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FACTORS AFFECTING MORBIDITY AND MORTALITY OF GASTRECTOMY CASES WITH SPLENECTOMY

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Abstract: Gastric cancer is a worldwide health problem. The addition of splenectomy to gastrectomy is a controversial issue, especially in cases located on the greater curvature. In this study, it is aimed to find the factors affecting morbidity and mortality in gastrectomy cases with splenectomy. Patients who underwent surgery for gastric cancer in Van Yuzuncu Yil University, Department of General Surgery between January 2010 and January 2018 were retrospectively selected. Splenectomy cases were filtered out in all gastrectomy patients. Preoperative, intraoperative and postoperative data of the patients were collected. The effects of the collected parameters on morbidity and mortality were evaluated. A p value of less than 0.05 was considered statistically significant. 45 patients were included in the study. The mean age of all patients was 64.2 years (32-85) and the male to female ratio was 27/18. Thirty seven cases (82.2%) were operated under elective conditions. The most common tumor location was cardia (n=24, 53.3%) and the most common surgical method (n=39) was total gastrectomy (86.7%). Morbidity and mortality rate of the study were 46.6% (n=21) and 17.8% (n=8), respectively. Mortality increased in patients who were operated in emergency conditions and received neoadjuvant therapy, p=0.002 and P=0.044, respectively. While surgery under emergency conditions increased mortality, preoperative neoadjuvant treatment decreased mortality. However, there was no factor affecting morbidity. Splenectomy in gastric cancer surgery, if possible, should be performed under elective conditions and after neoadjuvant therapy to reduce mortality.

Keywords: Emergency surgery, Gastrectomy, Morbidity, Mortality, Neoadjuvant therapy, Splenectomy

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1. Introduction

Gastric cancer is a major health problem all over the world. Due to Cancer Statistics 2019 report of Siegel et.al, 27510 new cases of gastric cancer were thought to be seen in the USA. Also, at the same cancer report it was estimated that 11140 people will die due to gastric cancer in the USA (Siegel and Miller, 2019).

Gastric cancer is the 5th mostly seen cancer all around the world (Collaborators, 2016). Because not to know the mechanism of gastric cancer completely, unfortunately patients present at advanced stages (Correa, 2013; Thrumurthy et al., 2013). In gastric cancer treatment, depending on localization and extent of cancer, surgery is the only potentially curative treatment for all T1b-T4 stage, and D2 lymphadenectomy should be recommended as standard of care in resectable cancer cases. Surgical treatment of liver-limited metastases and hyperthermic intra peritoneal chemotherapy for peritoneal carcinosis are fascinating frontiers (Orditura et al., 2014).

Splenectomy is the surgical procedure to remove spleen because of various indications. One of the most important indications is splenectomy, especially in gastric cancer located in the greater curvature (Coco and Leanza, 2019). Though preoperative chemotherapy has a role in gastric cancer, it is not the substitute for radical gastrectomy with D2 lymphadenectomy which is still the gold standard treatment especially in high-volume centers (Purkayastha et al., 2020). Lymph node station 10 dissection is the routine procedure in D2 lymphadenectomy (Wohnrath and Araujo, 2019). Because of splenic hilum or parenchyma invasion, splenectomy is required for proper D2 lymphadenectomy. Splenectomy is also required as a result of vascular or parenchymal injuries during dissection (D1 or D2 lymphadenectomy).

In the presented study, it was aimed to find the factors affecting morbidity and mortality in gastrectomy cases with splenectomy.

2. Material and Methods

2.1. Patient Selection

After ethical committee approval, patients who had been operated because of gastric cancer in Van Yuzuncu Yil University, Faculty of Medicine, Department of General Surgery between January 2010 and January 2018 were filtered for the study retrospectively from the hospital records. 174 patients were operated due to gastric

cancer during the study period. Splenectomy cases were choosed among these gastrectomy patients. There were 45 patients who underwent splenectomy during gastrectomy. Patients who developed complications in the 30 days after surgery were considered the morbidity-positive (+) group, and the patients without complications were considered the morbidity-negative (-) group. On the other hand, patients who died in the 30 days after surgery were considered the mortality-positive (+) group, and the patients who survived were considered the mortality-negative (-) group.

Preoperative, intraoperative, and postoperative data of the patients were gathered. Patients who were treated at external centers and referred to our center (n=12) were not included in the study.

2.2. Method

Demographic features (age, gender), preoperative comorbidity and habits, American Society of Anesthesiologists Classification (ASA) score, Mallampati score, surgical urgency and presence of neoadjuvant chemotherapy were evaluated. Also, indications of emergency surgeries were evaluated.

Tumor locations, type of abdominal incisions, type of surgery, presence of D2 lymphadenectomy, and indications for splenectomy were checked. Pathology reports of the patients, postoperative complications, hospital length of stay, morbidity, and mortality status were evaluated.

