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The impact of postoperative complications on health-related quality of life in older patients with rectal cancer; a prospective cohort study

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ABSTRACT

Objectives: As result of the aging population and increasing rectal cancer incidence, more older patients undergo treatment for rectal cancer. This study compares treatment course, postoperative complications, and quality of life (QOL) between older and younger patients with rectal cancer and evaluates the impact of postoperative complications on QOL in the elderly.

Materials and Methods: Patients with rectal cancer participating in a prospective colorectal cancer cohort and referred for radiotherapy between 2013 and 2016 were included. QOL was assessed with the cancer questionnaire of the European Organisation for Research and Treatment of Cancer (EORTC QLQ-C30) before treatment and at three, six, and twelve months. Outcomes were compared between older patients (≥70 years) and younger patients (<70 years) and stratified by presence of postoperative complications.

Results: In total, 115 (33%) older patients and 230 (67%) younger patients were included. Compared to younger patients, older patients underwent significantly more often short-course radiation with delayed surgery (6.1% and 19.1% respectively) and less often chemoradiation (62.6% and 39.1% respectively), and were more likely to undergo a Hartmann procedure with permanent stoma (3.5% and 13.0% respectively) instead of sphincter-sparing surgery (43.9% and 29.6% respectively). Postoperative complication rates were similar (38.5% in older patients versus 34.7% in younger patients). Older patients had worse physical functioning at six and twelve months after diagnosis compared to younger patients. Presence of postoperative complications had a significant stronger impact on physical- and role functioning in older patients.

Conclusion: Older patients undergo more often a tailored treatment approach for rectal cancer than younger patients. With this tailored approach, similar postoperative complication rates and QOL are achieved. However, postoperative complications have a larger negative impact on physical- and role functioning in older patients which indicates a need for better prediction of postoperative complications in the elderly.

1. Introduction

In the Netherlands, 4684 patients were diagnosed with rectal cancer in 2015, of which approximately 40% were over 70 years of age [1]. Due to aging of the population and increasing rectal cancer incidence, the number of older patients is expected to rise [1,2].

Rectal cancer treatment, consisting of surgery often in combination with neoadjuvant (chemo)radiotherapy, accounts for a considerable risk on morbidity including postoperative complications and functional problems [3]. Older patients in particular may be more prone to treatment-related risks due to frailty and presence of comorbid conditions [4,5]. Multiple comorbidities and poorer physical and mental health are associated with decreased functioning which makes older patients less

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able to cope with adverse events compared to younger patients [6]. Clinicians often need to weigh treatment risks against patients' prognosis and quality of life (QOL) when treating older patients with rectal cancer. Consequently, standard rectal cancer treatment is frequently tailored in older patients, with the aim to reduce the risk of complications and preserve functioning and QOL.

Previous studies have shown higher postoperative complication and mortality rates in older patients with rectal cancer compared to younger patients [7,8]. A systematic review on the impact of frailty on postoperative outcomes in the elderly undergoing elective surgery for colorectal cancer, concluded that frail older patients have a significantly higher risk of postoperative complications compared to the non-frail older patients [9]. Frailness and a tumor located in the rectum were previously reported as independent predictors of severe complications in older patients [10]. The impact of postoperative complications on QOL in older patients with rectal cancer is still unknown, while this is likely to be a very relevant outcome in this group of patients.

In the present study we aim to describe differences in rectal cancer treatment, occurrence of postoperative complications and their effect on QOL in patients over 70 years of age versus younger patients with rectal cancer.

2. Materials and Methods

This observational study was conducted within the Dutch Prospective Data Collection Initiative on Colorectal Cancer (in Dutch: Prospectief Landelijk ColoRectaal Carcinoom cohort (PLCRC) ClinicalTrials.gov: NCT02070146) which has been approved by the Medical Research Ethics Committee of the University Medical Center (UMC) Utrecht, the Netherlands [31]. PLCRC includes adult patients with histological proven colorectal cancer of all stages. For each patient, clinical data, biomaterial and patient reported outcome measures are collected. For the present study, cohort participants with rectal cancer referred to the Department of Radiation-Oncology of the UMC Utrecht between February 2013 and January 2016 were selected. Patients referred for radiotherapy treatment of recurrent rectal cancer (N = 16) or lost to follow-up (N = 1) were excluded.

