A phase II trial was started in Japan to evaluate the safety of laparoscopy-assisted distal gastrectomy (LADG) for clinical stage I gastric cancer. A total of 170 patients will be enrolled in this study by expert surgeons for laparoscopy from 16 institutions over 1 year. The primary endpoint is incidence of anastomotic leak and pancreatic fistula. The secondary endpoints are overall survival, relapse-free survival, proportion of completion of LADG, proportion of conversion from LADG to open gastrectomy, surgical morbidity and short-term clinical outcomes.

**Key words:** gastric cancer — laparoscopy assisted gastrectomy — phase II study

**INTRODUCTION**

The proportion of early gastric cancer is more than 50% in major institution in Japan. The Japanese guideline allows laparoscopy-assisted gastrectomy for early gastric cancer as investigational treatment, considering patients’ performance status. Since Kitano et al. (1) reported the first experience of laparoscopy-assisted gastrectomy in 1994, it has attracted attention of surgeons. Nationwide survey of laparoscopic surgery for gastric cancer showed that the total number of patients who were treated with laparoscopic technique increased and that the increase was remarkable in the patients with cT1N0 (Stage IA), cT1N1 (Stage IB) and cT2N0 (Stage IB) tumors.

Recently, technique for laparoscopy-assisted distal gastrectomy (LADG) with D1 plus suprapancreatic node dissection has been established among expert surgeons for laparoscopy. Although there is a concern whether it is an appropriate modality for cancer treatment, the technical difficulties for LADG have been solved gradually. Several retrospective and small prospective studies have reported that LADG brings faster recovery of bowel movement, less pain, shorter hospital stay and better cosmetic outcomes than open distal gastrectomy (ODG) (2–5). There has never been, however, a prospective study with adequate sample size to investigate the benefit of LADG. Some studies also reported that LADG had higher risk of surgical morbidities, such as anastomotic leak, stenosis and pancreatic fistula than ODG (6,7). Here, the Gastric Cancer Surgical Study Group of the Japan Clinical Oncology Group (GCSSG/JCOG) conducts a multi-institutional, phase II trial (JCOG0703) to evaluate the safety of LADG for clinical stage I gastric cancer. The JCOG Protocol Review Committee approved the study protocol in September 2007, and the study was activated in November 2007.

**JCOG 0703 PROTOCOL**

**PURPOSE**

The aim of this study was to evaluate the safety of LADG with nodal dissection for clinical stage I gastric cancer patients.

**STUDY SETTING**

A multi-institutional (16 specialized centers), single-arm phase II trial.

**RESOURCES**

This study was supported by the Grants-in-Aid for Cancer Research (17S-3, 17S-5, 17-11) from the Ministry of Health, Labor and Welfare, Japan.

**ENDPOINTS**

The primary endpoint is incidence of anastomotic leak and pancreatic fistula. The secondary endpoints are overall survival, relapse-free survival, proportion of completion of LADG, proportion of conversion from LADG to open gastrectomy, surgical morbidity and short-term clinical outcomes.
survival (OS), relapse-free survival (RFS), proportion of completion of LADG, proportion of conversion from LADG to ODG, surgical morbidity and short-term clinical outcomes.

In this trial, anastomotic leak is diagnosed radiologically and is recorded regardless of its clinical significance. Pancreatic fistula is diagnosed when fluid with a high amylase concentration drains from the peripancreatic area and induces infection. The OS is defined as the time from registration to death. The RFS is defined as the time from registration to either the first event of recurrence or death from any cause. All LADG cases that required skin incision >6 cm are counted as conversion to ODG. The completion of LADG is defined as the curative surgery without conversion to ODG. The short-term clinical outcomes are proportion of use of analgesics, duration from surgery to flatus, highest body temperature during hospitalization and during the first 3 days after surgery.

