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ORIGINAL ARTICLE

Short-term and long-term outcomes after robot-assisted versus laparoscopic distal pancreatectomy for pancreatic neuroendocrine tumors (pNETs): a multicenter comparative study

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Abstract

Purpose Minimally invasive surgery has increasingly gained popularity as a treatment of choice for pancreatectomy with encouraging initial results in robotic distal pancreatectomy (RDP). However, few data are available on the comparison between RDP and laparoscopic distal pancreatectomy (LDP) for pancreatic neuroendocrine tumors (pNETs). Our aim, thus, is to compare perioperative and long-term outcomes as well as total costs of RDP and LDP for pNETs.

Methods All RDPs and LDPs for pNETs performed in four referral centers from 2008 to 2016 were included. Perioperative outcomes, histopathological results, overall (OS) and disease-free survival (DFS), and total costs were evaluated.

Results Ninety-six RDPs and 85 LDPs were included. Demographic and clinical characteristics were comparable between the two cohorts. Operative time was 36.5 min longer in the RDP group ($p = 0.009$) but comparable to LDP after removing the docking time (247.9 vs 233.7 min; $p = 0.6$). LDP related to a lower spleen preservation rate (44.7% vs 65.3%; $p < 0.0001$) and higher blood loss (239.7 ± 112 vs 162.5 ± 98 cc; $p < 0.0001$). Advantages in operative time for RDP were documented in case of the spleen preservation procedures (265 ± 41.52 vs 291 ± 23 min; $p = 0.04$). Conversion rate, postoperative morbidity, and pancreatic fistula rate were similar between the two groups, as well as histopathological data, OS, and DFS. Significant advantages were evidenced for LDP regarding mean total costs (9235 (± 1935) € vs 11,226 (± 2365) €; $p < 0.0001$).

Conclusions Both RDP and LDP are safe and efficacious for pNETs treatment. However, RDP offers advantages with a higher spleen preservation rate and lower blood loss. Costs still remain the main limitation of the robotic approach.

Keywords Robot-assisted pancreatectomy · Pancreatic neuroendocrine tumors · Long-term outcomes · Minimally invasive

Introduction

The minimally invasive approach used in the treatment of pancreatic neuroendocrine tumors (pNETs) has gradually increased over the last decade [1].

Since its first application as a surgical option for islet cell tumors [2], reports have been published on the laparoscopic treatment of pNETs. However, most of these data are provided based on limited experiences and limited long-term follow-up studies [3–6]. As compared to the open access, evident

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advantages were reported in terms of length of hospital stay and reduced intraoperative blood loss whereas an equivalent rate of complications was demonstrated postoperatively [7].

Recently, a step towards a major surgical precision has been made through the development of the robotic surgical system. The first case of robotic distal pancreatectomy (RDP) was reported in 2002 [8], leading to a new era of minimally invasive pancreatic surgeries. Its high-definition and three-dimensional vision, as well as the seven degrees of freedom and improved ergonomics, have allowed to overcome some laparoscopy-related limits [9] and to even more improve the spleen preservation rate [9–16].

The first application of pNET resection was published in 2003 [17]. However, most state-of-the-art data on the robotic treatment of pNETs can only be retrieved from a larger RDP series. In addition, no randomized clinical studies can be found in the literature to demonstrate the potential benefits of robotic pNET treatment over laparoscopic and open approaches.

We assumed that, in comparison with laparoscopy, RDP would guarantee better perioperative and, at least, similar long-term outcomes in the treatment of pNETs.

To accomplish this purpose, we report the results of a multicenter Italian study of comparison between RDP and laparoscopic distal pancreatectomy (LDP) in the treatment of pNETs to assess the robot-assisted feasibility and outcomes in a large series and to discuss the results obtained as compared to the laparoscopic approach.

Material and methods

The study population comprised a cohort of 181 patients diagnosed with pNET and who underwent minimally invasive distal pancreatectomy in four tertiary Italian referral centers from December 2008 to December 2016. A total of five surgeons, with an already extensive experience in both laparoscopic and robot-assisted distal pancreatectomy, performed all the cases. All centers involved in the study are classified as high-volume, performing more than 50 pancreatic resections per year.

All data were retrospectively collected from prospectively maintained databases at each center and subsequently put together to be analyzed. An approval from the institutional review board of each center was obtained.

