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Evaluating clinicopathological profiling and treatment outcomes in Gastric cancer patients: a single institution experience

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Abstract: Background: Stomach cancer remains a major health problem in Egypt despite developments in diagnostic and therapeutic modalities with poor prognosis mainly due to its late-stage presentation, which is why it carries a burden on health and society. **Aim of the study:** to evaluate the incidence rate of gastric cancer among the patients treated at Kasr Al-Ainy Center of Clinical Oncology and Nuclear medicine (NEMROCK) as well as to correlate with patient's demographic and clinico-pathological characteristics and treatment outcome. **Patients and methods:** this is a retrospective study to evaluate the gastric cancer patients and their characteristics who received treatment at NEMROCK during the period from 2016 till 2020 and their data were extracted from the electronic database archive. **Results:** our series included 89 patients, Males and females have almost equal proportions among the included patients 50.6% versus 49.4% respectively where their median age was 54 years at the time of diagnosis, 56.2% of the included patients presented at an advanced stage with metastasis at their first presentation. Our study confirmed the impact of surgical resection on improving the survival where the median OS of patients who underwent surgical resection was 17.4 months Vs 8.4 months for those who didn't have surgical resection, we also observed that neoadjuvant therapy used in the locally advanced disease cases improved the median OS to 16.7 months (p value 0.0009). **Conclusion:** Surgical resection, use of neoadjuvant chemotherapy and poor histo-pathologic features correlate with the treatment outcomes in gastric cancers treated at our institution.

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1. Introduction:

Gastric cancer is the 5thmost frequently diagnosed cancer and the 3rdleading cause of cancer death (after lung cancer, breast cancer, prostate cancer, and colorectal cancer in incidence, after lung cancer and colorectal cancer in mortality) according to GLOBOCAN 2018 estimates⁽¹⁾.

Stomach cancer rates are reported to be decreasing in developed countries due to improved nutrition, better food preservation, better prevention, earlier diagnosis, and better treatment modalities. However, the scenario in Egypt is different, as most patients present at an end-stage with an impact on their overall survival and quality of life.

Globally it is the 12thmost common cancer in both sexes, accounting for 1.6% of all cancers with approximately 1,271 new patients in 2015. GC is the 12th leading cause of cancer death, accounting for 2.2% of all cancer deaths in Egypt. As reported in several Egyptian population-based cancer registries, the mean age of patients with GC is 56 years, while the incidence increases with age, 55% of cases occurring from 50 years of age. to 70 years ⁽²⁾. The majority of gastric cancers are associated with a variety of pathogenic infections, including but not limited to Helicobacter pylori (*H. pylori*) and Epstein-Barr virus (EBV). Strategies are being pursued to prevent the development of gastric cancer, such as the eradication of *H. pylori*, which helped to prevent in a significant proportion of gastric cancer cases ⁽³⁻⁴⁾.

It is recently believed that Gastric cancer is a very heterogenous disease, there are three subtypes according to Lauren classification (well differentiated, poorly differentiated and mixed disease) and four subtypes according to the WHO classification system (papillary, tubular, signet ring and mucinous)⁽⁵⁻⁶⁾, in addition to molecular markers such as HER2 status ⁽⁷⁻⁸⁾.

Surgery is the most effective treatment for the non-metastatic gastric cancer and the cure rate for T1 can reach 90% after surgery. However, many patients with locally advanced stomach cancer, even those with R0 resection will experience tumor recurrence within one year of surgery ⁽⁹⁻¹⁰⁾.

Numerous studies have demonstrated the importance of neoadjuvant treatment and its impact on

local control with reduction of lymph node metastasis rate, the aim of the neoadjuvant treatment is to achieve down-staging of the tumor, improvement of the tumor resection rate (R0), prolong the postoperative overall survival and progression-free survival for locally advanced resectable cases when combined with surgery ⁽¹¹⁻¹³⁾.

Stomach cancer is still a burden on health and society as it carries poor prognosis with an overall survival of around 25% worldwide ⁽¹⁴⁾ as most of the cases are diagnosed at an advanced stage leading to poor overall outcome with metastases and chemotherapy resistance. These data suggest the need for more effective molecular therapeutic strategies, especially with the success and challenges of newly available therapeutic agents emerging.

