RESEARCH ARTICLE

Pattern of Health-Related Quality of Life and its Association among Patients with Colorectal Cancer

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Abstract

Aim: Research on patient-reported outcomes in colorectal cancer are scarce in Malaysia. We aimed to determine pattern of health-related quality of life and its associations among patients with colorectal cancer. **Methods:** A cross-sectional study of 324 patients. Data were drawn from patient's records and interviews. Research tools included the locally validated European Organization for Research and Treatment of Cancer (EORTC) core QLQ-C30 and colorectal-cancer specific QLQ-CR29 questionnaires. **Results:** The mean (±standard deviation) age of patients was 62.5 (±13.6) years. Majority of them were Chinese (62.3%) followed by Malays (19.8%), Indians (14.8%) and others (3.1%). Colon cancer was 7-fold more common than rectal cancer (87% vs 13%). Majority of them were presented at Stage II (29.6%) and III (28.1) of TNM Staging. The mean (±SD) score for global health status/quality of life (GHS/QOL) was 73.13 (±14.19). Good overall functionality (mean scores ≥80) was observed for physical, emotional, role, cognitive and social/family for QLQ-C30; body image, anxiety and weight for QLQ-CR29. The mean score for sexual functioning in men (32.95±28.81) and women (17.56±25.60) were low. Commonest symptoms were fatigue (22.29±17.40), urinary frequency (21.96 ± 24.22) and insomnia (18.42 ± 23.32). Those with lower GHS/QOL had stoma (p=0.044) and were of Chinese ethnicity (p<0.001). On multivariate analysis, ethnicity was the only independent predictor of GHS/QOL (95% confidence interval, 2.589 to 6.139, p<0.001). **Conclusion:** Our results suggest that there is decrease in sexual functioning despite good overall GHS/QOL among our colorectal cancer survivors. Fatigue, sleep loss and urinary frequency were the common symptoms after cancer treatment. Chinese patients had the poorest quality of life.

Keywords: Quality of life- colorectal cancer- EORTC QLQ-C30- EORTC QLQ-CR29- global health status/quality of life

Introduction

Health-related quality of life (HRQOL) of colorectal cancer survivors is a growing public health concern, alongside conventional outcome measures that are disease-centric such as mortality and survival rate. Despite being the third most common cancer and the fourth leading cause of cancer-related deaths worldwide, the survival rate of colorectal cancer continues to increase substantially over the past decades [1]. The 5-year survival rates for both colon and rectal cancer have been reported to increase by at least 30% respectively over a 40-year duration [2]. Besides, colorectal cancer had the largest gain in surviving outcomes among several cancers studied from a population-based registries in Australia, Canada, Denmark, Norway, Swedish regions and UK where the survival rates have increased at a similar pace in these regions [3].

In Malaysia, colorectal cancer is the second leading cancer, accounts for 13.2% of all cancers [4]. It is now the most common cancer that replaced lung cancer in male and the second most common in female, comprising 14.6% and 11.1% of male and female cancers respectively. [4]. Comparing the three major ethic groups in Malaysia,

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those of Chinese ethnicity had the highest incidence (age-standardised rate of 21.1 per 100, 000) as compared to Malays (11.3 per 100,000) and Indians (10.3 per 100,000). Local studies reported that up to 76% and 60% of patients with colorectal cancer survived through the first and five years after diagnosis respectively [5-6]. As the long-term survival rate has improved over different regions, colorectal cancer survivors are therefore having higher expectations to optimize the quality on their well-being during the post-treatment period [7-8].

Understanding the pattern of HRQOL as well as the complexity of factors, characteristics or conditions that predict HRQOL is a significant step towards identifying patients who are at risk of poor HRQOL. Previous studies that have investigated the role of socio-demographic, medical, lifestyle behaviour, health system and various intervention in predicting the HRQOL of colorectal cancer patients have been inconsistent [9-12]. In addition, there are limited studies assessing the functionality and symptoms of colorectal cancer using the newest European Organization for Research and Treatment of Cancer (EORTC) Colorectal Cancer-specific Quality of Life Questionnaire (QLQ-CR29). Targeted interventions could be done effectively on potentially modifiable factors that are predictive of poorer HRQOL [9-11].

