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Improving the Nutritional Status of Patients with Colorectal Cancer Undergoing Chemotherapy through Intensive Individualised Diet and Lifestyle Counselling

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ABSTRACT

Introduction: Malnutrition is common among patients with cancer and it is also associated with their negative health outcomes. Generally, cancer patients undergoing chemotherapy have a high risk of malnutrition, secondary to both the disease and the treatment. It is important that patients maintain a good nutritional status to improve the effects, and minimise the side effects of cancer treatment. A good nutritional status should be maintained for patients through nutritional intervention during cancer treatment. There appears to be no published studies on the effects of intense dietary counselling versus usual dietary care on the nutritional status of colorectal cancer (CRC) patients undergoing chemotherapy alone. Furthermore, there have been no randomised controlled trials (RCT) undertaken in Malaysia, where CRC is increasing. It is therefore important to undertake a RCT of a dietary and lifestyle counselling intervention of CRC outpatients undergoing chemotherapy. **Methods:** The intervention study was an open (masking not used), prospective, and RCT to examine the effects of intensive individualised dietary and lifestyle counselling on dietary intake and nutritional status in CRC patients undergoing chemotherapy. It was designed as an 8-week program of intensive, individualised dietary and lifestyle counselling followed up with another 8-week post-intervention period without dietary and lifestyle counselling, and compared to a control arm given the usual care. A total of forty-two participants took part in this study and were randomised into two groups, namely, the intervention group (IG) (n=22) and the control group(CG) (n=20) at Kuala Lumpur Hospital and SelayangHospital, Malaysia. **Results:** In this study, 67% of CRC patients were malnourished at baseline. In the IG, the prevalence of malnutrition dropped from 72.7% at baseline to 27.3% eight weeks after the intervention. This repesents a large, and clinically meaningful shift. In the CG, the prevalence of malnutrition, or at risk of malnutrition, was still at 75% at the end of the sixteen weeks. **Conclusion:** Intensive, individualised dietary and lifestyle counselling resulted in improved nutritional status in patients with CRC undergoing chemotherapy.

Key words: Chemotherapy, colorectal cancer, dietary counselling, nutritional status

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INTRODUCTION

Globally, colorectal cancer (CRC) is the third and second most frequent cancer affecting men and women, respectively (Jemal *et al.*, 2011). Approximately, 15 million new cancer cases are diagnosed each year, and about half of those patients affected died within five years. In Malaysia, CRC is the second most common cancer among both men and women after breast cancer. The incidence of CRC rises with age with the group aged 70-years and above having the highest age-standardised rate (ASR) of 17.4 per 100,000 in 2007 (Zainal & Nor Saleha, 2011). Based on ethnicity, CRC incidence was highest among the Chinese with 34.0%,followed by 17.7% and 17.1%, respectively among Malays and Indians.

Cancer treatments generally include surgery, radiotherapy, and chemotherapy (either alone or in combination)(Paccagnella *et al.*, 2010). All of these treatments can result in damage to normal tissues, and at the same time produce intense side effects that often affect nutritional status. Cancer therapies may affect nutritional status through alterations to the metabolic system and/or reductions in food intake.

The incidence of malnutrition in patients with cancer is observed to range from 40% to 84% (Brown, Capra & Williams, 2008), while studies of hospitalised patients with cancer indicate that 56% to 76% of patients are either malnourished or at risk of being malnourished (Bauer, Capra & Ferguson, 2002; De Luis *et al.*, 2006). Meanwhile, about 42.4% of cancer patients receiving chemotherapy are suspected of being malnourished (Heredia *et al.*, 2008), 52% being in in stages III or IV of CRC (Gupta *et al.*, 2006), and 30% as outpatient CRC patients (Triantafillidis *et al.*, 1995). Furthermore, almost 20% of cancer patients have been reported to die from the effects of malnutrition, or its complications, rather than the cancer diagnosed (Wu *et al.*, 2009).

Malnutrition evidence during cancer treatments has highlighted the need for early identification and appropriate intervention in CRC patients. The extent of malnutrition should be identified early, followed by the implementation of strategies that can generate positive outcomes for the patient. This study was designed to add to the literature by contributing scientific evidence about effects of intensive, individualised diet and lifestyle counselling to overcome the deterioration of CRC patients' nutritional status when undergoing treatment.