This study assesses the incidence of gastric cancer and examines the demographic and clinical pathological characteristics of patients and the impact of various therapies used at our center on overall survival and progression-free survival. The impact of neoadjuvant therapy was studied as well.

2. Material and methods:

This is a Retrospective study of Gastric cancer patients treated at Kasr Al-Ainy center of Clinical Oncology and Nuclear medicine during the period from January 2016 to December 2020. The study design and documents were approved by the institutional review board of the Kasr al Ainy center of Clinical Oncology and nuclear medicine (NEMROCK). (Ethical committee number MS-492-2021).

We accessed the database to extract the file number of the patients. Our series included 89 patients. Data were retrieved from patients' records, including age at diagnosis, year of diagnosis, gender, demographic features, clinical and histo-pathological data, neoadjuvant therapy and other treatment modalities as well as the date of the last follow up. The disease stage was determined according to the 8th edition of the UICC/AJCC TNM classification. Patients with insufficient data were excluded.

Overall survival (OS) was defined as the time in months from the date of diagnosis till the date of death, last date known to be alive, or date of the study cut off. Progression-free survival (PFS) was defined as the time in months from the start of treatment till the date of progression of disease or death.

Inclusion criteria:

- Adult patients aged> 18 years old
- Pathologically proven gastric and gastroesophageal adenocarcinoma.
- All patients received active therapy for their disease (whether surgery, Radiation or Chemotherapy).

- Different stages of the disease (early, locally advanced, or metastatic).
- Patients with controlled co-morbidities such as diabetes Mellitus were included in this study.

Exclusion criteria:

- Patients with incomplete or missing data.
- Patients with another histopathology (e.g., GIST or lymphoma).

The primary outcome of this analysis was to identify the prevalence of gastric cancer at our institution during the period of the study (2016-2020), define the clinico-pathological features of various stages of gastric cancer and to correlate between different treatment protocols used to treat patients with gastric cancer according to the stage (surgery, radiotherapy, and chemotherapy) and its impact on progression-free survival (PFS) and overall survival (OAS).

Statistical analysis:

Statistical analysis was conducted using SPSS (statistical package for the social science) 22nd edition. Quantitative variables were presented in mean \pm standard deviation and range, qualitative variables were presented in frequency and percentage, and were compared using Chi2 test. Log-rank test was used to assess risk factors associated with poor survival outcomes. Multivariate cox hazard proportional test was conducted to assess the hazard ratio for the development of poor survival outcomes. Kaplan Meier curves were constructed to visualize the survival rates among study groups. A probability value (P-value) less than 0.05 will be considered significant.

3. Results:

In this study, we reviewed the medical files of 102 patients diagnosed with primary gastric adenocarcinoma who sought medical advice at Kasr AL-Ainy center of clinical oncology and nuclear medicine during the period from the beginning of 2016 till the end of 2020. Only 89 patients with complete clinical records and follow-up data were included in this study. The relative frequency of gastric cancers of all patients who were diagnosed with GIT malignancies for the sample period was 1%.

The demographic data

Of the 89 patients, Males and females have almost equal proportions among the included patients 50.6% versus 49.4% respectively. The mean age was 53.5 ± 13.9 years old, and the range was 23-82 years. The Median age was 54 years at diagnosis and most of the patients' ages lied between the age group of 40 to 60 years old.

Most of our patients were nonsmokers, where smokers represented only 23.6% of the included patients, 27% of the patients had co-morbidities and hypertension was the commonest co-morbidity. All demographic data are shown in the table (1).

		Mean± SD/	Rang
		Count	e / %
	Mean \pm SD,	53.5 ± 13.9	23-82
A	range		
Age	Below 40 years	16	18%
	40-60 years	44	49.5%
	Above 60 years	29	32.5%
Condon	Female	45	50.6%
Gender	Male	44	49.4%
es	None	65	73.0%
liti	Hypertension		13.5%
bid	HTN and	5	5.6%
IOU	diabetes		
Jon	Diabetes	7	7.9%
5	mellitus		
Smoking	No	68	76.4%
SHICKING	Yes	21	23.6%

Table 1:Demographics of the included patients

The majority of the reported cases were adenocarcinoma, 57.3% of them had signet ring appearance subtype. The majority of patients had grade 3 tumors (53.9%), most of the tumors were located at the lower third of the stomach (43.8%) and 7 patients had linitis plastica where the whole stomach was affected.