2.3. Statistical Analysis

Statistical analyses were performed using SPSS V22.0 (IBM, Armonk, NY, USA). Quantitative variables were expressed as mean ± standard deviation, and minimum-maximum. Qualitative variables were reported as numbers and percentages (%). The Shapiro-Wilk test was used to assess the normality distribution of quantitative variables. While the mean and standard deviations were used for homogenous distributions, median and range were given for heterogeneous distributions. Chi-Square test and Likelihood ratio test were used to compare qualitative variables. A p-value below 0.05 was considered statistically significant.

The effect of preoperative, intraoperative and postoperative parameters on morbidity and mortality was evaluated statistically.

3. Results

45 cases were included in the study. The mean age of all patients was 64.2 (32-85) and the male/female ratio (27/18) was 3/2. Thirty-one patients (68.9%) had at least one comorbid disease or habit. 13 patients were operated after neoadjuvant therapy, and 37 cases (82.2%) were operated in elective conditions. The remaining eight patients underwent emergency surgery due to perforation in three patients, due to massive bleeding that did not respond to medical treatment in three patients, due to gastric outlet obstruction in one patient, and due to simultaneously bleeding and perforation in one patient. The clinical findings of the patients are shown in Table 1.

Table 1. Clinicopathological variables of the patients

Variables	Value or n (%)
Age (mean, year)	64.2 (32-85)
<65 years	21 (46.7%)
≥65 years	24 (53.3%)
Gender	
Male	27 (60%)
Female	18 (40%)
ASA Score	
ASA 1	7 (15.6%)
ASA 2	29 (64.4%)
ASA 3	9 (20%)
Comorbid Diseases and Habits*	
Cigarette usage	12 (26.7%)
Hypertension	6 (13.3%)
Lung problems	5 (11.1%)
Cardiac interventions	4 (8.9%)
Diabetes mellitus	3 (6.7%)
Cardiac stent	1 (2.2%)
None	14 (31.1%)
Mallampati Score	
Mallampati 1	35 (77.8%)
Mallampati 2	9 (20%)
Mallampati 3	1 (2.2%)
Neoadjuvant Therapy	
Yes	13 (28.9%)
No	32 (71.1%)
Surgical Emergency	
Elective	37 (82.2%)
Urgent	8 (17.8%)
Type of Abdominal Incisions	
UMI	25 (55.5%)
UMI and LMI	16 (35.6%)
Anterior thoraco phreno-laparotomy (TPL) (left-sided)	4 (8.9%)
DL	4 (8.9%)
Tumor Localization	
Cardia	24 (53.3%)
Corpus	11 (24.4%)
Antrum	6 (13.3%)
Cardio-esophageal junction	3 (6.7%)
Fundus	1 (2.2%)
Type of Surgery	
Total Gastrectomy	39 (86.7%)
Completion Gastrectomy	3 (6.7%)
Distal Subtotal Gastrectomy	1 (2.2%)
Wedge Resection**	1 (2.2%)
Wedge Biopsy***	1 (2.2%)

Table 1. Clinicopathological variables of the patients (continue)

Variables	Value or n (%)
Splenectomy Indication	
Invasion	30 (66.7%)
Bleeding	15 (33.3%)
D_2 lymphadenectomy	
Yes	20 (44.4%)
No	25 (55.6%)
Pathology of Gastrectomy Specimen	
Adenocarcinoma	40 (88.9%)
Non-adenocarcinoma	5 (11.1%)
Pathological Tumor Invasion (pT)	
pT_1	1 (2.2%)
pT_2	3 (6.7%)
pT_3	18 (40%)
pT_4	14 (31.1%)
pT_x	9 (20%)
Pathological Node Invasion (pN)	
pN_0	8
pN_1	8
pN_2	5
pN_3	15
pN_x	9
Tumoral Invasion at Splenectomy Specimen	
Yes	0 (0%)
No	45 (100%)
Overall Morbidity	
Yes	21 (46.6%)
No	24 (53.4%)
Overall Mortality	
Yes	8 (17.8%)
No	37 (82.2%)
LOS (mean, days)	15.3 (3-63)

ASA= American society of anesthesiologists, UMI= upper midline incision, LMI= lower midline incision, TPL= thoraco phreno-laparotomy, DL= diagnostic laparoscopy, LOS= length of stay. *5 patients were not included due to missing data, **gastrointestinal stromal tumor located at fundus, ***unresectable tumor.

Midline laparotomy was used in all cases. Diagnostic laparoscopy was used for first step evaluation in only four patients to evaluate tumor degree. Upper midline incision was the most common incision type. The most common tumor localization was cardia (n=24, 53.3%). Other tumor locations were as follows: 11 in the corpus (24.4%), six in the antrum (13.3%), three in the cardio-esophageal junction (6.7%), and one in the fundus. The most common surgery type (n=39) was total gastrectomy (86.7%). In addition, completion gastrectomy was performed in three patients because of proximal border positivity. Another indications for completion gastrectomy were tumor relapse after distal subtotal gastrectomy 18 months later, anastomosis necrosis after proximal gastrectomy.

