Assessing the Quality of Life and Survival of Iraqi Patients with Metastatic Colorectal Cancer Receiving Bevacizumab and Chemotherapy

Rasha M. Faris*, Mohammed M. Mohammed*, Ayman A. Rafea**
College of Pharmacy, Mustansiriyah University, Clinical Pharmacy department, Baghdad / Iraq
**** Anbar Specialized Center for Oncology, Department of health Anbar, Anbar / Iraq***

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Corresponding Author email:
Pharm.drmhdclinical@uomustansiriyah.edu.iq
Orcid: https://orcid.org/0000-0002-1205-4829

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Abstract:

Background: The second most common reason for mortality from cancer is colorectal carcinoma. One of cancer patients' increasingly significant outcome measures is their health-related quality of life.

Objective This cross-sectional study in Iraq aims to examine Quality of life for Iraqi patients who had advanced colorectal cancer (CRC and receiving (chemotherapy + bevacizumab) in addition to find the correlation between Quality-of-life QOL scores and patients' survival

Methods All patients diagnosed with metastatic colorectal cancer and received bevacizumab in association with chemotherapy from three hospitals in Iraq took involved in this study: Oncology teaching hospital Baghdad Iraq, AL-Anbar center for oncology and AL-Fallujah hospital. All patients were questioned by the researcher from September 2022 to November 2023. The Arabic version Quality-of-Life Questionnaire (QLQ-C30) from the (European Organization for Research and Treatment of Cancer) was utilized for assessment.

Result The global health score of 107 QOL patients with metastatic colorectal cancer is low with a mean 56.54± 5.14. Regarding the Functional scales the Emotional functioning EF was the lowest score of 33.10±27.89. On the other hand, the generic symptoms, financial difficulties and appetite loss were the worst symptom, followed by fatigue. At the same time, there were significant statistical association between several QOL scores and the progression -free -survival (PFS) and the overall- survival (OS).

Conclusion Evaluating the QOL of patients with mCRC is crucial to recognize and managing symptoms associated with the disease as well as treatment by developing a comprehensive care plan and making improvements to their quality of life, as there is a substantial correlation between lower QoL and shorter survival.

Key wards quality of life, metastatic colorectal cancer, EORTC QLQ-C30, bevacizumab, Global- health status

نوعية الحياة والبقاء على قيد الحياة للمرضى العراقيين المصابين بسرطان القولون والمستقيم النقيلي الذين تم علاجهم باستخدام بيفاسيزوماب والعلاج الكيميائي

رشا محروس فارس*، محمد محمود محمد*، ايمن عدنان رافع**

كلية الصيدلة قسم الصيدلة السريرية، الجامعة المستنصرية, بغداد / العراق

**مركز الانبار التخصصي للأورام، دائرة صحة الانبار*

خلاصة

الخلفية: السبب الثاني الأكثر شيوعا للوفاة من السرطان هو سرطان القولون والمستقيم. أحد مقاييس النتائج ذات الأهمية المتزايدة لمرضى السرطان هو نوعية حياتهم المتعلقة بالصحة.

الهدف تهدف هذه الدراسة المقطعية إلى فحص نوعية الحياة للمرضى العراقيين الذين أصيبوا بسرطان القولون والمستقيم المتقدم ويتلقون (العلاج الكيميائي + بيفاسيزوماب) بالإضافة إلى إيجاد العلاقة بين درجات جودة الحياة وبقاء المرضى على قيد الحياة لتحديد العوامل المساهمة في رعاية مرضى سرطان القولون والمستقيم والتطورات المستقبلية في العرا ق

الطرق شارك في هذه الدراسة كل المرضى الذين تم تشخيص إصابتهم بسرطان القولون والمستقيم النقيلي وتلقوا بيفاسيزوماب بالإضافة الى العلاج الكيميائي في ثلاثة مستشفيات في العراق: مستشفى بغداد التعليمي لعلاج الأورام، مركز الانبار التخصصي للأورام ومستشفى الفلوجة العام. تم استجواب جميع المرضى من قبل الباحث في الفترة من سبتمبر 2022 إلى نوفمبر 2023. وتم استخدام استبيان جودة الحياة من (المنظمة الاوربية لأبحاث وعلاج السرطان) للتقييم.

