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Results of 100 consecutive laparoscopic distal pancreatectomies: postoperative outcome, cost-benefit analysis, and quality of life assessment

Marco Braga · Nicolò Pecorelli · Denise Ferrari · Gianpaolo Balzano · Walter Zuliani · Renato Castoldi

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Abstract
Background Laparoscopic distal pancreatectomy (LDP) has been recently proposed as the procedure of choice for lesions of the pancreatic body and tail in experienced centres. The purpose of this study is to assess the potential advantages of LDP in a consecutive series of 100 patients.
Methods Propensity score matching was used to identify patients for comparison between LDP and control open group. Match criteria were: age, gender, ASA score, BMI, lesion site and size, and malignancy. All patients were treated according to an early feeding recovery policy. Primary endpoint was postoperative morbidity rate. Secondary endpoints were operative time, blood transfusion, length of hospital stay (LOS), hospital costs, and quality of life.
Results Thirty patients of the LDP group had pancreatic adenocarcinoma. Conversion to open surgery was necessary in 23 patients. Mean operative time was 29 min shorter in the open group ($p = 0.002$). No significant difference between groups was found in blood transfusion rate and postoperative morbidity rate. LDP was associated with an early postoperative rehabilitation and a shorter LOS in uneventful patients. Economic analysis showed € 775 extra cost per patient of the LDP group. General health perception and vitality were better in the LDP group one month after surgery.
Conclusion Laparoscopic distal pancreatectomy improved short-term postoperative recovery and quality of life in a consecutive series of both cancer and non-cancer patients. Despite the extra cost, the laparoscopic approach should be considered the first option in patients undergoing distal pancreatectomy.

Keywords Pancreatic cancer · Pancreatectomy · Quality of Life · Costs · Laparoscopy

M. Braga (✉) · N. Pecorelli · D. Ferrari · G. Balzano · W. Zuliani · R. Castoldi
Department of Surgery, San Raffaele Hospital, Vita-Salute San Raffaele University, Via Olgettina 60, 20132 Milan, Italy
e-mail: braga.marco@hsr.it

Laparoscopic distal pancreatectomy (LDP) is one of the most challenging abdominal operations lasting on average 3–4 h, with a high morbidity rate being found also in experienced centers [1–3]. LDP has been described either in association with splenectomy [4] or as spleen-preserving procedure with or without splenic vessels ligation [5–7].

Large series in high volume hospitals reported an increasing confidence with the laparoscopic approach translating in a reduction of operative time, and the extension of indications including both cancer and high complication risk score patients [8, 9].

In several systematic reviews and meta-analyses [10–12], LDP has been associated with reduced operative bleeding and transfusion rate, and shorter length of hospital stay (LOS) compared to the open procedure. However, the quality of studies included in the meta-analyses is suboptimal because of non-consecutive series featuring patients selected to undergo laparoscopy, retrospective collection of data, and small sample size. Moreover, hospital costs and postoperative quality of life were not extensively assessed in the previous studies. Therefore, the real advantages of LDP still represent an open issue.

The purpose of this study is to assess the potential advantages of LDP over open distal pancreatectomy (ODP) in a consecutive series of both cancer and non-cancer patients. Primary endpoint was postoperative morbidity rate. Secondary endpoints were operative time, blood transfusion rate, LOS, hospital costs, and quality of life.

Patients and methods

Between April 2010 and April 2013, 170 consecutive adult patients undergoing distal pancreatectomy for either benign or malignant pancreatic lesion localized to the pancreatic body or tail were considered for laparoscopic approach. Seventy (41.2 %) patients were excluded from laparoscopic surgery due to one of the following: borderline resectable cancer at CT scan staging ($n = 46$); cardiovascular dysfunction (New York Heart Association class > 3) ($n = 7$); respiratory dysfunction (arterial $pO_2 < 70$ mmHg) ($n = 4$); BMI > 35 ($n = 8$); and refusing consensus to laparoscopy ($n = 5$). The remaining 100 patients undergoing LPD were included in the study after signing a written informed consent.

All parameters included in our Institutional pancreatic database have been prospectively collected in our Institution. Propensity score matching was used to identify patients for comparison between LDP and control open group. A propensity score was generated for each patient by performing a logistic regression using the type of surgical approach as the independent variable [13]. The following variables were used for propensity score calculation: age (±5 years), gender, ASA grading (1–2 vs. 3–4), BMI grading (<24, 24–30, >30), site of lesion (body or tail), lesion size (<40 mm vs. ≥40 mm), and malignancy. If multiple patients were identified, the closest one in time was selected.

