

Application of laparoscopy in the diagnosis and treatment of gastric cancer

Ziyu Li, Jiafu Ji

Department of Gastrointestinal Surgery, Peking University Cancer Hospital & Institute, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Beijing 100142, China

Correspondence to: Ziyu Li. Department of Gastrointestinal Surgery, Peking University Cancer Hospital & Institute, Key laboratory of Carcinogenesis and Translational Research (Ministry of Education), Beijing 100142, China. Email: ligregory@outlook.com.

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Introduction

The advantages and feasibility of laparoscopic surgeries have been widely recognized in recent years. In China, most gastric cancer cases are already in their advanced stages. Thus, the rational application and promotion of laparoscopic surgeries have become one of the priorities in the management of gastric cancer. First, the roles of laparoscopy in the diagnosis and efficacy evaluation of gastric cancer have not been fully recognized. While laparoscopic surgeries have been the standard treatment for the early gastric cancer, surgeons must have a solid knowledge of the indications of endoscopic and laparoscopic surgeries for the early gastric cancer and strictly obey them, so as to avoid excessive treatment. For patients with advanced gastric cancer, the laparoscopic surgeries still lack convincing evidences and require further validation in clinical trials. Currently, many studies on the laparoscopic surgeries for gastric cancer have been conducted in China; however, relevant training, access, and monitoring mechanisms still have not been established or applied. While the patients' rights and interests should always be prioritized, the learning curves of laparoscopic surgeries as well as the indications of these surgeries for advanced gastric cancer are still problematic. Based on my personal training and experiences, I would like to share my understandings about the rational application of laparoscopy in the diagnosis and treatment of gastric cancer.

Diagnosis

In fact, the role of laparoscopy in diagnosing gastric cancer has not been fully recognized in China, which is mainly

because this technique is still relatively new in our country. In addition, along with the rapid economic development in China, the standardized management of clinical conditions has become an important task. Nowadays more Chinese hospitals have become qualified to carry out laparoscopic surgeries; however, the diagnostic role of laparoscope is often neglected. Both the United States NCCN Clinical Practice Guidelines on gastric cancer and the Japanese Gastric Cancer Treatment Guidelines recommend that patients with clinically diagnosed advanced gastric cancer should routinely receive diagnostic laparoscopy; in addition, intraperitoneal free cancer cells should also be detected to further confirm the etiology and rule out any potential peritoneal metastasis.

Up to now, no other imaging method has been available for detecting the peritoneal metastases of gastric cancer. It has been reported that the positive rate of diagnostic laparoscopy in detecting the metastasis was around 20% (1); it may be higher when used for detecting the cT4 or Borrmann type IV gastric cancer (2). Such a diagnostic value can not be neglected. Since the treatment of gastric cancer is still based on staging, improper diagnosis will directly affect the treatment option and prognosis, not to mention its role in ensuring the success of relevant clinical trials. However, although the diagnostic value of laparoscopy has been included in the relevant guidelines, its specific applications and indications remain controversial.

Under the leadership and supervision of Dr. Jiafu Ji, our center has listed the diagnostic laparoscopy as a routine examination item. Patients who have been diagnosed with locally advanced gastric cancer by endoscopy, endoscopic ultrasonography, and computed tomography (CT) must be

further examined by laparoscopy before receiving treatment (surgery or pre-operative radiotherapy/chemotherapy). Some problems may exist before the initiation of this examination. At times, the patients may not understand its value, and the other departments may be reluctant to cooperate. However, since this examination does benefit the patients, its value will ultimately be recognized and accepted after a certain period of hard work.

