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Original Research

The gap in postoperative outcome between older and younger patients with stage I-III colorectal cancer has been bridged; results from the Netherlands cancer registry

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Abstract ***Aim of the study:*** Previous studies have shown that older patients benefited less than younger patients from surgical treatment for colorectal cancer (CRC). However, CRC care has advanced over time, and it is time to assess whether the difference in postoperative mortality between older and younger CRC patients is still present.
Methods: Patients with primary stage I-III CRC diagnosed between 2005 and 2016 were selected from the Netherlands Cancer Registry (N = 111,778). Trends in postoperative mortality and 1-year postoperative relative survival (RS) were analysed, stratified according to age (<75 versus ≥75 years) and tumour location (colon versus rectum). One-year postoperative RS was analysed to correct for background mortality in the older population.
Results: Between 2005 and 2016, 30-day postoperative mortality showed a stronger decrease for older patients (from 10.0% to 4.0% for colon cancer [$p < 0.001$] and from 8.3% to 2.7%

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for rectal cancer [$p < 0.001$]) compared with younger patients (from 2.0% to 0.9% for colon cancer [$p < 0.001$] and from 1.4% to 0.7% for rectal cancer [$p = 0.01$]). Between 2005 and 2016, also 1-year RS increased more for older patients (from 84.8% to 94.6% for colon cancer and from 86.1% to 97.2% for rectal cancer) compared with younger patients (from 94.0% to 97.8% for colon cancer and from 96.3% to 98.8% for rectal cancer).

Conclusion: Between 2005 and 2016, differences in postoperative mortality between older and younger CRC patients decreased. One-year postoperative RS was almost equal for older and younger patients in 2015–2016. This information is crucial for shared decision-making on surgical treatment.

1. Introduction

With over 50% of colorectal cancer (CRC) cases occurring in those over the age of 70 years, CRC is a disease of older patients [1]. Given the aging of Western societies, the number of older CRC patients will increase even further in the coming decades.

The older CRC population has great variety among their individual health statuses, with comorbidities mainly developing in those between 70 and 75 years of age [2]. This matter results in a population that includes patients who experience increased disabilities and comorbidities, patients with excellent health status and many in between these extremes.

The heterogeneity of the older population and the lack of specific data on older patients, because of their underrepresentation in clinical trials [3], make it difficult to establish treatment strategies. For CRC patients without distant metastases, surgical resection is the best option for curative treatment, and improvements in perioperative care, surgical techniques and the introduction of multimodality treatment have made surgery feasible for the majority of patients. However, there seems to be a tendency to offer surgical resection less in older compared with younger patients [4,5]. This reservations can be explained by previous studies, which state that older patients benefit less from surgical treatment for CRC as reflected in the higher postoperative morbidity and mortality rates after surgical resection [6,7]. Owing to these inferior outcomes in older patients, there has been an increasing focus on their frailty, i.e. their state of increased vulnerability and the incorporation of geriatric assessment in the oncology treatment decision-making [8,9].

However, surgical treatment of CRC patients has advanced with improved surgical techniques (e.g. minimally invasive surgery), subspecialisation and better perioperative care, in efforts to decrease postoperative mortality rates. Information on present-day postoperative mortality rates of older patients is important for shared decision-making regarding surgical treatment. Therefore, the aim of the present study is to investigate trends in postoperative mortality over time and to assess whether the difference in postoperative mortality between younger and older CRC patients is still present in the current practice.

2. Methods

2.1. Data collection

In the Netherlands, all newly diagnosed malignancies are registered by the Netherlands Cancer Registry (NCR). The NCR mainly receives notification from the Dutch pathology reporting system, and the National Registry of Hospital Discharge Diagnoses completes case ascertainment. Trained registry personnel gather data on patient, tumour and treatment characteristics directly from the medical records, following notification.

From the NCR, patients with stage I-III CRC who were diagnosed between 2005 and 2016 were selected for our study ($N = 111{,}778$). The anatomical subsite of a tumour was coded according to the International Classification of Diseases for Oncology [10]. The tumour-node-metastasis (TNM) classification was used for stage notification of the primary tumour, according to the edition valid at the time of the cancer diagnosis [11]. Pathological TNM staging took precedence over clinical staging, except in the case of missing pathological data (0.5% of patients).

The study period was divided into 6 time periods of 2 years each (2005–2006, 2007–2008, 2009–2010, 2011–2012, 2013–2014 and 2015–2016). Patients were stratified according to tumour localisation and age, specifically colon and rectum (rectosigmoid and rectum) as well as younger patients (0–74 years of age) and older patients (≥75 years), respectively. The age of 75 years and above was chosen to define older patients, as the prevalence of multimorbidity increases with age and more than 50% of the people aged 75 years and older suffer from at least two chronic diseases [12,13].