Before surgery demographics, ASA score, serum levels of glucose, albumin, hemoglobin, and primary diagnosis were recorded in all patients. All procedures were performed by the same surgical team with large experience in both open pancreatic surgery and other laparoscopic GI procedures [14, 15]. LDP with splenectomy and standard lymphadenectomy was performed in all cancer patients.

Laparoscopic surgical technique was the same previously reported by Melotti and colleagues [7]. A multifrequency laparoscopic ultrasound probe was used to identify small deep lesions. In case of spleen-preserving procedure, the dissection moved from the body to the tail of pancreas after identification of the splenic vein. Then, the dissection of the splenic artery moved from the tail to the body of pancreas. In case of LDP with splenectomy, a retropancreatic tunnel was opened at the neck level, and then, both splenic artery and vein were divided before splenopancreatic dissection. In both spleen-preserving and splenectomy-associated procedures, the first option for pancreas division was mechanical linear stapler with 4.1-mm staples. One drain was routinely placed close to the pancreatic stump.

Duration of surgery and operative blood loss were recorded in all patients. The volume of operative blood loss was calculated by adding the blood aspirated to the weight of the gauzes used during surgery. In cancer patients, resection margin status and the number of lymph nodes retrieved were also recorded.

Postoperative analgesia was ensured by continuous epidural infusion of 0.2 % ropivacaine (4–6 mL/h) or, when contraindicated, by intravenous morphine hydrochloride (patient-controlled administration) at a maximum of 4 mg/h with a single dose of 1 mg and free interval of 10 min. In both groups, recovery of oral fluids and solid food intake was scheduled on postoperative days 1 and 2, respectively [16]. Abdominal drain was removed on postoperative day 3, after a pancreatic fistula was ruled out (drain amylase value was less than 3 times the serum value).

Primary endpoint was postoperative morbidity rate. Secondary endpoints were operative time, blood transfusion rate, LOS, hospital costs, and quality of life.

Postoperative complications were a priori defined according to our previous study [17]. Microbiological analysis and positive culture proved all infectious complications. Pancreatic fistula was defined according to ISGPF criteria [18]. Postoperative complications were graded according to Clavien–Dindo classification [19], which has been validated in pancreatic surgery [20]. Major complications have been defined as Clavien–Dindo grade 3–5.

Patients were discharged after meeting the following criteria: absence of fever (<37.5 °C for more than 48 h), good pain control with oral analgesics, adequate oral food intake, recovery of gut function, valid mobilization, and acceptance of discharge by the patient.

Follow-up for infectious and non-infectious complications was carried out for 30 days after hospital discharge. Readmission within 30 days after discharge was also recorded.

Postoperative quality of life was assessed by the SF-8 questionnaire at one and three months after surgery [21].

Cost–benefit analysis was based on the following costs: surgical instruments (including re-usable trocars and harmonic scalpel), operative room (€ 502 per hour), routine surgical care, diagnosis and treatment of postoperative complications. Operative room costs included healthcare personnel, medications, and structure costs. To calculate the cost of each postoperative complication, the following items were assessed: laboratory and microbiology analysis; medical, technical, and diagnostic services; surgical and therapeutic interventions; medications; prolonged LOS; and outpatient clinic follow-up. The mean LOS of uncomplicated patients was the basis to calculate the prolonged LOS in each patient with complication. In patients who developed multiple complications, resources used to treat each complication were recorded separately.

Table 1 Demographics and preoperative variables

	Open ($n = 100$)	LDP ($n = 100$)	p-value
Age (years)	61.0 (13.8)	61.4 (13.5)	0.802
Gender			
Men	44	44	1.000
Women	56	56	
ASA[a] score			
I–II	88	83	0.315
III–IV	12	17	
BMI			
<24	47	30	
24–29.9	43	57	0.127
30–34.9	10	13	
Lesion site			
Body	66	66	1.000
Tail	34	34	
Lesion size			
<40 mm	71	72	0.874
Pancreatic adenocarcinoma	34	30	0.544
Serum Haemoglobin (g/L)	133 (17)	134 (14)	0.560
Serum Albumin (g/L)	39.3 (4.8)	40.8 (3.7)	0.082
Diabetes	24	21	0.611

Data are number of patients or mean (SD)

