Clinics in Surgery

Research Article
Published: 20 Nov, 2019

The Evaluation of Laparoscopic Radical Pancreaticoduodenectomy for Pancreatic Head Cancer with Programmed Process

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Abstract

Objective: To evaluate the safety and availability of laparoscopic radical pancreaticoduodenectomy following programmed process.

Methods: 38 cases with pathologically confirmed pancreatic ductal adenocarcinoma who had undergone Laparoscopic Radical Pancreaticoduodenectomy (LRPD) in Sun Yet-Sen Memorial Hospital from January 2016 to May 2018 were retrospectively analyzed. Several indicators of perioperative period were analyzed.

Results: 38 cases were successfully performed under total laparoscopy. The average operation time was (281.0 ± 76.0) min, blood loss was (138.2 ± 144.0) ml, acquired lymph node was (15.1 ± 9.0), the postoperative exhaust time was (50.4 ± 12.1) h, and the average postoperative hospital stay was (11.3 ± 3.3) days. No grade C pancreatic fistula was found in the group.

Conclusion: Followed accurate preoperative evaluation, procedural procedure of laparoscopic radical pancreaticoduodenectomy is safe and feasible.

Keywords: Laparoscopic surgery; Pancreatic head cancer; Pancreaticoduodenectomy; Programmed process

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Received Date: *28 Oct 2019*
Accepted Date: *13 Nov 2019*
Published Date: *20 Nov 2019*

Citation:
Guolin L, Shangyou Z, Iusheng W, Qing L, Quanbo Z, Rufu C. The Evaluation of Laparoscopic Radical Pancreaticoduodenectomy for Pancreatic Head Cancer with Programmed Process. Clin Surg. 2019; 4: 2663.

Introduction

Pancreatic cancer remains to be one of the highest lethal malignancies. Pancreaticoduodenectomy is the standard method for the treatment of pancreatic head cancer, and it is the only possible method to cure pancreatic head cancer. With the development of surgical techniques, the safety and effectiveness of laparoscopic pancreaticoduodenectomy have been recognized by most experts. However, based on the neurotropic characteristics of pancreatic cancer, radical operation of pancreatic head cancer has put forward higher requirements for traditional pancreaticoduodenectomy. We are one of the earliest members to perform Laparoscopic Pancreaticoduodenectomy (LPD) in China; over 400 cases of LPD had been successfully performed from the very beginning. Benefit from the long-time experience in practice, we had gradually formed characteristic surgical process for LPD with programmed design, and gradually applied the procedural procedure in laparoscopic radical pancreaticoduodenectomy. Here we summarize 38 cases of PDAC patients who underwent Laparoscopic Radical Pancreaticoduodenectomy (LRPD) in our institution. The primary purpose of this study is to verify the feasibility and safety for programmed LRPD and study the benefits of perioperative and overall survival from this novel programmed laparoscopic resection for pancreatic head cancer.

Materials and Methods

General data

The complete data of 38 patients with pathologically confirmed pancreatic ductal adenocarcinoma who had undergone laparoscopic radical pancreaticoduodenectomy in Sun Yet-Sen Memorial Hospital from January 2016 to May 2018 were retrospectively analyzed. Details including gender, age, jaundice, diabetes, the existence of lumbago, etc.

