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Laparoscopic resection for gastric neuroendocrine and stromal tumors: a single-center prospective study

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Abstract
In stomach, the majority of the endocrine system neoplasm is situated in the corpus or the fundus, constituting a collection of non-functioning, enterochromaffin similar cell, and proper differentiated carcinoid. The golden standard in gastric GIST and NET is always operational removal whenever possible. In this study, we aimed to exhibit our outcomes by experience on laparoscopic resection of GIST and NETs, each one in the stomach. The current study was prospectively designed in our hospital to assess the likelihood and the safeness of the laparoscopy for individuals with GISTs and NETs, between January 2012 and 2014. Partial gastric resection was applied to eleven individuals (6 males /5 females) who were clinically determined as stomach-located GIST and NETs. The mean value of the tumor diameter was 4.2±1,36 cm (range: 2.5-6.8, median:4.3 cm). Tumor locations were around the fundus (n:2;%18.1), the antrum (n:3;%27.3), and the corpus (n:6; %54.5). The mitotic counts of the tumors were found to be <5/50 HPF in 7 patients, 5-10/50 HPF in 2 patients and >10/50 HPF in 2 patients. All 7 GISTs were c-KIT (CD117), DOG1 or CD34 positive (n:7). All 4 NETs were both Synaptophysin and Chromogranin positive. The main presenting symptom was abdominal pain (n:6, %54). In this article, the results supported that the laparoscopic way on the treatment of gastric GISTs and NETs is a secure and profitable selection for individuals if treated properly.

Keywords: Gastrointestinal stromal tumor, neuroendocrine tumor, laparoscopic resection

Introduction

Neuroendocrine Tumors (NETs) of the gastro-intestinal system are believed to originate from the tissues of the disperse neuro-endocrine structure of the gastro-intestine system. In the stomach, the majority of the endocrine system neoplasm is situated in the corpus or the fundus, constituting a collection of non-functioning, enterochromaffin-similar cell, and proper differentiated carcinoid[1]. The neoplasm of the gastro-intestinal stroma (GIST) is mesenchymal neoplasm resulting from the interstitial tissues of the Cajal neighborhood within the wall structure of the gastro-intestine path. GISTs demonstrate a predilection for the stomach, the place where they compose the most of the mesenchymal malignant neoplasm [1,2].

GISTs were noticed to coexist with a number of different neoplasms. The proportion of these kinds of conditions varies from 4.5% to 33%; in such type of instances, the stomach is regarded as a regular destination of GIST [3]. Protoncogene mutation of KIT is stated in the overwhelming majority of GISTs. That results in neoplasm recognition through widespread expression (95%) of CD117, the section of the KIT receptor [4]. Around 60% to 70% of GISTs might display immune-positivity for CD34 that is more usual in the colorectal and esophagus. The most frequently observed coexisting unknown growth is adenocarcinoma of the gastrointestinal system; the other forms are; lymphoma, leukemia, pancreas, breast carcinoma, prostate, adrenocortical or lung adenoma. Likewise, existing research has shown the relationship between GI and NETs; and synchronous or metachronous epithelial malignant tumors are responsible for around 9% to 48% of the events [5].

Each GIST is recognized as being quite possibly cancerous. Whenever a gastric submucosal neoplasm could not be separated with superior assurance, this is steadily advised to extract the unknown growth by the majority of recommendations, particularly cancerous growth bigger than 2 cm [3]. Scaled-down growths might be identified due to the minimum risk of cancers, although sufferers must be enlightened on the prospects for cancer despite the modest neoplasm dimension. Principles of NCCN recommend operational excision of modest GISTs lesser than 2 cm size whether they are followed with superior liable Endoscopic Ultrasound capabilities like an unnatural boundary, cystic areas, ulceration, or heterogeneity **[6].**

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The golden standard in regional GIST and NET is always operational removal whenever possible. A surgical procedure should accomplish total tumor resection because it is the most crucial prognostic point [7]. Laparoscopic surgical procedure is currently regarded as a legitimate procedure for the therapy of these kinds of neoplasms because requirements for excessive resection can be accomplished by using this method [8]. It needs watchful intraoperative management to prevent the split of the neoplasm capsule and the circumstantial spilling of the cellular material. In this research, we herewith exhibit the situations of GIST and well-differentiated NETs, each one in the stomach. We expect to reveal our practical experience by showing that laparoscopy is an effective alternative associated incursive surgical treatment with its own higher convenience and is very easily carried out in this kind of sufferers who certainly require surgical treatment.

