

# Association of social support, functional status, and psychological variables with changes in health-related quality of life outcomes in patients with colorectal cancer

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## Abstract

**Background:** The aim of this study was to explore the association of social support received, and functional and psychological status of colorectal cancer patients before surgery with changes in health-related quality of life (HRQoL) outcomes measured by EORTC QLQ-C30 at 1-year post-intervention.

**Methods:** Consecutive patients that were because of undergo therapeutic surgery for the first time for colon or rectum cancer in nine hospitals in Spain were eligible for the study. Patients completed questionnaires before surgery and 12 months afterwards: one HRQoL instrument, the EORTC QLQ-C30; a social network and social support questionnaire, the Duke-UNC Functional Social Support Questionnaire; the Hospital Anxiety and Depression Scale, to assess anxiety and depression; and the Barthel Index, to assess functional status; as well as questions about sociodemographic information. General linear models were built to explore the association of social support, functional status, and psychological variables with changes in HRQoL 12 months after intervention.

**Results:** A total of 972 patients with colorectal cancer took part in the study. Patients' functional status, social support, and anxiety and depression were associated with changes in at least one HRQoL domain. The higher functional status, and the higher social support, the more they improved in HRQoL domains. Regarding anxiety and depression, the more anxiety and depression patients have at baseline, less they improve in HRQoL domains.

**Conclusions:** Patients with colorectal cancer who have more social support and no psychological distress may have better results in HRQoL domains at 1 year after surgery.

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## Background

Colorectal cancer (CRC) is one of the major causes of morbidity and mortality, particularly in the developed world [1]. In Spain, it is the second most common neoplasia in men and women after lung and breast cancer, respectively [2].

Because of improvements in early detection and treatment, survival rates have increased slowly over recent decades [3,4]. Health-related quality of life (HRQoL) have shown to be a length of survival predictor variable [5], and the evaluation of this variable could be very helpful for clinical decision-making and patient management [6].

Another variable that has been affected by this increased survival rate was functional status [7,8]. The continuously extending lifespan lead to an increasing number of patients with CRC experiencing limitations in their activities of daily living [9].

The social environment is an important determinant of patients with cancer' ability to cope with stressful

situations during their illness [10–12]. Social support has shown to be related with HRQoL, can act as an important promoter of mental health, and has shown to be negatively correlated with depression [13].

Anxiety and depression are common in patients with CRC [14]. Therefore, having a good understanding of such psychological problems and the implementation of preventive treatments may contribute to improving survival and HRQoL in patients with cancer [15–17].

Several studies have examined the association of social networks and social support with HRQoL in patients with cancer [9,10,18], but none has examined this relationship together with psychological and functional status. The objective of this study was to determine the association of social support and functional and psychological status of patients with CRC before surgery with changes in HRQoL measured by the European Organisation for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire (QLQ-C30) at 1-year post-intervention. Our hypothesis is that the more social support, better functional

and psychological status patients with CRC have, the more they would improve in HRQoL at 1 year.

## Methods

This study was conducted in nine hospitals in three Spanish regions: Andalusia, Catalonia, and Basque Country. The corresponding Institutional Review Boards approved the study. Written informed consent was obtained from participating patients.

Consecutive patients because of undergo therapeutic surgery for the first time for colon or rectum cancer between March 2010 and March 2012 were eligible for the study. Patients were excluded if they were diagnosed with colon or rectum carcinoma *in situ*, required urgent intervention or did not complete all the study questionnaires.

Patients were sent a letter informing them about the study and asking for their voluntary participation. We then sent questionnaires to each participant before surgery. Reminder letters were sent 15 days after each mailing to those who had not replied. The baseline questionnaire measured HRQoL with the EORTC QLQ-C30, social support with the Duke-UNC Functional Social Support Questionnaire (FSSQ), anxiety and depression with the Hospital Anxiety and Depression Scale (HADS), and functional status with Barthel Index (BI), plus questions requesting sociodemographic information. Cancer location was extracted from medical records. The 12-month survey included the same questionnaires. The data analyzed are from patients who completed preoperative and postoperative questionnaires.