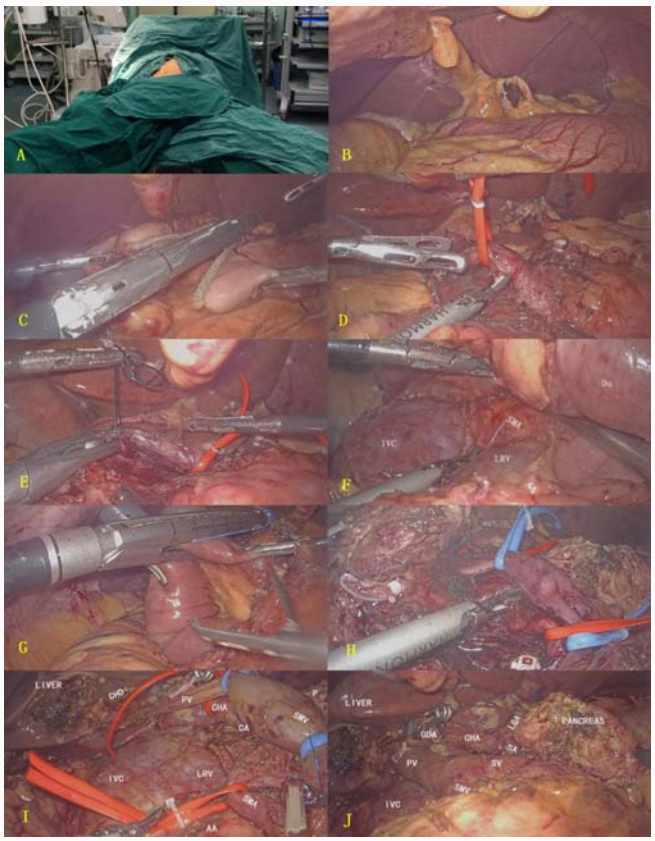

Figure 1: Brief surgical procedure for LRPD.
A: Supine, straddle and reverse Trendelenburg position, B: Suspend the ligamentum teres hepatis and left liver, C: Transect the stomach with GIA, D: Identify and tape CHA, E: Management of GDA, F: Expose IVC, LRV and the origin of SMA, G: Transect the jejunum with GIA, H: Separate the unciform process from the mesenteric vessels, I,J: Surgical field after resection.
LPRD: Laparoscopic Radical Pancreaticoduodenectomy; CHA: Common Hepatic Artery; GDA: Gastroduodenal Artery; IVC: Inferior Vena Cava; LRV: Left Renal Vein; SMA: Superior Mesenteric Artery; SMV: Superior Mesenteric Vein; PV: Portal Vein; CHD: Common Hepatic Duct; AA: Aorta abdominalis; CA: Coeliac Artery; LGA: Left Gastric Artery; SA: Spleen Artery; SV: Spleen Vein

Pre-operative assessment and management

Tumor markers including CA19-9, CEA, AFP and CA12-5 were measured. Computed Tomography with Angiography (CTA) and Magnetic Resonance imaging with Cholangiopancreatography (MRCP) were routinely performed. Preoperative bile drainage was performed in patients with a serum Total Bilirubin (TB) level of ≥ 220 μmol/L.

Surgical strategy and procedure

According to our laparoscopic experience on pancreatic head cancer, simplify the operative procedure is of great importance, individualized surgical approach and programmed surgical dissection are deserved to become the standard specification for laparoscopic radical pancreaticoduodenectomy. In our programmed surgical procedure, The PV-SMV axis or its projection could almost be seen throughout the surgical process, which is also called "PV-SMV approach". At the same time, the CHA and SMA are taken as the axis to perform the nerve & lymph dissection.

- The brief surgical procedures (without vessel resection) were showed bePlace the patient in a supine, straddle and reverse Trendelenburg position (30°-45°) (Figure 1A). Usually 5 trocars are needed. The surgeon stands on the right side of the patient while the assistant stands on opposite side, and the scope holder stands between the patient's legs.

- Establish pneumoperitoneum and then thoroughly explore the abdomen to exclude metastasis. Suspend the ligamentum teres hepatis and left liver to gain a better surgical exposure (Figure 1B). Orderly naked the greater curvature and lesser curvature then transect the stomach with GIA (Figure 1C).

Dissect the upper margin of the pancreas; identify the iconic lymph nodes in order to locate the CHA and portal vein. After taping the vassal, dissection can be performed towards the left side until the celiac trunk and its branches are all exposed into view (Figure 1D). Then dissection is turned to the right side and the gastroduodenal artery is management (Figure 1E), followed by skeletonization of the front and left side of ligament hepatoduodenal.

Anatomize the inferior margin of the pancreas and recognize the superior mesentery vein, create a post-pancreatic tunnel along the surface of SMV. Then transect the pancreas.

Sufficient Kocher maneuver is performed to isolate the duodenum, expose inferior vena cava, left renal vein and the origin of superior mesenteric artery (Figure 1F). Divide the Treitz ligament and transect the jejunum from the right side (Figure 1G).

