Mal J Nutr 23(3): 375 - 384, 2017

Relationship between Quality of Life and Nutritional Status in Colorectal Cancer Patients Undergoing Chemotherapy

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ABSTRACT

Introduction: Malnutrition is associated with poorer outcomes following treatment for colorectal cancer (CRC). This study evaluates the relationship between nutritional status using scored Patient Generated-Subjective Global Assessment (PG-SGA) with the validated European Organisation for Research and Treatment of Cancer questionnaire (EORTC-QLQ C30) which consists of five functional scales, three symptoms scales and one item of global health/quality of life (QOL). **Methods:** A total of 42 CRC patients at oncology outpatient clinics from two hospitals in Malaysia participated in the study from March 2011 to March 2012. The participants were classified as either well-nourished (PG-SGA A) or malnourished (PG-SGA B and C). **Results:** The majority of patients were Chinese, male, with a mean age of 57.1 ± 9.8 years and had been diagnosed with stage 2 CRC. Well-nourished patients had statistically significantly better QOL scores on symptom scales: fatigue (p<0.001), nausea and vomiting (p<0.05), and pain (p<0.001) compared to malnourished patients. PG-SGA was strongly correlated with the main domains of the QOL: global health status (r = -0.395, p<0.05), fatigue (r = 0.816, p<0.001), nausea and vomiting (r = 0.730, p<0.001) and pain (r = 0.629, p<0.001). The better the nutritional status (lower total mean score of PG-SGA), the higher the QOL (high mean score of global health status). **Conclusion:** The scored PG-SGA is suitable for use as a nutrition assessment tool to identify malnutrition and it is associated with QOL among this population.

Key words: Chemotherapy, colorectal cancer patient, malnutrition, nutritional status, PG-SGA score, quality of life

INTRODUCTION

Colorectal cancer (CRC) is one of the most insidious cancers and the third most commonly occurring cancer worldwide among men and the second in women. Approximately 1.3 million new CRC cases and 694,000 deaths are estimated to have occurred in 2012. It is the fourth most common cause of death from cancer (Ferlay *et al*., 2015). The incidence of CRC

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is increasing in South-east Asian countries due to the adoption of a Western diet and lifestyle (Pourhoseingholi, 2012).

Treatment for CRC patients includes surgery, radiation and chemotherapy, either alone or in combination. All of these treatments can produce side effects that affect nutritional status through alterations in the nutrient absorption and/or reduction in food intake. Over time this can lead to malnutrition (Takenaka *et al*., 2014).

Malnutrition is a common feature among cancer patients and is associated with lower survival rate, decreased quality of life (QOL), increased risk of infection, and various medical complications (Zalina *et al*., 2016). There may be a greater prevalence of weight loss and malnutrition in patients with an advanced stage of disease but nutrient and energy depletion may still occur with patients in early stage disease (Khalid *et al*., 2007). Regardless of stage of disease, patients with cancer, and particularly cancers of the lower gastrointestinal tract, are at high risk of weight loss and subsequent malnutrition.

QOL in cancer patients reflects their general health status, which in turn is determined by a range of nutritional factors. A study on the role of nutritional status in predicting QOL demonstrated a strong association between these two variables in the cancer population which shows that depletion of nutritional reserves and significant weight loss subsequently leads to decreased QOL among patients with cancer (Lis *et al*., 2012; Prevost *et al*., 2014; Zalina, Lee & Kandiah, 2012).

Generally, malnutrition is prevalent among cancer patients but its impact on the QOL of patients has not been adequately studied, particularly within a local oncology setting. To the best of our knowledge, there are a few studies that have addressed malnutrition in advanced cancer but not in the early stage of cancer (Lis *et al*., 2012; Prevost *et al*., 2014). Furthermore, specific information on the association of nutritional status and QOL among CRC undergoing chemotherapy is also notably lacking. Additionally, the present symptoms, nutritional status, and treatment-related factors may play critical roles in patients' QOL (Mohammadi *et al*., 2013). Even though nutritional deterioration is associated with worse well-being and higher morbidity, there is scant evidence to support interactions between nutritional status and QOL in these patients, who are commonly reported to be malnourished.

