Title: Laparoscopic distal pancreatectomy. The new gold standard for benign and malignant diseases of the pancreatic body and tail?

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ABSTRACT

Introduction: Laparoscopic surgical technique has been evolving since the end of the 20th century. Benign and malignant diseases of the pancreas have been treated laparoscopically. Open surgery is gradually being replaced by laparoscopy. The aim of this review is to examine data from comparative studies of laparoscopic distal pancreatectomy versus open pancreactomy.

Methods: Pubmed and Medline databases were searched for comparative studies from 2006 until October 2012. Twenty-two studies were identified that included a total of 2138 patients, 866 in the LDP group and 1272 in the ODP group.

Results: There was no difference regarding the operating time for laparoscopic distal pancreatectomy (LDP) and open distal pancreatectomy (ODP). The conversion rate was 9.4%. The rate of pancreatic fistula was similar in both groups. Laparoscopic distal pancreatectomy was associated with significantly higher spleen preservation rate, lower intraoperative blood loss, lower morbidity and shorter hospital stay.

Conclusion: Laparoscopic distal pancreatectomy is considered superior than the open procedure in terms of reduced blood loss, increased rate of spleen preservation when possible, shorter hospital stay, faster ambulation especially in patients with benign or low malignant potential pancreatic pathology. For patients with malignant pathology, longer follow up is needed to establish the role of LDP in such patients.

ΠΕΡΙΛΗΨΗ

Εισαγωγή: Η πρόοδος των λαπαροσκοπικών τεχνικών και μέσων είναι ραγδαία από τα τέλη του προηγούμενου αιώνα. Καλοήθεις και κακοήθεις παθήσεις του παγκρέατος έχουν αντιμετωπιστεί λαπαροσκοπικά. Η λαπαροσκοπική αντιμετώπιση τείνει να αντικαταστήσει την ανοικτή χειρουργική. Ο σκοπός της παρούσης ανασκόπησης είναι να αναλύσουμε τα δεδομένα από συγκριτικές μελέτες της λαπαροσκοπικής περιφερικής παγκρεατεκτομής (ΛΠΠ) και της ανοικτής περιφερικής παγκρεατεκτομής (ΑΠΠ).

Μέθοδος: Η έρευνα πραγματοποιήθηκε στις βάσεις δεδομένων Pubmed και Medline για συγκριτικές μελέτες από το 2006 έως τον Οκτώβριο 2012. Ανευρέθησαν 22 μελέτες που πληρούσαν τα κριτήρια που τέθησαν οι οποίες περιελάμβαναν 2138 ασθενείς, 866 στην ομάδα της ΛΠΠ και 1272 στην ομάδα της ΑΠΠ.

Αποτελέσματα: Δεν ανεδείχθησαν διαφορές σχετικά με το χειρουργικό χρόνο για την πραγματοποίηση ΛΠΠ και ΑΠΠ. Το ποσοστό μετατροπή της ΛΠΠ σε ΑΠΠ ήταν 9,4%. Η πιθανότητα ανάπτυξης παγκρεατικού συριγγίου ήταν παρόμοια και στις δύο ομάδες. Η λαπαροσκοπική περιφερική παγκρεατεκτομή σχετίζεται με υψηλότερα ποσοστά διατήρησης του σπληνός, μικρότερη διεγχειρητική απώλεια αίματος, χαμηλότερη νοσηρότητα και μειωμένη διάρκεια παραμονής στο νοσοκομείο.

Συμπέρασμα: Η λαπαροσκοπική περιφερική παγκρεατεκτομή υπερτερεί της ανοικτής σε δείκτες όπως η μικρότερη απώλεια αίματος, τα υψηλά ποσοστά διατήρησης του σπληνός, τη μειωμένη διάρκεια παραμονής στο νοσοκομείο και την ταχύτερη κινητοποίηση του ασθενούς ιδιαίτερα στις περιπτώσεις καλοήθων και χαμηλή κακοήθειας παθήσεων του παγκρέατος. Για τη διερεύνηση του ρόλου της λαπαροσκοπικής παγκρεατεκτομής χρειάζονται περισσότερες μελέτες με μακρά διάρκεια παρακολούθησης.

