# **RESEARCH ARTICLE**

# **Quality of Life and Psychological Well-Being of Colorectal Cancer Survivors in Jordan**

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# Abstract

Background: Colorectal ranked first among cancers reported in males and ranked second amongst females in Jordan, accounting for 12.7% and 10.5% of cancers in males and females, respectively. Colorectal cancer patients can suffer several consequences after treatment that include pain and fatigue, constipation, stoma complications, sexual problems, appearance and body-image concerns as well as psychological dysfunction. There is no published quantitative data on the health-related quality of life and psychological wellbeing of Jordanian colorectal cancer survivors. Method: This project was a cross-sectional study of colorectal cancer survivors diagnosed in 2009 and 2010. Assessment was performed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), the colorectal cancer specific module (EORTC QLQ-CR 29) and the Hospital Anxiety and Depression Scale (HADS). Data on potential predictors of scores were also collected. Results: A total of 241 subjects completed the study with mean age of 56.7±13.6. Males represented 52.3% of study participants. A majority of participants reported good to high overall health; the mean Global health score was 79.74± 23.31 with only 6.64% of study participants scoring less than 33.3%. The striking result in this study was that none of the study participants participated in a psychosocial support group; only 4 of them (1.7%) were even offered such support. The mean scores for HADS, depression score, and anxiety score were 8.25±9, 4.35±4.9 and 3.9±4.6, respectively. However, 77.1% of study participants were within the normal category for the depression score and 81.7% were within this category for anxiety score; 5.4% of participants had severe anxiety and 5.4% of them had severe depression. Discussion: Patients with colorectal cancer in Jordan have a good quality of life and psychological wellbeing scores when compared with patients from western countries. None of the colorectal cancer patients managed at the Ministry of Health received any formal counselling, or participated in psychological or social support programmes. This highlights the urgent need for a psychosocial support programme, psychological screening and consultations for patients diagnosed with colorectal cancer at the Ministry of Health Hospitals.

Keywords: Colorectal cancer - quality of life - psychological well-being - hospital anxiety and depression scale - Jordan

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# Introduction

Cancer is a major public health problem in Jordan. In 2009 it was the second leading cause of death among Jordanians contributing to 14.6% of deaths (Ministry of Health, June, 2012). In the year 2010, colorectal cancer ranked first among cancers reported in males and second among cancers reported in females, accounting for 14.2% and 9.2% of cancers in males and females, respectively. Its overall Age-standardized Incidence Rate (ASR) was 17.3 per 100,000 (ASR for males was 20.6 per 100,000 and for females was 13.7 per 100,000) (Non-communicable Diseases Directorate, 2010).

In this document, colorectal cancer (CRC) refers to

cases of colon cancer, rectal cancer or colorectal cancer. Cancer symptoms or symptoms secondary to treatment, such as diarrhea, constipation, fatigue and loss of appetite are very common and has significant negative effects on the quality of life (QoL) (Steginga et al., 2009; Gray et al., 2011; Pan and Tsai, 2012). Consequently, colorectal cancer patients have significantly poorer physical and mental quality of life scores when compared with the general population or with patients without cancer (Smith et al., 2008).

The main reported important predictors of the patients' quality of life scores are the stage and site of colorectal cancer at diagnosis and the surgical procedures used (Schmidt et al., 2005b; Paika et al., 2010; Cardin et al.,

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2012). In addition, some studies showed that the presence of a stoma also has a major negative impact on the quality of life (Rispoli et al., 2009). However, other studies failed to show a statistically significant difference in the quality of life of patients who had stoma and those who underwent a sphincter-saving resection (Smith-Gagen et al., 2010; Campos-Lobato et al., 2011).

In order to assess the short and long term effects of colorectal cancer on the quality of life, several cancerspecific health-related quality of life (HRQL) measures have been developed such as the Functional Assessment of Cancer Therapy (FACT) scale, the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 instrument, the Functional Living Index-Cancer (FLIC) scale and the Cancer Rehabilitation Evaluation System (CARES) instrument (Bowling, 2001).

The most widely used instrument is the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) which has been developed to assess the health-related quality of life of cancer patients (European Organization for Research and Treatment of Cancer). This questionnaire was translated and validated in different languages, including the Arabic language (Awad et al., 2008). Moreover, few instruments have been specifically developed and validated for the assessment of the HRQL of colorectal cancer patients. An example is the FACT scale which consists of a core instrument (FACT-G) and various subscales, including a subscale for colorectal cancer (FACT-C) (McDowell, 2006). Other examples are the EORTC colorectal cancer-specific quality of life questionnaire module (QLQ-CR29)

Moreover, few questionnaires have been specifically developed for the assessment of the HRQL of colorectal cancer patients. There are valid instruments that are in use at present. An example is the FACT scale which consists of a core instrument (FACT-G) and various sub-scales, including a subscale for colorectal cancer )FACT-C) (McDowell, 2006). Other instruments are the colorectal cancer specific module EORTC QLQ-CR29 and liver metastasis from colorectal cancer module EORTC QLQ-LMC 21 (Whistance et al., 2009).

General psychological well-being (subjective wellbeing) is a broad term. It covers negative aspects of the quality of life related to psychological morbidity such as depression, anxiety and emotional distress and positive aspects such as happiness, life satisfaction, morale, selfesteem and sense of coherence (Bowling, 2004).

Psychological well-being assessment for colorectal cancer patients is important in order to have a comprehensive assessment of the health-related quality of life. Previous studies, using screening questionnaires, showed that colorectal cancer patients have distress, anxiety and depression following diagnosis and treatment (Ramsey et al., 2002; Deimling et al., 2006). Compared with the general population of similar age, they have a higher prevalence of depression (Ramsey et al., 2002). These findings could be justified by fear from recurrence or from a second cancer occurrence (Deimling et al., 2006).

