Older is worse? Elderly patients who underwent gastrectomy:



Ann. Ital. Chir., 2023 94, 3: 268-273 pii: S0003469X2303823X

A single-center study.

Tevfik Kıvılcım Uprak*, Muhammer Ergenç**

*Department of General Surgery, Marmara University School of Medicine, Istanbul, Turkey **Department of General Surgery, Istanbul Sultanbeyli State Hospital, Istanbul, Turkey

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AIM: Gastric cancer is common cancer, and its incidence remains relatively high in elderly patients with increasing life expectancy. However, few studies have examined the clinical and prognostic characteristics of elderly gastric cancer patients undergoing gastrectomy. This study aimed to evaluate the clinical and prognostic features of elderly gastrectomy patients. MATERIALS AND METHODS: Patients over 65 years of age who underwent gastric cancer surgery at Marmara University were retrospectively analyzed. The patients' demographics, American Society of Anesthesiologists scores, prognostic nutritional index (PNI), complications, intensive care unit duration, and length of stay were examined. The patients were divided into two groups: young-old (65-74 years old) and old-old (\geq 75 years old). Two groups were compared in terms of postoperative outcomes and overall survival.

Results: Two hundred sixty-three patients were analyzed. The mean age was 79 years, and the female to male ratio was 85/178. Reoperation rates and hospital mortality were significantly higher in the old-old group (p=0.001 and p=0.01, respectively). The hospital stay was significantly longer in the old-old group (5.8 vs. 7.8 days, p=0.02). Complications were significantly higher in the group with a PNI < 40 (49% vs. 23%, p=0.005). There was a significant difference between the two groups regarding 5-year overall survival (33% vs. 55%, p=0.002).

CONCLUSIONS: Gastrectomy can be performed on the elderly. However, an increase in complications and in-hospital mortality is recognized over 75. These problems should be considered in this old-age group.

KEY WORDS: Aged, Carcinoma stomach, Elderly, Gastric cancer, Gastrectomy

Introduction

Gastric cancer is the fifth most common type of cancer diagnosed worldwide and the fourth leading cause of cancer death ¹. Along with surgical resection, perioperative chemotherapy or chemoradiotherapy are the primary treatment methods ²⁻⁴.

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The incidence of gastric cancer remains relatively high, and with increasing life expectancy, the incidence of gastric cancer in elderly patients is increasing ^{1,5,6}. The characteristics of elderly patients, such as reduced physiological function, poor nutritional status, and surgical trauma from radical gastrectomy, seem to result in higher postoperative morbidity, a longer length of hospital stay, increased healthcare costs, and higher postoperative mortality ^{7,8}. Elderly patients may have a worse prognosis than younger patients, primarily because of the postoperative complications. increased risk of Perioperative nutritional support and preoperative rehabilitations are beneficial for elderly patients with gastric cancer and may reduce surgical complications and mortality. Although some studies state that radical surgery can be performed for those aged 80 and over, some have argued that complications increase in elderly patients and that surgery should be limited 3, 9-11.

Pervenuto in Redazione Aprile 2022. Accettato per la pubblicazione Maggio 2022

Correspondence to: Muhammer Ergenç, MD, Department of General Surgery, Istanbul Sultanbeyli State Hospital, Battalgazi Mah. Pasakoy Cd. No:60 Sultanbeyli, 34935, Istanbul, Turkey (e-mail: muhammerergenc@gmail.com)

This study aimed to evaluate the clinical and prognostic features of elderly patients who underwent gastrectomy for gastric cancer. We also planned to compare elderly patients among themselves.

Material and Methods

Patients who underwent gastric cancer surgery at the Marmara University Hospital General Surgery Clinic between January 2014 and December 2020 were retrospectively analyzed. This study was approved by the Marmara University Faculty of Medicine Clinical Research Ethics Committee (Number: 08.10.2021.1144) and registered with ClinicalTrials.gov (NCT05071755). Patients aged 65 and over were included. Stage 4 patients who underwent palliative resection were excluded from the study.

