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HEALTH-RELATED QUALITY OF LIFE IN RECTAL CANCER PATIENTS DURING ACTIVE TREATMENT

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Abstract

Objective: The aim of this exploratory prospective observational study was to evaluate changes in Health-related Quality of Life (HRQoL) in rectal cancer patients (RCPs) during active cancer treatment, i.e. after diagnosis, after preoperative (chemo)radiotherapy and after surgical resection. Furthermore, the study aims to investigate which physical and psychosocial factors better predict HRQoL in the different treatment phases. Deepening the understanding of the positive and negative predictive factors for patients' HRQoL at different phases could indeed improve screening programs for early detection and intervention.
Methods: 43 RCPs, expected to be treated with preoperative (chemo)radiation and surgery, were enrolled after diagnosis and assessed at three different time points: diagnosis (T0), one month after the end of preoperative treatment (T1), and one month after resection surgery (T2). HRQoL (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, EORTC-QLQ-C30 and its disease-specific supplementary, the QLQ-CR29), psychological distress (Hospital Anxiety and Depression Scale, HADS), coping (Mini-Mental Adjustment to Cancer Scale, Mini-MAC), affectivity (Positive and Negative Affect Scale, PANAS), alexithymia (Toronto Alexithymia Scale, TAS-20) and social support (Multidimensional Scale of Perceived Social Support Scale, MSPSS) were evaluate at the different time points.
Results: The data showed that HRQoL decreased over time, especially between T1 and T2 (p=.005). Over time, patients' body image (p<.001) and urinary (p<.001), mouth (p=.015) and sexual (p<.001) symptoms worsened. Health anxiety (p<.001) and negative affectivity state (p=.037) improved after preoperative treatment, as did psychological distress (p<.001), although this increased again at T2 (p=.003).
Baseline intestinal symptoms (p<.001) and negative affectivity trait (p=.03) were found to be significant predictors of HRQoL at T0. Baseline pain (p<.001), intestinal (p=.003) and urinary (p=.009) symptoms at T1 significantly predicted HRQoL at T1. Finally, a fatalistic coping style at T1 (p=.013), psychological distress (p=.003) and mouth symptoms (p=.001) at T2 significantly predicted HRQoL at T2.
Conclusion: Our results suggest that several physical and psychological factors are involved in the changes occurring after diagnosis in RCPs' HRQoL, which decreases during active treatments. These data emphasise the importance of active screening, early diagnosis, and preventive psychological interventions immediately after diagnosis to improve HRQoL and psychological health outcomes.

Keywords: *Colorectal cancer, longitudinal study, active treatment, psychological distress, quality of life.*

1. Introduction

Rectal cancers account for 30% of colorectal cancers (CRC), which are the second most common type of cancer worldwide (Sung et al., 2021).

The diagnosis and treatment of rectal cancer can have a negative impact on patients' Health-related Quality of Life (HRQoL; Bours et al., 2016; Sales et al., 2014; Simillis et al., 2023). Various psychological aspects can influence the HRQoL of cancer patients, including those related to psychological distress, affective experience, alexithymia and coping strategies (De Vries et al., 2012; Kang & Son, 2019; Sales et al., 2014; Voogt et al., 2005). However, it is important to specifically analyze the combined role of these psychological and clinical aspects in patients with rectal cancer (RCPs), as they have specific characteristics that differ from other cancers.

This exploratory study aims to assess the changes in HRQoL of RCPs during active cancer treatments, i.e., after diagnosis during the appointment with the radiation oncologist where patients received the indication for treatment (T0), after preoperative (chemo)radiotherapy (T1) and after surgical resection (T2). In addition, the study will investigate which physical and psychosocial factors better predict HRQoL in the different treatment phases.

2. Methods

2.1. Participants and procedure

The participants were recruited in the Department of Radiation Oncology" of the Hospital "Città della Salute e della Scienza" in Turin. Inclusion criteria were: Age > 18 years, recent diagnosis of rectal cancer, indication for preoperative (chemo)radiotherapy and surgical resection, good knowledge of the Italian language and no severe cognitive or psychopathological disorders.

The sociodemographic, clinical, psychological and HRQoL data were collected during the appointment with the radiation oncologist when the patients received the indication for treatment (T0 - diagnosis). Except for alexithymia and trait affectivity, the psychological and HRQoL variables were collected again at T1 (at least one month after the end of preoperative treatment) and at T2 (at least one month after surgical resection), on average 3 and 6 months after diagnosis, respectively.

The study was approved by the institution's ethics committee (protocol number 0017109, procedure number CS2/1118) and conducted in accordance with the Declaration of Helsinki. All patients had given written informed consent.

2.2. Measures

The validated Italian versions of the following self-assessment scales were used.

