Minimally invasive pancreatic surgery – a review

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Abstract

During the past 20 years the application of a minimally invasive approach to pancreatic surgery has progressively increased. Distal pancreatectomy is the most frequently performed procedure, because of the absence of a reconstructive phase. However, middle pancreatectomy and pancreatoduodenectomy have been demonstrated to be safe and feasible as well. Laparoscopic distal pancreatectomy is recognized as the gold standard treatment for small tumors of the pancreatic body-tail, with several advantages over the traditional open approach in terms of patient recovery. The surgical treatment of lesions of the pancreatic head via a minimally invasive approach is still limited to a few highly experienced surgeons, due to the very challenging resection and complex anastomoses. Middle pancreatectomy and enucleation are indicated for small and benign tumors and offer the maximum preservation of the parenchyma. The introduction of a robotic platform more than ten years ago increased the interest of many surgeons in minimally invasive treatment of pancreatic diseases. This new technology overcomes all the limitations of laparoscopic surgery, but actual benefits for the patients are still under investigation. The increased costs associated with robotic surgery are under debate too. This article presents the state of the art of minimally invasive pancreatic surgery.

Key words: *laparoscopy, robotic surgery, robot-assisted surgery, pancreatic surgery, minimally invasive surgery, pancreatectomy.*

Introduction

Pancreatic surgery is one of the most challenging and complex fields in general surgery, due to the deep position of the organ inside the abdominal cavity and its close proximity to major vasculature; so the application of a minimally invasive (laparoscopic and robotic) approach to pancreatic resections came late and slowly when compared to most abdominal operations.

Accepted advantages of minimally invasive surgery are the cosmetic results and reduction of blood loss, pain, length of hospital stay and time for recovery. Since the first laparoscopic cholecystectomy more than 20 years ago, laparoscopic surgery has gone on to become the gold standard for cholecystectomy and also anti-reflux surgery and bariatric surgery.

1994 was the year when two different groups described the first laparoscopic pancreatoduodenectomy (LPD) [1] and the first laparoscopic distal pancreatectomy (LDP) [2]. Laparoscopic pancreatoduodenectomy never gained widespread popularity, because of the challenging resection (in particular the retroperitoneal margin), even more in the case of malignancy, but surely the biggest barrier is the complex reconstructive phase with three major anastomoses. Nowadays even in the biggest pancreatic centers the minimally invasive approach for pancreatoduodenectomy represents a small minority of the entire surgical volume, considering the lacking of scientifically proven advantages over conventional open surgery. On the other hand, LDP does not need a complex reconstructive phase, so it is widely per-

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formed, with thousands of patients undergoing the operation. At least for benign or borderline tumors, it is almost considered a standard of care thanks to its advantages over the traditional open approach: reduced blood loss and length of hospital stay [3–5].

In the second half of the 1990s, military research developed a new technology: robotic platforms designed to allow remote operations, e.g. in the battlefield or in space. The first prototypes were designed to be used outside the medical field, but later a medical device was developed and popularized. It was designed to reproduce the movements of the surgeon's hands positioned far away the operating table. Today only one system is available worldwide: the Da Vinci Surgical System, by Intuitive Surgical; from 1997 when it was launched, different models have been released: S, Si and recently Xi. It consists of three fundamental elements: a surgeon's console (where the surgeon is seated viewing the surgical field via a 3D visor and generating the movements by grasping the master controls with his hands), a patient-side cart (where the movements of the surgeon are reproduced by 4 articulated arms inside the patient) and a vision-control system similar to the laparoscopic column. Maintaining moreover all its advantages, robotic technology shows many advantages over traditional laparoscopy: restoration of hand-eye coordination, reduction of natural tremors with no fulcrum effect, three- instead of bi-dimensional vision, introduction of seven instead of three degrees of freedom of the instruments (Endowrist technology), and an improvement in ergonomics for the surgeon with a more comfortable position.

Clinical applications of robotic technology concern most surgical fields. In some cases, the robotic approach still remains almost experimental, while in some other cases, e.g. prostatectomy, it is now recommended. In 2003 Melvin *et al.* [6] described the first case of robotic distal pancreatectomy (RDP), and in the same year Giulianotti *et al.* [7] published his personal experience including five RDPs and eight robotic pancreatoduodenectomies (RPD). Since all the pancreatic procedures are safe and feasible via a robotic approach, many authors have reported their experience and the number of patients treated is increasingly quickly.

