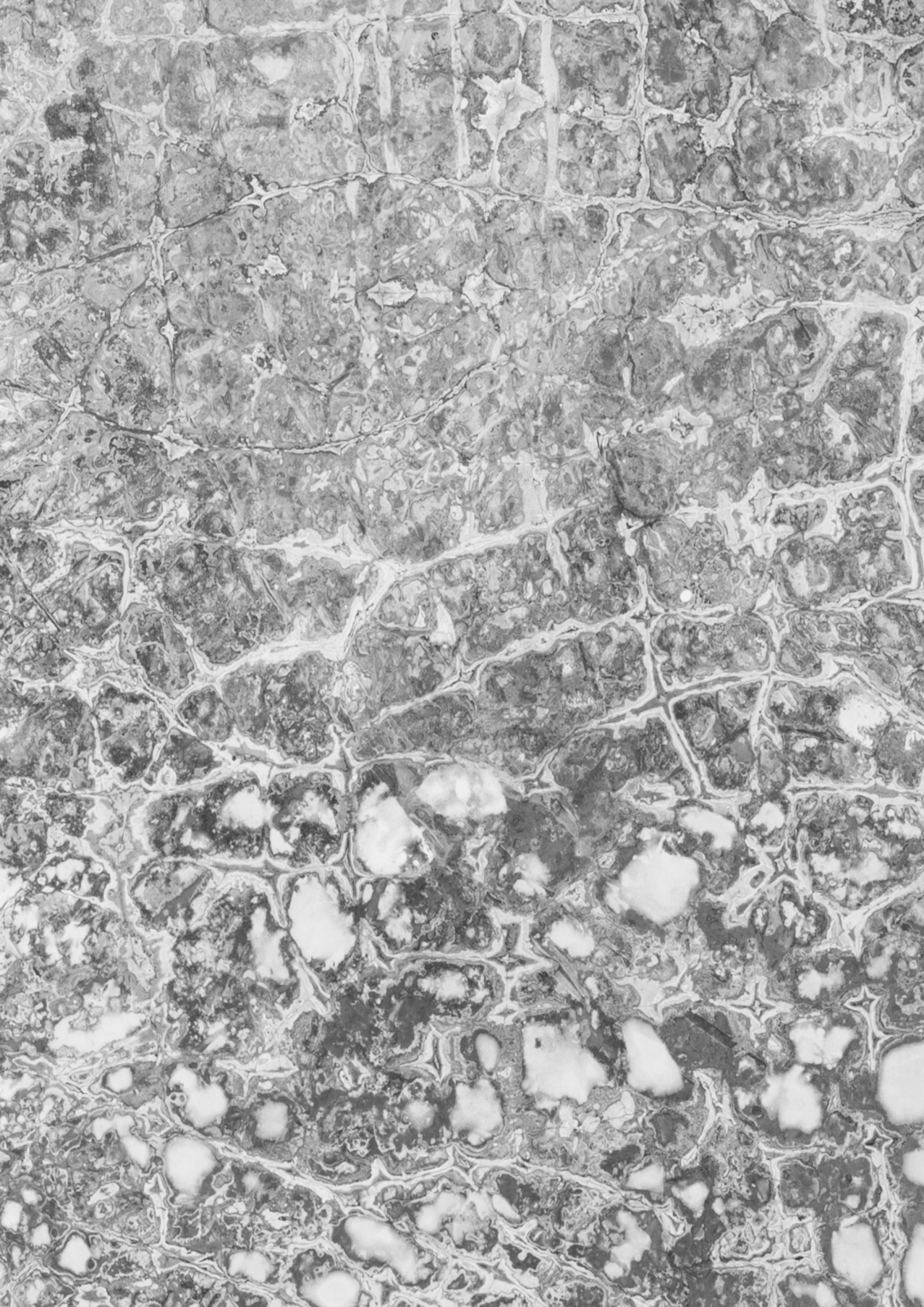
Improving colorectal cancer care: treatment and outcomes of patients with colorectal cancer

Breugom, A.J.