The Hospital Anxiety and Depression Scale (HADS) is a self-administered questionnaire with the ability to detect

minor psychiatric impairment. It is a screening instrument for anxiety and depression and has been validated in different settings for the general population and patients with a wide range of medical conditions (Zigmond and Snaith, 1983), including colorectal cancer (Tsunoda et al., 2005). There is a validated Arabic version of this questionnaire (El-Rufaie and Absood, 1987).

To the best of our knowledge, there are no published studies on the HRQL and psychological well-being of colorectal cancer patients in Jordan. Therefore, we conducted a survey on colorectal cancer survivors, one to three years after diagnosis, to assess their quality of life and psychological well-being. This study would help in evaluating the current management of colorectal cancer patients in Jordan particularly in the absence of a psychosocial support program for colorectal cancer survivors at the Ministry of Health hospitals, where the majority of colorectal cancer patients are primarily treated. Other objectives of the study were to measure the proportion of patients with undiagnosed depression or anxiety, to identify the predictors of the quality of life and psychological well-being scores and to assess the participation of colorectal cancer patients in psychosocial support programs.

### **Materials and Methods**

### Study design

This project was a cross-sectional study conducted among colorectal cancer patients diagnosed in the period from January 1, 2009 and December 31, 2010. The assessment was therefore at 12 to 36 months after the initial diagnosis. This allowed for the assessment of intermediate-onset (one to three years after diagnosis) consequences of colorectal cancer like pain, coping with stoma, sexual problems and psychosocial dysfunction. The study did not investigate immediate post-treatment effects of colorectal cancer management.

The data for this study were collected at the Radiation Oncology Department at Al-Bashir hospital in the period from July 2012 until October 2013. Al-Bashir hospital is the largest Jordanian governmental hospital and is located in Amman, the capital of Jordan. Since 2009, it has become the primary hospital for treating colorectal cancer patients insured by the Ministry of Health. Patients are surgically treated in the rest of governmental hospitals and then all are referred to Al-Bashir hospital for follow-up and to receive chemotherapy and radiotherapy, if needed. It is therefore believed that the selected sample is to a large extent representative of colorectal cancer patients in Jordan.

### Eligibility criteria

Inclusion criteria were being a colorectal cancer patient diagnosed in the period from the 1st of January 2009 and the 31st of December 2010, being aged between 18 and 65 years, living permanently in Jordan, having no history of other cancers, not having received therapy for a minimum of six months prior to the interview and finally, signing the study's informed consent form. Exclusion criteria were being unable to attend or complete the interview due to time constraints, refusing to participate in the study or choosing later to withdraw from it.

### Study outcomes primary endpoints

The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Core 30 (EORTC QLQ-C30) and the EORTC colorectal cancerspecific quality of life questionnaire module (QLQ-CR29).

# The hospital anxiety and depression scale (HADS)

The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and the EORTC colorectal cancerspecific quality of life questionnaire module (QLQ-CR29) have been widely used. These questionnaires were translated and validated in different languages, including the Arabic language.

# General psychological well-being (Subjective Well-being)

The HADS is a self-administered questionnaire that can detect minor psychiatric impairment. A score of 0 to 7 is categorized as normal, a score of 8 to 10 suggests possible anxiety or depressive disorder and a score of 11 or above indicates a probable anxiety or depressive disorder (Zigmond and Snaith, 1983). Depression and anxiety scores were also classified separately into four groups: normal (0-7), mild (8-10), moderate (11-14) and severe (15-21). This questionnaire was also validated on Arab populations, including on colorectal cancer patients.

# Methodology

Data were collected through a face-to-face interview and through chart review forms.

Eligible participants who consented to participate in our study were interviewed alone by a research assistant, unless they preferred to be accompanied by a friend or a family member. The research assistants received extensive training on the study questionnaires and forms.

Participants were free not to answer any question or to withdraw from the interview without being questioned. Research assistants were instructed to thank the withdrawals for their time and participation. For illiterate patients, a third party such as a family member or a friend of the participant was available when consenting.

# Scientific and ethics committees approvals

Scientific and Ethical approvals were obtained from Ethics Committee of the Faculty of Medicine at Mutah University and from the Ministry of Health. All participants signed an informed consent form prior to being interviewed. For illiterate patients, a third party such as a family member or a friend of the participant was available when consenting.

# Sample size calculation and data analysis

The reported cases of colorectal cancer in Jordan for the years 2009 and 2010 were 558 and 554, respectively. Using the Kish formula for sample size estimation (Al-Subaihi, 2003), the estimated sample size was 218. This is the smallest sample size possible based on the assumption of a 90% significance level and a 5% margin of error.

# Plan for statistical analysis

Analysis was conducted using SPSS software version 19.0 (SPSS Inc., Chicago, IL, USA). In addition to calculating the quality of life scores, data on the predictors of the quality of life scores were collected through a standardized interview questionnaire and a clinical chart review form. The interview questionnaire and chart review forms covered socioeconomic variables, histopathological findings, the stage and grade of colorectal cancer, treatment and current medical conditions.

Student's t-test was used to compare the means of continuous variables for two groups and one-way analysis of variance was used to compare the means of continuous variables for three or more groups (Bland, 2000).

Multiple linear regressions were used to relate the quality of life scores to their predictors. A stepwise selection method was used to select the best regression model with alpha-to-enter of 0.05 and alpha-to-remove of 0.1.