Patients' survival status was obtained by linking the NCR to the Municipal Personal Records Database, which records information on their inhabitants' vital

status. For all patients, a follow-up was completed at least 1 year after surgery.

2.2. Statistical analyses

Patients were stratified according to age group and primary tumour localisation, and only patients who underwent resection, with exception of patients who underwent local excision (e.g. polypectomy or TEM), were included (N = 104,185). Data on patient and tumour characteristics were analysed, and the significance of differences in their characteristics was analysed using the χ^2 test.

Crude 30-day mortality rates were analysed. Because previous studies showed that 30-day mortality highly underestimates the risk of dying in the first year after surgery [14], crude postoperative mortality rates for 90-day and 1-year mortality were reported as well. Multivariable logistic regression analyses were applied to estimate odds ratios (ORs) with 95% confidence intervals (CIs) to determine the association between time period and postoperative mortality. Besides the period of diagnosis, the variables included in the model are gender, tumour-stage, subsite of the tumour (colon cancer), histology, social economic status and the administration of chemotherapy (colon cancer) or radiotherapy (rectal cancer).

To estimate cancer-specific survival, 1-year relative survival (RS) was calculated. We define 1-year RS as the ratio of the absolute survival observed among the cancer patients and the survival that would have been expected for a comparable group from the general population (same age, gender and period).[15] Expected survival was calculated from population life tables from the Netherlands. Next, to analyse whether changes in 1-year RS estimates were because of changes in acute or subacute mortality, conditional 1-year RS was calculated, on the condition of being alive 30 or 90 days after resection.

For patients with multiple dates of resection, the last date of resection was included for RS and multivariable logistic regression analyses. For patients with multiple resections on the same date, the tumour with the most advanced TNM-stage was used for these analyses.

For analyses on surgical resection rates, all patients with stage I-III CRC were included, with the exception of patients who underwent local excision. The trends over time for the proportions of patients undergoing surgical resection were reported for the different time periods, and the Cochrane Armitage trend test was used to analyse the significance of trends over time. Trends over time for surgical resection rates stratified according to the presence or absence of comorbidities were added as Supplementary figures.

P values below 0.05 were considered statistically significant. Analysis was performed using SAS/STAT® statistical software (SAS system 9.4, SAS Institute, Cary, NC) and SPSS Statistics for Windows (version 22.0, IBM Corp, Armonk, NY).

3. Results

Between 2005 and 2016, 111,778 stage I-III CRC patients were diagnosed, of whom 104,185 (93.2%) underwent resection. 73,065 were colon cancer patients and 31,120 were rectal cancer patients.

The characteristics of patients who underwent resection are shown in Table 1. For colon cancer patients, the proportion of stage I tumours increased. The proportion of elective surgical procedures remained between 91 and 93% for both age groups. The use of a laparoscopic surgical approach in colon cancer patients increased between 2009 and 2016, specifically from 30% to 71% for younger patients and from 23% to 61% for older patients. For rectal and colon cancer patients, similar trends over time were demonstrated, but with an even larger increase in the use of laparoscopic approach for rectal cancer patients.

3.1. Postoperative mortality

30-day postoperative mortality decreased from 2.0% to 0.9% for younger colon cancer patients and from 1.4% to 0.7% for younger rectal cancer patients. A larger decrease in mortality was seen for older patients from 10.0% to 4.0% for colon cancer and from 8.3% to 2.7% for rectal cancer (Fig. 1).

The odds of dying within 30 days, 90 days or 1 year decreased significantly from 2005–2006 to 2015–2016 (Table 2). For 30-day mortality for colon cancer, ORs amounted to 0.48 (95% CI 0.36–0.64) for younger patients and 0.38 (95% CI 0.32–0.46) for older patients. For those with rectal cancer, ORs were found to be 0.50 (95% CI 0.32–0.79) for younger patients and 0.30 (95% CI 0.20–0.44) for older patients. Similar trends were found for 90-day and 1-year mortality.

3.2. One-year relative survival

Between 2005 and 2016, 1-year RS increased for both younger as well as older CRC patients (Fig. 2A). For younger patients, the 1-year RS increased from 94.0% to 97.8% for those with colon cancer and from 96.3% to 98.8% for those with rectal cancer. For older patients, a larger increase in 1-year RS was demonstrated. The 1-year RS increased from 84.8% to 94.6% for the older patients with colon cancer and from 86.1% to 97.2% for the older patients with rectal cancer.