Another problem is the lack of standardized detection method and uniform indications. Therefore, based on the foreign and domestic literature and the practices in our center, we developed the Standard Operation Procedures of Diagnostic Laparoscopy (see the Appendix), with the indications mainly targeting at the clinically diagnosed locally advanced gastric cancer (cT2-4NanyM0). Few literature has published on this regard, which may due to the relatively low prevalence of gastric cancer in Western countries and the high proportion of early gastric cancer in Japan and Korea. In China, more than half of the gastric cancer patients are in the advanced stage, which makes the research on this aspect particularly important. Dr. Ji has lead relevant multicenter study in Beijing, with an attempt to further verify the clinical values and indications of diagnostic laparoscopy. While the laparoscopy has an irreplaceable value in diagnosing the advanced gastric cancer, it also exerts a unique role in evaluating the treatment efficacy. Currently the role of neo-adjuvant therapy in treating the advanced gastric cancer has been well recognized. However, so satisfactory method or standards has been available for evaluating its efficacy. Laparoscopic inspection naturally can be a useful supplement to the imaging modes in clinical efficacy evaluation.

Treatment

The laparoscopic surgery was initially applied for early gastric cancer, and adequate evidences have been accumulated in studies on the early gastric cancer (3-5), making it one of the standard treatment options for the early gastric cancer. Along with the maturation of the laparoscopic D2 radical gastrectomy for gastric cancer, the application of laparoscopic techniques for advanced gastric cancer has increasingly been accepted (6-12). The learning curve is particularly important during the adoption of the laparoscopic surgery for gastric cancer. In this stage, selection of patients with early gastric cancer is as important as the patients' body weight and tumor location. When trying to grasp this technique, the doctors should

never forget the essential principle of tumor treatment, i.e., maintaining the patients' interests and following the requirements of medical ethics (13-17). Currently, many treatment options have been available for the early gastric cancer. The absolute indications of endoscopic treatment has been clearly described for the early gastric cancer, and quite a few clinical trials have explored the extended indications of endoscopic treatment for the early gastric cancer (18-23). For surgeons who are interested in carrying out laparoscopic surgery for gastric cancer, a solid knowledge of the indications of this procedure for early gastric cancer should be grasped and followed, so as to avoid the loss of a more minimally invasive treatment under the endoscope. For patients with the tumor localized within the mucous layer (T1a) and with good differentiation, endoscopic treatment should be preferred if condition allows. A surgery just for the purpose of performing laparoscopic surgery should be avoided.

In 2006, I began to receive training on laparoscopic techniques under the supervision of Dr. Ji. Since then I was able to carry out laparoscopic D2 radical gastrectomy for gastric cancer. In the first year, I was privileged to be trained a number of workshops on laparoscopic techniques, and meanwhile I also read many relevant training materials. The pioneers in this field included Dr. Peiwu Yu, Dr. Chengzhu Zheng, and Dr. Guoxin Li. Their lectures were always very interesting and informative. Furthermore, although the experimental animal resources were limited, they were more useful than the simulation test for me. In 2007, after I had successfully performed endoscopic surgeries for two cases of colorectal cancer, thanks to the supports of Dr. Ji and my colleagues, I successfully conducted my first laparoscopy-assisted distal gastrectomy in a female patient with early gastric cancer. In the coming years, I always followed the principle of performing endoscopic gastric surgery in patients with early gastric cancer only. The learning curve was relatively long due to the limitation in patient selection. Luckily, we also carried out laparoscopic colorectal surgeries, which helped our team to be more familiar with the endoscopic techniques. In 2009, we began to participate in the clinical trial (CLASS-01) led by Dr. Guoxin Li, during which I had passed my personal learning curve period and began to perform laparoscopic surgeries for advanced gastric cancer. With more cases treated, my faith and doubt on laparoscopic surgeries also increase. Like many other colleagues, I always have new feelings and insights after performing every dozens of laparoscopic surgeries. Before 2013, like many other operators in China,

I preferred to stand at the left side of the patient. In recent years, however, I am no longer tangled on the position; rather, I would like to timely change my position based on the anatomy and body shape. For me, changing the position can be a good way to relax my physical and mental statuses. A comfortable position favors the smooth operation. Initially, we also insisted that the digestive tract reconstruction after the endoscopic surgery must be conducted via the auxiliary incision; we believed it would be safer and meanwhile the specimens needed to be harvested through the small incision. However, we gradually recognize the advantages of total laparoscopic reconstruction, particularly for patients with large body weight.

The development of new surgical instruments and sutures also has made the laparoscopic anastomosis more convenient. Along with the maturation of our operation team, the digestive tract reconstruction in our center is mainly completed under laparoscopy, which is believed to be simpler and safer.

