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Demographic and clinical characteristics of gastric cancer patients in north of Iran, Mazandaran province, 2008-2014

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Abstract

Gastric cancer has been known as a poor prognosis disease with a high degree of mortality. In Iran, it has been increased during the previous two decades, especially in northern part of the country. The aim of this study was to determine the demographic and clinical characteristics of gastric cancer in Mazandaran province. All patients with gastric cancer diagnosis treated in the Imam Khomeini educational hospital or Touba Polyclinic, a university affiliated center, from March 2008 to March 2014 were included. Demographic data, the symptoms at the time of presentation, tumor size, type of tumor, lymph node involvement, status in terms of metastatic disease, therapeutic plan and type of chemotherapy regimens were gathered from patients' medical records. Statistical analysis was performed using SPSS, version 16. Totally, 643 patients were investigated. The mean age of patients was 64.34 years and men were more affected than women. "Time to relapse" and "time to progression" were 13 and 6.5 months, respectively. The most common initial symptoms at diagnosis were nausea, vomiting and epigastric pain (47.4%). Only in 6.3%, the disease was diagnosed at the initial stages. The most common site of involvement was cardia (almost 40%) and antrum (32%). More than 91% of tumors were adenocarcinoma. DCF (Docetaxel, Cisplatin, 5FU) (43.3%), Xeloda (15.2%), DOX (Docetaxel, Oxaliplatin) (13.8%) and ECF (Epirubicin, Cisplatin.5FU) (9.2%) were the most common used regimens. There was a trend for improved survival with DCF regimen (P = 0.08). Most gastric cancer patients were referred in the advanced stage or metastatic disease. The demographic characteristics are consistent with other previous reports. DCF regimen may have some advantages over other chemotherapy regimens.

Keywords: Gastric cancer, demographic, chemotherapy, DCF, Mazandaran

Introduction

Gastric cancer has been known as a poor prognosis disease with a high degree of mortality. It is one of the most common cancers with a diverse geographic variability worldwide. Latin America, Eastern Asia, parts of Europe and Middle East are among regions with a high incidence of gastric cancer, while the lowest rates are in parts of Africa and North America. Patients are often diagnosed in the advanced stages (1). Seventy percent of gastric cancer occurs in the developing countries, with a higher incidence in men compared to women. In Iran, it is the most common cancer in men and the second frequent cancer in women after breast cancer. Worldwide, it was the leading cause of mortality of cancer deaths until three decades ago.

As other part of the world, the high incidence and poor prognosis of gastric cancer is still a great health system concern in the country. Considering the cancer mortality in both sexes, gastric cancer is the most common cancer-related mortality in Iran (2,3,4). Although the incidence and mortality of gastric cancer has been declined in many countries including United States, the absolute number of new cases

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per year is increasing, mainly due to aging of the world population. In our country, there was an increase in the incidence of gastric cancer especially at the Northern provinces such as Mazandaran (5).

Treatment of cancer usually is accompanied with different modalities such as surgery, radiation therapy and chemotherapy. In Gastric cancer, the type of treatment should be selected based on the stage of the disease, clinical status of the patients, his or her comorbidities and preference (6). Worldwide, gastrectomy is the most widely used approach for treatment of gastric cancer. Chemotherapy has been widely used in treatment of different stage of gastric cancer. Over eighty percent of patients who die of gastric cancer experience a local recurrence of the disease. This is the basis for adjuvant chemotherapy. Neoadjuvant chemoradiotherapy or preoperative chemoradiotherapy may also be selected for gastric cancer, based on the location of the tumor. The decision which chemotherapy regimen is a better choice for a given patient is based on the stage of disease and the patients' baseline characteristics. Commonly, regimens based on the 5-fluorouracil (5-FU), Oxaliplatin, Cisplatin, Docetaxel and Paclitaxel are used as monotherapy or combination chemotherapy (7,8). To update the demographic and clinical characteristics of gastric cancer patients, this study has been conducted in Mazandaran province of Iran.

Materials and methods

This study was a descriptive observational study. All patients with gastric cancer diagnosis who were been treated in the Emam Khomeini educational hospital or Touba polyclinic, a university affiliated center, from March 2008 until March 2014 were included. The study was approved by ethics committee of Mazandaran University of Medical Sciences. Different demographic and clinical characteristics including sex, age, weight, height, job, the date of first visit, patient's symptoms at the time of diagnosis, macro and microscopic data of the tumor including the anatomic location of involvement (cardia, antrum, fundus, etc), tumor size, type (adenocarcinoma or other type), tumor invasion to lymph nodes or distant metastasis, the plan of treatment selected including surgery, radiation therapy and or chemotherapy and type of chemotherapy gathered. "Time to relapse" and "time to

progression" and survival were compared for different chemotherapy regimens. Statistical analysis has been done with SPSS version 16. Descriptive statistics were used to express the results. Analysis of variance (ANOVA) was executed to compare different regimens in terms of "time to relapse", "time to progression" and survival rate. $P < 0.05$ was considered as a significant difference.