Therefore, we embarked on this study to assess patient's perceived global health status and quality of life (GHS/QOL), functional outcomes and symptoms as measured by the Malaysian versions of Quality of Life Questionnaire core (QLQ-C30) and QLQ-CR29; and to determine factors among demographics, clinical factors, treatment and scales of the QLQ-C30/ QLQ-CR29 that were associated with of GHS/QOL in patients with colorectal cancer.

Materials and Methods

Study design and subjects

This was a cross-sectional study conducted at the University Malaya Medical Centre (UMMC), which is a tertiary hospital. Ethics approval was obtained from the Medical Research Ethics Committee (MREC ID: PPUM/ UPP/300/02/02, MEC 770.2). Colorectal cancer survivors were sampled via the Electronic Medical Record (EMR) system from the medical centre. Patients were eligible for the study if 1) they were Malaysian citizens or permanent residents, 2) aged 18 years and above at the time of diagnosis, 3) diagnosis were primary cancer of colon/ rectum, and 4) they received at least one form of treatment (surgery, chemotherapy or radiotherapy). Those with mental impairment or mental illness and those unable to read or understand any of the two languages (Malaysian national language, Malaysian Chinese) were excluded from the study. The protocol of this study were validated and published elsewhere [13]. Informed consent was obtained from each patient before data collection.

Sample size

Sample size was calculated based on previous literature by Neil W Scott et al., considering Malaysian colorectal

patients had global health mean score of 10 points higher than the reference values of 60.7 (SD 23.4) as reported in the literature [14]. The formula in the reference manuals of the EORTC QLQ-C30 was used. P-value of <0.05 was considered as significant and power was considered as 80%. To achieve this, 174 patients were needed to enrol into the study.

Data collection

Data collection was conducted between May and June 2013. Information on baseline socio-demographic and medical conditions, index cancer clinical features, treatment characteristic and the consequences of the disease and its treatments were obtained from the EMR system. While the functional scales, symptoms and single item scales of the EORTC QLQ-C30 and QLQ-CR29 questionnaires were obtained through the phone interviews. A total of four experienced research assistants were recruited, two for Malaysian national language and two for Malaysian Chinese language. During the phone interviews, patients were given detailed explanation on the purpose and methods of study, the right to participate or refuse and the language of preference for the questionnaire. Patients were requested to respond to the questionnaire themselves with no proxies allowed.

Study instruments

HRQOL scales were measured using locally validated questionnaire of the EORTC QLQ-C30 and CR-29. Validation of EORTC QLQ-C30 and QLQ-CR29 were necessary due to different cultural settings and languages in Malaysia. This has been translated into Malaysian national language [15-17] and Malaysian Chinese [18] and were validated.

The QLQ-C30 is one of the most widely used questionnaire in clinical cancer research [19]. It comprises of 30 items, representing five functioning sub-scales, three symptoms scales, GHS/QOL scale, six single items. The QLQ-CR29 is the newest colorectal cancer specific module comprising 29 items [20]. The questionnaire was administered with QLQ-C30. It consists of one multi-item function scale, four single items assessing functioning, three symptoms scale, single item symptoms and sexual pleasure. High score in functioning scales represents better level of functioning whereas high score in symptom scales represents worse or severe symptoms.

Data analysis

All statistical analyses were conducted using SPSS version 22.0 for Windows (SPSS Inc., and Chicago, Illinois, USA). Exploratory analysis was performed to examine the accuracy and completeness of our data as well as to guide the choice of statistical methods. Raw scores from the QLQ-C30 and QLQ-CR29 were transformed into a scale of 0-100 according to the developer's guidelines. The profile of patients' HRQOL was presented using mean and standard deviation (±SD)

Univariate analysis was performed to compare the difference in patients' GHS/QOL, functionality and symptoms experience according to patients'

characteristics, comorbidities and treatment modalities. Independent sample t-test and one-way analysis of variance (ANOVA) with Bonferroni post-hoc tests of contrasts were used. Chi-square test was used to compare proportions between categorical variables. Pearson correlations coefficient, Kruskal Wallis tests were used to compare mean in different HRQOL scales and correlation coefficient (r) with corresponding p-value were presented accordingly. Variables with p values of less than 0.25 were included in the multivariate analysis. Stepwise multiple linear regression analysis (3 levels) modelling was conducted with all the potential predictors and the outcome variable.

