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ORIGINAL ARTICLE

The Clinical Frailty Scale is a useful tool for predicting postoperative complications following elective colon cancer surgery at the age of 80 years and above: A prospective, multicentre observational study

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Abstract

Aim: Identification of the risks of postoperative complications may be challenging in older patients with heterogeneous physical and cognitive status. The aim of this multicentre, observational study was to identify variables that affect the outcomes of colon cancer surgery and, especially, to find tools to quantify the risks related to surgery.

Method: Patients aged ≥80 years with electively operated Stage I–III colon cancer were recruited. The prospectively collected data included comorbidities, results of the onco-geriatric screening tool (G8), Clinical Frailty Scale (CFS), Charlson Comorbidity Index (CCI) and Mini Nutritional Assessment-Short Form (MNA-SF), and operative and postoperative outcomes.

Results: A total of 161 patients (mean 84.5 years, range 80–97, 60% female) were included. History of cerebral stroke (64% vs. 37%, $p = 0.02$), albumin level 31–34 g/l compared with ≥35 g/l (57% vs. 32%, $p = 0.007$), CFS 3–4 and 5–9 compared with CFS 1–2

(49% and 47% vs. 16%, respectively) and American Society of Anesthesiologists score >3 (77% vs. 28%, P = 0.006) were related to a higher risk of complications. In multivariate logistic regression analysis CFS ≥3 (OR 6.06, 95% CI 1.88–19.5, p = 0.003) and albumin level 31–34 g/l (OR 3.88, 1.61–9.38, p = 0.003) were significantly associated with postoperative complications. Severe complications were more common in patients with chronic obstructive pulmonary disease (43% vs. 13%, p = 0.047), renal failure (25% vs. 12%, p = 0.021), albumin level 31–34 g/l (26% vs. 8%, p = 0.014) and CCI >6 (23% vs. 10%, p = 0.034).

Conclusion: Surgery on physically and cognitively fit aged colon cancer patients with CFS 1–2 can lead to excellent operative outcomes similar to those of younger patients. The CFS could be a useful screening tool for predicting postoperative complications.

KEYWORDS

aged patients, clinical frailty scale, colon cancer, postoperative outcome, surgery

INTRODUCTION

Colorectal cancer is the second leading cause of cancer death and the fourth most diagnosed malignancy in the world [1]. The risk of developing colorectal cancer increases with age. Thus, as the world's population ages, the number of patients experiencing colorectal cancer rises [2]. Colorectal cancer surgery in the aged is considered high risk for postoperative complications and compromised functional recovery [3]. The incidence of adverse events with colon cancer surgery ranges from 20% to 76% [4–7] It is more significant with advancing age and frailty, identified as a greater vulnerability in physical and cognitive status [7,8].

Old people are a heterogeneous group of patients, so the risk of postoperative complications cannot be judged by chronological age alone [9]. Preoperative risk estimation of postoperative complications, recognition of frailty and the identification of patients at greater risk of unfavourable treatment consequences are essential for optimizing aged patients for surgery and thereby improving postoperative outcomes [10,11].

Tools used in the preoperative comprehensive geriatric assessment of onco-geriatric surgical patients are often time-consuming and require special training and knowledge of gerontology [12]. The Clinical Frailty Scale (CFS) has been developed for rapid frailty screening without the need for specific geriatric expertise or functional testing [13]. The only prospective study concerning the CFS and postoperative complications in older patients after elective colorectal cancer surgery concluded that frail patients (CFS ≥ 4) had more severe postoperative complications, leading to higher mortality rates [14]. Otherwise there is a lack of prospective studies in elective colon cancer surgery with aged patients focusing on preoperative frailty and postoperative complications.

This prospective observational multicentre study aimed to identify those characteristics of aged colon cancer patients that affect postoperative morbidity and mortality. Special attention was focused on screening tools such as the CFS and their relationship to postoperative outcomes in patients aged 80 years and above.

What does this paper add to the literature?

This study showed that aged patients have high morbidity rates after curative colon cancer surgery despite modern achievements in operative treatment. However, the fittest patients had acceptable and similar operative outcomes to younger patients. The Clinical Frailty Scale appears to be a beneficial screening tool for predicting these adverse events.

PATIENTS AND METHODS

Study design

A multicentre, prospective observational cohort study of patients aged 80 years or older with Stage I–III colon cancer was designed to analyse the impact of surgery on functional ability, complications and mortality along with the predictors of these outcomes. Nine Finnish hospitals participated in the study. The total catchment area was 3.88 million people, representing 70.4% of Finland's population. Treatment of colon cancer in Finland is performed by public health care services. Patients were treated at precise hospitals based on their place of residence, so the study provided a nationwide spectrum of operative management of colon cancer in the aged.

This study followed the STROBE guidelines [15] (Appendix S1 in the Supporting Information). The Ethics Committee of Tampere University Hospital and the institutional review board at each study site approved the study protocol (reference approval

number R19028). The study was registered in ClinicalTrials.gov (NCT03904121) in April 2019.

