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Robotic gastric resection of large gastrointestinal stromal tumors

Jacopo Desiderio [a,*], Stefano Trastulli [a], Roberto Cirocchi [b], Carlo Boselli [b], Giuseppe Noya [b], Amilcare Parisi [a], Davide Cavaliere [c]

[a] Department of Digestive Surgery and Liver Unit, St. Maria Hospital, Terni, Italy
[b] Department of General and Oncologic Surgery, University of Perugia, Perugia, Italy
[c] Unit of Surgery and Advanced Oncologic Therapies, Forlì Hospital, Forlì, Italy

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ABSTRACT

Background: The stomach is the most common site for gastrointestinal stromal tumors (GIST) development. Surgical treatment consists of excision of the entire neoplastic mass, with sufficient surgical margins within healthy tissue. This can be achieved with different techniques ranging from wedge resections, typical gastric resections, right up to total gastrectomy. There aren't clear guidelines for the use of minimally invasive approach.
Materials and methods: From January 2011 to April 2012, 5 patients with presumed preoperative diagnosis of GIST were treated by robotic surgery at the Unit of Surgery and Advanced Oncologic Therapies, Forlì Hospital, Forlì, Italy. We report operative techniques, perioperative outcomes and follow-up.
Results: Lesions were localized at anterior wall of gastric antrum ($N = 2$) and near pyloric area ($N = 3$). Mean tumor size was 5 cm (range 4–7 cm). Surgical procedures were 5 distal gastrectomy. None intervention was converted to open surgery and there weren't major intraoperative complications. Median operative time was 240 min (range 210–300 min) and mean intraoperative blood loss was 96 ml (80–120 ml). All lesions had microscopically negative resection margins. Median follow-up was 13.5 months (range 12–15 months) with a disease-free survival rate of 100%.
Conclusions: Surgical robotic approach for large GISTs is feasibility and new evidences are needed to clarify the effective role of different surgical strategies.

1. Introduction

Gastrointestinal stromal tumors (GIST) are the most common intestinal mesenchymal tumors with an incidence of 20 cases per million.[1]

Surgical treatment allows neoplastic mass and gastric wall excision up to free margin. This can be achieved depending on tumor dimension and localization, through different techniques such as wedge resection for small GISTs, gastric resection, total gastrectomy in case of large dimension and localization near cardia.[2]

Laparoscopic interventions are limited by dimension and localization of the tumor and by the necessity to avoid intraoperative fragmentation and multi-visceral involvement.[3]

Recent studies on primitive gastric GISTs[4–7] seem encouraging with respect to cautions expressed by Consensus Conference that had limited laparoscopic approach only to GIST < 2 cm (National Comprehensive Cancer Network - NCCN),[8] or that had excluded this approach (European Society for Medical Oncology - ESMO - Consensus Conference, 2004)[9] because intraoperative lack of sense of touch may facilitate neoplastic tissue fragmentation.

Robotic surgery has started to have an important role in abdominal surgery and different studies on robot use for gastric diseases evidenced efficacy and feasibility of this mini-invasive approach.[10–12]

The aim of this study is to report our preliminary experience in robotic treatment for gastrointestinal stromal tumors of the stomach and evaluate surgical and oncologic short-term outcomes.

2. Materials and methods

From January 2011 to April 2012, 5 patients with presumed preoperative diagnosis of GIST that was confirmed by immunohistochemical study of the lesion, were treated by robotic surgery (Da Vinci; Intuitive Surgical, Inc., Sunnyvale, CA) and underwent follow up at the Unit of Surgery and Advanced Oncologic Therapies, Forlì Hospital, Forlì, Italy.

* Corresponding author. Department of Digestive Surgery and Liver Unit, St. Maria Hospital, Terni 05100, Italy.
E-mail addresses: djdesi85@hotmail.it (J. Desiderio), stefano.trastulli@hotmail.it (S. Trastulli), cirocchiroberto@yahoo.it (R. Cirocchi), carloboselli@yahoo.it (C. Boselli), gnoya@unipg.it (G. Noya), amilcareparisi@virgilio.it (A. Parisi), davidecavaliere@libero.it (D. Cavaliere).