The majority of the included patients presented by advanced disease (T3 and T4) (59.6%), while patients with early disease (T1 and T2) were 30.3%, and 9 (10.1%) patients could not be assessed for tumor size. The majority were node positive 54 (60.6%) and 35 cases were node negative (39.2%). (Figure 1&2)

The metastatic work up showed that more than half of the patients presented with metastasis (56.2%), and the most common site of metastasis was the Peritoneum followed by the liver and abdominal lymph nodes and multiple sites of metastasis were observed in 15.7% of the patients. The pathological data and TNM staging are outlined in Table 2.

Treatment modalities Surgery;

The aim of treatment was curative in 39 patients (43.8%) and palliative in 50 patients (56.2%). Surgery with curative intent was performed in 41 patients (46.1%). Subtotal gastrectomy was the commonest procedure (53.6%) and R0 resection could be achieved in all cases (100%). No Laparoscopic surgery was done for any patient, where all patients underwent open surgery.

Regarding nodal dissection, D1 dissection was the commonest procedure where it was conducted in 34 (82.9%) patients and D2 dissection in 7 (17.1%) cases.

		Count	%
Dethaleser	Adenocarcinoma	84	94.4%
Tuno	Anaplastic	5	5.6%
туре	carcinoma		
Signet ring	No	38	42.7%
appearance	Yes	51	57.3%
	Ι	1	1.1%
Crada	Π	25	28.1%
Graue	III	48	53.9%
	IV	15	16.9%
	Upper third	23	25.8%
	Middle third	20	22.5%
Tumor site	Lower third	39	43.8%
	Whole Stomach	7	7.00/
		/	1.9%
	(linitis Plastica)		
TNM stag	(linitis Plastica) ing	Count	%
TNM stag	(linitis Plastica) ing Tx	Count 9	% 10.1%
TNM stag T staging	(linitis Plastica) ing Tx Early disease	Count 9 27	% 10.1% 30.3%
TNM stag T staging	(linitis Plastica) ing Tx Early disease Late disease	Count 9 27 53	% 10.1% 30.3% 59.6%
TNM stag T staging	(linitis Plastica) ing Tx Early disease Late disease N0	Count 9 27 53 35 35	% 10.1% 30.3% 59.6% 39.3%
TNM stag T staging Nodal	(linitis Plastica) ing Tx Early disease Late disease N0 N1	Count 9 27 53 35 16	% 10.1% 30.3% 59.6% 39.3% 18.0%
TNM stag T staging Nodal status	(linitis Plastica) ing Tx Early disease Late disease N0 N1 N2	Count 9 27 53 35 16 28 28	% 10.1% 30.3% 59.6% 39.3% 18.0% 31.5%
TNM stag T staging Nodal status	(linitis Plastica) ing Tx Early disease Late disease N0 N1 N2 N3	Count 9 27 53 35 16 28 10	% 10.1% 30.3% 59.6% 39.3% 18.0% 31.5% 11.2%
TNM stag T staging Nodal status	(linitis Plastica) ing Tx Early disease Late disease N0 N1 N2 N3 M0	Count 9 27 53 35 16 28 10 39 39	% 10.1% 30.3% 59.6% 39.3% 18.0% 31.5% 11.2% 43.8%

Table 2: Pathological and TNM staging of the included patients

T stage



• Early disease (T1 and T2) • Advanced disease (T3 and T4) • Unknown (Tx) Figure 1: Pie chart showing the T stage among the included patients



Figure 2: Bar chart illustrating nodal stage at presentation

Radiation therapy:

Radiation was prescribed in 30 (33.7%) patients, where the aim of radiation was in an adjuvant setting for 25 patients with a dose assigned as 45 Gy/ 25fractions / 5weeks protocol concurrent with fluropyrdimine based chemotherapy.