Orderly dissect and tape SMV and SMA, carefully separate the uniform process from the mesenteric vessels, and perform dissection along the sheath of SMA towards the root, special attention should be given to the area between the original of SMA and CA, which is the most abundant area of the abdominal plexus and also the most frequent area for relapse (Figure 1H).

Fully skeletonize the hepatoduodenal ligament from the right and back side. Divide the gallbladder and transect hepatic duct, remove the whole specimen and finish the resection processes (Figure 1I and J).

Follow the child method to complete the digestive reconstruction (Pancreaticojejunostomy- Pancreaticojejunostomy-Gastrojejunostomy) after the reconstructions, two double-lumen drainages are emplaced, one in the hepatorenal recess, just posterior to the hepaticojejunostomy, and the other anterior to the pancreaticojejunostomy. It is better to put the tips of the two drainages cross each other.

Postoperative adjuvant therapy

Postoperative adjuvant chemotherapy was performed with standard GS regimen (Gemcitabine, D_1 and D_8 combined with S-1, D_1 to D_{14} (21 days per cycle, for six cycles). In the case of local recurrence or distant metastasis, appropriate treatment strategies were selected according to the latest NCCN Clinical Practice Guidelines in Oncology.

Follow-up

Strictly implement the concept of Enhanced Recovery after Surgery (ERAS) during the perioperative period, which including perioperative nutritional support, body fluid balanced, post-operative analgesia, management of various tubes, etc. Follow-up was performed at each cycle of chemotherapy and every 2-3 months thereafter. Routine blood tests, tumor markers, liver and kidney function, abdominal ultrasound and chest radiographs were routine examinations; enhanced CT/MR scans were performed for every

three cycles of chemotherapy or every 6 months.

Statistical analysis

Statistical analyses were performed using SPSS Statistics 16.0 (IBM Chicago, IL, USA). The Fisher's exact test for non-parametric variables, was considered statistically significant since two-sided value of P is smaller than 0.05.

Results

General data

Among these 38 patients, 20 were male and 18 were female, with an average age of (61.1 ± 9.2) years old. Among them, 14 patients had diabetes, 31 patients had jaundice of varying degrees, and 23 patients suffered obvious lumbago (Table 1).

Intra-operative conditions

The average operation time was (281.0 ± 76.0) min and the intraoperative blood loss was (138.2 ± 144.0) ml, of the 38 patients, only 6 (15.8%) required blood transfusion mainly due to moderate or severe anemia before surgery (Table 2).

Postoperative recover and complications

All 38 cases were pathologically diagnosed as pancreatic ductal adenocarcinoma. Diagnosis and grading of pancreatic fistula were based on the diagnostic criteria established by the International Study Group on Pancreatic Fistula (ISGPF). For the Pancreatic fistula complications, only seven patients (18.4%) developed biochemical leakage after the surgery, along with 4 (8.89%) in grade B, and 0 in grade C in the group. Other complications included bile leak (n=2, 5.26%), delayed gastric emptying (n=3, 7.89%), abdominal abscess (n=1, 2.63%), and wound infection (n=2, 5.26%). The acquired lymph nodes were (15.1 ± 9.0), the postoperative exhaust time was (50.4 ± 12.1) h, and the average postoperative hospital stay was (11.3 ± 3.3) days. Only one patient (2.63%) required reoperation due to bleeding of gastroduodenal stump during hospitalization, no perioperative death was found in three months after surgery (Table 3).

Survival

During the follow-up (range from 12 to 30 months) till April 2019, the 1-year survival rate was 76.3% and the 1-year disease-free survival rate was 63.2%.

Table 1: General data of 38 patients.

General data	Cases (n=38)
Sex, M:F	20:18
Age, mean ± SD, yr	**61.1 ± 9.2**
Diabetes	14 (36.8%)
Jaundice	31 (81.6%)
Lumbago	23 (60.5%)

Table 2: Intra-operative conditions in 38 patients.

Items	Results
Operative time (min, mean ± SD)	**281.0 ± 76.0**
Intraoperative blood loss (ml, mean ± SD)	**138.2 ± 144.0**
Percentage of patients requiring blood transfusion (n, %)	6, 15.8
Total retrieved LNs (mean ± SD)	**15.1 ± 9.0**

SD: Standard Deviation

Table 3: Morbidity and Mortality in 38 patients.