النتيجة: درجة الصحية العالمية لل 107 مريض المشخصين بسرطان القولون النقيلي منخفضة بمتوسط 56.54 ± 5.14فيما يتعلق بالمقاييس الوظيفية، حصل الأداء العاطفي على أقل درجة وهي 33.10±27.89. في المقابل، كانت الأعراض العامة والصعوبات المالية وفقدان الشهية هي أسوأ الأعراض، يليها التعب. في الوقت نفسه، كان هناك ارتباط إحصائي كبير بين العديد من درجات جودة الحياة والبقاء على قيد الحياة بدون تقدم والبقاء على قيد الحياة بشكل عام

الاستنتاج: يعد تقييم نوعية حياة المرضى المصابين بسرطان القولون والمستقيم النقيلي أمرًا بالغ الأهمية للتعرف على الأعراض المرتبطة بالمرض وإدارتها بالإضافة إلى العلاج من خلال وضع خطة رعاية شاملة وإدخال تحسينات على نوعية حياتهم، حيث يوجد ارتباط كبير بين انخفاض جودة الحياة وقصر فترة البقاء على قيد الحياة.

الكلمات المفتاحية: نوعية الحياة، سرطان القولون والمستقيم النقيلي، EORTC QLQ-C30، بيفاسيزوماب، الحالة الصحية العالمية.

Introduction

Approximately 10% of all cancer cases globally are colorectal cancer cases, making it the second most frequent malignancy and the second greatest cause of cancer-related death [1]. In the Iraqi Cancer Board report of 2012, colorectal cancer was the sixth most common among the top ten malignancies in the country in 2010 [2,3]. Even years after treatment finishes, cancer and its therapy have an important and prolonged impact on cancer survivors' QoL [4,5]. Additionally, assessing a patient's quality of life (QoL) aids in assessing the full effects of both the cancer disease and its therapy, as well as offering insights into how this illness influences the patient's life [6-8]. (HrQoL) has been introduced. A multidimensional health marker that covers the mental, emotional, and social elements of functioning and well-being [9]. A variety of tools have been created to evaluate (QoL) of patients with cancer; one significant tool is the quality-of-life questionnaires established by the European -Organization for -Research and -Treatment of Cancer (EORTC) [10,11]. The Arabic language was one of the languages in which this questionnaire was translated and also validated [12,13] The purpose of this

study is to assess life quality of CRC patients using the EORTC- (QLQ C-30) tool for assessment and supply vision to the impact of this burden on socio-demographic and disease characteristics in addition to find the correlation between QOL scores and progression- free- survival PFS and overall-survival OS to identify factors contributing to CRC patient care future improvements in Iraq. The study's significance lies in shedding insight on the variables influencing these patients' quality of life. Additionally, this will offer CRC caregivers with important data to assess how well their patients' problems are being managed. By raising medical professionals' knowledge of health-related quality of life.

Patients and Methods:

This cross-sectional analysis study involved hundred and seven individuals with metastatic colorectal cancer who were supplied with informed consent forms before to participating in this study. Data was collected from the three hospitals in Iraq: Oncology teaching hospital Baghdad Iraq, AL-Anbar center for oncology and AL-Fallujah hospital between September 2022 to November 2023. Each participant completed the research questionnaire for this study, and full disclosure was provided; participation was strictly by invitation. The ethical approval was obtained from The Scientific and Ethics- committee -of Mustansiriyah -University/ College of Pharmacy and from the research committee of Al-Anbar Health Directorate. The study's researcher formally contacted all eligible participants by face-to-face interview or telephone before sending them the online questionnaire via WhatsApp. The participants responded to the general QLQ-30 (https://qol.eortc.org/questionnaires/) questionnaire, which is a validated Arabic version of the EORTC [14]. The Arabic versions of the scoring guide and questionnaire were obtained by the researchers by getting in touch with the EORTC life quality group. Every answer scale was noted and converted into a score between 0 and 100 using a description. Subjects with a functional scale score of less than 33.3% have issues, whereas those with a score of more than 66.7% function well. Inclusion criteria were being the individuals of any gender who had a confirmed diagnosis of colorectal cancer (CRC) and were at least 18 years old. Patients who did not answer the questionnaire or declined to participate were excluded. All participants supplied informed consent, which was collected in conjunction with the questionnaire. To confirm the accuracy of the diagnosis, course of therapy, disease stage, and patient's current state, researchers also reviewed the patient's medical records. the patient’s response to bevacizumab treatment assessed according to Response evaluation criteria in solid tumors RECIST by oncologists.

