

Minimally Invasive Resection of Gastric GISTs: A Laparo-endoscopic Solution

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Abstract

Although the feasibility of minimally invasive resections of gastric gastrointestinal stromal tumors (GISTs) has been established, many aspects of this approach are still debated: in different scientific papers, gastroscopy during laparoscopy seems to be an effective technique for successful intraoperative tumor identification. 9 patients were referred to our institution for gastric GISTs. Preoperative work-up for all patients included medical history, standard blood tests, upper gastrointestinal endoscopy with endoscopic ultrasound examination and computed tomography scan. One of these patients underwent open surgery for acutely presentation (haemorrhage), and the other 8 underwent laparoscopic-endoscopic "rendez-vous" resection. The average operative time was 134.1 ± 59.3 min. The mean estimated blood loss was less than 62 ml (range, 10-174 ml). There were no episodes of tumor rupture or spillage, no major intraoperative complications and a conversion rate of 25%. At a mean follow-up of 25 months (range, 3-41) all patients are alive and disease free. There were no local recurrences. Given these findings, a minimally invasive approach should be the preferred surgical treatment in patients with small and medium-sized gastric GIST; moreover a selective approach to laparoscopic resection based on tumor location allows safe resection of these tumors with low morbidity and no compromise of oncologic principles.

Keywords: GIST; Laparoendoscopic resection; Subepithelial gastric masses; Endoscopically assisted laparoscopic wedge resection

Introduction

It is well established that gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms of the digestive tract with an estimated actual incidence higher than 0.4% [1-3]. They arise from pleuropotential intestinal pacemaker cells, the interstitial cells of Cajal, and they are characterised by overexpression of tyrosin kinase receptor KIT (CD 117 antigen), a c-kit proto-oncogene product, and CD 34, a human precursor cell antigen [4-8]. Although GISTs are found throughout the digestive tract, from the oesophagus to the rectum, the stomach is the most common site of occurrence in more than half of patients [7,9-11]. Furthermore clinical presentation of GISTs ranges from indolent, hardly proliferating to fast growing, recurring and metastasizing tumors [1,12].

It is difficult to predict GISTs metastatic potential: Fletcher et al. proposed a classification of aggressive behaviors for these neoplasms based on their maximum diameter and mitotic rate index [13]. Regarding treatment of GISTs two pivotal sets of guidelines have already been published from the United States (National Comprehensive Cancer Network-NCCN) and the European Union (European Society for Medical Oncology - ESMO) [14]. Notwithstanding same difference between the treatments proposed in such guidelines, surgery represents the main approach for nonmetastatic GISTs: an excision with negative margins without lymphadenectomy is recommended. Recently, in order to avoid the invasivity of a conventional open surgical technique, the laparoscopic wedge resection has been proposed as a less invasive option without compromising curability [2,15-18]. Although the feasibility of minimally invasive resections of gastric GISTs has been established, many aspects of this approach are still debated: wedge resection cannot be considered when a tumor is located near the cardia or pylorus, where the esophagocardiac junction or pyloric ring could be involved in the resection line [19]. The procedure would also be difficult if the tumor is located at the posterior wall. Another aspect of this approach is imminent: localization of intraparietal tumors during laparoscopy is only promising when approaching large lesions that protrudes into the abdominal cavity. In different scientific papers, gastroscopy during laparoscopy seems to be an effective technique

for successful intraoperative tumor identification and it is considered essential for laparoscopic resection of sub epithelial masses [20-22].

This retrospective analysis provides data regarding the outcome of patients undergoing a surgical resection for gastric GIST's at our institution.

Patients and Methods

Between January 2005 and December 2010 a total of 9 patients were referred to our institution (VIII Unit of General and Gastrointestinal Surgery - Second University of Naples) for gastric GISTs; 1 of these patients underwent open surgery for acutely presentation (hemorrhage), and the other 8 underwent laparoscopic approach: in 6 of them we performed a combined laparoscopic-endoscopic "rendez-vous" resection (in particular "endoscopically assisted laparoscopic wedge resection" - EAWR), while in 2 patients a conversion was necessary, performing open gastric resection.