The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and its disease-specific supplement (QLQ-CR29) were used to assess HRQoL and cancer-related symptoms. The QLQ-CR29 assesses 4 functional subscales (Body Image (BI), Anxiety (Anx), Weight (Wei), Sexual interest (SexInt)) and 18 symptoms scales categorized into the following groups: Urinary Symptoms (UrSy), Intestinal Symptoms (InSy), Pain Symptoms (PainSy), Mouth Symptoms (MoSy), Sexual Symptoms (SexSy). High scores indicate better HRQoL and a favorable outcome on the functional scale, but a greater symptom burden on the symptom scales.

The Hospital Anxiety and Depression Scale (HADS) was used to assess psychological distress (anxiety and depressive symptoms), with higher scores indicating high levels of symptoms.

The Mini-Mental Adjustment to Cancer Scale (Mini-MAC) was used to assess cancer-specific coping styles: cognitive avoidance (CA), fighting spirit (FS), fatalism (F), helplessness/hopelessness (HH), and anxious preoccupation (AP).

The Positive and Negative Affect Scale (PANAS) was used to assess positive and negative affectivity in both the trait (PANAS_PAtr and PANAS_NAtr) and state (PANAS_PAst and PANAS_NAst) versions.

The Toronto Alexithymia Scale (TAS-20) was used to assess alexithymia, with scores ranging from 20 to 100 and a cut-off point ≥ 61 indicating the presence of alexithymia.

2.3. Data analysis

Descriptive statistics were used for the variables collected at the three different time points. All variables were normally distributed (absolute values for skewness and kurtosis below 3.0 and 8.0 respectively). Repeated-measures analyses were used to assess changes in variables over time, applying the Greenhouse-Geisser correction when sphericity was violated. Post-hoc analyses with Bonferroni correction for significant main effects were then performed to assess differences between T1 and T0 and between T2 and T1.

Exploratory hierarchical multiple regression analyses were performed to investigate which variables better predicted HRQoL (QLQ-C30) at the different time points (T0, T1 and T2). Only significantly correlated variables (Pearson or Spearman bivariate correlations) were included in the regression models stepwise in the order of 1) clinical symptoms (QLQ-CR29 subscales), 2) psychological symptoms (TAS-20, PANAS, HADS, Mini-MAC) and chronologically (first T0, then T1 and then T2). Collinearity was assessed using the statistical factors of tolerance and Variance Inflaction Factor (VIF).

The Statistical Package for Social Sciences - 28.0 (IBM SPSS Statistics for Macintosh, Armonk, NY, USA: IBM Corp.) was used to perform the statistical analyses.

3. Results

At T0, 43 RCPs were enrolled (male: 29 (67.4%); female: 14 (32.6%); mean (SD) age: 61.6 (12.6); mean (SD) year of education levels: 11.35 (4.3); most were married/cohabiting: 32 (74.4%) and employed: 24 (55.8%)). Almost all patients (42 of 43) underwent preoperative chemotherapy with radiotherapy. 3 patients dropped out at T1 and 3 at T2. At T2, 38 patients (86.5%) had an ostomy (11 permanent, 21 temporary), and 17 patients (39.5%) underwent adjuvant chemotherapy.

The descriptive data and the results of the repeated measures ANOVAs are shown in Table 2. In particular, QLQ-C30 scores indicated overall HRQoL was maintained but decreased over time (p=.002), with post-hoc contrasts indicating significant differences between T1 and T2 (F(1,36)=8.86, p=.005).

The QLQ-CR29 showed a significant change in the QLQ-CR29_BI, with a decrease between T0 and T1 (F(1,36)=6.58, p=.015) and between T1 and T2 (F(1,36)=6, p=.019), and in the QLQ-CR29_SexInt, with a decrease between T1 and T2 (F(1,36)=18.37, p<.001). QLQ-CR29_UrSy, QLQ-CR29_MoSy, QLQ-CR29_SexSy worsened over time.

The QLQ-CR29_Anx improved over time, with a decrease between T0 and T1 (F(1,36)=14.31, p<.001). The PANAS_NAst decreased over time, especially between T0 and T1 (F(1,36)=4.71, p=.037). The HADS showed a fluctuating trajectory of symptoms, with post-hoc contrasts showing a decrease between T0 and T1 (F(1,36)=12.38, p<.001) and an increase between T1 and T2 (F(1,36)=9.79, p=.003).

Finally, for coping strategies, only Anxious Preoccupation changed over time, with a decrease between T0 and T1 (F(1,36)=6.31, p=.017) and between T1 and T2 (F(1,36)=6.56, p=.015).

Table 1. Repeated measures ANOVAs on health-related Quality of Life (QLQ-C30) at diagnosis (T0), after preoperative treatments (T1) and after surgical resection (T2).