The scored Patient Generated Subjective Global Assessment (PG-SGA) is a validated nutritional assessment tool and deemed to be the 'gold standard' for nutritional assessment in patients with cancer (Leuenberger, Kurmann & Stanga, 2010). The scored PG-SGA was adapted from the Subjective Global Assessment (SGA) and developed specifically for patients with cancer (Ottery, 2000). It is a method that correlates very well with objective nutritional criteria. The scored PG-SGA can be used as a screening tool for assessment of nutritional status and as a monitoring and an outcome measure. As this is a reproducible, easy-to-use, cheap, and non-invasive method, it would therefore be a simple method to be introduced into the clinical setting such as in the oncology wards. It also correlates highly with quality of life (Bapuji & Sawatzky, 2010).

This study is therefore justifiably designed and aimed to identify the extent of malnutrition using the scored PG-SGA and to investigate the relationship between nutritional status and QOL in CRC patients undergoing chemotherapy. Hence, a targeted assessment of the nutritional status and QOL of cancer patients may result in possible preventive methods for malnutrition and further improve the QOL. In addition, the results from this study not only provide cancer patients' adequate information about the importance of adherence to aggressive nutritional

interventions, but also enhance proficiency of oncologists on achieving better comfort and improve QOL of the patients who are undergoing chemotherapy.

METHODS

Subjects

A cross-sectional study was conducted in the Day Care Oncology Clinic at Hospital Kuala Lumpur and in the Day Care Oncology Clinic and Palliative Ward at Hospital Selayang, Malaysia from March 2011 to March 2012. Forty-two colorectal cancer patients (27 males; 15 females) completed the study. Inclusion criteria were diagnosis with CRC cancer, aged ≥18 years old, post-surgical and scheduled for chemotherapy and were willing to comply with study procedures and able to read and write in the Malay language. Patients were excluded from this study if they had a diagnosis of other cancer types or were involved in other research projects.

This study was registered with the Australian New Zealand Clinical Trials Registry (ANZCTR) (Universal Trial Number: U1111-1120-5586). The intervention study was approved by the Southern Adelaide Health Service/ Flinders University Human Research Ethics Committee (SAFUHREC) (Application number: 465.10) and the Medical Research Ethics Committee (MREC), Ministry of Health Malaysia (NMRR-11-285-8064). Permission to conduct the study was obtained from the director of Hospital Kuala Lumpur and Hospital Selayang, Malaysia. All participants provided written informed consent.

Measures

Interviewer-administered structured questionnaires were used in this study. Data were collected on socio-demographic profile (age, gender, and ethnic group), nutritional status of the patient based on the PG-SGA questionnaire, QOL based on The European Organisation for Research and Treatment of Cancer Care Quality of Life Questionnaire version 3.0 (EORTC QLQ C-30).

Instruments

Nutritional status was assessed from the scored PG-SGA, which consists of two sections. The first section of this assessment (weight history, food intake, nutrition impact symptoms and functional capacity) were completed by the patient using a check box format. The remaining questions in the second section which covered all relevant diagnoses, evaluation of metabolic stress such as fever, fever duration, use of corticosteroids, and finally the physical examination including muscle wasting (temporal areas, deltoids, and quadriceps with a loss of bulk and tone by palpation), loss of subcutaneous fat (triceps region and midaxillary line at the level of the lower ribs) and edema (ankle or sacral) or ascites were completed by the researcher.