INCLUSION CRITERIA

Patients are included in this trial if they meet all of the following criteria: (i) histologically proven stomach adenocarcinoma, (ii) eStage IA (T1N0) or IB (T1N1/T2N0) tumor according to the 13th edition of the Japanese Classification of Gastric Carcinoma (8), (iii) no indication of endoscopic mucosal resection according to the second version of the Japanese Endoscopic Treatment guideline, (iv) tumor located in the middle or lower third of the stomach which can be treated by distal gastrectomy, (v) no involvement of duodenum, (vi) aged 20–80 years, (vii) an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 or 1, (viii) body mass index (BMI) <30 kg/m², (ix) not recurrent tumor after endoscopic mucosal resection (EMR), (x) no prior upper abdominal surgery or intestinal resection, (xi) no prior chemotherapy or radiotherapy for any malignancy, (xii) adequate organ function and (xiii) written informed consent.

EXCLUSION CRITERIA

Patients are excluded if they meet any of the following criteria: (i) synchronous or metachronous (within 5 years) malignancy other than carcinoma in situ, (ii) pregnant or breast-feeding women, (iii) severe mental disease, (iv) systemic administration of corticosteroids, (v) unstable angina or myocardial infarction within 6 months of the trial, (vi) unstable hypertension, (vii) diabetes mellitus, uncontrolled or controlled with insulin or (viii) severe respiratory disease requiring continuous oxygen therapy.

REGISTRATION

After confirming the inclusion/exclusion criteria by telephoning or faxing the JCOG Data Center, the patients are registered into this JCOG0703 trial.

QUALITY CONTROL OF SURGERY

Initially, the 16 institutions among the Gastric Cancer Surgical Study Group of the JCOG participate in this trial. All participating surgeons agree to the technical details for LADG. Significant experience in gastric cancer surgery, especially in LADG and ODG, is a prerequisite for a surgeon’s participation in the trial. Surgeons with experience of more than 30 LADG and 30 ODG are selected. We, furthermore, perform central review of the surgical procedure by photographing all patients and by videotaping the arbitrarily selected patients. To assess the compliance with lymphadenectomy, the number of dissected nodes in all stations is recorded in the case report form, and the results were monitored.

TREATMENT METHODS

Laparoscopy-assisted distal gastrectomy with D1 plus suprapancreatic node dissection is performed. Extent of suprapancreatic node dissection is decided by surgical T and N stage of the tumor according to the second version of the Japanese Guideline of Gastric Cancer. If surgical finding of tumor is stage II or more advanced, the surgeon should convert LADG to ODG. We accept pylorus preserving distal gastrectomy. Total gastrectomy is not accepted. Size of minilaparotomy incision should be ≤6 cm. The reconstruction approach and method following resection is not specified.

FOLLOW-UP

All enrolled patients are followed up at least every 6 months for 5 years. Blood tests, upper gastrointestinal endoscopy and abdominal computed tomography are carried out every year.

STUDY DESIGN AND STATISTICAL METHODS

This trial determines the safety of LADG in terms of incidence of anastomotic leak and pancreatic fistula. If the incidence of these two postoperative complications is low as expected, the subsequent phase III trial is designed to evaluate non-inferiority of LADG to ODG in terms of long-term survival. In this phase II trial, the sample size was 170 cases, provided 90% power under the hypothesis of primary endpoint as the expected value of 3% and threshold value of 8% using one-sided testing at a 10% significance level.

This study was registered with UMIN-CTR, identification number UMIN000000874.

INTERIM ANALYSIS AND MONITORING

Interim analysis is not planned. If the number of cases with treatment-related death or severe (Grade 4) surgical morbidity reach six, the registration will be stopped unless the JCOG Data and Safety Monitoring Committee (DSMC) approves to continue this trial. The JCOG Data Center conducts data management, central monitoring and statistical analysis. This center also provides semi-annual monitoring.
reports, each of which is submitted to and reviewed by the JCOG DSMC. None of surgeons administering the interventions are involved in the data analysis. For quality assurance, site-visit audits are done by the JCOG Audit Committee.

Conflict of interest statement
None declared.

References