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Significant improvement in postoperative and 1-year mortality after colorectal cancer surgery in recent years

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ABSTRACT

Background: In earlier studies an association between older patients and higher morbidity and mortality after colorectal surgery is shown, especially in the first postoperative year. We conducted this study to investigate if there is improvement in postoperative morbidity and mortality in senior CRC patients over time.

Materials and methods: All patients, except those with distant metastasis, who received curative CRC surgery between 2006 and 2017 in the Catharina Hospital (Eindhoven, the Netherlands) were selected retrospectively. Differences in mortality and relative survival between different age groups (<75 and ≥ 75 years), period of surgery (2006–2012 and 2013–2017) and type of tumor (colon and rectum) were investigated.

Results: In total 2018 patients, of whom 57.4% is male, were selected (n = 1037 colon and n = 981 rectum). 615 (30.5%) patients were ≥75 years old. For electively treated CRC patients aged ≥75 years 30- and 90-day mortality improved from 5.8% to 1.2% (p = 0.004) and 9.1% to 4.6% (p = 0.043) respectively, in favour of the latest time period. Relative one-year survival rates of all electively treated CRC patients were not significantly different between younger and older patients in the latest time period (95.5% vs. 94.3%, p = n.s.)

Conclusions: This study shows significant improvement in postoperative morbidity and mortality over time for both age and treatment groups. Relative survival rates improved especially for older patients and no significant differences were seen between both age groups. Senior CRC patients should not be withheld curative treatment based on age or comorbidities alone.

Introduction

The incidence of colorectal cancer (CRC) increases with age. As worldwide age is increasing, more and more older patients are diagnosed with CRC [1]. With more senior patients affected by CRC, challenges originate in treatment choices. These patients are a heterogeneous group of patients with variations in fragility and comorbidities, and with inconsistencies between physical and chronological age [2]. They are at risk for complications with increased morbidity and post-operative mortality and if complications occur, they have more devastating consequences [3–5]. Furthermore, the percentage of seniors who receive surgery decreases with older ages [6]. In daily practice these findings could lead to withholding potentially curative treatment in the older population with an increased risk for undertreatment [7,8].

There is increasing evidence that older patients who are fit enough for surgery have the same benefit from potentially curative treatment as younger patients do [9,10]. They are able to withstand the surgical stressor better than commonly believed [9,10]. However, the risk of mortality in seniors during the first post-operative year is 20–23% [11]. If they survive the first year, their prognosis is equal to younger counterparts if they survive the first post-operative year [11].

In senior patients, one of the most important determinating factors in decision making is frailty. This is important because this condition, defined as a state of limited reserve to undergo physical stress, is a known risk factor for postoperative complications in

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colorectal cancer surgery [12]. In case of increased frailty or limited functional reserve, a prehabilitation program could be beneficial for senior patients to improve their condition prior to surgery [13]. However, until now evidence on the effect of prehabilitation on post-operative outcome is varying and inconclusive [13,14].

Improvement in earlier diagnosis, better staging, less invasive surgical techniques, pre- and postoperative care and centralization of complex cases have contributed to an improved outcome in the older patient [1]. Despite all these improvements, studies still report significant differences in 30-day and one-year mortality between older and younger CRC patients [11]. However, there is a possibility that these differences are changing over time.

The primary aim of this study is to investigate whether or not any improvement in short-term morbidity and mortality has occurred in senior CRC patients over the years treated in a high-volume center for complex CRC cases. The secondary aim is to compare these morbidity and mortality rates between younger and older CRC patients.