The aim of this study is to review the literature and to describe the trend of minimally invasive pancreatic surgery.

Minimally invasive distal pancreatectomy (MIDP) with or without splenectomy

Distal pancreatectomy (DP) is the most commonly performed pancreatic resection using minimally invasive techniques, thanks to the absence of a reconstructive phase. Today MIDP is considered safe and feasible and several studies have shown several advantages over open surgery: shorter hospital stay, decreased blood loss, fewer overall complications and faster recovery, in addition to being cost effective. The oncologic adequacy has been established too [8].

Indications

Distal pancreatectomy is indicated in the case of lesions of the pancreatic body-tail. Selection of the patient includes: evaluation of body mass index (BMI), history of previous laparotomy and cardio-pulmonary comorbidity. A high BMI is not a contraindication for MIDP, but visceral fat can make the procedure more challenging. Expected advantages of the minimally invasive approach in patients with high BMI are better access in the deep abdomen, less post-operative incisional pain, faster post-operative recovery and reduced incidence of incisional hernia. Lacking randomized trials, some argue that patients with cardiac and pulmonary comorbidities are ideal candidates for MIDP due a potentially greater benefit of an enhanced postoperative recovery, but major series include mostly patients with BMI < 30 kg/m^2, without severe comorbidities. Also tumor factors need to be evaluated in the selection of patients for MIDP. In the case of malignant, bulky and locally advanced tumors and those proximal to the pancreatic neck, the indication for a minimally invasive approach is questionable: referring the patient to an experienced center is advisable. Perhaps the robotic platform with its augmented vision and motion precision can extend the indications, once an adequate learning curve is reached.

Technique

Distal pancreatectomy can be performed with or without preservation of the spleen. The most feared risk after splenectomy is overwhelming post-splenectomy infection (OPSI), which has a low (< 1%) annual incidence but a high mortality (> 80%) [9]. The incidence is reducible if vaccination against capsulated bacteria (*S. pneumoniae*, *H. influenzae*, *N. meningitidis*) is carried out. The second risk to be taken into consideration is post-splenectomy thrombocytosis, which may increase the thrombotic global risk of the patient. Since the number of nodes removed is necessarily lower in spleen-preserving DP, this operation is preferred and advisable only for benign disease, when lymph node removal is not as crucial. Two techniques are described for spleen-preserving DP: Warshaw's and Kimura's. The Warshaw technique consists in the resection of the splenic artery and vein, leaving blood supply to the spleen only from short gastric vessels [10]. Kimura's preserves the spleen with its main vessels and is the most frequently applied technique [11]. Data from the literature report a spleen preserving rate superior for laparoscopic technique compared to open distal pancreatectomy (ODP) [12]. Moreover, some authors have reported superiority of the robotic approach over laparoscopy in order to save the spleen [12, 13], but drawing conclusions is difficult because of the high variability of the indication between different centers.

Outcomes

Variables to take into consideration are operating time, blood loss, conversion rate, incidence of fistula, length of hospital stay, oncologic outcomes, re-operation, morbidity, mortality and costs.

In different series, operating time is reported as longer [14–17], similar [18–25] or shorter [26–28] compared with the open approach: this may be explained by the difference in the surgeons' learning curve [29]. A series that compares operating time for LDP and ODP reports ranges of 180 [20] to 383 [30] min (LDP) and 152 [31] to 330 [30] min (ODP). Reported operating time for RDP is 164–458 min in major series [12, 13, 32–36].

Blood loss is lower for MIDP compared to ODP in all the series [3, 5]. It is one of the most important results of the advances in surgical techniques, vascular sealing devices and endomechanical staplers that have increasingly augmented the safety of minimally invasive pancreatic resections.

The conversion rate varies from 0% to 30% in major LDP series [3] and from 0% to 11.7% in major RDP series [5]. Some authors have reported a significant reduction in conversion rate associated with the robotic approach [32, 37]. Conversion to open surgery implies greater intraoperative blood loss [18, 21, 38] and longer operating time [26, 28]. Reasons for conversion include high BMI, adhesions, large and proximal lesions and intraoperative bleeding.

Pancreatic fistula after a DP is due to a later and incomplete closure of the pancreatic duct system after the resection of the parenchyma. Incidence of pancreatic fistula ranges from 0% to 70% independently of the approach [3, 5, 39]. Ranges are so large because different centers adopt different definitions and classifications of fistula, despite an international definition and classification being available (the International Study Group on Pancreatic Fistula, ISGPF [40]). Moreover, some series report the entire incidence, while others report only clinically relevant cases requiring interventions. A large meta-analysis also demonstrated that different treatment of the stump (stapler, suture or nothing) is not associated with variation of incidence of pancreatic fistula [41].