In 30 cases (66.7%), because of invasion, splenectomy was added to gastrectomy. Splenectomy was performed due to splenic laceration and bleeding in 14 cases (31.1%) and injury at splenic vein in one case. D2 lymphadenectomy was performed in 20 patient (44.4%). And, splenectomy was performed in only five cases due to hemorrhage during D_2 lymphadenectomy.

The main gastrectomy pathology was adenocarcinoma in 40 patients (88.9%). Less common gastric tumors were detected in the remaining five cases. Two cases were interpreted as gastrointestinal stromal tumor, one case as neuroendocrine carcinoma, one case as pleomorphic sarcoma and one case as leiomyoma. Depth of invasion of tumor was as follows: pT_1: 1, pT_2: 3, pT_3: 18, pT_4: 14, pT_x: 9 and lymph node metastasis was as follows: pN_0: 8, pN_1: 8, pN_2: 5, pN_3: 15, pN_x: 9.

At the reports of the splenectomy materials, hemorrhage and congestion was seen in 23 cases (51.5%). Normal splenic tissue were observed in 12 cases, and lacerated splenic tissue in three cases. The other rare pathologies in splenectomy materials were epidermal cyst and focal infarctus, mild congestion, mild autolysis, reactive changes, inflammation and fibrosis, and subcapsular hemorrhage.

Postoperative complications are shown in Table 2. The mean length of hospital stay was 15.3 days (3-63). Morbidity and mortality rate of the presented study were 46.6% (n=21) and 17.8% (n=8), respectively. Mortality increased in patients who were operated in emergency situations and received neoadjuvant therapy, P=0.002 and P=0.044, respectively. Mortality rate was 8.1% in elective surgery group, while 62.5% in emergency surgery group. While the mortality rate was 0% in patients who received neoadjuvant chemotherapy, it was 25.8% in the group not receiving neoadjuvant chemotherapy. Factors affecting morbidity and mortality are shown in Table 3.

Table 2. Postoperative complications.

Postoperative Complications	n (%)
Pleural effusion treated with chest tube and atelectasis*	4 (8.9%)
Roux-en-Y necrosis and leakage	4 (8.9%)
Esophagojejunal anastomosis leakage	4 (8.9%)
Abondan hemorrhage (one of them treated with re-exploration)	2 (4.4%)
Postoperative delirium	2 (4.4%)
Cerebrovascular disease and pulmonary embolism	1 (2.2%)
Surgical site infection	1 (2.2%)
Benign intracranial hypertension and papilledema	1 (2.2%)
Pleural effusion treated without chest tube and atelectasis	1 (2.2%)
Atelectasis	1 (2.2%)
Total	21 (46.6%)

*Only postoperatively inserted chest tubes were added to the study.

Table 3. Comparison of clinicopathological features of the patients with morbidity and mortality

PARAMETERS		morbidity (+) vs. morbidity (-) P value	mortality (+) vs. mortality (-) P value
Clinical Findings	Age (<65 vs ≥65)	0.905*	0.569*
	Gender	0.143*	0.119*
	ASA Score	0.911**	0.631**
	Hypertension[1]	0.673*	0.577*
	Diabetes Mellitus[1]	0.238*	0.662*
	Cigarette[1]	0.677*	0.627*
	COPD or Asthma[1]	0.598*	0.507*
	Cardiac Stent[1]	0.550*	0.875*
	Angiography[1]	0.114*	0.573*
Intraoperative Findings	Mallampati Score	0.556**	0.062**
	Surgical Urgency	0.443*	0.002*
	Neoadjuvant Treatment	0.322*	0.044*
	Type of Incision	0.551**	0.264**
	Type of Surgery	0.529*	0.222*
	Tumor Localization	0.492**	0.706**
	Splenectomy Indications	>0.999*	0.542*
	D_2 lymphadenectomy	0.161*	0.059*
Postoperative Findings	Main pathology (adenocarcinoma vs. others)	0.211*	0.652*
	Depth of invasion (pT)	0.617*	0.706*
	Lymph Node Metastasis (pN)	0.460*	0.792*

COPD= chronic obstructive pulmonary disease. [1]Evaluated at 40 patients, *Chi-Square test, **Likelihood ratio test.

4. Discussion

In this study, the splenectomy issue during gastric cancer treatment was evaluated in a different way. In splenectomy concomitant gastrectomy cases, we researched the factors affecting morbidity and mortality. There is no literature study on this subject. In the literature, studies were conducted by comparing the groups between splenectomy groups and non-splenectomy groups.