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Preoperative diagnosis, evaluation of tumor characteristics and staging were executed by esophagogastroduodenoscopy and computed tomography (CT), while endoscopic ultrasonography (EUS) and core-needle biopsy were performed only when clinically indicated.

Lesions were post-operatively diagnosed as GIST using immunohistochemistry that showed CD117 (KIT) positive cells.

Patients' characteristics and clinical presentation are reported in Table 1. Operative time was calculated as the time between skin incision and port-site closure. Measured perioperative parameters included estimated blood loss, intraoperative findings, morbidity, and length of hospitalization. In addition, tumor histopathologic characteristics including size, location, tumor marker status and mitotic activity were analyzed. All operations were performed by experienced laparoscopic and robotic surgeons.

According to Fletcher criteria,[13] tumors of less than 2 cm in diameter and with a mitotic count (MC) of less than 5 of 50 high-power fields (HPFs) were classified as very low risk tumors. Low risk was identified for size from 2 to 5 cm and MC less than 5 of 50 HPFs, intermediate risk for tumor size less than 5 cm and 6–10 MC of 50 HPFs or when the tumor size was 5–10 cm and the MC less than 5 of 50 HPFs, high risk was determined when tumor size was greater than 10 cm or the MC was greater than 10 of 50 HPFs or the tumor size was greater than 5 cm and the MC was greater than 5 of 50 HPFs.

Lesions localized mostly on the outer wall of the stomach have been defined as having an exophytic growth pattern, those predominantly located on the inner wall of the stomach were instead defined as endophytic growth pattern.[14]

The present series shows a surgical approach for tumors of the antrum and prepiloric area with distal gastrectomy performed because more limited approaches were not feasible.

All patients who underwent robotic treatment of gastric GIST were prospectively followed-up with routine visits, firstly one month after the operation, then every 6 months with computed tomography and gastroscopy in order to evaluate recurrence of disease.

2.1. Operative techniques

The "Da Vinci" Surgical System (Intuitive Surgical Inc, Sunnyvale, CA) is a telerobotic system controlled from a surgeon at remote console, while surgical team is close to operating table and follows the procedure through a service screen. In order to facilitate team coordination, we located operative console in a corner of the operating room.

Patient was supine with arms along the body. After pneumoperitoneum induction through peri-umbilical Veress needle, 12 mm Trocar for optics and other three 8 mm robotic Trocars were positioned.

After insertion of the ports, the patient was placed in a reverse Trendelenburg's position.

At the beginning of every intervention abdominal, conventional laparoscopic exploration was performed in order to rule out peritoneal seeding or hepatic metastasis.

During robot setup, console was connected to robot and automatic checkup verified correct functioning of robotic arms, then optic setup was done. At this point the correct position of robotic cart is fundamental so that robotic arms do not to interfere among themselves.

During the procedure we add 12 mm extra-port for accessory surgical instruments controlled by the assistant surgeon. In fact, a second experienced surgeon was at the bedside to exchange the robotic instruments, retract for exposure and assist with the procedure. Lesions were never directly manipulated with robotic instruments in order to avoid tumor rupture.

Intraoperative endoscopy was performed in all cases in order to facilitate localization of the lesion, evaluate appropriate surgical technique and assist in the identification of correct resection margins.

In the five cases reported, because of the intramural localization in the prepyloric area and GIST's dimensions, larger gastric resection was performed following a procedure that is described below.