Introduction

"Eat when you can, sleep when you can and don't mess with the pancreas". Every surgeon has heard that but all don't agree with the last bit. One of the most challenging areas in the field of the surgery of the digestive tract is the surgery of the pancreas. This is mainly due to the anatomy of the pancreas, its relation to surrounding structures and its complex physiology (both endocrine and exocrine). Since Cushieri[1] and Gagner[2] initial reports, laparoscopic distal pancreatectomy is performed more frequently for diseases of the body and tail of the pancreas[3]. The advantages of the laparoscopic procedure are the shorter hospital stay, decreased intraoperative blood loss, higher rate of splenic conservation, better cosmetic result and decreased incidence of incisional hernia[4].

Indications of laparoscopic distal pancreatectomy

Most laparoscopic distal pancreatectomies have been performed for benign lesions, neuroendocrine tumors (NET) and low grade malignancies especially cystic tumors[5]. Although some cases of pancreatic adenocarcinoma have been reported[6], the results of LDP are limited and the long term oncologic result is under discussion. Enucleation and distal pancreatectomy is the most frequently performed procedures[7] for NETs. In cases of potential malignant NET that are located in the body/tail region, LDP with splenectomy along with the splenic vessels and the associated lymph nodes is recommended[8]. Cystic lesions of the pancreas can be treated by LDP. Laparoscopic distal pancreatectomy is indicated in serous lesions when the differential diagnosis of a symptomatic serous cystic neoplasm from a malignant lesion is not possible[14],[16]. Intraductal papillary mucinous neoplasms (IPMN) are non-invasive mucin producing more often papillary epithelial neoplasms that arise either from the main pancreatic duct or

branch ducts[15]. Although intraductal papillary mucinous neoplasms occur more commonly in the head of the pancreas, LDP has been carried out for IPMNs of the body and tail[16]. Laparoscopic distal pancreatectomies have been performed in patients with invasive carcinoma of the pancreas. There is debate regarding the oncologic consequences of the laparoscopic approach for invasive carcinoma[17]. Koody et al[6] in a multicenter trial compared the cancer surgery outcomes regarding the procedure (number of lymph nodes and resection margins) and the survival and found similar results. Laparoscopic surgery has been performed in patients with chronic pancreatitis either as resection[12] or necrosectomy[13]. Pancreatic pseudocysts can be amenable to lapaparoscopic cystogastrostomy or cystojejunostomy[12]. Solitary pancreatic injuries can be treated with spleen preserving LDP if the main pancreatic duct is completely transected[11],[12].

Surgical Technique

Several techniques have been used for the conduction of LDP. Distal pancreatectomy has been traditionally coupled with splenectomy. A trend towards spleen preserving distal pancreatectomy has become increasingly common among pancreatic surgeons[10],[14],[17]. When comparing results of laparoscopic and open procedures, spleen preservation favors LDP over open distal pancreatectomy[19-20]. Warshaw et al[22] has described the preservation of the spleen in cases of distal pancreatectomy maintaining its blood supply via the short gastric vessels.

Supine and right lateral positioning of the patient are the most common choices. The standard number of trocars used for LDP is 4. The placement of the trocars varies among surgeon and depends on its own preference and the somatic characteristics of the patients. Hand assisted laparoscopic (HAL) technique has been used by surgeons for laparoscopic pancreatectomy[23-24].

Underlying pathology seems to play a crucial to the decision regarding the extent of resection. In cases of non-invasive MCN located in the tail of the pancreas, division of the pancreas medially to the lesion usually suffices. For chronic pancreatitis, the gland is typically divided at the pancreatic neck anterior to superior mesenteric vein[8]. Oncological radicality is very important in patients with IPMNs. In such circumstances extended resections may be necessary since IPMN pathology can vary from adenoma to invasive carcinoma[9].