	T0	**T1**	**T2**		
	N = 43	**N = 40**	**N = 37**	**F(df1,df2)**	**p**
QLQ-C30	86.89 (8.9)	87.20 (12.3)	80.52 (12.8)	F(1.5,54)=8.56	.002
QLQ-CR29_BI	92.51 (12.8)	86.11 (14.8)	78.38 (19.4)	F(2,72)=10.75	<.001
QLQ-CR29_Anx	46.51 (28.3)	65 (25)	68.47 (26)	F(2,72)=10.8	<.001
QLQ-CR29_Wei	89.15 (21.5)	85.83 (19.8)	84.68 (21.7)	F(2,72)=0.67	.514
QLQ-CR29_SexInt	25.58 (28)	30.83 (26.6)	13.51 (22.9)	F(2,72)=12.15	<.001
QLQ-CR29_SexSy	10.08 (18.6)	19.66 (30.3)	26.13 (36.1)	F(1.46,51.2)=4.1	.033
QLQ-CR29_UrSy	9.82 (13)	13.19 (15)	16.97 (16.6)	F(2,72)=9.60	<.001
QLQ-CR29_InSy	17.21 (13.8)	11.75 (12.7)	14.96 (13.2)	F(1.65,59.5)=2.29	.119
QLQ-CR29_PainSy	19.38 (16.9)	14.58 (14)	20.27 (13.8)	F(1.69,60.94)=2.68	.085
QLQ-CR29_MoSy	9.69 (13.2)	12.08 (16.9)	17.12 (20.2)	F(2,72)=4.45	.015
TAS-20	44.81 (10.5)				
PANAS_PAtr	36.98 (6.2)				
PANAS_NAtr	18.93 (5.8)				
PANAS_PAst	31.86 (6.4)	31.8 (6.1)	30.89 (5.9)	F(2,72)=1.19	.310
PANAS_NAst	18.38 (6.3)	16.22 (5.8)	15.89 (5.7)	F(1.7,61.3)=3.74	.036
HADS	10.07 (5.3)	7.67 (5.3)	9.81 (6.2)	F(1.66,59.8)=5.78	.008
Mini-MAC_F	2.93 (0.62)	2.96 (0.6)	2.96 (0.6)	F(2,72)=0.12	.887
Mini-MAC_FS	3.38 (0.44)	3.39 (0.5)	3.3 (0.4)	F(2,72)=0.58	.561
Mini-MAC_HH	1.56 (0.44)	1.54 (0.5)	1.54 (0.5)	F(2,72)=0.06	.942
Mini-MAC_AP	2.63 (0.61)	2.39 (0.6)	2.15 (0.6)	F(2,72)=12.04	<.001
Mini-MAC_CA	2.78 (0.76)	2.76 (0.7)	2.7 (0.8)	F(1.67,60)=0.33	.680

QLQ-CR29: EORTC colorectal cancer module: _BI: Body Image, _Anx: Anxiety, _Wei: Weight, _SexInt: Sexual Interest, functional scales; _SexSy: Sexual Symptoms; _UrSy: Urinary Symptoms, _InSy: Intestinal Symptoms, _PainSy: Pain Symptoms, _MoSy: Mouth Symptoms, subcales; TAS-20: Toronto Alexithymia Scale; PANAS: Positive and Negative Affect Scale, _PAtr: Positive Affect Trait; _NAst: Negative Affect Trait; _PAst: Positive Affect State; _NAst: Negative Affect State; HADS: Hospital Anxiety and Depression Scale; Mini-MAC: Mini-Mental Adjustment to Cancer scales, _F: Fatalism, _FS: Fighting Spirit, _HH: Helplessness/Hopelessness, _AP: Anxious Preoccupation, _CA: Cognitive Avoidance.

Before performing the regression analyses, correlation analyses were performed between HRQoL at T0, T1 and T2 and all other variables to identify potentially predictive variables.

The final models explained 68%, 80% and 71% of the variance in HRQoL at T0, T1 and T2, respectively.

Regarding HRQoL at T0, QLQ-CR29_InSy_T0 (β=-0.581, t(38)=-5.67, p<.001) and PANAS_NAtr_T0 (β=-0.215, t(38)=-2.25, p=.03) were found to be significant and negative predictors.

With regard to HRQoL at T1, QLQ-CR29_PainSy_T0 (β=-0.458, t(35)=-5.31, p<.001), QLQ-CR29_InSy_T1 (β=-0.322, t(35)=-3.25, p=.003) and QLQ-CR29_UrSy_T1 (β=-0.306, t(35)=-2.75, p=.009) as significant predictors.