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Decrease in 30-day and one-year mortality over time in patients aged ≥75 years with stage I-III colon cancer: a population-based study

A.J. Breugom
E. Bastiaannet
J.W.T. Dekker
M.W.J.M. Wouters
C.J.H. van de Velde
G.J. Liefers

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ABSTRACT

Background

Monitoring time trends of cancer mortality is essential. Thirty-day mortality is an important surgical outcome measure, though postoperative mortality exceeds to one year after surgery in patients with colorectal cancer. The aim of this nationwide observational study was to assess changes over time in 30-day and one-year mortality in patients with stage I-III colorectal cancer.

Methods

All surgically treated patients with stage I-III colorectal cancer, diagnosed between 2009 and 2013 were selected from the Netherlands Cancer Registry. Changes in 30-day and one-year mortality were assessed using logistic regression by tumour localisation (colon, rectum) and age group (<75 years, ≥75 years).

Results

Overall, 41,186 patients were included. Among patients with colon cancer ≥75 years, 30-day mortality decreased from 8.3% in 2009 to 6.2% in 2013 (p-value for trend =0.011), and one-year mortality from 18.5% in 2009 to 15.0% in 2013 (p-value for trend =0.007). No significant differences in mortality over time were observed for patients <75 years with colon cancer and for patients with rectal cancer.

Conclusion

Thirty-day and one-year mortality decreased over time in patients ≥75 years with stage I-III colon cancer, though the absolute decrease is small. However, 30-day mortality and in particular the one-year mortality are both still high in older patients with colorectal cancer and will need to be focused on to further improve outcomes for these patient subgroups.

INTRODUCTION

Colorectal cancer incidence increased with approximately one percent per year between 1989 and 2013 in the Netherlands, while a substantially higher increase was observed in 2014 as a result of the introduction of the national screening programme and a further increase in 2015 due to gradual implementation of the screening programme. With 15,400 patients diagnosed with colorectal cancer in 2016, it is currently the second most commonly diagnosed cancer in the Netherlands.[1]

Thirty-day postoperative mortality is widely used as an outcome measure after surgical procedures and is useful for benchmarking and quality assurance. However, previous studies suggested a continued effect of surgery on survival.[2-6] It was shown that 30-day mortality considerably underestimates postoperative mortality in patients with colorectal cancer, with one-year excess mortality (defined as one-year mortality adjusted for expected mortality in the general population) rates up to 30%.[5,6] Risk factors for excess mortality in the first postoperative year were comorbidity, stage III tumours, emergency surgery, and postoperative surgical complications.[6] Furthermore, age-related differences in colorectal cancer survival are mainly due to differences in mortality in the first postoperative year: patients ≥75 years who survived the first year had the same cancer-related survival compared to younger patients.[5] In the majority of patients with colorectal cancer, especially older patients, who died within the first year after surgery, the cause of death was attributed to the disease.[7] As it is unlikely that most of these patients had recurrent disease within the first year, the majority of these patients probably died as a result of cancer treatment.

Monitoring time trends of cancer mortality is important for cancer control. It might be possible to link changes in cancer mortality to changes in exposure to a particular risk factor, to changes in treatment guidelines, or to changes in health care including for example perioperative care for surgically treated patients, optimisation of care for specific subgroups, and non-surgical management.

Given the importance of the 30-day and one-year mortality as outcome measures after surgery for colorectal cancer, the aim of this nationwide observational study was to assess changes over time in both 30-day and one-year mortality in patients with stage I-III colorectal cancer.

METHODS

Patients

All surgically treated patients with stage I-III colorectal cancer (ICD-10 C18, C19, and C20), who were diagnosed between January 1, 2009 and December 31, 2013, were selected from the Netherlands Cancer Registry. Patients who underwent local resection of the tumour were excluded. The Netherlands Cancer Registry registers data of all newly diagnosed patients with cancer in the Netherlands. Patients are detected through the national pathology archive, after which trained registry personnel collect data from the medical records including patient, tumour, and treatment characteristics. Follow-up status is available through linkage with municipal population registers, and was complete until December 31st, 2014.