Demographic and clinical data were collected for each patient, notably gender, age, body mass index (BMI) at the time of the operation, the American Society of Anesthesiologists (ASA) score, symptoms, comorbidities, previous abdominal surgery, preoperative endoscopic ultrasonography (EUS) with or without fine-needle aspiration (FNA), previous pancreatitis, and tumor location. Surgical characteristics included the following: operative time (calculated based on the time between skin incision and skin closure), robotic docking duration, estimated intraoperative blood loss, and conversion rate.

Patients who underwent surgery before February 2012 were operated according to the ENETS Consensus Guidelines 2006 [18]. All the subsequent cases were treated according to the ENETS Consensus Guidelines 2012 [19].

The choice of the operative modality (laparoscopic or robot-assisted) was at the discretion of the operating surgeon and based on the robotic platform availability. If the robotic operating room was unavailable at the time of surgery, a laparoscopic left pancreatectomy was always performed.

In three out of four centers, the da Vinci Si platform was used in all cases, while in the remaining center, the Xi platform was employed from November 2014.

The type of procedure was planned before surgery. However, the final approach was decided upon during surgery, based on a combination of macroscopic and ultrasonographic findings whenever required.

Patients who underwent enucleation during the study period were excluded from the analysis, in order to guarantee a more homogenous comparison in terms of short- and long-term outcomes between the two study cohorts.

Trocar positioning, the number of trocars used, and the device used for pancreatic division (e.g., endostapler, ultrasonic scalpel, and Wirsung's duct suture) were at the surgeon's discretion. Splenectomy was performed in all cases of suspected malignant disease or when strong adhesions between the lesion and the splenic vessels were detected.

Morbidity and length of postoperative hospital stay were also analyzed. Postoperative complications were categorized according to the Clavien-Dindo classification [20] for intra-abdominal surgical complications. Postoperative pancreatic fistula (POPF) was defined and graded according to the International Study Group of Pancreatic Fistula (ISGPF) definition [21].

Post-pancreatectomy hemorrhage was defined according to the guidelines of the International Study Group of Pancreatic Surgery (ISGPS) [22]. Postoperative mortality was also recorded and defined as any death occurring within 30 days or during the index hospitalization after surgery.

Readmissions were defined as any hospitalization in any of the four centers included in our study or any admission to any health facility, excluding a subacute or rehabilitation admission, within 90 days from patient discharge.

Histopathological data were acquired according to the WHO 2010 classification for neuroendocrine neoplasms of the gastroenteropancreatic system [23] and the ENETS TNM classification [24]. In addition, resection status, tumor diameter, and number of lymph nodes harvested were recorded. The resection margin was defined as R1 when less than 1-mm tumor-free margin was encountered. Long-term outcomes, in terms of local and distant recurrence, and disease-specific and overall survival were evaluated.

Direct hospital costs were collected from economic offices. The acquisition and maintenance of the robotic device were excluded from the analysis. The calculated costs data were operating room costs (in terms of operating time per minute, surgeon, and anesthetist time per minute), surgical equipment such as robotic and laparoscopic instruments, energy devices and staplers, and hospital stay costs (including intensive care unit, floor, pharmaceutical, laboratory, pathology, and radiology costs). Costs were analyzed in Euros (€). Any 30-day hospital readmissions were not included.

Statistical analysis

Means and standard deviations (SDs) were used for all continuous data while numbers and percentages were calculated for all categorical data. Univariate analysis included Student's *t* tests, Mann-Whitney U test, χ^2 test, and Fisher's exact tests. All tests were two-tailed and a p value ≤ 0.05 was considered statistically significant for all analyses. To analyze improvements of the operative time over the years, the correlation coefficient (rho) and related p value were obtained using Spearman's rank correlation. Overall survival and disease-free survival were calculated using the Kaplan-Meier curves and 95% confidence intervals (CI). Every data was analyzed using SPSS for Windows, version 21 (SPSS Inc., Chicago, IL, USA).