Practice guidelines for the nutritional management of patients receiving radiotherapy have been based on strong evidence that nutrition support improves outcomes in patients with gastrointestinal or head and neck area cancer (Isenring *et al.*, 2008). The evidence highlights that dietary counselling by a dietitian, with or without the use of commercial nutritional supplements, is the most effective method of nutritional intervention that improves dietary intake (Isenring, Bauer & Capra, 2007; Ravasco *et al.*, 2005), nutritional status, and quality of life (QOL) in nutritionally-at-risk cancer patients undergoing radiotherapy (Ravasco *et al.*, 2005, Capra & Bauer, 2004; National Health and Medical Research Council grade of recommendation A; Isenring *et al.*, 2008).

Conversely, Bauer *et al.* (2008) report that there is currently insufficient evidence to routinely recommend dietary counselling in patients with cancer receiving chemotherapy due to a lack of well-designed, and high quality randomly controlled clinical studies. Most studies have investigated the effect of nutrition counselling on patients receiving radiotherapy or a combination of treatments, while one earlier study by Ovesen *et al.* (1993) report on the effects of nutritional counselling on patients receiving chemotherapy alone. However, Ovesen *et al.* (1993) used a non-validated tool to assess QOL, thus their findings may not be generalised to all populations,

and should not be included in meta-analyses(Bauer, Isenring & Ferguson, 2008). Bauer *et al.* (2008) recommend further research be conducted in this area.

Dietary counselling is the focus of this study as early intervention is warranted in order to combat malnutrition in patients with CRC undergoing chemotherapy. Research in this area is urgently required and the dietary counselling and lifestyle intervention strategies implemented in the study will also serve as a reference in designing intervention programs for the prevention and management of cancer in all clinical settings.

METHODS

Study design and study population

This interventional study was prospective and involved randomised controlled trials (RCT)that compared the effect of intensive individualised dietary counselling with the usual care on nutritional status in patients with CRC receiving chemotherapy. It was designed as an 8-week controlled trial of intensive, individualised dietary counselling followed by another 8-week period of post-intervention without dietary counselling. Nutritional status was measured using the Scored Patient Generated-Subjective Global Assessment (PG-SGA©), anthropometric measurements, as well as dietary intake.

At week eight, after the intervention period was over, dietary counselling was not offered and follow-up assessments were carried out at week sixteen. During the follow-up (post-intervention) visit, nutritional assessments used the Scored PG-SGA©, anthropometric data, and 2-day 24-hour dietary records.

Screening and recruitment of participants

Screening and recruitment of sequentially presenting patients was carried out simultaneously on patients who visited the Day Care Oncology Clinic at Kuala Lumpur Hospital and Day Care Oncology Clinic and Palliative Ward at Selayang Hospital, Malaysia during the study period. The recruitment was based on physicians' referrals. CRC patients aged 18-years and above, who were scheduled for chemotherapy, complied with the study protocols, and were able to read and write in Bahasa Malaysia were included in the study. The exclusion criteria included patients diagnosed with other cancer types, or had taken part in another study.

Screening of patients occurred during the clinic's operating hours to identify those eligibleto participate in this study. The selected patients were given a simple explanation from the oncologist about the study. Once the patients agreed, the oncologist informed the researcher. After eligibility was confirmed, the patients received a brief description of the study from the researcher, and if interested, more details were given. The explanation included the purpose of the study, the randomisation procedure, the follow-up schedule, and the potential benefits of the research study. The patients were also given time to read a patient information sheet, and to consider their participation before participating in the study. Willing participants were asked to endorse and return an informed consent form. The participants' baseline measurements were taken at a later date at the clinic.

Randomisation

The researcher was aware of the treatment allocation but the clinicians were blinded to these procedures. Allocation of participants into the two treatment groups was done by a permuted block method for a block size of four, with A for the intervention group (IG) and B for the control group (CG). This block of four had six different possible arrangements of two As and two Bs. A random number sequence was used to choose a particular block, which set the allocation order for the first four participants. Similarly, the treatment

group was allocated to the next four participants in the order specified by the next randomly selected block. The process was then repeated. Allocations were made by asking the participants to pull sealed envelopes out of a box. The envelope was opened on the spot, deciding which group the participant would be allocated to.

Intervention

This interventional study consisted of intensive, individualised dietary and lifestyle counselling involving the prescription of a modified therapeutic diet according to the individual participant's needs. The main goal of nutritional intervention is to enable every participant to maintain and/or achieve his or her calculated energy and protein requirements. The intervention carried out was on a one-to-one basis by the same research dietitian throughout the study.

