



# The Effect of Preoperative Nutritional Support on Postoperative Morbidity and Mortality in Patients With Gastric Cancer: A Single Center Retrospective Study

## Mide Kanserli Hastalarda Preoperatif Nütrisyonel Desteğin Postoperatif Morbidite ve Mortalite Üzerine Etkisi: Tek Merkezli Retrospektif Veri Analizi

<sup>1</sup>Korhan Tuncer<sup>1</sup>, <sup>2</sup>Ismail Sert<sup>2</sup>, <sup>3</sup>Gizem Kilinc<sup>1</sup>, <sup>4</sup>Cem Tugmen<sup>1</sup>, <sup>5</sup>Mustafa Emiroglu<sup>1</sup>

<sup>1</sup>Sciences Izmir Tepecik Training and Research Hospital, Department of General Surgery, Izmir, Turkey

<sup>2</sup>Izmir Egepol Hospital, Department of General Surgery, Izmir, Turkey

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### Abstract

**Aim:** Weight loss and malnutrition are frequently observed in patients with gastric cancer. Therefore, nutrition is important, especially in patients with gastric cancer. In this study, we aimed to identify the effect of preoperative nutritional support on postoperative morbidity and mortality in patients with gastric cancer.

**Material and Method:** A total of 110 patients underwent gastrectomy due to gastric cancer between December 2015 and December 2019 were retrospectively analyzed. It was determined whether the patients were given preoperative and postoperative nutritional support. Clinicopathological features and short-term results were compared.

**Results:** Overall morbidity was 29.1% (n=32) in patients who underwent gastrectomy. It was observed that the rate of major complications increased statistically with increasing age (p<0.001). Comorbidity was also found to be a risk factor for major complications (OR 3.917, 95% CI 1.423-10.781; p=0.006). The incidence of complications increases especially in patients with a diagnosis of diabetes (OR 3.743, 95% CI 1.201-11.666; p=0.040). While anastomotic leak developed in 6.7% (n=2) of the patients who were taken preoperative nutrition, anastomotic leak developed in 10% (n=8) of the patients who were not taken nutritional support (p=0.588). Likewise, the relationship between the postoperative length of stay, postoperative complications and mortality of patients receiving preoperative nutritional support could not be proven.

**Conclusion:** The present study reveals that preoperative nutrition in patients with gastric cancer was not associated with improved morbidity and mortality rates. Large, multicenter prospective studies focusing on preoperative nutritional support are needed to uncover the exact relation of preoperative nutrition and morbidity-mortality rates in patients with gastric cancer.

**Keywords:** Gastrectomy; nutritional support; gastric cancer

### Öz

**Amaç:** Mide kanserli hastalarda kilo kaybı ve malnütrisyon sıklıkla görülmektedir. Bu nedenle özellikle mide kanserli hastalarda beslenme önemlidir. Bu çalışmada mide kanserli hastalarda ameliyat öncesi beslenme desteğinin ameliyat sonrası morbidite ve mortalite üzerine etkisini belirlemeyi amaçladık.

**Materyal ve Metot:** Aralık 2015 ile Aralık 2019 tarihleri arasında mide kanseri nedeniyle gastrektomi yapılan toplam 110 hasta retrospektif olarak incelendi. Hastalara ameliyat öncesi ve sonrası beslenme desteği verilip verilmediği belirlendi. Klinikopatolojik özellikler ve kısa dönem sonuçları karşılaştırıldı.

**Bulgular:** Gastrektomi yapılan hastalarda genel morbidite %29.1 (n=32) idi. Yaş arttıkça majör komplikasyon oranının istatistiksel olarak arttığı görüldü (p<0.001). Komorbidite de majör komplikasyonlar için bir risk faktörü olarak bulundu (OR 3.917, %95 CI 1.423-10.781; p=0.006). Özellikle diyabet tanısı olan hastalarda komplikasyon insidansı artmaktadır (OR 3.743, %95 CI 1.201-11.666; p=0.040). Preoperatif beslenme alan hastaların %6.7'inde (n=2) anastomoz kaçağı gelişirken, beslenme desteği almayan hastaların %10'unda (n=8) anastomoz kaçağı gelişti (p=0.588). Aynı şekilde preoperatif nütrisyon desteği alan hastaların postoperatif yatış süresi, postoperatif komplikasyonlar ve mortalitesi arasındaki ilişki kanıtlanamamıştır.