Table 1 Demographic and clinical patients' characteristics

	RDP ($n = 96$)	LDP ($n = 85$)	p
Gender, *n* (%)			
Male	46 (47.9)	43 (50.5)	0.72
Female	50 (52.1)	42 (49.5)	
Age, *n* (%)			
< 65	61 (63.5)	62 (72.9)	0.17
>= 65	35(36.5)	23 (27.1)	
BMI, *n* (%)			
18.5 < BMI < 24.9	43 (44.8)	33 (38.8)	0.12
25 < BMI < 30	26 (27.1)	39 (45.8)	
BMI > 30	27 (28.2)	13 (15.2)	
ASA score, *n* (%)			
ASA 1	15 (15.6)	14 (16.5)	0.93
ASA2	57 (59.4)	53 (62.3)	
ASA 3	22 (22.9)	17 (20)	
ASA4	2 (2.1)	1 (1.2)	
Previous abdominal surgery, *n* (%)	47 (48.9)	35 (41.1)	0.3
Symptomatic patients, *n* (%)	27 (28.1)	29 (34.1)	0.1
Hypoglycemia	12 (12.5)	13 (15.3)	
Abdominal pain	10 (10.4)	10 (11.8)	
Dyspepsia	5 (5.2)	6 (7)	
Preoperative EUS, *n* (%)	22 (22.9)	14 (16.5)	0.42
Previous pancreatitis, *n* (%)	1 (1)	0	0.34
Tumor location, *n* (%)			
Body	25 (26)	22 (25.9)	0.98
Body-tail	40 (41.7)	36 (42.3)	
Tail	31 (32.3)	27 (31.8)	

Results

Demographic and preoperative characteristics

A minimally invasive distal pancreatectomy for pNETs was performed in a total of 181 patients during the 8-year study period. In particular, 96 underwent an RDP and 85 an LDP. Demographic and clinical characteristics of the patients are shown in Table 1. There were no differences in patient characteristics, previous surgeries, symptomatology, preoperative EUS, and tumor location.

Asymptomatic pancreatic lesions were found in 69 (71.9%) and 56 (65.9%) patients who underwent RDP and LDP, respectively ($p = 0.1$). A total of 4 patients (2 in the RDP and 2 in LDP groups) presented with non-functioning multiple tumors associated with MEN-1 syndrome.

Conversely, symptoms were documented in 27 (28.1%) and 29 (34.1%) patients of the RDP and LDP cohorts ($p = 0.1$), with similar rates of hypoglycemia, abdominal pain, and dyspepsia.

Preoperative EUS was equally performed in the two study cohorts (22 cases (22.9%) of RDPs and 14 cases (16.5%) of LDPs; $p = 0.42$) in order to better evaluate the exact tumor location, its size, and proximity to the main pancreatic duct. Preoperative FNA was performed in 10 patients of the RDP group as compared to 5 patients of the LDP cohort ($p = 0.56$) and turned out to be diagnostic in a total of 9 cases (7 and 2 cases of RDPs and LDPs, respectively; $p = 0.23$). One patient of the RDP group developed mild pancreatitis after the endoscopic procedure and recovered conservatively.

Intraoperative outcomes (Table 2)

Of the 96 robot-assisted procedures, 88 were performed with the da Vinci Si platform, while the Xi system was used in the remaining 8 cases.

When comparing the mean operative time, LDPs were shorter on average (233.7 (± 65.6) min) than RDPs (270.2 (± 90.2) min, with a mean docking time of 21.62 (± 13.5) min, available in 87 cases) ($p = 0.009$). However, no difference was found after removing docking time for each patient (RDP 247.9 min vs LDP 233.7 min; $p = 0.6$).

The evolution of the operative time for the RDP group over the years has been reported in Fig. 1. A significant reduction of the mean operative time has been evidenced between the year 2008 and 2016 (390 (± 45.5) vs 253 (± 19.3) min, respectively; $p < 0.0001$), with a rho correlation coefficient of 0.81 ($p < 0.0001$).

Table 2 Surgical characteristics

	RDP (*n* = 96)	LDP (*n* = 85)	*p*
Patient position, *n* (%)			
Modified supine	88 (91.7)	84 (98.8)	0.03
Lateral decubitus	8 (8.3)	1 (1.2)	
Operative time, min (± SD)	270.2 (± 90.2)	233.7 (± 65.6)	0.009
Docking duration[a], min (± SD)	21.62 (± 13.5)	–	
Intraoperative ultrasound, *n* (%)	35 (36.4)	39 (45.8)	0.2
Pancreatic transection, *n* (%)			
Stapler	44 (45.8)	44 (51.8)	0.47
Stapler + suture	24 (25)	15 (17.6)	
Ultrasonic scalpel	28 (29.2)	26 (30.6)	
Spleen and vessels preservation, *n* (%)	64 (65.3)	38 (44.7)	0.003
Vascular resections, *n* (%)	0		
Conversion to open access, *n* (%)	9 (9.4)	12 (14.1)	0.32
Intraoperative blood transfusion, *n* (%)	8 (8.3)	5 (5.8)	0.29
Estimated blood loss, mL (± SD)	162.5 (± 98)	239.7 (± 112)	< 0.0001

[a] Data available in 87 out of 96 patients

An intraoperative ultrasound (IOUS) was equally performed in the two groups (35 patients (36.4%) and 39 patients (45.8%) for RDP and LDP, respectively; $p = 0.2$). Accuracy was 100% in those cases. Similarly, the technique of pancreatic transection did not vary between the two cohorts ($p = 0.47$).