Preoperative work-up for all patients included medical history, standard blood tests, upper gastrointestinal (GI) endoscopy with endoscopic ultrasound examination and computed tomography (CT) scan. In some patients additional information was gained by taking biopsies of the lesion by means of conventional endoscopic tissue probing, even if preoperative histological confirmation of the diagnosis was not a prerequisite for inclusion. Patients were eligible for laparoscopic surgery if preoperative staging (endoscopy, endosonography and CT scan) showed a localized, non-metastatic extramucosal gastric lesion.

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Perioperative parameters measured included operative times, estimated blood loss, intraoperative findings, surgical techniques, morbidity, and length of hospitalization. Histological diagnosis of GIST was obtained from the resection specimen by means of hematoxylin and eosin staining and immunohistological assays for CD117 and CD34.

From a prospectively kept database, we extracted the following characteristics: age, sex, length of postoperative hospital stay, operation time, tumor location, tumor size, classification of aggressive behavior, histopathological assessment of resection margins, intraoperative blood loss, and incidence of perioperative complications (cardiac, pulmonary, septic, anastomotic failure, reoperation needed). We present single values as well as the median plus range or, where applicable, percentages, for the respective variables.

All patients with confirmed GIST were followed up regularly including upper GI endoscopy and abdominal CT scans every three to six months depending on the risk for malignant behavior and according to Scottish GIST guidelines. From these visits we assessed vital status and tumor recurrence.

Surgical methodology

All interventions were performed under general anesthesia with the patients in a supine and reverse-Trendelenburg position. After pneumoperitoneum was established with open laparoscopy technique, at least three trocars were inserted intra-abdominally: the optical trocar in a supraumbilical position and two trocars for the manipulating instruments in the left and right upper quadrants. A fourth (5 mm) trocar was inserted in the right epigastrium close to the costal arch for better exposition of the stomach. The abdominal cavity was exposed and identification of the gastric lesion was attempted. Upper endoscopy was then performed. Endoscopy was done after establishing the pneumoperitoneum to avoid injury to inflated organs. The endoscope was inserted perorally and advanced into the stomach, and the lesion, which usually protruded into the gastric lumen, was precisely localized. By the use of diaphanoscopy and manipulation along the gastric wall close to the lesion, the exact location of the subepithelial tumor was demonstrated to the laparoscopist, who observed the gastric wall from the outside. With this team approach, tumor targeting was accomplished and the decision was made for the best means of tumor resection. Depending on the localization of the tumor and according to the assessment of both actors, we ever perform Endoscopically Assisted Wedge Resection (EAWR), which can be applied to tumors in the anterior wall of the stomach or lesions located at the greater or lesser curvature. After localization of the tumor with the rendezvous technique, the surgeon elevates the part of the gastric wall that carries the lesion; this can be done by grasping the gastric wall with a traumatic forceps next to the lesion. As soon as the tumor is exposed that way, a linear stapler device is inserted intra-abdominally and positioned just beyond the lesion; after verifying the correct position of the stapler, with the tumor completely captured, the device is fired. After wedge resection of the tumor site, the specimen is recovered into a retrieval bag and extracted. Though the suture line is controlled from both sides, from endoluminal side by the endoscopist and externally by the laparoscopist; we believe that over suturing the stapler line to avoid bleeding is unnecessary. To assure a safe and leak-proof suture line, the endoscopist finally can insufflate air into the stomach or apply blue dye.

Results

Patient characteristics

From 2005 to 2010, 8 patients undergoing laparoscopic approach

for gastric GISTs were reviewed (3 male and 5 female). The average age was 61 ± 11.4 years (range, 42-79 years). The majority of these patients presented with symptomatic tumors, more than 50% of which had symptoms relating to blood loss. All patients had preoperative esophagogastroduodenoscopy; preoperative biopsy was carried out preoperatively with definitive diagnosis in all patients. In addition, all patients underwent an abdominal computed tomography scan and endoscopic ultrasonography.