Cases of anxiety and depression were defined using predefined HADS scores [19]. The HADS is designed specifically for individuals with a physical illness. It is divided into two subscales with seven questions pertaining to symptoms associated with anxiety and seven with depression. Each of the 14 items consists of a 4-point Likert scale (ranging from 0 to 3) that applies to the previous week. A total score for each subscale is then calculated, ranging from 0 to 21. As recommended [19] cut-off points, we considered scores <8 to be non-cases, scores between 8 and 10 borderline cases, and scores >10 probable cases (i.e., indicative of psychological distress). The HADS has been translated into and validated in Spanish [20].

The FSSQ [21], is composed of 11 items. Each item is rated on a five-point Likert scale, ranging from 1 to 5: the higher the score, the better the perceived social support. It assesses subjective social support in two domains: (1) Confidant support: 6 items (score range 6–30) and (2) Affective support: 5 items (score range 5–25), and provides an overall social support measure (score range: 11–55). The questionnaire has been translated into and validated in Spanish [22,23].

The BI consists of 10 items that assess the ability to perform certain activities without help. It has 2- and 4-point

response options summing to a score ranging from 0 (completely dependent) to 100 (completely independent), with intervals of 5 points [24]. The BI was translated into and validated in Spanish [25].

The EORTC QLQ-C30 is a 30-item instrument composed of five functional scales, three symptom scales, a quality of life scale, and six single items [26]. All of the scales and single-item measures range in score from 0 (worst) to 100 (best) on functioning scales, and from 0 (best) to 100 (worst) on symptom scales. When there are missing items, multi-item scores were calculated as the mean of non-missing items, provided that least half of the items from the corresponding scale had been completed [27]. The EORTC QLQ-C30 has previously been validated in Spain [28,29] and used in patients with CRC [6,14,30]. As in Skarstein et al. [31] and Tsunoda et al. [14], we used the following dimensions of the EORTC QLQ-C30: physical function (PF), role function (RF), emotional function (EF), cognitive function (CF), social function (SF), fatigue, pain, and global quality of life (QoL).

Disease stage and treatment are very important variables; however, in the present study we have analyzed variable which can be changed and we have followed the work of Skarstein et al. [31] and Tsunoda et al. [14], so we have analyzed the same variables in order to compare results, adding in our case the change in HRQoL and adjusting by other significant variables.

## Statistical methods

Descriptive data are expressed as frequencies and percentages, and means with standard deviations (SDs). We used the *t*-test or the nonparametric Wilcoxon test for quantitative variables and chi-squared test or Fisher's exact test for qualitative variables to assess the differences in baseline characteristics between patients who completed the questionnaires at both time points, or only at baseline.

EORTC QLQ-C30 changes were calculated as the difference between 12-month and baseline scores, with a positive result indicating a gain in HRQoL. General linear models were constructed to assess the association of patient functional status, social support, anxiety, and depression with changes in HRQoL 12 months after surgery. We studied the association of each variable with HRQoL changes in individual analyses considering HRQoL changes 12 months after surgery as the dependent variable, and functional status, social support, anxiety, and depression as independent variables. Given the importance of the baseline scores to HRQoL changes, we adjusted for the corresponding baseline dimension scores [6]. Patients were categorized into four groups by whether they showed anxiety and/or depression ('no anxiety–no depression', 'anxiety–no depression', 'depression–no anxiety' and 'depression–anxiety'). Then, we determined

the association of baseline functional status, social support, anxiety, and depression together with changes in HRQoL, adjusting for the corresponding baseline HRQoL scores and possible confounding variables, namely, gender, age, relapse, and cancer location. For the final models, only significant variables were retained. The magnitude of the effect was explained by the beta parameter, which represents the improvements on changes in HRQoL for each unit increase in the independent variable, if it is continuous. If the covariate is categorical, the beta parameter represents the difference in changes in HRQoL of a category with respect to the reference category. The explanatory power of final models was measured by the  $R^2$ .

