Effect of Oral Nutrition Supplementation on Quality of Life and Functional Outcomes in Gastrointestinal Cancer Patients Undergoing Chemotherapy: A Randomized Controlled Trial

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ABSTRACT

The purpose of this study was to investigate the efficacy of oral nutrition supplement ONS plus Dietary advice on the Muscle strength hand grip, quality of life (QoL) and related adverse events of gastrointestinal cancer patients undergoing chemotherapy. This study was randomized controlled trial RCT involved gastrointestinal cancer patients undergoing chemotherapy treatment. Malnutrition screening was done for all patients before the start of chemotherapy. Patients were randomized into two groups oral nutrition support group (ONS) (n=75) were given dietary guidance and oral nutrition supplements 500 kcal daily of ONS balanced formula for 12 weeks, while control group Non-ONS (n=75) received only dietary guidance. Basic demographics, Biochemical laboratory tests, Hand grip strength and health-related quality of life questionnaire EORTC QLQ-C30 scores (European Organization for Research and Treatment of Cancer to measure the health-related quality of life) were also collected and analyzed. Hand grip strength routinely measured each cycle every 3 weeks, in addition, the hematological adverse effect was collected according Common Terminology Criteria for adverse Events (CTCAE v5). In comparison to baseline measurements, the results indicated an enhancement in overall quality of life within the ONS group, encompassing the Global QLQ score (adjusted $\beta = 34.20$, SE = 3.80, $p < 0.001$), Symptoms QLQ (adjusted $\beta = 17.8$, SE = 3.00, $p < 0.001$), Functional QLQ (adjusted $\beta = 15.3$, SE = 2.7, $p < 0.001$), and Total QLQ score (adjusted $\beta = 22.4$, SE = 2.6, $p < 0.001$). Non-ONS showed a decrease in hand grip strength, was observed between Time 4 and Time 5 (mean difference = 0.350, p = 0.009), and between Time 3 and Time 5 (mean difference = 0.570, p = 0.033). In contrast, The ONS group showed maintenance in hand grip strength at all-time points, indicating preserving of muscle strength during follow up period. Early oral nutrition supplements for GIT cancer can significantly improve the nutritional risk profile and quality of life and was associated with preservation handgrip strength and lower incidence of treatment related adverse events predominant in the nutrition support group.

Keywords: Hand grip strength- Quality of life- Oral nutritional supplement- Gastrointestinal cancer- Malnutrition

INTRODUCTION

Controversial data exists about the endorsement of nutritional support therapy for patients with malignant gastrointestinal tumors, such as colorectal and gastric cancer. Cancer patients experience issues with insufficient food intake, diminished capacity to absorb and assimilate nutrients, and disrupted bodily homeostasis[1,2]. The significance of nutrition in cancer therapy must be addressed due to The extended and intensive nature of the treatment process that may entail a significant risk of malnutrition and other nutritional deficits in oncology patients[3].

The Malnutrition in individuals might substantially affect the immune system, leading to poorer treatment results and diminished clinical remission. In cases with incurable severe cachexia in patients with cancer of colon might led to median life expectancy is under three months. This patient has restricted oncological treatment options and a notably poor response to anti-cancer therapies is prevalent[4]. Gastrointestinal malignancies exhibit greater fatality rates than all other cancer types. In 2020, there were around 3.5 million fatalities globally, alongside an additional 5.0 million new diagnoses in that year[5]. Colorectal cancer (CRC) is the predominant form of gastrointestinal cancer, ranking third among all organ cancers, following lung and breast cancers. In contrast, gastric, esophageal, and pancreatic cancers which rated ranked fifth , eighth, and twelfth in terms of diagnosis frequency, respectively[6]. Patients with gastrointestinal cancer encounter diminished appetite, early satiety, oral lesions, alterations in taste and olfaction, epigastric discomfort, nausea, vomiting, constipation, and diarrhea. Collectively, these are referred to as nutrition impact symptoms (NIS)[3]. Nutritional Impact Symptoms (NIS) are associated with the initial phases of malnutrition and should be handled as gastrointestinal cancer prognostic indicators of nutritional status. The correlation between

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gastrointestinal cancer and nutrition has been thoroughly investigated, particularly regarding the influence of dietary composition as a risk factor for these specific oncological patients. Recently, numerous research have examined the impact of nutritional strategies as therapeutic interventions capable of preventing disease development and/or mitigating chemotherapy adverse effects[7]. Patients diagnosed with gastrointestinal cancer demonstrated signs of malnutrition upon hospital admission, attributable to compromised nutrient digestion and absorption. Undernourishment is significantly associated with worse prognosis, elevated incidence of chemotherapeutic problems, and increased morbidity, mortality. HGS has become such an important component of patient assessment may be the fact that muscle strength is typically a more relevant determinant of survival than muscle size. HGS could be by clinicians for the early identification of impairment or issues related to QoL. Also, patients with lower HGS may exhibit higher symptom burden. For these patients, early referrals through supportive or palliative care programs are indicated[8].

Malnutrition results from a deficiency of vital nutrients, resulting in inadequate protein consumption necessary for energy equilibrium and the preservation of muscle tone[9]. This study seeks to emphasize the significance of these measures, highlighting the nutritional support requirements of gastrointestinal cancer patients. Consequently, to effectively address this issue, the present randomized clinical trial (RCT) was formulated to examine the effects of ONS compared to dietary advice alone on primary endpoints, which include handgrip strength, quality of life and nutritional outcomes, as well as secondary endpoints such as chemotherapy tolerance and the incidence of adverse events.

MATERIALS AND METHODS

Study design: This was a prospective, and randomized controlled trial comparing ONS plus Nutrition advice versus with Nutrition advice alone in patients undergoing chemotherapy for gastrointestinal cancer for 12 weeks follow up. The study aimed to ascertain how oral nutrition supplements (ONS) affect GIT cancer patient's performance including hand grip and quality of life receiving chemotherapy ONS group in comparison to the control group (Non-ONS). Moreover, detailed adverse effect reported. Randomization was conducted in a 1:1 ratio via a web-based research randomizer[10].

This study was performed in Fayium Oncology Centre and the Oncology Department of Beni-Suef University Hospital and approved by institutional review board Research Ethical of the Faculty of Pharmacy of Beni-Suef University (F PH-BSU-HREC-000525) and Committee Faculty of Medicine Beni-Suef University (FM-BSU-REC/09072023/Rabie). This study registered at the clinical trials registry (ClinicalTrials.gov; NCT05980624). The study was conducted in compliance with the Declaration of Helsinki and its later amendments on ethical standards. This study investigating the use of ONS in gastrointestinal cancer patients undergoing chemotherapy[11].

Study population: The patients were enrolled if they were undergoing their first cycle of chemotherapy[19]. Cancer patients in the ONS group received nutritional guidelines and a daily oral intake of 500 mL of the balanced formula powder Ensure (Abbott Laboratories, USA) for 12 weeks during chemotherapy as nutritional support alongside regular meals. Balanced ONS offered a complete nutritional supplement of approximately 100 kcal energy, 3.72 g protein, 3.27g fat, 13.42 g carbohydrate, 1.01 g/100 mL of fiber, as well as vitamins and minerals per 100mL. Nutrition advice was defined as recommendations aimed at improving energy and nutrient intake through dietary changes, including the increase of protein-rich and high-fat foods. ONS Administered twice daily with the aim of attaining 500 mL each day[12,13]. All cancer patients were required to document their daily intake of ONS in a notebook, which was verified during their outpatient clinic visits, and refills were also computed to verify compliance. The control group patients received dietary guidance exclusively, which was similar to that provided to the ONS group. Furthermore, patients in both cohorts were monitored through weekly telephone interviews to assess and guide them regarding their specific interventions till their visit to the next chemotherapy cycle[14].