Patients were diagnosed and treated according to the Dutch colorectal cancer guideline (2014) [11] and were all reviewed by a colorectal cancer multidisciplinary team. Reference for neoadjuvant therapy was based on indication according to Tumour, Nodal and Metastasis Classification of Malignant Tumours (TNM) [12] in combination with tumor location and performance status. Patients with intermediate risk rectal cancer (cT1-3N1 or cT3c-dN0 and distance to the mesorectal fascia of >1 mm) underwent short-course radiotherapy (5 × 5 Gy) followed by immediate surgery. Patients diagnosed with a T2-3 N0 tumor and treated before the incorporation of the most recent guideline in 2014 also underwent short-course radiotherapy. Patients with high risk disease (cT3–4 with distance to the mesorectal fascia of ≤1 mm and/or cN2) underwent long-course chemoradiation (25 × 2 Gy with capecitabine two times daily 825 mg/m^2) followed by delayed surgery, usually after six to twelve weeks. Patients with high risk disease who were unfit for chemoradiation at the discretion of the medical-oncologist and radiation-oncologist, and patients requiring immediate resection for oligometastatic disease underwent short-course radiotherapy with delayed surgery as alternative to chemoradiation. Surgery was performed according to the principles of total mesorectal excision (TME) described by Heald [13], including low anterior resection (LAR) or abdominoperineal resection (APR) with permanent colostomy, and performed in different medical centers. A rectosigmoid resection with permanent colostomy (Hartmann procedure) was considered instead of LAR in patients with a high risk of anastomotic leakage including comorbid conditions such as diabetes, obesity, and/or use of corticosteroids. Patients with a preoperative poor sphincter function were more likely to receive a Hartmann. Surgical approach was either laparoscopic (robot or standard) or open. All referring medical centers have incorporated enhanced recovery after surgery (ERAS) protocols. Organ-sparing approaches, including local excision or wait-and-see, were performed in selected cases. According to the Dutch guidelines, no adjuvant chemotherapy is indicated in standard non-metastatic rectal cancer treatment [11].

Baseline patient-, disease-, treatment characteristics, and clinical outcomes, i.e. postoperative complications and mortality, were collected from electronic patient information systems. Presence and number of comorbidities were collected and categorized into malignancy, cardiac, vascular, diabetes, pulmonary, and other. Vital status was updated using linkage with the municipal personal records. Postoperative complications within 30 days after surgery were classified into surgical and non-surgical complications according to the criteria of the Dutch Surgical Colorectal Audit (DSCA) [14]. Surgical complications presented include anastomotic leakage, abscess, wound complication, ileus, bleeding, stoma-related complication, and other. The Clavien-Dindo classification (2004) of Surgical Complications was used to classify the severity of postoperative complications [15]. Non-surgical complications included cardiac, pulmonary, infectious, and other. Re-intervention was defined as a re-operation, e.g. laparoscopy, laparotomy or guided intervention.

Quality of life (i.e. physical-, emotional-, cognitive-, social- and role functioning, and global health) was assessed with the cancer questionnaire of the European Organization for Research and Treatment of Cancer (EORTC QLQ-C30) [16] before start of neoadjuvant therapy (baseline) and at three, six and twelve months afterwards. Data was collected within the Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship (PROFILES)-registry [17]. QOL outcomes of the older patients were compared to those of the Dutch general population including a cohort of older people (n = 329, age range 70 to 90 years and 63.5% male) provided by PROFILES.

2.1. Statistics

Patients were divided into an older patient group (≥70 years) and a younger patient group (<70 years). Independent *t*-tests or Mann–Whitney *U* tests, depending on distribution, were used to compare differences for continuous variables. Chi-square or Fishers exact tests were used to test differences in proportions. QOL data was handled according to the EORTC QLQ-C30 manual [18]. Scores of the functional QOL domains were linearly transformed into scores ranging from 0 to 100 and used as continuous outcomes. Higher scores indicate better functioning. Firstly, the unadjusted mean scores of older patients were compared with the mean scores of the Dutch elderly population (≥70 years) with use of Mann–Whitney *U* tests. Secondly, to observe change in QOL scores since baseline level within the older and younger patient group, outcomes were stratified by age group (<70 years and ≥70 years) and analyzed with linear mixed-effects models to take in account the correlation between repeated measurements within subjects. The models included a random intercept, time of measurement (as factor) and sex. An autoregressive covariance structure of the first order (AR1) was used to define the correlations among observations, assuming higher correlations between measurements that were closer in time, than those further apart (i.e. exponential decline) [19]. Results were presented as mean differences (MD) with 95% confidence intervals and p-value. Thirdly, to compare OQL scores between older patients and younger patients, we used linear mixed-effects models including a random intercept, age group, time of measurement (as factor), the interaction between age group and time, sex, baseline QOL score and an AR1 autocorrelation structure. Lastly, the effect of postoperative complications on QOL was assessed using stratification by presence of postoperative complications (yes/no). Due to limited sample sizes after stratification, QOL scores were only adjusted for baseline score and not for sex. A sensitivity analysis was performed excluding patients diagnosed with a clinical T4 tumor as these patients may have a higher risk on postoperative complications and impaired QOL. The level of significance was set at $p < 0.05$. Statistical

analyses were performed with Statistical Package for Social Sciences (SPSS) software (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp.).

3. Results

Between February 2013 and January 2016, 362 patients with rectal cancer were referred to the Department of Radiotherapy of the UMC Utrecht and included in PLCRC (Fig. 1). In total, 345 patients met the inclusion criteria, which consisted of 115 older (33.3%) and 230 younger (66.7%) patients.