Participants

Recruitment was initiated in April 2019 and, for this study, continued until July 2020. All patients aged 80 years or over with recently diagnosed Stage I–III colon cancer and referred to surgical units for consideration of operative treatment were eligible to participate in the study. Patients were informed of the study and gave written informed consent. If the patient was cognitively impaired, consent was provided by a legally authorized representative or family member. Patients with metastatic disease, emergency operations or an expected life expectancy of less than 6 months were excluded. Patients who consented to the study but were treated nonoperatively or had metastatic or benign disease at surgery were also excluded from the present analysis.

Data collection

Data were collected prospectively in the electronic case record forms using the RedCap (Research Electronic Data Capture) database [16]. The primary investigator, who was the managing surgeon at each study site, was responsible for data collection. The primary investigator or research nurses at each study site were charged to ensure that the patient questionnaires (Appendix S2) were completed. Operative data and postoperative outcomes were gathered prospectively during the hospital stay and at follow-up visits. Patient questionnaires were collected before and 1 month after surgery at outpatient clinics and surgical follow-ups conducted either by telephone call or by mail.

The collected clinical data included patient physical and functional characteristics, results of the onco-geriatric screening tool G8 [17] and CFS [13], comorbidities, nutritional status and characteristics of surgical treatment (Appendix S3). Postoperative complications were defined and determined using the Clavien–Dindo classification (CD) graded from 0 to V [18]. Class III–V complications were considered severe. Tumours were staged according to the Union for International Cancer Control (UICC) TNM classification [19]. The number of positive lymph nodes (LNs) and the total number of LNs were recorded in every case. The LN ratio [20] was calculated by defining the proportion of metastatic LNs from the total number of LNs examined.

Definition of variables

Age was analysed in three groups: 80–84 years, 85–89 years and ≥90 years. Body mass index (BMI) was categorized into three groups: <24 kg/m^2, 24-29 kg/m^2 and ≥30 kg/m^2 [21].

The G8 score ranged from 0 to 17. Geriatric evaluation is recommended for patients whose score is ≤14 [17]. For analyses, patients were divided into three groups according to their G8 score: <12, 12-14 and >14.

The CFS was subdivided and analysed in three groups: very fit or fit (1–2), independent but not regularly active in daily life or vulnerable (3–4), and frail with severe limitations in daily activities (5–9) [13].

The ASA risk score [22] and age-adjusted CCI [23] were used as measures of anaesthesiologist, comorbidity burden and mortality risk. Based on the ASA score, patients were analysed in three ASA groups: 2, 3 and 4 (the lowest score was 2, as all patients were 80 years or older). CCI scores ranged from 4 to 15 (solid tumour was ignored, all patients received four points for their age). Patients were analysed in two CCI groups: ≤6 and >6.

The Mini Nutritional Assessment–Short Form (MNA-SF) classifies nutritional status as normal (scores >11), risk of malnutrition (8–11) or malnourished (<8) [24].

Patients with haemoglobin ≤120 g/l (cut-off selected for clinical utility) were considered to have anaemia. Albumin was analysed in three groups: ≤30, 31–34 and >34 g/l for clinical relevance. Renal function was categorized in three groups based on the estimated glomerular filtration rate (GFR) calculated using the CKD-EPI equation [25]: normal to mildly decreased (≥60 ml/min), mildly to moderately decreased (45–60 ml/min) or moderately to severely decreased (<45 ml/min) renal function.

The LN ratio was analysed in three groups: <10% (LN ratio 1), 10%–25% (LN ratio 2) and >25% (LN ratio 3).

Outcomes

The primary outcome measures were postoperative morbidity and mortality 30 days after primary treatment. The complications were graded by the CD classification [18]. Outcome measures were assessed during the hospital stay and at the 1 month clinical follow-up visits. Multiple complications occurring in the same patient were independently rated, and the highest CD grade experienced was used in the analyses.

Sample size

The sample size calculation for postoperative complications was based on earlier studies [4–7] showing an incidence of complications in fit patients of 21% and in frail patients of 48%. To identify twofold differences in complication rates with an α-value of 0.05 and 80% power, it was calculated that 96 patients needed to be recruited and analysed.

Statistical analysis

Percentages were used to describe demographic data and the occurrence of outcomes. The median and range were calculated for age, preoperative laboratory values, BMI, operation time and

perioperative blood loss. Associations between the categorical variables were tested with the chi-square-test or Fisher's exact test, when appropriate. Uni- and multivariate analysis of the factors influencing morbidity and mortality were carried out using logistic regression. Results are shown as odds ratios (ORs) with 95% confidence intervals (95% CIs). All variables that were statistically significant ($p < 0.005$) in the univariate model were included in the multivariate model. Statistical analyses were performed using SPSS version 26.