We encouraged all patients to consume regular meals as much as possible. ONS treatment was suspended or the dosage was lowered due to adverse effects, including diarrhea, stomach discomfort, and emesis. Throughout the study period, all patients were instructed to document their daily ONS intake in a notebook, which would be verified during their outpatient clinic visits. Patients in the control group received identical dietary recommendations as those in the ONS group. It was important to highlight that ONS treatment would be commenced in the control group participants upon a subsequent weight loss of 5% occurring within one month. Furthermore, all patients in both groups were monitored weekly via telephone communication to verify and direct their specific treatment[15]. For the biochemical tests, the following data were gathered total lymphocyte count (×103/μL), absolute neutrophil count (×103/μL), hemoglobin (g/dL) and hematocrit (%). The biochemical test results obtained every 3 weeks at 12 weeks follow up.

Inclusion Criteria: The trial enrolled patients with gastrointestinal (GI) cancer at any point throughout their first course of chemotherapy. Through radiological and pathological testing or clinical evaluation, the patient was diagnosed with cancer, either at any stage or with metastases. They were receiving different chemotherapy protocols according to tumor site and stage. Patients were adults above 18 in age. It was ensured that any necessary follow-up medical examinations and chemotherapy treatments were available. The oral formula was suitable for the patient's acceptability and performance level. There could only be a maximum of two Eastern Cooperative Oncology Group (ECOG) Performance Statuses. A life expectancy of at least three months was required. The participant provided written consent and was prepared to complete health, nutrition, and quality of life questionnaires in accordance with the specific guidelines set forth by the local Ethics Committee.

Exclusion Criteria: Patients were excluded if there was a documented allergic reaction or intolerance to the experimental chemicals or contained components. Patients who did not comply with trial conditions due to factors such as cognitive impairment, psychiatric or mood disorders, or alcohol dependence. Inappropriate for those who are pregnant or lactating. Furthermore, the investigator suspected that the patient possesses a physical or psychiatric condition that could hinder their participation in the study or that informed permission was not acquired. Individuals under 18 years of age were omitted. This indicated the necessity for total parenteral nutrition (TPN) due to a full inability to consume food normally and incapacity to ingest oral nutritional supplements.

Hand grip strength: The hand dynamometer was used to measure Hand grip strength (HGS). The dynamometers were calibrated before the initial measurement. Participants were seated on a standard-height chair devoid of armrests and appropriately positioned. The dynamometer's grip handle was modified according to the participant's hand size to provide an appropriate grasp position. Participants were instructed to utilize the non-dominant hand initially, followed by the dominant hand[16]. Three measurements of HGS were taken for each

hand, with a 10–20-second rest between the measurements to avoid fatigue. The highest value of all three measurements from both hands was obtained, then the Average maximum value of both hands evaluated[17]. HGS were assessed every 3 weeks during 12 weeks of follow up period

Quality of Life: The quality of life questionnaire-core 30 (QLQ-C30) developed by the European Organization for Research and Treatment of Cancer (EORTC) was employed to evaluate the quality of life of patients[18]. The QLQ-C30 scores at admission and after chemotherapy were collected. The questionnaire had 30 questions covering physical function (physical, role, cognitive, emotional and social), cancer-related symptoms (fatigue, pain and nausea/vomiting, dyspnea, insomnia, anorexia, constipation and diarrhea), and overall health. Each of the questions concerning physical function and cancer-related symptoms was rated from 1 (never) to 4 (always), while that for overall health was rated from 1 (very poor) to 7 (excellent). After patients completed the questionnaire survey, the original scores of each field were recorded and then converted to standard scores ranging from 0 to 100. Elevated scores in overall health and physical function suggested an enhanced quality of life; conversely, we employed reversed scores for cancer-related symptoms, where a higher symptom score denotes a superior quality of life[18]. QoL measurements in the three time points W0 at baseline start of 1st cycle chemotherapy, W6 at 6 weeks and W12 at 12 weeks.

Primary Outcome Measures: Hand grip strength (HGS) were measured every three weeks along 12 weeks follow up period. Nutritional status scores and health of quality of life were measured every six weeks and. In addition to information about demographics, including age, gender, chemotherapy type, social status, and education level was documented for all patients.

Secondary Outcome Measures: Biochemical Laboratory data were taken every three weeks. Complete blood count liver and kidney function were measured to evaluate the nutritional and hematological health of patients together with the activity of the disease. Furthermore, to underscore the risk of therapy-related adverse events assessed by the Common Terminology Criteria for Adverse Events (CTCAE) v5.0[15]. These adverse events led to therapeutic delays that may indirectly affect disease outcomes.

Statistical analysis

Sample Size Calculation

The statistical program G*Power (Heinrich Heine University, Düsseldorf, Germany) was used for sample calculation. With an alpha value of 0.05 (two-tailed) and a statistical power of 80%, there was a required sample size of 150 patients to conduct this study to reject the null hypothesis[19]. The sampling technique used was convenience sampling, which included all patients who had received chemotherapy for GI cancer.

Descriptive and Inferential Statistics

The statistical analysis employed a range of methods to assess categorical and numerical variables, as well as to model continuous

Table 1. Baseline characteristics of cancer patients.

Variables		Non-ONS (n=75)		ONS (n=75)		Test value	p-value
		No.	%	No.	%		
BMI	Normal≥(18.5-24.99)	36	48	43	52.7	5.581	0.14
	Overwight ≥25	13	17.3	18	20.7		
	Obese≥ 30	16	21.3	7	15.3		
	Uderwight ≤18	10	13.3	7	11.3		
Social status	Single	2	2.67	2	2.67	7.35	0.06
	Married	66	88	73	97.33		
	Divorced	7	9.33	0	0		
Education	Illiterate	41	54.67	29	38.67	8.22	0.05
	Elementary or below	16	21.33	30	40		
	High scool	4	5.33	7	9.33		
	Universty graduate	14	18.67	9	12		
Living status	Alone	3	4	2	2.67	4.47	0.19
	Spouse	64	85.33	67	89.33		
	Chlidren	6	8	6	8		
	Parents	2	2.67	0	0		
Smoking	Never	50	66	47	62.67	14.32	0.08
	Former >10years	3	4	5	6.67		
	Current smoking	22	29.3	23	30.67		
No. of children (median)		4	3 – 5	4	3 – 6	-1.71	0.09
Family history	Positive	27	36	19	25.33	2.01	0.157
	Negative	48	64	56	74.67		
ECOG Baseline	Asymptomatic	59	78.66	67	89.33	3.18	0.118
	Symptomatic but ambulatory	16	21.34	8	10.67		
Chemotherapy type	0	47	62.7	52	69.33	10.87	0.09
	1	22	29.3	17	22.67		
	2	6	8	6	8		

type 0 = Capecitabine containing regimens 1 =5 FU containing regimens 2 =Gemcitabine/Cisplatin
* Significant p-value at 0.05 levels
NRS: nutrition risk Assessment, MNA: mini nutrition assessment short form, MUST: malnutrition universal nutrition tool, BMI: body mass index

outcomes over time. For categorical data, the Chi-square test was used to examine associations, while Fisher's exact test was applied in cases of small expected frequencies to provide accurate significance estimates. For numerical data, the independent samples t-test was conducted as a parametric method for comparing mean differences between two independent groups, assuming normality and homogeneity of variance. In cases where these assumptions were violated, the Mann-Whitney U test was used as a nonparametric alternative to assess distribution differences.

To predict changes in continuous outcomes, linear regression was applied to determine the relationships between independent variables and the dependent variable, with model assumptions including linearity, independence, homoscedasticity, normality of residuals, and absence of multicollinearity. For repeated measurements over time, repeated measures ANOVA was performed to evaluate the main effects of time and group, as well as interaction effects between these factors on the outcome variables. Pairwise group differences were examined using post hoc comparisons with Bonferroni-adjusted p-values to account for multiple comparisons following ANOVA. Assumptions for this analysis included sphericity, independence, and normality within groups. Statistical analyses were conducted using IBM SPSS Statistics version 28, ensuring robust computations and appropriate visualization of results.

RESULTS

Baseline characteristics

The ONS and Non-ONS groups exhibited no significant differences regarding BMI, living status, family history, number of children, and Eastern Cooperative Oncology Group (ECOG) performance, as detailed in Table 1 Mean age.

