



Robotic enucleations of pancreatic benign or low-grade malignant tumors: preliminary results and comparison with robotic demolitive resections

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Received: 5 April 2018 / Accepted: 2 November 2018 / Published online: 12 November 2018
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Abstract

Background The incidental detection of benign to low-grade malignant small pancreatic neoplasms increased in the last decades. The surgical management of these patients is still under debate. The aim of this paper is to evaluate the safety and feasibility of robotic enucleations and to compare the outcomes with non-parenchymal sparing robotic resections.

Methods The study included a total of 25 patients. Nine of them underwent a robotic enucleation (EN Group) and 16 patients received a robotic demolitive resection (DR Group). Perioperative and medium-term outcomes were compared between the two groups.

Results Patients' baseline characteristics were similar in the two groups except for presence of symptoms and tumor size, due to the inclusion criteria. Operative time was significantly shorter and postoperative results were better for EN group, including a significant shorter hospitalization (5 vs. 8 days, $p=0.027$), reduced pancreatic leaks (22% vs. 50%, $p=0.287$) and a better preservation of glandular function (100% vs. 62.5%, $p=0.066$). Mortality rate was zero in both groups, with all patients free from disease at a median follow-up of 18 months.

Conclusions The risks of under/overtreatment remain still unavoidable for benign to low-grade malignant small pancreatic neoplasms. Simple enucleation should be performed whenever oncological appropriate, to achieve the best postoperative outcomes. The adoption of robotic technique might widen the indications for parenchymal sparing, minimally invasive surgery.

Keywords Robotic surgery · Enucleation · Benign neoplasms · Demolitive resection

Pancreatic neuroendocrine tumors (pNETs) and pancreatic cystic neoplasms (PCNs) are a histologically heterogeneous group of lesions ranging from frankly benign lesions (mostly) to potentially more aggressive tumors with malignant behavior.

Globally, they are considered uncommon in the group of pancreatic neoplasms, pNETs accounting for less than 5% and cystic tumors 10% of all pancreatic neoplasms [1]. However, during the last two decades, the common use of high resolution imaging techniques had lead to the incidental detection of these tumors, up to sevenfold previous incidence. For the same reason, the size of these tumors at the time of diagnosis has markedly decreased [2, 3].

Most of pNETs are sporadic, while 10–30% are associated with a genetic syndrome, multiple endocrine neoplasia (MEN) type 1 being the most important [4].

Approximately, 90% of these tumors are non-functional pNETs (NF-pNETs). Functional pNETs (F-pNETs) present themselves with specific syndromes: the most common is that related to insulinoma (35–40% of F-pNET), while 16–30% are related to gastrinomas. Less common clinical manifestations are caused by glucagonomas, VIPomas, and somatostatinomas [4, 5].

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The four major types of pancreatic cystic neoplasms (PCNs) are intraductal papillary mucinous tumors (IPMN) accounting for 20–50% of all PCNs, mucinous cystic neoplasms (MCN, 10–45% of PCNs), serous cystadenomas (SCA, 32–39% of all PCNs), and solid-pseudopapillary neoplasm (SPN, less than 10% of all PCNs) [6].

In both the groups of pNET and PCN, there are no specific and unequivocal criteria to fully establish the behavior of these tumors, ranging from benign lesions to lesions with malignant potential with distant spread [5, 7–10]. Therefore, the risk of undertreat a patient missing the only opportunity of cure have to be balanced with the possibility to overtreat the patient performing an underrating pancreatectomy with risk of severe postoperative complications [11].

Even in the case of a surgical management, the extent of resection is also questioned [10, 12, 13]. The simple enucleation (EN) allowing parenchyma preservation is considered a good option for frankly benign neoplasms, while pancreaticoduodenectomy (PD) and distal pancreatectomy (DP) can be performed with low morbidity and mortality in high volume centres only [14, 15]. Nevertheless, both enucleations and parenchyma preserving operations together with pancreatectomies are at risk of severe postoperative complications, the most important being pancreatic fistula (postoperative pancreatic fistula, POPF).