Age was categorised as <75 years and ≥75 years. Tumour localisation was defined as colon or rectum. The information on TNM stage was based on pathological reports. If pathological data were missing, clinical TNM stage was used. Emergency surgery was recorded as no, yes, or as stent or stoma followed by planned surgery. Thirty-day and one-year mortality were defined as all-cause death at or before 30 days and one year after surgery for colorectal cancer.

Statistical analyses

Analyses were stratified by tumour localisation (colon, rectum) and age (<75 years, ≥75 years).

P-value for trend was obtained by logistic regression analyses. Moreover, we assessed if mortality changed over time using crude logistic regression models with 30-day or one-year mortality as dependent variable and year of diagnosis as independent variable, with the previous year used as a reference category. These analyses were additionally adjusted for stage, emergency surgery, and age. If data were missing, patients were analysed as a separate 'unknown' group within the same variable.

A p-value <0.05 was considered as statistical significant. All analyses were done with IBM SPSS Statistics, version 20.0.

RESULTS

Between January 1, 2009 and December 31, 2013, a total of 43,513 patients were identified. We excluded 2,327 patients who underwent local resection of the tumour. Data from the remaining 41,186 patients were included. Table 1 shows the characteristics

of the patients. Of all patients, 15,162 patients were aged ≥75 years. Moreover, over 70% of patients had a tumour located in the colon.

Table 1. Patient characteristics

	All patients (*n*=41,186)	**<75 years** (*n*=26,024)	**≥75 years** (*n*=15,162)
Age (median ±SD)	71.00 ±11.19	65.00 ±8.58	80.00 ±4.28
Gender			
Male	22,390 (54.4)	14,936 (57.4)	7,454 (49.2)
Female	18,796 (45.6)	11,088 (42.6)	7,708 (50.8)
Year of diagnosis			
2009	7,514 (18.2)	4,754 (18.3)	2,760 (18.2)
2010	8,282 (20.1)	5,123 (19.7)	3,159 (20.8)
2011	8,541 (20.7)	5,457 (21.0)	3,084 (20.3)
2012	8,577 (20.8)	5,428 (20.9)	3,149 (20.8)
2013	8,272 (20.1)	5,262 (20.2)	3,010 (19.9)
Tumour localisation			
Colon	30,022 (72.9)	17,798 (68.4)	12,224 (80.6)
Rectum	11,164 (27.1)	8,226 (31.6)	2,938 (19.4)
TNM stage			
I	9,829 (23.9)	6,474 (24.9)	3,355 (22.1)
IIA	13,930 (33.8)	8,175 (31.4)	5,755 (38.0)
IIB	2,083 (5.1)	1,160 (4.5)	923 (6.1)
IIIA	1,850 (4.5)	1,338 (5.1)	512 (3.4)
IIIB	8,209 (19.9)	5,272 (20.3)	2,937 (19.4)
IIIC	4,934 (12.0)	3,372 (13.0)	1,562 (10.3)
Unknown, but no metastases	351 (0.9)	233 (0.9)	118 (0.8)
Grade			
I	2,033 (4.9)	1,258 (4.8)	775 (5.1)
II	25,156 (61.1)	15,501 (59.6)	9,655 (63.7)
III	5,031 (12.2)	2,875 (11.0)	2,156 (14.2)
IV	50 (0.1)	22 (0.1)	28 (0.2)
Unknown	8,916 (21.6)	6,368 (24.5)	2,548 (16.8)
Emergency surgery			
No	27,578 (67.0)	16,340 (62.8)	11,238 (74.1)
Yes	2,209 (5.4)	1,328 (5.1)	881 (5.8)
Stent or stoma followed by planned surgery	185 (0.4)	120 (0.5)	65 (0.4)
Unknown	11,214 (27.2)	8,236 (31.6)	2,978 (19.6)

Data are presented as median ±SD or as *n* (%).

