Original article

Co-morbidity leads to altered treatment and worse survival of elderly patients with colorectal cancer

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Background: **The aim of this study was to evaluate the effects of co-morbidity on the treatment and prognosis of elderly patients with colorectal cancer.**
Methods: **The independent influence of age and co-morbidity on treatment and survival was analysed for 6931 patients with colorectal cancer aged 50 years or more diagnosed between 1995 and 2001 in the southern part of the Netherlands.**
Results: **Co-morbidity had no influence on resection rate. The use of adjuvant chemotherapy in patients with stage III colonic cancer was influenced by co-morbidity, especially a previous malignancy (odds ratio (OR) 0·2 (95 per cent confidence interval (c.i.) 0·1 to 0·6); $P = 0·002$) or chronic obstructive pulmonary disease (COPD) (OR 0·3 (95 per cent c.i. 0·1 to 0·9); $P = 0·043$). Co-morbidity also influenced use of adjuvant radiotherapy in patients with rectal cancer, especially the presence of hypertension in combination with diabetes (OR 0·5 (95 per cent c.i. 0·2 to 0·9); $P = 0·031$). Co-morbidity influenced survival (hazard ratio up to 1·6), when adjusted for age, sex, tumour stage and treatment. The greatest influence on survival of patients with colonic cancer was previous malignancy, cardiovascular disease and COPD, and that of patients with rectal cancer was COPD, hypertension, and hypertension in combination with diabetes.**
Conclusion: **Elderly patients with co-morbidity were treated less aggressively and had a worse survival than those with no concomitant disease.**

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Introduction

Colorectal cancer is the second most common cause of cancer death in industrialized countries[1,2]. Seventy-five per cent of incident tumours occur in persons aged 65 years or more. Colorectal tumours affect a large number of people who, because of their age, are likely to have other chronic disabling conditions (co-morbidity)[3]. In patients with serious co-morbidity, the practitioner might decide to alter standard oncological treatment because of increased risk of side-effects or limited life expectancy. Few data are available for treatment outcome in elderly patients with colorectal cancer who are also suffering from serious co-morbid conditions, as these patients are generally ineligible for clinical trials. Surgical, sometimes endoscopic, resection of the tumour is the only primary curative treatment for colorectal cancer. Total mesorectal excision (TME) and preoperative radiotherapy for stage II and III rectal cancer, and adjuvant chemotherapy for stage III colonic cancer, improve both disease control and patient survival[4–8]. These treatments have been recommended in the Netherlands since the mid-1990s. In this population-based study, carried out in medium to large general hospitals and two radiation therapy centres, the effect of co-morbidity on choice of treatment and survival of patients with colorectal cancer was investigated in association with other prognostic determinants.

Patients and methods

Analyses were based on data for all 6931 patients aged 50 years or more diagnosed with colorectal cancer from

1995 to 2001 in the registration area of Eindhoven Cancer Registry. This registry serves a large part of the southern Netherlands, with 2·4 million inhabitants; it is notified by six pathology departments, the hospital medical records departments of ten community hospitals, and two radiation therapy institutes. Despite lack of access to death certificates, the organization of Dutch healthcare facilities and notification procedures has enabled cancer registries to attain a completeness of data exceeding 95 per cent[9]. Prognostically relevant concomitant conditions were recorded from the medical records according to a slightly adapted version of the Charlson Index (*Table 1*)[10]; sources used included correspondence between specialists, medical history and preoperative reports. A patient's medical record is regarded as the most complete source of information on past and current health status[11].

Tumour site, stage and morphology were classified according to the International Classification of Diseases for Oncology. Patients with tumour stages I and II were considered as one group, because differences in treatment and 10-year survival were relatively small[12].

Primary treatment of colonic cancer was classified as surgery, surgery followed by chemotherapy, and other (palliative, radiotherapy alone, chemotherapy alone, radiotherapy plus chemotherapy) or no therapy. Rectal cancer treatment was classified as conventional surgery (without TME), surgery including TME (with or without radiotherapy), conventional surgery with radiotherapy, and other (palliative, radiotherapy alone, chemotherapy alone, radiotherapy plus chemotherapy) or no therapy. No differentiation was made betweem TME with and TME without radiotherapy because a large national trial comparing these two treatments was being conducted during the study period, and included a large proportion of patients in the region.