	Cases
Postoperative hospital stay (mean ± SD, d)	**11.3 ± 3.3**
In-hospital death (n, %)	0, 0
Re-operation (n, %)	1, 2.63
Postoperative exhaust time (mean ± SD, h)	**50.4 ± 12.1**
Complications	
Pancreatic fistula (ISGPF) (n, %)	
BL	7, 18.4
B	4, 10.5
C	0, 0
Bile leak (n, %)	2, 5.26
Delayed gastric emptying (n, %)	3, 7.89
Intra-abdominal bleeding (n, %)	1, 2.63
Intestinal fistula (n, %)	0, 0
Intra-abdominal abscess (n, %)	1, 2.63
Wound infection (n, %)	2, 5.26
Intractable diarrhea (POD 3 mo, n, %)	1, 2.63

ISGPF: International Study Group on Pancreatic Fistula; SD: Standard Deviation; POD: Postoperative Day

Table 4: Analysis of the short-term prognosis in 38 patients.

	Case (n, %)
Death within 1 post-operative year (n, %)	9, 23.7
Recurrence within 1 post-operative year (n, %)	14, 36.8

Discussion

Pancreatic cancer is one kind of highly lethal tumors. Surgical resection offers the only potential curative therapy for pancreatic malignant tumors. Although biological researches and diagnostic techniques of pancreatic cancer have been optimized, the overall rate of resectable operation and survival of pancreatic head cancer have not been improved [1,2]. In the past decades, successive generations of pancreatic surgeons have developed the radical surgical skills including extended lympadenectomy [3], synch ronous en bloc venous resections [4], and vascular resection [5,6] as so to improve the long-term survival. However, the benefit of long-term survival stays doubtful, which needs more convincing evidence. One of potential reasons is that lymphatic metastasis and perineural micrometastasis would happen in the small pancreatic tumors at the very early stage. Indeed, pancreatic cancer has extensive perineural invasion properties, and Perineural Invasion (PNI) exists in 90% to 100% of pancreatic head cancer [7,8]. The current researches suggested that the neurotropic property was one of inherent biological characteristics of pancreatic cancer, nothing to do with the diameter, location, histological grade of tumors or the situation of lymphatic involvement [9,10]. PNI plays an important role in local recurrence and is an independent prognostic factor even curative resection has been performed [11]. Peripancreatic nerve dissection may have important significance in the radical resection of pancreatic cancer. Since the first laparoscopic pancreaticoduodenectomy was reported in 1994 [12], the global enthusiasm for performing LPD has been increasing. Minimally invasion techniques for pancreatic head cancer was doubted for the potential benefits like less postoperative complications and shorter hospital stays, compared to the other gastrointestinal tumors [13,14]. However, some data from single high-volume pancreatic centers with well experienced pancreatic surgeons supported that LPD is feasible and safe when compared to