Materials and methods

Patients and treatment

The Catharina Hospital (Eindhoven, the Netherlands) is a specialized and high-volume center for treatment of CRC and is a referral center for locally advanced and recurrent colorectal cancer. For this study, all patients receiving curative surgery for primary non-recurrent colorectal cancer between 2006 and 2017 were selected. Almost all patients, except those undergoing emergency procedures, were adequately staged locally and systemically with histologically proven CRC and a pretreatment CT or MRI scan. Depending on location of the tumor and cancer stage, patients received neo-adjuvant and/or adjuvant treatment with (chemo) radiation, according to the Dutch National Guidelines for colorectal cancer [15]. Type of surgery (e.g. laparoscopic and open surgery) was used depending on the type and stage of the tumor and the preference of the surgeon. Patients with peritonitis carcinomatosis and distant metastasis at time of presentation were excluded in this study. All patients were assessed independently by a surgeon and an anesthesiologist to determine whether or not they were regarded fit for surgery. Besides the standard medical history regarding previous morbidities and co-existing morbidities, nutritional assessment, drug use and a somatic and psychogeriatric screening, also the support system at home and the requirements after surgery to return home were evaluated. If needed, other disciplines were involved.

Clinical data and follow-up

Clinical and demographic data were extracted retrospectively from medical records. Complications were scored using the Clavien-Dindo classification of surgical complications [16,17]. Follow-up data was extracted from medical records or by contacting the patient, the referring hospital or patients' general practitioner by telephone. Time to follow-up was calculated as the interval from the day of surgery to death or to the date of last contact. Minimum follow-up time of the surviving patients was at least one year. The vital status of all patients was assessed through linkage with Municipal Administrative Databases, which register all deceased and emigrated persons in the Netherlands. If a patient had died during follow-up the date and cause of death were noted.

Statistical analyses

Statistical analyses were performed using SPSS Statistics 25.0 software (IBM, Endicott, New York, USA). Patients were divided in two consecutive periods based on year of surgery: 2006–2012 and 2013–2017. All analyses were performed separately for both colon and rectal cancer. Survival analyses were performed only for CRC patients treated with elective surgery. Comparisons within these groups were based on age (<75 and ≥ 75 years). All survival analyses were also performed for patients <80 and ≥ 80 years, and shown in supplementary data. Intergroup comparisons were analyzed using chi-square tests or independent t-tests when appropriate. A p-value of <0.05 was considered statistically significant. Survival rates were analyzed for colon and rectal cancer separately and were stratified by age group using the Kaplan-Meier method. To calculate disease-specific survival we used relative survival rates, which was calculated as the absolute survival amongst CRC patients divided by the expected survival for the general population with the same sex and age structure.

Results

In total 2018 consecutive CRC patients were included. Of the 1037 colon cancer patients, 432 (41.7%) were ≥75 years old and of the 981 rectal cancer patients, 183 (18.7%) were ≥75 years old. Median follow-up time for colon cancer patients was 3.4 years and for rectal cancer patients 4.2 years. Senior (≥75 years) CRC patients had significantly more comorbidities compared to younger patients. Further clinical and demographic characteristics for both colon and rectal cancer patients are presented separately in Tables 1 and 2, respectively.

Postoperative morbidity and mortality

Senior colon cancer patients had significantly more pulmonary, cardiac and neurological complications compared to younger patients. Clavien-Dindo grade III complications were observed in 6.0% of the older and in 9.4% of the younger patients ($p = 0.046$). Clavien-Dindo grade IV complications occurred in 1.9% of the older and in 2.6% of the younger patients (p = n.s.). Post-operative mortality during admission was observed in 25 (5.8%) of the older and 11 (1.8%) of the younger patients ($p = 0.001$).

Senior rectal cancer patients also had significantly more pulmonary, cardiac and neurological complications. The incidence of other complications was similar compared to younger patients. Of the older patients, 11.5% and 4.9% of patients developed grade III or IV complications in comparison to 11.2% and 3.1% in younger patients, respectively (p = n.s.). Post-operative mortality during admission occurred in 8 (4.4%) older and in 9 (1.1%) younger patients ($p = 0.002$). A detailed description of the complications in both groups is presented in Table 3.