RESULTS

Patients and clinical characteristics

Of the 241 eligible patients, 180 (75%) consented to participate. Eleven patients were treated nonoperatively because of their age or personal refusal, reduced functional status or risk of anaesthesia due to severe comorbidities. Most of the patients treated nonoperatively were considered frail (CFS ≥ 5; 90%) and to have an increased risk of postoperative complications and recovery (G8 ≤ 14, 100%; ASA ≥ 3, 100%; CCI > 6, 70%). Eight patients were excluded because of metastatic or benign findings at operation or in the pathological sample. Figure 1 shows the patient flowchart.

Altogether 161 patients were included in the study. The median age was 84.5 years (range 80–97 years) and 60% were female. Most patients were classified as ASA 3 (67%) and had a CCI score ≤6 (62%). Almost all patients scored ≤14 (92%) in the G8 survey, and 77% were considered vulnerable or frail (CFS ≥ 3). Most of the patients (91%) were at risk of malnutrition or were malnourished (MNA-SF < 12). Table 1 shows the baseline patient characteristics.

TNM stages were as follows: Stage I, 29 patients (18%); Stage II, 86 patients (54%); Stage III, 45 patients (28%). The LN ratio was as follows: 84% ratio 1, 10% ratio 2 and 6% ratio 3. Postoperative adjuvant therapy was given to 27% (12/45) of the Stage III patients.

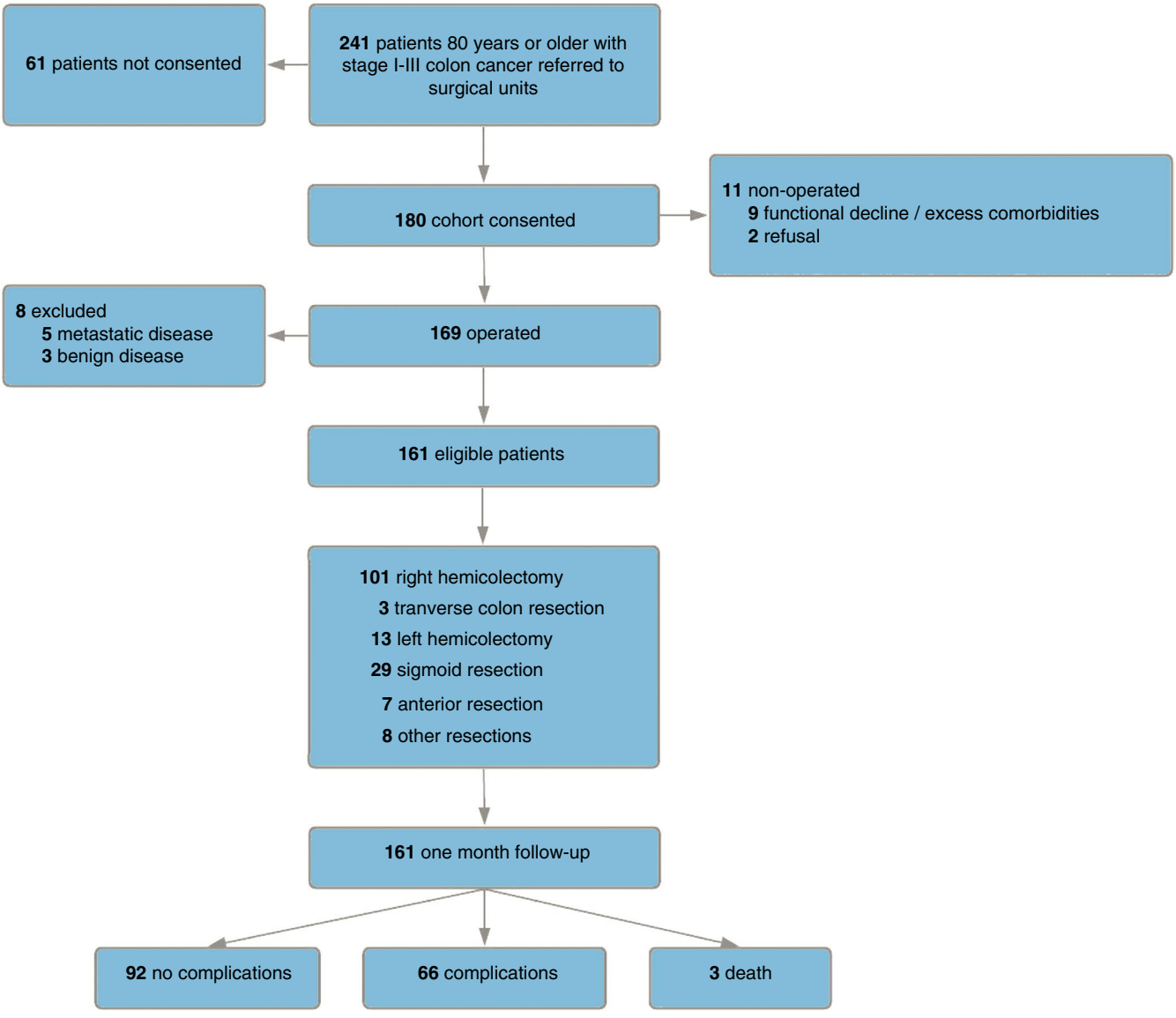

FIGURE 1 Patient flow-chart

TABLE 1 Baseline characteristics (n = 161)