Data regarding demographics, body mass indexes, smoking history, American Society of Anesthesiologists (ASA) scores, neoadjuvant treatment status of the patients, comorbidities, type of surgery, clinicopathological features of the tumor, complications developed during hospitalization, intensive care duration, and discharge dates were examined. The tumor stages were classified according to the American Joint Committee on Cancer (AJCC) 7th edition ¹². The Clavien-Dindo classification was used in the evaluation of postoperative complications ¹³.

All surgical procedures were performed by the same experienced general surgeons, with a standardized open surgical technique. D1 plus dissection was performed in patients with advanced tumors. Surgery was completed with D1 dissection in early-stage tumors ^{14,15}.

The patients were divided into two groups: young-old (65 to 74 years old) and old-old (\geq 75 years old). ¹⁶ In terms of overall survival, the time from the patient's operation to the date of death was evaluated.

The prognostic nutritional index (PNI) was calculated using the patients' pretreatment albumin and lymphocyte values. The prognostic nutritional index (PNI) was determined according to the following formula: $10 \times$ serum albumin concentration (g/dL) + 0.005 × total lymphocyte count (/mm3) ^{17,18}. According to the PNI scoring system, patients are divided ≥ 40 and < 40. Patients with a PNI < 40 was defined as severe malnutrition.

The primary outcome of this study was to determine whether there was a difference between the two groups in terms of postoperative complications, length of hospital stay, and overall survival. The second outcome was to examine the factors that affect survival in elderly gastric cancer patients.

STATISTICAL ANALYSIS

We performed statistical analysis using the Statistical Package for Social Sciences (Version 24 for Mac, IBM Corporation). Normally distributed data were expressed using the mean ± standard deviation, and nonnormally distributed data were defined using the median values. Chi-square was used to compare categorical data.

Student's t-test was used to compare parametric data, and the Mann–Whitney U test was used to compare nonparametric data. Progression-free survival was defined as the time from the start of primary treatment to the date of progression or, if no progression, to the date of death or last visit if the patient was still alive. Overall survival was defined as the time from the start of primary treatment to the date of exit or last visit if the patient was still alive (months). The Kaplan-Meier method was used in survival analysis, and the log-rank test was used in univariate analysis. The confidence interval for statistical significance will be accepted as 95%, and a bilateral p-value <0.05.

Results

After applying the exclusion criteria, a total of 263 patients were analyzed (Fig. 1). The mean age was 79, and 178 of the patients were male. One hundred twenty-four patients were classified as ASA 2. One hundred forty-four patients underwent subtotal gastrectomy, and as a result, patients with stage 3 tumors accounted for the majority (61%) (Table I). The incidence of any complications was 24% in total. Clavien-Dindo grade 3 and above were seen in 12% of these complications. While 39 patients were followed up in the intensive care unit (ICU), seven patients required reoperation. The median hospital stay was five days (Table II).

When the patients were divided according to age into two groups: 65-74 and \geq 75, no significant difference was found in terms of sex, operation type, tumor stage, and



Fig. 1: Flowchart of patient's selection.

