

Health-related quality of life in Slovenian patients with colorectal cancer: a single tertiary care center study

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Background. The aim of this study was to evaluate the influence of the surgical treatment on Slovenian colorectal cancer patients' health-related quality of life and to compare the results to the health-related quality of life of the general Slovenian population.

Patients and methods. A total of 413 patients with colorectal cancer operated on at the Abdominal Surgery Department at the Ljubljana University Medical Center between January 1st, 2016 and December 31st, 2017 were sent two standardized and validated questionnaires: the EORTC QLQ-C30 version 3 and EORTC QLQ-CR29. The questionnaires were returned by 197 patients.

Results. Compared to the general population, poorer physical ($p < 0.001$), role ($p = 0.002$), cognitive ($p = 0.021$), and social functioning ($p < 0.001$) with higher frequency of constipation ($p < 0.001$), diarrhea ($p < 0.001$), and financial difficulties ($p < 0.001$) were reported by the colorectal patients. Female patients reported lower cognitive ($p = 0.034$) and emotional ($p = 0.008$) functioning, as well as higher frequency of bloating ($p = 0.049$) and hair loss ($p = 0.01$). Compared to the younger group of patients, lower physical functioning ($p < 0.001$) and higher urinary frequency ($p = 0.007$), urinary incontinence ($p = 0.007$), buttock pain ($p = 0.007$), and anxiety regarding body weight ($p = 0.031$) were detected among the older group of colorectal patients.

Conclusions. The global health status of colorectal patients in Slovenia is comparable to that of the general Slovenian population, but there is a significantly lower level in some of the quality-of-life scales.

Key words: health-related quality of life; colorectal cancer; colorectal surgery; Slovenia

Introduction

Colorectal cancer (CRC) is an important cause of death as well as decreased quality of life. Worldwide, CRC is the third most commonly diagnosed malignancy and the fourth most common cause of death.¹ The incidence of CRC is higher in the developed countries.² The 5-year and 10-year

survival rates of operable and localized colorectal cancer are 60% and 50%, respectively.³

In Slovenia, 11,269 patients (56% men, 44% women) with CRC were still alive at the end of 2015. CRC is the fourth most commonly diagnosed malignancy among Slovenian cancer patients.⁴ In 2015, 1,356 patients were diagnosed with CRC (58% men, 42% women). Colon cancer was found

most frequently (63%), followed by cancer of the rectum and rectosigmoid junction. (37%).⁴

Impaired health-related quality of life (QoL) in CRC patients may result from the disease itself and/or treatment.⁵ It can be described as psychophysical, functional, and emotional disruption or social impairment.^{6,7} Standardized questionnaires are used to evaluate QoL in cancer patients.⁸ The most commonly used questionnaire for evaluating QoL in oncology is the EORTC QLQ-C30 questionnaire, launched by the European Organisation for Research and Treatment of Cancer (EORTC).⁹ It has been translated into many languages, including Slovenian.¹⁰ The reference values of the EORTC QLQ-C30 questionnaire for the general Slovenian population have already been obtained and published.¹¹ Moreover, the EORTC developed the colorectal QoL module EORTC QLQ-CR29, which has been used as an addition to the EORTC QLQ-C30 to evaluate QoL in CRC patients.¹²

The aim of this study was to evaluate QoL in CRC patients after colorectal surgery and to compare the results with the reference data from the general Slovenian population.

Patients and methods

Patients

QoL was evaluated for patients with CRC, stages I–IV, with and without metastatic disease, operated on at the Abdominal Surgery Department of the Ljubljana University Medical Center from January 1st, 2016 to January 31st, 2017. Patients still alive on January 1st, 2018 were included. A patient chart review was performed. A total of 413 patients met the inclusion criteria and were sent the questionnaire; of these, 197 patients (116 male, 81 female) returned the questionnaire. Patients at least one year and no more than two years from the initial operation were included in the study.

Questionnaires

For the purpose of this study, the standardized questionnaires EORTC QLQ-C30 and QLQ-CR29 were utilized. The questionnaires were translated into Slovenian.