	n or median	% or range
Gender		
Female	97	60.2
Male	64	39.8
Age (years)	85	80-97
80–84	91	56.5
85–89	48	29.8
≥90	22	13.7
BMI (kg/m^2)	25.7	16.5–40
<24	55	34.2
24–29	68	42.2
>29	38	23.6
Living status		
Home alone	86	53.4
Home with someone	72	44.7
Nursing home	3	1.9
Hospital admissions <6 months		
None	81	50.9
One or more	78	49.1
No. of medications		
<5	63	39.1
≥5	98	60.9
Comorbidities		
Hypertension	109	70.3
Cardiovascular disease	86	55.3
Diabetes	52	32.7
Renal failure	31	19.5
Cerebrovascular disease	22	13.8
Pulmonary disease	18	11.4
Dementia	14	9.1
Rheumatic disease	11	7.0
History of another cancer G8 score (0–17)	33	21.2
<12	74	46.0
12–14	74	46.0
>14	13	8.0
CFS (1–9)		
1–2	37	23.1
3–4	80	50.0
5–9	43	26.9
CCI (4–15)		
4–6	99	61.5
≥7	62	38.5
ASA score (2–4)		
2	40	25.5
3	105	66.9
4	12	7.6
MNA-SF (0–14)		
0–7 (malnutrition)	38	23.6
8–11 (risk of malnutrition)	109	67.7
≥12 (normal nutrition)	14	8.7
Haemoglobin (g/l)	112.5	66–169
≤120	106	66.3
>120	54	33.8
Albumin (g/l) (missing 16 values)	34.0	23–50
≤30	26	17.9
31–34	47	32.4
>34	72	49.7
Estimated GFR (ml/min)	61.0	19.8–93.1
<45	39	24.5
45–60	39	24.5
>60	81	51.0

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CCI, Charlson Comorbidity Index; CFS, Clinical Frailty Scale; GFR, glomerular filtration rate; MNA-SF, Mini Nutritional Assessment-Short Form.

Most of the operative procedures were performed for right-sided colon cancer (65%). An intended laparoscopic resection was performed in 122 patients (76%) and 15 cases (9.3%) were converted to open surgery for anatomical or technical reasons. The median operation time was 129 min (range 54–433 min) and median blood loss was 50 ml (range 0–2390 ml). The median length of stay in the operating hospital was 5 days (range 2–36 days). Ninety patients (56%) were discharged home with the remaining patients going to other hospitals or primary healthcare centre wards.

Morbidity and mortality

The overall postoperative morbidity was 41% (66/161), with 24% (39/161) of patients having surgical complications. The most common surgical complications were ileus (12%), anastomotic leakage (5%), superficial surgical site infection (3.6%) and wound dehiscence (2.5%). Four patients had iatrogenic bowel perforations and one patient had postoperative colon necrosis. Sixteen patients (10%) were reoperated on. The reasons for reoperations were anastomotic leakage (8/16), iatrogenic bowel perforation after the primary operation (4/16), wound dehiscence (2/16), colon necrosis after right hemicolectomy (1/16) and unclear abdominal infection (1/16). The most common nonsurgical complications were cardiovascular 6% (9/161) and pulmonary 8% (12/161). One patient had a massive cerebral stroke, causing permanent disability. Nine patients had both surgical and nonsurgical complications. According to the CD classification, 15% (24/161) of patients had severe complications. Table 2 shows

TABLE 2 Postoperative complications and mortality (n = 161)

	n	%
No complications	95	59.0
Complications (total)[a]	66	41.0
Postdischarge complications	5	3.1
Surgical complications	39	24.2
Postoperative ileus	20	12.4
Anastomotic leakage	8	5.0
Surgical site infection	6	3.6
Iatrogenic bowel perforation	4	2.5
Wound dehiscence	4	2.5
Surgical site bleeding	3	1.9
Colon necrosis	1	0.6
Nonsurgical complications	36	22.4
Respiratory failure/infection	12	7.5
Cardiovascular	9	5.6
Renal failure/urinary tract infection	5	3.1
Delirium	3	1.9
Thromboembolism	2	1.2
Cerebral stroke	1	0.6
Clavien–Dindo classification		
0	95	59.0
I–II	42	26.1
III–V	24	14.9
Thirty-day mortality	3	1.9

aNine patients with both surgical and nonsurgical complications.

postoperative complications and Figure 2 the incidence of complications compared with the CFS.

Readmission within 30 days of discharge occurred for 13 patients (8.1%). Nine had surgical and four had nonsurgical reasons for readmission. One patient needed reoperation because of new anastomotic leakage after primary relaparotomy with re-resection. The third operation was finished with formation of a protective stoma.

