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Single-centre comparison of robotic and open pancreatoduodenectomy: a propensity score-matched study

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Abstract

Background Pancreatoduodenectomy for pancreatic head and periampullary cancers is still associated with high perioperative morbidity and mortality. The aim of this study was to compare the short-term outcomes of robot-assisted pancreatoduodenectomy (RAPD) and open pancreatoduodenectomy (OPD) performed in a high-volume centre.

Methods A single-centre, prospective database was used to retrospectively compare the early outcomes of RAPD procedures to standard OPD procedures completed between January 2014 and December 2018. Of the 121 included patients, 78 underwent RAPD and 43 underwent OPD. After propensity score matching (PSM), 35 RAPD patients were matched with 35 OPD patients with similar preoperative characteristics.

Results There were no statistically significant differences in most of the baseline demographics and perioperative outcomes in the two groups after PSM optimization with the exception of the operative time (530 min (RAPD) versus 335 min (OPD) post-match, $p < 0.000$). No differences were found between the two groups in terms of complications (including pancreatic leaks, 11.4% in both OPD and RAPD), perioperative mortality, reoperations or readmissions. Earlier refeeding was obtained in the RAPD group vs. the OPD group (3 vs. 4 days, $p = 0.002$). Although the differences in the length of the hospital stay and blood transfusions were not statistically significant, both parameters showed a positive trend in favour of RAPD. The number of harvested lymph nodes was similar and oncologically adequate.

Conclusions RAPD is a safe and oncologically adequate technique to treat malignancies arising from the pancreatic head and periampullary region. Several perioperative parameters resulted in trends favouring RAPD over OPD, at the price of longer operating time. Data should be reinforced with a larger sample to guarantee statistical significance.

Keywords Robotic pancreatoduodenectomy · Pancreatic surgery · Robotic surgery

Pancreatic cancer (PC) is the fourth leading cause of death from cancer for females and the fifth leading cause for males in Western countries [1]. Its peak incidence occurs in the seventh and eighth decades of life, without significant sex differences [2]. Unfortunately, the incidence and mortality of PC in the United States have remained approximately stable over the past two decades [3], thus reflecting poor medical improvements. In a recent worldwide review of incidence and mortality in 185 countries, there were more than 400,000 annual newly diagnosed pancreatic cancer patients, and equal number was expected to die from the disease [4].

Despite the advances in modern chemoradiotherapy, the best and only chance of cure for patients with PC is an oncologically adequate surgical resection aimed at completely removing gross and microscopic disease (R0). An early curative intent surgery is the best predictor of outcome [5]. An integrated, multidisciplinary plan is mandatory to combine the benefits of surgery, chemotherapy and radiotherapy to obtain the best results [6, 7].

Unfortunately, less than 20% of patients suffering from PC are eligible for curative surgery, which has a 5-year survival rate of approximately 20% [7, 8]. Moreover, pancreatic surgery is still associated with a perioperative morbidity of

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45% and a mortality rate of less than 5% [9, 10]. Despite the high morbidity and mortality associated with the challenging pancreatoduodenectomy (PD), the centralization of major pancreatic resections to high-volume centres is expected to reduce perioperative complications and to improve survival [11]. However, PD for pancreatic head and periampullary cancers is one of the most challenging surgical procedures and requires the highest level of surgical expertise.

Since the first PD performed by Codivilla in 1898, many technical modifications have been undertaken in the procedure with the aim of improving patient outcomes [12]; however, almost none of these have demonstrated drastic differences over the others. For example, no difference in oncological outcomes, morbidity, mortality or survival has been noted between pylorus-preserving PD and the classic Whipple procedure or between pancreatojejunostomy and pancreaticogastrostomy [13, 14].

Interestingly, pancreatic surgery belonged exclusively to the field of open surgery until 1994, when the first laparoscopic PD (LPD) was performed by Gagner and Pomp [15]. Despite the theoretical benefits of a faster recovery and the potential oncological advantages related to a shorter interval to the receipt of adjuvant chemotherapy, only a few LPDs have been reported in the literature since then [16, 17]. Three randomized trials compared minimally invasive pancreatoduodenectomy with the open procedure. The first trial reported a shorter length of hospital stay after LPD in high-volume centres (> 40 LPD/OPD per year, > 150 LPDs performed), although it was underpowered to compare major morbidity [18]. A Spanish trial reported similar results [19]. In contrast, the third trial from the Netherlands (LEOPARD-2) was interrupted due to inferior results in the laparoscopic arm [20].

The intrinsic limitations of laparoscopy, such as non-articulated instruments, a lack of depth perception and its use in confined spaces, are the main obstacles to safely approaching the challenge of pancreatic surgery. Conversely, in the last decade, robotic surgery has been introduced to improve the feasibility of minimally invasive challenging procedures, such as pancreatic surgery, with encouraging results.

