

The Effect of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy on Quality of Life in Colorectal Originated Peritoneal Carcinomatosis

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Abstract: In this study, it was aimed to determine the symptoms experienced by patients undergoing cytoreductive surgery and hyperthermic intraperitoneal chemotherapy due to peritoneal carcinomatosis caused by colorectal cancer and the areas where their quality of life is affected. This study was carried using QLQ C30 and QLQ C29 form, out with patients who underwent SRC+HIPEC due to colorectal cancer in Cumhuriyet University Surgical Oncology Clinic. The QLQ-C30 quality of life scale is a globally used scale for patients with cancer. The scale consists of 30 questions for the past week. QLQ-CR29 is a quality of life questionnaire specifically designed for colorectal cancer. It consists of 29 questions evaluating disease symptoms, treatment side effects, body image, sexual status, and future prospects. The mean scores of the patients from the EORTC QLQ-C30 quality of life scale sub-dimensions; the general health score is 8.49 ± 2.54 functional scale 31.80 ± 2.18 and symptom scale 34.20 ± 3.32 . When the ranking of the items in the QLQ-C30 scale according to their average scores is examined, the antecedents of vomiting, need for rest, financial difficulty, difficulty while walking for long and feeling fatigue are the predecessors that received the most average, respectively. When the ranking of the items on the QLQ-C29 scale according to their average scores is examined, frequent urination during the night, pain in the anal area, mucus in bowel movements, hair loss are the predecessors that received the most average, respectively. Although aggressive surgery is performed in cytoreductive surgery and hyperthermic intraperitoneal chemotherapy, side effects and loss of function do not reduce the quality of life of patients. As a result of multidisciplinary studies, we believe that more progress will be made in improving the quality of life of patients.

INTRODUCTION

Peritoneal carcinomatosis is a common clinical picture that is seen in the advanced stages of peritoneal pseudomyxoma and peritoneal mesothelioma as well as gastrointestinal and gynecological cancer and affects long-term survival^{1,2}. Peritoneal carcinomatous (PC) is seen in 5-10% of patients with colorectal cancer at the time of initial diagnosis, in 15-30% in the presence of recurrent disease, and generally in 8-20%^{3,4}. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (SRC + HIPEC) are accepted as standard treatment in selected patients with a diagnosis of colorectal origin with a low peritoneal carcinomatous index (PCI) score. SRC+HIPEC is a highly successful treatment approach in terms of survival in selected patients despite high but acceptable mortality and morbidity rates⁵.

Considering the studies conducted, an important criterion that should be evaluated regularly in addition to evaluating symptoms in cancer patients with PC is the quality of life. Studies conducted to determine the quality of life in cancer patients with PC are very limited.

Management of disease and treatment-related symptoms affects quality of life in cancer patients. It is very important to identify and manage the symptoms frequently experienced by patients in order to increase the functional independence and quality of life of the patients^{6,7}. In this study, the quality of life of patients who developed PC due to colorectal cancer and underwent SRC + HIPEC was investigated.

MATERIALS and METHODS

This study was conducted with patients (n: 35) who underwent SRC+HIPEC due to colorectal cancer in Cumhuriyet University Surgical Oncology Clinic between January 2010 and January 2020.

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The data collection tools were filled in by interviewing the patients face to face and the interview took approximately 25-30 minutes. Ethical approval was obtained from the ethics commission of the university where the study was conducted, and verbal approval from the patients (2020-08/16 number and August 14,2020 data).

The EORTC QLQ-C30 version 3.0 quality of life scale is a scale developed by EORTC and used worldwide in cancer patients. The scale consists of three sub-dimensions: general health score (general well-being), functional scale and symptom scale, and includes 30 questions for the past week. The functional scale includes physical, role, cognitive, emotional and social functions. Symptom scale consists of subtitles of weakness, pain, nausea-vomiting, dyspnea, insomnia, loss of appetite, constipation, diarrhea and financial difficulty. The first 28 of the 30 items in the scale is a four-point Likert-type scale and the items are scored as None: 1, A little: 2, Quite: 3, Much: 4. In the 29th question of the scale, the patient is asked to evaluate his/her health with a scale from 1 to 7 (1: very bad and 7: excellent) and general quality of life in question 30. The 29th and 30th questions in the scale are questions that form the field of general well-being. Patients' high functional scale and general health scale scores; A low symptom scale score indicates a high quality of life⁸.

