



Review

Current status of surgical treatment of gastric cancer in the era of minimally invasive surgery in China: Opportunity and challenge



En-Hao Zhao, Tian-long Ling, Hui Cao*

Department of Gastrointestinal Surgery, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, 200127, Shanghai, China

HIGHLIGHTS

- MIS is now regarded as an accepted treatment for gastric cancer in China.
- Ongoing multicenter prospective studies aim to expand the indications of MIS for the treatment of gastric cancer.
- Improvement of techniques in laparoscopic gastrectomy has been developed in China.

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ABSTRACT

Gastric cancer is one of the most common cancers in China. In the past decade, with the developments in surgical instruments and technologies, minimally invasive surgery has rapidly become an accepted treatment for gastric cancer in China. Many Chinese surgeons and researchers have contributed to the rapid evolution of minimally invasive surgery for gastric cancer. Their efforts have transformed into unique laparoscopic technique, workshops, academic communications, education and international communications in China. Meanwhile, many retrospective comparative trials and randomized controlled trials have revealed the advantages in minimally invasive surgery for gastric cancer. However, multicenter randomized controlled trials are still needed to delineate significantly quantifiable differences between laparoscopic and open gastrectomy. With more and more experience has accumulated, laparoscopic gastrectomy has been performed on older and overweight patients. Moreover, advanced minimally invasive techniques, such as modified laparoscopic spleen-preserving splenic hilum lymphadenectomy, various laparoscopic gastric reconstruction methods and robotic gastrectomy have been developed. It seems that China owns the potential to keep up with her neighbor, Japan and Korea, to become one of leading countries utilizing minimally invasive surgery for gastric cancer.

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1. Introduction

Gastric cancer (GC) was newly diagnosed in 925,000 people worldwide in 2012, accounting for 6.8% of new cancers. It was the fifth leading cancer, following lung, breast, colorectal and prostate cancer. In addition, it was the third leading cause of cancer deaths worldwide, with approximately 723,000 deaths reported in 2012 according to GLOBCAN. Surgical resection with regional lymph node resection is the only curative therapeutic modality for patients with GC. However, the conventional laparotomy is sometimes associated with considerable morbidity, mortality, and impact on patient quality of life after surgery [1].

Minimally invasive surgery (MIS) for GC was developed in Japan. Kitano performed the first case of laparoscopy gastrectomy (LG) in 1991 [2]. In 1999, Uyama et al. [3] reported the first laparoscopy-assisted total gastrectomy (LATG) with distal pancreateosplenectomy for advanced gastric cancer (AGC). Since then, LG has become increasingly common in East Asia owing to the support of the instrument manufacturers, foundation of the technical authorization system, and activity of study groups that established the standard procedure and verified its technical and oncological feasibility. The latest Japanese GC treatment guideline (May 2014) defines laparoscopy-assisted distal gastrectomy (LADG) as an alternative procedure for cStage I GC.

China has the largest number of GC patients in the world, but more than 80% of patients are diagnosed with AGC. In the meantime, there is a lack of large-scale data regarding the outcomes for

* Corresponding author. Tel.: +86 21 68383731; fax: +86 21 58394262.
 E-mail address: caohuishcn@hotmail.com (H. Cao).

these patients, so the use of MIS for the treatment of AGC is still a contentious issue. This current status quo gives Chinese surgeons not only big challenges, but also numerous opportunities.

Today, because of surgical instrument innovations and technological advancements, several aspects of GC treatment are now shifting to a new era. These new MIS techniques for GC include modified laparoscopic spleen-preserving splenic hilum lymphadenectomy (LSPL), various laparoscopic gastric reconstruction methods and robotic surgery, which are all the achievements specifically developed in China.

2. History and development

In mainland China, the first case of laparoscopic subtotal gastrectomy for benign diseases was reported in 1993 in Shanghai [4], which was 2 years after Kitano of Japan performed first ever LG for GC. While this technique developed slowly over the following decade, most centers started LG after 2003. Chen et al. [4] looked into 447 papers on laparoscopic techniques treating gastric diseases recorded in China national knowledge infrastructure from January 1991 to January 2009 of which 65.5% (293/447) of the papers were published between 2003 and 2008. But this technique was still low in public recognition as compared to that in Japan and Korea. Due to the low proportion of early gastric cancer (EGC) in China, most Chinese surgeons could only begin to perform LG with D2 lymphadenectomy on patients with locally AGC. Furthermore, the unbalanced levels of regional economy and medical services across different areas in China were another reason for the slow development of MIS in GC. Patients needed to pay more for laparoscopic surgery because the instruments used in LG were not covered by the public medical insurance. So LG appeared to be accepted much better in cities along the eastern Chinese coastline which were more affluent than the inland areas. Recent years have witnessed the improvement of national economy and reform of public medical insurance, which in turn facilitated the popularization of LG in China.