Results

A total of 324 patients were recruited and included in the final analysis. Majority of them were of Chinese ethnicity (62.3%), followed by Malays (19.8%) and Indians (14.8%). They had a mean age (±SD) of 62.5 years (±13.6), with a mean duration of 62.8 months (±31.4) since diagnosis. Overall, 87% of our participants were diagnosed with colon cancer, up to 7-fold commoner than rectal cancer (13%). TNM staging at presentation to the hospital was as follows: Stage I (7.1%), Stage II (29.6%), Stage III (28.1%) and Stage IV (16.0%), while the remaining 19.1% was unknown. The most common treatment modality was surgery alone (42.9%). Stoma was present in about 10% of patients. The baseline characteristic of the overall patient cohort is shown in Table 1.

Health-related quality of life (HRQOL) in colorectal cancer patients

In general, majority of patients rated their HRQOL measures as high. About 89% of patients and 87% of patients rated their global health status (GHS) and overall quality of life (QOL) between score of 5 and 7 respectively on a scale of 1 to 7 (from 'very poor' to 'excellent'). After linear transformation from raw scores to a scale of 0-100, the mean score for GHS/QOL was 73.23.

A better functioning is represented by a higher score in functioning scales. With respect to the QLQ-C30 core module, high functioning abilities were observed in our patients with mean scores of above 80 in all aspects of functionality. Highest functioning score was reported for emotional functioning (mean= 88.17) whereas role functioning (mean= 83.02) scored the lowest. On the contrary, higher score in symptom scales represents a common/ worst symptom. Fatigue (mean= 22.29) was the most common/worst symptom, followed by sleep loss (mean 18.42), constipation (mean= 15.02) and pain (13.79). Financial difficulty (mean= 11.32) was perceived as relatively modest problem among colorectal cancer patients in term of lack of job and care-related expenditure.

Most patients were satisfied with their body image (mean= 94.27) as it scored the highest among the functioning scales covered in colorectal cancer specific QLQ-CR29 module. However, mean scores

for sexual dysfunction in both men (mean= 33.14) and women (mean= 17.56) were remarkably low, indicating significant sexual dysfunction in colorectal cancer patients. The most common/ worst symptoms specific to colorectal cancer reported by patients were urinary frequency (mean= 21.96), stoma care related problem (in patients with stoma) (mean= 20.00), impotence (in men) (mean= 18.49) and flatulence (mean= 16.87). Table 2 presents the mean scores and standard deviations for the GHS/QOL, functioning scales and symptoms experience.

Factors associated with HRQOL

On univariate analysis, presence of stoma and ethnicity were significantly associated with health-related quality of life among colorectal cancer patients. The mean score of GHS/QOL is significantly lower in Chinese (mean=70.13) than Malays (mean=77.73), Indians (mean= 78.65) and others (mean=80.83). Besides, there was significantly higher mean score observed among patients with stoma (mean= 73.63) than those without stoma (mean= 69.35). Results are shown in Table 1.

Variables with p-value of less than 0.25 were included in multivariate analysis. Factors included were gender, ethnicity, duration since diagnosis, hypertension, presence of stoma and treatment modality. Of these, ethnicity was the only independent predictor of GHS/QOL (95% confidence interval, 2.589 to 6.139, p<0.001). Further post-hoc analysis revealed that Indians and Malays had significantly higher scores compared to Chinese. Age, gender, body mass index (BMI), duration of diagnosis, comorbidities, anatomic site of tumour, TNM's staging, treatment modality and presence of stoma were not associated with GHS/QOL. Results are shown in Table 3.