RDP was associated with a significantly higher rate of spleen preservation (64 patients (65.3%) vs 38 patients (44.7%); $p = 0.003$). Of note, suspicious malignant disease and strong adhesions between the tumor and the splenic vessels were the causes of splenopancreatectomy in the remaining 32 patients of the RDP group. Conversely, bleeding along the splenic vessels was an additional cause of splenectomy in 18 out of 47 cases of the LDP cohort.

When comparing the mean operative time between robot-assisted and laparoscopic splenic preservation, a significant advantage was noted for RDP (265 (± 41.52) min) as compared to LDP (291 (± 23) min) ($p = 0.04$). No vascular resection was performed in any case.

Additional intraoperative variables including intraoperative blood transfusion and conversion rate were comparable between the two techniques. However, the estimated blood loss (EBL) was significantly lower in the RDP group (mean 162.5 ± 98 cc) as compared to the laparoscopic approach (239.7 ± 112 cc) ($p < 0.0001$).

The robot-assisted procedure was converted to laparotomy in 9 patients (9.4%) vs 12 patients (14.1%) of the LDP cohort ($p = 0.32$). Six and seven conversions in the RDP and LDP groups, respectively, were due to intraoperative bleeding, while an excess of visceral adipose tissue made robotic and laparoscopic dissection and retraction impossible in 2 and 5 cases, respectively. In the last robot-assisted patient, conversion was due to a tumor rupture.

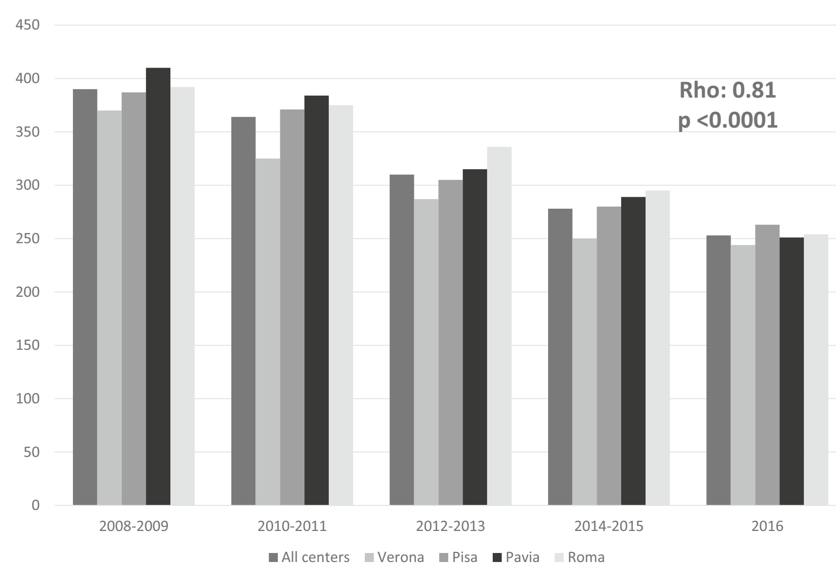

Fig. 1 Operative time over the study period

Postoperative outcomes (Table 3)

Postoperative outcomes were not significantly different between RDP and LDP in terms of length of stay (11 (± 8.8) and 10 (± 7.4) days, respectively; $p = 0.43$) postoperative morbidity incidence (46.9% for RDP and 44.7% for LDP, $p = 0.77$) and pancreatic fistula rate (40 patients (41.7%) and 34 patients (40%), respectively; $p = 0.82$). All grade A fistulas were managed conservatively. It meant that drains were left in place and no further treatment was required. Drains were removed when the output was minimal. Among patients presenting with a grade B fistula, 19 of them required a radiological drainage of fluid collections while 13 patients were treated with intravenous antibiotics only. The four patients with multiple non-functioning pNETs associated with MEN-1 syndrome did not present any postoperative complication, independently of the type of approach used.