Development of post-operative morbidity and mortality over time

In the period 2006–2012, 9.7% and 2.8% of the older and 12.8% and 3.5% of the younger CRC patients developed grade III or grade IV complications, respectively. Post-operative mortality during admission was observed in 8.8% of the older compared to 1.3% of the younger patients ($p < 0.001$).

In the period 2013–2017, no significant differences in complications or mortality between older and younger patients were seen. Grade III or IV complications occurred in 5.4% and 2.7% of the older and 7.7% and 2.3% of the younger patients, respectively. Post-operative mortality during admission in this period occurred in 1.7% of the older and 1.5% of the younger patients ($p = 0.842$).

Table 1
Demographic and clinical characteristics of all 1037 colon cancer patients stratified by age group and period of treatment.

	Colon n = 1037					
	<75 years			**≥75 years**		
	2006–2012 n = 287	**2013–2017 n = 318**	**p-value**	**2006–2012 n = 205**	**2013–2017 n = 227**	**p-value**
	n (%)	*n (%)*		*n (%)*	*n (%)*	
Mean age in years at time of surgery (range)	64.4 (24.4–74.9)	65.4 (30.3–74.9)	0.149	81.6 (75.1–96.1)	80.6 (75.0–95.2)	0.017
Median follow-up in years (±SD)	7.1 (3.1)	2.4 (1.4)		4.9 (3.4)	2.2 (1.4)	
Male	152 (53.0)	181 (56.9)	0.329	102 (49.8)	111 (48.9)	0.859
Comorbidity			0.083			0.008
None	92 (32.1)	120 (37.7)		31 (15.1)	65 (28.6)	
1 comorbidity	54 (18.8)	73 (23.0)		34 (16.6)	35 (15.4)	
2 comorbidities	47 (16.4)	48 (15.1)		38 (18.5)	38 (16.7)	
≥3 comorbidities	94 (32.8)	77 (24.2)		102 (49.8)	89 (39.2)	
ASA classification			0.330			0.417
I-II	218 (76.0)	254 (79.9)		100 (48.8)	123 (54.2)	
III	67 (23.3)	60 (18.9)		94 (45.9)	96 (42.3)	
IV	2 (0.7)	4 (1.3)		11 (5.4)	8 (3.5)	
Type of surgery			0.137			0.165
Right hemicolectomy	125 (43.6)	117 (36.8)		106 (51.7)	122 (53.7)	
Transversum colectomy	5 (1.7)	4 (1.3)		7 (3.4)	2 (0.9)	
Left hemicolectomy	36 (12.5)	62 (19.5)		22 (10.7)	36 (15.9)	
Sigmoid	109 (38.0)	125 (39.3)		68 (33.2)	64 (28.2)	
(Sub)total colectomy	12 (4.2)	10 (3.1)		2 (1.0)	3 (1.3)	
Initial type of intervention			<0.001			<0.001
Open surgery	184 (64.1)	105 (33.0)		158 (77.1)	86 (37.9)	
Laparoscopic	103 (35.9)	213 (67.0)		47 (22.9)	141 (62.1)	
Stoma during surgery			<0.001			<0.001
Yes	29 (10.1)	40 (12.6)		29 (14.1)	30 (13.2)	
No	236 (82.2)	276 (86.8)		159 (77.6)	197 (86.8)	
Missing	22 (7.7)	2 (0.6)		17 (8.3)	–	
Emergency surgery	32 (11.1)	35 (11.0)	0.955	40 (19.5)	37 (16.3)	0.384
Extended (multivisceral) resection	34 (11.8)	31 (9.7)	0.001	23 (11.2)	21 (9.3)	0.001
Missing	18 (6.3)	51 (16.0)		7 (3.4)	30 (13.2)	
Mean hospital stay in days (±SD)	9.7 (8.9)	9.0 (10.6)	0.381	12.6 (10.8)	9.6 (7.2)	0.001
Mean ICU stay in days (±SD)	0.7 (2.1)	1.1 (5.9)	0.466	2.2 (3.5)	1.0 (2.8)	0.020
Pathological T-stage			0.023			0.915
T0-T2	75 (26.1)	110 (34.6)		52 (25.4)	60 (26.4)	
T3	156 (54.4)	145 (45.6)		117 (57.1)	125 (55.1)	
T4	56 (19.5)	59 (18.6)		36 (17.6)	42 (18.5)	
Tx	–	4 (1.3)				
Pathological N-stage			0.428			0.572
N0	178 (62.0)	191 (60.1)		146 (71.2)	153 (67.4)	
N1	62 (21.6)	82 (25.8)		36 (17.6)	49 (21.6)	
N2	47 (16.4)	45 (14.2)		23 (11.2)	25 (11.0)	
Primary anastomosis	272 (94.8)	299 (94.0)	0.690	183 (89.3)	207 (91.2)	0.501
Radical resection (R0)	287 (100.0)	317 (99.7)	0.342	205 (100.0)	227 (100.0)	NA