The older patient group had a median age of 76 years (range 70–89) and 62.6% was male, whereas the younger group had a median age of 62 years (range 26–69) and 75.2% was male (Table 1). Older patients more often had previous abdominal surgery and (multiple) comorbidities compared to younger patients. Groups were similar in disease stage and tumor location. Two older patients did not undergo diagnostic magnetic resonance imaging (MRI) and therefore had an unknown disease stage and tumor location.

3.1. Treatment Patterns

Neoadjuvant therapy was administered to 112 older (97.4%) and 228 younger (99.1%) patients (Table 2). Older patients were more likely to undergo short-course radiation with delayed surgery (19.1% vs. 6.1% in younger patients) and less likely to undergo chemoradiation (39.1% vs. 62.6% in younger patients). Six (5.2%) older patients underwent palliative radiotherapy compared to seven (3.0%) younger patients. No neoadjuvant therapy was administered in three older patients (2.6%) and two younger patients (0.9%) due to personal preferences (n = 2), withdrawn indication for neoadjuvant therapy (n = 1), inflammatory bowel disease (n = 1) and previous prostate radiation treatment (n = 1).

Table 1
Baseline characteristics of younger (<70 years) and older (≥70 years) patients with rectal cancer.

	<70 years N = 230 (%)	≥70 years N = 115 (%)
Median age in years; range	62; 26–69	76; 70–89
Male sex	173 (75.2)	72 (62.6)
Previous abdominal surgery (yes)	69 (30.0)	47 (40.9)
Number of comorbidities		
None	95 (41.3)	24 (20.9)
1	70 (30.4)	38 (33.0)
2	41 (17.8)	21 (18.3)
≥3	24 (10.4)	32 (27.8)
Type of comorbidity[a]		
Malignancy	19 (8.3)	23 (20.0)
Cardiac	27 (11.7)	33 (28.7)
Vascular	70 (30.4)	48 (41.7)
Diabetes	27 (11.7)	25 (21.7)
Pulmonary	18 (7.8)	11 (9.6)
Tumor location		
Low (≤5 cm)	122 (53.0)	49 (42.6)
Medium (6–10 cm)	74 (32.2)	46 (40.0)
High (>10 cm)	34 (14.8)	18 (15.7)
Unknown	–	2 (1.7)
TNM-stage		
Stage 1	7 (3.0)	6 (5.2)
Stage 2	31 (13.5)	14 (12.2)
Stage 3	162 (70.4)	81 (70.4)
Stage 4	30 (13.0)	12 (10.4)
Unknown	–	2 (1.7)

cm: centimeter. TNM: Tumour, Nodal and Metastasis Classification of Malignant Tumours.
[a] Represents one comorbidity or a combination of types.

Surgery was performed equally often (83.5% older vs. 87.8% in younger patients). However, reason for no surgical treatment differed between the groups. Besides disease progression, poor performance

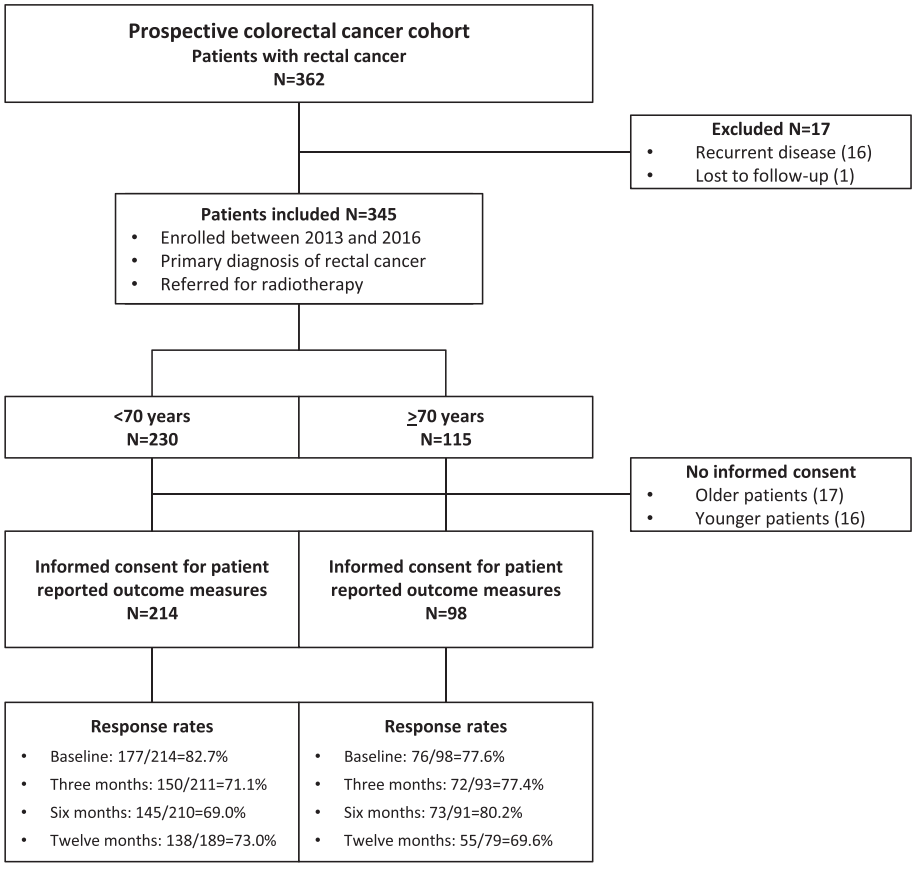

Fig. 1. Flowchart of selected patients and questionnaire response rates.

