ORIGINAL ARTICLE



Laparoscopic distal pancreatectomy in elderly patients: is it safe?

Giovanni Aprea¹ · Davide De Rosa¹ · Marco Milone² · Aldo Rocca¹ · Tommaso Bianco¹ · Guido Massa¹ · Rita Compagna¹ · Louis Banka Johnson³ · Alessandro Sanguinetti⁴ · Andrea Polistena⁴ · Nicola Avenia⁴ · Bruno Amato¹

Received: 4 September 2016/Accepted: 3 November 2016 © Springer International Publishing Switzerland 2016

Abstract

Background Laparoscopic distal pancreatectomy (LDP) appears to be safe and effective as open distal pancreatectomy (ODP) for benign or borderline malignant lesion. However, studies comparing LDP with ODP in elderly patients are limited. The purpose of this study is to compare the clinical outcomes of these two several approaches in elderly patients.

Methods A retrospective analysis was carried out by comparing laparoscopic (n = 7) and open (n = 15) distal pancreatectomy in elderly patients performed at the University of Naples "Federico II" and University of Perugia between January 2012 and December 2015. Demographic data, operative and postoperative outcomes were analyzed.

Results Demographic and tumor characteristics of laparoscopic and ODP were similar. There were also no significant differences in operating room time. Patients undergoing LDP had lower blood loss, first flatus time, diet start time and postoperative hospital stay. There were no

Aldo Rocca aldorocca@hotmail.it

- ¹ Division of General Surgery, Department of Clinical Medicine and Surgery, School of Medicine, University of Naples Federico II, via S. Pansini, 5, 80131 Naples, Italy
- ² Division of General Surgery, Department of Surgical Sciences and Nephrology, School of Medicine, University of Naples Federico II, Naples, Italy
- ³ Division of Colorectal Surgery, Department of Clinical Sciences, Pelvic Floor Centre, Malmö University Hospital, Lund University, Lund, Sweden
- ⁴ General Surgery and Surgical Specialties Unit, Medical School, S. Maria University Hospital, University of Perugia, Terni, Italy

significant differences in complication rates or 90-day mortality.

Discussion LDP is safe and feasible as ODP in selected elderly patients.

Keywords Distal pancreasectomy · Robotic surgery · Elderly

Introduction

The elderly population has increased in many countries, and the number of patients older than 70 years of age with resectable pancreatic neoplastic lesion is also predicted to rise in the future because of improved surgical techniques and medical management [1, 2]. Minimally invasive surgery has proved to be safe and effective and has largely replaced open surgery in many procedures. Despite this trend, laparoscopic pancreatic surgery has been slow to gain acceptance, but nowadays the laparoscopic technique is becoming increasingly popular among surgeons to perform distal pancreatectomy. A comparison between open surgery and laparoscopic distal pancreatectomy (LDP) confirms advantages commonly ascribed to minimal access surgery such as reduced postoperative pain, faster recovery and fewer wound-related and general morbidity [3, 4]. However, these outcomes are poorly defined in elderly population and the decision to perform this surgical procedure in an elderly patient can be difficult. The purpose of the present study was to evaluate the safety of LDP in patients older than 70 years and to show the influence of advanced age on the morbidity, long-term survival, length of hospital stay and mortality associated with this operation analyzing the differences with the open approach.

Materials and methods

At University "Federico II" of Naples, Italy, between January 2012 and December 2015, 22 consecutive patients who underwent elective distal pancreatectomy with an apparent diagnosis of benign or borderline malignant tumor were recruited into the current study. Preoperatively, ultrasonography (USG), computed tomography (CT) and magnetic resonance imaging (MRI) were routinely performed for the diagnosis of pancreatic benign or borderline malignant lesion. Seven patients underwent laparoscopic distal pancreatectomy (LDP) and 15 patients underwent open distal pancreatectomy (ODP). All possible advantages and disadvantages of both approaches were clearly explained to the patients. Written informed consent was obtained from each patient. Distal pancreas resection was defined as any resection of the pancreas parenchyma starting at the neck or distal to the neck with or without splenectomy. Retrospectively, the medical records were analyzed and compared between two groups for clinicopathologic characteristics such as age, gender, body mass index (BMI), ASA, tumor size and spleen preservation rate. In addition, the operative outcomes such as operation time, blood loss, return to normal bowel movement, return to adequate oral intake, length of hospital stay, pancreatic fistula rate and other complications, postoperative mortality and recurrence were compared between two groups. Postoperative complications were collected and graded according to the Clavien–Dindo complication scale [5]. Complications of Grades I and II were considered minor; those of Grades III to V were considered major. Pancreatic fistula, delayed gastric emptying and postpancreatectomy hemorrhage were defined according to the International Study Group of Pancreatic Surgery definitions [6–8].