We further stratified the dimensions of HRQOL by the ethnicity. It was found that all the domains including functionalities and symptoms in QLQ-C30 were significantly associated with different ethnic groups whereas some domains in QLQ-CR29 were significantly associated with ethnic groups. Chinese had significantly poorer GHS/QOL in all domains of QLQ-C30 core module as compared to Malays, Indians and others. Besides, Chinese had poorer functionalities (excluding sexual dysfunction in men) and experienced worst symptoms such as urinary frequency, bloated feeling, dry mouth, trouble with taste, hair loss and stoma care related problems than other ethnic groups according to the QLQ-CR29 module.

Discussion

Colorectal cancer and its temporal development in developing countries including Malaysia remains a significant health burden and public health concern. With increased post-treatment survival rate, research on the pattern of quality of life and its associated factors is crucial to guide physicians in choosing treatment options and to improve quality of life by giving proper intervention on modifiable factors [9-11]. In this study, we evaluated quality of life of colorectal cancer patients who received

Table 1. Baseline Characteristic and Its Association with Global Health Status/quality of Life (GHS/QOL) of Colorectal Cancer Patients. Total (n=324)

Characteristics	Number (Percentage)	Overall GHS/QOL *	p value
Age at diagnosis (years) *	62.45 (±13.64)		
Age at diagnosis (years)			0.437
≤ 60	131 (40.4)	73.79 (±15.09)	
≥ 61	193 (59.6)	72.80 (±13.51)	
Gender			0.198
Male	163 (50.3)	73.16 (±14.64)	
Female	161 (49.7)	73.29 (±13.76)	
Body mass index (kg/m²) *	22.35 (±4.99)		
Body mass index (kg/m²)			0.427
Normal weight (<25)	140 (43.2)	72.32 (±14.87)	
Overweight (25-30)	176 (54.3)	74.10 (±13.70)	
Obese (>30)	8 (2.5)	69.79 (±12.55)	
Ethnicity			< 0.001
Chinese	202 (62.3)	70.13 (±14.14)	
Malays	63 (19.8)	77.73 (±10.61)	
Indians	48 (14.8)	78.65 (±15.56)	
Others	10 (3.1)	80.83 (±11.15)	
Duration since diagnosis (months) *	62.78 (±31.36)		
Duration since diagnosis (months)			0.053
≤ 60	158 (48.5)	73.26 (±14.45)	
≥ 61	166 (51.5)	73.19 (±13.98)	
Comorbidities			
Hypertension			0.234
Yes	86 (26.5)	73.06 (±13.33)	
No	238 (73.5)	73.28 (±14.51)	
Diabetes			0.753
Yes	51 (15.7)	73.86 (±13.02)	
No	273 (84.3)	73.11 (±14.42)	
Anatomic site of tumour			0.713
Colon	282 (87.0)	73.20 (±14.39)	
Rectum	42 (13.0)	73.41 (±12.91)	
TNM Staging			0.746
I	23 (7.1)	73.55 (±11.95)	
II	96 (29.6)	72.92 (±14.20)	
III	91 (28.1)	74.54 (±14.18)	
V	52 (16.0)	71.15 (±12.18)	
Unknown	62 (19.1)	73.39 (±15.52)	
Treatment			0.085
Surgery alone	139 (42.9)	73.02 (±12.91)	
Surgery and chemo or radiotherapy	123 (38.0)	74.33 (±15.37)	
Surgery and chemo and radiotherapy	10 (3.1)	78.33 (±11.25)	
Chemo and/or radiotherapy	20 (6.2)	75.00 (±11.15)	
Palliative	32 (9.9)	67.19 (±16.11)	
Presence of stoma			0.044
Yes	31 (9.6)	69.35 (±13.16)	
No	293 (90.4)	73.63 (±14.25)	

Abbreviation, GHS/QOL, global health status/quality of life; * Values are expressed as mean (±standard deviation)

Table 2. Overall Scores for the Global Health Status/ Quality of Life (GHS/QOL), Functioning Scales and Symptoms Experience