QLQ-CR29 is a quality of life questionnaire specifically designed for colorectal cancer. It consists of 29 questions evaluating disease symptoms, treatment side effects, body image, sexual status and future expectation. Everyone answers the first 18 questions, and the questions after that are divided into sections according to gender, sexual function and colostomy status, and each patient fills in the appropriate parts for his/her own situation. The corresponding scores of function and global health status and symptoms are calculated in accordance with the EORTC QLQ-CR29 scoring manual. A high score on the functional scale indicates good health, while a high score on the symptom scale indicates an excess of symptoms, that is, a decrease in quality of life. EORTC QLQ-CR29 must always be used and completed with EORTC QLQ-C30.

Extra-abdominal metastasis, history of abdominal radiotherapy, massive small intestine and mesentery involvement, massive gastrohepatic ligament involvement, low performance patients were excluded from the study.

Statistical analysis

The data obtained from the study were analyzed with the SPSS (Statistical Package for Social Sciences, Chicago IL, USA) 21 package program. Percentage calculation and average measures (minimum, maximum) were used in the evaluation of the data. Spearman correlation analysis was performed to evaluate the relationship between the EORTC QLQ-C 29 and QLQ-C30 quality of life scale sub-dimensions. The significance level accepted in the study is $p < 0.05$.

RESULTS

The average age of the patients is 71.6 ± 0.5 (min: 65, max: 84). 64.8% of the patients are male and 81.6% are married. Regarding the cancer locations, 21 were from rectosigmoid, 7 from cecum and ascending colon, 4 from descending colon, and 3 from transverse colon. Cancer clinical stage is III in 38.7% of patients and IV in 33%. Almost half of the patients (51.9%) are primary-secondary school graduates. 89.6% of the patients live with their families, 71.7% are retired. The income level was evaluated as sufficient by 43.4% of the

patients. While the rate of those with chronic diseases is 68.9%, 67% of them have a drug that they use continuously. Considering the smoking and alcohol habits, 45.3% of the patients have smoked and quit before, and 73.6% have never used alcohol. The ECOG performance score of 44.3% of the patients is 1.

The median PCI score was 16 (range 0-27). Resection completeness score was 0 in ninety-six percent of patients. No postoperative complications were observed in 24 patients (68.5%). Grade 3 complications were observed in 3 (27.2%) of 11 patients who had complications, and grade 1 or 2 complications were observed in the other eight.

Average disease free survival was 12.9 months. Three-year overall survival was 57.2%. Kaplan-Meier survival analysis of the cases is given in Figure 1.

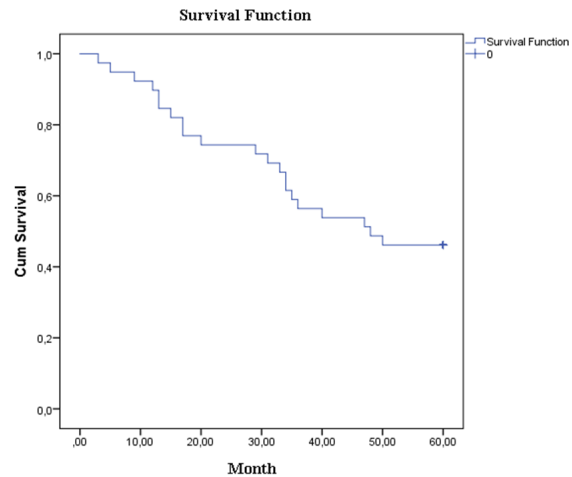


Figure 1. Kaplan-Meier analysis of survival

Hemicolectomy was performed in 12 of the cases, total colectomy in 10, and low-anterior resection in 13 cases. The number of patients who underwent permanent stoma was 7. Hematological toxicity due to HIPEC was seen in 18 (51.4%) patients. Early mortality was observed in three (8.5%) patients due to anastomotic leaks, sepsis and pneumonia.

The mean scores of the patients from the EORTC QLQ-C30 quality of life scale sub-dimensions; the general health score is 8.49 ± 2.54 , the functional scale is 31.80 ± 2.18 and the symptom scale is 34.20 ± 3.32 (Table 1).

Table 1. Distribution of EORTC QLQ C30 quality of life score averages of patients

Bottom Dimensions	Questions	Mean \pm SD*
Functional Scale		31.80 \pm 2.18
Physical Function	1-5	9.37 \pm 1.68
Role Function	6-7	3.31 \pm 0.83
Emotional Function	21-24	9.11 \pm 0.90
Cognitive Function	20-25	4.03 \pm 0.38
Social Function	26-27	5.97 \pm 0.89
General Health Score	29-30	8.49 \pm 2.54
Symptom Scale		34.20 \pm 3.32
Weakness	10,12,18	7.34 \pm 1.06
Nausea-Vomiting	14-15	5.57 \pm 0.74
Pain	9-19	6.11 \pm 0.87
Dyspnoea	8	2.23 \pm 0.43
Insomnia	11	2.49 \pm 0.51
Loss of Appetite	13	3.43 \pm 0.50
Constipation		3.37 \pm 0.84
Diarrhea	17	1.46 \pm 0.51
Financial Difficulty	28	2.20 \pm 0.41

When the ranking of the items in the QLQ-C30 scale according to their average scores is examined, the antecedents of vomiting, need for rest, financial difficulty, difficulty while walking for long and feeling fatigue are the predecessors that received the most average, respectively. The averages of the scores given in all these premises are between "a little" and "quite".