Postoperative complications

Postoperative complications of LDP include pancreatic fistula, peripancreatic fluid collection, bleeding, hematoma, splenic infarction, intrabdominal abscess, postoperative ileus, venous or pulmonary thromboembolism, cardiac ischemia and any complication that occur within 30 days after pancreatectomy[3].

Pancreatic fistula formation and peripancreatic fluid collections are the most common postoperative complications of LDP[17],[25].

Pancreatic fistula was defined in 2005 by the International Study Group on Pancreatic Fistula (ISGPF) Definition as the presence of any fluid output after the 3rd postoperative day with amylase content greater than three times the upper normal serum value[26]. In a series by Song et al the incidence of pancreatic fistula was 27.9%. Grade A,B and C pancreatic fistula were observed in 20.9%, 6.7% and 0.3% of patients respectively[3]. Risk factors that may contribute to fistula formation are the soft pancreatic parenchyma and the inability to selectively identify and ligate the main pancreatic duct[17],[25],[27-28].

Aim of the study

The aim of the study is to review the published literature that compares laparoscopic distal pancreatectomy (LPD) with open distal pancreatectomy in order to assess the possibility that LDP is the new gold standard in treating benign and malignant diseases of the distal pancreas. The number of available articles is limited, most being case reports, small case series and few multicentric large studies[6],[17],[29].

Method

Review of the literature was performed using PubMed and Medline order to identify studies published until 2012 that compared LDP vs ODP. The following terms were used “laparoscopy”, “laparoscopic”, “distal pancreatectomy”, “open”, “comparative study”, “left pancreatectomy”, “laparoscopic versus open pancreatectomy” and “minimal invasive”.

Articles that were included compared LDP and ODP for benign and malignant diseases, reported the indications for laparoscopic and open surgery, objectively evaluated of at least one of the outcome measures. Studies involving robotic procedures, laparoscopic procedures for trauma, necrosectomy or debridement for pancreatitis, enucleation procedures and non-english articles were excluded, as well as abstracts, reviews, case reports, letters, editorials and expert opinions.

Outcome of interest - definitions

The comparison between open and laparoscopic distal pancreatectomy was based upon several perioperative outcomes such as operative time, intraoperative blood loss, splenic preservation, postoperative recovery, oncologic radicality and postoperative complications.

Results

Twenty-two studies were identified from 2006 to 2012 that included a total of 2138 patients, 866 in the LDP group and 1272 in the ODP group. The mean LDP to ODP conversion rate was 9,4% and was more frequent in cases of incidental detection of malignancy, uncontrolled bleeding, poor exposure of the operating field, adhesions, lack of progress.

Operating time was reported in twenty-one studies (Table 1.). The mean operating time for LDP group was 225.6min (range: 160-342min) while for the ODP group was 215.8min (range: 145-281min). The difference is 10 min. The average splenic preservation rate was higher in the LDP group 31.2% (262/839 patients) versus 12.6% (149/1182 patients in the ODP group (Table 4.). This might be explained by the better operative exposure and reduced blood loss. During LDP for benign or low malignant potential lesions, splenic preservation must be the goal for the surgeon. This requires advanced technical skills and consumes a considerable amount of operating time[51].

Eighteen studies[18],[20-21],[25],[32-41],[43-45] reported the intraoperative blood loss. In the LDP group the mean intraoperative blood loss was 262.8ml (range: 33.6ml-667ml) and was significantly lower than in the ODP group (mean 607,6ml, range: 362ml-900ml) (Table 1.).

All studies reported the hospital stay which was lower in the LDP group (mean 8,04 range: 4-22 days) than in the ODP group (mean 12,6 range: 6-27 days) (Table 2.).

Twelve studies[18],[20],[25],[37-45] reported their results on pancreatic fistula after LDP or ODP based on the ISGPF classification[26]. The mean incident of pancreatic fistula formation among those studies was similar in both groups being 16,6% in the LDP group vs 17,5% in the ODP group (Table 3.).