The surgical management of these neoplasms by the minimally invasive approach, including laparoscopy or robotic technology, is promising although not broadly used in most hospitals worldwide and seldom reported in the current Literature [16–18].

The aim of this preliminary study was to investigate the feasibility and the early to medium-term outcomes of robotic enucleations of benign or low-grade malignant pancreatic lesions. A comparison of these results with robotic demolitive pancreatic resections was also attempted.

Materials and methods

Patients and settings

In 2014, a robotic structured program started at Careggi Main Regional and University Hospital. Most of the participating surgeons were well trained in pancreatic surgery, minimally invasive surgery, and robotics, although all the respective procedures were performed by a single surgeon with the largest previous experience (more than 50 robotic pancreaticoduodenectomies, distal pancreatectomies, and enucleations out of more than 1000 robotic visceral procedures over a 10 years period). Since then, all the patients who underwent a robotic procedure for a pancreatic lesion were prospectively collected in a dedicated database with demographic information, clinical parameters, preoperative

evaluations, perioperative outcomes, pathologic data, and medium-term outcomes. Patients with a confirmed histopathological response of benign- to low-grade malignant lesions were retrospectively analyzed in this study.

Patients were also aggregated according to the site of the primary lesion: tumors located in the head, including the uncinate process and neck of the pancreas and tumors located in body and tail, in order to compare EN for lesions located in pancreatic head versus PD and EN for lesions located in the body or tail of the pancreas versus DP.

Indications for surgery were given according to a multidisciplinary local meeting, based on the NCCN guidelines [13] (pNETs) and Fukuoka guidelines (PCNs) [19]. Patient wishes, concomitant illnesses and a doubtful preoperative characterization were also taken into consideration.

Routine preoperative work-up included triple-phase contrast-enhanced Computed Tomography and Magnetic Resonance. In selected cases, Positron Emission Tomography scan, and somatostatin receptor scintigraphy were added. Tumor markers such as CA19.9, chromogranin A, and neuron-specific enolase for pNETs and appropriate endocrine assessment were obtained in the suspicion of f-pNETs. Endoscopic ultrasonography with tumor biopsy and cystic fluid analysis with count of CEA was used to rule out mucinous neoplasms [4, 6].

The decision to perform an EN was undertaken in patients with a preoperative diagnosis or suspicion of a less than 3 cm pNET or PCN. Nevertheless, the decision to perform a robotic EN rather than a demolitive resection (DR) depended also on the distance between tumor and main pancreatic duct (MPD) being at least 3 mm in the absence of radiologic malignancy. The preoperative surgical plan was confirmed or changed after the exploration of the abdominal cavity and the intraoperative ultrasonography (IOUS) evaluation. This important final assessment was crucial to exclude the presence of mural nodules in cystic lesions or unexpected malignant features.

A procedure-specific detailed informed consent was obtained from all patients including a specific consent to the use of robotic assistance or the need for conversion.

Surgical technique

Both the da Vinci SI® and XI® Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) were used, depending on their availability. All patients received prophylactic antibiotic therapy and low-weight molecular heparin to prevent site infections and deep-venous thromboembolism, respectively.

The operating room was arranged with the patient in supine, mild reverse Trendelenburg position. The robotic cart and trocars' ports were displaced as shown in Fig. 1. In brief, the robotic procedures reflected the corresponding

