SURVIVAL RELATED FACTORS IN GASTRECTOMY SPECIMENS. A STUDY OF 65 CASES IN DUHOK CITY - IRAQ

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ABSTRACT

Background: Gastric cancer is one of the commonest malignancies and one of the most common causes of cancer deaths worldwide. This study aims to investigate the survival-related factors in gastrectomy specimens.

Method: This is a cross-sectional retrospective study that included 65 gastrectomy specimens in Duhok City-Iraq over a period of 6 years from January 2014- November 2019.

The parameters sought included age, gender, histological type, grade, lymph node status, tumor size, resection margin status, and lymphovascular and perineural invasions. Patients were grouped for their ages with an interval of 10 years and pathological parameters were expressed in frequencies and percentages.

Results: The male to female ratio was 1.1:1, and the most affected age group was between 60-69 years. The intestinal type adenocarcinoma represented 64.61% of cases, and the remainders were of the diffuse type. The resection margins were tumor-free in 78.5% of cases, and 80% had a lymphovascular invasion. Perineural invasion was seen in 35.38% of the included patients. Only 16.92% of patients were negative for lymph node involvement, and the nodal status was N0: 16.9%, N1:58.5%, N2: 18.5%, and N3:6.1%, and 66.15% of them fell in T3 category. The majority of patients had more than 4 adverse survival-related factors.

Conclusion: The present study showed that most of gastric carcinoma patients had multiple bad prognostic factors a fact that mostly correlated to their late presentation and a finding that indicates the gloomy outcome for patients at least in the near foreseen future unless a screening program is rapidly initiated.

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Keywords: Gastrectomy, Iraq, Survival Related Factors

Stomach carcinoma continues to be a major issue in oncology despite reducing its incidence globally[1], and still, it ranks 5th among others2. Until recently, its prognosis is gloomy and comes second to colorectal cancer as a cause of death from gastrointestinal cancers worldwide1. Gastric adenocarcinoma is multifactorial, with the possible interaction between genetic and environmental factors. Among the most important causes are; smoking, alcohol, dietary factors, infection with H. pylori, autoimmune gastritis, chronic atrophic gastritis, intestinal metaplasia, previous gastric surgeries, Peutz-Jeghers syndrome, Li-Fraumeni syndrome, and hereditary diffuse gastric cancer syndrome[3-6].

When all stages are combined, the 5 years survival still falls below 20%. The best option for treating stomach cancer is surgical removal with the lymph nodes plus the consideration of chemotherapy and or radiotherapy, which may have a good impact on the outcome[7]. Although remarkable progress has been made in

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gastric cancer treatment, gastrectomy with regional lymphadenectomy still remains the primary treatment for the resectable disease. Surgical resection alone with no pre-or postoperative treatment provides a five-year overall survival rate of approximately 20–30% [8,9].

Many factors affect the outcome of stomach adenocarcinoma. Knowledge about these factors enables us to assign the patient to a specific prognostic group and determine the most suitable therapeutic protocols to increase patients' survival and reduce the possible recurrence rate[7].

Advancing age was found to have a negative impact on survival, while gender does not have such an effect in one Korean series[10]. In contrast, in another study, it was found that females with gastric carcinoma were significantly younger and had more signet ring carcinoma histology than males. Furthermore, females had significantly poorer outcomes among young patients with signet ring carcinoma[11].

The tumor stage is the most significant factor post-surgically, according to the International Union against Cancer/ American Joint Committee on Cancer (UICC/AJCC)[12,13].

Tumor size is an important determinant of survival. The five-year survival rate was 84.3% in T1 tumors, 64.8% in T2 tumors, 48.9% in T3 tumors, and 29.2% in T4 tumors, according to one series12. Survival rates vary according to the T and N stage, being around 85–90% in T1 tumors and around 15–20% in T4 tumors and node-positive patients[14].

Lymph node metastasis has the most decisive influence on the prognosis of gastric cancer[15].

According to one huge meta-analysis of73 data, the diffuse type of gastric carcinoma has a worse prognosis than the intestinal type[16].