TABLE I - Pati	ents' demographics a	nd perioperative	clinical characteristics.
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Age (years, mean-range) 79 (65-90) Sex Female 85 (32) 55 (30) 30 (37) 0.23 Male 178 (68) 128 (70) 50 (63) 0.23 Diabetes Mellitus 72 (27) 50 (27) 22 (27) 0.9 Hypertension 130 (49) 85 (46) 45 (56) 0.1 Coronary Artery Disease 59 (22) 38 (21) 21 (26) 0.3 Chronic Obstructive Pulmonary Disease 26 (10) 15 (8) 11 (14) 0.1 American Society of Anesthesiologists Score 1 42 (15) 32 (17) 10 (13) 2 124 (48) 98 (54) 26 (32) 0.001 3 70 (26) 38 (21) 32 (40) 0.001 4 27 (10) 15 (8) 12 (15) 12 (15) Prognostic Nutritional Index Score	Parameters	Total n: 263 (%)	Age group 65–74 n: 183(%)	Age group ≥75 n: 80(%)	P-value
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$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Male	178 (68)	128 (70)	50 (63)	
Hypertension130 (49)85 (46)45 (56)0.1Coronary Artery Disease59 (22)38 (21)21 (26)0.3Chronic Obstructive Pulmonary Disease26 (10)15 (8)11 (14)0.1American Society of Anesthesiologists Score $42 (15)$ $32 (17)$ 10 (13)2124 (48)98 (54)26 (32)0.001370 (26)38 (21)32 (40)0.001427 (10)15 (8)12 (15)0.9Prognostic Nutritional Index Score 40 35 (21)24 (21)11 (21)0.9 ≥ 40 132 (79)91 (79)41 (79)0.61Operation Type $118 (45)$ $84 (46)$ $34 (43)$ 0.6Grade $7 (4)$ $6 (33)$ 22 (28)0.61TNM Stage $7 (4)$ $6 (396)$ 1 (1) $7 (4)$ $9 (11)$ TNM Stage 11 $48 (18)$ $39 (21)$ $9 (11)$ 0.24	Diabetes Mellitus	72 (27)	50 (27)	22 (27)	0.9
$\begin{array}{cccc} \hline \text{Coronary Artery Disease} & 59 (22) & 38 (21) & 21 (26) & 0.3 \\ \text{Chronic Obstructive Pulmonary Disease} & 26 (10) & 15 (8) & 11 (14) & 0.1 \\ \hline \text{American Society of Anesthesiologists Score} & & & & & & \\ \hline 1 & 42 (15) & 32 (17) & 10 (13) \\ 2 & 124 (48) & 98 (54) & 26 (32) & 0.001 \\ 3 & 70 (26) & 38 (21) & 32 (40) \\ 4 & 27 (10) & 15 (8) & 12 (15) \\ \hline \text{Prognostic Nutritional Index Score} & & & & & \\ < 40 & 35 (21) & 24 (21) & 11 (21) & 0.9 \\ \geq 40 & 132 (79) & 91 (79) & 41 (79) \\ \hline \text{Operation Type} & & & & \\ \hline \text{Total Gastrectomy} & 118 (45) & 84 (46) & 34 (43) & 0.6 \\ \hline \text{Subtotal Gastrectomy} & 118 (45) & 99 (54) & 46 (57) \\ \hline \text{Grade} & & & & \\ \hline \text{Poorly differentiated} & 173 (66) & 117 (64) & 56 (71) & 0.61 \\ \hline \text{Well-differentiated} & 173 (66) & 117 (64) & 56 (71) & 0.61 \\ \hline \text{Unknown} & 7 (4) & 6 (396) & 1 (1) \\ \hline \text{TNM Stage} & & & \\ \hline 1 & & & & & \\ 1 & & & & & & \\ 1 & & & &$	Hypertension	130 (49)	85 (46)	45 (56)	0.1