The first robotic-assisted PD (RAPD) was published in 2003 by Giulianotti and colleagues from a large community hospital [21]. Although the indication for robotic surgery in pancreatic disease is still controversial due to the lack of large oncological datasets, the preliminary experiences are encouraging [22].

Robotic surgery is expected to minimize the trauma created in the exposure and handling of tissues and may offer the opportunity to combine the advantages of both minimally invasive and open surgery. The main advantages of the robotic system are an optimal and ergonomic surgeon position, deeper and more stable high-definition 3D vision, endo-wrist arm technology (articulation of the instruments with 7 degrees of freedom), motion scaling and tremor filtration. Despite these theoretical advantages, RAPD remains a very challenging operation; its use is reserved to specialized centres with great experience in both pancreatic surgery and robotics.

The aim of this study was to compare the short-term outcomes RAPD and OPD performed in a high-volume centre.

Materials and methods

Patients and setting

In 2014, a structured robotics programme was started at Careggi Main Regional and University Hospital, Florence, Italy. A prospective database of all the robotic procedures was created to evaluate the results and the oncologic outcomes. According to the study's purposes, all consecutive patients who underwent elective RAPDs between 1 January 2014 and 31 December 2018 were collected and retrospectively compared with the open pancreatoduodenectomies (OPDs) performed during the same period.

The indication for surgery, for both open and robotic procedures, included malignant and borderline pancreatic nodules after a discussion at multidisciplinary oncology rounds (MOR). Briefly, the routine preoperative diagnosis of pancreatic disease was performed by conventional ultrasound, multidetector computed tomography (MDCT), magnetic resonance imaging (MRI), endoscopic ultrasonography, and Ca19-9 measurement. Fine-needle biopsy or cytology was obtained selectively.

The same experienced surgeon performed (or supervised using the second console) all the robotic procedures using both the da Vinci SI® and XI® Surgical System (Intuitive Surgical, Sunnyvale, CA, USA), while the open procedures were performed by the same surgeon and other experienced surgeons (more than 50 PD completed before 2014). The decision to perform a robotic operation or a laparotomy was balanced according to the preoperative imaging and patient characteristics. The only rigid exclusion criterion for RAPD was tumours with suspected vascular involvement at the preoperative imaging. Procedure-specific informed consent was obtained from all patients, including detailed consent to the use of the robotic assistance when needed.

Preoperative variables included baseline characteristics, such as age, sex, body mass index (BMI), comorbidities (Charlson comorbidity index) [23], past abdominal surgical history, MDCT/MRI-scan information (vascular/organ involvement), American Society of Anaesthesiologists (ASA) classification [24], and Eastern Cooperative Oncology Group (ECOG) performance status. Moreover, we divided patients into subgroups according to the tumour's location (head/uncinate, common biliary duct—CBD, duodenum or others).

Operative data were extracted by the operating theatre software, while the perioperative outcomes were collected from the clinical digital files. The International Study Group on Pancreatic Fistula definition (ISGPS) was used to classify Postoperative Pancreatic Fistula (POPF) [25]. The ISGPS definition was also used to classify post-pancreatectomy haemorrhage (PPH) [26]. Additionally, the incidence of delayed emptying syndrome (DGE) was collected according to the ISGPS definition [27]. The general complications (minor or major) were recorded based on the Clavien–Dindo Classification [28].

Patients were followed until discharge or 30 days postoperatively (whichever occurred later) during outpatient visits or by phone calls in selected cases. The primary objective was to assess the postoperative outcomes (limited to in-hospital or 30-day events). The final pathological report was obtained in all cases. The Union for International Cancer Control (UICC) TNM classification was used for pathological staging of the tumours [29].

Surgical technique

The OPD were performed according to a standardized Whipple-Kausch technique or by a pylorus-preserving method. Interestingly, the same steps were also followed during RAPD, with very few technical differences. In the RAPD, both the da Vinci SI® and XI® Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) procedures were used, depending on the availability.

Briefly, the operating room was arranged with the patient in the supine, mild reverse Trendelenburg position. The robotic cart and trocar ports were placed as shown in Fig. 1.

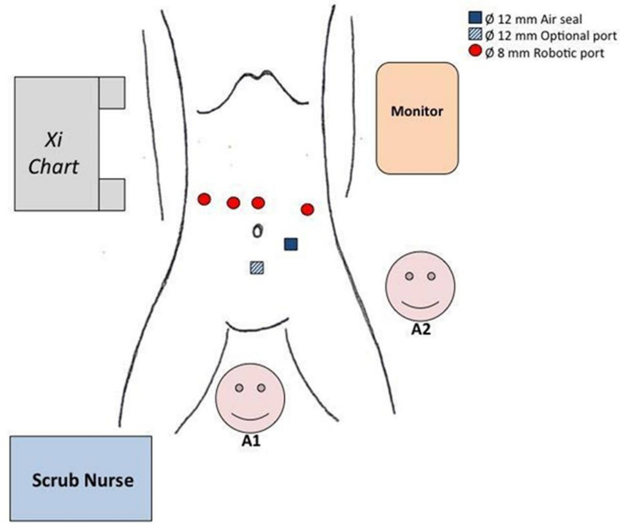

Fig. 1 Cart and trocar positioning and theatre arrangement during RAPD

The procedure was a fully robotic technique. In the presence of peritoneal adhesions, an operative laparoscopy was performed before docking the robotic system to allow adequate robotic port placement or to verify the absence of metastases or peritoneal carcinomatosis.