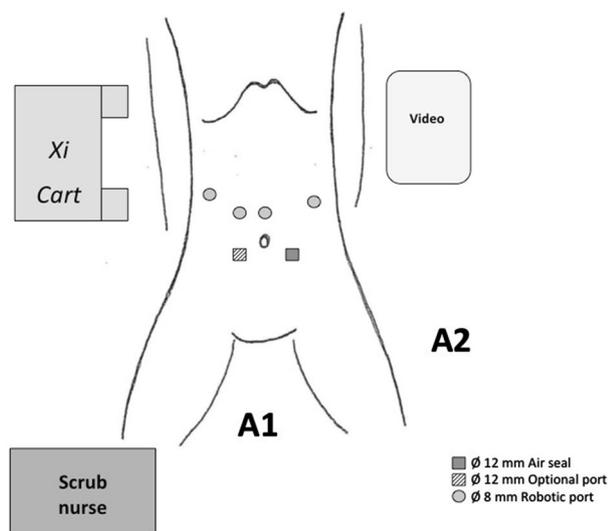


Fig. 1 Operative room setup (Ilenia Bartolini)

open steps, from the domolitive manoeuvres to the reconstructions. A duct-to-mucosa anastomosis was chosen for the pancreatic reconstruction in PD. For DP, the identification and selective ligation of MPD was achieved either with clip or a stitch. The first, crucial, point was to identify the lesion at pancreas surface using a robot-integrated ultrasound probe, especially during EN. The main pancreatic duct was also identified to prevent major leakage. Tissue dissection and tumors' enucleation was achieved by robotic monopolar scissors or harmonic scalpel, paying attention respect the healthy planes. Bleedings from the pancreas were secured with bipolar clamps or robotic hand-sewn stitches. Local topic hemostatic patches were also added in selected case. A drainage tube was also displaced on a routine basis. More technical details were discussed elsewhere [20].

Tissue dissection was achieved with the use of low energy bipolar forceps and monopolar scissor. The third robotic arm allowed a stable retraction of the structures reducing the possible collateral damages.

Postoperative management

Severity of any postoperative pancreatic fistula (POPF) was assessed according to the classification proposed by the International Study Group on Pancreatic Fistula (ISGPF) [21]. Amylase check from the drainage fluid was routinely collected on post-operative day (POD) 1, 3, and selectively in 5.

The Clavien-Dindo model [22] was used to classify all the postoperative complications. Mortality was defined as 90-day or in-hospital surgery-related death. The postoperative hospital stay was calculated from the day of surgery to the day of discharge. The Union for International Cancer

Control (UICC)—TNM classification [edge] was used for pathological staging of pancreatic tumors. New-onset diabetes was defined if requiring medical treatment. New-onset exocrine insufficiency was defined if needing of life-long pancreatic enzyme supplementation. Follow-up was performed in a multidisciplinary manner, involving the oncological team.

Analysis

Data were collected prospectively and reviewed retrospectively using the statistical package SPSS for Windows, vs. 18.0, (SPSS Inc., Chicago, Illinois, USA). Patient baseline characteristics, operative, and postoperative results and histological findings were compared between the patients who underwent robotic EN and those who underwent robotic DR. Continuous variables were analyzed using the non-parametric Mann–Whitney test, while discrete variables were compared using the χ^2 or Fisher's exact test when appropriated. Statistical significance was defined as p value < 0.05.

Results

From February 2014 to March 2017, nine consecutive patients who underwent a robotic EN and 16 patients who underwent a robotic DR with a final histopathological response of benign to low grade malignant lesions were collected. In the EN group, 3 patients had a lesion located in the head-neck-uncinate process of the pancreas ("Head" subgroup) and 6 patients had a lesion located in the body or tail of the pancreas ("Body/tail" subgroup). In DR group, there were 4 patients in "Head" subgroup (patients who underwent a PD) and 12 patients in "Body/tail" subgroup (patients who underwent a DP). The baseline and demographic preoperative characteristics of the patients are summarized in Table 1.

There were no statistically significant differences in the baseline demographics, except for the presence of symptoms at diagnosis and size of the tumor, between the EN and DR groups. Interestingly, almost all the symptomatic patients had an insulinoma that was treated with an EN. The median size of the lesions was smaller in the EN group.

The length of surgery was statistically significant shorter in the EN group, including the subgroups of "head" region and "body-tail" regions, if compared to the respective DR subgroup.