**Sonuç:** Bu çalışma, mide kanserli hastalarda ameliyat öncesi beslenmenin morbidite ve mortalite oranlarında iyileşme ile ilişkili olmadığını ortaya koymaktadır. Mide kanserli hastalarda ameliyat öncesi beslenme ile morbidite-mortalite oranları arasındaki kesin ilişkiyi ortaya çıkarmak için ameliyat öncesi beslenme desteğine odaklanan geniş, çok merkezli ileriye dönük çalışmalara ihtiyaç vardır.

**Anahtar Kelimeler :** Gastrektomi; nütrisyonel destek; mide kanseri

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**Sorumlu Yazar /Corresponding Author:** Korhan Tuncer, Sciences Izmir Tepecik Training and Research Hospital, Department of General Surgery, Izmir, Turkey, E-mail: [korhantuncer19@gmail.com](mailto:korhantuncer19@gmail.com)

## INTRODUCTION

Gastric cancer remains the fifth most common cancer type in worldwide and is the third leading cause of cancer-related deaths in the world (1). Gastrectomy is still remain as the main treatment method for gastric cancer though symptoms such as malabsorption, bacterial overgrowth, decreased gastric retention, rapid intestinal transit time and insufficient oral intake may occur in patients after surgery (2). Therefore gastrectomy is usually cause body weight loss in patients with gastric cancer. Weight loss in the first year after surgery was reported as 6% - 10% in patients who underwent subtotal gastrectomy and 15% - 18% in patients undergoing total gastrectomy (3,4). Preoperative malnutrition was reported as associated with increased morbidity (i.e. increased infection rate, delayed wound healing, pulmonary complications) and mortality in patients undergoing major surgery (5,6,7). Therefore, identification and treatment of malnutrition is important in the management of gastric cancer. Various guidelines such as ESPEN guidelines, German S3 Guidelines, and the North American Surgical Nutrition Summit recommend nutritional support for all patients with inadequate oral intake (8,9). Ding et al showed in a randomized controlled trial (RCT) of 106 patients who underwent gastrectomy that preoperative EN improves postoperative nutritional status, attenuates the inflammatory response, and facilitates recovery of patients (10). In this study, we aimed to identify the effect of preoperative nutritional support on postoperative morbidity and mortality in patients with gastric cancer.

## MATERIAL AND METHOD

### Demographics and Clinical Characteristics of The Patients

Patients underwent gastrectomy for gastric cancer between December 2015 and December 2019 were retrospectively analyzed. Patients that have the diagnosis of gastric adenocarcinoma and underwent R0 / R1 gastrectomy were included in the study. Patients who were considered inoperable and whose pathology result were not adenocarcinoma were excluded from the study. A total of 110 patients were detected. Patients' age, sex, comorbidities, American Society of Anesthesiology (ASA) scores, type of operation, TNM staging, histological type of tumor, presence of lymphovascular invasion, cerb-b2 positivity, preoperative level of albumin, whether preoperative or postoperative nutritional support was given, Clavien-Dindo scores, postoperative length of hospital stay, demographic and clinicopathological datas were collected. The study was approved by the ethics committee of the Ministry of Health University of Health Sciences Izmir Tepecik Training and Research Hospital (Approval number: 2020/9-2) and was adapted to the Helsinki Declaration.

### Statistical Analysis

Statistical analysis were done with IBM SPSS Statistics software, version 25.0. As the descriptive statistics, the number of units (n), percent (%), mean  $\pm$  standard

deviation ( $\bar{x} \pm ss$ ), Median (Q1-Q3) values were given. Pearson Chi-Square and Fisher's exact test were used to evaluate categorical variables. The results are reported as Odds ratios (ORs) with 95% confidence interval (CI). The normal distribution of data's continuous variables were evaluated by Shapiro Wilk, normality test and Q-Q graphs. In the comparison of the continuous variables of the two groups, the Independent Sample T test was used for variables with normal distribution, and Mann-Whitney U test for variables that did not fit the normal distribution.  $p < 0.05$  value was considered statistically significant.