$\begin{array}{c ccccc} \mbox{Chronic Obstructive Pulmonary Disease} & 26 (10) & 15 (8) & 11 (14) & 0.1 \\ \mbox{American Society of Anesthesiologists Score} & & & & & & & & & \\ 1 & 42 (15) & 32 (17) & 10 (13) & & & & & \\ 2 & 124 (48) & 98 (54) & 26 (32) & 0.001 \\ 3 & 70 (26) & 38 (21) & 32 (40) & & & \\ 4 & 27 (10) & 15 (8) & 12 (15) & & & \\ \mbox{Prognostic Nutritional Index Score} & & & & & & \\ < 40 & 35 (21) & 24 (21) & 11 (21) & 0.9 \\ \geq 40 & 132 (79) & 91 (79) & 41 (79) & & \\ \mbox{Operation Type} & & & & & \\ \mbox{Total Gastrectomy} & 118 (45) & 84 (46) & 34 (43) & 0.6 \\ \mbox{Subtoral Gastrectomy} & 118 (45) & 99 (54) & 46 (57) & & \\ \mbox{Subtoral Gastrectomy} & 118 (66) & 117 (64) & 56 (71) & & \\ \mbox{Subtoral Gastrectomy} & 7 (4) & 6 (38) & 1 (1) & & \\ \mbox{Well-differentiated} & 173 (66) & 117 (64) & 56 (71) & & \\ \mbox{Well-differentiated} & 173 (66) & 117 (64) & 56 (71) & & \\ \mbox{Well-differentiated} & 173 (66) & 117 (64) & 56 (71) & & \\ \mbox{Well-differentiated} & 7 (4) & 6 (38) & 1 (1) & & \\ \mbox{Well-differentiated} & 82 (31) & 60 (33) & 22 (28) & & \\ \mbox{Unknown} & 7 (4) & 6 (39) & 1 (1) & & \\ \mbox{TNM Stage} & & & & \\ \mbox{I} & & & \\ \mbox{I} & & \\ \mbox{I} & & $	Coronary Artery Disease	59 (22)	38 (21)	21 (26)	0.3
American Society of Anesthesiologists Score 42 (15) 32 (17) 10 (13) 2 124 (48) 98 (54) 26 (32) 0.001 3 70 (26) 38 (21) 32 (40) 4 27 (10) 15 (8) 12 (15) Prognostic Nutritional Index Score < 40	Chronic Obstructive Pulmonary Disease	26 (10)	15 (8)	11 (14)	0.1
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	American Society of Anesthesiologists Score				
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1	42 (15)	32 (17)	10 (13)	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2	124 (48)	98 (54)	26 (32)	0.001
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	3	70 (26)	38 (21)	32 (40)	
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$ \begin{array}{c} < 40 & 35 (21) & 24 (21) & 11 (21) & 0.9 \\ ≥ 40 & 132 (79) & 91 (79) & 41 (79) \end{array} $	Prognostic Nutritional Index Score				
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Subtotal Gastrectomy 145(55) 99(54) 46(57) Grade 173 (66) 117 (64) 56 (71) 0.61 Well-differentiated 82 (31) 60 (33) 22 (28) 0.61 Unknown 7 (4) 6 (3%) 1 (1) 10 TNM Stage 48 (18) 39 (21) 9 (11) 0.24	Total Gastrectomy	118(45)	84(46)	34(43)	0.6
Grade Poorly differentiated Well-differentiated Unknown TNM Stage I U U V V V V V V V V V V V V V	Subtotal Gastrectomy	145(55)	99(54)	46(57)	
Poorly differentiated 173 (66) 117 (64) 56 (71) 0.61 Well-differentiated 82 (31) 60 (33) 22 (28) 0.61 Unknown 7 (4) 6 (3%) 1 (1) 0.61 TNM Stage 48 (18) 39 (21) 9 (11) 0.24	Grade				
Well-differentiated 82 (31) 60 (33) 22 (28) 0.61 Unknown 7 (4) 6 (3%) 1 (1) TNM Stage 48 (18) 39 (21) 9 (11) I 58 (21) 35 (19) 23 (28) 0.24	Poorly differentiated	173 (66)	117 (64)	56 (71)	0.(1
Unknown 7 (4) 6 (3%) 1 (1) TNM Stage 1 48 (18) 39 (21) 9 (11) I 58 (21) 35 (19) 23 (28) 0.24	Well-differentiated	82 (31)	60 (33)	22 (28)	0.61
TNM Stage 48 (18) 39 (21) 9 (11) II 58 (21) 35 (19) 23 (28) 0.24	Unknown	7 (4)	6 (3%)	1 (1)	
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11	I	48 (18)	39 (21)	9 (11)	
$JO(\Delta I)$ $JJ(I)$ $\Delta J(\Delta I)$	II	58 (21)	35 (19)	23 (28)	0.24
III 157 (61) 109 (60) 48 (61)		157 (61)	109 (60)	48 (61)	