Perioperative outcomes

The laparoscopic procedure was the surgical approach of choice for all 8 patients: in 6 patients we performed an endoscopically assisted laparoscopic wedge resection, while in 2 patients a conversion to open surgery was necessary (conversion rate: 25%). Tumor identification and localization by single visual exploration and palpation of the abdominal cavity during initial laparoscopy was successful in 6 of 8 patients (75%), but in only two patients was it so exact that the resection could have been performed without additional targeting. This was due to the inability to define whether a lesion was located in the anterior or posterior aspect of the stomach, though the lesion itself appeared as protruding mass. However endoscopic tumor localization was applied in every case, and with the endoluminal view, all tumors were exactly located. The average operative time was 134.1 ± 59.3 min. The mean estimated blood loss was a little less than 62 ml (range, 10-174 ml). There were no episodes of tumor rupture or spillage, no major intraoperative complications, and no conversion to open surgery. Postoperatively, all patients required nasogastric tubes beyond the 24-hour period. Bowel function resumed between postoperative days 1 and 2 for all patients. Oral feedings started the day after radiologic control. No patient had any evidence of staple-line leak, stenosis and blood loss. The average length of hospitalization was 5.1 ± 1.1 days (range, 4-8 days). There were no postoperative complications or mortalities. There was no long-term morbidity related to wedge resection.

As regard cases that required a conversion to open surgery, in one patient the lesion was localized in correspondence of gastro-esophageal junction and was difficult to access (in this case we performed a total gastrectomy), while in the second one the tumor was nearest the pylorus and was once again difficult to access (in this one we performed distal gastrectomy).

Tumor gross and microscopic characteristics

The majority (75%) of tumors were found in the proximal third of the stomach, 4 on the anterior and 2 on the posterior aspect. One lesion was localized in the middle third of the stomach and another one was pyloric GIST. The average tumor size was 4.8 ± 0.9 cm (range, 2.5-5.9 cm). All lesions have a negative resection margin. Following the GIST risk criteria [13], of the 8 patients, none were high-risk, 6 intermediate-risk and 2 low-risk patients. Immunohistochemical analysis included CD117, CD34, S-100 and desmin. CD117 positivity was detected in all patients, and CD34 was positive in 2 (50%) patients. There were no positivity to S-100 and desmin.

Tumor related outcomes

Follow-up information was available for all patients. At a mean follow-up of 25 months (range, 3-41) all patients are alive and disease free. There were no local recurrences.

Discussions

Gastrointestinal stromal tumors are rare submucosal neoplasms that require complete surgical resection for achievement of definitive

treatment [9]. Thus, as defined by the GIST consensus conference, the goal of surgical therapy should be "complete resection of visible as well as microscopic disease, while avoiding tumor rupture and obtain negative margins" [9,23]. However the adequate surgical management of these submucosal lesions is still debated in fact, whereas lesions smaller than 2 cm are considered a clear indication for a minimally invasive approach, tumors larger than 3 - 5 cm in size are assigned to an increased risk for malignant behavior, and therefore some authors recommend open surgery, for oncological principles [24]. Moreover, laparoscopic resection for gastric GISTs had been proven to be feasible and safe with low complication rates for all tumor size, particularly when associating with intraoperative endoluminal endoscopy [7]: however this technique has not yet been evaluated. This article summarizes a single-center experience of 8 cases of laparoscopic procedure for gastric GISTs. The stomach is the most common site of GISTs, occurring in 52% to 60% of cases, with the proximal stomach involved in about two thirds of those patients [7,25-27], as encountered in our series. Moreover several studies [26,28] described that most patients with gastric GISTs present in their 6th or 7th decade, with only 10% of patients around 40 years of age; we found a comparable data. Only one of studied patients had lesion discovered incidentally during a work up of vague dyspeptic or reflux symptoms. On the other hand, anemia or frank gastrointestinal bleeding was encountered in more than 50%. Following upper endoscopy, an abdominal CT scan is usually the test of choice to further delineate the location and size of the lesion and to look for direct or metastatic spread. Endoscopic ultrasound can be very helpful to resolve diagnostic challenges [25,29].