3.3. Conditional relative survival

When the acute postoperative mortality (within 30 days) was excluded, the increase in survival between 2005 and 2016 was most pronounced for the older patients. An

Table 1
Patient, tumour and treatment characteristics of all patients diagnosed with stage I-III CRC between 2005 and 2016 who underwent resection by period of diagnosis. Patients were stratified according to age (<75 years or ≥75 years) and primary tumour location (colon or rectum).

Patient/tumour characteristics	Period of diagnosis											
	2005–2006		2007–2008		2009–2010		2011–2012		2013–2014		2015–2016	
Colon, <75 years												
Gender												
Male	3101	(54)	3220	(54)	3427	(54)	3747	(54)	4119	(55)	5629	(56)
Female	2617	(46)	2794	(46)	2974	(46)	3214	(46)	3387	(45)	4456	(44)
Stage												
Stage I	1042	(18)	1045	(17)	1153	(18)	1350	(19)	1588	(21)	3061	(30)
Stage II	2507	(44)	2555	(42)	2677	(42)	2798	(40)	3004	(40)	3418	(34)
Stage III	2169	(38)	2414	(40)	2571	(40)	2813	(40)	2914	(39)	3606	(36)
Histology												
Adenocarcinoma	4801	(84)	5032	(84)	5382	(84)	6000	(86)	6648	(89)	9113	(90)
Mucinous adenocarcinoma	868	(15)	903	(15)	931	(15)	902	(13)	779	(10)	888	(9)
Signet ring cell	49	(1)	79	(1)	88	(1)	59	(1)	79	(1)	84	(1)
Sublocalisation												
Proximal colon	2742	(48)	2909	(48)	3101	(48)	3355	(48)	3459	(46)	4494	(45)
Distal colon	2867	(50)	3007	(50)	3194	(50)	3456	(50)	3826	(51)	5462	(54)
Overlapping localisation	72	(1)	68	(1)	49	(1)	77	(1)	168	(2)	44	(0)
Colon, not otherwise specified	37	(1)	30	(0)	57	(1)	73	(1)	53	(1)	85	(1)
Social economic status												
Low	1435	(25)	1560	(26)	2109	(33)	2234	(32)	2014	(27)	2870	(28)
Medium	2610	(46)	2661	(44)	2302	(36)	2541	(37)	2748	(37)	4039	(40)
High	1651	(29)	1753	(29)	1953	(31)	2145	(31)	2718	(36)	3138	(31)
Unknown	22	(0)	40	(1)	37	(1)	41	(1)	26	(0)	38	(0)
(Neo)adjuvant chemotherapy												
Yes	2068	(36)	2351	(39)	2528	(39)	2722	(39)	2862	(38)	3424	(34)
No	3650	(64)	3663	(61)	3873	(61)	4239	(61)	4644	(62)	6661	(66)
Urgency[a]												
No, elective					5806	(91)	6313	(91)	6826	(91)	9377	(93)
Yes, emergency surgery					468	(7)	525	(8)	523	(7)	494	(5)
Construction stent/stoma, followed by planned surgery					36	(1)	39	(1)	65	(1)	37	(0)
Not applicable					33	(1)	23	(0)	31	(0)	0	(0)
Unknown					58	(1)	61	(1)	61	(1)	177	(2)
Approach[b]												
Laparoscopic surgery					1931	(30)	2903	(42)	4221	(56)	7204	(71)
Laparoscopic surgery with conversion					460	(7)	574	(8)	637	(8)	845	(8)
Open surgery					3945	(62)	3430	(49)	2564	(34)	1996	(20)
Not applicable					15	(0)	11	(0)	15	(0)	0	(0)
Unknown					4	(1)	43	(1)	69	(1)	40	(0)
Colon, ≥75 years												
Gender												
Male	1740	(44)	2019	(45)	2182	(47)	2218	(46)	2536	(49)	2388	(50)
Female	2260	(57)	2445	(55)	2507	(53)	2576	(54)	2632	(51)	2421	(50)
Stage												
Stage I	719	(18)	776	(17)	857	(18)	911	(19)	1182	(23)	1003	(21)
Stage II	1975	(49)	2128	(48)	2298	(49)	2275	(47)	2233	(43)	2229	(46)
Stage III	1306	(33)	1560	(35)	1534	(33)	1608	(34)	1753	(34)	1577	(33)
Histology												
Adenocarcinoma	3265	(82)	3675	(82)	3843	(82)	4080	(85)	4468	(86)	4191	(87)
Mucinous adenocarcinoma	686	(17)	743	(17)	784	(17)	657	(14)	644	(12)	561	(12)
Signet ring cell	49	(1)	46	(1)	62	(1)	57	(1)	56	(1)	57	(1)
Sublocalisation												
Proximal colon	2361	(59)	2623	(59)	2758	(59)	2779	(58)	2873	(56)	2901	(60)
Distal colon	1561	(39)	1762	(39)	1870	(40)	1922	(40)	2121	(41)	1855	(39)
Overlapping localisation	48	(1)	45	(1)	33	(1)	48	(1)	135	(3)	22	(0)
Colon, not otherwise specified	30	(1)	34	(1)	28	(1)	45	(1)	39	(1)	31	(1)
Social economic status												
Low	1172	(29)	1221	(27)	1695	(36)	1776	(37)	1581	(31)	1528	(32)
Medium	1736	(43)	1993	(45)	1693	(36)	1716	(36)	1883	(36)	1856	(39)
High	1079	(27)	1243	(28)	1287	(27)	1294	(27)	1685	(33)	1408	(29)
Unknown	13	(0)	7	(0)	14	(0)	8	(0)	19	(0)	17	(0)
(Neo)adjuvant chemotherapy												
Yes	279	(7)	380	(9)	385	(8)	454	(9)	564	(11)	510	(11)