Tumors larger than 3 cm in this location carry the risk of gastric outlet stenosis after wedge resection. We considered that in this case a limited approach was not feasible and distal gastrectomy was the best alternative. Therefore, section of gastro-colic ligament was performed (Fig. 1) with access to omental bursa (Fig. 2) after a precise evaluation of tumor location, followed by isolation and section with emolock clips of right gastric artery and right gastroepiploic vessels (Fig. 3), duodenal isolation and section distally to lesion with mechanical stapler (Fig. 4). Gastric resection was executed in the distal 2/3 of the stomach (Fig. 5). Finally surgical specimen was removed through endocatch.

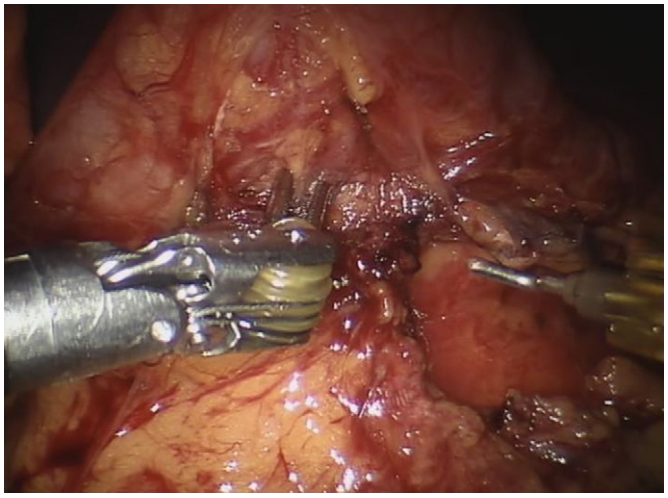

Fig. 1. Section of gastro-colic ligament.

A side-to-side one-row gastro-jejunal anastomosis is performed with running PDS 2-0 suture.(Figs. 6 and 7).

3. Results

This study reports characteristics of 5 patients with gastric GIST who underwent robotic surgical resection. There were 2 men and 3 women with mean age of 63.6 years (range 43–76 years). Three patients were asymptomatic and lesions were discovered after esophagogastroduodenoscopy, 1 patients referred abdominal discomfort and dyspepsia, 1 patient rectal bleeding with acute anemia.

The endoscopic investigations including EUS showed typical characteristics of GIST in all cases and their patterns of growth, the biopsy was performed preoperatively in three cases to increase the diagnostic accuracy but has not been performed in two patients at high risk of bleeding.

None patient underwent neoadjuvant therapy with tyrosine kinase inhibitor, Imatinib.

Lesions were localized at anterior wall of gastric antrum ($N = 2$) and near pyloric area ($N = 3$). One GIST presented exophytic pattern of grown. Mean tumor size was 5 cm (range 4–7 cm). Surgical procedures were 5 distal gastrectomy.

None intervention was converted to open surgery, nor there were tumor ruptures or spillage, nor major intraoperative complications and all lesions had microscopically negative resection margins that confirmed complete radicality of surgical intervention (R0). Estimated intraoperative bleeding has been negligible (mean of 96 ml, range 80–120 ml), and no blood transfusions were necessary in the perioperative period.

Histopatological analysis according to Fletcher criteria[13] classified 2 GISTs as low risk and 3 GISTs as intermediate risk.

Table 1
Characteristics of patients enrolled in the present study.

Patients	Gender	Age	Symptom/sign	Tumor location	Growth pattern	Size (cm)	Fletcher criteria
1	M	69	No symptoms	Antrum	Endophytic	5	Low risk
2	F	43	No symptoms	Antrum	Endophytic	4	Intermediate risk
3	M	71	No symptoms	Prepyloric	Endophytic	4	Low risk
4	F	59	Abdominal discomfort and dyspepsia	Prepyloric	Endophytic	7	Intermediate risk
5	F	76	Bleeding with acute anemia	Prepyloric	Exophytic	5	Intermediate risk