## RESULT

### Baseline Clinicopathological Characteristics

A total of 110 patients were found eligible for the inclusion criteria. The mean age was  $61.4 \pm 12.61$  (range, 28-88) and 73 (66.4%) of the patients were male. 57 (51.8%) of the patients that underwent gastrectomy were had various comorbidities. 7 (6.4%) patients were ASA 1, 66 (60.0%) patients were ASA 2, 32 (29.1%) patients were ASA 3 and 5 (4.5%) patients were ASA 4. 12 (10.9%) of the patients were taken neoadjuvant therapy. The mean of preoperative level of albumin was  $3.8$  (SD  $\pm 0.58$ ) g/dL. Total gastrectomy was performed in 78 (70.9%) patients while subtotal gastrectomy was performed in 32 (29.1%) patients. R0 or R1 resection was performed to all patients. In pathological materials, the majority of patients were T4 (n=59, 53.6%) or N3 (n=44, 40.0%). Lymphovascular invasion was detected in 81 (73.6%) patients and cerb-B2 expression was found in 19 (17.3%) patients. 7 (6.4%) of the patients were operated due to emergency reasons.

32 (29.1%) of the patients were presented overall morbidity. While the most common complications were pulmonary complications such as atelectasis and pneumonia (13.7%), other complications were anastomotic leakage (9.1%), surgical site infection (3.6%), bleeding (1.8%), and cerebrovascular disease (0.9%). Postoperative complications of the patients were classified according to Clavien-Dindo Classification. According to this classification, 25 patients with score of 3 and above were grouped as the major complication group, and 85 patients who did not develop complications or scored 1 or 2 according to Clavien-Dindo were grouped as without major complications. The effect of the clinicopathological characteristics of the patients on major complications is summarized in Table-1.

It was observed that the rate of major complications increased statistically with increasing age ( $p < 0.001$ ). Comorbidity was also found to be a risk factor for major complications (OR 3.917, 95% CI 1.423-10.781;  $p = 0.006$ ). The incidence of complications increases especially in patients with a diagnosis of diabetes (OR 3.743, 95% CI 1.201-11.666;  $p = 0.040$ ). Also the rate of complications increases according to the number of comorbidities of the patients ( $p < 0.001$ ). The level of albumin which is used as an indicator of malnutrition, was found to be significantly lower in patients with complications ( $p = 0.001$ ). The

Table 1. The clinical and pathological features				
	All patients (n=110)	without major complications (n=85)	with major complications (n=25)	p-Value
Age, years, mean $\pm$ SD	61.4 $\pm$ 12.61	59.0 $\pm$ 12.51	69.4 $\pm$ 9.37	<0.001
Gender, n (%)				0.776
Male	73 (66.4)	57 (67.1)	16 (64)	
Female	37 (33.6)	28 (32.9)	9 (36)	
Hypertension, n (%)	27 (24.5)	18 (21.2)	9 (36)	0.130
Diabetes mellitus, n (%)	15 (13.6)	8 (9.4)	7 (28)	0.040
Comorbidity, n (%)	57 (51.8)	38 (44.7)	19 (76)	0.006
ASA classification, n (%)				<0.001
1	7 (6.4)	7 (8.2)	0 (0)	
2	66 (60)	57 (67.1)	9 (36)	
3	32 (29.1)	20 (23.5)	12 (48)	
4	5 (4.5)	1 (1.2)	4 (16)	
ALB, g/dL, mean $\pm$ SD	3.8 $\pm$ 0.58	3.9 $\pm$ 0.51	3.4 $\pm$ 0.68	0.001
Neoadjuvant therapy, n (%)	12 (10.9)	11 (12.9)	1 (4)	0.291
Type of surgery, n (%)				0.101
Total gastrectomy	78 (70.9)	57 (67.1)	21 (84)	
Subtotal gastrectomy	32 (29.1)	28 (32.9)	4 (16)	
pT, n (%)				0.458
T1	10 (9.1)	9 (10.6)	1 (4)	
T2	11 (10)	10 (11.8)	1 (4)	
T3	30 (27.3)	22 (25.9)	8 (32)	
T4	59 (53.6)	44 (51.8)	15 (60)	
pN, n (%)				0.503
N0	26 (23.6)	21 (24.7)	5 (20)	
N1	16 (14.5)	14 (16.5)	2 (8)	
N2	24 (21.8)	19 (22.4)	5 (20)	
N3	44 (40)	31 (36.5)	13 (52)	
Tumor location, n (%)				0.110
Cardia	28 (25.5)	20 (23.5)	8 (32)	
Corpus	35 (31.8)	24 (28.2)	11 (44)	
Antrum	36 (32.7)	30 (35.3)	6 (24)	
Pylorus	11 (10)	11 (12.9)	0 (0)	
Lymphovascular invasion, n (%)	81 (73.6)	59 (69.4)	22 (88)	0.064
C-erb-B2 positivity, n (%)	19 (17.3)	16 (18.8)	3 (12)	0.555
Preoperative nutritional support, n (%)	30 (27.3)	21 (24.7)	9 (36)	0.265
Postoperative nutritional support, n (%)	78 (70.9)	54 (63.5)	24 (96)	0.002
Emergency operation, n (%)	7 (6.4)	3 (3.5)	4 (16)	0.046