TABLE II - Postoperative complications and clinical outcomes

Parameters	Total n: 263 (%)	Age group 65–74 n: 183(%)	Age group ≥75 n: 80(%)	P-value
Complications	64 (24)	40 (22)	24 (30)	
Anastomotic leaks	26 (9.9)	16 (9)	10 (13)	
Bleeding	9 (3)	6 (3)	3 (4)	0.16
Postoperative ileus	10 (4)	5 (3)	5 (6)	
Other	19 (7)	13 (7)	6 (7)	
Clavien Dindo Classification	0.10			
≥ Grade 3	33 (12)	19 (10)	14 (17)	0.10
Postoperative Intensive Care	39 (15)	23 (13)	16 (20)	0.11
Reoperation	7 (2)	2 (1)	5 (6)	0.01
Hospital Stay (median) (days)	5 (1-57)	5.8	7.8	0.02
Hospital Mortality	15 (5)	7 (3)	8 (10)	0.04

ICU care. However, the ASA score, reoperation rates, and hospital mortality were significantly higher in the older group (p=0.001, p=0.01, and 0.04, respectively). No significant difference was observed between the two groups in terms of the presence of any complications and Clavien-Dindo grade 3 or above. The length of hos-

pital stay was also significantly longer in the older group (5.8 vs. 7.8 days, p=0.02) (Table II).

One hundred sixty-seven patients' PNI scores were calculated. The cutoff value in the present study was set as 40, defined as moderate-to-severe malnutrition. There was no difference between age groups regarding PNI



Fig. 2: Overall survival curve of the patients

(Table I). Complications were significantly higher in the group with PNI < 40 (49% vs. 23%, p:0.005)

Multivariate analysis showed a significant relationship between the presence of any complication and PNI < 40 (p=0.02).

The median survival was 34 months in all patients. Survival analysis of age groups showed that the mean 5year overall survival in the 65-74 group was 55%, while it was 33% in the \geq 75 group (Fig. 2). There was a significant difference between the two groups (p=0.002). The median overall survival was 53 months in the 65-74 age group and 23 months in the \geq 75 age group. Multivariate analysis showed that age and disease stage had significant effects on overall survival (p=0.001 and p=0.03).

Discussion

Age is one of the most significant risk factors for cancer, and most solid tumors are considered age-related diseases. The incidence of gastrointestinal malignancies will increase, especially in the elderly ¹⁹. Older adults with stomach cancer have been shown to have lower overall survival than younger adults. This may be due to the lower availability of standard recommended treatment modalities and possible differences in disease biology. Although male, well-differentiated, and distal tumors are seen in elderly patients with gastric cancer, liver metastases are frequently observed. The more aggressive types are more common in younger patients 20-22. Therefore, differences in disease biology may not significantly explain the lower survival seen in the elderly. In a study, which compared those under 65 years of age and above, it was shown that age is not a prognostic factor ²³. In a study investigating the prognostic factors of patients over the age of 60, it was observed that the T stage and the ratio of lymph nodes significantly affected survival ⁶. In this study, the evaluation of patients over 65 years of age, it was observed that hospital mortality and complications increased in patients aged 75 years and older. In multivariate analysis, the TNM stage and age were effective on overall survival.