All effects were considered statistically significant at  $p < 0.05$ . All statistical analyses were performed using SPSS (SPSS Inc., Chicago, IL) version 18.0, and SAS for Windows version 9.2 (SAS Institute Inc., Cary, NC).

## Results

A total of 1496 eligible patients with CRC agreed to participate in the study and completed the baseline questionnaires. After surgery, 972 (64.97%) completed the follow-up questionnaires at 12 months. This is the sample included in the analysis. The mean age was 67.52 years (SD=10.39), 37.04% were women, 7.05% had a relapse, 60.13% had cancer located in the colon, 74.27% were married or living as a couple, and 62.22% were retired. Table 1 compares baseline data in patients that were and were not included. Patients who did not respond at 12 months, those 'not included', had worse scores on all EORTC QLQ-C30 domains, the FSSQ and the BI. In addition, there were significant baseline differences in anxiety and depression measured by HADS between these groups, with higher rates of anxiety and depression among those not included.

Regarding associations of functional status (BI), social support, anxiety, and depression with changes in HRQoL at 12 months adjusting for corresponding baseline HRQoL (Table 2), in general, the higher the functional status and social support, the higher the improvement in HRQoL domains. Further, regarding anxiety and depression, the more anxiety and depression patients had at baseline, the less they improved in HRQoL domains.

Specifically, the better the functional status, the greater the improvements in PF, RF, SF, and pain EORTC QLQ-C30 domains. With regards to social support, the more social support patients' had the more they improved in all EORTC QLQ-C30 domains, apart from RF, EF, and CF domains. The *depression-no anxiety* and *depression-anxiety* groups were regrouped in a single category '*depression*', given the small sample size and lack of significant differences between these categories in the main analyzed variables (gains in HRQoL). It was then found that patients with depression improved less than no anxiety-no depression patients in all EORTC

**Table 1.** Baseline patient characteristics of patients included and not included in the analysis

	Included (n = 972)	Not included (n = 524)	p-value
	n (%)	n (%)	
Age, years: mean (SD)	67.52(10.39)	67.80(11.70)	0.657
Gender			
Male	612(62.96)	337(64.31)	0.613
Relapse	64 (7.05)	63 (20.06)	<0.0001
Location			
Colon	567(60.13)	243(61.06)	0.627
Rectum	376(39.87)	155(38.94)	
Marital Status			
Single	71(7.64)	48(9.62)	0.048
Married	690(74.27)	340(68.14)	
Divorced/widowed	168(18.08)	111(22.24)	
Occupation			
Retired	578(62.22)	295(61.33)	0.041
Employed	213(22.93)	92(19.13)	
Others	138(14.85)	94(19.54)	
Barthel Index: Mean(SD)	95.32(11.85)	90.78(18.59)	<0.0001
Barthel Index categorized			
Total dependence	4(0.54)	7(2.02)	<0.0001
Severe dependence	17(2.29)	22(6.34)	
Moderate dependence	110(14.82)	69(19.88)	
Mild dependence	83(11.19)	36(10.37)	
Independence	528(71.16)	213(61.38)	
Social support (FSSQ): Mean(SD)			
Total score	48.12(8.02)	47.04(8.38)	0.029
Affective support	17.93(2.92)	17.75(3.03)	0.320
Confidant support	30.14(5.54)	29.30(5.85)	0.014
HADS			
Anxiety	359(37.91)	229(44.90)	0.010
Depression	185(19.56)	158(30.86)	<0.0001
Anxiety/Depression (HADS)			
No depression-no anxiety	556(58.77)	253(49.61)	<0.0001
Anxiety-no depression	205(21.67)	101(19.80)	
Depression-no anxiety	31(3.28)	28(5.49)	
Depression-anxiety	154(16.28)	128(25.10)	
EORTC QLQ-C30: mean (SD)			
Physical function	84.13(20.09)	76.61(26.54)	<0.0001
Role function	81.22(27.55)	72.43(33.99)	<0.0001
Emotional function	72.30(23.09)	66.03(26.68)	<0.0001
Cognitive function	87.35(19.47)	82.24(24.40)	<0.0001
Social function	82.27(24.64)	76.18(28.50)	<0.0001
Fatigue	28.47(25.94)	37.13(30.09)	<0.0001
Pain	21.92(25.97)	28.16(30.03)	<0.0001
Global quality of life	64.39(22.69)	60.20(26.69)	0.003