[a] American Society of Anesthesiologist

Table 2 Surgical variables

	Open ($n = 100$)	LDP ($n = 100$)	p-value
Duration of surgery (min)	213 (63)	239 (64)	0.003
Operative blood loss (mL)	685 (733)	464 (548)	0.016
Transfused patients	27	22	0.511
Pancreatic stump closure			
Stapler	8	86	<0.001
Handsewn	92	14	
Intraoperative ultrasound	8	22	0.024
Conversion to open	Not applicable	23	–

Data are number of patients or mean (standard deviation)

Statistical analysis

Descriptive data are reported as mean (standard deviation) and range or number of patients and percentage. Categorical variables were compared by the Chi square test and continuous variables by the Student's t test and non-parametric Mann–Whitney U test. The significance level was set at 0.05. Data analysis was performed using the Statistical Package for the Social Science (SPSS, Chicago, IL), version 20.

The study was registered at ClinicalTrials.gov on December 10, 2010 and had identifier NCT01258621.

Results

Demographics and preoperative variables are shown in Table 1. Matched patients in the open group underwent surgery between May 2007 and March 2010. Indications for surgery in the LDP group were primary pancreatic adenocarcinoma ($n = 30$), endocrine tumor ($n = 28$), mucinous cystadenoma ($n = 14$), IPMN ($n = 14$), large serous cystadenoma ($n = 3$), pancreatic metastasis derived from renal cell carcinoma ($n = 3$), others ($n = 8$). Indications for surgery in the open group were primary pancreatic adenocarcinoma ($n = 34$), endocrine tumor ($n = 29$), large serous cystadenoma ($n = 8$), IPMN ($n = 7$), mucinous cystadenoma ($n = 6$), pancreatic metastasis derived from renal cell carcinoma ($n = 5$), others ($n = 11$).

In the LDP group, conversion to open procedure was necessary in 23 patients. Reasons for conversion were lack of progress ($n = 12$), bleeding ($n = 6$), cancer involvement of celiac axis ($n = 4$), and cancer involvement of spleno-mesenteric vein confluence ($n = 1$).

Table 2 reports operative variables in the overall series. Duration of surgery was shorter in the open group ($p = 0.003$). In a higher proportion of patients who underwent LDP, intraoperative ultrasonography was necessary to detect the site of the lesion ($p = 0.024$). Operative blood loss was significantly lower in the LDP group but the reduction of transfusion rate was not significant. In patients with benign disease, spleen-preserving procedure without ligation of splenic vessels was successfully carried out in 36 out of 45 (80.0 %) LDP patients, and in 27 out of 41 (65.8 %) ODP patients (p-value = 0.140). The mean lengths of incision were 67.9 ± 40.9 mm in the LDP group and 192.2 ± 22.9 mm in the open group (p-value < 0.001).

In patients with primary pancreatic cancer, the mean numbers of lymph nodes collected were 14.6 ± 8.1 (range 6–32) in LDP patients and 15.0 ± 8.7 (range 6–26) in ODP patients (p-value = 0.850). Microscopic infiltration of resection margins was found in 8 (26.7 %) patients of the LDP group and in 11 (32.4 %) patients of the ODP group (p-value = 0.785).

Table 3 reports short-term postoperative outcome. No postoperative mortality occurred. Overall morbidity rate was similar in both groups, and a vast majority of postoperative events were minor complications. Major complications occurred in nine patients of LDP group and in six patients of the ODP group. Pancreatic fistula occurred in 53

Table 3 Postoperative morbidity

	Open ($n = 100$)	LDP ($n = 100$)	p-value
Overall morbidity	64	66	0.882
Complication grade[a]			
0—no complications	36	34	0.882
I	15	11	0.529
II	43	46	0.678
III	5	9	0.410
IV	1	0	0.327
V—mortality	0	0	1.000
Relaparotomy	1	4	0.174
Pancreatic fistula	51	53	0.888
Grade A	40	36	0.662
Grade B	10	14	0.412
Grade C	1	3	0.632
Bleeding	3	7	0.248
Peripancreatic fluid collection	1	5	0.211
Wound complications	3	4	0.703
Cardiorespiratory complications	11	9	0.815
Delayed gastric emptying	1	1	1.000

Data are number of patients (%)

Numbers of single type of complication do not add up to the number of overall complications within the two groups, in relation to the possible occurrence of more types of complication in some patients