Table 2
Differences in rectal cancer treatment between younger (<70 years) and older (≥70 years) patients.

	<70 years N = 230 (%)	≥70 years N = 115 (%)	p-Value
Neoadjuvant therapy			<0.001
SCRT and immediate surgery	58 (25.2)	39 (33.9)	
SCRT and delayed surgery	14 (6.1)	22 (19.1)	
Chemoradiation	144 (62.6)	45 (39.1)	
Palliative radiotherapy	7 (3.0)	6 (5.2)	
Other regimen	5 (2.2)	–	
None	2 (0.9)	3 (2.6)	
Surgical treatment			0.32
Yes	202 (87.8)	96 (83.5)	
No	28 (12.2)	19 (16.5)	
Reasons for no surgery			0.009
Disease progression	16 (7.0)	11 (9.6)	
Poor performance status	1 (0.4)	6 (5.2)	
Wait and see approach	11 (4.8)	2 (1.7)	
Surgical procedure			0.006
Low anterior resection	101 (43.9)	34 (29.6)	
Hartmann resection	8 (3.5)	15 (13.0)	
Abdominoperineal resection	87 (37.8)	45 (39.1)	
Local excision	3 (1.3)	1 (0.9)	
Unknown	3 (1.3)	1 (0.9)	
Stoma presence			0.04
Temporary deviating stoma[a]	83 (36.1)	27 (23.5)	
Permanent stoma[b]	95 (41.3)	60 (52.2)	
No stoma[c]	23 (10.0)	8 (7.0)	
Unknown	1 (0.4)	1 (0.9)	
Surgical approach			0.56
Laparotomy	39 (17.0)	15 (13.0)	
Laparoscopy	157 (68.3)	80 (69.6)	
Transanal	3 (1.3)	1 (0.9)	
Unknown	3 (1.3)	–	
Conversion (yes)	12 (5.2)	8 (7.0)	0.66
Median follow-up in months; range	26;2–46	20; 0–45	0.006
Overall mortality	36 (15.7)	27 (23.5)	0.08

SCRT: short-course radiotherapy.
[a] Represents patients who underwent a low anterior resection with temporary deviating stoma.
[b] Represents patients who underwent an abdominoperineal resection or Hartmann resection.
[c] Represents patients who underwent a low anterior resection or local excision.

status was a more common cause in older patients compared to younger patients. In those who underwent surgery, older patients were more likely to undergo a Hartmann procedure (13.0% vs. 3.5%) and less likely to undergo LAR (29.6% vs. 43.9%) compared to younger patients. Older patients received a permanent stoma more often and a temporary stoma or no stoma less often compared to younger patients (permanent stoma in 52.2% vs. 41.3%, temporary stoma in 23.4% vs. 36.0%, and no stoma in 7.0% vs. 10.0% respectively). Median follow-up time in older patients was significant shorter compared to younger patients (20 and 26 months respectively).

3.2. Postoperative Complications

No differences were observed in postoperative complications between older patients and younger patients (38.5% and 34.7% respectively, p = 0.46), also when stratified for surgical and non-surgical complications (Table 3). Of the older patients, 3.1% developed anastomotic leakage and 8.3% wound complications vs. 5.0% and 7.9% in the younger patients. After stratification by neoadjuvant regimen and surgical procedure, comparable results were obtained (see Table Supplemental Digital Content 1, including postoperative complications between older and younger patients stratified by LAR, APR, short-course radiotherapy and chemoradiation). Clavien-Dindo complication grades were similar between the groups. Grade 3 complications, including re-intervention, occurred in 9.4% of the older and in 10.9% in the younger patients. One patient in the younger patient group developed an anastomotic leakage and required intensive care management (grade 4). Two (2.1%) patients

Table 3
Differences in postoperative complications between younger (<70 years) and older (≥70 years) patients with rectal cancer.