Even if only a few Authors utilized preoperative endoscopic biopsies reporting limited results, conventional tissue probing was carried out in all patients, with definitive diagnosis in all patients [30]. Perhaps we considered an endoscopic ultrasound-directed needle biopsy not necessary. Although our series presenting an average tumor size of 4.8 cm (range, 2.5-5.9 cm), we can perform a laparoscopic wedge resection, with conversion rate to open surgery of 25%.

Evidence suggests that tumor size singularly is not a contraindication to the laparoscopic approach [20] is also supported by our laparoscopic removal of a 5.9 cm gastric GIST. The combination of a large tumor and difficult location (esophago-gastric junction/pylorus) can make laparoscopic approach all the more challenging: for tumors located in the fundus and along the greater curvature of the stomach, a laparoscopically stapled gastric wedge resection often is quite feasible given the significant redundancy and mobility of the stomach in these locations. Tumors in this locations are readily approached laparoscopically with a plan for a stapled wedge resection. Resections of tumors in other locations within the stomach are more challenging to accomplish with a simple stapled wedge resection [9]. Tumors of the gastric cardia in the peri-gastroesophageal junction region and pyloric tumors are limited by the risk of gastric inlet/outlet narrowing or the need for conversion to an open procedure [9]. If attempted laparoscopically, they can require extensive dissection for mobilization of the stomach or more complex techniques, such as manual sewing over an esophageal bougie [9]. In this study, those patients converted to an open procedure presented the lesion near the esophago-gastric junction and near the pylorus.

The use of intraoperative endoscopy (combined laparoscopic-endoscopic "rendez-vous" resection) is considered an indispensable precondition: we believe that it is probably the best method available for minimally invasive tumor localization [19,20,22,31-33]; this fact could be proved in our series, as a lesion of 2.5 cm was not identifiable by laparoscopic examination, but was exactly localized by intraoperative

endoscopy. A further advantage of intraoperative endoscopy is the assistance it provides during resection, allowing the laparoscopist to decide upon the best technique to be applied, to simultaneously verify a complete excision of the tumor, and to check for a leak-proof suture line. Sometimes the scope can also be used for improved exposition of the tumor, and the endoscopic view offers an additional angle of vision, which might be helpful for the step of tumor excision or the placement of the linear stapler device. As we encountered no complications associated with the additional use of intraoperative endoscopy, we recommend its use. Laparoscopic-endoscopic rendezvous resection is easy to perform, as demonstrated by relatively short operating times in our series 134.1 ± 59.3 min. By analyzing our perioperative data, blood loss was very low ranging from 10 to 174 ml; the resections were accomplished with none morbidity and mortality. A short in hospital stay ranging from 4 to 8 days was also demonstrated. In our series, the laparoscopic approach also was not necessarily limited by tumor size, as previously suggested by the GIST Consensus Conference [3]. Although previous authors have recommended limiting their approach to tumors smaller than 2.5 cm [9], we were able to perform the procedure successfully with larger tumors (up to 5 cm) while still achieving negative margins in all cases.

Long-term follow-up is fundamental for these patients because GISTs have an unpredictable biologic behavior. In the present series, laparoscopic-endoscopic rendezvous resection of gastric GISTs results in effective control of the disease with no morbidity and mortality and excellent long-term survival.

Given these findings as well as the advantages afforded by laparoscopic-endoscopic rendezvous, a minimally invasive approach should be the preferred surgical treatment in patients with small and medium-sized gastric GIST; moreover a selective approach to laparoscopic resection based on tumor location allows safe resection of these tumors with low morbidity and no compromise of oncologic principles.

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