Operative technique used for distal pancreatectomy

Laparoscopic distal pancreatectomy procedure

After general anesthesia, the patient was placed in a right semilateral decubitus position. The surgeon, the camera assistant and the scrub nurse were positioned to the right side of the patient, and the first assistant stood to the left side of the patient. A 12-mm trocar was first inserted through an infraumbilical minilaparotomy and pneumoperitoneum (12 mm Hg) was achieved by CO_2 insufflation. Under laparoscopic vision, three other trocars were inserted into the following locations: the epigastrium (5 mm) for the left hand of the surgeon; the midclavicular line below the costal arch (12 mm) for the right hand of the surgeon; and the left flank (5 mm) for assistance. The gastrocolic ligament was divided for entrance to the lesser sac using a harmonic scalpel and electrocautery. Laparoscopic ultrasonography probe was used through a 12-mm trocar and applied directly to the anterior surface of the pancreas to confirm the location of the tumor and identify its relationship to the splenic vessels. The mobilization of the pancreas began at the superior border until the proximal splenic artery was visualized. The pancreas was mobilized at the inferior border to visualize the superior mesenteric and splenic veins. After creating a tunnel behind the neck of the pancreas, the pancreas was transected with an endoscopic linear stapler. For spleen-preserving procedures, the distal pancreas was freely dissected from the splenic vessels by ligation of the small branches connected to the pancreas using a small Hem-o-lok or a harmonic scalpel. In the case of distal pancreatectomy with splenectomy, the splenic artery and splenic vein were divided. The spleen was resected with the pancreas. The specimen was then placed in a plastic retrieval bag and removed through a minimally extended umbilical port incision. Two closed suction drains were placed in the splenic fossa next to the remnant pancreas.

Open distal pancreatectomy procedure

Open distal pancreatectomy was performed using a conventional method. The patient was placed in the supine position, and a midline incision was made in the upper abdominal region. Pancreatic resection was performed using a blade and electrocautery. The main pancreatic duct was ligated with 4-0 black silk, and the pancreatic stump underwent multiple suture ligation with 2-0 black silk. Two closed suction drains were left in the pancreatic bed.

Statistical analysis

All results are expressed as media. Continuous variables were analyzed using Mann–Whitney U test, whereas categorical variables were analyzed using the Chi-square and/ or Fisher's exact test. A p value of <0.05 was considered significant.

Results

During the study period, a total of 22 patients underwent elective distal pancreatectomy for benign or borderline malignant tumors at our institution. Open and laparoscopic distal pancreatectomies were performed in 15 (68.2%) and 7 (11.6%) patients, respectively (Table 1). There last were 5 (71.4%) women and 2 (28.6%) men with a mean age of 73.6 \pm 2.5 years. All 7 patients who underwent LDP were completed laparoscopically without conversion and the rate