The robotic procedure started with the mobilization of the right colon; the lesser sac was opened and explored to exclude any tumour infiltration. The surgical steps reflected the standardized counter clockwise technique, including Kocher's manoeuvre, superior mesenteric vein (SMV) dissection, duodenum or stomach transection, cholecystectomy and common bile duct section, Treitz's section, and pancreatic division with dissection of the uncinate process, with the fourth robotic arm facilitating the retraction.

After the confirmation of negative resection margins, the reconstructive phase of the operation started, according to the classic clockwise approach (pancreatic anastomosis, biliary reconstruction and gastrointestinal anastomosis). The pancreatic texture was intraoperatively defined by the operating surgeon as either firm or soft. Because of the impossibility to palpate the gland during RAPD (despite the partial replacement of the tactile feedback by visual feedback), pancreatic texture was assessed or confirmed on the specimen. The pancreatic duct diameter was acquired intraoperatively by probing the ductal orifice with serial-sized dilators or estimated by preoperative radiological investigations. One or two drainage tubes were also placed in the upper abdominal quadrants at the end of the procedure.

Statistics

Statistical and descriptive analyses were performed using the Statistical Package for Social Science (SPSS) version 20 (SPSS Inc., Chicago, Illinois, USA).

All data were collected prospectively and reviewed retrospectively. Propensity score matching (PSM) was performed with the R package MatchIt procedure with the nearest-neighbour 1-to-1 method [30] to minimize the effects of preoperative selection biases between the OPD and RAPD groups.

Covariates were important parameters for the overall score of patients prior to the surgery (e.g. sex, age, BMI, smoking and alcohol consumption, CHA, ASA, ECOG). Cases with missing data in the matching variables were omitted from the analysis. After matching, 35 patients who received RAPD and 35 matched patients who received OPD were used for the statistical analysis.

Group and subgroup comparisons based on continuous data were performed using the non-parametric Mann–Whitney *U* test, while discrete variables were compared using the Chi-square or Fisher's exact test. The statistical level of significance was defined as a p value < 0.05.

Results

All 121 consecutive patients who underwent PD in our surgical department from January 2014 to December 2018 were prospectively collected. The entire cohort included 77 patients who underwent a planned OPD, 44 RAPD and 6 who started as RAPD but needed an early conversion to OPD (13.6%) due to intense adhesions. We decided to merge the converted RAPD with the group of OPD according to the study's purposes. The final analysis involved 83 OPDs to match 38 RAPDs.

An attempt to limit the obvious selection biases among robotic and open procedures was planned through a propensity score analysis to balance for possible preoperative confounders and to achieve balanced exposure groups at baseline. Overall, 13 preoperative variables were included in the model, reducing the initial cohort. Thirty-five of 38 RAPD were matched (1:1) to 35 of the 83 OPDs. Each variable was weighted as 1 in the final calculation. After matching, all variables were more homogeneous (Fig. 2).

The demographic and baseline characteristics, including age and BMI, were well matched among groups in the pre- and post-match comparisons. Comorbidities and performance indexes, including the Charlson, ECOG and ASA scores, were also similar. Other specific oncological parameters, such as CA19-9 level, jaundice, weight loss before surgery and the need for neoadjuvant chemotherapies, were not significantly different. Details of the matching for demographic and baseline characteristics are given in Table 1.

When considering the tumour characteristics, the only parameter that was significantly different in the pre-match and post-match comparison was the anatomic distribution of the primary lesion, which was mostly in the pancreatic head for the OPD cases (80 and 51.4%, $p = 0.006$, respectively). Tumour size, the number of harvested nodes and tumour staging were similar before and after matching. Nevertheless, the histopathologic final definition was significantly different in both the pre- and post-match comparisons (65.7 and 45.7%, $p = 0.04$, respectively) (Table 2).

When considering the perioperative results, the robotic group was reported to have a significantly longer operative time than the open group (median 560 min versus 367 min, $p < 0.000$) in the pre-match comparison, while the difference continued to be significant even after PSM (median 530 min versus 335 min, $p < 0.000$). Moreover, additional organ resections and vascular debridement were performed exclusively in the open group. Anastomotic (pancreatic) technique differences were also incomparable between the two groups because robotic operations included only duct-to-mucosa reconstruction, while in the open group, a larger spectrum of anastomosis was evaluated according to the surgeons' experiences. The consistency of the pancreatic gland was described as similar in the two groups pre- and post-matching (Table 2).