Length of hospital stay is shorter after an MIDP (RDP: 4–9 days [5, 39], LDP: 5–22 days [3]) compared to ODP (6–27 days) in major series [14–19, 21–28, 30, 42–45].

Patients undergoing MIDP tend to have a smaller lesion and rarely a malignant lesion, due to a pre-selection bias. Oncologic outcomes are difficult to compare between the different techniques due to the poor data reporting (R0/R1 resections and number of lymph node harvested) and the high variability of malignant cases in different series. However, the literature reports a margin positivity rate of 0–26% for LDP (similar to ODP when compared [14, 16, 18, 21, 46]) and generally 0% in RDP series [12, 32, 34, 36]. Numbers of lymph nodes harvested are 6–14 in LDP series (similar to ODP when compared [16, 21, 28, 40]) and 5–19 in RDP series [12, 32–34, 36]. Long-term results in terms of oncologic adequacy of minimally invasive technique for malignancy are not yet available.

Reoperation is generally < 10% after an LDP [14, 16, 19, 20, 27, 28, 42]; after an RDP it is 0% in most studies [7, 12, 33, 36], except one that reports 6.2% [34].

MIDP-related morbidity is generally high (12–70%), but lower than ODP in several studies [16, 27, 28]; although most series do not report any severity classification, most morbidity is of low-grade severity (e.g. pleural effusion).

Mortality is rare (< 1%) for LDP [3]. All RDP series report 0% mortality [12, 13, 32, 33, 36, 47].

Costs are one of the most debated aspects of MIDP, in particular for RDP, which requires a large initial investment and high maintenance costs too. Only a few articles analyze and compare costs, and the conclusions are not in agreement. Waters *et al.* [12] report intraoperative costs higher for RDP compared to LDP and ODP, but it was compensated by a shorter hospital stay after RDP, then total adjusted costs were advantageous for RDP ($11 904 vs. $12 900 and $15 521 for RDP, LDP and ODP respectively). Kang *et al.* [13] report a total cost higher for RDP than LDP ($8304 vs. $3861). It is difficult to compare costs of MIDP between different health systems, but in general a robotic procedure is considered more expensive than conventional open and laparoscopy.

In summary, MIDP up to now is considered safe and feasible. LDP has become the operation of choice for distal pancreatic lesions, except for bulky, locally advanced and proximal tumors. When indicated, the minimally invasive approach has better outcomes. Experience with RDP is quickly growing worldwide, but possible advantages are still under debate.

Minimally invasive pancreaticoduodenectomy (MIPD)

Pancreatoduodenectomy is considered one of the most challenging and complex operations in abdominal surgery, due to the necessity of very delicate manipulation during resection (considering the uncinate process, portal vein and mesenteric vessels) and very laborious reconstruction (considering biliary anastomoses and pancreatic anastomoses). This is the reason for the extremely low diffusion of a minimally invasive approach, including among pancreatic centers. So, since the demonstration of its feasibility by Gagner *et al.* in 1994 [1], LDP has never gained widespread application; indeed some of the first pioneers eventually concluded that there was no benefit for a minimally invasive approach for PD [48, 49]. Only 4 authors [50–53] have compared their experience between MIPD and open pancreatoduodenectomy (OPD); among them only two described a total laparoscopic technique. In this scenario the well-known technical advantages of the robotic platform were expected to be very useful in order to popularize the MIPD; this mirrors the experience with minimally invasive prostatectomy: the laparoscopic approach never gained popularity, but the advent of the robotic system changed the history of these operations. In fact, since the first small series [7] of robotic PD, the number of treated patients has slowly been increasing, although the experience is still in the hands of a few very skilled surgeons and only one series includes more than 100 cases [54].

Indications

Pancreatoduodenectomy is the surgical treatment of periampullary, duodenal and pancreatic head lesions. The earliest series [3, 39] of MIPD included patients with benign or low-grade malignant lesions, in the absence of local invasion of major vessels. So neuroendocrine tumors, cystic lesions and tumors of Vater's ampulla are ideal surgical candidates for MIPD. Patients affected by obesity, cardiac and pulmonary comorbidity are not excluded by traditional open PD. Experience with these patients operated via a minimally invasive approach is still too limited to establish a conclusion, but some surgeons state that it may have the most benefit.