of spleen preservation was 42.8% (n = 3). The tumors were located in the body (n = 2, 28.6%) and tail (n = 5, 28.6%)71.4%) of the pancreas, and the mean tumor size was 42.9 ± 4.7 mm. Two patients (28.6%) developed pancreatic fistula (grade A = 1, grade B = 1) according to the definition of ISGPF, and all patients were recovered with conservative management. The mean follow-up period was 6 months: All 22 patients were alive and disease-free. The operation time of the LDP group mean was 186.2 ± 11 min and that of the ODP group was 180.4 ± 7 min, the difference not being statistically significant. The estimated mean blood loss was lower in the LDP group $(212.30 \pm 62 \text{ ml})$ than in the ODP group $(342.3 \pm 104 \text{ ml}) (p = 0.0017)$. The mean time to normal bowel movement of the LDP group was significantly shorter than that of the ODP group $(2.14 \pm 0.3 \text{ vs.})$ 3.56 ± 0.9 days; p = 0.0006). Also, the mean diet start time in the LDP group was earlier than in the ODP group $(3.14 \pm 0.3 \text{ vs.} 5.53 \pm 0.74 \text{ days}; p = 0.013)$. The mean hospitalization period of the LDP group was 7.2 ± 1.2 days and that of the ODP group was 11.3 ± 4 days, which was significantly longer (p = 0.0187). No statistical difference was observed in the rate of the pancreatic fistula, 90-day mortality and recurrence (Table 2).

Discussion

Surgical approach represents the main option for treatment of benign or premalignant neoplasms of several organs of abdominal cavity or ectopically located in that region [9, 10]. Pre-neoplastic lesions often show genetic pathogenesis or expressing several specific markers [11–13]. A lot of these neoplasms can maybe useful treated using revolutionary approaches such as cell-based therapy or targeting therapies as demonstrated in oncologic [14–19] and non-oncologic diseases in aging patients [20, 21]. In this comparative study of clinical outcomes for LDP and ODP, we demonstrated that LDP is a feasible, safe and efficient approach for benign or premalignant pancreatic neoplasms also for elderly patients.

Table 1 Clinical characteristics of the patients

	LDP (n. 7)	ODP (n. 15)	p value
Sex (M:F)	2/5	5/10	0.3
Age (years)	73.6 ± 2.5	73.5 ± 2.3	0.97
BMI (Kg/m ²)	23.8 ± 1.9	23 ± 2	0.5
Tumor size (mm)	42.9 ± 4.7	43.9 ± 3.8	0.6
Spleen preservation (%)	42.86	46.67	0.86
ASA	1.5 ± 1	1.5 ± 1	1

The traditional surgical approach requires large abdominal incisions and involves possible postoperative complications such as wound infections, incisional hernia and alterations of respiratory mechanics. Laparoscopic surgery has the advantage of requiring smaller incisions and less bowel manipulation than does open surgery, thereby reducing pain postoperative, facilitating the earlier recovery of bowel function and ambulation [22]. Although several previous reports have shown safety of open distal pancreatectomy performed on elderly patients [23, 24], with the improvements of laparoscopic instruments and the accumulation of surgery experience, laparoscopic distal pancreatectomy could become an alternative to open surgery, as it is already happened in young patients [4, 25]. Nowadays laparoscopic distal pancreatectomy has not gained popularity in elderly patients, probably because of many comorbidities of these patients and of fear of not getting survival advantages, and in effect there are limited reports about this approach for these patients. On the contrary, in this study, we showed that both LDP and ODP have similar clinical outcomes in terms of operative times and perioperative complications, but that LDP is associated with advantages such as a shorter hospital stay, lower amount of intraoperative blood loss and earlier resumption of diet. These results confirm that LDP is safe and effective in elderly age. The most common major morbidity after distal pancreatectomy is pancreatic leakage, and the rate of pancreatic leakage after LDP is reported to range from 0 to 33% [26–29]. In the current study, it occurred in two laparoscopic patients (28.6%) and in five open patients (33.3%). This difference was not statistically significant. All the patients with a pancreatic fistula recovered with conservative management. Furthermore, quality of life should be considered when choosing the surgical procedure and LDP is thought to be an ideal procedure for a benign tumor and premalignant pancreatic lesions in elderly patients [30-33].

Conclusions

In conclusion, the findings in this study confirmed which LDP is feasible and safe also in elderly patients. It entails operative times and complication rates similar to those for ODP. In addition, LDP is associated with a lower blood loss, an earlier return to normal bowel movement and diet and shorter hospital stays than ODP. The indications for laparoscopic approach are essentially identical to those for conventional open procedure but requiring careful patient selection, as usual. Further studies with a large number of patients are need but LDP may be progressively adopted also in older selected patients.

