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Original Article

Preoperative Nutritional Status as a Determinant of Mortality in Patients with Gastric Cancer Undergoing Gastrectomy: A Prospective Study

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Abstract

Background: This study aimed to determine the prognostic factors related to three-year survival in patients with gastric cancer (GC) undergoing gastrectomy.

Methods: A total of 124 patients with GC undergoing gastrectomy were enrolled in this prospective study from September 2016 to October 2019. The three-year survival rate was assessed. Clinical records, the socioeconomic status (SES) questionnaire, and the Patient-Generated Subjective Global Assessment (PG-SGA) were used to evaluate tumor-related information, SES, and nutritional status, respectively. The Cox proportional hazard model was used to identify determinants of mortality.

Results: During the follow-up period, 29.03% of the patients died. Significant differences were observed between deceased and non-deceased patients regarding PG-SGA scores ($P=0.01$). The results of the univariate Cox regression models indicated that age (OR: 1.02, 95% CI: 1.03-1.04), tumor–node–metastasis (TNM) stage 3 (OR: 13.22, 95% CI: 4.30-42.26), poor pre-surgery nutritional status (OR: 2.57, 95% CI: 1.67-3.97), and a medium level of physical activity (PA) (OR: 0.62, 95% CI: 0.4-0.95) are the significant determinant of three-year mortality in patients with GC undergoing gastrectomy. In the multivariate model, only TNM stage 3 and poor nutritional status remained significant.

Conclusion: Based on the results, it is recommended that all patients with GC undergo a nutritional status assessments before gastrectomy, with suitable clinical management tailored accordingly.

Keywords: Gastrectomy, Nutritional status, Mortality, Neoplasm staging

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Introduction

Gastric cancer (GC) is the fifth most common malignancy worldwide, and its prognosis is poor.[1] Surgery is the main effective treatment for GC; however, it may be associated with changes in metabolic and endocrine functions, leading to high post-surgery morbidity rates.[2] Hence, identifying prognostic factors is essential for improving patient survival. In this regard, different studies have examined predictors of mortality after gastrectomy in patients with GC. The tumor–node–metastasis (TNM) stage was identified as a predictor of survival in GC patients undergoing gastrectomy.[3,4] Some studies have also shown that age is an important prognostic factor for gastrectomy mortality[5]; however, other studies have reported contradictory results.[6,7]

Poor dietary habits are considered the second-leading risk factor for mortality worldwide.[8] In patients with non-communicable disease, dietary factors were found to be associated with a substantial proportion of deaths.[9] Previous research indicated a high prevalence of malnutrition in patients with GC.[10] Malnutrition, sarcopenia, and cachexia were found to affect the survival and recovery of cancer patients.[11] Malnutrition or poor nutritional status is estimated to occur in about 80% of GC patients.[12] Suzuki et al demonstrated that malnutrition is associated with poor prognosis in elderly patients with GC undergoing gastrectomy.[13] Likewise, Sugawara et al showed that poor nutritional status influences survival outcomes in gastric carcinoma patients undergoing radical surgery,[14] with some studies reporting the same results.[15-17] However, other studies reported contradictory outcomes.[18]

In addition to dietary factors, lifestyle-related aspects such as physical activity (PA) have also been linked to surgery recovery in patients undergoing breast cancer[19] and abdominal surgeries.[20] However, a meta-analysis

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revealed that while prehabilitation programs improve exercise capacity after gastrointestinal surgery, they have no significant effect on mortality.[21]

As mentioned above, despite the prognostic value of demographic, disease-related, and lifestyle-related factors in patients with cancer, research on patients undergoing gastrectomy is limited. Moreover, the findings of the studies remain controversial. As such, we hypothesized that further research is needed with the prospective design to identify the prognostic factors of three-year mortality in patients with GC undergoing gastrectomy.

Methods

One hundred twenty-four consecutive patients with GC undergoing gastrectomy participated in the present prospective study from September 2016 to October 2019.

Measurements

Demographic information, including age, gender, residency, smoking history, family history, and other medical history was retrieved using a questionnaire. Clinical records were used to gather tumor-related information, including the number of lymph nodes, tumor location, and size. The TNM stage was categorized into four classes according to the latest edition of the American Joint Committee on Cancer (AJCC).

To determine socioeconomic status (SES), a validated questionnaire (SESIran) was applied.[22] Based on this score, participants were classified into four groups: very low, low, medium, and high SES.[22] The valid short form of the International Physical Activity Questionnaire (IPAQ) was used to categorize participants' PA levels into three categories: low, medium, and high.[23]

The Patient-Generated Subjective Global Assessment (PG-SGA) questionnaire, validated for Iranian cancerous patients,[24] was used to assess nutritional status.[25] Based on PG-SGA scores, the patients were classified as requiring no intervention (scores < 9) or requiring intervention (scores ≥ 9).