Statistical Analysis

Version 25 of the Statistical Package for Social Sciences (IBM Corp., Armonk, N.Y., USA) was used for all statistical analyses. The mean, range, or standard deviation (SD), were used for describing continuous variables. Frequency and percentage were used to represent categorical variables. Chi-square testing was used to compare the groups. When a cell's predicted value is less than 5, Fisher Exact was used. The quality-of-life values were correlated with their predictors using multiple linear regressions. The optimal regression model with an alpha-to-enter of 0.05 and alpha-to-remove of 0.1 was chosen using a stepwise selection procedure. The Cox proportional hazards regression model was used to identify the independent prognostic factors of QLQ-C30 domains. P value less than 0.05 was considered significant.

Results

Patient Characteristics

A cohort of 107 patients, with an average age of 54.4 ± 13.3, were evaluated for quality of life. Among them, 75% were below the age of 60, with a modest male predominance of 1.3:1. The range of patient BMI values was 15.47–44.27 kg per m2, with a median of 26.75 kg per m2. Thirty (28%) of the patients were smokers, whereas none consumed alcohol. While over 50% of the patients had an income below 500$, only 11 individual (10.3%) had an income of 1,000 $or more. A total of sixty cases (56.1%) reported a +ve family history of cancer, while 71 cases (66.4%) had comorbidities, as elaborated in Table 1. A healthy dietary regimen was adhered to to 76 patients (71.1%).

Table 1 characteristics of patients (n = 107)

Characteristic		No.	%
Age in years	60<	80	74.8
	≥60	27	25.2
Sex	Female	46	43.0
	Male	61	57.0
BMI	Median (range)	26.75	15.47-44.27
Alcohol status	No	100	93.5
	Yes	7	6.5
Smoking status	No	77	72.0
	Yes	30	28.0
Income/Month	<500$	60	56.1
	500-1000$	36	33.6
	≥1000$	11	10.3
Family history	Yes	60	56.1
	No	47	43.9
Fruits and Vegetables in food	Yes	76	71.1
	No	31	28.9
Comorbid disease	Hypertension	49	45.8
	Diabetes mellitus	20	18.7
	Inflammatory bowel disease	2	1.8

Disease Characteristic

Disease characteristic and association factors are described in Table 2. The majority of the patient had primary site colonic cancer 81 (75.7%), 44 (41.1%) were initially diagnosed before 12 -23 months of the survey while 27 (25.3%) were initially diagnosed within 6 months. A single site of metastasis was confirmed in 93 (86.9%) and liver metastasis constituted 38 (35.5%). Approximately two third the patients had grade 1 performance status and only 9 (8.4%) were grade 2. The most frequently used chemotherapy regimen used was Capecitabine and oxaliplatin CAPOX, 71 (66.4%) followed by Folinic acid, fluorouracil and oxaliplatin FOLFOX, 21 (19.6%) ranging between 3-41 cycles with a median of 16 cycles. Most of patients 82 (76.6%) complained of constipation.

Table 2 Disease Characteristic and association factors (n=107)

Characteristic		No.	%
Duration of disease	≥ 6 m	27	25.3
	≥ 12m	44	41.1
	≥ 24m	36	33.6
Primary tumor	Rectum	26	24.3
	Colon	81	75.7
No. of metastatic sites	1	93	86.9
	>1	14	13.1
Liver metastasis	No	69	64.5
	Yes	38	35.5
ECOG performance status	0	33	30.8
	1	65	60.7
	2	9	8.4
Bowel habits	Constipation	82	76.6
	Diarrhea	25	23.4
Chemotherapy regimen	FOLFOX	21	19.6
	CAPOX	71	66.4
	FOLFIRI	15	14.0
No. of treatment cycles	Median(range)	16	3-41

Responders to Bevacizumab therapy were 49 (45.8%), nine (8.4%) had complete response and 40 (37.4%) showed partial response while stable disease was observed on 17 (15.9%). Progression was seen in 41 (38.3%), as shown in Table 3. For the purpose of comparison, according to Response evaluation criteria in solid tumors RECIST criteria, stable disease and progressive disease were considered as non-responder [23]

Table 3 The response of patients to treatment, according to RECIST(n=107)

Response	Total	%
Responder		
Complete response	9	8.4
Partial response	40	37.4
Non-Responder		
Stable disease	17	15.9
Progressed disease	41	38.3