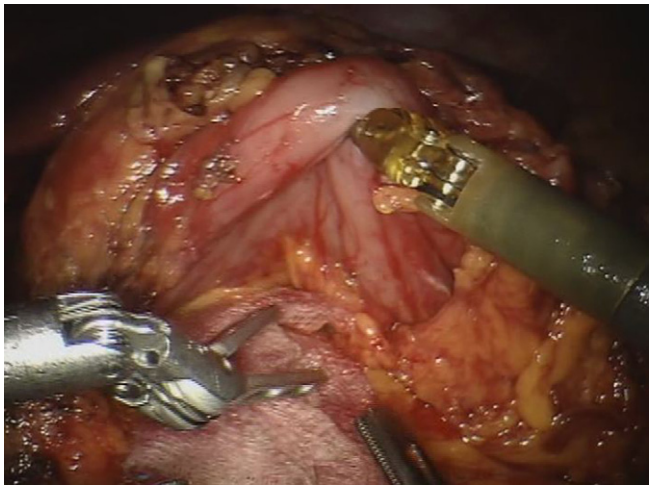

Fig. 2. Access to omental bursa.

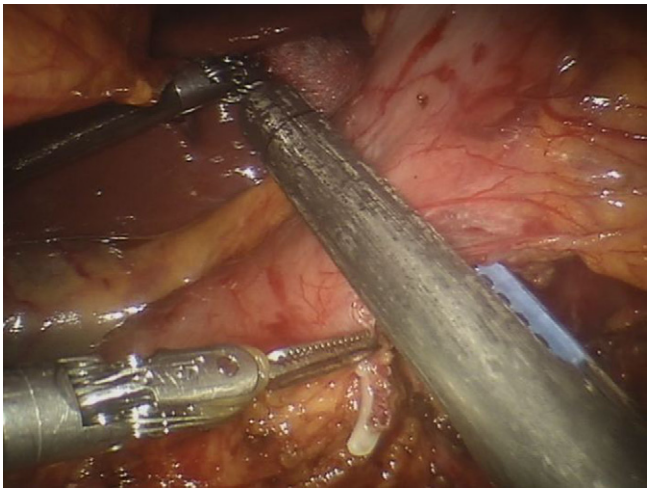

Fig. 4. Duodenal section with mechanical stapler.

Median operative time was 240 min (range 210–300 min).

There was no postoperative morbidity (such as bleeding or leaks) nor mortality and none patient experienced anastomotic stricture. Mean hospital stay (from surgical intervention to discharge) was 4.2 days (range 3–5 days). Median follow-up was 13.5 months (range 12–15 months) with a disease-free survival rate of 100%.

4. Discussion

Stomach is the most common site of GIST localization (65%) with an intraluminal or exophytic pattern of growth toward the lumen or the peritoneum with different biological behavior for aggressiveness, recurrence and tendency to metastasize.[15]

Lymph node involvement is very rare and lymphectomy is not necessary.[16] Recurrence is instead more frequent and is mostly peritoneal where tumor surface is directly in contact with coelomic cavity rather than in the thickness of visceral wall at the resection margin.[17]

Tumor pseudo-capsule displaces surrounding structures rather than infiltrate them and often presents clivage plane, but it is easily friable with peritoneal colonization that can be spontaneous or caused by surgical manipulation.[18]

Studies that investigated the relation between histologic positivity of resection margin and frequency of recurrence did not give univocal results, demonstrating absence of correlation in some cases,[19] while in others there was a negative effect on survival[20,21] but incomplete macroscopic removal of neoplastic tissue, as for example during palliative intervention for obstruction or bleeding that determined reduction in survival.[22]

