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Original article

Residual total pancreatectomy: Short- and long-term outcomes

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ABSTRACT

Background/objectives: Because of limited numbers of patients, there are limited data available regarding outcomes after residual total pancreatectomy (R-TP). This study aimed to assess outcomes after the R-TP *vs* the one-stage total pancreatectomy (O-TP), especially focused on the pancreatic adenocarcinoma cases.
Methods: From 2005 to 2014, all patients who underwent the R-TP ($n = 8$) and the O-TP ($n = 12$) for pancreatic primary malignancy were prospectively enrolled.
Results: The median time from the initial operation to the R-TP was 30 months. Ten patients in the O-TP group and 8 in the R-TP had pancreatic adenocarcinoma. Postoperative complications occurred in two O-TP patients and one R-TP patient. There was no in-hospital mortality. At 12 months after surgery, the median insulin dose was 27 U/day after the O-TP and 24 U/day after the R-TP, the median hemoglobin A1c was 7.2% after the O-TP and 6.9% after the R-TP. There was a significantly larger reduction in body weight after the O-TP than after the R-TP. Postoperative fatty liver disease occurred in about half of the patients in each group. In patients with pancreatic adenocarcinoma, the 2-year overall survival rate was not significantly different (68.6% after the O-TP vs 71.4% after the R-TP).
Conclusions: Although the postoperative morbidity and nutritional statuses should be improved, these favorable short- and long-term outcomes demonstrate that the R-TP is a feasible procedure for patients with malignant tumor in the remnant pancreas.

Introduction

Pancreatic resection is an important part of the multimodal therapy for pancreaticobiliary neoplasms. It remains the only treatment that may cure locoregional malignancy [1]. Standard pancreaticoduodenectomy (PD) and distal pancreatectomy (DP) are established procedures for the treatment of pancreaticobiliary neoplasms, but total pancreatectomy (TP) may be required for tumors that are locally advanced or located in the central part of the pancreas [2,3]. The Japanese National Clinical Database showed that TP was performed about 400 cases in a year in Japan, whereas PD and DP were performed about 10,000 and 3400 cases, respectively [4]. TP is performed for not only pancreatic adenocarcinoma, but also intraductal papillary mucinous neoplasm and pancreatic neuroendocrine tumor [5–7].

Advances in surgical techniques and perioperative management have reduced the mortality rate after pancreatic resection to <5% in high-volume centers, but the morbidity rate has not changed much and remains at 30–40% [8–10]. TP is associated with a high morbidity rate [2,3,11]. Recently, Hartwig et al. reviewed 434 cases who underwent TP for various pancreatic neoplasm, and indicated that 30-day mortality and in-hospital mortality were 3.7% and 7.8% [2]. They also showed that 5-year survival rates were 27.8% of all patients and 15.2% of patients with pancreatic adenocarcinoma [2]. Moreover, Johnston et al. analyzed the National Cancer Database and reported the outcomes of TP for 2582 patients with pancreatic adenocarcinoma [5]. They showed that 30-day mortality was 5.5% and 5-year survival rate was 13% [5]. These studies indicated on outcomes after the one-stage TP (O-TP), for such as pancreatic tumor which diffusely spread to whole pancreas.

The residual TP (R-TP) is required in patients who develop local recurrence or a new primary cancer in the pancreatic remnant. The

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R-TP is a challenging procedure because of adhesions and anatomical topography, and may be associated with a higher morbidity rate than the O-TP. However, there are limited data available regarding outcomes after the R-TP [12,13], because the reported number of patients who underwent this procedure was small. Kleff et al. reported 15 cases who underwent resection for recurrent pancreatic adenocarcinoma, including the only two R-TP cases [13]. Similarly, Miura et al. reported 3 patients who underwent the R-TP [12]. Thus, the indications for the R-TP and perioperative management have not been discussed in detail. In addition, detailed outcomes after the R-TP compared with the O-TP has been unclear in English literature.

The aim of this study was to compare short- and long-term outcomes in patients who underwent the R-TP *versus* the O-TP for pancreatic primary malignancy, especially focused on the pancreatic adenocarcinoma cases.

