ORIGINAL ARTICLE

Laparoscopic Hand-assisted Total Pancreatectomy: Single Institution Experience of Seven Patients

Sujit Kulkarni[1], Kaylene Barrera[2], Rick Selby[1], Dilipkumar Parekh[1]

[1]Department of Surgery, Keck Medical Center, University of Southern California, Los Angeles, United States

[2]SUNY Downstate Medical Center, New York City, New York, United States

ABSTRACT

Background In the past two decades, total pancreatectomy has been associated with improved postoperative and long-term outcomes due to the improvements in surgical technique, better enzyme preparations and diabetes control. While minimally invasive Whipple operation has enjoyed the attention in recent years, the safety and feasibility of a minimally invasive total pancreatectomy is still not established. **Methods** A retrospective review of minimally invasive total pancreatic resections. **Results** Seven patients underwent laparoscopic hand-assisted total pancreatectomy between 2005 and 2011. The mean patient age was 58.1 years (58.1 ± 6.45) and the median American Society of Anesthesiologist score was 3. Three patients had diffuse IPMN, two had multiple neuroendocrine tumors and two patients had large cystic lesions in head, body and tail of pancreas. Median operative time was 431 minutes (range 348-590) with 300 cc (range 150-1200) of blood loss. The 90 days postoperative complication rate of grade 2 or higher Clavien-Dindo classification was 14% and the mortality was 0. **Conclusion** The laparoscopic hand-assisted total pancreatectomy appears to be a safe and feasible procedure. It is a technically demanding procedure requiring expertise in both open and advanced laparoscopic pancreatic procedures and additional multi-institutional studies are necessary to further evaluate its role.

INTRODUCTION

Total Pancreatectomy (TP), first described in 1943 [1], enjoyed a brief period of popularity in the 1970's for the treatment of pancreatic adenocarcinoma which at the time was thought to be multi-centric in origin. It was also advocated in lieu of the Whipple operation to reduce postsurgical anastomotic complications. Substantial morbidity rates from exocrine and endocrine insufficiency and lack of data showing a survival advantage over a pancreaticoduodenectomy led to the abandonment of this procedure in patients with pancreatic adenocarcinoma [2, 3, 4]. Advances in the surgical techniques, new pancreatic enzyme preparations and improved control of diabetes have led to a wider application of total pancreatectomy in the past two decades. At present acceptable indications for total pancreatectomy include patients requiring prophylactic total pancreatectomy due to a history of familial pancreatic cancer, chronic pancreatitis patients undergoing a total pancreatectomy with autologous islet cell transplantation and patients with multicentric neoplasms of the pancreas such as main duct IPMN, and neuroendocrine tumors [2, 3, 4].

Complex laparoscopic pancreatic surgery has now evolved into mainstream practice with a number of centers in the USA and elsewhere performing advanced procedures such as the Whipple operation, distal pancreatectomy, tumor enucleation and pancreatic necrosectomy laparoscopically. It is our assessment that in the next decade, the vast majority of the pancreatic surgical procedures will be performed laparoscopically as expertise with advanced laparoscopic pancreas surgery is gained in the wider community of hepatobiliary and pancreatic surgeons. Advanced laparoscopic pancreatic surgery has been shown to be safe in the publications from several centers with large experience with similar or better outcomes than open surgery and for some procedures such as laparoscopic distal pancreatectomy, the minimally invasive technique appears to be associated with better outcomes compared to the open procedure [5]. Similar experience has been reported where the da Vinci robot system has been utilized for the minimally invasive approach to pancreatic resections. Total pancreatectomy is relatively uncommon procedure and only a few small series and anecdotal case reports have been published of minimally invasive total pancreatectomy [6, 7, 8, 9]. In this series we describe the largest experience to date