Quality of Life Analysis

In contrast to the symptoms scale, where greater scores indicate a poorer response, higher scores on the functional scales and indicate a better response. The mean score for global health on the QLQ-C30 was 56.54± 5.14, with a mere 3 (2.8%) of respondents achieving a score below 33.3%. Cognitive functioning received the maximum score (69.47±16.9) among functional scales with 85 (79.4%) of patients scored ≥ 66.7, while emotional functioning received the lowest score (33.10±27. global score 89) with 59 (55.1%) of the patients scored < 33.3. The symptoms of financial difficulties, appetite loss and Fatigue exhibited the highest mean scores on the QLQ-C30 scales, measuring 78.82 ±21.67, 74.45±26.92 and 69.37± 19.30 respectively. By contrast, dyspnea scores were the lowest with a mean of 14.95±24.33 Table 4.

Table 4 QLQ-C30 Scores for Participants with CRC Cancer (n=107)

Domain	Questions	Mean (±SD)	95% CI	QL< 33.3 N (%)	QL 33.3-66.6 N (%)	QL≥66.7 N (%)
Global- health status (GH)	2	56.54± 5.14	53.64 -59.44	3 (2.8)	65 (60.7)	39 (36.4)
Functional scales						
Physical functioning (PF2)	5	62.69±14.28	59.96-65.43	2 (1.9)	51 (47.7)	54 (50.5)
Role functioning (RF2)	2	42.21±25.83	37.26-47.16	25 (23.4)	56 (52.3)	26 (24.3)
Emotional functioning (EF)	4	33.10±27.89	27.76-38.44	59 (55.1)	29 (27.1)	19 (17.8)
Cognitive functioning (CF)	2	69.47±16.9	66.23-72.71	1 (0.9)	21 (19.6)	85 (79.4)
Social functioning (SF)	2	57.79±27.79	52.46-63.11	0	55 (51.4)	52 (48.6)
Symptom scales						
Fatigue (FA)	3	69.37± 19.30	65.67-73.06	5 (4.7)	28 (26.2)	74 (69.2)
Nausea and vomiting (NV)	2	48.29± 20.21	44.41-52.16	18 (16.8)	52 (48.6)	37 (34.6)
Pain (PA)	2	62.46±15.71	59.45-65.47	0	85 (79.4)	22 (20.6)
Dyspnea (DY)	1	14.95±24.33	10.29-19.62	71 (66.4)	36 (33.6)	0

Insomnia (SL)	1	58.57±23.28	54.11-63.03	7 (6.5)	90 (84.1)	10 (9.3)
Appetite loss (AP)	1	74.45±26.92	69.29-79.61	0	35 (32.7)	72 (67.3)
Diarrhea (DI)	1	33.33±24.66	28.61-38.06	22 (20.6)	70 (65.4)	15 (14.0)
Constipation (con)	1	52.02±21.56	47.89-56.16	8 (7.5)	32 (29.9)	67 (62.6)
Financial difficulties (FI)	1	78.82 ±21.67	74.66-82.97	0	10 (9.3)	97 (90.7)

Subjects with scores below 33.3% on functional scales have issues; those with scores above 66.7% have good functioning. Similarly, for symptom scales and symptoms, subjects with scores below 33.3% have good functioning and those with scores above 66.7% have issues. Better functioning is indicated by higher scores on functional assessments. Lower functioning is indicated by higher scores on symptom assessments.

There were no notable distinctions seen among the most demographic and clinical features of patients and the functional scores Table 5. However, global health score was positively associated with primary location in colon (P= 0.027) and negative correlation with liver metastasis (P=0.024). Physical functioning score was negatively correlated with the performance status (P=0.005. Role functioning was positively correlated with primary location in colon (P=0.008). Significant negative correlation between cognitive functioning and liver metastasis and positive correlation between social functioning and primary location in colon were observed, however, adjected R^2 were extremely low and the model was not significant, so the results should be interpreted cautiously.

In terms of symptom scores (Table 7), the adjected R^2 for most of the domains were extremely low with model P value > 0.05 except for pain where adjected R^2 = 0.42804 (P=0.029). Pain showed positive correlation with performance status grade 1 and more (P= 0.011).

