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Research Article

Colorectal Cancer in Octogenarians: Results of Treatment, a Descriptive Clinical Study

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Abstract

Background: Colorectal cancers (CRCs) often occur in octogenarians. However, data on treatment and survival are sparse. **Objectives:** Octogenarians were studied in order to gain data on treatment, outcomes, and survival related to CRC.

Patients and Methods: All consecutive octogenarians with CRC in the period of 2002-2008 were included. An extensive review of hospital records was carried out. Patients were divided into two groups, as follows: group 1 included patients who were alive after five years of follow-up, while group 2 comprised patients who died within 5 years of their diagnosis. Cause of death was determined and classified as related to cancer, non-related, or because of treatment.

Results: One hundred and eleven octogenarians were diagnosed with CRC (82 colon cancers and 29 rectal cancers). Patients in group 2 had a significantly higher disease stage compared with group 1(P < 0.001). Patients in group 1 more often underwent surgery with curative intent (P < 0.0001). There was no difference in clinical presentation or localization of the malignancy. In group 1, 14 patients died more than 5 years after surgery. The cause of death was not related to cancer in 100% of cases. In group 2, 29 (46.0%) died as a direct consequence of CRC, 14 (22.2%) due to the treatment, and 20 (31.7%) died due to non-cancer-related causes. The overall 5-year survival rate was 40% in colon cancer patients and 51.7% in rectal cancer patients. The Charlson age co-morbidity scores were significantly lower in colon cancer patients in group 1(P = 0.005). This was not the case in patients with rectal cancer.

Conclusions: The co-morbidity score is important in survival after surgery. Forty-four percent of octogenarians with CRC died because of non-tumor-related disease or illness. Fit elderly people can benefit from standard therapy for CRC.

Keywords: Octogenarians, Colorectal Cancer, Epidemiology, Survival, Recurrence

1. Background

Colorectal cancer (CRC) is one of the most frequently occurring malignancies in the Western world. Since people have a longer life expectancy, this type of cancer will also occur in octogenarians. Colonoscopy is the best diagnostic modality; in patients aged 80 years or more, this is a safe and effective procedure with a high diagnostic yield (1). There is also a significantly higher yield compared with patients younger than 80 years (2). In a previous study done in the Zaanstreek region, it was shown that 20% of CRCs occurred in patients above the age of 80 years. This number stayed rather constant over a period of 18 consecutive years (3).

Patients above the age of 80 years are excluded from large clinical trials. They do not have the potential life expectancy to gain enough follow-up years after treatment. However, in normal daily practice, the clinician has to deal with octogenarians and decide on the best treatment option. Surgery is the only curative treatment, but many older patients are frail, have significant co-morbidity, and are at risk for any type of surgery. Retrospective series have shown that older patients can have the same benefit from optimum treatment strategies as their younger counterparts. However, the lack of prospective data and increased toxicity rates seen in older patients lead to a reluctance to treat older patients adequately (4).

2. Objectives

Few data are present in the literature on the treatment and especially outcomes of treatment of CRC in octogenarians. For this reason, a study was carried out in consecutive octogenarians with CRC to gain data on treatment, outcomes, and disease-free survival.

3. Patients and Methods

All consecutive patients older than 80 years diagnosed with CRC in the Zaans medical centre, the community hospital of the Zaanstreek region in the Netherlands, were included in the study. The study period began in 2002 and

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ended in 2008. Evaluation was carried out in January 2014. Hence, there was at least 5 years of follow-up for every patient.

An extensive review of all hospital records (clinical files, endoscopy reports, and pathology reports) was carried out to study the presentation of the malignancy, disease stage (Dukes classification), treatment, recurrence, recurrence-free survival, and overall survival. In addition, co-morbidity was scored using the well-known Charlson age co-morbidity score (5-7).

For the sake of the study, patients were divided into two groups. Group 1 comprised patients who were alive after 5 years of follow-up, while group 2 included patients who died within 5 years after diagnosis and treatment. The cause of death was determined and classified as related to cancer, non-related, or because of treatment.

Statistical analysis was carried out using the chi-square test for contingency tabulations and the t-test. A value below 0.05 was considered statistically significant.