Data are given as frequency (percentage) unless otherwise stated.

FSSQ, Duke-UNC Functional Social Support Questionnaire; HADS, Hospital Anxiety Depression Scale; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer.

Score interpretation: FSSQ, higher scores indicating higher social support; Barthel Index, higher scores indicating greater independence; HADS, higher scores indicating higher level of mood disorder; EORTC QLQ-C30, higher scores for a functional scales (Physical, role, emotional, cognitive, and social function, and global quality of life) represents a *higher/healthy level of functioning* but a higher scores for a symptom scales/item (Fatigue and Pain) represents a *higher level of symptomatology/problems*.

QLQ-C30 domains, as did anxiety-no depression patients who improved less in RF, EF, and pain EORTC QLQ-C30 domains than no anxiety-no depression patients.

**Table 2.** General linear models analyzing the influence of psychological variables and other patient characteristics individually on changes in HRQoL at 12 months (n = 972)

	Change in EORTC QLQ-C30															
	PF		RF		EF		CF		SF		Pain		Fatigue		QL	
	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value
Barthel index	0.15	0.007	0.25	0.001	0.09	0.156	-0.01	0.839	0.18	0.013	0.17	0.010	0.09	0.169	0.05	0.463
Social support (FSSQ)	0.14	0.031	0.11	0.268	0.16	0.071	0.12	0.101	0.25	0.011	0.25	0.007	0.27	0.003	0.28	0.001
Anxiety/depression (HADS)																
Depression	-7.54	<0.0001	-12.20	<0.0001	-10.75	<0.0001	-3.84	0.021	-8.96	<0.0001	-8.88	<0.0001	-7.68	0.0001	-10.38	<0.0001
Anxiety-no depression	-2.52	0.061	-4.53	0.018	-5.08	0.005	-1.58	0.271	-1.43	0.444	-3.86	0.023	-2.58	0.097	-2.09	0.217
No anxiety-no depression	Ref		Ref		Ref		Ref		Ref		Ref		Ref		Ref	

All models have been adjusted for corresponding baseline HRQoL scores.

Ref: reference group.

FSSQ, Duke-UNC Functional Social Support Questionnaire; HADS, Hospital Anxiety Depression Scale; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer; PF, physical function; RF, role function; EF, emotional function; CF, cognitive function; SF, social function; QL, global quality of life.

Score direction: FSSQ, Confidant support score range 6–30, higher scores indicating higher social support; Barthel Index scores ranges from 0 (completely dependent) to 100 (completely independent); EORTC QLQ-C30 changes are calculated so that positive values indicate improvement and negative values worsening.

Table 3 shows the results of multivariate models assessing associations of baseline functional status, social support, anxiety, and depression together with changes in EORTC QLQ-C30 domains, adjusting for age, location, gender, and baseline HRQoL scores. Patients' functional status, social support, and anxiety and depression were associated with changes in at least one HRQoL domain. Patients with higher functional status had greater improvements only in the RF domain of EORTC QLQ-C30. Higher social support was associated with greater

improvements in four EORTC QLQ-C30 domains: SF, pain, fatigue, and QoL. Regarding psychological status, patients with depression tended to show less improvement in all EORTC QLQ-C30 domains and patients with only anxiety improved less in EORTC QLQ-C30 EF, pain, and fatigue domains than those without anxiety or depression. Concerning other variables, age appeared to influence HRQoL changes, there being less improvement in the PF but more in the SF domain with increasing age. Regarding gender and cancer location, Table 3 shows