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Abbreviations TP Total Pancreatectomy; EUS Endoscopic Ultrasound; SMV Superior Mesenteric Vein; PHA Proper Hepatic Artery; GDA Gastro-Duodenal Artery; CBD Common Bile Duct; SMA Superior Mesenteric Arterial; PCA Patient Controlled Analgesia; ASA American Society of Anesthesiology; IPMN Intraductal Papillary Mucinous Neoplasm; PSM Propensity Score Matching; NETs Neuroendocrine Tumours
Correspondence Sujit Kulkarni
Department of Surgery, Keck Medical Center,
University of Southern California, Los Angeles,
United States
Tel +323 442 7172
Fax +323 442 7173
E-mail Sujit.kulkarni@med.usc.edu

of laparoscopic hand-assisted total pancreatectomies reported from the USA.

PATIENTS AND METHODS

Patients

A total of twenty-one patients underwent TP during the period 2005 through 2011 at our institution by a team of five pancreatic surgeons. The choice of open or laparoscopic procedure was at the discretion of the individual surgeon. The seven patients who underwent laparoscopic hand-assisted TP by a single surgeon are included in this study. This is a retrospective review. Data collection was approved by the University Institutional Review Board and confidentiality was maintained according to the HIPPA guidelines. The operative indications were based on the multicentricity of the disease with diffuse involvement of the pancreas, the absence of tumor extension to the superior mesenteric vein, superior mesenteric artery or hepatic artery and the absence of bulky extra-pancreatic disease. Preoperative imaging workup included ultrasound, pancreatic protocol computed tomography and/or magnetic resonance imaging. Any patient under the age of 65 with cardiopulmonary disease and all patients over the age of 65 underwent a cardiopulmonary evaluation for preoperative clearance. Patients also underwent endoscopic ultrasound evaluation after 2009 since we did not have that facility prior to 2009. Indications and Endoscopic Ultrasound (EUS) findings are summarized in **Table 1**. The peri-operative data was acquired from the hospital electronic records and paper charts and postoperative complications were graded using the Clavien-Dindo classification.

Operative Technique

The patient was placed in a supine position and the surgeon stood on the right side of the patient, with the first assistant and the scrub-nurse standing on the left side and the right side of the patient, respectively. A right sub-costal incision (6-7cm) was made for a Gelport® and three trocars are placed as shown in the **Figure 1**. A diagnostic laparoscopy was initially performed to evaluate for the metastasis or locally advanced disease. Any suspicious lesions were biopsied and sent for intraoperative frozen section histology. The patient was placed in a reverse Trendelenberg position at 200 and slightly tilted to the right side. The cholecystectomy was performed in a usual fashion. The gastro-colic ligament was opened with a Harmonic™ scalpel (Ethicon Endo-surgery, Blue Ash, OH) to enter the lesser sac. This opening was extended from the first part of duodenum to the fundus of the stomach and the short gastric vessels were taken down with a Harmonic scalpel or a surgical stapler if splenectomy was performed. The splenic and hepatic flexures of the transverse colon were mobilized. The Kocher maneuver was performed. The inferior border of the pancreas at the neck of the pancreas was mobilized to expose the Superior Mesenteric Vein (SMV). A retro-pancreatic tunnel was created in front of the SMV. The hepato-duodenal ligament was dissected to identify the Proper Hepatic Artery (PHA), Gastro-Duodenal Artery (GDA) and the Common Bile Duct (CBD). The gastro duodenal artery was doubly clipped and divided between the clips or transacted with the surgical stapler. The common bile duct was transacted. The neck of pancreas was completely separated from the portal vein by completing the retro-pancreatic tunnel dissection. The right gastro-epiploic vessels and the right gastric vessels were divided between clips. Published studies with the Whipple operation have shown that there is no long-term functional or survival advantage with the pylorus-preserving procedure compared to a standard Whipple operation that incorporates an antrectomy. Furthermore, patients with a standard Whipple operation appear to have a lower incidence of gastro-paresis [10]. Based on

Table 1. Indications for laparoscopic TP and final pathologic diagnosis.