Additionally, nutritional prescriptions were based on the American Dietetic Association (ADA) Medical Nutrition Therapy (MNT) protocol for cancer patients (Hurst & Gallagher, 2006).

The dietary intervention was structured, and changes were only made to the energy and protein component of the diet. Individually tailored sample meal plans and recipe suggestions were provided as and when required during the visits. This process involved the prescription of a therapeutic diet modified based on individual needs, recognising personal eating patterns, feasible consistency, and preferences.

Dietary counselling strategies included providing advice on, and describing, treatment related symptoms that may negatively impact on dietary intake and nutritional status. Participants were also given practical advice on how to deal with these symptoms. A dietitian was on hand to answer any further queries or provide more information when requested.

Lifestyle counselling involved providing participants with general advice on ceasing or reducing smoking, and limiting alcohol consumption. The general advice given also emphasised physical activity. Participants already on an exercise program were advised to use a lower intensity and progress at a slower pace. The principal goal was to maintain activity as much as possible. Participants were reminded and encouraged to comply with their respective dietary interventions over the 16-week study period. Throughout the study, the participants were supported with scheduled visits to the clinics. Regular telephone calls were also made to develop a rapport to facilitate ongoing participation during the study period.

The intervention group(IG)

The IG received tailored, more intensive, and ongoing nutrition support and lifestyle advice as compared to the CG. They were counselled individually using the ADA MNT protocol for cancer patients. At the baseline visit, the researcher obtained their dietary intake using a 24-h dietary recall. Based on the estimated dietary intake, the researcher was able to determine if those in the IG met their daily nutritional needs. The energy requirement was calculated for each patient to be between 30 kcal/kg/day to a maximum of 35 kcal/kg/day based on their actual body weight, reported physical activity, presence of metabolic stress, abnormal losses, and current treatment. The protein requirement was between 1.2 g/kg/day to 1.6 g/kg/day (Hurst & Gallagher, 2006).

Participants in the IG were instructed to maintain a dietary intake based on the calculated energy and protein requirements. The distribution of macronutrients in the menu was such that 50% and 30% of total energy came from carbohydrates and fats, respectively. Participants were given a sample menu of 1,500 kcal and with modification to increase total energy to 1,800 kcal or 2,000 kcal.

Thereafter, an individualised, intensive nutritional plan was devised with a variety

of dietary interventions, which involved the prescription of a modified therapeutic diet based on the patients' needs. The patients were advised on healthy eating habits to reduce the side effects of their therapy that could affect their dietary intake and nutritional status. In brief, the first part of the consultation covered the basic concept of the malnutrition commonly seen in patients with CRC. This was then followed by a more intense dietary management intervention based on the recommendations of the ADA (Hurst & Gallagher, 2006). They also received written material i.e. the booklet containing information on nutrition and cancer in Malay and English languages.

The control group (CG)

The CG received the standard nutritional advice practised by the clinics, which involved general nutritional advice based on guidelines specifically focused on the treatment of symptoms such as nausea, vomiting, loss of appetite and diarrhoea, and how to deal with them through nutritional approaches. Basically, the advice was given by the oncologist or nurses. However, malnourished patients were referred to a service dietitian for dietary counselling, but this was not as tailored or as intense as the dietary and lifestyle advice given to the IG.

Those in the CG received the same information booklet as those in the IG. Information was delivered verbally, visually and in written form. The first part of the consultation covered the basic concept of malnutrition commonly seen in patients with CRC. This was then followed by discussing the aforementioned simple guidelines to help manage undesirable symptoms during the treatment.

Measured outcomes

Nutritional status

The Scored PG-SGA© consisted of two sections with seven domains. The first section, completed by the participant, was in the form of a checklist and comprised weight, food intake, symptoms, activities, as well as function. The second section was completed by the researcher as it covered the disease and its relation to nutritional requirements, determination of metabolic demands, and was followed by a nutrition-related physical examination, including subjective body composition (i.e.,fat, muscle, and fluid status).