Patients with colon cancer <75 years

Thirty-day mortality ranged from 1.4% in 2009 to 1.1% in 2013 for patients with colon cancer <75 years (p-value for trend =0.065, Figure 1a). Adjusted logistic regression showed no significant differences in 30-day mortality (Table 2).

One-year mortality was 5.0% in 2009 and 5.1% in 2013 (p-value for trend =0.058, Figure 1a). In 2010, the one-year mortality was higher compared to 2009 in adjusted analysis (OR 1.26, 95% CI 1.02-1.56, p=0.035, Table 2), and the one-year mortality in 2011 was lower compared to 2010 (adjusted OR 0.74, 95% CI 0.60-0.91, p=0.004, Table 2).

Table 2. Crude and adjusted Odds Ratios

	Year of diagnosis	Crude OR	95% CI*	p-value*	Adjusted OR	95% CI**	p-value**
Colon cancer <75 years							
30-day mortality	2009	1	(Reference)		1	(Reference)	
	2010	1.42	(0.97-2.09)	0.072	1.41	(0.96-2.07)	0.082
	2011	0.77	(0.54-1.11)	0.159	0.76	(0.53-1.08)	0.127
	2012	0.96	(0.66-1.40)	0.824	0.94	(0.64-1.37)	0.732
	2013	0.76	(0.50-1.14)	0.188	0.77	(0.51-1.17)	0.223
1-year mortality	2009	1	(Reference)		1	(Reference)	
	2010	1.27	(1.03-1.56)	0.027	1.26	(1.02-1.56)	0.035
	2011	0.77	(0.63-0.94)	0.011	0.74	(0.60-0.91)	0.004
	2012	1.16	(0.94-1.42)	0.164	1.15	(0.93-1.41)	0.193
	2013	0.90	(0.73-1.10)	0.286	0.91	(0.74-1.12)	0.375
Colon cancer ≥75 years							
30-day mortality	2009	1	(Reference)		1	(Reference)	
	2010	1.00	(0.81-1.23)	0.982	0.97	(0.79-1.20)	0.774
	2011	0.81	(0.66-1.00)	0.048	0.81	(0.65-1.01)	0.056
	2012	1.01	(0.81-1.26)	0.913	1.06	(0.85-1.32)	0.616
	2013	0.89	(0.71-1.11)	0.295	0.86	(0.68-1.08)	0.183
1-year mortality	2009	1	(Reference)		1	(Reference)	
	2010	0.98	(0.85-1.14)	0.815	0.94	(0.81-1.10)	0.456
	2011	0.89	(0.77-1.03)	0.111	0.89	(0.76-1.03)	0.117
	2012	0.99	(0.85-1.15)	0.895	1.05	(0.89-1.22)	0.581
	2013	0.90	(0.77-1.05)	0.181	0.86	(0.74-1.01)	0.072
Rectal cancer <75 years							
30-day mortality	2009	1	(Reference)		1	(Reference)	
	2010	1.10	(0.57-2.15)	0.776	1.09	(0.56-2.13)	0.807
	2011	1.11	(0.60-2.06)	0.737	1.16	(0.62-2.18)	0.638
	2012	0.94	(0.51-1.72)	0.830	0.97	(0.52-1.80)	0.927
	2013	0.78	(0.40-1.53)	0.466	0.77	(0.39-1.51)	0.440
1-year mortality	2009	1	(Reference)		1	(Reference)	
	2010	1.17	(0.83-1.64)	0.362	1.19	(0.85-1.68)	0.319
	2011	0.92	(0.67-1.27)	0.608	0.94	(0.67-1.30)	0.689
	2012	1.02	(0.73-1.41)	0.920	1.02	(0.73-1.42)	0.910
	2013	0.81	(0.57-1.15)	0.241	0.81	(0.57-1.16)	0.249
Rectal cancer ≥75 years							
30-day mortality	2009	1	(Reference)		1	(Reference)	
	2010	0.84	(0.51-1.40)	0.506	0.86	(0.52-1.44)	0.566
	2011	1.00	(0.60-1.68)	1.000	1.03	(0.61-1.75)	0.902
	2012	0.76	(0.44-1.31)	0.317	0.71	(0.41-1.23)	0.225
	2013	0.73	(0.39-1.37)	0.329	0.79	(0.42-1.49)	0.464
1-year mortality	2009	1	(Reference)		1	(Reference)	
	2010	0.84	(0.60-1.17)	0.311	0.86	(0.61-1.20)	0.369
	2011	1.06	(0.76-1.48)	0.732	1.11	(0.79-1.56)	0.568
	2012	1.01	(0.73-1.40)	0.934	0.96	(0.69-1.34)	0.803
	2013	0.81	(0.58-1.13)	0.218	0.85	(0.60-1.20)	0.355