Table 1 Classification of co-morbidity according to an adapted version of the Charlson Index[10]

Previous malignancy (except basal skin carcinoma and carcinoma *in situ* of the cervix)
Chronic obstructive pulmonary disease (COPD)
Cardiovascular disease (myocardial infarction, cardiac decompensation, angina pectoris, intermittent claudication, abdominal aneurysm, peripheral arterial disease)
Cerebrovascular disease (cerebrovascular accident, hemiplegia)
Hypertension
Diabetes mellitus
Digestive tract disease (stomach diseases, Crohn's disease, ulcerative colitis, liver cirrhosis, hepatitis)
Other (connective tissue disease, severe rheumatoid arthritis, kidney disease, dementia, tuberculosis, chronic infection)

It was not possible to differentiate between curative and palliative surgery; in stage IV disease, surgery was expected to be palliative. Chemotherapy given to patients with stage IV disease was classified as chemotherapy, not as palliative treatment.

To avoid bias due to changing guidelines, only recent data on therapy (1997–2001) were used when determining the influence of age and co-morbidity on adjuvant chemotherapy in patients with stage III colonic cancer, and adjuvant radiotherapy in patients with rectal cancer.

The prevalence of co-morbidity was analysed according to age (50–64, 65–79 and 80 or more years), sex and tumour site (colon or rectum). The independent influence of co-morbidity on adjuvant chemotherapy in patients with stage III colonic cancer, and adjuvant radiotherapy in patients with rectal cancer, was examined in a logistic regression analysis, controlling for age, sex and tumour stage (only for rectal cancer). The influence of co-morbidity on TME was also examined by logistic regression. The influence of age (50–64, 65–79 and 80 or more years) and number of co-morbid diseases on the rate of permanent stoma formation was analysed using the χ^2 test (excluding patients who had excision of the rectum).

The survival of patients at 1 January 2004 was assessed through civil municipal registries and the Central Bureau for Genealogy, which collects data on all Dutch citizens who die. Patients who left the Netherlands (estimated as 0·2 per cent) were lost to follow-up. A total of 3486 patients (50·3 per cent) died and 3445 (49·7 per cent) were still alive; the latter were censored at 1 January 2004. Crude survival was determined from date of diagnosis to death or end of study. The log rank test was used to compare survival between groups of patients. Multivariable proportional hazards regression methods were used to calculate hazard ratios adjusted for probable confounders. The likelihood ratio method was used to determine hazard ratios for death. The effects of co-morbidity were first evaluated in a model with the number of co-morbid conditions, age, tumour stage and sex, without treatment. Treatment was then included in the model, in order to investigate whether the prognostic effects of age and co-morbidity could be fully explained by less aggressive treatment. This procedure was repeated for each co-morbid condition (or combinations of conditions) in place of the number of co-morbidities. Patients who coded positive for a pair of conditions did not code positive for each condition singly. Univariate survival analysis (modelling a single explanatory variable) was stratified according to age at diagnosis. For facilitated application of the results in clinical practice, patients aged 65–79 years were stratified into 5-year age groups (50–64, 65–69, 70–74, 75–79 and 80 or more years).

Multivariable survival analysis was stratified according to tumour site (colon and rectum). All data analysis was performed using SAS/STAT® software, version 8 (SAS Institute, Cary, North Carolina, USA).

Results

The 6931 patients newly diagnosed with colorectal cancer between 1995 and 2001 had a mean age of 70 (maximum 98) years. Characteristics according to tumour site and age are shown in *Table 2*. Stage was more often unknown for older patients, especially those with rectal cancer. The number of co-morbid conditions increased with age. For all age groups the most frequent single concomitant diseases were hypertension (9·4 per cent of patients, decreasing with age), previous malignancy (7·1 per cent of patients, increasing with age) and cardiovascular disease (5·6 per cent of patients, increasing with age). The prevalence of COPD was 4·0 per cent, that of diabetes mellitus 3·4 per cent and digestive tract disease 1·9 per cent. The most frequent combination of co-morbid conditions was cardiovascular disease plus hypertension (3·3 per cent of patients). Combinations of hypertension with diabetes (2·1 per cent), previous malignancy with cardiovascular disease (up to 1·8 per cent of patients aged 80 years or more) and cardiovascular disease with COPD (up to 2·4 per cent of patients with rectal cancer aged 80 years or over) were also common. Women suffered more often from hypertension than men, and less often from concomitant cardiovascular disease and COPD. The prevalence of co-morbidity was similar in patients with colonic and rectal cancer. However, previous malignancy was more frequent in patients with colonic cancer aged 80 years or more (9·1 per cent *versus* 5·3 per cent of patients with rectal cancer), and COPD was more frequent in patients with rectal cancer aged 80 years or more (5·2 per cent *versus* 3·1 per cent of patients with colonic cancer). Previous malignancy consisted mainly of colorectal, genital and breast tumours (in women). The prevalence of co-morbidity was not related to tumour stage.