Surgical resection of localized gastric GISTs in absence of distant metastasis is the treatment of choice.[23] Besides, these tumors seldom develop loco-regional recurrence, which supports the practice of limited gastric resection with a 1- to 2-cm margin necessary for an adequate radicality[24] and authors agree that surgical purpose has to be complete resection with negative margins without routine lymphadenectomy.[25] For this reason wedge resection is indicated for the majority of gastric GISTs.[26,27] Anyway tumor size and location may dictate a more extensive surgery, including partial or total gastrectomy, as in our enrolled patients.[2] Laparoscopy is indicated as a safe and valid method from an oncological point of view,[28–30] however current guidelines[8] suggest that mininvasive approach should be reserved to tumor <2 cm. This recommendation derives from the impossibility of having a direct manipulation of lesion with the risk of rupture and dissemination that would represent a catastrophic consequence in terms of recurrence and survival of the patient.[23,31] In our series, mean tumor size was >2 cm (5 cm) but none patient underwent lacerations

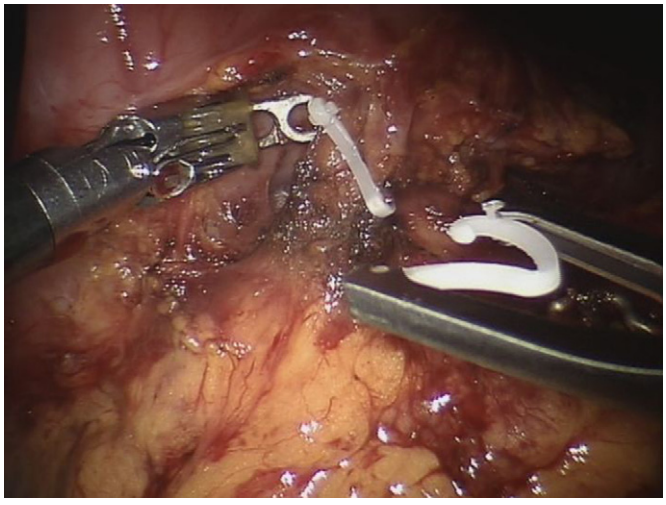

Fig. 3. Section with emolock clips of right gastroepiploic vessels.

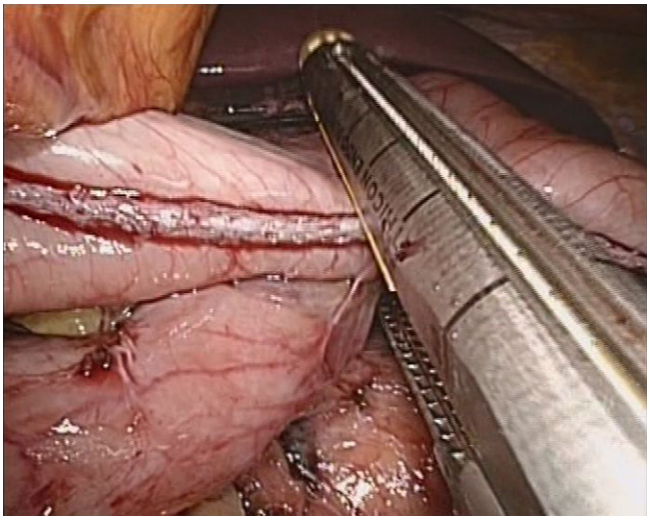

Fig. 5. Gastric resection in the distal 2/3 of the stomach.

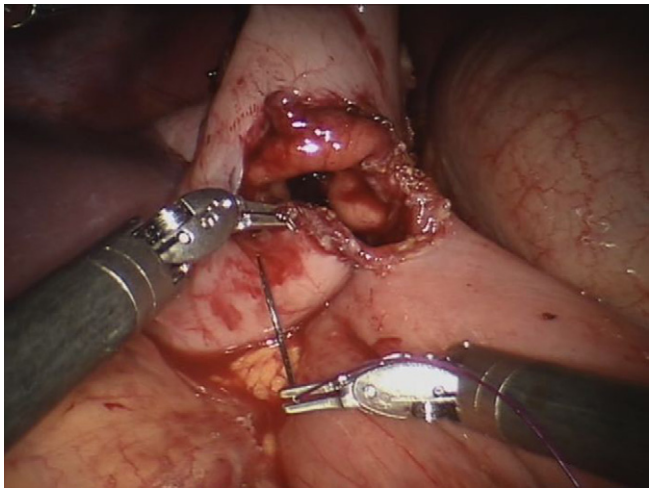

Fig. 6. View of the side-to-side gastro-jejunal anastomosis.