The overall 30-day mortality rate was 1.9% (3/161), but 8.3% (2/24) for those with CD grade III–IV complications. One patient died on the 23rd postoperative day after prolonged ileus and two reoperations due to wound dehiscence. One patient died on the 25th postoperative day after relaparotomy for anastomotic leakage and peritonitis. The third patient died on the 18th postoperative day from complications of ischaemic heart disease.

Predictors of postoperative complications

Postoperative complications were significantly more common in patients with a history of cerebral stroke (64% vs. 37%, p = 0.02), albumin level 31–34 g/l (57% vs. 32% in patients with albumin ≥35 g/l, p = 0.007), CFS 3–4 and 5–9 (49% and 47% vs. 16% in CFS 1–2, respectively) and ASA >3 (77% vs. 28%, p = 0.006). In patients with CFS 5–9, nonsurgical complications were more common than surgical complications (34% vs. 25%), whereas in patients with CFS 1–2 both types of complication were equally common (8% vs. 11%). Age, BMI, preoperative hospital admissions, polypharmacy, comorbidity burden, G8 score, nutritional status, anaemia, type of operation, duration of operation or operative blood loss were not associated with increased rates of complication. In multivariate logistic regression analysis CFS ≥3 (OR = 6.06, 95% CI 1.88–19.5, p = 0.003) and albumin level 31–34 g/l (OR = 3.88, 95% CI 1.61–9.38, p = 0.003) were significantly associated with postoperative complications. The area under the curve (AUC) for all complications was 0.747 (95% CI 0.67–0.83). Table 3 shows the predictors of postoperative complications.

Severe complications (CD III–V) were significantly more frequent in patients with chronic obstructive pulmonary disease (43% vs. 13%, p = 0.047), renal failure (25% vs. 12%, p = 0.021), albumin level 31–34 g/l (26% vs. 8% in patients with albumin >34 g/l, p = 0.014) and CCI score >6 (23% vs. 10%, p = 0.034). Patients with CFS 3–4 and 5–9 seemed to have more severe complications (OR 3.40, 95% CI 0.73–15.9, p = 0.121 and OR 4.63,

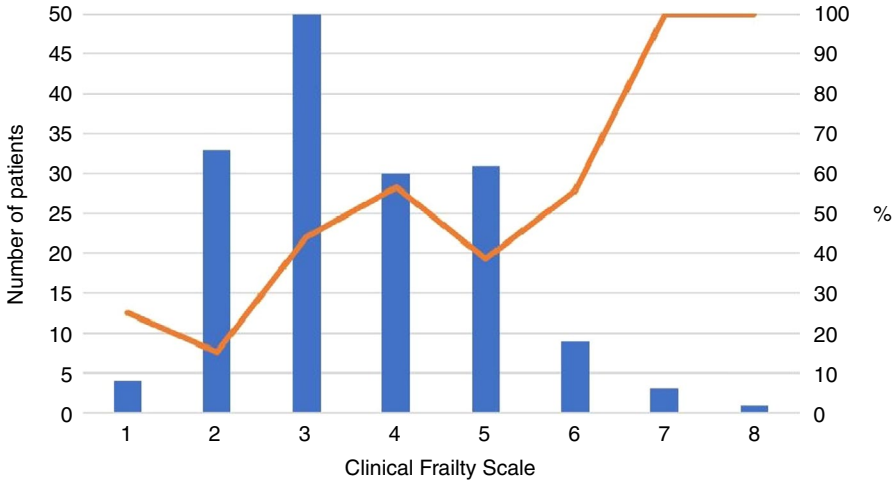

FIGURE 2 Clinical Frailty Scale (CFS) and percentages of complications. Blue bars represent the number of patients in CFS categories 1–9, and the yellow line represents portions of patients in each category with complications

TABLE 3 Predictors of 30-day postoperative complications

	No. of complications		Univariate analysis			Multivariate analysis		
	n	%	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Age (years)								
80–84	39	42.9	1					
85–89	17	35.4	0.73	0.36–1.51	0.396			
90-	10	45.5	1.11	0.44–2.83	0.825			
Gender								
Female	38	39.2	1					
Male	28	43.8	1.21	0.64–2.29	0.564			
BMI (kg/m^2)								
<24	22	40.0	1.01	0.49–2.09	0.974			
24–29	27	39.7	1					
>29	17	44.7	1.23	0.55–2.74	0.614			
Type of living								
Home	64	40.5	1					
Nursing home	2	66.7	2.94	0.26–33.1	0.383			
Hospital admissions <6 months								
None	31	38.3	1					
One or more	33	42.3	1.18	0.63–2.23	0.604			
No. of medications								
0–4	23	36.5	1					
≥5	43	43.9	1.36	0.71-2.60	0.354			
Congestive heart disease								
No	46	37.7	1					
Yes	16	53.3	1.95	0.87–4.34	0.104			
Coronary disease								
No	46	39.7	1					
Yes	16	43.2	1.15	0.55–2.43	0.712			
Hypertension								
No	14	30.4	1					
Yes	50	45.9	1.94	0.93–4.03	0.077			
COPD								
No	58	38.7	1					
Yes	5	71.4	4.01	0.75–21.3	0.104			
Diabetes								
No	39	36.4	1					
Yes	25	48.1	1.61	0.83–3.16	0.162			
Renal failure								
No	44	37.0	1					
Yes	16	51.6	1.82	0.82–4.03	0.141			
Cerebral stroke								
No	50	37.0	1			1		
Yes	14	63.6	3.05	1.20–7.76	0.020	2.53	0.85–7.52	0.096
Dementia								
No	57	43.5	1					
Yes	3	21.4	0.37	0.10–1.40	0.145			