A score ranging from 0 to 4 was given for each domain depending on the impact on the nutritional status. PG-SGA© scores that ranged from 0 to 35 reflected a greater risk of malnutrition, or indicated a lower nutritional status of the patient. These scores were transformed into global ratings - Stage A, Stage B and Stage C- which represented the states of being well-nourished, moderately malnourished, and severely malnourished, respectively. Then, the criticality of need for nutritional intervention was identified and classified based on the scores with 0 to 1 point requiring no intervention, health education for 2 to 3 points, dietetic intervention for 4 to 8 points, and nutrition support for ≥9 points. Participants' nutritional status was measured at baseline, weeks 4, 8, and 16.

Anthropometric measurements

The anthropometric measurements carried out in this study included body weight and height. These measurements were taken directly before the interview with all the participants and carried out during all visits. The measurements were taken with participants being shoeless and wearing lightweight clothing with empty pockets, without watches, or other accessories. Weight was determined to the nearest 0.1 kg using a digital weighing scale (SECA, British Indicators Ltd., United Kingdom). The machine was calibrated every morning with a standard weight before it was used. Height was measured in the standing position to the nearest 0.1 cm using a SECA 206 microtoise tape (Vogel and Halke GmbH & Co, Hamburg, Germany) which

was attached to the wall. The participants were asked to stand straight with the head in the Frankfort plane, feet together, knees straight, and heels, buttocks, and shoulder blades in contact with the vertical surface of the wall.

All anthropometric measurements were taken twice by the same investigators, and the average was used. Height measurement was only taken during the baseline visit. Weight and height measurements of the participants were then used to calculate the BMI (World Health Organisation [WHO], 2004).

Dietary intake

Dietary intake was measured through a 24-hour dietary recall at baseline and two days of 24-h dietary records (one weekday and one weekend) prior to each of the three subsequent clinic visits (at week four, week eight, and week sixteen). The participants were required to keep a record of all food and beverage intakes for each 24-h period of data collection.

Both groups were provided an explanation by the researcher on how to record their two-day intake in a food diary. They were also given a detailed set of instructions together with a food album. The food album lists commonly consumed food and includes details of portion sizes relative to typical household measurements (e.g., glass, cup, Chinese rice bowl, plate, tablespoon, and teaspoon) to facilitate recalls of serving size and improve accuracy. Details of food information and descriptions, which included brand names, preparation and cooking methods, as well as recipes of any mixed dishes eaten during the study period, were also recorded. In situations where foods and beverages were consumed away from home, the participants were encouraged to describe the quantities of foods and beverages consumed using the household measures as well.

Participants who had difficulty reading or writing were asked to seek assistance from their family members when completing their records. They were asked to complete the 2-day, 24-h dietary record of food intakes before each visit, which was used as the basis for their individualised dietary advice and also to assess compliance with dietary advice.

A computerised local dietary analysis program, Nutritionist Pro version 2.0(First Data Bank, The Hearst Corp. United States of America [USA]) was used to analyse the nutrient intakes of the patients. The foods and beverages consumed by the participants were coded by type and amount, and analysed for nutrient content primarily based on the Malaysian Food Composition Table (Tee *et al.*, 1997).

Nutritionist Pro was then used to calculate dietary intake at baseline (based on one 24-hour dietary recall), and at other subsequent assessment time points (based on average intake over each 2-day period of dietary record). Data obtained were analysed using the Statistical Package for Social Sciences (SPSS) version 19.0 (SPSS Inc, Chicago, USA).

Statistical analysis

The data collected were analysed by using the statistical software SPSS and checked for normality via 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.

Descriptive statistics, including percentages, mean values, and standard deviations (SD), were used to describe the baseline demographic data, stage of cancer, nutritional status level and anthropometric data, and dietary intake. The values from

both groups were compared by using an independent *t*-test, while the categorical data were analysed by using a chi-square test.

Nutritional status was the dependent variable in the primary analyses. The changes from baseline to week sixteen in anthropometric measurements, nutritional status, and dietary intake were computed. An intent-to-treat (ITT) analysis was performed to determine the effect of the intervention study on the assumption that participants adhered to the dietary advice and had baseline and endpoint values for the Scored PG-SGA©. The effects of the intervention between treatment groups based on primary outcomes were analysed using the SPSS General Linear Model (GLM) Repeated Measures procedure. The comparison of changes between the groups was made by an independent *t*-test, while the changes within the group were compared with a paired *t*-test. A *p*-value <0.05 was considered as being statistically significant.

