



## Survival among clinical stage I–III rectal cancer patients treated with different preoperative treatments: A population-based comparison



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### ABSTRACT

**Background:** Radical resection is regarded as the cornerstone of rectal cancer treatment. Preoperative (chemo)radiotherapy and adjuvant chemotherapy are often administered. This population-based study compares the survival in clinical stage I–III rectal cancer patients who received either preoperative radiotherapy, preoperative chemoradiotherapy or no preoperative therapy. As secondary research questions, the association of type of radical resection and adjuvant chemotherapy on survival is also investigated.

**Methods:** Patients diagnosed between January 2006 and December 2011 with stage I–III rectal adenocarcinoma were retrieved from the Belgian Cancer Registry database. Multivariable Cox proportional hazards regression models were applied to evaluate the association of preoperative treatment, type of radical resection and use of adjuvant chemotherapy with survival, adjusting for the baseline characteristics age, gender, WHO performance status and clinical stage.

**Results:** A total of 5173 rectal cancer patients were identified. Preoperative treatment was as follows: none in 1354 (26.2%), radiotherapy in 797 (15.4%) and chemoradiotherapy in 3022 (58.4%) patients. The patient group who did not receive preoperative therapy or radiotherapy followed by radical resection had a lower observed survival compared to the patient group receiving preoperative chemoradiotherapy. The patient groups who underwent abdominoperineal excision and those receiving adjuvant chemotherapy had a worse observed survival compared to the patient group treated with sphincter-sparing surgery and no adjuvant therapy respectively. These effects were age-dependent. Multivariable analysis demonstrated similar findings for the observed survival conditional on surviving the first year since surgery.

**Conclusion:** In this population-based study among clinical stage I–III rectal cancer patients treated with radical resection, a superior observed survival was noticed in the patient group receiving preoperative chemoradiotherapy compared to the patients groups receiving no or preoperative radiotherapy only, adjusting for case mix, type of radical resection and adjuvant chemotherapy. Additionally, higher adjusted observed survival was also detected for the patient groups with sphincter-sparing surgery or no adjuvant chemotherapy.

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## 1. Introduction

Colorectal cancer is the third most common cancer in men and the second in women and accounts for the fourth most common cause of cancer-related death worldwide [1]. About one-third of

these tumors are located in the rectum. Surgery is regarded as the cornerstone of rectal cancer treatment. With the implementation of total mesorectal excision (TME), which is a sharp dissection of the rectum and its surrounding mesorectum [2], local recurrence rates have dropped from above 20% to less than 10% [3,4]. Several large trials have demonstrated that the addition of preoperative (chemo)radiotherapy for locally advanced tumors further reduces local recurrences [5–10]. In analogy with colon carcinoma, adjuvant chemotherapy has been recommended, although its benefit for rectal cancer is heavily debated [11,12].

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It is not clear whether the improvements in outcome reported in standardized trials also translate into better outcomes at population level [13]. The elderly are generally underrepresented in clinical trials as older patients frequently comprise only a quarter to one third of study participants [15,16]. Guidelines based on relatively younger patients may therefore not be applicable to the entire rectal cancer population.

Analysis of population-based cancer registries shed light on the effect of treatment in daily practice. Systematic cancer registration is now mandatory in most European countries. Cancer registries are an important source of information since they provide accurate and comprehensive information on individual demographics, primary cancer sites and histology, cancer staging and surgical, radiation and systemic therapy. Dutch, Swedish, Danish and Norwegian cancer registries reported on colorectal cancer patients before [16–19]. However, little is known about the effect of preoperative and postoperative treatment and of the type of surgery on population-based rectal cancer survival in Belgium.

We primarily investigated the impact of preoperative radiotherapy, preoperative chemoradiotherapy and no preoperative therapy (upfront surgery) on the survival of clinical stage I–III rectal cancer patients registered in the Belgian Cancer Registry database. Additionally, the effect of type of radical resection and

adjuvant chemotherapy on survival at population level was investigated.

## 2. Patients and methods

### 2.1. Study population

Patients diagnosed between January 2006 and December 2011 with clinical stage I–III rectal adenocarcinoma as primary tumor were retrieved from the Belgian Cancer Registry database. Patients with lesions at the rectosigmoid were also included. Data on age, gender, WHO performance status, cTN-stage and pTN-stage were extracted from the Cancer Registry. Details on surgery and pre/postoperative therapy were obtained by coupling the Belgian Cancer Registry records with the Belgian Intermutualistic Agency (IMA) database [20]. Patients with unknown national social security identification number and patients who could not be retrieved in the IMA database were excluded from the analysis. Only patients who underwent a radical resection (sphincter-sparing surgery or abdominoperineal excision) were retained. Patients diagnosed with another cancer within 90 days around the rectum cancer incidence date and patients who received preoperative chemotherapy alone were also excluded.

**Table 1**  
Patient and tumor characteristics of rectal cancer patients who underwent radical resection according to the primary treatment, diagnosed between January 2006 and December 2011 in Belgium (n = 5173). Column percentages are given between brackets.

	All patients N (%)	Preoperative treatment group			p-value
		None N (%)	RT N (%)	CRT N (%)	
Total	5173	1354 (26)	797 (15)	3022 (58)	
Gender					<0.0001
Male	3199 (62)	756 (56)	497 (62)	1946 (64)	
Female	1974 (38)	598 (44)	300 (38)	1076 (36)	
Age					<0.0001
<65 years	2149 (42)	403 (30)	263 (33)	1483 (49)	
65–74 years	1589 (31)	363 (27)	231 (29)	995 (33)	
≥75 years	1435 (28)	588 (43)	303 (38)	544 (18)	
WHO PS					<0.0001
0	823 (16)	177 (13)	122 (15)	524 (17)	
1	3451 (67)	910 (67)	549 (69)	1992 (66)	
2+	436 (8)	174 (13)	68 (9)	242 (8)	
Missing	415 (8)	93 (7)	58 (7)	264 (9)	
Clinical stage					<0.0001
I	836 (16)	667 (49)	64 (8)	105 (4)	
II	1233 (24)	334 (25)	251 (32)	648 (21)	
III	3104 (60)	353 (26)	482 (61)	2269 (75)	
Pathological stage					#
0	276 (5)	0 (0)	24 (3)	252 (8)	
Is	33 (1)	1 (0)	5 (1)	27 (1)	
I	1457 (28)	486 (36)	221 (28)	750 (25)	
IIr	1393 (27)	356 (26)	240 (30)	797 (26)	
III	1569 (30)	446 (33)	256 (32)	867 (29)	
IV	84 (2)	19 (1)	17 (2)	48 (2)	
X	361 (7)	46 (3)	34 (4)	281 (9)	
Type of surgery					<0.0001
SSS	3883 (75)	1110 (82)	577 (72)	2196 (73)	
APE	1290 (25)	244 (18)	220 (28)	826 (27)	
Adjuvant chemotherapy					<0.0001
No	2711 (52)	942 (70)	563 (71)	1206 (40)	
Yes	2462 (48)	412 (30)	234 (29)	1816 (60)	

Abbreviations: APE = abdominoperineal rectum excision; CRT = chemoradiotherapy; NS = not specified; PS = performance status; RT = radiotherapy, SSS = sphincter-sparing surgery. The last column represents the *p*-value from the Pearson test for independence. # Pearson test not possible due to cells with zero counts.

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