Other important factors that influence patients' survival include lymphovascular invasion, grade, resection type, and performance status[8,9]. When both coexist, the lymphovascular and perineural invasion have a significant prognostic impact on disease-free survival and overall survival in patients with Stage II or III gastric cancer (17). Perineural invasion was found to be an independent prognostic factor (18). According to a multiple logistic regression model, depth of cancer invasion and lymphatic invasion were significantly correlated with lymph node metastases. Among the clinicopathological factors, depth of invasion and microscopically lymphatic invasion are important factors in predicting lymph node metastases. Thus, the ability to perform gastrectomy with dissection of lymph nodes represents a basic requirement for gastric cancer surgeons (15). The lymph node ratio is a predictor of survival for patients who underwent curative gastrectomy regardless of the number of lymph nodes examined. Thus, the lymph node ratio may be adopted as a new indicator for prognostic purposes19.

Prognostic score based on age, tumor size, and grade forms an independent predictor of survival after gastrectomy[20,21]. Involvement of the resection margins is another key prognostic[22].

This study aims to identify the main prognostic factors affecting survival and recurrence of gastric adenocarcinoma.

METHODS

This retrospective study included 65 cases of stomach adenocarcinoma in Duhok City from 2013-2019. Reports and slides were retrieved from many laboratories in Duhok. The patient privacy was maintained by giving a code for each patient. All the 65 cases had gastrectomy for stomach carcinoma. Patients were divided according to their gender and age groups using a 10 years interval. Then a search for all factors included in the reports and have relations to the prognosis was determined. These included age group, histological types, grade, resection margins involvement, lymphovascular invasion, perineural invasion, and lymph nodes status. The results of each variable were expressed in frequencies and percentages.

RESULTS

Figure 1 demonstrates the gender distribution of included patients, 31 females, and 34 males.

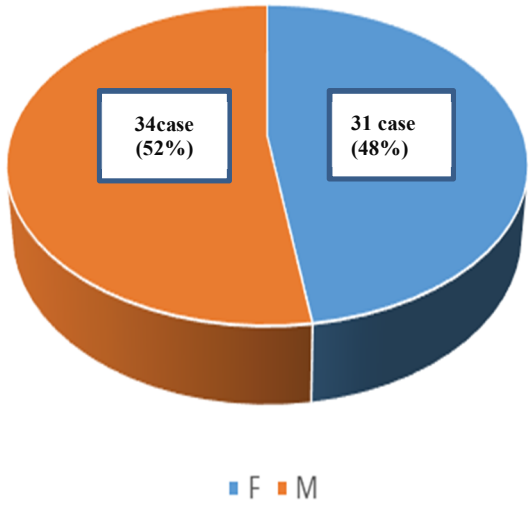

Figure 1: The gender distribution of the included patients.

The most affected age group ranges from 60-69 years, and figure 2 shows the age distribution of all the patients.

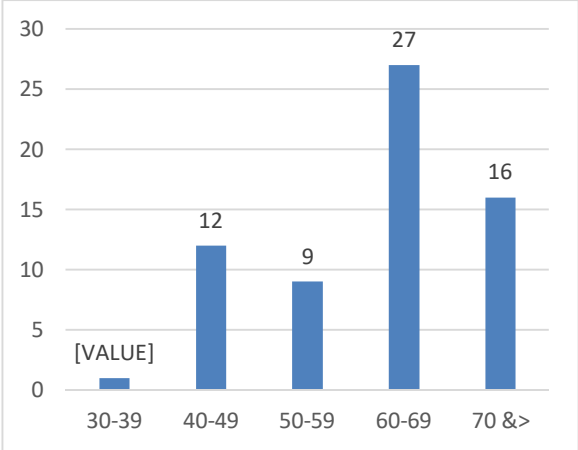

Figure 2: The age distribution of the included patients.

The intestinal type of gastric carcinoma was diagnosed in 42 (64.61%) patients, and table1 shows the histological types of gastric carcinoma.