Interestingly, the occurrence of overall intraoperative complications was a quite rare event in the open group

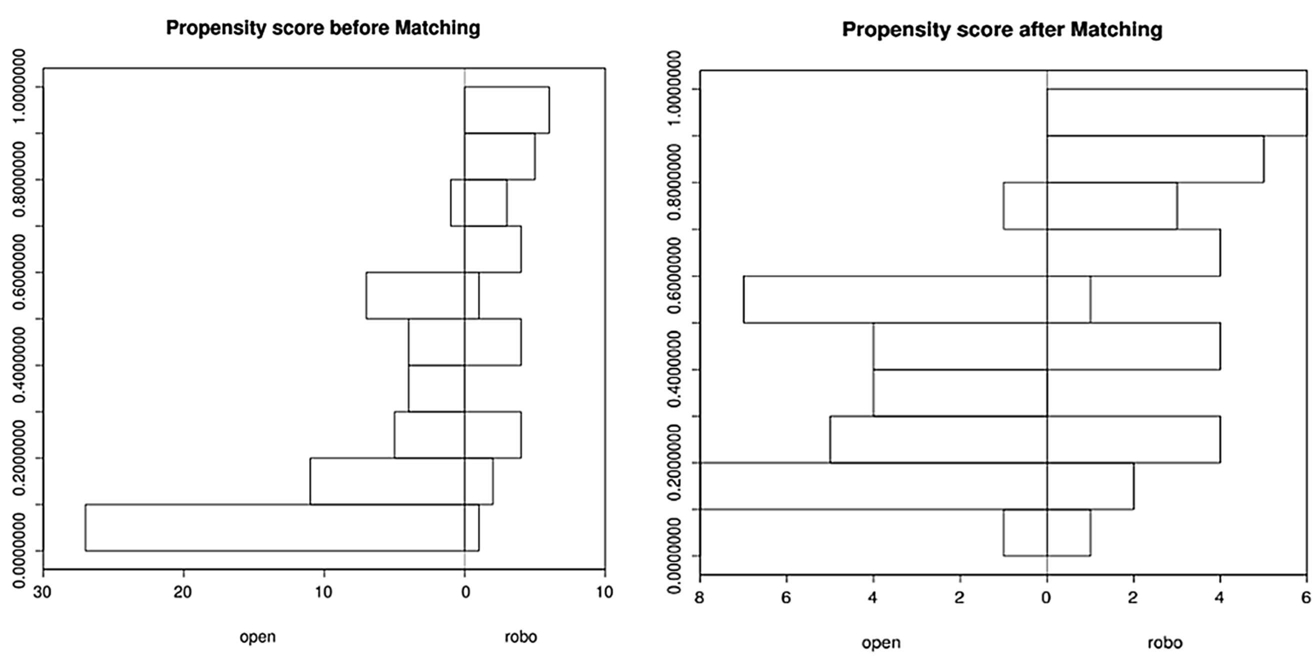

Fig. 2 Distribution of propensity score (pre- and post-matching)

Table 1 Baseline and demographic characteristics of the pre-match and post-match cohort of patients who underwent PD

Baseline characteristics	OPD pre $N=83$	RAPD pre $N=38$	p value	OPD post $N=35$	RAPD post $N=35$	p value
Age (years)	74 (56–91)	60 (42–73)	0.06	69 (50–88)	70.5 (42–85)	0.95
Sex, N (%)						
Female	39 (47)	16 (42.1)	0.69	19 (56.3)	16 (45.7)	0.51
Male	44 (53)	22 (57.9)		16 (45.7)	19 (56.3)	
BMI (kg/m^2)	24 (14–38)	26 (18–32)	0.07	24 (18–38)	26 (18–32)	0.19
CHARLSON score, N (%)						
2	33 (40.2)	17 (44.7)	0.92	18 (51.5)	16 (45.8)	0.86
3	13 (15.9)	8 (21.1)		7 (20)	7 (20)	
4	12 (14.6)	6 (15.8)		4 (11.4)	5 (14.3)	
5	15 (18.3)	6 (15.8)		6 (17.1)	6 (17.1)	
6	6 (7.3)	1 (2.6)		0 (0)	1 (2.8)	
7	2 (2.4)	0 (0)		0 (0)	0 (0)	
9	1 (1.2)	0 (0)				
ASA score, N (%)						
1	6 (7.2)	3 (7.9)	0.09	3 (8.6)	3 (8.6)	0.05
2	47 (56.6)	29 (76.3)		24 (68.6)	27 (77.1)	
3	28 (33.7)	5 (13.2)		8 (22.8)	5 (14.3)	
4	2 (2.4)	1 (2.6)		0 (0)	0 (0)	
ECOG performance score, N (%)						
0	69 (83.1)	37 (97.4)	0.19	34 (97.1)	34 (97.1)	1.000
1	8 (9.6)	0 (0)		0 (0)	0 (0)	
2	1 (1.2)	0 (0)		0 (0)	0 (0)	
3	4 (4.8)	1 (2.6)		1 (2.9)	1 (2.9)	
4	1 (1.2)	0 (0)		0 (0)	0 (0)	
MOR, N (%)	69 (83.1)	32 (84.2)	1.000	30 (85.7)	30 (85.7)	1.000
Pre-op diabetes, N (%)	22 (26.5)	7 (18.4)	0.36	6 (17.1)	7 (20%)	0.75
Previous abdominal surgery, N (%)	47 (56.6)	17 (44.7)	0.24	21 (60)	16 (45.7)	0.23
Pre-op stenting, N (%)	47 (56.6)	17 (44.7)	0.24	17 (48.6)	17 (48.6)	1.000
Pre-op jaundice, N (%)	55 (66.3)	24 (63.1)	0.83	21 (60%)	22 (62.8)	0.80
Weight loss (> 5 kg/6 m), N (%)	44 (53)	14 (36.8)	0.11	16 (45.7)	12 (34.3)	0.32
CA19.9 (U/mL)	102 (2–6642)	85 (2–1617)	0.3	70 (2–2617)	143 (2–1617)	0.80
Pre-op biopsy, N (%)	29 (34.9)	16 (42.1)	0.54	15 (42.8)	15 (42.8)	1.000
Neoadjuvant treatment, N (%)	7 (8.4)	1 (2)	0.43	0 (0)	0 (0)	1.000

