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Original Article

Effect of enteral nutritional support on nutritional status of patients with gastric cancer receiving chemoradiotherapy after gastrectomy

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Abstract

Aim: To evaluate the effects of enteral nutritional support in gastric cancer patients who received chemoradiotherapy (CRT) after gastrectomy.

Materials and Methods: Patients who underwent total/subtotal gastrectomy due to gastric cancer and received postoperative CRT between January 1, 2010 and December 31, 2015 at Zonguldak Bülent Ecevit University Faculty of Medicine General Surgery Clinic were included in the study. The nutritional risk of patients was recorded using NRS-2002. The values of patients at the scheduled routine clinical follow-up at the end of the first year were compared with baseline values.

Results: While 64.7% (n=22) of the patients continued to receive enteral nutritional support regularly (CNS group), 35.3% of the patients (n=12) discontinued nutritional support (DNS group). Patients in the DNS group had significantly lower baseline NRS-2002 scores (p=0.049). The NRS-2002 score of the CNS group decreased significantly at follow-up compared to the pre-CRT values. At the end of the first year, statistically significant increases were found in body weight, body mass index, transferrin level and vitamin D level of both patient groups. While the mean RBC count decreased significantly in the CNS group (p=0.002), there was no significant difference in the DNS group (p=0.382). When the amount of temporal change in RBC was evaluated, there was a significant difference between the DNS and CNS groups. Although vitamin B12 level and urea level increased in both groups, this increase was significant only in the DNS group (p = 0.049).

Conclusions: In this study, it was determined that gastric cancer patients who continued enteral nutrition in the first year after CRT had significantly higher nutritional risk before CRT. Enteral nutrition reduces nutritional risk and shows positive results on nutritional parameters such as body weight, ferritin, transferrin, vitamin D, vitamin B12.

Keywords: Enteral nutrition; chemoradiotherapy nutritional risk screening; stomach cancer

INTRODUCTION

Nutritional status is often negatively affected by chemoradiotherapy treatment after gastric cancer surgery. In addition to their direct detrimental effects, these treatments may significantly influence nutrition in the early and mid-term, furthering the negative effects suffered by patients; thereby worsening prognosis and reducing survival (1-4). Malnutrition after stomach cancer surgery leads to increases in mortality and morbidity. Therefore, clinicians aim to provide nutritional support to stomach cancer patients if possible (5).

Determining the nutritional risks of patients before surgery is important to evaluate the nutritional support needs of patients. Studies have shown that nutritional risk assessment results are related to the frequency of postoperative complications, duration of hospitalization, prognosis and survival of the disease (6,7). Nutritional Risk Screening 2002 (NRS-2002) is a widely used method in determining the nutritional risk of patients (8). With the nutritional risk screening performed in the early period, the nutritional risk level of patients can be determined before surgery / CRT. These results also contribute to the prediction of prognosis and the determination of post-treatment nutritional requirements of patients; so that the nutritional support options can be assessed and patients may receive the most appropriate support before and immediately after surgery, and also in the long-term (9,10). Critical nutritional support in cancer patients is considered as part of anti-cancer therapy (11). Moreover,

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it has been reported that the importance of an enriched diet in at-risk patients (even before scheduled treatments) can not be overstated; however, currently there is a lack of data on risk assessment and treatment adjustments of patients, especially in the long-term; thus, there is little evidence-based opinion on this matter (6,7).

In the multimodal oncological therapy process, monitoring of nutritional status is critical in preventing or minimizing treatment-related malnutrition. The aim of this study was to evaluate the effects of enteral nutritional support in gastric cancer patients who received CRT after gastrectomy.