Results

Totally six hundred and forty three patients were included in the study. Demographic characteristics of patients have been presented in table 1.

Table 1 Demographic and clinical characteristics of patients

Sex (male %)	68.3
Age (mean ± SD)	64.35 ± 14
Initial symptoms	
nausea, vomiting and epigastric pain	47.4%
fatigue, weakness and melena	34.2%
weight loss	10.5
dysphagia	2.6
Stages	
1	27 (6.3%)
2	57 (13.3%)
3	103 (24%)
4	243 (56.5%)
frequency (%) of surgery in different stages	
stage 1	24 (96%)
stage 2	48 (98%)
stage 3	79 (85.9%)
stage 4	53 (27.7%)
Tumor location	
Cardia	134 (39.6%)
Antrum	109 (32.2%)
Body	36 (10.7%)
Fundus	11 (3.3%)
Other	48 (14.2)
Type of tumor	
Adenocarcinoma	403 (91.2%)
other types	39 (8.8%)
Metastasis	
Liver	80 (46.9%)
Ascites and peritoneal involvement	45 (26.6%)
paraaort	14 (8.2%)
Lung	8 (4.7%)
Liver and paraaort	5 (2.9%)
Liver and Lung	2 (1.2%)
Others	16 (9.4%)

The men were two times most affected than women. The mean age of patients was 64.35 years. Time to relapse and time to progression were 13 and 6.5 months, respectively. The most common symptoms at the time of diagnosis were nausea, vomiting and epigastric pain (47.4%), followed by fatigue and weakness.

Cardia (40%) and antrum (32%) were sites most involved in gastric cancer. The type of tumor was adenocarcinoma in more than 91% of cases. Whereas only 6.3% of patients were in stage 1, the majority (56.4%) were in stage 4 at the time of referring to the oncology clinic. Liver was the most common site of metastasis (47% liver metastasis) and also there were cases that had simultaneously liver metastasis with peritoneum involvement, ascites and paraaortic metastasis. Totally, liver metastasis was occurred in almost 80% of gastric cancer patients. Sixty four percent of patients were undergone surgery before referring to oncologist. 191 patients were in stage 4, among them, 53 (28%) were undergone surgery. Neoadjuvant therapy was done for 39 (6%) of cases. Relapse was occurred in 10.1% of patients, whereas the liver was the most common site of relapse. Progression was documented in 28 medical records. Liver involvement and ascites were common features of progression. Time to relapse, Time to progression and overall survival were not statistically different between four common used regimens. Though, DCF was associated with a trend of improved overall survival (P=0.082) (Table 2).

Table 2 Outcome variables of different chemotherapy regimens

Variables/Regimens	ECF*	DOX*	Xeloda*	DCF*	Total	P-value*
Time to relapse	10.6 ± 2.302	11.57 ± 8.662	10.4 ± 7.701	14.83 ± 9.892	12.77 ± 8.432	0.643
Time to progression	NA	6.5 ± 3.464	4.67 ± 1.155	6.17 ± 3.403	5.91 ± 2.836	0.711
Number of courses	4.04 ± 1.255	3.62 ± 1.623	3.71 ± 3.189	3.63 ± 1.813	3.69 ± 2.094	0.825
Overall survival	21.4 ± 15.686	14.6 ± 10.036	19.62 ± 21.38	24.69 ± 22.088	21.13 ± 19.408	0.082

*DCF: Docetaxel.Cisplatin.5FU; DOX:Docetaxel.Oxaliplatin. Capecitabine; ECF: Epirubicin.Cisplatin.5FU; Xeloda: Capecitabine; P-value: ANOVA test between four chemotherapy regimens; NA: not available data

Discussion

This study which was designed to determine the demographic characteristics of gastric cancer in Mazandaran showed that the observed characteristics were in concordance with results of other studies.

In this study the number of male gastric cancer patients was 2.15 times more than females. This result is in agreement with the results of the study conducted by Biglarian and colleagues (9) (male: female ratio was 2.5) and is also similar to the results of the study performed by Shafigh and colleagues (10) (male:female ratio was (2.89). Mean age of the patients at the time of diagnosis was 65y for males and 63.7y for females. Mean age of the patients in Biglarian and colleagues (9) study was 59.39 for males and 56.22 for females. In three other studies conducted by Roshanayi and colleagues (11), Akhavan and colleagues (12) and Dehkordi and colleagues (13) mean age of the patients were 58.7, 59 and 46.2, respectively. These results are relatively similar to the results of the present study. As a general rule, age of the gastric cancer patients is an important prognostic factor. The more the age of the patient at the time of diagnosis is, the poorer prognosis of the patients will be (4). It seems that changes happened in the mean age of the population in our country have affected the prevalence of gastric cancer and its prognosis. This fact could be more important in areas of the country that the disease is more prevalent. In a study performed by Asmarian and colleagues (14) data gathered from 366 cities throughout the country between the 1382-1386 showed that gastric cancer is more prevalent in northern areas of the country especially in Mazandaran, Golestan, Ardabil and Kordestan provinces (14).