Predictors included in the regression model were classified into four groups:

*i*) Social and economic indicators: Age, city, age at diagnosis, marital status, place of living (with husband, family, others or alone), literacy, level of education, husband's education, employment status, average monthly family income (JD), number of children under 18 at home and smoking history.

*ii*) Medical indicators: Presence of chronic diseases, family history of cancer, number of pregnancies and if had reached menopause.

*iii*) Clinical indicators: cancer site (sigmoid including all other colon non-rectal sites, rectum including anorectal tumors and rectosigmoid tumors on junction between rectum and sigmoid colon), use of stoma, stage at diagnosis, pathological type, differentiation, tumor size at histological examination, recurrence since baseline, extent of disease, type of surgery, surgical margin, chemotherapy and its duration, radiation therapy and its duration, palliative chemotherapy and palliative radiotherapy.

*iv*) Psychosocial indicators: receiving psychological counseling after diagnosis, participation in a psychosocial support program, having suffered from traumatic events prior to the diagnosis with colorectal cancer, having suffered from traumatic events after diagnosis irrelevant to colorectal cancer, history of a diagnosis of depression, history of a diagnosis of anxiety, presence of current social problems causing major stress to the patient's life, presence of any financial difficulties that affect the patient's life and well-being and the total HADS score.

# Results

# Demographic, clinical and psychosocial characteristics of participants

Two hundred forty-one subjects completed the study with a mean age of  $56.7\pm13.6$ ; 52.3% were males with a mean age of  $59.0\pm13.0$  SD and 47.7% were females with mean age of  $54.0\pm14.0$  SD. Around two third of participants (64.0%) lived in Amman, while the rest lived in other governorates. The average number of children at



Figure 1.95% Confidence Interval for the Mean of Quality of Life Measures. Numbers represent the percentage of participates scoring "<33.3" and ">66.7" respectively

home was  $2.9\pm1.5$  SD. Regarding the employment status of patients, 17.4% were working on full-time basis, 14.5% were retired, 3.7% were working on a part-time basis, while the rest (64.4%) were unemployed. Consequent to their illness, 7.5% of patients changed their job of their own volition, while only 3.1% did that due to their bosses. Regarding the medical history of the participants, 25.3% of them had a history of type 2 diabetes and 26.3% had a history of hypertension. The smoking rate was 17.4%. Other reported common chronic conditions were rheumatoid arthritis, low back pain and ischemic heart disease. When asked about their ability to perform daily activities, 84.7% of the patients reported that they were able to do so on their own, 13.1% with a little help and 2.1% needed much help. Patients were asked about the presence of several relevant symptoms. Constipation was the most common with a prevalence of 23.3% followed by pain, reported by 20.0% of participants.

The analysis of clinical indicators revealed that 95.2% of participants had an invasive cancer. More than half of the cancers (59.8%) were sigmoidal (including all other colon types, but non-rectal sites), 22.8% of them were rectal including anorectal sites, while 17.4% were rectosigmoidal (i.e. tumors on the junction between rectum and sigmoid colon). The tumors were mostly moderately differentiated adenocarcinomas (85.3%), while the rest were either poorly differentiated or well-differentiated adenocarcinomas. Regarding the tumor, node, metastasis (TNM) staging system, 10.9% were stage 1, 38.0% were stage 2, 38.0% were stage 3 and 13.1% were stage 4. Only 3.5% (n=8) had no surgery, 2.6% (n=6) had local excision or simple polypectomy, while the rest had resection with or without anastomosis. Other treatments received were chemotherapy (88.0%) and radiotherapy (25.0%).



**Figure 2.** Percentage of Participants Classified as Normal, Mild, Moderate and Severe according to their (a) Anxiety score and (b) Depression score

Analysis of the psychosocial indicators showed a striking result that none of the participants participated in a psychosocial support group. Only four of them (1.7%) were offered such a support. Regarding the financial status of patient, 20.1% reported suffering from financial problems affecting their life.

### Quality of life assessment

The quality of life scores for all participants are shown in Figure 1. For the global score and functional scales, higher scores indicate a better response, while for the symptoms scales, higher scores mean a worse response. The mean global health score for the QLQ-C30 was  $79.7\pm23.31$  SD with only 6.6% of participants scoring less than 33.3%. Among functional scales, emotional functioning scored the highest  $83.0\pm24.3$  SD, whereas physical functioning scored the lowest  $75.5\pm24.5$  SD. The worst mean scores for the QLQ-C30 symptoms scales were for sleep disturbance, and financial difficulties, with means of  $23.4\pm31.7$ SD and  $20.7\pm27.1$  SD, respectively.