No planned robotic EN was shifted to resective surgery.

In one case of robotic PD, conversion to open surgery was needed because of anatomical reason. No intraoperative complications happened in both groups, median blood loss of less than 100 ml. The operative outcomes were summarized in Table 2.

Table 1 Patient characteristics

Patient characteristics	EN = 9	DR = 16	
Age (years)	58 (range 24–78)	66 (range 27–77)	<i>p</i> 0.496
Sex			<i>p</i> 0.397
Male	5 (56%)	5 (31%)	
Female	4 (44%)	11 (69%)	
BMI (kg/m ²)	27 (23–29)	26 (17–34)	<i>p</i> 0.652
ASA status			<i>p</i> 0.543
1–2	9 (100%)	15 (94%)	
3	–	1 (6%)	
Comorbidities	5 (56%)	14 (87.5%)	<i>p</i> 0.726
Diabetes	2 (22%)	2 (12.5%)	<i>p</i> 0.602
Hypertension	3 (33%)	12 (75%)	
Other	4 (44%)	12 (75%)	
Prev abdominal surgery	3 (33%)	9 (56%)	<i>p</i> 0.411
Clinical presentation			
Symptomatic	4 (44%)	1 (6%)	<i>p</i> 0.040
Incidental	5 (56%)	15 (94%)	
Site of tumor			<i>p</i> 0.673
Head/periampullary	3 (33%)	(25%)	
Body and tail	6 (67%)	12 (75%)	
Size of the tumor (mm)	15 (range 11–27)	31 (range 13–70)	<i>p</i> 0.018

Bold values indicate statistical significance (*p* < 0.05)

EN enucleation, DR demolitive resection, BMI body mass index, Prev previous

Associated procedures were performed in four patients (3 cholecystectomy for gallbladder stones—2 in EN group and 1 in DR group—and a wedge liver resection for a benign lesion in a patient of DR group). None of these experienced additional perioperative complications.

Frozen section examination was used in one patient of the EN group to confirm the suspicion of a well-differentiated NET and in two cases to rule out lymph node metastases. In the PD group, the frozen section was routinely employed to exclude malignancies in MPD and in bile duct, before the reconstructive step. During DP, frozen sections were required to assess the proximal pancreatic margin.

The need of Intensive Care Unit (ICU) stay during the postoperative period was statistically significant lower for the EN group, even when considering the “Head” subgroup of patients. General postoperative complications occurred in a lower, but not statistically significant percentage of the EN group (33% vs. 75%, *p* = 0.087). Two-third of the complication were POPF for both groups, mostly grade A or B according the ISGPF definition [21]. One patient in EN group discharged with the drainage left in situ was readmitted for fever but managed conservatively. According to the brand-new classification of POPF [23], POPF rate would decrease to 44% with 1 biochemical leakage, 6 POPF grade B and 1 POPF grade C in the DR group. No changes in the POPF rate would be collected in the EN group changing definition’s criteria. Other complications were mostly related to pulmonary infections or pleural mild effusions. One patient in EN group required a redo open surgery (distal pancreatectomy) because of abdominal pain and persistence of the lesion after a postoperative CT scan. Two additional patient of the DR group required a reintervention: one because of POPF grade C and another because of bowel obstruction. All these three patients fully recovered without further complications.

Restart of oral intake, bowel movements and discharge from hospital were significantly faster in the EN group and its “Head” subgroup. An overall description of the postoperative course is given in Table 3.

The preservation of organ function was higher but not statistically significant in EN group (0% vs. 37.5% for both endocrine and exocrine impairment, *p* = 0.066). The evaluation of endocrine and exocrine impairment is summarized in Table 4.