Table 1 (*continued*)

Patient/tumour characteristics	Period of diagnosis											
	2005–2006		2007–2008		2009–2010		2011–2012		2013–2014		2015–2016	
No	3721	(93)	4084	(91)	4304	(92)	4340	(91)	4604	(8)9	4299	(89)
Urgency[a]												
No, elective					4237	(90)	4376	(91)	4688	(91)	4387	(91)
Yes, emergency surgery					367	(8)	324	(7)	393	(8)	362	(8)
Construction stent/stoma, followed by planned surgery					28	(1)	24	(1)	32	(1)	17	(0)
Not applicable					21	(0)	29	(1)	18	(0)	0	(0)
Unknown					36	(1)	41	(1)	37	(1)	43	(1)
Approach[b]												
Laparoscopic surgery					1096	(23)	1574	(33)	2525	(49)	2940	(61)
Laparoscopic surgery with conversion					296	(6)	336	(7)	456	(9)	454	(9)
Open surgery					3255	(69)	2836	(59)	2142	(41)	1401	(29)
Not applicable					14	(0)	18	(0)	14	(0)	0	(0)
Unknown					28	(1)	30	(1)	31	(1)	14	(0)

	Period of diagnosis											
	2005–2006		2007–2008		2009–2010		2011–2012		2013–2014		2015–2016	
Rectum, <75 years												
Gender												
Male	2346	(66)	2289	(63)	2192	(64)	2239	(64)	2346	(66)	2868	(65)
Female	1192	(34)	1327	(37)	1249	(36)	1269	(36)	1192	(34)	1553	(35)
Stage												
Stage I	1077	(30)	1153	(32)	1153	(34)	1207	(34)	1279	(36)	1058	(24)
Stage II	1121	(32)	1105	(31)	1024	(30)	957	(27)	1017	(29)	911	(21)
Stage III	1323	(38)	1358	(38)	1264	(37)	1344	(38)	1242	(35)	2452	(55)
Histology												
Adenocarcinoma	3212	(91)	3294	(91)	3127	(91)	3246	(93)	3298	(93)	4194	(95)
Mucinous adenocarcinoma	291	(8)	303	(8)	296	(9)	247	(7)	220	(6)	207	(5)
Signet ring cell	18	(1)	19	(1)	18	(1)	15	(0)	20	(1)	20	(0)
Social economic status												
Low	885	(25)	896	(25)	1106	(32)	1121	(32)	921	(26)	1233	(28)
Medium	1609	(46)	1675	(46)	1313	(38)	1318	(38)	1342	(38)	1860	(42)
High	1006	(29)	1022	(28)	1003	(29)	1048	(30)	1267	(36)	1305	(30)
Unknown	21	(1)	23	(1)	19	(1)	21	(1)	8	(0)	23	(1)
(Neo)adjuvant radiotherapy												
Yes	2305	(65)	2258	(62)	2142	(62)	1944	(55)	1546	(44)	2672	(60)
No	1216	(35)	1358	(38)	1299	(38)	1564	(45)	1992	(56)	1749	(40)
Approach[b]												
Laparoscopic surgery					1007	(29)	1610	(46)	2314	(65)	3568	(81)
Laparoscopic surgery with conversion					207	(6)	266	(8)	292	(8)	290	(7)
Open surgery					2184	(63)	1571	(45)	887	(25)	561	(13)
Not applicable					5	(0)	14	(0)	5	(0)	0	(0)
Unknown					38	(1)	47	(1)	40	(1)	2	(0)
Rectum, ≥75 years												
Gender												
Male	758	(54)	761	(54)	748	(55)	756	(57)	787	(58)	746	(60)
Female	656	(46)	637	(46)	605	(45)	563	(43)	577	(42)	491	(40)
Stage												
Stage I	429	(30)	443	(32)	433	(32)	479	(36)	490	(36)	309	(25)
Stage II	485	(34)	486	(35)	441	(33)	433	(33)	427	(31)	325	(26)
Stage III	500	(35)	469	(34)	479	(35)	407	(31)	447	(33)	604	(49)
Histology												
Adenocarcinoma	1274	(90)	1217	(87)	1221	(90)	1225	(93)	1266	(93)	1170	(95)
Mucinous adenocarcinoma	127	(9)	173	(12)	124	(9)	90	(7)	91	(7)	65	(5)
Signet ring cell	13	(1)	8	(1)	8	(1)	4	(0)	7	(1)	3	(0)
Social economic status												
Low	404	(29)	378	(27)	477	(35)	487	(37)	403	(30)	380	(31)
Medium	628	(44)	623	(45)	492	(36)	460	(35)	514	(38)	520	(42)
High	378	(27)	394	(28)	379	(28)	370	(28)	442	(32)	337	(27)
Unknown	4	(0)	3	(0)	5	(0)	2	(0)	5	(0)	1	(0)
(Neo)adjuvant radiotherapy												
Yes	710	(50)	773	(55)	806	(60)	817	(62)	675	(49)	611	(49)
No	704	(50)	625	(45)	547	(40)	502	(38)	689	(51)	627	(51)