A total of 10 (5.5%) patients required reoperation, 6 (6.3%) in the RDP group and 4 (4.7%) in the LDP group ($p = 0.65$). Two patients with a grade C fistula (one per group) required reintervention for an intra-abdominal abscess, which was not drainable radiologically, and an open abdominal lavage and drainage were required. Three other patients with a grade C fistula (2 in the RDP group and 1 in the LDP cohort) underwent a re-laparotomy due to postoperative bleeding 12, 17, and 10 days after surgery, respectively. An active bleeder was identified at a branch of the splenic artery during the emergent exploratory laparotomy in 2 cases, while in the remaining patient, bleeding was due to the erosion of the splenic artery stump. Another patient of the RDP cohort developed a splenic ischemia and required a reoperation. An open splenectomy was subsequently performed. In three other cases (one in the RDP and two in LDP group), reoperation was mandatory due to bowel occlusion while the last patient required a re-laparotomy after RDP due to postoperative bleeding less than 24 h after the first surgery.

Mortality for the entire series was 1% (preoperatively evaluated as an ASA grade 3) because of the development of sepsis in response to a grade C pancreatic fistula and to intra-abdominal abscesses 93 days after RDP. No mortality was registered in the LPD cohort.

As a whole, readmission rate was 11% (20 patients) after a mean time of 67 (± 58) days from surgery. No difference was evidenced between the two groups of comparison (11 and 9 patients in the RDP and LDP groups, respectively; $p = 0.85$). No surgery was needed at readmission in any case.

Histopathological data and long-term outcomes

Pathological details are reported in Table 4. No significant differences were found between the two study groups in terms of tumor functionality, ENETS stage, grade of differentiation, mean number of harvested lymph nodes, and resection margin clearance. In one case of the RDP cohort, an ectopic spleen was found at histopathology. Of note, 39 (40.6%) patients of the RDP group presented a tumor dimension less than 2 cm as compared to 33 (38.8%) cases in the LDP group ($p = 0.77$).

Follow-up was available in 90 patients (93.7%) and 68 patients (80%) of the RDP and LDP cohorts, respectively, while a total of 22 patients were lost after surgery. Mean follow-up was 44 (± 26.3) (range, 10–104) and 41 (± 26.7) months (range, 11–156) for RDP and LDP patients, respectively ($p = 0.59$). Eighty-three (93.3%) and 64 patients (94.1%) were alive and disease-free on the last follow-up after RDP and LDP, respectively ($p = 0.84$). In the entire series, recurrence rate was 6.9% (one case of pulmonary metastases and six cases of hepatic metastases in the

Table 3 Postoperative outcomes

	RDP ($n = 96$)	LPD ($n = 85$)	p
Length of hospital stay (days), mean (± SD)	11 (±8.8)	10 (±7.4)	0.43
Postoperative morbidity, n (%)	45 (46.9)	38 (44.7)	0.77
Clavien grade 1–2	40 (88.8)	34 (89.5)	
Clavien grade 3–4	5 (11.2)	4 (10.5)	
POPF grade, n (%)	40 (41.7)	34 (40)	0.82
Grade A	20 (50)	17 (50)	
Grade B	17 (42.5)	15 (44.1)	
Grade C	3 (7.5)	2 (5.9)	
Postoperative hemorrhage, n (%)	3 (3.1)	3 (3.6)	0.87
Grade A	0	1 (1.2)	
Grade B	1 (1)	1 (1.2)	
Grade C	2 (2)	1 (1.2)	
Reoperation, n (%)	6 (6.3)	4 (4.7)	0.65
Overall perioperative mortality, n. (%)	1(1)	0	0.34
Readmission, n (%)	11 (11.4)	9 (10.6)	0.85

Table 4 Pathological findings

	RDP ($n = 96$)	LDP ($n = 85$)	p
Functional (%)	27 (28.2)	29 (34.1)	0.38
Non-functional (%)	68 (70.8)	56 (65.9)	
Other diagnosis	1 (1)	0	
Lesion size, cm, mean (± SD)	2.4 (± 2)	2.3 (± 1.3)	0.1
WHO 2010, *n* (%)			
G1	54 (56.2)	47 (55.3)	0.76
G2	33 (34.3)	33 (38.8)	
G3	8 (8.3)	5 (5.9)	
ENETS stage, *n* (%)			
I	48 (50)	34 (40)	0.4
II	32 (33.3)	38 (44.7)	
IIIA	10 (10.4)	9 (10.6)	
IIIB	5 (5.2)	3 (3.5)	
IV	0	1 (1.2)	
Lymph nodes removed, mean (± SD)	11.2 (± 13.75)	14 (± 10)	0.09
R status			
R0	96 (100)	84 (98.8)	0.28

RDP group vs 2 cases of hepatic metastases, one case of local recurrence, and one case of lymph node metastases in the LDP cohort) after a mean time of 23.4 (± 13.8) months. As a whole, recurrence was the late cause of death in 4 patients after a mean time of 17.8 months from surgery.