Radiation was prescribed on a palliative basis locally to the stomach in 5 patients to stop bleeding, three patients with a dose prescribed of 30 Gy / 10 fractions / 2 weeks. Whereas two patients with a dose prescribed of 20 Gy/ 5 fractions / 1 week.

Table 3: Modalities of treatment used in the treatment of the cohort of patients

Surgery		Count	%	
Summony	No	48	53.9%	
Surgery	Yes	41	46.1%	
Т	Sub-total	22	53.6%	
Type of surgery	Total	19	46.4%	
T 1 1 1	D1	D1 34		
Lympnadenectomy	D2	D2 7		
Radiotherapy		Count	%	
D - H- H-	No	59	66.3%	
Radiation	Yes	30	33.7%	
A	Adjuvant	25	83.3%	
Aim of radiation	Palliative	5	16.7%	
	2000/5#	2	6.7%	
Dose of Radiation	3000/10#	3	10.0%	
	45/25#	25	83.3%	
Type of	5FU	13	52.0%	
Concurrent	Xeloda	12	48.0%	
chemotherapy				
Chemotherapy		Count	%	
Chemotherapy	No	9	19.1%	
enemotiorup,	Yes	80	80.9%	
Aim of	Neoadjuvant	16	20.0%	
chemotherany	Adjuvant	15	18.7%	
enemotierupy	Palliative	49	61.3%	
	1	8	16.3%	
	2	3	6.1%	
D-111-41	3	13	26.5%	
chamatharany	4	6	12.2%	
Number of evelor	5	1	2.1%	
rumber of cycles	6	14	28.6%	
	8	3	6.1%	
	9	1	2.1%	

Chemotherapy:

Neoadjuvant chemotherapy was used in seventeen patients (19.1%), the neoadjuvant chemotherapy protocol was mainly a fluoropyrimidine based regimen (FOLFOX in most of cases) followed by ECF protocol (anthracycline-based regimen).

Fifteen patients received Adjuvant Chemotherapy; Anthracycline-based regimens were the first to be used but they were accompanied by great toxicity. Then Fluoropyrimidine based regimens were the commonly used.

Palliative chemotherapy was prescribed in 49 patients (55.1%), where fluoropyrimidine based chemotherapy was used in the majority of patients (59.2%) as first line, where FOLFOX was the commonest protocol used and the most tolerable one,

only 3 patients with a poor performance status were treated by single agents(Figure 3).

Eighteen patients received second line chemotherapy after progression on the first line and the Carboplatin/taxol regimen was the most commonly used. Table 2 illustrates the modalities used in treating the patients recruited in our study.



Figure 3: Chemotherapy regimens used on palliative basis as first line among the included patients



Figure 4: Kaplan Meier curves showing OS according to presence of signet ring appearance in pathology

Overall Survival analysis

Among the included cohort of patients, we observed a median of OS 10.7 months, with a 95% CI (8.3-13.2 months). There was a statistically significant difference in OS according to presence of signet ring appearance in the histopathology examination with a p-value of 0.005 (Figure 4).

Comparison of OS based on histological grade of the cancer cells showed that there was statistically significant difference in OS between groups with a pvalue of 0.004. Comparison of OS based with respect to the nodal status showed that there was statistically significant difference in OS between the study groups according to nodal status with a p-value of 0.0001. Comparing OS based on disease stage showed that, there was a statistically significant difference in OS between disease stages as an advanced disease stage was associated with shorter OS with p-values = 0.007. There was a statistically significant difference of OS based on metastatic disease as M1 disease was associated with significantly shorter OS with p-values = 0.008. Patients who underwent surgical resection had a significantly longer OS with p-values = 0.0001. Patients who received neoadjuvant chemotherapy showed significantly longer OS with p-values = 0.0009. Patients with stationary or regressive disease after first line chemotherapy was associated with longer OS compared to progressive disease with pvalues = 0.032.

Progression free survival analysis

In the current cohort of patients, the median PFS was 24.5 months (95% CI 12.5-36.5 months). Progression free survival showed a statistically significant difference between nodal positive and node negative disease with a p-value of 0.04 (Figure 5). PFS was significantly shorter among patients with progressive disease after first line of chemotherapy with a p-value of 0.012.

