Review Article

Minimally invasive gastrectomy for cancer: a review

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Abstract: Although current guidelines do not specifically delineate surgical technique in defining gastrectomy for cancer care, it is widely accepted that open surgical techniques are considered the standard of care. With the advent and increasing experience of minimally invasive techniques and technology, including laparoscopic and robotic platforms, the application of minimally invasive surgery (MIS) techniques has impacted outcomes in gastric cancer care. This review aims to provide an overview of short and long term outcomes as well as utilization of MIS techniques in gastric cancer surgery. Additionally, we address endoscopic techniques as this has become more prevalent, certainly for early stage cancers.

Keywords: Gastrectomy; minimally invasive surgery (MIS); laparoscopic surgery; robotic surgery

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Introduction

The ideal treatment for gastric cancer is in constant development. The goal of cure for each patient requires a multidisciplinary approach, utilizing advances in surgical technique, changes in chemotherapy options, radiation therapy, and possibly targeted treatments.

Surgical resection remains one of the mainstays of the treatment of gastric cancer, and the current "gold standard" remains open surgery. Conventional approaches to surgical resection for gastric adenocarcinoma are associated with a significant mortality rate of 4–13% and a morbidity rate of up to 46% (1). The advent of minimally invasive surgery (MIS), which includes laparoscopic, robotic, and endoscopic approaches, has the potential to decrease the morbidity and mortality of gastric resection. The benefits of the MIS approach are well documented for other disease states and malignancies; these include better visualization, reduced blood loss, less post-operative pain, earlier return to normal bowel function, earlier resumption of oral intake, earlier hospital discharge, and lower financial costs, mostly related to decreased length of stay (1-3). In addition, it has been suggested that MIS procedures may cause less surgical trauma as assessed in terms of acute inflammatory indices, improved nutrition, less impaired respiratory function, better quality of life, and reduced time to adjuvant therapy (1-3).

Despite these benefits, MIS gastrectomy has not been adopted as standard practice and indeed is not highly utilized in Western practice. Herein, the authors must acknowledge the unique demographic difference between gastric cancer prevalence in Eastern *vs.* Western countries. There is a significantly higher incidence of gastric cancer in Eastern countries; with the implementation of screening programs, this has led to detection of many cases at an earlier stage of disease. In Japan and South Korea, where the incidence of gastric cancer is highest in the world, screening is mandated for all citizens starting at the age of 40 (4). Unfortunately, screening programs have not been adopted in the U.S or Europe, and gastric cancer most often presents in advanced stages. This likely has led to hesitation regarding adoption of MIS approaches in Western

countries. This review aims to provide a general overview of MIS utilization, outcomes, and prospective directions for gastric cancer.

Utilization of laparoscopic surgery

As with many other oncologic procedures, minimally invasive gastrectomy has recently gained in popularity and utilization. Technologic advances with laparoscopic instrumentation and visualization, as well as increased familiarity with laparoscopic techniques, and the advent of robotic surgical technology has impacted and influenced much of the field of general and thoracic surgery. With respect to gastrectomy for gastric cancer, minimally invasive techniques are performed much less frequently than open surgery worldwide. The utilization of MIS techniques, however, does vary significantly between Eastern and Western institutions. In an analysis of the U.S. National Cancer Database from 2010–2012, 6,427 patients were identified as undergoing gastrectomy for cancer (5). Treatment groups were analyzed in an intention-to-treat manner. The majority (N=4,717, 73.4%) underwent open surgery, while 23.1% (N=1,487) underwent laparoscopic surgery, and 3.5% (N=223) underwent a robotic approach. The Dutch Upper GI Cancer Audit included 1,970 patients from 2011–2016. This included 1,138 (57.8%) undergoing distal gastrectomy and 832 (42.2%) undergoing total gastrectomy (6). Overall, the majority again underwent open surgery; 377 (33.1%) underwent minimally invasive distal gastrectomy, and 314 (37.7%) underwent minimally invasive total gastrectomy. In a breakdown of cases per year, the number of minimally invasive distal and total gastrectomy being performed steadily increased per year but is still performed far less than open surgery.

Minimally invasive surgery seems to be more prevalent in Asia, where gastric cancer is also more prevalent. However, this predilection for minimally invasive surgery is more pronounced in early stage disease. From the Japanese National Clinical Database, a nationwide clinical database, 40,875 patients with stage I cancer and 26,095 with stage II–IV cancers underwent distal gastrectomy between January 2012 and December 2013 (7). In patients with stage I cancer, 23,635 (57.8%) underwent laparoscopic distal gastrectomy; in those with advanced stage cancer, only 3,804 (14.6%) underwent laparoscopic surgery. Further investigation with MIS techniques in advanced cancer, however, is ongoing.