Muscle strength Hand grip strength

The results that were presented in Table 2 and Table 3 explored the differences in hand grip strength over time between the nutrition support group ONS and the control group Non-ONS, using repeated measures analysis of variance (ANOVA) and post hoc analysis. Table 3 showed Repeated ANOVA for Hand Grip over Time. The repeated measures ANOVA revealed that the time variable alone did not exert a significant impact on hand grip strength ($F = 1.641$, $p = 0.193$), suggesting that over the course of 12 weeks, there was no significant change in hand grip strength associated with time. Additionally, the interaction between time and group (ONS vs. Non-ONS) was not significant ($F = 1.021$, $p = 0.366$), meaning that the change in hand grip strength over time did not differ between the two groups. However, the main effect of the group (gp) was significant ($F = 5.627$, $p = 0.019$), suggesting that there were differences in hand grip strength between the nutrition support group ONS and Non-ONS group, regardless of the time factor.

Results of Post Hoc Hand Grip Analysis for each group over time provides detailed post hoc comparisons of hand grip strength between time points within each group presented in Table 4. Non-ONS group showed significant decrease in hand grip strength which was observed between Time 4 and Time 5 (mean difference = 0.350, $p = 0.009$), and between Time 3 and Time 5 (mean difference = 0.570, $p = 0.033$). ONS group showed non-significant changes in hand grip strength were observed within the nutrition support group ONS at any time points, as all p-values were greater than 0.05 as presented Table 5.

Nutritional scores outcomes and Quality of life

QOL scores at baseline (W0), week 6 (W6) and week 12 (W12) were presented in Table 2. The global health status scores were increased only in the ONS group. The ONS group demonstrated significant effects on the global health status score, with a consistent increase observed in the ONS group compared to a steady decrease in the Non-ONS group. Furthermore, the functional domain encompassing physical, role, emotional, and cognitive aspects demonstrated a significant improvement in ONS scores relative to the baseline, with no change in Non-ONS group over 12 week's follow-ups. Detailed summary of results represented in Table 5. Detailed QOL presented in Supplementary S1.

Table 6 summarized the results of separate linear regression models assessing the effect of a nutrition support intervention (independent variable) compared to a control group on various clinical and quality-of-life outcomes. Each outcome variable was analyzed individually using both univariate and multivariate linear regression models. The multivariate models were adjusted for potential confounders, including sex, age, baseline Nutritional Risk Screening (NRS) score, and the baseline value of each respective outcome variable. The results showed improvement in overall quality of life in ONS group, these included the Global QLQ score (adjusted $\beta = 34.20$, $SE = 3.80$, $p < 0.001$), Symptoms QLQ (adjusted $\beta = 17.8$, $SE = 3.00$, $p < 0.001$), Functional QLQ (adjusted $\beta = 15.3$, $SE = 2.7$, $p < 0.001$), and Total QLQ score (adjusted $\beta = 22.4$, $SE = 2.6$, $p < 0.001$). In terms of nutritional status, the intervention led to significant reductions in scores NRS and MUST. There was improving in nutritional status among participants receiving nutrition support. This was corroborated by significant improvements in standardized nutritional screening tools, including NRS (adjusted $\beta = -1.451$, $p < 0.001$), MUST (adjusted $\beta = -0.618$, $p < 0.001$). In addition, there was improvement and increased in ONS group MNA (adjusted $\beta = 2.681$, $p < 0.001$) showed in Table 6. There was maintenance of ECOG performance status in the nutrition group, whereas the control group exhibited a detectable decline into grades 2 and 3, as shown in Figure 1. The improvement in nutritional status within the ONS group compared to the Non-ONS group was demonstrated by statistically significant differences in scores for MNA, MUST, and NRS, as shown in Figures 2, 3, and 4.

Detailed adverse effect with Biochemical Laboratory data

Detailed adverse effect in both groups was presented in Table 7 and Table 8. For grade 3-4 gastrointestinal toxicities, a higher percentage was also observed in group Non-ONS than in group ONS. The difference between both groups was statistically significant. Except for diarrhea, which was classified as Grade 3-4, was observed in ONS. A GIT cancer patient was worsened grade 3 mucositis in Non-ONS group. Overall, high-grade hematologic toxicities were more commonly detected in the Non-ONS group than in the ONS group. The observed difference was statistically significant, with a P value of 0.006. For example, anemia was observed more frequently within the Non-ONS cohort. Moreover, ANC and leucopenia grade 4-5 more observed in Non-ONS group with statistically significant difference between both groups. The outcomes for these documented toxicities were shown in Table 7 and Table 8. Detailed biochemical laboratory data in both groups presented in table 9 and supplementary S2.

DISCUSSION

In order to ascertain the effectiveness of a 12-week oral nutrition supplement intervention on hand grip strengths, quality of life and nutritional status in gastrointestinal cancer patients undergoing treatment, we conducted a randomized clinical trial. Loss of muscle function and Low QOL scores, substantial weight loss, and appetite loss were all common side effects of cancer treatment. Gastrointestinal problems such nausea, vomiting, and mucositis brought on by medication can cause appetite loss[20]. Oral nutrition supplements ONS-based was the most effective nutrition intervention has been proposed

Table 2. Hand grip strenght comparison over time at each time point every 3 weeks

	Non-ONS		ONS		t-test	p-value
	Mean	SD	Mean	SD		
Hand Grip baseline w0	18.28	4.92	19.66	4.76	-1.74	0.084
Hand Grip w3	17.62	4.53	19.86	5.33	-2.78	0.006*
Hand Grip w6	18.34	4.85	20.24	5.62	-2.21	0.029*
Hand Grip w9	18.12	4.56	19.83	5.62	-2.04	0.043*
Hand Grip w12	17.77	4.33	19.84	6.40	-2.32	0.022*
Hand Grip difference w12-w0	-0.51	3.42	0.18	4.33	-1.08	0.280

* significant p-value at 0.05 level, w week indicated at time interval from baseline week 3,6,9,12

Table 3. Repeated ANOVA for hand grip over time between ONS group and Non-ONS over 12 weeks

Source	Type III Sum of Squares	Mean Square	F	p-value
Time	27.219	12.521	1.641	0.193
Time-gp interaction	16.931	7.788	1.021	0.366
Gp	646.612	646.612	5.627	0.019*

* significant p-value at 0.05 level

Table 4. Post hoc hand grip analysis for each group over time

Time 1	Time 2	Mean Difference (time1-time2)	Std. Error	p-value	95% Confidence Interval for Difference	
Non-ONS						
W0	W3	0.668*	0.23	0.048*	0.004	1.333
	W6	-0.06	0.359	1	-1.098	0.979
	W9	0.16	0.38	1	-0.938	1.259
	W12	0.51	0.394	1	-0.631	1.651
W3	W6	-0.728	0.279	0.109	-1.535	0.079
	W9	-0.508	0.313	1	-1.413	0.397
	W12	-0.158	0.342	1	-1.147	0.83
W6	W9	0.22	0.111	0.512	-0.101	0.541
	W12	.570*	0.188	0.033*	0.027	1.113
W9	W12	.350*	0.102	0.009*	0.056	0.644
ONS						
W0	W3	-0.202	0.312	1	-1.104	0.701
	W6	-0.576	0.505	1	-2.036	0.885
	W9	-0.167	0.445	1	-1.455	1.122
	W12	-0.18	0.5	1	-1.627	1.267
W3	W6	-0.374	0.301	1	-1.245	0.497
	W9	0.035	0.253	1	-0.698	0.768
	W12	0.022	0.351	1	-0.993	1.036
W6	W9	0.409	0.282	1	-0.406	1.224
	W12	0.396	0.417	1	-0.81	1.601
W9	W12	-0.013	0.221	1	-0.653	0.626

W=week, * significant p-value at 0.05 level,

Table 5. The follow up changes of the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30) scores in both groups.