	<70 years N = 202 (%)	≥70 years N = 96 (%)	p-Value
Postoperative complications			0.46
Yes	70 (34.7)	37 (38.5)	
No	126 (62.4)	55 (57.3)	
Unknown	6 (3.0)	4 (4.2)	
Surgical complications (yes)	51 (25.2)	23 (24.0)	0.85
Type of complications[a]			0.96
Anastomotic leakage	10 (5.0)	3 (3.1)	
Abscess	3 (1.5)	2 (2.1)	
Wound-related	16 (7.9)	8 (8.3)	
Ileus	5 (2.5)	4 (4.2)	
Bleeding	1 (0.5)	1 (1.0)	
Stoma-related	4 (2.0)	1 (1.0)	
Other	12 (5.9)	4 (4.2)	
Non-surgical complications (yes)	28 (13.9)	17 (17.7)	0.36
Type of complications[a]			0.84
Cardiac	6 (3.0)	5 (5.2)	
Pulmonary	5 (2.5)	2 (2.1)	
Infectious	7 (3.5)	4 (4.2)	
Other	10 (5.0)	6 (6.3)	
Clavien-Dindo classification			0.29
Grade 1	16 (7.9)	6 (6.3)	
Grade 2	12 (5.9)	7 (7.3)	
Grade 3	22 (10.9)	9 (9.4)	
Grade 4	1 (0.5)	–	
Grade 5	–	2 (2.1)	
Reintervention (yes)	23 (11.4)	10 (10.4)	0.67
90-day mortality	1 (0.5)	3 (3.1)	0.11

[a] Represents one complication or a combination of types.

in the older group died during hospital stay as result of multi-organ failure (grade 5). The 90-day mortality rate was 3.1% in the older patient group versus 0.5% in the younger patient group which was not significantly different.

3.3. Quality of Life

In total, 98 (85.2%) older patients and 214 (93.0%) younger patients consented to receive QOL questionnaires (Fig. 1). Non-responders were equally present in the older and younger groups (8.2% and 9.8% respectively, data not shown). The postoperative complication rate was similar between non-responders and responders in younger patients (33.0% and 37.1% respectively) and higher in older patients (60.0% and 39.5% respectively). Response rates ranged between 69.0 and 82.7% (Fig. 1).

Compared with the Dutch reference population of ≥70 years, pre-treatment (baseline) scores in older patients were similar, except for emotional functioning which was lower in older patients (Fig. 2). During and shortly after treatment, physical-, role-, and social functioning were significantly inferior to the reference group and remained so up to twelve months after diagnosis. Global health in older patients was poorer at three months but recovered to reference level at six months. Cognitive functioning showed no significant difference with the reference population and emotional functioning improved over time and was at similar level as the reference population at twelve months after diagnosis.

Relative to their baseline scores, older patients reported a significant decrease in global health, physical-, role- and social functioning at three months (Table 4, within scores). Global health recovered to baseline level at six months, whereas physical-, role- and social functioning remained significantly impaired up to twelve months. Younger patients reported lower scores for global health, role- and cognitive functioning up to six months, and physical-, social functioning up to twelve months compared to their baseline scores. Emotional functioning was significantly improved at twelve months in both older and younger patients.

Between older and younger patients, baseline functioning scores were similar (Table 4). Older patients reported significantly poorer physical