Variables	Scores *
EORTC QLQ-C30 module	
Overall GHS/QOL	73.23 (±14.19)
Functioning scales	
Physical	84.34 (±16.58)
Emotional	88.17 (±17.32)
Role	83.02 (±20.23)
Cognitive	83.90 (±19.99)
Social/ family	88.01 (±18.30)
Multi-item symptom scales	
Fatigue	22.29 (±17.40)
Nausea/ vomiting	7.30 (±13.43)
Pain	13.79 (±18.23)
Single item symptom scales	
Dyspnoea	10.70 (±18.79)
Sleep loss	18.42 (±23.32)
Appetite loss	13.07 (±20.08)
Constipation	15.02 (±22.43)
Diarrhoea	11.01 (±17.95)
Financial difficulty	11.32 (±17.26)
EORTC QLQ-CR29 module	
Functional scales	
Body image	94.27 (±12.59)
Anxiety	82.41 (±20.38)
Weight	91.05 (±16.76)
Sexual dysfunction in men	33.14 (±28.87)
Sexual dysfunction in women	17.56 (±25.59)
Multi-item symptom scales	
Urinary frequency	22.96 (±24.22)
Blood and mucus	1.03 (±5.92)
Stool frequency	5.14 (±15.04)
Single item symptom scales	
Urinary incontinence	4.63 (±13.97)
Dysuria	2.98 (±11.49)
Abdominal pain	4.63 (±13.21)
Buttock pain	1.85 (±8.89)
Bloated feeling	10.49 (±17.58)
Dry mouth	13.37 (±20.13)
Hair loss	14.19 (±23.96)
Trouble with taste	7.61 (±15.19)
Flatulence	16.87 (±21.71)
Faecal incontinence	3.60 (±14.03)
Sore skin	2.78 (±12.68)
Embarrassment	2.37 (±12.21)
Stoma care-related problem	20.00 (±31.91)
Impotence	18.49 (±26.74)
Dyspareunia	3.82 (±12.15)

Abbreviation, GHS/QOL, global health status/quality of life; EORTC, European Organisation for Research and Treatment of Cancer; * Values are expressed in mean (±standard deviation)

treatments in UMMC and to determine factors associated with quality of life.

The demographic, clinical and treatment characteristics of our patients were generally similar to those reported by previous studies from Malaysia and other countries in the South East Asian region [21-24]. The mean age of our participants was found to be around 62 years and up to 60% were of Chinese ethnicity. The number of male and female patients was almost equal. Besides, majority of patients included in this study presented with advanced stage cancer in which up to 45% were staged TNM's Stage III and IV. This could be due to the fact that most patients diagnosed with advanced cancer were usually referred to tertiary hospital such as our hospital.

Health-related quality of life among our patients was good with respect to the global health status and overall quality of life (GHS/QOL) with an overall mean score of 73. This is comparable with previous studies in which the reported mean score for global quality of life ranged from 60 to 75 [12, 25-30], and confirmed the findings from a smaller preliminary study in local cohort [31]. Apart from that, our patients reported relatively high scores (more than 80) for functionalities that include physical, emotional, role, cognitive, social/family for QLQ-C30 as well as body image, anxiety and body weight for QLQ-CR29. This could be explained by the better colorectal cancer management at our tertiary centre that involve multidisciplinary team such as colorectal surgeons, oncologists, palliative physicians and pain management team. Good overall functionalities were also reported elsewhere for QLQ-C30 [25-29] and QLQ-CR29 [30-32]. However, based on previous literature, there were substantial deficits observed for functioning in patients with colorectal cancer survivors as compared with normal population [27-33]. As we did not include normal population, we were not able to compare the difference in functioning between these two groups.

Of note, sexual dysfunction is one of the main concern among our patients with low mean scores of 33 in men and 17 in women respectively. Similar results were demonstrated in which the post-treatment sexual functioning scores were low, ranged from 15 to 40 [25-34, 35]. This confirms that sexual functioning is an essential component of quality of life that should be addressed adequately as it is one of the most common long-term effects of cancer treatment [36]. The impact of colorectal cancer treatments on sexual functioning is multifactorial and could be attributed to surgical scars, presence of stoma, urinary/faecal incontinence, fatigue and erectile dysfunction [36]. Patients often feel too embarrassed to raise sex-related health issues to healthcare providers [37]. Educating patients and providing them with treatment options could help to improve sexual functioning in colorectal cancer survivors [38].