Most patients with stage I–II colonic cancer received surgical treatment only (*Fig. 1*); less than 2 per cent of patients with stage II disease had adjuvant chemotherapy. For stage III colonic cancer, surgery followed by adjuvant chemotherapy was the most frequently used treatment for patients younger than 65 years (82·8 per cent). Adjuvant chemotherapy was given to 42·4 per cent of patients with stage III disease aged 65–79 years, but to only 1·2 per cent

Table 2 General characteristics of patients with colorectal cancer according to tumour site and age (1995–2001)

	Frequency (%)					
	Colonic cancer			Rectal cancer		
	50–64 years ($n = 1226$)	65–79 years ($n = 2331$)	≥ 80 years ($n = 842$)	50–64 years ($n = 865$)	65–79 years ($n = 1265$)	≥ 80 years ($n = 402$)
Sex						
M	54·2	50·9	39·0	62·6	60·0	45·3
F	45·8	49·1	61·0	37·4	40·0	54·7
Stage						
I–II	47·8	55·3	55·2	50·0	56·5	47·2
III	26·5	23·9	22·1	24·0	18·2	17·3
IV	23·4	16·8	13·6	17·1	15·2	11·5
Unknown	2·3	4·0	9·1	8·9	10·1	24·0
No. of co-morbid conditions*						
0	55·5	33·9	26·2	60·2	35·7	29·7
1	30·0	35·4	33·8	27·0	35·8	34·0
2	9·8	19·1	24·4	9·5	17·4	22·0
3	3·4	7·8	10·0	2·7	8·4	10·4
≥ 4	1·3	3·8	5·6	0·6	2·7	3·9
Unknown	10·8	8·2	9·9	8·5	7·0	9·1
Treatment						
Surgery alone	63·6	79·1	86·5	35·0	42·4	44·5
Surgery including TME ± radiotherapy				22·0	20·8	11·0
Surgery + adjuvant therapy†	29·5	12·3	0·2	34·3	23·5	11·1
Other or no therapy‡	6·9	8·6	13·3	8·8	13·3	33·4

*Proportion of patients excluding unknown co-morbidity. †Adjuvant chemotherapy for colonic and adjuvant radiation therapy for rectal cancer. ‡Other treatment comprises therapy not otherwise specified and metastasis-directed therapy such as metastasectomy and metastasis-directed radiotherapy, but not metastasis-directed chemotherapy, which is classified as chemotherapy.