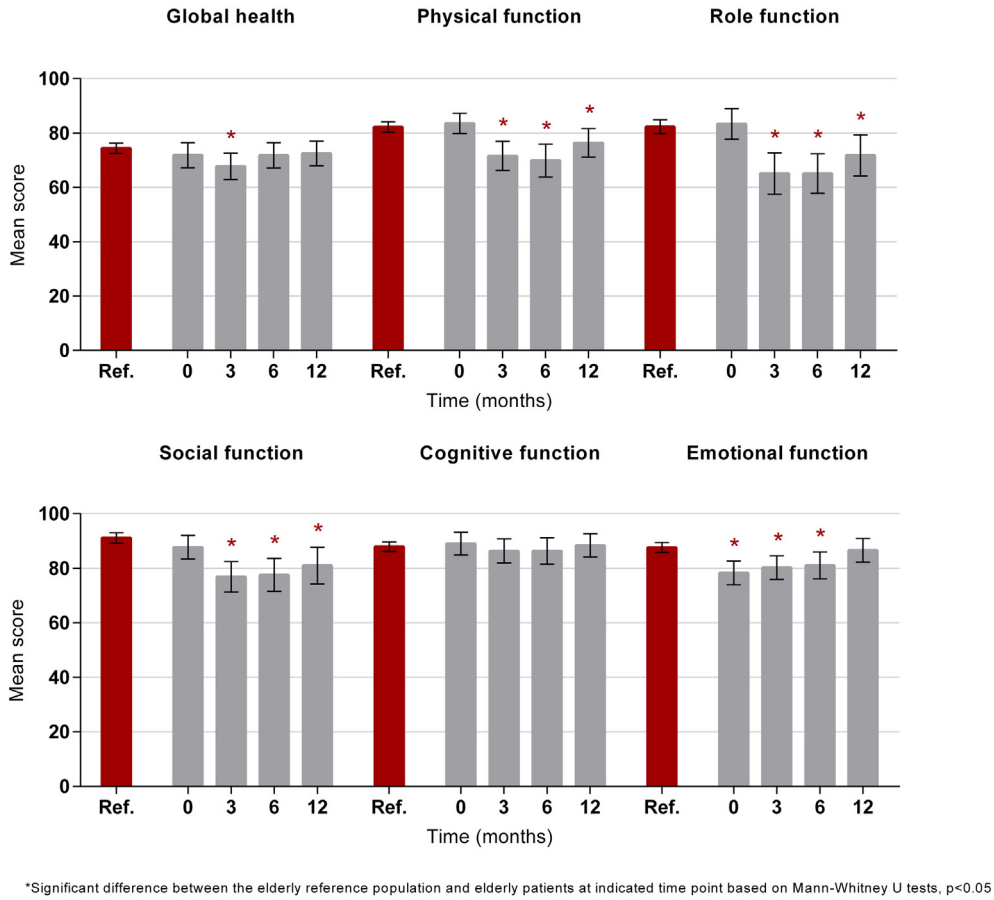

Fig. 2. Function domains and global health status in older (≥70 years) patients with rectal cancer compared with the Dutch population of ≥70 years (reference), assessed with the cancer questionnaire of the European Organization for Research and Treatment of Cancer (EORTC QLQ-C30). Results are presented in mean scores accompanied with the 95% confidence intervals. Higher scores indicate a better outcome.

functioning at six and twelve months after diagnosis compared to younger patients (MD −9.6, $p < 0.001$ and −7.0 respectively, $p = 0.02$, adjusted for baseline scores and sex), and a better cognitive functioning at three months (MD 5.4, $p = 0.03$). Global health, social-, role-, and emotional functioning were comparable between older and younger patients during the first year after diagnosis.

Stratification by postoperative complications showed a stronger negative impact on physical- and role functioning in older compared to younger patients (physical functioning at six months and twelve months MD −19.9, $p < 0.001$ and MD −12.3, $p = 0.04$ respectively, and role functioning at six months MD −20.5, $p = 0.01$, adjusted for baseline level) (Fig. 3 and see Supplemental Digital Content Table 2, including the differences in quality of life outcomes between older and younger patients with rectal cancer stratified by presence of postoperative complications). Global health, social-, cognitive-, and emotional functioning were comparable between older and younger patients who developed postoperative complications. In older and younger patients without postoperative complications, all QOL domains were similar during the first year after diagnosis. The sensitivity analysis excluding patients diagnosed with a clinical T4 stage showed similar outcomes for the unstratified and stratified QOL analysis (data not shown).

4. Discussion

This study shows that in older patients with rectal cancer, less invasive treatment approaches are often chosen including short-course radiotherapy with delayed surgery as alternative for chemoradiation and a Hartmann procedure as alternative for low anterior resection. Older and younger patients develop similar rates of postoperative surgical and non-surgical complications, with similar grade of severity. In both groups, patients' QOL deteriorates during and shortly after rectal cancer treatment, in particular physical-, role- and social functioning. One year after diagnosis, older patients experience worse physical functioning compared to younger patients and worse role-, social- and physical functioning compared to their pretreatment level and compared to the Dutch elderly reference population. Moreover, occurrence of postoperative complications has a stronger negative impact on physical- and role functioning in older patients than in younger patients.

Deviation from standard treatment in older patients with rectal cancer and comparable postoperative complication rates with younger patients are reported previously [7,20–22,24–26]. In contrast to our findings, several studies did observe less surgical treatment performed in older patients [7,8,20–24]. Also, higher rates of non-surgical complications, mainly cardiopulmonary, in older patients have been reported [7,8,20,26]. A possible explanation for these different findings is our selection of older patients referred for neoadjuvant therapy, as well as the less invasive regimens used in this group. Moreover, various cut-off ages are used in literature to define the older patient group which makes it hard to compare results. In a study which used the same cut-off age of 70 years and older, older patients underwent neoadjuvant radiotherapy and surgery less often, no or other treatment more often and developed more complications compared to patients of 60–69 years old (65% vs. 51%) [8]. Nevertheless, in this study complications within one year of diagnosis were counted instead of only postoperative complications.

Table 4
Function domains and global health status in younger (<70 years) and older (≥70 years) patients with rectal cancer assessed with the EORTC QLQ-C30 at baseline, three, six and twelve months after diagnosis. The between-group outcomes show the difference in mean score between the younger and older patient group adjusted for baseline score. The within-group outcomes show the change in mean score from baseline stratified by younger and older patients.