Variable	Non-ONS (n=75)			ONS (n=75)			p-Value		
	Mean ± SD			Mean ± SD					
	W0	W6	W12	W0	W6	W12	a	b	c
1-Global D	61.12±15.46	54.22±17.67	50.56±18.95	51.22±13.26	76.33±15.68	79.44±16.34	0.001*	0.001*	0.001*
Diff. w12-w0	-10.56±16.46			28.22±19.03			<0.0001*		
2- Functional	78.46±14.86	77.46±18.63	79.21±17.82	72.71±14.3	90.96±10.28	91.53±10.23	0.02*	0.001*	0.001*
Diff. w12-w0	0.76±11.435			18.81±13.89			<0.001*		
3- Symptoms	75.25±14.75	67.93±18.9	69.57±18.74	70.97±14.59	85.85±10.05	87.42±12.33	0.08	0.000*	0.000*
Diff. w12-w0	-5.68±13.11			16.44±14.03			0		
Total QOL	71.61±12.1	66.54±15.87	66.44±16.4	64.97±11.45	84.38±10.36	86.13±11.78	0.06	0.001	0.001*
Diff. w12-w0	-5.16±11.28			21.16±13.51			0.001*		

* Significant p-value at 0.05 level, D: domains, Financial difficulties, QOL Quality of Life

Supplementry S1. Detailed QOL Comparison in both groups

Variable	Non-ONS (n=75)			ONS (n=75)			p-Value		
	Mean ± SD			Mean ± SD					
	W0	W6	W12	W0	W6	W12	a	b	c
1-Global D	61.12±15.46	54.22±17.67	50.56±18.95	51.22±13.26	76.33±15.68	79.44±16.34	0.001*	0.001*	0.001*
Diff. w12-w0	-10.56±16.46			28.22±19.03			<0.0001*		
2- Functional	78.46±14.86	77.46±18.63	79.21±17.82	72.71±14.3	90.96±10.28	91.53±10.23	0.02*	0.001*	0.001*
Diff. w12-w0	0.76±11.435			18.81±13.89			<0.001*		
Physical	78.84±21.21	76.18±26.26	76.27±24.41	67.47±14.37	86.49±12.1	87.47±12.3	0.001*	0.001*	0.001*
Diff. w12-w0	-2.58±11.01			20±14.04			0.001*		
Role	73.11±26.55	75.11±26.19	77.33±23.35	64.22±24	90.44±19.41	90.89±19.24	0.03*	0.001*	0.001*
Diff. W12-W0	4.22±23.74			26.67±24.81			0.001*		
Emotional	75.22±24.2	75.67±24.56	77.67±23.28	75.11±2479	91.78±15.1	93.22±14.54	0.98	0.001*	0.001*
Diff. T3-T1	2.44±17.14			18.11±22.28			0.001*		
Cognitive	90.89±15.81	91.11±17.83	92±16.75	91.56±18.86	99.11±3.77	99.11±3.78	0.82	0.000*	0.00*
Diff. w12-w0	1.11±8.81			7.56±18.84			0.01*		
Social	76.89±24.18	72.67±23.99	68.89±26.89	70.67±19.34	92.89±13.75	91.33±17.62	0.08	0.000*	0.000*
Diff. w12-w0	-8±26.33			-20.67±22.4			0.000*		
3- Symptoms	75.25±14.75	67.93±18.9	69.57±18.74	70.97±14.59	85.85±10.05	87.42±12.33	0.08	0.000*	0.000*
Diff. w12-w0	-5.68±13.11			16.44±14.03			0		
Fatigue	65.48±24.48	59.55±27.26	63.26±25.77	61.63±20.36	79.7±17.65	84±20.03	0.29	0.000*	0.000*
Diff. w12-w0	-2.22±19.33			22.37±17.66			0.000*		
N/Vomiting	89.33±19.11	74.22±27.3	78.22±27.26	81.11±5.01	89.11±15.38	88.44±18.17	0.025*	0.001*	0.001*
Diff. w12-w0	-11.11±32.34			7.33±27.16			0.001*		
Pain	80.44±24.26	70.89±30.77	68.67±30.13	70.89±24.21	87.33±17.08	88.44±19.17	0.017*	0.001*	0.001*
Diff. w12-w0	-11.78±25.67			17.56±25.83			0.001*		
Dyspnea	79.56±31.43	80±32.42	80.89±30.1	84.89±26.45	92.89±15.78	92.±18.04	0.26	0.001*	0.01*
Diff. w12-w0	1.33±29.22			7.11±28.1			0.22		
Insomnia	48.89±39.26	46.67±41.37	45.78±41.65	46.67±40.27	82.22±28.12	84±26.49	0.73	0.001*	0.001*
Diff. w12-w0	-3.11±29.6			37.33±36.33			0.000*		
Anorexia	74.67±28.39	56.89±40.56	58.67±40.58	65.78±34.56	87.56±19.59	90.22±19.59	0.09	0.001*	0.001*
Diff. w12-w0	-16±31.12			24.44±35.23			0.000*		
Constipation	72±33.35	70.22±35.76	73.78±31.62	79.11±28.88	85.78±23.36	90.67±17.81	0.17	0.000*	0.001*
Diff. w12-w0	1.78±32.37			11.56±24.19			0.04*		
Diarrhea	96±16.4	92.89±16.71	95.11±17.06	85.78±31.08	87.11±24.44	84±25.91	0.01*	0.09	0.001*
Diff. w12-w0	-0.89±18.15			-1.78±29.96			0.83		
Financial	71.11±30.67	67.56±28.98	66.67±30.51	71.56±29.86	88.44±15.97	89.78±15.47	0.93	0.000*	0.001*
Diff. w12-w0	-4.44±19.25			18.22±31.14			0.0001*		
Total QOL	71.61±12.1	66.54±15.87	66.44±16.4	64.97±11.45	84.38±10.36	86.13±11.78	0.06	0.001	0.001*
Diff. w12-w0	-5.16±11.28			21.16±13.51			0.001*		

* Significant p-value at 0.05 level, D: domains, Financial difficulties, QOL Quality of Life

Table 6. Linear regression models to predict change in the following outcomes

Outcomes	Univariate linear regression				Multivariate linear regression			
	Beta	SE	p-value	95%CI	Adjusted Beta	SE	p-value	95%CI
Global QLQ	38.8	2.9	<0.001*	33.12,44.48	34.20	3.80	<0.001*	26.75,41.65
Symptoms QLQ	22.1	2.2	<0.001*	17.79,26.41	17.8	3.00	<0.001*	11.92,2368
Functional QLQ	18.1	2.1	<0.001*	113.98,22.22	15.300	2.700	<0.001*	10.01,20.59
Total QLQ	26.3	0.02	<0.001*	26.26,26.34	22.4	2.6	<0.001*	17.3,27.5
NRS	-1.853	0.26	<0.001*	-2.36, -1.34	-1.451	0.273	<0.001*	-1.99, -0.92
MUST	-0.853	0.166	<0.001*	-1.18, -0.53	-0.618	0.14	<0.001*	-0.89, -0.34
MNA	3.12	0.333	<0.001*	2.47,3.77	2.681	0.355	<0.001*	1.99,3.38

QLQ quality of life, NRS: nutrition risk Assessment, MNA: mini nutrition assessment short form, MUST: malnutrition universal nutrition tool. Beta, regression coefficient; SE, standard error; *, significant p-value at 0.05 level. CI confedence interval at 95%, The multivariate regression weights are adjusted to sex, age, baseline NRS, and baseline measured parameter.