Overall and relative survival analysis

Comparing the 2006–2012 and 2013–2017 period, the overall 30- and 90-day mortality for senior CRC patients decreased from 5.8% to 1.2% (p = 0.004) and from 9.1% to 4.6% (p = 0.043), respectively. For patients <75 years no differences in 30- and 90-day survival rates were seen between both time periods (Fig. 1). In contrast to the period 2006–2012, the most recent time period showed there were no significant differences in the 30- and 90-day mortality rate between both age groups for both colon and rectal cancer patients. The 30-day and 90-day mortality rate in this period was 1.1% and 4.2% for senior colon and 1.4% and 5.8% in senior rectal cancer patients, respectively. A more detailed description of the overall survival rates for all groups is presented in Table 4.

For all CRC patients, absolute one-year survival was 95.3% and 85.5% for younger and older patients in the 2006–2012 period compared to 94.9% and 89.2% in the 2013–2017 period, respectively (p = 0.002). In the most recent time period, no significant differences were found in overall one-year mortality between younger and older colon cancer patients (90.5% vs. 95.1%, respectively p = 0.055). In rectal cancer patients there were still significant differences between older and younger patients in overall one-year mortality for the same period (85.5% vs. 94.7%, p = 0.006).

The relative one-year survival for senior CRC patients improved from 88.4% in the 2006–2012 period to 94.3% in the latest time period and was not significantly different compared to younger patients for this latest time period. Improvement of the relative survival was observed for both colon and rectal cancer patients. Also in senior patients who underwent emergency surgery for CRC, similar relative one-year survival rates as their younger counterparts were seen in the period 2013–2017. The relative one-year survival rates are presented in Table 5.

Discussion

Potentially curative treatment for colorectal cancer is accompanied by acceptable morbidity and low mortality rates for all patients regardless of age [18–21]. However, earlier studies on this topic showed that morbidity in senior patients is most often higher than in their younger counterparts, and the risk for mortality is increased if a complication occurs [3,4]. Our cohort of consecutive CRC patients shows a major decrease in 90-day and one-year mortality in the older population. For the period 2006–2012, 9.1% patients aged ≥75 years died in the first 90 days compared to 4.6%

Table 2
Demographic and clinical characteristics of all 981 rectal cancer patients stratified by age group and period of treatment.