(Continues)

TABLE 3 (Continued)

	No. of complications		Univariate analysis			Multivariate analysis		
	n	%	OR	95% CI	*p*-value	OR	95% CI	*p*-value
G8 score								
<12	35	47.3	2.02	0.57–7.14	0.276			
12–14	27	36.5	1.29	0.36–4.60	0.692			
>14	4	30.8	1					
CFS								
1–2	6	16.2	1			1		
3–4	39	48.8	4.92	1.85–13.1	0.001	6.06	1.88–19.5	0.003
5–9	20	46.5	4.49	1.56–13.0	0.005	3.54	0.95–13.2	0.060
CCI								
4–6	36	36.4	1					
>6	30	48.4	1.64	0.86–3.13	0.132			
ASA score								
2	11	27.5	1			1		
3	43	41.0	1.83	0.83–4.05	0.137	0.94	0.36–2.48	0.904
4	10	76.9	7.91	1.80–34.7	0.006	3.08	0.57–16.8	0.193
MNA-SF								
0–7	18	47.4	3.30	0.79–13.7	0.101			
8–11	45	41.3	2.58	0.68–9.77	0.164			
≥12	3	21.4	1					
Haemoglobin (g/l)								
≤120	47	44.3	1.59	0.80–3.16	0.182			
>120	18	33.3	1					
Albumin (g/l)								
≤30	10	38.5	1.33	0.52–3.38	0.547	1.28	0.46–3.51	0.638
31–34	27	57.4	2.88	1.34–6.16	0.007	3.88	1.61–9.38	0.003
≥35	23	31.9	1			1		
Estimated GFR (ml/min)								
<45	16	41.0	1.25	0.57–2.73	0.580			
45–60	20	51.3	1.89	0.87–4.10	0.108			
>60	29	35.8	1					
Type of operation								
Laparoscopy	39	36.4	1					
Open	19	48.7	1.70	0.81–3.57	0.162			
Conversion	8	53.3	2.05	0.69–6.08	0.198			

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CCI, Charlson Comorbidity Index; CFS, Clinical Frailty Scale; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; MNA-SF, Mini Nutritional Assessment-Short Form.

95% CI 0.93–23.0, $P = 0.061$, respectively) compared with patients with CFS 1–2, but the differences were not statistically significant. In multivariate logistic regression analysis, albumin level 31–34 g/l (OR 4.39, 95% CI 1.31–14.7, $p = 0.017$) was the only significant variable causing postoperative complications. The AUC for severe complications was 0.756 (95% CI 0.65–0.86). Table 4 shows predictors of severe postoperative complications. Figure 3 shows distributions of all and severe postoperative complications, according to the CFS.

DISCUSSION

This prospective study demonstrated that CFS [13] predicts early postoperative complications following elective curatively aimed colon cancer surgery in aged patients. Patients who were vulnerable or frail with CFS scores ≥3 or had severe comorbidities had significantly more complications than fit patients with CFS scores 1–2, whereas age did not affect postoperative outcomes. On the contrary, fit patients managed exceptionally well and showed a very low

TABLE 4 Predictors of 30-day severe postoperative complications

	No. of complications		Univariate analysis			Multivariate analysis		
	n	%	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Age (years)								
80–84	14	15.4	1					
85–89	6	12.5	0.79	0.28–2.20	0.646			
≥90	4	18.2	1.22	0.36–4.16	0.748			
Gender								
Female	11	11.3	1					
Male	13	20.3	1.99	0.83–4.78	0.122			
BMI (kg/m^2)								
<24	9	16.4	1.71	0.59–4.92	0.324			
24–29	7	10.3	1					
>29	8	21.1	2.32	0.77–7.01	0.135			
Type of living								
Home	23	14.6	1					
Nursing home	1	33.3	2.94	0.26–33.7	0.387			
Hospital admissions ≤6 months								
No	10	12.3	1					
One or more	13	16.7	1.42	0.58–3.46	0.440			
No. of medications								
0–4	8	12.7	1					
≥5	16	16.3	1.34	0.54–3.35	0.529			
Congestive heart disease								
No	16	13.1	1					
Yes	8	26.7	2.52	0.96–6.62	0.060			
Coronary heart disease								
No	17	14.7	1					
Yes	6	16.2	1.15	0.42–3.17	0.787			
COPD								
No	20	13.3	1			1		
Yes	3	42.9	4.91	1.02–23.6	0.047	0.60	0.04–8.21	0.701
Hypertension								
No	8	18.2	1					
Yes	14	13.3	0.656	0.26–1.63	0.364			
Diabetes								
No	14	13.1	1					
Yes	10	19.2	1.58	0.65–3.85	0.312			
Renal failure								
No	14	11.8	1			1		
Yes	10	25.0	3.01	1.18–7.98	0.021	1.47	0.40–5.48	0.563
Cerebral stroke								
No	20	14.8	1					
Yes	4	18.2	1.30	0.40-4.24	0.664			
Dementia								
No	21	16.0	1					
Yes	2	14.3	0.89	0.19–4.27	0.888			