Table 5 Estimated Regression Coefficients for global and functional Scores of QLQ-C30

	Categories	Global-Health	P-value	Physical-functioning	P-value	Role-functioning	P-value	Emotional-functioning	P-value	Cognitive-functioning	P-value	Social-functioning	P-value
Age	<60	Reference											
	≥60	0.928	0.86	2.067	0.691	3.834	0.709	-5.725	0.494	-0.315	0.93	6.254	0.211
Gender	Male	Reference											
	Female	-7.416	0.108	2.586	0.457	-18.023	0.076	-14.110	0.06	-2.754	0.37	3.784	0.403
Family history	No	Reference											
	Yes	0.535	0.912	-1.385	0.709	-9.860	0.336	7.624	0.317	4.237	0.166	-5.567	0.233
PS(ECOG)	0	Reference											
	>1	-12.352	0.175	-28.016	0.005*	-27.296	0.144	-7.096	0.587	-8.379	0.159	-9.497	0.333
Primary location	Rectum	Reference											
	Colon	12.872	0.027*	7.233	0.061	32.349	0.008*	-1.709	0.843	2.531	0.467	14.625	0.008*
No. of metastatic sites	1	Reference											
	>1	-7.622	0.42	-8.650	0.209	2.073	0.867	20.531	0.079	-0.277	0.953	17.296	0.102
Liver metastasis	No	Reference											
	Yes	-11.839	0.024*	-2.702	0.484	-19.268	0.09	-12.740	0.138	-8.825	0.008*	-1.198	0.819
Model													
R^2		0.362		0.28		0.304		0.141		0.128		0.192	
Adjested R^2		0.230		0.175		0.191		0.055		0.049		0.063	
P-value		0.022		0.021		0.021		0.14		0.139		0.196	

The statistical model used Linear regression

P <.05 was designated as the cutoff value for statistical significance.

*The significant values

Table 6 Estimated Regression Coefficients for Symptom Scores of QLQ-C30

Description		Fatigue	P -value	Nausea and vomiting	P- value	Pain	P -value	Dyspnea	P -value	Insomnia	P -value	Loss of Appetite	P -value	Diarrhea	P -value	Constipation	P -value	Financial - difficulties	P -value
Age	60>	Ref																	
	≥60	0.97	0.82	16.45	**0.047**	-0.238	0.869	-4.894	0.367	-5.722	0.858	6.568	0.316	27.108	0.09	-2.78	0.651	5.25	0.185
Gender	Male	Ref																	
	Female	0.57	0.888	-9.92	0.161	1.429	0.266	4.428	0.35	-2.946	0.934	4.431	0.464	-2.701	0.853	-2.51	0.629	6.47	0.065
Family history	No	Ref																	
	Yes	2.82	0.481	-8.44	0.247	0.946	0.537	6.346	0.187	13.107	0.72	1.915	0.761	14.876	0.305	-1.55	0.765	-3.53	0.322
PS(ECOG)	0	Ref																	
	>1	4.08	0.539	9.09	0.49	6.823	**0.011**	15.294	0.076	135.03	0.122	10.59	0.257	85.947	**0.022**	8.29	0.389	-3.53	0.574
Primary location	Rectum	Ref																	
	Colon	-7.55	0.32	-17.8	**0.039**	0.199	0.886	-0.107	0.985	27.177	0.517	7.879	0.283	13.473	0.437	8.34	0.206	0.73	0.858
No. of metastatic sites	1	Ref																	
	>1	2.61	0.648	-22.47	0.052	3.105	0.093	16.771	**0.018**	77.602	0.081	1.19	0.897	-8.256	0.698	10.02	0.193	12.78	**0.013**
Liver metastasis	No	Ref																	
	Yes	5.20	0.212	0.23	0.98	-0.43	0.758	-2.42	0.641	20.89	0.51	-2.79	0.672	29.85	0.063	-3.97	0.478	-1.19	0.752
Model																			
R2		0.071		0.23767		0.61869		0.12338		0.42532		0.07139		0.333		0.061		0.114	
Adjected R2		-0.021		0.12413		0.42804		0.0614		-0.0217		-0.0302		0.172		-0.037		0.044	
P-value		0.61		0.063		**0.029**		0.064		0.515		0.669		0.08		0.737		0.136	

The statistical model used Linear regression

P <.05 was designated as the cutoff value for statistical significance.

Bold line refers to significant values

The life quality scores were compared between patients who response to Bevacizumab and those who did not, Table 7. No significant difference was observed in global health score between the two groups, Figure 1. However, high cognitive function score was significantly more frequent in responders 46 (93.90%) compared to none responders 39 (67.20%), P <0.001. Multiple domains in symptom scores showed significant difference between responders and non-responders. High pain and constipation scores were significantly more frequent in responders 15 (30.60%) and 39 (79.60%) compared to non-responders 7 (12.10%) and 28 (48.30%) respectively, whereas low dyspnea scores were significantly more frequent in responders 44 (89.80%) compared to non-responders 27 (46.60%), P<0.001.