In the initial phase, the published works mainly focused on case reports. However, few researches showed any signs of MIS burgeoning in China. Wang et al. [5] and Huang et al. [6] reported limited cases, less than 100, of GC treated with LG from March 2004 to May 2005 and from January 2007 to June 2008 respectively. Compared with open surgery, LG showed better short-term surgical outcomes such as less blood loss, less analgesic injections, faster recovery but longer operation time. The number of retrieved lymph nodes and the mean tumor margin in LG were also similar with those in the open surgery.

With the development of laparoscopic skills and instruments, more and more Chinese surgeons practiced LG, especially in large medical centers. As a result, studies involving large numbers of GC patients gradually become the mainstream of the phase. Among these, Chinese surgeons achieved promising short-term surgical outcome. Du et al. [7] reported their initial experience in 2009, where no significant differences were found between laparoscopic and open gastrectomy in terms of operation time. In 78 patients with AGC who underwent LG, there was no conversion to open surgery. Tang et al. [8] analyzed the intraoperative and postoperative complications of LG. The overall operative morbidity and mortality rates were 11.9% and 0.7% among 302 patients who underwent LG. Cui et al. [9] evaluated 131 patients who underwent LG with D2 lymphadenectomy and 78 patients who received open surgery, and no significant differences were found in surgical morbidity between the two groups. Mortality was zero in both groups. These results were quite similar to those in the meta-analysis of Japanese and Korean randomized controlled trials, of which the pooled complication and mortality rates were 9.9% and

0.9% [10].

Later, more and more reports began to focus on the long-term surgical outcomes of laparoscopic gastrectomy for gastric cancer. A retrospective study by Wang et al. [11] was performed to compare the outcomes of 54 patients who underwent LADG with another 54 patients who underwent open distal gastrectomy between October 2004 and October 2007. The pathologic stages between two groups were the same in which 55.6% (30/54) of the cases were in stage I. The follow-up duration was sufficient as the median follow-up duration was 60 months. The 1-, 3-, and 5-year disease-free survival and overall survival rates were statistically insignificant between two groups. Fang et al. [12] reported 87 consecutive AGC patients who underwent LG with D2 lymphadenectomy, compared with 87 AGC patients who had open gastrectomy during the same period. The 5-year cumulative overall survival rate in LG group was 59%, compared to 54% in the open group. This 5-year case-control study indicated that LG can provide an acceptable prognosis and may be applicable for AGC treatment. But the apparent downside of these studies was the relatively small sample size.

At present, surgeons in most medical centers of China have accumulated large number of cases and much clinical experience with LG, such as those in Beijing, Shanghai, Guangzhou, Fuzhou and Chongqing. Although there was still a huge difference between the amount of reported and actual cases in big medical centers, Chinese surgeons have already realized this problem and are trying to resolve this lack of high quality clinical studies. Recently, Lin et al. [13] reported the largest scale case-control study in mainland China till now. The study was comprised of 3580 patients who were treated with curative intent either by LG (2041 patients) or open gastrectomy (1539 patients) between January 2005 and October 2013. Regarding to perioperative characteristics, the operation time, time to first flatus and time to resumption of diet were similar between the two groups, whereas the blood loss, blood transfusion, time to ground activities, and postoperative hospital stay were significantly less in LG than in open gastrectomy. There was no statistically significant difference in postoperative morbidity (13.6% vs. 14.4%, $P = 0.526$) and mortality (0.3% vs. 0.2%, $P = 0.740$). No significant difference in the number of lymph nodes dissected was observed between these two groups. The 3-year disease-free and overall survival rates between the two groups were statistically insignificant. According to the UICC TNM classification of gastric cancer, the 3-year disease-free and overall survival rates were not statistically different at each stage. This large retrospective study will provide good data and basis to conduct a large randomized clinical trial in the future.

3. Prospective clinical trials in China and class group

LG for GC has become popular due to many advantages of MIS and innovation in surgical techniques. The results of several randomized controlled trials (RCT) in Japan and Korea have revealed the feasibility and safety of LG for EGC [14–16]. The recurrence and overall survival for EGC are also similar with those after open surgery [17]. To date, LADG has been the widely accepted modality for EGC in Japan and Korea. These RCTs have become powerful and strong evidence to support the development and promotion of this technique. With the international exchanges in nearly a decade, Chinese surgeons and researchers also realized the importance of RCTs. Recently there are several RCTs enrolling in China. A single-center study on laparoscopic distal subtotal gastrectomy for AGC was launched by Hongbo Wei from the Third Affiliated Hospital of Sun Yat-sen University in July 2014 (NCT02219854). The purpose of this ongoing study is to compare the long-term outcome between laparoscopic and open distal subtotal gastrectomy with D2 lymphadenectomy for locally AGC. The other single-center, randomized

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