In the EN group, the histopathological report of one patient (11%) demonstrated a benign cyst that was preoperatively classified as a PCN and selected for surgery. In the DR group, there were 5 (31%) cases of preoperative misdiagnosis: two ectopic splenic nodules preoperatively thought to be a NET, one serous cystadenoma (SCA) thought to be an IPMN with worrisome feature, 1 benign cyst thought to be a mucinous cystic neoplasm (MCN) and 1 benign lesion of the papilla thought to be a cancer. In one case of DP for

Table 2 Operative results

	EN = 9		DR = 16		<i>p</i> value	
	Head	Body/tail	Head	Body/tail	Head	Body/tail
N° of procedure	3 (33%)	6 (67%)	4 (25%)	12 (75%)		
Duration (min)	210 (180–225)	160 (130–250)	500 (435–525)	258 (205–390)	0.034	0.003
Conversion rate	–	–	1 (25%)	–	1.00	–
Associated procedure	1 (33%)	1 (17%)	–	2 (17%)		
Frozen section	–	3 (50%)	100%	2 (17%)		

Bold values indicate statistical significance (*p* < 0.05)

EN enucleation, DR demolitive resection

Table 3 Postoperative results

	EN = 9		DR = 16		p value	
	Head	Body/tail	Head	Body/tail	Head	Body/tail
N° of patients needing ICU in the post-op	1 (11%)	–	11 (69%)	7/12 (58%)	0.011	
Morbidity	–	1/6 (17%)	4/4 (100%)	–	0.029	0.152
	3 (33%)	–	12 (75%)	–	0.087	
	1/3 (33%)	2/6 (33%)	4/4 (100%)	8/12 (67%)	0.143	0.321
CD I–II	2 (22%)	–	8 (50%)	–		
CD III–IV	1 (11%)	–	4 (25%)	–		
POPF	2 (22%)	–	8 (50%)	–	0.287	
	1/3 (33%)	1/6 (17%)	3/4 (75%)	5/12 (42%)	0.486	0.600
Grade A	–	–	3 (19%)	–		
Grade B	2 (22%)	–	3 (19%)	–		
Grade C	–	–	2 (12.5%)	–		
Reoperation rate	1 (11%)	–	2 (12.5%)	–	1.00	
	–	1/6 (17%)	2/4 (50%)	–	0.429	0.333
Refeeding ^a	1	1 (1–3)	3.5 (3–19)	2 (1–6)	0.026	0.018
Gas ^a	2 (2–3)	2.5 (1–6)	4 (3–4)	3 (1–5)	0.040	0.767
Feces ^a	3.5 (3–4)	3 (1–6)	5.5 (4–13)	3 (2–6)	0.140	0.675
Length of hospital stay ^a (median)	5 (3–12)	–	8 (3–110)	–	0.027	
	5 (3–5)	5 (3–12)	12 (8–110)	6 (3–20)	0.032	0.254

Bold values indicate statistical significance ($p < 0.05$)

EN enucleation, DR demolitive resection, CD Clavien-Dindo classification, POPF post operative pancreatic fistula

^aExpressed as post-operative days

Table 4 Endocrine and exocrine impairment

	EN = 9		DR = 16		p value	
	Head	Body/tail	Head	Body/tail	Head	Body/tail
New onset DM	–	–	6 (37.5%)	–	0.066	
	–	–	–	6/12 (50%)	–	0.272
Endocrine impairment	–	–	6 (37.5%)	–	0.066	
	–	–	2/4 (50%)	4/12 (33%)	0.429	0.532
Follow-up (months)	19 (2–38)	–	18 (1–32)	–		

EN enucleation, DR demolitive resection, DM Diabetes Mellitus

NET G2, there was a positivity of 1 lymph node. The final histopathological findings are reported in Table 5.

After a median follow-up of 19 months for EN and 18 month for DR, all the patients were alive and free from recurrence.

Discussion

a. Indication for surgery

In case of pNETs, patients were scheduled for surgery according to the NCCN guidelines [13] while in presence of PCN, Fukuoka guidelines were followed [19]. Patients'

wishes or doubtful preoperative characterization were also taken into account.