Power calculation

The sample size formula for two group comparisons of means in a two-sided test was used to determine the sample size in this study. A previous study of intensive nutrition intervention by Isenring *et al.* (2007) was used as a reference. The sample size was calculated as 11 patients in each group. In order to detect a 20% difference in mean nutritional status between groups, 12 patients had to be included in each group. Allowing for a high drop-out rate of >20% and the fact that this type of study had not been conducted in a Malaysian setting previously, the study aimed to recruit a total of twenty-four patients per group to maximise the power to detect clinically significant differences.

Ethical approval

This study was registered with the Australian New Zealand Clinical Trials Registry (ANZCTR). The study was approved by the Southern Adelaide Health Service/Flinders University Human Research Ethics Committee (SAFUHREC) and the Medical Research Ethics Committee (MREC) of the Malaysian Ministry of Health. Additionally, permission to conduct the study was obtained from the directors of Kuala Lumpur Hospital and Selayang Hospital in Malaysia. Written consent was obtained prior to the commencement of the intervention

RESULTS

The researcher screened fifty potentially eligible patients with forty-two participants (84%) consenting to enter this study. Six patients were excluded because they did not meet the study's criteria and two refused to participate. Selected participants were randomised into the two groups (i.e., IG and CG). There were twenty-two participants in the IG and twenty participants in the CG who completed the intervention and presented at the follow-up eight weeks after the intervention.

The baseline characteristics of the study participants are presented in Table 1. There was no statistical difference in age between the two groups. The mean age of the participants was 58.91±8.63-years in the IG, and 55.00±10.80-years in the CG. The majority of them were men from the Chinese ethnic background. Twenty five (59.5%) were diagnosed with stage II cancer, whilst seventeen (40.5%) had stage III cancer. Most of the participants in both groups (59.1% IG, 60.0% CG) were diagnosed with stage II CRC.

The nutritional status of the IG and CG participants according to the Scored PG-SGA© and PG-SGA© global rating is shown in Table 1. Even though the nutritional status for the IG and CG did not differ significantly, there were more malnourished (Stage B and C) participants in the IG (n=16, 72.7%) compared to those in

CG (n=12, 60%). Nevertheless, ten (9.5%) of the patients required no intervention, and a further four (10%) were offered health education. The majority of the patients (66.7%) required dietetic intervention, but no critical intervention was required. Although low BMI and malnutrition are associated, 23 of the 36 participants in the normal or overweight/obese ranges in this study were at risk of malnutrition or severe malnutrition (Stages B and C) as shown in Table 2.

The prevalence of malnutrition is shown in Table 3. Across all participants, fourteen (33%) of were well-nourished (Stage A), whilst twenty-six (62%) were moderately malnourished (Stage B) and two (5%) were severely malnourished (Stage C) at baseline. By the end of the treatment, more participants in the IG were assessed as being well-nourished than malnourished and vice versa for the CG as shown in Table 3. This was statistically significant at week 8 (x^2 = 4.7, p<0.05) and again at week 16 (x^2=9.5, p<0.01), when the proportion of malnourished participants

Table 1. Baseline characteristics of the participants in the intervention group (IG) and control group (CG)

Characteristics	*IG (n = 22)*		*CG (n = 20)*		*p value*
Age (years)(Mean±SD)	*59.0±8.6*		*55.0±10.8*		*0.905*
PG-SGA scores(Mean±SD)	*8.7±1.9*		*7.9±1.6*		*0.36*
	n	*% of participants*	*n*	*% of participants*	*p value*
Gender					
Men	13	59.1	14	70.0	0.461
Women	9	40.9	6	30.0	
Ethnicity					
Malay	4	18.2	6	30.0	0.173
Indian	0	0.0	2	10.0	
Chinese	18	81.8	12	60.0	
Cancer stage					
Stage 2	13	59.1	12	60.0	0.952
Stage 3	9	40.9	8	40.0	
PG-SGA global rating					
A (well-nourished)	6	27.3	8	40.0	0.309
	n (%) of participants : 14 (33.3)				
B (suspected or moderately malnourished)	14	63.6	12	60.0	
	n (%) of participants : 26 (61.9)				
C (severely malnourished)	2	9.1	0	0.0	
	n (%) of participants : 2 (4.8)				
Triage intervention					
No intervention (Score of 0–1)	3	13.6	7	35	0.214
	n (%) of participants : 10 (23.8)				
Health education (Score of 2–3)	3	13.6	1	5	
	n (%) of participants : 4 (9.5)				
Dietetic intervention (Score of 4–8)	16	72.7	12	60	
	n (%) of participants : 28 (66.7)				
Critical interventions (≥ 9)	0	0	0	0	
	n (%) of participants : 0 (0.0)				

p>0.05, not significantly different from the CG with Chi-square

Table 2. Baseline body mass index (BMI) categories and PG-SGA global rating in colorectal cancer (CRC) participants