The Kaplan-Meier overall survival and disease-free survival are shown in Fig. 2. At 5 years, disease-free survival was 91% and 85.8% in the RDP and LDP populations ($p = 0.78$) while overall survival was 97% and 93.5%, respectively ($p = 0.86$).

Costs analysis

The overall mean total cost was higher in the robotic group (RDP, 11226 (± 2365) €) as compared to the laparoscopic group (9235 (± 1935) €) ($p < 0.0001$). The mean operating room costs were lower for LPD (2365.4 (± 918.8) € vs 3304.7 (± 1697) € in the robotic cohort; $p = 0.03$), as well as the mean costs of surgical equipment (2042.1 (± 736) vs 4538.2 (± 1246) € in the robotic group; $p = 0.001$). Conversely, no difference was evidenced in terms of hospital stay costs between the two techniques (3869.4 (± 1477) and 3636.5 (± 1602.7) € in the RDP and LDP groups, respectively; $p = 0.38$).

Discussion

Even though there is still a high controversy reported in the literature regarding the operative approach to pNETs,

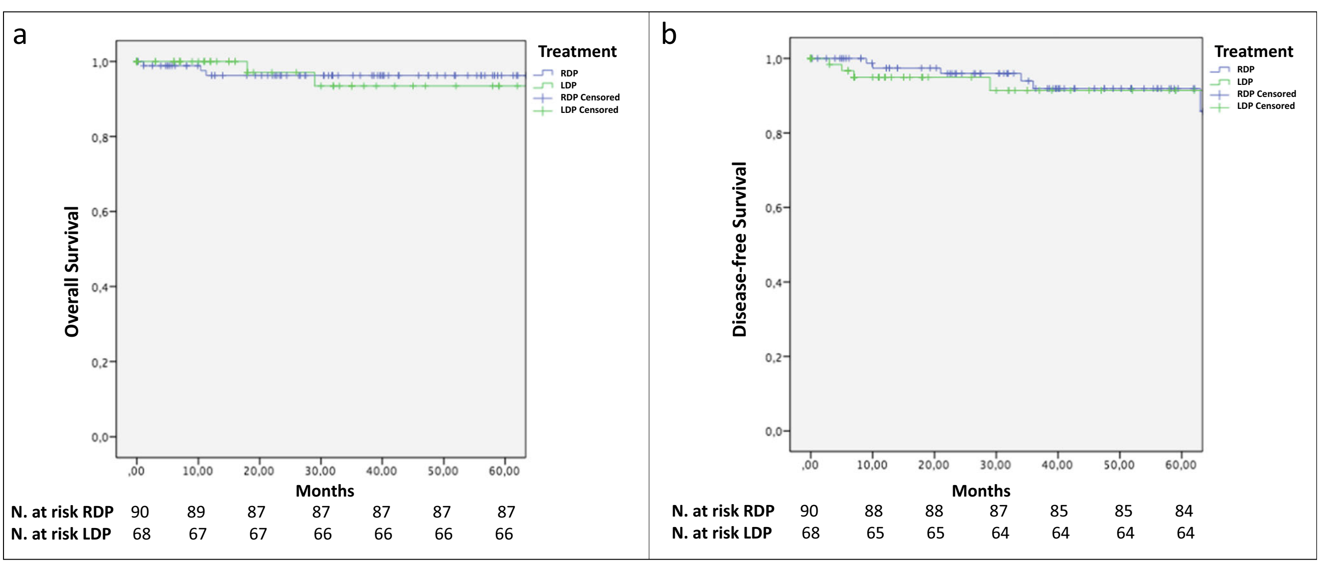

Fig. 2 Kaplan-Meier plots comparing overall survival (**a**) and disease-free survival (**b**) between RDPs and LDPs

minimally invasive techniques have been increasingly used for their treatment, leading to less surgical trauma, reduced intraoperative blood loss, reduced hospital length of stay, and a higher spleen preservation [7, 25, 26]. However, selective data on the robotic treatment of pNETs can only be extracted from more extensive reports on robotic pancreatic surgery, with consequent inconsistent results.

To our knowledge, this is the first case series that compares the robotic and laparoscopic treatments of pNETs, which specifically focused on short-term outcomes and, most importantly, on oncological safety and long-term life expectancy. From the results that we reported, three major findings can be outlined. Firstly, the robotic treatment of pNETs is a safe and feasible procedure, with an acceptable operative time when performed in high-volume centers. Secondly, postoperative outcomes turned out to be comparable between the two minimally invasive techniques. Finally, excellent results were obtained in terms of oncological radicality and long-term survival independently of the type of approach used.