Table 7 QLQ-C30 Scores for responders and none responders

Domain	QoL	responders		none responders		
		No	%	No	%	P value
GH Score	Low	1	2.00%	2	3.40%	0.238
	Intermediate	26	53.10%	39	67.20%	
	High	22	44.90%	17	29.30%	
PF Score	Low	1	2.00%	1	1.70%	0.455
	Intermediate	20	40.80%	31	53.40%	
	High	28	57.10%	26	44.80%	
RF Score	Low	13	26.50%	12	20.70%	0.083
	Intermediate	29	59.20%	27	46.60%	
	High	7	14.30%	19	32.80%	
EF Score	Low	30	61.20%	29	50.00%	0.337
	Intermediate	13	26.50%	16	27.60%	
	High	6	12.20%	13	22.40%	
CF Score	Low	0	0.00%	1	1.70%	**0.001**
	Intermediate	3	6.10%	18	31.00%	
	High	46	93.90%	39	67.20%	
SF Score	Low	0	0.00%	0	0.00%	0.333
	Intermediate	28	57.10%	27	46.60%	
	High	21	42.90%	31	53.40%	
Fa Score	Low	2	4.10%	3	5.20%	0.079
	Intermediate	8	16.30%	20	34.50%	
	High	39	79.60%	35	60.30%	
Nv Score	Low	7	14.30%	11	19.00%	0.116
	Intermediate	20	40.80%	32	55.20%	
	High	22	44.90%	15	25.90%	
Pas Score	Low	0	0.00%	0	0.00%	**0.029**
	Intermediate	34	69.40%	51	87.90%	
	High	15	30.60%	7	12.10%	
Dy Score	Low	44	89.80%	27	46.60%	**<0.001**
	Intermediate	5	10.20%	31	53.40%	
	High	0	0.00%	0	0.00%	
Sl Score	Low	2	4.10%	5	8.60%	0.447

	Intermediate	41	83.70%	49	84.50%	
	High	6	12.20%	4	6.90%	
Ap Score	Low	0	0.00%	0	0.00%	0.418
	Intermediate	14	28.60%	21	36.20%	
	High	35	71.40%	37	63.80%	
Di Score	Low	7	14.30%	15	25.90%	0.131
	Intermediate	37	75.50%	33	56.90%	
	High	5	10.20%	10	17.20%	
Co Score	Low	4	8.20%	4	6.90%	**0.001**
	Intermediate	6	12.20%	26	44.80%	
	High	39	79.60%	28	48.30%	
Fi Score	Low	0	0.00%	0	0.00%	0.105
	Intermediate	2	4.10%	8	13.80%	
	High	47	95.90%	50	86.20%	

Chi -Square test used

P <.05 was designated as the cutoff value for statistical significance

Bold line refers to significant values

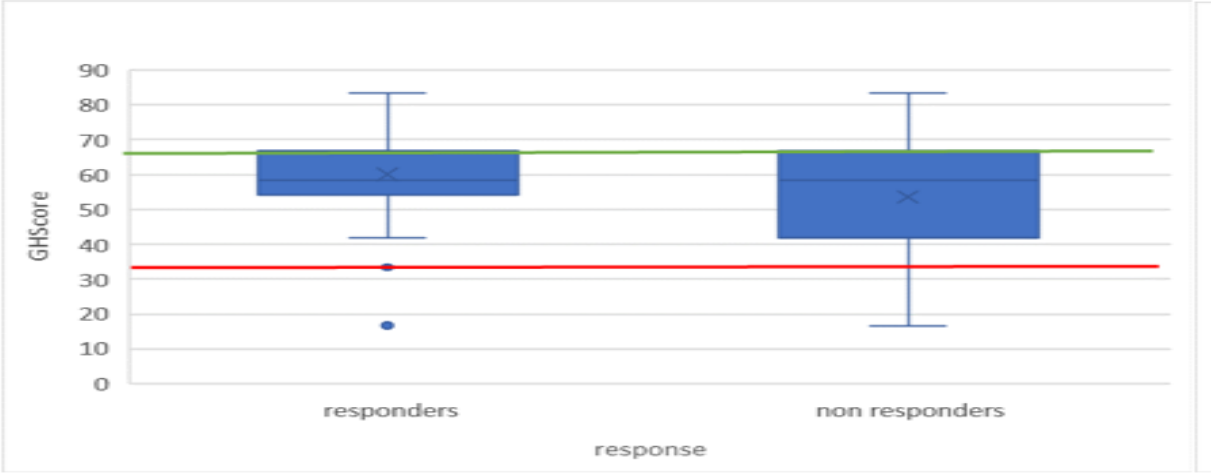

Figure 1 Global health score in relation to patient response to therapy. Green line denoted the cutoff for high quality life and red line is the cutoff for low quality life