Patient	Indication/Lesion type	Location	Range of size of lesions (cm)	EUS report with biopsy	Total Lymph nodes (positive for tumor)	Margins	Final Pathology
1	Diffuse main duct IPMN	Entire gland	0.5-3.5	Cysts with main duct IPMN, cytology inconclusive	29 (0)	Clear	Papillary adenocarcinoma from main duct IPMN
2	Multiple neuro-endocrine tumors	Entire gland	0.5-3.0	Not available	9 (0)	Clear	Islet cell tumor
3	Multiple neuro-endocrine tumors	Entire gland and liver	0.5-3.5	Not available	33 (28)	Clear	Carcinoid tumor (metastatic to liver)
4	Diffuse main duct IPMN	Head, Neck, Body	0.5-2.2	Main duct IPMN, atypical cells suspicious for cancer	24 (0)	Clear	Pancreatic adenocarcinoma associated with main duct IPMN
5	2 cystic lesions	Head and tail	6.0 and 7.2	Not available	18 (0)	Clear	Mucinous Cystadenomas
6	Diffuse main duct IPMN	Entire gland	0.7-2.2	Not available	36 (0)	Clear	Pancreatic adenocarcinoma at three locations (two in the head and one in tail) associated with main duct IPMN
7	2 Cystic lesions	Head, tail	2.0-3.2	Main duct IPMN, atypical cells suspicious for cancer	11 (0)	Clear	Main duct IPMN with pancreatic intraductal neoplasia Grade III, Chronic pancreatitis with dysplasia of ductal epithelium

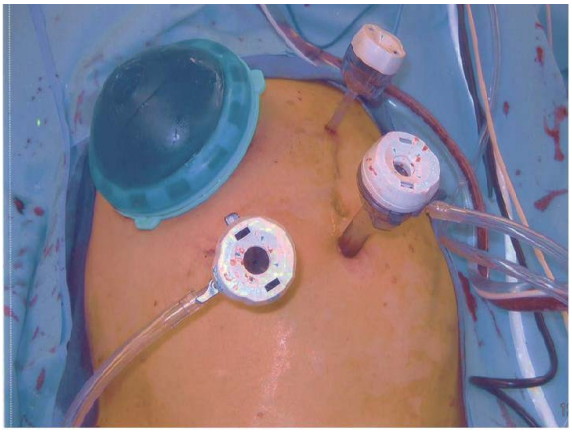

Figure 1. Port placement for surgery.

this reported experience an antrectomy was performed in preference to a pylorus-preserving procedure at the discretion of the senior author. The stomach was divided at the incisura angularis with an endoscopic stapler.

The spleno-renal and spleno-phrenic ligaments were divided. The spleen and the tail of pancreas were carefully dissected off of the retroperitoneum. The dissection was continued medially along the superior, inferior borders and retroperitoneal surface of the pancreas. The inferior mesenteric vein when draining into the splenic vein was divided between the clips. The coronary vein was preserved during all the cases. The distal pancreas and spleen were reflected to the right side to expose confluence of splenic vein and superior mesenteric vein. The splenic vein was dissected from the posterior surface of pancreas and was divided with a vascular stapler load. The splenic artery was identified along the superior border of pancreas and was divided close to the celiac trunk with a vascular stapler load. The proximal jejunum was divided with a stapler at 10 cm distance from the ligament of Treitz. The jejunal mesenteric vessels were divided with the harmonic scalpel or a vascular stapler to complete the duodenal derotation. The jejunum was passed under the mesenteric vessels and the entire specimen was flipped over to the right side of portal vein. The specimen was pulled to the right side to facilitate uncinate process dissection. The small venous branches were divided between clips. The Superior Mesenteric Arterial (SMA) pulsations were palpated and fibrocapsular layer over the uncinate process was opened with the harmonic scalpel close to the SMA. The uncinate process was separated from the SMA with a meticulous dissection. The crossing vessels were clipped and divided between the clips. The specimen was extracted through the Gelport®. The margins were checked with the frozen sections.