For each component of the PG-SGA, a score ranging from 0 to 4 was given depending on the impact on nutritional status. Typical total scores range from 0 to 35 and those with a higher score reflect a greater risk of malnutrition or indicate lower nutritional status of the patient (Ottery, 2000). These scores were applied to global assessment categories by assigning a global rating of Stage A (well-nourished), Stage B (moderately malnourished/moderately thin) or Stage C (severely malnourished/very thin). After this screening had been done, patients with special nutritional needs were identified and classified according to the attention needed: 0-1 points: no intervention; 2-3 points: health education; 4-8 points: dietetic intervention; ≥9 points: a critical need for nutrition intervention. Participants rated as Stage A did not have any weight loss or deficits in nutrition impact symptoms, dietary intake, functioning, and physical examinations. Those in Stage B had moderate deficits or showed recent

improvement in weight, nutrition impact symptoms, dietary intake, function and physical examinations. Participants with any severe PG-SGA categories (weight loss, nutrition impact symptoms, dietary intake, function and physical exam) were rated as severely malnourished.

The PG-SGA questionnaire was used for this research. On completion of translation, the questionnaires were examined by experts from the supervisory committee. Necessary modifications were done on the questionnaires based on the recommendations from the supervisory committee. In addition, a pre-test was conducted on the questions relating to the participants' nutritional status. The pre-test was carried out on a group of ten patients in Day Care Oncology Clinic and Palliative Ward, Hospital Selayang, Malaysia. The objective of this pre-test was to evaluate the clarity and readability of the questions and the overall structure of the questionnaire. The patients were requested to give comments on clarity and interpretability of the questionnaire. If there were comments from the patients, the questionnaires were reviewed and amended accordingly. The pre-test indicated that there was no need to re-structure the questionnaire.

The EORTC QLQ C-30 version 3.0 questionnaire comprises 30 items cancer-specific question which incorporate five functional scales (physical, role, emotional, cognitive, and social), three symptoms scales (fatigue, pain and nausea/vomiting) and one item of global health/QOL. All scales and single items are scored on a 4-point Likert scale (four response categories) with answers as follows: 1 (Not at all), 2 (A little), 3 (Quite a bit) and 4 (Very much) except for the global health scale which employs a 7-point ranging from 1 (very poor) to 7 (excellent) and a 1-week recall period. The QOL scores are calculated according to the EOR TC scoring manual (Fayers *et al*., 2001). Higher scores on the function scales and global health status scores (0 - 100) indicate higher level of QOL and better functioning, whereas higher scores on the symptom scales (100 - 0) denote increased symptoms. A difference of 5–10 points in the scores rep resents a s mall change, 10– 20 points a moderate change, and greater than 20 points a large clinically significant change from the patient's perspective. The EORTC QLQ C30 Questionnaire has been translated into Bahasa Melayu and validated among Malaysian women who had undergone breast cancer surgery with the value of the Cronbach's $\alpha > 0.75$ in almost all domains in the questionnaire (Yusoff, Low & Yip, 2010). This shows that the questionnaires have relatively high internal consistency.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 19 (SPSS Inc, Chicago, USA). For the purpose of this analysis, patients were classified as either well-nourished (PG-SGA A) or malnourished (PG-SGA B and C). Data were checked for normality by Kolmogorov-Smirnov analysis. All data were normally distributed as indicated by $p>0.05$ unless otherwise stated. If the data were not normally distributed, analyses were carried out on the natural logarithm of the values to improve the symmetry and homoscedasticity of the distribution. Still, if the data were not normally distributed even after logarithm transformation, then non-parametric analysis (Mann-Whitney test) was performed and presented as medians followed by the inter-quartile range (IQR).

Descriptive statistics included percentages, means and standard deviation. For skewed QOL data, the Mann-Whitney U-test was carried out to test the differences between groups for continuous data and Spearmen's Rank Order Correlation was performed to evaluate the association between the two numerical variables (The PG-SGA and QOL scores). A chi-square test was used

Table 1. Socio-demographics, cancer stage and BMI characteristics of CRC patients prior to chemotherapy