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Description (	Categories	Global health	Physical functioning	Role functioning	Emotional functioning	Cognitive functioning	Social functioning	
	Constant	-22 905	-70 983	-123.1	42 153	-81 104	-246 554	_
Site of cancer	Sigmoid	22.905	10.905	125.1	42.155	01.104	240.554	
	Rectum							
Pathological coding	invasive	28.224	52.832	46.69	27.382	57.852	30.049	
cancer	First	66.478	51.693	86.133				
Exten of disease	Distant_mets					23.075		
	Local							
SEER stage	Distant					-34.503		
Type of surgery	Resection and anasto	mosis	166.274					100.0
Surgical margin	Negative		10010					10010
Radiation therapy	No		-16.175	6.3	10.1 20.3	3		
Stoma	Current							
	Not_used		-18.848			25.0		75 20 0
Age at diagnosis	Numeric		75.0			-78.721		73.00.0
Educational level	5th-9th				17.952			
	Illiterate			56.3	46.8			
	1st-5th							
educational level for spouse	10th-12th		50.0		54.2	31.3		50.0
	5th-9th				-25.465	51.5		30.0
	College							
	Illiterate							
	1st-5th		25.0		-9 <mark>3.29</mark> 4		-66.265	25.0
Job status	Full_time				38.0			
	Housewife			31.3	-17.031 23 5	7 31.3		30.0
	Part_time				23.1		-48.969	
	Retired		0					0
Did your boss change job af	fter disease		0		0	-		U
	No			-\$봄 .692	ant nce	ior	17.537	one
Residence	Other		-53.67	Ĕ	rre	ilise		ž
Health Insurance	Military			eat	cui	eπ		
	Private			Ę.	t e	2	84.558	
	Uninsured			ont	i or lith			
	University			ith	d v			
History of psychological pro	oblem before diagnosis	s with colorectal	cancer	2	se			
	No			sec	Jno	66.208	135.72	
Do you suffer from social p	roblems causing daily	anxiety		йц	Pel		10.000	
	No			iag	>		48.682	
Suffering from financial pro	blems affecting your I	ife or health		p >				
1 / 1 / 1	No			1 Mi	ž <sup>12.287</sup>		52 419	
rheumatoid arthritis	NO N			Ne or	22,412		-53.418	
Migraine	INO No			42.980	-33.413			
Heart_problems	No			20 625				
hypertension	No			50.025			10 162	
low back pain	Alona						49.405	
you do daily activities	Little help				12 701	19 629		
loss of appetite	No		30 872		15./91	10.030		
depression	No		39.072		31 701			
diarrhaa	No	10 681		40.241	51.701			
hoarspess of voice	No	19.001		40.241	21 516			
constinution	No				21.010	18 663	11 502	
restlessness	No					11 568	11.374	
vomiting	No					11.500	89 231	
HADS	High			35 791		-32 692	57.251	
	Low		17.583	55.171		52.072	17.296	
R-squared		0.395	0.689	0.714	0.847	0.854	0.868	
R-squared adjusted		0.356	0.63	0.668	0.809	0.818	0.826	
P-value		< 0.001	< 0.001	< 0.001	< 0.001	<0.001	< 0.001	

 Table 1. Estimated Regression Coefficients for Global and Functional Scores of QLQ-C30

The most affected scales in terms of proportion of participants scoring more than 66.7% were constipation and sleep disturbance. For each of the above two scores independently, 8% of the participants scored above this rate.

The analysis of the QLQ-C30 score of different clinical parameters showed that patients with recurrent cancer had statistically significant lower scores than patients with a first episode in the global health (36.0 vs 81.0, p<0.05), physical functioning (52.2 vs 77.9, P<0.05) and role

functioning (52.8 vs 81.9, p<0.05) scales. Five of these six patients had Duke's stage C or D with only one of them at stage B. There was also a statistically significant difference by SEER stage in all scales, except global health and social functioning. As expected, patients with distant metastasis, compared with patients with no metastasis, had the lowest scores in all domains.

Analysis of the QLQ-C30 functional scales by socioeconomic indicators showed no statistically significant difference in the global health or physical

### Table 2. Estimated Regression Coefficients for the Symptom Scores of QLQ-C30

Description	Categories	Fatigue	Nausea & vomiting	Pain	Dyspnoea	n Sleep disturbance	Appetite loss	Constipation	Diarrhoea	Financial difficulties		
Site of cancer	Constant Sigmoid	142.413	78.079	242.21	100	18.653	93.651	48.786	-8.793	41.518 -31.579		
Pathological coding	Rectum	10 104	2.79	08 / 57	,							
Cancer	First	53 /62		-90.497				18 786				
Duke's stage	A	-55.402	11 136	-39.004	r			-40.700				
Duke s stage	B		11.150									
Radiation therapy	No									22 817		
Palliative chemo-therapy	No		10 198	10	0.0		88 889			10	0.0	
Living status	Alone	22 428	10.170	10	010		00.007			10		
Erving status	Family	22.720				6.3	10.1	20.3				6.3
	Others		20.344									
Job status	Full-time		-4.182	7					25.0	-		
	Housewife			12.451	5.0				23.0		5.00.0	
	Part-time						60.317					
	Retired					56.3	46.8			-16.725		56.3
Did vou change vour job af	ter diagnosis			_	~ ~			54.2				
	No		2.908	-26.962	0.0			54.2	31.3	5	0.0	
Monthly family income	(≥1000)			35.116							30.0	
5 5	(400-599)											
	(600-999)		-10.717									
	<200			2	5.0					2	5.0	
Residence	Other					93.885	38.0		24.2			
Number family members	Numeric		0.535			2.896		23.7	31.3		30.0	31.3
Living status	Rural								28.46			
C	Semi-urban				0	58.017	26.984					
Type of insurance	Governmen	t			U			(D	17فيو		<b>U</b>	>
	Military		-9.831			ent	ent	ů.	-1.2.253		ŭ	apta
	Private		-88.555			Ĕ	Ĩ	rre	Jise		Ž	<u>E</u>
	Uninsured					ea	ea	g	-3 <b>5</b> .078			ea Off
	University				42.222	t	đ	9	ĽĽ.			ent
Patient had psychological p	roblem before	diagnosis				no	vith	ō				СС,
	No				-82.222	-107.222	-93 <b>.6</b> 51	70 851	59.515			lth
Suffers from social problem	ns causing dail	y anxiety				~ ~	se	ster				~
	No	-18.041				sec	gno	rsi				sec
Rheumatoid arthritis	No					31 <b>.<u>8</u>19</b>	diac	Ъе		-27.011		ou I
DM (T2)	No		2.731			iag	_>					
Hypertension	No		-3.421			ر d	SW					⊳ ∧
Low back pain	No					N.	-82 <b>ಪೆ</b> 4					ž
Able to do daily activities	Alone					Ň						Ne
	Little help			-32.174	Ļ							
Loss of appetite	No			-18.043				-27.36				
Depression	No											
Diarrhoea	No	-25.899		-23.596	)				-58.48	-16.805		
Hoarseness of voice	No	-14.113	-5.866			-14.587		-38.675		-26.413		
Pain	No	-10.051		-22.687	7							
Nausea	No		-15.915						-31.042			
Vomiting	No		-75.293									
Other symptoms	No					63.974						
HADS	High					82.23						
	Low											
R-squared		0.768	0.99	0.793	0.249	0.807	0.617	0.489	0.84	0.7		
R-squared adjusted		0.73	0.985	0.748	0.218	0.771	0.574	0.444	0.804	0.634		
P value		< 0.001	< 0.001	< 0.001	0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001		