The EORTC QLQ-C30 questionnaire consists of three scoring scales that grade function, symptoms, and global health. The scales include one or more questions. Each question has four response options from 1 = not at all to 4 = very much. A higher score corresponds to a poorer result and more symptoms

present. On the other hand, global health status is categorized with seven-point scoring scale on which a higher score corresponds to greater well-being and higher quality of life.

The EORTC QLQ-CR29 questionnaire consists of two scoring scales that grade function and symptoms, and it has specifically been used to assess QoL in CRC patients. As for the EORTC QLQ-C30, the responses range from 1 to 4 and a higher score defines a poorer outcome, with exception of the response for sexual interest, for which a higher score correlates with a better result.

Statistical analysis

Because the scoring scales consist of one or more questions (anxiety on the EORTC QLQ-CR29 and cognitive functions on the EORTC-CR29), a raw score (RS) was calculated for each scoring scale. Linear transformation was used to standardize the RS and the transformed recorded answers into dimensions ranging from 0 to 100. Higher scores on functional scoring scales correlated with better functions in patients and, on the other hand, higher scores on symptom scoring scales correlated with poorer outcomes. For the linear transformation, the following formulas were applied:

- For functional scoring scales: $S =$;
- For symptom scoring scales: $S =$;
- For global health-status: $S =$.

The numerical variables were represented by means and standard deviations. The differences between numerical variables were tested using Student's *t*-test. For the purpose of the statistical analysis, patients were divided into two age groups according to the reported median age of 73 years. First group included patients from 39 to 73 years and the second group patients from 74 to 92 years. The association between age groups and sexes was tested using the Mann–Whitney test. A *p*-value < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS software (IBM Corp., version 24.0 Armonk, NY).

Approval for the study was obtained from the Medical Ethics Committee of the Republic of Slovenia, the Protocol Review Board (MZ 0120-48/2018-6). Written consent from all patients included was provided prior to study enrollment.

Results

A total of 413 patients received the questionnaire, and the response rate was 47.7% (197 patients).

Characteristics of the study population are shown in Table 1.

EORTC QLQ-C3 Scoring scale

When the average scores of the EORTC QLQ-C30 in the general Slovenian population and in patients with CRC were compared, statistically significant differences in QoL were detected. Physical, role, cognitive, and social functioning scores were significantly lower in patients with CRC compared to the general population. Compared to the general population, CRC patients more often experienced symptoms as constipation and diarrhea. Moreover, compared to general population, financial difficulties were also more often reported by the CRC patients. No other statistically significant differences were detected between CRC patients and the general population (Table 2).¹¹

When comparing QoL among CRC patients, statistically significant lower scores for cognitive and emotional functioning were detected in females. No other statistically significant differences between the sexes were detected (Table 3).

When comparing the different age groups of the CRC patients (younger group 39–73 years, older group 74–92 years), statistically significant lower physical functioning scores were reported among the older patients. In addition, insomnia and dyspnea were more often reported among the older patients compared to the younger ones (Table 4).

EORTC QLQ-CR29 Scoring scale

Females more often reported bloating and hair loss. No other statistically significant differences in the rate of reporting other symptoms and in the scoring for mental health were found between the sexes (Table 5).

Compared to younger patients, older patients more often reported symptoms such as urinary frequency, urinary incontinence, and buttock pain. Older patients were also more concerned regarding their weight (Table 6).

Discussion

QoL is a substantial factor when outcomes and effects of the disease on CRC patients after multimodal treatment are evaluated.¹³ In Slovenia, the evaluation of QoL in CRC patients is not yet systematically used. To the best of our knowledge, this is the first study evaluating QoL in CRC pa-