The transacted end of the jejunum was passed through the transverse mesocolon into the upper abdomen and at this point pneumoperitoneum was released. The hepatico-jejunostomy was performed through the Gelport® under direct vision using 5-0 PDS suture. The gastrointestinal continuity was re-established with an ante-colic, isoperistaltic stapled side to side gastro-jejunostomy. 10F flat JP drain was placed to drain the biliary anastomosis. Post-operatively, all the patients were admitted to the intensive care unit and started on insulin drip and gradually switched to long acting insulin doses. Pain was controlled with Patient Controlled Analgesia (PCA). Thromboprophylaxis with subcutaneous heparin (5000 Units every 8 hours) was started on post-op day 1. Urinary catheter was removed on post-op day 1 or 2. Upon return of bowel function, the patients were started on liquids and diet was gradually advanced as tolerated. All the patients received pancreatic enzyme supplements with diet. All the patients were seen by the endocrinology team during the post-operative period.

RESULTS

Seven patients underwent the laparoscopic hand-assisted total pancreatectomy (3 males and 4 females) with a mean age of 58.1 years (range, 44-63 years). The mean adult American Society of Anesthesiology (ASA) physical status was 2.8 (median 3, range 1-3). Three patients underwent TP for diffuse IPMN **(Figure 2)**, two had multiple neuroendocrine tumors and two patients had large cystic lesions in the head, body and tail of pancreas. The indications, EUS results and final pathological diagnoses are described in **Table 1**.

The intra-operative and post-operative results with complications are listed in **Table 2**. The median blood loss was 300 ml (range 150-1200). One patient had intraoperative bleeding secondary to adhesions from previous abdominal surgery and required blood transfusion. The median operating time was 431 minutes (range 348-590). The splenectomy was performed in 6 patients and the spleen was preserved in 1 patient. The median length of hospital stay was 10 days and intensive care unit monitoring required for 2 days (range, 1-6 days). The median time for ambulation and self-care was 3 days. The median duration for the nasogastric tube was 4 days. The nasogastric tube was removed and clear liquid diet was resumed upon passage of flatus. The patients received oral pancreatic enzyme supplements with diet. The median times to pass flatus and first bowel movement after surgery were 4 and 6 days respectively. The endocrinology team saw all the patients after the surgery. One patient had

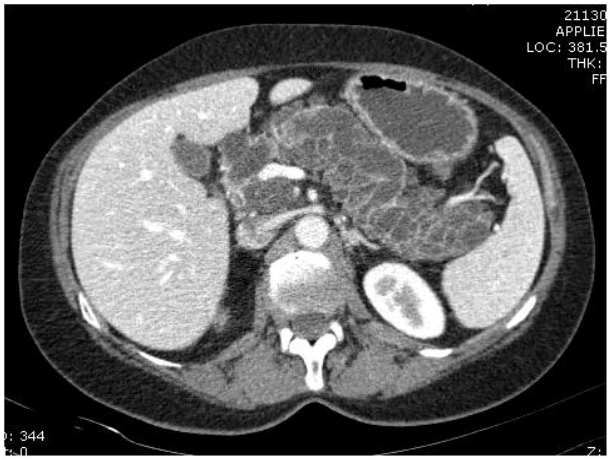

Figure 2. Diffuse Intraductal Papillary Mucinus Neoplasm (IPMN).

Table 2. Intra-operative and postoperative results of laparoscopic total pancreatectomy.