complications were also found increased in patients that underwent emergency surgery ( $p=0.046$ ).

### Impact of Preoperative Nutritional Support on Postoperative Complications and Length of Hospital Stay

5 (4.5%) of the patients were received nutritional support only in the preoperative period, 53 (48.2%) of them were received nutritional support only in the postoperative period and 25 (48.2%) of them were received nutritional support both in the preoperative and postoperative periods. 27 (24.5%) patients were not received any nutritional support during the perioperative period. The

effects of preoperative nutritional support on 30 patients' postoperative hospital stay, complications and mortality were summarized in Table-2. While anastomotic leak developed in 6.7% ( $n=2$ ) of the patients who were taken preoperative nutrition, anastomotic leak developed in 10% ( $n=8$ ) of the patients who were not taken nutritional support. However, it was not statistically significant ( $p=0.588$ ). Likewise, the relationship between the postoperative length of stay, postoperative complications and mortality of patients receiving preoperative nutritional support could not be proven.

**Table 2. The effect of nutritional support on mortality and morbidity**

	All patients (n=110)	to get preoperative nutritional support (n=30)	not to get preoperative nutritional support (n=80)	p-Value
<b>Postoperative length of hospital stay, days, mean <math>\pm</math> SD</b>	12.3 $\pm$ 12.42	13.1 $\pm$ 14.58	12.0 $\pm$ 11.60	0.692
<b>Any complication, n (%)</b>				0.123
Yes	32 (29.1)	12 (40)	20 (25)	
No	78 (70.9)	18 (60)	60 (75)	
<b>Anastomosis leakage, n (%)</b>				0.588
Yes	10 (9.1)	2 (6.7)	8 (10)	
No	100 (90.9)	28 (93.3)	72 (90)	
<b>Clavien-Dindo classification, n (%)</b>				0.227
0	78 (70.9)	18 (60)	60 (75)	
1	5 (4.5)	2 (6.7)	3 (3.8)	
2	2 (1.8)	1 (3.3)	1 (1.3)	
3	5 (4.5)	0 (0)	5 (6.3)	
4	10 (9.1)	5 (16.7)	5 (6.3)	
<b>Mortality, n (%)</b>				0.343
Yes	10 (9.1)	4 (13.3)	6 (7.5)	
No	100 (90.9)	26 (86.7)	74 (92.5)	

## DISCUSSION

It is important to provide nutritional support in patients with gastric cancer in order to reduce postoperative complications and increase long-term quality of life. Early enteral nutrition should be initiated after surgery and adequate nutritional support should be given before surgery in patients with gastric cancer. Nutritional support for these patients can be provided enterally and parenterally. Although total parenteral nutrition (TPN) provides a significant benefit to surgical patients, it has many complications. Studies have proven that intestinal permeability increases in patients after surgical trauma and therefore there is a risk of bacterial translocation in patients receiving only TPN (11). It has also been found that enteral nutrition preserves intestinal integrity and reduces septic complications and hospital stay (12,13). Enteral nutrition is safer, cheaper and more physiological

than parenteral nutrition. However, parenteral nutrition is mandatory in patients with gastrointestinal dysfunction.