Short- and long-term outcomes

In addition to multiple retrospective reviews, several randomized controlled trials (RCTs) and meta-analyses have demonstrated the safety and feasibility of laparoscopic approaches to gastric cancer. In 2002, Kitano *et al.* published a small RCT of 28 patients with gastric cancer who underwent laparoscopy-assisted distal gastrectomy (N=14) *vs.* open (N=14) for patients with early gastric cancer; the authors reported less blood loss, improved recovery of bowel function and ambulation, and lower post-operative pain scores for the laparoscopic group and equivalent pathologic outcomes, in terms of lymph node retrieval and margins (8).

Small studies in the US at major cancer centers reported comparable results between laparoscopic and open approaches across early and advanced stages of gastric cancer. At City of Hope National Medical Center, 78 gastric cancer patients (laparoscopic N=30, open N=48) were evaluated and found to have no difference in number of lymph nodes retrieved or complication rate, but did have lower blood loss, shorter length of stay, and increased operative times associated with laparoscopic approaches (9). A study of 60 patients (laparoscopic N=30, open N=30) at Memorial Sloan Kettering found no difference in surgical margins, lymph node retrieval, and short-term recurrence rates, but lower complication rates in the laparoscopic group (10). A retrospective study of the U.S. National Cancer Data Base analyzed 6,247 gastric cancer patients who underwent gastrectomy (laparoscopic N=1,487, robotic N=223, open N=4,717) and demonstrated no differences in R0 resection rates or perioperative mortality, inclusive of more advanced stage gastric cancers (5).

A Cochrane review published in 2016, described 2,794 participants in 13 trials, and concluded that there was no difference in short-term mortality and short-term or long-term outcomes, but noted that these conclusions were based on low quality evidence (11).

As experience with laparoscopic approaches increased and became more readily performed, the need for RCT demonstrating the safety and efficacy of minimally invasive approaches became more readily apparent. In 2003, the Korean Laparoscopic Gastrointestinal Surgery Study (KLASS) group initiated RCTs evaluating the technical safety and oncologic feasibility of employing laparoscopic approaches to gastric cancer resections. The multi-center KLASS-01 trial compared 1,416 patients, randomized

to laparoscopic (N=705) or open (N=711) approaches, in patients with stage 1 gastric cancer, and reported an overall lower complication rate, and wound complication rate, in the laparoscopic group (12). They reported a comparable major intra-abdominal complication rate and mortality between the two groups (12). In the subsequent KLASS-02 trial, 1,050 patients with early and advanced stage gastric cancer were randomly assigned to laparoscopic (N=526) or open (N=524) distal gastrectomy with D2 lymphadenectomy. A laparoscopic approach was associated with less estimated blood loss, overall complication rate, post-operative analgesic use and reported pain, earlier return of bowel function, and shorter hospital length of stay (13). The number of retrieved lymph nodes and 90-day mortality rate was comparable between the two groups (13). The Japan Clinical Oncology Study Group JCOG0912 trial, a RCT of 921 patients with clinical IA or IB gastric cancer comparing open (N=459) and laparoscopic (N=462) distal gastrectomies, demonstrated longer operative time, but lower blood loss in the laparoscopic group (14). They reported no difference in high-grade surgical complications and no mortalities (14).

The Japanese Laparoscopic Surgery Study Group JLSSG 0901 analyzed 180 patients with advanced gastric cancer, and demonstrated comparable anastomotic leak rate, pancreatic fistula rate, mortality and readmissions between laparoscopic (N=91) and open (N=89) approaches (15). A meta-analysis by Chen *et al.* reviewed 7,336 patients over 23 studies and reported comparable 5-year overall survival, recurrence, and gastric cancer related death (16).

Laparoscopic approaches to gastric cancer seem to offer many of the same benefits attributed to laparoscopy—shorter hospital length of stay, reduced analgesia, faster recovery time, while preserving the oncologic integrity of the operation. Related to the much higher incidence of gastric cancer in Eastern countries, clearly the MIS gastrectomy experience is more robust in Japan and Korea than in the U.S. and Europe.

Robotic surgery

Robotic technology has introduced wristed and articulated movement, increased dexterity, motion stabilization and three-dimensional visualization, and near infrared fluorescence imaging into the armamentarium of MIS. In some high-volume centers such as Yonsei University Health System in Seoul, South Korea, robotic gastrectomy has become as routine as laparoscopic gastrectomy, with surgeons there performing over 200 robotic gastrectomies a year (17). However, the benefit of the robotic platform comes with a high price and questionable benefit over laparoscopy. Larger series evaluating robotic *vs.* laparoscopic surgery across multiple disciplines has espoused the main benefit of robotic surgery being lower blood loss (18). Laparoscopic surgery was generally associated with lower operative times and lower operating cost (18). An analysis specifically evaluating laparoscopic *vs.* robotic gastrectomy found that the increased operating room time, and therefore cost, was mostly due to time involved in changing robotic instruments, adjusting the arms, or in other non-essential steps (19). As the advance in surgical efficiency and robotic technology improves, this aspect of robotic surgery may improve. Prospective trials are currently evaluating the oncologic efficacy of robotic surgery, evaluating surgical complication rates and oncologic outcomes (20).