4. Results

In the time period from of 2002 - 2008, a total of 111 octogenarians were diagnosed with colorectal cancer CRC (82 patients with colon cancer and 29 with rectal cancer). Table 1 shows the characteristics of the patients. There was no difference in gender between both the groups. Patients in group 2 had significantly more often a higher stage of disease significantly more often compared with than the group of long survivors (P < 0.001). In group 1, a higher percentage of patients underwent surgery with curative intent (P < 0.0001). There was no significant difference in clinical presentation, in the sense terms of patients.

There was no difference in the localization of the cancer between both the two groups.

In group 1, 14 patients died more than 5 years after surgery. The cause of death was not related to cancer in 100% of these cases. In group 2, all patients died within 5 years after the diagnosis. 29 (46.0%) as a direct consequence of the colorectal cancer, 14 (22.2%) due to the complications from treatment, and finally, 20 (31.7%) patients died due to non-cancer cancer-related causes. Of the Nonnon-cancer cancer-related deaths, was 28.7% occurred in patients with colon cancer and 42.9% in patients with rectal cancer. There was no significant difference between deaths of patients with colon cancer or and those with rectal cancer. The overall 5-year survival was 33 out of 82 (40%) patients with colon cancer and 15 out of 29 (51.7%) patients with rectal cancer. Figures 1 and 2 show the survival curves with overall survival but also cancer specific survival. There was no difference for colon or rectal cancer. Figure 3 shows

the time to recurrence of patients with colon cancer. In group 2 patients with rectal cancer from group 2, only one patient had recurrent disease 1.98 years after diagnosis; the other four already had metastases at the time of presentation.





Figure 2. Cancer-Specific Deaths in Patients With Colon and Rectal Cancer

The Charlson age co-morbidity score was significantly lower in colon cancer patients in group 1 (mean 5.73 [standard deviation (SD) 0.94] vs. 6.59 [SD: 1.53]; P = 0.005). This was not the case in patients with rectal cancer (mean 5.73 [SD: 0.88] vs. mean 6.5 [SD: 1.4]; P = ns).

None of the patients were treated with adjuvant chemotherapy in the case of colon cancer. However, 10 patients with rectal cancer and a survival exceeding 5 years were treated with neo-adjuvant radiotherapy, in comparison with only two patients who died within 5 years.

		Group 1 (n = 48)	Group 2 (n = 63)	P Value
Gender				Ns
Men		19 (39.5)	28 (44.4)	
Wom	nen	29 (60.5)	35 (55.6)	
Cause of death				
Tumo	or related		29 (46)	
Treat	ment related		14 (22.2)	
Non-	cancer related	14 (100)	20 (31.7)	
Dukes				< 0.0001
Duke	es A	11 (22.9)	5 (7.9)	
Duke	es B	28 (58.3)	18 (28.5)	
Duke	es C	7(14.6)	13 (20.6)	
Duke	es D		17 (26.9)	
Unkr	nown	1(4.2)	10 (16.4)	
Cura	tive surgery	47 (97.9)	40 (63.5)	< 0.0001
Localization of the tumor				Ns
Rectu	ım	15 (31.2)	14 (22.2)	
Sigm	oid	15 (31.2)	13 (20.6)	
Desce	ending colon		1(1.6)	
Trans	sverse colon	5 (10.4)	7 (11.1)	
Ascer	nding colon	6 (12.5)	9 (14.3)	
Cecu	m	7 (14.7)	19 (30.2)	
Complaints				
Bleed	ling	26 (54.2)	20 (31.7)	
Anen	nia	19 (39.6)	32 (50.8)	
Abdo	ominal pain	15 (31.3)	23 (36.5)	
Chan	iging bowel habits	21 (43.7)	32 (50.8)	

Table 1. Comparison of Octogenarians With a Follow-Up of More than 5 Years (Group 1) and Those who Died Within 5 Years After Diagnosis (Group 2)^{a,b}

Abbreviation: ns, not significant. ^aValues are expressed as No. (%).

^bStatistical analysis with chi-square test for contingency tabulations.

5. Discussion

It can be expected that the number of octogenarians with CRC will rise in the near future. In the United States, nearly 8% of all cancers diagnosed and 15% of cancer deaths occur in individuals aged 85 years and older (8, 9). However, probably due to the increasing number of adenomas that have been removed endoscopically, it also can be expected that the number of CRCs in octogenarians will ultimately decline (2, 3).