* Previous year is used as a reference category.

** Previous year is used as a reference category adjusted for stage, emergency surgery, and age.

Patients with colon cancer ≥75 years

For patients with colon cancer ≥75 years, 30-day mortality decreased from 8.3% in 2009 to 6.2% in 2013 (p for trend =0.011), and one-year mortality from 18.5% in 2009 to 15.0% in 2013 (p-value for trend =0.007, Figure 1b).

We did not demonstrate a significant improvement in 30-day and one-year mortality using the previous year as a reference category in adjusted logistic regression analysis (Table 2).

Patients with rectal cancer <75 years

We observed no significant differences in 30-day mortality (p-value for trend =0.901) and one-year mortality (p-value for trend =0.058) for patients with rectal cancer <75 years (Figure 1c). Thirty-day mortality ranged from 1.4% in 2009 to 1.1% in 2013, and one-year mortality ranged from 5.0% in 2009 to 5.1% in 2013. Adjusted logistic regression analysis with the previous year as a reference category also showed no significant improvement in 30-day and one-year mortality (Table 2).

Patients with rectal cancer ≥75 years

For patients with rectal cancer aged ≥75 years, 30-day mortality decreased from 6.1% in 2009 to 2.9% in 2013 (p for trend =0.107), and one-year mortality from 15.3% in 2009 to 11.7% in 2013 (p-value for trend =0.490, Figure 1d). Compared to the previous year, no significant differences in 30-day and one-year mortality were observed (Table 2).