Open Pancreaticoduodenectomy (OPD). Besides, LPD could lower the intraoperative blood loss and blood transfusion, decrease the intensive care unit stay and postoperative morbidity rate, and shorter the total hospital stay [15-17]. Although the appropriate patients are more likely to be selected for some surgeons in the learning curve of LPD, indications and contraindications of LPD are equal with OPD's for others with sufficient pancreatic surgical experience. Vascular resection and reconstruction and multi-visceral resection are also feasible and safe in LPD [18]. Beyond all doubt, minimally invasion pancreaticoduodenectomy is appropriate for radical surgical resection of Pancreatic Ductal Adenocarcinoma (PDAC). In 2014, Croome et al. [19] reported similar outcomes between LPD (n=108) and OPD (n=214) for PDAC. In except of benefits mentioned above, longer progression-free survival was found in the LPD group. The operative time, radical resection rate, resected lymph and positive nodes were similar between LPD and OPD. Instead, there was a significantly higher proportion of patients who had a delay to pursue adjuvant treatment in OPD group comparing to LPD. Technically speaking, LPD totally meets the criterions for radical resection of pancreatic head cancer, including the extent of lymph node resection and negative resection margin (R0). However, there are seldom researches involving in investigating the feasibility and safety of peripancreatic nerve dissection in LPD. In this paper we summarize 38 cases of PDAC patients who underwent Laparoscopic Radical Pancreaticoduodenectomy (LRPD) in our institution since January 2016 to July 2018. Based on our experience on peripancreatic nerve dissection, we put forward a novel programmed laparoscopic radical pancreaticoduodenectomy centering on Portal Vein-Superior Mesenteric vein (PV-SMV) axion among the resection process, and Common Hepatic Artery (CHA) axion and Superior Mesenteric Artery (SMA) axion among the dissection process. According to the preliminary results, the operation time of this group was slightly longer than that of conventional laparoscopic pancreaticoduodenectomy, and the blood loss was not significantly increased. The number of lymph nodes obtained by surgery was significantly higher than the required standard, postoperative exhaust time and postoperative hospital stay were respectively (50.4 ± 12.1) h and (11.3 ± 3.3)days, which were superior to OPD reported in the literature. At the same time, there was no significant increase in surgical complications, and no c-grade pancreatic fistula was found in this group. In addition, the short-term results such as the 1-year survival rate and the 1-year disease-free survival rate were better than that reported in the relevant literature. Based on the neurotropic characteristics of pancreatic cancer and the distribution of peritoneal nerve plexus, radical pancreaticoduodenectomy is significantly different from conventional pancreaticoduodenectomy in terms of neurolymphatic dissection. The celiac nerve plexus is mainly distributed in the area between the root of the celiac trunk and the superior mesenteric artery, which is an important cause of cancer pain and postoperative recurrence in patients with pancreatic head cancer. Therefore, it is necessary to carry out targeted dissection according to the anatomical characteristics, and design reasonable surgical approaches and operation procedures.

1. Benefit from abundant cases of LPD and open experience for pancreatic head carcinoma and, we gradually form our characteristic surgical process, this procedural process, take full advantages of the laparoscopic view, effective optimize the surgical details, and reduce the unnecessary exposure for each operative field. While guarantee the quality of operation, we obviously shorten the operation time. The innovation and key points of this procedure are showed belThe surgical resection is carried out closely around the PV-SMV axis, which can be seen in the surgical field almost throughout the operation.

2. The dissection process is carried out closely around the CHA axes and the SMA axes (which is in line with the distribution of celiac plexus).

3. Vessel suspension technique and arterial-venous crossing technique are helpful for dissection and protecting the vessels.

4. Maximizing the use of each surgical field and avoiding repeated exposure would be of great importance.

5. Reducing the interference in the lower colon region would be beneficial to postoperative recovery.

Because of the complex anatomical structure around the ampulla, normally the liver and stomach are covered on the surface of the pancreas, suspension of the left hepatic lift and ligamentum teres hepatis can provide perfect operative exposure. Preferential transaction of the stomach is beneficial to expose the common hepatic artery and celiac trunk, and it also provides great convenience for local dissection. The severed pancreas is conducive to fully exposing and protecting the PV-SMV axis, at the same time facilitating radical neurolymphatic dissection. By pulling and dividing the jejunum to the right side, interference for the intestine would reduce, which is conducive to postoperative recovery. On the other hand, the separation of the uncinate process from the upper mesenteric vessels is easier after the intestine is dislocated. Removing the gallbladder and separating the bile duct at last can minimize the bile pollution in the surgical field, reduce the incidence of postoperative abdominal infection, and avoid the possible damage of abnormal blood vessels to the greatest extent. The implementation of the procedural process is inseparable from the tacit cooperation of the surgical team, including the cooperation of the surgeon, the assistant, the surgical nurse, and the anesthesiologist. Tacit surgical cooperation cannot be cultivated overnight, which explains why LPD is recommended to be carried out orderly in large medical centers, preferably in large pancreatic centers. At the same time, strict individualized surgical planning before surgery is also one of the guarantees to ensure the smooth operation. However, this procedural surgical procedure is not suitable for all the cases of pancreatic head cancer. For those cases with obvious acute inflammation, vascular invasion, or relatively large tumors, there are deficiencies or imperfections in this surgical procedure. Therefore, different surgical approaches and resection methods should be selected according to the actual situation of each case, that is, procedural procedures for different cases.

Funding

This work was supported by the National Natural Science Foundation of China, No. 81802419.

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