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Does proximal gastrectomy work better versus total gastrectomy in proximal gastric cancers? A Comparative analytic study

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Summary

Background and aim: The ideal extent of resection in proximal gastric cancer is still controversial and there is no general consensus. Therefore, this study was designed to compare the results of proximal gastrectomy versus total gastrectomy in patients with proximal gastric cancer.

Methods: One hundred forty-six patients who underwent total (n=96) or proximal (n=50) gastrectomy due to proximal gastric cancer in Firoozgar Hospital, in Tehran, Iran in 2015 and 2021 were enrolled. Patients were classified and evaluated according to age, sex, duration of hospitalization, 30-day mortality, histological grading and stage, resection margin, lymph node involvement, and overall survival.

Results: Patients who underwent proximal gastrectomy had a significantly longer survival (P=0.025). There was no statistically significant difference between the two groups in terms of the number of lymph nodes removed and the status of resected margin. Cox regression analysis showed that the number of positive lymph nodes, undergoing splenectomy and grade of invasion were associated with decreased survival (P<0.05).

Conclusion: The optimal treatment for proximal gastric cancer is not yet known. Although patients with proximal gastric cancer who underwent proximal gastrectomy had better survival, it might be due to the confounding effect of a grade of invasion, which needs further investigations in this field.

EDN: FLJYFY

Keywords: Gastric cancer, Gastrectomy, Survival

Conflict of interests. The authors declare no conflict of interest.

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Эффективна ли проксимальная резекция желудка лучше, чем тотальная гастрэктомия при раке проксимального отдела желудка? Сравнительно-аналитическое исследование

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Резюме

Цель: Идеальный объем резекции при раке проксимального отдела желудка до сих пор остается спорным и не имеет общего согласия. Таким образом, это исследование было разработано для сравнения результатов проксимальной гастрэктомии и тотальной гастрэктомии у пациентов с проксимальным раком желудка.

Методы: В исследование были включены сто сорок шесть пациентов, перенесших тотальную (n=96) или проксимальную (n=50) гастрэктомию по поводу проксимального рака желудка в больнице Фирузгар в Тегеране, Иран, в 2015 и 2021 годах. Пациенты были классифицированы и оценены в соответствии с возрастом, полом, продолжительностью госпитализации, 30-дневной смертностью, гистологической классификацией и стадией, краем резекции, поражением лимфатических узлов и общей выживаемостью.

Результаты. Пациенты, перенесшие проксимальную гастрэктомию, имели значительно более длительную выживаемость (P=0,025). Статистически значимой разницы между двумя группами по количеству удаленных лимфатических узлов и состоянию резецированного края не было. Регрессионный анализ Кокса показал, что количество положительных лимфатических узлов, подвергшихся спленэктомии, и степень инвазии были связаны со снижением выживаемости (P<0,05).

Заключение: Оптимальное лечение рака проксимального отдела желудка пока не известно. Хотя пациенты с проксимальным раком желудка, перенесшие проксимальную гастрэктомию, имели лучшую выживаемость, это может быть связано с мешающим эффектом степени инвазии, что требует дальнейших исследований в этой области.

Ключевые слова: рак желудка, гастрэктомия, выживаемость

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Introduction

Gastric cancer (GC) is one of the most life threatening malignancies with a high mortality rate worldwide. According to the statistics, it is the fifth most common cancer which can affect a wide range of age groups. There are quite number of risk factors, such as smoking, infection with H-pylori and an unhealthy diet consisting of high salt intake and low fruits and vegetables [1–3].

Proximal gastric cancers and cancers of gastro-esophageal junction can be classified into three types; type I, consisting of distal oesophagus, type II, involving cardia and type III which involves the main stomach, distal to the cardia [4]. Based on histological classification, adenocarcinoma is the most common type [5]. In our country, Iran, GC is responsible for the most cancer related mortality, especially in men; nevertheless, there is no screening program for its early detection. Therefore, the principal option in treatment of these cancers is surgical resection [6].

Treatment of gastric cancer is based on gastrectomy following neoadjuvant chemotherapy. Since the outcome is poor, patient-centred treatments based on gene therapy might be a promising therapeutic option in near future of GC management [7]. Although total gastrectomy is a conventional treatment of choice for proximal gastric cancers, it can evolve significant morbidity and mortality. Partial gastric resection has been developed to remove some drawbacks according to physiologic and anatomic reasoning. On the other hand, disadvantages of partial gastric resection by proximal gastrectomy can be a violation of oncologic principles and developing gastro-esophageal reflux [8].