or tumor ruptures, however this situation is related to surgeon's experience and adequate used instruments. In fact, different studies report feasibility and safety of mininvasive techniques for lager GISTs, both laparoscopy[6,32,33] and robotics.[34]

In our experience, the correct identification of tumor localization was considered more important than tumor dimension in order to decide which would be the more adequate surgical approach and type of resection to be performed.

Laparoscopic surgery is now widely recognized and used as a mini invasive approach to many procedures, because it offers a variety of benefits when compared to open surgery.[35] These include less pain, faster postoperative recovery times, reduced morbidity and fewer complications.[36] Laparoscopic gastrectomy has been adopted in many centers, but has proved a complex procedure that introduces obstacles associated with the limited movement of instruments and the amplification of hand tremors and two-dimensional vision. Robotic gastric surgery was introduced to overcome these problems.[37] The majority of studies on the use of this technique are case series that have been limited through the small sample size and the insufficient data on the oncological outcomes that nevertheless highlight the practicality of using the robotic procedure.[38–40] There are however no studies to assess the advantages when compared with classic laparoscopic procedures.

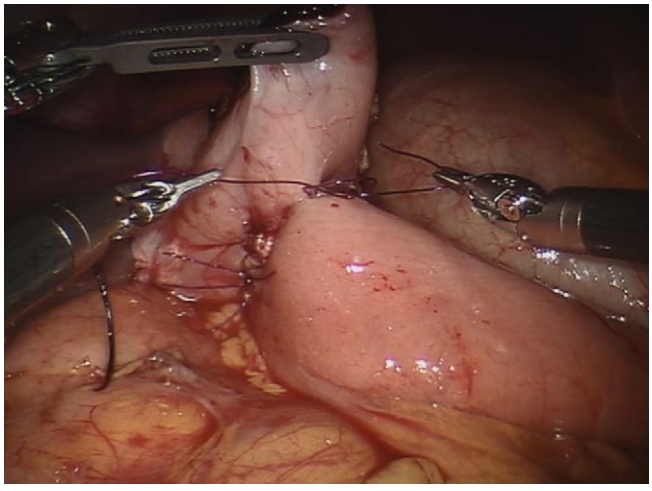

Fig. 7. Robotic suture of the aperture.

To date there are no RCTs and only three comparative studies[41–43] have been conducted on robotic oncological gastric surgery.

The published findings do not demonstrate any differences between the two treatment groups with regard to perioperative complications, conversion rates and postoperative stay. The three studies do however highlight that intraoperative blood loss was significantly less in the robotic group compared to the laparoscopic, a difference that is attributable to a clearer view of the operating area and the magnification of the image. However, the studies that have been analyzed are limited in as much as they do not provide data concerning long-term follow-up and this makes it necessary to produce new evidence and randomized trials.

Actually it's very difficult to try to determine whether there is any difference between robotic and laparoscopic gastrectomy for malignant disease. The fact that only three trials are suitable for comparative considerations shows the lack of data generally available.

The bibliographic research on surgical treatment of gastric GIST showed that several authors described laparoscopy,[6,28,29,44–47] while only one study reported cases treated with robotic system with adequate description of used technique.[34]

The current study is a case series of 5 patients who underwent robotic gastric resection.

Our personal experience evidences usefulness of robotic system to improve dexterity of a surgeon during complex mini-invasive procedures and to facilitate traditional laparoscopic approach.

Mini-invasive gastric surgery is considered not doable and risky for large and pre-pyloric GISTs because of the anatomic positioning, fragility of the tumor capsule and difficulties to perform laparoscopic sutures.[8]

We have shown that tridimensional image magnification and precise robotic arm movements with tremor filtering could help gastric resection for GISTs without intra-abdominal dissemination and margin-free specimen.

