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Original Research

Short- and mid-term outcomes of robotic versus laparoscopic distal pancreatosplenectomy for pancreatic ductal adenocarcinoma: A retrospective propensity score-matched study

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ABSTRACT

Background: Robotic distal pancreatectomy exhibits short-term benefits over laparoscopic distal pancreatectomy. The use of minimal invasive techniques to carry out distal pancreatosplenectomy (DPS) for pancreatic ductal adenocarcinoma (PDAC) remains controversial and has not gained popular acceptance. A comparative study was designed to analyze the short- and mid-term outcomes of robotic DPS (RDPS) versus laparoscopic DPS (LDPS) on patients with PDAC.

Methods: The baseline characteristics, perioperative outcomes and survival data among patients who underwent RDPS (n = 35) versus LDPS (n = 35) for PDAC between December 2011 and December 2015 were compared after a 1:1 propensity score matching.

Results: There were no significant differences in the operative time, blood loss, blood transfusion rate, and morbidity and pancreatic fistula rates between the RDPS and LDPS groups. RDPS significantly reduced the rate of conversion to laparotomy (5.7% vs. 22.9% when compared with LDPS, $p = 0.04$). There were no significant differences in R0 resection rates, number of harvested lymph nodes, positive to harvested lymph node ratios, and disease-free survival and overall survival rates between the two groups. A Cox proportional hazards analysis showed N1 stage to be significantly associated with worse survival and suggested that chemotherapy might prolong overall survival in these PDAC patients.

Conclusions: This single-center study demonstrated that RDPS was safe and efficacious in treatment of PDAC. When compared with LDPS, RDPS was associated with a reduced rate of conversion to open surgery. There were no significantly differences in oncological outcomes and mid-term survival rates between the groups of patients who underwent RDPS or LDPS.

1. Introduction

Pancreatic ductal adenocarcinoma (PDAC) is an aggressive malignancy characterized by late diagnosis and poor prognosis [1,2]. Surgical resection remains the only potential curative treatment for PDAC although it can be performed only in about 20% of patients [1–3]. Pancreatic surgery is one of the most challenging abdominal operations with high perioperative and mortality rates [1,4].

Recent developments in laparoscopic instruments and techniques has made laparoscopic pancreatic surgery to become widely accepted by surgeons [5]. As laparoscopic distal pancreatectomy only requires limited dissection around splenic vessels and it does not require any reconstruction, it has been more commonly applied in pancreatic cancers than laparoscopic pancreaticoduodenectomy [6,7]. Increasing evidence has shown that, when compared with open distal pancreatectomy, laparoscopic distal pancreatectomy significantly reduces blood loss, length of hospital stays and postoperative complication rates [8–11]. Recent data suggest that laparoscopic distal pancreatosplenectomy (LDPS) is safe and effective to treat distal PDAC, and the short- and long-term oncologic outcomes are not inferior to those in open

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procedures [11–16].

Robotic technology overcomes many inherent limitations of laparoscopic surgery [17]. An increasing number of studies have demonstrated that robotic distal pancreatectomy is technically safe and feasible when compared with laparoscopic distal pancreatectomy in clinical and pathological outcomes [18–20]. Nevertheless, very few studies have reported the oncological and survival outcomes after robotic distal pancreatosplenectomy (RDPS), and data comparing RDPS with LDPS to treat patients with PDAC are lacking. This 1:1 case–control study matched by propensity score was performed at a high-volume pancreatic center to compare the short- and mid-term outcomes of RDPS and LDPS for PDAC.

2. Patients and methods

From December 2011 to December 2015, 38 patients with PDAC underwent LDPS and 86 patients with PDAC underwent RDPS at our institution. All patients were preoperatively evaluated by two highly experienced surgeons (Dr. LR and Dr. ZZ) and had to be eligible for both minimally invasive approaches. After we explained the advantages and disadvantages, the possible complications and the costs of RDPS and LDPS to the patients, the patients made their decisions to receive either robotic or laparoscopic surgery and gave written informed consents for the operation and for their data to be used for research purposes.

The study was approved by the Institutional Review Board of Chinese People's Liberation Army (PLA) General Hospital. An 1:1 propensity score matching based on the patients' age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, and tumor size was conducted on 35 patients who underwent RDPS and 35 patients who underwent LDPS for PDAC. The work has been reported in line with the STROCSS criteria [21].