Interestingly, many different guidelines about the management of pancreatic borderline lesions were reported in Literature [24, 25]. The exact behavior of these tumors remains often unpredictable because of loss of specific evaluable criteria. However, the most used criteria are size of the tumor, radiological aspect, grade of cellular atypia or Ki-67 expression (for pNETs) [5, 7].

In the present study, the median size of the resected pNETs was 15 mm in EN group, while the median size of resected pNETs in the DR group was 54 mm. The statistically significant difference in the size of tumor between the two groups is a direct consequence of the chosen cut-off

Table 5 Histopathological findings

	EN=9	SR=16	
		PD=4	DP=12
Histological type			
NET	8 (89%)	–	5 (42%)
G1	7 (87.5%)	–	1 (20%)
G2	1 (12.5%)	–	4 (80%)
MCN	–	–	1 (8%)
SCA	–	1 (25%)	–
IPMN	–	–	1 (8%)
SPN	–	–	1 (8%)
Other	1 (11%)	3 (75%)	4 (34%)
Total <i>N</i> ^o lymph node	7 (0–36)	25 (19–28)	15 (1–31)

EN enucleation, DR demolitive resection, NET neuro endocrine tumor, G grade, MCN mucinous cystic neoplasm, SCA serous cystadenoma, IPMN intraductal papillary mucinous tumor, SPN solid-pseudopapillary neoplasm

of 3 cm to perform an EN. Nevertheless, histopathological reports showed a higher rate of NETs G1 in EN group and a higher number of NETs G2 in DR group. These findings are consistent with the fact that size seems to directly relate with the tumor behavior [13, 26].

While F-pNETs should be always resected, when technically feasible, to treat the endocrinopathy [13], in Literature, there is an on-going debate between observation versus resection in patients with small NF-pNETs.

Some Authors advocate for a careful nonoperative management of small NF-pNETs with little differences in the cut-off (1.5–2 cm) [9, 24, 26, 27]. On the contrary, others believe that surgical treatment, when the patient is fit for surgery, is the best possibility of cure, despite the size. According to them, surgery can provide longer survival rate [8, 28–30] because of the existence of small high-grade tumors with aggressive behavior. These authors also advocate that a proper histological examination of the tumor (including mitotic and Ki-67 indexes) is possible on the resected specimen only.

In the present study, 1 patient with a MD-IPMN of 3 cm underwent a DP. One patient with a MCN of 2.5 cm that appeared to be in very proximity of the MPD underwent a DP. In both patients, final histopathological report found low-grade dysplasia. The management of PCN is also questioned leading to the development of different guidelines, with the most used being that born in Sendai and revised in Fukuoka (Japan) [19]. This experts' panel reported a mean frequency of malignancy in MD-IPMN of 61.6%, with resection recommended for all surgically fit patients [19]. All MCNs should be resected in patients fit for surgery. For MCNs of < 4 cm without mural nodules, minimally invasive resections as well as parenchymal-sparing resections are

options [19]. Serous cystadenomas should not be resected unless in the presence of symptoms, size of greater than 4 cm and uncertainty about the diagnosis (i.e., in oligocystic lesion) [11]. All SPNs should undergo surgery, even in cases with local invasion, recurrences or metastases due to their long-term survival [31].

b. Extension of the resection

In the present study, the median size of pNETs treated by an EN was 15 mm. All F-pNETs were treated with an EN and were confirmed to be insulinomas at final pathological response. In the case of EN performed for NF-pNETs, lymph nodal sampling (median number of lymph nodes harvested of 9) was routinely performed.

Enucleation is considered safe for insulinomas in updated guidelines [13]. Otherwise, gastrinomas are indicated for demolitive resections, with a formal lymphadenectomy for the high risk of lymph node metastasis (60–90%). Enucleation is also acceptable for superficial NF-pNETs [10]. However, the tumor size is directly related with the probability of lymph node metastasis: NF-pNETs smaller than 2 cm have a 7–26% of risk of lymph node metastases, this leading to a formal cut-off value [13], although in some case-reports enucleation is used for tumors up to 4 cm [32].