OPD open pancreatoduodenectomy, *RAPD* robot-assisted pancreatoduodenectomy, *BMI* body mass index, *ASA* American Society of Anaesthesiologists, *ECOG* Eastern Cooperative Oncology Group, *MOR* multidisciplinary oncology rounds, *DM* diabetes mellitus

without a statistical significance in both the pre- and post-match comparisons, with a consistent trend to better results in the robotic group (8.4% vs. 0%, $p=0.09$ and 5.7% vs. 0%, $p=0.15$, respectively). Intraoperative results are summarized in Table 3. The overall morbidity and mortality rates were acceptable and highly comparable between open and robotic procedures for both the pre-match comparison and the post-match adjustment (Table 4).

The occurrence of POPF was 14.4% versus 13.1% between OPD and RAPD, respectively, in the pre-match comparison ($p=0.84$) and 11.4% vs. 11.4% in the post-match comparison ($p=1.00$); the POPF was equally distributed in grades B and C according to the brand-new classification of the International Study Group on Pancreatic Fistula definition (ISGPS). Other pancreatic-specific complications, such as post-pancreatectomy haemorrhage (PPH), the reoperation rate, readmissions and the need for blood transfusions, were also similar (Table 4).

The bowel canalization, including both gases and faeces, occurred with a similar median time in the early postoperative period. Nevertheless, the median day of resumption of solid foods (creams, yogurt or chopped meat) was earlier for the robotic group in the pre- and post-match test (3 vs. 4 days, $p=0.002$). Additionally, the overall length of

Table 2 Tumour characteristics of the pre-match and post-match cohort of patients who underwent PD

Tumour characteristics	OPD pre $N=83$	RAPD pre $N=28$	p value	OPD post $N=35$	RAPD post $N=35$	p value
Localization, N (%)						
Pancreas	58 (69.9)	20 (52.7)	**0.000***	28 (80)	18 (51.4)	**0.006***
Duodenum	9 (10.8)	17 (44.7)		4 (11.4)	16 (45.7)	
CBD	11 (13.3)	1 (2.6)		3 (8.7)	1 (2.8)	
Others	5 (6)	0 (0)		0 (0)	0 (0)	
Histology, N (%)						
Ductal adenocarcinoma	46 (55.4)	18 (47.4)	**0.01***	23 (65.7)	16 (45.7)	**0.04***
Duodenum adenocarcinoma	6 (7.2)	13 (34.2)		3 (8.6)	13 (37.1)	
CCK	11 (13.3)	1 (2.6)		3 (8.6)	1 (2.8)	
NET	6 (7.2)	2 (5.3)		4 (11.4)	2 (5.7)	
IPMN/MCN	5 (6)	2 (5.3)		2 (5.3)	1 (3.3%)	
Pancreatitis	1 (1.2)	–		–	–	
Other	8 (9.6)	2 (5.3)		–	2 (5.7)	
AJCC stage						
Not a cancer (confirmed)	14 (16.9)	6 (15.8)				
0	1 (1.2)	0 (0%)	0.33	3 (8.6)	5 (14.3)	0.27
Ia	7 (8.4)	2 (5.3)		6 (17.1)	2 (5.7)	
Ib	4 (4.8)	7 (18.4)		2 (5.7)	7 (20)	
IIa	18 (21.7)	10 (26.3)		6 (17.1)	8 (22.9)	
IIb	31 (37.3)	11 (28.9)		15 (42.9)	11 (41.4)	
III	6 (7.2)	2 (5.3)		3 (8.6)	2 (5.7)	
IV	2 (2.4)	0 (0%)		0 (0)	0 (0)	
Tumour size (mm)	35 (2–51)	30 (18–40)	0.2	37 (2–51)	30 (18–40)	0.92
Wirsung duct diameter (mm)	3 (2–10)	3 (2–12)	0.7	3.5 (2–7)	3 (2–12)	0.79
Lymph nodes harvested (N)	23 (2–67)	22 (7–60)	0.88	23 (3–62)	22 (7–60)	0.85
Lymph node ratio ($N+/N$)	0 (0–0.7)	0 (0–0.2)	0.16	0.3 (0–0.4)	0 (0–0.2)	0.18