Methods

Patients and characteristics

Twenty four patients underwent TP for primary or metastatic/recurrent pancreaticobiliary malignancy at the Department of Gastroenterological Surgery, Kumamoto University Hospital and Department of Surgery, Kumamoto Regional Medical Center between September 2005 and August 2014. Written informed consent was obtained from all patients before treatment. The study protocol was approved by the Institutional Review Board of Kumamoto University Hospital. Four patients were excluded from this study, two patients with intraductal papillary mucinous adenoma and two patients with pancreatic metastasis from renal cell carcinoma. Twelve of the patients underwent the O-TP and eight underwent the R-TP, including four who underwent the pancreatic head R-TP (hR-TP) after distal pancreatectomy and four who underwent the pancreatic tail R-TP (tR-TP) after pancreaticoduodenectomy. The main surgical indications for theO-TP were pancreatic adenocarcinoma which diffusely spread to almost whole pancreas. It included the cases in whom intraoperative pathological examination was positive at the pancreatic resection limit. Main duct or mixed type intraductal papillary mucinous carcinoma (IPMC) which spread from pancreatic head to tail were also included. The main surgical indications for the R-TP were pancreatic tumor which developed in the pancreatic remnant such as pancreatic adenocarcinoma. When pancreatic adenocarcinoma in the pancreatic remnant was accompanied by distant metastasis, systemic chemotherapy was given and the R-TP was not considered. All TP procedures for malignant disease included D2 lymph node dissection [14,15]. Venous resection and reconstruction were performed in patients with possible portal vein (PV) or superior mesenteric vein (SMV) invasion. For the O-TP and the hR-TP, the resection limit of the jejunum was passed upwards behind the colon through the incision in the right side of the transverse mesocolon, and hepaticojejunostomy and gastrojejunostomy were performed. A peritoneal drainage tube (6.3-mm J-VAC Suction Reservoir R; Johnson and Johnson, Somerville, NJ) was placed in all patients. After TP, patients routinely took orally pancreatic digestive enzyme drug (ex Lipacreon R, Abbott Laboratories, Abbott Park, IL). Adjuvant chemotherapy was performed regarding the previous studies [16,17]. Basically, gemcitabine (Gemzar R, Eli Lilly and Company, Indianapolis, IN.) was used until 2012 [16], after that S-1 (TS-1R, TAIHO Phamaceutical Co., Ltd, Tokyo, JAPAN) was used [17]. The median computed tomography (CT) attenuation value of the liver parenchyma was measured on plain CT using a five-point scale, preoperatively and at 6 and 12 months after TP. Fatty liver disease was defined as a hepatic CT number of <40 HU [18].

Data collection

Operative and postoperative data were prospectively collected and stored in an electronic database. The American Joint Committee on Cancer (AJCC) stage was recorded for each tumor. Postoperative complications of grade IIIa or higher according to the Clavien scale were recorded [8].

Statistical analysis

Descriptive statistics are presented as the median (range) or number (%). Data were analyzed using SAS software (version 9.1; SAS Institute Inc., Cary, NC). Parameters were compared between patient groups using the Mann–Whitney *U* test or Fischers' test. Overall survival was measured from the date of TP to the date of death from any cause or the last follow-up. Patients were censored at the last follow-up if they were still alive. Survival rates were calculated using the Kaplan–Meier method, and the statistical significance of differences was determined using the log-rank test. Differences were considered statistically significant at $P < 0.05$.

Results

Patient and tumor characteristics

Table 1 shows the patient and tumor characteristics. The median patient age and the sex distribution were not significantly different between the O-TP ($n = 12$) and the R-TP ($n = 8$) groups. The body weight and body mass index did not show significant differences between the two groups. The preoperative incidence of diabetes, hemoglobin A1c (HbA1c) and treatment of diabetes were not significantly different between the O-TP and the R-TP patients (Table 1). Table 2 indicates diagnosis for operation. In the R-TP group, the initial operation was for pancreatic adenocarcinoma in 7 patients (stage IIA in 4 patients, stage IIB in 4 patients), and IPMC in one patient (stage IB). The median time from the initial operation to the R-TP was 30 months (range, 21–86 months). In the O-TP group, 10 patients had pancreatic adenocarcinoma (stage IIA in 5 patients, stage IIB in 5 patients) and 2 patients had IPMC (stage IB). The R-TP was performed for pancreatic adenocarcinoma in 8 patients (stage IIA in 5 patients, stage IIB in 3 patients). The diagnoses and cancer stages were not significantly different between the two groups.

Operative outcomes

The operative findings are shown in Table 3. The operative time was not significantly different between the 4 patients who underwent the hR-TP (544 min, range 453–741 min) and the 12 patients who underwent the O-TP (586 min, range 378–784 min). However, the operative time was significantly shorter in the 4 patients who underwent the tR-TP (369 min, range 208–426 min) than in the patients who underwent the O-TP. Similarly, the amount of operative bleeding was not significantly different between patients who underwent the hR-TP (698 g, range 488–1317 g) and patients who underwent the O-TP (703 g, range 376–1266 g). However, the patients who underwent the tR-TP (318 g, range 82–678 g) showed significantly less bleeding than those who underwent the O-TP. TP was planned pre-operatively in 9 (7 pancreatic adenocarcinoma and 2 IPMC) of the 12 O-TP patients (75%) for extent tumors, the 4 hR-TP patients (100%) and the 4 tR-TP patients (100%), respectively. On the other hand, the O-TP as completion for margin positive disease were performed in 3 pancreatic adenocarcinoma patients. Splenectomy was performed in 9 of the 12 O-TP patients (75%) and the 4 tR-TP patients (100%), respectively. Resection and reconstruction of the PV and SMV were performed in 5 patients

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