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Signet ring	Modian OS	Std Ennon	95% Confidence Interval		P value	
appearance	Median OS	Stu. Error	Lower Bound	Upper Bound		
No	17.405 1.113 15.223 19.587		0.005			
Yes	13.067 0.684		11.726	14.409	0.005	
Grade	Madian OS	Std. Error	95% Confidence Inte	P value		
	Median OS		Lower Bound	Upper Bound		
Low grade (II)	16.985	1.564	13.920	20.050		
High grade (III- IV)	11.637	0.648	10.366	12.908	0.004	
Nodal status	Modian OS	Std Frror	95% Confidence Int	terval	P value	
	Methan 05	Stu. Error	Lower Bound	Upper Bound		
Node negative	17.531	1.646	14.304	20.758	0.0001	
Node positive	10.061	0.741	8.608	11.514	0.0001	
Stage	Median OS	Std. Error	95% Confidence Interval		P value	
-			Lower Bound	Upper Bound		
I-II	17.500	0.930	15.678	19.322	0.007	
III-IV	8.933	1.137	6.705	11.161	0.007	
			1			
Metastasis			95% Confidence Int	erval	P value	
11200000000	Median OS	Std. Error	Lower Bound	Upper Bound		
MO	16.100	4.008	8.244	23.956		
M1	9.833	1.237	7.409	12.258	0.008	
Overall	10.767	1.255	8.306	13.227		
0.000		Std. Error	95% Confidence Interval			
Surgery	Median OS		Lower Bound Unner Bound		P value	
No	8 467	0 944	6.617	10.316		
Yes	17 400	1 938	13.602	21 198	0.0001	
Overall	10.767	1.255	8 306	13 227	0.0001	
~ / vi un	10.707	1.200	5.500	13.227	1	
Neoadjuvant			95% Confidence In	nterval	P value	
chemotherapy	Median OS	Std. Error	Lower Bound	Upper Round	i value	
No	9.867	1.195	7.524	12.209		
Yes	16.567	3.859	9.003	24.131	0.009	
Overall	10.767	1.255	8.306	13.227		
Assessment nost	nost 05% Confidence Interval					
chemotherany	Median OS	Std. Error	Lower Bound	Unner Round	- P value	
Stationary	17 733	1 234	0 /3/	26.032		
Regression	17.755	7 163	3 126	20.032		
Drogression	0.967	1.105	7.021	12 702	0.032	
r rogression	9.007	1.447	9 206	12.702		
Overall	10.767	1.200	8.300	13.227	1	

Table 4: Factors influ	encing O	OAS among	the study	group

Cox hazard proportional test Overall survival:

Cox hazard proportional test showed that surgical resection was associated with a lower hazard of death with a p-value of 0.005, and HR 6.2 (95% CI 1.7-22.1).

Progression free survival:

Cox hazard proportional test showed that hypertension and progression after first line was an independent risk factor for shorter PFS with p-values = 0.022 and 0.046, and HR 11.2 (95% CI 1.4 – 89.2) and 20.8 (95% CI 1.05-409.8) respectively.



Figure 5: Kaplan Meier curves showing PFS according to nodal status

 Table 5:Cox hazard proportional test for overall survival among the included patients