Enteral immunonutrition (EIN) is an immune product enriched with arginine, glutamine, omega-3 fatty acids and ribonucleic acid. EIN is known as an alternative nutritional supplement that has emerged to modulate the metabolism and immune system and has attracted attention in recent years. However, its superiority over enteral nutrition is controversial. Gianotti et al. was compared the perioperative immunonutrition with standard enteral nutrition in patients undergoing major elective gastrointestinal surgery (14). This study showed that perioperative immunonutrition significantly reduced overall complications and length of hospital stay. However, it was found not associated with mortality. Song et al. reported in a meta-analysis that immunonutrition could effectively improve the nutritional and immunological

status of patients with gastric cancer who underwent surgical resection. On the other hand they couldn't find any association between immunonutrition and patients' postoperative complications and hospital stay (15).

It was shown that malnutrition can cause immunosuppression and poor prognosis in patients with gastric cancer. Therefore, nutritional support during the postoperative period is as important as preoperative nutrition. The ERAS protocol advocates that patients should take enteral nutrition as early as possible. However, some studies did not find a significant difference between early enteral nutrition and parenteral nutrition after total gastrectomy (16). Parenteral nutrition may be the only option especially for patients who are not suitable for enteral feeding. There are studies suggesting that parenteral nutrition can significantly improve patients' nutritional and psychological status, quality of life and immune functions (17). In addition, a study in an elderly patients undergoing surgery for gastric cancer showed that the combination of enteral and parenteral nutrition is superior to early enteral nutrition or total parenteral nutrition in promoting immune recovery (18). There are no separate guidelines for the management and treatment of elderly patients with gastric cancer. As expected, older patients typically have more medical comorbidities and higher American Society of Anesthesiologists (ASA) classification scores. Elderly patients should be evaluated carefully in the preoperative period considering the postoperative morbidity and mortality risks.

Fujiwara et al. (19) and Hsu et al. (20) reported higher rates of postoperative complications and mortality in elderly patients with gastric cancer. In our study it was observed that the rate of major complications increased statistically with increasing age. Also, age was found to be an independent factor negatively affecting postoperative mortality and morbidity in patients undergoing gastric resection. In our study, the increase in the number of comorbidities was also found to be associated with postoperative complications. We considered that this result is associated with the increase of various systemic diseases in elderly patients. When systemic diseases were examined separately, it was found that the incidence of complications increased in patients with diabetes mellitus. In a multicenter study, it was found that diabetic patients who underwent major surgery had a higher risk of infections and mortality than non-diabetic patients who had similar major surgery (21). There is an inverse correlation between serum levels of albumin and length of hospital stay and postoperative complications in patients with gastric cancer (22). We found that inverse correlation in our study either. This inverse correlation was due to both the decrease in albumin levels in the geriatric population and the fact that albumin was an indicator of malnutrition.

This study could not clearly show the effect of preoperative nutrition on postoperative mortality and morbidity. It is considered that the effect of preoperative nutrition could not be proven, since the majority of patients receiving

preoperative enteral nutrition were malnourished patients and the risk of complications in this group was higher than other patients. However, age, albumin level, diabetes and the presence of more than one comorbidity were found to be factors affecting the postoperative prognosis in gastric cancer. These findings support other similar studies. The retrospective nature of this study caused some limitations. The lack of malnutrition or sarcopenic data such as body mass index of the patients, limited information about the perioperative diet regimen of the patients, the difference in surgical experience and surgical resection types determine the limits of this study. Prospective randomized studies are needed to overcome these problems and to examine preoperative nutrition in more detail.

## CONCLUSION

The present study reveals that preoperative nutrition in patients with gastric cancer was not associated with improved morbidity and mortality rates. This result may stem from retrospective nature of this study and its limitations. Large, multicenter prospective studies focusing on preoperative nutritional support are needed to overcome these limitations and uncover the exact relation of preoperative nutrition and morbidity-mortality rates in patients with gastric cancer.

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