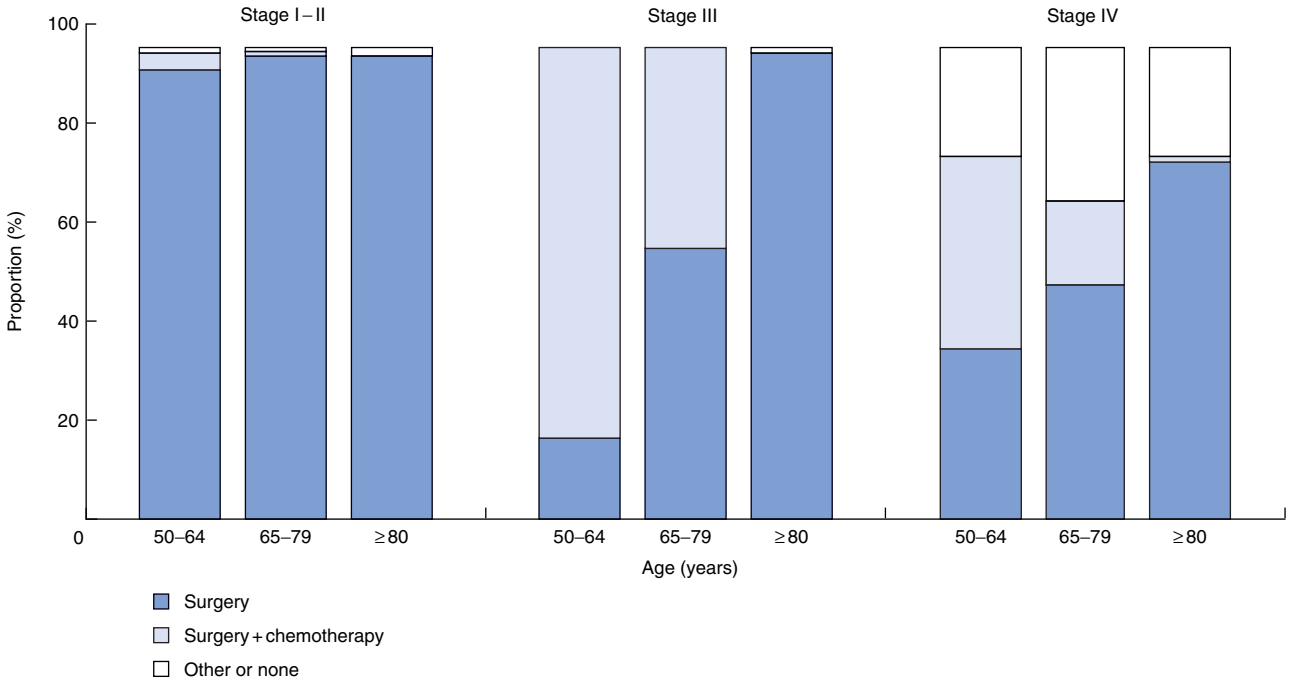

Fig. 1 Choice of therapy for patients with colonic cancer according to stage and age (1997–2001)

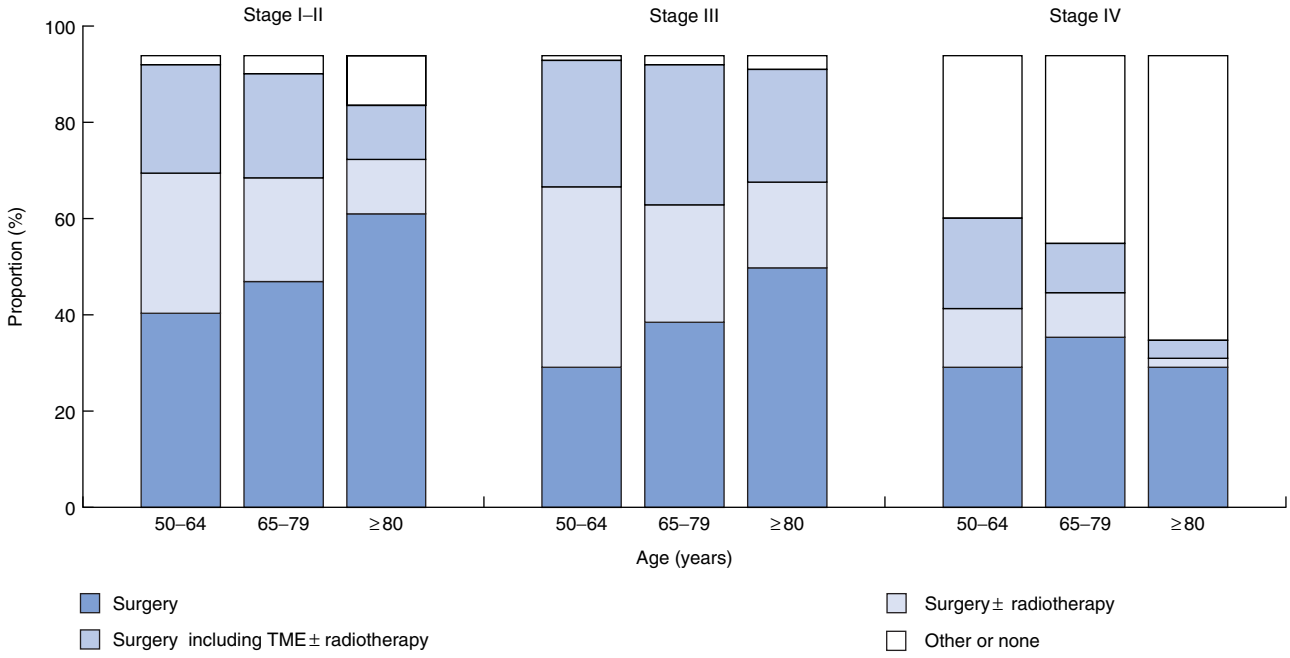

Fig. 2 Treatment of patients with rectal cancer according to stage and age (1997–2001). TME, total mesorectal excision

of those aged 80 years or more. For stage IV disease, the proportion receiving chemotherapy decreased from 41·3 per cent of patients aged 50–64 years to 1·8 per cent of those in the oldest age group.