MIS learning curve

Another barrier to the adoption of MIS techniques related to gastric cancer is the required skill set for laparoscopic resection while maintaining oncologic principles of resection. The more advanced tumors are often bulkier, with close proximity to vasculature or adjacent organs, making the dissection challenging in a minimally-invasive manner. A comprehensive lymphadenectomy is also one of the challenging portions of the operation laparoscopically and is critical to improved oncologic prognosis. Hu *et al.* reported the learning curve to be 40 cases to improve the operative time, reduce blood loss and increase the number of resected lymph nodes (21).

Endoscopic techniques

An even more recent development is the use of endoscopic therapies, specifically in early gastric cancer. Because the incidence of early gastric cancer is much higher in the Eastern world than in the Western world, endoscopic resection (ER) has yet to become a commonly used tool in the West. The incidence of nodal metastasis in intramucosal early gastric cancer is 3%, and in submucosal early gastric cancer is 20% (22). Lymphatic vessel invasion, histological ulceration of the tumor, and tumor diameter (>3 cm) are independent risk factors for regional lymph node metastasis (22,23). In the absence of these risk factors, the

incidence of nodal involvement in early gastric cancer is 0.36% (22), and these patients may be able to be managed with ER, namely endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD), rather than gastrectomy with lymphadenectomy (22). Indications for EMR include elevated cancers less than 2 cm in diameter, and small (<1 cm) depressed cancers without ulceration (24). The lesion must be differentiated cancer confined to the mucosa. In a retrospective analysis with propensity-score matching, Choi *et al.* found that the 5-year overall survival rates and recurrence rates did not differ between patients undergoing EMR and patients undergoing surgery (93.6% *vs.* 94.2% and 1.2% *vs.* 1.1%) (25). The risk of metachronous gastric cancer was higher in the EMR group than in the surgery group (5.8% *vs.* 1.1%), however all recurrences were successfully retreated (25). The cost of care in the EMR group was also significantly lower than in the gastrectomy group, P<0.001 (25).

One of the significant limitations of EMR is that complete resection of lesions larger than 2 cm in diameter is difficult, mostly due to limitations in the equipment, and the high risk of local recurrence due to piecemeal resection (2.3–36.5%) (26). Because of these limitations with regards to size restrictions, ESD techniques have become more popular. One of the benefits of ESD is that it allows better *en bloc* resection of early gastric cancers (25). A meta-analysis of 15 studies found that ESD, compared with EMR, had higher *en bloc* and curative resections rates (OR 13.9 and 3.5, respectively), as well as lower rates of local recurrence (OR 0.09) (27).

Currently the indication for ER for patients with early gastric cancer is differentiated cancers without evidence of lymphovascular invasion, including: mucosal cancer without ulceration, irrespective of tumor size; mucosal cancer with ulceration, less than 3 cm in diameter; and minimal (500 μm from the muscularis mucosa) submucosal invasive cancer less than 3 cm in size (24). Undifferentiated mucosal cancers should not be treated by EMR, as the risk of lymph node metastasis rises to 4% (27).

It is unclear whether these techniques could have any role in more advanced gastric cancers, and further study may be required to determine the utility of endoscopic techniques in these settings.

Conclusions

Minimally invasive gastrectomy has been increasing in prevalence, and many surgeons have now overcome their personal learning curve and have developed faster ways at overcoming the learning curve for their trainees. While initial experience with early stage gastric cancer showed improved recovery following laparoscopic gastrectomy compared to open surgery, this has now also been demonstrated in those with advanced gastric cancer. Laparoscopic gastrectomy in experienced centers is a reasonable alternative to open surgery, offering equivalent oncologic surgery and improved recovery. The robotic platform still lacks robust data but may offer surgeons not otherwise comfortable with laparoscopic surgery a MIS approach for gastrectomy. Endoscopic techniques also show great promise in treatment of early, localized gastric cancers. More work is being performed investigating endoscopic techniques in more advanced or higher risk tumors, including endoscopic full thickness gastric wall resections. The MIS platforms offer cost reduction and improved recover, with early data showing equivalent oncologic outcome. In conclusion, advanced MIS techniques should be incorporated into the multidisciplinary discussion, including modern chemotherapy, targeted therapy and advances in surgical technique, to offer patients with gastric cancer the most comprehensive options.

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Footnote

Conflicts of Interest: The authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ls.2018.10.14). The authors have no conflicts of interest to declare.

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