Bodyweight and height were measured using standard protocols and instruments, and body mass index (BMI) was calculated by dividing weight (kg) by height squared (m^2). Underweight was defined as a BMI < 18.5 kg/m^2, normal weight as a BMI of 18.5-24.9 kg/m^2, overweight as a BMI of 25-29.9 kg/m^2, and obese as a BMI > 30 kg/m^2. All questionnaires and measurements were conducted prior to gastrectomy. The three-year survival was calculated from the date of diagnosis to the date of death or last visit.

Statistical Analysis

The 19th version of the IBM SPSS software was used for statistical analysis (IBM Corporation, Armonk, NY, USA). The Kolmogorov-Smirnov test was used to assess the normal distribution of the studied variables. Continuous variables were reported as mean ± standard deviation, while categorical and nominal variables were presented as frequency and percentage, respectively. Between-group comparisons were analyzed using independent t-tests and chi-square tests where appropriate. The Cox proportional hazard model was utilized to determine the prognostic value of different variables in relation to three-year mortality. Different variables were considered in multivariate models, including age, gender, SES, PA level, smoking status, other diseases, type of surgery, time to surgery, and TNM stage. A two-sided P value of < 0.05 was considered statistically significant.

Results

The mean age of participants was 64.06 ± 10.49 years, with 66.9% of participants being male. As presented in Table 1, 16.9% of participants were in stage I of GC, and 60.4% underwent total gastrectomy. According to PG-SGA results, 82.5% of patients required nutritional intervention. During the three-year follow-up, 29.03% of patients died.

Significant differences were found between deceased and non-deceased patients regarding PG-SGA scores ($P = 0.01$). Moreover, the TNM stage was marginally significant between the two groups ($P = 0.05$). As illustrated in Table 2, the result of the univariate COX regression models indicated that age (OR: 1.02, 95% CI: 1.03-1.04), TNM stage 3 (OR: 13.22, 95% CI: 4.30-42.26), poor preoperative nutritional status (OR: 2.57, 95% CI: 1.67-3.97), and medium level PA (OR: 0.62, 95% CI:0.4-0.95) are significant determinant of three-year mortality in patients with GC undergoing gastrectomy. In the multivariate model, only TNM stage 3 (OR: 11.97, 95% CI: 3.63-39.46), and poor nutrition status (OR: 1.98, 95% CI: 1.13-3.47) remained significant.

Discussion

Surgery remains the main curative option for GC.[26] However, the survival rates of patients are low.[27] The results of the present prospective study show that three-year survival after gastrectomy is significantly associated with TNM stage and PG-SGA scores. These results are in line with the results of a recent study conducted in South Korea which demonstrated a significant relationship between the preoperative nutritional risk index and survival. Poor nutritional status has been found to influence survival outcomes in gastric carcinoma patients undergoing radical surgery.[14] Additionally, other studies have indicated that pre-surgery malnutrition can affect both cancer-related and non-cancer-related mortality.[28,29] Prior research suggested that in GC patients with malnutrition, nutritional support prior to surgery may decrease the risk of post-surgery infections[30] and increase the immune responses.[31] Moreover, nutritional status at the time of diagnosis was shown to be associated with survival rates.[32] To date, the precise mechanisms of association between poor nutritional status and mortality in GC patients have remained unclear. However, some studies have speculated that the association between nutritional status and cancer survival may be partly

Table 1. Demographic and Disease-Related Characteristics of Participants

Variables	Total (N = 124)	Alive (n = 88)	Deceased (n = 36)	*P* Value*
Age (y)				
< 65	74 (59.6)	52 (59.09)	22 (61.1)	0.83
≥ 65	50 (40.3)	36 (40.9)	14 (38.8)	
Gender				
Male	83 (66.93)	60 (68.1)	23 (63.8)	0.52
Female	41 (33.06)	28 (31.8)	13 (36.1)	
Residency				
Capital city	33 (26.6)	22 (25.0)	11 (30.5)	0.63
Suburb	91 (73.3)	66 (75.0)	25 (69.4)	
Smoking history				
Yes	25 (20.1)	16 (18.1)	9 (25.0)	0.23
No	99 (79.8)	72 (81.8)	27 (75.0)	
Other diseases				
No	93 (75)	68 (77.2)	25 (69.4)	0.47
Yes	31 (25)	20 (22.7)	11 (30.5)	
SES				
Very Low	11 (8.8)	11 (12.5)	0 (0)	
Low	107 (86.2)	74 (84.09)	33 (91.6)	0.13
Medium	6 (4.83)	3 (3.4)	3 (8.3)	
TNM Stage				
I	23 (18.5)	19 (21.5)	4 (11.1)	0.05
II	28 (22.5)	20 (22.7)	8 (22.2)	
III	59 (47.5)	43 (48.8)	16 (44.4)	
IV	14 (11.2)	6 (6.8)	8 (22.2)	
Tumor location				
Cardia	53 (42.7)	41 (46.5)	12 (33.3)	0.31
Non-cardia	71 (57.2)	47 (53.4)	24 (66.6)	
Extent of Gastrectomy				
Total	75 (60.4)	49 (59.03)	26 (63.4)	0.26
Partial	49 (39.5)	34 (40.9)	15 (36.5)	
PG-SGA				
No Intervention required	27 (21.7)	24 (27.2)	3 (0.08)	0.01
Intervention required	97 (78.2)	64 (72.7)	33 (91.6)	
Intent of resection				
Curative	93 (75)	67 (76.1)	26 (72.2)	0.20
Palliative	31 (25)	21 (23.8)	10 (27.7)	
Physical activity				
Low	82 (66.1)	60 (68.1)	22 (61.1)	
Medium	39 (31.4)	25 (28.4)	14 (38.84)	0.13
High	3 (2.4)	3 (3.4)	0 (2.4)	