In patients with stage I–II and III rectal cancer, surgery alone or in combination with radiotherapy was the most common treatment (*Fig. 2*). TME was performed in 20·1 per cent of patients with stage I–II disease and in 28·0 per cent of those with stage III. Most patients with stage IV rectal cancer received palliative therapy alone. For all stages of disease, the proportion receiving adjuvant radiotherapy decreased with increasing age.

The proportion of patients with stage II and III rectal cancer who received adjuvant chemoradiotherapy increased from 3·9 per cent in 1995–1999 to 15·9 per cent in 2001 (data not shown). Owing to small numbers in 1995–1999, adjuvant chemoradiotherapy was not taken into account in further analyses.

In logistic regression analysis of patients with stage III colonic cancer, controlling for age and sex, co-morbidity was associated with a lower probability of receiving adjuvant chemotherapy (*Table 3*). Previous malignancy (odds ratio (OR) 0·2 (95 per cent confidence interval (c.i.) 0·1 to 0·6); $P = 0·002$) and COPD (OR 0·3 (95 per cent c.i. 0·1 to 0·9); $P = 0·043$) were mainly responsible for this effect (subanalysis; data not shown). Older age was also clearly related to less frequent administration of adjuvant therapy. Patients with rectal cancer and co-morbidity had a lower probability of receiving adjuvant radiotherapy; previous malignancy and the combination of hypertension and diabetes had the greatest effect on treatment (OR 0·5 (95 per cent c.i. 0·2 to 0·9); $P = 0·031$). The use of adjuvant radiotherapy decreased with age. Elderly patients with rectal cancer and patients with co-morbidity were less likely to have TME (*Table 4*). The effect of co-morbidity was largely due to previous malignancy. The rate of permanent stoma formation increased with age, from 16·7 per cent of patients aged 50–64 years to 26·7 per cent of those aged 80 years or more ($P = 0·001$), but was not influenced by co-morbidity ($P = 0·298$; data not shown).

For colonic cancer, patients aged 50–64 years without recorded concomitant disease had a crude 5-year survival rate of 58·4 per cent. In patients aged 65–79 years without co-morbidity the survival rate was 58·4 per cent (age 65–69 years, 56·1 per cent; 70–74 years, 59·9 per cent; 75–79 years, 57·3 per cent), and in those aged 80 years and older 39·2 per cent (*Table 5*). Survival decreased with the number of co-morbid conditions. In a multivariable analysis, co-morbidity was a significant predictor of death even when adjusted for age, sex and disease stage. The inclusion of treatment in the model did

Table 3 Administration of adjuvant therapy for patients with stage III colonic cancer or rectal cancer diagnosed between 1995 and 2001; logistic regression model including all listed variables

	Odds ratio	*P**
Colonic cancer		
Age (years)		
50–64	1·0	
65–79	0·2 (0·1, 0·3)	< 0·0001
≥ 80	0·01 (0·001, 0·02)	< 0·0001
Sex		
M	1·0	
F	0·7 (0·5, 0·9)	0·045
No. of co-morbid conditions		
0	1·0	
1	0·8 (0·6, 1·1)	0·057
≥ 2	0·5 (0·3, 0·8)	0·001†
Rectal cancer		
Age (years)		
50–64	1·0	
65–79	0·7 (0·5, 0·9)	0·041
≥ 80	0·4 (0·2, 0·5)	< 0·0001
Sex		
M	1·0	
F	1·0 (0·8, 1·2)	0·970
Stage		
I–II	1·0	
III	1·3 (0·9, 1·6)	0·071
IV	0·5 (0·4, 0·7)	< 0·0001
No. of co-morbid conditions		
0	1·0	
1	0·9 (0·7, 1·2)	0·535
≥ 2	0·7 (0·5, 0·9)	0·040‡

Values in parentheses are 95 per cent confidence intervals. *Wald χ^2 test. †$P < 0·050$, ‡$P < 0·050$ (χ^2 test for trend).