Proximal gastric cancer is currently treated with total or proximal gastrectomy; the choice of each is based on the size and the stage of tumour, the amount of remaining stomach volume and also the surgeon's skills. Proponents of total gastrectomy believe that complete resection along with radical lymphadenectomy can lead to better therapeutic effects with free distal margins, while opponents suggest that the remaining gastric tissue in proximal gastrectomy can be beneficial [9, 10].

Finally, the ideal extent of resection in proximal gastric cancer is still controversial and there is no general consensus. Therefore, the aim of this study was to compare early results of upper third gastric cancer treatment with either total or proximal gastrectomy.

Patients and Method

In this cohort study, 146 patients with gastric cancer who had undergone gastrectomy, either total or proximal, in Firoozgar hospital, in Tehran, Iran from March 2015 to December 2020 entered the study. Patients were followed up till the time of study (2021). Exclusion criteria were as follows: Siewert–Stein type I adenocarcinoma, gastric remnant adenocarcinoma, anastomotic site recurrent carcinoma, gastrointestinal stromal tumours, neuroendocrine tumours, lymphomas, antro-pyloric lesions, synchronous primary, combined operation, liver failure and recent myocardial infarction within the previous 6 months.

The evaluated variables were age, sex, duration of hospitalization, 30-days mortality, histological type and stage, resection margin, lymph nodes, grade of invasion (T) and survival by reviewing the clinical records. In case of any doubt or missing data, a telephone call was made to compete data.

Data analysis

Results were expressed as mean and standard deviation (mean±SD) for quantitative variables and as a percentage for stratified qualitative ones. Independent t test and Mann-Whitney test were used to compare the variables between proximal and total gastrectomy groups. Chi square test was used to compare qualitative variables. Kaplan-Meier plot was used to compare survival between the groups and Cox regression analysis was run to predict survival. P value below 0.05 was considered as statistically significant. SPSS software version 21 (SPSS Inc. Chicago, Il, The USA) was used for data analysis.

Ethical issues

An informed consent was obtained from live participants or their legal guardians if died. The study protocol was approved by the ethics committee of Iran University of Medical Sciences (registration number IR.IUMS.FMD.REC.1398.522). The study steps were performed according to Helsinki declaration.

Results

Fifty (34.25%) of 146 patients had undergone proximal gastrectomy (group A) and the remaining 97 (65.75%) patient's total gastrectomy (group B). The mean age in group A and B were 65.06±10.9 and 61.4±11 years, respectively. There was no significant difference between the two groups in terms of age (P-value=0.057). Moreover, the two groups were not significantly different in terms of gender (P-value=0.720). According to inclusion and exclusion criteria, all patients had adenocarcinoma. Data regarding post-op permanent pathology, marginal, the number of removed lymph node and etc. were summarized in Tables 1 to 4.

Duration of surgery in Groups A and B were 3.52±0.38 and 4.33±1.33 hours, correspondingly. There was a significant difference between the two groups regarding the operation time (P-value<0.001). Days of hospitalization were 6.76±1.84 and 7.37±1.27 days in groups A and B (P-value=0.020) (Table 5). Two patients in each group died within 30 days after the operation (P-value=0.494) (Table 6). In addition, higher grades of invasion were reported in group B patients (P=0.008).

Patients were followed up for an average of 21.43±15 months. It was found that the median and mean survival of patients using Kaplan-Meyer in group A were 40 and 40.75±4.12 months, while in group B, they were 24 and 32.16±2.83 months, respectively (Figure 1).

In addition, patients undergoing proximal gastrectomy had a significantly longer survival (P-value=0.025) using log-rank method. Furthermore, number of positive lymph nodes, undergoing splenectomy and grade of invasion were associated with decreased survival by Cox regression method (P<0.05) (Table 7).