scales between participants living in Amman, the capital of Jordan, and those living in other governorates. In addition, the only statistically significant difference between males and females was in physical functioning domain, where males had better scores than females (72.1 vs 78.6, p<0.05). There was a statistically significant difference in role functioning and cognitive functioning scales by educational level of the participants.

Analysis of QLQ-C30 functional scales by psychosocial indicators revealed that participants who reported suffering from financial difficulties had worse scores in global health and all physical scales.

Analysis of the symptom scales of the QLQ-C30 by clinical indicators showed that patients with recurrent cancer had statistically worse scores in general, when compared with patients who had first time diagnosis of colorectal cancer. For example, the mean scores for fatigue were 44.4 vs 19.1, p<0.05, the mean scores for pain were 47.2 vs 15.5, p<0.05, the mean scores for appetite loss 33.3 vs 9.2, p<0.05, and the mean scores for constipation were 38.9 vs 13.0, p<0.05, respectively. In addition, patients at stage 4 in TNM staging had the lowest mean scores for nausea and vomiting, dyspnea, constipation and diarrhea, when compared with patients with milder

Description	Categories	Body	Anxiety	Weight	Sexual	Sexual
		Image			interest (men)	interest (women)
	Constant	42.97	112.717	-2.992	-9.12	22.517
Site of cancer	Sigmoid					
	Rectum	-17.113				
Pathological coding	Invasive			29		-12.65
Cancer	First		-26.893			
Tumour size at histological exam	Numeric				2.907	
Extent of disease	Distant metastasis	18.449				-37.508
	Local					
Metastasis	No					
TNM stage	Stage 1					8.792
	Stage 2					
Stoma	Current					-29.032
	Not used		11.706			
Type of insurance	Government					
	Military	12.669				
	Private	44.574	-52.49			
	Uninsured					
	University					
Patient is a smoker	No					99.873
Patient had change in weight	No					-71.474
Psychological problems before cancer diagnosis	No	-47.763				
History of anxiety	No	18.904				
Diabetes type 2	No					28.4
Migraine	No	-31.029				
Low back pain	No					-104.807
Able to do daily activities	Alone					
	Little help					
Loss of appetite	No					
Diarrhoea	No			-14.477		33.207
Hoarseness of voice	No	39.48		13.915		
Constipation	No	-5.987				
Vomiting	No	75.142		58.24		
Other symptoms	No					33.333
HADS	High	22.83	-37.14			
	Low			18.509		
R-squared		0.93	0.638	0.847	0.704	0.99
R-squared adjusted		0.906	0.585	0.814	0.658	0.981
P value		< 0.001	< 0.001	< 0.001	<0.001	< 0.001

# Table 3. Estimated Regression Coefficients for Functional Scales of QLQ-CR29

stages. In Duke's staging, patients with distant metastasis had worse means scores for fatigue, nausea and vomiting, sleep disturbance, diarrhea and financial difficulties, when compared with the remaining groups. Finally, patients who had palliative radiotherapy had statistically worse means scores for fatigue (88.9 vs 20.6, p<0.05), pain (83.3 vs 18.3, p<0.05) and appetite loss (66.7 vs 0.3, p<0.05).

Regarding colorectal cancer module (QLQ-CR29) questionnaire, the worst scores within the functional scales were for sexual interest for both men and women with mean scores of  $51.3\pm31.4$  SD and  $66.1\pm31.3$  SD, respectively.

Analysis of the functional scales of the QLQ-CR29 showed that patients with poorly differentiated cancer had worse body image and anxiety scores. Patients with metastatic cancer had also worse body image scores. Participants who had social problems, unrelated to their medical condition, had worse scores for body image (89.7 versus 67.1, p<0.001), anxiety (87.1 versus 76.4, p=0.04) and weight, when compared with participants without social problems, the (90.9 versus 76.4, p=0.001)

As shown in Figure 1, the symptoms scales within the QLQ-CR29 with the lowest scores were flatulence, impotence and stoma care problems with mean scores of  $37.9\pm36.8$  SD,  $34.6\pm33.9$  SD and  $32.3\pm35.4$  SD,

respectively. The percentage of participants who scored more than 66.7% in these scales was 18.7%, 12.7% and 7.9%, respectively.

Analysis of the QLQ-CR29 symptoms scales by clinical indicators showed that there was a statistically significant difference in the stool frequency by site of cancer. The mean scores for this scale were 14.3, 20.9 and 29.8 for sigmoid, rectum and recto-sigmoid cancers, respectively (p=0.002). Patients with recurrent colorectal cancer had statistically significant higher scores in blood and mucous in stool scale when compared with patients with first time-diagnosis with colorectal cancer (13.9 versus 3.3, p=0.013). Patients with distant metastasis on SEER staging, when compared with patient with localized or regional cancer, had worst scores in flatulence (p=0.04) and taste symptoms (0.02).