Materials and Methods

The current study was prospectively designed in our hospital to assess the likelihood and the safeness of the laparoscopy for individuals with GISTs and NETs, between January 2012 and January 2014. The informed consent of the study was provided by all individuals. We applied limited gastric resection to 11 individuals (6 males / 5 females) clinically determined as stomach-located GIST and NETs, and claimed that surgical resection should be applied after the assessment of the research laboratory, endoscopy and radiological imaging consequences (Figure 1). Individuals suffering from any specific additional procedures during a period of laparoscopy restricted the resection of the stomach, which was not effective for curing the intestinal capability (like enterolysis), and any sort of contra-symptoms to laparoscopic procedure were solved out from the investigation. Maintaining limitations are available for be the mean ± standard variant; nonetheless, statistical outcome evaluation was not carried out due to being a smaller sample size**.** As stated previously, the region and the improvement type of the unknown growth, along with the neoplasm dimension, were the important elements in determining trustworthiness through solely incursive strategies.

Exophytic cancerous growth around the larger curve, fundus and anterior gastric wall area were conveniently variable to limited resection; and 1 or 2 laparoscopy staplers (EndoGIA, North-Haven, CT, USA) were used to eradicate the neoplasm. Such cancerous growths placed in the backside structure/composition of the gastric wall were directly switched into the abdominal area [9]. Malignancy localized to the lumen was immediately removed with larger amount of resection to entry/extort neoplasm. The tumor around the pylorus was resected via distal gastric way by laparoscopy (Figure 2). A close-way suction drain was put around the operational area. Nasogastric-way drains were post-operatively implemented and plugged out at 12^{th} hour after the operation [10]. On the initial postoperative daytime, all individuals were requested to travel around and stay hydrated, and there was a couple of problems connected with the postoperative circumstances [11]. The individuals were released when they were able to endure a daily diet plan. Intraoperative neoplasm rupture was analyzed as the most crucial benefits. Subsequent points were the transformation procedure rate, operational length, expected blood loss, solid eating plans, duration of the post-operative medicinal assistance, vacation and the recurrence speed at the end of the follow-up [6].

Figure 1. Computed tomography image of a gastric gastrointestinal stromal tumor

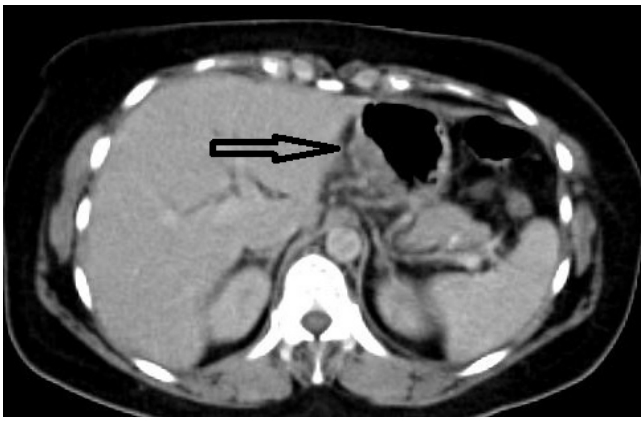
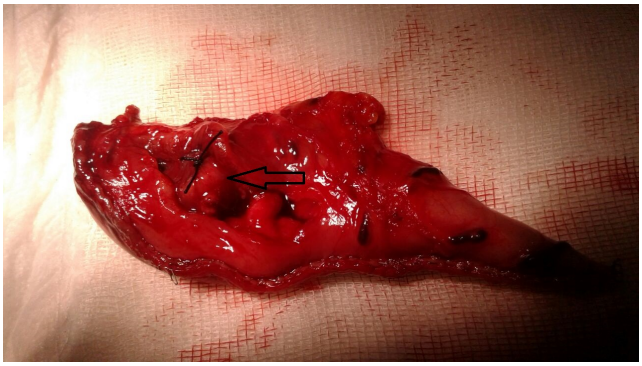


Figure 2. Laparoscopic partial gastric resection



Results

Considering the eligible patients, 11 patients were included in this study. The patients were 6 males and 5 females; and the ages ranged from 23 years to 70 years (50.5±16.2, median: 62). The mean value of the Body Mass Index for the patients was 23.9±2.9. All the cases were showing symptoms at presentation. The main presenting symptom was abdominal pain (n:6, 54%). Other symptoms were anemia with a hemoglobin of <12g/dl (n:3; 27%), gastro intestinal bleeding as hematemesis or melena (n:2; 18%), and incidental finding (n:4; 36%). The mean value of the tumor diameter was 4.2±1,36 cm (range:2.5-6.8, median:4.3 cm). The tumor locations were around the fundus (n:2; %18.1), the antrum (n:3; %27.3), and the

corpus (n:6; 54.5%). All the data regarding the characteristics of the patients are given in Table 1.