The present study described the clinical course in octogenarians diagnosed with CRC, and more specifically, survival after diagnosis. All patients with CRC are discussed in a multi-disciplinary meeting with gastroenterologists, oncologists, surgeons, radiologists, and radiotherapists. Based on clinical presentation, data from the literature and co-morbidity, the best therapeutic option was chosen. As clearly shown, the disease stage in older patients with CRC is an important predictor of survival (10).

The present study showed that co-morbidity expressed as the Charlson age co-morbidity score is important in survival after surgery. However, this was only the case in patients with colon cancer. Patients with rectal cancer have a longer or shorter survival after diagnosis irrespective of the Charlson age co-morbidity score. Why this is the case is not clear. This could be due to the small sample size. How-



ever, 10 out of 15 patients (67%) with rectal cancer underwent neo-adjuvant radiotherapy followed by surgery and were still alive after 5 years of follow-up in comparison with 2 out of 14 patients (14%) who died within 5 years. This indicates that neo-adjuvant radiotherapy in cases of treatable rectal cancer characterized by a lower clinical stage has fair results for octogenarians. This is in accordance with the results of another study (11).

None of the octogenarians with colon cancer received adjuvant chemotherapy. According to the literature, receiving adjuvant chemotherapy is a poor factor of overall survival for older patients with CRC (11). In a study of adjuvant 5FU based chemotherapy, it was found that this treatment did not benefit older cancer patients, while neoadjuvant radiotherapy improved the prognosis of older patients with stage III rectal cancer. (11). However, there are also different opinions in the literature. Several publications have suggested that geriatric patients can benefit from chemotherapy similarly to younger patients in the settings of both early and advanced-stage CRC (12).

Another interesting point in the present study is that 31.7% of octogenarians with colorectal cancer died because of non-tumor-related disease or illness. This certainly shows the limited life expectancy of elderly patients with co-morbidity. This is in accordance with another study from the Netherlands (13). In contrast, the prognosis of patients with CRC who underwent curative surgery improves with each additional year survived, with the largest improvements in the first years after diagnosis (13).

Management of cancer in the elderly is challenging, as is screening patients in the 80+ age group. Older patients with colorectal cancer are underrepresented in clinical trials. For this reason, the outcomes in elderly patients are unclear. A reduced life expectancy should lead to more conservative approaches. However, treatment outcomes for fit, elderly patients with colorectal cancer can be similar to those of younger patients, as shown in the present study. A consensus report expressed the hope that recommendations will pave the way for formal treatment guidelines based upon scientific evidence in the future (14).

Screening for frailty is useful. A study showed 1-year survival to be 80% in the frail group and 92% in the nonfrail group. Five-year survival was significantly lower in frail (24%) than non-frail patients (66%) (15). A palliative approach should be taken into consideration for frail elderly patients and for those with a short life expectancy (16). Data from studies specifically targeting older patients indicate that proper treatment planning and specific medical and geriatric assessment can achieve a safe and beneficial treatment result in older patients (17). Chronological age should not be an exclusion criterion for therapy. Careful patient selection, dose adjustments, close monitoring, and early intervention in the event of side effects are essential (17). It is important to realize that 22% of patients died because of treatment-related causes. Complications of surgery have a greater impact on frail patients.

In normal daily practice, the most important question is whether the life expectancy of the patient is long enough. Sometimes, treatment can be expected to be more hazardous than the original tumor. However, if fit elderly people are treated according to the standard applied in younger patients, the results can be beneficial. The benefits of treatment must be balanced with its potential side effects and the patient's wishes.

Footnote

Authors' Contribution: Elmer van Eeghen is a PhD student and carried out all of the research tasks. Sandra D Bakker is an oncologist and provided input for the manuscript. Ruud J.L.F Loffeld developed the concept, provided the data set, and wrote the paper.

References

- Arora A, Singh P. Colonoscopy in patients 80 years of age and older is safe, with high success rate and diagnostic yield. *Endoscopy*. 2004;60(3):408-13. doi: 10.1016/s0016-5107(04)01715-8.
- Loffeld RJ, Liberov B, Dekkers PE. Yearly diagnostic yield of colonoscopy in patients age 80 years or older, with a special interest in colorectal cancer. *Geriatr Gerontol Int.* 2012;12(2):298–303. doi:10.1111/j.1447-0594.2011.00769.x. [PubMed: 22050603].
- Loffeld RJLF, Dekkers PEP, Flens M. The Incidence of Colorectal Cancer Is Decreasing in the Older Age Cohorts in the Zaanstreek Region in the Netherlands: An Age-Cohort Effect. *ISRN Gastroenterology*. 2013;2013:1– 5. doi: 10.1155/2013/871308.