MATERIALS and METHODS

Patients who underwent total / subtotal gastrectomy due to gastric cancer and received postoperative CRT between January 1, 2010 and December 31, 2015 at Zonguldak Bülent Ecevit University Faculty of Medicine General Surgery Clinic were included in the study. The nutritional risk of patients was recorded using NRS-2002 before receiving CRT, and all the measurements in the tables were also recorded. Afterwards, enteral nutrition solution providing 330 kcal per serving (containing 11 g fat, 37 g carbohydrate, 20 g protein, 500 IU vitamin D, and calcium) was given 3 doses per day. All measures of patients were repeated at the routine clinical follow-up at the end of the first year, and comparison with baseline values was performed. When comparing, patients that discontinued enteral nutrition within one year were grouped as the "Discontinued Nutrition Support" (DNS) group, and patients who continued to receive enteral nutrition were grouped as "Continued Nutrition Support" (CNS) group. Patients who developed metastasis during follow-up were excluded from the study. Ethics committee approval was obtained from the Ethics Committee of Zonguldak Bulent Ecevit University (Approval no: 2020/04, Date: 19/02/2020). Informed consent was obtained from all individual participants included in the study.

Determination of nutritional risk (NSR 2002)

The first step in evaluating nutritional risk with the NRS-2002 is determining whether the patient in question fulfills any of the following criteria (8):

- BMI value less than 20.5 kg/m^2,
- Having lost weight in the last 3 months,
- Decreased food intake in the last week,
- Severe disease status (usually considered as ICU admission).

If none of these criteria are fulfilled, the patient is defined to have low risk. However, if any of these criteria are present, the second step of the NRS-2002 is performed by the evaluation of age the characteristics given in Table 1. A score lower than 4 indicate low risk, 4 points indicates at-risk, and greater than 4 points (up to a maximum of 7) indicates high risk.

Table 1. The Nutrition Risk Screening 2002 (NRS-2002) (8)

Nutritional Status		Severity of Disease	
Score	**Sign**	**Score**	**Sign**
0: Absent	Normal nutritional status	0: Absent	Normal nutritional requirements
1: Mild	Weight loss > 5% in 3 months or food intake below 50%–75% of normal requirements	1: Mild	Hip fracture, chronic patients, in particular acute complications: cirrhosis, COPD, chronic hemodialysis, diabetes, oncology
2: Moderate	Weight loss > 5% in 2 months + impaired general condition or food intake 25%–60% of normal requirement in preceding week	2: Moderate	Major abdominal surgery, stroke, severe pneumonia, hematological malignancy
3: Severe	Weight loss > 5% in 1 month (>15% 3 months) or BMI < 18.5 + impaired general condition or food intake 0%–25% of normal requirement in preceding week.	3: Severe	Head injury, bone marrow transplantation, intensive care patients (APACHE > 10)
Total score		Total score	

Calculate the total score: 1. Find score (0–3) for Impaired nutritional status (choose the highest score) and Severity of disease; 2. Add the two scores as total score; 3. If age ≥ 70 years: add 1 to total score above

Statistical Analysis

All analyses were performed on SPSS ver. 21 (SPSS Inc., Chicago, IL, USA). For the normality check, the Shapiro-Wilk test was used. Data are given as mean ± standard deviation or median (minimum - maximum) for continuous variables with regard to the normality of distribution, and as frequency (percentage) for categorical variables. Parametric tests were preferred for the comparison of normally distributed variables, and non-parametric tests were preferred for the comparison of non-normally distributed variables. Age comparisons were done with the independent samples t-test. Normally distributed variables with repeated measurements were analyzed with two-way repeated measures analysis of variances (ANOVA). Non-normally distributed variables were compared with the Wilcoxon Signed Ranks test for repeated measurements. Between-groups comparison of these variables was performed by analyzing differences between measurements with the Mann Whitney U test. Categorical variables were evaluated by the use of Chi-square tests or Fisher's exact test. Two-tailed p-values of less than 0.05 were considered statistically significant.

RESULTS

Of the 34 patients included in the study, 70.6% (n = 24) were male, 29.4% (n = 10) were female, and the mean age was 56.6 ± 9.7 years. While 64.7% (n = 22) of the patients continued to receive enteral nutritional support regularly (CNS group), 35.3% of the patients (n = 12) were found to have discontinued nutritional support (DNS group).