The unfavorable factor reported in several studies[48] is the increased operative time than laparoscopic approach caused by the placed and doked of the system's patient cart and the robot setup. However, in our series the mean operative time was 240 min, favorably if compared with data reported in literature for laparoscopic resection.[49–51]

Also, in our series we have observed no significant intraoperative blood loss (mean of 96 ml) and no need for transfusion, there were not major intraoperative complications or perioperative morbidity.

The advantages associated with the use of a robotic minimally invasive technique mainly concerned a hospital stay particularly short and regular: in first postoperative day all the patients started oral liquid intake and median referred Visual Analog Scale (VAS) score for pain[52] was 3. The mean hospital stay was 4.2 days and physical examination at discharge showed not painful, palpable abdomen, normal bowel functioning and hematological laboratory values. No complications were reported in all patients both perioperatively and at follow-up, a quick return to daily activities was demonstrated by the Short Form-12 (SF-12) assessment scale.[53] In particular this questionnaire was submitted one-month to surgical intervention. All patients answer not limitations in moderate activities or problems with work and other regular daily activities as a result of their physical health.

Furthermore, the goal of oncological radicality was reached with tumor-free margins (R0) and no recurrence in the short-term observation period.

Even if comparative studies are necessary to demonstrate real advantages of robotic approach with respect to classic laparoscopy, Da Vinci Surgical System allows large tridimensional field of view, a steady traction, tremor suppression, flexibility of the instruments and offers improved dexterity with an internal articulated

EndoWrist (Intuitive Surgical Inc., Sunnyvale, CA, USA) that allows seven degrees of freedom and therefore execution of precise and safe dissection of tissue and sutures.[38]

We think that minimally invasive surgery for large gastric GIST appear now more viable and safe in selected patients through the increasing experience of dedicated laparoscopy surgeons with development of the concept of "team approach" and technological improvements.[54] New guidelines and discussions we seem necessary.

Even if this study was not specifically realized to compare different surgical approaches, nevertheless it demonstrates the feasibility and efficacy of surgical robotic treatment. We believe further evidences are needed as well as comparative studies in order to clarify the effective role of different surgical strategies in the treatment of gastric GIST.

5. Conclusions

The NCCN Clinical Practice Guidelines for Optimal Management of Patients with GIST[8] suggests that laparoscopic techniques should be limited to tumors less than 2 cm, but some authors have reported successful and safe removal of larger GISTs.[6,28,33] So if laparoscopy appears very appealing, the main problem using the classical laparoscopic approach is inadequate resection margins or tumor spillage that can results in catastrophic consequences with disease progression, recurrence, and poor survival. Advantages of "Da Vinci" Surgical system are the dexterity of the Endowrist, that could extend the feasibility of a minimally invasive approach to patients requiring advanced suturing, precise tissue dissection and tridimensional visualization of the operative field. We suggest that both these characteristics allow overcoming lack of tactile feedback that is considered fundamental for GIST treatment.

However, the literature contains no evidences on the correct management of large GISTs and in particular on the validity and role of the minimally invasive surgery.

We studied the feasibility of the robotic procedure to provide a mean for the design of future studies that could evaluate benefits of this approach versus open and laparoscopic surgery.

The present series demonstrates that robotic resection for gastric GIST can be safely adopted not only for its advantages of minimally invasive surgical technique but also because it was associated with a favorable perioperative outcome without compromising oncologic safety and with encouraging results in terms of earlier return of bowel function, earlier resumption of diet, decreased duration of the use of analgesia and shorter postoperative hospitalization.

Ethical approval

Ethical Approval was given by the University of Perugia.

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None.

Author contribution

All authors contributed equally to this work, read and approved the final manuscript.

Conflicts of interest

None.

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