Enucleation of other benign or borderline malignant cystic neoplasms such as BD-IPMN, SCA, MCN, and SPN is also accepted in the absence of clear signs of malignancies [14, 19, 32–34]. Nevertheless, to be approachable by EN, lesions should be at least 2–3 mm far from main pancreatic duct to avoid injuries and severe leaks [33, 35–37].

The need and importance of lymph node sampling or clearance associated with EN is still under debate [10, 13, 28].

In the present study, all parenchymal sparing procedures resulted in shorter operative time, ICU postoperative monitoring, hospital stay and faster recovery. There was a trend to a lower, although not statistically significant, incidence of complications when compared to demolitive resections. The best benefits were shown in the “head” subgroup of patients. POPF rate in the EN group was 22%, graded B according to the classic and more recent ISGPF classifications [21, 23]. Interestingly, the incidence of POPF in EN group was lower than in the DR group (22% and 50%, respectively). Anyway, the small number of patients in the DR group may represent a bias, in a wider series of robotic PD and DP published by the same Authors, POPF rate was 18% and 14%, respectively, indeed [20].

In the current Literature, the incidence of POPF is reported to be superior after EN respect to DR (18%–50% vs. 12%) [12, 34, 38, 39]. However, they are mostly graded as A and B and managed conservatively [33]. There are many possible explanations to this higher rate of POPF. Firstly,

these lesions are often associated with a non-dilated pancreatic duct and a soft and friable pancreas. Secondly, centralization of the patients in high volume hospitals, that are reported to have better outcomes, is of crucial importance to reduce complications. Finally, in case of head or uncus location of the tumors, in order to try to avoid a challenging PD that may be also associated with high morbidity and mortality rates, surgeons may try to go beyond technical indications (i.e., enucleation for lesions located at less than 3 mm from MPD). This fact may be a cause of higher POPF rate compared to POPF rate after DP.

One of the major advantages of parenchyma-preserving resections is the maintenance of organ function [12, 14, 33, 34, 38, 40]. In the present study, none of the patients of the EN group developed new onset diabetes or exocrine impairment, while the rates of these complications for DR group were both 37.5% ($p = 0.066$).

In his systematic review, Zhou collected 1316 pancreatic EN (19.3% of them carried out by minimally invasive surgery) for pNETs (65.6%), IPMN (9.3%), SCA (8.1%) and MCN (7.4%). He demonstrated an overall morbidity rate of 50.3%, a POPF rate of 38.1%, reoperation rate of 3.7%, mortality rate of 0.3% and recurrence rate of 2.3%. Endocrine and exocrine insufficiency was observed in 2.4% and 1.1% of the patients, respectively. Compared with demolitive resections, perioperative outcomes were at least equal if not superior except for higher rate of POPFs. Compared with open enucleation, minimally invasive enucleation had a shorter operation time and a shorter length of hospital stay [36].

Despite the short follow-up period, the oncologic results were excellent with all the patients of both groups being alive and free from recurrence.

c. Minimally invasive techniques

From a theoretical perspective, parenchymal sparing resection performed in a minimally invasive fashion would be the ideal procedure in selected patients. However, the use of these techniques in pancreatic surgery is far from being a gold standard. The indications for minimally invasive resections are the same as for open pancreatic resections, although the advent of the minimally invasive technologies could have increased the number of surgical candidates.

