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Complications and their correlation with prognosis in patients undergoing total gastrectomy with splenectomy for treatment of proximal advanced gastric cancer

Masahiro Watanabe, Takahiro Kinoshita*, Masanori Tokunaga, Akio Kaito, Shizuki Sugita

Gastric Surgery Division, National Cancer Center Hospital East, 6-5-1 Kashiwanoha, Kashiwa, Chiba, 277-8577, Japan

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ABSTRACT

Introduction: Spleen-preserving surgery is a mainstay in the treatment of proximal advanced gastric cancer according to the results of several clinical studies. However, total gastrectomy with splenectomy (TGS) still plays a role in the treatment of aggressive tumors invading the greater curvature line or adjacent structures, in spite of its high morbidity. The aim of this study was to identify the risk factors for morbidity and the association between the occurrence of postoperative complications and long-term outcomes.

Methods: We retrospectively analyzed 430 patients with gastric cancer who underwent curative TGS from 1992 to 2010. In total, 134 patients encountered grade ≥III postoperative complications (C group), and risk factors for morbidity were analyzed. Patients in the C group were matched 1:1 with patients selected from among 296 patients without complications (matched non-C group, n = 134) using propensity score estimation, to compare relapse-free survival (RFS) between the two groups.

Results: The overall grade ≥III complication rate was 31.2%. Multivariable analysis identified pancreatic resection (odds ratio [OR], 5.65), male sex (OR, 1.77), and an operation time of ≥240 min (OR, 1.69) as independent predictors of postoperative complications after TGS. The RFS was not significantly different between the C-group and matched non-C group (46.9% vs. 45.0%, respectively; hazard ratio, 0.98).

Conclusions: Pancreatic resection, male sex, and a longer operation time are risk factors for morbidity after TGS, and a precise surgical technique is required for such patients. However, postoperative complications of TGS may have little impact on long-term outcomes.

Introduction

Total gastrectomy with splenectomy (TGS) was historically performed as a standard surgical procedure for complete removal of the splenic hilar lymph nodes (LNs) in the treatment of advanced proximal gastric cancer in Japan. This procedure had been recommended in the guideline of the Japanese Gastric Cancer Association until the 3rd English version [1] and was termed D2 total gastrectomy. However, the final result of a multi-institutional randomized trial conducted in Japan (JCOG 0110) was recently published. This trial compared splenectomy versus non-splenectomy in patients with tumors not involving the greater curvature line and showed higher morbidity in the splenectomy than non-splenectomy group (30.3% vs. 16.7%, respectively), and splenectomy provided no survival benefit with respect to relapse-free survival (RFS) or overall survival (OS) [2]. Therefore, the current consensus in Japan is that splenectomy should not be performed unless the tumor involves the greater curvature line. For tumors involving the greater curvature line, whether splenectomy should be performed for complete removal of the splenic hilar LNs in spite of the high morbidity rate remains controversial. Our previous retrospective study indicated that splenic hilar LN dissection provides a survival benefit in patients with tumors involving the greater curvature [3]. In clinical practice, TGS must be performed if the tumor directly invades the splenogastric ligament or is associated with gross nodal metastasis at the splenic hilum. In this context, the number of TGS procedures that are performed is expected to decrease. However, TGS still plays a role in the treatment of proximal advanced gastric cancer.

* Corresponding author.
E-mail addresses: maswatan@east.ncc.go.jp (M. Watanabe), takkinos@east.ncc.go.jp (T. Kinoshita), mtokunag@east.ncc.go.jp (M. Tokunaga), akaito@east.ncc.go.jp (A. Kaito), shisugit@east.ncc.go.jp (S. Sugita).

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TGS is associated with a high morbidity rate. Morbidity definitely diminishes the patient's quality of life; furthermore, some researchers have suggested a significant correlation between postoperative complications and a subsequent poor prognosis in patients who have undergone radical surgery for gastric cancer [4–6]. To date, however, no studies have evaluated the correlation between morbidity and prognosis with a focus on TGS. It also seems possible that the patient's weakened immune function after splenectomy influences the oncological outcomes.

In our institution, TGS was performed as a standard surgical procedure for proximal advanced gastric cancer from 1992 to 2009. In the current study, we retrospectively reviewed our clinical database of patients who underwent TGS to identify the risk factors for morbidity and the association between the occurrence of postoperative complications and long-term outcomes.