Table 4 Total mesorectal excision for patients with rectal cancer diagnosed between 1995 and 2001; logistic regression model including all listed variables

	Odds ratio	*P**
Age (years)		
50–64	1·0	
65–79	1·0 (0·8, 1·3)	0·898
≥ 80	0·6 (0·4, 0·9)	0·038
Sex		
M	1·0	
F	0·9 (0·7, 1·1)	0·762
Stage		
I–II	1·0	
III	1·5 (1·2, 1·9)	0·016
IV	1·1 (0·8, 1·5)	0·294
No. of co-morbid conditions		
0	1·0	
1	0·7 (0·5, 0·9)	0·008
≥ 2	0·8 (0·6, 1·1)	0·192

Values in parentheses are percentages. *χ^2 test.

Table 5 Univariate and multivariable analyses for overall survival of patients with colonic cancer according to age, and relative survival (1995–2001)

	5-year survival rate (%)*			Multivariable analysis†	
	50–64 years	65–79 years	≥ 80 years	Hazard ratio	*P*#
Age (years)					
50–64	55·8 (1)			1·0	
65–79		46·2 (1)		1·3 (1·2, 1·5)	< 0·0001
≥ 80			28·1 (2)	2·0 (1·8, 2·4)	< 0·0001
Sex					
M	55·5 (2)	43·3 (1)	27·7 (3)	1·0	
F	56·6 (2)	49·9 (1)	28·4 (2)	0·9 (0·8, 0·9)	0·008
Stage					
I–II	80·0 (2)	63·2 (1)	39·3 (3)	1·0	
III	54·5 (3)	39·0 (2)	24·7 (3)	2·1 (1·9, 2·3)	< 0·0001
IV	9·0 (2)	3·8 (1)	3·7 (2)	5·2 (4·7, 5·9)	< 0·0001
Treatment					
Surgery	66·0 (1)	51·5 (1)	32·0 (2)	1·0	
Surgery + chemotherapy	45·8 (2)	40·5 (3)	§	0·7 (0·7, 0·9)	< 0·0001
Other or none	§	2·1 (1)	§	1·5 (1·3, 1·8)	< 0·0001
No. of co-morbid conditions					
0	58·4 (2)	55·1 (1)	39·2 (4)	1·0	
1	55·4 (3)	44·2 (1)	27·2 (3)	1·2 (1·1, 1·3)	0·0003
≥ 2	49·6 (4)	37·9 (2)	22·1 (3)	1·4 (1·2, 1·5)	< 0·0001
Co-morbid condition‡					
Previous malignancy	60·8 (6)	39·9 (3)	30·4 (6)	1·3 (1·1, 1·5)	0·002
Cardiovascular disease	45·9 (7)	42·9 (4)	21·2 (6)	1·3 (1·1, 1·8)	0·008
COPD	55·2 (9)	39·3 (5)	34·0 (11)	1·3 (1·1, 1·7)	0·010
Diabetes	58·3 (11)	44·5 (5)	33·7 (11)	1·1 (0·9, 1·4)	0·386
Hypertension	59·0 (5)	55·5 (3)	29·0 (7)	1·1 (0·9, 1·2)	0·074
Digestive tract disease	58·9 (10)	44·5 (5)	31·2 (8)	0·9 (0·7, 1·4)	0·049

*Univariate analysis of crude actuarial survival; values in parentheses are standard errors. †Model included age, sex, tumour stage, treatment and number of co-morbid conditions or single concomitant diseases; values in parentheses are 95 per cent confidence intervals. ‡Includes patients with the respective concomitant disease alone; patients with no co-morbidity formed the reference group (hazard ratio 1·0). §Sample size too small to complete analysis. COPD, chronic obstructive pulmonary disease. #χ^2 likelihood ratio test.

not affect the significance of co-morbidity. Patients with previous malignancy, cardiovascular disease, COPD, the combination of previous malignancy and COPD (hazard ratio (HR) 1·8 (95 per cent c.i. 1·1 to 1·7)), and the combination of hypertension and diabetes (HR 1·6 (95 per cent c.i. 1·2 to 2·0)) had a worse survival.