**Table 3.** Multivariate general linear models analyzing the influence of functional status, anxiety and depression, and social support on changes in HRQoL at 12 months (n = 972)

	Changes in EORTC QLQ-C30															
	PF		RF		EF		CF		SF		Pain		Fatigue		QL	
	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value
Baseline HRQoL	-0.56	<0.0001	-0.72	<0.0001	-0.76	<0.0001	-0.60	<0.0001	-0.76	<0.0001	0.77	<0.0001	0.61	<0.0001	-0.81	<0.0001
Age	-0.22	<0.0001							0.22	0.003						
Location																
Rectum	Ref		Ref		Ref			Ref								
Colon	2.74	0.012	5.50	0.001	4.85	0.0002			6.15	<0.0001	4.30	0.003	3.63	0.014	4.84	0.0005
Gender																
Male	2.86	0.011			4.69	0.0006	2.61	0.028			4.48	0.003	3.16	0.037	3.47	0.014
Female	Ref				Ref		Ref			Ref		Ref		Ref		Ref
Barthel Index			0.17	0.026												
Social support (FSSQ)								0.21	0.031	0.19	0.040	0.22	0.020	0.22	0.013	
Anxiety/depression (HADS)																
Depression	-6.57	<0.0001	-10.25	<0.0001	-10.40	<0.0001	-3.38	0.043	-8.80	0.0001	-7.50	0.0004	-6.21	0.004	-9.38	<0.0001
Anxiety-No depression	-2.55	0.058	-3.68	0.079	-4.49	0.012	-1.35	0.347	-1.63	0.398	-4.19	0.019	-3.86	0.033	-2.12	0.214
No anxiety-No depression	Ref		Ref		Ref		Ref		Ref		Ref		Ref		Ref	
R <sup>2</sup>	0.288		0.404		0.393		0.292		0.400		0.472		0.354		0.448	

Ref: reference group.

FSSQ, Duke-UNC Functional Social Support Questionnaire; HADS, Hospital Anxiety Depression Scale; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer; PF, physical function; RF, role function; EF, emotional function; CF, cognitive function; SF, social function; QL, global quality of life.

Score interpretation: FSSQ, Confidant support score range 6–30, higher scores indicating higher social support; Barthel Index scores ranges from 0 (completely dependent) to 100 (completely independent); EORTC QLQ-C30 changes are calculated so that positive values indicate improvement and negative values worsening.

significant differences in nearly all domains, except for RF and SF in the case of gender and except for CF in the case of cancer location, men and patients with colon cancer improving more in EORTC QLQ-C30 domains than women or patients with rectum cancer. The explanatory power of the models ranged from 28.8 to 47.2% depending on the domain analyzed.

## Conclusions

Our prospective study offers insight into the association of patients with CRC' social support, functional and psychological status, with changes in HRQoL outcomes at one year post-surgery. We observed that patients with more social support and no anxiety or depression improved more in HRQoL (EORTC QLQ-C30), adjusted for age, gender, location, and HRQoL baseline scores. Regarding functional status, this had a minor impact on HRQoL changes in our sample.

Several studies have measured the association of HRQoL in patients with CRC with social support [10], functional status [9], or anxiety and depression [14] but, to our knowledge, ours is the first to examine the association between changes in HRQoL and social support, functional and psychological status together in patients with CRC at one year after surgery.

In this study, depression together with baseline HRQoL was the variables most strongly associated with changes in HRQoL 12 months after surgery, patients with depression showing lower gains in all HRQoL domains analyzed than patients without anxiety or depression. Previous research has indicated that baseline HRQoL commonly predicts HRQoL at later time points [6], and further, that poorer HRQoL is related to increased psychological distress, although in all cases the analysis was performed without adjusting for potential confounders [14,32,33]. Supporting these results, in our study, these associations were maintained after adjusting for other main variables, namely, baseline HRQoL, age, location, gender, functional status, social support, anxiety, and depression.