Series (Yr)	Total (Primary TPs)	Median Length of Stay (d)	Median Estimated Blood loss (ml)	Median OR time (min)	Spleen preservation	Total morbidity (%)	Mortality (%)
Current	7 (7)	10	300	431	01-Jul	14	0
Boggi Lap Robot (2015)	11 (11)	27 (mean)	220 (mean)	600	03-Nov	63	0
Zureikat (Robotic) (2013)	5(5)	10	1000	503	-	100	0
Muller (2007)	147 (124)	11	1000	380	39/124	44	6
Crippa (2010)	65 (25)	12	-	430	Feb-25	36	0
Janot (2010)	63 (45)	21	800	420	-	50.8	6.25
Billings (2005)	99 (80)	-	-	-	-	32	5

liver metastasis from carcinoid tumor which was resected at later time. There was major 90-days morbidity (Clavien grade 2) in a patient who had deep venous thrombosis and pulmonary embolism requiring anticoagulation. One other patient developed common bile duct stricture after 6 months, which was treated with endoscopic interventions. Mortality within 90 days was zero. Median length of follow up was 36 months (12-40 months). One patient died after one year due to hypoglycemic attack. One patient died after three years due to widespread metastasis of neuroendocrine tumor. One patient died at home because of failure to thrive and possible hypoglycemia after two years.

DISCUSSION

There has been a paradigm shift on the indications for total pancreatectomy. In the late 70's and 80's a belief in the section of the surgical community that pancreatic cancer is multi-centric led to a brief popularity of total pancreatectomy for pancreatic adenocarcinoma. The purported advantage of avoiding a pancreatic anastomosis was proposed as an added advantage for a total pancreatectomy at the time. Total pancreatectomy as the primary treatment for patients with pancreatic adenocarcinoma however rapidly fell into disrepute since there was no demonstrable survival benefit and the complications associated with brittle diabetes and pancreatic enzyme insufficiency were extremely difficult to manage [2, 3, 4, 6]. At the present time, the primary indications for total pancreatectomy are limited to diffuse main duct IPMN, multifocal Neuroendocrine Tumours (NETs), familial pancreatic cancer and patients with chronic pancreatitis who are candidates for a total pancreatectomy with autologous islet cell transplantation [2, 3, 4, 6]. In the past two decades surgery for main duct IPMN and TP with autologous islet cell transplantation for chronic pancreatitis have emerged as the primary indications for total pancreatectomy. At present approximately 12 centres in the United States have an islet isolation laboratory and a recent review reported on over 400 patients with total pancreatectomy and autologous islet transplantation [11]. Similarly, in the past two decades there has been an epidemic of IPMN cases. The incidence of carcinoma in main duct IPMN has been reported to range from 25% to 65% and therefore surgery is recommended for all cases of main duct IPMN [12]. Furthermore, a recent study showed that pancreatic malignancy occurred in 36% of patients with a mean of 33 months after diagnosis in a cohort of patients who were not treated surgically [13]. Patients with segmental main duct IPMN are appropriately treated with localized resection procedures such as the Whipple operation or distal pancreatectomy. Patients with diffuse main duct IPMN are candidates for TP. In our study four of the seven patients requiring TP had main duct IPMN and in three of four (75%) microscopic invasive cancer was found in the final pathological specimen. The cytology from EUS in two out of these three patients had shown atypical cells suspicious for malignancy.

Complex laparoscopic pancreatic surgery has now evolved into mainstream practice with a number of centres in the USA and elsewhere performing advanced laparoscopic procedures such as the Whipple operation, distal pancreatectomy, tumor enucleation and pancreatic necrosectomy. A sheer volume of studies over the past decade have shown that left-sided pancreatectomy performed laparoscopically has advantages compared to the open approach with shorter hospital stay, less pain, less blood loss and reduced complications [14, 15]. A recent study from 69 medical centres in Japan using a sophisticated statistical method (Propensity Score Matching (PSM)) comparing laparoscopic distal pancreatectomy to open distal pancreatectomy underscores this. Key findings after PSM showed that laparoscopic distal pancreatectomy was associated with significantly lower blood loss, fewer blood transfusions, fewer grade B or C pancreatic fistulae, and a higher percentage of splenic reservations and a shorter length of stay. The study had power as there were over 700 patients in each arm [16]. Laparoscopic and robotic pancreaticoduodenectomy has also shown to be feasible and safe in several large series of patients reported from around the world [9, 17, 18, 19]. On the other hand, there are only a few anecdotal publications and two small series of laparoscopic TP [6, 7, 8, 9]. Zureikat et al. reported on their experience with five robotic TP [9] and the 30- and 90-day mortality was 0%, Clavien grade 3 or higher morbidity was 20%, operating time was 503 minutes, there was one conversion and the mean length of stay of 10 days (7-18 d). Boggi et al. reported a case-matched series of 11 laparoscopic robot-assisted total pancreatectomy cases with 11 open TP from Italy [6]. The overall morbidity, Clavien Grade 3 or more complications, spleen preserving procedures, number of transfused patients, ICU stay and 90-day mortality was not significantly different between the two procedures. Only the mean blood loss and mean