Patients are at risk of deterioration in organ function and body composition, decreased efficacy of anticancer treatments, and increased toxicity with increasing age. Many of the elderly present comorbidities that present a higher potential risk of complications from surgery or systemic therapies ²⁴. Negative characteristics of older people affect the surgical decision and results. Many studies have been conducted to predict gastrectomy results in elderly patients using various parameters ^{6,25}. The authors have compared different age groups for surgical outcomes ^{23,25}. In this study, we used well-known parameters such as comorbidities, ASA scores, complications, and PNI and compared 65 to 74-year-old and \geq 75year-old patients. The incidence of severe complications was 12%. This result was consistent with the literature ^{3,26}. Although there was no difference in the type of surgery and tumor characteristics in the two groups, the complications and hospital mortality were higher in the \geq 75-year-old group. This study shows that the older group has higher complication rates and is consistent with previous studies ^{11,27,28}. However, in another study evaluating patients aged 69 years and older, it was observed that patients aged 80 years and older who underwent gastrectomy had the same survival and postoperative morbidity as younger patients. However, it was observed that the elderly group received less chemotherapy and had less survival, especially in stage 2 tumors. This difference may have been observed because less chemotherapy was recommended with age or patients refused chemotherapy 29. It was also observed that the survival of the elderly group who could receive chemotherapy was longer than that of those who could not ^{30,31}.

Del Rio et al showed that postoperative complications and mortality increased over the age of 75 but were not statistically significant when compared below 75 3 .

PNI is an important indicator of prognosis in gastric cancer, as in many other types of cancer, reflecting the patient's nutritional condition and immune index. This study shows that complications are more common in patients with low PNI scores, but there is no difference between the two groups regarding hospital mortality. In another study comparing those over and under 75 years of age, it was shown that the overall survival of the elderly group was low due to causes other than gastric cancer. In particular, multiple comorbidities and low PNI scores have been significant risk factors for death ³². As in other studies, we could not show that high PNI scores are related to a good prognosis ³³⁻³⁶. These results may be related to our small study cohort.

Our study has certain limitations. It is a single-center and low-volume study. Larger multicenter studies will be required to further evaluate and compare the prognostic factors for gastric surgery patients.

Conclusions

Gastrectomy can be safely performed on the elderly. However, an increase in complications and in-hospital mortality is recognized over the age of 75. We should closely monitor patients over 75 years of age and be prepared for these complications. The surgical and postoperative care decisions should be made carefully according to the patient's condition.

Riassunto

Il cancro gastrico è un tumore comune e la sua incidenza rimane relativamente alta nei pazienti anziani con un'aspettativa di vita in aumento. Tuttavia, pochi studi hanno esaminato le caratteristiche cliniche e prognostiche dei pazienti anziani con cancro gastrico sottoposti a gastrectomia. Questo studio mira a valutare le caratteristiche cliniche e prognostiche dei pazienti anziani con gastrectomia.

MATERIALI E METODI: Sono stati analizzati retrospettivamente i pazienti di età superiore ai 65 anni che hanno subito un intervento chirurgico per cancro gastrico presso l'Università di Marmara. Sono stati esaminati i dati demografici dei pazienti, i punteggi dell'American Society of Anesthesiologists, l'indice nutrizionale prognostico (PNI), le complicanze, la durata dell'unità di terapia intensiva e la durata della degenza. I pazienti sono stati divisi in due gruppi: giovani (65-74 anni) e anziani (≥ 75 anni). Due gruppi sono stati confrontati in termini di esiti postoperatori e sopravvivenza globale.

RISULTATI: Sono stati analizzati duecentosessantatre pazienti. L'età media era di 79 anni e il rapporto tra femmine e maschi era di 85/178. I tassi di reintervento e la mortalità ospedaliera erano significativamente più alti nel gruppo di anziani (p=0,001 e p=0,01, rispettivamente). La degenza ospedaliera è stata significativamente più lunga nel gruppo di anziani (5,8 vs 7,8 giorni, p= 0,02). Le complicanze erano significativamente più alte nel gruppo con un PNI < 40 (49% vs. 23%, p=0,005). C'era una differenza significativa tra i due gruppi per quanto riguarda la sopravvivenza globale a 5 anni (33% vs. 55%, p=0,002).

CONCLUSIONI: La gastrectomia può essere eseguita sugli anziani. Tuttavia, si riconosce un aumento delle complicanze e della mortalità intraospedaliera sopra i 75 anni. Questi problemi dovrebbero essere considerati in questa fascia di età avanzata.

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