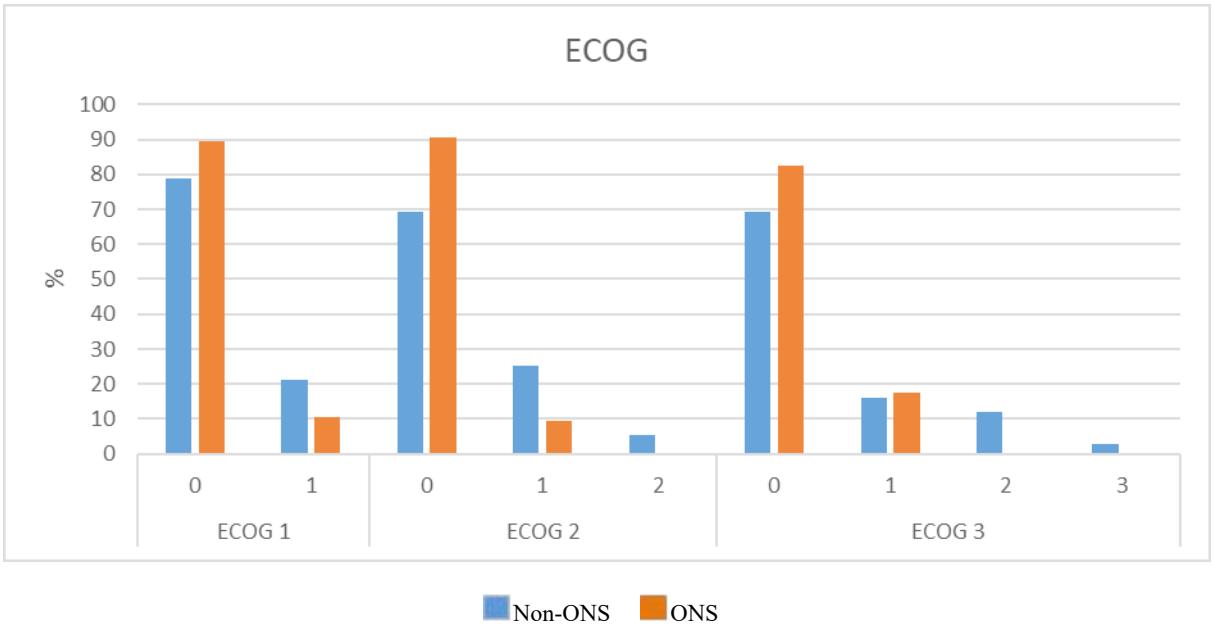

Figure 1. comparison ECOG performance in both groups

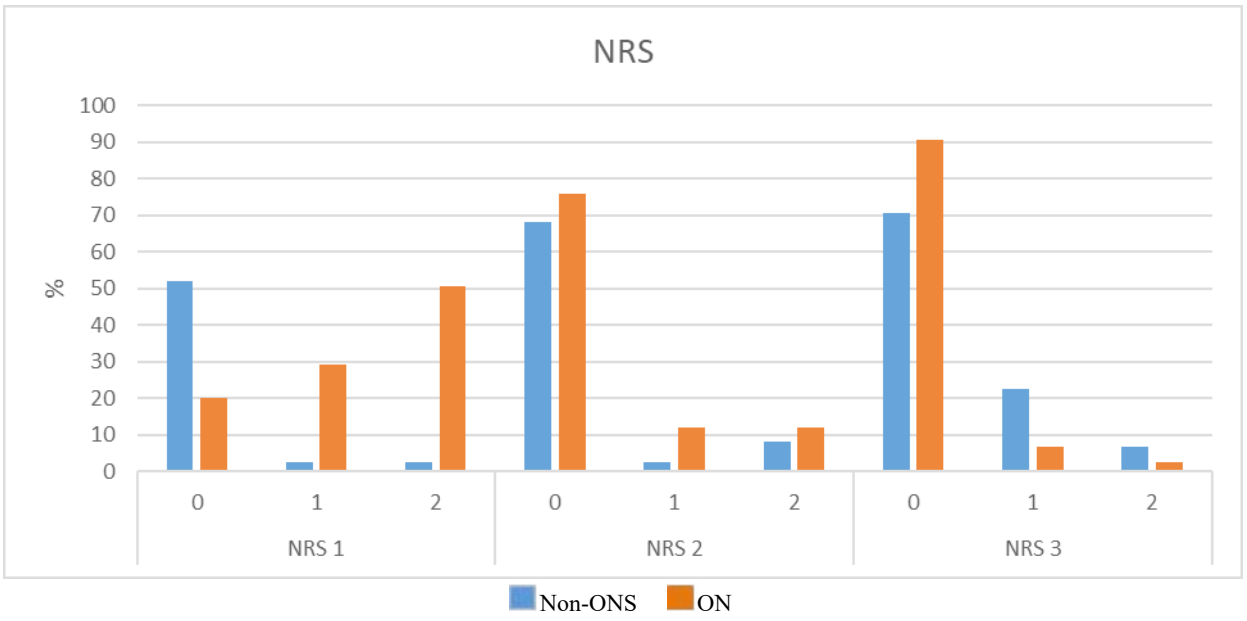

Figure 2. Nutrition risk score in both groups, NRS2002 nutritional risk screening 0= no risk/ low 1 = at risk 2 = High risk

to reduce these symptoms. In cases of cancer cachexia, severe weight loss and malnutrition frequently result in the cessation of cancer treatment, which lowers cancer survival. Thus, severe malnutrition and the related cancer fatalities may be avoided with nutrition screening and early nutrition management[21].

Muscle atrophy and diminished strength impact 20–70% of cancer patients, leading to tiredness, functional impairment, poor treatment tolerance, and heightened mortality risk[22]. Our findings indicate that one group, most likely the ONS group, had a better performance in hand grip strength than the Non-ONS group across all time points. Non-ONS group showed significant decrease in hand grip strength was observed this suggests that participants in the control group showed worsening in hand grip strength in the later stages of the study, with notable changes between the final time points. ONS group showed steady state in hand grip strength through any time points, as all. This indicates that the intervention-maintained hand grip strength over the 12 weeks when compared to baseline measurements. Moreover, it prevented worsening and maintained the hand grip strength this similar to the previous research[22]. These finding was matched with our previous published study which that indicated improvement in lean body mass in nutrition group[23].

Numerous QOL domains and subdomains improved after 12 weeks of ONS administration. One of the most crucial tools for cancer patients' pre-treatment concerns is their quality of life score. Previous literature that looked at the effectiveness of ONS undernourished cancer patients found that ONS arm group significantly improved QOL scores[24]. Scores related to role function, fatigue symptoms, nausea and vomiting, insomnia, and constipation all demonstrated improvements. According to a previous meta-analysis conducted to assess the effectiveness of home enteral nutrition on the quality of life (QOL) of gastrointestinal patients who are discharged, the nutrition group experienced enhancement in patient fatigue levels when compared to the control group similar with our result[25]. In line with earlier research,

we also discovered that ONS intervention reduced gastrointestinal symptoms like nausea, vomiting, and constipation[21]. Few researches look at the effectiveness of nutritional supplements on therapy-associated linked GI side events, even though numerous studies have found a positive correlation between nutritional supplements and QOL. Without affecting other metrics, nutrition intervention helped palliative cancer patients with their patient-rated nausea and vomiting symptoms. These findings imply that nutritional supplements may enhance certain aspects of quality of life, which require a mechanistic explanation supported by data[26].

With the exception of the oral balanced formula supplements supply in ONS group, which included instruction on how to improve total oral intake by consuming foods with elevated nutrient density and augmenting the frequency of meals and/or snacks. The ONS and Non-ONS groups in our trial got the same nutritional support. We postulated that ONS could help individuals who have had chemotherapy maintain their nutritional status. We showed that ONS oral nutrition supplement may, in fact, aid in improving the EORTC QLQ-C30's fatigue symptom and nutritional status scores. These side effects were particularly noticeable during the initial treatment cycle. The findings show that a variety of outcomes were positively and statistically significantly impacted by the nutrition support intervention. Most significantly, there were notable and substantial increases in quality of life outcomes as reported by patients. The Global QLQ score, Symptoms QLQ, Functional QLQ, and Total QLQ score were among them[11,27]. After 12 weeks, patients in the ONS had a higher chance of receiving 34.2 better global quality than those in the Non-ONS group, when baseline NRS, baseline total quality, gender, and age were considered. After 12 weeks, patients in the ONS had a larger chance of achieving 15.3 better function quality than those in the control group, when baseline NRS, baseline total quality, gender, and age were considered. Furthermore,