Bold and astericks values with statistic significance ($p < 0.05$)

OPD open pancreatoduodenectomy, *RAPD* robot-assisted pancreatoduodenectomy, *AJCC* American Joint Committee on Cancer

hospital stay was similar for robotic operations and open procedures (8 vs. 10, $p=0.09$ in the pre-match and 8 vs. 10, $p=0.13$ in the post-match).

Discussion

The role of robotics in pancreatic surgery has been discussed in several papers [12, 31, 32], although its wide application is far from reality. Nevertheless, a minimally invasive approach to pancreatic malignancies could have a crucial impact in the oncologic perspective, reducing the interval between surgery and adjuvant therapies. Moreover, improved results in hand-sewn anastomoses, lymphadenectomy and the management of major bleeding are facilitated by the magnified 3D intraoperative view and the articulate endoscopic instruments. Furthermore, the availability of a second console is crucial in enhancing dedicated training in pancreatic surgery, including more and more challenging steps, and facilitating both senior and younger surgeons. Unfortunately, large robotic series are still lacking, and the supposed benefits of the technique have never been demonstrated. Retrospective/prospective series with accurate data analyses are considered precursors to quality controlled large observational studies if the general principles of oncologic surgery are maintained.

Interestingly, the capabilities of the da Vinci Surgical System® can overcome the technical limitations of laparoscopy to reproduce complex open procedures pointing towards the failed spread of laparoscopic PD. Therefore, in our centre, laparoscopic PD has never been performed, and any effort is directed towards robotic applications. Nevertheless, major laparoscopic pancreatic resection continues to be adopted at a slower pace and only in a few highly selective centres. Indeed, whereas less than 500 laparoscopic PD have been reported in the literature in almost 20 years [16, 17], more than 350 robot-assisted PD have been published in the last few years [33, 34].

Table 3 Intraoperative results (pre-match and post-match cohort)

Intraoperative results	OPD pre $N=83$	RAPD pre $N=38$	p value	OPD post $N=35$	RAPD post $N=35$	p value
Operative time (min)	367 (270–520)	560 (465–670)	**0.000***	335 (220–565)	530 (405–660)	**0.000***
Type of resection, N (%)						
Pylorus-preserving PD	58 (69.8)	17 (44.8)	**0.008***	24 (69)	16 (46)	0.053
Whipple PD	25 (30.2)	21 (55.2)		11 (31)	19 (54)	
Additional organs resected, N (%)	11 (13.3)	0 (0)	**0.01***	2 (5.7)	0 (0)	0.15
Vascular resection, N (%)	20 (24.1)	0 (0)	**0.001***	8 (22.8)	0 (0)	**0.003***
Type of anastomosis, N (%)						
Pancreatojejunostomy	11 (13.3)	0 (0)	**0.02***	7 (20)	0 (0)	**0.007***
Duct-to-mucosa	61 (73.5)	36 (94.7)		23 (65.7)	33 (94.3)	
Pancreatogastrostomy	8 (9.6)	2 (5.3)		5 (14.3)	2 (5.7)	
None	3 (3.6)	0 (0)		0 (0)	0 (0)	
Consistency of the pancreas, N (%)						
Hard/firm pancreas	37 (44.6)	16 (42.1)	0.96	17 (48.6)	16 (45.7)	0.94
Soft pancreas	37 (44.6)	18 (47.4)		18 (51.4)	15 (42.8)	
Unknown	9 (10.8)	4 (10.5)		0 (0)	0 (0)	
Intraoperative complications, N (%)	7 (8.4)	0 (0)	0.09	2 (5.7)	0 (0)	0.15

Bold and astericks values with statistic significance ($p < 0.05$)

OPD open pancreatoduodenectomy, *RAPD* robot-assisted pancreatoduodenectomy, *POPF* postoperative pancreatic fistula, *PPH* post-pancreatectomy haemorrhage, *DGS* delayed gastric syndrome

Nonrandomized studies and meta-analyses comparing minimally invasive techniques with open pancreatic resections show comparable complications (including the incidence of POPF), reoperations, mortality, and numbers of harvested lymph nodes as a surrogate of good oncologic outcome [35-37]. Wound infections, hospital stay length, blood loss, transfusion rate and R1 resections were significantly lower in patients who underwent minimally invasive resections [35].