The current epidemiology of gastric cancer is quite different from those in Japan and Korea. In particular, the proportion of early gastric cancer is relatively lower in China. Therefore, the laparoscopic surgeries in China must have certain Chinese characteristics. The laparoscopic surgeries for the advanced gastric cancer is a hot topic in the clinical research on gastric surgeries. The corresponding phase III multi-center randomized controlled trials (RCTs) have been conducted in China, Japan, and Korea (24-26). Before adequate evidences have been obtained from evidence-based medicine, the corresponding work must be done in clinical trials. Patients with advanced gastric cancer are the main populations receiving surgical treatment in the departments of gastric surgery in China. The proportion is even higher than 50%. The rationality of the treatment will directly affect the prognosis of the whole patient population (27). After years of controversy in this regard, the D2 radical surgery has gradually been recognized as the standard surgery for the advanced gastric cancer. However, the D2 has relatively high technical requirements (19,28,29), and the laparoscopic surgeries were also introduced during this period. Based on its natural advantages in surgical communications (the collection and dissemination of surgical video), the minimally invasive laparoscopic surgeries rapidly attract much attention. Under the laparoscopy, the enlarged surgical field is much clearer, which is more feasible for lymph node dissection and many other fine surgical operations. This challenges the traditional ideas of surgeons, in particular those who

are specialists in tumor management: the efficacies of treatments for the advanced gastric cancer are low, and the studies on the perioperative treatment are always changing the traditional surgical treatment modes. Laparoscopic gastric surgery has been introduced in China for 10 years. Its technical features/advantages are quite impressive for both doctors and patients. An increasing number of hospitals in China have embraced this technique. Recent studies have indicated that the laparoscopic D2 lymphadenectomy for advanced gastric cancer showed no significant difference with the open surgeries in terms of the completeness of tumor resection, tumor resection margin, and amount of the dissected lymph nodes. It can achieve radical resection and has impressive advantage for its minimal invasiveness after the surgery (30-35).

According to the Chinese Guidelines on the Laparoscopic Surgery for Gastric Cancer, in gastric cancer patients with massive serosal layer invasion, or with tumors sized larger than 10 cm, or with lymph node metastatic site fusing or surrounding major blood vessels, and/or with tumors excessively infiltrating the surrounding tissues, the laparoscopic surgery can be challenging (36). The contraindications of laparoscopic surgery for gastric cancer include: (I) the lymph node metastatic sites fuses and surrounds the major blood vessels; (II) the tumor extensively invades the surrounding tissues/organs; (III) the patient can not tolerate long-term pneumoperitoneum due to conditions such as severe heart and lung diseases or severe infections. The relative contraindications of the laparoscopic techniques included pathological obesity and extensive abdominal adhesions. These guidelines were developed by surgeons with rich experiences in laparoscopic surgery for gastric cancer, the indications of the laparoscopic surgeries showed no significant differences with the open surgeries, which also indicates their joint expectations for the application of laparoscopic surgeries in treating gastric cancer.

The indications of the laparoscopic surgeries for advanced gastric cancer are based on the comparison with the open surgeries. Analysis on the technical features of these two different surgical modes may yield good findings. Factors such as body mass index and teamwork may affect the learning curves, but will not fundamentally affect the surgical indications. The latter mainly depends on the “consistency” between the tumor itself and the technical features. Compared with the open surgeries, the laparoscopic surgeries are performed using two-dimensional and indirect visual field. However, its zoom-in effect makes it become inferior to the open surgeries.