All HRQoL domains were associated with depression but only changes in EF, pain, and fatigue domains with anxiety. Hence, in general, HRQoL seems to be more influenced by depression than anxiety. Associations of PF, RF [14,31], CF [14,31], SF [34], pain, and fatigue [35–37] with depression have been observed in previous studies, although again the analysis was not adjusted. Notably, our study has shown associations between all of these EORTC QLQ-C30 domains, even after adjusting for other variables.

This strong association between depression, measured by HADS, and changes in HRQoL, measured by EORTC QLQ-C30, adjusted for the other variables suggests that the importance of depression needs to be assessed and treated. On the other hand, the question of whether

psychological interventions with patients with cancer can influence disease outcome has been widely debated in cancer research [15,38,39]

In our study, we also found an association between anxiety and change in some HRQoL domains, namely, EF, pain, and fatigue, contrasting with no relationship between anxiety and HRQoL being observed in previous studies [14,31]. Specifically, as with depression, anxiety was associated with less improvement in these HRQoL domains.

Functional status was weakly related to HRQoL changes, the only domain associated with this variable being RF. Disease-related functional status is associated with patient difficulties in carrying out daily activities, the greater independence patients have the more able they are to perform these activities. The poor association observed could be due, in part, to a ceiling effect, with 71.16% patients in our sample being classified as 'independent'. We conclude that this variable is not suitable for this population.

Among people with cancer, there is evidence [9,10] that support from others may maximize their resilience and enhance their experience post-treatment, thereby improving their HRQoL. Sapp et al. [10] showed that social networks may play a vital role in maintaining or improving HRQoL among surgically-managed patients. We found that social support was associated with improvements in SF, pain, fatigue, and QoL, even adjusting for psychological variables, functional status, age, gender, and location. These findings could be of interest to health-care providers, researchers, and surgically managed patients to improve HRQoL among this growing population.

To interpret changes in scores over time we have followed the values given in physical, emotional, social functioning, and global quality of life domains by Osoba et al [40], the values of the change found between baseline and HRQoL outcomes at 1 year showed that in these domains patients reported 'none' or 'a little' change for better. For physical and social functioning domains no change was found, despite of the statistically significant differences between baseline and HRQoL outcomes at 1 year in the case of social functioning domain. Regarding emotional functioning (basal mean value 72.15 (23.12) and 80.56 (21.40) at one year) and global health status (basal mean value 64.40 (22.71) and 73.49 (21.41) at 1 year) patients reported a little change for better. These authors did not show values of change for the other domains or symptoms.

A limitation of our study is the relatively high percentage of patients not included in the analysis. Overall, 64.97% patients completed the questionnaires at 12 months. We recognize that given the length of the battery used, completion of the questionnaires required considerable effort from patients. Despite the losses, however, our sample is still

relatively large compared with those used in other similar studies. Like most of this kind of studies we found differences between included and non-included patients. Patients who do not answer to the questionnaires at one year tend to be worse than patients who complete them. However, in some cases, likely because of this relatively large sample size, we found differences between included and non-included patients, including a difference of less than 1 point in the social support total scores and confidant support domains. In relation to this, the response rate may also have impacted on, for example, the prevalence of anxiety and depression, in terms of underrepresenting those with more advanced cancer and possibly also those who were more depressed or anxious (as they may have declined to participate).

This study to our knowledge is unique in its consideration of sociodemographic, medical, psychological, and lifestyle-related variables as associated variables with gains in HRQoL.

In conclusion, the data indicate that patients with colon or rectum cancer with more social support and no anxiety or depression tend to have better HRQoL at one year after surgery, adjusted for baseline HRQoL, age, location, and gender. These findings could highlight the need for regular distress and social support screening for patients with CRC. Therefore, our results could suggest important implications in clinical practice. Healthcare professionals may promote interventions as the use of support groups to help increase patients' social support, and anxiety and depression can be improved by appropriate case management.

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