Our series represents one of the few and large experiences with RAPD. Although the present study suffers from being inherently retrospective, highly selective and subject to early learning curves with a high cost burden, these early short-term results are within optimal parameters. Patients with a very advanced pancreatic neoplasm with proven or suspected vascular involvement or who received neoadjuvant chemotherapy for locally advanced stages were excluded a priori from a minimally invasive approach, thus representing an obvious bias. Conversely, periampullary small tumours in younger patients were considered an excellent target for RAPD. Another limitation of the present study was the inclusion of converted RAPD in the open group, according to the limits of the pre-determined aim. This choice was based on the fact that all the conversions were decided in the early step of the interventions due to severe adhesions or the presence of advanced disease. Of note, all converted patients were excluded by the PSM process.

The more interesting findings of the present study were that, in both the pre- and post-matched comparisons, early feeding and several perioperative minor outcomes tended to favour RAPD compared to OPD. After the propensity score calculation, the subgroups of patients remained substantially similar in the relevant aspects, including the incidence of POPF, morbidity, mortality and hospital stay length (Table 1). Interestingly, in our study, the entire postoperative course of each patient was followed by the same team (surgeons, anaesthesiologists, nurses, dieticians and physiotherapists) until the time of discharge, reducing any bias in postoperative management.

Overall, no significant differences were found between the two groups in terms of complications and perioperative mortality, with a similar percentage of POPF demonstrated in the two groups (11.4% after PSA adjustment), which was consistent with the current literature [34]; "biochemical leak" (defined in the previous nomenclature as grade A by ISGPS [25] was the most common event with minimal impact on the perioperative course. Although no significant difference between the two groups was observed in terms of B/C POPF, the RAPD group presented with a higher risk of fistulas due to the different types of histology and location of the neoplasms (more adenocarcinomas of the pancreatic head versus periampullary location, Table 2). According to the work of Callery and colleagues [38], the pancreatic texture in the malignancies of the pancreatic gland is more consistent than the periampullary lesions (due to the

Table 4 Outcomes and postoperative complications (pre-match and post-match cohort)

Postoperative complications (30 days/in-hospital)	OPD pre $N=83$	RAPD pre $N=38$	*p* value	OPD post $N=35$	RAPD post $N=35$	*p* value
Overall morbidity, *N* (%)	43 (51.8)	20 (52.6)	1.000	15 (42.8)	17 (48.5)	0.63
Mortality, *N* (%)	4 (4.8)	1 (2.6)	1.000	0 (0)	1 (2.9)	1.000
Clavien–Dindo classification			0.30			0.61
0	24 (28.9)	17 (44.7)		14 (40)	17 (48.6)	
I	16 (16.9)	6 (15.8)		8 (22.8)	6 (17.1)	
II	21 (25.3)	4 (10.5)		7 (20)	4 (11.4)	
IIIa	7 (8.4)	2 (5.3)		2 (5.7)	2 (5.7)	
IIIb	7 (8.4)	5 (13.2)		3 (8.6)	3 (8.6)	
IVa	1 (1.2)	2 (5.3)		0 (0)	2 (5.7)	
IVb	5 (6)	1 (2.6)		1 (2.9)	0 (0)	
V	4 (4.8)	1 (2.6)		0 (0)	1 (2.9)	
POPF *N* (%)	12 (14.4)	5 (13.1)	0.84	4 (11.4)	4 (11.4)	1.00
Grading of POPF, *N* (%)						
B	5 (6)	3 (7.9)	0.78	2 (5.7)	2 (5.7)	1.00
C	7 (8.4)	2 (5.2)		2 (5.7)	2 (5.7)	
PPH, *N* (%)	8 (9.6)	4 (10.5)	1.000	4 (11.4)	3 (8.6)	0.69
Grading of PPH, *N* (%)						
A	0 (0)	1 (2.6)	0.25	0 (0)	1 (2.8)	**0.03***
B	1 (2.5)	2 (5.2)		0 (0)	2 (6.7)	
C	7 (87.5)	1 (2.6)		4 (11.4)	0 (0)	
DGS, *N* (%)	12 (14.4)	5 (13.1)	0.84	5 (14.2)	4 (11.4)	0.72
Blood transfusion, *N* (%)	32 (38.6)	7 (18.4)	**0.03***	8 (22.8)	6 (17.1)	0.55
Refeeding (days)	3.5 (2–8)	3 (2–7)	**0.002***	4 (2–19)	3 (1–5)	**0.002***
Gas canalization (days)	3 (1–9)	4 (2–7)	0.5	3 (1–7)	3 (2–7)	0.36
Faeces canalization (days)	4 (1–10)	5 (3–7)	0.46	4 (3–8)	5 (2–9)	0.29
Reoperation, *N* (%)	14 (16.9)	8 (21.1)	0.61	4 (11.4)	6 (17.1)	0.49
Readmission, *N* (%)	7 (8.4)	3 (7.9)	1.000	4 (11.4)	3 (8.6)	0.69
Hospital stay (days)	10 (6–110)	8 (6–68)	0.09	10 (7–110)	8 (6–40)	0.13

Bold and astericks values with statistic significance ($p < 0.05$)

OPD open pancreatoduodenectomy, *RAPD* robot-assisted pancreatoduodenectomy, *POPF* postoperative pancreatic fistula, *PPH* post-pancreatectomy haemorrhage, *DGS* delayed gastric syndrome

fibrosis associated with ductal cancer). The equal percentage of POPFs in both groups could suggest a relatively better outcome with the robotics. Moreover, this result could be sustained by the reduced blood loss and the technical advantages offered by robotic surgery, which allows the anastomosis of a very small pancreatic duct.

