.68 | 1.26–2.22 | < 0.001 | 1.52 | 0.99–2.34 | 0.055 |
| Tumour stage | | | | | | |
| 1–2 | 1 | | | 1 | | |
| 3 | 1.61 | 1.23–2.12 | 0.001 | 2.04 | 1.48–2.81 | < 0.001 |
| Type of operation | | | | | | |
| Laparoscopy/conversion | 1 | | | 1 | | |
| Open | 1.35 | 1.02–1.78 | 0.038 | 1.37 | 1.00–1.88 | 0.051 |
| Postoperative complications | | | | | | |
| CD 0–II ^b | 1 | | | | | |
| CD III–V | 1.17 | 0.78–1.77 | 0.450 | | | |
| Surgical complication | | | | | | |
| No | 1 | | | | | |
| Yes | 1.23 | 0.88–1.71 | 0.228 | | | |
| Non-surgical complication | | | | | | |
| No | 1 | | | | | |
| Yes | 1.04 | 0.71–1.54 | 0.836 | | | |

ASA, American Society of Anesthesiologists; BMI, body mass index; CCI, Charlson Comorbidity Index; CD, Clavien–Dindo classification; HR, hazard ratio.

findings propose that surgery in aged patients diagnosed with colon cancer can lead to acceptable long-term outcomes, comparable with younger patients.

In conclusion, this study extends our earlier findings [8] and suggests that aged colon cancer patients who are physically and functionally fit to survive surgery can achieve acceptable long-term outcomes and survival with radical surgical treatment and additional chemotherapy. Further prospective studies are required to identify patients who are at risk of complications and able to recover from them as well as the effects of colon cancer surgery on the quality of life in long-term follow-up.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

References

- 1 Finnish Cancer Registry. www.cancerregistry.fi (accessed March 2020).
- 2 GBD 2017 Colorectal Cancer Collaborators. The global, regional, and national burden of colorectal cancer and its attributable risk factors in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Gastroenterol Hepatol* 2019; **4**: 913–33.
- 3 Neuman HB, O'Connor ES, Weiss J *et al.* Surgical treatment of colon cancer in patients aged 80 years and older: analysis of 31,574 patients in the SEER-Medicare database. *Cancer* 2013; **119**: 639–47.
- 4 Merkel S, Weber K, Matzel KE, Agaimy A, Göhl J, Hohenberger W. Prognosis of patients with colonic carcinoma before, during and after implementation of complete mesocolic excision. *Br J Surg* 2016; **103**: 1220–9.
- 5 Jafari MD, Jafari F, Halabi WJ *et al.* Colorectal cancer resections in the aging US population: a trend toward decreasing rates and improved outcomes. *JAMA Surg* 2014; **149**: 557–64.
- 6 Mothes H, Bauschke A, Schuele S, Eigendorff E, Altdorf-Hofmann A, Settmacher U. Surgery for colorectal cancer in elderly patients: how can we improve outcome? *J Cancer Res Clin Oncol* 2017; **43**: 1879–89.
- 7 Oh BY, Huh JW, Kim HC *et al.* Oncologic outcome of colorectal cancer patients over age 80: a propensity score-matched analysis. *Int J Colorectal Dis* 2018; **33**: 1011–8.
- 8 Niemeläinen S, Huhtala H, Ehrlich A, Kössi J, Jämsen E, Hyöty M. Risk factors of short-term survival in the aged in elective colon cancer surgery: a population-based study. *Int J Colorectal Dis* 2020; **35**: 307–15.
- 9 Papamichael D, Audisio RA, Glimelius B *et al.* Treatment of colorectal cancer in older patients: International Society of Geriatric Oncology (SIOG) consensus recommendations 2015. *Ann Oncol* 2015; **26**: 463–76.
- 10 Bos ACRK, Kortbeek D, van Erning FNT *et al.* Postoperative mortality in elderly patients with colorectal cancer: the impact of age, time-trends and competing risks of dying. *Eur J Surg Oncol* 2019; **45**: 1575–83.
- 11 Sheridan J, Walsh P, Kevans D *et al.* Determinants of short- and long-term survival from colorectal cancer in very elderly patients. *J Geriatr Oncol* 2014; **5**: 376–83.
- 12 Tominaga T, Nonaka T, Takeshita H *et al.* The Charlson Comorbidity Index as an independent prognostic factor in older colorectal cancer patients. *Indian J Surg* 2018; **80**: 54–60.
- 13 Souwer ETD, Oerlemans S, van de Poll-Franse LV *et al.* The impact of colorectal surgery on health-related quality of life in older functionally dependent patients with cancer – a longitudinal follow-up study. *J Geriatr Oncol* 2019; **10**: 724–32.
- 14 Giannotti C, Sambuceti S, Signori A *et al.* Frailty assessment in elective gastrointestinal oncogeriatric surgery: predictors of one-year mortality and functional status. *J Geriatr Oncol* 2019; **10**: 716–23.
- 15 Samuelsson KS, Egenvall M, Klarin I, Lökk J, Gunnarsson U, Iwarzon M. The older patient's experience of the healthcare chain and information when undergoing colorectal cancer surgery according to the enhanced recovery after surgery concept. *J Clin Nurs* 2018; **27**: e1580–e88.
- 16 Lahti RA, Penttilä A. The validity of death certificates: routine validation of death certification and its effects on mortality statistics. *Forensic Sci Int* 2001; **115**: 15–32.
- 17 Chang CM, Yin WY, Wei CK *et al.* Age-adjusted Charlson Comorbidity Index score as a risk measure of perioperative mortality before cancer surgery. *PLoS One* 2016; **11**: e0148076.
- 18 HUS FICAN working committee. Finnish National Guidelines for the treatment of colorectal cancer. 2019.
- 19 Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; **240**: 205–13.
- 20 Fagard K, Casaer J, Wolthuis A *et al.* Postoperative complications in individuals aged 70 and over undergoing elective surgery for colorectal cancer. *Colorectal Dis* 2017; **19**: O329–38.
- 21 Aquina CT, Mohile SG, Tejani MA *et al.* The impact of age on complications, survival, and cause of death following colon cancer surgery. *Br J Cancer* 2017; **116**: 389–97.
- 22 Statistics Finland. www.tilastokeskus.fi (accessed March 2020).
- 23 Holleczeck B, Rossi S, Domenic A *et al.* Ongoing improvement and persistent differences in the survival for patients with colon and rectum cancer across Europe 1999–2007. Results from the EURO-CARE-5 study. *Eur J Cancer* 2015; **51**: 2158–68.
- 24 Bhangu A, Kiran RP, Audisio R *et al.* Survival outcome of operated and non-operated elderly patients with rectal cancer: a Surveillance, Epidemiology, and End Results analysis. *Eur J Surg Oncol* 2014; **40**: 1510–6.
- 25 Bethune R. What happens when we do not operate? Survival following conservative bowel cancer management. *Ann R Col Surg* 2016; **98**: 409–12.
- 26 Au S, Venham NT, Yalamarathi S, Manimaran N. Colorectal cancer outcomes in nonagenarian patients: a case series. *Int J Surg* 2018; **55**: 139–44.
- 27 Halonen P, Raitanen J, Jämsen E, Enroth L, Jylhä M. Chronic conditions and multimorbidity in population aged 90 years and over: associations with mortality and long-term care admission. *Age Ageing* 2019; **48**: 564–70.
- 28 Okabe H, Ohsaki T, Ogawa K *et al.* Frailty predicts severe postoperative complications after elective colorectal surgery. *Am J Surg* 2019; **217**: 677–81.
- 29 Brown SR, Mathew R, Keding A, Marshall HC, Brown JM, Jayne DG. The impact of postoperative complications on long-term quality of life after curative colorectal cancer surgery. *Ann Surg* 2014; **259**: 916–23.
- 30 Weerink LBM, Gant CM, van Leeuwen BL, de Bock GH, Kouwenhoven EA, Faneyte IF. Long-term survival in octogenarians after surgical treatment for colorectal cancer:

