

Notes on laparoscopic gastrointestinal surgery—current status from clinical studies of minimally invasive surgery for gastric cancer

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Abstract: To establish high-quality evidence of laparoscopic gastrectomy (LAG) in the field of gastric cancer treatments, large-scale, prospective randomized controlled trials have been performed in Japan, Korea and China. Furthermore, as advanced laparoscopic techniques have been developed, prospective clinical studies are being performed with regard to laparoscopy-assisted total gastrectomy and robotic gastrectomy. This review summarizes the current status of minimally invasive surgeries for gastric cancer based on the latest ongoing clinical trials.

Keywords: Laparoscopic gastrectomy (LAG); randomized clinical trials; advanced gastric cancer

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Introduction

Since laparoscopy-assisted distal gastrectomy (LADG) with lymph node dissection for early gastric cancer (EGC) was developed in 1991 in Japan, this procedure has been widely accepted (1,2). Initially, major efforts were made to improve the technical safety and improve the standardization of laparoscopic gastrectomy (LAG) (3-7). In order to improve the laparoscopic technique, the Japan Society for Endoscopic Surgery (JSES) established the Committee for the Endoscopic Surgical Skill Qualification System in 2001 (8,9). It is considered that establishment of the system is one of the reasons why quality of laparoscopic surgery is guaranteed so far in Japan.

Although advances in techniques and improvement of instruments have led to the standardization of LAG with lymph node dissection among experienced surgeons, surgeons should evaluate as to whether the laparoscopic approach to gastric cancer is adequate and beneficial for cancer treatment. Therefore, large-scale, prospective

studies are needed to answer several clinical questions. Here we review the current status of the latest studies.

Ongoing clinical studies of LAG for gastric cancer

To provide answers to the clinical questions, prospective clinical studies are ongoing. These contain multicenter prospective randomized trials and a large-scaled prospective cohort study.

LADG for gastric cancer

So far, most of these studies were limited by having a small sample size-, and a short-term follow-up period (10). Therefore, a retrospective, multicenter study was conducted to know whether LAG for EGC is a safe procedure or not in terms of short- and long-term outcomes (11). According to some retrospective studies with large samples,

LAG for EGC is considered to be feasible treatment in terms of technical and oncological aspects. With regard to prospective studies, a randomized controlled study (JCOG0912) was performed to confirm the non-inferiority of relapse-free survival of LADG to ODG in patients with the same inclusion criteria used in the phase II study (JCOG0703) (12). Regarding short-term outcome, there were no significant differences between two groups in terms of intra-operative adverse events (G3-4) and in-hospital, non-hematological adverse events (G3-4) (13). The authors concluded that LADG performed by the credentialed surgeons was safe as ODG for cStage I cancer. A large-scale, multicenter randomized trial (KLASS01) regarding the safety of LADG for cStage I cancer from Korea has mentioned that this procedure confers the benefit of a lower occurrence of wound complications compared with conventional ODG (14). Therefore, LADG is safe in terms of short-term outcomes, at least for patients with cStage I cancer. Regarding the non-inferiority of LADG in terms of long-term outcome, the result should be anticipated from each country.

In order to feedback for surgeons the real-time clinical data, a nationwide surgical patient registration system named the National Clinical Database (NCD) was initiated from 2011 in Japan. Recently, retrospective- and prospective-cohort studies have been conducted to clarify a risk model of LAG using the NCD (15). These results based on mega-data will be expected to cover the fields of exclusive criteria in our prospective RCT for LAG, such as age (elderly patients), and high BMI.

The extent of lymph node dissection in advanced gastric cancer (AGC) remains controversial. In Asian countries, D2 lymph node dissection is routinely carried out in AGC, the main advantages of D2 lymph node dissection being considered to include prolonged survival and improved staging accuracy (16,17). Recent retrospective studies and meta-analysis comparing laparoscopic D2 gastrectomy and open D2 gastrectomy for AGC demonstrated that the laparoscopic procedure may be feasible (18-20). A phase III trial to confirm the non-inferiority of this procedure to open gastrectomy in terms of long-term outcomes is ongoing. In East Asia, large-scale, multicenter RCTs are currently ongoing in Japan (UMIN00003420) (21), Korea (KLASS 02: NCT01456598) (22) and China (CLASS 01: NCT01609309) (23). Regarding to short-term outcomes from the Korean and Chinese trials, favorable outcomes in LADG as well as ODG for AGC have been demonstrated.

These data may contribute to make a decision of indication for LAG.

LATG for gastric cancer

There are a lot of concerns of LATG because of its technical difficulty, particularly for esophagojejunostomy (24-26). So far, no RCT data on LATG are available, because the standardization of techniques for esophagojejunal anastomosis has proved difficult even for experienced surgeons. Recently, a multicenter, non-randomized confirmatory study of LATG with lymph nodal dissection for clinical stage I gastric cancer (JCOG1401) was carried out in terms of technical safety-, and short-term surgical outcomes (registered number, UMIN 000017155). In Korea, a feasibility study of LATG in EGC (KLASS03) was performed, and patient enrollment has already finished (NCT01584336). The primary endpoint of the KLASS03 study was to evaluate the incidence of postoperative morbidity and mortality. These studies will lead to the confirmation of the technical safety of LATG for EGC. On the other hand, several issues related to the technical and oncological feasibility still exist regarding LATG for AGC. For standardization of these procedures, it will be needed to expand the indication of LATG step by step at this moment.

Robotic gastrectomy for gastric cancer

Although a number of robotic systems is rapidly increasing, several issues remain to be solved regarding clinical indication, short- and long-term outcomes, cost-effectiveness, and stress of surgeons (27-29). Recently, prospective cohort study of robotic gastrectomy for gastric cancer conducted (registered number, UMIN000015388). These results will be expected to inform decisions on the future direction of robotic gastrectomy for gastric cancer.

Future perspective

Since the first LADG for gastric cancer was introduced, many surgeons have made efforts to improve the technical and oncological safety of LAG. With a view to standardizing LAG, multicenter clinical studies have also been launched to establish high-quality evidence from Japan, Korea and China. The fruitful data from these studies are expected to decide future directions for the use of LAG for gastric cancer. International cooperation and

sharing of information on current issues regarding LAG for gastric cancer will be required.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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