With regard to the intraoperative data, RDP showed clear advantages in terms of spleen preservation ($p = 0.003$) and intraoperative blood loss ($p < 0.0001$), although a more prolonged operative time has been documented as compared to laparoscopy ($p = 0.009$).

The mean operative time in the RDP cohort was 36.5 min longer than in the LDP group. However, before drawing any conclusion, two main factors should be taken into consideration when evaluating this outcome for robot-assisted procedures: firstly, the docking time and, secondly, the learning curve of this more recent approach. For instance, the robotic set-up took a mean time of 21.6 min, representing 8% of all the procedure duration. When removing this value, RDPs and LDPs presented a comparable operative time (247.9 min and 233.7 min, respectively; $p = 0.6$).

In addition, the progressive experience gained with the robotic platform has led to a significant reduction of the operative duration over the study period (Fig. 1), reaching in the last year a similar value as compared to the laparoscopic approach (253 (± 19.3) vs 233.7 (± 65.6) min, respectively; $p = 0.3$). In order to evaluate potential additional factors influencing the whole operative time, we additionally conducted a subanalysis of the procedure duration in case of spleen preservation for both RDPs and LDPs. According to multiple studies, spleen-saving distal pancreatectomy relates to a prolonged operative time [27, 28] due to its high complexity. Of note, in our case series, RDP related to a significantly lower operative time as compared to laparoscopy (265 (± 41.52) and 291 (± 23) min, respectively; $p = 0.04$).

Even though the benefits of spleen preservation are widely known (up to a 5% reduction in post-splenectomy sepsis and a significantly reduced mortality), it remains a challenging procedure to be performed [4, 29–31]. In a recent meta-analysis on the laparoscopic treatment of pNETs, its success rate was reported to be 46% [32], in line with the 44.7% obtained in our case series. In comparison with these data, we reported a significantly higher preservation in the RDP group with a rate up to the 65.3% of cases ($p = 0.003$), validating robotic effectiveness in spleen preservation, as already documented in other studies [33, 34].

Despite the high rate of spleen-preserving procedures, mean intraoperative blood loss was significantly lower for RDPs. The mean value that we documented was 162.5 (± 98) cc, as compared to 239.7 (± 112) cc in the laparoscopic group ($p < 0.0001$). Clear advantages have been also evidenced in comparison with the laparoscopic experiences demonstrated by Zhou et al. and Gumbs et al. [35, 36] with a mean value of 217 ± 141 mL in a total of 18 procedures and 378 ± 240 mL in 206 patients, respectively.

There are several potential explanations for these advantages we evidenced for the RDP group, which are mainly related to robotic platform characteristics. The 3D vision, enhanced visual control, ergonomics, and the seven degrees of freedom motion of the robotic platform have made it possible to selectively suture the splenic vein and artery branches, leading to a higher rate of spleen preservation with a minimum blood loss and a reduced operative time for spleen-preserving procedures as compared to laparoscopy.

With regard to the conversion rate, Daoudi et al. [9] demonstrated that RDP significantly reduces the risk of conversion to open surgery in comparison with laparoscopy. However, in our case series, a similar rate was documented between the two approaches. This might be justified by the extensive experience in LDP already gained by the authors at the time of the study.

An additional interesting analysis would have been the comparison of the intraoperative outcomes between the Si and Xi platform. However, since the transition from one robotic system to the more recent one was documented in only one of the centers involved, solid conclusions cannot be drawn. However, a reduced arm collision but a slightly worse visualization was noted by the authors with the Xi platform as compared to the Si system.

As a counterpart, intraoperative benefits did not show better short-term outcomes as compared to laparoscopy. A morbidity rate reaching up to 46.9% and 44.7% for RDP and LDP, respectively, was documented ($p = 0.77$), which is notably higher in comparison to case series present in the literature [37–39]. However, two main aspects should be underscored in this respect. First, the different complication classifications used in the literature do not allow to perform homogeneous comparisons. Second, 88% of our patients in the RDP group and 89.5% in the LDP group presented only with mild complications (grades 1–2, according to the Clavien classification [20]), especially grade A fistulas, not affecting total recovery time. Indeed, when considering patients with the Clavien-Dindo grade 3–4 complications only, the incidence rate drops to 11.2% (5 patients) and 10.5% (4 patients) in the robot-assisted and laparoscopic cohorts, respectively, which is even lower as compared to the results of a recent meta-analysis [40]. With regard to the POPF incidence, no significant difference was noted between the two approaches. For instance, a rate of 41.7% (40 patients) was evidenced in the robotic cohort, not significantly different as compared to the laparoscopic approach (40%, 34 patients) ($p = 0.82$) and to other series on the minimally invasive treatment of pNETs [36, 41]. Additionally, the type of pancreatic remnant closure did not influence the pancreatic leak rate as already confirmed in a large meta-analysis [31] where POPF after distal pancreatectomy ranged from 0 to 45.7%, without any differences between stapler and suture closure of the pancreatic remnant.