A nearly constant result is a longer operative time in the robotic series, in line with the majority of published studies (335 versus 530 min for OPD and RAPD, respectively, after PSM, $p>0.001$). This aspect, together with the increased costs of supplies and operative room employment, is recognized drawbacks of robotic technology, although these aspects are expected to be reduced as the surgical teams gain experience.

According to recent studies, patients undergoing PD for pancreatic adenocarcinoma require perioperative transfusions in 20% of cases [10]. In our series, the blood transfusion rate was lower for RAPD (38.6 (OPD) and 18.4% (RAPD), $p=0.03$ in the unmatched cohort); while not statistically significant after PSM (22.8 (OPD) and 17.1% (RAPD), $p=0.55$), the trend favoured RAPD.

Refeeding in the RAPD group started significantly faster (one day) than in the OPD group before and after PSM, although the rate of DGE in both groups was similar (and low) (Table 4). Moreover, the length of the hospital stay was similar in the two groups, with a median value that was higher in the OPD group (not statistically significant).

The number of harvested lymph nodes was comparable and oncologically adequate according to the AJCC guidelines [29], with a median number for the post-match results of 23 for the OPD group and 23 for the RAPD group. The few patients with < 12 lymph nodes harvested were not affected by confirmed malignancies without the need for an extended lymphadenectomy.

A recent similar retrospective multicentre PSM cohort study comparing minimally invasive (including both robotic, laparoscopic and hybrid procedures) and open PD found no differences in the 30-day major morbidity, mortality and length of stay between the two groups. However, minimally invasive PD was associated with a doubled rate of POPF and longer operative times [32]. In addition to the approach itself, other factors could have influenced this outcome, such as an insufficient balance between the groups at baseline (residual confounding), underreporting in some registry data and the presence of many operating surgeons from different countries. Furthermore, the 2005 ISGPF definition of POPF can be interpreted in many ways, and the POPF registration after discharge may not be accurate in registry studies.

A large systematic review and meta-analysis suggested advantages of robotic pancreatectomy over the open approach in several aspects. First, a significantly lower overall complication rate and a reduced reoperation rate were observed. No significant differences were observed in POPF or mortality between robotic surgery and open surgery. However, the long-term survival rate and lymph node retrieval were not evaluated due to incomplete data [39].

Interestingly, a lymph node ratio (LNR) > 0.4 has been associated with a risk of death comparable to that due to the presence of a metastatic disease [40]. In this case series, the LNR of patients who underwent OPD was 0.3, while the LNR of patients treated with RAPD was 0 in the absence of statistical significance ($p = 0.18$). The excellent and comparable lymph node clearance with both techniques reflects the consistent standardization achieved with a dedicated oncological-oriented surgical team.

Our data confirmed that robotic pancreatectomy can be performed safely and according to current oncological standards (adequate resection margins and appropriate lymphadenectomy), with comparable results to those obtained for open pancreatectomy, except for the duration of surgery. Moreover, many perioperative parameters (refeeding, hospital stay length, blood transfusions) seemed to favour RAPD over OPD.

Conclusions

The advent of robotic technology might circumvent the technical limitations of laparoscopic pancreatic surgery. Many of the advocated advantages regarding the robotic platform are more evident when dealing with challenging pancreatoduodenectomy, while the distal pancreatectomies are easily approached by pure laparoscopy. However, a minimally invasive approach to pancreatic malignancies could have a crucial impact in the oncologic perspective, reducing the interval between surgery and adjuvant therapies. Furthermore, the availability of a second console is crucial in enhancing dedicated training in pancreatic surgery, including more and more challenging steps, and facilitating both senior and younger surgeons.

Our data confirmed that robotic pancreatectomy can be performed safely and according to current oncological standards in selected patients, and several perioperative parameters (refeeding, hospital stay length, blood transfusions) seem to favour RAPD over OPD, although at the price of longer operating times.

Although large, randomized controlled trials are very difficult to design (if not impractical and/or impossible) due to the need for local expertise, wide caseloads and problems of informed consent, further studies are of crucial importance to assess the definitive superiority of one technique over another.

Compliance with ethical standards

Disclosures Drs Lapo Bencini, Federica Tofani, Claudia Paolini, Carla Vaccaro, Paolo Checcacci, Mario Annecchiarico, Luca Moraldi, Marco Farsi, Simone Polvani and Andrea Coratti have no conflicts of interest or financial ties to disclose.

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