Variable	*Well-nourished PG-SGA (A)*	*Malnourished PG-SGA (B and C)*	*P value*
Age (year), median (IQR)	51.50 (44.75 - 65.50)	60.50 (50.00 – 65.00)	0.131*
Gender, *n* (%)			
Male	9 (64.3)	18 (64.3)	1.00***
Female	5 (35.7)	10 (35.7)	
Ethnic group, *n* (%)			
Malay	2 (14.3)	8 (28.3)	0.417***
Indian	1 (7.1)	1 (3.6)	
Chinese	11 (78.6)	19 (67.9)	
Stage of cancer, *n* (%)			
Stage II	9 (64.3)	16 (57.1)	0.660***
Stage III	5 (35.7)	12 (42.9)	
BMI, mean (SD)	21.93 ± 2.97	21.21 ± 2.55	0.426**

SD, Standard deviation; IQR, interquartile range; *p* values are based on independent sample *t*-test for symmetric continuous data**, Mann-Whitney test for skewed data* and chi-square test for proportions ***

to see the significant differences between groups for categorical data (gender, ethic group and stage of cancer). A statistical probability of $p<0.05$ was considered as significant.

RESULTS

Participant characteristics are presented in Table 1. During the clinic day, 50 patients were screened for eligibility to participate in this study. Forty two of the 50 eligible patients consented to the study. Eight participants had been excluded because they did not meet the study's criteria (n=6) or refused to participate (n=2). There were nine males (64.3%) and five females (35.7%) in the well-nourished group. In the malnourished group, there were 18 males (64.3%) and 10 females (35.7%). Mean age of the subjects was 57.1 $\pm$ 9.8 years, with all subjects (100%) aged less than 70 years. The majority of the participants were Chinese across all groups. More than half (60%) were diagnosed with Stage 2 cancer in both groups (64.3% in well-nourished group; 57.1% in malnourished group respectively), while 5 participants (35.7%) in the well-nourished group and 12 (42.9%) in the malnourished group had Stage 3 cancer.

The prevalence of malnutrition as determined by the PG-SGA is shown in Table 2. Fourteen (33.3%) of the participants were well-nourished (SGA = A), 26 (61.9%) were moderately malnourished (SGA = B), and 2 (4.8%) were severely malnourished (SGA = C) based on the PG-SGA global rating. Ten (23.8%) of the participants required no intervention. Health education was offered to four (9.8%) of them. The majority of the participants (66.7%) required dietetic intervention. Critical intervention was not required for any of the participants.

Participants' QOL scores are shown in Table 3. There were no differences for global health status and functional scales/ items within the CRC groups and between well-nourished and malnourished patients, all of which were within the range of established reference values (Vergara *et al.*, 2013). However, symptom scales and symptoms single items score showed significant difference between well-nourished and malnourished, (fatigue ($p<0.01$), nausea and vomiting ($p<0.05$)

Table 2. Characteristics of colorectal cancer (CRC) participants prior to chemotherapy

Characteristics	*n (%)*
PG-SGA global rating	
A (well-nourished)	14 (33.3)
B (suspected or moderately malnourished)	26 (61.9)
C (severely malnourished)	2 (4.8)
Triage intervention	
No intervention (Score of 0–1)	10 (23.8)
Health education (Score of 2–3)	4 (9.5)
Dietetic intervention (Score of 4–8)	28 (66.7)
Critical interventions (≥ 9)	0 (0.0)

and pain (p<0.01), with the malnourished showing the highest symptoms scores, particularly fatigue.

Table 4 shown the relationship between PG-SGA and QOL scores among the CRC patients. There was a significant correlation between nutritional status (PG-SGA score) and global QOL score (r= -0.395, p<0.05) and between nutritional status and symptoms (fatigue, nausea and vomiting, and pain (r= 0.816, p<0.01; r= 0.730, p<0.001; r= 0.629, p<0.001), indicating better nutritional status is linked to better QOL.