operative time was significantly lower for open TP. The length of stay was 27 days (12-88 days) for robotic cases and 17 days (12-34 days) for open TP (differences not significant), both these values are much higher than the length of stay reported for open TP in the United States. The length of stay data, from the studies from Europe and Asia, are not comparable to the USA due to cultural and medical practice differences. This small study showed that outcome of robotic TP appeared to be similar to open TP. Similarly our results in a small cohort of seven patients demonstrate that laparoscopic-assisted total pancreatectomy is a safe procedure and our results are comparable to outcomes published in the literature of patients who underwent open total pancreatectomy with respect to the blood loss, OR time, blood transfusion requirements, postoperative 30 and 90 day morbidity and mortality and length of stay **(Table 3)**. Of two patients who were candidates for a spleen preserving total pancreatectomy in this study, it was preserved in one patient with a mucinous cystadenoma of the pancreas. In the second patient with diffuse neuroendocrine tumors of the pancreas attempted splenic preservation failed due to bleeding from splenic vein. Since there is a high incidence (this is 75% in the present series) of occult malignancy in patients with main duct IPMN, we do not attempt splenic preservation in this group of patients. Splenic preservation is important in the young patient; however, in the older patient the advantage of splenic preservation has to be weighed against the additional difficulty of the dissection added to the laparoscopic surgical procedure. It is unclear whether the small benefit of splenic preservation outweighs the risk in this situation.

The laparoscopic hand-assisted technique has some advantages over a totally laparoscopic or robotic approach. The incision for the hand port is fairly small (6-7cm) and can be used for the specimen retrieval. A thorough exploration of abdominal cavity can be performed with the combination of palpation and laparoscopy [8]. If there is an injury to the portal vein or SMV during dissection, then bleeding can be quickly controlled and the vessel can be repaired. The hepaticojejunostomy is also easily performed through the hand port incision. There are no comparative studies of complex pancreatic surgery performed totally laparoscopically, with the hand-assisted laparoscopic approach or robotically.

The small sample size and length of follow up in this series are not adequate to assess the oncologic outcomes. Quality indicators of adequate oncologic resection include status of radial and resection margins and total lymph node yield. Our study suggest that complete oncologic resection is possible laparoscopically since the radial and transected margins were negative, furthermore the lymph node yield in this study is similar to that reported in previous open studies of total pancreatectomy **(Table 1)**. Laparoscopic total pancreatectomy is a complex procedure and was performed on the patients in this study after an extensive experience with open and laparoscopic distal pancreatectomies and Whipple operations. Similarly, the excellent outcomes reported in the literature of advanced minimally invasive pancreatic procedures particularly Whipple operation and total pancreatectomy have come from centres with extensive expertise in minimally invasive pancreatic surgery. Translation of these results to a wider community of surgeons is not clear.

CONCLUSION

Laparoscopic hand-assisted TP appears to be a safe and feasible procedure that can be performed with morbidity and mortality rates that are similar to that reported for open TP. Laparoscopic hand assisted TP is a technically demanding procedure and expertise in both open and advance laparoscopic pancreatic procedures is necessary. Additional multi-institutional studies are necessary with larger numbers and long-term follow-up to further evaluate its role as an alternative to open total pancreatectomy.

Conflicts of Interest

All named authors hereby declare that they have no conflicts of interest to disclose.

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