Table 2. Summary of patients' characteristics and some blood values with regard to nutrition support status

	Nutrition Support		
	Discontinued (n=12)	Continued (n=22)	p (between groups)
Age	51.67 ± 12.34	59.32 ± 6.72	0.065
Gender, Male	9 (75.00%)	15 (68.18%)	1.000
Chronic Disease	3 (25.00%)	10 (45.45%)	0.292
Surgery			
Total	5 (41.67%)	3 (13.64%)	0.098
Subtotal	7 (58.33%)	19 (86.36%)	
Osteoporosis	5 (41.67%)	9 (40.91%)	1.000
Follow-up Time	4 (2 - 8)	4 (2 - 6)	0.709
NRS-2002			
Before	0.5 (0 - 3)	2 (0 - 4)	0.309
After	0 (0 - 3)	1 (0 - 4)	
p (within groups)	0.157	**0.013**	
Weight			
Before	64.5 (48 - 120)	54.5 (33 - 70)	0.136
After	67.5 (50 - 120)	56.5 (37 - 70)	
p (within groups)	**0.011**	**<0.001**	
Body Mass Index			
Before	24.02 ± 5.61	20.16 ± 3.55	0.100
After	24.76 ± 5.23	21.47 ± 3.38	
p (within groups)	**0.010**	**<0.001**	
WBC			
Before	6.65 (3.1 - 9.2)	5.4 (2.5 - 14.1)	0.901
After	6.4 (4.8 - 12.7)	6.05 (3.5 - 9.6)	
p (within groups)	0.146	0.101	
Haemoglobin			
Before	12.03 ± 1.08	12.45 ± 1.44	0.157
After	12.52 ± 1.00	12.30 ± 1.39	
p (within groups)	0.172	0.585	
RBC			
Before	4.15 ± 0.58	4.29 ± 0.61	**0.010**
After	4.24 ± 0.53	4.03 ± 0.52	
p (within groups)	0.382	**0.002**	
Serum Iron			
Before	77.29 ± 27.13	73.82 ± 35.72	0.953
After	92.67 ± 31.81	90.00 ± 31.99	
p (within groups)	0.169	0.053	
Ferritin			
Before	18.65 (5.4 - 545)	45.7 (5 - 344.7)	0.074
After	26.35 (5 - 374)	50.45 (5.4 - 653.7)	
p (within groups)	0.638	**<0.001**	
Transferrin			
Before	177.5 (97 - 217)	181 (57 - 307)	0.131
After	199 (104 - 253)	203 (45 - 298)	
p (within groups)	**0.002**	**0.004**	

Data are given as mean ± standard deviation or median (minimum-maximum) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables

Table 3. Summary of patients' measurements with regard to nutrition support status

	Nutrition Support		
	Discontinued (n=12)	Continued (n=22)	p (between groups)
Vitamin D			
Before	7.65 (2.5 - 59.9)	8.2 (4 - 21.8)	0.191
After	28 (8.7 - 75.9)	30.6 (6.4 - 41.5)	
p (within groups)	**0.002**	**<0.001**	
Vitamin B12			
Before	177.5 (60 - 1500)	282 (75 - 1099)	0.606
After	224.5 (72 - 2000)	429 (100 - 1288)	
p (within groups)	**0.049**	0.064	
Folate			
Before	11.7 (0.8 - 21.36)	19.01 (8.35 - 24)	0.217
After	11.45 (8.72 - 20.1)	16.53 (7.59 - 24)	
p (within groups)	0.441	0.126	
Calcium			
Before	9.11 ± 0.56	9.04 ± 0.83	0.892
After	9.24 ± 0.40	9.15 ± 0.84	
p (within groups)	0.358	0.310	
Albumin			
Before	3.95 (3.3 - 4.7)	4 (1.7 - 4.8)	0.901
After	3.95 (3.1 - 4.6)	4 (1.7 - 4.8)	
p (within groups)	0.305	0.141	
Total Protein			
Before	7 (5.5 - 11.26)	6.9 (5.5 - 7.9)	0.845
After	6.85 (5.3 - 7.8)	6.8 (4.5 - 7.9)	
p (within groups)	0.183	0.076	
LDL			
Before	197 (131 - 250)	191.5 (131 - 243)	0.102
After	182 (131 - 310)	189 (127 - 336)	
p (within groups)	0.530	0.194	
HDL			
Before	61.5 ± 20.43	60.14 ± 18.44	0.796
After	64.00 ± 22.64	63.76 ± 16.19	
p (within groups)	0.472	0.173	
Triglyceride			
Before	74.5 (43 - 142)	79 (36 - 494)	0.365
After	69 (41 - 124)	78 (43 - 254)	
p (within groups)	0.409	0.520	
Urea			
Before	30.50 ± 9.47	30.86 ± 9.64	0.177
After	35.83 ± 12.01	31.73 ± 8.70	
p (within groups)	**0.049**	0.657	
Creatinine			
Before	0.85 (0.5 - 1.5)	0.8 (0.5 - 1.5)	0.231
After	0.85 (0.6 - 1.3)	0.7 (0.5 - 1.4)	
p (within groups)	1.000	**0.004**	