(*continued on next page*)

Table 1 (*continued*)

	Period of diagnosis							
	2005–2006	2007–2008	2009–2010		2011–2012		2013–2014		2015–2016	
Approach[b]										
Laparoscopic surgery			350	(26)	544	(41)	855	(63)	978	(79)
Laparoscopic surgery with conversion			91	(7)	140	(11)	128	(9)	93	(8)
Open surgery			902	(67)	617	(47)	366	(27)	167	(13)
Not applicable			1	(0)	4	(0)	4	(0)	0	(0)
Unknown			9	(1)	14	(1)	11	(1)	0	(0)

CRC, colorectal cancer.
Data are absolute numbers with percentages inside parentheses.
[a] Data was only available for colon cancer patients and from 2009 onward.
[b] Data was available from 2009 onward.

increase from 94.0% to 98.4% for those with colon cancer and from 93.9% to 99.9% for those with rectal cancer was seen (Fig. 2B).

When not only the acute but also the subacute postoperative mortality (within 90 days) was excluded, the increase in survival of the older patients between 2005 and 2016 was less pronounced than for the 30-day conditional survival (Fig. 2C).

3.4. Resection rates

Resection rates decreased significantly over time ($p < 0.001$) for both colon and rectal cancer as well as for younger and older patients (Fig. 3). For rectal cancer patients, a larger decrease in resection rates can be seen compared with colon cancer patients, especially in the older (>75 years) patients for whom we found a decrease from 89.6% to 66.2% ($p < 0.001$).

Supplementary figure 1 shows trends in resection rates for both colon and rectal cancer patients, stratified according to age and the presence of comorbidities. For younger colon cancer patients, resection rates decreased with 6.9% for patients without comorbidities compared with 8.2% for patients with comorbidities. For older colon cancer patients, the resection rates decreased with 9.8% for patients without comorbidities compared with 7.9% for patients with comorbidities. For younger rectal cancer patients, resection rates decreased more, with 14.1% for patients without comorbidities compared with 17.6% for patients with comorbidities. For older patients, this was slightly more pronounced with a decrease of 18.9% for patients without comorbidities compared with 24.8% for patients with comorbidities.

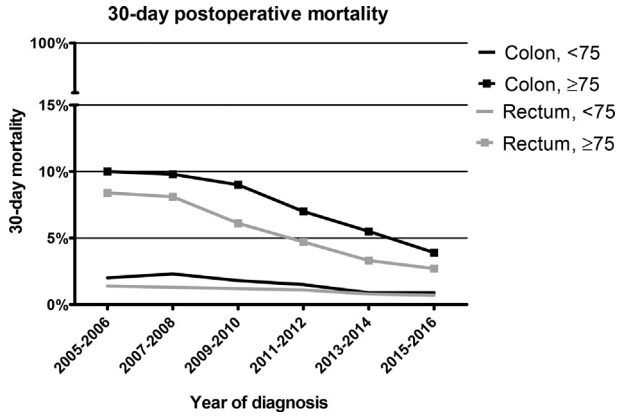

Fig. 1. 30-day postoperative mortality for stage I-III colon and rectal cancer patients, according to age (<75, ≥75).