Technique

Since the beginning, two techniques have been described for MIPD: the total laparoscopic [50, 52] and the hybrid [51, 53] approach. The first consists of resection and anastomosis performed totally laparoscopically; in contrast, in the hybrid technique the reconstructive phase is performed through a small incision which is also used for specimen extraction. With the advent of the robotic system the authors described different approaches: hybrid laparoscopic/robotic technique [55] (laparoscopic resection and robotic reconstruction) or fully robot-assisted [56], as advocated by the pioneers of RPD. Independently of the technique, LPD and RPD are now accepted as safe operations, with morbidity and mortality similar to the traditional open surgery.

Outcomes

Compared to OPD, LPD demonstrated a longer operative time [50, 52] (456–541 min vs. 372–401 min, similar between hybrid and totally laparoscopic methods), a reduction of blood loss [50, 51] and a shorter length of hospital stay [50] (8 vs. 12.4 days, only one study). In a review of the literature including 285 patients [57], 87% of procedures were totally laparoscopic, with a 9% rate of conversion to open. The main reasons for conversion are bleeding (mostly from the portal vein), difficult dissection, adhesions and tumor infiltration of local vascular structures [51, 53, 58]. Overall incidence of complications was 48%, including a 15% pancreatic fistula rate and a 2% (0–8.8%) overall mortality rate.

Comparison of results across series is very difficult because each department may have different practices and enhanced recovery programs in post-operative pain management, diet advancement, drain management and criteria for discharge; moreover, there are big differences in surgeons' learning curves. In addition, there is tremendous bias in patient selection, since malignant, large and locally advanced tumors and morbidly obese patients are frequently excluded, so the results may appear in favor of MIPD over OPD.

Robotic series are still small: only 3 included more than 50 patients, and only 4 studies compared the results of RPD with those of OPD [59–62]. No prospective randomized clinical trials comparing LPD and RPD are available. Several studies demonstrate a reduction in blood loss and a trend towards reduced length of hospital stay vs. OPD. Morbidity rates range between 0% and 75%, including 0–35% incidence of pancreatic fistula; mortality was between 0% and 4.5%, similar to the open approach. In a meta-analysis on RPD vs. OPD an advantage in terms of 12% reduction of morbidity in robotic patients was demonstrated [63].

Since the major indications for PD are periampullary and pancreatic head cancers, the oncologic outcome of the resection is one of the key points of the success of different approaches. Comparison of results is once again compromised by enormous selection bias; nevertheless, negative margins are achieved in most LPD series [64–66], with an adequate number of lymph nodes harvested [50, 53]. Robotic pancreatoduodenectomies series obtained a R0 resection in 89–100% of cases [60, 67], while the median number of lymph nodes harvested in some series [55, 60, 61] was not adequate according to current guidelines [68].

Only one paper in the literature compares the mean costs of RPD vs. OPD, showing an excess of €6200 with the robotic approach [69].

Even though these results are encouraging, it is important to observe that they are obtained by only a few very skilled minimally invasive surgeons and, as such, cannot be considered a standard of care, including for high volume pancreatic centers. Given that in experienced centers the results of pancreatoduodenectomy via the open traditional approach are excellent, it may be hard to justify the increased operative time, efforts and resource utilization for MIPD.

Minimally invasive total pancreatectomy (MITP)

Major indications of total pancreatectomy (TP) are the tumor involving most of or the entire gland (e.g. intraductal papillary mucinous neoplasms), positivity of the pancreatic resection margin during pancreatoduodenectomy for ductal adenocarcinoma, multiple primitive (e.g. neuroendocrine) or metastatic tumors (e.g. from renal cancer), and chronic pancreatitis with refractory pain. In selected patients laparoscopy with or without robotic assistance proved advantageous, although experience with MITP is still confined to small series [54, 70–73]. Total pancreatectomy with auto-transplant of islet cells has been described in patients with chronic pancreatitis [74, 75]. Characteristics of TP are the absence of risk of pancreatic fistula by definition, the delicate dissection of the uncinate/posterior margin as it is in pancreatoduodenectomy and the difficult biliary anastomoses due to the presence of a non-dilated bile duct in most patients.

In a series of 5 robotic total pancreatectomies (RTPs) by Zureikat *et al.* [54], operative time was 503 min, conversion rate 20%, complication rate 100%, and length of hospital stay was 10 days with 1 readmission.