Data are given as mean ± standard deviation or median (minimum - maximum) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables

With regard to groups, 75.0% of the patients in the DNS group were male (n = 9), and the average age was 51.67 ± 12.34 years. Whereas, 68.2% of patients in the CNS group were male (n = 15), and they had an average age of 59.32 ± 6.72 years (Table 2).

Patients in the DNS group had significantly lower baseline NRS-2002 scores (p = 0.049, Figure 1). The NRS 2002

scores of patients in the CNS group were found to have decreased significantly at follow-up compared to pre-CRT (p = 0.013). This difference was not significant between DNS and CNS groups (p = 0.309). At the end of the first year, body weight, BMI, transferrin level, vitamin D level of both patient groups increased significantly (p<0.05). The average red blood cell count (RBC) of patients in the CNS group decreased from 4.29 ± 0.61 to 4.03 ± 0.52 x 10^6 (p = 0.002). In the DNS group, no significant difference was found between the two RBC values.

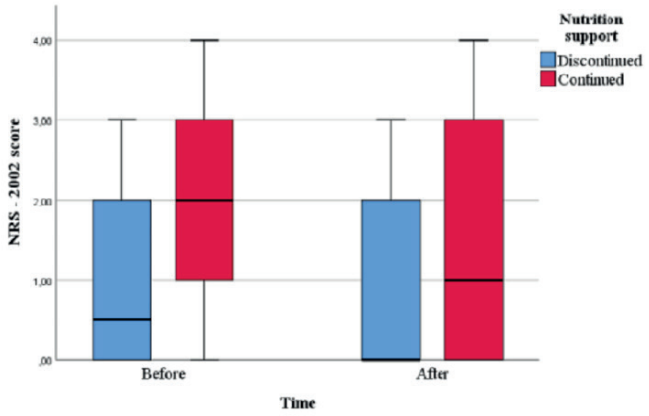

Figure 1. NRS – 2002 scores regard to support status

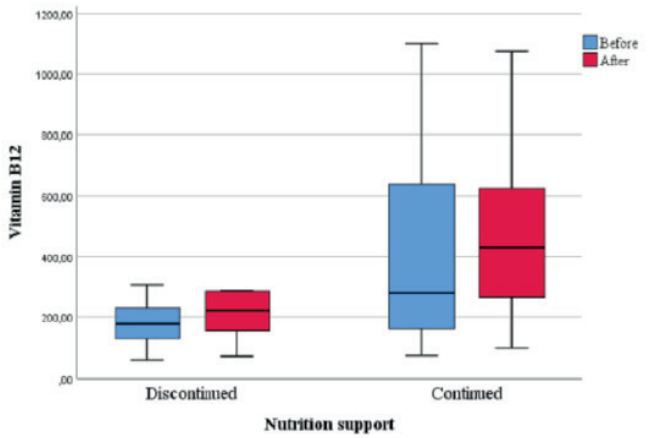

Figure 2. Vitamin B12 levels regard to support status

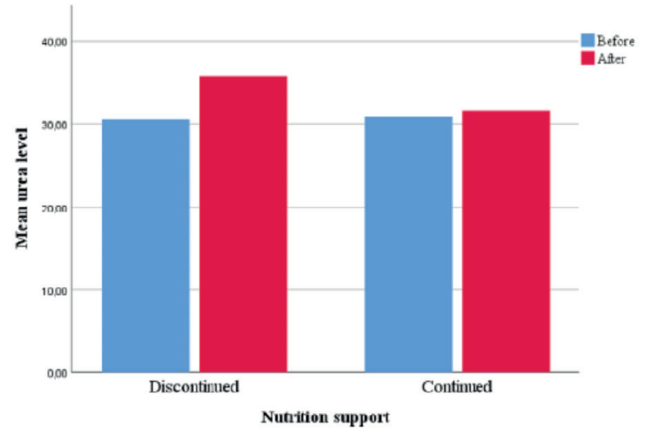

Figure 3. Urea levels regard to support status

The amount of temporal change in RBC in the DNS and CNS groups demonstrated a statistically significant difference (p = 0.010). Although vitamin B12 and urea levels increased in both groups, this increase was statistically significant only in the DNS group (p = 0.049, Figure 2, Figure 3). While the creatinine level of patients in the CNS group decreased significantly (p = 0.004), the creatinine level of patients in the DNS group did not change significantly (Table 2, Table 3).

DISCUSSION

It is known that gastric cancer patients receiving adjuvant CRT after surgery should be carefully monitored for malnutrition, especially during the first year after the operation. In this study, in which the effects of enteral nutritional supplement initiated before CRT (after gastrectomy) on treatment results were examined, nutritional risk was determined to be significantly decreased at the end of 1 year in the CNS group. While there was a statistically significant increase in the weight, BMI, transferrin, vitamin D, vitamin B12, urea levels of patients in the DNS group, no significant change was observed in other parameters. In the CNS group, the increase in weight, BMI, transferrin, ferritin, vitamin D parameters and decrease in NRS-2002 score, RBC value, and creatinine levels were statistically significant. Although not clinically significant, it was determined that only the amount of change in RBC showed a significant difference between groups.