4. Discussion

This large population-based study demonstrates a significant decrease in postoperative colorectal cancer mortality between 2005 and 2016, especially for older patients: 30-day mortality rates decreased from 10.0% to 4.0% for colon cancer patients and from 8.3% to 2.7% for rectal cancer patients. Compared with younger patients with stage I-III colorectal cancer, 1-year RS and 1-year RS on the condition that patients survived the first 30 postoperative days are almost equal and equal for older patients with stage I-III colorectal cancer, respectively.

Decreased mortality rates are most likely because of quality and safety improvements in colorectal cancer care, with more standardised operation procedures and an increasing proportion of laparoscopic procedures [16,17]. Although it can be argued that better patient selection over time could also play a role in the lower mortality rates, it is unlikely that it is the main cause. This notion is based on the Supplementary figure, showing equal resection rates over time for colon cancer patients with and without comorbidities. For rectal cancer, resection rates for older patients with comorbidity decreased with 6% more compared with those without comorbidity which could be considered as patient selection. However, for younger rectal cancer patients, this trend was also evident with a 3.5% larger decrease in resection rates for patients with comorbidities. Therefore, it is unlikely that better patient selection can fully explain the catch-up of older CRC patients with younger CRC patients regarding postoperative mortality. A previous study that used data from the Dutch Surgical Colorectal Audit also showed nearly equal proportions of surgically treated CRC patients

Table 2
Logistic regression analyses for 30-day, 90-day and 1-year postoperative mortality among stage I-III CRC, stratified according to tumour location (colon, rectum) and age (<75, ≥75).

Patient/tumour characteristics	N (total)	30-day mortality			90-day mortality			1-year mortality		
		Crude %	OR	95%-CI	Crude %	OR	95%-CI	Crude %	OR	95%-CI
Colon carcinoma, <75 years										
Period of diagnosis										
2005–2006	5718	2.0	1.00		3.3	1.00		7.6	1.00	
2007–2008	6014	2.3	1.20	(0.93–1.55)	3.5	1.07	(0.87–1.32)	7.0	0.91	(0.78–1.05)
2009–2010	6401	1.8	0.94	(0.72–1.23)	2.9	0.91	(0.74–1.13)	6.2	**0.81**	**(0.70–0.94)**
2011–2012	6961	1.5	0.79	(0.60–1.03)	2.3	**0.72**	**(0.58–0.90)**	5.4	**0.70**	**(0.61–0.81)**
2013–2014	7506	0.9	**0.50**	**(0.37–0.67)**	1.6	**0.51**	**(0.40–0.64)**	4.7	**0.62**	**(0.53–0.72)**
2015–2016	10,085	0.9	**0.48**	**(0.36–0.64)**	1.5	**0.48**	**(0.38–0.60)**	3.4	**0.47**	**(0.40–0.54)**
Colon carcinoma, >75 years										
Period of diagnosis										
2005–2006	4000	10.0	1.00		13.8	1.00		22.0	1.00	
2007–2008	4464	9.8	0.98	(0.85–1.14)	13.1	0.95	(0.83–1.08)	21.0	0.94	(0.84–1.04)
2009–2010	4689	9.0	0.89	(0.78–1.03)	11.9	**0.85**	**(0.75–0.96)**	19.3	**0.85**	**(0.76–0.94)**
2011–2012	4794	7.0	**0.68**	**(0.58–0.79)**	9.4	**0.66**	**(0.57–0.75)**	16.5	**0.70**	**(0.63–0.78)**
2013–2014	5168	5.5	**0.54**	**(0.46–0.63)**	7.3	**0.51**	**(0.44–0.59)**	13.3	**0.56**	**(0.50–0.62)**
2015–2016	4809	4.0	**0.38**	**(0.32–0.46)**	5.5	**0.37**	**(0.32–0.43)**	11.6	**0.47**	**(0.42–0.53)**
Rectal carcinoma, <75 years										
Period of diagnosis										
2005–2006	3521	1.4	1.00		2.3	1.00		5.1	1.00	
2007–2008	3616	1.3	0.95	(0.64–1.43)	2.2	0.97	(0.71–1.33)	4.9	0.95	(0.77–1.18)
2009–2010	3441	1.2	0.86	(0.57–1.31)	1.7	0.74	(0.53–1.04)	4.6	0.89	(0.71–1.11)
2011–2012	3508	1.1	0.80	(0.52–1.22)	1.7	0.72	(0.51–1.02)	4.2	0.82	(0.66–1.03)
2013–2014	3538	0.8	**0.53**	**(0.34–0.67)**	1.5	**0.67**	**(0.47–0.95)**	3.5	**0.68**	**(0.53–0.86)**
2015–2016	4421	0.7	**0.50**	**(0.32–0.79)**	1.0	**0.40**	**(0.27–0.58)**	2.4	**0.43**	**(0.33–0.55)**
Rectal carcinoma, >75 years										
Period of diagnosis										
2005–2006	1414	8.3	1.00		11.7	1.00		20.2	1.00	
2007–2008	1398	8.2	0.99	(0.75–1.29)	12.2	1.06	(0.84–1.34)	19.3	0.96	(0.80–1.16)
2009–2010	1353	6.1	**0.73**	**(0.54–0.97)**	8.9	**0.74**	**(0.58–0.95)**	14.5	**0.68**	**(0.56–0.83)**
2011–2012	1319	4.7	**0.56**	**(0.40–0.77)**	7.5	**0.62**	**(0.48–0.81)**	14.5	**0.70**	**(0.57–0.86)**
2013–2014	1364	3.3	**0.37**	**(0.26–0.53)**	5.9	**0.47**	**(0.36–0.63)**	10.7	**0.48**	**(0.39–0.60)**
2015–2016	1238	2,7	**0.30**	**(0.20–0.44)**	4.0	**0.29**	**(0.21–0.41)**	8.1	**0.33**	**(0.26–0.42)**