Factors	Correlation	D voluo	IID	95.0% CI	95.0% CI	
	coefficient	P value	нк	Lower	Upper	
Gender	0.597	0.052	1.816	0.995	3.315	
Comorbidities (DM)	-0.296	0.831	0.744	0.049	11.290	
Comorbidities (HTN and DM)	-0.024	0.988	0.976	0.047	20.321	
Comorbidities (HTN)	-0.046	0.978	0.955	0.037	24.400	
Signet ring appearance	0.262	0.484	1.299	0.625	2.701	
Grade (I)	1.017	0.306	2.765	0.394	19.410	
Grade (II)	0.128	0.780	1.136	0.463	2.787	
Grade (III)	-0.554	0.141	0.575	0.275	1.202	
T1	-1.382	0.029	0.251	0.073	0.866	
T2	-1.463	0.029	0.232	0.062	0.859	
T3	-0.422	0.410	0.655	0.240	1.789	
T4	-0.643	0.171	0.526	0.210	1.320	
NO	0.092	0.901	1.097	0.255	4.718	
N1	0.171	0.819	1.187	0.273	5.165	
N2	0.806	0.185	2.240	0.679	7.384	
M1	0.505	0.496	1.657	0.388	7.083	
Stage (I)	0.287	0.849	1.332	0.069	25.673	
Stage (II)	1.505	0.109	4.502	0.714	28.403	
Stage (III)	-0.276	0.719	0.759	0.168	3.424	
Surgery	1.823	0.005	6.188	1.733	22.095	
Neoadjuvant chemotherapy	1.242	0.090	3.462	0.823	14.560	
Relapse	-0.409	0.542	0.664	0.179	2.472	

Table 6:Cox hazard proportional test for progression free survival among the included patients

Factors	Correlation coefficient	P value	HR	95% CI	
ractors				Lower	Upper
Gender	2.490	0.007	12.060	1.944	74.811
DM	-0.125	0.911	0.883	0.099	7.851
DM and HTN	0.130	0.908	1.138	0.128	10.133
HTN	2.424	0.022	11.290	1.428	89.256
Pathology	-13.670	0.989	0.000	0.000	0.000
Signet ring appearance	-1.629	0.085	0.196	0.031	1.251
Grade II	-0.084	0.925	0.920	0.159	5.309
Grade III	-1.007	0.243	0.365	0.068	1.978
Surgery	-10.684	0.990	0.000	0.000	0.000
Neoadjuvant chemotherapy	-0.241	0.724	0.786	0.207	2.990
Stationary	-0.040	0.959	0.961	0.211	4.371
Progression	3.036	0.046	20.825	1.058	409.814
Regression	0.583	0.532	1.792	0.288	11.168

4. Discussion

In Egypt, Gastric cancer is the 12thmost common cancer in both sexes, accounting for 1.6% of al cancers with approximately 1,271 new patients in 2015. GC is the 12thleading cause of cancer death, accounting for 2.2% of all cancer deaths in Egypt. As reported in several Egyptian population-based cancer registries ⁽²⁾.

The importance of our study is that it shows the relative frequency of gastric cancer patients treated at Kasr Al-Ainy center of Clinical Oncology and Nuclear medicine, the different clinico-pathological features of Gastric cancer patients, and the impact of the different treatment modalities used on their PFS and OS as Gastric cancer is a burden on health and society.

In our study, 102 cases with Gastric cancer were retrieved from our medical records in the period from the start of 2016 till the end of 2020.And only 89 patients with complete data were included in the study. The median age of patients at our study was 54 years with extremes of 23 and 79 years of age but most of the included patients' age lied between the age group of 40-60 years which is consistent with recent studies that predict the incidence of gastric cancer tends to be in younger age groups (younger than 50 years old)⁽¹⁵⁾

Hypertension among the included patients was an independent prognostic risk factor for shorter PFS. Moreover, most of the patients in this study had signet ring appearance subtype (57.3%), in our series the presence of signet ring appearance was associated with median OS 11.8 months VS 8.4 months for those with No signet ring appearance. However, there was no statistically significant difference between the two groups. The impact of the signet ring pathology on the prognosis in advanced cases is controversial but it is commonly known to be poor of prognosis as proven by many studies ^(7,16-18). Other small studies didn't indicate a significantly worse prognosis of the signet ring subtype ^(19,20). It was also observed that lymph node involvement is an important prognostic predictor of gastric cancer, as patients with lymph node positive disease were associated with a shorter median OS and PFS compared to those with lymph node negative disease which matches with the results of previous studies (21)

Regarding the location of the tumor, the lower third of the stomach was the most commonly affected site in our study representing 43.9% of the included patients who had the antrum and pylorus affected by the tumor. Our results regarding the site are similar to many previous studies ^(22,23). This could be explained by the prevalence of H.pylori infection and other precancerous lesions which induce gastric mucosal inflammation eventually leading to atrophy, and these atrophic mucosal changes progress from the antrum upwards to the body of the stomach along the lesser curvature, this could explain the higher incidence of Gastro-esophageal cancer in the lower portions of the stomach^(24,25).