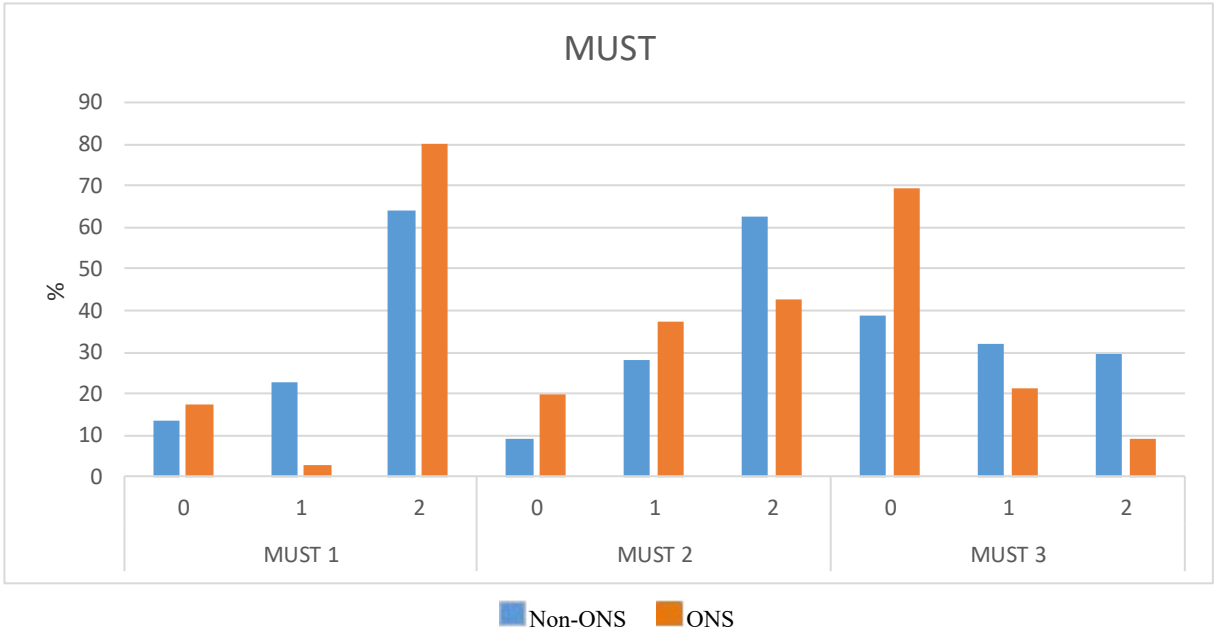

Figure 3. MUST Score in both groups 12 week, (0= no risk 1 = Moderate risk 2 = High risk)

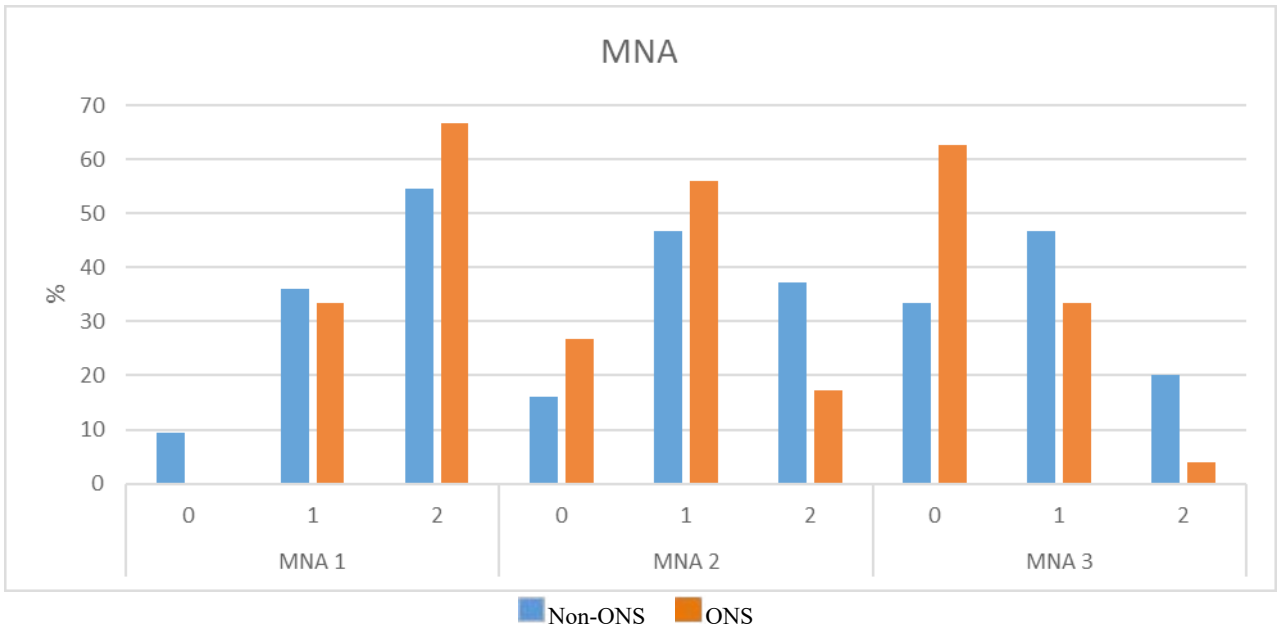

Figure 4. MNA score in both groups, (0= Normal nutrition atatus 1 = at risk of malnutrition 2 = Malnourished)

Table 7. GIT side effects in both groups

		Non-ONS (n=75)		ONS (n=75)		Test value	P-value
		No.	%	No.	%		
Nausea	N	21	28	29	38.7	21.89	<0.001*
	G1	29	38.7	43	57.3		
	G2	16	21.3	3	4		
	G3	6	8	0	0		
	G4	3	4	0	0		
Vomiting	N	22	29.33	45	60.00	19.9	<0.001*
	G1	28	37.33	23	30.67		
	G2	17	22.67	4	5.33		
	G3	5	6.67	3	4.00		
	G4	3	4.00	0	0.00		
Diarrhea	N	62	82.67	46	61.33	22.7	<0.001*
	G1	7	9.33	24	32.00		
	G2	6	8.00	0	0.00		
	G3	0	0.00	3	4.00		
	G4	0	0.00	2	2.67		
Constipation	N	44	58.67	55	73.33	9.72	0.014*
	G1	14	18.67	16	21.33		
	G2	15	20.00	4	5.33		
	G3	2	2.67	0	0.00		
Mucositis	N	62	82.67	72	96.00	7.75	0.034*
	G1	2	2.67	0	0.00		
	G2	9	12.00	3	4.00		
	G3	2	2.67	0	0.00		
Taste change	G1	5	6.67	2	2.67	1.35	0.44
Dry mouth	G1	23	30.67	22	29.33	0.03	0.86

N: not present, G1: grade 1, G2: geade 2, G3: grade 3, G4: grade 4.
* significant p-value at 0.05 level,

Table 8. Heamatological toxicity in both groups

variable		Non-ONS (n=75)		ONS (n=75)		Test value	P-value
		No.	%	No.	%		
Neutropenia							
Total Neutropenia	Y	24	32	23	30.67	0.03	0.86
	N	51	68	52	69.33		
Frequency	1	11	14.67	17	22.67	4.56	0.23
	2	11	14.67	4	5.33		
	4	2	2.67	2	2.67		
Neutropenia	G2	16	21.34	19	25.33	0.335	0.562
Frequency	1	11	14.67	15	20	3.84	0.262
	2	3	4	6	8		
	3	2	2.67	0	0		
Neutropenia	G3	4	5.33	4	5.33	0	1
Frequency	1	4	5.33	2	2.67	2.67	0.45
	2	0	0	2	2.67		
Neutropenia	G4	4	5.33	0	0	8.45	0.006*
Frequency	1	2	2.67	0	0	8.45	0.007*
	2	6	8	0	0		
Anemia							
Anemia G2	G2	47	62.67	45	60	0.112	0.74
Frequancy	1	9	12	7	9.33	8.14	0.15
	2	11	14.67	16	21.33		
	3	8	10.67	14	18.67		
	4	17	22.67	6	8		
	5	2	2.67	2	2.67		