BMI category	*PG-SGA global rating*			*Total (n)*
	A	*B*	*C*	
Underweight (< 18.5 kg/m²)	1 (7.1%)	5 (19.2%)	0 (0.0%)	6 (26.3%)
Acceptable weight (18.5–24.9 kg/m²)	11 (78.6%)	20 (76.9%)	2 (100.0%)	33 (78.6%)
Overweight/obese (≥25 kg/m²)	2 (14.2%)	1 (3.8%)	0 (0.0%)	3 (7.1%)

in the CG remained more than pre-treatment levels. Over the sixteen weeks, the mean Scored PG-SGA decreased in the IG and increased in the CG indicating an improved nutritional status in the IG and a decreased nutritional status in the CG (p<0.001 time*group interaction, repeated measures analysis of variance)as shown in Figure 1.

In all, forty-two participants completed the 24-h dietary recall at baseline. The baseline energy and nutrient intakes of the participants in both groups are shown in Table 4. The baseline energy and protein intakes for the IG and CG were 1363±278 kcal/day and 51±14 g/day, and 1382±365 kcal/day and 52±15 g/day, respectively. Both energy and protein intakes were within the acceptable requirement limits for the participants. Additionally, the energy and protein intakes for the participants in both groups at baseline were comparable and not statistically different.

The effects of eight weeks of intensive, individualised dietary counselling and lifestyle intervention on dietary intake of the participants is shown in Table 5. The mean values for nutrient intake (±SD) were calculated from the baseline 24-h dietary recall as well as from the 2-day food records from week 4, week 8, and week 16. At baseline, both the IG and CG had comparable energy and protein intakes. At week 16, the IG and CG consumed 1365±263 and 1289±320 kcal/day, respectively. Although the mean values for energy and protein intake for the IG and CG did not differ significantly, during the 16-week study, the IG increased their energy and protein intake during the first four weeks of treatment, but then maintained an intake similar to that consumed at baseline. In contrast, the CG had a steady decrease in their energy and protein intake, which only started to increase at week 16. However, this was still 93 kcal/day and 5 g/day less than at baseline.

DISCUSSION

This study demonstrated that intensive dietary and lifestyle counselling improved the nutritional status of CRC patients after eight weeks of starting their chemotherapy compared to those receiving the usual care in a clinical setting. The prevalence of malnutrition or suspected malnutrition in this study was high with twenty-eight (66.7%) participants being either malnourished or at risk of being malnourished as shown in Table 1. Similar findings were obtained from other studies that determined the nutritional status of cancer patients (Read *et al.*, 2006; Bauer *et al.*, 2002). Additionally, previous studies on patients with cancer using the PG-SGA© also reported 42.4% to 76% patients either being malnourished or at risk of being malnourished (Bauer *et al.*, 2002;De Luis *et al.*, 2006). Although the prevalence of malnutrition in CRC patients varied between studies, this, nevertheless, demonstrates that malnutrition is a

Table 3. Changes in PG-SGA global rating categories of the participants in the intervention group (IG) and control group (CG) over 8-week intervention trial and a follow-up visit at week 16

Nutritional status	*Baseline (n=42)*		*Week 4 (n=42)*		*Week 8 (n=42)*		*Week 16 (n=42)*	
	IG n (%)	*CG n (%)*	*IG n (%)*	*CG n (%)*	*IG n (%)*	*CG n (%)*	*IG n (%)*	*CG n (%)*
PG-SGA global rating								
A (well-nourished)	6 (27.3)	8 (40.0)	9 (40.9)	7 (35.0)	14 (63.6)	6 (30.0)	16 (72.7)	5 (25.0)
B (suspected or moderately malnourished)	14 (63.6)	12 (60.0)	13 (59.1)	13 (65.0)	8 (36.4)	14 (70.0)	6 (27.3)	15 (75.0)
C (severely malnourished)	2 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
p value[1]	0.026		0.121		0.011		0.001	