As time passed, the subject of gastric cancer treatment has gained new dimensions and the addition of splenectomy to the surgical modality has been a subject of discussion, especially in tumors located in the greater curvature. Despite the continuous comparison between spleen-preserving surgeries and spleen-resecting surgeries in the literature, concurrent splenectomy is still debated issue in gastric cancer treatment.Especially, concurrent splenectomy is recommended in cases of gastric cancer with greater curvature involvement (Usui et al., 2016; Watanabe et al., 2016).

In the prospective study of Japan Clinical Oncology Group (JCOG0110), concurrent splenectomy has been shown to have no advantage over oncological outcomes in cases without greater curvature involvement, but rather to increase morbidity (Sano et al., 2017). So that, in Eastern countries such as Japan applies concurrent splenectomy in suitable gastric cancer cases (Jp, 2011; Association, 2017). However, in Western countries, concurrent splenectomy is not applied as often as Eastern countries because of higher complication rates (Wagner et al., 2017). In the study of Ohkura et al. (2017) there were a significant increase in blood loss and pancreatectomy related complications in cases with splenectomy. At the randomized controlled trial of Toge et al. (1985) splenectomy had positive effect on overall survival compared to the non-splenectomy group (71.7% vs 56%). However, at some retrospective studies, splenectomy had a negative effect on overall survival (Ito et al., 2013; Nashimoto et al., 2012; Zhang et al., 2014).

Another important issue is station 10 lymph node dissection. Up to 10% of patients with advanced proximal gastric cancer have station 10 lymph node metastasis (Chen et al., 2014; Huang et al., 2014; Hong et al., 2017; Jeong et al., 2019). In the literature, the efficacy of station 10 lymph node dissection with splenectomy is under investigation. In this studies splenectomy showed either a negative impact or no impact on survival (Ajani et al., 2013; Ji et al., 2016; Wang et al., 2013).

In the literature, the number of cases in studies varied between 10 and 260 (Oh et al., 2009; Tsuda et al., 2015; Galizia et al., 2015; Son et al., 2017; Jeong et al., 2018). There are 45 cases in this study; unfortunately, this number of cases was below the literature average. Mean age of patients of this study is suitable with literature data (in the literature mean age range: 52.7-65 year). As in the present study, incidence of male gender is higher

in the studies (Csendes et al., 2002; Zhang et al., 2007; Li et al., 2009; Galizia et al., 2015; Son et al., 2017; Jeong et al., 2018; Hyung et al., 2019), except the study of Fujita et al. (1996) (Male to female ratio was 4/6).

In the literature, the morbidity rate of splenectomy performed during gastric cancer surgery varies between 2.3% and 50%, while the mortality rate varies between 0% and 6% (Csendes et al., 2002; Zhang et al., 2007; Li et al., 2009; Oh et al., 2009; Galizia et al., 2015; Son et al., 2017; Jeong et al., 2018). The morbidity and mortality rate of the present study were 46.6% and 17.8%, respectively. While the morbidity rate of our study was within the range of the literature, the mortality rate was higher than the range of the literature. Because patients in the present study had more advanced tumor pathologic stages (pT_3-pT_4: 71.1%; pN_2-pN_3: 44.4%).

Emergency gastrectomy, with or without splenectomy, has higher morbidity and mortality. In addition, emergency gastric cancer is associated with advanced stage disease at presentation, lower rates of operability, and peritoneal contamination (Vasas et al., 2012). However, there were studies showed that there was no correlation between the presence of complications and resection of spleen (Valenti et al., 2011; Ciesielski et al., 2017). In this study, emergency surgery did not affect morbidity, but had effect on mortality. In our study, we found that neoadjuvant therapy had a protective effect on postoperative mortality. We attributed this to the tumor down-sizing effect of neoadjuvant therapy.

Except for laparoscopic studies (Son et al., 2017; Usui et al., 2016), mean of hospital stay was higher than 10 days like recent study (Li et al., 2009; Oh et al., 2009; Galizia et al., 2015; Son et al., 2017; Jeong et al., 2018).

5. Conclusion

Splenectomy during gastric cancer surgery is still a debated issue. Because there are studies in English literature evaluating morbidity, mortality and survival, and the results of which are controversial. The authors of this study recommend that splenectomy in gastric cancer surgery be performed, if possible, in elective conditions and after neoadjuvant therapy. But, more studies are needed to investigate new factors determining morbidity and mortality in gastrectomy cases with splenectomy.

Author Contributions

All authors had equal contribution and authors reviewed and approved the manuscript.

Conflict of Interest

The author declared that there is no conflict of interest.

Ethical Approval/Informed Consent

Ethics committee approval was received from Non-invasive Clinical Research Ethics Committee of Van Yuzuncu Yil University (Decision Number/Date: 2021/03-02/19.02.2021).

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