The last aspect that we analyzed concerned the oncological radicality and safety of the robotic approach in terms of lymph nodes harvested, R0 resections, and long-term survival. We demonstrated an appropriate number of lymph nodes harvested with both approaches (11.2 (± 13.75) and 14 (± 10) in the RDP and LDP cohorts, respectively; $p = 0.09$), in line with the experience of Butturini et al. [42]. In this last series of 43 patients who underwent minimally invasive distal pancreatectomy, the authors reported a mean number of 15 (range, 1–47) lymph nodes harvested in the case of laparoscopy and 11.5 (range, 0–37) in the case of the robotic approach. This would suggest a similar accuracy in terms of lymphadenectomy between the two minimally invasive techniques. Such an equivalent efficacy among the techniques (also including the open approach) was additionally confirmed by Magge et al. [43]. In addition to the similar lymph node radicality, comparable beneficial results were also gained in terms of R0 resection for both the minimally invasive techniques ($p = 0.28$), confirming the feasibility of the robot-assisted approach in obtaining margin clearance. This led to evident benefits over the open approach, where an R0 resection was reported in only up to 94% of cases [44].

At the completion of the oncological safety analysis and overall and disease-free survival were also assessed. Up to now, contrasting results have been reported in the comparison between laparoscopy and open surgery due to small series generally included, with no homogeneous population of comparison. For instance, in the minimally invasive group, most comparative case series between an open and a laparoscopic access mainly included smaller tumors with a lower grade and with less lymphovascular invasion. Conversely, no data are present in the literature specifically focusing on the long-term outcomes in case of the robot-assisted pNET treatment.

Two of the most extensive reports on the laparoscopic approach were reported by Xoufaras et al. and Haugvik et al. [38, 45]. Both authors documented a 5-year survival of 90% in the laparoscopic treatment of pNETs. These results are significantly more advantageous as compared to the open approach. In fact, Phan et al. [46] reported a 5-year survival of only 65% in their series of 125 open treatments. Superior and more meaningful long-term outcomes can be evidenced in our case series. We reached a 5-year overall survival of 97% and 93.5% ($p = 0.86$) and a disease-free survival of 91% and 85.8% ($p = 0.78$) for RDP and LDP, respectively, reflecting the equivalency of the two minimally invasive approaches in the long-term oncological radicality.

With regard to the cost analysis, the economic impact of the robot-assisted procedures is still under debate with controversial data reported in the literature [12, 15, 42]. We found that total costs, mean operating room, and surgical equipment costs of RDP were more expensive than LDP (11,226 vs 9235 €, $p < 0.001$; 2356.4 vs 3304.7 €, $p = 0.03$; 2042.1 vs 4538.2 €, $p = 0.001$, respectively) but with no significant difference concerning hospital stay costs (3869.4 vs 3636.5; $p = 0.38$).

Based on the results we obtained, costs still remain the main limitation of the robotic approach. However, we do believe that the introduction in the near future of new robotic/digital platforms with reduced related costs will hopefully path the way to the routine use of robotic systems for pancreatectomy.

Despite the evident superiority reached in terms of spleen preservation and intraoperative blood loss for RDP, the limitation of the study should be underlined. Although it is the most extensive case series reported on the robotic treatment of pNETs, its retrospective and multicenter design over an 8-year period represented the main biases. Even though all operations were performed by highly skilled surgeons (more than 50 pancreatic procedures per year) in pancreatic robot-assisted surgeries, a standardized procedure was difficult to obtain. In addition, confounding by indication cannot be entirely excluded, as the choice of the operative modality (laparoscopic or robot-assisted) was at the discretion of the surgeon and based on the availability of the robotic platform.

These are the main reasons demonstrating the need for further prospective randomized trials to obtain a final confirmation of the feasibility of the robotic approach for the treatment of pNETs.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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. For this type of study, formal consent is not required.

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