TABLE 1. Characteristics of the study population

	Responders n 197	Non-responders n 216	p-value
Median age (IQR)	72 (62–79)	74 (65–81)	0.016
Sex			
Male (%)	116 (58.9)	133(61.5)	0.603
Female (%)	81 (41.1)	83 (38.5)	
Complications			
Not reported	175 (88.8)	150 (69.4)	<0.001
Severe* (%)	15 (7.6)	32 (14.8)	
Operation			
Right hemicolectomy	80 (40.6)	101 (46.8)	0.208
Extended right hemicolectomy	8(4.1)	17(7.9)	0.033
Left hemicolectomy	26 (13.2)	19 (8.8)	0.152
Hartmann's procedure	10 (5.1)	14 (6.5)	0.542
Rectosigmoid resection	4 (2)	8 (3.7)	0.312
Low anterior resection	13 (6.6)	8 (3.7)	0.181
Sigmoid resection	46 (23.4)	38 (17.6)	0.147
Subtotal colectomy	2 (1)	5 (2.3)	0.298
Total colectomy	5 (2.5)	3 (1.4)	0.396
Segmental resections of the colon	4(2)	2(0.9)	0.007
Other procedures	1 (0.5)	2 (0.9)	0.613

*Clavien–Dindo classification 3 to 5; IQR = interquartile range; n = number of patients

tients after surgery and comparing it with QoL for the general Slovenian population.

This study found no statistical differences in the reported global health score between CRC patients and the general Slovenian population. The results are comparable to other similar studies.^{6,14–17} On the other hand, compared to the general Slovenian population, our CRC patients reported poorer physical, cognitive, and social functioning. Moreover, they also more frequently reported symptoms such as constipation, diarrhea, and financial difficulties compared to the general Slovenian population. Similar results have been observed in other published studies.^{15,17} A comparable discovery was made by Rauch *et al.*, in which patients more frequently reported lower physical functioning but also had greater levels of pain than the general population.¹⁴

When comparing the responding and non-responding group of CRC patients, a higher rate of major postoperative complications was observed in the non-responding group. Postoperative complications that lead to reoperation, longer hospitalization, or stoma formation can greatly alter QoL in CRC patients. In our study, the reported satisfaction with QoL in the responding group may therefore be due to the lower rates of major postoperative complications. Nevertheless, patients in

TABLE 2. Comparison of the scores for all scales of the EORTC QLQ-C30 between CRC patients and the general Slovenian population

	Colorectal patients					General Slovenian population M (SD)	p-value
	Min	Max	M (SD)	Me (IQR)	n		
Functional scoring scale							
Physical functions	0	100	83 (20.2)	87 (80–100)	197	91.8 (14)	< 0.001
Role functions	0	100	82.7 (26.8)	100 (67–100)	196	88.7 (20.1)	0.002
Cognitive functions	0	100	87.2 (18.1)	100 (83–100)	197	90.2 (16)	0.021
Emotional functions	0	100	83.4 (16.2)	83 (75–100)	197	82 (18.5)	0.239
Social functions	0	100	82.1 (24)	100 (67–100)	197	90.9 (17.3)	< 0.001
Symptom scoring scale							
Dyspnea	0	100	6.2 (16.1)	0 (0–0)	197	5.3 (15.3)	0.928
Insomnia	0	100	22.4 (27.5)	0 (0–33)	197	19.8 (25.1)	0.182
Loss of appetite	0	100	5.6 (17.2)	0 (0–0)	195	5.3 (15.5)	0.791
Nausea and vomiting	0	50	2.9 (8.1)	0 (0–0)	195	3.3 (10.6)	0.524
Constipation	0	100	13.2 (22.5)	0 (0–33)	196	6.9 (16.9)	< 0.001
Diarrhea	0	100	12.6 (22.7)	0 (0–33)	196	4.2 (13.6)	< 0.001
Fatigue	0	100	22.2 (22.2)	22 (0–33)	197	19.8 (19.8)	0.126
Pain	0	100	13.8 (21.8)	0 (0–17)	195	14.5 (20.2)	0.633
Financial impact of disease	0	100	14.2 (26.6)	0 (0–33)	196	6.6 (17.5)	< 0.001
Global health status							
Global health status	17	100	68.3 (20.5)	67 (50–83)	197	71.1 (21.4)	0.058

IQR = interquartile range; Max = maximum value; Me = median; Min = minimal value; SD = standard deviation; n = number of patients

TABLE 3. Comparison of the scores for all the scales of the EORTC QLQ-C30 by sex.