Mean overall postoperative morbidity was 28,6% (range 0%-48,2%) in the LDP group and 32,7% (range 0%-69%) in the ODP group (Table 2.). The LDP group experienced less surgical site infections than the open surgery probably because of the less invasive procedure[18-21],[25],[30-33],[35-43]. There was no significant difference regarding the mortality between the LDP group and the ODP group 0,17% and 0,54% respectively.

Fifteen out of 331 (4,5%) in LDP pancreatic resection margins and 45 out of 514 (8,8%) in ODP were positive as it was shown in four studies[21],[38-39],[46]. Mehta et al[20] and Baker et al[18] reported higher mean total lymph node count with ODP compared to LDP (14 and 9,4 vs 11 and 5,2). Di Nocia et al[38] and Jayaraman[39] et al reported no significant difference in lymph node harvesting in either the laparoscopic or the open procedures.

Three studies by Kim et al[19], Nakamoura et al[25] and Matsoumoto et al[36] studied the effect of minimally invasive surgery to first flatus and oral intake. The LDP group had first flatus and oral intake at 2,4 days (mean) and 2,9 days (mean) vs 4,2 days (mean) and 5,9 days (mean) in the ODP group.

Discussion

Minimally invasive surgery represents one of the most important advances in the field of surgery. Cushieri[1] and Gagner[2] performed the earliest attempts at laparoscopic distal pancreatectomy in humans. Since then numerous reports show the advantage of LDP in minimizing trauma, shortening the hospital stay and speeding recovery. Restrictions for the wider use of LDP are the high postoperative morbidity, especially in the management of pancreatic fistulae. Briggs et al[47] in 2009 published the first review on minimal invasive pancreatic resection and Nigri et al[48] in the first meta-analysis comparing LDP and ODP (2010) reviewed 10 studies, all retrospective with a total of 729 patients showed that LDP did better in terms of less blood loss, shorter length of hospital stay, lower incidence of overall complications, less surgical site infections and pancreatic fistula. Reoperation rate and mortality had no significant difference between the two procedures.

Two thousand one hundred thirty eight (2138) patients from 22 retrospective studies were included of whom 866 (40,5%) underwent LDP and 1272 (59,5%) ODP. The results indicate that LDP compared to ODP has lower blood loss, lower postoperative complication rate, less surgical site infections, reduced length of hospital stay. Five studies[20],[38-39],[44-45] reported readmission rates that were lower in the laparoscopic than in the open surgery group. Only Mehta et al[20] reported higher readmission rate in the LDP group (16,6% vs 10%).

Laparoscopic distal pancreatectomy is associated with lower blood loss than ODP which was a consistent finding in all studies. This may be due to the less invasive nature of the procedure and the magnification which allows better visualization and cleaner dissection.

Although laparoscopic procedures take more time to complete than the open procedures considering the setup time, the number of instruments used and their handling during surgery we observed that ODP procedures took only about 10 minutes longer than LDPs. Kooby et al[21] in a series of 342 matched patients showed no statistically significant difference between the LDP and ODP regarding the operating time and the possible effect of tumor size that might have on it.

Many authors suggest that laparoscopic pancreatectomy is contraindicated in malignant pancreatic neoplasms because of concerns about long term survival, lymph node harvesting and tumor margins. In 15 studies[18],[20-21],[25],[30-31],[36-46] both malignant

and benign pathology was reported. There was no difference in positive radial margins or lymph node harvest. In a multicenter study by Kooby et al[49] survival was shown to depend on advanced age, tumor size, positive tumor margins and node positive disease. The method of resection did not affect survival which was 16 months for both the laparoscopic and the open group.

When LDP group and ODP group were studied focusing on hospital stay there was a significant difference of a mean 4 days. This can be explained by the fact that both the time to oral intake and the time to passing first flatus were less in LDP group. Patients also benefit from the reduced postoperative stress associated with laparoscopic procedures and the absence of a long subcostal incision that would cause enough pain to restrict normal activity.