2.1. Selection of the procedure

Computer tomography (CT) and/or magnetic resonance imaging (MRI) were used for preoperative diagnoses and to evaluate resectability of PDAC [3]. The inclusion criteria were: 1) over 18 years old, 2) resectable ductal adenocarcinoma of the pancreatic body and tail in accordance with the National Comprehensive Cancer Network (NCCN) guidelines, and 3) compliance with the American Society of Anesthesiologists score (ASA) of < 3. The exclusion criteria were: 1) neoadjuvant therapy, 2) extensive intra-peritoneal or extra-peritoneal metastases, and 3) presence of associated serious cardiopulmonary or hepatorenal insufficiency. Tumor invasion of adjacent organs was not considered a contraindication to surgery.

2.2. Perioperative details

The demographic data, perioperative outcomes and survival data were prospectively entered into a database and they were retrospectively analyzed. These data included: gender, age, ASA, body mass index (BMI), largest tumor size, estimated blood loss (EBL), blood transfusion, rate of conversion to open surgery, operation time (OT), resection margin status, number of harvested lymph nodes, positive to harvested lymph node ratio, postoperative complications, postoperative pancreatic fistula (POPF), length of postoperative hospital stay (PHS) after surgery, readmission rate within 90 days, 90-day mortality rate, and overall survival (OS) and disease-free survival (DFS) rates.

2.3. Definitions

Postoperative complications were graded using the Clavien–Dindo classification. Major complications were defined as events requiring surgical, endoscopic, or radiological intervention (Clavien–Dindo classification ≥3) [22]. The grading for postoperative pancreatic fistula was based on the International Study Group of Pancreatic Fistula (grades A, B, and C) [23]. R1 resection was defined when the tumor extension was within 1 mm of the resection margin. The TMN staging followed the American Joint Committee on Cancer [24].

2.4. Treatment and follow up

For distal pancreatic adenocarcinoma, the radical antegrade modular pancreatosplenectomy approach was used to achieve better oncological surgical clearance [25,26]. Our surgical procedures of RDPS and LDPS have been described previously [11,27]. In patients who had tumor invasion to adjacent organs, extended en bloc resection of these adjacent organs was performed.

All robotic surgical procedures were performed using the Da Vinci Si Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) by an assigned surgical team including three highly experienced pancreatic surgeons. All laparoscopic DP were performed by the same surgical team to reduce the performance bias in this study. At the start of the study, we had already performed 50 LDPS and 10 RDPS.

Systemic chemotherapy was routinely offered to all the patients who were physically fit enough to receive it between 4 and 8 weeks after surgery. If the patients consented to receive adjuvant therapy, intravenous infusion of gemcitabine was given at a dose of 1000 mg/m^2 on day 1, day 8 and day 15, followed by a resting period of 1 week. Treatment was continued until unacceptable toxicity, patient refusal, documented progressive disease or a maximum of six cycles had been given, whichever happened first.

All patients were followed up once every 3 months in the first year and then at 6-month intervals thereafter. All patients who failed to attend the outpatient visits were contacted by telephone. Recurrences or metastasis were diagnosed using a combination of imaging examinations and serum tumor biomarkers. These patients were followed up until death or the date when this study was censored on June 30, 2017.

2.5. Statistical analysis

Continuous variables were presented either as mean ± SD or as median, interquartile range (IQR) as appropriate. The student's *t*-test was applied to compare normally distributed variables, whereas the Mann–Whitney *U* test was used for non-normally distributed variables. Categorical data were analyzed using the Chi-squared test or the Fisher's exact test. Survival analyses were performed using the Kaplan–Meier method and validated using the log-rank test. A Cox proportional hazards analysis was applied to investigate prognostic factors of overall survival after surgery. Patients who were lost to follow up or those who had died from non-cancer-related causes were censored.

To minimize the impact of potential confounders and selection bias, the propensity score analysis was used to compensate the differences in baseline patient characteristics between the two groups of patients. A propensity score was calculated by logistic regression, and covariates like age, sex, body mass index (BMI), ASA score and tumor size were matched. An 1:1 nearest neighbor matching was used to select the participants in the two groups of patients. All statistical analyses were performed using SPSS v22.0 (SPSS Inc., Chicago, IL, USA). A P value < 0.05 was considered as statistically significant.

3. Results

3.1. Patient characteristics

Before matching, patients in the LDPS group were predominantly male (65.8% vs. 46.5%, $p < 0.05$) and had a smaller tumor size (4.35 ± 2.3 cm vs. 5.16 ± 1.96 cm, $p < 0.05$) than those in the RDPS group. There were no significant differences between the two groups in age, BMI, and ASA score. This propensity score matching study