(Continues)

TABLE 4 (Continued)

	No. of complications		Univariate analysis			Multivariate analysis		
	n	%	OR	95% CI	*p*-value	OR	95% CI	*p*-value
G8 score								
<12	15	20.3	0.5	-	-			
12–14	9	12.2	1	-	-			
>14	0	0	-					
CFS								
1–2	2	5.4	1			1		
3–4	13	16.3	3.40	0.73–15.9	0.121	8.16	0.89–75.0	0.064
5–9	9	20.9	4.63	0.93–23.0	0.061	7.69	0.70–85.1	0.096
CCI								
4–6	10	10.1	1			1		
>6	14	22.6	2.6	1.07–6.28	0.034	1.96	0.48–7.95	0.346
ASA score								
2	4	10.0	1			1		
3	16	15.2	1.62	0.51–5.17	0.417	0.48	0.10–2.23	0.345
4	4	33.3	4.50	0.92–21.9	0.063	0.90	0.10–8.08	0.924
MNA-SF								
0–7	7	18.4	2.94	0.33–26.3	0.336			
8–11	16	14.7	2.24	0.27–18.3	0.453			
≥12	1	7.1	1					
Haemoglobin (g/l)								
<120	15	14.2	1.21	0.49–2.99	0.674			
≥120	9	16.7	1					
Albumin (g/l)								
≤30	3	11.5	1.44	0.33–6.21	0.629	1.34	0.27–6.72	0.719
31–34	12	25.5	3.77	1.30–10.9	0.014	4.39	1.31–14.7	0.017
>34	6	8.3	1			1		
Estimated GFR (ml/min)								
<45	7	17.9	1.55	0.54–4.45	0.412			
45–60	7	17.9	1.55	0.54–4.45	0.412			
>60	10	12.3	1					
Type of operation								
Laparoscopy	11	10.4	1					
Open	9	23.1	2.59	0.98–6.85	0.055			
Conversion	4	26.7	3.14	0.85–11.6	0.085			

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CCI, Charlson Comorbidity Index; CFS, Clinical Frailty Scale; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; MNA-SF, Mini Nutritional Assessment-Short Form.

complication rate and mortality. Altogether these results emphasize the importance of patient assessment irrespective of chronological age [26].

The study sample represented only colon cancer patients as they have homogeneous treatment strategies compared with rectal cancer patients. Our study showed a higher frequency of right-sided colon cancers and female patients, which is in line with previously reported studies of aged patients [6,27]. Colon cancer surgery is performed in Finland by surgeons who specialize exclusively in colon operations following uniform, standardized protocols for colon cancer treatment [28]. The study sample is nationally representative, providing realistic and novel information on postoperative outcomes of aged patients.

Our study showed high morbidity rates in the early postoperative period. Almost 41% of the patients developed postoperative complications and 15% had severe complications. These figures are comparable to other studies of colon cancer surgery in the aged [5–7]. Complications were overrepresented in patients who were

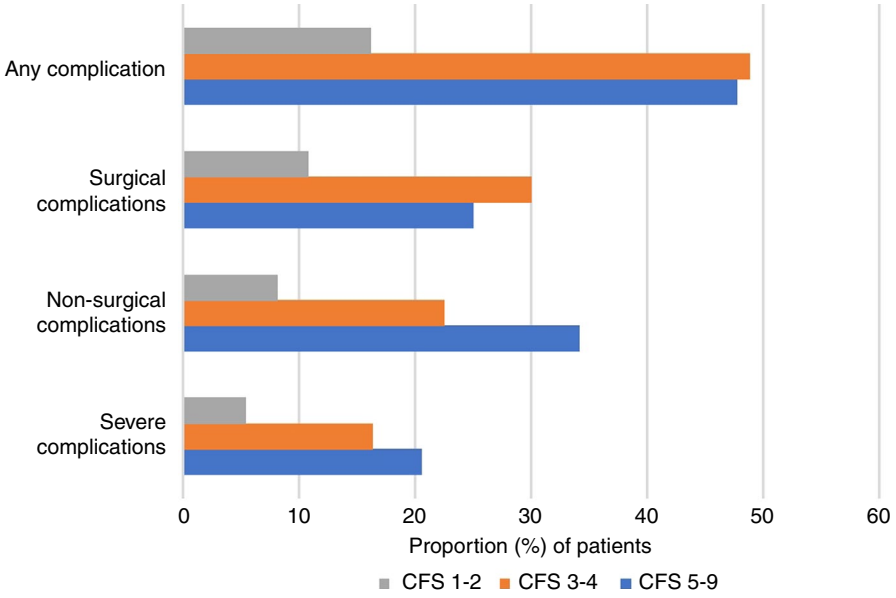

FIGURE 3 Distribution (%) of postoperative complications according to Clinical Frailty Scale (CFS): patients grouped in three categories (CFS 1–2, 3–4 and 5–9)