[1]chi-square tests

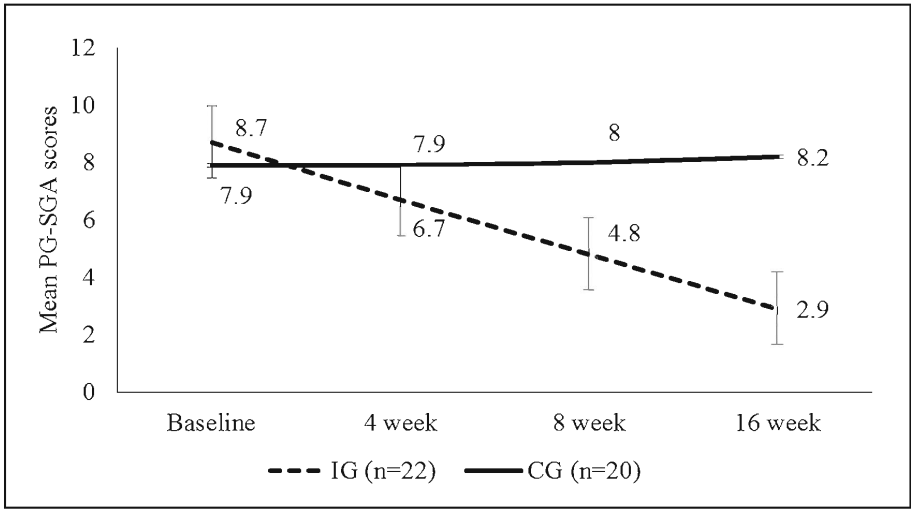

Figure 1. Mean (±SD) changes in PG-SGA scores from baseline to week 16 in the intervention group (IG) and control group (CG).*Significantly different from the CG group, with repeated measures analysis of variance with $p < 0.001$. **Statistical analyses were performed on log-transformed.

Note: Higher score for the scored PG-SGA represents the greater the risk for malnutrition or indicated lower nutritional status of the patients

Table 4. Comparisons of estimated daily nutrient intake of key nutrients between the intervention group (IG) and control group (CG) at baseline, as measured by 24-hour food recall

*Nutrient intake**		*IG (n = 22)*		*CG (n = 20)*		*p value*
		Mean ± SD	*Range*	*Mean ± SD*	*Range*	
Energy, kcal	1363 ± 278	1023–2254	1382 ± 365	734–2016	0.840	
Protein, g	51 ± 14	19–90	52 ± 15	27–88	0.970	
Protein, as % of energy	15%	7-22%	15%	12-21%	0.771	

p>0.05 not significantly different from the CG with Independent T-Test
*Statistical analyses were performed on log-transformed data

Table 5. Comparisons of nutrient intake (mean ± SD) calculated from two-day food records of the participants in the intervention group (IG) and control group (CG) over 16-weeks

Nutrient intake *per day2*	*IG (n=22)*				*CG (n=20)*				*p value1*		
	Baseline	*4 week*	*8 week*	*16 week*	*Baseline*	*4 week*	*8 week*	*16 week*	*Group*	*Time*	*Time*group*
Energy, kcal	1363 ± 278	1364 ± 187*	1344 ± 257	1365 ± 263	1382 ± 365	1258 ± 330*	1328 ± 366	1289 ± 320	0.598	0.374	0.580
Energy, kJ	5707 ± 1165	5636 ± 784	5630 ± 1078	5715 ± 1104	5787 ± 1529	5270 ± 1383	5560 ± 1534	5396 ± 1339	0.598	0.374	0.580
Protein, g	51 ± 14	51 ± 11	48 ± 12	53 ± 12	52 ± 15	44 ± 10*	44 ± 9	47 ± 21	0.08	0.825	0.127

[1] Repeated measures analysis of variance
[2] Statistical analyses were performed on log-transformed data
* p<0.05 significantly different from baseline within a group with paired t-test

common occurrence amongst cancer patients. Moreover, studies by Bauer *et al.* (2002) and Pirlich *et al.*(2006) found that patients with cancer had the highest prevalence of malnutrition among those hospitalised.

Even though this study was conducted among patients with CRC, which is not considered as a very cachectic tumour (Dewys *et al.*, 1980), the fact that the 66.7% of the participants were suffering from some kind of malnutrition (Stages B and C) before starting chemotherapy is of concern because it is known that patients receiving chemotherapy may have several toxic side effects that could negatively influence their nutritional status by interfering with their ability to eat (Santarpia, Contaldo & Pasanisi, 2011). Moreover, Read *et al.* (2006) found a similar result among oncology outpatients as a higher prevalence of malnutrition was revealed before the start of treatment. Therefore, identifying patients at risk of malnutrition and optimising symptom management to reverse or prevent malnutrition during treatment is essential in patient care (Watterson *et al.*, 2009).