Table 1. Characteristics of patients with gastric GIST and NETs who received partial laparoscopic resection

Characteristics	Value
Mean age (range), years	50.5±16.2 (23-70)
Gender (male/female)	6 / 5
Body Mass Index	23.9±2.9
Presenting symptoms, n (%)	
Anemia	3 (27.2)
Gastrointestinal bleeding	2 (18.1)
Abdominal pain	6 (54.5)
Incidental finding	4 (36.4)
Preoperative tumor diagnosis, n(%)	
Tumor size (range), cm	4.2±1.36 (2.5-6.8)
Tumor location, n (%)	
Fundus	2 (18.1)
Antrum	3 (27.3)
Corpus	6 (54.5)

Abbreviations: GIST, Gastrointestinal tumor, NETs: Neuroendocrine tumors

The tumors were two types as GIST (n: 7) and NETs (n: 4). The mitotic counts of the tumors were found to be <5/50HPFin 7 patients, 5-10/50HPF in 2 patients and >10/50HPF in 2 patients. All 7 GIST were c-KIT (CD_{117}), DOG_1 or CD_{34} positive (n: 7). All 4 NETs were both Synaptophysin and Chromogranin positive (Table 2). The volume of the blood drainage ranged between 30 and 100 ml for all cases. The surgery duration varied from 60 to 180 minutes, which took 135 minutes for the operation time. The post-operative feeding took 2-3 days. The median clinic stay time was 6 days (4-9 days). The rest of the patients were followed-up for a period ranging from 6 to 18 months with a mean of 11.2±3.9 months.

Table 2. Tumor characters of GIST and NETs

Parameters	N (%)
Cell type	
Spindle	6 (54.5)
Epithelioid	2 (18.1)
Mixed	3 (27.3)
Mitotic rate, /50 HPF	
≤5	7 (63.6)
5‑10	2 (18.1)
≥10	2 (18.1)
Positive for	
CD_{117}	7 (63.6)
DOG_1	7 (63.6)
CD_{34}	7 (63.6)
S‑100	0
Synaptophysin (NETs)	4 (36.3)
Chromogranin (NETs)	4 (36.3)
Ki‑67 index, %	
<10	7 (63.6)
≥10	4 (36.3)

Abbreviations: CD, cluster of differentiation; DOG1, discovered on GIST-1; GIST, gastrointestinal stromal tumor; HPF, high-power fields

Discussion

In this article, we reported our laparoscopic outcomes on the gastric tumors including GISTs and NETs. Our results supported that the laparoscopic way on the treatment of the gastric GIST and NETs is a secure and profitable selection for individuals if treated properly. Nonetheless, the resection via surgical way is currently the golden procedure for the treatment in recent guidelines. The fundamentals regarding the laparoscopic treatment should contain no trauma against pseudocapsul and negative macroscopic border. In our study, we cautiously dissected submucosal mass under the augmented laparoscopic watch, and evaluated histological examination to determine the presence of the tissue of the marginal submucosa. This kind of method for dissection must be complicated to opened operation, since human eye resolution is unable to identify enough layers for dissection. In this aspect, laparoscopy permits us to specifically separate the tissue of the submucosa and to encounter any microscopically injurious investment.

Based upon the newest recommendations, Neuroendocrine Cancers (NETs) have different treatment method practices. In the event that the diameter of NETs is smaller than 1 cm, tumor resection and endoscopic view should be the initial options. If equal or higher than 1 cm, larger endoscopic submucosal resection should be executed. If the neoplasm reaches the submucosal wall and misses the R_0 resection with endoscopic submucosal resection, operation entrances is escapable [12]. However, not much literature is accessible on the laparoscopic management of the gastric NETs. There is little proof presenting that laparoscopic partial gastrectomy with or without lymph node dissection for cancer is safe, and includes all the features of laparoscopy in comparison with open resection [13]. Our results for 4 patients promote the use of laparoscopic gastrectomy in NETs obtaining significant effect in those kinds of conditions.

In a study of 25 patients, Hoteya et al. [14] mentioned about the possibility and the protection of old-fashioned laparoscopic method of gastric submucosal tumors. The study of Qiu et al. [15] and Tsujimoto et al. [16] exhibited the probability and suitable results of laparoscopic gastrectomy of GIST. Benefits of the traditional laparoscopic gastrectomy process remain strong for preventing intense gastric wall resection. Another study revealed that the traditional laparoscopic gastrectomy diminished the operational sample as even now offering an adequate operational option for efficient GIST treatment [17]. Moreover, the traditional laparoscopic gastrectomy method is not influenced by tumor position, like the locality of the pyloric circle or the eusophogastric junction [18]. In all these reports, the operation time varied between 156 and 169 minutes by mean values. The research of De Vogelae reported lessened wide afflictions and morbidity [19]. In this cohort study, he suggested that the resection by laparoscopy was a reliable and strong choice for curing GISTs in spite of the neoplasm length and width. Another similar study conducted by Ronellenfitsch showed that the tumor dimension did not determine the possibility of the

laparoscopic wedge resection [20]. A diameter-matched research project indicated that laparoscopy for GISTs>5 cm had advantages against the opened procedure with regards to the operative interval, blood loss, liquid supplement, and postop-stay.