managing well but inactive or mildly frail (CFS 3–4) and frail (CFS 5–9) compared with fit patients (CFS 1–2) with complication rates of 49% and 47%, respectively, versus 16%. This indicates that fit aged patients can manage invasive surgical treatments like their younger counterparts [4]. On the other hand, particularly vulnerable patients might benefit from preoperative medical optimization and comprehensive geriatric assessment [29].

Previous studies verified that aged patients with severe complications have a disproportionately high risk of 30-day and 1-year mortality [3,6]. In this study, the 30-day mortality rate was 1.9% (8.3% in patients with severe complications), showing a remarkable decline from mortality rates previously reported in Finland and the Netherlands [6,30]. The enhanced recovery after surgery (ERAS) protocol and mini-invasive surgery were well-established in the recruiting hospitals [31,32]. Thus, the significant improvement in mortality rates indicates improved preoperative risk assessment and optimization, counselling and awareness of frailty together with nationwide standardization and advances in modern multidisciplinary treatment.

Nutritional prehabilitation was implemented at some of the study hospitals [33] but is not standard nationwide and may not cover all patients. This might explain excess complications in patients with a mildly reduced albumin level (31–34 g/l) compared with patients with clearly abnormal albumin, suggesting probable malnutrition. On the other hand, BMI had no effect, and thus it should not be used alone for evaluation of nutritional state.

Frailty is identified as a significant predictor of postoperative complications, leading to greater health care utilization and higher mortality [8,14]. Our study focused on the growing population of colon cancer patients aged 80 years or over with even more significant heterogeneity in physical and cognitive status. Notably, most patients lived at home before surgery, but only 56% returned directly to home after operative treatment, emphasizing the major impact of surgery on functional recovery. Our findings demonstrated that patients with pre-existing frailty and morbidity express an excess number of complications, corroborated by a recently published meta-analysis [34].

The CFS proved to be a beneficial tool for assessing preoperative daily physical and cognitive activities and independence. At present, only a few surgical units have readily available geriatric services for comprehensive assessment, so easily implemented frailty screening tools are helpful for surgeons. We grouped patients in three categories (CFS 1–2, 3–4 and 5–9) as we wanted to demonstrate the importance of identifying patients with possible vulnerable physical status. CFS ≥3 was the only screening parameter which showed a significant association with adverse outcomes. Patients with CFS 3–4 can be challenging for a surgeon to identify as they can manage well independently and live with mild frailty.

Although an observational study cannot answer the question of whether the surgery is beneficial or not, performing a randomized trial in this patient group is not realistic. Instead, it is clinically more relevant to study outcomes in an observational setting with less selection bias and more relevance to real-life settings. The strengths of this study included the fact that it examined a representative, nationwide cohort treated at several secondary and tertiary care hospitals instead of single-centre analysis with uniform and standardized protocols during the perioperative period (ERAS protocol).

There are some limitations to this study. It was acknowledged that the tests used (G8, CFS and MNA-SF) are screening tests, and geriatric evaluation would be needed for precise diagnosis of frailty and other geriatric syndromes. Although we did not do cognitive testing, the CFS gives some insight into cognition, and it can be anticipated that patients with CFS 1–2 had no or only mild cognitive impairment. The sample size was not quite sufficient for the analysis of predictors of severe complications. More extensive patient data are needed to confirm the possible prognostic trends such as with CFS, ASA, MNA-SF and GFR. Moreover, a longer follow-up would be necessary to evaluate the complete impact of invasive cancer treatment

[3,35]. Future studies using these multicentre data will focus on long-term results with outcomes, and especially functional recovery.

In conclusion, this study showed that aged patients have high morbidity rates after curative colon cancer surgery. However, the fittest patients had excellent operative outcomes similar to their younger counterparts. Surgeons should not abstain from curative surgery based on age or comorbidities alone. Conversely, modern treatment decision-making should complement preoperative risk assessment with the considered use of the CFS and counselling jointly with patients and their families.

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CONFLICT OF INTEREST

The authors declare, that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

The study was designed by SN, HH, JK, MH and EJ. SN was the principal investigator and major contributor in writing the manuscript. All authors participated in writing and revising the manuscript. All authors read and approved the final manuscript.

ETHICAL STATEMENT

Regional Ethics Committee of the Expert Responsibility area of Tampere University Hospital has approved the study and its consent to participate (number R19028). Each study hospital has approved the study by institutional review boards of at their unit.

DATA AVAILABILITY STATEMENT

The datasets generated or analysed during the current study are not publicly available due to Finnish laws on privacy protection.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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