An important problem in gastric cancer is that most patients are diagnosed in late stages of the disease so it is difficult to treat them effectively and this delay in diagnosis significantly decreases survival time of the patients. In our study population only 6% of the patients were diagnosed at stage I and in 80% of metastatic cases, liver metastasis were present which in turn predispose the patient to a poor prognosis.

Results of studies conducted in other area of the country show similarities in stage of the disease at the time of the diagnosis of the patients. Biglarian and colleagues (9) reported that in their study population only 26.8 % of patients diagnosed at stage I of the disease and 37% of them diagnosed at stage IV. Keyhanian and colleagues (15) study showed that in Ramsar, 46.5% of patients were at stage IV and 18.8 % were at stage III when diagnosed. 31.9% of the patients had metastasis and among them 78% had liver metastasis. In Davudabadi and colleagues study 60% of patients diagnosed at late stages (16). Similar results were found by Somi and colleagues in East Azarbayjan (17).

These results indicate that unfortunately and as a common problem, in majority of gastric cancer patients the disease is diagnosed at late stages. The reason for this is probably difficulty in making a differential diagnosis at early stages of the disease and lack of proper and cost-effective screening program for diagnosis of the patients. These factors seemingly contribute in high mortality of gastric cancer patients.

Studying chemotherapeutic regimen of our patients revealed that DCF regimen is prescribed more than ECF, DOX and Xeloda. Furthermore there was a trend toward longer "mean survival time" in patients receiving DCF regimen although mean "time to recurrence" and mean "time to progression" were not significantly different. These findings indicate relative superiority of DCF regimen to other chemotherapeutic regimens. However, because of high cost of this regimen (mainly because of high cost of docetaxel) and because this superiority is not an unchangeable fact for all patients it is not recommendable to use DCF for all gastric cancer patients. In other studies, adding docetaxel to CF regimen resulted in more favorable outcomes. For example in a phase 3 clinical trial performed by Cutsem and colleagues (18), adding docetaxel to CF regimen lead to improvement in quality of life, time to progression and survival time of the patients (p < 0.001). In an another study conducted in MD Anderson Cancer Center by Ajani(19) it has been shown that the rate of complete response, time to progression, overall survival and quality of life were significantly better in patients received DCF rather than CF regimen. In this study "time to progression" was 5.6 and 3.7 for DCF and CF groups, respectively. Mean survival time were 9.2 in DCF group versus 8.6 in CF group. These statistical differences do not necessarily mean a significant clinical superiority of DCF regimen. Especially when taking into account limitations in financial resources exists for health systems, it is not reasonable to consider high cost DCF regimen as the first choice in all gastric cancer patients.

Cutsem et al (18) also showed that in their study population the most common sites involved in gastric cancer were body (44%), anthrum (25%) and fundus (12%), respectively. Keyhanian and colleagues (15) reported antrum (45.1%) and cardia (29.2%) as the most common sites of involvement in gastric cancer patients and 98.8% of tumors were diagnosed as adenocarcinomas.

In Sumi and colleagues(17) study population, 41.1% of tumors were at proximal third, 25.3% were at medial third and 25.3% were at distal third of the stomach (17). In this study 96% of tumors were of adenocarcinoma type. Unlike the above mentioned studies, cardia was the most common site of involvement in our study, followed by antrum. Similar to other reports, adenocarcinoma type was very common in our gastric cancer patients. An important factor which affects the prognosis of the patients and response to treatment is the site of tumor. According to the previous studies tumors of the cardia show a poorer response to the treatment relative to tumors located at more distal parts of the stomach and mortality rate is also higher in cardia tumors (7). A comparison between the results of the present study with results of the studies performed in other areas of the country shows that unfortunately most gastric tumors develop at sites of the stomach that respond poorly to the treatment.

In the present study the most prevalent symptoms among the patients when first came to the clinic were nausea, vomiting, epigastric pain (47.4%) and the most prevalent clinical presentations were weakness, tiredness, melena (34.2%) and weight loss (10.5%). So our results were similar to the results of other studies. Sumi and colleagues (17) reported abdominal pain (26.7%), dysphagia(30%) and loss of appetite (28%) as the most prevalent symptom of their patients. In Sharifi and colleagues (20) study, 85.6% of the gastric cancer patients reported epigastric pain as their first symptom.

Conclusion

Most aspects of the demographic characteristics are consistent with other studies. Unlike some previous reports, cardia was the most common site on involvement on our study. Most gastric cancer patients referred in the advanced stage or metastatic disease. DCF regimens was prescribed more than ECF, DOX and Xeloda.

This regimen may have some advantage over the other chemotherapy regimens. There was a trend toward longer "mean survival time" in patients receiving DCF regimen although mean "time to recurrence" and mean "time to progression" were not significantly different.

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Conflict of interest

The authors declared no potential conflict of interest with respect to the authorship, and/or publication of this study.

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