Anemia G3	G3	12	16	8	10.67	0.923	0.337
	1	6	8	14	18.67		
Frequency	2	2	2.67	0	0	9.23	0.011*
	3	4	5.33	0	0		
	0	63	84	61	81.33		
Anemia G4-5	G4-5	5	6.67	0	0	5.17	0.058
Frequency	1	5	6.67	0	0	5.17	0.058
T. Anemia	Y	45	60	43	57.33	0.11	0.74
	N	30	40	32	42.67		
Frequency	1	9	12	7	9.33	21.5	<0.001*
	2	5	6.67	10	13.33		
	3	4	5.33	18	24		
	4	10	13.33	2	2.67		
	5	17	22.67	6	8		
Leucopenia							
Leucopenia	G2	16	21.33	18	24	0.152	0.7
Frequency	1	8	10.67	18	24	11.88	0.003*
	2	6	8	0	0		
	3	2	2.67	0	0		
Leucopenia	G3	10	13.33	8	10.67	0.25	0.62
Frequency	1	8	10.67	8	10.67	2.03	0.6
	3	2	2.67	0	0		
Leucopenia	G4	6	8	0	0	6.25	0.028*
Frequency	0	69	92	75	100	6.25	0.028*
	1	6	8	0	0		
Leucopenia	Y	22	29.33	22	29.33	0	1
	N	53	70.67	53	70.67		
Frequency	1	6	8	18	24	14.57	0.002*
	2	10	13.33	4	5.33		
	3	4	5.33	0	0		
	4	2	2.67	0	0		
Thrombocytopenia	G1	3	3.99	2	2.67	1.007	1
Frequency	1	2	2.67	2	2.67	1	1
	2	1	1.33	0	0		
Thrombocytopenia	G2	72	96	73	97.33	0.207	1
Frequency	1	3	4	2	2.67	0.2	1

N: not present, Y: present , NO: number, G1: grade 1, G2: grade 2, G3: grade 3, G4: grade 4,. * significant p-value at 0.05 level

Table 9. Prediction of the change in the biochemical laboratory. Delta change w15-w0 using ONS intervention as an independent variable versus Non-ONS

	Univariate analysis					**Multivariate analysis**				
	Beta	**SE**	**95% CI**		**p-value**	**Beta**	**SE**	**95% CI**		**p-value**
Heamoglobin g/dl	-0.07	0.2	-0.47	0.33	0.73	-0.33	0.26	-0.85	0.19	0.206
ANC /µL	-161.85	598.86	-1345.6	1021.84	0.787	349.94	604.96	-845.54	1545.42	0.564
WBCs(10^3 /µL)	-0.91	0.58	-2.05	0.24	0.119	-0.5	0.64	-1.76	0.76	0.434
Platelets (10^3 /µL)	39.57	22.05	-4.02	83.15	0.075	21.8	26.62	-30.8	74.4	0.414

Beta, regression coefficient; SE, standard error; *, significant p-value at 0.05 level. The multivariate regression weights are adjusted to sex, age, baseline NRS, and baseline measured parameter. WBC white blood cell, ANC absolute neutrophil count

Supplementry S2. Detailed laboratory data every three weeks in both groups.

	NON-ONS		ONS		t	p-value
	Mean	**SD**	**Mean**	**SD**		
HB 0	10.436	1.279	11.044	1.833	-2.356	0.020*
HB 1	10.293	1.119	10.781	1.500	-2.259	0.025*
HB 2	10.457	1.427	10.893	1.580	-1.774	0.078
HB 3	10.373	1.024	10.912	1.436	-2.645	0.009*
HB 4	10.379	1.157	10.651	1.472	-1.259	0.210
HB 5	10.296	1.164	10.573	1.318	-1.362	0.175
Delta	**-0.140**	**1.246**	**-0.471**	**1.888**	**1.269**	**0.207**
HCT 0	32.732	4.194	34.938	5.923	-2.632	0.009*
HCT 1	31.683	5.960	33.515	5.460	-1.963	0.052
HCT 2	32.085	6.773	34.384	5.004	-2.364	0.019*
HCT 3	32.801	4.901	34.500	4.853	-2.134	0.035*
HCT 4	31.912	6.105	34.181	5.270	-2.437	0.016*
HCT 5	31.455	6.400	33.307	5.828	-1.853	0.066
Delta	**-1.277**	**6.846**	**-1.631**	**7.718**	**0.297**	**0.767**
PLT 0	309.790	149.660	348.090	174.277	-1.444	0.151
PLT 1	286.670	113.739	315.050	155.809	-1.274	0.205
PLT 2	266.080	97.214	334.730	175.099	-2.969	0.004*
PLT 3	282.840	126.412	300.680	124.801	-0.870	0.386
PLT 4	266.450	133.308	295.720	118.171	-1.423	0.157
PLT 5	234.510	105.656	294.610	137.646	-3.000	0.003*
Delta	**-75.280**	**163.682**	**-53.480**	**162.308**	**-0.819**	**0.414**
WBC 0	6.293	2.503	7.231	3.187	-2.003	0.047*
WBC 1	5.665	2.383	6.166	2.686	-1.208	0.229
WBC 2	4.671	2.375	5.553	2.293	-2.314	0.022*
WBC 3	4.662	2.055	5.926	3.448	-2.727	0.007*
WBC 4	4.901	2.171	5.655	2.852	-1.823	0.071
WBC 5	5.180	3.094	5.618	3.349	-0.831	0.407
Delta	**-1.113**	**3.955**	**-1.613**	**3.838**	**0.785**	**0.434**
NEUT% 0	60.141	14.276	59.104	15.678	0.424	0.672
NEUT% 1	61.549	15.839	55.872	14.574	2.284	0.024*
NEUT% 2	54.472	17.867	54.986	16.440	-0.183	0.855
NEUT% 3	54.995	17.394	55.339	15.305	-0.129	0.898
NEUT% 4	59.050	17.493	60.188	13.267	-0.449	0.654
NEUT% 5	53.373	15.648	60.062	15.789	-2.606	0.010*
Delta	**-6.769**	**17.631**	**0.958**	**17.372**	**-2.704**	**0.008***
LYMPH% 0	30.348	11.591	31.240	12.823	-0.447	0.656
LYMPH% 1	29.069	12.059	35.276	13.511	-2.968	0.004*
LYMPH% 2	34.656	17.162	34.309	16.598	0.126	0.900
LYMPH% 3	33.974	15.473	33.781	13.894	0.080	0.936
LYMPH% 4	31.361	15.529	32.376	15.727	-0.398	0.691
LYMPH% 5	35.369	13.465	30.726	15.189	1.981	0.049*
Delta	**5.021**	**11.959**	**-0.514**	**16.690**	**2.335**	**0.021***
NLR RATI 0	2.638	1.981	2.355	1.437	1.001	0.319
NLR RATI 1	2.816	1.915	2.166	1.828	2.124	0.035*
NLR RATI 2	2.265	1.781	2.251	1.583	0.052	0.958
NLR RATI 3	2.203	1.628	2.138	1.445	0.258	0.797
NLR RATI 4	2.829	2.233	2.522	1.811	0.924	0.357
NLR RATI 5	2.284	1.900	3.155	2.603	-2.340	0.021*
Delta	**-0.354**	**2.146**	**0.799**	**2.366**	**-3.128**	**0.002***
RBCS 0	4.014	0.609	4.272	0.939	-1.998	0.048*
RBCS 1	3.905	0.489	4.168	0.533	-3.148	0.002*
RBCS 2	3.850	0.862	4.183	0.552	-2.820	0.006*
RBCS 3	3.870	0.549	4.124	0.526	-2.896	0.004*
RBCS 4	3.754	0.553	3.994	0.562	-2.643	0.009*
RBCS 5	3.859	0.693	4.005	0.532	-1.442	0.152