In gastric cancer cases, various nutritional problems are encountered as a result of the disease and its indirect effects. These problems manifest by various symptoms, the most probable being weight loss. Although depending on the amount of decrease, the loss of weight seen in these patients negatively affects the prognosis of the disease and survival (1,12). After the operation, the continuation of nutritional problems bring with it varying degrees of weight problems. Davis et al., in their study where they examined factors affecting weight loss after gastrectomy, reported that BMI and weight reduction that developed within 12 months after gastrectomy were associated with preoperative BMI and extensive gastric resection (2). In different studies, it has been shown that the decrease in BMI observed after gastric cancer surgery is associated with CRT and may affect the prognosis of the disease (3,4,13). Routine dietary support was not provided in these studies. Patients who were followed up with enteral nutrition support after gastrectomy have been shown to improve their acute and long-term nutritional status (14,15). Although the effect of enteral nutrition on the nutritional status and weight of patients is positive (with regard to supportive characteristics and patient compliance), this type of support has only been shown to decrease the amount of weight loss (16). In addition, while the nutritional status very often worsens in the early period after gastrectomy, it was reported that patients recovered from this state within a year (9). In our study, it was determined that body weight and

BMI values in both groups significantly increased in the first year after surgery. This situation was observed in both groups, probably due to the fact that patients who discontinued nutritional support had received nutritional support for a certain period of time. In addition, weight loss can be observed after stomach cancer operations due to postoperative complications (17). In this study, postoperative complications were not examined, which is a limitation. At this point, it is important to note that the extent of gastrectomy (total or subtotal) has little to no effect on weight change (18).