OR, odds ratio; CI, confidence interval; CRC, colorectal cancer.
Variables included in the logistic regression analyses are period of diagnosis, gender, stage of the tumour, subsite of the tumour, histology, social economic status, (neo)adjuvant chemotherapy for colon and (neo)adjuvant radiotherapy for rectum.
OR's were regarderd as significant when the 95%-CI did not include 1.00.

with high comorbidity scores between 2009 and 2016 [18]. Furthermore, frailty screening is currently implemented only to a limited extent in the Netherlands and internationally [19].

Our results are in contrast with previous Dutch studies [6,20], in which much higher mortality rates among older patients with rectal cancer compared with younger patients were reported. Unfortunately, there is no recent comparable evidence from other Western countries, because studies analysing both differences in postoperative mortality between older and younger patients, as well as trends over time, are very scarce. Those that do mention differences between older and younger patients are limited by reporting overall cancer mortality or including age only as a risk factor in their multivariable analysis [21,22].

As mentioned by Speelman *et al.*, there might be risk-avoiding behaviour of clinicians and therefore the possibility that older patients are being undertreated at the moment [5]. In the present study, we noticed decreasing resection rates over time with age-related disparities. Patients aged 75 years and older had a more pronounced decrease in resection rates, mainly when they had rectal cancer (89.6% in 2005, 66.2% in 2016). In contrast, in a Dutch cohort diagnosed between 1995 and 2004, almost all patients with stage I-III colon or rectal cancer underwent surgery (92–99%), regardless of age [23]. The decreasing resection rates in the current study are in accordance with more recent studies and could be because of the availability of other non-surgical treatment options, such as radiotherapy. Also, the Dutch national screening program was introduced in 2014, leading to the earlier detection of CRC and an increase in the proportion of patients undergoing local excision. Because we excluded local excisions from our study, this could be an additional explanation for the decreasing resection rates in our study. However, rectal cancer curative surgery might be omitted too often, and instead palliative radiotherapy is proposed to older patients. One should bear in mind that age itself should not be