Table 1.
Gastric cancer pathology types

Pathology	Surgery type	
	Proximal gastrectomy No. (%)	Total gastrectomy No. (%)
Adenocarcinoma (Non-specified)	20 (40)	43 (44.3)
Well-differentiated Adenocarcinoma	7 (14)	17 (17.5)
Moderate-differentiated Adenocarcinoma	15 (30)	15 (15.5)
Poor-differentiated Adenocarcinoma	8 (16)	21 (21.6)
Total	50 (100)	96 (100)

Table 2.
Marginal involvement in tissue samples

Type of gastrectomy	Non-involved margin	Involved margin	Total
Total gastrectomy	93 (96.9%)	3 (3.1%)	96 (100)
Proximal gastrectomy	49 (98%)	1 (2%)	50 (100)
Total	142 (97.26%)	4 (2.74%)	146 (100)

Table 3.
Number of removed lymph nodes during the operation

Type of surgery	Number of lymph nodes	Number of involved lymph nodes
Total gastrectomy	21.06±7.71	4.25±7.26
Proximal gastrectomy	18.82±7.53	6.69±8.53
P-value	0.095	0.072

Table 4.
Concomitant splenectomy during gastrectomy

Type of surgery	Splenectomy	Total
Total gastrectomy	15 (15.5)	96 (100)
Proximal gastrectomy	5 (10)	50 (100)
Total	20 (13.6)	146 (100)

Table 5.
Comparison of surgery duration and days of hospitalization in both groups

Type of surgery	Duration of surgery (hour)	Days of hospitalization (day)
Total gastrectomy	4.33±1.33	7.37±1.27
Proximal gastrectomy	3.52±0.64	6.76±1.84
P-value	<0.001*	0.020*

* Significant at 0.05, independent t test.

Table 6.
Grade of invasion between the two groups (No. and %)

Type of surgery	Response to chemotherapy	T1	T2	T3	T4	Total
Total gastrectomy	21 (21.9)	10 (10.4)	7 (7.3)	50 (52.1)	8 (8.3)	96 (100)
Proximal gastrectomy	14 (28)	4 (8)	19 (38)	11 (22)	2 (4)	50 (100)

Table 7.
Cox regression analysis for prediction of survival

Predictor (unit)	Hazard ratio (HR)	95% confidence interval	P-value
Positive lymph nodes (1 number)	1.051	1.019, 1.084	0.002*
Splenectomy (yes)	2.185	1.166, 4.092	0.015*
Grade of invasion (1 grade)	1.300	1.050, 1.610	0.016*

* Significant at 0.05, backward method. HR >1 indicates reduced survival. For grade of invasion, complete response to chemotherapy was considered as 0.

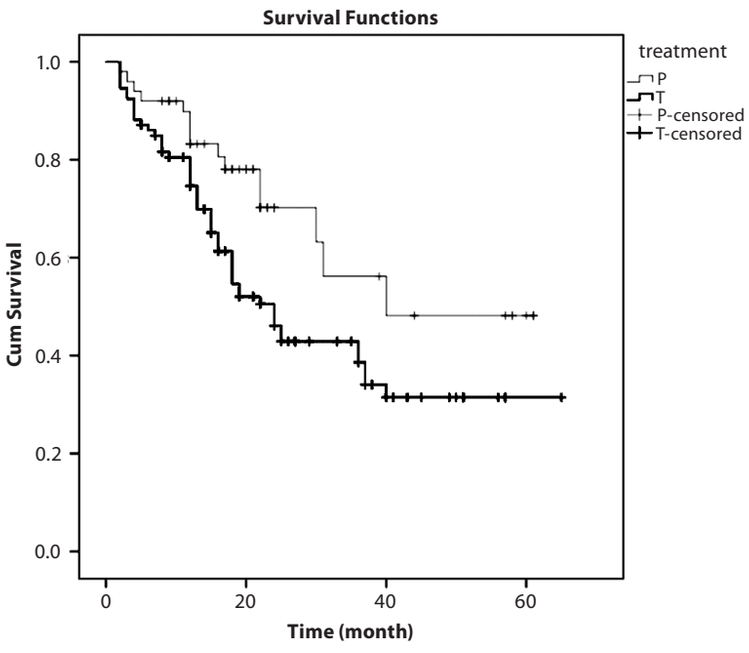

Figure 1. Patient survival chart by Kaplan-Meyer analysis

Discussion

According to the latest reports from the Ministry of Health, gastric adenocarcinoma is the deadliest cancer in Iran. The maximum prevalence is in the seventh decade of life in men and older women, as the prevalence of the disease is increasing by age [11].