Table 2	Operative	variables
and comp	olications	

	LDP (n. 7)	ODP (n. 15)	p value
Mean operative time (min)	186.2 ± 11	180.4 ± 7	0.12
Blood loss (ml)	212.30 ± 62	342.3 ± 104	0.0017
First flatus time (days)	2.14 ± 0.3	3.56 ± 0.9	0.0006
Diet start time (days)	3.14 ± 0.3	5.53 ± 0.74	0.0013
Postoperative hospital stay (days)	7.2 ± 1.2	11.3 ± 4	0.00187
Postoperative complications (%)	28.6	33.3	0.8
Intra-abdominal abscess (%)	0	0	
Delayed gastric emptying (%)	0	0	
Pulmonary complications (%)	0	0	
Pancreatic fistula	28.6	33.3	0.8
Grade A	1	4	
Grade B	1	1	
Mortality	0	0	
Recurrence	0	0	

Compliance with ethical standards

Conflict of interest All authors listed have contributed sufficiently to the project to be included as authors, and to the best of our knowledge, no conflict of interest, financial or other exists.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent For the radiological and surgical procedure, the processing of personal data was obtained from each individual study participant. In accordance with Italian Drug Agency (AIFA) guide-lines, observational studies using retrospective data or materials do not require formal approval by the local ethics committee.

References

- Hankey BF, Ries LA, Kosary CL et al (2000) Partitioning linear trends in age-adjusted rates. Cancer Causes Control 11:31–35
- 2. Balcom JH 4th, Rattner DW, Warshaw AL et al (2001) Ten-years experience with 733 pancreatic resections: changing indications, older patients and decreasing length of hospitalization. Arch Surg 136:391–398
- Briggs CD, Mann CD, Irving GR et al (2009) Systematic review of minimally invasive pancreatic resection. J Gastrointest Surg 13:1129–1137
- Nigri GR, Rosman AS, Petrucciani N et al (2011) Metaanalysis of trials comparing minimally invasive and open distal pancreatectomies. Surg Endosc 25:1642–1651
- Clavien PA, Barkun J, de Oliveira ML et al (2009) The Clavien– Dindo classification of surgical complications: five-year experience. Ann Surg 250:187–196
- Bassi C, Dervenis C, Butturini G et al (2005) International Study Group on Pancreatic Fistula Definition: postoperative pancreatic

fistula: an international study group (ISGPF) definition. Surgery $138{:}8{-}13$

- 7. Wente MN, Bassi C, Dervenis C et al (2007) Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 142:761–768
- Wente MN, Veit JA, Bassi C et al (2007) Post-pancreatectomy hemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition. Surgery 142:20–25
- Rocca A, Calise F, Marino G et al (2014) Primary giant hepatic neuroendocrine carcinoma: a case report. Int J Surg 12(Suppl 1):S218–S221
- Guerra G, Cinelli M, Mesolella M et al (2014) Morphological, diagnostic and surgical features of ectopic thyroid gland: a review of literature. Int J Surg 12S1:S3–S11
- 11. Truta B, Allen BA, Conrad PG et al (2005) A comparison of the phenotype and genotype in adenomatous polyposis patients with and without a family history. Fam Cancer 4:127–133
- Thirlwell C, Howarth KM, Segditsas S et al (2007) Investigation of pathogenic mechanisms in multiple colorectal adenoma patients without germline APC or MYH/MUTYH mutations. Br J Cancer 96:1729–1734
- Rippa E, Altieri F, Chiara Di Stadio S et al (2015) Ectopic expression of gastrokine 1 in gastric cancer cells up-regulates tight and adherens junction proteins network. Pathol Res Pract 211:577–583
- 14. Dragoni S, Turin I, Laforenza U et al (2014) Store-operated ca(2 +) entry does not control proliferation in primary cultures of human metastatic renal cellular carcinoma. Biomed Res Int 2014:739494
- Moccia F, Zuccolo E, Poletto V et al (2015) Endothelial progenitor cells support tumour growth and metastatisation: implications for the resistance to anti-angiogenic therapy. Tumour Biol 36:6603–6614
- Dragoni S, Reforgiato M, Zuccolo E et al (2015) Dysregulation of VEGF-induced pro-angiogenic Ca²⁺ oscillations in primary myelofibrosis-derived endothelial colony forming cells. Exp Hematol 43:1019–1030.e3
- 17. Zuccolo E, Bottino C, Diofano F et al (2016) Constitutive storeoperated Ca^{2+} entry leads to enhanced nitric oxide production and proliferation in infantile hemangioma-derived endothelial colony forming cells. Stem Cells Dev 25:301–319
- Poletto V, Dragoni S, Lim D et al (2016) Endoplasmic reticulum Ca²⁺ handling and apoptotic resistance in tumor-derived endothelial

