Safety of Laparoscopic Resection for Gastrointestinal Stromal Tumor on Unfavorable Anatomic Site of Stomach：a multicenter prospective trial (CLASS-06)

Study Protocol

Applying party：Renji Hospital affiliated to Shanghai Jiaotong University School of Medicine

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V1.6

2021.07.01

Agree to comply with SOP in the study

Name	Position	Unit	Adress	Signature

By providing the signature, participants have agreed the following disclaimers

Confidentiality Statement:

The information contained in this clinical protocol is only available to the investigators, the Ethics Committee and relevant agencies for review. Without approval from the principal investigator (PI), no information shall be given to a third party irrelevant to this study.

Abstract

Protocol Titile	Safety of Laparoscopic Resection for Gastrointestinal Stromal Tumor on Unfavorable Anatomic Site of Stomach：a multicenter prospective trial
Protocol Version	V1.6
PI	Cao Hui
Research Centers	Renji Hospital affiliated to Shanghai Jiaotong University School of Medicine Nanfang Hospital, Southern Medical University Peking University Cancer Hospital Zhongshan Hospital, Fudan University The First Affiliated Hospital of Nanjing Medical University Fujian Medical University Union Hospital Peking University People's Hospital Ruijin Hospital affiliated to Shanghai Jiao Tong University School of Medicine Union Hospital, Tongji Medical College, Huazhong University of Science and Technology West China Hospital, Sichuan University The First Affiliated Hospital, Sun Yat-Sen University Liaoning Cancer Hospital and Institute Chinese PLA General Hospital
Indications	Patients with gastrointestinal stromal tumor (GIST) at stomach whose diameter is ≥2cm and ≤5cm at unfavorable anatomic sites. Note: Favorable anatomic sites are defined as greater curvature and anterior wall of stomach by Soft Tissue Sarcoma, NCCN Clinical Practice Guidelines in Oncology (version 2. 2020). Accordingly, the unfavorable anatomic sites are defined as all the anatomic locations of stomach except greater curvature and anterior wall, including less curvature, posterior wall, and area near pylorus or cardia.
Research Purpose	The aim of this trial is to evaluate the safety of laparscopic resection for GIST whose diameter is ≥2cm and ≤5cm at unfavorable anatomic sites of stomach

Rsearch Design	Prospective, multicenter, open-label, single-arm
Case Grouping	Study group: laparoscopic resection for GIST at unfavorable anatomic sites of stomach
Determination of Sample Size	The reference group proportion is 0.9800 according to the 3-year disease free survival rate reported in the previous literature on the subject of gastric GIST with maxium diameter between 2 to 5cm. -0.06 is set to detect a non-inferiority margin. The test statistic used is the one-sided Z test (unpooled). The significance level of the test is 0.025. The target Power is 0.80. The inconsistency rate between preoperative and postoperative pathological diagnosis of GIST from literature is about 30%The dropout rate during follow-up is assumed to be 10%. The sample size needed by the study group was 182.
Number of Research Centers	13
Inclusion Criteria	Diagnosed as gastrointestinal stromal tumor at unfavorable anatomic sites of stomach preoperatively by endoscopy, ultrasound endoscopy, CT or MRI; Diameter of tumor size is ≥2cm and ≤5cm confirmed by contrast CT or MRI; Patients whose tumor is resectable by laparoscopic techniques at preoperative assessment; No evidence of distant metastasis and tumor invading nearby organs at preoperative assessment; Performance status of 0 or 1 on ECOG (Eastern Cooperative Oncology Group) scale; ASA (American Society of Anesthesiology) score I, II, or III; Written informed consent.

Exclusion Criteria	Women during pregnancy or breast-feeding; Severe mental disorder; History of previous upper abdominal surgery (except laparoscopic cholecystectomy); History of other malignant disease within the past five years; History of previous neoadjuvant imatinib therapy; History of unstable angina or myocardial infarction within the past six months History of cerebrovascular accident within the past six months; History of continuous systematic administration of corticosteroids within the past month; Requirement of simultaneous surgery for other disease; Emergency surgery due to complication (bleeding, obstruction or perforation); FEV1 < 50% of predicted value. Patients with GIST locates at favorable anatomic sites detected by contrast CT, MRI or ultrasound endoscopy at preoperative assessment; Patients with GIST diameter < 2cm or>5cm detected by contrast CT or MRI; Presence of distant metastasis or tumor invading nearby organs at preoperative assessment
Withdrawal Criteria	Patients postoperatively confirmed as non-GIST case by pathology; ● GIST Patients diagnosed with GIST at unfavorable anatomic site preoperatively but confirmed at favorable anatomic site intraoperatively; Patients confirmed as spontaneous tumor rupture, metastasis or invading nearby organs intraoperately; ● Requirement of simultaneous surgery for other disease; Sudden severe complications during the perioperative period (intolerable

	surgery or anesthesia), which renders it unsuitable or unfeasible to implement the study treatment protocol as scheduled; Patients confirmed to require emergency surgery by attending physicians due to changes in the patient's condition after enrolled into this study; Patients who voluntarily quit or discontinue treatment for personal reasons at any stage after enrolled in this study; Treatment implemented is proven to violate study protocol.
Intervention	Laparoscopic resection for GIST at unfavorable anatomic site of stomach will be conducted
Endpoints	Primary Endpoint: 3-year disease-free survival rate (DFS) Second Endpoints: Success rate of laparoscopic surgery Rate of intraoperative complication Rate of Postoperative complication 3-year overall survival rate (OS) Postoperative recovery course
Stastical considerations	Statistical software SAS (version 9.4) will be used for statistical analysis. The efficacy will be tested for non-inferiority with historical comparison and the safety indicators adopts descriptive analysis.All statistical tests will be conducted by bilateral test. The test level with statistical significance is 0.05. The interval estimation of parameters is 95% confidence interval. K-M survival analysis and Cox regression model will be used for analysis of survival time data. Central effect analysis: mixed-effect model for quantitative measures, CMH method for qualitative measures, and hierarchical logistic regression model for grade variables, survival time variables will be evaluated and adjusted using a Cox regression model. The central effect analysis and subgroup analysis will be carried out according to the specific situation. Interim analysis of this study will be carried out.