	Male			Female			p-value
	M (SD)	Me (IQR)	n	M (SD)	Me (IQR)	n	
Functional scoring scale							
Physical functions	82.9 (19.1)	87 (80–100)	116	83.1 (21.8)	93 (80–100)	81	0.584
Role functions	84.1 (23.2)	100 (67–100)	115	80.7 (31.2)	100 (67–100)	81	0.982
Cognitive functions	89.8 (15.2)	100 (83–100)	116	83.5 (21)	83 (67–100)	81	0.034
Emotional functions	85.7 (14.9)	92 (75–100)	116	80 (17.5)	83 (75–92)	81	0.008
Social functions	81.5 (22.7)	83 (67–100)	116	82.9 (25.8)	100 (67–100)	81	0.329
Symptom scoring scale							
Dyspnea	6 (16.2)	0 (0–0)	116	6.5 (16.1)	0 (0–0)	81	0.570
Insomnia	21.2 (26.9)	0 (0–33)	116	24.2 (28.4)	33 (0–33)	81	0.450
Loss of appetite	4.3 (15.6)	0 (0–0)	115	7.5 (19.1)	0 (0–0)	80	0.115
Nausea and vomiting	3.1 (8.7)	0 (0–0)	115	2.7 (7.3)	0 (0–0)	80	0.934
Constipation	13.6 (22.9)	0 (0–33)	115	12.7 (22)	0 (0–33)	81	0.903
Diarrhea	12.8 (22)	0 (0–33)	115	12.3 (23.8)	0 (0–33)	81	0.641
Fatigue	19.9 (21)	11 (0–33)	116	25.5 (23.5)	22 (0–33)	81	0.110
Pain	12.3 (19.8)	0 (0–17)	114	15.8 (24.4)	0 (0–22)	81	0.338
Financial impact of disease	13.5 (26.7)	0 (0–33)	116	15.4 (26.5)	0 (0–33)	80	0.441
Global health status							
Global health status	68.1 (21.4)	67 (50–83)	116	68.6 (19.3)	67 (50–83)	81	0.903

IQR = interquartile range; M = mean; Me = median; n = number of patients SD = standard deviation

TABLE 4. Comparison of the scores for all the scales of the EORTC QLQ-C30 by age groups

	Age 39–73 years			Age 74–92 years			p-value
	M (SD)	Me (IQR)	n	M (SD)	Me (IQR)	n	
Functional scoring scale							
Physical functions	87.5 (16.3)	93 (80–100)	98	78.6 (22.7)	87 (67–93)	99	0.001
Role functions	82.2 (28.7)	100 (67–100)	97	83.2 (24.9)	100 (67–100)	99	0.724
Cognitive functions	89.3 (15)	100 (83–100)	98	85.1 (20.5)	100 (83–100)	99	0.268
Emotional functions	85 (14.7)	83 (75–100)	98	81.7 (17.5)	83 (75–92)	99	0.218
Social functions	84.7 (23.3)	100 (67–100)	98	79.5 (24.5)	83 (67–100)	99	0.069
Symptom scoring scale							
Dyspnea	3 (9.6)	0 (0–0)	98	9.4 (20.2)	0 (0–0)	99	0.014
Insomnia	16.6 (23.5)	0 (0–33)	98	28.2 (29.9)	33 (0–33)	99	0.004
Loss of appetite	6.4 (18.3)	0 (0–0)	98	4.8 (15.9)	0 (0–0)	97	0.511
Nausea and vomiting	2.9 (7.9)	0 (0–0)	98	2.9 (8.4)	0 (0–0)	97	0.993
Constipation	11.6 (22.6)	0 (0–33)	97	14.7 (22.4)	0 (0–33)	99	0.177
Diarrhea	10.8 (20.9)	0 (0–33)	97	14.4 (24.3)	0 (0–33)	99	0.286
Fatigue	20.9 (22.7)	22 (0–33)	98	23.6 (21.7)	22 (0–33)	99	0.228
Pain	11.5 (21.6)	0 (0–17)	98	16.1 (21.9)	0 (0–33)	97	0.061
Financial impact of disease	18.7 (29.9)	0 (0–33)	98	9.8 (22)	0 (0–0)	98	0.025
Global health status							
Global health status	69.8 (22.4)	75 (50–83)	98	66.8 (18.5)	67 (50–83)	99	0.132