[a] Complications are graded according to Clavien-Dindo classification

Table 4 Postoperative recovery

	Open ($n = 100$)	LDP ($n = 100$)	p-value
Bowel function recovery	3.1 (1.1)	2.4 (1.0)	0.013
First oral fluids intake	2.8 (1.0)	1.9 (0.9)	0.001
First solid food intake	3.9 (1.2)	2.8 (1.0)	0.001
Intravenous fluids suspension	4.6 (1.6)	3.7 (1.8)	0.002
Mobilization on POD 1 (min)	84 (51)	149 (60)	0.001
LOS in uneventful patients	6.9 (1.4)	6.2 (1.5)	0.047
LOS in patients with complication grade 0–II	8.6 (2.1)	8.6 (3.0)	0.904
LOS in patients with complication grade III–V	18.2 (9.4)	15.2 (6.2)	0.008

Data are number of patients (%) or mean postoperative day (standard deviation)

POD postoperative day, *LOS* length of hospital stay

patients of the LPD group and in 51 patients of the ODP group. The majority of patients with pancreatic fistula had a grade A fistula (36/53, 67.9 % in the LDP group and 40/51, 78.4 % in the ODP). Reoperation was necessary in four patients in the LDP group (bleeding $n = 3$, peripancreatic abscess $n = 1$) and in one patient in the open group (bleeding). Abdominal drain was removed before discharge in 44 patients of the LDP group and in 47 patients of the ODP group (p-value = 0.777).

Table 5 Economic analysis of the LDP group

Operative room		Postoperative outcome	
Surgical equipment	+751	LOS in uneventful patients	−222
Longer operative time	+228	Cost of complications	+18
Overall	+979	Overall	−204
Balance	+775		

Data are reported in Euros per patient

Table 4 reports postoperative recovery in both groups. Recoveries of both oral feeding and bowel function, mobilization, and suspension of i.v. fluids occurred significantly earlier in the LDP group. Consequently, LDP reduced hospital stay in uneventful patients (p-value = 0.047). Readmission occurred in eight patients of LDP group because of peripancreatic fluid collection requiring percutaneous drainage ($n = 6$) and bleeding ($n = 2$), and in seven patients of the ODP group because of peripancreatic fluid collection requiring percutaneous drainage ($n = 6$), and bleeding ($n = 1$).

Considering the LDP group, we compared the subgroup of converted patients with the subgroup of patients who had a successful laparoscopic procedure. A significant reduction in the successful subgroup was found in duration of surgery (227.5 vs. 279.5 min, p-value < 0.001), blood transfusion rate (15.6 vs. 43.5 %, p-value = 0.009), and LOS (7.7 vs. 10.4 days, p-value < 0.001). Comparing successful laparoscopic subgroup versus open group, duration of surgery was similar (p-value = 0.120), while blood transfusion rate was higher (p-value = 0.027), and LOS was longer in the open group (p-value = 0.046).

Table 5 summarizes the extra charges and the savings associated to laparoscopic approach. The mean extra charge of laparoscopic surgical instruments was €751 per patient. Operative room (OR) occupancy cost resulted in €228 as additional charge per patient of LDP group. Therefore, the additional OR charge in the LDP group was €979 per patient. Fifty patients had an uneventful postoperative course (LDP $n = 24$, ODP $n = 26$). In these patients, the mean cost of routine care was the same in both groups (€318/day), while the mean postoperative stay was 6.2 days in the LDP group and 6.9 days in the ODP group. This translated to €222 saving per patient of LDP group. The costs of postoperative complications were €56,012 in the LDP group and €54,190 in the ODP group. This resulted in a saving of €1,822 in the ODP group (€ 18 per patient). Therefore, the net balance was €775 extra cost per patient in the LDP group.