Regarding HRQoL at T2, HADS_T2 (β=-0.394, t(31)=-3.26, p=.003) and QLQ-CR29_MoSy_T2 (β=-0.369, t(31)=-3.56, p=.001) were found to be significant and negative predictors and Mini-MAC_F_T1 (β=0.040, t(31)=2.65, p=.013) was the only positive predictor.

Table 2. Hierarchical multiple regressions with health-related Quality of Life (QLQ-C30) at the different times as dependent variables.

	Predictor	R^2	Adj R^2	F	F- ΔR^2	B	SE B	β	p
	QLQ-C30 at T0								
4	(Constant)	0.71	0.68	23.33***	5.05*	98.93	3.49		<.001
	QLQ-CR29_InSy_T0					-0.38	0.07	-0.581	<.001
	QLQ-CR29_PainSy_T0					-0.11	0.06	-0.199	.082
	QLQ-CR29_Anx_T0					0.06	0.03	0.185	.054
	PANAS_NAtr_T0					-0.33	0.15	-0.215	.030
	QLQ-C30 at T1								
4	(Constant)	0.82	0.80	40.93***	7.58**	101.17	1.42		<.001
	QLQ-CR29_PainSy_T0					-0.33	0.06	-0.458	<.001
	QLQ-CR29_UrSy_T0					-0.06	0.11	-0.063	.569
	QLQ-CR29_InSy_T1					-0.31	0.10	-0.322	.003
	QLQ-CR29_UrSy_T1					-0.25	0.09	-0.306	.009
	QLQ-C30 at T2								
5	(Constant)	0.75	0.71	18.97***	10.65**	92.21	8.45		<.001
	TAS-20					-0.18	0.13	-.143	.181
	PANAS_NAst_T0					-0.39	0.20	-.195	.056
	Mini-MAC_F_T1					5.15	1.95	.240	.013
	QLQ-CR29_MoSy_T2					-0.23	0.07	-.369	.001
	HADS_T2					-0.81	0.25	-.394	.003

**p-value < .05; ** p-value <.01; ***p-value < .001*

QLQ-CR29: EORTC colorectal cancer module: _InSy: Intestinal Symptoms, _PainSy: Pain Symptoms, _Anx: Anxiety; _UrSy: Urinary Symptoms; _MoSy: Mounth Symptoms; PANAS_NAtr: Positive and Negative Affect Scale_Negative Affect trait scale; PANAS_NAst: Positive and Negative Affect Scale_Negative Affect state scale; TAS-20: Toronto Alexithymia Scale; Mini-MAC_F: Mini-Mental Adjustment to Cancer scales_Fatalism; HADS: Hospital Anxiety and Depressive Scale.

4. Discussion and conclusion

The present exploratory longitudinal study sought to assess changes in HRQoL of RCPs during active treatment phases and to investigate which physical and psychosocial factors predict HRQoL at different time points.

Few previous studies examining some of these factors provided separate data for RCPs. Our study showed that HRQoL was preserved at the time of diagnosis and patients had few physical symptoms, which is consistent with the results of two studies on CRC patients (Orive et al., 2022; Qaderi et al., 2021). However, RCPs reported high levels of health anxiety and psychological distress, which decreased after preoperative treatments, as in Rades et al. (2023). This finding may be explained by the initial burden of the diagnosis and preoperative treatments, of which the side effects of radiotherapy in particular are a concern for patients as they are not fully aware of them (Hernández Blázquez & Cruzado, 2016; Stiegelis et al., 2004). In contrast to some recent longitudinal studies on CRC patients that recruited patients who had already undergone major treatments (Orive et al., 2022; Qaderi et al., 2021), our data showed a significant decrease in HRQoL, especially after surgery. Only one study came to a similar conclusion (Reudink et al., 2022).

The exploratory analyses showed the different weight of physical and psychosocial factors on HRQoL depending on the treatment phases. Indeed, physical symptoms have a strong impact on HRQoL in RCPs, especially at diagnosis and after preoperative treatment, confirming previous research findings (Murata et al., 2008; Reudink et al., 2022). However, the psychological response in the early phases has a greater weight in predicting HRQoL of RCPs after active treatments than during the early phases themselves.

From a clinical perspective, the data from the present study suggest that physical and psychological screening programs for RCPs need to be improved from diagnosis and in all subsequent treatment phases. In this way, support services should be better tailored, taking into account the treatment phase, and preventive and prehabilitative measures after diagnosis should be improved, which will have an impact on HRQoL and mental health in the medium to long term. In fact, psychological adjustment to the diagnosis and initial treatments of rectal cancer seems to explain HRQoL more than physical symptoms after surgery, so promoting early adoption of active coping styles and prevent distress could be a key practice for better HRQoL in the medium term.

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