Current stoma users, when compared with non-users or ex-users, had the worst scores in the sore skin scale and embarrassment scale. The mean scores for the sore skin scale were 32.1, 13.7 and 25.0, respectively (<0.001). For the embarrassment scale, the mean scores were 44.0, 22.0 and 36.5, respectively (<0.001). Ex-users of stoma had worse scores on fecal incontinence scale when compared with current or non-users. The mean scores for this scale were 16.7, 13.8 and 4.8, respectively (<0.001).

### Table 4.1. Estimated Regression Coefficients for QLQ-CR29 Symptoms Scores

Description	Categories	Urinary frequency	Blood and mucus in stool	Stool frequency	Urinary incontinence	Dysuria	Abdominal pain	Buttock pain	Bloating	Dry mouth	Hair loss	Taste
	Constant	116.607	57.301	29.708	180.352	82.28	118.605	-1.107	106.696	37.958	83.893	-28.189
Site of cancer	Sigmoid Rectum										23.676	8.174
Pathological coding	Invasive				-50.208	-37.822	-29.429					-75.795
Morphology	Poorly*				-17.239							
	Moderately?	k									21.952	
Cancer	First				-129.448	-66.071	-50.411					
Tumour size at histologic	cal exam											
	Numeric										-0.443	
Extent of disease	Distant meta Local	astasıs	-2.597		-47.777							
Metastasis	No	18.529	-3.831		-52.371							
TNM stage	Stage 1 Stage 2									17.341		
Duke's stage	A			18.201	17.045							
	В										25.378	
SEER stage	Distant			53.625								
Surgical margin	Negative											-19.473
Radiation therapy	No											
Palliative chemotherapy	No			38.343			59.591	124.019				49.039
Type of insurance	Governmen	tal					-20.36					8.242
	Military											
	Private		10.556		07.45	52 200						
	Uninsured		18.556		-97.45	-52.299						
Patient had change in we	ight		-1.023									
I attent had change in we	No									27.071		
Psychological problems	before cancer	diagnosis								27.071		
r oj enologieta problemo	No	-67 94	-50 103								-104 906	24 821
Social problems causing	daily anxiety											
1 0	No						-20.992					
Migraine	No		-3.26			24.938		-32.972	-70.39			55.863
Heart problems	No				-20.899							
Low back pain	No	-35.137			22.397							
Able to do daily activitie	s											
	Alone		2.441		24.947	15.073						
	Little help											
Loss of appetite	No	-24.198			7.246		-17.773			-47.495	-27.356	-12.636
Depression	No			10.425								
Diarrhoea	No			-19.435		17.007	25 100	70.400				20.255
Hoarseness of voice	No No		1 152			-17.097	-35.189	-72.496				-29.255
Consupation	No		-1.155				17 602					
Pattlacepace	No						-17.095	24.070				
Nausea	No							-41 497				
Vomiting	No							-11.177				-41 246
Other symptoms	No				41 582							59 801
HADS	High				.1.002				62.414			25.32
-	Low								-			
R-squared		0.457	0.978	0.508	0.948	0.732	0.767	0.673	0.367	0.455	0.801	0.967
R-squared adjusted		0.41	0.972	0.465	0.922	0.674	0.715	0.637	0.327	0.42	0.744	0.949
P value		< 0.001	< 0.001	< 0.001	< 0.001	<0.001	< 0.001	< 0.001	< 0.001	<0.001	< 0.001	< 0.001

\*differentiated

Patients who had palliative radiotherapy had a statistically significant worse dysuria score when compared with participants who did not have the same intervention (66.7 vs 8.8, p < 0.05).

### *Predictors of the quality of life scores*

Results of the stepwise method are shown in Table 1 for the global and functional scores of the QLQ-C30. Pathological coding was a statistically significant predictor for all scales in this questionnaire. The statistically significant predictors for the global quality of life score were the pathological type cancer recurrence and the diarrhea mean score (R-squared adjusted = 0.356, p<0.05). The physical functioning scales were predicted by cancer recurrence, resection and anastomosis surgery, radiation therapy, stoma use, residence outside Amman, loss of appetite and the total HADS scale score. Statistically significant predictors of the symptoms scales of the QLQ-C30 are shown in Table 1.

The extent of the disease was a statistically significant predictor for body image, sexual interest (in women), blood and mucous in stool, urinary incontinence, fecal incontinence and impotence scales. Interestingly, neither the type of surgery nor the SEER stage predicted any of the physical or symptoms scales of the QLQ-CR29.

#### Psychological Well-being Assessment

Analysis of the HADS questionnaire showed that the mean scores for the HADS, depression and anxiety were 8.25±9 SD, 4.35±4.9 SD and 3.9±4.6 SD, respectively, with no statistically significant difference in the mean scores by gender.

Figure 2 shows that 77.1% of participants were within the normal category for the depression score, while 5.4% of them were within the severe category. Regarding the anxiety score, 81.7% of participants were within the normal category, while 5.4% of them were within the severe category.