In this study, the majority of the patients (59.6%) presented with advanced disease (T3 and T4 according to TNM staging). There was a statistically significant difference in the OS between the different disease stages as advanced disease stages were associated with shorter OS with p values = 0.013. This is because this disease becomes symptomatic in advanced stages, moreover, there are no mass screening programs in Egypt for Gastric cancer as it is expensive, and these programs are recommended only in regions with a high incidence as East Asia⁽²⁶⁾

In our study, 56.2% of the included patients presented with metastasis, where the most common site affected is the peritoneum followed by the liver and this could be correlated with the presence of signet ring appearance in 57.3% of the cohort as the rates of peritoneal dissemination in advanced patients with signet ring cell subtype is higher than those with no signet ring appearance, and this is matched with previous studies with similar results ^(27,28).

In our cohort of patients, Subtotal gastrectomy with D1 lymphadenectomy was the commonest procedure done, where all patients underwent open surgery (not laparoscopic) and R0 (negative margins) could be achieved in all patients, surgical resection had a great impact on the OS where there was a statistically significant difference in OS between those who underwent surgical resection and those who didn't, with median OS 17.4 months vs 8.4 months respectively. On the other hand, D2 lymph node dissection was less widely used, it was performed in 7 patients only and this correlates with the results of previous studies reported that D2 dissection was accompanied by higher rates of mortality and morbidity, and it is a difficult procedure that should be performed by experienced surgeons at highly equipped centers ⁽²⁹⁾. Moreover, according to a highly cited Dutch trial (DGCT) there was no difference in the 5 years survival between the two groups $(D1 \text{ vs } D2)^{(30)}$.

In our study, neoadjuvant chemotherapy was used in 20 patients, and it was proven to have a significant impact on overall survival, where patients who received neoadjuvant chemotherapy showed significantly longer OS with p values=0.0009 and a median OS of 16.5 months versus 9.8 months for those who didn't receive neoadjuvant therapy. This matches with the data extracted from previous studies which confirmed the impact of perioperative chemotherapy in improving PFS and OS ^(31,32).

Moreover, chemotherapy was prescribed on a palliative basis in the metastatic setting for 49 patients (55.1%) and fluoropyrimidine-based protocols were the commonest. FOLFOX was the most frequently used protocol as first line, as it was tolerable by most

of the patients, while only 3 patients received single agent chemotherapy due to poor performance status. Anthracycline-based chemotherapy was used at first in the adjuvant setting for 20% of the patients then shifted to the fluoropyrimidine-based regimens as they are less toxic to the patients with fewer side effects. After progression on the first line chemotherapy which was used in the metastatic setting, eighteen patients received 2^{nd} line chemotherapy, where Carboplatin/Paclitaxel was the most commonly used regimen which was an effective regimen with acceptable toxicity and this matches with data from numerous studies that showed the efficacy of this regimen in the metastatic setting $^{(33,34)}$. In this study, the patients who responded favorably after receiving the first line chemotherapy had a prolonged OS compared to patients who progressed on the first line and the survival benefit was significant with a p-value of 0.032. The patients who progressed on the first-line chemotherapy had shorter PFS as well and it was statistically significant with a p-value of 0.012. Finally, we found that the median OS was10.7 months and regarding the PFS the median survival was 24.5 months in our series of cases

Conclusion and recommendations:

Surgical resection, use of neoadjuvant chemotherapy and poor histo-pathologic features correlate with the treatment outcomes in gastric cancers treated at our institution. Early and proper treatment of precancerous lesions such as H.pylori infection is recommended as it will lead to a decline in the incidence of gastric cancer.

Author's contribution

Conception or design: KM, MR, MN and EH; Acquisition, analysis or interpretation of data: KM, MR, MN and EH; Drafting the manuscript: KM, MN and EH: revising it critically: KM, MR, MN and EH; Final approval of the manuscript version to be published: KM, MN and EH; Agreement to be accountable for all aspects of the work: KM,MR,MN and EH.

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