Patients and methods

Patients

In total, 430 patients with gastric cancer underwent curative TGS from 1992 to 2010 at the National Cancer Center Hospital East in Japan, and their medical records were retrospectively reviewed. Patients with remnant gastric cancer, double cancer, and intraoperatively confirmed metastasis to the para-aortic LNs were excluded.

Surgical procedure and follow-up

Standard Japanese D2 TGS was performed by surgeons experienced in laparotomy. The pancreas was basically preserved, leaving the splenic artery and vein as distal as possible to maintain vessel communication with the pancreas tail. Simultaneous pancreas resection was performed only in cases of direct invasion of the pancreas by the tumor or metastatic LNs. The pancreas was transected with a knife and sutured or transected with an ultrasonically activated scalpel or linear stapling device [7]. Patients usually started meals on postoperative day 3. The drain was removed after starting meals. Since 2007, S-1 has been the standard postoperative chemotherapy regimen based on the results of the ACTS-GC trial in Japan [8]; therefore, postoperative adjuvant chemotherapy was carried out when the final tumor stage was consistent with the ACTS-GC criteria.

Definition of postoperative complications

The Clavien–Dindo grading system was used to classify postoperative complications within 1 month after the operation [9]. Postoperative complications were defined as those of grade ≥III. Univariable and multivariable analyses were carried out to identify risk factors for postoperative complications.

Matching of patients

Patients were divided into two groups: those with postoperative complications (C group, n = 134) and those without postoperative complications (non-C group, n = 296). Matching of patients was performed by propensity score estimation to generate two comparable groups, in which sex, age, and American Society of Anesthesiologists physical status were used as covariates. After the matching, patients in the C group and matched non-C group were re-evaluated with respect to the following clinicopathologic factors: sex, age, preoperative albumin concentration, body mass index (BMI), American Society of Anesthesiologists physical status, blood loss, pathological T and N stage, and presence of adjuvant chemotherapy. Tumor progression and stage were recorded according to the 7th TNM classification of gastric cancer [10]. The OS and RFS durations were compared between the two groups.

Statistical analysis

All statistical analyses were performed using JMP version 11 (SAS Institute, Cary, NC). The chi-square test, Student's *t*-test, and Wilcoxon's signed-rank test were used for the statistical analysis. Survival curves were constructed by the Kaplan–Meier method, and the log-rank test was used to assess survival differences. We also estimated the hazard ratio (HR) with stratified Cox proportional hazard regression. Factors that might affect postoperative complications were evaluated by multivariate logistic regression analysis. All *P* values of <0.05 were considered statistically significant.

This study was approved by the Institutional Review Board of the National Cancer Center, Japan (IRB file No. 018, approval date: April 28, 2015).

Results

Details of postoperative complications

Among all 430 enrolled patients (male/female, 314/116; median age, 63 years), the complication rate (grade ≥III) was 31.2% (134/430). Infectious postoperative complications were observed in 28.6% (123/430) of patients. Among these complications, pancreatic fistula was the most frequently observed (Table 1). Three (0.7%) patients died of postoperative intra-abdominal hemorrhage, pneumonia, and subarachnoid hemorrhage, respectively.

Clinicopathologic characteristics

The clinicopathologic characteristics of the C group (n = 134) and non-C group (n = 296) before matching are shown in Table 2. The C group contained significantly more male patients with a high BMI and significantly more patients with advanced-stage cancer. Additionally, the operation time was longer, the blood loss volume was higher, and additional pancreatic resection was more frequently performed in the C than non-C group. There was no significant difference in the percentage of patients who received adjuvant chemotherapy between the two groups.

Risk factors for postoperative complications

The univariable analysis indicated that the predictors of postoperative complications were male sex, old age (≥65 years), a long operation time (≥240 min), a large intraoperative blood loss volume (≥700 ml), performance of pancreatic resection, ≥pT3, and pN+. These items were transferred to the multivariable analysis, which revealed the following independent predictors of postoperative

Table 1
Details of postoperative complications.

	All postoperative complications n = 134 (31.2%)
Infectious complications	123 (28.6%)
Pancreatic fistula	88 (20.5%)
Anastomotic leakage	27 (6.3%)
Intra-abdominal abscess	13 (3.0%)
Pneumonia	10 (2.3%)
Ileus	4 (0.9%)
Intra-abdominal bleeding	6 (1.4%)
Others	5 (1.2%)

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