	Rectum n = 981					
	<75 years			**≥75 years**		
	2006–2012 n = 454	**2013–2017 n = 344**	**p-value**	**2006–2012 n = 113**	**2013–2017 n = 70**	**p-value**
	n (%)	*n (%)*		*n (%)*	*n (%)*	
Mean age in years at time of surgery (range)	61.8 (27.0–74.9)	62.2 (28.8–74.9)	0.519	79.3 (75.0–88.6)	79.7 (75.0–90.6)	0.531
Median follow-up in years (±SD)	7.1 (3.2)	2.7 (1.4)		4.5 (3.2)	1.8 (1.4)	
Male	277 (61.0)	223 (64.8)	0.270	68 (60.2)	45 (64.3)	0.578
Comorbidity			0.117			0.024
None	180 (39.6)	139 (40.4)		18 (15.9)	25 (35.7)	
1 comorbidity	107 (23.6)	70 (20.3)		23 (20.4)	10 (14.3)	
2 comorbidities	90 (19.8)	56 (16.3)		22 (19.5)	11 (15.7)	
≥3 comorbidities	77 (17.0)	79 (23.0)		50 (44.2)	24 (34.3)	
ASA classification			0.686			0.253
I-II	392 (86.3)	292 (85.2)		68 (60.2)	48 (68.6)	
III	61 (13.4)	49 (14.2)		42 (37.2)	22 (31.4)	
IV	1 (0.2)	1 (0.3)		3 (2.7)	–	
Neo-adjuvant treatment			<0.001			0.659
None	51 (11.2)	59 (17.2)		33 (29.2)	17 (24.3)	
Short course radiotherapy (5 × 5 Gy)	85 (18.7)	47 (13.7)		32 (28.3)	24 (34.3)	
Chemoradiation	298 (65.6)	237 (68.9)		44 (38.9)	28 (40.0)	
Long course radiotherapy	20 (4.4)	1 (0.3)		4 (3.5)	1 (1.4)	
Type of surgery			0.489			0.263
Low anterior resection	270 (59.5)	212 (61.6)		56 (49.6)	43 (61.4)	
Abdominoperineal resection	171 (37.7)	121 (35.2)		45 (39.8)	24 (34.3)	
(Sub)total resection	2 (0.4)	–		2 (1.8)	–	
TEM	11 (2.4)	11 (3.2)		10 (8.8)	3 (4.3)	
Initial type of intervention			<0.001			<0.001
Open surgery	432 (95.2)	263 (76.5)		99 (87.6)	51 (72.9)	
Laparoscopic	11 (2.4)	70 (20.3)		4 (3.5)	16 (22.9)	
Ostomy during surgery			0.001			0.628
Yes	379 (83.5)	270 (78.5)		90 (79.6)	55 (78.6)	
No	55 (12.1)	69 (20.1)		17 (15.0)	13 (18.6)	
Missing	20 (4.4)	5 (1.5)		6 (5.3)	2 (2.9)	
Emergency surgery	6 (1.3)	4 (1.2)	0.842	3 (2.7)	1 (1.4)	0.581
Clinical T-stadium			0.990			0.633
T1-T2	67 (14.8)	50 (14.5)		23 (20.4)	16 (22.9)	
T3	183 (40.3)	136 (39.5)		48 (42.5)	24 (34.3)	
T4	203 (44.7)	157 (45.6)		39 (34.5)	29 (41.4)	
Tx	1 (0.2)	1 (0.3)		3 (2.7)	1 (1.4)	
Clinical N-stadium			<0.001			<0.001
N0	164 (36.1)	92 (26.7)		54 (47.8)	29 (41.4)	
N1	88 (19.4)	102 (29.7)		20 (17.7)	22 (31.4)	
N2	102 (22.5)	141 (41.0)		10 (8.8)	19 (27.1)	
Nx	19 (4.2)	8 (2.3)		4 (3.5)	–	
Missing	81 (17.8)	1 (0.3)		25 (22.1)	–	
Extended (multivisceral) resection	145 (29.7)	121 (35.2)	0.006	34 (30.1)	29 (41.4)	0.098
Missing	36 (7.9)	10 (2.9)		11 (9.7)	2 (2.9)	
Mean admission time in days (±SD)	11.6 (10.7)	9.4 (6.7)	0.001	14.5 (12.8)	12.7 (10.6)	0.329
Mean admission time on ICU in days (±SD)	1.7 (7.5)	0.9 (1.8)	0.129	1.9 (3.3)	2.1 (3.6)	0.798
Primary anastomosis	264 (58.1)	200 (58.1)	0.684	41 (36.3)	32 (45.7)	0.205
Radical resection (R0)	446 (98.2)	340 (98.8)	0.491	108 (95.6)	69 (98.6)	0.269

Table 3
Complications in both colon and rectal cancer patients, stratified by age groups.