When the ranking of the items on the QLQ-C29 scale according to their average scores is examined, frequent urination during the night, pain in the anal area, mucus in bowel movements, hair loss are the predecessors that received the most average, respectively. The averages of the points given in all these premises are collected in the "a little" option.

When the average of the answers given to the other items of the QLQ-C30 and QLQ-C29 scales are examined, it is seen that there is an average of almost 2. In other words, it can be said that patients experience very few complaints from these substances. The mean and standard deviation values of the items belonging to the QLQ-C30 and QLQ-C29 scales are given in Tables 2 and 3.

When the average of the answers given to the questions by the patients with stoma bags are examined, it is seen that the most problem is the involuntary gas discharge, followed by frequent bag changes. The factor that least decreases the quality of life in this regard is frequent bag changes during the night. The fact that patients without stoma bags frequently have bowel movements throughout the day, is the subject that patients in this group complain most and suffer from the disease the most. The mean and standard deviation values of the responses of the patients with and without stoma bags to the 49th and 55th items of the scale are given in Tables 4 and 5. As can be seen from the table, patients who do not have a stoma bag have higher life satisfaction and lower average responses to precursors that reduce the quality of life. Since the patients did not want to answer questions about sexuality at a very high rate, the 56-59. questions were excluded from the study.

DISCUSSION

Colorectal is a complex of surgery that includes surgical resection with hyperthermic peritoneal perfusion, local resection of peritoneal surfaces and intraperitoneal chemotherapy in the treatment of hyperthermic peritoneal carcinomatosis secondary to cancers. SRC+HIPEC has many positive aspects, especially reducing systemic toxicity and increasing survival, in addition to multiple organ resections, long operation time and intraperitoneal chemotherapy, some of the patients received neoadjuvant chemotherapy, had more than one abdominal intervention and makes peritoneal carcinomatosis patients a high-risk group for complications. Factors associated with morbidity and mortality rates include the extent of the disease, comorbidities, the extent of cytoreduction, the number of removed organs, age, perioperative blood loss, and operation time^{9,10}.

In patients who develop PC due to colorectal cancer, the quality of life decreases due to the physiological changes seen in the common disease due to PC, comorbidity and complications related to treatment. The increase in life expectancy in these patients brings up the issue of quality of life¹¹. The aim of this study was to evaluate the relationship between the symptoms and quality of life experienced by patients with PC due to colorectal cancer.

Our article is important for the literature because it is one of the few studies to focus solely on patients with peritoneal carcinomatosis from colorectal cancer.

While CRS and HIPEC for PC from colorectal cancer can provide good long-term overall and disease-free survival for patients, the

benefit of this procedure must be weighed against possible mortality, morbidity, and changes in quality of life.

The rate of severe morbidity after cytoreductive surgery and hyperthermic intraoperative chemotherapy varies between 20.8% and 53.3% in various sources^{5,12,13}. This severe morbidity rate, which was 27.2% in our study, was found to be compatible with other studies. However, while the total morbidity rate was reported as 39% in the study conducted by Canda et al. 5, this rate was calculated as 31.4% in our study.

According to Müller H. et al. after cytoreductive surgery, major mortality and morbidity rates were reported as 19-56% and 0-12%, respectively¹⁴. In a multi-center study conducted by Glehen et al. in 506 patients, the post-procedure mortality rate was reported as 4.1%¹⁵. A study conducted by Verwaal et al. on 102 patients also showed a mortality rate of 7.8%¹⁶. In the study conducted in our clinic, the mortality rate was found to be 8.5%, which is partially higher than the related studies. Low performance of patients and comorbid diseases can be listed as the reason for this situation.

PKI is the appropriate patient selection criterion for HIPEC application in colorectal cancer with peritoneal spread. In the study conducted by Elias et al., The 5-year survival rate was 70% for the group with a PKI below 15; It was found to be 12% in the group with a PKI of 15 or more 17. In our study, the mean PKI was found to be 16. The five-year survival rate was found to be 68% for the group with PKI below 16, and 17% for the group with PKI 16 and above.