Table1: The histological types of gastric carcinoma

Histological type	No.	%
Intestinal	42	64.61
Diffuse	21	32.31
Mucinous	1	1.54
In-situ	1	1.54

Table 2: The histological grading of the 42 cases of the intestinal type adenocarcinoma.

Tumor grade	No	%
Well differentiated	2	4.76
Moderately differentiated	22	52.38
Poorly differentiated	18	42.86
Total	**42**	**100**

Only 2 (4.76%) cases out of the 42 cases were well-differentiated (Table 2). The resection margins were tumor-free in 51 (78.5%) cases and involved by the tumors

in the rest 14 (21.5%) cases. Lymphovascular invasion was detected in 52 (80%) of cases. Perineural invasion was detected in 23 (35.38%) cases.

About the lymph node status table 3 shows that only 11 (16.92%) cases had no lymph node involvement, and the rest of the patients have variable lymph node involvement.

Table 3: Lymph node status in all the included cases.

Number of LN involved	No. of patients	%	Nodal status	%
0	11	16.92	N0	16.9
1	6	9.23		
2	6	9.23	N1	58.5
3	7	10.76		
4	8	12.30		
5	8	12.30		
6	3	4.61		
7	3	4.61		
8	1	1.53		
9	1	1.53	N2	18.5
10	2	3.07		
11	2	3.07		
12	1	1.53		
13	1	1.53		
14	1	1.53		
16	1	1.53		
17	1	1.53	N3	6.1
18	1	1.53		
24	1	1.53		
Total	**65**	**100**		**100**

In consideration of the tumor size (T) in the TNM staging system, 43 (66.15%) patients fell in the T3 category (Table 4).

Table 4: The T variable in the pTNM staging.

T variable in TNM	No.	%
T0	1	1.54
T1	3	4.62
T2	12	18.46
T3	43	66.15
T4	6	9.23
Total	**65**	**100**

When an age over fifty years and female gender are considered as poor prognostic factors, and with the consideration of other adverse factors (Diffuse histology, high grade, lymph node involvement, large tumor size, presence of lymphovascular invasion, perineural invasion, and resections margin involvement), the results of this study show that 15 patients had 4 adverse prognostic factors, 10 patients had 5 adverse factors and 17 patients had 6 adverse factors (Table 5).

Table 5: The number of adverse prognostic factors in all the included patients.

Number of adverse prognostic factors	Number of patients	Percentage
1	1	1.53
2	3	4.62
3	7	10.77
4	15	23.08
5	10	15.39
6	17	26.15
7	7	10.77
8	5	7.69
9	0	0
Total	**65**	**100**

DISCUSSION

Gastric cancer, one of the commonest malignant tumors worldwide, causes thousands of deaths annually[19,23,24,25] and represents the fifth most common cancer all over the world and the second leading cause of cancer mortality. There is marked geographical variation in its highest incidence in Japan, China, other East Asian countries, Eastern Europe, and South America. Over the past sixty years, there was a marked decline in the West incidence but an unfortunate increment in gastroesophageal ones[26].

There is also significant variation in the outcome and survival rates, which reaches 70% in East Asian countries (including Japan) while remains low in most western countries despite the great advancement in the diagnosis and treatment with an overall survival rate of less than 30% [10,27].

The burden of gastric cancer is mostly bear by the developing countries, having more than 70% of the total world cases; most of these being in East Asia, which bear about 50% of total cases in the world[2, 28]. Extension of patients' lives after curative resection remains the consistent goal. Therefore, prognostic factors were studied extensively globally[19].

Many studies confirmed the male predominance of gastric carcinoma[12,20,28,29], and this study is not an exception demonstrating a male to female ratio is 1.1:1.

The peak incidence in this series was in the 6th decade of life; this is similar to what was reported by Zeraati et al. in one Iranian series[20] and higher than reports from Turkey, Kuwait, and Egypt[12,26,29]. While USA, Australia, China, Korea, and UK, the peak incidence was in the 8th decade of life[30,31,32,33,34,35].

Histologically, the intestinal type of gastric adenocarcinoma represented 64.61% of cases in this series, and this is in agreement with many other workers' reports[17,28,29].