DISCUSSION

Cancer patients are especially at risk for malnutrition since they have elevated metabolic requirements due to tumour burden, poor or reduced food intake due to treatment and inherently altered taste and smell (Lis *et al.*, 2012). In this study, 28 (66.7%) patients presented with malnutrition or were suspected of malnutrition (Table 2). These results appear to be similar to previous studies carried out exclusively on oncology patients using the PG-SGA which reported 42.4–76% of these patients to be malnourished or at risk of malnutrition (Du *et al.*, 2017; Gavazzi *et al.*, 2016; Zalina *et al.*, 2016).

CRC is a disease burden that is increasing in developing countries. A few studies have shown that cancer affects not only patients' health but also their QOL (Polanski *et al.*, 2017; Prevost *et a*l., 2014). On the other hand, several studies have demonstrated that the scores of QOL outcomes in malnourished patients are worse compared to well-nourished patients (Du *et al.*, 2017; Lis *et al.*, 2012). Therefore, assessment of CRC patients' QOL is essential and of benefit to patients as well as to the clinicians as the results can guide patients to the treatment options while informed decisions can be made by the clinician. Even though QOL is a subjective perception of cancer patients' symptoms, function and side effects of treatment, the results may help guide clinicians in making treatment decisions.

The scores for the symptom scales showed significant difference between well-nourished and malnourished, fatigue, nausea and vomiting, and pain. The symptoms score with the biggest difference was fatigue where malnourished patients reported the worse cancer related fatigue with a median score of 55.56, compared to a median score of 33.33 in well-nourished patients (Table 3). Cancer related fatigue is defined as a distressing, persistent, subjective sense of tiredness related to cancer and cancer treatment that interferes with usual functioning (National Cancer Comprehensive Network, 2011). Cancer

Table 3. Median (IQR) for QOL scores according to the nutritional status of 42 patients obtained using the PG-SGA global rating

Variable	*Overall (n=42)*	*Well-nourished PGSGA (A) (n=14)*	*Malnourished PGSGA (B and C) (n=28)*	*P value*
*Global health status/QOL	66.67 (62.50 – 66.67)	66.67 (66.67 – 66.67)	66.67 (50.00 – 66.67)	-
Functional scales				
Physical functioning	86.67 (86.67 – 93.33)	90.00 (86.67 – 93.33)	86.67 (81.67 – 93.33)	0.31
Role functioning	66.67 (33.33 – 66.67)	66.67 (33.33 – 66.67)	66.67 (33.33 – 66.67)	0.80
*Emotional functioning	100.00 (100.00 – 100.00)	100.00 (100.00 – 100.00)	100.00 (100.00 – 100.00)	-
*Cognitive functioning	100.00 (100.00 – 100.00)	100.00 (100.00 – 100.00)	100.00 (100.00– 100.00)	-
Social functioning	66.67 (66.67 – 66.67)	66.67 (66.67 – 75.00)	66.67 (66.67 – 66.67)	0.40
Symptom scales				
Fatigue	50.00 (33.33 – 66.67)	33.33 (33.33 – 33.33)	55.56 (47.22 – 66.67)	<0.001
Nausea and vomiting	50.00 (33.33 – 54.17)	33.33 (33.33 – 37.50)	50.00 (50.00 – 66.67)	0.03
Pain	33.33 (33.33 – 50.00)	33.33 (33.33 – 33.33)	50.00 (33.33 – 50.00)	<0.001
Appetite loss	33.33 (33.33 – 66.67)	33.33 (33.33 – 41.67)	33.33 (33.33 – 66.67)	0.42

p-values are based on non-parametric median test.
p<0.05 shows the significant difference between well-nourished PG-SGA (A) and malnourished PG-SGA (B and C) group
*all values are less than or equal to the median so median test cannot be performed.
PG-SGA, the scored patient generated subjective global assessment; iqr, interquartile range
Note: high score for global health status/QOL represents a better QOL; high score for functional scale represents a high/healthy level of functioning; high score for symptom scale/item represents a high level of symptomatology/problems

Table 4. Correlation between PG-SGA total score and independent variables (*n*=42)