Note. SES: Socioeconomic status; TNM: Tumor, node, and metastasis; PG-SGA: Patient generated-subjective global assessment;
* *P* value of chi-square

attributed to malnutrition's impact on lymphocyte counts.[33] Lee et al showed that higher peripheral lymphocyte counts before surgery are associated with better survival outcomes in early-stage cervical cancer.[34] Additionally, lower serum albumin levels were associated with higher risks of surgical complications and mortality.[35] Albumin is considered an indicator of malnutrition.[36] Moreover, patients undergoing gastrectomy are at higher risk of infections, which may affect treatment responses.[37]

The current study did not find any significant relationship between PA level and mortality in GC patients undergoing gastrectomy in the multivariate model. A meta-analysis conducted by Lau et al revealed that while prehabilitation programs improve exercise capacity both before and after gastrointestinal surgery, it had no significant effect on mortality.[21] Conversely, pre-surgery PA has been identified as a predictor of postoperative functional recovery in patients undergoing gastrointestinal cancer surgeries.[38] Another study on patients with abdominal surgery revealed that preoperative PA has a protective effect against post-surgery pulmonary complications.[38] Pre-surgery PA level has been reported as significant predictors of recovery in patients undergoing breast cancer surgery.[19] The controversies in findings across various reports may be due to differences in the types of cancer surgeries and the specific outcomes assessed.

One of the important limitations of our study was the low sample size. Additionally, data were collected from a single center, which may affect the generalizability of the results. Moreover, some important co-factors related to systematic inflammation and immunity were not measured. We also did not consider the complications after gastric surgery.

Conclusion

In conclusion, the result of this prospective study indicates that pre-surgery nutritional status, assessed using PG-SGA, and TNM stage are independently associated with mortality in patients with GC undergoing gastrectomy. Therefore, all GC patients undergoing gastrectomy need to be checked for any necessary nutritional interventions prior to surgery. However, due to the study's limitations, further cohort and experimental investigations need to be conducted to approve these initial findings. In addition, future studies should assess the effects of pre-surgery and post-surgery chemotherapy on the survival of patients with GC.

Ethics statement

The study adhered to the Declaration of Helsinki guidelines and received ethical approval from the Ethics Committee of Tabriz University of Medical Sciences (Ethics code: IR.TBZMED.REC.1395.465).

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Table 2. Association Between Demographic, Disease-Related, and Nutritional Factors and Mortality in Patients Undergoing Gastrectomy

Variables	Univariate Model			Multivariate Model		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Age	1.03	1.02-1.04	<0.001	1.01	0.99-1.03	0.17
Gender						
Male	1	-	-	1	-	-
Female	1.09	0.70-1.43	0.96	0.92	0.56-1.57	0.77
SES						
Very low	1	-	-	1	-	-
Low	0.95	0.48-1.88	0.88	1.43	0.53-3.70	0.48
Medium	0.74	0.27-2.05	0.56	1.27	0.33-4.88	0.72
Smoking history						
No	1	-	-	1	-	-
Yes	0.92	0.58-1.47	0.74	0.61	0.34-1.13	0.08
Other diseases						
No	1	-	-	1	-	-
Yes	1.33	0.88-1.99	0.15	0.40	0.83-2.38	0.20
TNM stage						
I	1	-	-	1	-	-
II	2.92	0.75-11.33	0.12	3.49	0.87-14.04	0.11
III	2.64	0.77-9.08	0.12	2.38	0.66-8.54	0.18
IV	13.22	4.13-42.26	<0.001	11.97	3.63-39.46	<0.001
Gastrectomy type						
Total	1	-	-	1	-	-
Partial	0.42	0.14-1.20	0.10	0.52	0.10-1.26	0.08
Time to surgery	1.002	0.99-1.006	0.46	1.04	0.89-1.08	0.58
PG-SGA						
No Intervention required	1	-	-	1	-	-
Intervention required	2.57	1.67-3.97	<0.001	1.98	1.13-3.47	0.01
Physical activity						
Low	1	-	-	1	-	-
Medium	0.62	0.40-0.95	0.02	1.50	0.56-3.98	0.41

Note. OR: Odds ratio; CI: Confidence interval; SES: Socioeconomic Status; TNM: Tumor, node, and metastasis; PG-SGA: Patient generated-subjective global assessment.

Conflict of interests declaration

The authors declare no conflict of interests.

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Data availability statement

Data will be available upon request from corresponding author.

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Consent for publication

Not applicable.

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