	Colon n = 1037			**Rectum n = 981**		
	<75 years n = 605	**≥75 years n = 432**	**p-value**	**<75 years n = 798**	**≥75 years n = 183**	**p-value**
	n (%)	*n (%)*		*n (%)*	*n (%)*	
Pulmonary	44 (7.3)	59 (13.7)	0.001	62 (7.8)	25 (13.7)	0.011
Cardiac	20 (3.3)	47 (10.9)	<0.001	35 (4.4)	18 (9.8)	0.003
Infectious	52 (8.6)	30 (6.9)	0.332	92 (11.5)	27 (14.8)	0.228
Neurological	13 (2.1)	37 (8.6)	<0.001	18 (2.3)	18 (9.8)	<0.001
Thrombosis	7 (1.2)	3 (0.7)	0.452	13 (1.6)	1 (0.5)	0.265
Clavien-Dindo grade			<0.001			<0.001
None	385 (63.6)	248 (57.4)		398 (49.9)	65 (35.5)	
Grade I-II	136 (22.5)	125 (28.9)		277 (34.7)	80 (43.7)	
Grade IIIa	13 (2.1)	9 (2.1)		29 (3.6)	2 (1.1)	
Grade IIIb	44 (7.3)	17 (3.9)		60 (7.5)	19 (10.4)	
Grade IV	16 (2.6)	8 (1.9)		25 (3.1)	9 (4.9)	
Grade V	11 (1.8)	25 (5.8)		9 (1.1)	8 (4.4)	

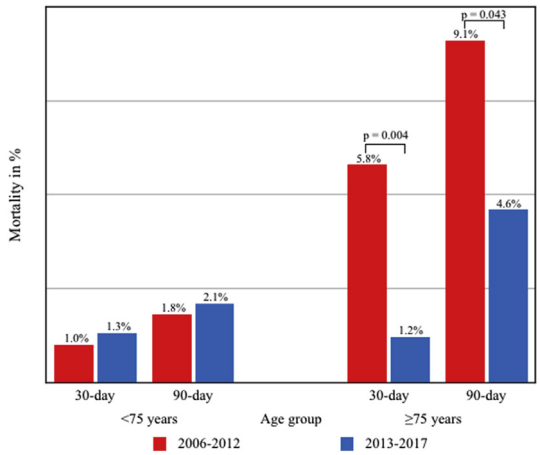

Fig. 1. Improvement of short-term mortality for elderly colorectal cancer patients over the years.

in the most recent period. After correcting absolute mortality for age-related background mortality (relative survival), one-year survival rates were almost equal for younger and older patients: 95.5% and 94.3%, respectively. Although overall mortality in senior patients is higher, the impact of current CRC treatment on mortality is equal between both patient groups. We believe that improvement in peri-operative and post-operative care have contributed to this positive effect. Since senior patients had significantly more comorbidities than younger patients, the differences in overall mortality between ages are most probably accountable on other diseases which affect these patients.