Very few comparable studies and no prospective randomized controlled studies are available in Literature, matching laparoscopic, robotic and open pancreatic resections. Nevertheless, many of the published papers investigating the role of minimally invasive surgery mix the laparoscopic and robotic approach, limiting the power of any comparison. However, the minimally invasive approaches are reported to be feasible, safe and effective, with many advantages with respect to open surgery [16, 32, 37, 41]. Moreover, the robotic surgery seems to be feasible and at least equal

if not superior to conventional laparoscopic surgery for all types of commonly performed pancreatic resections [17]. There are many additional advantages of robotic technology in pancreatic surgery. The presence of four stable arms with 7° of freedoms and a 3D view allowing a sharp dissection are well known. Moreover, the availability of an integrated flexible ultrasound probe moved by the console surgeon with the images seen in a picture-in-picture mode may lead to a partial overcoming of the absence of tactile sense [35]. The use of the near-infrared technology (so called Firefly®) for lesion detection is of great help for guiding enucleations.

The longer duration of surgery is one of the main drawbacks of robotic surgery. Interestingly, most of the published studies comparing open and robotic EN report shorter duration of surgery for the robotic one [32, 34, 36, 37]. The ongoing discussion is still focused on the survival benefits of surgery, the good long-term survivals and the risks of surgery, rather than the issues of costs and other technical aspects [5, 18].

Unfortunately, the experience with robotic EN (REN) is very limited, mostly related to single centre case-series. To date, the largest experience on robotic pancreatic surgery was that published by Zureikhat in 2013. Of a total of well-studied 250 resections, only 10 were REN. No conversions were collected with a mean duration of surgery of 204 min. The total number of POPF was 3, none of grade C (33%) [16].

d. Other technical considerations

Interestingly, none of the planned robotic EN were converted to more resective procedures intraoperatively, due to sonographic findings, according to a rigorous preoperative imaging. Nevertheless, one patient of the EN group did not receive the correct surgery at the first time, requiring a further resective procedure. This is a major issue of enucleation that should be discussed with the patient. Unfortunately, the patient had a pseudonodular lesion very close to the tumor that was not properly identified at IOUS examination and frozen section examination was not available in that moment. This event remarks the importance of performing a deep preoperative study, discussing all the options with the patient. However, the missing of a deep small lesion could not be excluded neither during robotic surgery nor during open operations. Interestingly, a minimally invasive previous procedure could reduce peritoneal adhesions, this facilitating a further redo surgery.

The problem of misdiagnosis leading to unnecessary surgery has been previously reported in Literature [42, 43]. In the present study, a global misdiagnosis rate of 24% was collected. A more detailed preoperative study, completed during a dedicated Hospital's Multidisciplinary Meeting with periodical revisions could lead to a reduction of failures.

The major drawback of this study is the small number of patients included, leading to the need of a careful statistical interpretation. Secondly, the oncological follow-up is considered short, when dealing with slow growing tumors. Thirdly, this is a nonrandomized retrospective study with an inherent selection bias. Lastly, there is a lack of comparison with other surgical approaches (traditional or laparoscopic) and, definitely, to surveillance in small NF-pNETs or other small cystic lesions.

In conclusion, the increase in incidental diagnosis of small pancreatic neoplasms with a broad and not always predictable oncological behavior leads to many challenging clinical decisions. The risks of under/overtreatment and the potential morbidities related to surgery should be discussed carefully with patients. The limits of the present study and the scarcity of published papers avoid definitive conclusions. However, parenchymal sparing surgery allows better postoperative course and higher chance of conserving pancreatic function with similar long-term outcomes, if compared to demolitive pancreatectomies. Enucleations are best indicated for young patients who better tolerate a surgical complication (such as POPF) and for lesions located in pancreatic head.

The recent introduction of robotic technology is of valuable help during pancreatic surgery. This preliminary study confirmed the good outcomes of robotic enucleation of pancreatic lesions with few mild complications and short duration of hospital stay. Large comparative studies are needed to investigate the real advantages over open and laparoscopic surgery.

Funding No funding has been received.

Compliance with ethical standards

Disclosures Drs. Ilenia Bartolini, Lapo Bencini, Marco Bernini, Marco Farsi, Massimo Calistri, Mario Anneschiarico, Luca Moraldi, and Andrea Coratti have no conflicts of interest or financial ties to disclose.

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