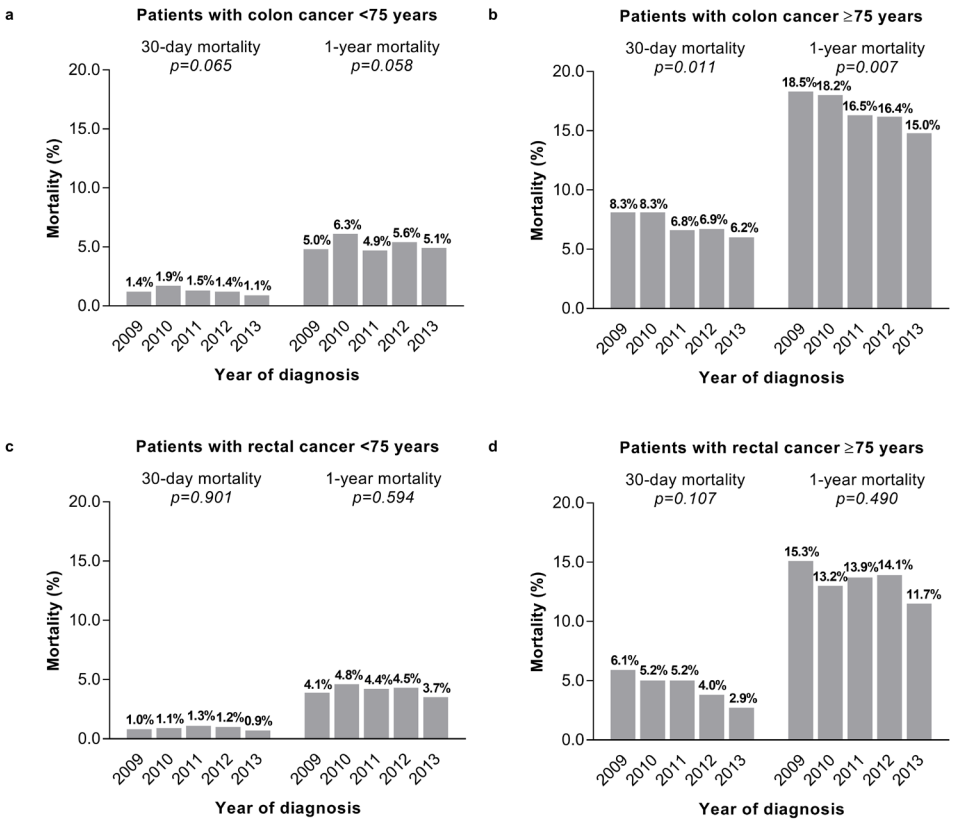

Figure 1. Time trends in 30-day and 1-year mortality for patients with a. colon cancer <75 years, b.colon cancer ≥75 years , c. rectal cancer <75 years, d. rectal cancer ≥75 years

P-values were calculated using logistic regression, and represent p for trend for year of diagnosis.

DISCUSSION

This study shows a 25% relative decrease in 30-day and a 19% relative decrease in one-year mortality over time in patients with stage I-III colon cancer aged ≥75 years, while the absolute decrease was 2.1% in 30-day mortality and 3.5% in one-year mortality.

Improving quality and safety of colorectal cancer care is an important issue. Survival improved markedly over time for patients with colorectal cancer in Europe, whilst incidence rates increased modestly.[1,8-10] The increase in survival has been mainly attributed to improvements in for example staging, access to treatment, effective treatment options, standardising care, and the introduction of high-volume care.[8,11,12] Moreover, several European countries initiated surgical audits which may also have contributed to improved survival by measuring quality of care, and reflecting on the effects of any

changes in the quality of care over time.[13] These factors could have contributed to the decrease in 30-day and one-year mortality that we observed. Moreover, in older patients, more individual selection for preoperative and postoperative treatment might have been improved over time.

For patients with rectal cancer, we observed no significant decrease over time in both 30-day and one-year mortality. Outcome of patients with rectal cancer already improved considerably over the past decades mainly as a result of the introduction of standardised total mesorectal excision, more accurate staging with MRI, and the use of preoperative (chemo)radiotherapy.[12,14-17] In this study, we demonstrated that for example the 30-day mortality rate for patients with rectal cancer <75 years was only 0.9% in 2013. However, although slightly lower than in patients with colon cancer aged ≥75 years, 30-day and one-year mortality are still high among older patients with rectal cancer.

Henneman et al. demonstrated that the mortality rate in patients with a severe complication is higher in patients with colon cancer than in patients with rectal cancer, although patients with rectal cancer have a higher complication rate.[18] In a study by van der Sijp et al., it was also shown that complications account for a higher one-year excess mortality in patients with colon cancer.[19] In our study, we observed higher 30-day and one-year mortality in patients with colon cancer, which is in line with the findings of these studies.

For patients aged younger than 75 years, we observed no significant changes over time in 30-day mortality and one-year mortality for both colon and rectal cancer, with especially low 30-day mortality rates. This indicates that a further reduction in mortality would be difficult to achieve. Moreover, there is substantial more evidence for younger patients from randomised controlled trials regarding optimal treatment compared to older patients who are often excluded from randomised controlled trials.[20] However, although not significant, it is worth noticing that in patients <75 years with colon cancer, one-year mortality did not decrease at all over time. While 30-day mortality is very low in this group, one-year mortality is still over five percent. This suggests that there might be a continued effect of surgery on survival for younger patients as well. A possible explanation could be that younger patients will be fit enough to survive complications in the acute phase, but may die during the first year after surgery as a late result of their severe complications, while older patients will also die more often in the acute phase after a complication.