Older studies focusing on outcome in the older CRC population report 30-day mortality rates up to 7% in patients aged 75 years or older and one-year mortality rates of 19–26% [18,22–25]. However, this study, showed a 30-day mortality rate of 1.1% in senior colon and 1.4% in senior rectal cancer patients for the most recent period. In a population based study from The Netherlands, including patients surgically treated for CRC between 2009 and 2013, an improvement was observed in 30-day and one-year mortality for patients ≥75 years old over the years [26]. They reported mortality rates in patients ≥75 years that were slightly higher compared to our rates, 2.9–6.2% and 11.7–15.0%, respectively for one-month and one-year mortality [26]. Another recent population-based cohort study across four North European countries also showed somewhat higher 30-day, 90-day and overall one-year mortality rates for octogenarian colon and rectal cancer patients [27]. For octogenarian colon cancer patients they reported 30-day and one-year mortality rates of 5.5–11.4% and 17.1–23.6%, respectively [27]. For the octogenarian rectal cancer patients these rates were 4.7–7.5% and 13.6–22.1%, respectively [27]. This study also showed that short-term mortality improved over the years, which varied substantially between different countries [27]. These rates were even slightly higher than we found for patients ≥80 years old in our cohort (shown as supplementary data). A small single institution study of 85 patients from the United Kingdom including CRC patients showed a 30-day mortality rate for patients ≥75 years of 6.5%, which was almost equal to that of younger patients [23]. Others studies focusing on survival rates over the years have also shown improved survival rates in senior CRC patients [1,22,28,29].

The reported survival rates in this study are promising, particularly as a significant proportion of the senior rectal cancer patients have locally advanced cases. These patients require intensive treatment regimens with neo-adjuvant treatment and in about one third of the cases multivisceral resections. Possible explanations for improvement in short-term survival rates in senior colon cancer patients are probably due to increasing use of minimal invasive techniques and peri-operative measures. However in rectal cancer patients there is not a clear surgical explanation as most patients

Table 4
Absolute survival rates of both colon and rectal cancer patients with elective surgery, stratified by age groups.

	Colon n = 893			
	<75 years		**≥75 years**	
	2006–2012 n = 255	**2013–2017 n = 283**	**2006–2012 n = 165**	**2013–2017 n = 190**
1-month	0.98	0.99	0.94	0.99
3-month	0.97	0.98	0.90	0.94
6-month	0.96	0.97	0.88	0.90
1-year	0.95	0.95	0.86	0.85
	Rectum n=967			
	<75 years		**≥75 years**	
	2006–2012 n=448	**2013–2017 n=340**	**2006–2012 n=110**	**2013–2017 n=69**
1-month	0.99	0.99	0.94	0.99
3-month	0.98	0.98	0.92	0.94
6-month	0.98	0.97	0.90	0.90
1-year	0.95	0.95	0.85	0.85

Table 5
Relative one-year survival rates, stratified by age and period of surgery.

	Relative one-year survival					
	2006–2012			**2013–2017**		
	<75 years	**≥75 years**	**p-value**	**<75 years**	**≥75 years**	**p-value**
	%	**%**		**%**	**%**	
All CRC patients	96.5%	88.4%	<0.001	95.5%	94.3%	0.429
Colon	96.5%	87.3%	<0.001	95.3%	94.7%	0.429
Rectum	96.3%	89.4%	0.003	95.3%	91.2%	0.176
Emergency surgery	100%	69.8%	<0.001	87.2%	92.1%	0.479

are treated with open surgery due to the locally advanced nature of most cases. However, increased expertise in these cases with improved perioperative care and awareness of complications will probably attribute to these improved outcomes. Another possible explanation for better short-term outcomes is the introduction and standardization of the Enhanced Recovery After Surgery (ERAS) program, that showed promising results in the postoperative phase [27].