Delta	**-0.154**	**0.931**	**-0.267**	**0.992**	**0.717**	**0.474**
ANC 0	3970.727	2051.874	4461.260	2802.641	-1.223	0.223
ANC 1	3693.054	2254.857	3301.139	1373.724	1.285	0.201
ANC 2	2654.986	1864.651	3070.905	1692.710	-1.430	0.155
ANC 3	2638.176	1435.113	3586.413	2606.851	-2.760	0.007*
ANC 4	3032.187	1907.129	3692.858	2569.698	-1.788	0.076
ANC 5	3036.572	2534.964	3877.047	3788.465	-1.597	0.113
Delta	**-934.155**	**3609.060**	**-584.213**	**3797.768**	**-0.578**	**0.564**
creat 0	0.948	0.154	0.977	0.181	-1.041	0.300
creat 1	0.934	0.170	1.030	0.178	-3.403	0.001*
creat 2	0.900	0.135	0.991	0.169	-3.605	<0.001*
creat 3	0.942	0.156	1.034	0.156	-3.605	<0.001*
creat 4	0.939	0.164	1.008	0.151	-2.665	0.009*
creat 5	0.918	0.161	1.002	0.158	-3.218	0.002*
Delta	**-0.030**	**0.141**	**0.025**	**0.145**	**-2.363**	**0.019***
UREA 0	27.554	8.347	25.455	10.040	1.393	0.166
UREA 1	26.849	7.740	27.194	9.281	-0.247	0.805
UREA 2	25.619	8.024	23.986	7.199	1.312	0.192
UREA 3	25.280	7.274	27.916	10.285	-1.812	0.072
UREA 4	26.383	6.150	25.416	6.432	0.940	0.349
UREA 5	26.378	6.038	24.035	4.947	2.600	0.010*
Delta	**-1.176**	**8.387**	**-1.420**	**10.358**	**0.158**	**0.874**
ALT 0	27.221	16.314	24.760	15.061	0.960	0.339
ALT 1	34.532	34.352	25.180	18.136	2.085	0.039*
ALT 2	28.711	21.158	24.321	14.724	1.475	0.143
ALT 3	26.424	12.636	26.637	12.425	-0.104	0.917
ALT 4	27.224	11.779	27.155	16.482	0.029	0.977
ALT 5	26.145	12.944	26.461	17.597	-0.125	0.901
Delta	**-1.425**	**18.382**	**1.701**	**24.574**	**-0.882**	**0.379**
AST 0	25.728	14.237	25.539	17.236	0.073	0.942
AST 1	36.019	27.582	30.150	12.072	1.688	0.094
AST 2	32.537	19.572	29.068	10.060	1.365	0.175
AST 3	34.330	18.501	32.358	14.589	0.725	0.470
AST 4	33.496	13.770	32.264	13.966	0.544	0.587
AST 5	32.733	14.365	32.996	14.269	-0.113	0.911
Delta	**7.005**	**15.034**	**7.457**	**21.688**	**-0.148**	**0.882**
BIL DIRE 0	0.179	0.089	0.198	0.119	-1.135	0.259
BIL DIRE 1	0.213	0.081	0.198	0.100	1.052	0.294
BIL DIRE 2	0.238	0.148	0.655	2.892	-1.247	0.216
BIL DIRE 3	0.206	0.119	0.200	0.130	0.249	0.803
BIL DIRE 4	0.196	0.089	0.177	0.084	1.359	0.176
BIL DIRE 5	0.203	0.087	0.201	0.101	0.156	0.877
Delta	**0.025**	**0.130**	**0.003**	**0.147**	**0.966**	**0.336**
BILR TOTAL 0	0.611	0.272	0.521	0.226	2.216	0.028*
BILR TOTAL 1	0.670	0.373	1.764	7.375	-1.283	0.203
BILR TOTAL 2	0.695	0.301	0.554	0.274	2.988	0.003*
BILR TOTAL 3	0.490	0.223	0.503	0.235	-0.349	0.728
BILR TOTAL 4	0.657	0.294	0.522	0.221	3.176	0.002*
BILR TOTAL 5	0.582	0.248	0.606	0.219	-0.621	0.535
Delta	**-0.029**	**0.360**	**0.085**	**0.264**	**-2.218**	**0.028***

The independent t-test was used; *, significant p-value at 0.05 level. HB hemoglobin, HCT hematocrit, WBC white blood cell, ANC absolute neutrophil count, Lymph lymphocyte, Neutrophil, NLR neutrophil lymphocyte ratio, creat. serum creatinine, direct bilirubin, total bilirubin total, ALT alanine Alanine Aminotransferase, AST Aspartate Aminotransferase, (0) baseline, (1) week three, (2) week 6, (3) week 9,4-week (12), (5) week 15. Delta difference (w15-w0).

Patients in the ONS group had a greater chance of seeing a 17.8 improvement in their symptoms. These results imply that nutrition support has a significant and wide-ranging effect on enhancing patients' overall functioning, symptom burden, and perceived well-being. Only weariness in the symptomatic scales category exhibited the ONS-specific effect when the EORTC QLQ-C30 (version 3.0) was employed to assess quality of life. Cancer patients most frequently feel fatigue during treatment, which impairs everyday functioning and lowers overall quality of life[28]. This aligns partially with prior reports indicating that the Office for National Statistics (ONS) noted improvements in fatigue and appetite loss among cachectic cancer patients receiving palliative care[28,29], thereby enhancing the overall quality of life for patients with unresectable pancreatic tumor[18].

In our study, the physical function and role function scores of the ONS group following nutritional therapy were significantly higher than those of the Non-ONS group. This finding corresponds with a previous study indicating that the improvement of physical function scores in nutritional intervention groups resulted from increased muscle strength in gastrointestinal cancer patients[30]. Patients in the ONS group may reduce the risk of physical impairment and demonstrate enhanced performance status and role function in their daily activities.

Addressing the symptom scale, individuals in the ONS group reported a reduction in postintervention scores for fatigue, pain, and insomnia, in contrast to the Non-ONS group. Our findings align with prior studies, which demonstrated that nutritional therapy interventions help alleviate pain and appetite loss, as well as enhance tiredness symptoms and overall quality of life in cachectic cancer patients[11,29]. The majority of advanced-stage cancer patients typically experience diminished appetite, exhaustion, pain, and weakness, forming a recognizable symptom cluster for cancer anorexia-cachexia. In addition to physical symptoms, cancer-related fatigue is associated with cognitive impairments, sleeplessness, and mental health issues such as anxiety and depression, as well as diminished quality of life. Our study suggests that an early individualized nutritional intervention during chemotherapy is feasible to improve the dietary intake as well as the QoL, especially among those prone to suffer from malnutrition and to report the worse QoL.

In terms of nutritional status, the intervention led to significant reductions indicating improved nutritional status among participants receiving nutrition support. This was corroborated by significant improvements in standardized nutritional screening tools, including NRS, MUST and MNA[31,32]. Although the malnutrition resulting from cancer cachexia is distinct from other disease-related or age-related malnutrition, there is a lack of nutrition screening methods specifically tailored for cancer patients. This study revealed a substantial difference in nutritional status scores between the two groups[33].

A different research investigation indicated that cancer patients undergoing nutritional intervention exhibited elevated white blood cell and platelet counts in comparison to those getting standard therapy alone. (Yang et al., 2020) in concordance with our study showed grade 4 neutrophilia and leucopenia with more frequent predominant in Non-ONS group. On the other hand, thrombocytopenia did not show significant different. Malnutrition in cancer patients correlates with diminished treatment tolerance, heightened risk of infections and complications, extended hospital stays, and elevated mortality rates[34].

This study had several limitations. Initially, the study participants were diagnosed with varied forms of gastrointestinal cancer, which may have led to disparate reactions to nutritional intervention, resulting in significant variances in numerous markers, despite good compliance among those who completed the trial. The findings were assessed within a brief timeframe, specifically three months post-intervention. Consequently, future nutritional intervention studies may employ the Randomized Controlled Trials design with a substantial sample size to enhance the reliability of the results. The findings of this study offer significant evidence for physicians, public health practitioners, and policymakers to implement early individualized nutritional counseling that improves both patients' nutritional metrics and their quality of life. Nutritional therapy markedly enhanced the quality of life of the intervention group. We were unable to compute the calorie values of the patients' daily meals post-discharge. The distinction in total caloric intake between the ONS and Non-ONS groups remains ambiguous; there may be a bias in the treatment arm, as patients in the ONS group might have consumed more calories than those in the control group, not due to the nutrition formula itself, but rather due to heightened nutritional awareness.

CONCLUSION

Nutritional treatment supplements preserve muscle strengths and enhance the quality of life across all dimensions and diminished unpleasant symptoms in individuals with gastrointestinal cancer. Early personalized dietary assistance, in conjunction with specialist nutritionists during chemotherapy, was essential for enhancing patients' quality of life and treatment results. These data robustly endorsed the implementation of ONS alongside dietary guidance for patients with GIT cancer.

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