In the study by Hill et al., using the FACT and SF-36 questionnaires and after 3 months of surgery, they showed impairment in quality of life, but improved close to or above baseline by 12 months. Emotional scores improved significantly at 3 months and then remained above baseline. In addition, they showed that there was no significant difference between patients with and without stoma¹⁸. However, the FACT and SF-36 questionnaires may not be as rigorous and comprehensive in inquiry as the widely adopted EORTC questionnaires. In the study of Hill et al., they examined a total of 62 patients who underwent HIPEC due to colonic peritoneal carcinomatosis. According to this study, overall survival was 71.3% in 1 year and 47% of the patients reported normal activity according to their performance status¹⁸. In our study, overall survival was 84% at the 1st year and 56% of the patients reported normal activity according to their performance status.

In the study conducted by Nowak et al., the difference between gender and patients with and without ostomy was examined in the study with colorectal cancer of the QLQ-CR29 quality of life module of EORTC. According to the results of the study, the difference in quality of life of the scale by gender was not found to be statistically significant, while a difference was observed in body image scale and stool leakage items in individuals without ostomies¹⁹. In the study conducted by Bruscia et al., they reported that women with colorectal cancer had a higher rate than men, but the level of satisfaction did not differ significantly according to gender²⁰. In our study, the difference in quality of life by gender was not statistically significant ($p > 0.05$).

In the study of Peng et al., QLQ-30 and QLQ-CR29 scales were applied to patients with rectal cancer and who were treated. In the study, the results of individuals with and without ostomy were evaluated with different treatment modules. According to the results of the study, having a stoma bag decreases the quality of life²¹. On the other hand, in our study, even though the quality of life of individuals with ostomy was lower than those without ostomies, this difference was not statistically significant ($p > 0.05$).

Table 2. Average and standard deviation values of substances belonging to QLQ-C30 scales

	Not at All		A Little		Quite a Bit		Very Much		Mean \pm SD*
	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	
Q1	5	14,29	19	54,29	11	31,43	0	0,00	8,75 \pm 8,18
Q2	3	8,57	29	82,86	2	5,71	1	2,86	8,75 \pm 13,52
Q3	18	51,43	16	45,71	0	0,00	1	2,86	8,75 \pm 9,57
Q4	0	0,00	31	88,57	4	11,43	0	0,00	8,75 \pm 14,95
Q5	19	54,29	14	40,00	2	5,71	0	0,00	8,75 \pm 9,22
Q6	3	8,57	27	77,14	5	14,29	0	0,00	8,75 \pm 12,34
Q7	28	80,00	5	14,29	2	5,71	0	0,00	8,75 \pm 13,00
Q8	0	0,00	27	77,14	8	22,86	0	0,00	8,75 \pm 12,74
Q9	0	0,00	0	0,00	20	57,14	15	42,86	8,75 \pm 10,31
Q10	2	5,71	19	54,29	14	40,00	0	0,00	8,75 \pm 9,22
Q11	2	5,71	20	57,14	13	37,14	0	0,00	8,75 \pm 9,43
Q12	2	5,71	13	37,14	19	54,29	1	2,86	8,75 \pm 8,73
Q13	0	0,00	0	0,00	20	57,14	15	42,86	8,75 \pm 10,31
Q14	3	8,57	15	42,86	10	28,57	7	20,00	8,75 \pm 5,06
Q15	2	5,71	32	91,43	1	2,86	0	0,00	8,75 \pm 15,52
Q16	15	42,86	9	25,71	4	11,43	8	22,86	9,00 \pm 4,55
Q17	3	8,57	12	34,29	1	2,86	19	54,29	8,75 \pm 8,34
Q18	0	0,00	28	80,00	7	20,00	0	0,00	8,75 \pm 13,25
Q19	0	0,00	11	31,43	24	68,57	0	0,00	8,75 \pm 11,41
Q20	20	57,14	15	42,86	0	0,00	0	0,00	8,75 \pm 10,31
Q21	0	0,00	18	51,43	17	48,57	0	0,00	8,75 \pm 10,11
Q22	2	5,71	17	48,57	16	45,71	0	0,00	8,75 \pm 9,00
Q23	0	0,00	19	54,29	16	45,71	0	0,00	8,75 \pm 10,18
Q24	10	28,57	23	65,71	2	5,71	0	0,00	8,75 \pm 10,44
Q25	2	5,71	23	65,71	10	28,57	0	0,00	8,75 \pm 10,44
Q26	1	2,86	21	60,00	10	28,57	3	8,57	8,75 \pm 9,03
Q27	0	0,00	2	5,71	23	65,71	10	28,57	8,75 \pm 10,44
Q28	2	5,71	31	88,57	2	5,71	0	0,00	8,75 \pm 14,86
Q29									4,11 \pm 1,23
Q30									4,37 \pm 1,42