Description	Categories	Flatulence i	Faecal incontinence	Sore skin	Embarrassment	Stoma care problems	Impotence	Dyspareunia
Pathological coding	Invasive	-48.171						
Extent of disease	Distant metastasis						-33.333	
	Local		-14.384					
Duke's stage	А		45.475					
	В		17.705					
Surgical margin	Negative							-33.333
Radiation therapy	No						33.333	
Stoma	Current				24.367		100	
	Not used							
Type of insurance	Governmental					16.667		
	Military			-32.314			-100	33.333
	Private			-41.385				
	Uninsured							
	University		-23.107	26.517				
Are you a smoker	No							-33.333
Had you change in weight	No							33.333
Psychological problem before	e diagnosis colon ca	ancer						
	No					66.667		
History of anxiety	No		47.546					
Social problems causing dail	ly anxiety							
	No		-6.862					
DM (T2)	No							-66.667
Hypertension	No						-33.333	
Depression	No		-19.478					
Diarrhoea	No					-25		
Hoarseness of voice	No		-11.563			-8.333		
Constipation	No		5.765		-23.209			-33.333
Pain	No					-8.333		33.333
Restlessness	No					-8.333		
Nausea	No		-26.059	-34.404				
HADS	High		17.249					
	Low	-56.008		-32.527	-51.652	-50		
R-squared		0.673	0.957	0.787	0.576	1	1	1
R-squared adjusted		0.645	0.935	0.752	0.538	1	1	1
P value		<0.001	<0.001	< 0.001	<0.001	< 0.001	<0.001	< 0.001

<b>Fable 4.2.</b>	Estimated	Regression	Coefficients	for QLQ	-CR29 Sym	ptoms Scales

The results of the stepwise regression analysis for predictors of the HADS score, anxiety score and depression score showed that the statistically significant predictors for the total HADS score were: living status, changed job after cancer diagnosis, monthly family income, smaller number of family members, patients who has no health insurance, suffered from psychological problems before cancer diagnosis, suffer from social problems causing daily anxiety, rheumatoid arthritis and HADS. For depression score, the statistically significant predictors were stoma use, changing job after cancer diagnosis, smaller number family members, living in rural area, patients with no health insurance, presence of rheumatoid arthritis, reported diarrhea symptoms and HADS total score. Finally, anxiety scores were predicted by the following factors: extent of disease, presence of social problems causing daily anxiety, low back pain, presence of other chronic diseases, reported diarrhea symptoms, hoarseness of voice and HADS total score.

Regarding the effect of the presence of symptoms, which were assessed through the QLQ-C30 and QLQ-CR29, on the psychological status, statistically significant predictors of total HADS score were emotional functioning scale (QLQ-C30), fatigue score (QLQ-C30), anxiety scale within the CR-29 and embarrassment scale within the CR-29. While anxiety score was predicted by the mean fatigue score (QLQ-C30) and embarrassment scale within the CR-29. Finally, the depression score was predicted by the mean emotional functioning scale (QLQ-C30) and anxiety scale within the CR-29.

### Discussion

This project was the first quantitative study to assess the quality of life and psychological well-being for intermediate colorectal cancer survivors (One to three years post-diagnosis) in Jordan. A total of 241 were interviewed and their mean age was  $56.7\pm13.6$  SD. The majority of the study participants had a good to high overall health with a mean global health score of  $79.7\pm23.31$  SD and only 6.64% of participants scoring less than 33.3%.

The striking result in our study is that none of the participants participated in a psychosocial support group; only four of them (1.7%) were offered such support. Results from different studies provide a strong evidence that psychosocial interventions are often efficacious in decreasing patients' distress and improving their quality of life (Shin et al., 2013). In addition, participation in psychosocial support programs can often lead to saving of resources (Tsai and Tsao, 2014).

The mean global score of the QLQ-C30 ( $79.7\pm23.3$  SD) is similar to that reported in a recent study from Malaysia (Natrah et al., 2012), but is higher than that reported in regional and international figures; the mean global score in a recent study from Egypt was  $64.5\pm11.9$  SD (Hokkam

et al., 2013) and was in a study from Germany 62.8±22.4 SD (Arndt et al., 2004). The mean ages of participants in the previous two studies were 61.6±8.2 SD (Hokkam et al., 2013) and 65.0±9.9 SD (Arndt et al., 2004), respectively. In a study from China, the mean global score was 67.0 with a mean age close the mean age of our sample (Peng et al., 2011). The higher reported scores in our study might be justified by the ten-year-difference in the mean age of our sample when compared with the Egyptian and German studies (Arndt et al., 2004; Hokkam et al., 2013). This was shown in other studies (Williams, 1977). However, in a study among patients within the same age group from Germany, the results were also lower than findings in our study (Arndt et al., 2004). There are small differences in the German study and our study in the stage of the disease. The proportions of patients with local, regional and distant stages in the Germany study were 51.7%, 31.6% and 16.7%, respectively, while they were in our study 47.4%, 40.5% and 12.1%, respectively. However, such a difference does not justify the detected quality of life variations (Arndt et al., 2004).

The mean emotional functioning in our study was 83, while in the German study it was 67 (Arndt et al., 2004). Differences were small between these two studies when comparing scores of the remaining scales. Unfortunately, we did not perform a follow-up study on patients after diagnosis in order to obtain a more comprehensive picture about the quality of life of colorectal cancer patients in Jordan. According to 2010 report of the Jordan cancer registry, 34.0% of colorectal cases were localized tumors, 30.0% were regional, 12.0% showed distant metastasis, while the remaining 24.0% of the cases were labeled as unknown stage (Non-communicable Diseases Directorate, 2010). This indicates that our sample is not different from distribution of cases at diagnosis and all stages are well represented in proportions relevant to this baseline distribution. However, we have no data on those individuals who declined to take part in the study or those who died. Results from the United States showed that advanced age, but not advanced stage of the disease predicts the response to such surveys (Ramsey et al., 2000).

The mean global score for rectal cancer patients in our study shows better results than those reported in western countries. In our sample, the mean score was  $80.8\pm23.6$  SD, while the mean scores for results from France, Norway and Germany were  $72.2\pm20.1$  SD,  $72.4\pm3.0$  SD and  $63.5\pm5.0$  SD, respectively. Similar to the above results, we expect the difference in age to justify these findings (Rauch et al., 2004).