Although we observed an improved 30-day and one-year mortality over time for patients with colon cancer ≥75 years, 30-day mortality and especially one-year mortality are still high for older patients with colon or rectal cancer, which is in line with previous studies.[5,6]

These studies concluded that the focus should be on the first postoperative year to improve outcomes after colorectal cancer surgery.

Comorbidity, stage III tumours, emergency surgery, postoperative surgical complications, and readmission were already identified as important factors influencing one-year mortality.[6,19,21] Moreover, older patients are at increased risk to dehydration and electrolyte abnormalities, especially when there is physiological stress, as a result of age-related pathophysiological changes combined with iatrogenic causes.[22] In older patients admitted to hospital as medical emergencies, dehydration is associated with a greater risk of in-hospital mortality.[23] Dehydration may therefore be a factor influencing 30-day mortality after surgery for colorectal cancer in older patients. Geriatric consultation can be of help in treatment decision making for older patients and may lead to more individualised and optimised treatment.[24] Further insight in modifiable risk factors for 30-day and one-year mortality in patients ≥75 years is necessary. Moreover, the period after hospital discharge will also be of great importance to improve the quality of colorectal cancer care.

The main strength of this study is the well-registered and quality assured data from the Netherlands Cancer Registry of a large number of unselected patients with stage I-III colorectal cancer. This made it possible to assess time trends of 30-day and one-year mortality, providing insight in mortality rates over time. On the contrary, we were unfortunately not able to incorporate specific patient characteristics such as comorbidity and clinical condition, as these data are not registered in the Netherlands Cancer Registry. This limits detailed analysis on specific subgroups. Moreover, no information on cause of death, as well as toxicity or complications of treatment was available. In this study, we used all-cause 30-day and one-year mortality as outcomes. However, it was previously shown that excess mortality was high among patients with colorectal cancer who died within the first postoperative year.[5,6]

In conclusion, 30-day and one-year mortality decreased over time in patients with stage I-III colon cancer aged ≥75 years. However, 30-day mortality and in particular one-year mortality are both still high in older patients with colorectal cancer and will need to be focused on to further improve outcomes for these patient subgroups.