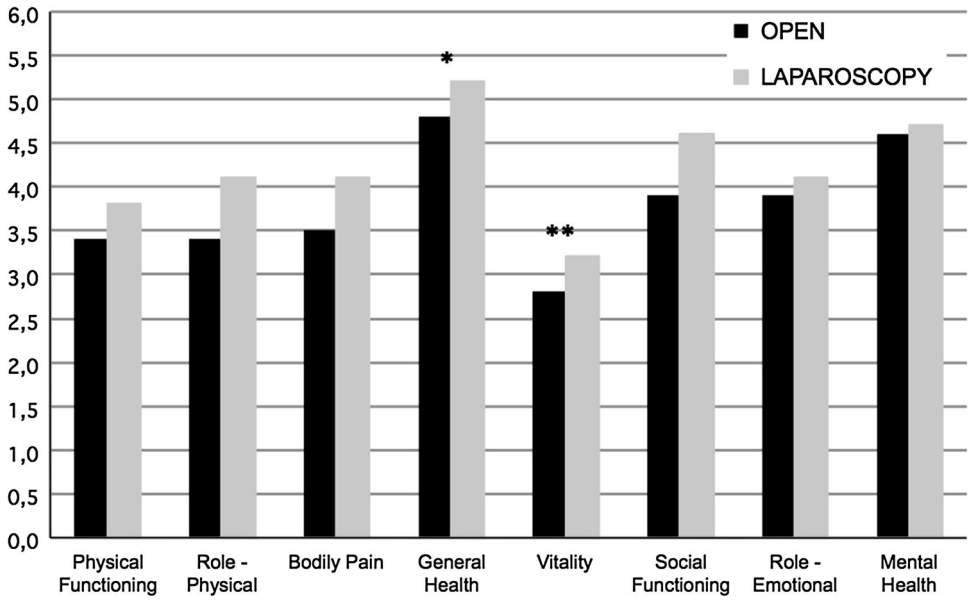

Fig. 1 Quality of life parameters 1 month after surgery. Comparison between laparoscopy and open surgery. $*p = 0.03$; $**p = 0.008$

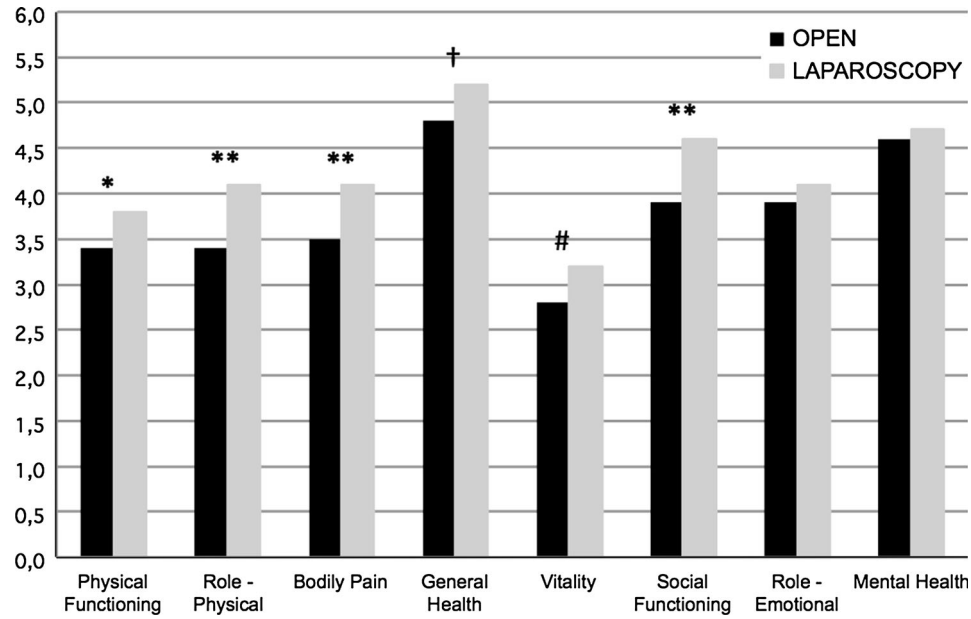

Fig. 2 Quality of life parameters 1 month after surgery. Comparison between patients discharged with or without abdominal drain. $*p = 0.005$; $**p < 0.001$; $^{\dagger}p = 0.024$; $^{\#}p = 0.001$

A separate analysis in patients with benign or malignant diseases did not result in substantial short-term outcome and cost–benefit differences in comparison with the overall series (data not shown).

Figure 1 shows quality of life parameters one month after surgery. A slight but significant improvement in the LDP group was found in both general health perception and vitality. The most important factor impairing quality of life parameters was the presence of abdominal drain at home, regardless of surgical technique (Fig. 2). Three months after surgery, no difference in any quality of life parameters was found between LDP and open groups.

Discussion

In recent years, LDP has gained popularity among experienced pancreatic surgeons. No postoperative mortality has been reported, and both major complication and pancreatic fistula rates were similar to previous open series in high volume centers [22–24]. Strict selection criteria, high-volume hospital, and the presence of an experienced team in pancreatic surgery have been reported as the most relevant factors to shorten the learning curve [25].