Both groups had a mean BMI within the normal range as shown in Table 2. Sarhill *et al.* (2003) found a similar result in a study of 346 advanced cancer patients where most of them (87%) had normal or high BMIs. However, Sarhill *et al.* (2003) also found that some patients suffered severe post-illness weight loss even though most patients had a normal BMI, which they explain by suggesting the existence of pre-illness obesity. This may be caused in part by the surgery being performed, including extensive resection of the small bowel which can lead to the malabsorption of nutrients.

Isenring *et al.*(2007) reported that the BMI for both participants from IG and CG (25.2 vs 26.4 kg/m^2) indicated slight overweight. Um *et al.*(2014) found that of 87 cancer patients undergoing radiotherapy at baseline, approximately 74.6% were classified as either overweight or obese. Bye *et al.* (2013) explain that patients' higher body weights could be partially due to an increase in extra cellular water in ascites and oedemas, rather than an increase in fat or muscle mass.

This study found that the effect of early intensive nutrition intervention improved the nutritional status among CRC patients when compared to normal nutritional care as shown in Figure 1. The benefits of early intensive nutrition intervention have been demonstrated in several studies (Isenring *et al.*, 2007; Um *et al.*, 2014; Isenring *et al.*, 2004). Individualised dietary counselling has been shown to be effective in improving and maintaining patients' nutritional status, dietary intake, and QOL (Ravasco *et al.*, 2005, Isenring *et al.*, 2007).

Isenring *et al.*(2007) report that among 60 gastrointestinal or head and neck cancer outpatients on radiotherapy receiving nutritional intervention resulted in significantly increased dietary intake, as well as improved QOL and nutritional status level. A similar positive result due to individualised nutrition intervention was found by Ravasco, Monteiro-Grillo & Camilo(2012) on 89 CRC ambulatory patients undergoing neo-adjuvant radiotherapy. Van den Berg *et al.*(2010) highlight that maintaining an optimal nutritional status through nutritional intervention during cancer treatment is important for promoting better patient outcomes.

This study finding that both energy and protein intakes were significantly increased in the IG throughout the study period when compared with the CG is consistent with those of Isenring *et al*, (2007). Lua *et al.* (2012) also recorded protein intake above the recommended level among breast cancer patients during chemotherapy. Patients normally require diet alterations toward a low residue diet, especially if they were experiencing chemotherapy-related symptoms such as diarrhoea. This might account for the intake of certain dietary

items such as fibre being lower than that recommended(Van Loon *et al.*, 2013). Read *et al.*(2007) demonstrated that acute side effects of chemotherapy exert a negative influence on advanced cancer patients' food intake patterns. Therefore, changes in dietary intake tend to follow the natural progression of side effects among patients undergoing chemotherapy.

The timing of nutritional advice could be important. Increasing dietary intake just before treatment might also not be acceptable to patients undergoing chemotherapy. Studies on mice and in cell culture show that short-term fasting (48 h) can protect normal cells but not cancer cells from chemotherapy agents (Raffaghello *et al.*, 2010). However, the situation in head and neck cancer patients undergoing radiotherapy may be different from that in those given chemotherapy where several trials found an improvement in dietary intake (Isenring *et al.*, 2007), and nutritional status (van den Berg *et al.*, 2010).

This study has some important strengths and limitations. The RCT adapted for the implementation of intervention was the most suitable design for measuring its efficacy. It was also sufficiently powered to detect the large effect of the intervention, compared with the CG. Recruitment of patients through referral by physicians had a significant influence in reaching the targeted number of participants and improving response rate, as evidenced by there being no participant drop-out. The small numbers of subjects limits the generalisation of the findings to other clinical settings and CRC populations. Food diary recording could be very time consuming and taxing for the participants, especially oncology patients who are undergoing treatment, and this might impact on the quality of the food diary.

CONCLUSION

This study found evidence that intensive, individualised diet and lifestyle counselling conferred beneficial effects in improving the nutritional status and QOL of CRC patients undergoing chemotherapy, compared to the usual nutritional care offered to them.

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Conflict of Interest

The authors declare no competing interests.

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