Table 3. Average and standard deviation values of substances belonging to QLQ-C29 scales

	Not at All		A Little		Quite a Bit		Very Much		Mean \pm SD*
	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	
Q31	5	14,29	12	34,29	16	45,71	2	5,71	8,75 \pm 6,40
Q32	5	14,29	19	54,29	9	25,71	2	5,71	8,75 \pm 7,41
Q33	9	25,71	15	42,86	9	25,71	2	5,71	8,75 \pm 5,32
Q34	16	45,71	13	37,14	4	11,43	2	5,71	8,75 \pm 6,80
Q35	5	14,29	15	42,86	12	34,29	3	8,57	8,75 \pm 5,68
Q36	8	22,86	19	54,29	7	20,00	1	2,86	8,75 \pm 7,50
Q37	2	5,71	14	40,00	11	31,43	8	22,86	8,75 \pm 5,12
Q38	2	5,71	16	45,71	15	42,86	2	5,71	8,75 \pm 7,80
Q39	12	34,29	17	48,57	5	14,29	1	2,86	8,75 \pm 7,14
Q40	8	22,86	16	45,71	11	31,43	0	0,00	8,75 \pm 6,70
Q41	11	31,43	15	42,86	9	25,71	0	0,00	8,75 \pm 6,34
Q42	12	34,29	14	40,00	7	20,00	2	5,71	8,75 \pm 5,38
Q43	3	8,57	8	22,86	16	45,71	8	22,86	8,75 \pm 5,38
Q44	5	14,29	14	40,00	12	34,29	4	11,43	8,75 \pm 4,99
Q45	2	5,71	7	20,00	17	48,57	9	25,71	8,75 \pm 6,24
Q46	8	22,86	14	40,00	10	28,57	3	8,57	8,75 \pm 4,57
Q47	12	34,29	12	34,29	9	25,71	2	5,71	8,75 \pm 4,72

Table 4. Mean and standard deviation values of substances belonging to QLQ-C29 scales in patients with stomae

	Not at All		A Little		Quite a Bit		Very Much		Mean \pm SD*
	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	
Q49	3	8,57	5	14,29	7	20,00	6	17,14	5,25 \pm 1,71
Q50	2	5,71	8	22,86	6	17,14	5	14,29	5,25 \pm 2,5
Q51	2	5,71	7	20,00	7	20,00	5	14,29	5,25 \pm 2,36
Q52	1	2,86	4	11,43	6	17,14	10	28,57	5,25 \pm 3,77
Q53	4	11,43	8	22,86	9	25,71	0	0,00	5,25 \pm 4,11
Q54	4	11,43	4	11,43	7	20,00	6	17,14	5,25 \pm 1,5
Q55	0	0,00	4	11,43	7	20,00	3	8,57	3,5 \pm 2,89

Table 5. Mean and standard deviation values of substances belonging to QLQ-C29 scales in patients without stoma

	Not at All		A Little		Quite a Bit		Very Much		Mean ± SD*
	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	
Q49	1	2,86	1	2,86	5	14,29	7	20,00	3,5±3
Q50	3	8,57	4	11,43	4	11,43	3	8,57	3,5±0,58
Q51	1	2,86	4	11,43	7	20,00	2	5,71	3,5±2,65
Q52	1	2,86	2	5,71	5	14,29	6	17,14	3,5±2,38
Q53	5	14,29	6	17,14	3	8,57	0	0,00	3,5±2,65
Q54	2	5,71	4	11,43	4	11,43	4	11,43	3,5±1

In the study conducted by Benzten et al., they examined the deteriorated health-related quality of life in anal cancer patients after chemotherapy and conducted a cohort study with 128 survivors after cancer. The long-term health-related quality of life of the sample in the study was measured with the QLQ-C30 and QLQ-CR29 scales published by the EORTC. According to the results of the study, it has been reported that cancer patients have difficulty in performing their social and role functions in a statistically significant way²². In our study, the most prominent symptoms were loss of appetite, diarrhea, and pain.

Conclusion

Although aggressive surgery is performed in SRC+HIPEC, side effects and loss of function do not reduce the quality of life of patients. As a result of multidisciplinary studies, we believe that more progress will be made in improving the quality of life of patients.

Conflict of interest

The authors declare that they have no conflict of interest.

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