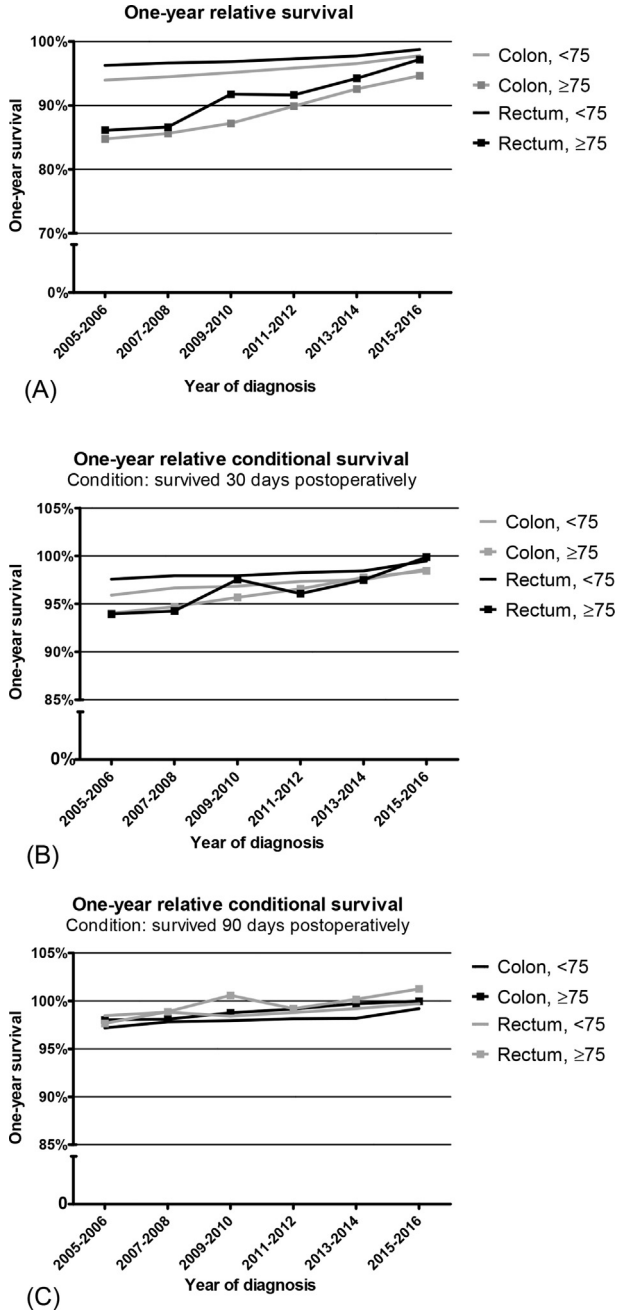

Fig. 2. One-year relative survival for stage I-III colon and rectal cancer patients, according to age (<75, ≥75). (A) Without any condition. (B) On the condition that patients survived the first 30 postoperative days. (C) On the condition that patients survived the first 90 postoperative days.

considered a risk factor for postoperative mortality [24]. Therefore, personalised strategies for older patients based on shared decision-making should be pursued after adequate frailty screening [25].

The need for adequate preoperative frailty screening is further emphasised by the knowledge that cancer-related survival can be the same for older and younger patients, not only after 1-year survival as previously mentioned in the literature [26] but already after 30 days

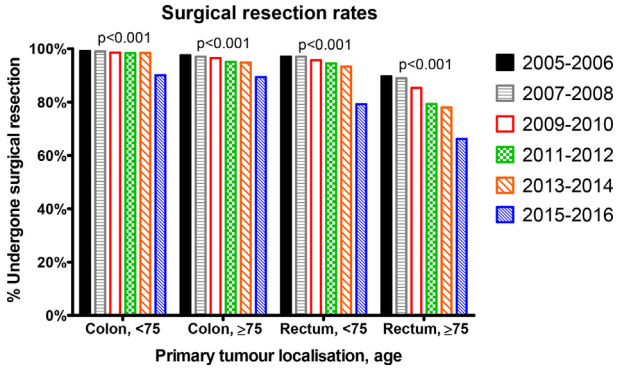

Fig. 3. Resection rates for stage I-III colon and rectal cancer patients, according to age (<75, ≥75) and period of diagnosis. P-values for trends over time are shown.

postoperative. This knowledge showcases the possible benefits of upcoming prehabilitation programs. These multidisciplinary programs, by reducing vulnerability and increasing resilience to postoperative risks, could enhance postoperative clinical outcomes and thereby lead to further survival improvement, especially for older, frail patients [27,28].

The lack of complete and adequate information on comorbidity and of correction for emergency surgery are obvious limitations of this study, as both are associated with increased postoperative morbidity and mortality. Although the proportion of patients undergoing emergency surgery has remained stable over time and was fairly equal between older and younger patients, the impact of an emergency surgery is larger for older and multimorbid patients [29]. Not correcting for this factor could account for the remaining difference in mortality between older and younger patients.

Although we have seen an increase in survival rates, it is not clear what the impact of colorectal surgery is on postoperative functional outcomes. Older patients often give higher priority to these functional outcomes than to survival [30]. Further research should therefore focus not only on further increasing postoperative survival rates in older patients but also on quality of life and improvement of postoperative physical functioning. Prehabilitation programs could play a role in achieving this goal [31].

In conclusion, postoperative colorectal cancer mortality rates significantly decreased over time, especially for older patients with an almost equal 1-year RS compared with younger patients. Clinicians should bear in mind that previous literature is no longer representative of the current clinical practice when informing patients during shared decision making on surgical treatment. With adequate preoperative frailty screening and shared decision-making, there is no need for unnecessary risk-avoiding behaviour in older CRC patients.

Conflict of interest statement

None declared.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejca.2019.04.036.

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