- Power DG, Lichtman SM. Chemotherapy for the elderly patient with colorectal cancer. *Cancer J.* 2010;16(3):241–52. doi: 10.1097/PPO.0b013e3181e07690. [PubMed: 20526103].
- Kastner C, Armitage J, Kimble A, Rawal J, Carter PG, Venn S. The Charlson comorbidity score: a superior comorbidity assessment tool for the prostate cancer multidisciplinary meeting. *Prostate Cancer Prostatic Dis.* 2006;9(3):270–4. doi: 10.1038/sj.pcan.4500889. [PubMed: 16770340].
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *Journal of Chronic Diseases*. 1987;40(5):373–83. doi: 10.1016/0021-9681(87)90171-8.
- Ouellette JR, Small DG, Termuhlen PM. Evaluation of Charlson-Age Comorbidity Index as predictor of morbidity and mortality in patients with colorectal carcinoma. *J Gastrointest Surg.* 2004;8(8):1061–7. doi: 10.1016/j.gassur.2004.09.045. [PubMed: 15585394].
- Thakkar JP, McCarthy BJ, Villano JL. Age-specific cancer incidence rates increase through the oldest age groups. *Am J Med Sci.* 2014;**348**(1):65– 70. doi: 10.1097/MAJ.00000000000281. [PubMed: 24805784].
- 9. McCleary NJ, Dotan E, Browner I. Refining the chemotherapy approach for older patients with colon cancer. *J Clin Oncol.* 2014;**32**(24):2570–80. doi: 10.1200/JCO.2014.55.1960. [PubMed: 25071118].
- Uyeturk U, Turker I, Bal O, Demirci A, Uysal Sonmez O, Helvaci K, et al. Treatment decision plans matter in elderly patients with gastrointestinal cancer: suboptimal or optimal?. *J BUON*. 2014;19(2):365-71. [PubMed: 24965393].

- Yang L, Ma Q, Yu YY, Wang C, Meng WJ, Adell G, et al. Efficacy of surgery and adjuvant therapy in older patients with colorectal cancer: a STROBE-compliant article. *Medicine (Baltimore)*. 2014;93(28):eee266. doi: 10.1097/MD.00000000000266. [PubMed: 25526455].
- Xiao H, Lichtman SM. Management of colorectal cancer in older patients. Oncology (Williston Park). 2006;20(7):741–50. [PubMed: 16841797].
- van Erning FN, van Steenbergen LN, Lemmens VE, Rutten HJ, Martijn H, van Spronsen DJ, et al. Conditional survival for long-term colorectal cancer survivors in the Netherlands: who do best?. *Eur J Cancer.* 2014;**50**(10):1731–9. doi: 10.1016/j.ejca.2014.04.009. [PubMed: 24814358].
- Papamichael D, Audisio R, Horiot JC, Glimelius B, Sastre J, Mitry E, et al. Treatment of the elderly colorectal cancer patient: SIOG expert recommendations. *Ann Oncol.* 2009;20(1):5-16. doi: 10.1093/annonc/mdn532. [PubMed: 18922882].
- Ommundsen N, Wyller TB, Nesbakken A, Jordhoy MS, Bakka A, Skovlund E, et al. Frailty is an independent predictor of survival in older patients with colorectal cancer. *Oncologist.* 2014;19(12):1268–75. doi: 10.1634/theoncologist.2014-0237. [PubMed: 25355846].
- Berretta M, Benedetto F, Francia R, Menzo E, Palmeri S, Tirelli U, et al. Colorectal Cancer in Elderly Patients: From Best Supportive Care to Cure. Anti-Cancer Agents Med Chem. 2013;13(9):1332–43. doi: 10.2174/18715206113136660350.
- Kordatou Z, Kountourakis P, Papamichael D. Treatment of older patients with colorectal cancer: a perspective review. *Ther Adv Med Oncol.* 2014;6(3):128–40. doi: 10.1177/1758834014523328. [PubMed: 24790652].