In the LDP group mean overall postoperative morbidity was 28,7% versus 32,7% in the ODP group. Surgical site infection rate was significantly lower in the LDP group. The most serious complication of pancreatic surgery is the formation of pancreatic fistula. Almost all studies reported the incidence of pancreatic fistula in both the open and the laparoscopic surgery group. Studies that reported pancreatic fistula based on ISGPF[18],[20],[25],[37-45] showed similar results. The most commonly used methods for transecting the pancreatic parenchyma are the Ligasure vessel sealer, harmonic scalpel, EndoGIA stapler and bipolar cautery. Nakamura et al[50] described a peri-firing compression method using the Echelon stapler to transect the pancreas in order to prevent pancreatic leakage.

The mean postoperative mortality was low in both groups yielding a rate of 0,15% and 0,54% for the LDP and ODP groups respectively. Pulmonary embolism (PE) and myocardial ischemia were the leading causes of postoperative mortality. Vijan et al[41] reported 4 deaths overall. Three patients died due to pulmonary embolism (2 in the LDP group and 1 in the ODP group) and 1 patient died due to pancreatic leak complications

Conclusion

This review shows that laparoscopic distal pancreatectomy is considered superior than the open procedure in terms of reduced blood loss, increased rate of spleen preservation when possible, shorter hospital stay, faster ambulation especially in patients with benign or low malignant potential pancreatic pathology. It should be considered the new gold standard among pancreatic surgeons and high volume institutions. Selected

patients with malignant tumors of the pancreatic body and tail may also be considered candidates for the laparoscopic approach since there is evidence that LDP is not inferior to ODP in terms of oncologic radicality and long term survival. Further studies are needed to resolve these controversies.

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Table 1. Operative outcomes of comparative studies of laparoscopic vs open distal pancreatectomy

Study [ref] (year)	No of patients		Operating time (min)		Conversion (%)	Estimated Blood loss (ml)	
	LAP	OPEN	LAP	OPEN		BL LAP	BL OPEN
Velanovich et al [30] (2006)	15	15	NA	NA	20	NA	NA
Shimura et al [32] (2006)	5	8	160	179,8	NA	33,6	439,3
Teh et al [34] (2007)	12	16	212	278	16,7	193	609
Tang et al [33] (2007)	9	5	180	210	0	100	450
Kooby et al [21] (2008)	142	200	232	216	12,6	357	588
Bruzoni et al [35] (2008)	7	4	182	152	0	214	362
Matsumoto et al [36] (2008)	14	19	290	213,8	7,1	247,1	400,3
Kim et al [19] (2008)	93	35	195	190	NA	NA	NA
Eom et al [31] (2008)	31	62	217	194.6	NA	NA	NA
Baker et al [18] (2009)	27	85	236	253	3,7	219,4	612,6
Nakamura et al [25] (2009)	20	16	308,4	281,5	4,7	249	714,1
Casadei et al [40] (2010)	22	22	225	145	0	510	900
Aly et al [37] (2010)	40	35	342	250	10	363	606
Waters et al [46] (2010)	18	22	224	234	11	667	681
Di Norcia et al [38] (2010)	71	168	250	270	25,3	150	900
Vijan et al [41] (2010)	100	100	214	208	4	171	519
Jayaraman et al [39] (2010)	74	236	194	164	30	100	350
Butturini et al [42] (2011)	43	73	180	180	0	NA	NA
Abu et al [43] (2011)	35	16	200	225	0	200	394
Limongelli et al [45] (2012)	16	29	204	160	6	160	365
Mehta et al [20] (2012)	30	30	188	226	na	294	726
Fox et al [44] (2012)	42	76	304	281	11.91	375	375

Table 2. Postoperative outcomes of comparative studies of laparoscopic vs open distal pancreatectomy