Regarding grade of the intestinal type, only 2 (4.76%) cases out of the 42 cases are well-differentiated, which is very similar to what was reported from Korea, Turkey, and Egypt[10,12,29]. The most likely explanation for this finding is that most cases of gastric carcinoma present lately and because of the absence of screening programs.

The resection margins in this work were tumor-free in 51 (78.5%) cases and involved by the tumors in the rest 14 (21.5%) cases; in a similar study done in North East Turkey, the resection margins were positive in 11.7% [36].

Unfortunately, the lymphovascular invasion was detected in 52 (80%) of our cases, a much higher than what was reported from North East Turkey36 and Korea10. This fact could be attributed again to the late presentation in our patients.

Perineural invasion was linked to poor differentiation and advanced stage[17], and in our study, the perineural invasion was detected in 23 (35.38%) cases, and this is lower than what is reported from a multicenter meta-analysis which reported 40.9%[18].

Lymph node stage (N stage) is one of the foremost prognostic factors[37,38,39]. It was considered as an independent prognostic factor[40]. In this study, only 11 patients (16.9%) were negative for lymph node involvement, and the lymph node stage

was as follows N0: 16.9%, N1:58.5%, N2: 18.5%, and N3:6.1%. Darwish et al reported a nodal stage of N0: 10.9%, N1: 39.1%, N2: 44.6%, N3: 5.4% ([29]) and Canyilmaz E et al reported a nodal status of N0:19.5%, N1:25.3%, N2 59:23% N3A: 26.1%, N3B:6.2%[36]. Data from one study in Iran showed that 55.8% of their patients had no lymph node involvement[20], and from Korea 46.2% were negative for lymph node involvement[10].

This study showed that 66.15% of cases had T3, which is an advanced T parameter in the staging system. Many other workers also demonstrated advancement in the T parameter[12,29,36].

The conclusion which could be made from this study is that still, stomach cancer presents in advanced stages with multiple bad prognostic factors. This fact necessitates introducing a screening program to diagnose cases in early stages with less adverse prognostic factors.

CONFLICT OF INTEREST

We – the authors of this research- declare that there is no conflict of interest

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پوختە

فاکتڕێن ژیانێ یین پەیواندیدار د نمونێن گاستروانتستاین. لێکولینك ل سەر 65 بویارێن ل باژێرێ دهوکێ– عیراق

ئێشەکی: پەنچەشێرا گەدێ دهێتە هژمارتن وەک ئێک ژ بەربەلاڤترین پەنچەشێرێن ڕق پیس و ئێک ژ ئەگەرێن سەرەکی یێن مرنێ ژ نەخوشیا پەنچەشێرێ لهەمی جیهانێ ، ئارمانجا مە لڤێ ڤەکولینێ ئەو بوو کو دیڤچوون بهێتە کرن لسەر فاکتەرێن گرێدای هەبوونێ د نموونێت راکری یێن گەدێ دا.

ڕێکێن ڤەکولینێ: ئەڤ ڤەکولینە یا بەندبرە و کونخوازە و 65 نموونێت گەدێ یێن نیشتەرگەریێ بخووڤە دگرێتن لباژێرێ دهوکێ/عراق بو ماوێ 6 ساڵان مەها ئێک 2014- مەها یازدە 2019

پیڤەرێن پێویست. ژی، توخم، جورێ شانێ، پلە، بارێ گرێیێن لمفاوی، قەبارێ گرێ یێ، بارێ کەنارێ راکرنێ، داگیرکرنا لمفاوی و بورییێن خووینێ و دەماران . نەخوش هاتنە دابەش کرن لدویڤ ژیێ وان و بجوداهیا 10 ساڵان تیژیێن نەخوشیێ هاتنە دیار کرن و ناف دووبارەبوون و رێژا سەدی دا

دەرئەنجام: رێژا توخمێ نێر وو مێ 1.1:1 و ژیێ پتر هەمیان بەرکەفتی دناڤ بەرا 60_69 سالی دا بوون و 64.61% ژ جورێ ریخوڵان بوو و یێن دیتر ژیک ژ جورێ بەرەڵاڤ بوون