QLQ-C30 as a Predictor for Progression - Free and Overall -Survival

Cox regression was conducted to evaluated the association of QLQ-C30 domains and PFS and OS, Table 8. Global health score did not show significant association with PFS, however, higher GH scores associated with longer OS HR= [0.829], 95%CI [0.726-0.946], P= 0.005. Looking at each functional and symptomatic score individually, two symptomatic scores showed association with PFS. As shown in Table 8, increased pain and insomnia scores associated with longer PFS, P=0.013 and 0.009 respectively while high fatigue scores associated with shorter PFS. On the other hand, increased role and emotional fatigue and functioning scores, constipation and scores of financial difficulties associated with shorter OS while higher cognitive and scores of social function, pain, dyspnea, appetite and diarrhea scores associated with longer OS.

Table 5 The hazard ratio for QLQ-C30 domains

QLQ-C30	PFS				OS			
	HR	**95%CI**		***P-value**	**HR**	**95%CI**		***P -value**
GH Score	0.985	0.953	1.017	0.357	0.829	0.726	0.946	**0.005**
PF Score	0.983	0.951	1.015	0.292	1.099	0.988	1.224	0.083
RF Score	1.012	0.992	1.032	0.243	1.121	1.036	1.214	**0.005**
EF Score	1.009	0.994	1.023	0.239	1.1	1.017	1.189	**0.017**
CF Score	0.973	0.942	1.005	0.1	0.765	0.647	0.906	**0.002**
SF Score	0.981	0.962	1	0.053	0.896	0.822	0.977	**0.013**
FA score	1.063	1.03	1.096	**<0.001**	1.31	1.081	1.587	**0.006**
Nv score	0.976	0.951	1.001	0.064	1.039	0.962	1.122	0.327
Pa score	0.96	0.929	0.992	**0.013**	0.785	0.635	0.97	**0.025**
Dy score	1.005	0.987	1.023	0.597	0.941	0.889	0.996	**0.037**
SL score	0.968	0.944	0.992	**0.009**	1.062	0.998	1.13	0.059
Ap score	1.011	0.992	1.031	0.271	0.887	0.815	0.966	**0.006**
Co score	0.99	0.966	1.014	0.406	1.079	1	1.164	**0.049**
DI score	0.987	0.966	1.008	0.228	0.992	0.923	1.066	0.829
Fi score	1.004	0.985	1.023	0.69	1.124	1.039	1.216	**0.004**

*Cox proportional hazards regression
P <.05 was designated as the cutoff value for statistical significance
Bold line refers to significant values

Discussion

Assessing patients' quality of life (QOL) becomes crucial for helping physicians in making decisions and helping patients in selecting the appropriate treatment [16-18]. In Iraq, this is the first research that, to the best of our knowledge, assesses QOL in CRC following bevacizumab treatment. A descriptive study in Iraq was carried out to evaluate the quality of life in a group of patients with colorectal cancer using the EORTC Quality of Life- Questionnaires—Core30 (QLQ-C30) which showed troubles with symptom scales and financial difficulties interfering with everyday life[19] ,while global previous studies showed that the three main symptoms that have the biggest impact on colorectal cancer patients' scores which are diarrhea, constipation, and fecal control[20-24] .Another research revealed that the most significant predictors were fatigue and appetite loss[25,26]. This study showed alarming results of low overall quality of life in Iraq. The QLQ-C30's mean global score (56.54± 5.14SD) with a mere 3 (2.8%) of patients achieving a score below 33.3% Table 4. These outcomes are similar to those of a recent Saudi study 56.91 ±31.32 SD [27] and is lower than the values provided in other regions and countries, the mean of global score in a study from Egypt was 64.5±11.9 SD [28] and from Malesia (85.16 ±17.58) SD [29] and 62.8 ± 22.4 SD [30] from Germany .In the three earlier trials, the mean age of the subjects was (61.6±8.2 SD), (58.47±12.04 SD) and (65.0±9.9 SD) respectively But the Saudia trial had a mean age of (53.3±11.6 SD) [27], which is too close to our sample's age (54.4 ± 13.3). In comparison to the Egyptian, Malysia, and German investigations, our sample's mean age differed by several years, which could account for the lowest reported scores in our study. Cognitive functioning received the maximum mean score (69.47±16.9) among functional scales with 85 (79.4%) of patients scored ≥ 66.7, while emotional functioning received the lowest mean score (33.10±27.89) with 59 (55.1%) of the patients scored < 33.3 with a score below 33.3% have good functioning and those with a score above 66.7% have issues.[31]