Advantages of robotic (RTP) vs. open total pancreatectomy (OTP) have been described in a case-matched study by Boggi *et al.* [76]. Eleven patients underwent RTP for benign (1) or malignant disease and were compared to 11 patients with similar indications but without the availability of the robotic system at the time of scheduled surgery. They had a 0% conversion rate, 2 vascular resections in each group, a longer operative time but reduced blood loss in the robotic series. The length of hospital stay was similar between the two groups, but all the parameters evaluating the recovery were advantageous for RTP.

Enucleation (EN)

Pancreatic enucleation is an "extreme" parenchyma-sparing procedure and is indicated for benign pancreatic tumors (e.g. insulinomas, small neuroendocrine tumors or benign cystic lesions, not requiring lymph node evaluation) or solitary metastases from renal cell carcinoma. Enucleation is characterized by the maximal preservation of pancreatic parenchyma, the absence of dissection and reconstruction, low blood loss, but a high incidence of pancreatic fistula. Preoperative imaging and intraoperative ultrasound assessment are crucial in ensuring that the tumor can be resected with negative resection margins and leaving the main pancreatic duct intact [3, 77].

Laparoscopic series reported a 13–38% incidence of fistula [78], which is lower than the incidence in open enucleation series [79]. Length of stay is about 6–9 days [77, 79], shorter than the 10-14 days of open series. Zureikat *et al.* [54] reported 10 robotic enucleations, with no perioperative mortality and a 30% incidence of pancreatic fistula. Mean operative time was 206 min, length of stay was 5 days, and readmission was 30%.

Middle pancreatectomy (MP)

Middle pancreatectomy is a rare but interesting procedure, indicated in cases of benign or low-grade malignant tumors located in the pancreatic neck or proximal body, where the surgical purpose is to achieve a radical removal preserving full exocrine and endocrine pancreatic function [80]. The minimally invasive approach for this procedure has not been widely described in the literature, and there are only a few reports available on laparoscopic and robotic MP. Results of robotic MP compared to open MP were evaluated in a small series by Kang *et al.* [81]: no differences were observed in terms of overall complication rate, perioperative mortality and length of hospital stay; the robotic group had a lower blood loss, but a longer operative time compared to the open group. The approach described by Kang was hybrid for 3 patients out of 5 (laparoscopic resection and robotic reconstruction), with pancreaticogastrostomy preferred over pancreaticojejunostomy. Giulianotti *et al.* [82] described the first series of three totally robotic MPs. The mean operative time was 320 min, and the mean length of hospital stay was 9 days for patients with no complications and 27 days for patients complicated by a grade B (according to ISGPF) pancreatic fistula. There were no conversions and the mortality was nil. Zureikat *et al.* [54] in his series of 13 robotic MPs had a 92% incidence of pancreatic fistula, mean operative time was 394 min, they had 2 conversions to open surgery and one reoperation, and length of hospital stay was 8 days. All the series reported a 0% incidence of pancreatic or endocrine insufficiency during follow-up [5].

Conclusions

During the last 20 years the history of pancreatic surgery has undergone a revolution thanks to the introduction and diffusion of minimally invasive surgery. Traditionally the laparoscopic approach was limited to distal pancreatectomies and enucleations; conversely, laparoscopic pancreaticoduodenectomy never gained wide diffusion because of the very challenging reconstructive phase. The introduction of the robotic platform more than 10 years ago elicited an increased interest in minimally invasive pancreatic surgery. The main advantages of the robot are the restoration of eye-hand coordination, enhanced 3D vision, augmented precision in movements and improved ergonomics. The robot eventually allows one to perform a procedure more similar to open surgery but via a minimally invasive approach.

Laparoscopy is accepted as a gold standard approach for small tumors of the pancreatic body-tail thanks to its many advantages: reduced blood loss, reduced length of hospital stay and perhaps a reduction in overall complications (pancreatic fistula excluded). The robot can obtain similar outcomes, but clear advantages over the traditional laparoscopic approach are difficult to demonstrate. On the other hand, robotic surgery is commonly criticized for the costs involved. Randomized clinical trials are not available in the literature, while comparative studies are contradictory and compromised by strong bias in patient selection and data analysis. Surgery of the pancreatic head is very challenging with the laparoscopic and robotic approach too. The learning curve with this procedure is very long, so even though results are encouraging, a large and extensive diffusion is still far away. Young patients with benign or low-grade malignant pancreatic lesions are perhaps the most suitable candidates for this type of surgery.

Conflict of interest

The authors declare no conflict of interest.

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