کەنارێ راکرنێ یێ پاقژ بوو ژ پەنچەشێرێ ل 78.5٪ و داگیرکرنا بورییێن خووینێ و دەماران ل 80٪ و داگیرکرنا دوردەماری ل 35.38٪ نەخووشان هەبوو. و لدەف 16.92٪ داگیرکرنا گرییێن لمفاوی نەبوو، و بارێ گرییێن لمفاوی بڤی شێوەی بوو N0 16.9 و 58.5٪ N1و N2 18.5 %و N3 6.1و 66.15٪ دهاتنە هژمارتن. T3لدەف پتریا نەخوشان زێدەتر ژ چار فەکتەرێن نەرێنی هەبوون گرێدای بەردەوام بوونا ژیانێ بوون.

کوتای یان دەرکەفتن: ئەڤ ڤەکولینە نوکە دیار دکەتن کو رێژەیا هەرە زور یا نەخوشێن پەنچەشێرا گەدێ گەلەک فەکتەرێن نەرێنی یێت هەین، ئەڤە ژیک دبیتە ڕاستیەک گرێدای نیشانێن نەخوشیێ یێن درەنگ، و ئەنجام دیاردکەن پاشەروژ یا تاریە لبەر نەخوشان ب کێمی ل پاشەروژا دیتی دا ئەگەر چ بەرنامێن بلەز نەهێنە دانان بو دەست نیشانکرنا نەخوشیا بەروەخت.

الخلاصة

عوامل البقاء على قيد الحياة ذات الصلة في عينات الجهاز الهضمي. دراسة 65 حالة في مدينة دهوك – العراق

الخلفية والأهداف: يعد سرطان المعدة أحد أكثر الأورام الخبيثة شيوعًا وأحد الأسباب الأكثر شيوعًا لوفيات السرطان في جميع أنحاء العالم. الهدف من هذه الدراسة هو التحقيق في العوامل المرتبطة بالبقاء في عينات استئصال المعدة.

طرق البحث: هذه دراسة مقطعية بأثر رجعي تضمنت 65 عينة استئصال معدة في مدينة دهوك – العراق على مدى 6 سنوات من كانون الثاني 2014 الى تشرين الثاني 2019

المعايير المطلوبة هي العمر ، والجنس ، والنوع النسيجي ، والدرجة ، وحالة العقدة الليمفاوية ، وحجم الورم ، وحالة هامش الاستئصال ، والغزوات اللمفاوية و الوعائيه الدمويه والعصبية. تم تصنيف المرضى حسب أعمارهم بفاصل 10 سنوات. تم التعبير عن المعلمات المرضية في التكرارات والنسب المئوية.

النتائج: كانت نسبة الذكور إلى الإناث 1.1: 1 وكانت الفئة العمرية الأكثر تضررا بين 60–69 سنة. النوع المعوي يمثل 64.61٪ من الحالات والباقي من النوع المنتشر. كانت هوامش الاستئصال خالية من الورم في 78.5٪ وكان 80٪ غزو الأوعيةالدمويه و اللمفاوية. شوهد الغزو حول العصب في 35.38٪ من المرضى المشمولين. كان 16.92 ٪ فقط من المرضى سلبيين للانتشار الى العقد الليمفاوية وكانت الحالة العقدية N0: 16.9٪ ، N1: 58.5٪ ، N2: 18.5 ٪ و N3: 6.1 ٪ و 66.15 ٪ منهم تقع في فئة T3 كان لدى غالبية المرضى أكثر من 4 عوامل سلبية مرتبطة بالبقاء على قيد الحياة.

الخلاصة: تُظهر الدراسة الحالية أن معظم مرضى سرطان المعدة لديهم عوامل تنبؤية سيئة متعددة ، وهي حقيقة ترتبط في الغالب بالعرض المتأخر والنتائج تشير إلى المستقبل القاتم للمرضى على الأقل في المستقبل المنظور ما لم يبدأ برنامج الفحص المبكر بسرعة .