Independent variables	*Relationship (r)*	*Significance (p)**
Global health status/QOL	-0.395	0.010
Symptom scales		
Fatigue	0.816	<0.001
Nausea and vomiting	0.730	<0.001
Pain	0.629	<0.001

*Spearmen's rho

related fatigue is the most prevalent cancer symptom, which has been reported in 50 – 90% of cancer patients (Campos *et al.*, 2011). Fatigue, depression, anxiety, and pain can also result in weight loss (Polanski, 2017). It is well known that feeding difficulties and weight loss due to the course of the disease and/or its therapies have a significant negative impact such as poor QOL (Borges *et al.*, 2010), and low energy intake in patients with cancer.

Assessment of QOL scores against nutritional status as measured by PG-SGA scores showed that there was a significant association between impaired QOL in global health status and symptom scales (fatigue, nausea and vomiting, and appetite loss) (Table 4). This study is in agreement with Polanski *et al.* (2017). They conducted a study among 180 patients with non-small lung cancer. They found that there was a significant correlation between PG-SGA score and QOL score which means that malnutrition is significantly associated with a poorer QOL (Polanski *et al.*, 2017). This result is line with a study conducted by Tong *et al.* (2009) on 219 medical oncology patients who had commenced chemotherapy at the centre within the past four weeks. They reported that patients with higher PG-SGA score and higher nutritional symptoms, such as constipation, diarrhoea, vomiting and bad taste in the mouth, had lower QOL and life satisfaction score (Tong, Isenring & Yates, 2009).

Patients with cancer are at high risk of weight loss and malnutrition. Health care professionals need to be aware of the effects of malnutrition on patients' outcome. Therefore, early identification and nutritional status assessment should be carried out at the beginning and during cancer treatment for all patients which may benefit from nutrition intervention to prevent further deterioration in their nutritional status. In addition, the scored PG-SGA is a well established and validated tool in identifying the degree of malnutrition in patients with cancer. The findings showed that the scored PG-SGA is undoubtedly a convenient choice of nutritional status assessment as it is significantly associated with QOL. Thus, this highlights the need and importance of early identification of malnutrition in CRC patients as the first step toward providing appropriate nutritional management during cancer treatment.

However, several potential limitations in the current study require acknowledgement. A potential limitation was the small sample size which might not have been large enough to accommodate the number of comparisons made within this study. Moreover, this present study was conducted through two study centres only and might therefore not be entirely representative of all CRC patients, thereby limiting generalisation of our findings. Still this present study has generated preliminary evidence on current nutritional status and QOL of CRC patients to serve as a basis for future research.

This study has several strengths which include the use of the validated scored PG-SGA and QOL questionnaires. The scored

PG-SGA has been validated for nutritional assessment in patients with cancer. Also the QOL questionnaires have been used widely in many international trials and research on cancer. The questionnaires have been translated and validated in Europe and other parts of the world and are considered as the strength of this study.

In conclusion, CRC patients have shown a relationship between nutritional status, and QOL. This relationship shows the importance of dietary management in CRC patients. A targeted assessment of the nutritional status and QOL of cancer patients done routinely may result in possible preventive methods for malnutrition and further improve their QOL.

ACKNOWLEDGEMENTS

The authors wish to express their sincere gratitude to all the enthusiastic study participants who extended their cooperation during the study. The authors acknowledge Dr Gerald Lim Chin Chye (Head, Department of Radiotherapy and Oncology), Dr Lau Kah Liew (Clinical Oncologist) from Hospital Kuala Lumpur, Dr Lim Boon Leong (Head, Department of Palliative Care), Dr Farhan Hadi (Consultant Oncologist) from Hospital Selayang, as well as the clinical staff of Day Care Oncology Clinic at Hospital Kuala Lumpur and Day Care Oncology Clinic and Palliative Ward at Hospital Selayang, Malaysia for their cooperation and assistance throughout the course of the study.

Conflict of interest

The authors declared no conflict of interest with respect to their authorship or the publication of this article and financial source. The study is a non-funded study.

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