All patients with CRC need to be adequately staged and performance status needs to be assessed. It is known that frailty is a relevant risk factor for postoperative complications, longer hospital stay, readmission rates and lower long-term survival [30,31]. In order to prevent adverse outcomes in older CRC patients it is important to recognize frailty to determine the most appropriate therapeutic regimen. It is still a discussion how frailty should be adequately identified in the individual patient, as no specific tool is able to identify all heterogeneous aspects of frailty [8,32]. Montroni et al. recommend focusing on main predictors as functional and nutritional status and comorbidities as these are targets for prehabilitation programs [8]. Since 2012, as part of a National Patient Safety Program in the Netherlands, all patients over 70 years should be subjected to a short evaluation of four domains: undernutrition, physical impairment, delirium risk and fall risk. This short screening method is easy and less time consuming than a full geriatric assessment, but provides some important prognostic information about outcome and morbidity [33]. When patients seem to be at risk for frailty it is important to perform a complete geriatric assessment in these patients. The most eligible tool to identify frail from fit patients in the geriatric oncological group appears to be the Comprehensive Geriatric Assessment (CGA) [32]. CGA uses a more multidimensional approach than ASA score does, assessing functional, psychosocial and physical health status, polypharmacy and cognition. Although time consuming, CGA has been shown to be a useful predictor for postoperative complications in senior patients [32]. In our institution all patients are seen by the surgeon and anesthesiologist to asses peri-operative risk and to shortly evaluate the four geriatric domains. If increased risk is considered, patients are referred for a full geriatric assessment. If indicated, in some of these patients, prehabilitation programs were initiated. Nevertheless, all senior patients were advised to increase protein intake and to try to double their standard physical exercise in the waiting period for surgery.

Intense prehabilitation programs as standard care for all CRC patients have not shown to be of value yet, although in selected patients enhancing preoperative condition with prehabilitation programs could be useful in decreasing postoperative complications and improved recovery [34,35]. Studies performed in frail patients undergoing intra-abdominal surgery showed that prehabilitation decreases postoperative complications with 40–50%. Other promising results were achieved in orthopedic and cardiac surgery patients [13,36–38]. It is believed that the frailest patients benefit most from these programs, but they are often excluded from studies and therefore the effect of these programs on older and frail CRC patients is still uncertain [12]. In addition, as our results show major improvement in postoperative mortality and outcome in the current era, and we did not implement prehabilitation programs in all patients, the effect of prehabilitation for the majority of the older population is probably small. The challenge is to find which patient in daily practice could be planned for surgery and which will benefit most from a prehabilitation program. Hopefully future studies focusing on this topic will provide more insight in the selection of patients.

The strength of this study lies in the availability of many clinical variables in a large population of patients with a low prevalence of missing values. Limitations of this study are based on its retrospective character. The report on minor complications could be underestimated due to a lack of documentation. However, we believe that the underestimation of complications was kept to a minimum by accurate studying of medical records, contact with referral hospitals and general practitioners and direct contact with patients by telephone. Assessment and screening for frailty has been implemented gradually since 2012 as it was part of a national health program. If frailty was suspected, the patients were referred for geriatric assessment. Therefore, only a few patients were assessed with a CGA and subjected to a prehabilitation program, thus we do not know the impact of prehabilitation on postoperative outcomes as this was not standard care. Over the years, we found slightly lower incidences of $\geq$3 comorbidities in senior patients. We believe this is due to a difference in documentation of comorbidities, rather than that outcomes have been influenced by only selecting the best patients for treatment.

As most of our rectal cancer patients are referred, there could also be an effect of selection bias for this specific patient group. Therefore, we believe that all patients with locally advanced rectal cancer cases should be discussed in a regional multidisciplinary team meeting (MDT) or should be referred to a tertiary center before declining curative treatment.

This study shows that relative survival in the first year for senior patients undergoing CRC surgery has improved greatly over the past years. Their relative survival is even equal to that of younger patients. Therefore, all senior patients regardless of age should be adequately staged and discussed in a MDT meeting and when in doubt of frailty, patients should be referred to a geriatrician prior to declining treatment. We believe that the outcomes of this study are promising and senior patients should not be withheld curative treatment based on age or comorbidities alone.

Conclusion

Postoperative morbidity in senior CRC patients has decreased and survival has improved over the latest years. Currently, 30- and 90-day mortality and relative 1-year survival are almost equal for older and younger CRC patients. All senior CRC patients should be adequately staged and screened before any treatment plan is determined. Clinicians should not withheld senior patients from curative treatment based on age or comorbidities alone.

Conflict of interest statement

None.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ejso.2019.06.017.

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