Study [ref] (year)	Hospital stay (days)		Pancreatic Fistula (%)		Postoperative morbidity %		Mortality (cases)	
	LAP	OPEN	LAP	OPEN	LAP	OPEN	LAP	OPEN
Velanovich et al [30] (2006)	4,4	9,2	9,1	18,2	20	26	0	0
Shimura et al [32] (2006)	10	22,5	27,9	13,7	0	0	0	0
Teh et al [34] (2007)	6,2	10,6	18	20	9 events	2 events	0	0
Tang et al [33] (2007)	7	11	12	17	33,3	0	na	na
Kooby et al [21] (2008)	5,9	9	11,1	18,2	40	57	0	1
Bruzoni et al [35] (2008)	6,2	9	13,3	13,3	14,2	0	0	0
Matsumoto et al [36] (2008)	12,9	23,8	26	32	7	21	0	0
Kim et al [19] (2008)	10	16	11,3	14,1	24,7	29	0	0
Eom et al [31] (2008)	11,5	13,5	16,7	13,3	35,5		0	0
Baker et al [18] (2009)	4	8,6	17	17	37	35	0	1
Nakamura et al [25] (2009)	10	25,8	22	14	0	18.8	0	0
Casadei et al [40] (2010)	8	11	14,2	0	27,2	27,2	0	0
Aly et al [37] (2010)	22	27	0	12,5	20	31	0	0
Waters et al [46] (2010)	6	8	0	10,5	33,3	18,1	0	0
Di Norcia et al [38] (2010)	5	7	8,3	6,2	28,2	43,8	0	1
Vijan et al [41] (2010)	6,1	8,6	8,6	14,3	34	29	3	1
Jayaraman et al [39] (2010)	5	7	9,7	6,5	18	40	0	2
Butturini et al [42] (2011)	8	9	22,2	0	48,2	45,2	0	0
Abu et al [43] (2011)	7	11	29	44	40	69	0	1
Limongelli et al [45] (2012)	6.4	8.6	8	13	25	41	0	1
Mehta et al [20] (2012)	8,7	12,6	28,6	13,2	50	43	0	1
Fox et al [44] (2012)	5	7	0	0	21.42	19.7	NA	NA

Table 3. Pancreatic Fistula rates in LDP and ODP (according to ISGPF)

Study [ref] (year)	LAP (%)	OPEN (%)
Baker et al [18] (2009)	22	14
Nakamura et al [25] (2009)	0	12,5
Di Norcia et al [38] (2010)	11,3	14,1
Jayaraman et al [39] (2010)	8	13
Vijan et al [41] (2010)	17	17
Casadei et al [40] (2010)	9,1	18,2
Aly et al [37] (2010)	12	17
Abu et al [43] (2011)	29	44
Butturini et al [42] (2011)	27,9	13,7
Fox et al [44] (2012)	28,6	13,2
Mehta et al [20] (2012)	16,7	13,3
Limongelli et al [45] (2012)	18	20

Table 4. Spleen preservation cases in open and laparoscopic pancreatectomy groups

Study [ref] (year)	No of Patients		Spleen preserving	
	LAP	OPEN	LAP	OPEN
Casadei et al [40] (2010)	22	22	4	4
Butturini et al [42] (2011)	43	73	19	8
Limongelli et al [45] (2012)	16	29	5	3
Aly et al [37] (2010)	40	35	13	3
Waters et al [46] (2010)	18	22	5	3
Velanovich et al [30] (2006)	15	15	0	0
Kooby et al [21] (2008)	142	200	43	24
Di Norcia et al [38] (2010)	71	168	11	26
Mehta et al [20] (2012)	30	30	21	9
Vijan et al [41] (2010)	100	100	25	
Bruzoni et al [35] (2008)	7	4	0	0
Nakamura et al [25] (2009)	20	16	7	5
Matsumoto et al [36] (2008)	14	19	1	0
Teh et al [34] (2007)	12	16	5	1
Kim et al [19] (2008)	93	35	38	2
Eom et al [31] (2008)	31	62	13	
Tang et al [33] (2007)	9	5	4	
Abu et al [43] (2011)	35	16	14	3
Jayaraman et al [39] (2010)	74	236	14	33
Fox et al [44] (2012)	42	76	15	17
Shimura et al [32] (2006)	5	8	5	8