For rectal cancer, patients without recorded co-morbidity aged 50–64 years had a crude 5-year survival rate of 60·0 per cent (*Table 6*). In patients without co-morbidity aged 65–79 years the survival rate was 53·9 per cent (age 65–69 years, 52·8 per cent; 70–74 years, 55·9 per cent; 75–79 years, 52·4 per cent), and in those aged 80 years or more 32·9 per cent. Survival decreased with number of concomitant diseases. In a multivariable analysis, age, stage and co-morbidity were prognostic factors in patients with rectal cancer; these factors remained significant after the inclusion of treatment in the model. Patients with COPD, hypertension, and the combination of hypertension and diabetes (HR 1·8 (95 per cent c.i. 1·2 to 2·7)) had a worse survival.

Discussion

In this study of the influence of prognostically relevant co-morbidity on choice of treatment and long-term survival of unselected patients with colorectal cancer, the proportion of patients with co-morbidity varied from almost 40 per cent patients aged 50–64 years to more than 70 per cent in those aged 80 years or older. The most common concomitant diseases were hypertension, cardiovascular diseases and previous malignancy.

The proportion of patients undergoing surgery was not affected by age or co-morbidity. This can be explained by the fact that resection is the only primary curative treatment for colorectal cancer, and is often necessary to prevent obstruction. This contrasts with

Table 6 Univariate and multivariable analyses for overall survival of patients with rectal cancer according to age, and relative survival (1995–2001)

	5-year survival rate (%)*			Multivariable analysis†	
	50–64 years	65–79 years	≥ 80 years	Hazard ratio	*P*#
Age (years)					
50–64	57·8 (2)			1·0	
65–79		44·9 (2)		1·4 (1·2, 1·6)	< 0·0001
≥ 80			24·3 (2)	2·1 (1·7, 2·5)	< 0·0001
Sex					
M	57·6 (2)	40·7 (2)	20·1 (3)	1·0	
F	58·3 (3)	49·8 (2)	27·1 (3)	0·9 (0·8, 1·0)	0·057
Stage					
I–II	79·4 (1)	62·0 (2)	37·7 (2)	1·0	
III	54·5 (4)	35·9 (3)	25·8 (6)	1·9 (1·5, 2·4)	< 0·0001
IV	4·5 (2)	2·4 (1)	6·3 (4)	5·1 (4·7, 6·6)	< 0·0001
Treatment					
Surgery	64·2 (3)	51·3 (2)	35·4 (4)	1·0	
Surgery + radiotherapy	60·1 (3)	49·9 (3)	24·3 (7)	1·0 (0·8, 1·2)	0·889
Surgery including TME ± radiotherapy	64·7 (4)	55·2 (3)	44·1 (8)	0·8 (0·7, 0·9)	0·009
Other or none	8·0 (3)	6·4 (1)	3·2 (2)	1·9 (1·5, 2·3)	< 0·0001
No. of co-morbid conditions					
0	60·0 (2)	53·9 (2)	32·9 (5)	1·0	
1	61·1 (4)	43·8 (2)	20·2 (4)	1·3 (1·1, 1·5)	0·001
≥ 2	43·4 (5)	32·7 (2)	19·3 (4)	1·6 (1·4, 1·9)	< 0·0001
Co-morbid condition‡					
Previous malignancy	45·9 (8)	54·0 (5)	§	1·2 (0·9, 1·6)	0·125
Cardiovascular disease	64·8 (8)	37·3 (6)	§	1·3 (0·9, 1·6)	0·082
COPD	59·2 (11)	41·3 (7)	16·9 (10)	1·4 (1·1, 1·9)	0·021
Diabetes	67·2 (11)	49·1 (9)	§	1·1 (0·8, 1·6)	0·554
Hypertension	63·4 (7)	40·0 (5)	35·4 (11)	1·3 (1·1, 1·6)	0·014
Digestive tract disease	59·8 (10)	35·4 (6)	§	1·3 (0·8, 2·1)	0·210

*Univariate analysis of crude actuarial survival; values in parentheses are standard errors. †Model included age, sex, tumour stage, treatment and number of co-morbid conditions or single concomitant diseases; values in parentheses are 95 per cent confidence intervals. ‡Includes patients with the respective concomitant disease alone; patients with no co-morbidity formed the reference group (hazard ratio 1·0). §Sample size too small to complete analysis. TME, total mesorectal excision; COPD, chronic obstructive pulmonary disease. #χ^2 likelihood ratio test.

resectable non-small cell lung cancer, for example, in which the proportion of patients undergoing surgery decreases with age[13]. However, the rate of permanent stoma formation in the present study increased with rising age.