The financial issues scale's mean score (78.82 ±21.67) is the worst score in comparison with the other studies (16.01 ±28.81) in Saudia [27], (47.6 ± 20.4) in Egypt [28], (20.9± 31.7) in Germany [30] and (17.71 ±26.94) in Malysia [29]. Financial implication of CRC was not affected by age group. But affected by number of metastatic sites of disease, where with more metastatic sites, the median score for the financial implications of colorectal cancer increased. Accordingly, advanced patients were more likely to have negative economic effects from the illness. The results of this scale would be influenced by variations in price of therapy for cancer. In Iraq, Free medical care is provided to cancer patients for the treatment, but Sometimes treatment is not available in health institutions, so treatment must be purchased from outside the hospital. Not all patients can afford the treatment and this will affect the quality of life of patients as well as the response to treatment and survival of patients. Regarding predictors of quality-of-life scores. Role function and social function were positively correlated with primary location in the colon p-value was (0.027, 0.008, 0.008 respectively) while global health and Cognitive function were negatively correlated with the liver metastasis. In terms of symptom scores (Table 6), Pain showed positive correlation with performance status grade 1 and more (P= 0.011). Patients displayed a markedly loss of appetite, fatigue and Constipation symptoms linked to receiving chemotherapy regimens as a side effect in patients with mCRC [32] There were also reports of increased pain, which could be related to the development or progression of the disease. at the beginning of treatment, neuropathic pain due to oxaliplatin treatment [33] The quality-of-life scores were compared between patients who response and those who did not Table 7. High cognitive function score was significantly more frequent in responders 46 (93.90%) compared to non- responders 39 (67.20%) Our findings are strengthened by studies showing that after six months of treatment with Bevacizumab cognitive function is improved by four points. [34]. In our study we evaluated the association between QLQ-C30 domains and PFS and OS Table 8. regarding functional scores increased Role and Emotional functioning scores associated with shorter OS while higher Cognitive and Social functioning scores associated with longer OS. On the other hand, increased pain and insomnia scores associated with longer PFS, P=0.013 and 0.009 respectively, while high fatigue scores associated with shorter PFS and increased constipation and financial difficulties scores associated with shorter OS, regarding symptom scores dyspnea, constipation, pain, appetite loss, and financial difficulties scores associated with shorter OS and diarrhea scores associated with longer OS. Low- and middle-income nations have trouble providing high-quality cancer care because of their weak infrastructure, lack of funding, and lack of medical experts with sufficient education and experience. This could lead to delay in diagnosing the disease and administering the appropriate therapy, which would lower the quality of life for survivors. The project's findings show that, in comparison to regional or global data, colorectal cancer patients in Iraq often have poor quality of life scores. The primary limitation of this study includes the inability to compare quality of life before and after therapy, and the broad nature of the QoL assessments was restricted in the absence of more focused questionnaires for psychological well-being. Consequently, it was suggested to assess QoL both before and after the treatment and to focus on psychological well-being questionnaires.

Conclusions

The present study's findings demonstrated that lower quality of life ratings is related to disease metastasis, late illness diagnosis, financial difficulties, and the patient's age.

The symptoms (appetite loss, fatigue and financial difficulties) in addition to Emotional and Role functions were most strongly associated with the under-investigation factors. Healthcare professionals should pay extra attention to patients who are likely to score poorly on these tests and target them with supportive care techniques. Hopefully, the study's findings may give care providers for CRC useful information to evaluate the management of their patients' conditions. By increasing awareness of healthcare professionals in health-related quality of life that is detected could reduce long term role and emotional and burden of cancer and helpful in the managing a patient's symptoms with CRC in the future as well as encourage more study in this field of study.

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