Five-year survival rate is 10–30% according to the studies in European countries, which is similar to the United States at about 15% to 28%. In recent decades, the most common site of gastric cancer has shifted from distal to the proximal part of the stomach [12, 13]. This shift in gastric cancers has prompted incentives to review the upper gastric cancer protocol for the extent of resection; total gastrectomy versus proximal gastrectomy. Gastric reservation by considering surgical oncologic principals is the most important goal of proximal gastrectomy [14].

On the other hand, metastasis to the lymph nodes of the supra and infrapiloric is very rare in cancers of the proximal stomach, and removing them has little effect on survival [15]. The number of lymph nodes removed in proximal gastrectomy (PG) was less than total gastrectomy (TG), but no significant difference was observed between the overall survivals of the two groups [16]. In our study as well, on average 21.06 lymph nodes were removed in group B, in which 4.25 lymph nodes had cancerous involvement. In group A, on average 18.82 lymph nodes were removed, in which 6.69 lymph nodes had metastatic invasion, however, the difference was not statistically significant. Although, Lymph node dissection in each group was not significantly associated with survival rate.

A negative margin after tumour resection is a main principle of gastric cancer surgery. In total gastrectomy, a safe distal margin is provided. However in PG, frozen section during operation can confirm distal free margin [17]. In our study, proximal margin involvement was observed in 2 and distal margin in 1 patient who underwent TG, while in PG there was one patient with proximal margin involvement. This low rate probably indicates the surgeon judgment to convert PG to TG and considering intraoperative frozen section to ensure a free distal margin. Moreover, the existence of positive margin in each group had no significant relationship with survival rate. In our centre as a high load cancer surgery hospital, frozen section is almost always performed during gastrectomy.

Duration of operation and the amount of bleeding depend on the number of anastomoses and distal perigastric node dissection. According to existing studies, the duration of operation in the PG group is shorter than the TG group [18].

Moreover, the duration of hospitalization and postoperative mortality were the same in both groups, but the rate of splenectomy was higher in the TG group [17]. The duration of operation in patients who underwent TG was 4.33 hours and in the PG group was 3.52 hours. Patients were hospitalized for an average of 7.37 days in TG group while it was 6.76 days in PG group, which was significantly less than total gastrectomy patients.

Surgical management of patients with proximal gastric cancer is still controversial regarding the extent of resection. The best surgical procedure for gastric cancer should adhere to the following characteristics; first, a complete tumour removal, second a safe and patent jujeno-esophageal anastomosis and third a free margin and finally a complete regional lymph node dissection. Based on several studies, total gastrectomy can provide better outcomes regarding the above goals, while in some others there were not significant differences between the two options. Other factors such as the duration of operation, days of hospitalization, 30-days mortality and 5-years survival rate are also important. According to different studies, we could not yet declare whether proximal gastrectomy is more efficient than total gastrectomy [17, 19–25].

Another important issue in gastric cancer surgery is quality of life (QOL). It seems that QOL in proximal gastrectomy is better regarding nutritional status and digestion compared with total gastrectomy. However, gastroesophageal reflux is a common complication

in PG which can be prevented by modified anterior antireflux procedure. More studies should be performed on these subjects.

In this study, the number of lymph nodes removed and the margin involvement were not significantly different between the two groups, Moreover, the amount of lymph node dissection and positive margin involvement were not significantly associated with survival. Duration of operation and the days of hospitalization in TG were longer than the PG group, with statistically significant difference.

Several studies have shown that there is no significant difference between the two groups in terms of survival [10, 25, 26]. Survival between the two groups was compared by log-rank method. It was found that patients undergoing proximal gastrectomy had a significantly longer survival.

Lower survival rate in total gastrectomy is probably due to larger tumour and more advanced stage of the disease. In addition, in the study of factors affecting patient survival by Cox regression the number of positive lymph nodes, concurrent splenectomy and grade of invasion were associated with decreased survival. It shows that higher grades of invasion in total gastrectomy may be associated with decreased survival.

Conclusion

Patients with proximal gastric cancer had a shorter hospitalization and surgical duration and a longer survival. Actually, proximal gastrectomy is not inferior to total gastrectomy, while future studies should be considered to focus on patient's postoperative function and quality of life. Both procedures can be suggested as safe methods.

Conflicts of interest and disclosure. The authors declare that there is no conflict of interest regarding the publication of this article.

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Authors' contribution. ICMJE criteria for authorship were followed.

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