A prospective study of Novitsky et al. [21] with 50 individuals, who underwent laparoscopic or laparoendoscopic treatment of GISTs, exposed that laparoscopic procedure might perhaps be the preferred resection method in the majority of the cases with smaller scale and moderate-sized stomach GISTs. The diameters of the patient's lesions are the same with our study. The tumor size was around 4.4 cm (1.0-8.5 cm) with much of the neoplasms positioned in the proximal stomach. Moreover, the neoplasms in our analysis were within 2.5-6.8 by a mean value of 4.2 cm. However, most of the lesions were placed in the corpus. Surgical instance, blood decrease and the course of hospital stays were usually similar to our research, as well as the study outcomes. We did not encounter operative complications or mortality as well as in the study that was conducted by Novitsky et al. In an equivalent analysis, Cao et al. [10] investigated the resection for gastric GISTs bigger than 5 cm in terms of essential security of laparoscopy. As a conclusion, they declared that laparoscopic surgical procedures should be considered as the regular method in all events, irrespective of the neoplasm dimension and/or locality.

Leukaszczyk et al. [22] verified that laparoscopic methods were sufficient to realize the array of resection; they did not hurt the tumor, and might possibly minimize the recurrence frequency of the closest tumor. Nguyen et al. [23] reported that choosing resection through laparoscopy for gastric stromal tumors is secure and contributes quicker restoration, lesser postoperative clinic staying, timelier running of the gastro-intestinal system, and less reaches in contrast to open resection. Our outcomes are in accordance with the latest surgical experiences demonstrating that laparoscopic surgical procedure of the gastric stromal malignant tumors is protected and also practical, and contributes to far less tension and more rapid healing. Laparoscopy surgery procedure of GISTs and NETs leads to both much less damage and quicker postoperative healing. This also delivers the following capabilities: the functioning area of the scene is more lucid, decision and remedy may appear concurrently as well as the surgery tending to be much more accurate. Since the laparoscopic imaging could be increased and the device is light, portable and adjustable, a far more accurate procedure is possible.

Laparotomic surgical treatment produces pose an elevated likelihood of postoperative intestinal tract blockage, and it might lead to the tearing of the splenic capsule and blood loss. The use of laparoscopic staplers furthermore lowers the compression on the growth and eliminates the potency neoplasm split after the compress setting. One of the drawbacks to the laparoscopic method is that the normal entire hospital stay expense for the laparoscopy team was moderately greater than that of the accessible resection group. Surgeons' enhanced procedure abilities and the improved reputation of laparoscopic surgical treatment are going to lessen the performance instances, postoperative healing instances, and clinic stays, lowering overall hospital stay expenses and alleviating patients' financial problems.

There are many restrictions to the current research. Firstly, the few situations have bounded the worth of the decisions. Secondly, the malignant cancerous growth contained in this study was primarily placed around the fundus and the corpus of the stomach, which were simple goals for laparoscopic surgical treatment.

In addition to the literature, our results proved that using laparoscopy for curing GISTs and NETs carries various benefits, such as substantially less damage, more rapid postoperative healing, quicker clinic remain, lucid intraoperative optical area, concurrent medical diagnosis and cure. This process may prevent huge accidental injuries induced by hands or wrists, metallic retractors, and clogs triggered by the gauze throughout the procedure allowing it to decrease the compress on the neoplasm and reduce the chance of compression-induced tumor rupture; hence, it truly is assumed to adhere to the tumor-free procedure requirements superior to open resection does indeed. Thus, the laparoscopic surgical procedure of GISTs is risk-free, achievable, and effectual. The augmented reputation of laparoscopic surgical treatment and surgeons' enhanced operating abilities are going to lessen the operating instances, rate postoperative recuperation, and minimize clinic accommodation, consequently lowering hospital stay expenses and eliminating patients' financial problems.

As a result, the laparoscopic partial resection is a safe and applicable method for non-metastatic small tumors of GIST or NETs, which are positioned in tough localizations of the stomach and unsuitable to endoscopic procedures.

Conflict of Interest: The authors declare that they have no conflict of interest.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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