Nutritional problems often bring with them deficiencies in essential nutrients. In cases where enteral nutrition support is not provided after gastrectomy, parameters such as transferrin, ferritin and B12 have been shown to decrease (19,20). Seo et al. showed that vitamin B12 and ferritin levels did not change during the follow-up after gastrectomy, while transferrin level increased over time. They also reported that the use of supplements provided effective support for gastrectomy patients (21). The change in acidic composition after gastrectomy disrupts iron absorption, and decreased intrinsic factor negatively affects the absorption of vitamin B12 (19). There are studies in which low levels of iron and vitamin B12 parameters are shown in different types of gastrectomy operations (18). The most frequent nutritional defects reported by these studies are vitamin B12, folate, iron, calcium and vitamin D (22,23). Therefore, it is important to provide these components with enteral nutrition support in the early period to prevent or reduce deficiencies of these essential nutrients (24). In the postoperative period, enteral supplement support rapidly regulates these parameters (24,25). In our study, it was determined that transferrin and vitamin D values were significantly increased in both groups, ferritin increased only in the CNS group and vitamin B12 increased only in the DNS group. Malnutrition encountered after gastrectomy is affected by factors such as surgical procedure, age, CRT dose, duration of treatment, and preoperative nutritional status (19,26). In addition, it was reported that the patients who received enteral nutrition support in the preoperative period had better postoperative results, which seems to be an additional advantage (27). The effect of these variables on the results was not evaluated in our study.

Positive changes in various parameters are observed as a reflection of the treatment after successful gastric cancer treatment. Mutawa et al. reported that the frequency of patients with low RBC levels increased after gastrectomy by 7% in the first 6 months, and by 15% after 5 years (28). Nozali et al. reported that RBC, hemoglobin and hematocrit values continued to decrease for 3 years in patients who underwent total gastrectomy (29). In different studies, the postoperative decrease in RBC value was shown in patients undergoing gastrectomy for gastric cancer (30). In our study, it was determined that the RBC value of the patients in the CNS group decreased significantly, while the RBC value of the patients in the DNS group did not decrease significantly. It was thought that this difference between the two groups may be due to the small number of patients evaluated in the study, or that the patients in the DNS group did not continue enteral nutrition because they had better regression of RBC decrease. In addition, patients in the DNS group had significantly lower nutritional risk levels before CRT. In several studies, high nutritional risk has been associated with negative results after gastrectomy (6,7). This may have contributed to the lower RBC level in the CNS group.

After stomach cancer treatment, the nutritional risk of patients who receive regular nutritional support will decrease. In studies conducted with patients with gastric cancer, nutritional risk assessed by NRS-2002 in the pre-treatment period was found to be related to postoperative well-being of the patients and benefited prognosis (6,7). In the literature review, there was not any study evaluating nutritional risk with NRS-2002 before and 1 year after treatment. In our study, it was determined that the NRS-2002 scores of patients in the CNS group decreased significantly. It was determined that the nutritional risk scores evaluated at the beginning were worse in the CNS group, and the score in the DNS group was very close to '0', which is the lowest level of the scale. The decrease in the NRS 2002 score in the DNS group was not significant, probably because the pre-CRT NRS 2002 score of this group was quite close to the lowest value that can be obtained from the scale. The severity of the disease and nutritional status, which are the parameters examined in NRS 2002, improved positively in both groups after gastric cancer treatment.

LIMITATIONS

The retrospective design and single-centeredness of this study are important limitations. Since patients with metastasis and those that died were excluded from the study, the results of the patients evaluated in the study may seem to be better relative to studies including all such patients. These patients were excluded from the study in order to be able to accurately assess results in a comparable manner. Similarly, postoperative complication development status, which is effective in prognosis, was not evaluated in the study. Patients in the DNS group were also largely unclear on exactly how long they had continued enteral nutrition before discontinuation; thus we could not assess results with regard to this parameter. This situation may have also caused temporal heterogeneity in the effect of nutrition in DNS group results. Finally, a higher initial baseline NRS-2002 score in the CNS group may have affected adverse outcomes.

CONCLUSION

In this study, it was determined that gastric cancer patients who continued to receive enteral nutrition in the first year after CRT significantly reduced their nutritional risk compared to baseline values. Enteral nutrition also shows positive results on nutritional parameters including body weight, ferritin, transferrin, vitamin D and vitamin B12. In

future studies, we believe researchers could benefit from employing the cohort study design, in which the results of patients with similar nutritional risk at the beginning of the study can be evaluated prospectively; thus, the duration of nutritional support and its effects on the results can be examined in more detail.

Competing Interests: The authors declare that they have no competing interest.

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Ethical Approval: Ethics committee approval was obtained from the Ethics Committee of Zonguldak Bulent Ecevit University (Approval no: 2020/04, Date: 19/02/2020).

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