Domains		Baseline			Three months						Six months						Twelve months					
			Between			Within[a]			Between[b]			Within[a]			Between[b]			Within[a]			Between[b]	
		N	Mean	95% CI	N	MD	95% CI	p	MD	95% CI	N	MD	95% CI	p	MD	95% CI	N	MD	95% CI	p	MD	95% CI
Global health	<70	174	73.3	70.1; 76.4	149	−7.5	−10.9; −4.1	<0.001	Ref.		144	−4.6	−8.1; −1.0	0.011	Ref.		138	−0.4	−4.0; 3.2	NS	Ref.	
	≥70	76	71.4	66.9; 75.8	72	−5.0	−10.0; −0.1	0.045	2.7	−2.7; 8.2	72	−0.9	−6.1; 4.3	NS	1.6	−3.9; 7.0	56	0.07	−5.6; 5.7	NS	−1.6	−7.5; 4.3
	p-Value		NS						NS						NS						NS	
Physical function	<70	177	87.0	84.1; 89.8	150	−10.7	−13.6; −7.8	<0.001	Ref.		145	−6.7	−9.6; −3.9	<0.001	Ref.		138	−4.1	−7.0; −1.3	0.005	Ref.	
	≥70	75	82.6	78.5; 86.7	72	−13.3	−18.2; −8.5	<0.001	−4.2	−9.5; 1.0	73	−13.9	−18.9; −8.9	<0.001	−9.6	−14.9; −4.4	56	−9.5	−14.9; −4.0	0.001	−7.0	−12.6; −1.3
	p-Value		NS						NS						<0.001						0.02	
Role function	<70	177	77.4	73.0; 81.9	150	−17.8	−23.1; −12.5	<0.001	Ref.		145	−13.9	−19.5; −8.2	<0.001	Ref.		138	−4.4	−10.2; 1.3	NS	Ref.	
	≥70	75	83.1	76.6; 89.6	72	−19.6	−27.5; −11.7	<0.001	−0.1	−8.7; 8.5	73	−19.4	−27.8; −11.0	<0.001	−5.1	−13.7; 3.5	56	−12.7	−21.9; −3.5	0.007	−4.0	−13.4; 5.4
	p-Value		NS						NS						NS						NS	
Social function	<70	175	82.2	78.3; 86.0	149	−14.4	−18.9; −9.9	<0.001	Ref.		144	−10.5	−15.2; −5.9	<0.001	Ref.		138	−6.4	−11.1; −1.7	0.008	Ref.	
	≥70	76	87.4	81.8; 93.0	72	−11.3	−17.8; −4.8	0.001	6.5	−1.0; 14.0	72	−11.0	−17.8; −4.2	0.002	−0.3	−7.8; 7.3	56	−7.4	−14.8; −0.1	0.047	2.0	−6.1; 10.2
	p-Value		NS						NS						NS						NS	
Cognitive function	<70	175	87.4	84.4; 90.3	149	−6.5	−9.4; −3.6	<0.001	Ref.		144	−5.5	−8.4; −2.5	<0.001	Ref.		138	−2.1	−5.1; 0.9	NS	Ref.	
	≥70	76	88.2	84.0; 92.4	72	−3.0	−7.6; 1.7	NS	5.4	0.5; 10.3	72	−3.7	−8.2; 0.8	NS	1.4	−3.5; 6.3	56	−1.9	−6.8; 3.0	NS	0.6	−4.7; 5.9
	p-Value		NS						0.03						NS						NS	
Emotional function	<70	175	75.3	72.2; 78.5	149	−0.2	−3.2; 2.7	NS	Ref.		144	3.1	−0.2; 6.5	NS	Ref.		138	6.0	2.5; 9.5	0.001	Ref.	
	≥70	76	77.7	73.3; 82.2	72	1.4	−2.9; 5.6	NS	2.3	−3.0; 7.6	72	1.8	−2.7; 6.3	NS	−0.6	−5.9; 4.6	56	7.0	2.1; 12.0	0.006	2.0	−3.7; 7.7
	p-Value		NS						NS						NS						NS	

CI: confidence interval. EORTC QLQ-C30: cancer questionnaire of the European Organization for Research and Treatment of Cancer. MD: mean difference. NS: non-significant. p: p-value. Ref: reference group.
[a] Change in mean scores between baseline and follow-up measurements stratified by younger and older patients and adjusted for sex, based on linear mixed-effect models with a random intercept.
[b] Difference in mean scores between younger and older patients at three, six and twelve months adjusted for sex and baseline score, based on linear mixed-effect models with a random intercept.

In both older and younger patients, the strongest impact of rectal cancer treatment was observed in physical-, social- and role functioning during or shortly after treatment. Similar results were found in other studies with longitudinal QOL measurements [27–29] and confirmed by a systematic review of 23 studies regarding the changes in physical- and role functioning after colorectal cancer treatment [30]. Also, worse postoperative physical functioning in older patients compared to younger patients was described previously [7,32–37]. Our results may add that older patients still report poor physical-, social-, and role functioning up to one year after diagnosis compared to their pretreatment level and compared to the reference population, indicating slow recovery or permanently affected functioning.

This is the first study describing the effect of postoperative complications on older patients' QOL. We found a stronger negative impact on physical- and role functioning in older patients with postoperative complications compared to younger patients with statistical and clinical significant differences in mean scores, while older patients without postoperative complications showed similar QOL when compared to younger patients. Poor physical and role functioning in the elderly may result in patients' inability to perform daily activities or self-care, and therefore emphasizes the need to predict this subgroup at risk for postoperative complications to take precautions in clinical, pre- or post-treatment care. A pretreatment frailty assessment may be of added value to estimate risks and benefits of perioperative management [9] and thereby to predict functioning after treatment. Frailty, which indicates the progressive disability resulting from a generalized decline in multiple physiological systems, negatively affects functional reserves and increases vulnerability to adverse outcomes [38]. Frail older adults may benefit from prehabilitation programs before elective surgery to enhance functional capacity and mental health [39,40]. Studies are needed to evaluate the effect of these interventions in older patients with rectal cancer. Furthermore, organ-sparing approaches in rectal cancer treatment may be of important value in frail older patients to avoid surgery-related treatment risks.