Also, the operator and the assistant can share the clearly magnified surgical field, which can not only promote the teamwork during the surgery and also facilitate the teaching process. The tactile sensation is a major aspect that makes the laparoscopic surgeries different from or weaker than the open surgeries. An accurate tactile sensation not only facilitates the division operations but also is beneficial for the protection of tumors. For surgeries during which the tactile sensation is particularly important, the laparoscopic surgeries will be difficult. Although such condition are only seen in a limited number of patients, sufficient attention should be paid. It is reasonable that some foreign and domestic authors remain cautious about the application of laparoscopic surgeries for advanced gastric cancer with serous membrane invasion (T4a). Good exposure of the surgical field is important for the success of laparoscopic or open surgeries. If the tumor is relatively large or involves the serous membrane, the operator and the assistant has to take special care when holding or pulling the tissues/organs, which may affect the efficacy of exposure and thus make the surgery more difficult. This may be a bit different in obese patients, in whom the exposure of the surgical field may also be difficult, and it may take longer time to search for the proper layers due to the impact of excess adipose tissues. In these patients, there may be more exudates in the surgical field, which, however, will not affect the safety of the surgery for tumors. Nevertheless, the impacts of the repeated stimulations on the tumor by surgical instruments such as grasping forceps warrant further investigation in well-designed clinical trials. Thus, some surgeons, both in China and abroad, still only apply the laparoscopic surgeries in treating gastric cancer with an invasion depth within T2.

When the clinical trials on the laparoscopic surgeries for the early gastric cancer were on the way in some advanced countries, the laparoscopic surgeries were still newly introduced in China. In addition, the proportion of early gastric cancer remains low in China. Therefore, no large Chinese RCT has explored the role of laparoscopic surgeries in treating the early gastric cancer. Fortunately, a multi-center RCT on the laparoscopic surgeries for the advanced gastric cancer has been conducted in China, which may provide evidences for the development of more tailored clinical guidelines. This study was initiated by the Chinese Laparoscopic Gastrointestinal Surgery Study (CLASS) group, which recently has published a multi-center retrospective analysis (37). This article analyzed the data of 1,184 patients who had undergone laparoscopic-assisted surgery from 2003 to 2009 and found that the 3-year

overall survival (OS) and disease-free survival (DFS) were 75.3% and 69.0%, respectively; more specifically, the OS and DFS were 89.7% and 88.9% in stage I patients, 85% and 77% in stage II patients, and 60% and 59.3% in stage III patients. The analysis indicated that the laparoscopic-assisted surgery has satisfactory short-term efficacy for the locally advanced gastric cancer. However, it also found that a tumor size of larger than 40 mm and a later stage were the independent risk factors for the relapse and survival, as demonstrated in other studies (38). Therefore, for patients with phase T4 gastric cancer, the potential effect of tumor size on the laparoscopic surgery can not be neglected. When actively conducting the laparoscopic surgeries, it is also important to discover new surgical indications, so as to promote the smooth development of this work.

Nevertheless, the laparoscopic surgery has been well explored, and its advantages and feasibility has been widely recognized. In China, most gastric cancer cases are already in their advanced stages. Thus, the rational application and promotion of laparoscopic surgeries have become one of the priorities in the management of gastric cancer. While laparoscopic surgeries have been the standard treatment for the early gastric cancer, surgeons must have a solid knowledge of the indications of endoscopic and laparoscopic surgeries for the early gastric cancer and strictly obey them, so as to avoid excessive treatment and miss the chance for more minimally invasive treatment. For patients with advanced gastric cancer, the laparoscopic surgeries still require further validation in clinical trials. Currently, many studies on the laparoscopic surgeries for gastric cancer have been conducted in China; however, relevant training, access, and monitoring mechanisms still have not been established or applied. The learning curves of laparoscopic surgeries for advanced gastric cancer are still problematic. If the patients during the learning curve period are only those with early gastric cancer, the low proportion of early gastric cancer in China will make the learning curve unnecessarily long, which may hamper the application and promotion of laparoscopic surgeries. For patients with advanced gastric cancer, in addition to the patient's body weight and the tumor location, tumors with smaller size (<40 mm) and/or without serous membrane invasion should be selected; of course, which should also be further verified in clinical trials. The patients' interests should always be a priority. In the clinical settings, it is particularly important to carefully select the proper patients and follow the principles of the radical treatment of malignancies, so as to ensure the laparoscopic surgeries for gastric cancer, with an advantage

of “minimally invasive”, can achieve the comparative long-term efficacy with the open surgeries. Of course, further determination of the indications of the laparoscopic surgeries for gastric cancer remains an urgent task.