Despite good overall GHS/QOL and functionalities, some symptoms seem to persist among our patients. We found that our patients suffered from long-lasting physical symptoms such as fatigue and sleep loss, genitourinary symptoms such as urinary frequency as well as bowel symptoms such as constipation. Several

Table 3. Association between Global Health Status/quality of Life (GHS/QOL) and Baseline Characteristic of Patients

Dependent variable	Covariates	Regression coefficient, R		95% confidence interval	
		B (SE)	p value	Lower bound	Upper bound
GHS/QOL	Gender	.173 (1.529)	0.113	-2.836	3.181
	Ethnicity	4.241 (.907)	<0.001	2.456	6.025
	Duration since diagnosis	.343 (1.635)	0.834	-2.874	3.561
	Hypertension	-.372 (1.750)	0.832	-3.815	3.071
	Presence of stoma	-3.372 (2.759)	0.222	-8.800	2.055
	Treatment modality	-.641 (.611)	0.295	-1.844	0.561

Abbreviation, GHS/QOL, global health status/quality of life; SE, standard error

studies also reported persistent physical symptoms in colorectal cancer survivors such as reduction in energy [26-39], genitourinary symptoms such as frequency and incontinence [35] and bowel problem including constipation and diarrhoea [29-40]. Not only that, psychological distress and depression have been found to be a significant problem among long-term colorectal cancer survivors even after they achieved remission for years [41].

Presence of stoma is likely to impair patients' quality of life. The association between stoma and poorer quality of life have been studied and was further demonstrated when the quality of life improved consistently after reversal of stoma [42]. Patients with stoma have been shown to have limited functioning in their daily activities related to work and hobbies. Apart from that, they would feel less satisfied with body image and this further impaired their family and social functioning [28]. In this study, the mean score for GHS/QOL in patients with stoma is lower than those without stoma (69 vs 74) but it was not statistically significant on multivariate analysis. This might be due to the small number (10%) of our patients who had stoma during recruitment.

To our surprise, ethnicity is the only independent predictor of health-related quality of life among colorectal cancer survivors. No association between ethnicity and quality of life were reported previously except that there is one study reported a trend for higher psychological quality of life among African American survivors than Caucasion survivors [43]. We found that Chinese had the poorest quality of life in comparison with Malays and Indians. After stratifying the QLQ-C30 and QLQ-CR29 module according to different ethnic groups, Chinese was found to have poorer quality of life in all domains in functioning as well as symptoms scales that were examined in QLQ-C30 core module. Besides, some domains in the QLQ-CR29 were significantly more impaired in Chinese patients than Malay and Indian patients. The reason for this observation might be the cultural factors and traditional beliefs among different ethnic groups that possess different perceptions towards quality of life. Socio-cultural factors such as education, income, family/social support might play a role in determining the perception of quality of life.

This study demonstrated that the quality of life among our colorectal cancer survivors is comparable with other studies. However, there were several limitations that should be addressed while interpreting our results. Firstly, there

may be sampling bias as the data were obtained from only one institution and therefore may not be generalised to the general population of colorectal cancer patients. Besides, as half of our patients survived more than five years, this may not reflect the situation for those who died before the five-year follow-up. On the other hand, the strength of our study includes the use of well-established instruments to assess HRQOL among colorectal cancer survivors, in which comparisons can be made with studies from both local and international settings. We also highlighted that despite good overall GHS/QOL, sexual dysfunction is prevalent among Malaysian patients which need to be addressed in future.

In conclusion, our results suggest that there is decrease in sexual functioning despite good overall GHS/QOL among our colorectal cancer survivors. Fatigue, sleep loss, urinary frequency and constipation were the common symptoms after cancer treatment. Chinese had poorer quality of life among colorectal cancer survivors.

Acknowledgments

Conflict of interest
The authors declare no conflict of interest.

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