colony forming cells. J Cell Biochem 117:2260–2271. doi:10.1002/ jcb.25524

- Moccia F, Zuccolo E, Poletto V et al (2016) Targeting Stim and Orai proteins as an alternative approach in anticancer therapy. Curr Med Chem 23:3450–3480. doi:10.2174/092986732366616 0607111220
- 20. Berra-Romani R, Avelino-Cruz JE, Raqeeb A et al (2013) Ca²⁺dependent nitric oxide release in the injured endothelium of excised rat aorta: a promising mechanism applying in vascular prosthetic devices in aging patients. BMC Surg 13(Suppl 2):S40
- 21. Moccia F, Dragoni S, Cinelli M et al (2013) How to utilize Ca²⁺ signals to rejuvenate the repairative phenotype of senescent endothelial progenitor cells in elderly patients affected by car-diovascular diseases: a useful therapeutic support of surgical approach? BMC Surg 13(Suppl 2):S46
- 22. Matsumoto T, Shibata K, Ohta M et al (2008) Laparoscopic distal pancreatectomy and open distal pancreatectomy: a non-randomized comparative study. Surg Laparosc Endosc Percutan Tech 18:340–343
- Scurtu R, Bachellier P, Oussoultzoglou E et al (2006) Outcome after pancreaticoduodenectomy for cancer in elderly patients. J Gastrointest Surg 10:813–822
- Fong Y, Blumgart LH, Fortner JC et al (1995) Pancreatic or liver resection for malignancy is safe and effective for the elderly. Ann Surg 222:426–437
- 25. Kooby DA, Chu Ck (2010) Laparoscopic management of pancreatic malignancies. Surg Clin North Am 90:427–446

- 26. Di Norcia J, Schrope BA, Lee MK et al (2010) Laparoscopic distal pancreatectomy offers shorter hospital stays with fewer complications. J Gastrointest Surg 14:1804–1812
- 27. Dicitore A, Caraglia M, Gaudenzi G et al (2014) Type I interferon-mediated pathway interacts with peroxisome proliferator activated receptor-γ (PPAR-γ): at the cross-road of pancreatic cancer cell proliferation. Biochim Biophys Acta Rev Cancer 1845:42–52. doi:10.1016/j.bbcan.2013.11.003
- Benassai G, Desiato V, Benassai G et al (2014) Adrenocortical carcinoma: what the surgeon needs to know. Case Rep Lit Rev Int J Surg 12:22–28
- 29. Eom BW, Jang JY, Lee SE et al (2008) Clinical outcomes compared between laparoscopic and open distal pancreatectomy. Surg Endosc 22:1334–1338
- 30. Amato B, Sivero L, Vigliotti G et al (2013) Surgery for cancer in the elderly: state of the art. Chirurgia 26:313–315
- Rispoli C, Rocco N, Iannone L, Amato B (2009) Developing guidelines in geriatric surgery: role of the grade system. BMC Geriatr 9(Suppl.1):A99
- 32. Compagna R, Vigliotti G, Rispoli C et al (2013) Carotid screening with Duplex ultrasound in elderly asymptomatic patients candidate to general surgery. Chirurgia 26:291–294
- Amato B, Donisi M, Rispoli C et al (2013) Enhanced recovery after surgery (ERAS) program in the elderly: is it feasible? Chirurgia 26:307–308