IQR = interquartile range; M = mean; Me = median; SD = standard deviation; n = number of patients

TABLE 5. Comparison of the scores for all the scales of the EORTC QLQ-CR29 by sex

	Male			Female			p-value
	M (SD)	Me (IQR)	n	M (SD)	Me (IQR)	n	
Symptom scoring scale							
Urinary frequency	29.4 (2.8)	33 (0–50)	115	28.1 (24.4)	33 (17–33)	81	0.670
Urinary incontinence	9.1 (18.3)	0 (0–0)	116	9.1 (17.5)	0 (0–0)	80	0.941
Dysuria	4.6 (13.1)	0 (0–0)	115	2.4 (8.7)	0 (0–0)	81	0.266
Abdominal pain	10.5 (16.7)	0 (0–33)	116	12.7 (19.4)	0 (0–33)	81	0.548
Buttock pain	12.3 (22.2)	0 (0–33)	116	8.6 (20.3)	0 (0–0)	81	0.123
Bloating	18.9 (24.5)	0 (0–33)	116	25.4 (26)	33 (0–33)	81	0.049
Blood & mucus in stool	3.4 (11.7)	0 (0–0)	116	3.5 (11.1)	0 (0–0)	81	0.939
Dry mouth	21 (25.2)	16.5 (0–33)	116	24.7 (28.8)	0 (0–33)	81	0.503
Hair loss	1.4 (6.7)	0 (0–0)	116	5.7 (15.5)	0 (0–0)	81	0.010
Taste	6 (16.2)	0 (0–0)	116	11.6 (24.3)	0 (0–0)	80	0.090
No stoma							
Flatulence	25.7 (29.8)	33 (0–33)	88	27.1 (29.1)	33 (0–33)	70	0.651
Fecal incontinence	6.7 (18.2)	0 (0–0)	89	7.1 (16.8)	0 (0–0)	70	0.569
Sore skin	14 (22.4)	0 (0–33)	88	18.5 (25.1)	0 (0–33)	70	0.212
Stool frequency	11.8 (18.3)	0 (0–17)	89	11.6 (16.4)	0 (0–17)	71	0.772
Embarrassment	8.3 (18.3)	0 (0–0)	88	9.3 (20.6)	0 (0–0)	68	0.925
Mental health							
Anxiety	57.1 (29.1)	67 (33–67)	114	49.8 (26.6)	67 (33–67)	81	0.069
Weight	78.7 (28.1)	100 (67–100)	115	79.9 (29.2)	100 (67–100)	81	0.563
Body image	86.5 (20.2)	100 (78–100)	115	87.3 (21)	100 (78–100)	81	0.708

IQR = interquartile range; M = mean; Me = median; SD = standard deviation; n = number of patients

TABLE 6. Comparison of the scores for all the scales of the EORTC QLQ-CR29 by age groups

	Age 39–73 years			Age 74–92 years			p-value
	M (SD)	Me (IQR)	n	M (SD)	Me (IQR)	n	
Symptom scoring scale							
Urinary frequency	24.7 (25.2)	17 (0–33)	97	33 (23.3)	33 (17–50)	99	0.007
Urinary incontinence	5.9 (15.1)	0 (0–0)	98	12.4 (19.9)	0 (0–33)	98	0.007
Dysuria	3 (9.6)	0 (0–0)	98	4.4 (13.2)	0 (0–0)	98	0.607
Abdominal pain	8.8 (14.6)	0 (0–33)	98	14.1 (20.2)	0 (0–33)	99	0.087
Buttock pain	7.8 (20.2)	0 (0–0)	98	13.7 (22.3)	0 (0–33)	99	0.007
Bloating	19.6 (23.3)	0 (0–33)	98	23.5 (27.1)	33 (0–33)	99	0.404
Blood & mucus in stool	4.1 (14)	0 (0–0)	98	2.8 (8.2)	0 (0–0)	99	0.938
Dry mouth	18.7 (24.2)	0 (0–33)	98	26.2 (28.7)	33 (0–33)	99	0.069
Hair loss	4.4 (14)	0 (0–0)	98	2 (7.9)	0 (0–0)	99	0.193
Taste	7.1 (17.4)	0 (0–0)	98	9.5 (22.4)	0 (0–0)	98	0.648
No stoma							
Flatulence	22.2 (27.3)	3 (0–33)	81	30.7 (31)	33 (0–33)	77	0.068
Fecal incontinence	5.3 (14.4)	0 (0–0)	81	8.5 (20.4)	0 (0–0)	78	0.329
Sore skin	14.9 (23)	0 (0–33)	80	17 (24.4)	0 (0–33)	78	0.566
Stool frequency	12.3 (18.2)	0 (0–17)	82	11.2 (16.7)	0 (0–17)	78	0.860
Embarrassment	7.8 (17.7)	0 (0–0)	81	9.7 (21)	0 (0–0)	75	0.550
Mental health							
Anxiety	51.4 (30.1)	67 (33–67)	98	56.8 (26.1)	67 (33–67)	97	0.227
Weight	74.6 (30.8)	100 (67–100)	98	83.7 (25.4)	100 (67–100)	98	0.031
Body image	84.9 (22.8)	100 (78–100)	98	88.8 (17.7)	100 (78–100)	98	0.156