In Jordan, there is no colorectal cancer control program and initiatives for colorectal cancer early detection or screening are lacking. This could explain why around half of the study subjects had stage three or greater on TNM staging. This is consistent with results from other developing countries where such program is not available (Safaee et al., 2012; Hajmanoochehri et al., 2014).

In our study, the worst reported symptom within the QLQ-C30 questionnaire was sleep disturbance (mean score= 23.4). However, this score is better than that reported for German patients (32.1) (Arndt et al., 2004)

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or Egyptian patients (39.8) (Hokkam et al., 2013).

The mean score of the financial difficulties scale (20.7) is close to that reported in Germany (20.9) (Arndt et al., 2004), but better than that reported in Egypt where the mean score was 47.6 (Hokkam et al., 2013). Variations in the cost of cancer treatment and differences in the social security system might alter the outcomes of this scale. In Jordan, cancer patients receive free health insurance for cancer management and a small proportion of our participants changed their job after cancer diagnosis on their own volition (7.5%) or by their employers' decision (3.1%).

As a consistent trend with the above findings, financial difficulties affected the global score and all physical scales of the QLQ-C30. Participants who were suffering from financial difficulties had worse scores in global health and all physical scales. These results are consistent with previous studies where patients with deprivation indicators had a poor quality of life (Kong et al., 2010; Loh et al., 2013).

Fatigue had the second worst mean score after financial difficulties. However, the mean score for our sample is lower than that reported in other regional or international studies (Li et al., 2014) (Arndt et al., 2004; Peng et al., 2011; Hokkam et al., 2013).

For the QLQ-CR29 questionnaire, the worst scores within the functional scales were for sexual interest for both men and women. Sexual interest of women was predicted by factors such as the presence of low back pain, smoking, presence of type 2 diabetes mellitus, extent of the disease and presence of stoma. This is similar to results of previous studies (Schmidt et al., 2005a; Di Fabio et al., 2008; Den Oudsten et al., 2012). Patient education and counseling are essential to improve the outcomes of this domain (Moriya, 2006). Regarding sexual interest in men, its mean score was better and the only statistically significant predictors of it were tumor size and site of cancer. Results from Egypt are similar to ours (Hokkam et al., 2013), while body image was the worst functional scale for Chinese patients (Peng et al., 2011). In our study, the proportion of patients who were current users of stoma was 23.2%, while it was 48.7% in the Chinese study. Although in our study there was no statistically significant difference in body image between stoma and non-stoma users, previous studies showed statistically significant difference between them. A study from Germany showed that this difference persisted at end of years one, two and three post-diagnosis (Engel et al., 2003).

The worst scores for the QLQ-CR29 symptoms scales were for flatulence, impotence and stoma care problems. These results are consistent with the results of the Egyptian study (Hokkam et al., 2013). In the Chinese study, impotence was the worst symptom, followed by fecal incontinence and dyspareunia (Ramsey et al., 2002).

Patients who received palliative radiotherapy had a statistically significant worse dysuria score when compared with patients who did not receive it. The development of hemorrhagic cystitis secondary to radiotherapy could justify these findings (Andriole et al., 1987; Chong et al., 2005).

Patients who were current stoma users had worse scores

than non-users or ex-users in sore skin and embarrassment, while the ex-users had worse fecal incontinence mean scores. The prevalence of early complications of stoma varied from 13.1% to 69.4% (Kann, 2008), while the prevalence rates of late complications varied from a low of 6% to a high rate exceeding 76% (Husain and Cataldo, 2008). There are several approaches to reduce such high complications rates (Husain and Cataldo, 2008; Kann, 2008). Preventive measures should be applied and patients need support and counseling to reduce feelings of embarrassment.

Regarding predictors of quality of life scores, the pathological type, cancer recurrence and the mean score of diarrhea were the statistically significant predictors of the global quality of life score of the QLQ-C30. Educational level, educational level of the spouse, job status, current financial problems, residence outside Amman, presence of migraine, ability to perform daily activities, pathological coding, cancer recurrence, type of surgery, radiation therapy, stoma use, loss of appetite, reported diarrhea symptom and HADS score were also important predictors of the quality of life scores for QLQ-C30 and QLQ-CR29. These are consistent with results from other countries (Tsunoda et al., 2007; Gray et al., 2011; Hung et al., 2013). Results from the UK showed that sex, stage of the disease, symptoms, beliefs about consequences, lower income and presence of other comorbidities were the main predictors for the quality of life scores (Gray et al., 2011). The effect of symptoms on the quality of life scores was explored in several studies. One study showed that diarrhea, fecal control and constipation were the most important symptoms that affect the quality of life scores, while other studies showed that fatigue and loss of appetite were the most important predictors (Tsunoda et al., 2007; Gray et al., 2011).

For psychological wellbeing assessment using depression, anxiety and the total HADS scores, our results are consistent with a recently published study from Scotland where the mean score for depression was 4.07 and the mean score for anxiety was 4.32 (Gray et al., 2014). The proportion of participants with abnormal depression score or abnormal anxiety score in our study was 18% and 23% respectively. In a study from the United States, investigators used the Brief Symptom Inventory as a screening tool for anxiety and depression. Results of that study showed prevalence rates of 35% for distress, 24% for anxiety and 19% for depression (Zabora et al., 2001).

The main limitation of our study was that we could not get information from the patients who were diagnosed in 2010 and died, those who did not come for follow-up, those receiving treatment in the private sector and those older than the age of 65 years.

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