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Department of Gastrointestinal Surgery, Beijing Cancer Hospital

Technical Guidance on the Diagnostic Laparoscopy for Gastric Cancer

1st Edition

Indications and contraindications

Indications

- (I) Pre-treatment diagnosis of locally advanced gastric cancer (cT2-4NanyM0);
- (II) Detection of the suspected peritoneal metastasis of gastric cancer;
- (III) Efficacy evaluation after the pre-operative chemotherapy/radiotherapy for locally advanced gastric cancer;
- (IV) Efficacy evaluation after the converted treatment (radiotherapy/chemotherapy/intraperitoneal chemotherapy).

Contraindications

- (I) With a previous history of surgery, or, with suspected severe abdominal adhesions that make the patient can not tolerate a laparoscopic surgery;
- (II) With cardiopulmonary insufficiency that make the patient can not tolerate anesthesia or surgery.

Surgical procedures

Patient position

The patient is typically on a supine position, and the operating table can be adjusted during the surgery.

Establishment of pneumoperitoneum:

- (I) Puncturing with the veress needle; and
 - (II) Open method.
- The abdominal pressure is maintained at 10-12 cmH₂O.

Placement of trocar

Typically one camera port and two operation ports (left and right) were created. One or two operation ports may be

added if needed.

- (I) Camera port (10-12 mm trocar): a camera port was usually made under the umbilicus. In patients with a previous history of abdominal surgery, other sites may be chosen.
- (II) Right operation port (10-12 mm trocar): this port is often made 2 cm below the intersection between the right anterior axillary line and the right costal arch. Left operation port (5-10 mm trocar): This port is symmetrical to the right operation port.
- (III) The second operation port at the right side (5-10 mm trocar): it is typically located at the right anterior axillary line and is about one fist away from the first operation port at the right side.

Detection of free peritoneal cancer cells

To avoid the inflammatory cell aggregation due to peritoneal inspection and biopsy and the contamination of the ascites or peritoneal lavage fluid due to epithelial cell shedding, the ascites or peritoneal lavage fluid should be collected immediately after the creation of operation ports.

- (I) In patients with sufficient ascites, cytology may be performed after collecting ascites from the pouch of Douglas (39-41).
- (II) In patients without ascites or the volume of ascites is less than 200 mL, peritoneal lavage may be performed using 250 mL of warm normal saline in the following sequence: bilateral diaphragm, subhepatic region, greater omentum, bilateral paracolic sulcus, and pouch of Douglas.

The body position may be adjusted to Trendelenburg position or reverse Trendelenburg position. Direct rinsing of the primary tumor site should be avoided if possible. No less than 100 mL of lavage fluid should be collected from the bilateral subdiaphragmatic region, subhepatic region, and pouch of Douglas for cytological examination (42-44).

Abdominal inspection

- (I) The inspection begins from the right upper quadrant and then is performed in the clockwise direction. The following structures are then inspected in sequence: right diaphragm, right hepatic lobe, hepatic round ligament, left diaphragm, left hepatic lobe (the hepatogastric ligament may be dissected to expose the caudate lobe of liver), left parietal peritoneum, and descending colon. The pelvic cavity and pouch of Douglas can be inspected at the Trendelenburg position. For females, the bilateral ovary, right parietal peritoneum, ascending colon, and greater omentum should be inspected; meanwhile, the greater omentum and transverse colon should be lifted to inspect the transverse colon and colonic mesentery, and the anterior abdominal wall is inspected by inserting the camera from the right operation port. Then back to the camera port, and the primary tumor site and the perigastric lymph nodes are inspected. For tumors located at the posterior gastric wall, the gastrocolic ligament is dissected to inspect the lesser omental bursa, including the transverse mesocolon and dorsal pancreatic membranes. Biopsy should be performed for the suspected intra-abdominal lesions.
- (II) The location, size, invasion of the serous membrane, and invasion of the surrounding organs of the tumor are recorded. Peritoneal metastasis is assessed using the Peritoneal Cancer Index (PCI) score.
- (III) All the laparoscopic inspection is videotaped.

The incision is closed

Incisions larger than 10 mm should be closed under direct vision, so as to avoid damaging the abdominal viscera.

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