A limitation of our study is the selection by indication as we selected patients referred for neoadjuvant therapy to our clinic. We have therefore missed patients who were not referred for (chemo) radiotherapy because of a poor performance status at diagnosis or patients' personal preference but have received surgery. This situation is most probable in the group of older patients with intermediate risk disease and indication for short-course radiotherapy since the rationale for neoadjuvant therapy in these patients may be less strong. Older patients with locally advanced disease but unfit for chemoradiation are more likely to undergo neoadjuvant short-course radiotherapy with delayed surgery to allow downsizing of the tumor. Also, in this study only outcomes on QOL until one year after diagnosis are reported. The longer-term impact of postoperative complications on QOL in the elderly remains still unclear. Lastly, non-responders had a higher rate of postoperative complications than responders in the older patient group. However, as non-responders were only 8% of the older study population, the number of complications was small. We therefore assume that its effect on the validity of our results is low.

A strength of this study is the high generalizability of cohort participants. All patients with rectal cancer at the Radiation-Oncology Department were asked to participate, with a high participation rate of 86%. Furthermore, response rates to QOL questionnaires were reasonably good and comparable between older and younger patients.

In conclusion, we showed that older patients more often than younger patients undergo a tailored treatment approach for intermediate or high risk rectal cancer. According to this current patient selection, similar postoperative complication rates and QOL are observed between older and younger patients. However, there is a need to predict older patients who develop postoperative complications as these patients are at risk for poor role- and physical functioning after rectal cancer surgery.

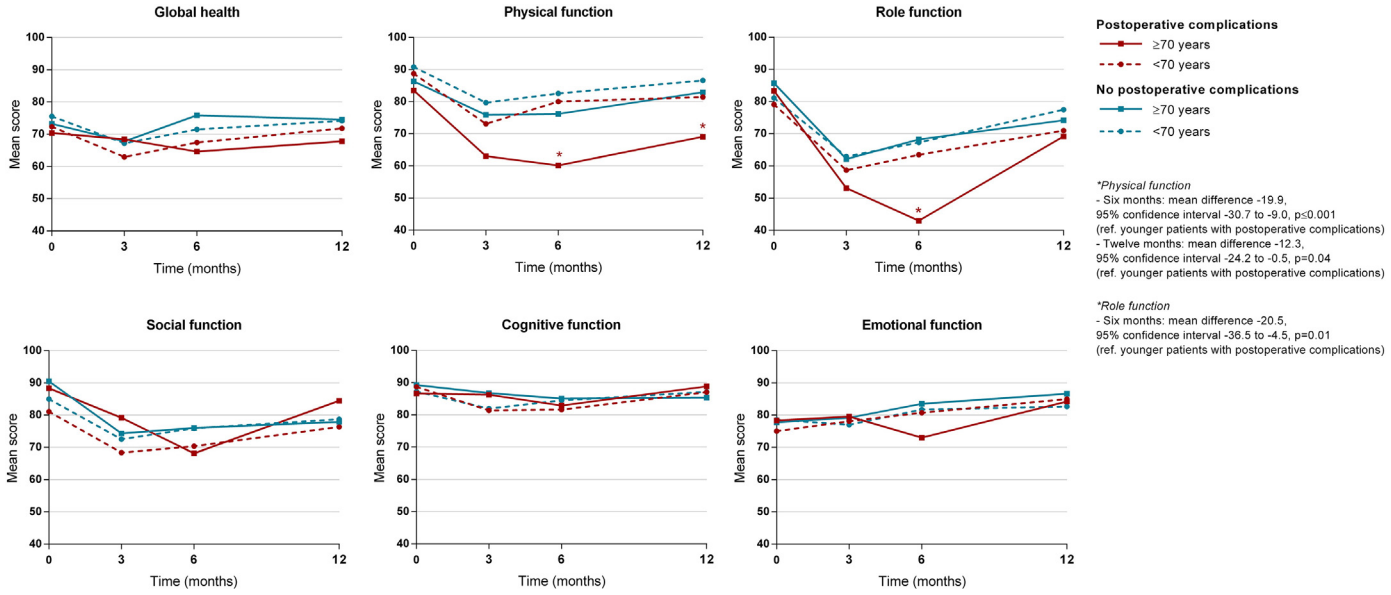

Fig. 3. Function domains and global health status in older (≥70 years) and younger (<70 years) patients with rectal cancer stratified by presence of postoperative complications, assessed with the cancer questionnaire of the European Organization for Research and Treatment of Cancer (EORTC QLQ-C30). Results are presented in mean scores accompanied with the 95% confidence intervals. Higher scores indicate a better outcome.

Disclosures and Conflict of Interest Statements

All authors declare they have no conflicts of interest.

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Appendix A. Supplementary Data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jgo.2017.09.005.

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