Adjuvant chemotherapy is recommended in treatment guidelines for patients with stage III colonic cancer, whereas adjuvant radiotherapy is recommended for patients with stage II and III rectal cancer[5,14]. However, the use of adjuvant therapy decreased strongly with increasing age for both colonic and rectal cancer, as has been shown previously[15–20], for several reasons. As well as co-morbidity and the decrease in patients' general condition and cognitive ability, data on the efficacy of chemotherapy and radiotherapy in patients older than 70 years are limited. In addition, elderly patients are more likely to decline adjuvant treatment, especially in the absence of supportive caregivers[17,21,22].

In agreement with previous studies, patients with co-morbidity were less likely to be offered adjuvant therapy[16,17,19,20]. A history of previous malignancy contributed particularly to this effect, presumably because of a less favourable risk : benefit balance for patients with a second tumour. Patients with rectal cancer who also had a combination of hypertension and diabetes were less likely to receive adjuvant radiotherapy, which may be explained by the increased likelihood of radiotherapy-related complications in patients with these conditions[23,24]. The combination of adjuvant chemoradiation in patients with stage II and III rectal cancer increased from 3·9 per cent in 1995–1999 to 15·9 per cent in 2001. These rates contrast with the results of a SEER (Surveiliance, Epidemiology, End Results)–Medicare-based study (1992–1996), in which 37 per cent of patients aged 65 years or more with stage II and III disease received adjuvant chemoradiotherapy[25].

TME-based surgical resection is strongly recommended for all resectable cancers of the mid or lower rectum[14]. TME was performed less often in older patients and those with co-morbidity, especially previous malignancy. The effect of co-morbidity on TME surgery could be explained partly by the fact that a large national trial on the management of rectal cancer (the Dutch TME trial) was ongoing between 1996 and 1999; previous malignancy was an exclusion criterion for this study[26].

Age and co-morbidity were independent prognostic factors after adjustment for stage, sex and mode of treatment. Previous malignancy, cardiovascular diseases, COPD, the combination of previous malignancy and COPD, and the combination of hypertension and diabetes increased the risk of postoperative mortality in patients with colonic cancer. For patients with rectal cancer, increased mortality was associated mainly with COPD, hypertension, and the combination of hypertension and diabetes.

The presence of concomitant disease had an impact on both crude and relative survival rates, an effect not mediated purely by changes in treatment[27]. However, information was not available on possible dose reductions for adjuvant therapy in patients with co-morbidity. A negative effect of co-morbidity on survival of patients with colorectal cancer was demonstrated in an earlier population-based study in which 2-year survival was affected by high-impact cardiac-related co-morbid conditions, COPD, renal failure and liver disease[28].

The present population-based study has the advantage of avoiding selection bias, but detailed information on performance status of the patient (as measured by means of the Karnofsky scale[29]), dosages of chemotherapy and radiotherapy, and treatment-related complications was not available. Although performance status and co-morbidity are both predictive factors for survival in patients with cancer, they are independent of one another[30,31]. These and other factors, such as socioeconomic status, cognitive disorders and frailty, also play a role in the selection of patients in terms of the administration of effective and safe treatment[32].

The recording of co-morbidity in patients with colorectal cancer diagnosed between 1995 and 1999 and registered in the Eindhoven Cancer Registry was validated in a subset of 507 patients[33]. Agreement of almost 70 per cent was found between the registry data and the findings of a medical doctor plus an epidemiologist; differences related mostly to minor co-morbidity and to a lesser extent vascular diseases, which tended to be underscored in the registry. This may have led to an underestimation of the prognostic effects of co-morbidity in the present study.

Co-morbidity did not affect the resection rate of patients with colorectal cancer, but led to less frequent use of adjuvant chemotherapy in patients with colonic cancer and of adjuvant radiotherapy in patients with rectal cancer, especially in those with previous malignancy. Co-morbidity was also an independent negative prognostic factor, with previous malignancy and COPD having the greatest negative effect. Future studies on the treatment and outcome of elderly patients with colorectal cancer suffering from co-morbidity should also take account of treatment dosages and complications, as well as broader geriatric assessment.

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