IQR = interquartile range; M = mean; Me = median; SD = standard deviation; n = number of patients

the responding group were also younger (median age 73 years, compared to 75.5 years in the non-responding group, respectively; $p = 0.016$), which can also be an important factor contributing to reported better QoL in this group of patients. As determined in a study by Velenik *et al.*, reported QoL in the general Slovenian population decreases with age.¹¹

In the general Slovenian population, a comparison of QoL between the sexes showed a statistically significant difference in reported physical functioning, which was poorer among females ($p < 0.000$). No other statistically significant differences in functioning were reported.¹¹ On the other hand, when comparing CRC patients by sex, female CRC patients more frequently reported lower cognitive and emotional functioning compared to males ($p = 0.034$ and 0.008 , respectively). Females also more frequently reported bloating and hair loss, and the difference was statistically significant ($p = 0.049$ and 0.01 , respectively). No other statistically significant differences were observed between the sexes. Similar to our study, Adams *et al.* discovered that female CRC patients, compared to males, more often reported lower cognitive and emotional functioning, and also lower physical and social functioning.¹⁸ As the results show, female patients may

need more emotional support following treatment. Therefore open discussion of the symptoms and suitable referrals for additional support or mental health treatments should be made during follow-ups.¹⁹

Reported QoL in the general Slovenian population is lower among the elderly.¹¹ This phenomenon has also been reported by other European researchers.^{20–22} Comparing QoL of different age groups shows lower physical functioning of older patients. ($p = 0.001$). Our results correlate with similar reports in the literature.^{23–25} Statistically significant differences between age groups were discovered when reporting the frequency of symptoms of urinary frequency, urinary incontinence, and buttock pain. On the other hand, Japanese and American studies discovered better QoL in elderly patients.^{26,27} One can conclude that society and environment significantly influence individual evaluations of QoL.

Our study has limitations. First of all, the response rate was low (47.7%). For optimal results, the respond rate should be above 85%. This could be achieved by systematically distributing the questionnaire to CRC patients at follow-ups. Therefore, not only the feedback but also immediately addressing patients' key issues with possible

additional referrals could be achieved. Another limitation is that the study was performed at a single tertiary center in Slovenia. For better results and optimal insight into QoL in CRC patients, a systematic multicenter study including all tertiary and regional centers in Slovenia should be carried out. The questionnaires should be given to CRC patients prior to surgery or neoadjuvant treatment, 1 month after surgery, and 1 and 5 years after treatment. In this way, comprehensive insight into QoL in CRC patients could be obtained, evaluating not only the influence of surgery but also the influence of neoadjuvant treatment on QoL in these patients.

Conclusions

This is the first Slovenian study comparing QoL in CRC patients with the general Slovenian population. The global health status of CRC patients in Slovenia is comparable to that of the general Slovenian population, but there is a significantly lower score on some of the QoL scales. For further research, a systematic multicenter study, including CRC patients from all Slovenian tertiary centers, should be performed with the aim of improving QoL for these patients with multidisciplinary follow-up treatment.

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