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REFERENCES

1. http://cijfersoverkanker.nl. *Accessed October* 2017.
2. Visser BC, Keegan H, Martin M, Wren SM. Death after colectomy: it's later than we think. *Arch Surg* 2009; **144**(11): 1021-7.
3. Faiz O, Haji A, Bottle A, Clark SK, Darzi AW, Aylin P. Elective colonic surgery for cancer in the elderly: an investigation into postoperative mortality in English NHS hospitals between 1996 and 2007. *Colorectal Dis* 2011; **13**(7): 779-85.
4. Mamidanna R, Almoudaris AM, Faiz O. Is 30-day mortality an appropriate measure of risk in elderly patients undergoing elective colorectal resection? *Colorectal Dis* 2012; **14**(10): 1175-82.
5. Dekker JW, van den Broek CB, Bastiaannet E, van de Geest LG, Tollenaar RA, Liefers GJ. Importance of the first postoperative year in the prognosis of elderly colorectal cancer patients. *Ann Surg Oncol* 2011; **18**(6): 1533-9.
6. Gooiker GA, Dekker JW, Bastiaannet E, et al. Risk factors for excess mortality in the first year after curative surgery for colorectal cancer. *Ann Surg Oncol* 2012; **19**(8): 2428-34.
7. Dekker JW, Gooiker GA, Bastiaannet E, et al. Cause of death the first year after curative colorectal cancer surgery; a prolonged impact of the surgery in elderly colorectal cancer patients. *Eur J Surg Oncol* 2014; **40**(11): 1481-7.
8. Karim-Kos HE, de VE, Soerjomataram I, Lemmens V, Siesling S, Coebergh JW. Recent trends of cancer in Europe: a combined approach of incidence, survival and mortality for 17 cancer sites since the 1990s. *Eur J Cancer* 2008; **44**(10): 1345-89.
9. Brenner H, Bouvier AM, Foschi R, et al. Progress in colorectal cancer survival in Europe from the late 1980s to the early 21st century: the EUROCARE study. *Int J Cancer* 2012; **131**(7): 1649-58.
10. Holleczek B, Rossi S, Domenic A, et al. On-going improvement and persistent differences in the survival for patients with colon and rectum cancer across Europe 1999-2. *Eur J Cancer* 2015.
11. Birkmeyer JD, Siewers AE, Finlayson EV, et al. Hospital volume and surgical mortality in the United States. *N Engl J Med* 2002; **346**(15): 1128-37.
12. Heald RJ, Ryall RD. Recurrence and survival after total mesorectal excision for rectal cancer. *Lancet* 1986; **1**(8496): 1479-82.
13. Breugom AJ, Boelens PG, van den Broek CB, et al. Quality assurance in the treatment of colorectal cancer: the EURECCA initiative. *Ann Oncol* 2014; **25**(8): 1485-92.
14. Taylor FG, Quirke P, Heald RJ, et al. Preoperative magnetic resonance imaging assessment of circumferential resection margin predicts disease-free survival and local recurrence: 5-year follow-up results of the MERCURY study. *J Clin Oncol* 2014; **32**(1): 34-43.
15. van Gijn W, Marijnen CA, Nagtegaal ID, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer: 12-year follow-up of the multicentre, randomised controlled TME trial. *Lancet Oncol* 2011; **12**(6): 575-82.
16. Sauer R, Becker H, Hohenberger W, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. *N Engl J Med* 2004; **351**(17): 1731-40.
17. Gérard JP, Conroy T, Bonnetain F, et al. Preoperative radiotherapy with or without concurrent fluorouracil and leucovorin in T3-4 rectal cancers: results of FFCD 9203. *J Clin Oncol* 2006; **24**(28): 4620-5.
18. Henneman D, Ten Berge MG, Snijders HS, et al. Safety of elective colorectal cancer surgery: non-surgical complications and colectomies are targets for quality improvement. *J Surg Oncol* 2014; **109**(6): 567-73.
19. van der Sijp MP, Bastiaannet E, Mesker WE, et al. Differences between colon and rectal cancer in complications, short-term survival and recurrences. *Int J Colorectal Dis* 2016; **31**(10): 1683-91.
20. Zulman DM, Sussman JB, Chen X, Cigolle CT, Blaum CS, Hayward RA. Examining the evidence: a systematic review of the inclusion and analysis of older adults in randomized controlled trials. *J Gen Intern Med* 2011; **26**(7): 783-90.
21. Greenblatt DY, Weber SM, O'Connor ES, LoConte NK, Liou JI, Smith MA. Readmission after colectomy for cancer predicts one-year mortality. *Ann Surg* 2010; **251**(4): 659-69.
22. El-Sharkawy AM, Sahota O, Maughan RJ, Lobo DN. The pathophysiology of fluid and electrolyte balance in the older adult surgical patient. *Clin Nutr* 2014; **33**(1): 6-13.
23. El-Sharkawy AM, Watson P, Neal KR, et al. Hydration and outcome in older patients admitted to hospital (The HOOP prospective cohort study). *Age Ageing* 2015; **44**(6): 943-7.

24. Verweij NM, Souwer ETD, Schiphorst AHW, et al. The effect of a geriatric evaluation on treatment decisions for older patients with colorectal cancer. *Int J Colorectal Dis* 2017.