Two single-center [26, 27] and one multicenter [28] case–match trials reported that LDP was associated with

a significant reduction of LOS compared to open procedure, despite no difference in both overall postoperative morbidity and pancreatic fistula rates being reported. In the past few years, systematic reviews and meta-analyses [10–12] have been carried out. LDP has been associated to lower operative blood loss and transfusion rate, shorter LOS, and earlier recovery of oral feeding. In the largest meta-analyses LDP was also associated to a lower risk of both grade B–C pancreatic fistula [10, 12] and wound infection [12]. However, due to the suboptimal quality of the studies included in the meta-analyses, the real advantage of LDP still represents an open issue.

Recently, the introduction of novel perioperative care protocols has allowed for a faster postoperative rehabilitation and considerable benefits on postoperative outcome. In colorectal surgery, the implementation of these protocols also in open surgery limited the advantages of laparoscopy on hospital stay [29]. In the present study, the impact of LDP on outcome has been assessed within a fast-track recovery pathway, which was applied in the open group too.

Duration of LDP was longer when compared with a larger consecutive series reported by Song et al. (average 195 min), who included only 10 % patients with primary adenocarcinoma in comparison with 30 % in our series [8]. As previously reported, LPD was longer compared to the open procedure [10, 11]. Intraoperative detection of pancreatic lesion required an ultrasonography examination in 22 % of patients compared to 8 % during the open approach, and this contributed to a lengthier procedure. According to previous studies [10–12], LDP was associated to a lower operative blood loss; however, this did not translate into a significant reduction of transfusion rate in our series. When the analysis was restricted to patients who had laparoscopic procedure successfully completed, blood transfusion rate was significantly lower in comparison with the open group.

Even if not statistically significant, LDP was associated with a higher chance of successful spleen-preserving procedure than the open technique in patients with benign diseases. In both groups, unplanned splenectomy occurred more frequently in patients with a higher BMI and larger lesions. According to Nakamura's meta-analysis [12], oncologic outcome of LDP was not different from ODP. In fact, both the number of lymph nodes collected and the rate of microscopic infiltration of the resection margin were similar in both groups.

The conversion rate in our study was higher than in other series, probably being related to the higher percentage of cancer resections performed in the laparoscopic group [8]. Since we performed an intention to treat analysis, the relatively high conversion rate may have also limited the potential advantages of the laparoscopic approach in postoperative recovery.

Overall morbidity rate is comparable with other large series of LDP [2, 3, 7, 8, 30, 31]. Laparoscopic approach did not reduce either the overall morbidity rate or grade B–C pancreatic fistula in the present series. The different pancreatic stump closure technique used in the two groups had no impact on the occurrence of pancreatic fistula. This is consistent with previous reports showing comparable pancreatic fistula rates following different pancreatic stump closure techniques in patients who underwent ODP [22, 23, 32].

Laparoscopic approach has been associated to an earlier postoperative rehabilitation resulting in a shorter LOS in the subgroup of uneventful patients. Shortening of LOS in the laparoscopic group was limited compared with previous studies [10–12], probably because early recovery of oral feeding substantially shortened hospital stay in the open group when compared to previous standard postoperative care [23]. LOS in the LDP group was slightly longer than that in other laparoscopic series. This could be explained by two main factors: (i) about 40 % of patients in our series came from Central or Southern Italy, and they completed postoperative recovery before being discharged; and (ii) 36 % of LDP patients had cancer, whereas the vast majority of patients in the other series had benign disease [10–12].

Two small-sized comparative trials [33, 34] reported similar hospital costs between LDP and ODP, as savings due to better short-term postoperative outcome balanced the extra charge of laparoscopic instruments. In our series, laparoscopy did not reduce postoperative morbidity rate and severity, thus the savings related to shorter LOS in the LDP group were lower than those in the previous studies. Therefore, the operative room extra charge due to laparoscopic approach was only partially balanced.

Cost–benefit analysis was focused on hospital costs only, though other important issues such as cosmesis and quality of life after discharge should also be considered in order to assess the role of laparoscopy for patients undergoing distal pancreatectomy. The high rate of patients discharged with abdominal drain in both groups reduced the potential advantages of LDP on physical and social activities early after discharge. Nevertheless, the shorter incision length not only improved cosmesis, but it was probably also the main determinant for a better general health perception and vitality in the laparoscopic group.

In conclusion, LDP approach improved postoperative recovery, cosmesis, and quality of life in a consecutive series of both cancer and non-cancer patients. No significant difference was found in overall morbidity and LOS. The relatively high conversion rate and considerable number of cancer patients probably limited the potential advantages of laparoscopy on short-term postoperative

outcome. Despite the extra cost, laparoscopic approach should be considered as the first option in patients undergoing distal pancreatectomy.

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