- prevention of postoperative complications is key. *Ann Surg Oncol* 2018; **25**: 3874–82.
- 31 Vallribera Valls F, Landi F, Espín Basany E *et al.* Laparoscopy-assisted versus open colectomy for treatment of colon cancer in the elderly: morbidity and mortality outcomes in 545 patients. *Surg Endosc* 2014; **28**: 3373–8.
- 32 Roscio F, Boni L, Clerici F, Frattini P, Cassinotti E, Scandroglio I. Is laparoscopic surgery really effective for the treatment of colon and rectal cancer in very elderly over 80 years old? A prospective multicentric case–control assessment. *Surg Endosc* 2016; **30**: 4372–82.
- 33 Devoto L, Celentano V, Cohen R, Khan J, Chand M. Colorectal cancer surgery in the very elderly patient: a systematic review of laparoscopic versus open colorectal resection. *Int J Colorectal Dis* 2017; **32**: 1237–42.
- 34 Tan KK, Koh FH, Tan YY, Liu JZ, Sim R. Long-term outcome following surgery for colorectal cancers in octogenarians: a single institution's experience of 204 patients. *J Gastrointest Surg* 2012; **16**: 1029–36.
- 35 Osterman E, Glimelius B. Recurrence risk after up-to-date colon cancer staging, surgery, and pathology: analysis of the entire Swedish population. *Dis Colon Rectum* 2018; **61**: 1016–25.
- 36 Bertelsen CA, Neuenschwander AU, Jansen JE *et al.* Disease-free survival after complete mesocolic excision compared with conventional colon cancer surgery: a retrospective, population-based study. *Lancet Oncol* 2015; **16**: 161–8.
- 37 Delgado MV, Serrano CS, de la Fuente EC *et al.* Efficacy of adjuvant chemotherapy for elderly patients with colon cancer. *Ann Oncol* 2018; **29**(Suppl 5): v65.
- 38 Kawamura H, Morishima T, Sato A, Honda M, Miyashiro I. Effect of adjuvant chemotherapy on survival benefit in stage III colon cancer patients stratified by age: a Japanese real-world cohort study. *BMC Cancer*. 2020; **20**: 19.